

nQuery Advisor[®]

Version 5.0

User's Guide

Janet D. Elashoff

Statistical Solutions Ltd.

8 South Bank

Crosse's Green

Cork, Ireland

Tel: +353 21 319629 Fax: +353 21 319630

<http://www.statsol.ie>

In Boston, MA, USA: 1-800-262-1171

<http://www.statsolusa.com>

info@statsolusa.com

The correct bibliographic citation for this document is as follows:
Janet D. Elashoff (2002). **nQuery Advisor Version 5.0 User's Guide.**
Los Angeles, CA

Copyright © 2002 by Janet D. Elashoff
Program Copyright © 2002 by Janet D. Elashoff
All Rights Reserved Worldwide

October, 2002

Printed in Republic of Ireland

Edited by Virginia Lawrence.

Development of nQuery Advisor® was supported in part by SBIR grant number 2-R44-RR07555-02 from NIH Center for Research Resources.

Computational methods developed in part by Michael Ray Oliver.

Windows, Windows Calculator, Windows 95, Windows 98, and Windows NT, Windows 2000, Windows ME, Windows XP are trademarks of the Microsoft Corporation.
Microsoft Word is a trademark of the Microsoft Corporation.
WordPerfect is a trademark of the WordPerfect Corporation.

Third party copyrights: Integrated within nQuery Advisor are the following products provided by third parties, who own copyrights to these products. The products are trademarks or trade names of their respective owners:

Dixon soft fonts are licensed from Elfring Consulting, Inc. 4N899 West Mary Drive, St. Charles, IL 60175.

wct32d.dll, © 1994, 1997 Quinn-Curtis, Incorporated.

Microsoft runtime support files © 1993-1999 Microsoft Corporation.

Spreadsheet ss32x25.ocx © 1998 Farpoint, Incorporated.

Table of Contents

1. INTRODUCTION	1-1
Running nQuery Advisor for the First Time.....	1-1
Uninstalling nQuery Advisor from Standalone Computer	1-2
Uninstalling nQuery Advisor from Client Computer	1-2
Getting Started with nQuery Advisor	1-3
New Features and Tables in nQuery Advisor 5	1-4
New features:	1-4
New Sample Size Tables:	1-5
Customizing Regional Settings.....	1-7
Troubleshooting	1-8
 2. TUTORIAL.....	 2-1
Step 1. Formulate the study.....	2-1
Detail the study design.....	2-1
Choose the outcome summary	2-2
Specify the analysis method	2-2
Step 2. Specify Parameters for Planned Analysis.....	2-9
Using Mouse Buttons in Data Entry	2-10
Right-click Menus.....	2-11
Step 3. Specify Effect Size for Test	2-11
Specifying the difference in means expected for the two groups	2-12
Specifying the common standard deviation	2-13
Step 4. Compute: Sample Size or Power	2-14
Step 5. Sensitivity Analysis	2-16
a. Edit Values in Filled-in Column	2-16
b. Edit a Column Name.....	2-17
c. Use Plot Options	2-19
d. Fill Table Rows.....	2-20

Using Fill Right and Specify Multi-Factor Table	2-20
Step 6. Choose Sample Size, Write Statement	2-23
Buttons in the Statement Dialog Box	2-24
Summary	2-27
 3. THE FILE AND OPTIONS MENUS	 3-1
File Menu - Initial	3-1
New	3-1
Going Beyond the Study Goal and Design Box	3-3
Open	3-3
Print Setup	3-4
Recent File.....	3-4
Exit	3-4
File Menu - From a Sample Size Table	3-4
Close.....	3-5
Save	3-5
Save As.....	3-5
Print	3-6
Print Active View	3-7
Print Table to Clipboard	3-7
Using the Right-Click Menu to Print the Table.....	3-9
Printing the Sample Size Justification Statement	3-10
Exit	3-11
Options Menu.....	3-12
Change Minimum Expected Cell Count.....	3-12
Auto Recalculation	3-13
Preferences	3-15
 4. THE EDIT MENU.....	 4-1
Undo	4-1
Clear... ..	4-1
Cut	4-2

Copy.....	4-2
Paste.....	4-4
Paste Unformatted	4-5
Fill Right.....	4-6
Specify Multi-factor Table.....	4-6
Create Statement	4-8
Edit Row Names	4-11
Edit Column Names.....	4-12
Special Characters.....	4-14
Using Right-Click Menu to Access Edit Options	4-15
5. THE ASSISTANTS MENU	5-1
Unequal n's	5-1
Finite Population Adjustment.....	5-3
Data Entry	5-4
Compute Effect Size.....	5-4
Sample Size Tables Offering Side Tables.....	5-8
Conversion between Parameters.....	5-9
Estimate SD	5-11
Specify SIGMA, Covariance Matrix	5-12
Distribution Functions.....	5-13
Windows Calculator	5-14
6. THE PLOT MENU	6-1
Example 1	6-1
Example 2	6-6
Example 3	6-10
Example 4	6-14
Example 5	6-17
Plot File Menu	6-20
New.....	6-20

Open	6-20
Save as Metafile	6-20
Save as Old-style Metafile.....	6-21
Print Current Page	6-21
Printer Setup	6-21
Printing Options.....	6-21
Summary of Ways to Print a Plot	6-23
Plot Edit Menu	6-23
Copy	6-23
Plot Graphs Menu.....	6-23
Parameters	6-24
Plot Assistants Menu	6-25
Editing Within the Plot.....	6-25
Edit Plot Text.....	6-25
Edit Plot Axis Labels.....	6-26
Edit Plot Parameters	6-28
Edit Plot Legend Parameters	6-29
 7. THE VIEW AND WINDOWS MENUS	 7-1
View Menu-Initial	7-1
Toolbar	7-1
Status Bar.....	7-1
View Menu - From a Sample Size Table.....	7-2
Guide	7-2
Window Menu	7-5
New Window	7-6
Cascade.....	7-6
Tile.....	7-6
Arrange Icons	7-6
List of Open Tables	7-6
Contents of Study Goal and Design Dialog Box	7-6

Unequal n's	7-8
Finite Population	7-8
Abbreviation Codes.....	7-8
 8. SAMPLE SIZE TABLES FOR MEANS.....	 8-1
Sample Size Tables for Means in nQuery Advisor	8-1
One-group Tests and Confidence Intervals.....	8-2
Two-group Tests and Confidence Intervals.....	8-2
One and two group paired, crossover, & repeated measures designs, tests and confidence intervals	8-3
One and two group and crossover designs, equivalence and bio-equivalence tests	8-4
Multiple group tests and confidence intervals	8-4
Example 1	8-5
Example 2	8-9
Two-sample Confidence Interval (MTC1)	8-9
Example 3	8-11
Confidence Interval for percentile of a normal distribution (MOC5).....	8-11
Example 4	8-13
Two group Satterthwaite t-test of equal means (unequal variances) (MTT0uv)	8-13
Example 5	8-15
Two group t-test for fold change assuming log-normal distribution (MTT0cv)	8-15
Example 6	8-18
Two group t-test of equal fold change with fold change threshold (MTT0fct)	8-18
 9. DETERMINING A VALUE FOR STANDARD DEVIATION .	 9-1
Data Entry (SD calculator).....	9-2
Using One of the Estimate SD Options.....	9-6
1. From Standard Error	9-6

2. From SD1 and SD2 (pooled SD)	9-8
3. From Range	9-10
4. From Percentile	9-11
5. From Coefficient of Variation	9-13
6. From Upper Confidence Limit	9-15
7. From SD1, SD2, Correlation	9-17
8. For Cluster Sampling	9-19
9. For Specified x-values	9-23
10. Of Residuals	9-26
Using the Specify Covariance Matrix Option.....	9-27
1. Specify Full Covariance Matrix	9-28
2. Specify Standard Deviations	9-30
3. Specify Correlations	9-31
Summary	9-35
 10. UNEQUAL N'S	 10-1
Finding Sample Size for Unequal n's Design.....	10-2
Caveat.....	10-5
 11. DEMONSTRATING EQUIVALENCE	 11-1
One-sided (non-inferiority) tests for difference of means.....	11-1
Two one-sided tests (TOST) for difference or ratio of means.....	11-1
One-sided non-inferiority tests for difference of proportions.....	11-2
Difference of proportions in paired or two-group design.....	11-2
Equivalence testing	11-2
One-sided, non-inferiority equivalence testing for difference in means	11-3
Example 1	11-4
Two-sided, "neither better nor worse", bio-equivalence testing	11-6
TOST for difference in means	11-6
Example 2	11-8
Example 3	11-11

Two-sided, "neither better nor worse", bio-equivalence testing.....	11-15
Example 4	11-16
Example 5	11-18
Example 6	11-20
Two-sided, "neither better nor worse", bio-equivalence testing.....	11-22
Example 7	11-23
Example 8	11-24
Relationships between sample size methods for standard tests, confidence intervals, and equivalence tests	11-26
Test for equality of two means	11-26
Confidence interval for difference in two means.....	11-28
 12. SIDE TABLES/COMPUTE EFFECT SIZE.....	 12-1
Compute Effect Size.....	12-1
Side Table Name.....	12-1
Example 1	12-1
Side Table Buttons.....	12-4
Right-click Menu Options	12-6
Continuing Example 1	12-9
Example 2	12-10
Example 3	12-14
Example 4	12-16
Example 5	12-19
Summary.....	12-21
 13. REPEATED MEASURES AND CROSSOVER DESIGNS ...	 13-1
Paired Designs, Tests, Confidence Intervals, and Equivalence Tests	13-2
2x2 Crossover Designs, Tests and Equivalence Tests.....	13-2
Designs with Two or More Repeated Measures	13-3

Crossover Designs	13-3
Example 1	13-4
Example 2	13-8
Example 3	13-12
Example 4	13-14
Repeated Measures Designs	13-15
Example 5	13-16
Example 6	13-18
Example 7	13-20
 14. NONPARAMETRIC TESTS	 14-1
Wilcoxon/Mann-Whitney rank-sum test (continuous outcome) (MTT1)	14-1
Wilcoxon/Mann-Whitney rank-sum test (ordered categories) (MTT2)..	14-4
 15. SAMPLE SIZE TABLES FOR PROPORTIONS	 15-1
Tests, Confidence intervals, and Equivalence Tests for single proportions or for differences in paired proportions in a single sample:	15-2
Tests, Confidence Intervals, and Equivalence tests for comparisons of proportions in two independent groups:.....	15-3
Tests for more than two groups.....	15-4
Example 1	15-4
Example 2	15-6
Example 3	15-12
Example 4	15-17
Example 5	15-21
Example 6	15-23
Example 7	15-25
Example 8	15-29
Example 9	15-32
Equivalence and Bioequivalence for Paired Proportions	15-32
Example 10	15-40
Example 11	15-46

Equivalence and Bioequivalence for Independent Proportions (TOST procedure).....	15-46
---------------------------------------------------------------------------------------------	--------------

16. SURVIVAL ANALYSIS TABLES 16-1

Log-rank test for equality of survival curves.....	16-2
-----------------------------------------------------------	-------------

Test based on exponential survival, accrual period STT0.....	16-3
---------------------------------------------------------------------	-------------

Test based on exponential survival, accrual period, dropouts STT2.....	16-3
-------------------------------------------------------------------------------	-------------

Log-rank test with user specified survival, hazard, accrual, dropout rates, simulation STT3.....	16-3
-------------------------------------------------------------------------------------------------------------	-------------

Example 1	16-3
-----------------	------

Example 2	16-6
-----------------	------

Example 3	16-9
-----------------	------

Example 4	16-14
-----------------	-------

Example 5	16-21
-----------------	-------

Example 6	16-23
-----------------	-------

Example 7	16-26
-----------------	-------

Using the Multi-period Side Tables with Simulation Survival Table ... 16-30

Opening a Survival Table and its Side Table.....	16-31
--------------------------------------------------	-------

Colors for Side Table Names	16-31
-----------------------------------	-------

Changing a Side Table Name	16-31
----------------------------------	-------

17. AGREEMENT TABLES 17-1

Dichotomous outcome methods using Intraclass Kappa	17-1
-----------------------------------------------------------------	-------------

Continuous outcome methods using Pearson r.....	17-1
--------------------------------------------------------	-------------

Continuous outcome methods using Lin's concordance coefficient.....	17-2
----------------------------------------------------------------------------	-------------

Example	17-2
---------------	------

18. REGRESSION TABLES 18-1

Choosing a Regression Table 18-1

Dichotomous y (Logistic Regression)	18-1
-------------------------------------------	------

Continuous y	18-2
--------------------	------

Logistic Regression	18-4
Example 1	18-4
Example 1a	18-4
Example 1b	18-7
Example 2	18-7
Example 3	18-12
Linear Regression	18-14
Example 4	18-14
Example 5	18-18
 19. SAMPLING FROM FINITE POPULATIONS.....	 19-1
Means, One group, Test	19-1
Means, One group, Confidence Interval.....	19-1
Proportions, One Group, Test	19-2
Proportions, One Group, Confidence Interval.....	19-2
Example.....	19-2
 20. DISTRIBUTION FUNCTION TABLES.....	 20-1
Example	20-1
 21. APPENDIX - REFERENCES AND FORMULAS	 21-1
Section 1.....	21-1
Methods of computation for each table	21-2
Section 2.....	21-20
Central functions (computing cumulative distribution function)	21-20
Non-Central functions (computing cumulative distribution function)	21-22
Percentage points and non-centrality parameters	21-23
Use of distribution functions in computing power, sample size, and effect size, or interval width and sample size	21-26
 Index	 I-1

1. Introduction

nQuery Advisor assists you in choosing an appropriate sample size for your research studies. nQuery Advisor also helps you to provide the standard deviation and effect size information which you need to make sample size and power computations.

The nQuery Advisor program was designed by professional statisticians with many years of experience in study design. They have created the nQuery Advisor program so that research investigators can compute appropriate sample sizes easily.

Running nQuery Advisor for the First Time



1. When you first run the nQuery Advisor software, a dialog box informing you that you have not registered nQuery Advisor will be displayed. Click on **Register...** to enter the license key that you have received from Statistical Solutions Ltd or to view your license number before contacting Statistical Solutions so that they can issue a license key.



-
2. The Register Product dialog allows you enter the license key that you have received from Statistical Solutions Ltd. Enter the license key and click **Continue** to unlock nQuery Advisor.



3. **Perpetual License.** If you have purchased a perpetual license, the **Thank you for registering your perpetual licensed copy of nQuery Advisor** message will be displayed before you can run nQuery Advisor.
3. **Annual License.** If you have purchased an annual license, a message containing the expiration date of your license will be displayed before you can run nQuery Advisor.

Uninstalling nQuery Advisor from Standalone Computer

Go to Add/Remove Programs in the Control Panel, click on **nQuery Advisor (Standalone Installation)** and then click on the **Add/Remove** button. Alternatively, you can run **setup.exe** again from either your CD or the web page, and setup will uninstall nQuery Advisor.

Uninstalling nQuery Advisor from Client Computer

Go to Add/Remove Programs in the Control Panel, click on **nQuery Advisor (Network - Client Installation)** and then click on the Add/Remove button. Alternatively, contact your administrator to find out the directory where the server version of nQuery Advisor has been installed and execute **setup.exe** from the \NetSetup folder off this directory.



Getting Started with nQuery Advisor

You have installed the nQuery Advisor program. Now you can spend a few minutes getting acquainted with the program.

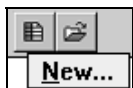
You should start by doing the tutorial in Chapter 2. If you use the program to follow the tutorial, you can learn the basics of nQuery Advisor in a short period of time.

The Chapter 2 tutorial may provide enough information for many users, but if you still have questions, you should follow the Analysis of Variance Tutorial in Chapter 12 while using nQuery Advisor.

As questions arise, you can use the other chapters of this manual for reference. However, you have more than just this manual to help you understand nQuery Advisor. Each sample size table screen provides four different aids to understanding the workings and requirements of the program:

The guide card for each row of each sample size table and many side tables.

When you open a sample size table (and many of the side tables), the guide card for that table displays a short description of the type of entry expected for the row.



The tag for each icon.

When your cursor remains on an nQuery Advisor icon briefly, a tag appears with a description of that icon. For example, when you depress the File menu New option, you get the tag shown above.



The status line description for each menu item.

When your cursor lies on an icon or a menu item, a short description of that item appears on the left end of the status bar at the bottom of the screen.

The Help system.

When you choose the Help menu, you can access the Help Topics option to use the Contents, Index, or Find options.

New Features and Tables in nQuery Advisor 5

The nQuery Advisor 5.0 program delivers 32 bit Windows architecture for Windows 98/NT/2000/XP.

New features:

- **References**
References for every sample size table are shown in a separate pane below the table and can be copied and pasted into reports.
- **Column names**
You can assign names (e.g. Outcome A, Outcome B, or Low SD, High SD, etc.) to each column in a table. These names will display on the screen and in the plot legends, as well as in the printed or pasted tables.
- **RTF Copy and Paste with user font choice for tables and side-tables**
You can copy and paste tables from nQuery Advisor into user documents in the user-selected font using Rich Text Format. The table structure, formatting, and Greek symbols are preserved (without use of the Dixon font.)
- **RTF Copy and Paste with user font choice for statements, user notes, references and guides**
You can copy nQuery Advisor statements, user notes, references, and guides. Then you can paste them into user documents in your selected font using Rich Text Format. This process preserves formatting and Greek symbols (without use of the Dixon font.)



New Sample Size Tables:

- **t-tests**

New table to compute power and sample size for the two group t-test with *unequal variances* (Satterthwaite's t-test)

Two group Satterthwaite t-test of equal means (unequal variances) (equal and unequal n's) (MTT0uv, MTT0uvU)

New table to compute power for detection of specified *fold-change* when the CV is specified (especially useful for planning *DNA microarray* studies)

Two group t-test for fold change assuming log-normal distribution (equal and unequal n's) (MTT0cv, MTT0cvU)

New table to compute probability of detection of specified fold-change when the CV is specified and the result must exceed a specified *fold-change threshold* (especially useful for planning *DNA microarray* studies)

Two group t-test of equal fold change with fold change threshold (equal and unequal n's) (MTT0fct, MTT0fct)

- **Proportions**

For the two group Chi-square, and continuity corrected Chi-square, you can now solve for the proportion which is detectably different from a specified proportion.

Two group χ^2 test of equal proportions – Compute one of two proportions (PTT0p)

Two group continuity corrected χ^2 test of equal proportions – Compute one of two proportions (PTT1p)

- **Equivalence**

Separate tables are available for two-group and crossover designs

Two-group t-tests (TOST) of equivalence in means (equal n's)
(MTE1tg, the same table structure as the former MTE1)

t-tests (TOST) of equivalence in means for crossover design
(MTE1co)

Two-group t-tests (TOST) for ratio of means (using log scale) (equal
n's) (MTE2tg, the same table structure as the former MTE2)

t-tests (TOST) of equivalence in ratio of means for crossover
design (natural log scale) (MTE2co)

- **Survival**

The total number of required events is now calculated for these
survival tables:

Log-rank test for equality of survival curves (STT0)

Test based on exponential survival, accrual period (STT1)

Test based on exponential survival, accrual period, dropouts
(STT2)

- **Standard Deviation Calculator**

A new table has been added to the Assistants menu, Estimate SD
option, to calculate the pooled standard deviation from two
independent samples.



Customizing Regional Settings

You can change Windows settings to suit your locale, and if you tell Windows 98/2000/NT/XT that you want to use commas instead of periods for the decimal point, nQuery Advisor will honor your request. This is called internationalization or localization.

You do this in one of two ways:

1. From the **Start** menu, choose **Control Panel**. Within **Control Panel**, double click to activate **Regional Settings**. Choose the **Regional Settings** tab and choose a language/region in the drop-down box.

or

2. From the **Start** menu, choose **Control Panel**. Within **Control Panel**, double click to activate **Regional Settings**. Choose the **Number** tab. When you see the dialog box under the Number tab, enter your preferred decimal symbol in the **Decimal symbol** field.

Considerations:

- a) If you use option 2 above, your edits change the system's configuration for that language. That is, if you're working in English (United States) and you change the decimal symbol to &, then change the language to French (France) and then back to English (United States), your decimal symbol will remain &. You can, however, return to the Number tab dialog box to change the Decimal symbol again.
- b) The remaining settings in the dialog box under the Number tab have no apparent effect on the displays in the nQuery Advisor program. These are: No. of digits after decimal, Digit grouping symbol, No of digits in group, Negative sign symbol, Negative number format, Display leading zeroes, Measurement system, and List separator.
- c) Files saved by nQuery Advisor should be entirely independent of the regional settings. This means that when you use commas as your decimal symbol, and you send a saved file to someone who uses periods, when he opens the file on his computer, the numbers will have periods.
- d) Testing has uncovered no problems, but if you are changing the decimal symbol to any symbol other than the period or the comma, you may run into complications.
- e) The printed date in the lower right corner of printed nQuery output respects the choices you make in Regional settings. As with decimal points, you can change

the style in which the date is presented either by changing the language in the Regional Settings tab, or by making the change on the Date tab dialog box.

Please see Chapter 3, *The File and Options Menus*, to read about the Preferences menu and its effect on your regional settings.

Troubleshooting

Some users experienced installation or runtime problems with the previous version of nQuery Advisor. Those problems were traced to particular versions of support DLLs and OCXs on their system. In order to resolve any future such problems quickly and effectively, we have provided a tool which determines the exact versions of all such files which nQuery Advisor is using on your system.

To use the troubleshooting tool:

Choose the **Help** menu **About nQuery** option.

In the **About nQuery Advisor** dialog box, click on the **Advanced Version Information** button.

The **Advanced Version Information** box will appear. This box lists the paths, versions and dates of the files which nQuery Advisor needs as those files exist on your computer.

Click on the **Save** button to save this information to a text file.

Send the saved text file to us so that we can advise you on any necessary updates to the files.

For this tool to work, you must have a particular file in the same folder as the executable file, nQuery50.exe. The file you need depends on the operating system you are using.

Operating System	File Required
Windows® 98	AdvVer.exe
Windows® NT	AdvVerNT.exe
Windows™ 2000	AdvVer.exe or AdvVerNT.exe
Windows™ XP	AdvVer.exe or AdvVerNT.exe

2. Tutorial

Determination of the appropriate sample size is a crucial part of study design. We must choose sample size correctly to allow a study to arrive at valid conclusions for the scientific question. A study which is too small may produce inconclusive results, while a study which is too large will waste scarce resources.

Answering the question “What sample size do I need?” requires six steps. Using an actual example of determining sample size for the two-sample t test, this chapter takes you through a step-by-step tutorial demonstrating some of the nQuery Advisor features. This chapter is not meant to be an exhaustive demonstration of nQuery Advisor options. Rather, the tutorial demonstrates the general methods of nQuery Advisor through one complete example. For a tutorial illustrating the use of the Compute Effect Size side tables, see Chapter 12, *Side Table & Compute Effect Size*.

Ideally, evaluations of obtainable power or interval width are made prior to the start of a study. This is done to ensure that the chosen sample size is neither too small to be likely to detect important effects nor so large that the study is longer and more costly than necessary. However, evaluation of the power of a completed study which failed to find significance can be useful in deciding whether the intervention is ineffective or whether further study may be justified. The results of the completed study can provide information about variance. Nevertheless, the “effect size” used in retrospective power analyses should not be the effect size observed in the study, but should be an effect size that would be important to detect.

Step 1. Formulate the study

The study question is: Does the new drug reduce anemia in elderly women after hip fracture?

Detail the study design


A two-group, randomized, parallel, double-blind study is planned. Patients will be studied for two weeks; each patient will be randomly assigned to receive either new drug or placebo 3 times per week. The sample sizes in the two groups will be equal.

Choose the outcome summary

The primary outcome measure will be the mean change in hematocrit level from pre-treatment to post-treatment. These changes will be compared between the two groups.

Specify the analysis method

The mean change in hematocrit level will be compared between the two groups of patients using the two-sample t test. The null hypothesis states that the mean change in hematocrit is the same in both groups.

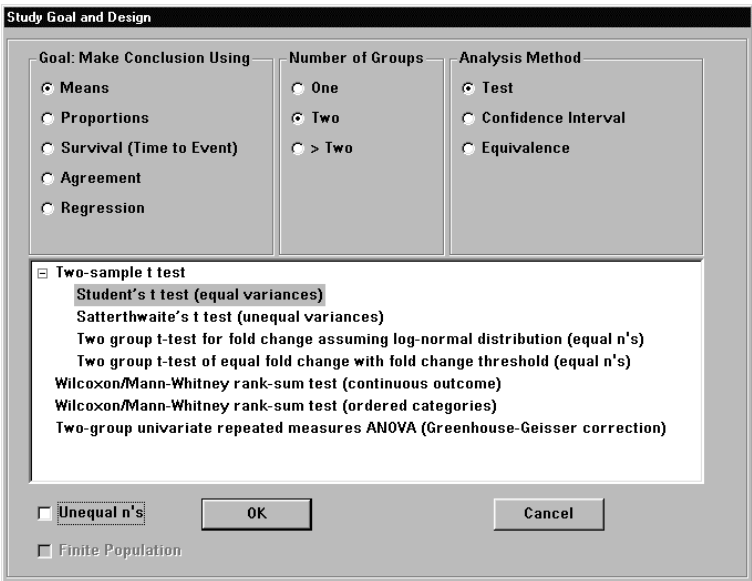
Select **File menu New** option or click on the **New** button . In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.

In the Study Goal and Design box below, the selections result initially in seven choices in the lower half of the Study Goal and Design dialog box.



Study Goal and Design

Goal: Make Conclusion Using

- ☒ Means
- ☐ Proportions
- ☐ Survival (Time to Event)
- ☐ Agreement
- ☐ Regression

Number of Groups

- ☐ One
- ☒ Two
- ☐ > Two

Analysis Method

- ☒ Test
- ☐ Confidence Interval
- ☐ Equivalence

☐ Two-sample t test

- Student's t test (equal variances)**
- Satterthwaite's t test (unequal variances)
- Two group t-test for fold change assuming log-normal distribution (equal n's)
- Two group t-test of equal fold change with fold change threshold (equal n's)
- Wilcoxon/Mann-Whitney rank-sum test (continuous outcome)
- Wilcoxon/Mann-Whitney rank-sum test (ordered categories)
- Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)

☐ Unequal n's

☐ Finite Population

OK Cancel

Different selections under “Goal” or “Number of Groups” or “Analysis Methods” bring up different lists of available sample size tables.



Note: This manual uses the ordering of the analyses within the Study Goal and Design box to determine an abbreviation for each analysis type. In this example, you are choosing analysis type MTT0. For a detailed explanation of the table abbreviation codes, please read the *Contents of the Study Goal and Design Dialog Box* section of Chapter 7, *The View and Windows Menus*.

(If you have set your screen resolution to a setting which is less than optimal for your monitor, some of the words in your display of the following figure may be cut off. The solution is to set the video display settings to the optimum for your monitor.)

Note that the Two-sample t test listing has a - sign beside it. To hide the listings under **Two-sample t test**, click on the – sign.

Select the Student's t test (equal variances) and click on the **OK** button to accept the choice. You will see the following screen:

	1	2	3	4
Test significance level, α				
1 or 2 sided test?				
Group 1 mean, μ_1				
Group 2 mean, μ_2				
Difference in means, $\mu_1 - \mu_2$				
Common standard deviation, σ				
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$				
Power (%)				
n per group				

Two-sample t-test (equal n's)
Enter a value for alpha, α , the significance level for the t-test, and select a one or two-sided test. Specify two of effect size, power and sample size and nQuery Advisor will compute the third.

Test significance level, α
Alpha is the probability of rejecting the null hypothesis of equal means when it is true (the probability of a Type I error).

Suggestion:
Enter 0.05, a frequent standard

Acceptable entries:
0.001 to 0.20

USER NOTES for MTT0-1

REFERENCES for MTT0-1:
Dixon, W.J., Massey, F.J. **Introduction to Statistical Analysis. 4th Edition** McGraw-Hill (1983)
O'Brien, R.G., Muller, K.E. **Applied Analysis of Variance in Behavioral Science** Marcel Dekker, New York (1983) pp. 297-344

STORED STATEMENTS for MTT0-1:

For Help, press F1 AUTO RECALC OFF

This is the sample size table for the two group t test of equal means with equal n's. Before continuing with the example, this section discusses the general structure of the nQuery Advisor screen.

Title Bar

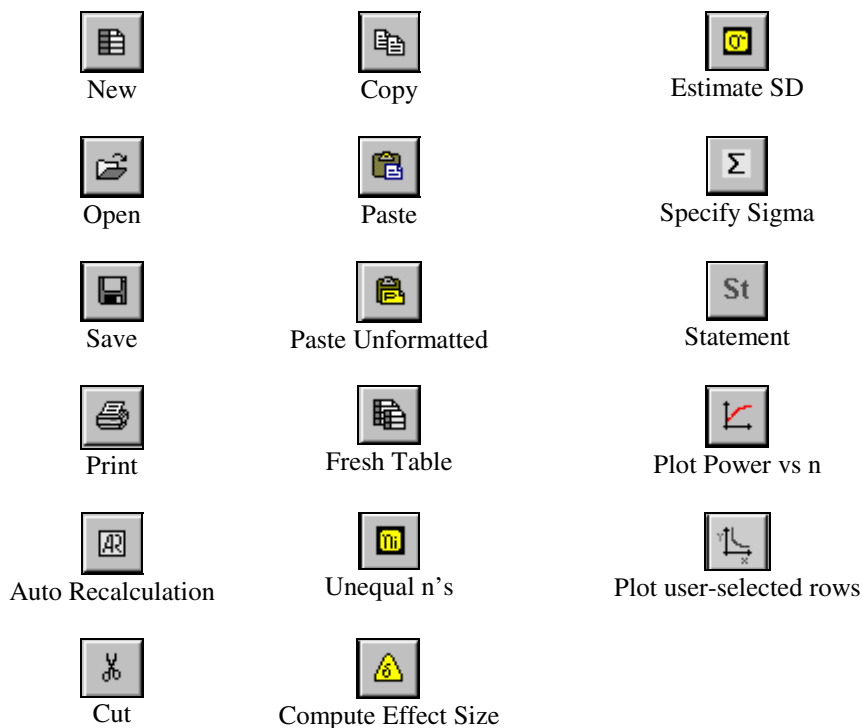
The title bar on the top of the sample size table window displays the name of the sample size table. The default name is the table abbreviation plus the number of the table. If you save the table using a different name, the next time you open the table, the title bar will display the name you used to save the table. For details on the nQuery table name abbreviations, see Chapter 7, *The View and Windows Menus*.

Menu Bar

The sample size table displays eight menus in the menu bar at the top of the window. The menus are: File, Edit, View, Options, Assistants, Plot, Window, Help.

Icon Bar

Note that the icon bar beneath the menu bar offers 17 icon buttons. You can click on each of those icon buttons to gain direct access to the represented program option, rather than selecting the menu option. The icons are:





If you rest the cursor on one of the icons, you will see a tag with a short description of the icon. A description of each icon also appears in the status line on the bottom of the window.

Table Title

Just below the icon buttons, the screen displays the title for this table: Two group t test of equal means (equal n's).

Column Numbers

Each column in the sample size table is labeled with a column number. You can change these default column names by using the Edit Column Names option from the Edit menu. Each table allows up to 20 columns for use. See Chapter 4 *The Edit Menu* for details.

Row Names

Below the table title, the screen displays nine row names. Each row name specifies the type of value to be found in the row, whether you enter the value, or the program calculates the value for you.

Changing Row Names or Labels

You can change the row labels to replace **Group 1** and **Group 2** with the specific names for your groups. This option allows you to enter customized row labels for the groups. Your new row labels will appear both on the screen and in the saved and printed versions of your sample size table.

To edit row names:

Click on the **Edit** menu **Edit Row Names** option. The Edit Row Name dialog box will appear.



Click on **Group 1 mean, μ_1** and Group 1 will appear in the white rectangle in the center of the dialog box. Note that **mean, μ_1** appears to the right of the white rectangle so that you always know which mean you are specifying.

In the white rectangle, type New drug to replace Group 1, then click on the **Accept Edit Row** button.

Click on **Group 2 mean, μ_2** , enter **Placebo** in the white rectangle, and click on the **Accept Edit Row** button. The dialog box will show your new row name entries.

Click on the **Update Table Row Name** button to update the table, and the sample size table will appear with the new row names. You will see those names in the next figure, as you specify parameters in Step 2.

Note: You can use up to a maximum of 20 characters for the editable part of the row name.

Status Bar

The Status Bar lies at the bottom of your nQuery Advisor window. The Status Bar toggle in the View menu controls the display of the Status Bar. The bar presents a short description of each icon button as your cursor goes over the icon button. The status bar also presents the on/off status of the automatic recalculation option, along with the exact contents of any cell selected by the cursor.

Note: The status bar may show more significant figures than you can see in the cell, depending on the number in the cell.



Colors in the Sample Size Table

The rows for power, sample size, effect size, interval width which provide the answers to your sample size queries are highlighted with yellow on the screen. In the sample size tables shown in grayscale in this manual, the yellow highlighting shows as a pale gray.

For example, Effect size, Power, and n per group are yellow when you have the table for the Two group t test on your screen. If you enter all required information in the white rows, you can fill in any two of the three yellow rows, and nQuery will compute the third. For this example, enter the group means and the common standard deviation, nQuery will compute the corresponding effect size. Then enter either power or n per group, and nQuery Advisor will calculate the other.

Any rows appearing white on your screen are the rows you can ignore, if you wish.

When you set the Auto Recalc option to **On**, the row(s) to be automatically recalculated will display green. For details on the Options menu Auto Recalc option, see Chapter 3, *The File and Options Menus*.

Guide Cards

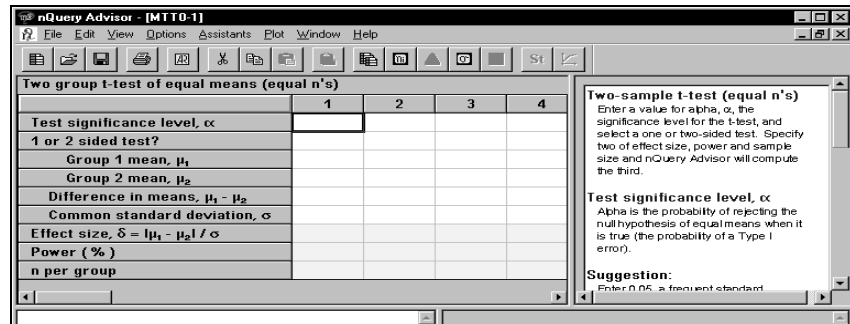
The guide cards in the right pane of the nQuery Advisor window provide statistical information on the row in which your cursor lies. If you are unfamiliar with the analytic procedure or with doing sample size computations, or you want some help with how to proceed while filling in values for the table, refer to the guide cards.

The default Guide toggle is set to **On** when you have an open sample size table. Thus, every new table appears with its guide card on. You can toggle the guide card to **Off** by choosing the **View** menu **Guide** option.

To view the guide card:

Click on any spreadsheet cell in the first row.

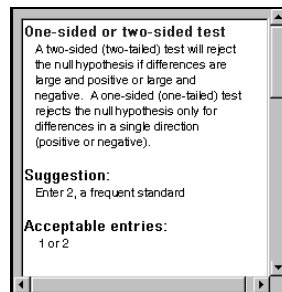
The guide card for the first row will appear in the upper right of the window.



Note that the guide card corresponding to the top row provides general information about how to use the table. As you move the cursor from row to row, the guide cards display information appropriate for each row. You also get suggestions for row values, details on limits for the values you can enter, and reminders about other helpful nQuery Advisor features.

To bring up the guide card for a different row:

Click on a cell in the second row, and the guide card will change to the card for the second row.



Every new table appears on the screen with its guide card On unless you turn off the guide card in the View menu.

To turn off the guide card:

Click on the **View** menu **Guide** option. The guide card pane will disappear from the window. (The guide card has been turned off for the rest of this example.)

To turn on the guide card after you have turned it off:

Click on the **View** menu **Guide** option. The guide card pane will appear in the window.



For details on copying, pasting and printing the Guide cards, please see the *Guide* section of Chapter 7, *The View and Windows Menus*.

References

The References pane is directly below the Guide Card pane of the nQuery Advisor window. There you will find the references for the current sample size table.

Statements

The Statements pane is directly below the References pane of the nQuery Advisor window. That pane is available for storing sample size justification statements generated by nQuery; these stored statements will be saved with the sample size table. This tutorial will demonstrate how to request Statements and store, print, or copy them to clipboard for pasting into other Windows applications.

Notes

The Notes pane is directly below the sample size table pane of the nQuery Advisor window. In the Notes pane you can enter all necessary notes to be saved with the sample size table.

Step 2. Specify Parameters for Planned Analysis

For the two group t test example (MTT0), the parameters you must specify for the analysis method being planned are:

- the significance level for the test
- whether the test procedure is to be one or two-sided.

Plans call for a 5% ($\alpha = .05$) significance level and a two-sided test.

To enter the values:

Click on the first cell of column 1. Enter **.05** into that cell.

Press <Enter> or the down arrow to register your entry. Your cursor will move to the cell in the second row.

Type **2** and press <Enter>.

The next screen shows the new values entered into the table after we have turned the Guide card option to Off. Note that the center section of the status bar at the bottom of the screen shows the exact contents of the chosen cell. The status bar will usually show more decimal places than appear in the table.

nQuery Advisor - [MTT0-1]

File Edit View Options Assistants Plot Window Help


Two group t-test of equal means (equal n's)


	1	2	3	4	5	6
Test significance level, α	0.050					
1 or 2 sided test?	2					
New drug mean, μ_1						
Placebo mean, μ_2						
Difference in means, $\mu_1 - \mu_2$						
Common standard deviation, σ						
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$						
Power (%)						
n per group						


In preparation for the next step, repeat your row entries of .05 and 2 for columns 2 and 3. The next section will use the three columns.

To copy the values:

Use your cursor to select the first two rows of the first column.

Click on the **Edit** menu **Copy** option or use the Copy icon, , in the icon bar, or use the <Ctrl><C> keyboard shortcut.

Select column two and use the Paste icon, , in the icon bar, or click on the **Edit** menu **Paste** option, or use the <Ctrl><V> keyboard shortcut.

Select column three and use the Paste icon, , in the icon bar, or click on the **Edit** menu **Paste** option, or use the <Ctrl><V> keyboard shortcut.

The row entries will display in columns two and three.

Using Mouse Buttons in Data Entry

When you are entering data into a sample size table, you can select the cell in two ways:

- Use the left mouse button to single click on the cell. You can immediately start entering a value. Your new value will replace any existing cell contents.



- Use the left button to double click on the cell. Any existing number will be selected. You can press <Delete> to remove the number, or simply start typing the new number. In either case, the original number in the cell will disappear.

Right-click Menus

If you right click within the sample size table (or within other panes or views,) you will get a right-click menu. These menus provide another way to access the Undo, Copy, Cut, Paste, Paste Unformatted, Print, Print Table to Clipboard, Create Statement, and Edit Row Name, and Edit Column Names options.

U <u>ndo</u>	Ctrl+Z
C <u>o</u> py	Ctrl+C
C <u>u</u> t	Ctrl+X
P <u>a</u> ste	Ctrl+V
Paste U <u>n</u> formatted	
<hr/>	
P <u>r</u> int	
<hr/>	
Print Table to Clipboard	
<hr/>	
Create S <u>t</u> atement	
Edit R <u>o</u> w Names	
Edit C <u>o</u> lumn Names	

These Edit options function in the same way whether you access them from the Edit menu or through the right-click menu for the sample size table.

Note that the right-click menus for the Guide Card, Statement, References, and User Notes panes differ from the menu shown above. Those right-click menu options include pane-specific options, such as Special Characters in the User Notes pane, Hide in the Guide Card pane, and Create Statement in the Stored Statements pane. See Chapter 4, *The Edit Menu* for details on the options available in the right-click menus.

Step 3. Specify Effect Size for Test

Specifying the effect size is often the hardest part of study planning.

For the two-sample t test, specifying the effect size has two parts: specifying the expected difference in means you would like to detect, and specifying the standard deviation expected within each group.

Specifying the difference in means expected for the two groups

You should specify the expected mean changes, the worthwhile mean changes, or the important mean changes. People often say, “This study has never been done before, so how do I know what will happen?” However, previous use of the intervention is not the important question.

The important question is what is known about the outcome measure. What would be an important effect of treatment? What kinds of effects might be expected, given other information?

In this example, there was information on hematocrit from four prior studies:

1. From a small pilot study in six elderly females after hip fracture, the mean hematocrit was 32.3%. In the same institution, in 32 healthy elderly females, the mean hematocrit was 33.5%.
2. Two previous studies tested different doses of the new drug in other patient groups. In those studies, the placebo group showed no change in hematocrit. The treated group showed changes of 2.5% to 5%.

These data taken together suggest that we can expect a change of 0% in the placebo treated group, with treatment group changes lying in the range 2.5 to 5%. Thus, a conservative estimate of the possible effect of the new drug in elderly females might be in the range 2.0% to 2.4%. Such increases would be of real value to the patient.

To enter means:

Click on the cell in the first column of the **New drug mean** row and enter **2.0**.

Press the right arrow to move to the second column of the **New drug** row.

Enter **2.2**.

Press the right arrow to move to the third column of the **New drug** row.

Enter **2.4** and press <Enter>.

You have entered the treatment means.

Click on the first column of the **Placebo** mean row and type **0**.

Press the right arrow to move to the second column of the **Placebo** row.

Type **0** in the second and third columns of the **Placebo** row.

Note that nQuery Advisor automatically calculates the difference in means, as you can see in the next screen.



Two group t-test of equal means (equal n's)						
	1	2	3	4	5	6
Test significance level, α	0.050	0.050	0.050			
1 or 2 sided test?	2	2	2			
New Drug mean, μ_1	2.000	2.200	2.400			
Placebo mean, μ_2	0.000	0.000	0.000			
Difference in means, $\mu_1 - \mu_2$	2.000	2.200	2.400			
Common standard deviation, σ						
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$						
Power (%)						
n per group						

Specifying the common standard deviation

The next row in the table is **Common standard deviation**, so we must obtain information about variability between individuals within a group. The two-sample t test assumes that variability in the two groups is the same, so you enter a single value.

In determining the value of the common standard deviation, we again refer to previous studies. Standard deviations for hematocrit values were 3.2% in elderly females, and 3 to 6% for other groups.

The current study, however, requires the standard deviation for change in hematocrit, and less information is available. The information reported here required some additional calculations from the values given in the references. The standard deviation of change in hematocrit in the various placebo and treated groups ranged from about 1.5% to 2.5%. These data suggest that we can reasonably expect a standard deviation for change in hematocrit of about 2%.

The nQuery Advisor program helps you to utilize information from a variety of formats to obtain an estimate of the standard deviation. For details, see Chapter 9, *Determining a Value for the Standard Deviation*.

To enter Common standard deviation:

Click on the cell in the first column of the **Common standard deviation** row and enter **2.0**.

Type **2.0** in the second and third columns of the **Common standard deviation** row.

Note that nQuery Advisor automatically calculates the **Effect** size.

At this point, you may wish to enter notes concerning the origin of these values for the mean and standard deviation so that you can document them in your report. You can

save any notes with the table, then print them out or copy them to the clipboard for future reference.

To add a note to the table:

Click in the white rectangle in the lower left of your screen below the title, USER NOTES for MTT0-1

Type: **References 1-5 suggest change in hematocrit due to the new drug treatment of 2% to 5% and standard deviations of change from 1.5 to 2.5%.**

Your nQuery Advisor table should look like the following screen.

The screenshot shows the nQuery Advisor software window titled "nQuery Advisor - [MTT0-1]". The main window contains a table for a "Two group t-test of equal means (equal n's)". The table has columns for parameters and six data points (1-6). The parameters listed are: Test significance level, α ; 1 or 2 sided test?; New drug mean, μ_1 ; Placebo mean, μ_2 ; Difference in means, $\mu_1 - \mu_2$; Common standard deviation, σ ; Effect size, $\delta = |\mu_1 - \mu_2| / \sigma$; Power (%); and n per group. The values entered are: $\alpha = 0.050$; 1 or 2 sided test? = 2; $\mu_1 = 2.000$; $\mu_2 = 0.000$; $\mu_1 - \mu_2 = 2.000$; $\sigma = 2.000$; $\delta = 1.000$; Power = 1.100; and n per group = 1.200. Below the table, there are three sections: "USER NOTES for MTT0-1" containing the text "References 1-5 suggest change in hematocrit due to the new drug treatment of 2% to 5% and standard deviations of change from 1.5 to 2.5%."; "REFERENCES for MTT0-1:" listing two references: "Dixon, W.J., Massey, F.J. Introduction to Statistical Analysis, 4th Edition McGraw-Hill (1983)" and "O'Brien, R.G., Muller, K.E. Applied Analysis of Variance in Behavioral Science Marcel Dekker, New York (1983) pp. 297-344"; and "STORED STATEMENTS for MTT0-1:" which is currently empty. The status bar at the bottom shows "For Help, press F1", "1.200000", and "AUTO RECALC OFF".

	1	2	3	4	5	6
Test significance level, α	0.050	0.050	0.050			
1 or 2 sided test?	2	2	2			
New drug mean, μ_1	2.000	2.200	2.400			
Placebo mean, μ_2	0.000	0.000	0.000			
Difference in means, $\mu_1 - \mu_2$	2.000	2.200	2.400			
Common standard deviation, σ	2.000	2.000	2.000			
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.000	1.100	1.200			
Power (%)						
n per group						

USER NOTES for MTT0-1

References 1-5 suggest change in hematocrit due to the new drug treatment of 2% to 5% and standard deviations of change from 1.5 to 2.5%.

REFERENCES for MTT0-1:

Dixon, W.J., Massey, F.J. **Introduction to Statistical Analysis, 4th Edition** McGraw-Hill (1983)

O'Brien, R.G., Muller, K.E. **Applied Analysis of Variance in Behavioral Science** Marcel Dekker, New York (1983) pp. 297-344

STORED STATEMENTS for MTT0-1:

Step 4. Compute: Sample Size or Power

Choose the value of power required for the study. The power is the probability that the results of your study will be statistically significant at the specified significance level if your assumptions about means, standard deviations, and effect size are true. The significance level is 5% for this example, and we are assuming that the values you have entered for means and standard deviation are the true values (not necessarily those observed in your study).



Investigators typically request study powers between 80% and 95%. The higher the required power, the larger the required sample size. Here, we assume that the investigator chooses 90% power.

To enter a value for Power:

Click on the cell in the first column of the Power row and type **90**.

Press the right arrow to move to the second column.

Type **90** into the second and third columns of the Power row.

Note that, when you type the value **90** into the power row and press <Enter> or the right arrow, nQuery Advisor computes the necessary sample size and completes the column.

The screenshot shows the nQuery Advisor software window titled "nQuery Advisor - [MTT0-1]". The main window contains a table for a "Two group t-test of equal means (equal n's)". The table has 7 columns (1-6) and 11 rows. The data entered is as follows:

	1	2	3	4	5	6
Test significance level, α	0.050	0.050	0.050			
1 or 2 sided test?	2	2	2			
New drug mean, μ_1	2.000	2.200	2.400			
Placebo mean, μ_2	0.000	0.000	0.000			
Difference in means, $\mu_1 - \mu_2$	2.000	2.200	2.400			
Common standard deviation, σ	2.000	2.000	2.000			
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.000	1.100	1.200			
Power (%)	90	90	90			
n per group	23	19	16			

Below the table, there are two panels. The left panel is titled "USER NOTES for MTT0-1" and contains the text: "References 1-5 suggest change in hematocrit due to the new drug treatment of 2% to 5% and standard deviations of change from 1.5 to 2.5%." The right panel is titled "REFERENCES for MTT0-1:" and lists two references: "Dixon, W.J., Massey, F.J. Introduction to Statistical Analysis, 4th Edition McGraw-Hill (1983)" and "O'Brien, R.G., Muller, K.E. Applied Analysis of Variance in Behavioral Science Marcel Dekker, New York (1983) pp. 297-344". Below the references is a section titled "STORED STATEMENTS for MTT0-1:" which is currently empty. At the bottom of the window, there is a status bar with the text "For Help, press F1" and "AUTO RECALC OFF".

For the range of hypothesized changes in the new drug group, a sample size per group of 16 to 23 would be required (total study sample sizes of 32 to 46.) In the next section we illustrate easy ways to evaluate a variety of possibilities for other scenarios and sets of analysis parameters.

Step 5. Sensitivity Analysis

A sensitivity analysis allows you to assess variability as in required sample size or in resulting power or interval width for a range of plausible parameter values. This section will discuss three approaches to sensitivity analysis.

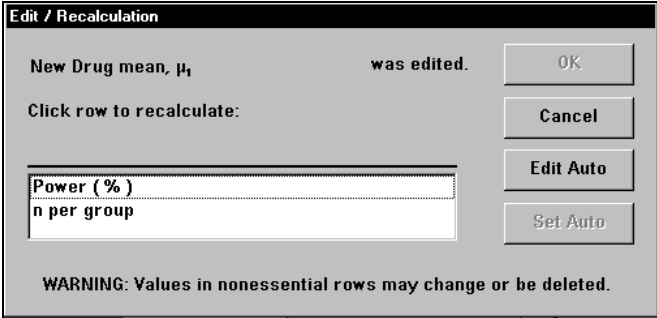
a. Edit Values in Filled-in Column

You might use this method after you have filled a sample size table and reviewed the results. For example, you might look at the screen above and wonder how the answer would change if the New drug mean were only 1.8. You can quickly get the answer to that question.

To edit a value in a filled-in column:

Click on the cell in the first column at the **New drug** row, type **1.8** and press <Enter>.

The **Edit/Recalculation** dialog box will appear.



The dialog box titled "Edit / Recalculation" has a grey background. At the top, it says "New Drug mean, μ_1 was edited." To the right of this text are three buttons: "OK", "Cancel", and "Edit Auto". Below this, it says "Click row to recalculate:". Below that is a table with two rows: "Power (%)" and "n per group". To the right of the table are two buttons: "Edit Auto" and "Set Auto". At the bottom, there is a warning message: "WARNING: Values in nonessential rows may change or be deleted."

Because you have edited the New drug row, either the value for **Power** or the value for **n per group** must change. The choice is yours. In this example, we want to keep the power at 90%.

Click on **n per group**. The **OK** button and the **Set Auto** button will be enabled.

You could click on **Set Auto** to cause nQuery Advisor to automatically recalculate n per group every time you edit a row value. See Chapter 3, *The File and Options Menus*, for more details on that feature.



Edit / Recalculation

New Drug mean, μ_1 was edited.

Click row to recalculate:

n per group

Power (%)

WARNING: Values in nonessential rows may change or be deleted.

Click on **OK** to finish selecting the **n per group** row for recalculation. You can see the recalculated screen in the next figure. A New drug mean of 1.8 would require 27 per group to achieve 90% power.

nQuery Advisor - [MTT0-1]

File Edit View Options Assistants Plot Window Help

Two group t-test of equal means (equal n's)

	1	2	3	4
Test significance level, α	0.050	0.050	0.050	
1 or 2 sided test?	2	2	2	
Group 1 mean, μ_1	1.800	2.200	2.400	
Group 2 mean, μ_2	0.000	0.000	0.000	
Difference in means, $\mu_1 - \mu_2$	1.800	2.200	2.400	
Common standard deviation, σ	2.000	2.000	2.000	
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	0.900	1.100	1.200	
Power (%)	90	90	90	
n per group	27	19	16	

b. Edit a Column Name

Before you use the Plot options, you may want to edit a column name so that the column name will appear in the plot legend.

To change a column name:

Select the **Edit** menu **Edit Column Names** option or the right-click menu **Edit Column Names** option.

The **Edit Column Name** dialog box will appear. This box lists the column names that you can change in your sample size table. Column names are restricted to a maximum of 25 characters each; the names will not wrap.

#

Column name (25 chars max)

1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
11	11
12	12
13	13
14	14
15	15
16	16
17	17
18	18
19	19
20	20

Copy Name(s)

Paste Name(s)

To add a name:

click on name and type

To edit a name:

double-click on name and edit

OK

Cancel

Click on the second column name and type in the desired name. In this case, the name is Diff = 2.2, SD= 2.0. (If you wanted to use Special Characters in the column names, you would select the Special Characters box and paste the selected character into the notes, then copy it and paste it into the column name box. See Chapter 4, *The Edit Menu*.)

#

Column name (25 chars max)

1	1
2	Diff = 2.2, SD= 2.0
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
11	11
12	12
13	13
14	14
15	15
16	16
17	17
18	18
19	19
20	20

Copy Name(s)

Paste Name(s)

To add a name:

click on name and type

To edit a name:

double-click on name and edit

OK


Cancel

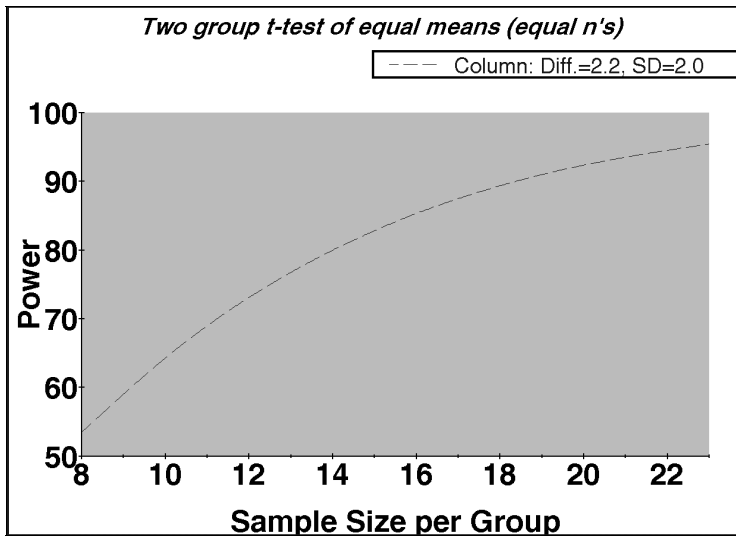
c. Use Plot Options

To use the Plot option to see n per group for different powers:

Use the mouse to highlight the entire second column of your sample size table.

Click on the **Plot** menu **Plot Power vs n** option or the **Plot Power vs n Plot**

icon . The plot for the chosen column will appear.



To use the Plot option to plot user-selected rows:

When you prefer more choice in axis parameters, you could choose the **Plot** menu **Plot User-selected rows** option or the **Plot User-selected rows**

icon . See Chapter 6, *The Plot Menu*, for details on using the Plot option.


If you want to re-label your plot axes or title or change the appearance of the plotted lines or the background, read Chapter 6, *The Plot Menu*, for details.

d. Fill Table Rows

Using Fill Right and Specify Multi-Factor Table


If you have been following this tutorial, you now have a table with three filled columns. Since we want an empty table for the next demonstration, you can open a New table, open a Fresh Table, or Clear the present table.

To open a new table using the File menu New option:

Choose the **File** menu **New** option or click on the **New** icon . The Study Goal and Design box will appear.

Select your analysis and click **OK**. The new table will appear.

To open a new table using the Fresh Table option:

Choose the **File** menu **Fresh Table** option or click on , the Fresh Table icon to get a new table for the same type of analysis as the current table. The new table window will appear; the table will contain no entries.

To clear the existing table:

Click on the **Edit** menu **Clear** option. A box will appear, prompting you to confirm that you want to clear the table.

Click on the **No** button if you want to refrain from clearing the table before you save it.

Click on the **Yes** button, and nQuery Advisor will clear your table.

The sample sizes necessary to detect differences in mean hematocrit change of 2.0, 2.2, 2.4 with a standard deviation of 2.0 were 23, 19, 16, respectively. Based on these values, the investigator decided to enroll 20 subjects per group. The investigator now wants to confirm that 20 subjects per group will give adequate power for these expected differences even for standard deviations larger or smaller than 2.0. The Edit options, Fill Right and Specify Multi-Factor Table, provide shortcuts for obtaining power or sample size for multiple sets of values.

Fill Right will quickly enter your chosen values in specified rows when you want to enter identical values in every column of any given row. The Specify Multi-Factor Table option accepts one-time entry of row values to be combined, then creates one column in your table for every combination of row values. These two options can



substantially reduce the typing necessary to evaluate many sets of parameters or effect size values.

To use the Fill Right option:

Enter **.05** in the cell in the first row of the first column.

Enter **2** in the second row of the first column.

Enter **20** in the bottom row of the first column, n per group.

Select the first column.

Choose the **Edit** menu **Fill Right** option, and nQuery Advisor will enter the value from each of the three rows into every column of the table.

To use the Specify Multi-factor Table option:

Choose the **Edit** menu **Specify Multi-factor Table** option. The Specify Multi-factor Table dialog box will appear.

The dialog box is titled "Specify Multi-Factor Table". It contains the instruction: "Set up multiple columns with all possible combinations of values you specify for each row." Below this, it says "Select a row (up to 4 rows):" and "Type value(s) for row and press enter after each one:". On the left is a list box with the following items: "Test significance level, α ", "1 or 2 sided test?", "New Drug mean, μ_1 ", "Placebo mean, μ_2 ", "Difference in means, $\mu_1 - \mu_2$ ", "Common standard deviation, σ ", "Effect size, $\delta = |\mu_1 - \mu_2| / \sigma$ ", and "Power (%)". To the right of the list box is a large text entry field. To the right of the entry field are four buttons: "Save Row", "OK", "Delete Value", and "Cancel". Below these buttons are two more buttons: "Delete Row" and "Clear". At the bottom of the dialog box, it says "Saved rows and values (max of 4 rows and 20 columns)" followed by a large empty rectangular area.

This option allows you to specify several values for one or more rows. The program will enter the values into your table in all possible combinations.

Click on **New drug mean**, and the cursor will blink in the value entry field in the second column.

Enter **2** and press <Enter>. The program will write the 2 to the column below the entry box.

Enter **2.2** and press <Enter>.

Enter **2.4** and press <Enter>.

Now that you have entered all three values, click on the **Save Row** button, and the three entries will be recorded in the bottom of the dialog box.

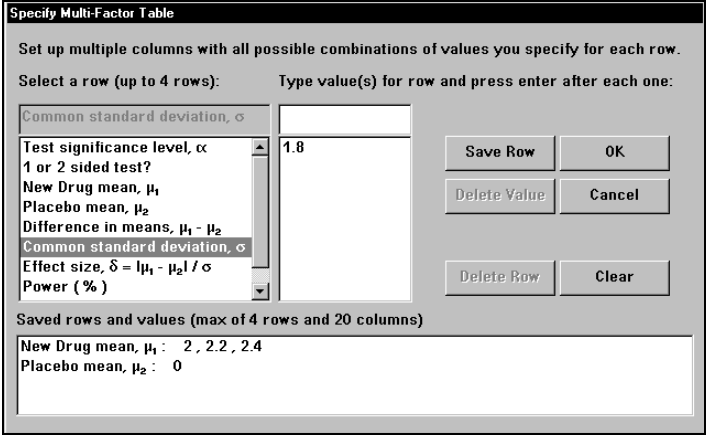
Click on **Placebo mean**.

Type **0** and press <Enter>.

Click on **Save Row**.

Click on **Common standard deviation**.

Type **1.8** and press <Enter>. The dialog box will be similar to the following figure. The bottom section displays the values entered for New Drug mean and Placebo mean.



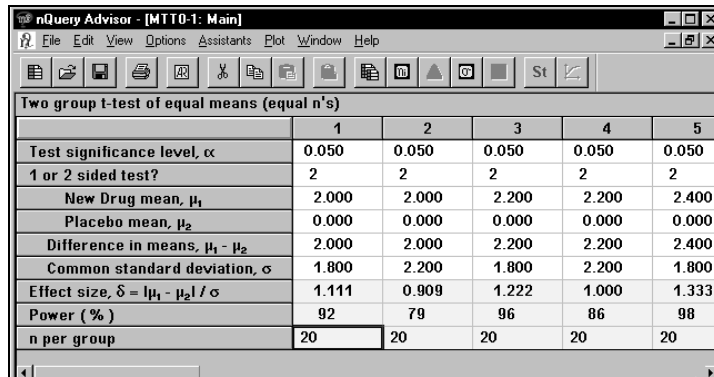
The dialog box is titled "Specify Multi-Factor Table". It contains instructions: "Set up multiple columns with all possible combinations of values you specify for each row." Below this, it says "Select a row (up to 4 rows):" and "Type value(s) for row and press enter after each one:". A list of parameters is shown on the left, with "Common standard deviation, σ " selected. The value "1.8" is entered in the adjacent text field. To the right of the text field are four buttons: "Save Row", "OK", "Delete Value", and "Cancel". Below these are two more buttons: "Delete Row" and "Clear". At the bottom, a section titled "Saved rows and values (max of 4 rows and 20 columns)" displays the following text: "New Drug mean, μ_1 : 2 , 2.2 , 2.4" and "Placebo mean, μ_2 : 0".

Type **2.2** and press <Enter>.

Click on the **Save Row** button.

Click on **OK** to finish the entries and send them to the table. Your sample size table will appear with the columns filled as you have specified. Note that the nQuery Advisor Specify Multi-Factor Table option fills only as many columns as necessary to form all combinations.

Note: Values for the last row specified will change in the fastest moving fashion while values for the first row specified will change in the slowest moving fashion as they fill in the columns. See the screen below.



The screenshot shows the nQuery Advisor software interface. The title bar reads "nQuery Advisor - [MTT0-1: Main]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains icons for file operations, editing, and a button labeled "St". The main window displays a table titled "Two group t-test of equal means (equal n's)".

	1	2	3	4	5
Test significance level, α	0.050	0.050	0.050	0.050	0.050
1 or 2 sided test?	2	2	2	2	2
New Drug mean, μ_1	2.000	2.000	2.200	2.200	2.400
Placebo mean, μ_2	0.000	0.000	0.000	0.000	0.000
Difference in means, $\mu_1 - \mu_2$	2.000	2.000	2.200	2.200	2.400
Common standard deviation, σ	1.800	2.200	1.800	2.200	1.800
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.111	0.909	1.222	1.000	1.333
Power (%)	92	79	96	86	98
n per group	20	20	20	20	20

Now that your table is almost completely filled in, you can see how the power varies with the changes in the mean difference and standard deviation.

Use the scroll bar to display columns lying to the right. Note that columns 7-20 contain the significance level, test sidedness, and n per group. That's because we used the Fill Right option for ease of filling the table. Since the Specify Multi-Factor Table option only filled columns 1-6, we should clean up the table.

To clean up the table:

Use the mouse to select columns 7-20.

Choose the **Edit** menu **Cut** option. The entries in columns 7-20 will be cut, and your table will contain only the columns necessary for the full multi-factor combinations.

Step 6. Choose Sample Size, Write Statement

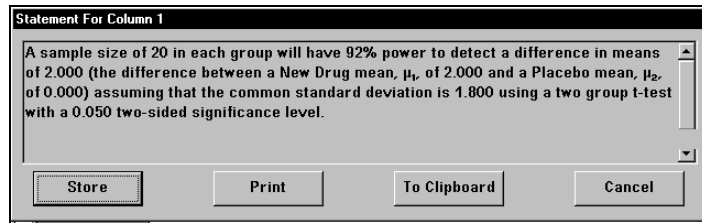
The nQuery Advisor program writes up the sample size decision for any chosen column. This feature makes it easy for you to report your sample size decisions in correct language.

To create a sample size justification statement:

Select any single completed column in your sample size table. For this example, select the first column.



Click on **St**, the **Create statement** button, or the **Edit** menu **Create Statement** option. The statement will appear in the Statement dialog box.



Buttons in the Statement Dialog Box

Store

To store the statement with the sample size table:

Click on the **Store** button to send the statement to the Statement pane of the sample size table.

	1	2	3	4	5	6
Test significance level, α	0.050	0.050	0.050	0.050	0.050	0.050
1 or 2 sided test?	2	2	2	2	2	2
New drug mean, μ_1	2.000	2.000	2.200	2.200	2.400	2.400
Placebo mean, μ_2	0.000	0.000	0.000	0.000	0.000	0.000
Difference in means, $\mu_1 - \mu_2$	2.000	2.000	2.200	2.200	2.400	2.400
Common standard deviation, σ	1.800	2.200	1.800	2.200	1.800	2.200
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.111	0.909	1.222	1.000	1.333	1.091
Power (%)	92	79	96	86	98	91
n per group	20	20	20	20	20	20

USER NOTES for MTT0-1

REFERENCES for MTT0-1:

Dixon, W.J., Massey, F.J. *Introduction to Statistical Analysis*. 4th Edition McGraw-Hill (1983)

O'Brien, R.G., Muller, K.E. *Applied Analysis of Variance in Behavioral Science* Marcel Dekker, New York (1983) pp. 297-344

STORED STATEMENTS for MTT0-1:

A sample size of 20 in each group will have 92% power to detect a difference in means of 2.000 (the difference between a New drug mean, μ_1 , of 2.000 and a Placebo mean, μ_2 , of 0.000) assuming that the common standard deviation is 1.800 using a two group t-test with a 0.050 two-sided significance level.

Now when you save the sample size table, you will save the statement with the table.

After you have stored the statement with the sample size table, you can choose to print the statement or not, whenever you print the table.



Note: A stored statement is permanently associated with the sample size table and cannot be erased from the Stored Statements pane. For more information, see the Create Statements section of Chapter 4, *The Edit Menu*.

Print

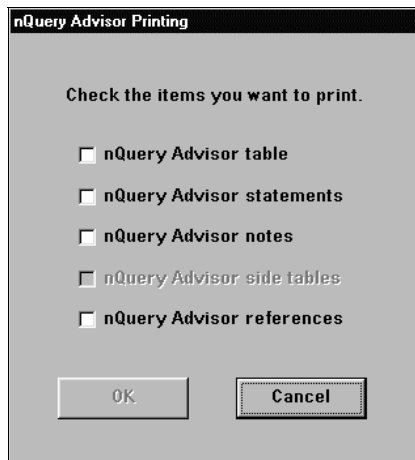
To print the statement from the Statement dialog box:

Click on the **Print** button to bring up the **Print** dialog box.

Click **OK** to print the statement.

To print the stored statement and the table:

Choose the **File** menu **Print** option, and you will see the following dialog box. Note that the nQuery Advisor statements, notes, and side tables options will be grayed out when you have no statements, notes, or side tables for the current table.



Click in the appropriate check box to select **nQuery Advisor table** and **nQuery Advisor statements** for printing.

Click on **OK** to bring up the **Print** dialog box.

Click **OK** to print the statement and table.

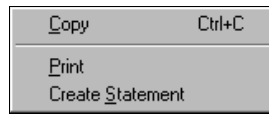
To Clipboard

To use the statement in the statement dialog box with another Windows application:

Click on the **To Clipboard** button to send the statement to the clipboard for pasting into another Windows application.

To use the statement stored in the Statement pane with another Windows application:

Click on the right mouse button in the **Statement** pane to bring up the right-click menu.



Click on the **Copy** option to send the statement to the clipboard. The Font selection for pasting dialog box will appear. This box contains instructions on how to switch fonts. For details on this option, see Chapter 4, *The Edit Menu*.

Click on the **OK, Complete Copy** button to save the fully formatted statement to the Clipboard.

Move to Microsoft Word or another word processing program, then paste the statement into the Windows word processing document. (Note that you can also paste to your sample size table from Windows applications. For details, see Chapter 4, *The Edit Menu*.)

The following figure shows the printed table.

nQuery Advisor						
Two-group t test of equal means (equal n's)						
Column	1	2	3	4	5	6
Test significance level, α	0.050	0.050	0.050	0.050	0.050	0.050
1 or 2 sided test?	2	2	2	2	2	2
New Drug mean, μ_1	2.00	2.00	2.20	2.20	2.40	2.40
Placebo mean, μ_2		0.00	0.00	0.00	0.00	0.00
0.00						
Difference in means, $\mu_1 - \mu_2$	2.00	2.00	2.20	2.20	2.40	2.40
Common standard deviation, s	1.80	2.20	1.80	2.20	1.80	2.20



Effect size, $\delta= \mu_1-\mu_2 /\sigma$	1.11	0.91	1.22	1.00	1.33	1.09
Power (%)	92	79	96	86	98	91
n per group	20	20	20	20	20	20

STORED STATEMENTS for MTT0-1

A sample size of 20 in each group will have 92% power to detect a difference in means of 2.000 (the difference between a New Drug mean, μ_1 , of 2.000 and a Placebo mean, μ_2 of 0.000) assuming that the common standard deviation is 1.800 using a two group t-test with a 0.050 two-sided significance level.

MTT0-1 9/09/02 Page 1

Cancel

To exit from the statement dialog box:

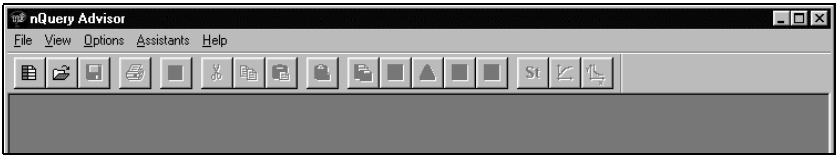
Click on **Cancel** to discard the statement.

Summary

This tutorial has introduced you to several of the nQuery Advisor features by using one complete example. You should now have a good overview of the nQuery Advisor program and its mode of operation. However, please keep in mind that nQuery Advisor offers many features not discussed in detail or even mentioned in this chapter. See the other chapters of this manual for details and examples of the other available options.

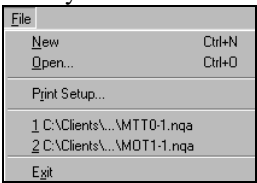
3. The File and Options Menus

The first nQuery Advisor screen contains a menu bar with five choices: File, View, Options, Assistants, and Help. The File, and View menus on this first screen are the initial menus. These initial menus are shorter than the File and View menus available after you open a table. The next figure shows the first nQuery Advisor screen, excluding the Tips dialog box. See Chapter 5 for a description of the Assistants menu and Chapter 7 for a description of the View menu.



File Menu — Initial

The initial File menu allows you to start a new sample size table, open an existing sample size table, perform print setup, or exit from the nQuery Advisor program. After you have saved a table, the File menu lists recent saved files.



New



The New option on the File menu allows you to start a new sample size table by selecting from the Study Goal and Design dialog box.

Study Goal and Design

Goal: Make Conclusion Using	Number of Groups	Analysis Method
<input checked="" type="radio"/> Means	<input type="radio"/> One	<input checked="" type="radio"/> Test
<input type="radio"/> Proportions	<input checked="" type="radio"/> Two	<input type="radio"/> Confidence Interval
<input type="radio"/> Survival (Time to Event)	<input type="radio"/> > Two	<input type="radio"/> Equivalence
<input type="radio"/> Agreement		
<input type="radio"/> Regression		

☒ Two-sample t test

- Student's t test (equal variances)
- Satterthwaite's t test (unequal variances)
- Two group t-test for fold change assuming log-normal distribution (equal n's)
- Two group t-test of equal fold change with fold change threshold (equal n's)
- Wilcoxon/Mann-Whitney rank-sum test (continuous outcome)
- Wilcoxon/Mann-Whitney rank-sum test (ordered categories)
- Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)

☐ Unequal n's

☐ Finite Population

The Study Goal and Design dialog box provides an organized index to the available sample size tables.

Choosing an analysis type in the Study Goal and Design Dialog Box:

Note that this dialog box contains three columns. For each sample size table, you will click on one radio button in each column to make your selection of analysis type.

Click on one of the five **Goal** radio buttons. You can decide to base your conclusions on Means, Proportions, Survival, Agreement, or Regression.

Click on the radio button specifying the **Number of Groups** as One, Two, or Greater than Two.

Click on the radio button specifying the **Analysis Method**, Tests, Confidence Interval, or Equivalence.

The list box at the bottom of the dialog box will display types of analyses for which nQuery sample size tables are available for each combination of radio button choices.

When you see an analysis type listed with a + sign to the left, click on the + sign to display the selections available under that analysis type.

Click on the name of the preferred analysis method to select it.



Note the two checkboxes in the lower left corner: Unequal n's and Finite Population.

Click on the **Unequal n's** checkbox if you want unequal n's. (If you decide to use unequal n's after opening the sample size table, the analysis types which accept unequal n's offer an unequal n's button in the sample size table for later selection.)

Some goal and analysis combinations for one-group designs can be modified for sampling from a finite population. When the Finite Population checkbox is active, you can check the box to modify your one-group design. Click on the **Finite Population** checkbox to specify a finite population.

Click **OK**. Your chosen sample size table will appear.

To get details on your choices in the Study Goal and Design dialog box:

Read the *Contents of the Study Goal and Design Dialog Box* in Chapter 7, *The View and Windows Menus*.

Going Beyond the Study Goal and Design Box

The Study Goal and Design dialog box offers you a wide range of analysis designs. However, statistically sophisticated users may be planning a design or analysis not considered here. If you have a formula for some sample size problem that nQuery Advisor does not automatically cover, you can go beyond the default designs. You can obtain distribution function values to insert in your own sample size equation. For details, see the *Distribution Function Menu* section in Chapter 5, *The Assistants Menu*, and see examples of its use in Chapter 20, *Distribution Function Tables*.

Open

The File menu Open option allows you to open any sample size table created and saved by nQuery Advisor.

To use the Open option:

Choose the **File** menu **Open** option or the **Open** icon to bring up the **File Open** dialog box.

In the **File Open** dialog box, select the appropriate drive and directory.

Click on the name of the desired file and click on **OK**.

Print Setup

The Print Setup option brings up the Windows Print Setup dialog box. You can use the dialog box to choose the printer and paper orientation, as well as paper size and source.

Recent File

The File menu will also display the names of recently-saved files. Those names will appear in the space above the Exit option.

To use the Recent File option:

Click on **File** menu and review the listed files.

Click on the name of the desired file to open the file.

Exit

The Exit option on the File menu allows you to exit from the nQuery Advisor program. When you choose this option, you will be prompted to save any unsaved sample size tables or plots.

File Menu — From a Sample Size Table

This menu offers you the New, Open, Exit and Recent Files options, as on the initial File menu. This menu also offers ways to open a new table of the same type, close a table, save or print your table, print it to clipboard, or change the printer setup.

File		
N	New	Ctrl+N
F	resh table	Ctrl+F
O	pen...	Ctrl+O
C	lose	
S	ave	Ctrl+S
A	Save As...	
P	rint...	Ctrl+P
	Print Active View...	
	Print Setup...	
	Print Table to Clipboard	
1	C:\Clients\...\MTC1-1.nqa	
2	C:\Clients\...\MTT0-1.nqa	
	Exit	



Fresh Table

The Fresh Table option on the File menu opens a new, empty copy of the current table.

To use the Fresh Table option:

Click on the **File** menu **Fresh Table** option or click on the **Fresh Table** icon. Your current sample size table will remain open in nQuery, and a new, empty version of the current sample size table will appear.

The new table will be identified with a higher number than the first table. For example, if the first table was MTC0U-1, the second table will be MTC0U-2.

Close

The Close option on the File menu closes the active sample size table.

To use the Close option:

Click on the **File** menu **Close** option. The current sample size table will close.

Save

The Save option on the File menu saves the active sample size table.

To use the Save option:

Click on the **File** menu **Save** option or the **Save** icon. If you have not saved this sample size table previously, you will be prompted to give a name and a directory for the file.

After you enter a directory and name for the file, click on **OK**.

Save As

The Save As option on the File menu prompts you for a name for the file and saves the active sample size table.

To use the Save As option:

Click on the **File** menu **Save As** option. You will be prompted to give a name and a directory for the file.

After you enter a directory and a name for the file, click on **OK**.

Print

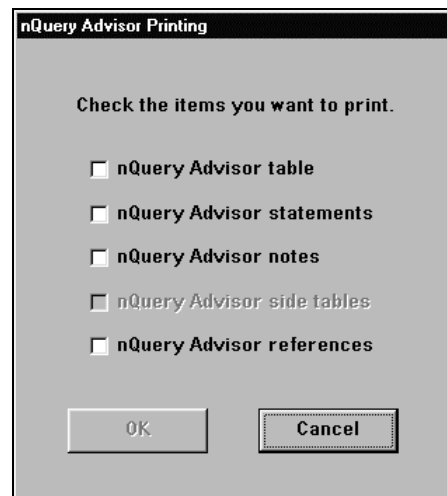


The Print option on the File menu will print your sample size table, including its title, the row names, and the column values; it also allows printing of attached side tables, and any saved notes or sample size justification statements.

To use the File menu Print option:

Create a sample size table and enter row values in at least one column of the table.

Click on the **File** menu **Print** option or the **Print** icon. The nQuery Advisor Printing dialog box will appear.



The dialog box gives you five check boxes. The table and references options are always active. The side table option is active when you have an active side table. The notes and statements options are active whenever you have information in the Notes and Statements panes.

You can click in a check box to choose the **nQuery Advisor table**, the **nQuery Advisor statements**, **nQuery Advisor notes**, **nQuery Advisor side tables** connected with the main table, and/or **nQuery Advisor references**. Check your preferred items and the OK button becomes active.

Click **OK**.



The Windows Print dialog box will appear.

Click **OK** to send your selected items to the printer.

Print Active View

The File menu Print Active View option will print whichever pane has the focus, whether the table, the notes, the statements, or the guide cards. Thus, this option is essentially the same as the Print option in the right-click menu. This option is not active for side tables; they have their own Print button.

Print Table to Clipboard

The Print Table to Clipboard option on the File menu copies your complete sample size table, including Greek letters and equations, to the Clipboard as a table in RTF format. The table in the Clipboard will include the table title, the row names and all column values with tabs between columns.

Note: When the active table is a side table, you can use the Print Table to Clipboard option to copy the side table to the Clipboard as a table.

You can use this option for later pasting into various Windows applications. For example, you might want to paste the complete table into Microsoft Word or WordPerfect or into a spreadsheet. The table is pasted into a word processing document as a table.

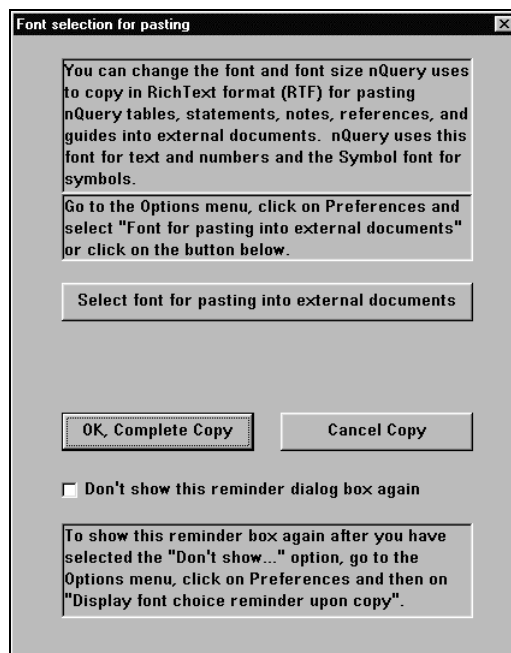
To use the Print Table to Clipboard option:

If you have more than one sample size table open, use the **Window** menu to make the desired table the current table.

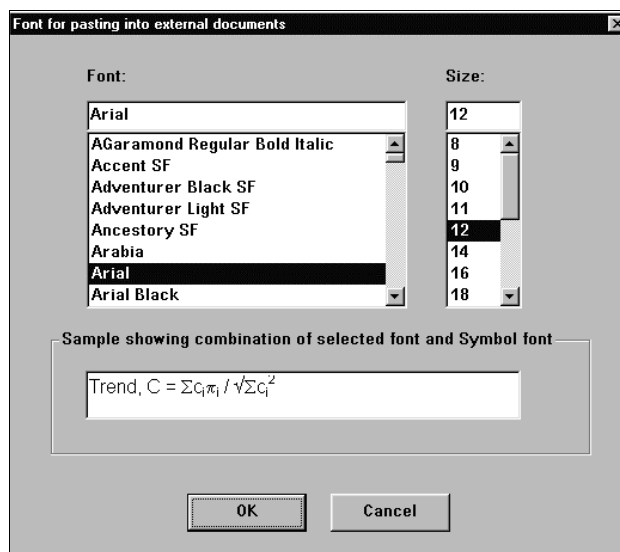
Select the **File** menu **Print Table to Clipboard** option.

Or, you can right click in the table to bring up the right click menu, then click on the **Print Table to Clipboard** option.

The **Font selection for pasting** dialog box will appear.



The default font is the Arial font. To select a different font, click on **Select font for pasting into external documents**. The **Font for pasting into external documents** dialog box will appear.





The default font, Arial, will be highlighted. Select the font and font size you prefer and click on **OK**. Symbols will appear in the document in Windows symbol font.

In the **Font selection for pasting** box, click on the **OK, Complete Copy** button.

The current table will be sent to the clipboard for use with other programs.

Move to a word processing document and paste the contents of the clipboard into the document.

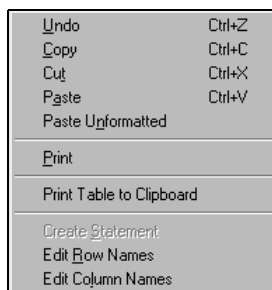
Note: Print Table to Clipboard will copy the Greek letters and any equations used in the table. When you paste the contents of the clipboard into Microsoft Word, Word Perfect, or another word processing program, your document will display the contents of the table faithfully. If you want to paste the table contents into a spreadsheet, you should first paste into a word processing document. Then copy from that document and paste into the spreadsheet.

If you are interested in copying Notes, Statements, or References to Clipboard, these panes have a right-click menu containing a Copy option. For details, see the Copy option described in Chapter 4, *The Edit Menu*.

If you want to copy the contents of the Guide card to Clipboard, you can use the guide card right-click menu containing a Copy option. For details, see the Guide section of Chapter 7, *The View and Windows Menus*.

Using the Right-Click Menu to Print the Table

If you right click within the sample size table (or within other panes or views), you will get the right-click menu. The right-clicks menus will differ from each other, but all include a Print option. The right-click menu below is the menu for the sample size table.



Choose the Print option, and you will see the usual Windows Print dialog box.

Printing the Sample Size Justification Statement

There are several ways to print the customized statement for the selected column in the sample size table.

To print a statement from the statement dialog box:

Create a sample size table and enter row values in at least one column of the table.

With your cursor in one cell of the filled column of the sample size table, you can create a statement in three ways:

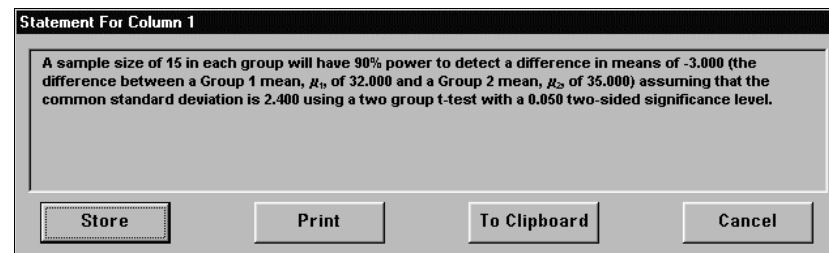
Click on the Create Statement icon .

Click on the **Edit** menu **Create Statement** option.

Right click within the sample size table to bring up the right-click menu, then click on the **Create Statement** option.

The customized statement will appear.

The statement will describe the results in the chosen column. For example:



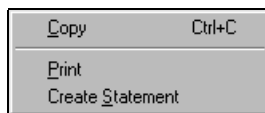
While you are viewing the statement, click on the **Print** button on the Statement window.

The Print dialog box will appear. Click on **OK** to print the statement.

To print a stored statement from the right-click menu:

While you are viewing the statement, click on the **Store** button on the Statement window. The statement will be stored in the Statement pane of the sample size table window.

Right click in the Stored Statements pane, and the Statements right-click menu will appear.



Choose the **Print** option, and the Windows Print dialog box will appear.

To print a stored statement using the File menu Print Active View option:

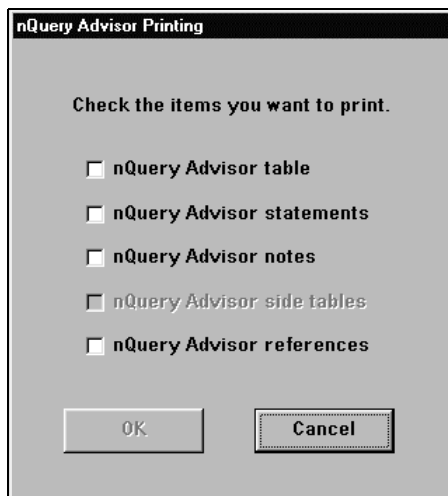
Left click in the Stored Statements pane.

Choose the File menu Print Active View option.

The Windows Print dialog box will appear.

To print a stored statement and/or its table using File menu Print:

Choose the **File** menu **Print** option, and you will see the following dialog box.



Click on nQuery Advisor statements and click on **OK**.

Whenever you have a stored statement, you can use the File menu Print option and this dialog box to print that statement.

Exit

The Exit option on the File menu shuts down the nQuery Advisor program. It also closes any open sample size tables.

To use the Exit option:

Select the **File** menu **Exit** option or click in the X in the upper right hand corner of the table.

If you have one or more open tables which have not been saved since the last change to the table, you will see the following prompt:

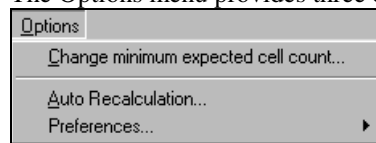


Click on the **Yes** button to save the table. The Windows **Save as** dialog box will appear.

Enter a name and directory for the file and click on **OK**. The nQuery Advisor program will shut down and save your file.

Options Menu

The Options menu provides three choices:



Change Minimum Expected Cell Count

The formulas for sample sizes for many of the proportions tables are designed for large samples. The nQuery Advisor program checks that the minimum expected cell size (number of counts expected for each of successes and failures in a group) is greater than a preprogrammed default value.

When you see the warning box stating that minimum expected cell size is not large enough, you must check that the sample size n which has been computed by Query Advisor will really be large enough for your study. For further details, see *Example for Two group χ^2 test (PTT0) and Sample Too Small Warning*, in Chapter 15, *Sample Size Tables for Proportions*. In some cases, the minimum expected cell size used for the warning box may be too conservative. When that is the case, you may wish to customize the minimum cell count for the current session using the Change Minimum Expected Cell Count option.



To use the Change Minimum Expected Cell Count option for the current session:

Click on **Options** menu, then on **Change Minimum Expected Cell Count**. The Change Minimum Expected Cell Size dialog box will appear.

The dialog box has a title bar 'Change Minimum Expected Cell Size'. Inside, it says 'For proportions tables, change default value for minimum expected cell size (for this session) to:' followed by a text input field. Below the input field, it explains the default value: 'Default value is the square of the 100(1-α/s) percentage point of the normal (Gaussian) distribution, where s=1 for a one-sided test or interval and 2 for a two-sided test or interval.' At the bottom are three buttons: 'OK', 'Cancel', and 'Reset to Default'.

Enter the new **minimum expected cell size** for this proportion sample size table. Enter **0** if you do not want nQuery Advisor to check for minimum cell size.

Click on **OK**.

To change the Change Minimum Cell Size back to the default for the current session:

Click on **Options** menu, then on **Change Minimum Cell Count**. The Change Minimum Cell Count dialog box will appear, showing your designated cell size.

Click on **Reset to Default**. The dialog box will disappear and the minimum cell size will be the default minimum cell size.

Auto Recalculation



The Auto Recalculation option specifies the sample size table row to be recalculated as you make changes to your entries. The Auto Recalculation option is a particularly handy toggle. You can turn it on when you want to edit or change numbers in columns that have been previously filled in.

When Auto Recalculation is On, the specified row in any sample size table column will be recalculated as soon as you edit a number in the column and press <Enter>.

You can then see how the new entry will be reflected in the effect size, power, or n per group for tests. When you are working with confidence intervals, you will see the change in interval width or n per group.

If you do not have the Auto Recalculation option On, you will be asked to select the row to be recalculated every time you change a value in a completed column.

To use the Auto Recalculation option:

Use the **File** menu **New** option to create a new sample size table or use the **Open** option to open a sample size table.

Click on the **Options** menu **Auto Recalculation** option. The **Set Automatic Recalculation** dialog box for your sample size table will appear. The example below is the dialog box for a confidence interval table.

The dialog box is titled "Set Automatic Recalculation". It contains three main sections. The first section, "Row selected for automatic recalculation:", has an empty text box. The second section, "Click row for automatic recalculation:", contains a list box with two items: "Distance from mean to limit, ω " (which is highlighted) and "n". The third section contains three buttons: "Auto On", "Auto Off", and "Cancel".

The **Click row for automatic recalculation** field will display the rows available for recalculation for the current sample size table. Click on a row description to select it.

This dialog box is identical to the one above, but the "Row selected for automatic recalculation:" text box now contains the text "Distance from mean to limit, ω ". The "Auto On" button is now enabled (it has a darker background), while the "Auto Off" button is disabled (it is grayed out).

The name of the selected row will appear in the **Row selected for automatic recalculation** field. The **Auto On** button will be enabled.

Click on **Auto On** to turn on the auto recalculation and close the dialog box.



When Auto Recalc is On, you can use the Auto Recalculation while you are editing your sample size table. For example, you might have chosen **Distance from mean to limit** as the row to be automatically recalculated. This means that you can edit any other entry in the table, press <Enter> and automatically see the recalculated **Distance from mean to limit** for that column.

Note: After you choose a row for recalculation and turn on Auto Recalculation, the row for the value to be recalculated will display green. Thus, you will always be aware of the row selected for Auto Recalculation.

Note: You can view the status of the Auto Recalculation toggle at any time. As long as you have the Status Bar on, you can see the words AUTO RECALC ON or AUTO RECALC OFF in the lower status bar of your nQuery Advisor window.

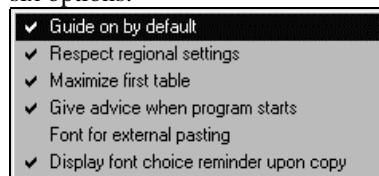


If the Auto Recalculation option is Off when you change a number in a calculated column of a sample size table, you will get a dialog box prompting you to specify the row to be recalculated. You can also turn on the Auto Recalculation option at this point.

Note: Some unequal n's tables for two-sample problems will not be as well-behaved as the equal n's tables with regard to the automatic recalculation of values. That is, some unequal n's tables may simply recalculate one particular row rather than providing you with a choice of rows for recalculation. You should avoid setting the Auto Recalculation option to On when you have two-sample unequal n's problems.

Preferences

When you choose the Options menu Preferences option, you get another menu with six options.



Five of the options are toggles, and they are On by default. The sixth option brings up a dialog box.

Guide on by default

When **Guide on by default** is checked (**On**), nQuery displays the guide card for every newly-opened sample size table. When Guide on by default is not checked (**Off**), the change does not affect the current table. However, all tables opened in future will omit the display of the guide cards.

To turn on the guide card after you have turned it off:

Click on the **View** menu **Guide** option. The guide card pane will appear in the window.

Respect regional settings

When **Respect regional settings** is checked (**On**), nQuery displays numbers and dates according to the regional settings which are selected in your computer's Control Panel Regional Settings.

When Respect regional settings is unchecked (**Off**), nQuery displays numbers and dates in standard U.S. English format regardless of any changes you may have made in the Control Panel Regional Settings. That is, nQuery uses the period as the decimal symbol in number representations and the abbreviated date (month/day/year) in date representations.

Maximize first table

When **Maximize first table** is checked (**On**), the first table and subsequent tables displayed after opening nQuery will be maximized. That is, they will be expanded to fill the available space within the nQuery window. When Maximize first table is unchecked (**Off**), tables will not be maximized. Changing the toggle does not affect the display of tables during the rest of the current session.

Give advice when program starts

If **Give advice when program starts** is checked (**On**), nQuery displays the nQuery Advice window every time the program starts.

Font for external pasting

If you click on **Font for external pasting**, nQuery displays the **Font for pasting into external documents** dialog box. You can choose a font and a font size in that box. Your choice will be the default font for external pasting.



Display font choice reminder upon copy

If **Display font choice reminder upon copy** is checked (**On**), nQuery displays the **Font selection for pasting dialog box** every time you select the copy option for sample size tables, side-tables, notes, statements, references, and guides.

4. The Edit Menu

This chapter describes the Edit menu and its options. The Edit Menu provides eleven options for use in manipulating your sample size table. The options are:

Edit	
Undo	Ctrl+Z
Clear ...	
Cut	Ctrl+X
Copy	Ctrl+C
Paste	Ctrl+V
Paste Unformatted	
Fill Right	
Specify Multi-factor Table ...	
Create Statement	
Edit Row Names ...	
Edit Column Names ...	
Special Characters ...	

Undo

The Undo option on the Edit menu allows you to undo your last action in the sample size table.

To use the Undo option:

Click on the **Edit** menu **Undo** option or use the Undo hotkey combination, <Ctrl><Z>. The last action will be undone.

Clear...

The Clear option on the Edit menu allows you to clear all data from the current sample size table.

To use the Clear option:

Click on the **Clear** option in the **Edit** menu. A message will appear, confirming that you want to clear the table.

Click **Yes** to clear all data from the table.

Cut



The Cut option on the Edit menu allows you to cut selected values from the current sample size table. Note that due to computational relationships among the rows, in some cases when you remove a value, the value will automatically be recomputed. For example, if your sample size table displays the difference between means, that difference will be automatically recalculated after you remove the difference value. Thus, it may be necessary to cut two or more values at once. In the case of a difference between two means, you must remove one mean along with the difference between means.

To use the Cut option:

To select cells for cutting, start with your cursor in one corner of the block of cells to be cut. Hold down the mouse button and drag the cursor across all cells containing values which you want to cut.

Choose the **Edit** menu **Cut** option, the **Cut** icon, or the **Cut** hotkey combination, **<Ctrl><X>**, to remove the cell contents from the table.

Copy



The Copy option on the Edit menu and in the right click menu for the table allows you to copy the values in selected cells from the current sample size table. Those values go into the Clipboard where they are available to be pasted into other columns or other tables.

The Copy option on the Edit menu and in the right click menu for each pane also allows you to copy the text from the Guide Cards, User Notes, Statements, or References to paste into the notes or into external documents.

As stated above, the Copy option copies only selected values. You may prefer to copy an entire table or side table in order to paste it into an external document. To print an entire table or side table, use the Print to Clipboard option in the File menu or in the table's right click menu.

To use the Copy option for specific values within the sample size table:

To select cell(s) for copying, start with your cursor in a corner of the block of cells to be copied. Hold down the mouse button and drag the cursor across all cells containing values which you want to copy.

Choose the **Copy** option, the **Copy** icon, or the Copy hotkey combination, **<Ctrl><C>**, to copy the cell contents from the table.



When copying from a table, you are using a “smart” or formatted copy option. The Copy option “knows” the appropriate row for each cell copied. Thus, using the Paste option will paste cell values only into the appropriate rows. To paste values into different rows, use the **Paste Unformatted** option.

When you use Copy to copy numeric values from Notes, Statements, a sample size table with different row names, or another application, Copy is not a “smart” or formatted copy option. That is, the Paste option will paste cell values into the selected rows unless the values are out of range for the rows. In some cases, it will be necessary to use Paste Unformatted to paste in a value from a different table.

To use the Copy option to copy the entire sample size table or side table:

Click within the sample size table or side table, then click on the right mouse button to bring up the right click menu. Click on the **Copy** option to copy the entire sample size table to the clipboard.

To use the Copy option within the Notes, Statements, References, or Guide Card panes:

In Statements, References, and Guide Card panes, simply click the mouse in the pane. Then choose the **Copy** option, the **Copy** icon, the Copy hotkey combination, **<Ctrl><C>**, or the **Copy** option from the right-click menu to copy the selected contents or the entire contents of the pane.

In Notes, use the cursor to select the text to be copied. Then choose the **Copy** option, the **Copy** icon, the Copy hotkey combination, **<Ctrl><C>**, or the **Copy** option from the right-click menu to copy the selected contents or the entire contents of the pane.

Note: When you select the Copy option for the first time, you will see a dialog box stating that you can select the font you want to use for pasting. For more details on your font options, see the discussion for the Options menu Preferences option in Chapter 3 *The File and Options Menus*.

Whenever you use the Copy option, you can paste the copied information into another Windows application.

Rich Text Format

The text in nQuery panes is in Rich Text Format, so formatting will be preserved when it is pasted into external documents. In addition, you can select a default font and font size to be used for pasting. Greek symbols will paste in the symbol format in applications like Word. However, such symbols may show up as strange characters in Excel. To remedy this problem, paste the selection into Word, then copy and paste it into Excel.

Paste

The Paste option on the Edit menu allows you to paste cell values into the appropriate cells in your sample size table. You can access this option only after you have cut or copied the cell(s) containing values of interest.

To use the Paste option within the sample size table:

To use the **Paste** option, you should first use the **Copy** command to copy the contents of one or more sample size table cells to the Clipboard.

In the current sample size table, select one cell of the column into which you want to paste.

Choose the **Edit** menu **Paste** option, the right-click menu **Paste** option, the **Paste** icon, or the Paste hotkey combination, <Ctrl><V>.

Note that there is no need to select a specific target cell, because the nQuery Advisor Paste option is a “smart” or formatted pasting option. This option automatically pastes each cell value into its appropriate row.

For example, you might copy the Test significance from row 1 and sidedness from row 2 of column 1 in a t test sample size table. Then place your cursor in the cell in row 4, column 2. When you select Paste, nQuery Advisor pastes the number for Test significance into row 1, column 2, and the value for sidedness into row 2, column 2, disregarding the row position of the cursor.

Note that, when you have copied values from your Notes pane or from a Windows application, you can paste those values into the cells of the sample size table when the values are appropriate.



To use the Paste option within the Notes, Statements, References or Guide Cards pane:

Start by using the cursor to select the words or values to be copied, then use the **Edit** menu **Copy** option. The chosen information can come from an nQuery Advisor table, Notes, Statements, References or Guide Cards, or from a different program running under Windows.

Choose the **Edit** menu **Paste** option, the **Paste** icon, or the Paste hotkey combination, <Ctrl><V>, to paste the selected contents within the Notes.

Paste Unformatted



The Paste Unformatted option on the Edit menu pastes the contents of the clipboard into the selected cell(s). This paste option removes the information about the rows from which values were copied and pastes copied values into the current cursor position.

Paste Unformatted vs. Paste

The Paste option “knows” the correct row for each copied or pasted number. Regardless of the position of the cursor in the column, the Paste option pastes the cut or copied values into the appropriate rows.

In contrast, the Paste Unformatted option starts by pasting the first value in the first selected cell, the second value in the next cell, etc. As it pastes, the Paste Unformatted option evaluates each value and accepts or rejects the value as acceptable for the selected cell.

Since the Paste Unformatted option is simply pasting the number found in the clipboard, this option does not “know” where the number belongs. Thus, the program tries to paste the number at the selected cell in the sample size table. However, if you try to Paste Unformatted an inappropriate number, such as .05 in the row for Power, you will get an error message.

To use the Paste Unformatted option within the sample size table:

You must first use the **Copy** option to place some information in the Clipboard. That information can come from nQuery Advisor or from a different program running under Windows.

Note that, when you have copied values from your Notes pane or from a Windows application, you can paste those values into the cells of the sample size table when the values are appropriate.

Select the cell into which you want to paste the information.

Click on the **Edit** menu **Paste Unformatted** option, the **Paste Unformatted** icon, or the **Paste Unformatted** option in the sample size table right click menu. The contents of the Clipboard will be pasted into the selected location in your table.

To use the Paste Unformatted option within the Notes pane:

Start by copying the words or values to be copied. The chosen information can come from an nQuery Advisor table, Notes, Statements, References or Guide Cards or from a different program running under Windows.

Click to place the cursor within the Notes or Statements pane.

Choose the **Paste Unformatted** option or the **Paste Unformatted** icon to paste the selected contents within the Notes or Statements.

Fill Right

The Fill Right option on the Edit menu allows you to duplicate specific row values across all columns in the sample size table quickly and easily. You might, for example, fill in column 1. You can then select one or more contiguous rows in column 1 and use the Fill Right option to fill columns 2-20.

The Fill Right option will fill only the cells in the same row as the selected cell. For example, you might want to set a significance level of .05 and a 2-sided test for all columns. Just enter .05 and 2 in the appropriate rows, then select those two rows and choose the Edit menu Fill Right option. Every column will display .05 and 2 in their respective rows.

To use the Fill Right option:

In the column of interest, select each cell to be duplicated across the row. If you are selecting more than one cell, drag the cursor across the contiguous cells to select them.

Choose the **Edit** menu **Fill Right** option. The sample size table will fill all columns to the right with the information from the chosen column rows.

Specify Multi-factor Table

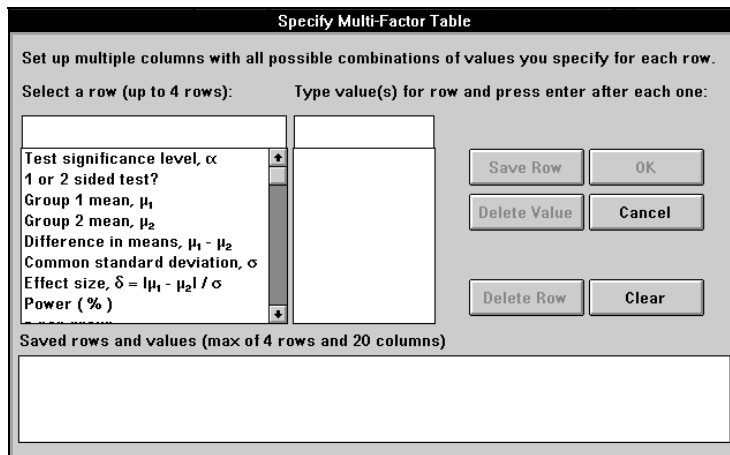
The Specify Multi-factor Table option on the Edit menu allows you to fill selected rows and columns of your sample size table with a range of specific row values. For example, you might want to fill in column rows for every combination of .01 and .05 significance values, along with 1- and 2-tailed tests.



To use the Multi-factor Table option:

Start with the sample size table of interest as the current table.

Choose the **Edit** menu **Multi-factor Table** option and you get the **Specify Multi-factor Table** dialog box.

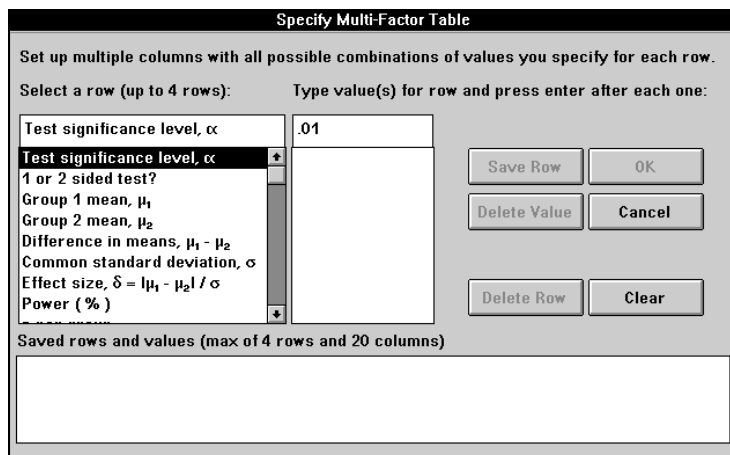


The dialog box is titled "Specify Multi-Factor Table". It contains the following elements:

- Instructions: "Set up multiple columns with all possible combinations of values you specify for each row."
- Two input areas: "Select a row (up to 4 rows):" and "Type value(s) for row and press enter after each one:".
- A list of statistical parameters with a scroll bar: "Test significance level, α ", "1 or 2 sided test?", "Group 1 mean, μ_1 ", "Group 2 mean, μ_2 ", "Difference in means, $\mu_1 - \mu_2$ ", "Common standard deviation, σ ", "Effect size, $\delta = |\mu_1 - \mu_2| / \sigma$ ", and "Power (%)".
- Buttons: "Save Row", "OK", "Delete Value", "Cancel", "Delete Row", and "Clear".
- A section labeled "Saved rows and values (max of 4 rows and 20 columns)" with an empty table area.

In that dialog box, click on the name of one row which you want to propagate. The row name will appear in the top left box.

Your cursor will be in the upper right box. Enter the first value for that row.



The dialog box is shown with the following updates:

- The "Test significance level, α " row is selected in the list.
- The value ".01" is entered in the "Type value(s) for row" box.
- The "Save Row" button is highlighted.

Press <Enter>, and the new value will move to the lower box. Enter the second value and press <Enter>, etc.

Specify Multi-Factor Table

Set up multiple columns with all possible combinations of values you specify for each row.

Select a row (up to 4 rows): Type value(s) for row and press enter after each one:

Test significance level, α	
Test significance level, α	.01
1 or 2 sided test?	.025
Group 1 mean, μ_1	.05
Group 2 mean, μ_2	
Difference in means, $\mu_1 - \mu_2$	
Common standard deviation, σ	
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	
Power (%)	

Save Row OK

Delete Value Cancel

Delete Row Clear

Saved rows and values (max of 4 rows and 20 columns)

--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

When you have finished entering the values for that row, click on the **Save Row** button. Your choices will move to **the Saved Rows and Values** box.

You can specify up to four rows. When you have finished entering information into this dialog box, click on **OK**.

Your sample size table will appear with the designated rows filled in order. For example, consider choosing significance levels of .01, .025, and .05, with power equal to 80 and 90. The first column would display .01 and 80, the second .01 and 90, the third .025 and 80, etc.

When you have created your multi-factor table, you can finish the table by entering any remaining information into the sample size table.

Create Statement


The Create Statement option on the Edit menu allows you to view the customized sample size justification statement created by nQuery Advisor for any completed column in your sample size table.

To use the Create Statement option:

Fill in one column of a sample size table, letting the program calculate the last number.

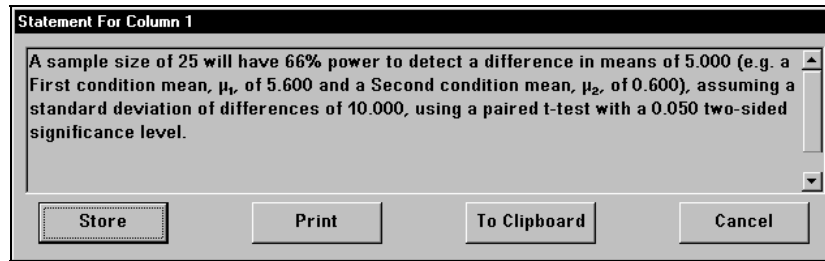
Place your cursor in any cell of the completed column on the sample size table.

Choose the **Edit** menu **Create Statement** option, the right click menu **Create**

Statement option, click on , the Statement icon, or right click in the Stored Statements panel and choose **Create Statement**.



A complete statement will appear in its own panel, describing the contents of that column.



The Statement window has four buttons: **Store**, **Print**, **To Clipboard**, and **Cancel**.

Store

The Store button on the Statement window stores the statement for the selected column with the sample size table. If you click on the Store button on the Statement window, your statement will appear in the Stored Statements panel of the sample size table. The stored statement is linked to its sample size table. Since the statement has been linked to the sample size table, when you save the table, you save the statement with it. Thus, when you open the table later, you will see the stored statement in the Stored Statements pane.

Note: A stored statement is permanently associated with the sample size table and cannot be erased from the Stored Statements pane. However, new stored statements are appended below statements which have already been stored in the Stored Statements pane. If you are testing and evaluating different values in the sample size table, you might prefer to place your statements in the Notes pane so that you can edit them and/or reorder them and delete some.

To do that, use the **Edit** menu **Create Statement** option, and click on the **To Clipboard** button in the **Statement** dialog box. Move to the sample size table and place the cursor in the **Notes** pane. Use the **Edit** menu **Paste** option to paste the statement into the **Notes** pane. You can compare statements in the **Notes** pane and later **Cut** any unnecessary statements.

To print a stored statement:

You can print your statement any time after you have stored it.

To quickly print any stored statement, click in the **Stored Statements** pane and right click to bring up the right click menu. Click on the **Print** option, and you

will see the usual Windows Print dialog box. Click on **OK** to print only the contents of the Stored Statements pane.

To print a stored statement plus the contents of other panes, select the **File** menu **Print** option, then click on the **Print** option. The **nQuery Advisor Printing** dialog box will appear.

The **nQuery Advisor Printing** dialog box lets you choose to print the sample size table, as well as its associated notes and statement(s), along with any connected side tables.

Print

The Print button on the Statement window prints the customized statement for the selected column in the sample size table.

To print a statement from the Statement window:

While you are viewing the statement, click on the **Print** button on the Statement window.

You will see the usual Windows Print dialog box. Click on **OK** to print only the contents of the Statement window.

To Clipboard

The To Clipboard button on the Statement window copies the displayed sample size justification statement to the Clipboard.

To send the statement to the Clipboard from the Statement window:

Click on the **To Clipboard** button.

Note: When you select the **To Clipboard** option for the first time, you will see a dialog box stating that you can select the font you want to use for pasting. For more details on your font options, see the discussion for the Options menu Preferences option in Chapter 3 *The File and Options Menus*.

You can then paste the Clipboard contents into an external document document. The statements are in RTF (Rich Text Format) and you can choose the font to be used when the text is pasted into the document. For applications like Word, formatting will appear as it does on the screen, and Greek symbols will appear using the Symbol font. For some applications like Excel, if you paste a statement or table directly from nQuery Advisor, you will see strange symbols in place of the Greek symbols. To remedy this problem, paste the selection into Word, then copy and paste it into Excel.



Cancel

The Cancel button on the Statement window closes the Statement window without storing, printing, or saving the customized statement for the selected column in the sample size table.

Edit Row Names

The Edit Row Names option on the Edit menu allows you to change the names of particular rows, such as Group 1 and Group 2 in the table for the Two Group Student's t test (MTT0). This option is available only in certain sample size tables.

To use the Edit Row Names option:

Select the **Edit** menu **Edit Row Names** option.

The **Edit Row Name** dialog box will appear. This box lists the row names that you can change in your sample size table.

Note: The changeable rows will depend on the sample size table chosen.

Click on a row name to bring the name to the editing field on the right side of the dialog box.

The dialog box is titled "Edit Row Name". It contains a list of row names on the left: "Group 1 mean, μ_1 " and "Group 2 mean, μ_2 ". The first row is highlighted. To the right of the list is an editing field containing the text "Group 1 mean, μ_1 ". Below the editing field are three buttons: "Accept Edit Row", "Update Table Row Name", and "Cancel".

Type the new name in the editing field.

The dialog box is titled "Edit Row Name". It contains the same list of row names on the left. The editing field now contains the text "Treatment mean, μ_1 ". The buttons remain the same: "Accept Edit Row", "Update Table Row Name", and "Cancel".

Click on the **Accept Edit Row** button.

Click on the next row name to be changed, etc.

When you have finished changing the row names, click on the **Update Table Row Name** button. You will return to your table, updated with new row names. The new names which you see on screen will also appear in the printed version of the table and in any statements which you create.

Note: The editable section of each row name accepts a maximum of 20 characters.

Edit Column Names

The Edit Column Names option on the Edit menu allows you to change the names of particular columns from 1, 2, etc. to names such as Outcome A, Outcome B, Low SD, High SD etc. The new names may include special characters. The new column names will appear in the printed tables, pasted tables, and plot legends.

To use the Edit Column Names option:

Place the cursor anywhere within the sample size table.

Select the **Edit** menu **Edit Column Names** option or the right-click menu **Edit Column Names** option.

The **Edit Column Name** dialog box will appear. This box lists the column names that you can change in your sample size table. Column names are restricted to a maximum of 25 characters each; the names will not wrap.

#	Column name (25 chars max)
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
11	11
12	12
13	13
14	14
15	15
16	16
17	17
18	18
19	19
20	20

Copy Name(s)

Paste Name(s)

To add a name:
click on name and type

To edit a name:
double-click on name and edit

OK Cancel

Enter the new name and press <Enter> to move to the next column field.



Dialog box titled "Edit column names".

#	Column name (25 chars max)
1	Outcome A
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	

Buttons: Copy Name(s), Paste Name(s), OK, Cancel.

Instructions:
To add a name: click on name and type
To edit a name: double-click on name and edit

When you have finished entering column names, click **OK**. You will return to your sample size table, updated with the new column names.

You can use the **Edit Column Name** dialog box to copy a column name for pasting elsewhere.

To copy column names and paste into different columns:

Select the column name(s) to be copied and click on the **Copy Name(s)** button.

Select the column(s) to be renamed, and click on the **Paste Name(s)** button.

You can also use the Paste Name(s) button to paste names from other Windows programs.

To paste column names from a Windows program:

Make sure that you have one column name per line.

Copy the column names in the Windows program.

In the **nQuery Edit Column Names** dialog box, select the column(s) to be renamed, and click on the **Paste Name(s)** button. The names will be pasted into the column name boxes.

Special Characters

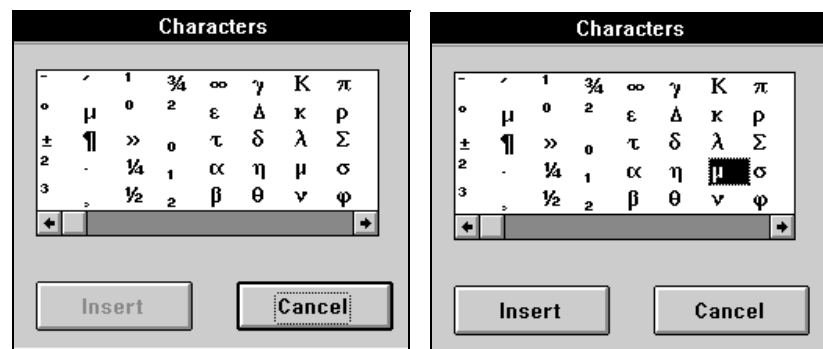
The Special Characters option on the Edit menu provides Greek letters and other symbols which you may find useful in writing your notes.

To use the Special Characters option:

Start writing your notes in the Notes pane in the lower left area of your sample size table screen.

When you get to a spot in your notes where you need a special character, choose the **Edit** menu **Special Characters** option or right click within the **Notes** pane to bring up the menu and choose **Special Characters**.

The **Characters** dialog box will appear.



Click on any single character in this box to select it. The **Insert** button becomes active.

Click on the **Insert** button. The character will appear in your notes.

You can Copy your Notes and paste the Clipboard contents into a word processor document.

Note: The notes may lose the Dixon font when pasted into an Excel document. Such a loss would change the Greek figures to strange characters. To remedy this problem, paste the selection into Word, then copy and paste it into Excel.



Using Right-Click Menu to Access Edit Options

If you right click within the sample size table, you will get the right-click menu. The following example is the right-click menu for the sample size table.

<u>U</u> ndo	Ctrl+Z
<u>C</u> opy	Ctrl+C
<u>C</u> ut	Ctrl+X
<u>P</u> aste	Ctrl+V
Paste U <u>n</u> formatted	
<u>P</u> rint	
Print Table to Clipboard	
Create <u>S</u> tatement	
Edit <u>R</u> ow Names	
Edit <u>C</u> olumn Names	

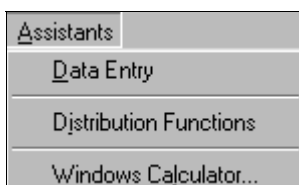
Choose any of the available Edit menu options: Undo, Copy, Cut, Paste, Paste Unformatted, Print, Print Table to Clipboard, Create Statement, Edit Row Names, or Edit Column Names. These Edit options function in the same way whether you access them from the Edit menu or through the right-click menu for the sample size table.

Note that the right-click menus for the Guide Card, Statement, and User Notes panes differ from the menu shown above. Those right-click menu options include pane-specific options, such as Special Characters in the User Notes pane, Hide in the Guide Card pane, and Create Statement in the Stored Statements pane.

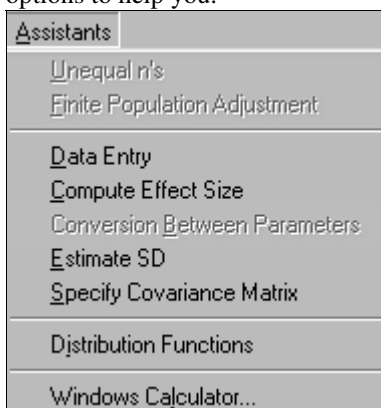
5. The Assistants Menu

This chapter describes the Assistants menu and its options.

When you are in the first nQuery Advisor window, before you open a sample size window, the Assistants menu contains only three options.



While you are working with a sample size table, the Assistants menu provides nine options to help you.



Unequal n's

The Unequal n's option on the Assistants menu allows you to change your chosen sample size table from the default equal n's to unequal n's. You can select the Unequal n's version of your analysis type in either of two ways:

- from the Study Goal and Design dialog box
- from the current sample size table.

Note that some sample size tables do not allow unequal n's. When you choose those analyses, the Unequal n's option will not be available.

See Chapter 10, *Unequal n's*, for detailed examples using unequal n's.

To use the Unequal n's option in the Study Goal and Design dialog box:

Start in the Study Goal and Design dialog box.

Study Goal and Design

Goal: Make Conclusion Using

- ☒ Means
- ☐ Proportions
- ☐ Survival (Time to Event)
- ☐ Agreement
- ☐ Regression

Number of Groups

- ☐ One
- ☒ Two
- ☐ > Two

Analysis Method

- ☒ Test
- ☐ Confidence Interval
- ☐ Equivalence

Two-sample t test

- Student's t test (equal variances)**
- Satterthwaite's t test (unequal variances)
- Two group t-test for fold change assuming log-normal distribution (equal n's)
- Two group t-test of equal fold change with fold change threshold (equal n's)
- Wilcoxon/Mann-Whitney rank-sum test (continuous outcome)
- Wilcoxon/Mann-Whitney rank-sum test (ordered categories)
- Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)

☐ Unequal n's


☐ Finite Population

OK Cancel

After you select the design for your sample size table, check the **Unequal n's** box in the lower left corner of the Study Goal and Design dialog box. After you click on **OK**, your sample size table will appear, and it will be set up for unequal n's.

To use the Unequal n's option from an existing sample size table:

Start with your chosen sample size table as the active window.

Select the **Assistants** menu **Unequal n's** option or  the Unequal n's icon. You will obtain a new unequal n's sample size table for your goal, design, and analysis.



Finite Population Adjustment

The Finite Population Adjustment option on the Assistants menu allows you to make inferences to populations with a specified number of subjects. You can select the Finite Population version of your analysis type in either of two ways:

- from the Study Goal and Design dialog box
- from the current sample size table.

For full details on the use of this option, see Chapter 19, *Sampling from Finite Populations*.

Note that most sample size tables do not have a version allowing the use of the Finite Population option. When you choose those analyses, the Finite Population option will not be active.

To use the Finite Population Adjustment option in the Study Goal and Design dialog box:

Start in the Study Goal and Design dialog box.

The screenshot shows the 'Study Goal and Design' dialog box. It has three main sections: 'Goal: Make Conclusion Using', 'Number of Groups', and 'Analysis Method'. The 'Goal' section has radio buttons for Means (selected), Proportions, Survival (Time to Event), Agreement, and Regression. The 'Number of Groups' section has radio buttons for One (selected), Two, and > Two. The 'Analysis Method' section has radio buttons for Test (selected), Confidence Interval, and Equivalence. Below these sections is a list box containing the following options: 'One-sample t test', 'Paired t-test for difference in means' (highlighted), 'Univariate one-way repeated measures analysis of variance', 'One-way repeated measures contrast', and 'Univariate one-way repeated measures analysis of variance (Greenhouse-Geisser)'. At the bottom left, there are two checkboxes: 'Unequal n's' and 'Finite Population' (checked). At the bottom right are three buttons: 'OK', 'Last', and 'Cancel'.

After you select the design for your sample size table, check the Finite Population Adjustment box in the lower left corner of the Study Goal and Design dialog box. After you click on **OK**, your sample size table will appear, and it will be set up for finite population adjustment.

To use the Finite Population Adjustment option from an existing sample size table:

Start with your chosen sample size table as the active window.

Select the **Assistants** menu **Finite Population Adjustment** option. You will obtain a new finite population adjustment sample size table for your goal, design, and analysis.

Data Entry

The Data Entry option on the Assistants menu allows you to enter a small data set to compute mean and standard deviation. See the full description of Data Entry in Chapter 9, *Determining a Value for Standard Deviation* and an example of its use in Chapter 18, *Regression Tables*.

The Estimate SD option provides an alternate route to the Data Entry table. Select the **Assistants** menu **Estimate SD** option, then select the **For specified values** option, and the Data Entry table will appear.

Compute Effect Size



For sample size tables requiring input of multiple outcome parameters, the Compute Effect Size option brings up a side table specific to the current sample size table. The Compute Effect Size option in the Assistants menu provides automatic calculations of effect size from user input of expected outcome parameters and design features. For example, Compute Effect size will automatically calculate:

- ◆ an effect size from the expected group means for one-way and two-way analysis of variance, and repeated measures analysis of variance
- ◆ an expected contrast value from group means and contrast coefficients for analyses of contrasts
- ◆ effect sizes from expected proportions for paired and multi-group designs
- ◆ effect sizes from the components of agreement measures

The Compute Effect Size option will incorporate unequal sample size ratios in the computation of effect sizes for sample size tables allowing unequal n 's. In addition, the Compute Effect Size option allows user input of accrual, hazard, survival, and dropout rates to be used in simulation of power for the log rank test.



Side Table Access

To bring up a side table for the current sample size table, use the Assistants menu Compute Effects Size option.

To use the Compute Effect Size option:

Create a sample size table and enter the number of groups or factors. If the table is one that allows you to compute effect size, the Compute Effect Size option will be accessible in the Assistants menu. Both the menu option and the icon button will be active.

Click on the **Assistants** menu **Compute Effect Size** option. If you have not yet entered the necessary values in your sample size table, you may see a prompt reminding you to enter the number of groups or factors.

A dialog box titled "Compute Effect Size Initialization". It contains the text "Compute Effect Size side table cannot be accessed until values are specified for:". Below this text is a rectangular box containing two labels: "Number of factor A levels" and "Number of factor B levels". At the bottom of the dialog is an "OK" button.

After you have entered the appropriate values in your sample size table, choosing the **Compute Effect Size** option brings up the Compute Effect Size side table. The structure of the side table will be specific to your chosen sample size table.

The example side table below is for the two-way analysis of variance with two levels for factor A and three levels for factor B.

Note: Side tables for kappa, concordance, and McNemar's test need no design parameter; most other tables require specification of the number of groups.

MGT2-1: Aid for col 1 -- Two-way analysis of variance (equal n's)					
Compute	Transfer	Close	Restore	Clear	Cut Copy Paste Print
	B1	B2	B3	Row Mean	
A1					
A2					
Column Mean					
Variance in means, V_A					
Variance in means, V_B					
Variance in means, V_{AB}					

The title bar of the Compute Effect Size side table displays the name of the sample size table. The title bar also specifies the column for which the effect size is being computed.

Use the dialog box to enter the values necessary for computing effect sizes.

MGT2-1: Aid for col 1 -- Two-way analysis of variance (equal n's)								
Compute	Transfer	Close	Restore	Clear	Cut	Copy	Paste	Print
	B1	B2	B3	Row Mean				
A1	20.000	22.000	25.000	22.333				
A2	18.000	18.000	21.000	19.000				
Column Mean	19.000	20.000	23.000	20.667				
Variance in means, V_A								
Variance in means, V_B								
Variance in means, V_{AB}								

When you have finished entering the means, the **Compute** button will be enabled. Click on the **Compute** button to make the calculation.

Note: Some Compute Effect Size dialog boxes do not include a Compute button. Those boxes perform the calculation automatically as soon as you have entered all necessary values.

MGT2-1: Aid for col 1 -- Two-way analysis of variance (equal n's)								
Compute	Transfer	Close	Restore	Clear	Cut	Copy	Paste	Print
	B1	B2	B3	Row Mean				
A1	20.000	22.000	25.000	22.333				
A2	18.000	18.000	21.000	19.000				
Column Mean	19.000	20.000	23.000	20.667				
Variance in means, V_A	2.778							
Variance in means, V_B	2.889							
Variance in means, V_{AB}	0.222							

After the effect size has been calculated, the **Transfer** button will be enabled.

Click on the **Transfer** button. The effect(s) will be written to the appropriate cells of your sample size table, and the focus will return to the main sample size table.



Note: Side tables with the MTT2, the PTT4, and the STT3 sample size tables behave in a different manner. You start with the sample size table and enter the number of levels or strata. Select the Assistants menu Compute Effect Size menu to bring up the side table. After you fill out the side table and click on the Transfer button, the side table name will be inserted into the Side table name row in the sample size table. You can then copy and paste the Side table name to other columns. Note that the information in the side table will be available to the main table, but will not be displayed in that sample size table. For details, refer to Example for MTT2 in Chapter 14 and Example 7 for PTT4 in Chapter 15, and Examples 4, 5, and 6 for STT3 in Chapter 16.

Unless you close the effect size side table, it will remain available. You can come back to the side table to edit it, print it alone, or print it with the main table. You can also copy the entire side table and paste it into user notes or an external document by using the Print Table to Clipboard options in the side-table right click menu. When you save the main sample size table, the associated side tables will be saved with it.

Effect size side table tutorial

In Chapter 12, *Side Tables/Compute Effect Size*, you will find a detailed tutorial on using effect size side tables. This tutorial explains the functions of the side table buttons: Compute, Transfer, Close, Restore, Clear, Cut, Copy, Paste, and Print. It also explains the functions available in the side table right-click menu options: Copy, Cut, Paste, Print, Print Table to Clipboard.

Sample Size Tables Offering Side Tables

The following is a list of nQuery Advisor sample size tables which have a side table to assist you in entering parameters describing the effect size in your study. A few of these side tables operate like ordinary sample size tables, but most operate like the special side tables described in the preceding pages. The following list uses the nQuery Advisor shorthand description for each of these sample size tables.

MOT2	Univariate one-way repeated measures analysis of variance
MOT3	One-way repeated measures contrast
MOT4	Univariate one-way repeated measures ANOVA (Greenhouse-Geisser)
MOC4	Confidence interval for one-way repeated measures contrast
MTT1	Wilcoxon/Mann-Whitney rank sum test (continuous outcome)
MTT2	Wilcoxon/Mann-Whitney rank sum test (ordered categories)
MTT3	Two-group univariate repeated measures ANOVA (Greenhouse-Geisser)
MGT0	One-way analysis of variance (equal or unequal n's)
MGT1	Contrast in one-way analysis of variance (equal or unequal n's)
MGT2	Two-way analysis of variance (equal n's)
MGC0	Confidence interval for one-way contrast (equal or unequal n's)
MGC1	Confidence interval for one-way contrast (coverage probability) (equal or unequal n's)
POT1	McNemar's test (χ^2) of equality of paired proportions
POT1x	Exact sign test of equality of paired proportions
POT2	Chi-square test of specified proportions in C categories
POE1	Paired test of equivalence in proportions using confidence interval: a) Lower confidence limit for difference in paired proportions (simulation), b) Upper confidence limit for difference in paired proportions (simulation), c) Two-sided confidence limits for difference in paired proportions (simulation)
POC1	Confidence interval for odds ratio of paired proportions
PTT3	Two-group Chi-square test comparing proportions in C categories
PTT4	Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata (with and without continuity correction)
PGT0	χ^2 for G x 2 table (equal or unequal n's)
PGT1	Test for linear trend in G x 2 table—logistic model (equal or unequal n's)



PGT2	G-group Chi-square test comparing proportions in C categories (equal or unequal n's)
STT3	Log-rank test, user-specified survival rates, accrual, dropout (simulation)
AOT0	Agreement between two dichotomous ratings (intraclass Kappa)
AOT2	Large sample test that Lin's Concordance Coefficient = K_0
AOC0	Confidence interval for intraclass Kappa
AOC2	One-sided large sample confidence interval for Lin's Concordance Coefficient

For details on the side table for each of these sample size tables, see the Side Tables topic in the online Help system.

Conversion between Parameters

The Conversion between Parameters option on the Assistants menu provides a conversion to alternate rates for exponential survival curves. This option is available only for the survival tables: STT0, STT1, STT2, STT3.

Examples 2 and 3 in Chapter 16 Survival Analysis Tables illustrate how to use this Conversion between Parameters table in connection with the Survival Analysis tables.

To use the Conversion between Parameters option:

Create a sample size table for comparison of survival curves. You might use STT1, the two-group test of equal exponential survival.

Select the Assistants menu **Conversion between Parameters** option. You will see the sample size table for **Conversion to Alternate Rates for Exponential Survival Curves**.

Conversion to alternate rates for exponential survival curves					
Time t					
Group 1 proportion π_1 at time t					
median survival					
exponential parameter, λ_1					
Group 2 proportion π_2 at time t					
median survival					
exponential parameter, λ_2					
Hazard ratio, $h = \ln(\pi_1)/\ln(\pi_2) = \text{med}_2/\text{med}_1 = \lambda_1/\lambda_2$					

Suppose you want to find the exponential parameters corresponding to one-year survival rates of 90% and of 70%.

Enter **1** in the **Time** row and press <Enter>.

For each group, you can enter proportion, median survival or exponential parameter. The table will calculate the remaining two values for the group. For example, if you enter **.9** for **Group 1 proportion**, the table will immediately show:

Conversion to alternate rates for exponential survival curves				
Time t	1.0			
Group 1 proportion π_1 at time t	0.900			
median survival	6.579			
exponential parameter, λ_1	0.1054			
Group 2 proportion π_2 at time t				
median survival				
exponential parameter, λ_2				
Hazard ratio, $h=\ln(\pi_1)/\ln(\pi_2)=\text{med}_2/\text{med}_1=\lambda_1/\lambda_2$				

If you enter **.7** for **Group 2 proportion**, the table will immediately show:

Conversion to alternate rates for exponential survival curves				
Time t	1.0			
Group 1 proportion π_1 at time t	0.900			
median survival	6.579			
exponential parameter, λ_1	0.1054			
Group 2 proportion π_2 at time t	0.700			
median survival	1.943			
exponential parameter, λ_2	0.3567			
Hazard ratio, $h=\ln(\pi_1)/\ln(\pi_2)=\text{med}_2/\text{med}_1=\lambda_1/\lambda_2$	0.295			

This table can also be used to convert median survival values to survival proportions or exponential rates. You can also use this table to find out what survival proportions or median survival values correspond to specific exponential parameters.

See Examples 2 and 3 in Chapter 16, *Survival Analysis Tables*, for details of how to copy information from this table to the Survival Analysis tables.



Estimate SD

The Estimate SD option on the Assistants menu provides a way to estimate the standard deviation of a variable from other information. The Estimate SD options allow you to calculate an estimate of the standard deviation from: the standard error, SD1 and SD2 (pooled SD), the range, percentiles, coefficient of variation, upper confidence limit, pre and post standard deviations and the correlation coefficient, or for cluster sampling from between and within cluster variances, for specified x values, and for the standard deviation of residuals (errors).

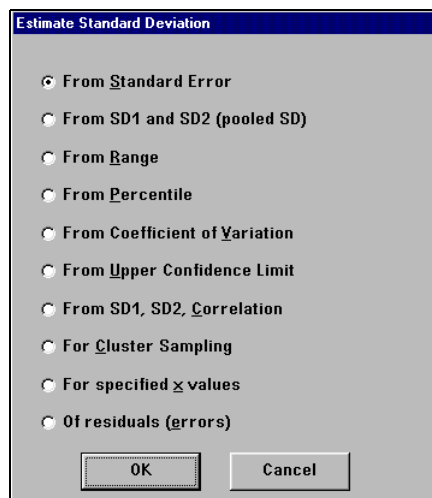
This section describes the Estimate SD option in general terms.

Note: The Estimate SD menu leads to ten different dialog boxes. See Chapter 9 for details and examples of the use of each of the ten dialog boxes used for estimating the standard deviation.

To use the Estimate SD option:

Choose **Estimate SD** on the **Assistants** menu.

The **Estimate Standard Deviation** dialog box will appear.



Click on the radio button beside the method you need, then click on **OK**. The estimation dialog box will appear for your chosen method.

See Chapter 9, *Determining a value for Standard Deviation* for examples.

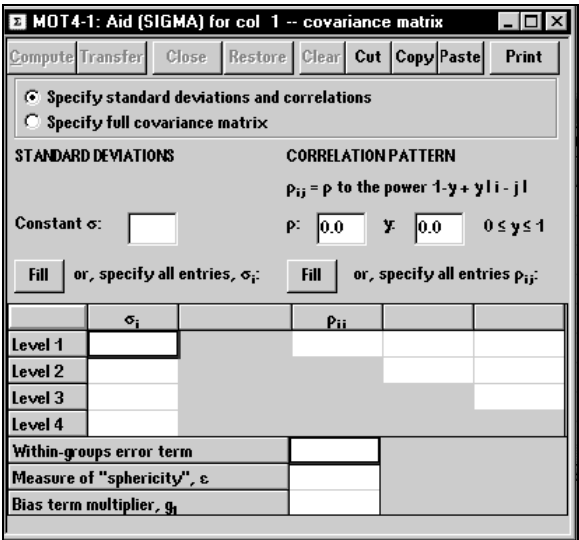
Specify SIGMA, Covariance Matrix

For tables MTT3, Two-group univariate repeated measures ANOVA (Greenhouse-Geisser), and MOT4, Univariate one-way repeated measures ANOVA (Greenhouse-Geisser), you must specify the covariance matrix for the repeated measures. Use the Specify Covariance Matrix button to specify the structure of the covariance matrix and to compute and transfer the within-group error term and the Greenhouse-Geisser correction terms. Use of this option is described in Chapter 9, *Determining a Value for Standard Deviation*. See also Example 7 in Chapter 13, *Repeated Measures and Crossover Designs*.

To use the Specify Covariance Matrix option:

In MTT3 [Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)] or MOT4 [Univariate one-way repeated measures analysis of variance (Greenhouse-Geisser approximation)], choose **Specify Covariance Matrix** on the **Assistants** menu or click on the **Specify Covariance Matrix** button.

The Aid (SIGMA) dialog box will appear.



	σ_i	p_{ii}
Level 1		
Level 2		
Level 3		
Level 4		
Within-groups error term		
Measure of "sphericity", ϵ		
Bias term multiplier, g_1		

Click in the radio button to choose Specify standard deviations and correlations or Specify full covariance matrix.

For details, see Chapter 9, *Determining a Value for Standard Deviation*.



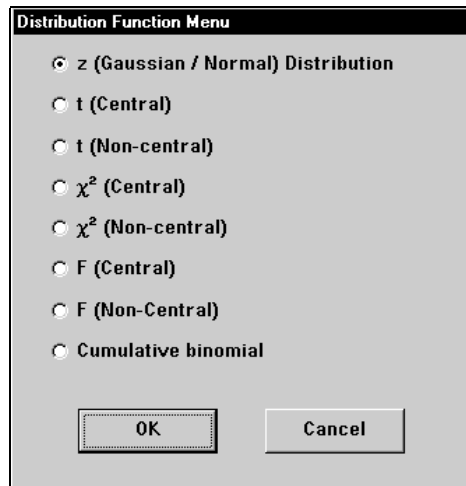
Distribution Functions

The Study Goal and Design dialog box offers you a wide range of analysis designs. However, statistically sophisticated users may be planning a design or analysis not presented in the dialog box. If you have a formula for some sample size problem that nQuery Advisor does not automatically cover, you can go beyond the default designs. You can obtain distribution function values to insert in your own sample size equation by choosing the appropriate distribution function from the Distribution Function Menu option in the Assistants menu.

To use the Distribution Function Menu option:

Select the **Assistants** menu **Distribution Function Menu** option to specify that you want to create a distribution function sample size table.

The Distribution Function Menu dialog box will appear, giving you a choice of eight possible distributions.



To use the Distribution Function Menu Dialog Box:

Click on the radio button beside the distribution name, then click **OK** to obtain the distribution function table. The table specialized for your chosen distribution will appear.

See Chapter 20, *Distribution Function Tables*, for more details.

Windows Calculator

The Assistants menu includes an easy path to the Microsoft Windows Calculator.

To call up the Windows Calculator:

Select the **Assistants** menu **Windows Calculator** option. The Windows Calculator will appear.

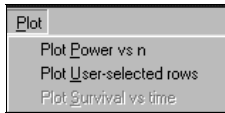
Use the calculator as necessary. You can copy the result to the Clipboard using the **Edit** menu **Copy** option, then use the **Edit** menu **Paste** option to paste the value into your sample size table.

Note: The Windows Calculator View menu allows you to choose the scientific calculator or the standard calculator.

When you have finished using the Windows calculator, click on the gray square in the upper left corner to close that window. You will return to nQuery Advisor.

6. The Plot Menu

The Plot menu on the sample size table has three options:



This chapter discusses the first two options in detail. For an example using the Plot Survival vs time option, see Chapter 16, *Survival Analysis Tables*, Example 7.

To use one of the first two options, highlight one to four completed columns in a sample size table and select one of these options from the **Plot** menu or click on one of the two plot buttons on the toolbar. The first option, **Plot Power vs n**, provides an automatic plot of power on the Y-axis (scaled from 50 to 100%) versus sample size (n or N) on the X-axis. The second option, **Plot User-selected rows**, allows you to select any of the yellow calculable rows (effect size or interval width, power, sample size) to plot on the Y-axis and one of the other rows in the table to plot on the X-axis. You must specify the range of values to plot for X.

You have considerable flexibility in changing the look of the plot. You can change the plot legend directly (see Example 1) or by editing the column names in the table (see Example 1). You can change the text or font size or color for the table title or axis labels (see Examples 1, 2, 5). You can change the attributes of the plotted lines (see Example 3) and the plot area background (see Example 3). You can choose the way you want your printed plot to look (see Example 4) or paste the plot file into a document (see Example 5).

Example 1

Plot Power vs. n for MOT1

To use the Plot Power vs n option:

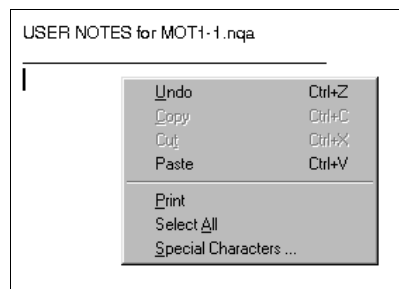
We start with the example for the paired t-test (MOT1) from Chapter 8. We have specified one additional column in which $\alpha=.01$.

Paired t-test of mean difference equal to zero				
	1	2	3	4
Test significance level, α	0.050	0.010		
1 or 2 sided test?	2	2		
First condition mean, μ_1	6.000	6.000		
Second condition mean, μ_2	3.000	3.000		
Mean difference, $\mu_d = \mu_1 - \mu_2$	3.000	3.000		
Standard deviation of differences, σ_d	5.250	5.250		
Effect size, $\delta = \mu_d / \sigma_d$	0.571	0.571		
Power (%)	85	64		
n	30	30		

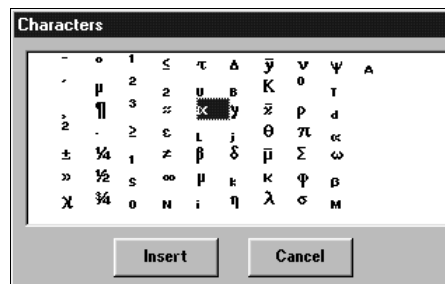
First we change the column names so that our plot will be appropriately labeled.

Since we prefer to identify these columns with the significance level, we want to use α , a Greek letter, in the column name. To use Greek letters in column names, we first build our column names in the Notes panel.

Right click within the Notes panel to bring up the **right click menu**.



Select the **Special Characters** option and click on α .



Click on the **Insert** button, and the Greek letter α appears in the **Notes** panel.



USER NOTES for MOT1-f.nqa

α

Finish writing the column name, $\alpha=0.50$ (2) $\delta=0.5721$.

Copy the first column name in preparation for pasting it into the **Edit Column Names** dialog box.

Right click on the sample size table to bring up the **right click menu**.

Select the **Edit Column Names** option, and the Edit Column Names dialog box appears.

#	Column name (25 chars max)
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
11	11
12	12
13	13
14	14
15	15
16	16
17	17
18	18
19	19
20	20

Copy Name(s)

Paste Name(s)

To add a name:
click on name and type

To edit a name:
double-click on name and edit

OK Cancel

To paste the new column name into the Edit Column Names dialog box, click on the first column name, then click on the **Paste Name(s)** button.

Click on **OK**, and the column name appears in the sample size table.

To use the first column name as the basis for the second, select the first name.


First, copy the name: click on the **Copy Name(s)** button.

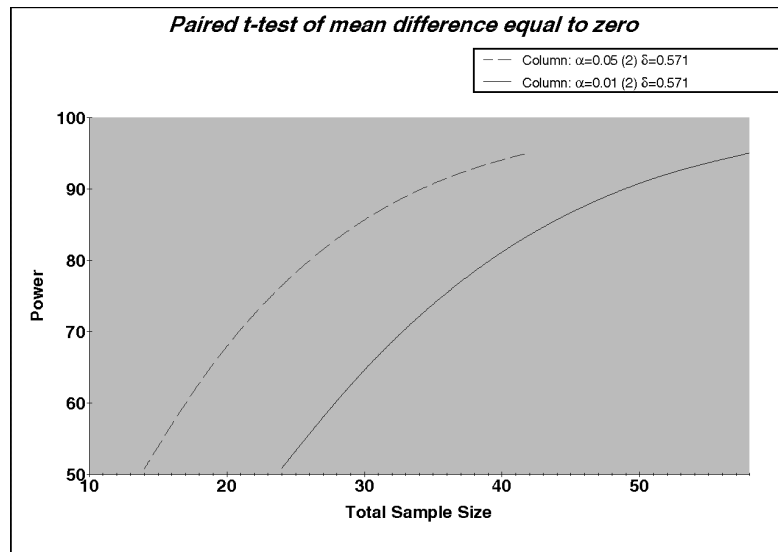
Second, paste the name: select the second column name and click on the **Paste Name(s)** button.

Double click on the second name to edit it.

To begin the plot, highlight the two adjacent columns in your sample size table, then choose the **Plot** menu **Plot Power vs n** option or choose the **Plot Power vs n**

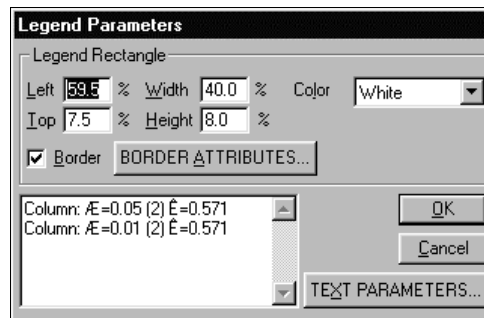


icon, . After you select **Plot Power vs n**, your power versus sample size plot will appear on your screen.



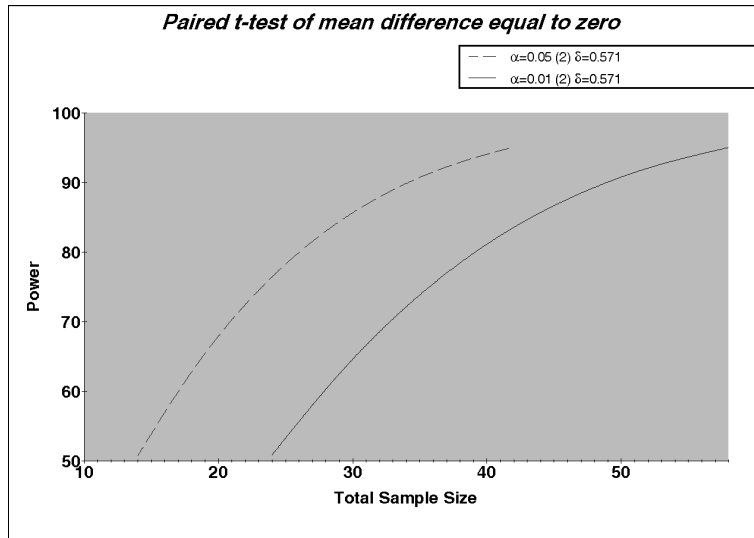
To remove the characters “Column:” from the plot legend:

Double click on the legend. The Legend Parameters dialog box will appear.



Remove the characters you prefer to omit, then click **OK** to see the updated plot.

Note: The plot legend is limited to 40 characters.



Note that the **Plot Power vs n** option used in this example plots your results automatically. In contrast, the **Plot User-selected rows** option allows you to choose the rows to plot, and you must specify a range for the X-axis parameter.

Note: For sample size tables in which n cannot be calculated, this automatic **Plot Power vs n** option is not available. However, you can still plot power versus n by choosing the Plot User-selected rows option, selecting power as the Y-axis, selecting n as the X-axis, and specifying a range for n.

To change the title text or font on the plot:

Double click on the title. The **Text Parameters** dialog box will appear.

Text Parameters

Text:

Font:

Color:

Size:

☒ Bold ☒ Italic ☐ Underline

You can use the **Text Parameters** box to edit the text, change the font, the font size, and the color of the text.

To change text or font for an axis title on the plot:

Double click on the axis label. The **Text Parameters** dialog box will appear.

You can use the **Text Parameters** box to edit the text, change the font, the font size, and the color of the text. Make your changes and click **OK** to see the updated plot.

To change text or font for an axis label on the plot:

Double-click on the axis label. The appropriate **Axis Labels** dialog box will appear.

Click on one of the radio buttons to specify **Labels Position**.

Click on one of the radio buttons to specify **Format** as **Decimal**, **Scientific**, or **Engineering**. You can also determine the number of decimal places in each label by entering the number in the **# Places** box.

Click on a radio button to specify the **Last Label** as **On**, **Off**, or **Text**. If you choose **Off**, the plot will appear without a label on the last tick mark. If you choose **Text**, you can enter a small amount of text as a label for the last tick mark.

Example 2

Plot User-selected rows for MOT1

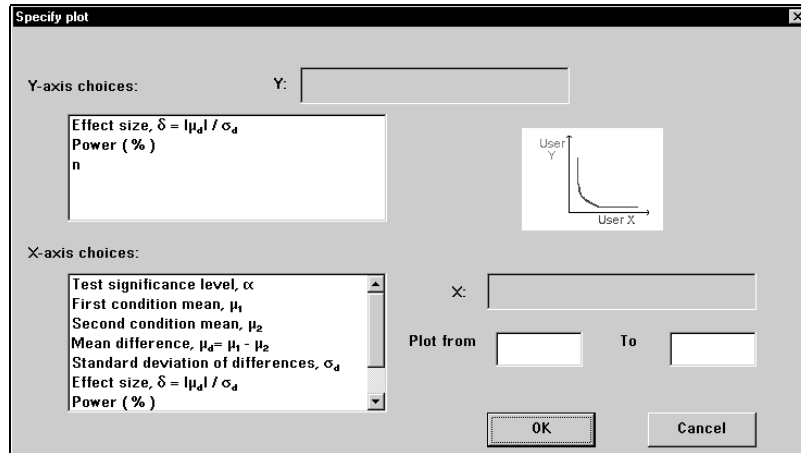
To use the Plot User-selected rows option to plot power vs. the mean difference:

We use the example for the paired t-test (MOT1) from Chapter 8. We have specified one additional column in which $\alpha=.01$. See Example 1 above.

Select the two adjacent columns in your sample size table, then choose the **Plot** menu **Plot User-selected rows** option or choose the **Plot User-selected rows**



icon. After you select **Plot User-selected rows**, the Specify Plot dialog box will appear.



The 'Specify plot' dialog box contains the following elements:

- Y-axis choices:** A list box with 'Effect size, $\delta = |\mu_d| / \sigma_d$ ', 'Power (%)', and 'n'. 'Power (%)' is highlighted in yellow.
- Y-axis label:** A text box labeled 'Y:'.
- X-axis choices:** A list box with 'Test significance level, α ', 'First condition mean, μ_1 ', 'Second condition mean, μ_2 ', 'Mean difference, $\mu_d = \mu_1 - \mu_2$ ', 'Standard deviation of differences, σ_d ', 'Effect size, $\delta = |\mu_d| / \sigma_d$ ', and 'Power (%)'. 'Mean difference, $\mu_d = \mu_1 - \mu_2$ ' is highlighted in yellow.
- X-axis label:** A text box labeled 'X:'.
- Plot range:** Two text boxes labeled 'Plot from' and 'To'.
- Buttons:** 'OK' and 'Cancel' buttons.
- Preview:** A small graph showing a curve with 'User Y' on the vertical axis and 'User X' on the horizontal axis.

This dialog box allows you to choose your preferred parameters for the Y- and X-axes. The Y-axis can be any calculable row highlighted by yellow in the table. The X-axis can be any other row with some exceptions. For example, the X-axis cannot be a row such as 1 or 2 sided, number of groups, # of categories, side table name, # factors, etc. Also, if Y is an effect size row, then X cannot be a component of effect size, such as mean difference, since their relationship is unaffected by power or n.

Note: Since plots are based on only 7 points, and an automatic method is used for connecting points, plots with n on the Y-axis may not always appear monotone.

For this example, click on **Power** for your Y-axis choice and **Mean difference** for your X-axis choice.

Specify a range from **2** to **4** in the **Plot from** and **To** fields. The dialog box will display your choices.

Specify plot

Y-axis choices: Y:

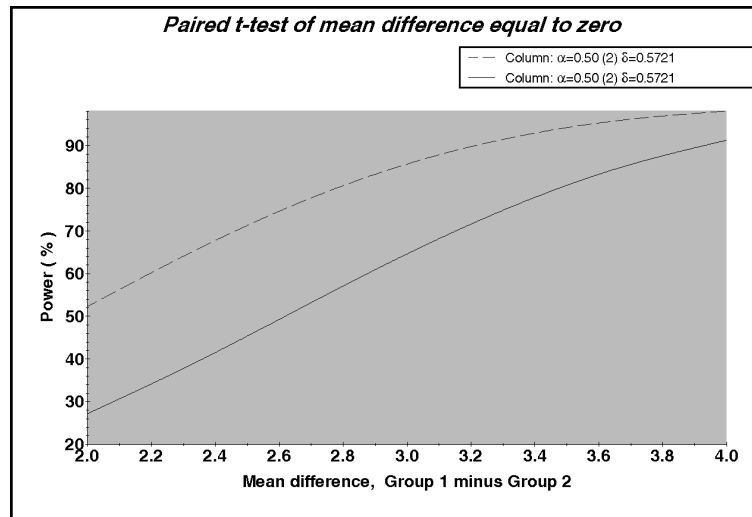
Effect size, $\delta = |\mu_d| / \sigma_d$
 Power (%)
 n

X-axis choices: X:

Test significance level, α
 First condition mean, μ_1
 Second condition mean, μ_2
 Mean difference, $\mu_d = \mu_1 - \mu_2$
 Standard deviation of differences, σ_d
 Effect size, $\delta = |\mu_d| / \sigma_d$
 Power (%)

Plot from To

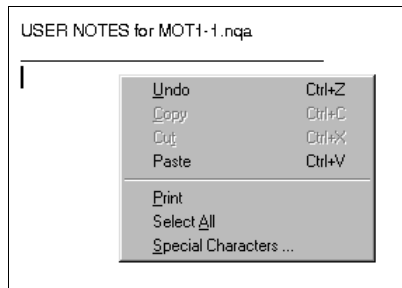
Click on the **OK** button to create the plot.



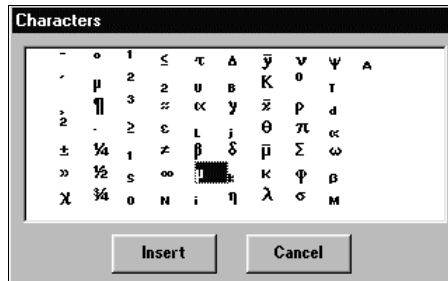
To edit the X-axis label:

Since we prefer to include Greek letters in the X-axis label, we first build our label in the Notes panel.

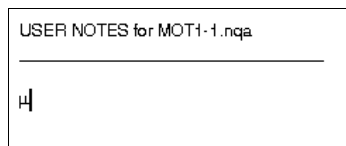
Move to the MOT1 sample size table and right click within the Notes panel to bring up the **right click menu**.



Select the **Special Characters** option and click on μ .



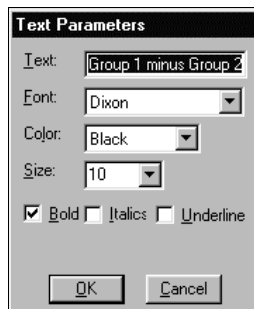
Click on the **Insert** button, and the Greek letter μ appears in the **Notes** panel.



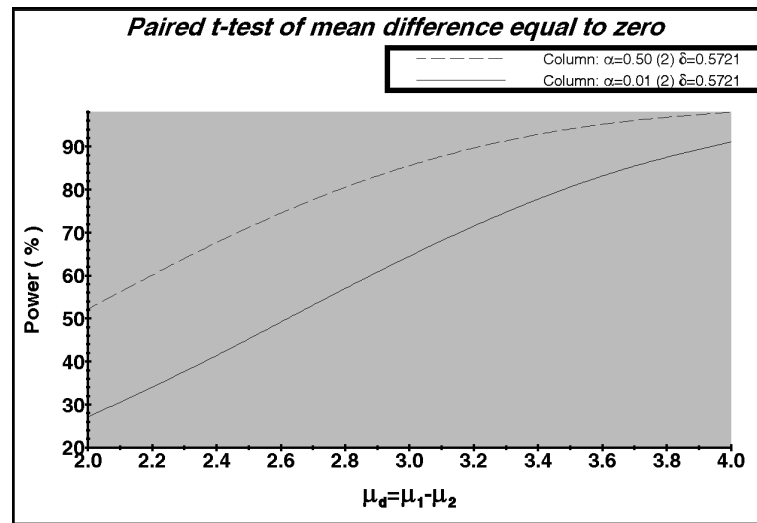
Finish writing the X-axis label, $\mu_a = \mu_1 - \mu_2$.

When you have the equation written properly, copy the equation.

Move to the plot. In the plot, double click on the X-axis label. The **Text Parameters** dialog box will appear.



Paste the new equation in the **Text** field in place of “Mean Difference, Group 1 minus Group 2.” Click on **OK** to see the updated plot.



You can easily go back to your nQuery table and request another plot.

Note: Additional prompts appear occasionally. Sometimes you will see the Edit/Recalculation dialog box after selecting the parameters for the X- and Y- axes. If you see that dialog box, just click on the **OK** button to complete the plot. (It may be necessary to click on it several times.)

You may see a **Power too high** message as shown in Example 3. Just click on the **OK** button each time to complete the plot.

Example 3

Plot User-selected rows for MTT0

To use the Plot User-selected rows option to plot power vs. effect size:

We use the example for the group t-test (MTT0) from Chapter 2.



Two group t-test of equal means (equal n's)					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Group 1 mean, μ_1	2.000				
Group 2 mean, μ_2	0.000				
Difference in means, $\mu_1 - \mu_2$	2.000				
Common standard deviation, σ	2.000				
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.000				
Power (%)	86				
n per group	20				

To begin the plot, highlight the first column and choose the **Plot** menu **Plot**



User-selected rows option or choose the **Plot User-selected rows** icon.

After you select **Plot User-selected rows**, the Specify Plot dialog box will appear.

Select **Power** for the Y-axis and **Effect size** for the X-axis. Enter a range of **.5** to **1.5** for the X-axis.

Specify plot

Y-axis choices:

Y: Power (%)

Effect size, $\delta = |\mu_1 - \mu_2| / \sigma$
Power (%)
n per group

X-axis choices:

X: Effect size, $\delta = |\mu_1 - \mu_2| / \sigma$

Plot from 5 To 1.5

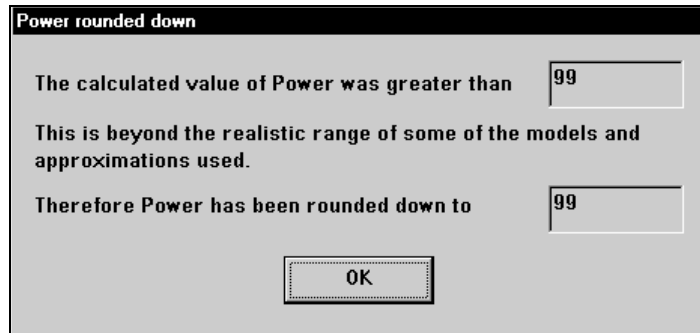
OK

Cancel

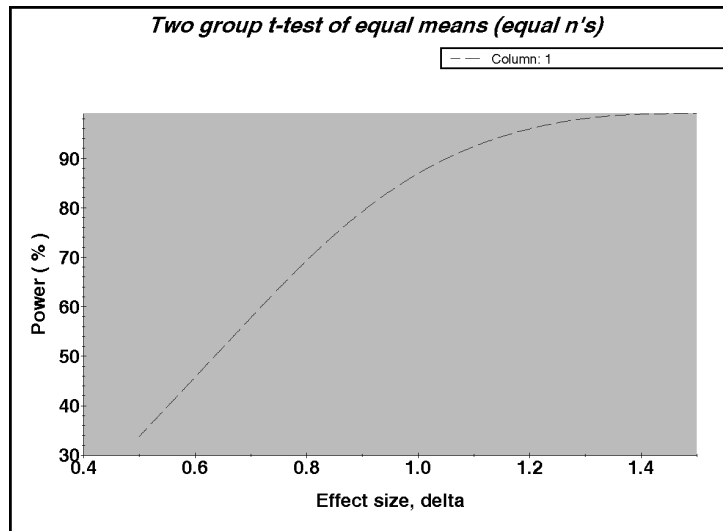
User Y

User X

Click on the **OK** button. When power is very high for X values in the specified range, you may see the following power dialog box one or more times; simply click on **OK** each time and the plot will appear on your screen.



Click on the **OK** button, and your power versus effect size plot will appear on your screen.

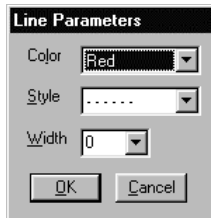


To change the dotted line to a solid line:

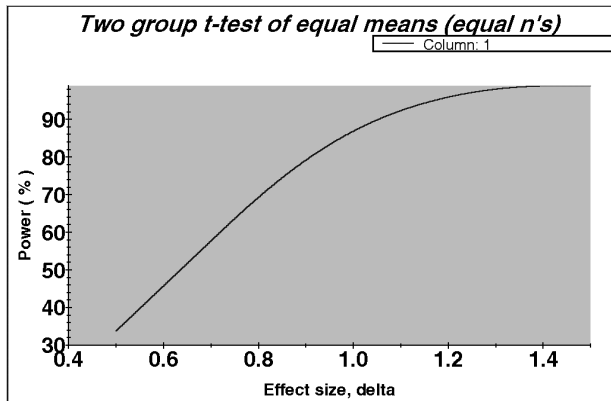
Double click on the line to bring up the **Plot Parameters** dialog box.



Click on the **Line Attributes** button to bring up the **Line Parameters** dialog box.

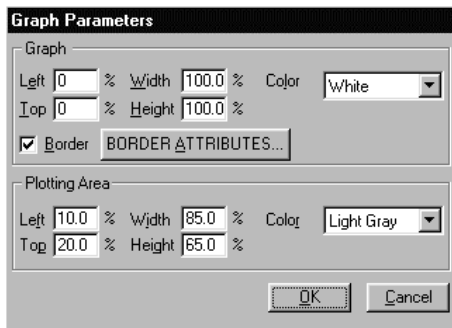


In the **Style** field, choose **Solid**, and in the **Width** field choose **2**. Click on **OK** in each dialog box to see the plot with the updated line.

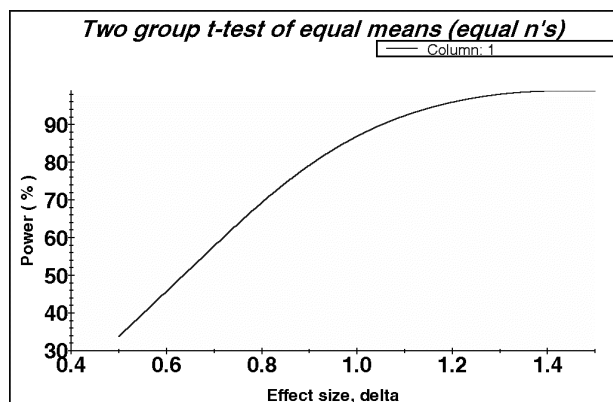


To change the plot background to off white:

Click on the **Graphs** menu **Parameters** option to bring up the **Graph Parameters** dialog box.



In the **Plotting Area Color** field, select **Off White**. Click **OK** to view the completed plot.



Example 4


Plot User-selected rows for PTT0

To use the **Plot User-selected rows** option to plot n versus the odds ratio:

We use the example for the two group χ^2 test (PTT0) from Example 3 in Chapter 15.

Two group χ^2 test of equal proportions (odds ratio = 1) (equal n's)				
	1	2	3	
Test significance level, α	0.050	0.050		
1 or 2 sided test?	2	2		
Group 1 proportion, π_1	0.450	0.450		
Group 2 proportion, π_2	0.650	0.650		
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	2.270	2.270		
Power (%)	95	90		
n per group	158	128		

Select both columns and choose the **Plot** menu **Plot User-selected rows** option

or the **Plot User-selected rows** icon, . The Specify Plot dialog box will appear.

Select **Power** for the **Y-axis** and **Odds ratio** for the **X-axis**.

Enter an X-axis range from **1.0** to **3.0**.

Specify plot

Y-axis choices: Y:

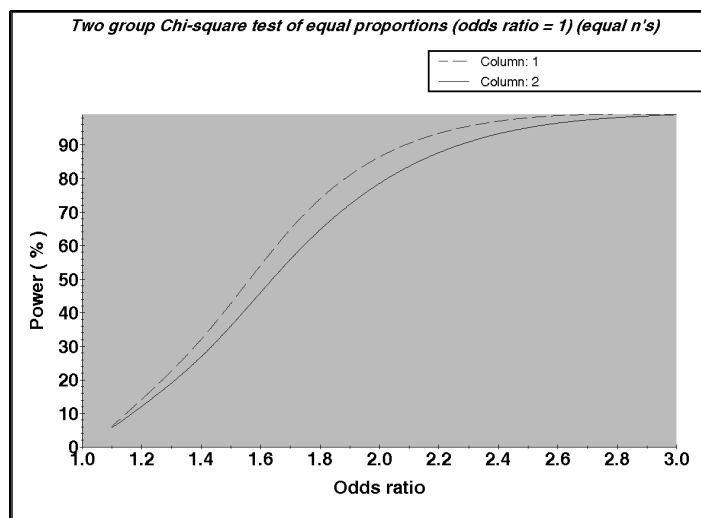
Power (%)
n per group

X-axis choices:

Test significance level, α
Group 1 proportion, π_1
Group 2 proportion, π_2
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$
Power (%)
n per group

Plot from To

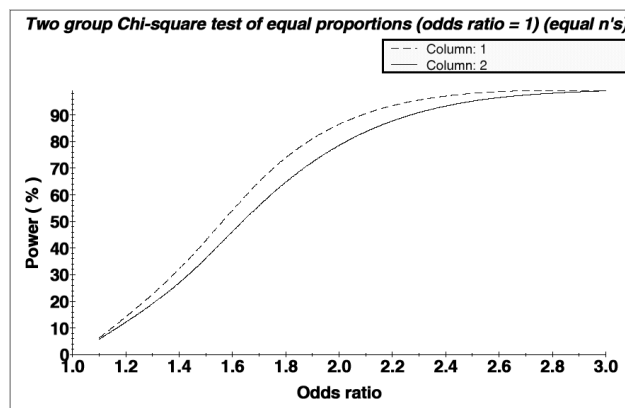
Click on the **OK** button to create the plot.



Note: Since plots are based on only 7 points and an automatic method is used for connecting points, plots with n on the Y-axis may not always appear monotone.

To print the plot:

Select the **File** menu **Print current page** option. Using the default settings, the printed plot will be white and will appear similar to the following plot. This is a reduced version of an actual landscape printed plot that fills up the entire page.



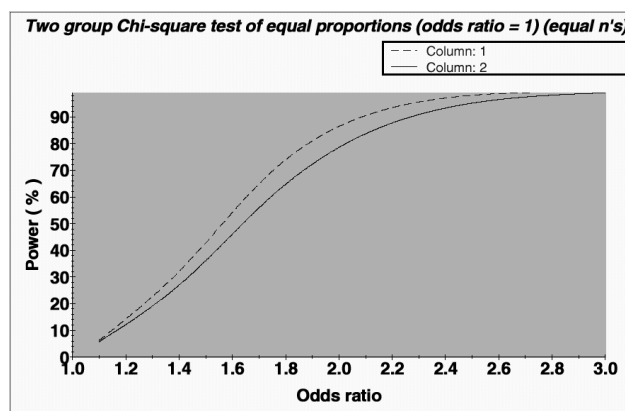
Note: The default settings cause the plot to print without the plot area background.

To print the plot with the plotting area background:

Choose the **File** menu **Printing Options** option to bring up the **Print Parameters** dialog box.

Click in the check box **Plotting Area Background** checkbox.

Click on **OK**, and your printed plot will look like the following plot. This is a reduced version of an actual landscape printed plot that fills up the entire page.





Example 5

Plot User-selected rows for MTC1


To use the **Plot User-selected rows** option to plot interval width versus n :

We use the example for the two-sample confidence interval (MTC1) from Example 2 in Chapter 8.

Confidence interval for difference of two means (coverage probability) (equal n's)					
	1	2	3	4	
Confidence level, $1-\alpha$	0.950	0.950			
1 or 2 sided interval?	2	2			
Coverage probability, $1-\gamma$	0.900	0.800			
Common standard deviation, σ	6.000	6.000			
Distance from difference to limit, ω	1.500	1.500			
n per group	138	134			

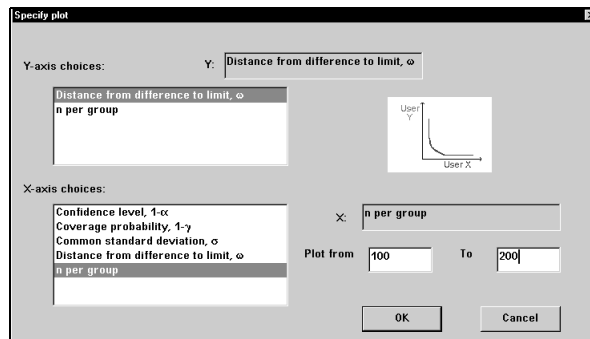
To plot these columns:

Select the filled column and choose the **Plot** menu **Plot User-selected rows**

option or the **Plot User-selected rows** icon, . The Specify Plot dialog box will appear.

Select **Distance from difference to limit** for the **Y-axis** and **n per group** for the **X-axis**.

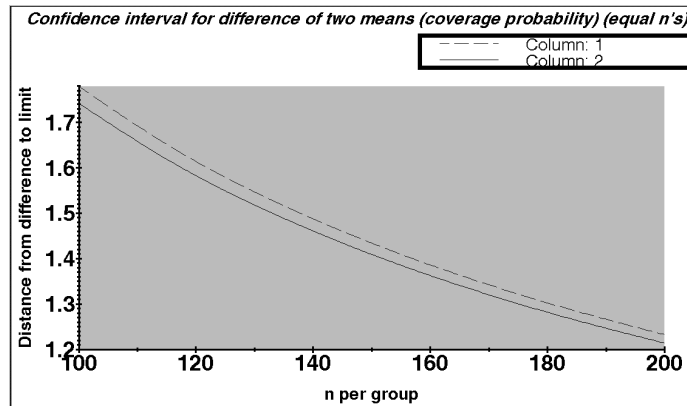
Enter a range from **100** to **200** for the X-axis.



The Specify plot dialog box shows the following configuration:

- Y-axis choices:** Distance from difference to limit, ω
- X-axis choices:** n per group
- Plot from:** 100
- To:** 200
- OK** and **Cancel** buttons are at the bottom.

Click on the **OK** button to create the plot.



To edit the legend:

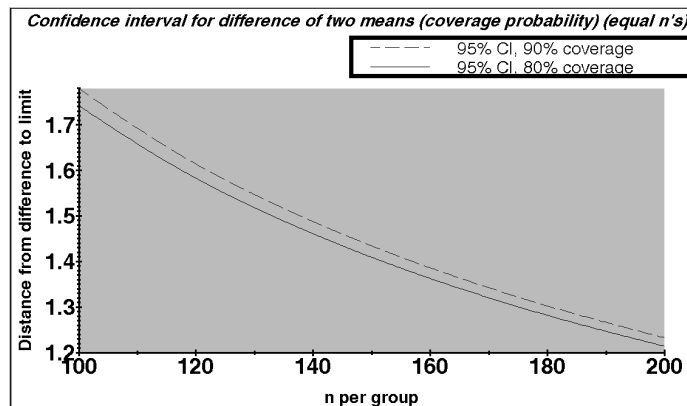
Double click on the legend to bring up the Legend parameters dialog box.

The 'Legend Parameters' dialog box has two main sections. The 'Legend Rectangle' section includes fields for Left (49.5 %), Width (50.0 %), Top (7.5 %), Height (9.5 %), and Color (White). There is a checked 'Border' checkbox and a 'BORDER ATTRIBUTES...' button. The 'Text' section shows 'Column: 1' and 'Column: 2' in a list box, with 'OK', 'Cancel', and 'TEXT PARAMETERS...' buttons at the bottom.

In place of Column: 1, type 95% CI, 90% coverage.

In place of Column: 2, type 95% CI, 80% coverage.

Click **OK** to see the updated plot.





Note: The plot legend is limited to 40 characters.

To paste this plot into a document in a Windows application:

Click on the **Edit** menu **Copy** option to copy the plot to the clipboard.

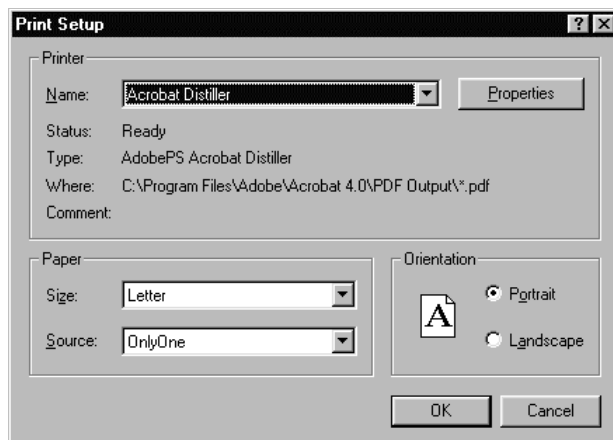
Move to the document in the Windows application and click on the **Edit** menu **Paste** option.

If you have the full Adobe Acrobat program, you can print your plots to pdf format for use alone or in other Windows applications.

To print this plot to an Adobe Acrobat pdf document:

Click on the menu **Printer setup** option to specify the use of Adobe acrobat rather than your usual printer.

In the **Printer Name** field, change to **Acrobat Distiller**.

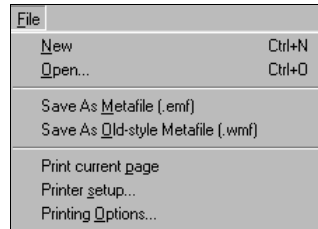


Click **OK**.

Select the File menu Print current page option. When prompted, specify a name and location for the file.

Plot File Menu

The Plot File menu displays seven options for use with the plot:



New

The New option on the Plot window File menu brings up the Study Goal and Design box so that you can specify a new sample size table.

Open

The Open option on the Plot window File menu brings up the Open dialog box so that you can open an existing sample size table file.

Save as Metafile

The Save as Metafile option on the Plot window File menu allows you to save your plot as a Windows metafile, a file with the .emf extension. The .emf files can be inserted into Word documents.

To use the Save as Metafile option:

Select the **File** menu on the Plot window.

Select the **Save as Metafile** option. The Save as Metafile dialog box appears.

The default name will be a numbered plot, such as **plot0.emf**. Change the file name and directory as necessary.

Click on **OK** to save the file.



Save as Old-style Metafile

The Save as Old-style Metafile option on the Plot window File menu allows you to save your plot as an older type of Windows metafile, a file with the .wmf extension. The .wmf files can be inserted into Word documents. The .wmf files can also be converted to .jpg, .gif, .bmp, and other formats using a graphics conversion program such as Conversions Plus from DataViz.

To use the Save as Old-style Metafile option:

Select the **File** menu on the Plot window.

Select the **Save as Old-style Metafile** option. The Save as Metafile dialog box appears.

The default file name will be a numbered plot, such as **plot0.wmf**. Change the file name and directory as necessary.

Click on **OK** to save the file.

Print Current Page

The Print Current Page option on the Plot window File menu allows you to send the current page to the printer.

To use the Print Current Page option:

Select the **File** menu on the Plot window.

Select the **Print Current Page** option. The page will start to print, and you will see a dialog box allowing you to cancel the printing.

Printer Setup

The Printer Setup option on the Plot window File menu brings you to the usual Windows Printer Setup dialog box.

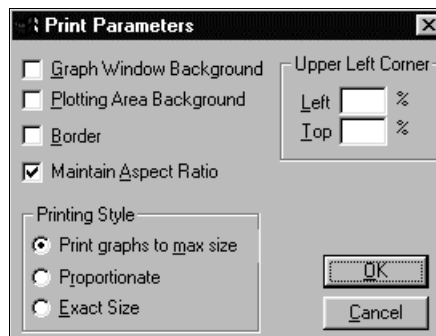
Printing Options

The Printing Options choice on the Plot window File menu provides a selection of printing options for your graph.

To use the Printing Options:

Select the **File** menu on the Plot window.

Select the **Printing Options**. The Print Parameters dialog box appears.



Check the appropriate checkbox to choose backgrounds, border, and whether you want to maintain the aspect ratio.

Click on a radio button to choose the printing style for your graph.

We suggest that you add a check to the following options:

- **Plotting Area Background** to get a background similar to that on the screen
- **Maintain Aspect Ratio** to retain the ratio of the lengths of the x and y axes
- **Exact Size** to print at the same size as the plot on the screen.

Note: By default, the **Plotting Area Background** box is not checked. This means that the plot will not print the background that you see on the screen. If you prefer to print the background, you must check **Plotting Area Background**.

Then enter **20** in the Left % and Top % boxes. If you have also used the **Printer Setup** to select a **Landscape** setting, these choices will bring you a plot nicely centered in the middle of your page. The printed plot will display a gray background in the plotting area if you have kept the default setting for the plotting area background.

Click on **OK** to finish specifying the printing options for the file.

Choose **Print Current Page** to print the graph.



Summary of Ways to Print a Plot

The nQuery Advisor program and the Windows interface offer four ways for you to print your plot.

File Menu Print Option

The File menu Print Current Page option will print your plot directly.

File Menu Print Option Printing to PDF

If you have Adobe Acrobat, and you first choose Acrobat Distiller as your printer, the File menu Print Current Page option will print your plot to an Acrobat pdf file.

File Menu Save as Metafile Option

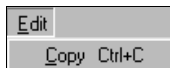
The File menu Save as Metafile option creates an .emf file which you can insert into other Windows applications for printing.

File Menu Save as Old-style Metafile Option

The File menu Save as Old-style Metafile option creates a .wmf file which you can insert into other Windows applications for printing.

Plot Edit Menu

The Plot Edit menu provides one option for use while viewing a plot:

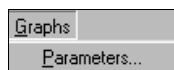


Copy

The **Copy** option on the Plot window Edit menu copies the graph to the Clipboard for use with other Windows programs.

Plot Graphs Menu

The Plot Graphs menu provides one option for use while viewing a plot:



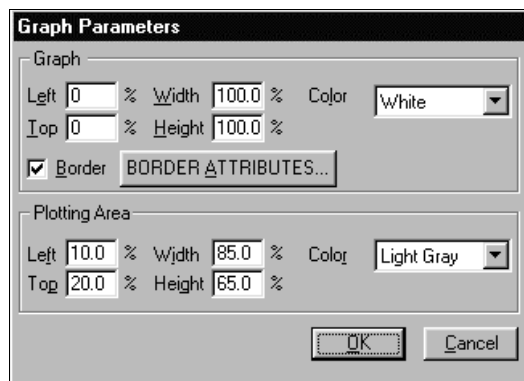
Parameters

The **Parameters** option on the Plot window **Graphs** menu offers several ways to customize your graph on the screen.

To use the **Parameters** option:

Select the **Graphs** menu on the Plot window.

Select the **Parameters** option. The Graph Parameters dialog box appears.



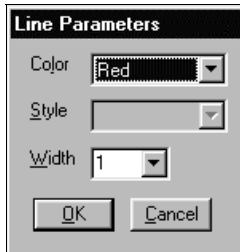
Enter a number into each of the Graph boxes: **Left%**, **Top%**, **Width%**, and **Height%**. These numbers determine the size and position of the graph in the Plot window.

Enter a number into each of the Plotting Area boxes: **Left%**, **Top%**, **Width%**, and **Height%**. These numbers determine the size and position of the plotting area within the graph.

Note: The defaults in the figure above, combined with the Printing Options recommendations will produce pleasing graphs.

You can also specify the color for the graph and a different color for the plotting area.

Click on the **Border Attributes** button if you want to bring up the **Line Parameters** dialog box.

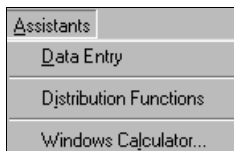


You can use the Line Parameters box to specify the **Color** and **Width** for the border lines. Click **OK** when you finish specifying the line parameters. Note that the **Style** option has been disabled.

Click **OK** when you have finished choosing your graph parameters. The graph will appear with your specifications.

Plot Assistants Menu

While viewing a plot, the Assistants menu allows you access to three of the usual nine Assistants menu options. For details on these options, see Chapter 5, *The Assistants Menu*.



Editing Within the Plot

The nQuery Advisor Plot window provides several additional ways to edit the contents of your plot. In general, when you want to edit a particular section of the plot, double click on that section.

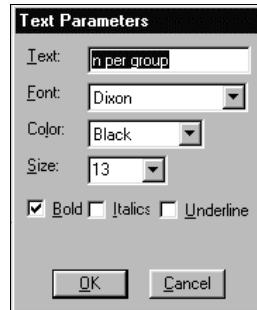
Edit Plot Text

You can edit the text on your plot. You can also change the font style, color, and size.

Note: The default font is the Dixon font. This font will form special characters which you may find useful.

To edit a section of text, such as a title or axis label:

Double click on the text on your plot. The **Text Parameters** dialog box will appear.



Edit the words in the text by editing the **Text** field. If you want to use special characters, use the Notes pane of the sample size table to write those characters using the Special Characters option. See Example 2 in this chapter for an example using Greek characters in an axis title.

Use the down arrow to choose a font in the **Font** field.

Use the down arrow to choose a color for the text in the **Color** field.

Use the down arrow to choose a size for the text in the **Size** field.

Click to activate **Bold**, **Italics**, and/or **Underline**.

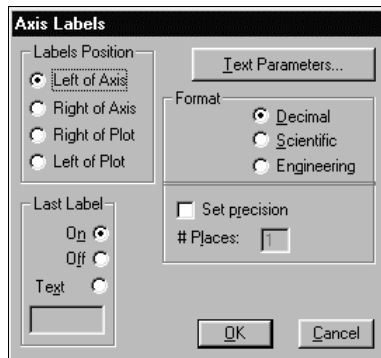
When you have finished customizing the text, click **OK**.

Edit Plot Axis Labels

You can edit the axis labels on your plot. You can set the position, format, precision, as well as the text parameters.

To edit an axis label:

Double-click on the axis label. The appropriate **Axis Labels** dialog box will appear.



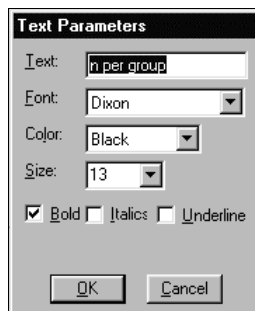
Click on one of the radio buttons to specify **Labels Position**.

Click on one of the radio buttons to specify **Format** as **Decimal**, **Scientific**, or **Engineering**. You can also determine the number of decimal places in each label by entering the number in the **# Places** box.

Click on a radio button to specify the **Last Label** as **On**, **Off**, or **Text**. If you choose **Off**, the plot will appear without a label on the last tick mark. If you choose **Text**, you can enter a small amount of text as a label for the last tick mark.

To edit the text of the plot axis labels:

Click on the **Text Parameters** button. The Text Parameters dialog box will appear.



The **Text** field is disabled.

Change the font in the **Font** field.

Change the color in the **Color** field.

Change the size in the **Size** field.

Click in the appropriate check box to add bold, italics, and/or underline.

Click **OK** to close the **Text Parameters** dialog box.

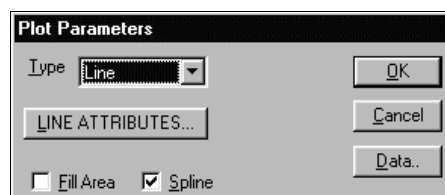
When you have finished customizing the tick mark labels, click **OK**. Your plot will display the changes.

Edit Plot Parameters

You can change the characteristics of the plotted lines in your graph.

To edit a plotted line:

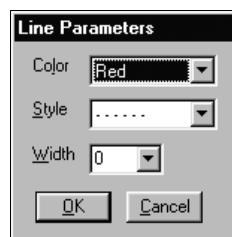
Double click on the plotted line. The **Plot Parameters** dialog box will appear.



Keep the default **Spline**, which draws a smooth curve through the plotted points, or click to remove the check in the **Spline** box.

Click on the **Fill Area** box to change the plot to a fill area plot.

If you want to change the plotted line itself, click on **Line Attributes** button to bring up the **Line Parameters** dialog box.



You can use this box to change the color, style, and width of the plotted line. Click **OK** to close the **Line Parameters** dialog box.

When you have finished customizing the plotted line, click **OK**. Your plot and the legend box will display the changes.

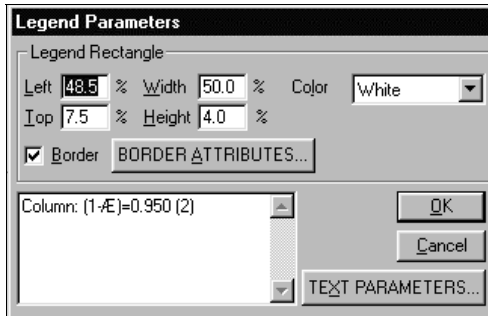


Edit Plot Legend Parameters

You can change the characteristics of the legend in your graph.

To edit the legend:

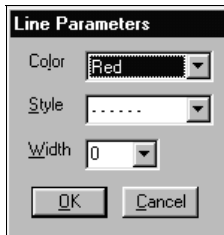
Double click on the legend. The **Legend Parameters** dialog box will appear.



Click in one or more of the **Legend Rectangle** fields and enter new numbers to change the size of the legend rectangle.

Click on the down arrow in the **Color** field, then choose a color.

Click to specify a border. You can then click on the **Border Attributes** button to bring up the **Line Parameters** dialog box.



In this box, you can change the color, style, and width of the line. Click **OK** to close the **Line Parameter** box.

In the lower left of the dialog box, you can see the legends themselves, although the special characters may not be recognizable. You can edit them here; click to place your cursor, then edit. However, it is better to edit the legends in the **Text Parameters** dialog box.

To edit the text of the legends:

Click on the **Text Parameters** button. The **Text Parameters** dialog box will appear.



Edit the text in the **Text** field. You can then change the font, color, and size, adding bold, italics, and/or underline.

Click **OK** to close the **Text Parameters** dialog box.

When you have finished customizing the legend, click **OK**. Your plot legend box will display the changes.

Note: The plot legend is limited to 40 characters.

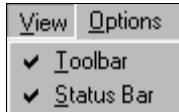
7. The View and Windows Menus

This chapter describes the View and Windows menus and their options.

The initial View menu contains only two options. The View menu which appears while you have an open sample size table offers three options.

View Menu—Initial

The initial View menu offers two toggle options:



Toolbar

The Toolbar option toggles between displaying and hiding the toolbar directly below the menu bar in the nQuery Advisor window.

To use the Toolbar option:

Choose the **View** menu.

The Toolbar option is a toggle. If the **Toolbar** option has a check mark beside it, the toolbar is On and displayed in the nQuery Advisor window. When you select the On **Toolbar** option, the toolbar will disappear from the nQuery Advisor window.

If the **Toolbar** option has no check mark beside it, the toolbar is Off and it is not displayed in the nQuery Advisor window. When you select the Off **Toolbar** option, the toolbar will appear in the nQuery Advisor window.

Status Bar

The Status Bar option toggles between displaying and hiding the status bar. The status bar lies at the bottom of your nQuery Advisor window. The bar displays a short description of each icon button as you select the icon button. The status bar also displays the status of the automatic recalculation option, along with the value of any cell selected by the cursor. Generally, the status bar will display more significant digits than appear in the sample size table cell.

To use the Status Bar option:

Choose the **View** menu.

If the **Status Bar** option has a check mark beside it, the Status Bar is On and displayed in the nQuery Advisor window. When you select the On **Status Bar** option, the status bar will disappear from the nQuery Advisor window.

If the **Status Bar** option has no check mark beside it, the status bar is Off and it is not displayed in the nQuery Advisor window. When you select the Off **Status Bar** option, the status bar will appear at the bottom of the nQuery Advisor window.

View Menu — From a Sample Size Table

The View menu which you see while you are working with your sample size table is similar to the initial View menu. Both menus include the two toggle options, Toolbar and Status Bar. The working version of the View menu, however, also includes one additional option, Guide.



Guide

The Guide card option is a toggle which is available only when you have an open sample size table. When the Guide Card option in the View menu is checked (default), the guide card appears in the pane on the right side of the sample size table.

The guide cards provide statistical information concerning the row in which your cursor lies. For example, the cards include information on limits for the values you can enter. Thus, if you have any questions concerning your input into the row of a sample size table, the guide card for that row will describe the contents of the row, as well as the acceptable entries.

The guide card pane displays the name of the row in a blue heading, followed by the description of the row. The pane will include a Suggestion for appropriate use of the row, as well as the Acceptable entries for the row. Some panes include additional topics concerning the row, such as a Shortcut or a Special Feature.



As you move the cursor from row to row, the guide card displays the information appropriate for the designated row. This option is particularly useful if you have any question concerning your entry for the selected row.

To use the Guide card option:

In an open sample size table, click on a spreadsheet cell in the row of interest.

If the Guide card is on, the sample size table will display the guide card for the selected row.

Use the arrow keys to move the cursor to another row. The guide card will change to reflect your choice.

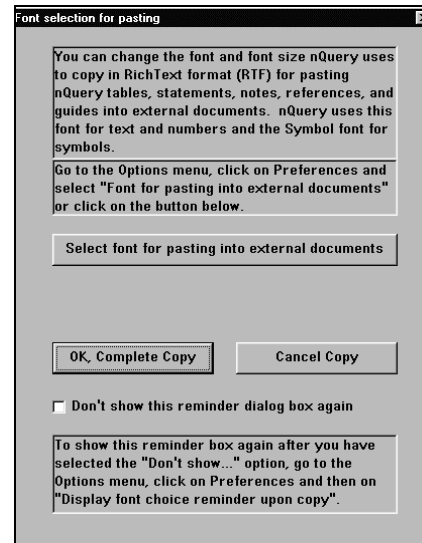
To turn off the guide card, click on the **View** menu **Guide** option or right click on the guide card and choose the **Hide** option in the guide card menu.

To copy the complete contents of the Guide card, retaining the guide card formatting for pasting into Windows applications:

Right click on the guide card of interest. The guide card right click menu will appear.

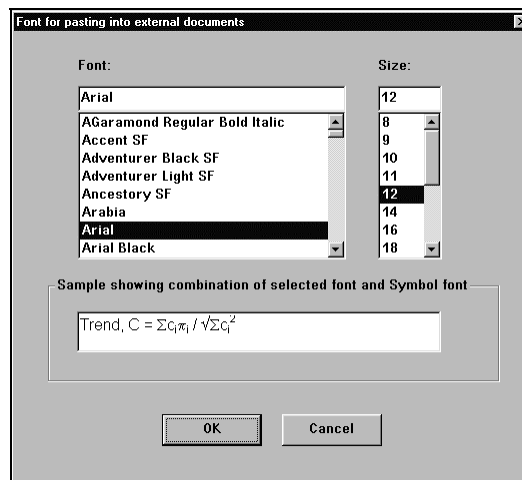
Click on the guide card menu **Copy** option.

The first time you select the Copy option from the guide card right click menu, you will see a message screen telling you how to change the font for the pasted text.



Click **OK Complete Copy** to accept the default Arial font.

If you prefer to select a different font, click on **Select font for pasting into external documents**. You will see the **Font for pasting into external documents** dialog box.



Select a font and a font size, then click **OK** to print to the clipboard.



After you have selected the font you want, you can choose not to see the reminder box again by clicking in the checkbox for **Don't show this reminder dialog box again**. Note that the symbols will appear in the Windows symbol font.

You can change the selected font at any time by using the **Option** menu **Preferences** option, and selecting **Font for External Pasting**. You can choose to display the font reminder box again by selecting the **Options** menu **Preferences** option **Display font choice reminder upon copy** option. See Chapter 3. *The File and Options Menus* for full details.

After copying, move to your word processing program and use the **Paste** option to paste the contents of the clipboard. The text below shows guide card contents pasted using the Arial font.

Two-sample t-test (equal n's)

Enter a value for alpha, α , the significance level for the t-test, and select a one or two-sided test. Specify two of effect size, power and sample size and nQuery Advisor will compute the third.

Test significance level, α

Alpha is the probability of rejecting the null hypothesis of equal means when it is true (the probability of a Type I error).

Suggestion:

Enter 0.05, a frequent standard

Acceptable entries:

0.001 to 0.20

Shortcuts:

To duplicate values across any row, see the Edit menu.

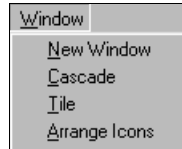
To print the complete contents of the Guide card:

Right-click on the guide card of interest. The guide card right click menu will appear.

Click on the guide card menu **Print** option. The usual Windows Print dialog box will appear. Click on **OK** to print.

Window Menu

The Window menu performs the usual Window menu functions for Microsoft Windows. You can use it to move among the open sample size table windows.



New Window

The New window option on the Window menu opens an exact duplicate of current sample size table complete with entered values.

Cascade

The Cascade option on the Window menu displays the open windows in nQuery Advisor in a staggered fashion. One window lies on top of the other, slightly offset so that you can view the table names.

Tile

The Tile option on the Window menu displays as much as possible of every open window in nQuery Advisor. This option tiles the nQuery Advisor window with the currently-open table windows.

Arrange Icons

The Arrange icons option on the Window menu will rearrange the icons for your minimized tables. You might use this option if you have several open tables and you minimize those tables. You can grab the table icons and move them around on the screen. After moving the icons, you can use the Arrange icons option to arrange the icons neatly.

List of Open Tables

The Window menu lists each table by its abbreviation title or if saved, by its file name.

Note: The tables are initially listed by their table abbreviations. Please read the next section to understand the table abbreviations.

Contents of Study Goal and Design Dialog Box

The Study Goal and Design dialog box allows you to choose the sample size table you want to use.



Study Goal and Design

Goal: Make Conclusion Using	Number of Groups	Analysis Method
<input checked="" type="radio"/> Means	<input type="radio"/> One	<input checked="" type="radio"/> Test
<input type="radio"/> Proportions	<input checked="" type="radio"/> Two	<input type="radio"/> Confidence Interval
<input type="radio"/> Survival (Time to Event)	<input type="radio"/> > Two	<input type="radio"/> Equivalence
<input type="radio"/> Agreement		
<input type="radio"/> Regression		

☒ **Two-sample t test**

- Student's t test (equal variances)
- Satterthwaite's t test (unequal variances)
- Two group t-test for fold change assuming log-normal distribution (equal n's)
- Two group t-test of equal fold change with fold change threshold (equal n's)
- Wilcoxon/Mann-Whitney rank-sum test (continuous outcome)
- Wilcoxon/Mann-Whitney rank-sum test (ordered categories)
- Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)

☒ Unequal n's ☐ Finite Population

OK Cancel

The nQuery Advisor program provides a sample size table for more than 75 different types of study plans. Codes will help you to find the analyses quickly.

The first letter of the code represents a goal from the first column:

Means, **P**roportions, **S**urvival, **A**greement, or **R**egression.

The second letter of the code represents the Number of Groups from the second column:

One, **T**wo, or **G**reater than two.

The third letter of the code represents the analysis method from the third column:

Test, **C**onfidence Interval, or **E**quivalence.

The fourth character in the code is the sequence number of the listed analyses, starting with 0.

For example, in the screen above, the code for Two-sample t test is MTT0. Most combinations of choices offer one or more analysis types for your selection, but a few do not.

Note that the Two-sample t test listing has a + sign beside it. In this case the sub-listings have already been expanded, but for other such menu items, you can click on the + to see the sub-listings.

Unequal n's

If your chosen analysis type has an unequal n's option, the Unequal n's checkbox in the lower left of the Study Goal and Design dialog box will be enabled. If you want unequal n's, click on the Unequal n's checkbox and click **OK**.

Finite Population

If your chosen analysis type has a Finite Population option, the Finite Population checkbox in the lower left of the dialog box will be enabled. If you want to specify Finite Population, click on the Finite Population checkbox and click **OK**.

The following tables have versions allowing for a finite population correction: MOT0, MOT1, MOC0, MOC1, MOC2, MOC3, POT0, POC0.

Abbreviation Codes

The abbreviation codes are:

MOT0	One-group t test that a mean equals user-specified value
MOT1	Paired t test of mean difference equal to zero
MOT2	Univariate one-way repeated measures analysis of variance (constant correlation)
MOT3	One-way repeated measures contrast (constant correlation)
MOT4	Univariate one-way repeated measures analysis of variance (Greenhouse-Geisser approximation)
MOC0	Confidence interval for mean based on z (n large)
MOC1	Confidence interval for mean based on t (with coverage correction)
MOC2	Confidence interval for difference in paired means based on z (n large)
MOC3	Confidence interval for difference in paired means based on t (coverage correction)
MOC4	Confidence interval for one-way repeated measures contrast (constant correlation)
MOC5	Confidence interval for percentile of a normal distribution
MOE0	Paired t test of equivalence of means
MTT0	Two group t test of equal means (equal or unequal n's)



MTT0uv	Two group Satterthwaite t test of equal means (unequal variances) (equal or unequal n's)
MTT0cv	Two group t test for fold change assuming log-normal distribution (equal or unequal n's)
MTT0fct	Two group t test of equal fold change with fold change threshold (equal or unequal n's)
MTT1	Wilcoxon (Mann-Whitney) rank-sum test that $P(X<Y)=.5$ (continuous outcome)
MTT2	Wilcoxon (Mann-Whitney rank-sum test that $P(X<Y)=.5$ (ordered categories) (equal or unequal n's)
MTT3	Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)
MTC0	Confidence interval for difference of two means based on z (large equal or unequal n's)
MTC1	Confidence interval for difference of two means (coverage probability) (equal or unequal n's)
MTE0	Two-group t test of equivalence in means (equal or unequal n's)
MTE1tg	Two-group t test (TOST) of equivalence in means
MTE1co	t-tests (TOST) of equivalence in means for crossover design
MTE2tg	Two-group t-tests (TOST) for ratio of means (using log scale)
MTE2co	t-tests (TOST) of equivalence in ratio of means for crossover design (natural log scale)
MTE3	Two-group t-tests (TOST) for ratio of means (using original scale)
MTE4	Crossover design TOST for ratio of means (using original scale)
MGT0	One-way analysis of variance (equal or unequal n's)
MGT1	Single one-way between means contrast (equal or unequal n's)
MGT2	Two-way analysis of variance
MGC0	Confidence interval contrast between means (equal or unequal n's)
MGC1	Confidence interval for one-way contrast (large equal or unequal n's)
POT0	One group χ^2 test that proportion equals user specified value (normal approximation)

POT0x	Exact test for single proportion.
POT1	McNemar's test (χ^2) of equality of paired proportions
POT1x	Exact sign test of equality of paired proportions
POT2	Chi-square test of specified proportions in C categories
POC0	Confidence interval for proportion using normal approximation (n large)
POC1	Confidence interval for $\ln(\Psi_m)$, odds ratio for paired proportions (n large)
POC2	Confidence interval for probability of observing a rare event.
POE0	Paired test of equivalence in proportions (n large)
POE1	Paired test of equivalence in proportions using confidence interval: a) Lower confidence limit for difference in paired proportions (simulation), b) Upper confidence limit for difference in paired proportions (simulation), c) Two-sided confidence limits for difference in paired proportions (simulation)
PTT0	Two-group χ^2 test of equal proportions (odds ratio=1) (equal or unequal n's)
PTT0p	Two-group χ^2 test of equal proportions (equal or unequal n's)
PTT1	Two-group continuity corrected χ^2 test of equal proportions (odds ratio=1) (equal or unequal n's)
PTT1p	Two-group continuity corrected χ^2 test of equal proportions (odds ratio=1) (equal or unequal n's)
PTT2	Two-group Fisher's exact test of equal proportions (odds ratio=1)(equal or unequal n's)
PTT3	Two-group Chi-square test comparing proportions in C categories
PTT4	Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata
PTT4cc	Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata (continuity corrected)
PTC0	Confidence interval for difference of two proportions (large equal or unequal n's)
PTC1	Confidence interval for difference of two proportions (continuity corrected) (large equal or unequal n's)
PTC2	Confidence interval for $\ln(\Psi)$ (large equal n's)



PTE0	Two-group test of equivalence in proportions (large equal or unequal n's)
PTE1	Two group test of equivalence in proportions using confidence interval: a) Lower confidence limit for difference in proportions (simulation), b) Upper confidence limit for difference in proportions (simulation), c) Two-sided confidence limits for difference in proportions (simulation) (equal or unequal n's)
PGT0	χ^2 test of equal proportions in G groups (equal or unequal n's)
PGT1	Trend across proportions, logistic model (equal or unequal n's)
PGT2	G-group Chi-square test comparing proportions in C categories (equal or unequal n's)
STT0	Log-rank test of survival in two groups followed for fixed time, constant hazard ratio
STT1	Two-group test of equal exponential survival (n large) no dropouts
STT2	Two-group test of equal exponential survival (n large), exponential dropout
STT3	Log-rank test of survival in two groups, simulation with specified rates (equal or unequal n's)
AOT0	Agreement between two dichotomous ratings (intraclass kappa)
AOT1	Correlation test that $\rho=\rho_0$ for x and y bivariate normal
AOT2	Large sample test that Lin's concordance coefficient = K_0
AOC0	Confidence interval for intraclass Kappa (n large)
AOC1	One-sided confidence interval for ρ for x and y bivariate normal
AOC2	One-sided large sample confidence interval for concordance coefficient
ROT0	Logistic regression, test that $\beta=0$ for one normally distributed covariate, x
ROT1	Logistic regression, test that $\beta=0$ for one covariate, x, after adjustment for prior covariates
ROT2	Linear regression test that $\rho=0$ for one normally distributed covariate, x
ROT3	Multiple linear regression, test that $R^2=0$ for k normally distributed covariates

ROT4	Multiple linear regression, test 0 increase in R^2 for B covariates adjusting for A covariates
ROT5	Linear regression test that $\beta=\beta_0$ for one x
ROC0	Linear regression confidence interval for β
RTT0	Linear regression test that $\beta_1=\beta_2$ for one x
RTC0	Linear regression confidence interval for $\beta_1-\beta_2$

8. Sample Size Tables for Means

The nQuery Advisor program provides a variety of sample size tables for determining sample size in problems where the group mean is the summary measure for analysis. To select the appropriate sample size table, you first identify:

- the study design
- one, two, or multiple groups
- the intended analysis, test, confidence interval, or equivalence test.

Sample size tables for most designs with two or more groups allow sample size computations for designs utilizing unequal sample sizes in the groups. For an example, see Chapter 10.

For every sample size table used for analysis of group means, the nQuery Advisor program requires an estimate of the within-group standard deviation. If you need help in determining an estimate of the standard deviation, refer to Chapter 9.

1. The most commonly used design for comparison of means is the two-group (independent sample) design.

The most common analysis method is the two-group (two-sample) t test. The nQuery Advisor table choice would be:

MTT0 Two-group t test of equal means

See Chapter 2, *Tutorial*, for a detailed tutorial on this table.

2. Another common design is one in which each subject is tested under two conditions. The usual analysis is the paired t test when each subject is tested under two conditions or provides a pre and post measurement.

MOT1 Paired t test of mean difference equal to zero

See Example 1 later in this chapter.

Sample Size Tables for Means in nQuery Advisor

This section of the Sample Size Tables for Means chapter briefly outlines all sample size tables available for analysis of means and refers you to examples in the manual.

One-group Tests and Confidence Intervals

MOT0	One group t test that a mean equals a user-specified value
MOC0	Confidence interval for mean based on z (n large)
MOC1	Confidence interval for mean based on t (with coverage probability)
MOC5	Confidence interval for percentile of a normal distribution See Example 3 in this chapter.

Versions of tables MOT0, MOC0, MOC1, are available for sampling from finite populations. See Chapter 19, *Sampling from Finite Populations*, for details.

Two-group Tests and Confidence Intervals

MTT0	Two group t test of equal means See the example in Chapter 2, <i>Tutorial</i> . See this table used in a crossover design in Example 1 in Chapter 13, <i>Repeated Measures and Crossover Designs</i> .
MTT0uv	Two group Satterthwaite t-test of equal means (unequal variances) This table is for situations where a comparison between two means using the t-test would be applicable, but the variances for the two groups are expected to be unequal. See Example 4 in this chapter.
MTT0cv	Two group t-test for fold change assuming log-normal distribution This table is for situations where a comparison between two means using the t-test would be applicable, but the distribution is expected to be log-normal and the user wants to specify the expected fold-change and the CV rather than means and standard deviations after log transformation. This table is of special interest for planning and interpreting <i>DNA microarray</i> studies. See Example 5 in this chapter.



MTT0fct	Two group t-test of equal fold change with fold change threshold This new table computes the probability of detection of specified fold-changes when the CV is specified and the result must exceed a specified <i>fold-change threshold</i> . This table is of special interest for planning and interpreting <i>DNA microarray</i> studies, see Example 6 in this chapter.
MTT1	Wilcoxon (Mann-Whitney) rank-sum test that $P(X<Y)=0.5$ (continuous outcome) See example in Chapter 14, <i>Nonparametric Tests</i>
MTT2	Wilcoxon (Mann-Whitney) rank-sum test that $P(X<Y)=0.5$ (ordered categories) See example in Chapter 14, <i>Nonparametric Tests</i> .
MTC0	Confidence interval for difference of two means based on z
MTC1	Confidence interval for difference of two means (coverage probability) See Example 2 in this chapter.

One and two group paired, crossover, & repeated measures designs, tests and confidence intervals

MOT1	Paired t test of mean difference equal to zero See Example 1 in this chapter
MOT2	Univariate one-way repeated measures analysis of variance (constant correlation)
MOT3	One-way repeated measures contrast (constant correlation)
MOT4	Univariate one-way repeated measures analysis of variance (Greenhouse-Geisser approximation)
MOC2	Confidence interval for difference in paired means based on z (n large)
MOC3	Confidence interval for difference in paired means based on t (coverage probability)
MOC4	Confidence interval for one-way repeated measures contrast (constant correlation)
MTT3	Two-group univariate repeated measures analysis of variance (Greenhouse-Geisser correction) See Example 7 in Chapter 13.

Versions of tables MOT1, MOC2, MOC3, are available for sampling from finite populations. See Chapter 19, *Sampling from Finite Populations*, for details.

One and two group and crossover designs, equivalence and bio-equivalence tests

MOE0	Paired t test of equivalence of means
MTE0	Two-group t test of equivalence in means See Example 1 in Chapter 1, <i>Demonstrating Equivalence</i> .
MTE1tg	Two-group t tests (TOST) of equivalence in means for two-group design See Examples 2 and 4 in Chapter 11, <i>Demonstrating Equivalence</i> .
MTE1co	t tests (TOST) of equivalence in means for crossover design See Example 3 in Chapter 11, <i>Demonstrating Equivalence</i> .
MTE2tg	Two-group t-tests (TOST) for ratio of means (using log scale) See Example 5 in Chapter 11, <i>Demonstrating Equivalence</i> .
MTE2co	t-tests (TOST) for ratio of means for crossover design (natural log scale) See Example 6 in Chapter 11, <i>Demonstrating Equivalence</i> .
MTE3	Two-group t-tests (TOST) for ratio of means (using original scale) See Example 7 in Chapter 11, <i>Demonstrating Equivalence</i> .
MTE4	Crossover design TOST for ratio of means (using original scale) See Example 8 in Chapter 11, <i>Demonstrating Equivalence</i> .

Multiple group tests and confidence intervals

MGT0	One-way analysis of variance See Example 1 in Chapter 12, <i>Analysis of Variance Tutorial</i> .
MGT1	Single One-way between means contrast See Example 3 in Chapter 12, <i>Analysis of Variance Tutorial</i> .
MGT2	Two-way analysis of variance
MGC0	Confidence interval contrast between means (large n's)
MGC1	Confidence interval for one-way contrast (with coverage probability)



Example 1

Paired t test (MOT1)


This chapter provides an example for a paired t test with an expected mean difference of zero. The example uses data from a cancer chemotherapy study.

Patients with cancer receive repeated chemotherapy cycles. During each chemotherapy cycle, the number of neutrophils (a type of white blood cell) decreases. “Neutropenia” occurs when the number of neutrophils decreases below a fixed cutoff value.

The study plan is to compare a new therapy intended to reduce the number of days of neutropenia with a placebo. Each patient will receive the new therapy during one chemotherapy cycle and placebo during another chemotherapy cycle. (Although the study is to be a crossover study, we ignore that aspect of the design in the sample size planning for this example).

The study will analyze the data using a 5% level, two-sided, paired t test to test the null hypothesis that the mean duration of neutropenia following the drug is the same as following the placebo. The investigator thinks it will be feasible to recruit 30 patients and wants to know if that number of patients will provide adequate power.

To bring up the correct sample size table:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **One** group.

Under **Analysis method**, select **Test**.

The box in the lower portion of the Study Goal and Design box will display several design choices. The highlighted design is **Paired t test for difference in means**.

Click on **OK** to accept the highlighted choice.

You will get the sample size table for the **Paired t test for difference in means**. Your table will appear with no numbers. This example shows a table containing .05 in the test significance level row, 2 in the 1 or 2 sided test row, and 30 in the n row.

Paired t-test of mean difference equal to zero					
Test significance level, α	0.050				
1 or 2 sided test?	2				
First condition mean, μ_1					
Second condition mean, μ_2					
Mean difference, $\mu_d = \mu_1 - \mu_2$					
Standard deviation of differences, σ_d					
Effect size, $\delta = \mu_d / \sigma_d$					
Power (%)					
n	30				

Information on duration of neutropenia is available from two sources:

- 1) A published study reported a median of eight days of neutropenia in a control chemotherapy period with median durations of three and four days for two combination therapies.
- 2) Pilot data from four patients receiving two cycles of chemotherapy with no treatment intervention showed median durations of about six days and a standard deviation of differences in duration between the two cycles of 7.5.

Based on these data, the investigator wants to be able to detect a drop in the duration of neutropenia from six days for control to three days for the new therapy. The investigator decided to use a smaller estimate, 5.25, for the standard deviation of differences based on the information about range and standard deviation of neutropenia duration for a single period.

Note: The investigator has customized row titles for the means. See Chapters 2 and 3 for details on how to customize row names by selecting **Edit Row Names** from the **Edit** menu or the right click menu.


Paired t-test of mean difference equal to zero					
Test significance level, α	0.050				
1 or 2 sided test?	2				
Placebo mean, μ_1	6.000				
Treatment mean, μ_2	3.000				
Mean difference, $\mu_d = \mu_1 - \mu_2$	3.000				
Standard deviation of differences, σ_d	5.250				
Effect size, $\delta = \mu_d / \sigma_d$	0.571				
Power (%)	85				
n	30				

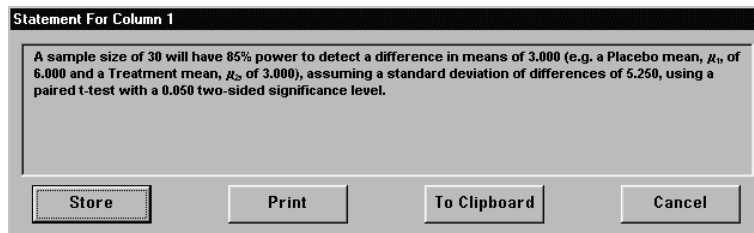
After the investigator enters the values for the means and for the standard deviation of differences, nQuery solves for the effect size and the expected power, 85% in this case.

nQuery Advisor provides automated customized sample size justification statements.

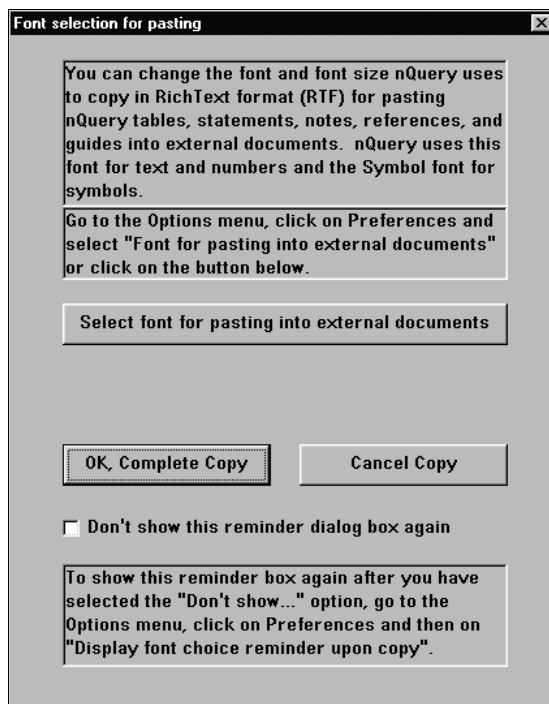


To obtain this statement and copy it to Notes or another Windows application:

With the cursor in the column of interest, click on , the **Create Statement** button. The Statement dialog box will appear.



When you have the statement for this column, click on the Statement window's **To Clipboard** button to copy that statement. The Font selection for pasting dialog box will appear.



You can use this dialog box to specify the font to be used to copy the Statement in Rich text Format. Click on the **Select font for pasting into external**

documents button. After you have selected a font, click on the **OK, Complete Copy** button.

To paste the newly-copied statement to USER NOTES:

Place the cursor in the USER NOTES pane and select the Edit menu **Paste** option or the Paste button or **<Ctrl><V>**.

To paste to Windows application: Place the cursor in a Windows application and use that application's **Edit** menu **Paste** option to paste the statement. Using the default Arial font, the statement will look like this:

A sample size of 30 will have 85% power to detect a difference in means of 3.000 (e.g. a Placebo mean, μ_1 , of 6.000 and a Treatment mean, μ_2 , of 3.000), assuming a standard deviation of differences of 5.250, using a paired t-test with a 0.050 two-sided significance level.

To paste a previously-stored statement into USER Notes for editing:

Select the text in the Statements pane.

Click on the **Edit** menu **Copy** option or the Copy button or **<Ctrl><C>**.

Click to place the cursor in the desired location of the **NOTES** pane.

Click on the **Edit** menu **Paste** option or the Paste button or **<Ctrl><V>** to paste the copied statement.

You can print the user notes directly or copy them and paste them into a Windows document. Below we give an example showing a statement which has been pasted into the user notes and then edited. The user notes also contain information on the data from the published study.

USER NOTES for MOT1-1

A sample size of 30 will have 85% power to detect a difference in mean duration of neutropenia of 3 days (e.g. a mean duration of neutropenia under placebo of 6 days and a mean duration under the new drug of 3 days), assuming a standard deviation of differences in duration of 5.250 days, using a paired t-test with a 0.050 two-sided significance level.

Data on duration of neutrophil count less than $0.5 \times 10^9/L$ in 50 cycles in 36 patients from Brugger W. et al (1992) Sequential administration of interleukin-3 and granulocyte-macrophage colony-stimulating factor following standard dose combination chemotherapy with etoposide, ifosamide, and cisplatin. J. ClinOncology 10:1452-1459.



To copy the User Notes for pasting into other Windows applications:

Highlight the text you want to copy.

Choose **Copy** from the **Edit** menu or the right click menu or click on the Copy icon in the toolbar.

Example 2

Two-sample Confidence Interval (MTC1)

The following example illustrates the use of the tables for confidence interval for two groups. Consider a trial in which a Placebo, the current Standard drug, and a New Drug will all be compared for their ability to reduce blood pressure. The standard deviation for reduction in blood pressure is estimated from previous studies with the Standard drug as about 6mmHg. In the past, the Placebo has resulted in reductions of about 5mmHg, and the Standard drug in reductions of about 12 mmHg.


The study as a whole will be analyzed using a one-way analysis of variance. For details on analysis of variance, see the tutorial in Chapter 12.

As one of their goals, the investigators wish to establish that the New Drug and the Standard provide essentially the same reduction in blood pressure. Two approaches are of interest in this study:

- A. To obtain a very good estimate of any differences between the New Drug and the Standard in blood pressure reduction, and decide whether these differences are in the acceptable range.
- B. To define an upper limit on acceptable differences and use a test of equivalence, see Chapter 11, *Demonstrating Equivalence*, for an example of this approach.

The investigator wants to know the sample size necessary so that a 95% confidence interval for the difference in mean blood pressure reduction for the New Drug and the Standard extends no farther than 1.5 mmHg above and below the observed difference.

To bring up the correct sample size table:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Confidence Interval**.

Select the second analysis type, Confidence interval for difference between two means, coverage probability.

Click on **OK**.

The table will come up empty. The following table shows our entries of 0.95 for the confidence level, and 2 for a two-sided confidence interval.

Confidence interval for difference of two means (coverage probability) (equal n's)					
Confidence level, $1-\alpha$	0.950				
1 or 2 sided interval?	2				
Coverage probability, $1-\gamma$					
Common standard deviation, σ					
Distance from mean to limit, ω					
n per group					

The standard deviation actually observed in your planned study may be larger or smaller than the expected standard deviation used for study planning. As a result, the confidence interval distance which you compute at the end of the study may be larger or smaller than the distance specified. Therefore, we must specify how sure we want to be that the observed confidence interval will be shorter than the specified length.

Here the investigator chooses **90%** for the desired probability that the observed confidence interval width will be shorter than that specified, so he enters **.90**. Then he enters the value **6** for the standard deviation. For the confidence width (distance from mean to limit), he enters **1.5** to set the desired value to ± 1.5 . As soon as you enter **1.5** and press <Enter>, nQuery Advisor solves for the required sample size in each group.

Confidence interval for difference of two means (coverage probability) (equal n's)					
Confidence level, $1-\alpha$	0.950				
1 or 2 sided interval?	2				
Coverage probability, $1-\gamma$	0.900				
Common standard deviation, σ	6.000				
Distance from mean to limit, ω	1.500				
n per group	138				

This example produced the n per group necessary to obtain a good estimate of differences between the New Drug and the Standard in blood pressure reduction.



Example 3

Confidence Interval for percentile of a normal distribution (MOC5)

Investigators frequently wish to estimate “normal limits” for some new test. In our example, we assume that the investigator wishes to define a cut-point which only 10% of the normal population will exceed and to use this in identifying those for whom further investigation is needed; in this case we want an estimate of the 90th percentile. The Pth percentile of a normal distribution is estimated as the sample mean + k (sd) where sd is the sample standard deviation of the distribution and k is chosen to satisfy $\text{Prob}(z < k) = P$.

We suppose that 100 subjects have been studied and that the sample mean is 143 and the sample standard deviation is 15.

To estimate the Pth percentile from the data, we use the observed mean and standard deviation of the sample of normals under study, and determine k by using the Distribution Functions option.

To estimate the Pth percentile from the data:

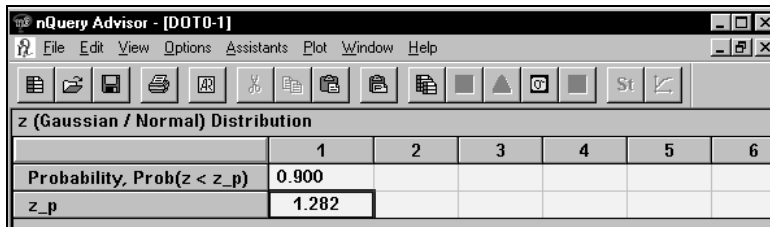
In the **Assistants** menu select **Distribution Functions**. In the **Distribution Function** menu, select **z (Gaussian/Normal) Distribution**.

Click **OK**.

The z (Gaussian/Normal) Distribution table appears.

To get the estimate for the 90th percentile, enter **0.9** for **Probability**.

nQuery solves for the value of z.




z (Gaussian / Normal) Distribution						
	1	2	3	4	5	6
Probability, Prob(z < z_p)	0.900					
z_p	1.282					

The value of z is 1.282 in this case. Thus, the estimated upper 90th percentile of the distribution of normals is

$$\text{mean} + 1.282 (\text{sd}) = 143 + 1.282(15) = 162.23.$$

To determine the expected width of the confidence interval for the Pth percentile

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

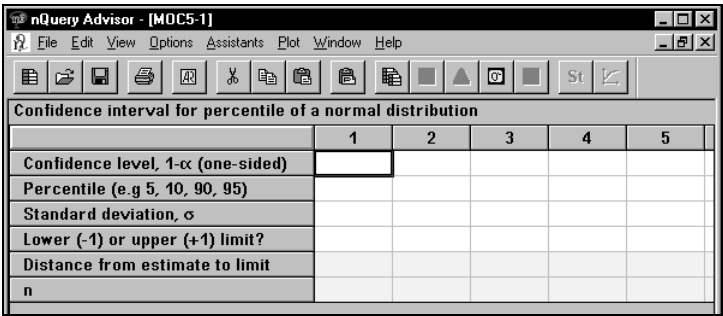
Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **One** group.

Under **Analysis method**, select **Confidence Interval**.

Select the sixth analysis type, Confidence interval for percentile of a normal distribution.

Click on **OK** to bring up the MOC5 sample size table.



	1	2	3	4	5
Confidence level, 1- α (one-sided)					
Percentile (e.g 5, 10, 90, 95)					
Standard deviation, σ					
Lower (-1) or upper (+1) limit?					
Distance from estimate to limit					
n					

To complete all three illustrated columns, enter **.95** in the **Confidence level** row of the first three columns of the sample size table.

Enter **90** in the **Percentile** row of the first three columns.

Enter **15** in the **Standard deviation** row of the first three columns.

To determine distances from the estimate to the limits, enter **1** in **Lower or upper limit** row of column 1 and **-1** in this row for column 2. Then enter a sample size of 100 for both column 1 and column 2.

We see that with a sample size of 100 and a standard deviation of 15, a 95% confidence interval for the 90th percentile of a normal distribution can be expected to extend about 3.7 units above and 3.1 units below the estimate.

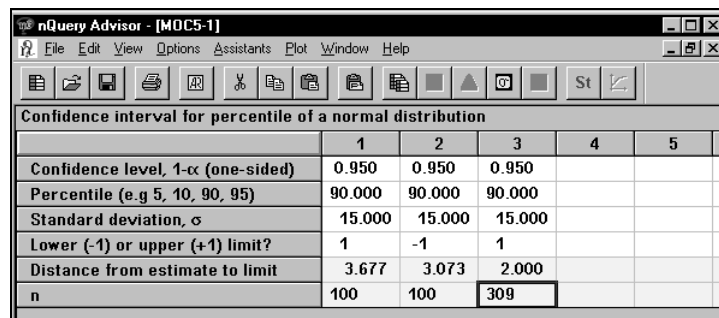
Suppose the investigator wants to estimate the 90th percentile to within no more than 2 units.

Enter **1** in **Lower or upper limit** row of column 3.

Enter **2** in the **Distance from estimate to limit** row of the third column.



Then nQuery calculates a required sample size of 309.



	1	2	3	4	5
Confidence level, 1- α (one-sided)	0.950	0.950	0.950		
Percentile (e.g. 5, 10, 90, 95)	90.000	90.000	90.000		
Standard deviation, σ	15.000	15.000	15.000		
Lower (-1) or upper (+1) limit?	1	-1	1		
Distance from estimate to limit	3.677	3.073	2.000		
n	100	100	309		

Using MOC5, the upper limit of the 95% confidence interval for the 90th percentile is $162.23 + 3.677$ or 165.9 and the lower limit is $162.23 - 3.073$ or 159.15. To assure that the 90th percentile is known to within ± 2 would require more than 300 subjects.

Example 4

Two group Satterthwaite t-test of equal means (unequal variances) (MTT0uv)

One of the assumptions of the ordinary two-group Student's t-test is that the underlying population variances (standard deviations) are equal. When the sample sizes are also equal and reasonably large, the effect of violation of this assumption on the probability of Type I error and on power is not large. However, when both the variances and the sample sizes are markedly unequal, the effects on the Type I error and on power can be large.


For example, when the ratio of variances is 10 to 1 (ratio of SDs is 3.16), and the ratio of sample sizes is also 10 to 1 (the group with the larger variance also has a larger sample), then the probability of a Type I error can be less than .001 when the nominal alpha level is .05 and the power will also be reduced. On the other hand, when the ratio of variances is 10 to 1 and the ratio of sample sizes is 1 to 10 (the group with the larger variance has the smaller sample size), then the probability of a Type I error can be as large as .38 when the nominal alpha level is .05 and the power is higher than it should be.

When the variances in the two groups are expected to differ markedly, power and sample size should be computed for a version of the t-test (Satterthwaite's t) which will take the expected ratio of variances into account; this will be especially important when sample sizes are also expected to differ. Alternatively, for many outcomes variables, a transformation might be expected to stabilize variances, and

therefore sample size and power computations can be based on use of the transformed data in the table for ordinary Student's t-test.

Suppose that preliminary data on a hormonal measurement suggests that the mean for the control group will be about 300 with an SD of 150 and that the mean for the intervention group will be about 1200 with an SD of 600. The investigator wants to know if it will be possible to keep the sample size in the control group small.

To bring up the sample size table for the Satterthwaite t test:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

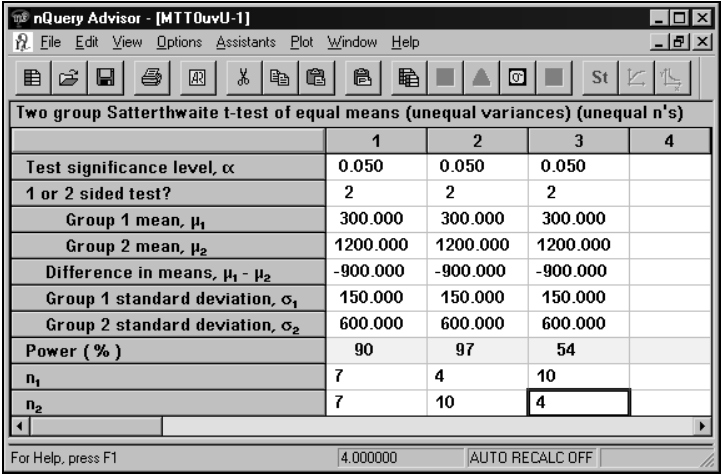
Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.

Under **Two-sample t-test**, select the second analysis type, **Satterthwaite's t test (unequal variances)**.

Check the **Unequal n's** box.

Click on **OK**.



The screenshot shows the nQuery Advisor software window titled "nQuery Advisor - [MTT0uvU-1]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons for file operations and analysis. The main window displays a table titled "Two group Satterthwaite t-test of equal means (unequal variances) (unequal n's)". The table has four columns labeled 1, 2, 3, and 4. The rows include parameters for the t-test, such as Test significance level, Group means, standard deviations, difference in means, Power, and sample sizes (n1, n2). The values for column 1 are 0.050, 2, 300.000, 1200.000, -900.000, 150.000, 600.000, 90, 7, and 7. The values for column 2 are 0.050, 2, 300.000, 1200.000, -900.000, 150.000, 600.000, 97, 4, and 10. The values for column 3 are 0.050, 2, 300.000, 1200.000, -900.000, 150.000, 600.000, 54, 10, and 4. The status bar at the bottom indicates "For Help, press F1", "4.000000", and "AUTO RECALC OFF".

	1	2	3	4
Test significance level, α	0.050	0.050	0.050	
1 or 2 sided test?	2	2	2	
Group 1 mean, μ_1	300.000	300.000	300.000	
Group 2 mean, μ_2	1200.000	1200.000	1200.000	
Difference in means, $\mu_1 - \mu_2$	-900.000	-900.000	-900.000	
Group 1 standard deviation, σ_1	150.000	150.000	150.000	
Group 2 standard deviation, σ_2	600.000	600.000	600.000	
Power (%)	90	97	54	
n_1	7	4	10	
n_2	7	10	4	

In column 1, the investigator has specified that 7 subjects will be assigned to each group and finds that the power will be about 90%. With this same total sample size, if the investigator assigns only 4 of the 14 subjects to Group 1 and 10 to Group 2,



the power will still be high. However, if the investigator were to assign 10 subjects to Group 1 and 4 to Group 2, the power would be very low.


For this example, the CV (coefficient of variation) is about 0.5 for both groups, this suggests that a log transform would stabilize the variances and that an ordinary t-test could be applied. The investigator could consider using table MTT0cv to make sample size and power computations, see Example 5. Or the investigator could actually transform the pilot data and use the transformed means and SDs in the table for Student's t-test, see tutorial in Chapter 2.

Example 5

Two group t-test for fold change assuming log-normal distribution (MTT0cv)

Suppose preliminary data on a hormonal measurement suggests that the mean for the control group will be about 300 with an SD of 150 and the mean for the intervention group will be about 1200 with an SD of 600. The investigator wants to know if it will be possible to keep the sample size in the control group small. The coefficient of variation (SD/mean) is about 0.5 in both groups, which suggests that a log transform would stabilize the variances so that an ordinary Student's t-test could be used on the log transformed data. The expected fold-change (ratio of means) is 4.

To bring up the correct sample size table:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.

Under **Two-sample t-test**, select the third analysis type, **Two group t-test for fold change assuming log-normal distribution**.

Check the **Unequal n's** box.

Click on **OK**.

nQuery Advisor - [MTT0cvU-1]

File Edit View Options Assistants Plot Window Help

Two group t-test for fold change assuming log-normal distribution (unequal n's)

	1	2	3	4
Test significance level, α				
1 or 2 sided test?				
Expected Fold-Change, FC				
Coefficient of variation, $CV = \sigma / \mu$				
Power (%)				
n_1				
n_2				

To calculate the Power, enter all values except Power in the following table.

nQuery Advisor - [MTT0cvU-1]

File Edit View Options Assistants Plot Window Help

Two group t-test for fold change assuming log-normal distribution (unequal n's)

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Expected Fold-Change, FC	4.000			
Coefficient of variation, $CV = \sigma / \mu$	0.500			
Power (%)	99			
n_1	7			
n_2	7			

When the calculation finishes, you will see a message box stating that the power has been rounded down to 99.

Power rounded down

The calculated value of Power was greater than

This is beyond the realistic range of some of the models and approximations used.

Therefore Power has been rounded down to

OK

Select the rows from Test Significance level through Coefficient of variation. Click on the Edit menu Fill right option to place those values in the remaining columns in the table.



Two group t-test for fold change assuming log-normal distribution (unequal n's)				
	1	2	3	4
Test significance level, α	0.050	0.050	0.050	0.050
1 or 2 sided test?	2	2	2	2
Expected Fold-Change, FC	4.000	4.000	4.000	4.000
Coefficient of variation, $CV = \sigma / \mu$	0.500	0.500	0.500	0.500
Power (%)	99			
n_1	7			
n_2	7			

Enter values of n for columns 2 and 3.

Two group t-test for fold change assuming log-normal distribution (unequal n's)				
	1	2	3	4
Test significance level, α	0.050	0.050	0.050	0.050
1 or 2 sided test?	2	2	2	2
Expected Fold-Change, FC	4.000	4.000	4.000	4.000
Coefficient of variation, $CV = \sigma / \mu$	0.500	0.500	0.500	0.500
Power (%)	99	99	99	
n_1	7	4	10	
n_2	7	10	4	

For this example, the expected power using a t-test on log transformed data is over 99% for all three cases. In general, if the data are truly log-normally distributed and analysis is done using the log scale, the power can be expected to be higher than it will be when the data are analyzed in the original scale and adjustments for unequal variances are made in the Satterthwaite t-test, see Example 4.

In the following example, we expect the intervention to produce only a doubling of the mean. This example shows us, that even when variances are equal and the ordinary Student's t-test will be used, the power is lower for the same total sample size when the n's are unequal. See Chapter 10 for further details.

Two group t-test for fold change assuming log-normal distribution (unequal n's)				
	1	2	3	4
Test significance level, α	0.050	0.050	0.050	0.050
1 or 2 sided test?	2	2	2	2
Expected Fold-Change, FC	2.000	2.000	2.000	2.000
Coefficient of variation, $CV = \sigma / \mu$	0.500	0.500	0.500	0.500
Power (%)	97	69	69	
n_1	15	5	10	
n_2	15	10	5	

Example 6

Two group t-test of equal fold change with fold change threshold (MTT0fct)

Planning and interpreting DNA microarray studies is complicated by the fact that many different genes are being evaluated in the same study and that the expense of the studies tends to keep sample sizes low. It is typically assumed that data will be analyzed in the log scale so that alternative hypotheses are expressed in terms of fold changes (ratio of largest to smallest mean) and variability information is expressed in terms of the CV (coefficient of variation, SD/mean).


Because of the multiplicity of testing, alpha levels (significance levels) are kept low and investigators may also wish to specify that no change smaller than a specified threshold is of interest. Therefore the planned detection rule is a combination of “statistical significance” and “clinical or biological significance”.

To plan studies not involving a fold-change threshold, you can use the table **Two group t-test for fold change assuming log-normal distribution** (MTT0cv), see Example 5.

For this example, we assume that a gene expression study has already been conducted and analyzed, and that results for each gene were compared between two groups (with 3 microarrays each) using a two-sided 1% t-test. Of the genes with significant differences, only those genes for which the observed fold-change is greater than or equal to 2 will be studied further. The investigator wants to know what the detection rates for genes with various fold-changes would be using these detection rules with this sample size assuming a CV of 0.25.



To bring up the correct sample size table:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

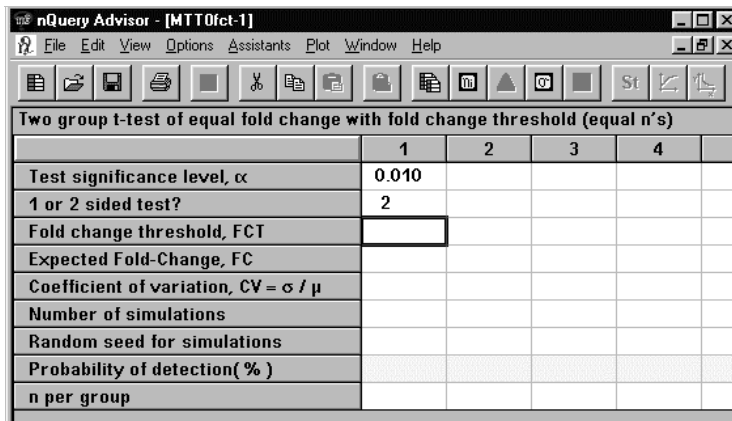
Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.

Under **Two-sample t-test**, select the fourth analysis type, **Two group t-test of equal fold change with fold change threshold**.

Click on **OK**.

The table will come up empty, but we show a table with 0.01 already filled in for the significance level and 2 for a two-sided test.



	1	2	3	4
Test significance level, α	0.010			
1 or 2 sided test?	2			
Fold change threshold, FCT				
Expected Fold-Change, FC				
Coefficient of variation, $CV = \sigma / \mu$				
Number of simulations				
Random seed for simulations				
Probability of detection(%)				
n per group				

Then enter the fold change threshold of 2, the CV (coefficient of variation) of 0.25 and the sample size in each group of 3.

In this first example, we are interested in the detection rate for genes whose expected true fold change is 2.

Two group t-test of equal fold change with fold change threshold (equal n's)					
	1	2	3	4	
Test significance level, α	0.010				
1 or 2 sided test?	2				
Fold change threshold, FCT	2.000				
Expected Fold-Change, FC	2.000				
Coefficient of variation, $CV = \sigma / \mu$	0.250				
Number of simulations					
Random seed for simulations					
Probability of detection(%)					
n per group	3				

Then you must specify the desired number of simulations and a random seed. The random seed can be any integer greater than or equal to 0.

The precision of the estimate of the probability of detection depends on the number of samples in the simulation. In the following table, we show the width of the 95% confidence interval for the estimated probability.

Number of samples in simulation	Estimate of the probability of detection
1000	within $\pm 2\%$ for probabilities near 90%,
1600	within $\pm 2\%$ for probabilities near 80%
10000	Within $\pm 1\%$ at the widest

For this example, we specify 10000 simulations and a random seed of 24. When everything in the column except the **Probability of detection** is filled in, nQuery Advisor will make an estimate of the time required to complete the requested number of simulations on your computer. (This estimate is based on making a small number of preliminary simulations.)

As soon as you enter the last value, the simulations will begin. You will see a box like the following.



Progress of simulations

██████

Simulations completed: 1799 / 10000

Time elapsed: 7.1

Estimated power: 23.07

95% confidence interval for power, normal approximation

Lower limit: 21.12

Upper limit: 25.03

Cancel Minimize

At this point, you can choose to cancel the simulation, run nQuery Advisor minimized during computation of the simulations, or take a brief break while you wait.

You can follow or cancel the progress of the simulation in the **Progress of simulations** dialog box. Unless you want to cancel the simulation or minimize the dialog box, there are no necessary steps for you to take. Simply watch or ignore the simulations until they have finished and the Probability of detection appears in the table. (Simulations are reasonably fast; this example took about 40 seconds on a 600 MHz computer.)

For genes with an expected fold-change of 2, only 24% are likely to be detected as statistically significant at the 1% level as well as having an observed fold change greater than 2.

Note: When the fold change threshold is set equal to the expected true fold change the probability of detection will never be greater than 50% since no more than half of experiments are expected to have a mean difference greater than the true mean difference.

Two group t-test of equal fold change with fold change threshold (equal n's)						
	1	2	3	4	5	6
Test significance level, α	0.010					
1 or 2 sided test?	2					
Fold change threshold, FCT	2.000					
Expected Fold-Change, FC	2.000					
Coefficient of variation, $CV = \sigma / \mu$	0.250					
Number of simulations	10000					
Random seed for simulations	22					
Probability of detection(%)	24					
n per group	3					

The investigator also wants to know the detection rates for expected fold-change values of 2.5, 3, 4, 5, and 6. To replicate to other columns values which stay the same in each example, select the rows from **Test significance level** through **Fold change threshold**. Then click on the **Edit** menu **Fill Right** option. Select **Coefficient of variation** and **Number of simulations** and choose **Fill Right**. Select the **n per group** row and choose **Fill Right** again.

Enter a new value for **Random seed for simulations** for each column.

Your sample size table will look like this:

Two group t-test of equal fold change with fold change threshold (equal n's)						
	1	2	3	4	5	6
Test significance level, α	0.010	0.010	0.010	0.010	0.010	0.010
1 or 2 sided test?	2	2	2	2	2	2
Fold change threshold, FCT	2.000	2.000	2.000	2.000	2.000	2.000
Expected Fold-Change, FC	2.000					
Coefficient of variation, $CV = \sigma / \mu$	0.250	0.250	0.250	0.250	0.250	0.250
Number of simulations	10000	10000	10000	10000	10000	10000
Random seed for simulations	22	23	24	25	26	27
Probability of detection(%)	24					
n per group	3	3	3	3	3	3

Enter the **Expected Fold-Change** in each column. When the simulations for the last column are complete, you will see a message box:

Power rounded down

The calculated value of Power was greater than

This is beyond the realistic range of some of the models and approximations used.

Therefore Power has been rounded down to



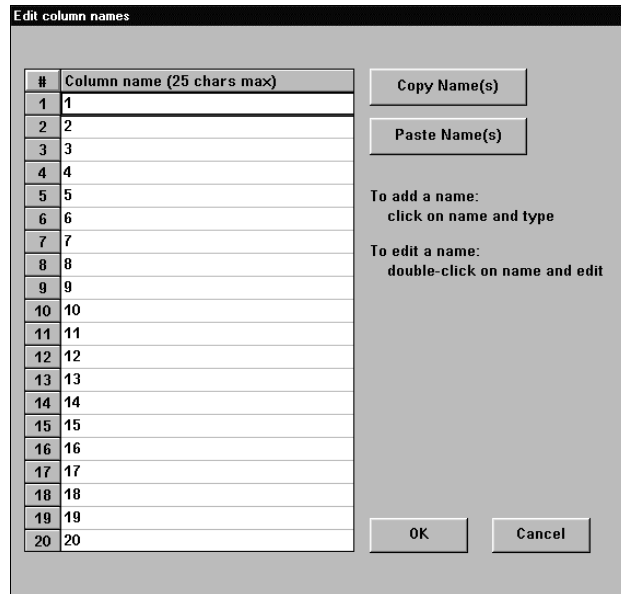
Click **OK** to complete the sample size table.

To label the columns using the Edit Column Names option:

Place the cursor anywhere within the sample size table.

Select the **Edit** menu **Edit Column Names** option or the right-click menu **Edit Column Names** option.

The **Edit Column Name** dialog box will appear. This box lists the column names that you can change in your sample size table. Column names are restricted to a maximum of 25 characters each; the names will not wrap.



The dialog box titled "Edit column names" contains a table with 20 rows and 2 columns. The first column is labeled "#" and the second is labeled "Column name (25 chars max)". The rows are numbered 1 through 20. To the right of the table are two buttons: "Copy Name(s)" and "Paste Name(s)". Below these buttons are two instructions: "To add a name: click on name and type" and "To edit a name: double-click on name and edit". At the bottom of the dialog are "OK" and "Cancel" buttons.

#	Column name (25 chars max)
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
11	11
12	12
13	13
14	14
15	15
16	16
17	17
18	18
19	19
20	20

Click on the first column name and type the new column name, **FC = 2**. Click on the **Copy Name(s)** button.

Click on the second column name and click on the **Paste Name(s)** button to paste the name. Paste the name into the remaining four column name fields.

For the second column name, double click on the second column name and edit it to say **FC = 2.5**.

Edit the remaining column names to agree with the following table.

Two group t-test of equal fold change with fold change threshold (equal n's)						
	FC = 2	FC = 2.5	FC = 3	FC = 4	FC = 5	FC = 6
Test significance level, α	0.010	0.010	0.010	0.010	0.010	0.010
1 or 2 sided test?	2	2	2	2	2	2
Fold change threshold, FCT	2.000	2.000	2.000	2.000	2.000	2.000
Expected Fold-Change, FC	2.000	2.500	3.000	4.000	5.000	6.000
Coefficient of variation, $CV = \sigma / \mu$	0.250	0.250	0.250	0.250	0.250	0.250
Number of simulations	10000	10000	10000	10000	10000	10000
Random seed for simulations	22	23	24	25	26	27
Probability of detection(%)	24	54	72	91	96	99
n per group	3	3	3	3	3	3

The researcher can conclude that for studies of this size, the selection rule in this example would have found more than 90% of the genes with a true fold-change of 4 or more. The rule would have found only 24% of genes with a true fold-change of 2.

To display this information, you can choose to plot it.

To bring up the plot:

Highlight the first column in the table and click on the Plot button,



In the **Specify Plot** screen, the **Y-axis** is set to Probability of detection (%). Under the **X-axis** choices, select **Expected Fold-Change, FC**, and specify the range **2** to **6**.

Specify plot

Y-axis choices:
Y:
Probability of detection(%)

Probability of detection(%)

X-axis choices:

Test significance level, α
Fold change threshold, FCT
Expected Fold-Change, FC
Coefficient of variation, $CV = \sigma / \mu$
n per group

X:
Expected Fold-Change, FC

Plot from
2
To
6

OK
Cancel

Click on **OK**.

Plots may take some time, as they are based on simulations for seven points. You will see the time estimate and progress of simulations boxes for each point.



Progress of simulations

Simulations completed: 3105 / 10000

Time elapsed: 10.7

Estimated power: 24.83

95% confidence interval for power, normal approximation

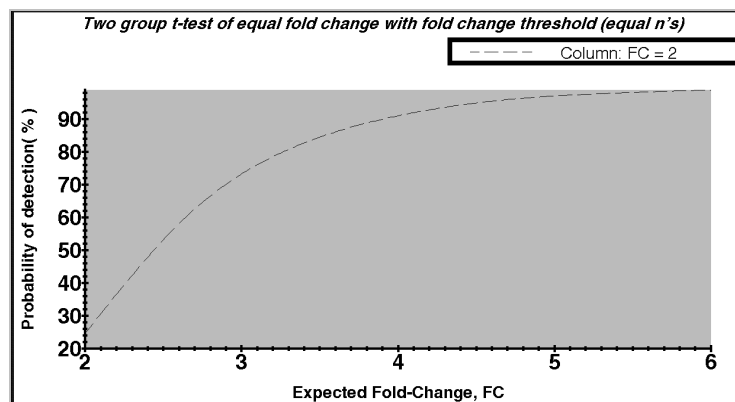
Lower limit: 23.31

Upper limit: 26.35

Cancel Minimize

The simulations may take a minute or two to complete.

Your plot will then appear as follows:



If you double-click on the plot legend, you can edit the text in the legend. See Chapter 6 for details.

To change the look of the line:

Double click on the line to bring up the **Plot parameters** dialog box.

Plot Parameters

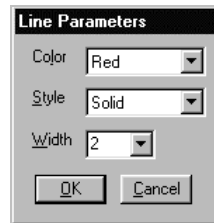
Type: Line

LINE ATTRIBUTES...

☐ Fill Area ☒ Spline

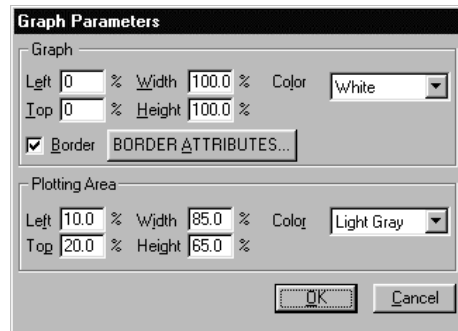
OK Cancel Data..

Click on the **Line Attributes** button to bring up the **Line Parameters** dialog box. Change the **Style** to **Solid** and change the **Width** to **2**.



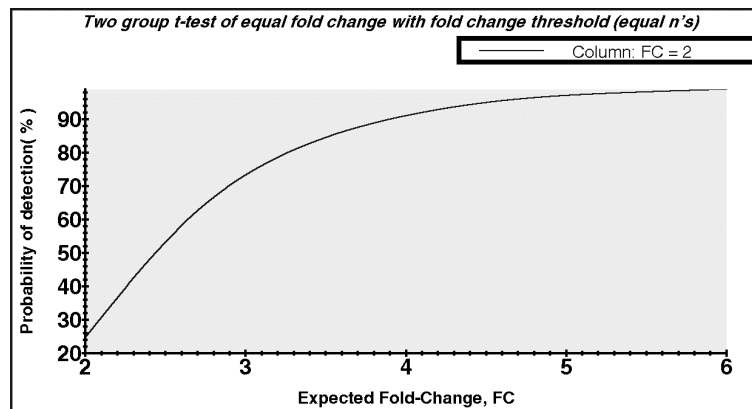
Click **OK** in each dialog box to display the changed plot.

To change from the gray in the plot area background, select the **Graphs** menu **Parameters** option to get the **Graph Parameters** dialog box.



If you want a lighter gray when the plot is displayed in grayscale, choose **Yellow** as your **Plotting Area Color**.

Click **OK** to complete the change.






9. Determining a Value for Standard Deviation

When you want to estimate the required sample size for tests or confidence intervals involving means (or regression slopes), you must provide an estimate of the within-group standard deviation (or standard deviation of residuals). You can base this standard deviation on a pilot study or use reported values of the standard deviation from previous studies with the same outcome measure. Typically, it is not necessary to have a standard deviation from a group treated with the planned intervention.

If you can find a direct report of the standard deviation, you can use that value in the appropriate sample size table. When you cannot find a reported standard deviation, you may have other information which you can use to determine a reasonable value for the standard deviation. You can use nQuery Advisor options in the Assistants menu to estimate the standard deviation with information in a variety of formats.

The Assistants menu includes three useful options for estimation of a standard deviation:

- **Data Entry (SD calculator)** when individual subject values are available (or click on , the SD button and choose **For Specified x values** from the Estimate Standard Deviation dialog box)
- **Estimate SD** to convert information from other formats; these options can also be accessed by clicking on , the SD button and choosing one of the ten options from the Estimate Standard Deviation dialog box)
- **Specify Covariance Matrix** to specify the covariance matrix for repeated measure designs for use with tables MTT3, Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction), and MOT4, Univariate one-way repeated measures analysis of variance (Greenhouse-Geisser approximation.) This option can also be accessed by clicking on the toolbar button marked , the Specify covariance matrix icon.


Data Entry (SD calculator)

If you have measurements on several individuals from a pilot study or from a paper listing individual data points, use the **Assistants** menu **Data Entry** option. The Data Entry option on the Assistants menu allows you to enter a small data set to compute mean and standard deviation. This option is also useful in the context of estimating SDx for a predictor variable with equally spaced values, see Example 8 later in this chapter, and Example 5 in Chapter 18 *Regression Tables*.

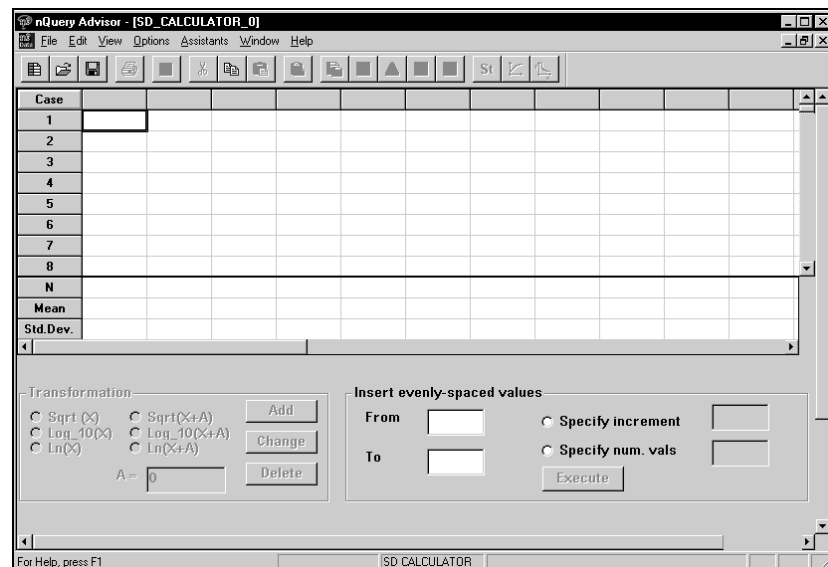
To use the Data Entry option:

Start with your chosen sample size table as the active window.

Select the **Assistants** menu **Data Entry** option.

Or click on , the SD button and choose For Specified x values from the Estimate Standard Deviation dialog box.

The Data Entry spreadsheet will appear with the cursor in the data cell for the first row and the first column.





You must enter data column-wise. To enter data in one column, type the first data point and press the <Enter> key or the down arrow on your keyboard. The cursor will move to the second row of the first column. You can use the mouse to move the cursor to the first row of the second column to enter a new set of data.

We will enter six hematocrit values from elderly women with hip fracture: 32, 29, 31, 30, 33, 38.

To enter one column of data:

Type **32** in the **Case 1** cell in the first column and press <Enter>. The table will display your entry, as well as the **N** and **Mean** for that column. As you enter the value for each case, nQuery Advisor will update the **N**, **Mean**, and **Std. Dev.** values.

The screenshot shows the nQuery Advisor window with the following data:

Case	X0										
1	32.00										
2											
3											
4											
5											
6											
7											
8											
N	1.00										
Mean	32.00										
Std.Dev.											

Enter the remaining numbers in the first column, pressing <Enter> after each value. The table will display **N**, **Mean**, and **Standard Deviation** for the column.


The screenshot shows the nQuery Advisor window with the following data:

Case	X0										
1	32.00										
2	29.00										
3	31.00										
4	30.00										
5	33.00										
6	38.00										
7											
8											
N	6.00										
Mean	32.17										
Std.Dev.	3.19										

Now that nQuery Advisor has calculated the standard deviation for this data set, you can use this standard deviation as an estimated standard deviation for the planned study.

To move the standard deviation from the Data Entry table to the sample size table:

Click on the **Std. Dev** cell in the first column to select that cell for copying.

Select the **Edit** menu **Copy** option or click on , the Copy button, or **<Ctrl><C>** to copy the cell contents.

You can use the **Window** menu list of open tables to select the sample size table as the current table.

Click on the cell in the standard deviation row to which you want to paste the standard deviation. Select one of the **Edit** menu **Paste** options or one of the Paste buttons, or **<Ctrl><V>** to paste the standard deviation value into the sample size table.

When a column in the Data Entry (SD calculator) window contains data, you can easily find the mean and standard deviation of a transform of that data.

Transformation in Data Entry

The Transformation button in the Data Entry window allows you to transform your data using square root, \log_{10} or natural log transformations. Such transforms are often helpful for improving homogeneity of variances. In addition, you can customize each transformation with an added constant.

To use the transformation function:

Click on the title of the column of interest or on any value in the column to select the column.

Click on a Transformation radio button to select the desired transformation.

If you have selected a transform including an added constant, enter the value for that constant in the box marked A=.

The Add button will become active.

Click on the **Add Transformation** button.



nQuery Advisor - [SD_CALCULATOR_0]

File Edit View Options Assistants Window Help

Case	X0	Log X0																		
1	32.00	1.51																		
2	29.00	1.46																		
3	31.00	1.49																		
4	30.00	1.48																		
5	33.00	1.52																		
6	38.00	1.58																		
7																				
8																				
N	6.00	6.00																		
Mean	32.17	1.51																		
Std.Dev.	3.19	0.04																		

Transformation

☐ Sqrt (X) ☐ Sqrt(X+A) ☐ Log_10(X) ☐ Log_10(X+A) ☐ Ln(X) ☐ Ln(X+A)

A = 0

Insert evenly-spaced values

From To

☐ Specify increment

☐ Specify num. vals

Execute

For Help, press F1

SD_CALCULATOR

The transformed column of data will appear in blue for square root or green for a log transform in the first empty column to the right. The column name will reflect the transformation and the name of the original column. The column name will not include any information about an added constant.

To delete a transformation:

Click on any cell in the column of transformed data. The Delete button will become active.

Click on the **Delete** button.

The column containing the transformed data will be cleared.

To change a transformation:

Click on any cell in the column of transformed data and choose a different transformation. The Change button will become active.


Click on the **Change** button.

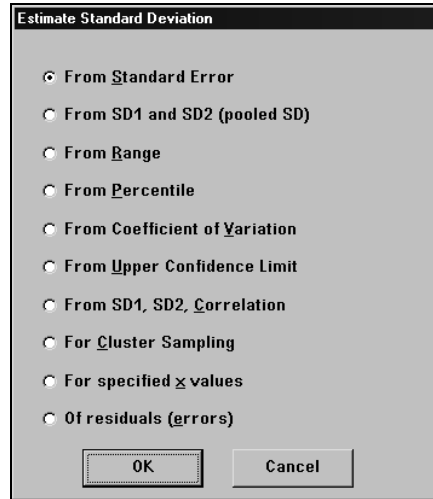
The column will display the new transformation.

Using One of the Estimate SD Options

The nQuery Advisor program provides methods for converting several different kinds of information into an estimate of the standard deviation.

To estimate standard deviation:

Select the **Assistants** menu **Estimate SD** option, or click on  the SD button. The Estimate Standard Deviation dialog box will appear.



Click on the radio button for the information you want to use to compute the standard deviation.

1. From Standard Error

To estimate standard deviation from standard error:

Click on the **From Standard Error** radio button.



Estimate Standard Deviation

☒ From Standard Error

☐ From SD1 and SD2 (pooled SD)

☐ From Range

☐ From Percentile

☐ From Coefficient of Variation

☐ From Upper Confidence Limit

☐ From SD1, SD2, Correlation

☐ For Cluster Sampling

☐ For specified x values

☐ Of residuals (errors)

OK Cancel

Click **OK** to bring up the standard error table.

Estimating standard deviation from standard error						
	1	2	3	4	5	
n						
Standard error (s.e.)						
Estimate of standard deviation, σ						

The Tutorial in Chapter 2 discussed a study to evaluate a new drug to raise hematocrit; one group of 24 patients showed a pre-donation hematocrit of 35.2% with a standard deviation of 4.4%. If that report had provided only the standard error of the mean, .898, we could have converted that standard error to the standard deviation. The formula is:

$$\text{S.D.} = \sqrt{n} \text{ S.E.}$$

To calculate the estimated standard deviation for this study:

Enter **24** in the **n** row and press <Enter>.

Enter **.898** in the **Standard error** row and press <Enter>. The nQuery Advisor program will calculate the estimated standard deviation.

Estimating standard deviation from standard error					
	1	2	3	4	
n	24				
Standard error (s.e.)	0.898				
Estimate of standard deviation, σ	4.399				

Click on the cell containing the estimated standard deviation.

Select the **Edit** menu **Copy** option or the **Copy** button.

Use the **Windows** menu to switch to the sample size table.

Click on a cell in the standard deviation row.

Select the **Edit** menu **Paste Unformatted** option or the **Paste Unformatted** button. The estimated standard deviation will appear in your sample size table.

2. From SD1 and SD2 (pooled SD)

To estimate the common standard deviation by pooling estimates of standard deviations from two independent groups, s_1 and s_2 :

Click on the **From SD1 and SD2 (pooled SD)** radio button.

Estimate Standard Deviation

☐ From Standard Error
☒ From SD1 and SD2 (pooled SD)
☐ From Range
☐ From Percentile
☐ From Coefficient of Variation
☐ From Upper Confidence Limit
☐ From SD1, SD2, Correlation
☐ For Cluster Sampling
☐ For specified x values
☐ Of residuals (errors)

OK Cancel

Click **OK** to bring up the pooled standard deviation table.



Estimating common standard deviation by pooling s_1 and s_2					
	1	2	3	4	
n_1					
n_2					
Standard deviation of Group 1, s_1					
Standard deviation of Group 2, s_2					
Common standard deviation, σ					

You can use this table if you have estimated standard deviations from two independent groups and wish to pool them to provide an estimate of the common standard deviation. The formula is:

$$\sigma = \sqrt{\frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2 - 2}}$$

In the study of anemia in elderly women after hip fracture covered in the Tutorial, we had estimates of the standard deviation in the two groups from pilot studies. In a small pilot study of six elderly females after hip fracture, the standard deviation of hematocrit level was 3.2%, and in a treated group of 10 females, the standard deviation was 5%.

To calculate the pooled standard deviation for this study:

Enter **6** in the n_1 row and press <Enter>.

Enter **10** in the n_2 row and press <Enter>.

Enter **3.2** in the **Standard deviation of Group 1, s_1** row and press <Enter>.

Enter **5** in the **Standard deviation of Group 2, s_2** row and press <Enter>. The nQuery Advisor program will calculate the common standard deviation.

Estimating common standard deviation by pooling s_1 and s_2					
	1	2	3	4	
n_1	6				
n_2	10				
Standard deviation of Group 1, s_1	3.200				
Standard deviation of Group 2, s_2	5.000				
Common standard deviation, σ	4.442				

Click on the cell containing the common standard deviation.

Select the **Edit** menu **Copy** option or the **Copy** button.

Use the **Windows** menu to switch to the sample size table.

Click on a cell in the standard deviation row.

Select the **Edit** menu **Paste Unformatted** option or the **Paste Unformatted** button. The estimated common standard deviation will appear in your sample size table.

3. From Range

To estimate standard deviation from range:

Click on the **From Range** radio button.

Estimate Standard Deviation

☐ From Standard Error

☐ From SD1 and SD2 (pooled SD)

☒ From Range

☐ From Percentile

☐ From Coefficient of Variation

☐ From Upper Confidence Limit

☐ From SD1, SD2, Correlation

☐ For Cluster Sampling

☐ For specified x values

☐ Of residuals (errors)

OK

Cancel

Click **OK** to bring up the range table.

Estimating standard deviation from range (assuming normality)						
	1	2	3	4	5	
n						
Minimum observed value						
Maximum observed value						
Range						
Estimate of standard deviation, σ						

As a demonstration of the use of the range in estimating the standard deviation, we will use the results of a pilot study. That study measured impaired glucose tolerance using the glucose infusion rate in mg/kg/min. The study reported a range of 1.8 to 9.1 in 19 individuals, but the standard deviation was not reported. When you enter the values, you can enter the minimum and maximum and let nQuery Advisor compute the range, or you can enter the range directly.

Note that this procedure assumes that the data have a normal (Gaussian) distribution.



To calculate the estimated standard deviation for this study:

Enter **19** in the **n** row and press <Enter>.

Enter **1.8** in the **Minimum observed value** row and press <Enter>.

Enter **9.1** in the **Maximum observed value** row and press <Enter>. The nQuery Advisor program will calculate the range and the estimated standard deviation.

Estimating standard deviation from range (assuming normality)						
n	19					
Minimum observed value	1.800					
Maximum observed value	9.100					
Range	7.300					
Estimate of standard deviation, σ	2.00					

Click on the cell containing the estimated standard deviation.

Select the **Edit** menu **Copy** option or the **Copy** button.

Use the **Windows** menu to switch to the sample size table.

Click on a cell in the standard deviation row.

Select the **Edit** menu **Paste Unformatted** option or the **Paste Unformatted** button. The estimated standard deviation will appear in your sample size table.

4. From Percentile

To estimate standard deviation from percentile:

Click on the **From Percentile** radio button.

Estimate Standard Deviation

☐ From Standard Error
 ☐ From SD1 and SD2 (pooled SD)
 ☐ From Range
 ☒ From Percentile
 ☐ From Coefficient of Variation
 ☐ From Upper Confidence Limit
 ☐ From SD1, SD2, Correlation
 ☐ For Cluster Sampling
 ☐ For specified \bar{x} values
 ☐ Of residuals (errors)

OK

Cancel

Click on **OK** to bring up the percentile table.

Estimating standard deviation from sample percentiles					
Percentile (e.g., 5%, 10%)					
Lower observed value					
Upper observed value					
Difference of upper and lower values					
Estimate of standard deviation, σ					

In some cases, there may be no direct information available about the standard deviation for an outcome measure, but for variables such as SAT scores or for medical laboratory measurements percentile values may be available. To provide an example, we consider data for cholesterol from a large screening trial. The 10th percentile for cholesterol was reported as 167 and the 90th percentile as 263. We can use these values to determine an estimate of standard deviation provided the data come from a normal (Gaussian) distribution. When we have more than one set of percentiles available, we expect the estimated standard deviation to be the same whichever set is used when the normality assumption is satisfied.

To calculate the estimated standard deviation for this study:

Enter **10** in the **Percentile** row and press <Enter>.

Enter **167**, the 10th percentile, in the **Lower observed value row** and press <Enter>.

Enter **263**, the 90th percentile (or upper 10th percentile), in the **Upper observed value row** and press <Enter>.

The nQuery Advisor program will calculate the difference of upper and lower values and the estimated standard deviation.



Estimating standard deviation from sample percentiles					
Percentile (e.g., 5%, 10%)	10.00				
Lower observed value	167.000				
Upper observed value	263.000				
Difference of upper and lower values	96.000				
Estimate of standard deviation, σ	37.45				

Click on the cell containing the estimated standard deviation.

Select the **Edit** menu **Copy** option or the **Copy** button.

Use the **Windows** menu to switch to the sample size table.

Click on a cell in the standard deviation row.

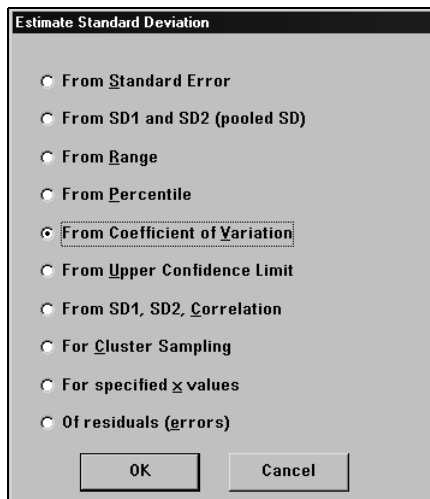
Select the **Edit** menu **Paste Unformatted** option or the **Paste Unformatted** button. The estimated standard deviation will appear in your sample size table.

5. From Coefficient of Variation

To estimate standard deviation from coefficient of variation:

Click on the **From Coefficient of Variation** radio button.

Click on **OK** to bring up the coefficient of variation table.



The dialog box titled "Estimate Standard Deviation" contains a list of radio buttons for different estimation methods. The "From Coefficient of Variation" option is selected and highlighted with a dashed border. At the bottom are "OK" and "Cancel" buttons.

- ☐ From Standard Error
- ☐ From SD1 and SD2 (pooled SD)
- ☐ From Range
- ☐ From Percentile
- ☒ From Coefficient of Variation
- ☐ From Upper Confidence Limit
- ☐ From SD1, SD2, Correlation
- ☐ For Cluster Sampling
- ☐ For specified \bar{x} values
- ☐ Of residuals (errors)

OK Cancel

Click on **OK** to bring up the coefficient of variation table.

Estimating standard deviation from coefficient of variation (assuming log-normality)					
Coefficient of variation, $CV = s / \bar{x}$					
Estimated σ in log scale					
Observed mean, \bar{x}					
Estimated mean, μ , in log scale					

To demonstrate using the coefficient of variation in estimating the standard deviation, we will use information on a diagnostic test as reported in an abstract. Eighteen hypertensive Mexican/American males had a mean of 3.3 and a reported standard deviation of 1.3. The 75 non-hypertensive males had a mean of 5.2 and standard deviation of 2.5.

Note that many biological measurements show a pattern in which groups with a larger mean response also have a larger standard deviation. That is, larger measurements are more variable. When the standard deviation is proportional to the mean across groups, we also typically see measurements in each group skewed toward larger values and the log transformed measurements appear to have a nearly normal distribution within groups. Also, the standard deviations of the transformed values are nearly constant across groups.

Standard tests and confidence intervals for group means are based on the assumption that the standard deviation is constant. Thus, we must make sample size computations on the transformed data.

When the original data from a previous or pilot study are available, you can use Data Entry to enter the individual values. That option will then compute mean and standard deviation for log transformed values.

If the original data are not available, but means and standard deviations are reported, you can compute the coefficient of variation, SD/mean . You can then use that coefficient of variation to estimate the standard deviation for the log transformed scale. (Sometimes you may have a direct estimate of the coefficient of variation.)

In this example, the coefficient of variation is .394 for hypertensives and .48 for non-hypertensives. If we used an in-between value such as .45, we could get an estimate of the standard deviation. We could also estimate the possible value for each mean in the log scale. We can then copy those values to the appropriate sample size table to be used in computing sample size.

To calculate the estimated standard deviation from coefficient of variation (assuming log-normality):

Enter **.45** in the first column of the **Coefficient of variation** row and press <Enter>. The program will calculate the **Estimated σ in log scale**.



Enter **3.30** in the first column of the **Observed mean** row and press <Enter>. The program will calculate the **Estimated mean, μ , in log scale** for that column.

Enter **.45** in the second column of the **Coefficient of variation** row and press <Enter>. The program will calculate the **Estimated σ in log scale**.

Enter **5.20** in the second column of the **Observed mean** row and press <Enter>. The program will calculate the **Estimated mean, μ , in log scale** for that column.

Estimating standard deviation from coefficient of variation (assuming log-normality)					
Coefficient of variation, $CV = s / \bar{x}$	0.45	0.45			
Estimated σ in log scale	0.4294	0.4294			
Observed mean, \bar{x}	3.30	5.20			
Estimated mean, μ , in log scale	1.1017	1.5565			

Use the **Edit** menu **Copy** option and the Paste **Unformatted** option to copy the estimated standard deviation to your sample size table. See details in sections 1 through 3 of this chapter.

6. From Upper Confidence Limit

When we estimate the standard deviation based on only a few cases, the standard deviation may not be very precise. This is a special concern in sample size estimation, because the standard deviation used might be too small, leading to a sample size that is too small for the study.

If you select an upper confidence limit, you have a way to take the uncertainty in the estimation of the standard deviation into account and determine a conservative estimate.

Note: For other approaches to taking uncertainty in estimates of the standard deviation into account in computing power or sample size, see Taylor, D. J. and Muller, K. E. (1995) Computing confidence bounds for power and sample size of the general linear univariate model. *American Statistician*, 49, 43-47. Taylor, D. J. and Muller, K. E. (1996) Bias in linear model power and sample size calculations due to estimating noncentrality. *Communications in Statistics: Theory and Methods*, 25, 1595-1610. Muller, K. E., and Pasour, V. B. (1997) Bias in linear model power and sample size due to estimating variance. *Communications in Statistics: Theory and Methods*, 26, 839-851.

To estimate the upper confidence limit for a standard deviation estimated from a small sample:

Click on the **From Upper Confidence Limit** radio button.

The dialog box titled "Estimate Standard Deviation" contains the following options:

- ☐ From Standard Error
- ☐ From SD1 and SD2 (pooled SD)
- ☐ From Range
- ☐ From Percentile
- ☐ From Coefficient of Variation
- ☒ From Upper Confidence Limit
- ☐ From SD1, SD2, Correlation
- ☐ For Cluster Sampling
- ☐ For specified \bar{x} values
- ☐ Of residuals (errors)

Buttons: OK, Cancel

Click on **OK** to bring up the Estimating upper limit for standard deviation table.

Estimating upper limit for standard deviation from confidence interval					
n					
Observed standard deviation, s					
Confidence level, 1- α					
Upper limit for σ					

To demonstrate the estimation of the standard deviation from a confidence interval, refer back to the data entry example using pilot data on hematocrit values in elderly women with hip fractures. The standard deviation of those six values was 3.19. For a conservative estimate of the population standard deviation, you might want to use the upper 80% confidence limit.

This procedure assumes that the data have a normal (Gaussian) distribution.

To calculate the estimated standard deviation from confidence interval:

Enter 6 in the n row and press <Enter>.

Enter 3.19 in the Observed standard deviation row and press <Enter>.

Enter .8 in the Confidence level row and press <Enter>. the nQuery Advisor program will calculate the upper limit for σ .



Estimating upper limit for standard deviation from confidence interval					
n	6				
Observed standard deviation, s	3.190				
Confidence level, 1- α	0.800				
Upper limit for σ	4.661				

Use the **Edit** menu **Copy** option and the Paste **Unformatted** option to copy the estimated standard deviation to your sample size table. See details in sections 1 through 3 of the Using One of the Estimate SD Options section of this chapter.

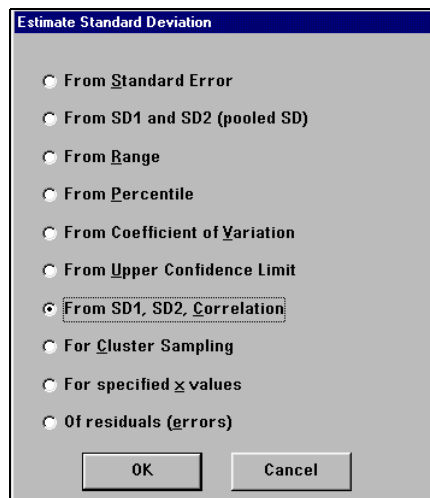
7. From SD1, SD2, Correlation

Frequently, the outcome measure is a change from pre-treatment to post-treatment. Alternatively, for studies in which each subject is tested under two conditions, the outcome measure is the difference in response between the two conditions. To plan the necessary sample size for such studies, we need the standard deviation of differences between the two measures.

Unfortunately, many such studies reported in the literature provide means and standard deviations for each condition, but do not report the standard deviation of differences. In such cases, we can make an estimate of the standard deviation of differences using the standard deviation for each condition with an estimate of the correlation coefficient.

To estimate standard deviation from SD1, SD2, and Correlation:

Click on the **From SD1, SD2, Correlation** radio button.



The dialog box titled "Estimate Standard Deviation" contains a list of radio buttons for selecting the method to estimate standard deviation. The options are: From Standard Error, From SD1 and SD2 (pooled SD), From Range, From Percentile, From Coefficient of Variation, From Upper Confidence Limit, From SD1, SD2, Correlation (which is selected), For Cluster Sampling, For specified x values, and Of residuals (errors). At the bottom are "OK" and "Cancel" buttons.

Click on **OK** to bring up the Estimating Standard Deviation table.

Calculating standard deviation of differences from SD1, SD2, and correlation				
First condition standard deviation, σ_1				
Second condition standard deviation, σ_2				
Correlation coefficient, ρ				
Standard deviation of differences, σ_d				

For this example, consider a study of triglyceride level with men tested under a regular diet and a low fat diet. The mean and standard deviation were 106 and 38.5 under the low fat diet and 79 and 24.5 under the high fat diet.

The planned study will use a paired t-test to test whether the effect of dietary fat on triglyceride level is significant. No estimate of the correlation between triglyceride levels under the two diets was provided in the abstract, but a study carried out with identical twins reported correlations between members of a twin pair in three twin groups as: .41, .48, .68. Time-to-time correlations within an individual are probably higher than those found in the twin study. However, since larger values of ρ give smaller values for the standard deviation of differences, the investigator decided to be somewhat conservative and use $\rho=.6$.

To calculate the estimated standard deviation from SD1, SD2, and correlation for this study:

In the first column of the σ_1 row, enter **38.5** and press <Enter>.

In the first column of the σ_2 row, enter **24.5** and press <Enter>.

In the first column of the ρ row, enter **.6** and press <Enter>. The program will calculate the estimated σ_d , the estimated standard deviation of the differences.

Calculating standard deviation of differences from SD1, SD2, and correlation				
	1	2	3	4
First condition standard deviation, σ_1	38.500			
Second condition standard deviation, σ_2	24.500			
Correlation coefficient, ρ	0.600			
Standard deviation of differences, σ_d	30.832			

Use the **Edit** menu **Copy** option and the Paste **Unformatted** option to copy the estimated standard deviation to your sample size table. See details in sections 1 through 3 of this chapter.

Standard deviation of differences ANOVA Mean Squared Error

For pre and post measurements, x_i and y_i , the differences are $d_i = y_i - x_i$. The standard deviation of the differences is the standard deviation of the d_i ; $SD(d_i)$ is the square root of the variance of the d_i .



$\text{Var}(d_i) = \text{Var}(x_i) + \text{Var}(y_i) - 2r \text{SD}(x_i) \text{SD}(y_i)$ where r is the correlation coefficient.

To test $H_0: \mu_x = \mu_y$ using a paired t test, the standard deviation of the differences must be computed. When H_0 is tested using a Repeated Measures ANOVA (or a crossover ANOVA), the within-group error mean square will be equal to $\text{Var}(d_i)/2$. If an estimate of this mean square is available, then use $\sqrt{2}\sqrt{MSE}$ as an estimate of the standard deviation of differences.

8. For Cluster Sampling

Cluster randomization, or randomization of intact groups, is often used in the design of community intervention studies. The cluster constitutes the unit of randomization; it may be a household, classroom, school, clinic, worksite, city, or other natural unit. Cluster randomization is often much simpler logistically than other methods, but it is less efficient from a statistical point of view. That is, when using cluster randomization, more individuals must be studied to obtain the same power.

Standard sample size formulas and nQuery Advisor tables can be used to compute necessary sample size, power, or interval widths for designs in which the unit being randomized is a cluster. However, a value for the cluster standard deviation must be used in place of the ordinary within group standard deviation.

Our first example is taken from a paper by David M. Murray and Peter J. Hannan (1990) Planning for the Appropriate Analysis in School-Based Drug-Use Prevention Studies. *J. Consulting and Clinical Psychology*. 53:458-468.

The study to be planned involves the evaluation of a school-based drug-use prevention program. Schools will be randomized to intervention or control groups, and the prevention program will be applied to 7th and 8th grade students over a two-year period. There are approximately 100 students in each grade in each school.

The outcome is smoking prevalence among 9th grade students. Previous studies have indicated a 15% smoking prevalence among 9th graders; the intervention will be considered a success if the smoking prevalence is reduced to 10%.

How many schools must be randomized to each of the intervention and control programs to obtain 80% power for a two-sided 5% level test? Although the outcome measure is dichotomous, we can analyze such a study by using a two-sample t -test where the school level outcome is the proportion of 9th graders who smoke.

To run this example:

Open the nQuery Advisor table for the two-sample t test; see Chapter 2, *Tutorial*, for details.

To make values for means and standard deviations easier to read, we enter number of smokers per 100 students, instead of the proportion of smokers.

Use the **Edit** menu **Edit Row Names** option. Fill in the information about test parameters and expected smoking prevalence to obtain the table shown in the following screen.

Two group t-test of equal means (equal n's)						
	1	2	3	4	5	
Test significance level, α	0.050					
1 or 2 sided test?	2					
Cont/100 mean, μ_1	15.000					
Inter/100 mean, μ_2	10.000					
Difference in means, $\mu_1 - \mu_2$	5.000					
Common standard deviation, σ						
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$						
Power (%)	80					
n per group						

We want to obtain the cluster standard deviation appropriate for school-based clusters of 100 students.

To estimate standard deviation from Cluster Sampling:

Select the **Assistants** menu **Estimate SD** option, or click on , the SD button.

Estimate Standard Deviation

- ☐ From Standard Error
- ☐ From SD1 and SD2 (pooled SD)
- ☐ From Range
- ☐ From Percentile
- ☐ From Coefficient of Variation
- ☐ From Upper Confidence Limit
- ☐ From SD1, SD2, Correlation
- ☒ For Cluster Sampling
- ☐ For specified \bar{x} values
- ☐ Of residuals (errors)

OK
Cancel

Click on the **For Cluster Sampling** radio button.



Click on **OK** to bring up the table for computing the cluster standard deviation. We have already filled in the number of 9th grade students per cluster (school).

Estimating standard deviation for cluster sampling					
	1	2	3	4	5
Between-cluster variance, σ_B^2					
Within-cluster variance, σ_i^2					
Intraclass correlation, ρ					
Subjects per cluster, m	100				
Estimate of standard deviation, σ					

Specify the between and within cluster variances, or the intraclass correlation and either one of these variances, along with the number of subjects within each cluster. With that information, nQuery Advisor will compute the cluster standard deviation.

The average proportion of students expected to be smokers is .125 (the average of .15 and .10.) Thus, the expected within school per student variance is (pq) or $(.125)(.875) = 0.109375$ (based on the binomial.)

When we use prevalence per 100 students, the variance is multiplied by 10,000 to obtain 1093.75. We enter this value in the row marked **Within-cluster variance**.

Murray and Hannan report that values of the intraclass correlation for previous studies involving smoking prevalence ranged from 0 to 0.05. Therefore, we estimate the cluster standard deviation for the three values of the intraclass correlation evaluated in their paper, 0.0, 0.02, 0.05.

The standard deviation for clusters is the square root of the sum of the within cluster variance and the between cluster variance divided by m .

When the intraclass correlation is 0.0, the cluster standard deviation is the within-cluster standard deviation divided by the square root of the number of subjects per cluster, in this case, 33.07 divided by 10, or 3.307.

Having calculated the first cluster standard deviation, we will use nQuery to estimate the cluster standard deviation only for the remaining two values of the intraclass correlation, 0.02 and 0.05. To make our estimates, we use Murray and Hannan's between-cluster variances of 22.321 and 57.566.

Estimating standard deviation for cluster sampling					
	1	2	3	4	5
Between-cluster variance, σ_b^2	22.321	57.566			
Within-cluster variance, σ_i^2	1093.750	1093.750			
Intraclass correlation, ρ	0.020	0.050			
Subjects per cluster, m	100	100			
Estimate of standard deviation, σ	5.767	8.277			

Use the cluster standard deviations computed here in the standard deviation row of the appropriate sample size table.

To copy the calculated standard deviations to the sample size table:

Highlight the Estimate of standard deviation in column 1, and select the **Edit** Menu **Copy** Option.

Use the **Window** menu to make the sample size table active.

Use the **Edit** menu **Paste Unformatted** option to paste the Estimate of standard deviation value in the Common standard deviation row of column 1 in the two-sample t-test table.

Use the **Window** menu to make the Estimating standard deviation for cluster sample table active.

Highlight the Estimate of standard deviation in column 2, and select the **Edit** Menu **Copy** Option.

Use the **Window** menu to make the sample size table active.

Use the **Edit** menu **Paste Unformatted** option to paste the Estimate of standard deviation value in the Common standard deviation row of column 2 in the two-sample t-test table.

Fill in the rest of column2 as shown below.



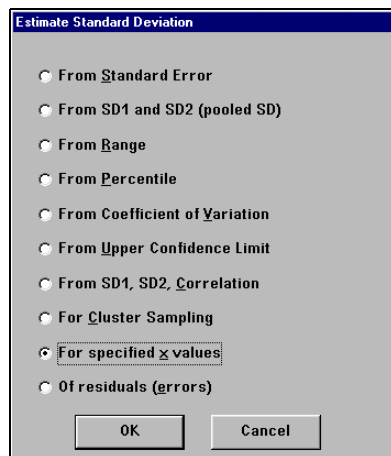
Two group t-test of equal means (equal n's)					
	1	2	3	4	5
Test significance level, α	0.050	0.050			
1 or 2 sided test?	2	2			
Cont/100 mean, μ_1	15.000	15.000			
Inter/100 mean, μ_2	10.000	10.000			
Difference in means, $\mu_1 - \mu_2$	5.000	5.000			
Common standard deviation, σ	5.767	8.277			
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	0.867	0.604			
Power (%)	80	80			
n per group	22	44			

As we can see, very small values of the intraclass correlation can have a large impact on the required sample size. For realistic values of the intraclass correlation such as 0.02, we must assign 22 schools to the control group and 22 to the intervention group.

9. For Specified x-values

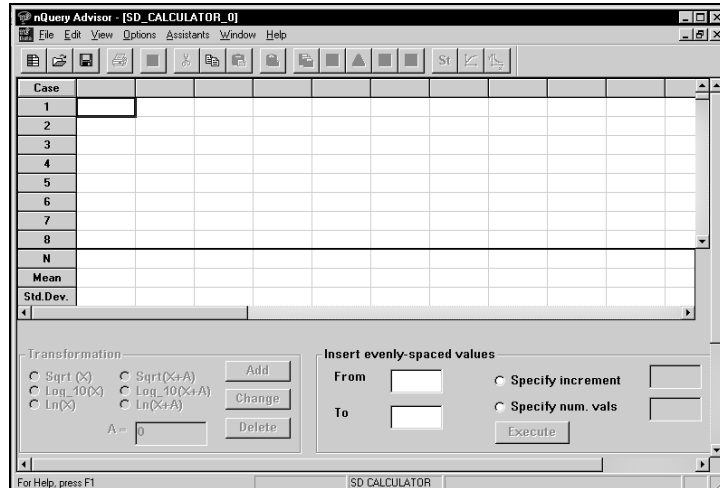
To estimate standard deviation for specified x-values:

Click on the **From Specified x-values** button.



The dialog box titled "Estimate Standard Deviation" contains a list of radio buttons for different methods to estimate standard deviation. The options are: "From Standard Error", "From SD1 and SD2 (pooled SD)", "From Range", "From Percentile", "From Coefficient of Variation", "From Upper Confidence Limit", "From SD1, SD2, Correlation", "For Cluster Sampling", "For specified x-values" (which is selected), and "Of residuals (errors)". At the bottom, there are "OK" and "Cancel" buttons.

Click on **OK** to bring up the Data Entry (standard deviation calculator) table.



As described in the Data Entry section of this chapter, you enter the actual data values column-by-column. As you enter the values, nQuery will calculate the standard deviation.

You can select a transform for the data; see discussion at the beginning of this chapter and see Example 5 in Chapter 18 *Regression Tables*.

Equally-spaced x values

There are easy options for entering equally spaced x values.

To enter equally-spaced x values, specifying number of values:

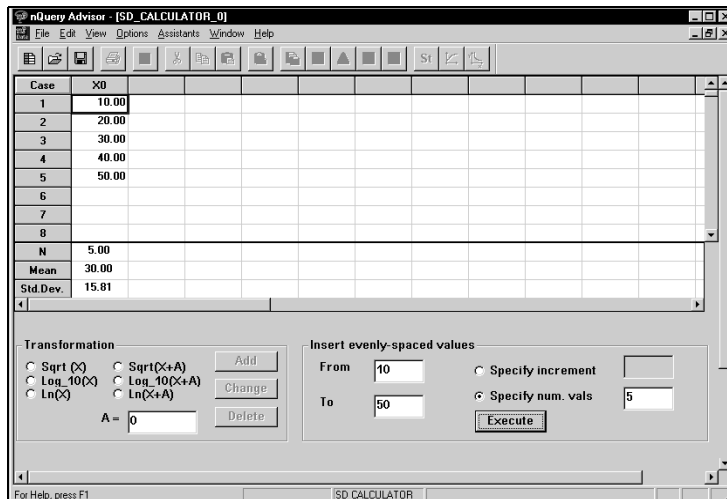
For example, to specify five equally spaced values from 10 to 50, enter **10** in the **From** box.

Enter **50** in the **To** box.

Select **Specify num. values**.

Enter **5** in the **Specify num. values** box to specify that you want 5 values.

Click on **Execute**.



To enter equally-spaced x values, specifying the increment:

For example, to specify the equally spaced values 6,12,18,...36, enter **6** in the **From** box.

Enter **36** in the **To** box.

Select **Specify** increment.

Enter **6** in the **Specify increment** box to specify that you want values incremented by 6.

Click on **Execute**.

nQuery Advisor - [SD_CALCULATOR_0]

File Edit View Options Assistants Window Help

Case	X0
1	6.00
2	12.00
3	18.00
4	24.00
5	30.00
6	36.00
N	5.00
Mean	18.00
Std. Dev.	9.49

Transformation

☐ Sqrt (X) ☐ Sqrt(X+A)
☐ Log_10(X) ☐ Log_10(X+A)
☐ Ln(X) ☐ Ln(X+A)

A =

Insert evenly-spaced values

From ☐ Specify increment
 To ☐ Specify num. vals

For Help, press F1

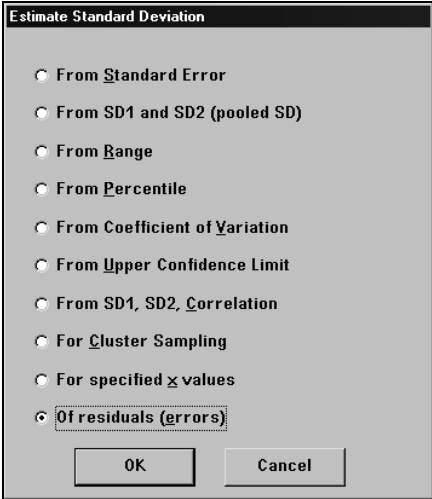
[SD_CALCULATOR]

10. Of Residuals

For regression problems, it will be necessary to specify the standard deviation of residuals (also called the root mean square error, or the standard deviation around the line.) When a direct estimate of this value is not available, it is possible to estimate it, using other information about the regression line.

To estimate standard deviation of residuals:

Click on the **of residuals (errors)** button.

A dialog box titled "Estimate Standard Deviation" with a list of radio buttons. The options are: "From Standard Error", "From SD1 and SD2 (pooled SD)", "From Range", "From Percentile", "From Coefficient of Variation", "From Upper Confidence Limit", "From SD1, SD2, Correlation", "For Cluster Sampling", "For specified x values", and "Of residuals (errors)". The "Of residuals (errors)" option is selected. At the bottom are "OK" and "Cancel" buttons.

Estimate Standard Deviation

- ☐ From Standard Error
- ☐ From SD1 and SD2 (pooled SD)
- ☐ From Range
- ☐ From Percentile
- ☐ From Coefficient of Variation
- ☐ From Upper Confidence Limit
- ☐ From SD1, SD2, Correlation
- ☐ For Cluster Sampling
- ☐ For specified x values
- ☒ Of residuals (errors)

OK Cancel

Click on the **OK** button, and the Residual Standard Deviation around the line for one predictor table will appear.

Residual (error) standard deviation around the line for one predictor x							
	1	2	3	4	5	6	
Regression coefficient, β							
Correlation coefficient, ρ							
Standard deviation of x , $\sigma(x)$							
Standard deviation of y , $\sigma(y)$							
SD of residuals (errors), σ							

Enter values into any three of the first four rows. The nQuery program will calculate the fourth and the standard deviation of residuals. For a detailed example, see Example 4 in Chapter 18 *Regression Tables*.



Using the Specify Covariance Matrix Option

For analysis of repeated measures designs, users must specify the within group covariance matrix for the M levels of the repeated measures factor. Remember, the repeated measures tables are:

MTT3 Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)

MOT4 Univariate one-way repeated measures analysis of variance (Greenhouse-Geisser approximation)

When a repeated measures sample size table is open, and the number of levels, M, has been specified select Specify Covariance Matrix from the Assistants menu or click on the Σ icon.

The resulting side table will be attached to the active column in the main sample size table and will transfer summary values for the covariance matrix back to the main table.

The Specify Covariance Matrix side table offers two main options for specifying information about the covariance matrix:

- specify standard deviations and correlations
- specify full covariance matrix

If you select the first option to specify standard deviations and correlations, you can specify standard deviations in one of two ways:

- specify a standard deviation for each level
- fill in a constant standard deviation for each level.

If you select the first option to specify standard deviations and correlations, you can specify correlations in one of two ways:

- specify each correlation,
- specify a correlation pattern in which all correlations are equal, correlations follow an autoregressive pattern, or correlations follow an intermediate pattern.

Whichever option you choose, all standard deviations and correlations, and all variances and covariances are available for editing.

In the following example, you will see examples of several of these options, using the side-table which appears when invoked from the main sample size table MTT3, Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction).


1. Specify Full Covariance Matrix

For this example, there are three repeated measures levels.

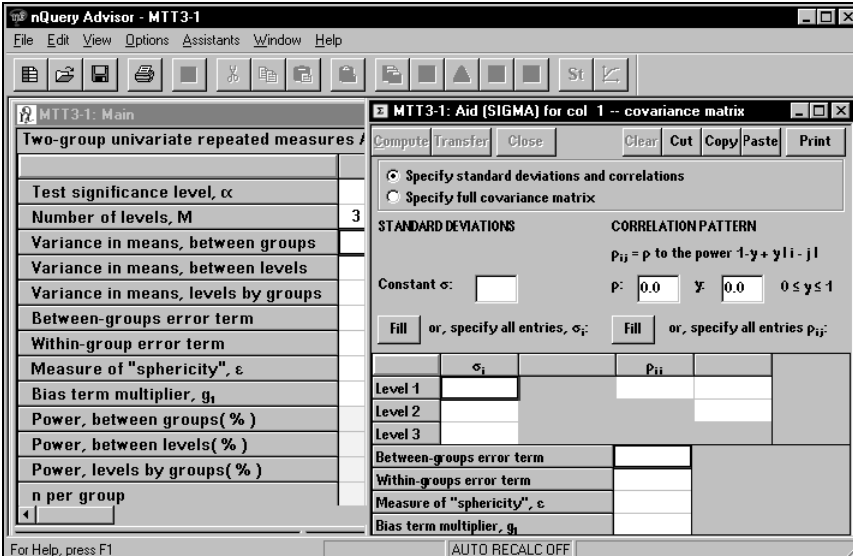
To bring up the specify the covariance matrix side table:

Open the MTT3 repeated measures sample size table.

In the **Number of levels, M** row, enter **3**.

Click on , the Specify covariance matrix icon, or select the **Assistants** menu **Specify Covariance Matrix** option.

The following table appears.



	σ_i	p_{ij}
Level 1		
Level 2		
Level 3		

The figure above shows tables as they appear using **Print Table to Clipboard** from the **File** menu. Within the side table, click the radio button for **Specify Full Covariance Matrix** to obtain the alternate version of the table.



MTT3-1: Aid (SIGMA) for col 1 -- covariance matrix

Compute Transfer Close Clear Cut Copy Paste Print

☐ Specify standard deviations and correlations
☒ Specify full covariance matrix

	$\sigma_1\sigma_2\rho_{12}$		
Level 1			
Level 2			
Level 3			
Between-groups error term			
Within-groups error term			
Measure of "sphericity", ϵ			
Bias term multiplier, g_1			

Enter the variances **25**, **64**, **36** in the diagonal cells of the table.

Enter the covariances (**16**, **12**) of the first measure with the two subsequent measures into columns 2 and 3 for the Level 1 row.

Enter **30** in column 3 for the Level 2 row. This value is the covariance of the second and third measures.

Select **Compute** to obtain the summary values.

MTT3-1: Aid (SIGMA) for col 1 -- covariance matrix

Compute Transfer Close Clear Cut Copy Paste Print

☐ Specify standard deviations and correlations
☒ Specify full covariance matrix

	$\sigma_1\sigma_2\rho_{12}$		
Level 1	25.000	16.000	12.000
Level 2		64.000	30.000
Level 3			36.000
Between-groups error term			8.963
Within-groups error term			4.726
Measure of "sphericity", ϵ			0.928
Bias term multiplier, g_1			-1.192

Click on the **Transfer** button to return the required summary values to the main table for sample size computation.

MTT3-1: Main			
Two-group univariate repeated measures ANOVA (Greenhouse-Geisser)			
	1	2	3
Test significance level, α			
Number of levels, M	3		
Variance in means, between groups			
Variance in means, between levels			
Variance in means, levels by groups			
Between-groups error term	8.96		
Within-group error term	4.73		
Measure of "sphericity", ϵ	0.93		
Bias term multiplier, g_1	-1.19		
Power, between groups(%)			
Power, between levels(%)			
Power, levels by groups(%)			
n per group			

2. Specify Standard Deviations

If you select the first option to specify standard deviations and correlations, you can specify standard deviations in one of two ways:

- specify a standard deviation for each level
- fill in a constant standard deviation for each level.

You can simply enter the standard deviations for each level as shown:

covariance matrix	
σ_1	
Level 1	5.000
Level 2	8.000
Level 3	6.000

Alternatively, you can fill in a constant value for the standard deviations for each level. To do that, enter a single value in the box marked **Constant σ** and click on the button marked **Fill** immediately below it.



MTT3-1: Aid (SIGMA) for col 1 -- covariance matrix

Compute Transfer Close Clear Cut Copy Paste Print

☒ Specify standard deviations and correlations
☐ Specify full covariance matrix

STANDARD DEVIATIONS CORRELATION PATTERN

$\rho_{ij} = \rho$ to the power $1 - \gamma + \gamma|i - j|$

Constant σ_i : ρ : γ : $0 \leq \gamma \leq 1$

or, specify all entries, σ_i : or, specify all entries ρ_{ij} :

	σ_i	ρ_{ii}
Level 1	7.000	
Level 2	7.000	
Level 3	7.000	
Between-groups error term		
Within-groups error term		
Measure of "sphericity", ϵ		
Bias term multiplier, g_1		

3. Specify Correlations

If you select the first option to specify standard deviations and correlations, you may specify correlations in one of two ways:

- specify each correlation
- specify a correlation pattern in which all correlations are equal, correlations follow an autoregressive pattern, or correlations follow an intermediate pattern.

For this example, we will go to the second column and specify that there are seven levels: basal, and six doses of a drug given in increasing order to each animal. You can specify each individual correlation or specify a patterned correlation matrix.

nQuery Advisor provides a choice of patterned correlation matrices defined by:


$$\rho_{ij} = 1 - \gamma + \gamma|i - j|$$

Note: This patterned correlation model was recommended by Keith Muller. The model is discussed in Murray SC, Helms RW (1990) Linear Models with Generalized AR(1) Covariance Structure for Irregularly-Timed Data. *Department of Biostatistics, University of North Carolina at Chapel Hill. Institute of Statistics Mimeo Series No. 1876.*

To bring up the specify the covariance matrix side table:

Open the MTT3 repeated measures sample size table.

In the **Number of levels, M** row, enter 7.

Click on , the Specify covariance matrix icon, or select the **Assistants** menu **Specify Covariance Matrix** option.

The following table appears.

	σ_i	ρ_{ij}					
Level 1							
Level 2							
Level 3							
Level 4							
Level 5							
Level 6							
Level 7							
Between-groups error term							
Within-groups error term							
Measure of "sphericity", ϵ							
Bias term multiplier, g_1							

To specify the standard deviations for each repeated measures level, enter the desired values in the σ_i column; for example, enter the values 3, 5, 7, 7, 7, and 8 for levels 1 through 7 respectively.

To obtain a patterned correlation matrix in which all correlations are equal:

Enter the desired constant correlation in the box marked ρ , say **0.9**.

Leave the **0.0** value in the box marked γ .

Click on the button marked **Fill** immediately below.



MIT3-1: Aid (SIGMA) for col 1 -- covariance matrix

Compute Transfer Close Clear Cut Copy/Paste Print

☒ Specify standard deviations and correlations
☐ Specify full covariance matrix

STANDARD DEVIATIONS

Constant σ :

Fill or, specify all entries, σ_i :

CORRELATION PATTERN

$\rho_{ij} = \rho$ to the power $1-y + y|i-j|$

ρ : γ : $0 \leq y \leq 1$

Fill or, specify all entries ρ_{ij} :

	σ_i	ρ_{ii}					
Level 1	3.000	0.900	0.900	0.900	0.900	0.900	0.900
Level 2	5.000		0.900	0.900	0.900	0.900	0.900
Level 3	6.000			0.900	0.900	0.900	0.900
Level 4	7.000				0.900	0.900	0.900
Level 5	7.000					0.900	0.900
Level 6	7.000						0.900
Level 7	8.000						
Between-groups error term							
Within-groups error term							
Measure of "sphericity", ϵ							
Bias term multiplier, g_i							

To obtain a patterned correlation matrix in which correlations follow a first-order autoregressive pattern:

Enter the desired constant correlation in the box marked ρ , say **0.9**.

Enter **1** in the box marked γ .

Click on the button marked **Fill** immediately below.

MIT3-1: Aid (SIGMA) for col 1 -- covariance matrix

Compute Transfer Close Clear Cut Copy/Paste Print

☒ Specify standard deviations and correlations
☐ Specify full covariance matrix

STANDARD DEVIATIONS

Constant σ :

Fill or, specify all entries, σ_i :

CORRELATION PATTERN

$\rho_{ij} = \rho$ to the power $1-y + y|i-j|$

ρ : γ : $0 \leq y \leq 1$

Fill or, specify all entries ρ_{ij} :

	σ_i	ρ_{ii}					
Level 1	3.000	0.900	0.810	0.729	0.656	0.590	0.531
Level 2	5.000		0.900	0.810	0.729	0.656	0.590
Level 3	6.000			0.900	0.810	0.729	0.656
Level 4	7.000				0.900	0.810	0.729
Level 5	7.000					0.900	0.810
Level 6	7.000						0.900
Level 7	8.000						
Between-groups error term							
Within-groups error term							
Measure of "sphericity", ϵ							
Bias term multiplier, g_i							

We see that correlations decrease from .9 to .534 as observations get farther apart in time.

To obtain a patterned correlation matrix in which correlations follow a pattern in which they do not decrease as fast as for a first-order autoregressive pattern:

Enter the desired constant correlation in the box marked ρ , say **0.9**.

In the box marked γ , enter a value between 0 and 1.

Click on the button marked **Fill** immediately below.

The two figures below use values of .2 and .5 for γ .

MTT3-1: Aid (SIGMA) for col 1 -- covariance matrix

Compute Transfer Close Clear Cut Copy Paste Print

☒ Specify standard deviations and correlations
☐ Specify full covariance matrix

STANDARD DEVIATIONS CORRELATION PATTERN
 $\rho_{ij} = \rho$ to the power $1 - \gamma + \gamma|i - j|$

Constant σ : ρ : γ : $0 \leq \gamma \leq 1$

Fill or, specify all entries, σ_i : Fill or, specify all entries ρ_{ij} :

	σ_i	ρ_{ij}						
Level 1	3.000	0.900	0.881	0.863	0.845	0.827	0.810	
Level 2	5.000		0.900	0.881	0.863	0.845	0.827	
Level 3	6.000			0.900	0.881	0.863	0.845	
Level 4	7.000				0.900	0.881	0.863	
Level 5	7.000					0.900	0.881	
Level 6	7.000						0.900	
Level 7	8.000							0.900

Between-groups error term

Within-groups error term

Measure of "sphericity", ϵ

Bias term multiplier, g_0



MTT3-1: Aid (SIGMA) for col. 1 -- covariance matrix

Compute Transfer Close Clear Cut Copy/Paste Print

☒ Specify standard deviations and correlations
☐ Specify full covariance matrix

STANDARD DEVIATIONS CORRELATION PATTERN
 $p_{ij} = \rho$ to the power $1-y + y|i-j|$

Constant σ : ρ : y : $0 \leq y \leq 1$

or, specify all entries, σ_i : or, specify all entries p_{ij} :

	σ_i	p_{ii}					
Level 1	3.000	0.900	0.854	0.810	0.768	0.729	0.692
Level 2	5.000		0.900	0.854	0.810	0.768	0.729
Level 3	6.000			0.900	0.854	0.810	0.768
Level 4	7.000				0.900	0.854	0.810
Level 5	7.000					0.900	0.854
Level 6	7.000						0.900
Level 7	8.000						
Between-groups error term							
Within-groups error term							
Measure of "sphericity", ϵ							
Bias term multiplier, g_1							

Summary

Sample size calculations for tests and confidence intervals for means require an estimate of the within-group standard deviation. The nQuery Advisor program provides several ways to estimate the standard deviation from available information. You can use the Data Entry option or one of the Estimate SD options in the Assistants menu to determine a reasonable estimate for standard deviation from the information you have. You can use the Specify Covariance Matrix option to specify the covariance matrix, standard deviations, or correlations.

10. Unequal n's

Generally speaking, one prefers designs with equal sample sizes in each group. For tests on means, assuming that the standard deviation is the same in each group, for a specified total sample size the power will be maximized for designs in which the sample sizes are equal. Achieving the same power with unequal n's will require a larger total sample size.

In some cases, however, a design with unequal sample size may be unavailable or even undesirable. For example, considerable information may already be available about the control group. In a study comparing placebo, new drug, and standard drug, comparisons with the placebo group will have high power anyway. Thus, it may be undesirable to treat too many patients with a placebo when a known effective drug is available.


The nQuery Advisor program provides sample size computations for designs with unequal n's for:

- most of the Means tables for two or more groups,
- ♦ most of the Proportions tables for two or more groups
- ♦ one of the Survival Analysis tables—Log-rank test, user-specified survival rates, accrual, dropouts (simulation)

To access a sample size table with unequal n's when you are initially selecting a sample size table:

Check the Unequal n's box in the Study Goal and Design dialog box.

To access the unequal n's version of the current appropriate table with equal n's:

Select the **Assistants** menu **Unequal n's** option or click on  the Unequal n's icon.

Finding Sample Size for Unequal n's Design

To illustrate finding a sample size for a design planned with unequal n's, we use the example from the tutorial in Chapter 2.

To reiterate the Chapter 2 example:

Select the **File** menu **New** option.

In the **Study Goal and Design** box, Select the **MTT0** design: **Means**, **Two** groups, **Test**, first listed method.

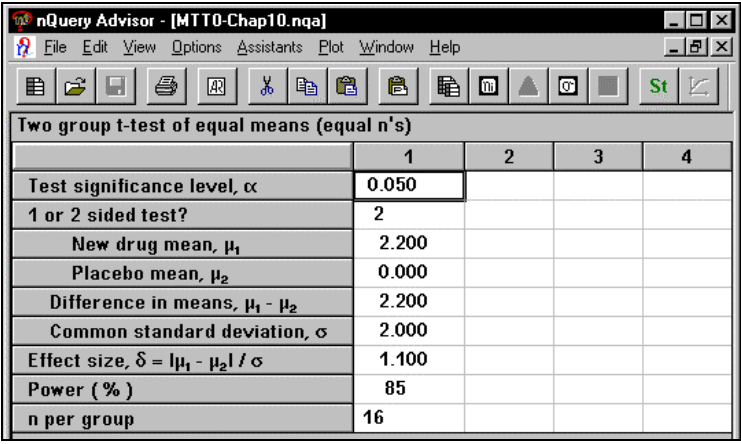
In the sample size table, use the **Edit** menu **Edit Row Labels** option to change Group 1 and Group 2 to **New drug** and **Placebo**, respectively.

Enter **.05** for significance level and **2** for 1 or 2 sided test.

Enter **2.2** for **New drug** mean.

Enter **0** for **Placebo** mean.

Enter **2** for Common standard deviation and **85** for Power. Press <Enter> and nQuery Advisor will calculate the n per group.



The screenshot shows the nQuery Advisor window titled "nQuery Advisor - [MTT0-Chap10.nqa]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons for file operations and analysis. The main window displays a table titled "Two group t-test of equal means (equal n's)". The table has five columns: a label column and four numerical columns labeled 1, 2, 3, and 4. The data entered in the table is as follows:

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
New drug mean, μ_1	2.200			
Placebo mean, μ_2	0.000			
Difference in means, $\mu_1 - \mu_2$	2.200			
Common standard deviation, σ	2.000			
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.100			
Power (%)	85			
n per group	16			

The total sample size required is 32.

Since we want to see the effect of using unequal n's, we will open an unequal n's table. First, copy part of the current table.



To copy several rows:

Use the mouse to select the first seven rows of the first column.

Choose the **Edit** menu **Copy** option or click on the **Copy icon**, or use the keyboard shortcut **Ctrl-C**.

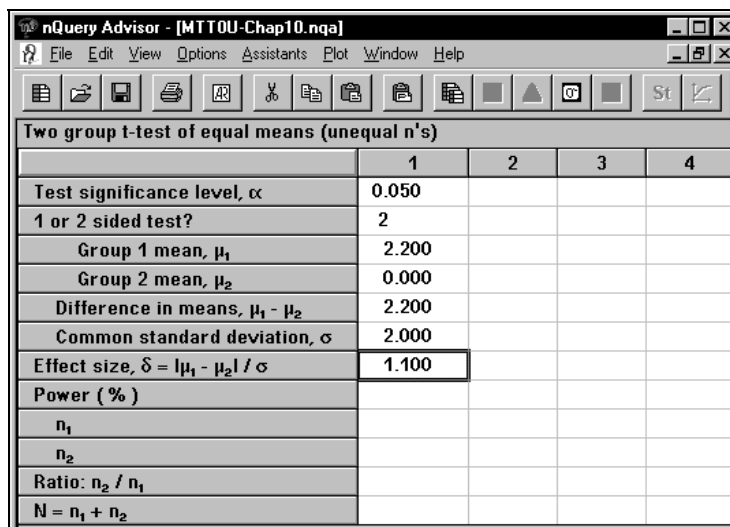
To create the unequal n's version of the current table:

Click on the **Assistants** menu **Unequal n's** option or click on the Unequal n's icon.

The unequal n's table will appear.

Click on the first cell of the first column.

Choose the **Edit** menu **Paste** option or click on the **Paste icon**, or use the keyboard shortcut **Ctrl-V**. The first seven rows of the unequal n's table will fill.



The screenshot shows the nQuery Advisor software window titled "nQuery Advisor - [MTT0U-Chap10.nga]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons for file operations and calculations. The main window displays a table titled "Two group t-test of equal means (unequal n's)". The table has five columns: a label column and four data columns numbered 1, 2, 3, and 4. The first column is filled with the following labels: Test significance level, α ; 1 or 2 sided test?; Group 1 mean, μ_1 ; Group 2 mean, μ_2 ; Difference in means, $\mu_1 - \mu_2$; Common standard deviation, σ ; Effect size, $\delta = |\mu_1 - \mu_2| / \sigma$; Power (%); n_1 ; n_2 ; Ratio: n_2 / n_1 ; and $N = n_1 + n_2$. The first seven rows of the data columns are filled with the values 0.050, 2, 2.200, 0.000, 2.200, 2.000, and 1.100, respectively. The remaining five rows of the data columns are empty.

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Group 1 mean, μ_1	2.200			
Group 2 mean, μ_2	0.000			
Difference in means, $\mu_1 - \mu_2$	2.200			
Common standard deviation, σ	2.000			
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.100			
Power (%)				
n_1				
n_2				
Ratio: n_2 / n_1				
$N = n_1 + n_2$				

At this point, you can fill in power and the desired ratio between the sample sizes of the two groups, then nQuery Advisor will solve for the n's. Alternatively, you can fill in any two of the four n rows and nQuery Advisor will solve for power.

In the first column, suppose that we want 85% power and twice as many cases in the new drug group as in the placebo group. Type in 85 for power and .5 for ratio and see the solution below.

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Group 1 mean, μ_1	2.200			
Group 2 mean, μ_2	0.000			
Difference in means, $\mu_1 - \mu_2$	2.200			
Common standard deviation, σ	2.000			
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.100			
Power (%)	85			
n_1	24			
n_2	12			
Ratio: n_2 / n_1	0.500			
$N = n_1 + n_2$	36			

With these unequal n's, the total sample size required has increased from 32 to 36.

If you wanted to have 20 in the first group and 15 in the second group, what power would be obtained?

To calculate power for group sizes of 20 and 15:

Copy the first 7 rows to the second column.

Enter **20** and **15** in the n_1 and n_2 rows, respectively.



Two group t-test of equal means (unequal n's)				
	1	2	3	4
Test significance level, α	0.050	0.050		
1 or 2 sided test?	2	2		
Group 1 mean, μ_1	2.200	2.200		
Group 2 mean, μ_2	0.000	0.000		
Difference in means, $\mu_1 - \mu_2$	2.200	2.200		
Common standard deviation, σ	2.000	2.000		
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.100	1.100		
Power (%)	85	87		
n_1	24	20		
n_2	12	15		
Ratio: n_2 / n_1	0.500	0.750		
$N = n_1 + n_2$	36	35		

By making the sample sizes in the two groups somewhat closer in size, we were able to get slightly higher power with a slightly lower total sample size.

Caveat

When you want to see the effect of changing values in the more complex tables allowing unequal n's for two groups, you must avoid editing the filled-in values. Rather, you should copy the rows to be retained. Then paste the rows into another column. Using the new column, you can enter the new values.

This methodical approach provides you with an audit trail, so that you can compare the effects of your differing choices. This method also avoids the possibility of:

- deleting values other than values you intended to delete
- recalculating a row other than the row you intended to recalculate.

11. Demonstrating Equivalence

In this chapter we provide an introduction to sample size issues in equivalence testing, and give examples for sample size tables for equivalence testing for means . . . At the end of the chapter we review the interrelationships between tests, confidence intervals, and equivalence demonstrations. Examples for equivalence tests for differences in proportions are given in Chapter 15 *Sample Size Tables for Proportions*; see examples 9, 10, 11 in that chapter.

nQuery Advisor provides sample size tables for the following equivalence testing situations.

One-sided (non-inferiority) tests for difference of means

- MTE0 **Two-group t test of equivalence in means**
See Example 1 in this chapter.
- MOE0 **Paired t test of equivalence of means**

Two one-sided tests (TOST) for difference or ratio of means

- MTE1tg **Two-group t tests (TOST) of equivalence in means**
See Examples 2 and 4 in this chapter.
- MTE2tg **Two-group t tests (TOST) for ratio of means (using log scale)**
See Example 5 in this chapter.
- MTE3 **Two-group t tests (TOST) for ratio of means (using original scale)**
See Example 7 in this chapter.
- MTE1co **t tests (TOST) of equivalence in means for crossover design**
See Example 3 in this chapter.
- MTE2co **t-tests (TOST) of equivalence in ratio of means for crossover design (natural log scale)**
See Example 6 in this chapter.
- MTE4 **Crossover design TOST for ratio of means (using original scale)**
See Example 8 in this chapter.

One-sided non-inferiority tests for difference of proportions

PTE0	Two-group test of equivalence in proportions (large n) See Examples 10 and 11 in Chapter 15.
PTE1	Two group test of equivalence in proportions using confidence interval: a) Lower confidence limit for difference in proportions (simulation) See Example 10 in Chapter 15. b) Upper confidence limit for difference in proportions (simulation)
POE0	Paired test of equivalence of proportions (n large) See Example 9 in Chapter 15.
POE1	Paired test of equivalence in proportions using confidence interval: a) Lower confidence limit for difference in paired proportions (simulation) See Example 9 in Chapter 15. b) Upper confidence limit for difference in paired proportions (simulation)

Difference of proportions in paired or two-group design

PTE1	Two group test of equivalence in proportions using confidence interval: c) Two-sided confidence limits for difference in proportions (simulation) See Example 11 in Chapter 15.
POE1	Paired test of equivalence in proportions using confidence interval: c) Two-sided confidence limits for difference in paired proportions (simulation)

Equivalence testing

We distinguish between two types of equivalence demonstration:

- 1) **one-sided** the intent is to demonstrate that the new drug is not inferior to the standard, a typical clinical equivalence goal
- 2) **two-sided** the intent is to demonstrate that the dose delivered by the new drug is close to that delivered by the standard, a typical quality control, equi-potency, or bioequivalence goal



Equivalence testing hypotheses may be specified in terms of differences in means, ratios of means, or in terms of differences, ratios, or odds ratios of proportions.

The most commonly used designs for equivalence testing are two independent groups and the 2 x 2 crossover design.

One-sided, non-inferiority equivalence testing for difference in means

To simplify the following discussion, we assume that higher means are more desirable. Consider a trial comparing new test drug (T), and a standard (reference) drug (S). We want to demonstrate that the test drug is as least as good as the standard (reference) ($T \geq S$).

For example, consider a clinical trial comparing a standard drug and a new test drug designed to reduce blood pressure. Previous studies suggest that the average reduction in resting diastolic blood pressure in a four-week study is 12 mmHg for the standard drug, with standard deviations for these reductions of about 6 mmHg.

We want to demonstrate that the new drug is not inferior to the standard: Specifically, we want to demonstrate that the average reduction of blood pressure for the test drug is no more than 1.5 mmHg less than for the standard.

Note: Selection of an equivalence limit difference may be aided by considering the difference between the expected reduction in blood pressure for the standard drug and that for the placebo. For this example, the reduction in blood pressure for the standard drug is expected to be 12 mmHg, and the reduction for placebo treated patients is expected to be 5 mmHg. This is a difference in reduction of 7 mmHg. Here we have stated that the test and standard drugs will be considered equivalent if the difference in their means is less than a quarter of the difference between standard and placebo means.

Define:

μ_s = standard, reference (control) drug mean

μ_T = test, new, (experimental) drug mean

Then

$$H_0: \mu_T - \mu_s \leq \Delta_0 \text{ or } H_0: \mu_T \leq \mu_s + \Delta_0 \text{ or } H_0: \mu_T - \mu_s - \Delta_0 \leq 0$$

$$H_A: \mu_T - \mu_s > \Delta_0$$

In the context of our example $\Delta_0 = -1.5$ and we would write the null hypothesis as:

$$H_0: \mu_T - \mu_s \leq -1.5 \text{ or } \mu_T \leq \mu_s - 1.5 \text{ or } \mu_T - \mu_s + 1.5 \leq 0$$

In other words, the null hypothesis states that the standard (reference) is better than the test treatment by some stated amount Δ_0 . That is, the new drug is inferior to the standard. We wish to test the null hypothesis that there is an important difference between the two drugs (they are not equivalent) and reject the null hypothesis in favor of the alternative hypothesis that the new drug is not inferior to the standard.

The specific alternative value of $\mu_T - \mu_S$ usually used in power and sample size calculations for equivalence testing is $\mu_T - \mu_S = 0$.

This formulation of the hypotheses for equivalence testing leads back to the same power and sample size calculations as for classical testing approach of $H_0 = 0$ with a one-sided alternative $H_A: \mu_T - \mu_S = \Delta_0$ with Type I and Type II errors reversed. See discussion in a later section in this chapter, *Relationships between sample size methods for standard tests, confidence intervals, and equivalence tests*.

This equivalence testing approach can also be put in the context of confidence interval estimation. We reject the null hypothesis of non-equivalence at the 5% level when the one-sided 95% confidence interval for $\mu_T - \mu_S$ does not include the value -1.5, that is, when its lower bound is > -1.5 . For further discussion, see *Relationships between sample size methods for standard tests, confidence intervals, and equivalence tests*.

Note: We should note here that even if equivalence between treatments is accepted, we cannot directly conclude the *effectiveness* of the test treatment. Even if the standard (reference) was shown to be superior to placebo in previous trials, there is no guarantee that either treatment would have out-performed placebo in the current study, had there been a placebo group. Inferring efficacy on the basis of equivalence to a treatment previously shown to be superior to placebo should be done cautiously. A placebo group from a previous trial is now only an historical control.

Example 1


One-sided, non-inferiority test for difference in means Two group t test of equivalence in means (MTE0)

In this example, we assume that the null hypothesis of non-inferiority is to be tested for a new drug versus the standard using a two group design with equal sample sizes in the two groups. If sample sizes will be unequal, select the Unequal n's option on the Goal and Design box before clicking OK. If you decide on unequal n's after opening the table you can click on the unequal n's button in the toolbar for the equal n's sample size table.



We wish to demonstrate that the standard drug does not reduce blood pressure by 1.5 mmHg more than the test drug (see previous section.) We fix the one-sided alpha level at 0.05 and desire a power of 80% when the true means of the two drugs are the same.

To bring up a table appropriate for this example:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

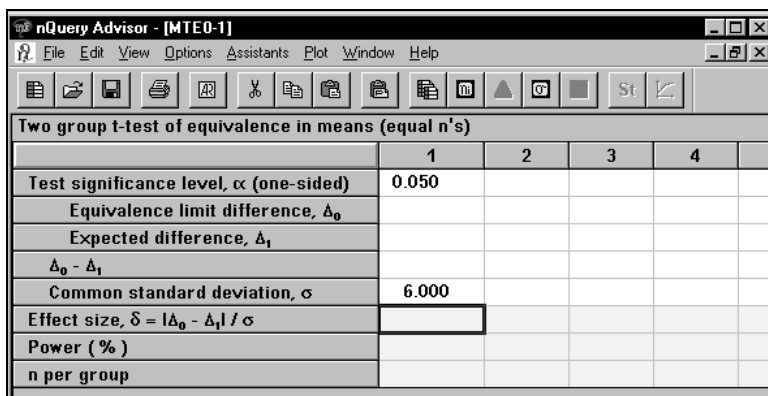
Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Equivalence**.

Select the first choice among the listed analyses, **Equivalence of two means**, and click on **OK**.

The table will come up empty. The following table shows the entries for the desired significance level and the expected value of the standard deviation.



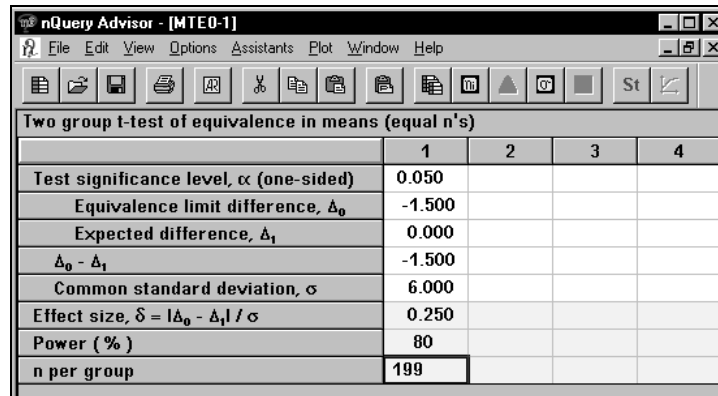
	1	2	3	4	
Test significance level, α (one-sided)	0.050				
Equivalence limit difference, Δ_0					
Expected difference, Δ_1					
$\Delta_0 - \Delta_1$					
Common standard deviation, σ	6.000				
Effect size, $\delta = \Delta_0 - \Delta_1 / \sigma$					
Power (%)					
n per group					

The null hypothesis for a one-sided equivalence test for a difference in means is generally the one-sided hypothesis that the two treatments are **not** equivalent, i.e. that the test drug is worse than the standard (reference) by some specified amount.

In this case, the null hypothesis states that the mean reduction in blood pressure produced by the test drug minus the mean reduction produced by the standard drug is less than -1.5 mmHg. Therefore, the equivalence limit difference is -1.5.

The manufacturers of the test drug believe that it will, in fact, produce exactly the same reduction in blood pressure as the standard drug, so the expected difference is

0.0. The investigators want 80% power to reject the null hypothesis of lack of equivalence if the two drugs do in fact have the same effect on blood pressure.



The screenshot shows the nQuery Advisor window with the title "nQuery Advisor - [MTE0-1]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons for file operations and analysis. The main window displays a table for a "Two group t-test of equivalence in means (equal n's)".

	1	2	3	4
Test significance level, α (one-sided)	0.050			
Equivalence limit difference, Δ_0	-1.500			
Expected difference, Δ_1	0.000			
$\Delta_0 - \Delta_1$	-1.500			
Common standard deviation, σ	6.000			
Effect size, $\delta = \Delta_0 - \Delta_1 / \sigma$	0.250			
Power (%)	80			
n per group	199			

For this example, a sample size of about 200 per group (400 total) would be necessary to have 80% power to demonstrate that the new drug is not inferior to the standard when their true means are in fact equal.

The nQuery Advisor statement for this sample size calculation has been copied to clipboard and pasted into this document:

When the sample size in each group is 199, a two group 0.050 one-sided t-test will have 80% power to reject the null hypothesis that the test and standard are not equivalent (the difference in means, $\mu_T - \mu_S$, is -1.500 or farther from zero in the same direction) in favor of the alternative hypothesis that the means of the two groups are equivalent, assuming that the expected difference in means is 0.000 and the common standard deviation is 6.000.

See Chapter 2 *Tutorial* and Chapter 4 *The Edit Menu* for details on using nQuery Advisor's automated sample size justification statements.

Two-sided, “neither better nor worse”, bio-equivalence testing

TOST for difference in means

This type of equivalence testing occurs when there is a requirement to have enough but not too much. For example, one might be testing a generic drug versus a standard (reference) drug to be sure that the drug blood levels achieved are the same with both formulations.



For example, suppose that we want to make sure that the test drug produces the same blood levels at steady state as the standard. Published results for the standard show steady state levels about 16 with a standard deviation of 2.8.

We want to demonstrate that the steady state blood levels are essentially the same, that the test drug produces blood levels which are neither markedly higher nor markedly lower.

The standard strategy for showing equivalence of two means is to demonstrate that the difference is within acceptable limits. To test for equivalence, we must first specify a range of differences that we consider small enough for the treatments or drugs to be considered essentially the same.

Equivalence is concluded if the confidence interval for the difference in means is contained completely within the equivalence limits. To compute required sample size in this situation, we must:

- ◆ establish two hypotheses
- ◆ compute the sample size required to have specified power to reject both hypotheses when equivalence is true

Difference in means

We first discuss the situation in which the equivalence limits are expressed in terms of a difference in means, and we believe in exact equivalence. That is, we want to establish that the difference in means is within the interval (Δ_L, Δ_U) .

The hypotheses are stated as:

$$H_{01}: \mu_T - \mu_S \leq \Delta_L \text{ or } H_{01}: \mu_T - \mu_S - \Delta_L \leq 0$$

$$H_{02}: \mu_T - \mu_S \geq \Delta_U \text{ or } H_{02}: \mu_T - \mu_S - \Delta_U \geq 0$$

$$H_A: \mu_T - \mu_S = 0$$

The two one-sided tests (TOST) procedure for differences in means tests the null hypotheses for the upper and lower limits separately, each with a one-sided α level test. Only when both hypotheses are rejected may one conclude that the two means are equivalent.

The resulting TOST procedure is an α level test (see caveat below). The results correspond to a $100(1-2\alpha)\%$ confidence interval. If the confidence interval is contained completely within (Δ_L, Δ_U) , then the alternative hypothesis that the two formulations are equivalent is accepted.

Note: The Type I error for the TOST procedure may be less than α when the sample size per group is not large enough so that the total confidence

interval width is less than $\Delta_U - \Delta_L$. In large samples when $\Delta_L = -\Delta_U$, this requires that n per group satisfy the inequality

$$n > \frac{2z_{1-\alpha}^2 \sigma^2}{\Delta_U^2}$$

See Examples 2 and 3 for sample sizes for TOST procedures for differences in means for two-group and crossover designs.

Example 2

TOST for difference in means

Two-group t tests (TOST) of equivalence in means (MTE1tg)

In this example we assume that the null hypothesis of non equivalence is to be tested for a new drug versus the standard using a two group design with equal sample sizes in the two groups. We want to demonstrate that the standard drug and the test drug have similar steady state blood levels. In a published study evaluating the standard, the mean steady state blood level was about 16, and its standard deviation was 2.8. We must specify values for Δ_L and Δ_U . For example we might specify that the difference in means should be within 15% of the mean for the standard (in this case, $16(.15) = 2.4$). We would then rewrite the two null hypotheses as

$$H_{01}: \mu_T - \mu_S \leq -2.4 \text{ or } H_{01}: \mu_T - \mu_S + 2.4 \leq 0$$

$$H_{02}: \mu_T - \mu_S \geq 2.4 \text{ or } H_{02}: \mu_T - \mu_S - 2.4 \geq 0$$

The composite null hypothesis is that the two formulations produce doses of unequal strength (differing steady state blood levels). The alternative hypothesis is that the delivered dose is equivalent for the test and standard.


Reject H_{01} if the observed difference in the two means is too large. That is, reject if the lower bound for two-sided $100(1-2\alpha)\%$ confidence interval for $\mu_T - \mu_S$ is greater than -2.4.

Reject H_{02} if the observed difference in means is too small. That is, reject if the upper bound for the two-sided $100(1-2\alpha)\%$ confidence interval for $\mu_T - \mu_S$ is less than 2.4.

We fix the one-sided alpha levels at 0.05 for each of the two one-sided tests and desire a power of 80% when the two drugs produce the same true mean blood levels.



To use TOST for difference in means using MTE1tg:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

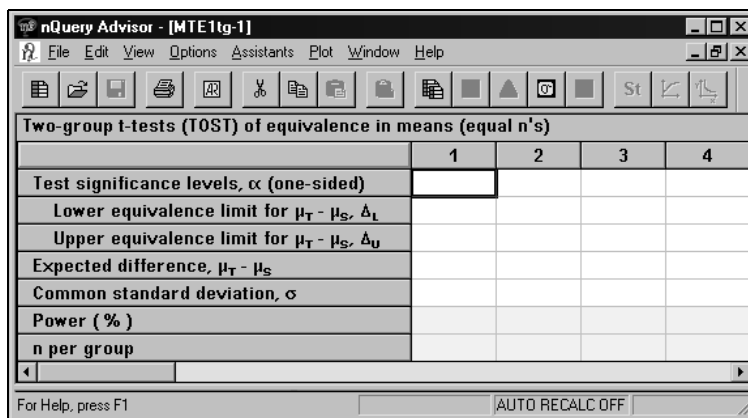
Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Equivalence**.

Click on the + sign next to the second choice among the listed analyses, **Two one-sided equivalence tests (TOST) for two-group or crossover designs**, and then select **Two one-sided equivalence tests (TOST) for two group design**.

Click on **OK**.



The screenshot shows the nQuery Advisor window with the title bar 'nQuery Advisor - [MTE1tg-1]'. The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons for file operations and analysis. The main window displays a table titled 'Two-group t-tests (TOST) of equivalence in means (equal n's)'. The table has 5 columns: a label column and four data columns numbered 1 through 4. The rows are: Test significance levels, α (one-sided); Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$; Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$; Expected difference, $\mu_T - \mu_S$; Common standard deviation, σ ; Power (%); and n per group. The table is currently empty, with all data cells highlighted in light gray. At the bottom of the window, there is a status bar with the text 'For Help, press F1' and 'AUTO RECALC OFF'.

	1	2	3	4
Test significance levels, α (one-sided)				
Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$				
Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$				
Expected difference, $\mu_T - \mu_S$				
Common standard deviation, σ				
Power (%)				
n per group				

The table will come up empty.

In column 1, enter **.05** in the **Test significance levels** row.

Enter **-2.4** in the **Lower equivalence limit** row.

Enter **2.4** in the **Upper equivalence limit** row.

Enter **0** in the **Expected difference** row.

Enter **2.8** in the **Common standard deviation** row.

Enter **80** in the **Power** row, and nQuery calculates the n per group.

	1	2	3	4
Test significance levels, α (one-sided)	0.050			
Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$	-2.400			
Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$	2.400			
Expected difference, $\mu_T - \mu_S$	0.000			
Common standard deviation, σ	2.800			
Power (%)	80			
n per group	25			

For Help, press F1 25.00000 AUTO RECALC OFF

Now, if the test drug were actually a bit more potent than the standard, the n required per group would be greater than 25.

To choose sample size to demonstrate equivalence for a test drug which is more potent than the standard:

Select the first three rows of column 1 and choose the **Edit** menu **Copy** option or press <Ctrl><C> or choose the Copy icon.

To paste the contents of the three rows of column 1 into column 2, place the cursor in column 2 and choose the **Edit** menu **Paste** option or press <Ctrl><V> or choose the Paste icon. The “smart” Paste will paste the values into the appropriate rows.

Enter **.5** in the **Expected difference** row.

Enter **2.8** in the **Common standard deviation** row.

Enter **80** in the **Power** row, and nQuery calculates the n per group.



Two-group t-tests (TOST) of equivalence in means (equal n's)				
	T = S	T > S	3	4
Test significance levels, α (one-sided)	0.050	0.050		
Lower equivalence limit for $\mu_T - \mu_S$, Δ_L	-2.400	-2.400		
Upper equivalence limit for $\mu_T - \mu_S$, Δ_U	2.400	2.400		
Expected difference, $\mu_T - \mu_S$	0.000	0.500		
Common standard deviation, σ	2.800	2.800		
Power (%)	80	80		
n per group	25	29		

When we have an expected difference of .5, we need a group size of 29.

Note that for this example, we have used the **Edit Column Names** option to label the columns in the table. See Chapter 4 *The Edit Menu* for details on the this option.

Example 3

TOST for difference in means crossover


t-tests (TOST) of equivalence in means for a crossover design (MTE1co)

For the study discussed in Example 2 above, suppose that a crossover design were planned instead of a two-group design.

If a balanced 2 x 2 crossover design is to be used instead of a two-group design, and it can be assumed that there are no carryover effects, table MTE1co can be used to determine the necessary sample size.

For a 2 x 2 crossover design, n per group is the number of subjects in each sequence group (AB and BA), so the total sample size is 2n.

To use the appropriate table for this example:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

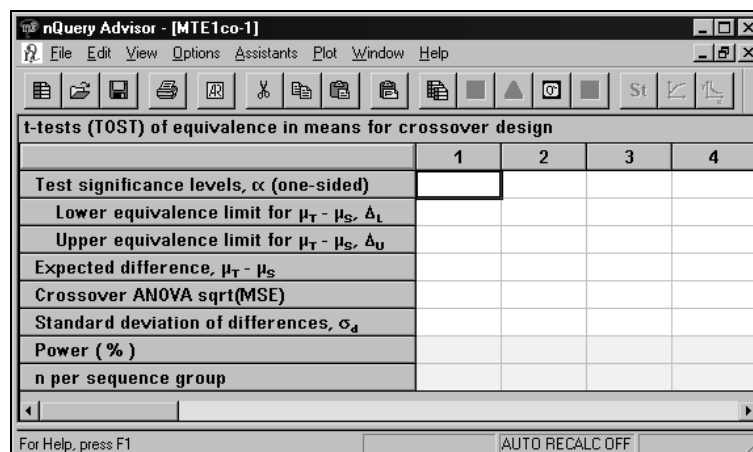
Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Equivalence**.

Click on the **+** sign next to the second choice among the listed analyses, **Two one-sided equivalence tests (TOST) for two-group or crossover designs**, and then select **Two one-sided equivalence tests (TOST) for crossover design**.

Click on **OK**.



	1	2	3	4
Test significance levels, α (one-sided)				
Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$				
Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$				
Expected difference, $\mu_T - \mu_S$				
Crossover ANOVA sqrt(MSE)				
Standard deviation of differences, σ_d				
Power (%)				
n per sequence group				

In column 1, enter **.05** in the **Test significance levels** row.

Enter **-2.4** in the **Lower equivalence limit** row.

Enter **2.4** in the **Upper equivalence limit** row.

Enter **0** in the **Expected difference** row.

Then enter either the square root of the Mean Squared Error from the crossover Analysis of Variance or the standard deviation of differences depending on the information you have available. Whichever value is entered, nQuery will compute the other.

For this example, we assume that the investigator does not have information on the crossover ANOVA MSE, but has performed a small, paired pilot study of two different doses of the new drug. In that study, the standard deviation for each dose was about 2.8 and the correlation between blood levels during the two different periods was observed to be 0.55.

To calculate the standard deviation of differences:

Select **Estimate SD** from the **Assistants** menu, or click on the σ button to get the Estimate Standard deviation dialog box.



Estimate Standard Deviation

☒ From Standard Error

☐ From SD1 and SD2 (pooled SD)

☐ From Range

☐ From Percentile

☐ From Coefficient of Variation

☐ From Upper Confidence Limit

☐ From SD1, SD2, Correlation

☐ For Cluster Sampling

☐ For specified x values

☐ Of residuals (errors)

OK Cancel

Select **From SD1, SD2, Correlation** and click **OK** to bring up the side table.

Calculating standard deviation of differences from SD1, SD2, and correlation				
	1	2	3	4
First condition standard deviation, σ_1				
Second condition standard deviation, σ_2				
Correlation coefficient, ρ				
Standard deviation of differences, σ_d				

Enter the value **2.8** for the **First** and **Second** condition standard deviations.

Enter **0.55** for the **Correlation coefficient**.

Calculating standard deviation of differences from SD1, SD2, and correlation				
	1	2	3	4
First condition standard deviation, σ_1	2.800			
Second condition standard deviation, σ_2	2.800			
Correlation coefficient, ρ	0.550			
Standard deviation of differences, σ_d	2.656			

We find that the expected standard deviation of differences would be 2.656.

To copy the estimated the standard deviation differences calculated in this side table, click on **2.656** and use the **Copy** option. Then switch to the sample size table. Use the **Edit** menu **Paste Unformatted** option to paste the value 2.656 into the Standard deviation of differences row in the crossover equivalence table.

Note: Chow and Liu (1992, pages 52 and 53) define the period differences as $(1/2)(y_{1i} - y_{2i})$, so that their "standard deviation of differences" is $\sigma_d/2$.

Enter **80** in the **Power** row, and nQuery calculates the n per sequence group. Since there are two sequence groups in a standard 2x2 crossover, the total sample size required would be 14.

The screenshot shows the nQuery Advisor window with the title bar 'nQuery Advisor - [MTE1co-1]'. The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons for file operations and calculations. The main window displays a table titled 't-tests (TOST) of equivalence in means for crossover design'. The table has columns for parameters and four sequence groups (1, 2, 3, 4). The parameters listed are: Test significance levels, α (one-sided); Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$; Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$; Expected difference, $\mu_T - \mu_S$; Crossover ANOVA sqrt(MSE); Standard deviation of differences, σ_d ; Power (%); and n per sequence group. The values for sequence group 1 are: 0.050, -2.400, 2.400, 0.000, 1.878, 2.656, 80, and 7. The status bar at the bottom shows 'For Help, press F1', '7.000000', and 'AUTO RECALC OFF'.

	1	2	3	4
Test significance levels, α (one-sided)	0.050			
Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$	-2.400			
Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$	2.400			
Expected difference, $\mu_T - \mu_S$	0.000			
Crossover ANOVA sqrt(MSE)	1.878			
Standard deviation of differences, σ_d	2.656			
Power (%)	80			
n per sequence group	7			

If a crossover design is appropriate, and our assumptions about the correlation between results for the two periods are correct, this crossover design could use 14 instead of the 50 subjects required for the two-group design.

Note that other references for sample size for differences in means for the crossover design may use the coefficient of variation, $CV = \sigma_e / \mu_s$, where $\sigma_e = \sqrt{MSE}$ from the crossover analysis of variance, for table and figure entry. Some references may provide total sample size instead of sample size per sequence group. The following table shows how to reproduce three examples from Phillips' Table 1 (see reference pane for table MTE1co) . Test and standard are considered equivalent if the mean difference is within 20% of the standard; the crossover ANOVA \sqrt{MSE} is 20% or 30%. The total sample sizes are 24, 70, 20.

t-tests (TOST) of equivalence in means for crossover design (MTE1co)

	1	2	3
Test significance levels, α (one-sided)	0.050	0.050	0.050
Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$	-0.200	-0.200	-0.200
Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$	0.200	0.200	0.200
Expected difference, $\mu_T - \mu_S$	0.000	0.100	0.000
Crossover ANOVA sqrt(MSE)	0.200	0.200	0.300
Standard deviation of differences, σ_d	0.283	0.283	0.424
Power (%)	90	90	80
n per sequence group	12	35	20

To paste an entire nQuery table into a document as we have done here, select **Print Table to Clipboard** in the **Edit** menu or the right click menu for the table. The table formatting



and Greek symbols will be preserved, and you can select the font and font size for the table. See Chapter 4 *The Edit Menu* for details.

Two-sided, “neither better nor worse”, bio-equivalence testing

TOST for Ratio of means (analysis in log scale)

Investigators may prefer to express equivalence bounds in terms of the ratio of test to standard means. When the data in their original scale have a log-normal distribution, it will make sense to make a log transformation and to analyze the data in the log scale. (We assume throughout that natural logs have been taken).

Hypotheses about the ratio of means in the original scale can then be expressed in terms of hypotheses about the difference of means in the log scale.

The hypotheses are stated as:

$$H_{01}: \mu_T / \mu_S \leq \Delta_L$$

$$H_{02}: \mu_T / \mu_S \geq \Delta_U$$

which correspond to:

$$H_{01}: \ln(\mu_T / \mu_S) = \ln(\mu_T) - \ln(\mu_S) \leq \ln(\Delta_L)$$

$$H_{02}: \ln(\mu_T / \mu_S) = \ln(\mu_T) - \ln(\mu_S) \geq \ln(\Delta_U)$$

These hypotheses are tested using two one-sided t tests for data in the log scale.

For two group designs, when information on the value of the relevant standard deviation is available in the log scale, use table MTE1tg Two-group t tests (TOST) of equivalence in means. See Example 4 in this chapter.

When information about variability is only available in the original scale (the CV for the original scale is known), use Table MTE2tg Two-group t-tests (TOST) for ratio of means (using log scale.) See Example 5 in this chapter.

For crossover designs, use MTE2co Crossover t tests (TOST) for ratio of means (using logscale). See Example 6 in this chapter.

Example 4

Two-group t tests TOST for ratio of means using log scale (MTE1tg)

You can use MTE1tg to obtain sample size or power for a two group TOST equivalence test for the ratio of means when the analysis will be in the log scale and a standard deviation of differences is available for the log transformed data.

To evaluate whether the blood level profile for two different dosage forms is equivalent, a two group design with equal n's is to be conducted.


The dosage forms are:

1. two capsules of 250 mg
2. one capsule of 500 mg plus one capsule of placebo

The outcome measure is AUC (area under the curve) for 48 hours after administration of the dose. Previous studies with the standard (two 250 mg capsules) gave a mean $\ln(\text{AUC})$ of 5.4 with a standard deviation of $\ln(\text{AUC})$ of 0.20.

The investigator wants to establish that the ratio of means (in the original scale) is within the interval (.8, 1.25) which corresponds to an interval for the difference of means in the natural log scale of (-.223, .223).

To use the appropriate table for this example:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Equivalence**.

Click on the + sign next to the second choice among the listed analyses, **Two one-sided equivalence tests (TOST) for two-group or crossover designs**, and then select **Two one-sided equivalence tests (TOST) for two group design**.

Click on **OK**.



nQuery Advisor - [MTE1tg-1]

File Edit View Options Assistants Plot Window Help

Two-group t-tests (TOST) of equivalence in means (equal n's)

	1	2	3	4
Test significance levels, α (one-sided)				
Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$				
Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$				
Expected difference, $\mu_T - \mu_S$				
Common standard deviation, σ				
Power (%)				
n per group				

For Help, press F1

AUTO RECALC OFF

Enter **.05** for the test significance levels.

Enter lower and upper and lower equivalence limits of **-.223** and **+.223**.

Enter expected difference of **0** ($\ln(1) = 0$) since we assume that the two dosage forms do in fact have the same mean blood levels.

nQuery Advisor - [MTE1tg-1]

File Edit View Options Assistants Plot Window Help

Two-group t-tests (TOST) of equivalence in means (equal n's)

	1	2	3	4
Test significance levels, α (one-sided)	0.050			
Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$	-0.223			
Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$	0.223			
Expected difference, $\mu_T - \mu_S$	0.000			
Common standard deviation, σ				
Power (%)				
n per group				

For Help, press F1

AUTO RECALC OFF

Enter common standard deviation of **.2**, and Power equal to **90**.

Two-group t-tests (TOST) of equivalence in means (equal n's)				
	1	2	3	4
Test significance levels, α (one-sided)	0.050			
Lower equivalence limit for $\mu_T - \mu_S, \Delta_L$	-0.223			
Upper equivalence limit for $\mu_T - \mu_S, \Delta_U$	0.223			
Expected difference, $\mu_T - \mu_S$	0.000			
Common standard deviation, σ	0.200			
Power (%)	90			
n per group	19			

Then nQuery calculates the n per group to be 19.

Example 5

TOST for ratio of means using log scale

Two-group t-tests TOST for ratio of means (using log scale) (MTE2tg)

Returning to the study under discussion in Example 4, we now suppose that the original data were not available so that the standard deviation in the log scale could not be estimated directly. However, the mean and standard deviation for AUC in the original scale had been reported as 230 and 45, respectively, yielding a coefficient of variation for the standard ($CV = \sigma_s / \mu_s$) of $45/230 = 0.196$.

When the standard deviation in log scale is not known, table MTE2tg uses the fact that when data are log-normally distributed, the variance in the log scale equals the $\ln(1+CV^2)$ where $CV = \sigma/\mu$.

Note: In some references on computing sample size for this situation, the approximation $\sigma \approx CV$ is used, since for small CV , $\ln(1+CV^2) \approx CV$.

(If you wished to express everything in the natural log scale you could use table MTE1tg as in Example 4. To convert the CV to an estimate of the standard deviation in the log scale, you could select **Estimate SD** from the **Assistants** menu or click on the icon [σ] and select **From Coefficient of Variation**. Then enter the CV and nQuery will compute an estimate of the standard deviation in the log scale; see Chapter 9 *Determining a Value for Standard Deviation*, Example 5 for details.)



To use the appropriate table for this example:



Choose the **File** menu **New** option or click on the New icon button.

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Equivalence**.

Click on the + sign next to the third choice among the listed analyses, **(TOST) for ratio of means (log scale) for two-group or crossover designs**, and then select **TOST for equivalence for ratio of means (logscale) for two-group design**.

Click on **OK**.

The screenshot shows the nQuery Advisor software window. The title bar reads "nQuery Advisor - [MTE2tg-1]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons for file operations and analysis. The main window displays a table titled "Two-group t-tests (TOST) for ratio of means (using log scale) (equal n's)". The table has four columns labeled 1, 2, 3, and 4. The rows are: Test significance levels, α (one-sided); Lower equivalence limit for μ_T / μ_S , Δ_L ; Upper equivalence limit for μ_T / μ_S , Δ_U ; Expected ratio, μ_T / μ_S ; Coefficient of variation, σ_S / μ_S ; Power (%); and n per group. The bottom status bar shows "For Help, press F1" and "AUTO RECALC OFF".

	1	2	3	4
Test significance levels, α (one-sided)				
Lower equivalence limit for μ_T / μ_S , Δ_L				
Upper equivalence limit for μ_T / μ_S , Δ_U				
Expected ratio, μ_T / μ_S				
Coefficient of variation, σ_S / μ_S				
Power (%)				
n per group				

Enter **.05** for the test significance level.

Enter Lower equivalence limit of **.8**, upper equivalence limit **1.25**.

Enter Expected ratio of **1** since we assume that the two drugs are in fact equivalent, and enter Coefficient of variation of **.196**.

Finally, enter **90** for Power, and nQuery calculates an n per group equal to 18.

Two-group t-tests (TOST) for ratio of means (using log scale) (equal n's)				
	1	2	3	4
Test significance levels, α (one-sided)	0.050			
Lower equivalence limit for μ_T / μ_S , Δ_L	0.800			
Upper equivalence limit for μ_T / μ_S , Δ_U	1.250			
Expected ratio, μ_T / μ_S	1.000			
Coefficient of variation, σ_S / μ_S	0.196			
Power (%)	90			
n per group	18			


Example 6

TOST for ratio of means using log scale

t-tests (TOST) of equivalence in ratio of means for crossover design (natural log scale) (MTE2co)

The investigator wishes to demonstrate that the ratio of the test mean to the standard means is no lower than 0.8 and no higher than 1.25. Data are assumed to be log normally distributed. Based on a pilot crossover study, the MSE for the log transformed data was observed to be 0.03922, its square root is 0.198.

To use the appropriate table for this example:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Equivalence**.

Click on the + sign next to the third choice among the listed analyses, **(TOST) for ratio of means (log scale) for two-group or crossover designs**, and then select **TOST for equivalence for ratio of means (logscale) for crossover design**.

Click on **OK**.



nQuery Advisor - [MTE2co-1]

File Edit View Options Assistants Plot Window Help

t-tests (TOST) of equivalence in ratio of means for crossover design (natural log scale)

	1	2	3	4
Test significance levels, α (one-sided)				
Lower equivalence limit for $\mu_T / \mu_S, \Delta_L$				
Upper equivalence limit for $\mu_T / \mu_S, \Delta_U$				
Expected ratio, μ_T / μ_S				
Crossover ANOVA, $\sqrt{\text{MSE}}$ (ln scale)				
SD differences, σ_d (ln scale)				
Power (%)				
n per sequence group				

Enter **.05** for the test significance level.

Enter Lower equivalence limit of **.8**, upper equivalence limit **1.25**.

Enter Expected ratio of **1** since we assume that the two drugs are in fact equivalent, and enter the square root of Crossover ANOVA Mean Squared Error, **.198**. nQuery will compute the SD differences of **.280**.

Finally, enter **90** for Power, and nQuery calculates an n per sequence group equal to 10, so the total sample size for this crossover design will need to be 20.

In the second column, we use a larger value for the square root MSE, 0.2934.

To start filling column 2, select the first four rows in column 1, and choose the **Edit** menu **Copy** option.

Place your cursor in column 2 and choose the **Edit** menu **Paste** option to fill the first four rows..

Enter **.294** for the square root of the crossover ANOVA MSE. nQuery will compute the SD differences of **.416**.

Finally, enter **90** for Power, and nQuery calculates an n per sequence group equal to 20. So a total of 40 subjects would be required for this 2x2 crossover design.

The screenshot shows the nQuery Advisor interface for a crossover design. The table below represents the data entered in the software.

t-tests (TOST) of equivalence in ratio of means for crossover design (natural log scale)				
	1	2	3	4
Test significance levels, α (one-sided)	0.050	0.050		
Lower equivalence limit for $\mu_T / \mu_S, \Delta_L$	0.800	0.800		
Upper equivalence limit for $\mu_T / \mu_S, \Delta_U$	1.250	1.250		
Expected ratio, μ_T / μ_S	1.000	1.000		
Crossover ANOVA, $\text{sqrt}(\text{MSE})$ (ln scale)	0.198	0.294		
SD differences, σ_d (ln scale)	0.280	0.416		
Power (%)	90	90		
n per sequence group	10	20		

This example is taken from the paper by Diletti, E., Hauschke, D., Steinijans, V.W. (1991) (See References pane.) To compare these results to those in the Diletti, Hauschke, Steinijans paper, note that these authors transform MSE to "CV" for table entry using the formula " $\text{CV} = \sqrt{[\exp(\text{MSE}) - 1]}$ ".

Two-sided, “neither better nor worse”, bio-equivalence testing

Ratio of means (analysis in original scale)

Investigators may prefer to express equivalence bounds in terms of the ratio of test to standard means.

Hypotheses about the ratio of means in the original scale can be expressed as:

$$H_{01}: \mu_T / \mu_S \leq \Delta_L$$

$$H_{02}: \mu_T / \mu_S \geq \Delta_U$$

When the data in their original scale have a normal distribution, the two one-sided t tests differ somewhat from the standard form of the t test. See the Appendix and the reference panes for the relevant tables for references.

The (Sasabuchi) t-statistic of H_{01} is given by:

$$t = \frac{\bar{x}_T - \Delta_L \bar{x}_S}{s_p \sqrt{\frac{1}{n_T} + \frac{\Delta_L^2}{n_S}}}$$

The corresponding confidence interval is given by use of Fieller's approach.



Example 7 shows sample size computations for a two-group design, while Example 8 shows sample size computations for a crossover design.

Example 7

TOST for ratio of means using original scale for two-group design (MTE3)


We return to the study discussed in Example 2, but we now state the hypotheses directly in terms of the ratio of means

$$H_{01}: \mu_T / \mu_S \leq .85$$

$$H_{02}: \mu_T / \mu_S \geq 1/.85 = 1.1765$$

The coefficient of variation for the standard is assumed to be $CV = 2.8/16 = 0.175$.

To use the appropriate table for this example:

Choose the **File** menu **New** option or click on the New icon button .

In the Study Goal and Design Box, you will see three columns of options.

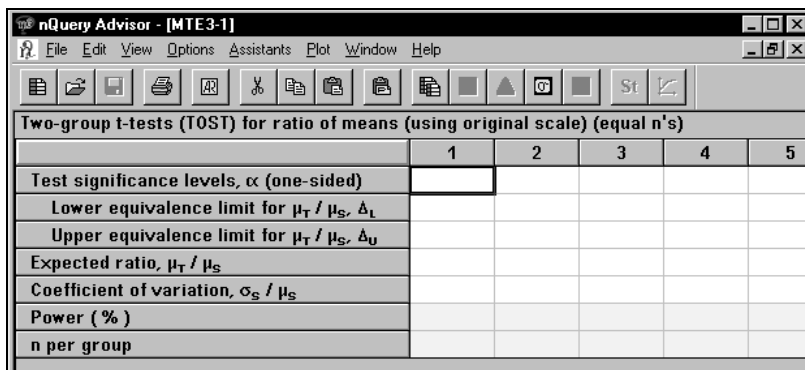
Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Equivalence**.

Select the fourth choice among the listed analyses, **TOST for ratio of means for two-group design (original scale)**.

Click on **OK**.



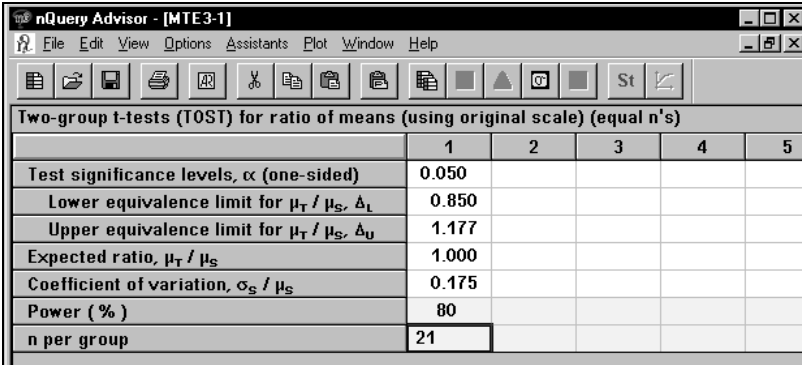
	1	2	3	4	5
Test significance levels, α (one-sided)					
Lower equivalence limit for μ_T / μ_S , Δ_L					
Upper equivalence limit for μ_T / μ_S , Δ_U					
Expected ratio, μ_T / μ_S					
Coefficient of variation, σ_S / μ_S					
Power (%)					
n per group					

Enter **.05** for the test significance level.

Enter Lower equivalence limit of **.85**, upper equivalence limit **1.1765**.

Enter Expected ratio of **1**, and Coefficient of variation of **.175**.

Finally, enter **80** for Power, and nQuery calculates an n per group equal to 21.



The screenshot shows the nQuery Advisor window titled "nQuery Advisor - [MTE3-1]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains icons for file operations, calculations, and plotting. The main window displays a table for "Two-group t-tests (TOST) for ratio of means (using original scale) (equal n's)".

	1	2	3	4	5
Test significance levels, α (one-sided)	0.050				
Lower equivalence limit for $\mu_T / \mu_S, \Delta_L$	0.850				
Upper equivalence limit for $\mu_T / \mu_S, \Delta_U$	1.177				
Expected ratio, μ_T / μ_S	1.000				
Coefficient of variation, σ_S / μ_S	0.175				
Power (%)	80				
n per group	21				

Note that the sample size required for this formulation of the problem is a bit smaller than that seen in Example 2, since the upper limit here is a bit wider than the 2.4 used for the upper limit there ((1.1765) 16 = 18.824, so 18.824-16 = 2.824).

Example 8

TOST for ratio of means using original scale for crossover design (MTE4)

For this example we use the data from Table 3.6.1 in Chow SC, Liu JP (1992) *Design and Analysis of Bioavailability and Bioequivalence Studies*, Marcel Dekker, Inc in which a tablet form of the dose (test) was to be compared to an oral form (standard or reference) using a crossover design with the AUC for the first 32 hours as the outcome of interest. In this case, the data were felt to be reasonably normal in the original scale.

The mean for the standard was about 82, the intra-subject MSE was 167.25, which yields an intra-subject CV of $12.9/82 = .158$, and the inter-subject MSE was 736.89, so that $2\sigma_s^2$ is estimated as $736.89-167.25$ and $\sigma_s^2 = 284.82$ (see Table 3.5.1 in Chow and Liu), and the between-subject CV as $16.88/82 = .206$. We are planning a new study of the oral form (standard) in comparison with a different tablet formulation. How many subjects will be required for a crossover design to establish that the ratio of means is in the interval (.90, 1.111)?



To use the appropriate table for this example:



Choose the **File** menu **New** option or click on the New icon button.

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Equivalence**.

Select the fifth choice among the listed analyses, **TOST for ratio of means for crossover design (original scale)**.

Click on **OK**.

	1	2	3	4
Test significance levels, α (one-sided)				
Lower equivalence limit for $\mu_T / \mu_S, \Delta_L$				
Upper equivalence limit for $\mu_T / \mu_S, \Delta_U$				
Expected ratio, μ_T / μ_S				
Coefficient of variation between subjects, CV_B				
Coefficient of variation, intrasubject, CV_i				
Power (%)				
n per group				

Enter **.05** for significance level.

Enter Lower equivalence limit of **.90**, upper equivalence limit **1.111**.

Enter Expected ratio of **1**, and Coefficient of variation between subjects of **.206**.

Enter Coefficient of variation intra-subject of **.158**.

Finally, enter **90** for Power, and nQuery calculates an n per sequence group equal to 26. So the 2x2 crossover design will require a total of 52 subjects.

Crossover design TOST for ratio of means (using original scale)				
	1	2	3	4
Test significance levels, α (one-sided)	0.050			
Lower equivalence limit for μ_T / μ_S , Δ_L	0.900			
Upper equivalence limit for μ_T / μ_S , Δ_U	1.111			
Expected ratio, μ_T / μ_S	1.000			
Coefficient of variation between subjects, CV_B	0.206			
Coefficient of variation, intrasubject, CV_i	0.158			
Power (%)	90			
n per group	26			

Note that sample size and power will be more sensitive to changes in the intrasubject CV than in the intersubject CV.

Relationships between sample size methods for standard tests, confidence intervals, and equivalence tests

What are the interrelationships between tests, confidence intervals and equivalence demonstrations? How do required sample sizes differ, depending on the method of analysis planned for the study? We discuss these questions in the context of a two-group design with equal sample sizes where means are to be compared.

Investigators sometimes ask why the sample size required for a test of equivalence between two means is markedly larger than that required for a confidence interval for the difference in means when the parameters used in the calculations appear to be the same. The explanation lies in the fact that the confidence interval approach does not take into account the observed value of the difference in means but only the interval width. In contrast, the equivalence test takes into account both the observed value of the difference in means and the interval width. To simplify the presentation, we will use mainly large sample formulas, but the logic is the same for large or small samples.

Test for equality of two means

The standard test for comparison of means is the two-sample t test.

The usual null hypothesis is that the means in the two groups are the same:

$$H_0: \mu_1 - \mu_2 = 0.$$



An alternative hypothesis for a one-sided level α test is $H_1: \mu_1 - \mu_2 = \delta\sigma$.

The null hypothesis will be rejected if the observed difference in means is greater than or equal to

$$t_{1-\alpha, 2(n-1)} s_p \sqrt{\frac{2}{n}}$$

The probability that the observed difference in means will be greater than the value stated above is:

α when the null hypothesis is true

$1-\beta$ the power of the test, when the specified alternative hypothesis is true.

We choose the sample size n so that $1-\beta$ will equal a desired power, such as 0.90.

For example, for $\alpha = .05$, and $1-\beta = 0.9$, and $\sigma = 6$ and $\delta = 0.5$, then the required sample size is 70 per group. For $\alpha = .10$, and $1-\beta = 0.95$, and $\sigma = 6$ and $\delta = 0.5$, then the required sample size is 69 per group. See nQuery table (MTT0) below.

Note: When n is large, reversal of the values for α and β will not change the required sample size.

For the rest of this chapter, we will display sample size table results as they appear in Print Table to Clipboard output, since we are interested in demonstrating the relationships between methods rather than the operation of the program. (For details on the Print Table to Clipboard option, see Chapter 4, *The Edit Menu*. That chapter also discusses how to select the font for the output.)

Two group t-test of equal means (equal n's)

	$\alpha = .05, \beta = .10$	$\alpha = .10, \beta = .05$
Test significance level, α	0.050	0.100
1 or 2 sided test?	1	1
Difference in means, $\mu_1 - \mu_2$	3.000	3.000
Common standard deviation, σ	6.000	6.000
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	0.500	0.500
Power (%)	90	95
n per group	70	69

If the alternative hypothesis were $H_1: \mu_1 - \mu_2 = -\delta\sigma$, then the one-sided level α test would reject when the observed difference in means is less than or equal to

$$-t_{1-\alpha, 2(n-1)} s_p \sqrt{\frac{2}{n}}$$

For a two-sided level α test, we commonly divide the α level in half and reject the null hypothesis if the observed difference in means is less than or equal to

$$-t_{1-\alpha/2, 2(n-1)} s_p \sqrt{\frac{2}{n}}$$

or greater than or equal to

$$t_{1-\frac{\alpha}{2}, 2(n-1)} s_p \sqrt{\frac{2}{n}}$$

Confidence interval for difference in two means

The $100(1-\alpha)\%$ one-sided confidence interval for $\mu_1 - \mu_2$ will have lower bound

$$\bar{x}_1 - \bar{x}_2 - t_{1-\alpha, 2(n-1)} s_p \sqrt{\frac{2}{n}}$$

If this confidence interval does not include the value 0.0, then the null hypothesis that the difference in means is 0.0, would be rejected at the $100\alpha\%$ level.

A two-sided $100(1-\alpha/2)\%$ confidence interval for $\mu_1 - \mu_2$ will typically have upper and lower limits given by

$$\bar{x}_1 - \bar{x}_2 \pm t_{1-\frac{\alpha}{2}, 2(n-1)} s_p \sqrt{\frac{2}{n}}$$

Sample size methods for confidence intervals focus only on the size of the distance between the observed mean difference and the end of the confidence interval; for the one-sided interval case, this difference is

$$t_{1-\alpha, 2(n-1)} s_p \sqrt{\frac{2}{n}}$$

In the large sample case where we can substitute a z value for the t value and assume that the standard deviation is known so we can substitute σ for s_p and this distance becomes

$$z_{1-\alpha} \sigma \sqrt{\frac{2}{n}}$$

The sample size required to obtain an interval for which this distance is ω is

$$n = \frac{2z_{1-\alpha}^2 \sigma^2}{\omega^2}$$



For the example above, we use table MTC0 to request a 95% one-sided confidence interval to have width 3.0 when $\sigma = 6$; this will require a sample size of 22 per group. The MTC0 table below uses the large sample formula.

Confidence interval for difference of two means based on z (large equal n's)

	1
Confidence level, $1-\alpha$	0.950
1 or 2 sided interval?	1
Common standard deviation, σ	6.000
Distance from mean to limit, ω	3.000
n per group	22

When the standard deviation σ is not known and must be estimated from the data, the distance from the observed mean difference to the end of the confidence interval will vary, depending on the observed value of s_p . About half of the confidence interval widths will be shorter, and about half will be longer than required. To obtain the sample size necessary to ensure an interval which will be shorter than required with a specified probability requires an iterative method rather than a simple formula.

The next table, MTC1, utilizes coverage probability. For the interval width to be shorter than 3 with 85% probability, it would be necessary to have a sample size of 27 per group.

Confidence interval for difference of two means (coverage probability) (equal n's)

	1	2
Confidence level, $1-\alpha$	0.950	0.950
1 or 2 sided interval?	1	1
Coverage probability, $1-\gamma$	0.500	0.850
Common standard deviation, σ	6.000	6.000
Distance from difference to limit, ω	3.000	3.000
n per group	23	27

What do these results mean in terms of power? We can use the Two-group t test of equal means (MTT0) to estimate the power of this design. (Note that we have edited out the unused rows for the two group means.)

Two group t-test of equal means (equal n's)

	1	2	3	4
Test significance level, α	0.050	0.050	0.050	0.050
1 or 2 sided test?	1	1	1	1
Difference in means, $\mu_1 - \mu_2$	3.000	3.000	3.000	3.000
Common standard deviation, σ	6.000	6.000	6.000	6.000
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	0.500	0.500	0.500	0.500
Power (%)	90	49	50	56
n per group	70	22	23	27

With 22 per group, the test would have 49% power, and with 27 per group, the test would have 56% power. The power is near 50% in both cases, because half the time the observed difference in means will be less than 3, even when the true difference is equal to 3.

An interval which corresponds to the test situation is an interval which has chance $1-\beta$ of excluding the null hypothesis value for $\mu_1 - \mu_2$ when a specified alternative is true. To obtain such an interval, we would need the same sample size as for the test. That is, we are requiring that, when the true difference in means is 3, the lower limit of the one-sided 95% confidence interval will be greater than 0.0 with probability $1-\beta$.

Using MTC1 again for a sample size of 70, we get the following table. For this example, a sample size of 70 results in a confidence interval which extends no more than 1.675 below the observed difference in means in 50% of studies and no more than 1.781 below in 85% of studies.

Confidence interval for difference of two means (coverage probability) (equal n's)

	1	2
Confidence level, $1-\alpha$	0.950	0.950
1 or 2 sided interval?	1	1
Coverage probability, $1-\gamma$	0.500	0.850
Common standard deviation, σ	6.000	6.000
Distance from difference to limit, ω	1.675	1.781
n per group	70	70

12. Side Tables/Compute Effect Size

This advanced tutorial uses analysis of variance examples to illustrate use of the side tables which are designed to help you compute the effect sizes required for more complex sample size tables.

You can get specific Compute Effect Size tables when you are using nQuery Advisor tables for more than two groups, as well as several other sample size tables. To access the Compute Effect Size tables, use either the Assistants menu Compute Effect Size option or the icon:



Compute Effect Size

Compute Effect Size side tables allow you to enter details of the alternative hypothesis and have nQuery compute the necessary summary values for you.

This tutorial illustrates the simplest type of Compute Effect Size side table for an example using the analysis of variance. See examples for other tables in the relevant chapters in the manual.

Side Table Name

For side tables requiring specification of a Side table name, see examples in Chapters 14, 15, and 16.

Example 1


One-way analysis of variance (MGT0)

This chapter uses a blood pressure example to illustrate the nQuery Advisor One-way analysis of variance (MGT0) table and its effect size side table. Note that Chapter 8 also used this blood pressure example to illustrate the determination of necessary sample sizes for two-group confidence intervals and equivalence testing.

In this trial, we are comparing the reduction in blood pressure resulting from use of a Placebo, the current Standard drug, and a New Drug. From previous studies with the Standard drug, we have an estimate of about 6mmHg for the standard deviation for reduction in blood pressure. In the past, the Placebo has resulted in reductions of about 5mmHg, and the Standard drug in reductions of about 12mmHg.

The study as a whole will be analyzed using a one-way analysis of variance at the .05 significance level.

To access the one-way analysis of variance sample size table:

Select the **File** menu **New** option or click on the **New** button .

In the Study Goal and Design Box, you will see three columns of options. You will select analysis **MGT0**:

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **>Two** groups.

Under **Analysis method**, select **Test**.

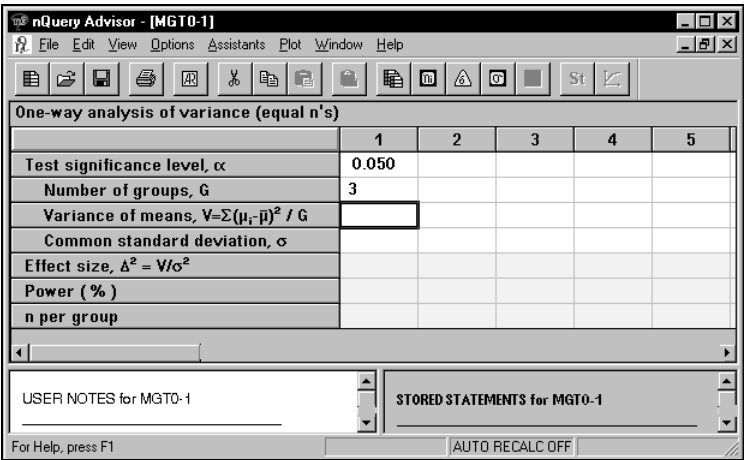
Select **One-way analysis of variance**.

Click on the **OK** button to accept your choice. The empty analysis of variance table will appear.

To use the one-way analysis of variance sample size table:

Enter **.05** in the **Test significance level** row and press <Enter> or the down arrow.

Enter **3** in the **Number of groups** row and press <Enter> or the down arrow. Your sample size table will look like the following table.



The screenshot shows the nQuery Advisor software interface. The title bar reads "nQuery Advisor - [MGT0-1]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. Below the menu bar is a toolbar with various icons. The main window displays a table titled "One-way analysis of variance (equal n's)". The table has columns for parameters and five columns for sample sizes (1, 2, 3, 4, 5). The parameters listed are: Test significance level, α (0.050), Number of groups, G (3), Variance of means, $V = \sum (\mu_i - \bar{\mu})^2 / G$, Common standard deviation, σ , Effect size, $\Delta^2 = V/\sigma^2$, Power (%), and n per group. The rows for Effect size, Power, and n per group are highlighted in yellow. At the bottom of the window, there are sections for "USER NOTES for MGT0-1" and "STORED STATEMENTS for MGT0-1", and a status bar indicating "For Help, press F1" and "AUTO RECALC OFF".

	1	2	3	4	5
Test significance level, α	0.050				
Number of groups, G	3				
Variance of means, $V = \sum (\mu_i - \bar{\mu})^2 / G$					
Common standard deviation, σ					
Effect size, $\Delta^2 = V/\sigma^2$					
Power (%)					
n per group					

This figure does not show the yellow highlighting that appears on your screen. nQuery Advisor can provide answers for any of the highlighted yellow rows. For example, Effect size, Power, and n per group are yellow when you have the One-




way analysis of variance table on your screen. The nQuery Advisor program can calculate any of the three rows: Power, n per group, or Effect size when you enter values for the other two after entering values for all other required rows.

The analysis of variance tests the null hypothesis that the means in all G groups are equal. The alternative hypothesis is that the means in the G groups are not all equal.

In general, you will know what means you expect for each group, but you will not have computed the variance of these means, the measure of how far apart the three means are. The nQuery Advisor program offers the Compute Effect Size option to compute the variance of means for you. In a two-step procedure, you bring up the Compute Effect Size side table, then you enter the expected mean for each group and the variance of means is computed automatically.

To calculate the variance of means by using the Compute Effect Size option:

Select the **Assistants** menu, **Compute Effect Size** option, or click on , the **Compute Effect Size** icon. You will see the Compute Effect Size table for the One-way analysis of variance.

MGT0-1: Aid for col 1 -- One-way analysis of variance (equal n's)	
Transfer Close Restore Clear Cut Copy Paste Print	
Group	Mean
1	
2	
3	
Variance of means, $V = \sum (\mu_i - \bar{\mu})^2 / G$	

The Compute Effect Size side table appears in the lower right of the nQuery Advisor window. If your table is not expanded to its full size, you may find it necessary to expand the window in order to see the Compute Effect Size table.

Note that the table shows three groups. Your entry of 3 in the Number of groups row of the sample size table determined the number of groups in this side table.

To record the expected mean for the Placebo group, enter **5** in the **Group 1** row and press <Enter> or the down arrow.

To record the expected mean for the Standard group, enter **12** in the **Group 2** row and press <Enter> or the down arrow.

Here we expect the New Drug to produce about the same changes as the Standard.

To record the expected mean for the New Drug group, enter **12** in the **Group 3** row and press <Enter> or the down arrow. The side table will calculate the variance of the means automatically.

MGT0-1: Aid for col 1 -- One-way analysis of variance (equal n's)							
	Transfer	Close	Restore	Clear	Cut	Copy	Paste
Group	Mean						
1	5.000						
2	12.000						
3	12.000						
Variance of means, $V = \sum(\mu_i - \bar{\mu})^2 / G$	10.889						

Note that the side table is fully labeled with the abbreviation name of the sample size table, the full name of the sample size table, and the number of the column being calculated. Thus, you can have one Compute Effect Size side table for each column in the sample size table.

You can clear, cut, copy, paste, and print the contents of the side table. See the next section of this chapter, *Side Table Buttons*, for details. This example continues on page 12-7.

When you save the sample size table, any open Compute Effect Size side table associated with the sample size table will also be saved. This is true even when you have multiple side tables, one for each of several columns.

Side Table Buttons

Although the table in the example above calculates the result automatically, some Compute Effect Size side tables display a Compute button. When you are using a table with a Compute button, click on **Compute** after you have made your entries.

The Compute Effect Size side table displays eight buttons: Transfer, Close, Restore, Clear, Cut, Copy, Paste, and Print.

Transfer Button

The Transfer button copies required values back to the main sample size table and returns the focus to the main table. When you save the sample size table, nQuery saves the contents of the side tables for each column. That information will reappear if you call the table again with the same design parameter values.

Note: The Transfer button becomes active only when the side table is complete.



Close Button

Close will close the side table without transferring the computed values. It does save the entries, so that you can see them the next time you open the side table.

Restore Button

The Restore button is active after effect size results have been transferred to the main table. If you clear all the data from the table using the Clear button, or if you change some entries in the table (with or without clicking on Compute), clicking on the Restore button will restore all the data in the side table to the values which were transferred.

Clear Button

Deletes all the entries and computed values from the side table. A dialog box will appear to confirm that you want to clear the data.

Cut Button

Deletes any highlighted data. The data will be available for pasting within the side table and to other Windows applications.

Copy Button

Copy will copy selected entries to the clipboard for use in an nQuery Advisor sample size table or a side table or any other Windows program.

To use the values from one side table within the next side table:

If you open a side table from another column and want to use the same values as the earlier table, you can copy the values from the first side table and paste them into the new one.

In the first side table, select the entered values and click on the **Copy** button.

In the second side table, place the cursor in the topmost cell, and click on the **Paste** button. The values will be pasted into the side table. (Note that **<Ctrl><V>** does not work here.)

The Paste button on the side table does not act like a “smart” Paste. Thus, when copying and pasting the values from several cells, be sure to place the cursor in the topmost cell, corresponding to the topmost cell selected for copying.

If you want to copy the entire side table for use in a Windows application, you can do that in either of two ways. You can use the menu Print Table to Clipboard

option, or you can use the right click menu Print Table to Clipboard option.. Then you can paste the contents of the side table into another document.

Paste Button

Pastes data which has been Copied to the Clipboard from a Windows application. The Paste button pastes the data into the upper portion of the side table starting from the cursor position. You can not paste into the lower section of a side table.

Print Button

Prints the side table. Clicking on this button will produce the Windows Print dialog box.

When the main sample size table is active you can print the attached side tables without returning the focus to them by selecting Print in the File menu. The nQuery Advisor Printing checklist will appear and you can select printing of the side tables. After you specify which items are to be printed, press OK,. The Windows Print dialog box will appear.

Right-click Menu Options

The right-click menu for the side tables offers the same Edit functions (Copy, Cut, and Paste) as the side table buttons. It also offers the functions Print and Print Table to Clipboard options from the File menu. The Copy, Cut, Paste, and Print options work just the same as described above for the Side Table Buttons.

Copy Entire Side Table to Clipboard for Pasting into External Documents using Print Table to Clipboard option

You can copy side tables from nQuery Advisor and paste them into your Windows application documents. You select the font to be used in the Rich Text Format. The tabular structure, formatting, and Greek symbols are preserved even when you do not retain the Dixon font.

Use the Print Table to Clipboard option to print the entire side table to the Clipboard for pasting into Windows applications, such as Word



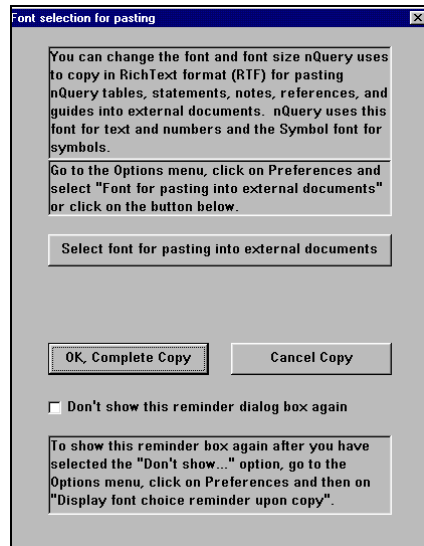
To export the side table with its values to Word or to a different Windows application:

You will use the **Print Table to Clipboard** option in the **Right Click** menu.

To use the **Right Click** menu from the side table, place the cursor anywhere within the side table. Click on the right button on your mouse. The **Right Click** menu appears.

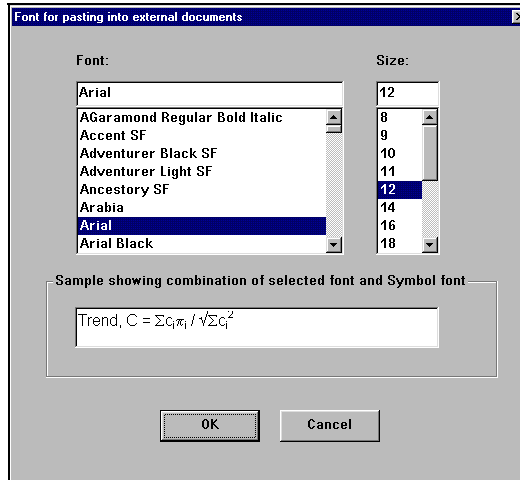
Select **Print Table to Clipboard**.

The first time you select the Print Table to Clipboard option, you will see a message screen telling you how to change the font for the pasted text.



Click **OK Complete Copy** to accept the default Arial font.

If you prefer to select a different font, click on **Select font for pasting into external documents**. You will see the **Font for pasting into external documents** dialog box.



Select a font and a font size, then click **OK** to print to the clipboard.

After you have selected the font you want, you can choose not to see the reminder box again by clicking in the checkbox for that option. You can change the selected font at any time by using the **Option** menu **Preferences** option, and selecting **Font for External Pasting**. You can choose to display the font reminder box again by selecting the **Options** menu **Preferences** option **Display font choice reminder upon copy** option. See Chapter 3. *The File and Options Menus* for full details.

Move to your word processing program and use the **Paste** option to paste the contents of the clipboard. The panel below shows the pasted side table using the Ariel 9 font.

MGT0-1: Aid for col 1 -- One-way analysis of variance (equal n's)

Group	Mean
1	5.000
2	12.000
3	12.000

Variance of means, $V = \sum (\mu_i - \mu)^2 / G$ 10.889

(This Print Table to Clipboard option is also available for the main sample size tables. From a sample size table, you can access the option in two ways: from the **File** menu **Print Table to Clipboard** option or from the **Right Click** menu **Print File to Clipboard** option.)



Continuing Example 1

To transfer the Variance of the means back to the analysis of variance sample size table:

Click on the **Transfer** button. The sample size table will display the calculated variance. The sample size table will become the active table, while the side table becomes inactive.

	1	2	3	4
Test significance level, α	0.050			
Number of groups, G	3			
Variance of means, $V = \sum(\mu_i - \bar{\mu})^2 / G$	10.889			
Common standard deviation, σ				
Effect size, $\Delta^2 = V/\sigma^2$				
Power (%)				
n per group				

	1	2	3	4
2		12.000		
3		12.000		
Variance of means, $V = \sum(\mu_i - \bar{\mu})^2 / G$	10.889			

For Help, press F1 10.88900 AUTO RECALC OFF

We have an estimated standard deviation of 6 and we want 90% power.

To compute the effect size and the sample size:

Enter **6** in the **Common standard deviation** row and press <Enter>. The nQuery Advisor program will compute the Effect Size.

MGT0-1: Main				
One-way analysis of variance (equal n's)				
	1	2	3	4
Test significance level, α	0.050			
Number of groups, G	3			
Variance of means, $V = \sum(\mu_i - \bar{\mu})^2 / G$	10.889			
Common standard deviation, σ	6.000			
Effect size, $\Delta^2 = V/\sigma^2$	0.3025			
Power (%)				
n per group				

Enter **90** in the **Power** row and press <Enter> or press the down arrow. The program will compute the n per group.

MGT0-1: Main				
One-way analysis of variance (equal n's)				
	1	2	3	4
Test significance level, α	0.050			
Number of groups, G	3			
Variance of means, $V = \sum(\mu_i - \bar{\mu})^2 / G$	10.889			
Common standard deviation, σ	6.000			
Effect size, $\Delta^2 = V/\sigma^2$	0.3025			
Power (%)	90			
n per group	15			

This study would require a sample size of 15 in each group, for a total of 45 patients.

Example 2

A different set of means

What if the New Drug does not work as well as the Standard? The means **5**, **12**, and **10** for Groups **1**, **2**, and **3**, respectively, will give the required sample size if the New Drug does not work quite as well as the Standard.

To try a different set of means in the second column:

In the second column of the sample size table, enter **.05** for the **Test significance level** and **3** for the **Number of groups**.

Click on the **Compute Effect Size** icon to bring up the side table.

To use the values from the first side table within the second side table:

Use the Window menu to select the first side table, labeled **Aid for Col 1**.

In the first side table, select the first two values and click on the **Copy** button.



In the second side table, place the cursor in the topmost cell, and click on the Paste button. The values will be pasted into the side table. (Note that this is not a “smart” paste, so you must select the appropriate topmost cell for pasting, and <Ctrl><V> does not work here.)

Enter **10** as the mean for Group 3, and the table will calculate the new Variance of means.

MGT0-1: Aid for col 2 -- One-way analysis of variance (equal n's)		
	Transfer	Close
	Restore	Clear
	Cut	Copy
	Paste	Print
Group	Mean	
1	5.000	
2	12.000	
3	10.000	
Variance of means, $V = \sum(\mu_i - \bar{\mu})^2 / G$	8.667	

Click on the **Transfer** button to bring the variance of means to the second column of the sample size table.

Enter **6** for **Common standard deviation**. The nQuery Advisor program will calculate the Effect size.

Enter **90** for **Power**. The program will calculate the sample size.


MGT0-1: Main				
One-way analysis of variance (equal n's)				
	1	2	3	4
Test significance level, α	0.050	0.050		
Number of groups, G	3	3		
Variance of means, $V = \sum(\mu_i - \bar{\mu})^2 / G$	10.889	8.667		
Common standard deviation, σ	6.000	6.000		
Effect size, $\Delta^2 = V/\sigma^2$	0.3025	0.2407		
Power (%)	90	90		
n per group	15	19		

To be on the safe side, an investigator may decide to enter 20 patients in each group.


To determine the power of this study with 20 per group in the third column:

Use the mouse to select the first five rows of the second column.




Click on the **Edit** menu **Copy** option or , the **Copy** icon, or <Ctrl><C>.

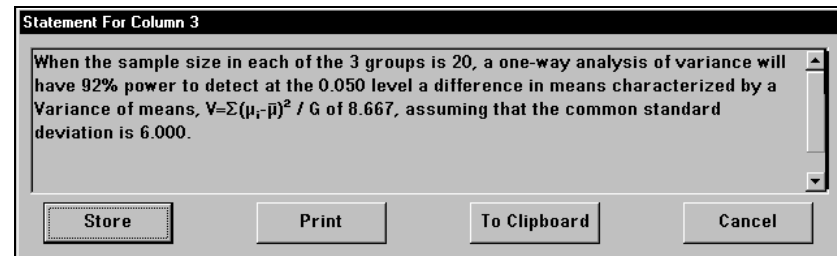
Click on the first cell of the third column.

Click on the **Edit** menu **Paste** option or the **Paste** icon , or <Ctrl><V>. The third column will contain the pasted values for the first five rows.

Enter **20** in the **n per group** row and press <Enter>. The nQuery Advisor program will calculate the power for this study.

To create and customize the statement:


With the cursor in the third column of the sample size table, click on , the **Create Statement** button or right click to bring up the right-click menu and choose the Create Statement option. The statement will appear.




Click on the **Store** button to store the statement with the sample size table. The statement will remain ready for later use, and the Statement box will close.

You are ready to customize the statement, but you cannot edit the statement while it lies in the statement pane. However, you can copy the statement and paste it into the editable Notes section.

Use your cursor to select the statement in the Statement pane.

Click on the **Edit** menu **Copy** option or , the **Copy** icon, or <Ctrl><C>.

Click in the **USER NOTES for MGT0-1** pane to designate the position for the information about to be pasted.

Click on the **Edit** menu **Paste** option or the **Paste** icon , or <Ctrl><V>. The statement will appear in the User Notes pane.



Edit the statement as shown in the following figure.

The screenshot shows a software window titled "MGT0-1: Main" with a tab labeled "One-way analysis of variance (equal n's)". The window contains a table with 5 columns and 8 rows of statistical data. Below the table are two text areas: "USER NOTES for MGT0-1" and "STORED STATEMENTS for MGT0-1".

	1	2	3	4	5
Test significance level, α	0.050	0.050	0.050		
Number of groups, G	3	3	3		
Variance of means, $V = \sum(\mu_i - \bar{\mu})^2 / G$	10.889	8.667	8.667		
Common standard deviation, σ	6.000	6.000	6.000		
Effect size, $\Delta^2 = V/\sigma^2$	0.3025	0.2407	0.2407		
Power (%)	90	90	92		
n per group	15	19	20		

USER NOTES for MGT0-1

When the sample size in each of the 3 groups is 20, a one-way analysis of variance will have 92% power to detect at the 0.050 level a difference in means characterized by an expected Placebo mean reduction of 5 mmHg, and reductions of 12 mmHg for the Standard and 10 mmHg for the New Drug, assuming that the common standard deviation is 6.000.

STORED STATEMENTS for MGT0-1

When you edit the statement within the User Notes section, not only can you edit while viewing the sample size table, but you can also keep the edited statement with the sample size table. When you save the table, you save the edited statement in the Notes section too.

To print Notes or Statements directly:

Right click on the Notes pane or the Statements pane. The right-click menu will appear.

U <u>ndo</u>	Ctrl+Z
C <u>opy</u>	Ctrl+C
C <u>ut</u>	Ctrl+X
P <u>aste</u>	Ctrl+V
P <u>rint</u>	
S <u>elect All</u>	
S <u>pecial Characters ...</u>	

Choose the **Print** option and you will see the Print dialog box.

To print Notes or Statements Using the File Menu Print Option:

Click on the **File** menu **Print** option.

The nQuery Advisor Printing dialog box will appear.

Click to select the **Notes** and/or the **Statement**.

Click on **OK**, and the Print dialog box will appear.

You can, of course, copy and paste the statement into any other program running under Windows. This option allows you to use the statement in wordprocessing, desktop publishing, or presentation software.


Example 3

One-way analysis of variance contrast (MGT1)

Consider a trial similar to the one described earlier in this chapter, but in which we compare a Placebo, a low dose of the new drug, and a high dose of the new drug with the Standard drug in their ability to reduce blood pressure. We expect that the Placebo will result in a reduction of 5mmHg, the Standard in a reduction of 12 mmHg, and the low and high doses of the new drug in reductions of 10.5 and 13.5 mmHg respectively.

Again, we assume that the standard deviation of blood pressure reduction is about 6 mmHg. We want to make sure that the group sizes will be large enough that analysis of variance contrasts can detect differences between Placebo and low dose of the new drug and also between low and high dose of the new drug. The test of a contrast uses an estimate of standard deviation pooled from all the groups studied.

To access the single one-way contrast table:

Select the **File** menu **New** option or click on the **New** button . In the Study Goal and Design Box, you will see three columns of options. You will select analysis **MGT1**:

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **>Two** groups.

Under **Analysis method**, select **Test**.

Select **Single one-way contrast**.

Click on the **OK** button to accept your choice. The empty contrast table will appear.

You will get the sample size table for the **Single one-way between means contrast**. Your table will come up with no numbers. This example shows a table containing .05 in the test significance level row, 2 in the 1 or 2 sided test row, 4 in the Number of groups, G row, and 90 in the power row.



Single one-way between means contrast (equal n's)					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Number of groups, G	4				
Contrast, $C = \sum c_i \mu_i$					
Scale, $D = \text{SQRT}(\sum c_i^2)$					
Common standard deviation, σ					
Effect size, $\Delta = C /(\sigma D)$					
Power (%)	90				
n per group					

To compute effect size:



Click on , the Compute Effect Size icon to bring up the effect size side table.

In the **Means** column, enter **5, 10.5, 13.5, 12** for groups 1 through 4, the placebo group, the low dose of the new drug group, the high dose of the new drug group, and the standard drug group, respectively.

In the **Coefficient** column, enter contrast coefficients of **0, -1, 1, 0** for groups 1 through 4, respectively. This set of coefficients will allow us to contrast the low dose and high dose groups.

Press the **Compute** button in the side table to calculate the Contrast and Scale.

MGT1-1: Main					
Single one-way between means contrast (equal n's)					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Number of groups, G	4				
Contrast, $C = \sum c_i \mu_i$					
Scale, $D = \text{SQRT}(\sum c_i^2)$					

MGT1-1: Aid for col 1 -- Contrast in one-way analysis of variance (equal n's)								
Compute	Transfer	Close	Restore	Clear	Cut	Copy	Paste	Print
Group	Mean	Coefficient						
1	5.000	0.000						
2	10.500	-1.000						
3	13.500	1.000						
4	12.000	0.000						
Contrast, $C = \sum c_i \mu_i$	3.000	$\sum C_i = 0.000$						
Scale, $D = \text{SQRT}(\sum c_i^2)$	1.414							

Press the **Transfer** button in the side table to transfer the Contrast and Scale values to the Single one-way between means contrast table.

Enter **6** in the **Common standard deviation** row and press <Enter>.

The program will calculate the n per group.

MGT1-1.nqa: Main					
Single one-way between means contrast (equal n's)					
	1	2	3	4	
Test significance level, α	0.050				
1 or 2 sided test?	2				
Number of groups, G	4				
Contrast, $C = \sum c_i \mu_i$	3.000				
Scale, $D = \text{SQRT}(\sum c_i^2)$	1.414				
Common standard deviation, σ	6.000				
Effect size, $\Delta = \text{ICI}/(\sigma D)$	0.354				
Power (%)	90				
n per group	85				


A sample size of 85 per group would be required to distinguish between the low and high doses (which differ by 3.0) with 90% power (a total of 340 subjects).

Example 4

One-way analysis of variance contrast (MGT1) (unequal n's)

In Example 3, the placebo and low dose differ by 5.5. We'd like to contrast the placebo group to the low dose group. What sample size would be required if we assigned only half as many subjects to the placebo group? We will use the unequal n's version of the table to answer that question.

To access the single one-way contrast table for unequal n's:

Select the **File** menu **New** option or click on the **New** button . In the Study Goal and Design Box, you will see three columns of options. You will select analysis **MGT1U**:

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **>Two** groups.

Under **Analysis method**, select **Test**.

Select **Single one-way contrast**.

Click on the **Unequal n's** box to select it.



Click on the **OK** button to accept your choice. The empty analysis of variance table will appear.

(If you had the MGT1 sample size table open, and you decided to use MGT1U for unequal n's, it is not necessary to use the File menu New option. You can choose the Assistants menu Unequal n's option to bring up the MGT1U sample size table.) You will get the **MGT1U** sample size table for the **Single one-way between means contrast (unequal n's)**. Your table will come up with no numbers. The following figure shows a table containing .05 in the test significance level row, 2 in the 1 or 2 sided test row, 4 in the Number of groups, G row, and 90 in the power row.

Single one-way between means contrast (unequal n's)					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Number of groups, G	4				
Contrast mean, $C = \sum c_i \mu_i$					
Scale, $D = \text{SQRT}(\sum c_i^2 / r_i)$					
Common standard deviation, σ					
Effect size, $\Delta = C /(\sigma D)$					
Power (%)	90				
N as multiple of n_1 , $\sum r_i = \sum n_i / n_1$					
Total sample size, N					

To compute effect size:



Click on , the Compute Effect Size icon to bring up the effect size side table.

In the **Means** column, enter **5, 10.5, 13.5, 12** for groups 1 through 4, respectively.

In the **Coefficient** column, enter contrast coefficients of **-1, 1, 0, 0** for groups 1 through 4, respectively. This set of coefficients will allow us to contrast the placebo group to the low dose group.

In the r_i column, enter 1, 2, 2, 2 for groups 1 through 4, respectively, to specify that the placebo group will have half the sample size of the experimental groups.

Press the **Compute** button in the side table to calculate the Contrast and Scale values.

MGT1U-1: Main

Single one-way between means contrast (unequal n's)

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Number of groups, G	4			

MGT1U-1: Aid for col 1 -- Contrast in one-way analysis of variance (unequal n's)

Compute Transfer Close Restore Clear Cut Copy Paste Print

Group	Mean	Coefficient	n_i	$r_i = n_i/n_1$
1	5.000	-1.000		1.000
2	10.500	1.000		2.000
3	13.500	0.000		2.000
4	12.000	0.000		2.000
Contrast, $C = \sum c_i \mu_i$	5.500	$\sum C_i = 0.000$		
Scale, $D = \text{SQRT}(\sum c_i^2 / r_i)$	1.225			
Total sample size, N				
N as multiple of n_1 , $\sum r_i = \sum n_i / n_1$				7.000

Press the **Transfer** button to send the Contrast mean and the Scale value to the Simple one-way between means table.

Enter **6** in the **Common standard deviation** row and press <Enter>.

Single one-way between means contrast (unequal n's)

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Number of groups, G	4			
Contrast mean, $C = \sum c_i \mu_i$	5.500			
Scale, $D = \text{SQRT}(\sum c_i^2 / r_i)$	1.225			
Common standard deviation, σ	6.000			
Effect size, $\Delta = C /(\sigma D)$	0.748			
Power (%)	90			
N as multiple of n_1 , $\sum r_i = \sum n_i / n_1$	7.000			
Total sample size, N	134			

A total of 134 subjects would be required if we want to have 90% power for this specific contrast; using 20 in the placebo group and 40 in each of the other three groups (140 total) would be adequate for the comparison of placebo to low dose.



Example 5

One-way analysis of variance contrast (MGT1) (unequal n's)

Using 140 subjects and allowing for unequal sample sizes, what power would be obtained for the comparison between low and high doses?

To determine power for the low and high dose comparison:

In the second column of the MGT1 table from Example 4, enter **.05** in the **test significance level** row, **2** in the **1 or 2 sided test** row, **4** in the **Number of groups, G** row, and **90** in the **power** row.

To compute effect size:



Click on , the Compute Effect Size icon to bring up the effect size side table.

In the **Means** column, enter **5, 10.5, 13.5, 12** for groups 1 through 4, respectively.

In the **Coefficient** column, enter contrast coefficients of **0, -1, 1, 0** for groups 1 through 4, respectively. This set of coefficients will allow us to contrast the low dose group to the high dose group.

In the **n_i** column, enter **20, 40, 40, 40** for groups 1 through 4, respectively, to specify that the placebo group will have half the sample size of the experimental groups.

Press the **Compute** button in the side table to calculate the Contrast and Scale.

MGT1U-1.nqa: Main

Single one-way between means contrast (unequal n's)

	1	2	3	4
Test significance level, α	0.050	0.050		
1 or 2 sided test?	2	2		
Number of groups, G	4	4		

MGT1U-1.nqa: Aid for col 2 -- Contrast in one-way analysis of variance (unequal n's)

Compute Transfer Close Restore Clear Cut Copy Paste Print

Group	Mean	Coefficient	n_i	$r_i = n_i/n_1$
1	5.000	0.000	20.000	1.000
2	10.500	-1.000	40.000	2.000
3	13.500	1.000	40.000	2.000
4	12.000	0.000	40.000	2.000
Contrast, $C = \sum c_i \mu_i$	3.000	$\sum C_i = 0.000$		
Scale, $D = \text{SQRT}(\sum c_i^2 / r_i)$	1.000			
Total sample size, N			140.000	
N as multiple of n_1 , $\sum r_i = \sum n_i / n_1$				7.000

Press the **Transfer** button to send the Contrast Mean and Scale values to the Single one-way between means contrast table, unequal n's.

Enter **6** in the **Common standard deviation** row and press <Enter>.

We get a power of 60%.

MGT1U-1.nqa: Main

Single one-way between means contrast (unequal n's)

	1	2	3	4
Test significance level, α	0.050	0.050		
1 or 2 sided test?	2	2		
Number of groups, G	4	4		
Contrast mean, $C = \sum c_i \mu_i$	5.500	3.000		
Scale, $D = \text{SQRT}(\sum c_i^2 / r_i)$	1.225	1.000		
Common standard deviation, σ	6.000	6.000		
Effect size, $\Delta = \text{ICI} / (\sigma D)$	0.748	0.500		
Power (%)	90	60		
N as multiple of n_1 , $\sum r_i = \sum n_i / n_1$	7.000	7.000		
Total sample size, N	134	140		

Although a total sample size of 140 was adequate for the comparison between placebo and low dose, it would not have sufficient power for the comparison between low and high doses.



Remember that you can print the sample size table, the side tables, notes, or statements. You can also copy the contents of the sample size table, the side tables, notes, or statements for use in other Windows applications.

Summary

This chapter has led you through a complete tutorial based on a one-way analysis of variance, together with contrasts. You learned how to calculate the variance of the means by using the Compute Effect Size side table, then transfer the calculated value back to the sample size table. You saw that cutting and pasting cell contents can cut down on the number of keystrokes required for additional calculations. Finally, you created and edited the statement for the chosen sample size.

After following this tutorial and the tutorial in Chapter 2, you should have a good grounding in the use of the nQuery Advisor program. As questions arise, you can use the Help system and the other chapters of this manual as references. Remember, the sample size table screen provides four different aids to understanding:

1. The guide card for each row of each table. When you access the guide cards through the View menu Guide option, you can view a short description of the type of entry expected for the row.
2. The name tags for each icon. When your cursor remains on an icon briefly, the name tag appears with a description of the icon.
3. The status line description for each menu item. When your cursor lies on a menu item, a short description of that item appears on the left end of the status bar at the bottom of the screen.
4. The Help system. When you choose the Help menu, you can access the Contents option to get to the Full Index, or you can use the Search option to search the system by keyword.

Note that you will find additional descriptions of the use of side tables in Chapter 5, Chapter 13, Chapter 14, Chapter 15, Chapter 16, and Chapter 17.

13. Repeated Measures and Crossover Designs

In this chapter, we discuss computing sample size and power for designs involving one or more groups of subjects in which the same continuous outcome variable is measured more than once. This is often called a repeated measures study. The simplest example of this type of study is a design with two measurements per subject where the two measurements occur sequentially in time as in a pre-post design, in which subjects are measured before and after an intervention. Other examples of repeated measures designs are:

- measurements are made at multiple sites in the same individual, such as measurements of visual acuity in both right and left eyes,
- a case-control study with individually pair-matched cases and controls,
- acid output is evaluated after a low dose of an acid suppressing drug and then after a high dose,
- subjects have been paired on background variables and then randomized so that one receives intervention A and one receives intervention B, or subjects have been surgically paired, such as in studies of pair-fed rats,
- measurements can be geographically contiguous as in split-plot designs,
- crossover studies in which each subject receives all interventions, but different groups of subjects receive the interventions in different orders.

nQuery Advisor has a number of sample size tables applicable for planning sample size for repeated measures designs.

The following categorization of repeated measures tables reflects their most common usage. However, it should be noted that tables for two or more repeated measures can also be used for power calculations for crossover designs, and some problems might properly be approached with any one of several different sample size tables. When based on the same underlying model, all of these approaches will give the same required sample size. The correspondences between approaches are illustrated in the examples in this chapter and in Chapter 11, *Demonstrating Equivalence*.

Paired Designs, Tests, Confidence Intervals, and Equivalence Tests

MOT1	Paired t test of mean difference equal to zero See Example 4 in this chapter and Example 1 in Chapter 8, <i>Sample Size Tables for Means</i> .
MOC2	Confidence interval for interval in paired means based on z (n large)
MOC3	Confidence interval for difference in paired means based on t (coverage probability)
MOE0	Paired t test of equivalence of means
POT1	McNemar's test (χ^2) of equality of paired proportions
POT1x	Exact sign test of equality of paired proportions
POC1	Confidence interval for $\ln(\Psi_M)$, odds ratio for paired proportions (n large)
POE0	Paired test of equivalence in proportions (n large)
POE1abc	Paired test of equivalence in proportions using confidence interval: a) Lower confidence limit for difference in paired proportions (simulation), b) Upper confidence limit for difference in paired proportions (simulation), c) Two-sided confidence limits for difference in paired proportions (simulation)

2x2 Crossover Designs, Tests and Equivalence Tests

MTT0	Two group t test of equal means See Example 1 in this chapter. See also examples in Chapter 2, <i>Tutorial</i> , and Chapter 18, <i>Regression Tables</i> .
MTE0	Two-group t test of equivalence in means See example in Chapter 11, <i>Demonstrating Equivalence</i> .
MTE1co	Two-group or crossover t test (TOST) of equivalence in means See example in Chapter 11, <i>Demonstrating Equivalence</i> .
MTE2co	Two-group or crossover t tests (TOST) for ratio of means (using log scale) See example in Chapter 11, <i>Demonstrating Equivalence</i> .
MTE4	Crossover design TOST for ratio of means (using original scale) See example in Chapter 11, <i>Demonstrating Equivalence</i> .



Designs with Two or More Repeated Measures

- MOT2 Univariate one-way repeated measures analysis of variance (constant correlation)**
See Examples 2 and 5 in this chapter.
- MOT3 One-way repeated measures contrast (constant correlation)**
See Examples 2, 3 and 6 in this chapter.
- MOT4 Univariate one-way repeated measures analysis of variance (Greenhouse-Geisser correction)**
- MOC4 Confidence interval for one-way repeated measures contrast (constant correlation)**
- MTT3 Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)**
See Example 7 in this chapter

Crossover Designs

nQuery Advisor can easily provide sample size information for common crossover designs where outcome means will be compared. In Example 1, we show how to use the nQuery Advisor table for the two-sample t test (MTT0) to compute sample size for the 2 x 2 crossover (AB,BA) design. For equivalence testing for the 2 x 2 crossover design, see Chapter 11. Examples 2,3,4 show how to use nQuery for crossover designs with more than two periods (a three period three treatment design with all possible sequences, and an ABB, BAA crossover design). Example 7 illustrates the use the sample size table for the two-group repeated measures analysis of variance (MTT3) which can also be used for the 2 x 2 crossover.

Crossover studies are studies in which each subject receives two or more treatments in sequence. Thus, crossover studies are a type of repeated measures study. For example, consider a study to compare the effects of a heartburn relieving drug (Drug A) with a placebo (Drug B). In such a study, we might ask patients with regular heartburn to take the study medication when they have an attack of heartburn and to record their degree of relief using a continuous scale.

Week 1: Patients will take the first study medication for their first heartburn attack.

Week 2: Patients will take no medication to avoid any possible carryover or residual effects of the first drug.

Week 3: Patients will take the second study medication for their first heartburn attack.

Week 1 is the first period in the design and week 3 is the second period in the design. Half the patients will be randomly assigned to receive drug A first and drug B second (sequence AB), while the other half of the patients will receive drug B first and drug A second (sequence BA). We would refer to this study design as a two-treatment, two-period crossover design with sequences AB and BA.

You can use nQuery Advisor to compute sample sizes for crossover designs in which the following assumptions are satisfied.

- **The design is uniform with respect to period effects.** This means that period effects do not appear in the contrasts estimating treatment effects.
- **No carryover or residual effects.** It will usually make no sense to plan a crossover study if carryover or residual effects are expected. In any case, the testing of such effects would seldom be the basis for powering the study.
- **Error variance.** It is assumed that the within-subject covariance matrix satisfies the conditions in which the between subject standard deviation is the same for each treatment/period and that the correlation between pairs of treatments/periods is constant. Under these conditions, the within-subject standard deviation is given by $\sigma_e = \sigma_B \sqrt{1-\rho}$. You must provide an estimate of the within-subject standard deviation, σ_e , or the between subject standard deviation, σ_B , and the between period/treatment correlation, ρ , or of the standard deviation of differences, $\sigma_d = \sqrt{2} \sigma_e = \sqrt{2} \sigma_B \sqrt{1-\rho}$.
- **Note that the standard deviation of differences equals $\sqrt{2} \sqrt{MSE}$** where MSE is the within-group mean squared error from the crossover ANOVA.

Example 1

2 x2 crossover (two-period, two treatment AB,BA) crossover using table for two-sample t (MTT0)

The study design has a total sample size of $2n$ with n subjects receiving sequence AB, and n receiving BA. Thus, the A-B contrast is free of period effects on the average. The basis for the test of treatment effects will be the difference between treatments within each subject, $y_{\text{diff}} = y_1 - y_2$ where y_1 is the period 1 response and y_2 is the period 2 response.

The table for the two-sample t is used to compare the mean difference between the periods for sequence group 1 to the mean difference between the periods for sequence group 2.

Note that, in this context, you must provide an estimate of the standard deviation of differences, $\sigma_d = \sqrt{2} \sigma_e = \sqrt{2} \sigma_B \sqrt{1-\rho}$ where σ_e is the square root of the mean squared error from the crossover ANOVA.



Patients with cancer receive repeated chemotherapy cycles during which the number of neutrophils (a type of white blood cell) decreases. *Neutropenia* occurs when the number of neutrophils decreases below a fixed cut-off.

The study plan is to compare a new therapy to reduce the mean number of days of neutropenia with a placebo, using a 5% level two-sided t test appropriate for a crossover design. Each patient will get the new therapy during one chemotherapy cycle and placebo during another chemotherapy cycle. A new cycle of chemotherapy is not instituted until any previous neutropenia has resolved, and we assume that there are no carryover or residual effects.

The investigator asks whether 30 patients will provide adequate power to detect a drop of 3 days in the duration of neutropenia due to the new therapy. A previous study reported a median of 8 days of neutropenia in a control chemotherapy period with median durations of 3 and 4 days for two combination therapies. A small pilot study for patients receiving two cycles of chemotherapy with no treatment intervention showed median durations of about 6 days and a standard deviation of differences in neutropenia duration between the two cycles of 5.2.

To run this example:

In nQuery Advisor, choose the **File** menu **New** option or click on the **New** Icon button to obtain the Study Goal and Design dialog box.

Click on **Means**, **Two** group, and **Test** and select **Two-sample t test**.

The sample size window for two-group t test of equal means appears.

	1	2	3	4	5
Test significance level, α	.05				
1 or 2 sided test?					
Group 1 mean, μ_1					
Group 2 mean, μ_2					
Difference in means, $\mu_1 - \mu_2$					
Common standard deviation, σ					
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$					
Power (%)					
n per group					

In the significance level row, enter .05.

Enter 2 for a two-sided test.

In sequence group 1, with order “New, Placebo”, we expect that the difference between days of neutropenia for the two periods (Period 1 - Period 2 = New - Placebo) will average -3.0.

In sequence group 2, with order “Placebo, New” we expect that the difference between days of neutropenia for the two periods (Period 1 - Period 2 = Placebo - New) will average +3.0.

Enter -3 in Group 1 mean row.

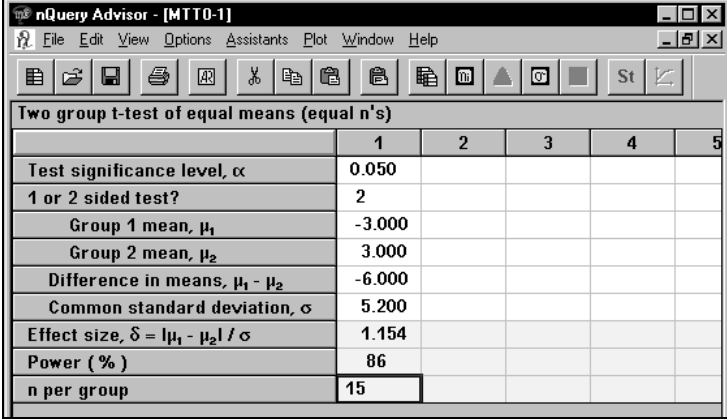
Enter 3 in Group 2 mean row.

The difference in means will be calculated.

The relevant standard deviation is the standard deviation of differences estimated to be 5.2. We want to assess power for a total sample size of 30, so the sample size per sequence group would be 15.

Enter 5.2 in Common standard deviation row, and Effect size will be calculated.

Enter 15 in the n per group row, and we find a power of 86%.



Two group t-test of equal means (equal n's)					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Group 1 mean, μ_1	-3.000				
Group 2 mean, μ_2	3.000				
Difference in means, $\mu_1 - \mu_2$	-6.000				
Common standard deviation, σ	5.200				
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.154				
Power (%)	86				
n per group	15				

Alternatively, you can use the same approach as used in the sample size tables for equivalence testing for crossover designs.

To do this:

Select the first two rows of column 1.

Use the **Edit** menu **Copy** option or the **Copy** icon or **<Ctrl><V>** to copy the row values.

Place the cursor in the second row.



Use the **Edit** menu **Paste** option or the **Paste** icon or **<Ctrl><V>** to paste the row values into column 2.

Enter the mean duration of neutropenia expected for the New treatment (3 days) and the mean for the Placebo (6 days), then input $\sigma_d/2$ for the common standard deviation to obtain the same effect size. See results in Column 2 of the sample size table below.

Two group t-test of equal means (equal n's)				
	1	2	3	4
Test significance level, α	0.050	0.050		
1 or 2 sided test?	2	2		
Group 1 mean, μ_1	-3.000	3.000		
Group 2 mean, μ_2	3.000	6.000		
Difference in means, $\mu_1 - \mu_2$	-6.000	-3.000		
Common standard deviation, σ	5.200	2.600		
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	1.154	1.154		
Power (%)	86	86		
n per group	15	15		

Required sample size for this crossover design can also be obtained using table MTT3, Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction). See example 7.

If an estimate of the standard deviation of the differences is not directly available, but estimates of the between subject standard deviation and the between treatment/period correlation are available:

- Click on the **Assistants** menu item **Estimate S.D.** or the button labeled σ and select the item **Estimate Standard Deviation from SD1, SD2, Correlation**. nQuery Advisor will do the calculations for you. See Chapter 9, Determining a Value for Standard Deviation, Example 6.

If an estimate of the within group mean squared error from the crossover (or repeated measures) ANOVA is available:

- Use the equation, $\sigma_d = \sqrt{2} \sigma_e = \sqrt{2} \sigma_B \sqrt{(1-\rho)}$ where σ_e is the square root of the mean squared error from the crossover ANOVA.

Example 2

M period, M treatment crossover ($2 \leq M \leq 8$) (MOT2)

In an M period, M treatment crossover design, treatments are given in all possible sequences or balanced as in a Latin square. All sequences have the same number of replicates, and sequences are chosen so that no confounding occurs between treatment and period effects.

Use the nQuery Advisor table for one group repeated measures analysis of variance to obtain power or sample size for the treatment effect. As an alternative, you can use the nQuery Advisor table for repeated measures contrasts to obtain power or sample size for contrasts between treatments.

The current standard drug and two doses of a new drug will be compared for their ability to reduce blood pressure in a three-treatment three-period crossover design with an adequate washout period. An equal number of subjects will be assigned to each of the 6 possible drug sequences, ABC, ACB, BAC, BCA, CAB, CBA.

The standard deviation for reduction in blood pressure is estimated from previous studies with the standard drug as about 6 mmHg. The correlation between reductions observed in successive time periods is small, since baselines have been removed, about 0.20 and is expected to be the same for all pairs of periods.

In the past, the standard drug has resulted in reductions of about 12 mmHg. Investigators expect the lower dose of the new drug to be about the same as the standard, and the high dose to reduce blood pressure by about 14 mmHg. They plan a repeated measures analysis of variance with testing at the 5% level, and wish to obtain 90% power.

To obtain the required sample size for the overall main effect treatment comparison between all three treatments:

Open the Study Goal and Design box.

Click on **Means**, **One** group, **Test**, and select **Univariate one-way repeated measures analysis of variance**.

Enter the values for significance level, number of treatments (levels), the standard deviation and correlation, and the desired power into the table. (If between subject standard deviation and between period correlation are not available, the within-subject standard deviation must be estimated directly and entered into the row for σ , with the value zero entered for ρ .)



nQuery Advisor - MOT2-1

File Edit View Options Assistants Plot Window Help

MOT2-1: Main

Univariate one-way repeated measures analysis of variance (constant correlation)

	1	2	3	4	5
Test significance level, α	0.050				
Number of levels, M	3				
Variance of means, $V = \sum(\mu_i - \mu)^2 / M$					
Standard deviation at each level, σ	6.000				
Between level correlation, ρ	0.200				
Effect size, $\Delta^2 = V / [\sigma^2(1-\rho)]$					
Power (%)	90				
n					

To enter the expected means for each treatment and have nQuery Advisor compute the variance of means:

Click on Assistants menu item **Compute Effect Size** or the button labeled δ .

Enter the expected means, **12, 12, 14**, into the side table (only one sequence need be entered).

nQuery Advisor - MOT2-1

File Edit View Options Assistants Window Help

MOT2-1: Main

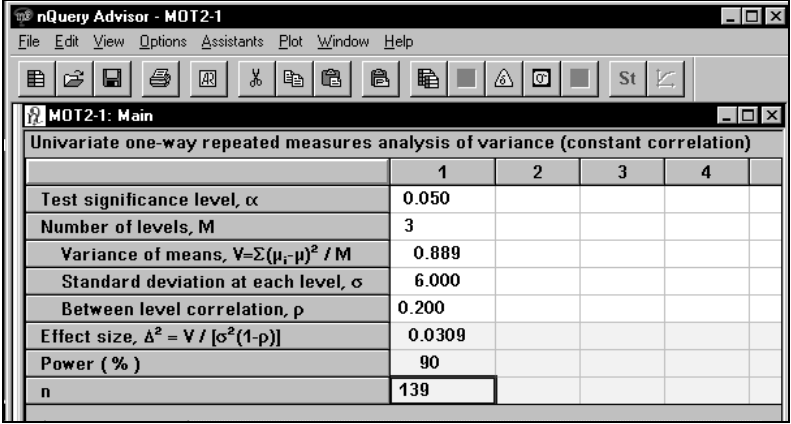
Univariate one-way repeated measures analysis of variance (constant correlation)

	1	2	3	4	5
Test significance level, α	0.050				
Number of levels, M	3				
Variance of means, $V = \sum(\mu_i - \mu)^2 / M$					
Standard deviation at each level, σ	6.000				
Between level correlation, ρ	0.200				
Effect size, $\Delta^2 = V / [\sigma^2(1-\rho)]$					
Power (%)	90				
n					

MOT2-1: Aid for col 1 -- One-way repeated measures analysis of variance

Level	Mean
1	12.000
2	12.000
3	14.000
Variance of means, $V = \sum(\mu_i - \mu)^2 / M$	0.889

Click on the **Transfer** button to copy the computed variance of means back to the main sample size table.



The screenshot shows the 'nQuery Advisor - MOT2-1' window. The 'Main' tab is active, displaying a table titled 'Univariate one-way repeated measures analysis of variance (constant correlation)'. The table has columns for parameters and four empty columns labeled 1, 2, 3, and 4. The parameters and their values are as follows:

	1	2	3	4
Test significance level, α	0.050			
Number of levels, M	3			
Variance of means, $V = \sum (\mu_i - \mu)^2 / M$	0.889			
Standard deviation at each level, σ	6.000			
Between level correlation, ρ	0.200			
Effect size, $\Delta^2 = V / [\sigma^2(1-\rho)]$	0.0309			
Power (%)	90			
n	139			

Then nQuery finishes the calculation in this table.

The figure above shows that a total of 139 subjects would be required for 90% power. Since all 6 sequences will be assigned with equal sample sizes, a total of 144 subjects (6 x 24) must be planned.

To obtain power for the specific contrast between high dose and low dose of the new drug:

Open the Study Goal and Design box.

Click on **Means, One group, Test**, and select **One-way repeated measures contrast**.

Enter the values for significance level and M into the sample size table.

Choose the Assistants menu Compute Effect Size option to bring up the side table as seen in the next figure.



nQuery Advisor - MOT3-1

File Edit View Options Assistants Window Help

MOT3-1: Main

One-way repeated measures contrast (constant correlation)

	1	2	3	4	5
Test significance level, α	0.050				
Number of levels, M	3				
Contrast, $C = \sum c_i \mu_i$					
Scale, $D = \text{SQRT}(\sum c_i^2)$					
Standard deviation at each level, σ					
Between level correlation, ρ					
Effect size, $\Delta = C / [D\sigma \text{SQRT}(1-\rho)]$					
Power (%)					
n					

MOT3-1: Aid for col 1 -- One-way repeated measures contrast

Compute Transfer Close Clear Cut Copy Paste Print

USER

Level	Mean	Coefficient
1		
2		
3		
Contrast, $C = \sum c_i \mu_i$		
Scale, $D = \text{SQRT}(\sum c_i^2)$		

Enter the values for means and for the coefficients for the contrast of interest.
Click on **Compute**.

MOT3-1: Aid for col 1 -- One-way repeated measures contrast

Compute Transfer Close Clear Cut Copy Paste Print

Level	Mean	Coefficient
1	12.000	0.000
2	12.000	-1.000
3	14.000	1.000
Contrast, $C = \sum c_i \mu_i$	2.000	$\sum C_i = 0.000$
Scale, $D = \text{SQRT}(\sum c_i^2)$	1.414	

Click on the **Transfer** button to move the result to the sample size table.

Enter the remaining values to obtain the power for the specific contrast, as shown in the next table. A power of 90% will require an n of 153.

nQuery Advisor - MOT3-1					
File Edit View Options Assistants Plot Window Help					
MOT3-1: Main					
One-way repeated measures contrast (constant correlation)					
	1	2	3	4	
Test significance level, α	0.050				
Number of levels, M	3				
Contrast, $C = \sum c_i \mu_i$	2.000				
Scale, $D = \text{SQRT}(\sum c_i^2)$	1.414				
Standard deviation at each level, σ	6.000				
Between level correlation, ρ	0.200				
Effect size, $\Delta = C / [D\sigma \text{SQRT}(1-\rho)]$	0.264				
Power (%)	90				
n	153				

Example 3

M period crossover (MOT3)

The design can require each treatment to appear the same number of times in each sequence, (AABB, for example) or can use sequences such as ABA. It is assumed that sequences are chosen so that no confounding occurs between treatment and period effects (the design is balanced.) In such cases, the table for repeated measures contrasts can be used to compute power for specific treatment contrasts.

Return to Example 1 in which a new drug for reduction in neutropenia is to be evaluated. Now assume that the investigator plans to use the three period, two treatment design ABB and BAA.

To obtain the required sample size for the overall main effect treatment comparison in the three period two treatment design:

Open the Study Goal and Design box.

Click on **Means**, **One** group, **Test**, and select **One-way repeated measures contrast**.

Enter the Test significance level and the Number of levels, as shown in the following sample size table. Then choose the **Assistants** menu **Compute Effect Size** option.

Enter the means and coefficients as shown below and click on **Compute**.



nQuery Advisor - MOT3-1

File Edit View Options Assistants Window Help

MOT3-1: Main

One-way repeated measures contrast (constant correlation)

	1	2	3	4	5
Test significance level, α	0.050				
Number of levels, M	3				
Contrast, $C = \sum c_i \mu_i$					
Scale, $D = \text{SQRT}(\sum c_i^2)$					
Standard deviation at each level, σ					
Between level correlation, ρ					
Effect size, $\Delta = C / [D\sigma \text{SQRT}(1-\rho)]$					
Power (%)					
n					

MOT3-1: Aid for col 1 -- One-way repeated measures contrast

Compute Transfer Close Clear Cut Copy Paste Print

USER

Level	Mean	Coefficient
1	6.000	2.000
2	3.000	-1.000
3	3.000	-1.000
Contrast, $C = \sum c_i \mu_i$	6.000	$\sum C_i = 0.000$
Scale, $D = \text{SQRT}(\sum c_i^2)$	2.449	

Click on **Transfer** to transfer the calculated value for Contrast and Scale to the sample size table.

Enter the values for the Standard deviation and the Between level correlation. The program will calculate the Effect size.

Note that in Example 1 we were given the standard deviation of differences which we have converted to the within standard deviation, 3.677. (We have divided σ_d by $\sqrt{2}$ to get an estimate of $\sigma_e = \sigma_B \sqrt{(1-\rho)}$. We have also substituted 0 for ρ and $\sigma_d / \sqrt{2} = 5.2 / \sqrt{2} = 3.677$ for σ_e .)

Enter 30 for the requested sample and nQuery will compute the power, in this case 94%.

One-way repeated measures contrast (constant correlation)					
	1	2	3	4	
Test significance level, α	0.050				
Number of levels, M	3				
Contrast, $C = \sum c_i \mu_i$	6.000				
Scale, $D = \text{SQRT}(\sum c_i^2)$	2.449				
Standard deviation at each level, σ	3.677				
Between level correlation, ρ	0.000				
Effect size, $\Delta = C / [D\sigma \text{SQRT}(1-\rho)]$	0.666				
Power (%)	94				
n	30				

Example 4

M period crossover second approach (MOT1)

As an alternative to the one-way repeated measures contrast in Example 3, we can use the table for the paired t test to obtain power or sample size for contrasts between pairs of treatments. Also, we can adjust the value entered for σ_d based on the design. Let $\sigma_c = \sqrt{f} \sigma_e$ be the standard deviation for the contrast using an estimate of the within subject standard deviation, σ_e , or $\sigma_c = \sqrt{f} \sigma_B \sqrt{(1-\rho)}$ if estimates of the between subject standard deviation and the correlation are available. Table 1 provides the multiplier f for a variety of designs.

Table 1. Multiplier f in $\sigma_c = \sqrt{f} \sigma_e$ or $\sigma_c = \sqrt{f} \sigma_B \sqrt{(1-\rho)}$ for crossover designs for contrasts between pairs of treatments			
Number of periods, M	Number of treatments, t	Design sequences	f
2	2	AB, BA	2
2	2	ABB, BAA	4.5/3 = 1.5
3	3	ABC, ACB, BAC, BCA, CAB, CBA	2
3	2	AABB, BBAA, ABBA, BAAB	1
4	4	ABCD, BDAC, CADB, DCBA	2

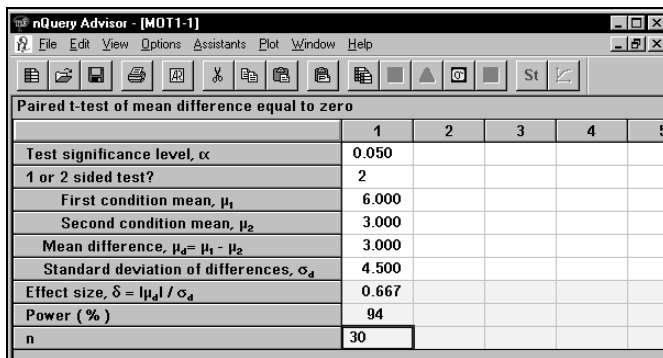


To obtain sample size for the Example 3 design using the paired t test sample size table:

Open the Study Goal and Design box.

Click on **Means, One** group, **Test**, and select **Paired t test**.

Enter the same values into the table as for Example 1, except that the value entered for the standard deviation of differences should be $\sqrt{1.5} [5.2] / \sqrt{2} = 4.5$.



	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
First condition mean, μ_1	6.000				
Second condition mean, μ_2	3.000				
Mean difference, $\mu_d = \mu_1 - \mu_2$	3.000				
Standard deviation of differences, σ_d	4.500				
Effect size, $\delta = \mu_d / \sigma_d$	0.667				
Power (%)	94				
n	30				

This design will have a power near 94% for a sample of size 30.

Repeated Measures Designs

The general repeated measures design may have one, two, or more than two groups, and may have one or more factors defining the levels of the repeated measures. Such designs may be analyzed using univariate analysis of variance or multivariate ANOVA methods.

Univariate analysis of variance methods are appropriate when the covariance matrix of the repeated measures responses satisfies the sufficient (but not necessary) condition of compound symmetry (that is, all response variances are equal and all response intercorrelations are equal). nQuery Advisor provides three sample size tables appropriate for situations where the covariance matrix satisfies conditions of compound symmetry.

MOT2 Univariate one-way repeated measures analysis of variance (constant correlation)

MOT3 One-way repeated measures contrast (constant correlation)

MOC4 Confidence interval for one-way repeated measures contrast (constant correlation)

See Examples 5 and 6 in this chapter.

Univariate analysis of variance methods may still be approximately correct when the covariance matrix is not restricted to be compound symmetric if the degrees of freedom for tests involving the repeated measures factor are multiplied by a correction factor before assessing significance.

nQuery Advisor provides two sample size tables appropriate for situations where the covariance matrix need not be compound symmetric and the Greenhouse-Geisser correction is to be used. See Muller, KE, Barton CN (1989) Approximate Power for Repeated-Measures ANOVA lacking Sphericity, *Journal of the American Statistical Association* 84:549-555 for details of the methods used.

**MOT4 Univariate one-way repeated measures analysis of variance
(Greenhouse-Geisser correction)**

**MTT3 Two-group univariate repeated measures ANOVA (Greenhouse-
Geisser correction)**

See Example 7 in this chapter

Example 5

One-way repeated measures analysis of variance (MOT2)

A psychologist plans to conduct a study of a three month intervention aimed at raising self-esteem in children. Self-esteem will be measured before, after 1 month, after 2 months, and after 3 months of the intervention, using a 100 point scale.

In a small pilot study of 10 children who had self-esteem measured once and again a week later with no intervention, the correlation between measures was 0.7, and standard deviation across children at times 1 and 2 was about 10. The beginning score was 55. The investigator hopes to raise the initial score to 59.5 over the course of the unit.

To run the one-way repeated measures analysis of variance example:


Open the Study Goal and Design box.

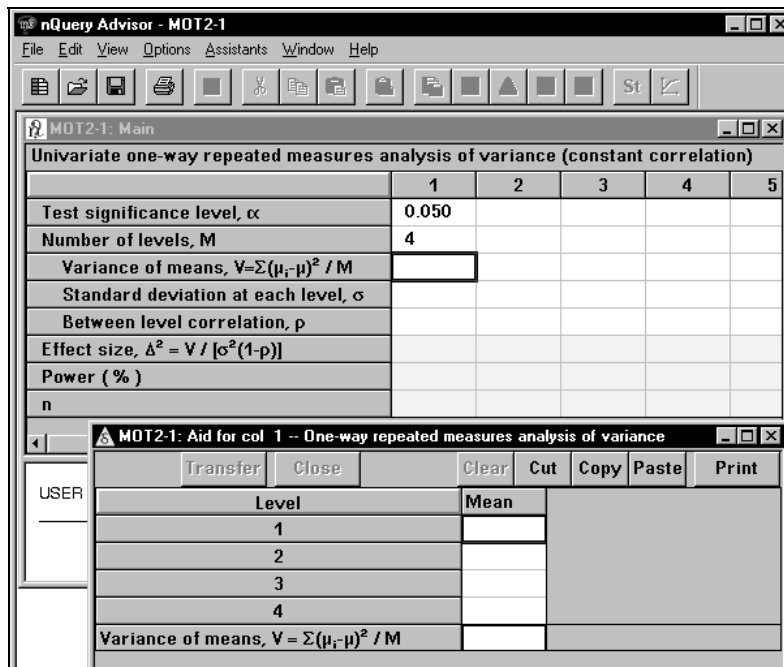
Click on **Means**, **One** group, **Test**, and select **Univariate one-way repeated measures analysis of variance**.

Enter **0.05** for a 5% significance level.

Measurements will be made at 4 time points so enter 4 in the Number of levels row.



After you have entered the number of levels, click on , the **Compute effect size** button to obtain the side table shown below.



nQuery Advisor - MOT2-1

File Edit View Options Assistants Window Help

MOT2-1: Main

Univariate one-way repeated measures analysis of variance (constant correlation)

	1	2	3	4	5
Test significance level, α	0.050				
Number of levels, M	4				
Variance of means, $V = \sum(\mu_i - \mu)^2 / M$					
Standard deviation at each level, σ					
Between level correlation, ρ					
Effect size, $\Delta^2 = V / [\sigma^2(1-\rho)]$					
Power (%)					
n					

MOT2-1: Aid for col 1 -- One-way repeated measures analysis of variance

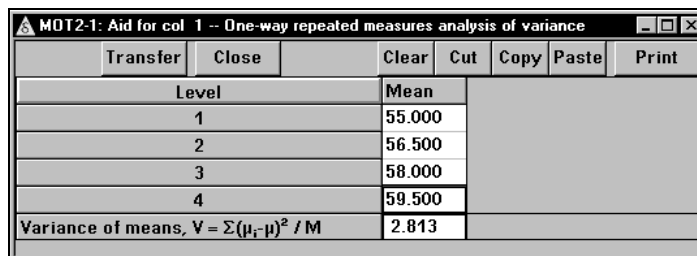
Transfer Close Clear Cut Copy Paste Print

USER

Level	Mean
1	
2	
3	
4	
Variance of means, $V = \sum(\mu_i - \mu)^2 / M$	

Enter **55** for the pre-test self-esteem score, and **59.5** for the post test self-esteem score.

Enter sensible intermediate values for the results you expect to see at the one and two month tests. Then nQuery Advisor will compute the Variance of means.



MOT2-1: Aid for col 1 -- One-way repeated measures analysis of variance

Transfer Close Clear Cut Copy Paste Print

Level	Mean
1	55.000
2	56.500
3	58.000
4	59.500
Variance of means, $V = \sum(\mu_i - \mu)^2 / M$	2.813

Click on the **Transfer** button to transfer this value to the main table.

Enter **10** for the Standard deviation at each level and **0.7** for the correlation between successive tests.

Enter the required power, and nQuery Advisor will solve for the necessary sample size. The resulting table is shown below.

The screenshot shows the nQuery Advisor - MOT2-1 window. The main table is titled 'Univariate one-way repeated measures analysis of variance (constant correlation)'. It has columns for parameters and four levels (1, 2, 3, 4). The parameters and their values are as follows:

	1	2	3	4
Test significance level, α	0.050			
Number of levels, M	4			
Variance of means, $V = \sum (\mu_i - \mu)^2 / M$	2.813			
Standard deviation at each level, σ	10.000			
Between level correlation, ρ	0.700			
Effect size, $\Delta^2 = V / [\sigma^2(1-\rho)]$	0.0937			
Power (%)	90			
n	40			

To have 90% power to obtain a significant result in the one-way repeated measures analysis of variance when self-esteem scores are expected to rise gradually from 55 to 59.5, would require 40 children.

Example 6

One-way repeated measures contrast (MOT3)

The investigator expects that self-esteem scores will increase monotonically over time. Thus, she will probably wish to test the linear contrast following the repeated measures analysis of variance and assess what sample size will be necessary for the contrast to have 90% power.

To run the one-way repeated measures contrast example:

Open the Study Goal and Design box.

Click on **Means**, **One** group, **Test**, and select **One-way repeated measures contrast**.

Enter the numbers as shown in the following table.



nQuery Advisor - MOT3-1

File Edit View Options Assistants Window Help

MOT3-1: Main

One-way repeated measures contrast (constant correlation)

	1	2	3	4	5
Test significance level, α	0.050				
Number of levels, M	4				
Contrast, $C = \sum c_i \mu_i$					
Scale, $D = \text{SQRT}(\sum c_i^2)$					
Standard deviation at each level, σ					
Between level correlation, ρ					
Effect size, $\Delta = C / [D\sigma \text{SQRT}(1-\rho)]$					
Power (%)					
n					

MOT3-1: Aid for col 1 -- One-way repeated measures contrast

Compute Transfer Close Clear Cut Copy Paste Print

Level	Mean	Coefficient
1	55.000	-3.000
2	56.500	-1.000
3	58.000	1.000
4	59.500	3.000
Contrast, $C = \sum c_i \mu_i$	15.000	$\sum c_i = 0.000$
Scale, $D = \text{SQRT}(\sum c_i^2)$	4.472	

Click on the **Assistants** menu **Compute Effect Size** option and enter the Means and Coefficients as shown in the above table. These coefficients are appropriate to test for a linear trend in self-esteem.

Click on **Compute** to calculate the Contrast and Scale parameters.

Click on **Transfer** to transfer the Contrast and Scale values to the sample size table.

Enter the Standard deviation and Between level correlation. The program will calculate the Effect Size.

Enter the Power of **90**, and the program calculates the required sample size.

nQuery Advisor - MOT3-1					
File Edit View Options Assistants Plot Window Help					
MOT3-1: Main					
One-way repeated measures contrast (constant correlation)					
	1	2	3	4	
Test significance level, α	0.050				
Number of levels, M	4				
Contrast, $C = \sum c_i \mu_i$	15.000				
Scale, $D = \text{SQRT}(\sum c_i^2)$	4.472				
Standard deviation at each level, σ	10.000				
Between level correlation, ρ	0.700				
Effect size, $\Delta = C / [D\sigma \text{SQRT}(1-\rho)]$	0.612				
Power (%)	90				
n	29				

For the test of the linear contrast to have 90% power the study design requires only 29 children.

Example 7

Two-group repeated measures ANOVA (Greenhouse-Geisser correction) (MTT3)

We return to the study outlined in Examples 5 and 6, and we now suppose that the investigator believes that correlations will decrease over time and wants to design a study comparing the intervention group to a no treatment control group. The investigator plans to analyze the data using univariate analysis of variance with the Greenhouse-Geisser correction. That is, an ordinary univariate analysis of variance will be computed. Then the Greenhouse-Geisser correction factor (an estimate of the measure of lack of sphericity ϵ) will be computed. (When the assumption of compound symmetry is satisfied ϵ equals 1.0; its minimum value is $1/(M-1)$ where M is the number of repeated measures levels.) The F statistics for the significance tests for levels or levels by groups will be compared to critical values of F with degrees of freedom obtained by multiplying the nominal degrees of freedom by the Greenhouse-Geisser correction factor.



To run the two-group repeated measures analysis of variance example:

Open the Study Goal and Design box.

Click on **Means, Two group, Test**, and select **Two-group univariate repeated measures ANOVA**.

Enter **0.05** for a 5% significance level.

Measurements will be made at 4 time points so enter 4 in the Number of levels row.

After you have entered the number of levels, click on the **Compute effect size** button to obtain the side table shown below.

For group 1, we enter the same means across the four time levels as we used in Example 5 and assume that the control group will show no change over time.

The screenshot shows the nQuery Advisor interface. The main window displays the 'Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)' table. Below it, a sub-window titled 'MTT3-1.nqa: Aid for col 1 -- Means for groups by levels' is open, showing the 'Means for groups by levels' table.

	1	2	3	4	5
Test significance level, α	0.050				
Number of levels, M	4				
Variance in means, between groups					
Variance in means, between levels					
Variance in means, levels by groups					

	Level 1	Level 2	Level 3	Level 4	Row Mean
Group 1	55.000	56.500	58.000	59.500	57.250
Group 2	55.000	55.000	55.000	55.000	55.000
Column Mean	55.000	55.750	56.500	57.250	56.125
Variance, between groups	1.266				
Variance, between levels	0.703				
Variance, levels by groups	0.703				

Click on **Compute** to get the numbers shown in the figure above.

Click on the **Transfer** button to transfer the "Variances" back to the main table.

nQuery Advisor - MTT3-1.nqa					
File Edit View Options Assistants Plot Window Help					
MTT3-1.nqa: Main					
Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)					
	1	2	3	4	5
Test significance level, α	0.050				
Number of levels, M	4				
Variance in means, between groups	1.266				
Variance in means, between levels	0.703				
Variance in means, levels by groups	0.703				
Between-groups error term					
Within-group error term					
Measure of "sphericity", ϵ					
Bias term multiplier, g_1					
Power, between groups(%)					
Power, between levels(%)					
Power, levels by groups(%)					
n per group					



Click on the button, or click on the **Assistants** menu **Specify covariance matrix** option to bring up the Specify Covariance side table. (You will find details on using the Specify Covariance option in Chapter 9, *Determining a Value for Standard Deviation*.)

Enter **10** for **Constant σ** and click on **Fill**.

Enter **.7** for **ρ** and **.5** for **γ** to get a pattern of correlations which decrease with distance between measurements.

Click on **Fill**.

Click on **Compute** to get the result.



nQuery Advisor - MTT3-1.nqa

File Edit View Options Assistants Window Help

MTT3-1.nqa: Main

Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)

Test significance level, α

Number of levels, M

Variance in means, between groups

Variance in means, between levels

Variance in means, levels by groups

Between-groups error term

Within-group error term

Measure of "sphericity", ϵ

Bias term multiplier, g_1

Power, between groups(%)

Power, between levels(%)

Power, levels by groups(%)

n per group

MTT3-1.nqa: Aid (SIGMA) for col 1 -- covariance matrix

Compute Transfer Close Clear Cut Copy Paste Print

☒ Specify standard deviations and correlations
☐ Specify full covariance matrix

STANDARD DEVIATIONS

Constant σ : 10.0

CORRELATION PATTERN

$\rho_{ij} = \rho$ to the power $1 - |y + y_i - j|$

ρ : 0.70 γ : 0.50 $0 \leq y \leq 1$

Fill or, specify all entries, σ_i : Fill or, specify all entries ρ_{ij} :

	σ_i	ρ_{ij}
Level 1	10.000	0.700 0.586 0.490
Level 2	10.000	0.700 0.586
Level 3	10.000	0.700
Level 4	10.000	
Between-groups error term	16.973	
Within-groups error term	6.108	
Measure of "sphericity", ϵ	0.885	
Bias term multiplier, g_1	-1.984	

Click on **Transfer** and enter the required power, say 85% for the levels by groups interaction, and have nQuery compute n.

nQuery Advisor - MTT3-1.nqa

File Edit View Options Assistants Plot Window Help

MTT3-1.nqa: Main

Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)

	1	2	3	4	5
Test significance level, α	0.050				
Number of levels, M	4				
Variance in means, between groups	1.266				
Variance in means, between levels	0.703				
Variance in means, levels by groups	0.703				
Between-groups error term	16.97				
Within-group error term	6.11				
Measure of "sphericity", ϵ	0.88				
Bias term multiplier, g_1	-1.98				
Power, between groups(%)	42				
Power, between levels(%)	85				
Power, levels by groups(%)	85				
n per group	90				

For this study, the effect sizes for the between levels and levels by group interaction are equal, but this will not generally be the case.

Note: Due to use of the estimated Greenhouse-Geisser correction, the actual significance level of the test may be somewhat lower than the nominal level which can affect the computed power.

14. Nonparametric Tests

A nonparametric approach to analysis of a two-group design uses the Wilcoxon/Mann-Whitney rank-sum test. The rank-sum test is a test of the null hypothesis that $P(X < Y) = 0.5$, where X is an observation from Group 1 and Y an observation from Group 2. It is equivalent to a test of equality of means when the two distributions have the same shape and equal variances. When the two distributions are normally distributed with equal variances, the rank-sum test will require about 5% more observations than the two-sample t-test to provide the same power against the same alternative.

For nonnormal populations, especially those with long tails, the rank-sum test may not require as many observations as the two-sample t-test. For example, the rank-sum test requires only about 80% of the sample size required by the t-test when the data are distributed like a t with 5 degrees of freedom.

Two nQuery Advisor tables are available for nonparametric tests, depending on whether the outcome variable is continuous or ordered categorical.

Example 1


Wilcoxon/Mann-Whitney rank-sum test (continuous outcome) (MTT1)

To illustrate finding a sample size for a two-group design to be analyzed using the Wilcoxon/Mann-Whitney rank-sum test, we use the example from the tutorial in Chapter 2.

A two-group, randomized, parallel, double-blind study is planned. Patients will be studied for two weeks; each patient will be randomly assigned to receive either new drug or placebo 3 times per week. The sample sizes in the two groups will be equal. A two-sided 5% level rank-sum test will be used to analyze the outcome measure, the change in hematocrit level from pre-treatment to post-treatment.

One hypothesized outcome scenario is that the difference in means between the two groups would be 2.2, while the standard deviation of change within groups would be 2.0. Using the table for the two-sample t-test, we found that 19 subjects per group would be required to obtain 90% power.

To bring up the sample size table:

Choose the **File** menu **New** option or click on , the **New** icon button.

In the **Study Goal and Design Box**, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.


Select **Wilcoxon/Mann-Whitney rank-sum test (continuous outcome)** in the selection box.

Click on **OK**.

The table will come up empty. The following table shows the entries for the test parameters and the desired power.

nQuery Advisor - [MTT1-1]						
File Edit View Options Assistants Plot Window Help						
Wilcoxon (Mann-Whitney) rank-sum test that $P(X < Y) = .5$ (continuous outcome)						
	1	2	3	4	5	
Test significance level, α	0.050					
1 or 2 sided test?	2					
$p_1 = P(X < Y)$						
Power (%)	90					
n per group						

You may have a value for $p_1 = P(X < Y)$ from pilot data or other information. Or, you might wish to select a value for p_1 using Cohen's definition of small ($\delta = 0.2$, $p_1 = 0.556$), medium ($\delta = 0.5$, $p_1 = 0.638$), and large effect sizes ($\delta = 0.8$, $p_1 = 0.714$) for sampling from a normal distribution. Or, you may wish to compute p_1 from the values expected for the means and standard deviation using the **Compute Effect Size** option.

Select the **Assistants** menu, **Compute Effect Size** option, or click on the  icon. You will see the side table shown below. The table will come up empty, but we have entered the values for means and standard deviations and nQuery Advisor has already computed p_1 .



nQuery Advisor - [MTT1S-1]					
File Edit View Options Assistants Plot Window Help					
Estimate of $p_1 = P(X < Y)$ from means and SD assuming normality					
	1	2	3	4	5
Group 1 mean, μ_1	0.000				
Group 2 mean, μ_2	2.200				
Difference in means, $\mu_1 - \mu_2$	-2.200				
Common standard deviation, σ	2.000				
Effect size, $\delta = (\mu_1 - \mu_2) / \sigma$	-1.100				
$p_1 = P(X < Y)$	0.782				

Select the value for p_1 .



Use the **Edit** menu **Copy** option or the **Copy** icon, or the **Copy** keyboard shortcut, **<Ctrl><C>**, to copy to clipboard.

Return to the main table by using the list of open tables in the **Windows** menu or by using the **<Ctrl>-<Tab>** keys on your keyboard to toggle between the table displays.



Use the **Edit** menu **Paste** option or the **Paste** icon, or the **Paste** keyboard shortcut, **<Ctrl><V>**, to paste the value in the appropriate row. nQuery Advisor will compute the required sample size.

nQuery Advisor - [MTT1-1]					
File Edit View Options Assistants Plot Window Help					
Wilcoxon (Mann-Whitney) rank-sum test that $P(X < Y) = .5$ (continuous outcome)					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
$p_1 = P(X < Y)$	0.782				
Power (%)	90				
n per group	23				

The large sample approximation used for computing power and sample size for the rank-sum test is based only on the value of p_1 and does not take into account knowledge you have about the shape of the underlying distribution.

Example 2


Wilcoxon/Mann-Whitney rank-sum test (ordered categories) (MTT2)

For this table, nQuery Advisor computes power based on approximating the unconditional distribution of the Wilcoxon rank-sum test statistic under the null and alternative hypotheses using the first four moments of the distribution. See an outline of the method in the Appendix.

To illustrate finding a sample size for a two-group design with an ordered categorical outcome which will be analyzed using the Wilcoxon/Mann-Whitney rank-sum test, we use an example from a paper by E.I. Lesaffre, I. Scheys, J. Frohlich, E. Bluhmki (1993) Calculation of Power and Sample Size with Bounded Outcome Scores. *Statistics in Medicine* 12:1063-1078.

A two-group, randomized, parallel, double-blind study is planned. Patients will be randomly assigned to receive either a placebo or a new drug. The sample sizes in the two groups will be equal. A two-sided 5% level rank-sum test will be used to analyze the outcome measure, a coded version of a quality of life scale. The expected proportions in each of five categories: 0, 5-30, 35-65, 70-95, 100 are approximately .23, .08, .10, .14, .45 for Group 1, and .13, .06, .10, .16, .55 for Group 2. Researchers evaluated power for a sample size in each group of 150.

To bring up the sample size table:

Choose the **File** menu **New** option or click on , the New icon button

In the **Study Goal and Design Box**, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Means**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.

Select **Wilcoxon/Mann-Whitney rank-sum test (ordered categories)** in the selection box.

Click on **OK**.

The table will come up empty. The following table shows the entries for the test parameters, the number of categories and the desired sample size in column 1.



Enter the values shown in the table below, and leave your cursor in the first column.

Wilcoxon (Mann-Whitney) rank-sum test that $P(X < Y) = .5$ (ordered categories)						
	1	2	3	4	5	6
Test significance level, α	0.050					
1 or 2 sided test?	2					
Number of categories, k	5					
Side table name						
$p_1 = P(X < Y)$						
Power (%)						
n per group	150					

You must specify the proportions expected under the alternative hypothesis in each of the k categories for each group in order for nQuery to compute power. To do this, you must use the **Assistants** menu **Compute Effect Size** option.



Select the **Assistants** menu **Compute Effect Size** option, or click on the icon.

You will see an empty side table associated with column 1 of the main table.

MTT2-1: Aid table E1 -- Specification of probabilities in groups, categories		
Category	Proportion in Group 1 (X)	Proportion in Group 2 (Y)
1		
2		
3		
4		
5		
$\sum \pi_i$		
$p_1 = P(X < Y)$		

Enter the proportions expected in each category for each group in the table. Note that nQuery updates the sum of the p_i as you enter a proportion value for each category.

Click on the **Compute** button to calculate the p_1 value and the other information necessary for the approximation, see reference in the Appendix.

For this example, we have entered the values for the proportions expected in each category under the alternative hypothesis in the Lesaffre et al example, and clicked on the **Compute** button.

MTT2-1: Aid table E1 -- Specification of probabilities in groups, categories		
Compute	Transfer	Close
Restore	Clear	Cut
Copy	Paste	Print
Category	Proportion in Group 1 (X)	Proportion in Group 2 (Y)
1	0.230	0.130
2	0.080	0.060
3	0.100	0.100
4	0.140	0.160
5	0.450	0.550
$\sum \pi_i$	1.000	1.000
$p_1 = P(X < Y)$	0.570	

Click on the **Transfer** button. The main MTT2 table will reappear and the side table name and the value for p_1 will display in the appropriate cells in the first column of the sample size table. The program will compute the power for an n per group of 150—here the computed power is 62%. When the number of categories is large, it may require a few seconds to complete the computation.

MTT2-1: Main						
Wilcoxon (Mann-Whitney) rank-sum test that $P(X < Y) = .5$ (ordered categories)						
	1	2	3	4	5	
Test significance level, α	0.050					
1 or 2 sided test?	2					
Number of categories, k	5					
Side table name	E1					
$p_1 = P(X < Y)$	0.570					
Power (%)	62					
n per group	150					

The “exact” power computed in the Lesaffre paper using all 21 categories and a smoothed alternative was 55% for an n per group of 150. nQuery uses an approximation to the conditional power based on the first four moments, see reference in the Appendix and the guide card for the first row.

Since a power of 62% is not sufficient, we use the second column to calculate the power for a larger sample.



To use the side table from the first column also for the second column:

Use the **Edit** menu **Copy** option to copy the first four rows in the first column.

Click on the first row of the second column and use the **Edit** menu **Paste** option to paste the values into the second column. Using the contents of side table E1, nQuery will enter the p_1 value and provide the other necessary values for the second column.

Enter **300** into the **n per group** row in the second column. nQuery will calculate the power of 89%.

MTT2-1: Main						
Wilcoxon (Mann-Whitney) rank-sum test that $P(X < Y) = .5$ (ordered categories)						
	1	2	3	4	5	
Test significance level, α	0.050	0.050				
1 or 2 sided test?	2	2				
Number of categories, k	5	5				
Side table name	E1	E1				
$p_1 = P(X < Y)$	0.570	0.570				
Power (%)	62	89				
n per group	150	300				

To use a new side table for the third column:

To create a new side table similar to E1 but with some changes in the proportions, use the **Edit** menu **Copy** option to copy the first three rows in the first column.

Click on the first row of the third column and use the **Edit** menu **Paste** option to paste the values into the third column.

To bring up a side table for the third column, select the **Assistants** menu



Compute Effect Size option, or click on the icon.

Enter the proportions into this side table by hand, or use the **Window** menu to select E1, the side table for column 1, **Copy** those values, return to E2, and **Paste** the values into E2, the side table for column 3. You can then edit these proportions as desired.

Click on **Compute**.

Click on **Transfer** to transfer the computed value to the third column.

Enter the desired sample size into the **n per group** row in the third column, and nQuery will compute the power.

15. Sample Size Tables for Proportions

Sample size tables for proportions assist you in determining the necessary sample size for studies in which:

- the outcome variable measure is dichotomous (success/failure, alive/dead, yes/no)
- you want to estimate or make tests on the proportion of “successes.”

A number of sample size tables for proportions provide power using exact computations or simulation. However formulas used by nQuery Advisor for sample sizes for many of the proportions tables use a normal approximation and are thus designed for large samples. For these, nQuery Advisor checks that the minimum expected cell size for the 2x2 or Gx2 table is greater than a preprogrammed default value. You will see a warning box if the minimum cell size falls below this value. If you see this box, you must check that the sample size computed by nQuery Advisor will be adequate; see Example 4 for the two-group χ^2 test later in this chapter. In some cases, the default value used by nQuery may be too conservative and lead to an unnecessarily large sample size. You may want to use the Change Minimum Expected Cell Count option from the Options menu to reduce the required minimum cell count for your nQuery Advisor session.

The nQuery Advisor program provides the following tables appropriate to studies in which the outcomes are proportions. Some of these tables have a version appropriate for sampling from finite populations. Those tables are denoted by an F at the end of the table code; see Chapter 19, *Sampling from Finite Populations*, for further details.

Note that for exact tests, the actual probability of rejecting the null hypothesis when it is true is less than or equal to alpha, and in some cases may be markedly less than the specified nominal level. For a two-sided test, nQuery uses the highest possible actual significance level for which the probability is less than or equal to $\alpha/2$ in both tails. Due to the fact that the attainable alpha level depends on the specified sample size, note that computed power may not increase monotonically with sample size for exact tests. See references for specific tables for details and advice.

Tests, Confidence intervals, and Equivalence Tests for single proportions or for differences in paired proportions in a single sample:

POT0	One group χ^2 test that proportion equals user specified value (normal approximation)
POT0x	Exact test for single proportion
POT1	McNemar's Test (χ^2) of equality of paired proportions See Example 2 in this chapter.
POT1x	Exact sign test of equality of paired proportions See Example 2 in this chapter.
POT2	Chi-square test of specified proportions in C categories
POC0	Confidence interval for proportion using normal approximation (n large) See Example 1 in this chapter and example in Chapter 19.
POC1	Confidence interval for $\ln(\Psi_M)$, odds ratio for paired proportions (n large)
POC2	Confidence interval for probability of observing a rare event
POE0	Paired test of equivalence in proportions (n large) See Example 9 in this chapter.
POE1	Paired test of equivalence in proportions using confidence interval: a) Lower confidence limit for difference in paired proportions (simulation), b) Upper confidence limit for difference in paired proportions (simulation), c) Two-sided confidence limits for difference in paired proportions (simulation) See Example 9 in this chapter.

See Chapter 19 *Sampling from Finite Populations* for details for versions POT0F and POC0F.



Tests, Confidence Intervals, and Equivalence tests for comparisons of proportions in two independent groups:

PTT0	Two group χ^2 test of equal proportions (odds ratio = 1) (Compute power or sample size) See Examples 3 and 4 in this chapter.
PTT0p	Two group χ^2 test of equal proportions (Compute one of two proportions) See Example 3 in this chapter.
PTT1	Two group continuity corrected χ^2 test of equal proportions (odds ratio = 1) (Compute power or sample size) See Example 4 in this chapter.
PTT1p	Two group continuity corrected χ^2 test of equal proportions (Compute one of two proportions)
PTT2	Two-group Fisher's exact test of equal proportions (odds ratio=1) See Example 4 in this chapter.

Sample size and power for PTT0 are derived using the large sample normal approximation. Those obtained from PTT1 use a correction factor designed to approximate results for Fisher's Exact Test, and sample sizes will be larger and power lower than obtained using PTT0. Answers given by PTT2 are obtained using exact methods and will typically lie between those for PTT0 and PTT1.

PTT3	Two-group Chi-square test comparing proportions in C categories See Example 6 in this chapter.
PTT4	Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata See Example 7 in this chapter.
PTT4cc	Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata (Continuity Corrected)
PTC0	Confidence interval for difference of two proportions
PTC1	Confidence interval for difference of two proportions (continuity corrected)
PTC2	Confidence interval for ln(odds ratio) See Example 5 in this chapter.
PTE0	Two group test of equivalence in proportions (large n) See Examples 10 and 11 in this chapter.

-
- PTE1** **Two group test of equivalence in proportions using confidence interval:**
a) Lower confidence limit for difference in proportions (simulation),
b) Upper confidence limit for difference in proportions (simulation),
c) Two-sided confidence limits for difference in proportions (simulation)
See Examples 10 and 11 in this chapter.
- MTT2** **Wilcoxon (Mann-Whitney) rank-sum test that $P(X < Y) = 0.5$ (ordered categories)**
See Example 2 in Chapter 14, *Nonparametric Methods*.

Tests for more than two groups

- PGT0** χ^2 test of equal proportions in G groups
- PGT1** **Trend across proportions, logistic model**
See Example 8 in this chapter.
- PGT2** **G group Chi-square test comparing proportions in C categories**

All the proportions tables for two or more groups have versions allowing for unequal sample sizes.

Example 1

Confidence interval for proportion normal approximation (n large) (POC0)

In educational institutions, administrators frequently need to estimate the percent of students satisfied with some aspect of the institutional program, for example, “What percent of eligible students plan to return next year?” To address this question, a sample survey will be mounted in which a random sample of students is selected from the undergraduate study body and asked about their intentions. Each student will be asked to answer the question (and others) with either a yes or a no.


The estimated proportion of students who plan to return will be reported, together with a 95% confidence interval. The investigators want to know how many students must be questioned to estimate the retention rate to within $\pm 5\%$. It is hoped that the retention rate will be 60%.

For this example, we assume that the student body is very large. See Chapter 19 for the solution to this same question when the size of the undergraduate student body is small and a finite sampling correction is required.



To bring up the sample size table for a confidence interval for a single proportion:



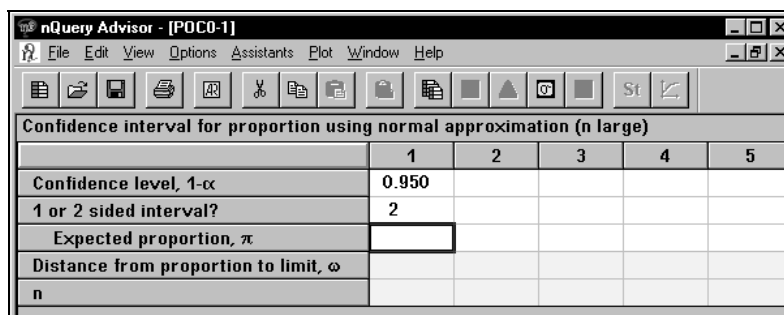
Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **One** group, **Confidence Interval**.

Select the top entry from the choices in the lower half of the box.

Click **OK**. The sample size table for **Confidence interval for proportion using normal approximation (n large)** will appear.

The following table shows the confidence level, and two-sided interval all filled in.



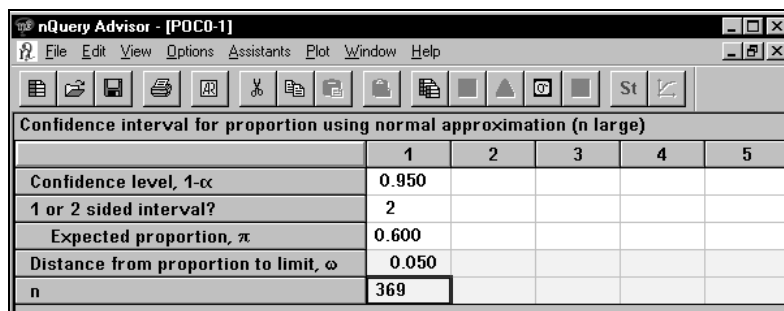
	1	2	3	4	5
Confidence level, $1-\alpha$	0.950				
1 or 2 sided interval?	2				
Expected proportion, π					
Distance from proportion to limit, ω					
n					

To complete the table, enter the expected proportion and the desired precision of the estimate:

Enter **.60** as the expected proportion.

Enter **0.05** for the distance from the estimated proportion to the end of the confidence interval.

nQuery Advisor will compute the required sample size.



	1	2	3	4	5
Confidence level, $1-\alpha$	0.950				
1 or 2 sided interval?	2				
Expected proportion, π	0.600				
Distance from proportion to limit, ω	0.050				
n	369				

For this example, a sample of 369 students would be necessary.

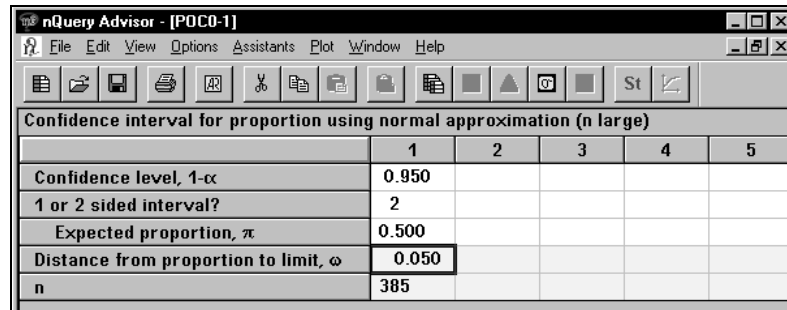
To get the statement for this column:

Click on any cell in the calculated column.

Click on the **Create Statement** button. The statement will appear and can be saved to clipboard, printed directly, or stored in the Stored Statements panel of your screen. Note that you can select the font to be used for the statement in Windows applications. See Chapter 3, *The File and Options Menus* for details.

When the sample size is 369, a two-sided 95.0% confidence interval for a single proportion using the large sample normal approximation will extend 0.050 from the observed proportion for an expected proportion of 0.600.

Frequently, the investigator really doesn't know what proportion of students are likely to express satisfaction, or the survey instrument will contain a variety of questions, and the investigator wants to have precision of at least $\pm 5\%$ for every question. Since the required sample size for a specified confidence interval width is largest when the expected proportion is 0.50, the investigator can solve for the required sample size using an expected proportion of 0.5.



The screenshot shows the nQuery Advisor software window. The title bar reads "nQuery Advisor - [POC0-1]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. Below the menu bar is a toolbar with various icons. The main window displays a table titled "Confidence interval for proportion using normal approximation (n large)". The table has columns for confidence level, 1- α , and 1 or 2 sided interval?, and rows for Expected proportion, π , Distance from proportion to limit, ω , and n. The values in the table are: Confidence level, 1- α = 0.950; 1 or 2 sided interval? = 2; Expected proportion, π = 0.500; Distance from proportion to limit, ω = 0.050; n = 385.

	1	2	3	4	5
Confidence level, 1- α	0.950				
1 or 2 sided interval?	2				
Expected proportion, π	0.500				
Distance from proportion to limit, ω	0.050				
n	385				

The required sample size will be 385 for precision of $\pm 5\%$ for a 95% two-sided confidence interval.

Note: This has given rise to the rule of thumb that a sample survey should have a sample size of 400.

Example 2

McNemar's test of equality of paired proportions (POT1)

Exact sign test of equality of paired proportions (POT1x)

To address the question of whether taking a certain diet drug combination increased the likelihood of requiring valve surgery, investigators wanted to design a retrospective case-control study.




The cases would be patients who had had valve surgery in a defined two-year period, and the controls would be pair-matched using age, gender, and body-mass index. Cases and controls would be asked to fill out a survey to determine whether they had taken the diet drugs in question.

It was expected that about 5% of controls would have taken the diet drugs. What sample size would be necessary to have 90% power to detect an increase to 10% among the cases?

We start by using the table for McNemar's test.

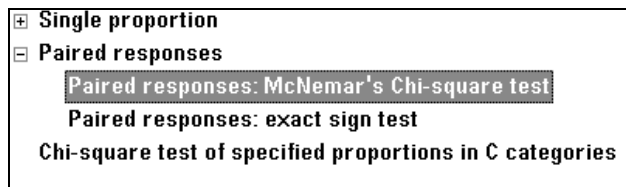
To bring up the sample size table for McNemar's test:

Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **One group**, **Test**.

Double click on the entry **Paired responses**, or click on the + sign to the left of that entry.

Then select the top entry **Paired responses: McNemar's Chi-square test** from the two choices below the heading **Paired responses**.



Click **OK**. The sample size table for **McNemar's test of equality of paired proportions** will appear.

The following table shows two rows filled in: significance level, and one or two-sided test.

POT1-1: Main		
McNemar's test (χ^2) of equality of paired proportions		
	1	2
Test significance level, α	0.050	
1 or 2 sided test?	2	
Difference in proportions, $\delta = \pi_1 - \pi_2 $		
Proportion of discordant pairs, $\eta = \pi_{10} + \pi_{01}$		
Power (%)		
n (number of pairs)		

To obtain a side table to allow you to enter the proportions of paired cases and controls expected to show each response pattern, select the **Assistants** menu **Compute Effect Size** option or click on the δ button in the toolbar.

You will see the following side table:

POT1-1: Aid for col 1 -- McNemar's test of equality of paired proportions			
<div> <div>Compute</div> <div>Transfer</div> <div>Close</div> <div>Restore</div> <div>Clear</div> <div>Cut</div> <div>Copy</div> <div>Paste</div> <div>Print</div> </div>			
Proportions	Case yes	Case no	Row proportion, π_1
Control yes			
Control no			
Column Proportion, π_2			
Difference, $\delta = \pi_1 - \pi_2 $			
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$			
Odds ratio, $\psi_M = \pi_{10} / \pi_{01}$			
Proportion, π_{01} (in blue cell)			
$P = 0.5 + 0.5 \delta / \eta$			

Since the cases and controls are paired, you must specify:

- the proportion of pairs in which both case and control are expected to use the diet drugs
- the proportions in which only the case or only the control would be expected to be using the diet drugs.

We postulate that 3% of pairs will have both case and control using the drug, and that a total of 5% of the controls and 10% of the cases are users of the diet drug. So we will:

- enter .03 in the upper control-yes, case-yes cell of the 2x2 table
- enter .02 in the control-yes, case-no cell
- enter .07 in the control-no, case-yes cell.

Then click on the button marked **Compute**, and nQuery will fill in the rest of the table.



POT1-1: Aid for col 1 -- McNemar's test of equality of paired proportions			
Compute	Transfer	Close	Restore
Clear	Cut	Copy	Paste
Print			
Proportions	Case yes	Case no	Row proportion, π_1
Control yes	0.030	0.020	0.050
Control no	0.070	0.880	
Column Proportion, π_2	0.100		
Difference, $\delta = \pi_1 - \pi_2 $	0.050		
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$	0.090		
Odds ratio, $\psi_{11} = \pi_{10} / \pi_{01}$	0.286		
Proportion, π_{01} (in blue cell)	0.070		
$P = 0.5 + 0.5 \delta / \eta$	0.778		

The actual hypothesis being tested is that among discordant pairs, half are expected to be in the control-yes, case-no and half in the control-no, case-yes cells. Thus, the required sample size depends only on the proportions entered for the discordant cells.

Click on the **Transfer** button to transfer these values back to the main table.

The screenshot displays the nQuery Advisor software interface. The title bar reads "nQuery Advisor - POT1-1". The menu bar includes "File", "Edit", "View", "Options", "Assistants", "Plot", "Window", and "Help". Below the menu bar is a toolbar with various icons for file operations and analysis. The main window is titled "POT1-1: Main" and contains a table for McNemar's test results.


	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Difference in proportions, $\delta = \pi_1 - \pi_2 $	0.050			
Proportion of discordant pairs, $\eta = \pi_{10} + \pi_{01}$	0.090			
Power (%)				
n (number of pairs)				

Since the investigator wanted 80% power, enter **80** as the required power. nQuery reports that **262** case-control pairs would be required.

nQuery Advisor - POT1-1				
File Edit View Options Assistants Plot Window Help				
POT1-1: Main				
McNemar's test (χ^2) of equality of paired proportions				
	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Difference in proportions, $\delta = \pi_1 - \pi_2 $	0.050			
Proportion of discordant pairs, $\eta = \pi_{10} + \pi_{01}$	0.090			
Power (%)	80			
n (number of pairs)	262			

However, since only 9% (an expected number of 24 in a sample of 262) of the case-control pairs are relevant to the test of equality of paired proportions, the investigator wants to re-compute the required sample size, assuming that the exact sign test will be used for testing.

To get the Exact sign test of equality of paired proportions table:

Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **One group**, **Test**.

Double click on the entry **Paired responses**, or click on the + sign to the left of that entry.

Then select the second entry **Paired responses: Exact sign test** from the two choices below the heading **Paired responses**.

Click **OK**. The sample size table for **Exact sign test of equality of paired proportions** will appear.

This table will look the same as the previous table, except that only one row is highlighted in yellow. Note that you cannot solve for n in this table, but only for power given n. Therefore you cannot type in a value for power.

In this new table, enter the same values which were used in the first four rows of the table above. Enter 262 as the number of pairs. nQuery reports that the power for the exact sign test is only expected to be 73%. The sign test is an exact binomial test that the proportions in the two discordant cells of the 2 x 2 table are equal with a sample size equal to the observed number of discordant pairs.



POT1x-1				
Exact sign test of equality of paired proportions				
	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Difference in proportions, $\delta = \pi_1 - \pi_2 $	0.050			
Proportion of discordant pairs, $\eta = \pi_{10} + \pi_{01}$	0.090			
Power (%)	73			
n (number of pairs)	262			

After trying several values for n in the second column, we find that 305 case-control pairs would provide 80% for an exact test.

Note that for exact tests, the actual probability of rejecting the null hypothesis when it is true is less than or equal to alpha. As a consequence, the attainable alpha level depends on the specified sample size. Therefore, computed power may not increase monotonically with sample size. For details and advice, see the references for this table as listed in the references pane.

POT1x-1					
Exact sign test of equality of paired proportions					
	1	2	3	4	5
Test significance level, α	0.050	0.050			
1 or 2 sided test?	2	2			
Difference in proportions, $\delta = \pi_1 - \pi_2 $	0.050	0.050			
Proportion of discordant pairs, $\eta = \pi_{10} + \pi_{01}$	0.090	0.090			
Power (%)	73	80			
n (number of pairs)	262	305			

To get the statement for this column:

Click on any cell in the calculated column.

Click on the **Create Statement** button. The statement will appear, and you can save it to clipboard, print the statement directly, or store the statement in the Stored Statements panel of your screen. Note that you can select the font that you want the statement to appear in, see Chapter 3. *The File and Options Menus* for details.

A sample size of 305 pairs will have 80% power to detect a difference in proportions of 0.050 when the proportion of discordant pairs is expected to be 0.090 and the method of analysis is a sign test of equality of paired proportions with a 0.050 two-sided significance level. (The sign test is an exact binomial test that the proportions in the two discordant cells of the 2 x 2 table are equal with a sample size equal to the observed number of discordant pairs.)

Example 3

Two group χ^2 test (PTT0) – Compute power or sample size

Two group χ^2 test (PTT0p) – Compute one of two proportions

An investigator is planning a four-week clinical trial. He wants to compare a new drug to a placebo for effectiveness in healing duodenal ulcers. The proportion healed after four weeks of treatment will be compared between the two treatment groups using a Chi-square test at the 5% level.


Many previous trials suggest that 45% of those receiving the placebo will be healed at four weeks, and 75% of patients receiving standard H2 blockers will heal by four weeks. The investigator wants to have 95% power for the trial even if the new drug results in the healing of only 65% of patients.

There are three appropriate tables for this design:

- Two group χ^2 test of equal proportions (odds ratio = 1)
- Two group continuity corrected χ^2 test of equal proportions (odds ratio = 1).
- Fisher's exact test.

See Example 4 for illustrations of the latter two tables.

To bring up the PTT0 sample size table for the Two group χ^2 test of equal proportions:

Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **Two group**, **Test**.

Click on the + sign next to **Chi-square test to compare two proportions** and select the first option, **Compute power or sample size**.

Click **OK**. The **Two group χ^2 test of equal proportions (odds ratio=1)** table will appear.

The following table shows the significance level, 2-sided test, and power already filled in.

Note: The standard χ^2 test is, of course, automatically two-sided, and you should select a two-sided test in sample size tables for χ^2 . If you selected a one-sided test, you would get approximate sample sizes for the normal approximation test, rather than the χ^2 .



nQuery Advisor - [PTT0-1]

File Edit View Options Assistants Plot Window Help

Two group χ^2 test of equal proportions (odds ratio = 1) (equal n's)

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Group 1 proportion, π_1				
Group 2 proportion, π_2				
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$				
Power (%)	95			
n per group				

To customize and complete:

Select the **Edit** menu **Edit Row Names** option.

Rename **Group 1** as **Placebo** and **Group 2** as **New drug**.

Click on the **Update Row Name** button.

In the spreadsheet, enter **.45** for the **Placebo** proportion.

Enter **.65** for the **New drug** proportion. The nQuery Advisor program will calculate the odds ratio and n per group.

nQuery Advisor - [PTT0-1.nqa]

File Edit View Options Assistants Plot Window Help

Two group χ^2 test of equal proportions (odds ratio = 1) (equal n's)

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Placebo proportion, π_1	0.450			
New Drug proportion, π_2	0.650			
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	2.270			
Power (%)	95			
n per group	158			

To complete the second column using one proportion and the odds ratio:

Select the first three rows of column 1.

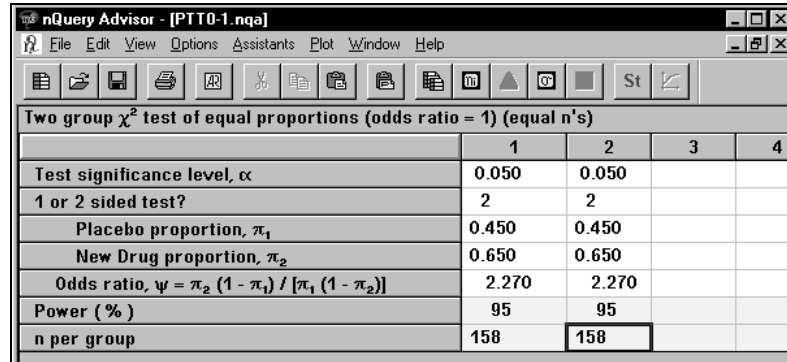
Use the **Edit** menu **Copy** option or **<Ctrl><C>** or the **Copy** button to copy those rows.

Click in the second column and use the **Edit** menu **Paste** option or the **Paste** icon in the toolbar or **<Ctrl><V>** to paste the values into column 2.

Enter the odds ratio and press <Enter>. The nQuery Advisor program will calculate the proportion for the second group.

Enter the Power and press <Enter>.

Then nQuery will calculate n per group.



The screenshot shows the nQuery Advisor window titled "nQuery Advisor - [PTT0-1.nqa]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons for file operations and analysis. The main window displays a table titled "Two group χ^2 test of equal proportions (odds ratio = 1) (equal n's)".

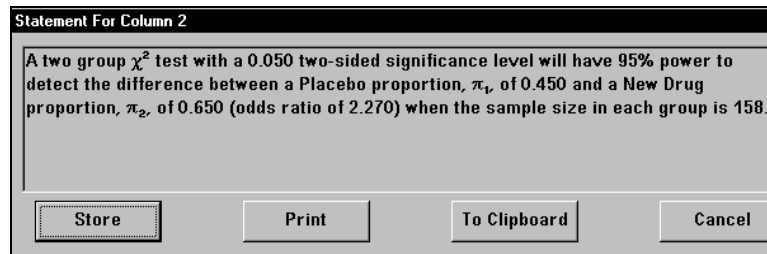
	1	2	3	4
Test significance level, α	0.050	0.050		
1 or 2 sided test?	2	2		
Placebo proportion, π_1	0.450	0.450		
New Drug proportion, π_2	0.650	0.650		
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	2.270	2.270		
Power (%)	95	95		
n per group	158	158		

Whether you enter two proportions or one proportion and the odds ratio, you can see that this study will require 158 subjects per group to achieve 95% power.

To get the statement for this column:

Click on any cell in the calculated column.

Click on the **Create Statement** button. The statement will appear.



The screenshot shows a dialog box titled "Statement For Column 2". It contains a text area with the following statement:

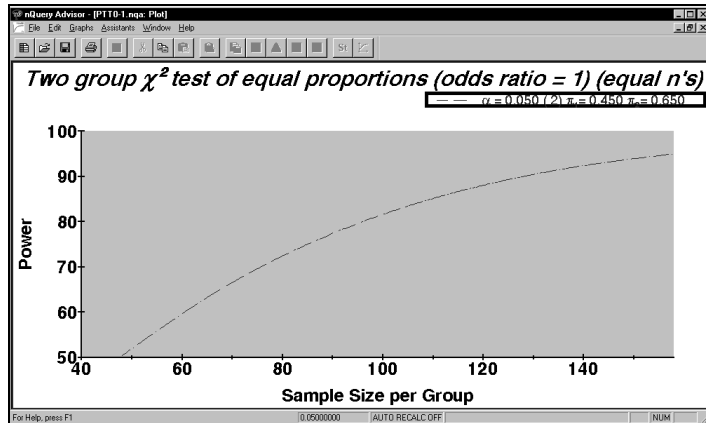
A two group χ^2 test with a 0.050 two-sided significance level will have 95% power to detect the difference between a Placebo proportion, π_1 , of 0.450 and a New Drug proportion, π_2 , of 0.650 (odds ratio of 2.270) when the sample size in each group is 158.

At the bottom of the dialog box are four buttons: Store, Print, To Clipboard, and Cancel.

To get a plot of power versus sample size for this column:

Select the calculated column.

Click on the **Plot** menu **Plot power vs n** option or use the left-most of the two **Plot** icon buttons. The following plot will appear. For other plot options, select **Plot user-selected rows** or the right-most of the two **Plot** icon buttons.



Note that the plot above displays Greek characters. See Chapter 6, *The Plot Menu* for details on including Greek characters in the legend.


Compute one of two proportions

If you want to solve for the detectable difference between two proportions, rather than for power or sample size, then you can use table **PTT0p**

For example, say that the investigator had only 90 patients available per group for this clinical trial. Given that the previous trials suggested that 45% of those receiving the placebo would be healed at four weeks, he wants to find the difference detectable with a power of 95%.

To bring up the PTT0p sample size table for the Two group χ^2 test of equal proportions:



Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **Two group**, **Test**.

Click on the + sign next to **Chi-square test to compare two proportions** and select the second option, **Compute one of two proportions**.

Click **OK**. The **Two group χ^2 test of equal proportions** table will appear.

The following table shows the significance level, 2-sided test, and power already filled in.

nQuery Advisor - [PTT0p-1]

File Edit View Options Assistants Plot Window Help

Two group χ^2 test of equal proportions (equal n's)

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Smaller proportion, π_1				
Larger proportion, π_2				
Power (%)	95			
n per group				

For Help, press F1

AUTO RECALC ON

Enter **.45** for the **Smaller proportion**, and enter **90** for n per group. The nQuery Advisor program will calculate the larger proportion, which for this example turns out to be **.711**. That is, with a sample size of 90 in each group, the power will be 95% to detect the difference between a proportion of .45 and one of .711 using a 5% level Chi-square test.

nQuery Advisor - [PTT0p-1]

File Edit View Options Assistants Plot Window Help

Two group χ^2 test of equal proportions (equal n's)

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Smaller proportion, π_1	0.450			
Larger proportion, π_2	0.711			
Power (%)	95			
n per group	90			

For Help, press F1

95.00000 AUTO RECALC ON



Example 4

Two group χ^2 test (PTT0) and
Sample Size Too Small Warning

Two group continuity corrected χ^2 test
of equal proportions (PTT1)

Two-group Fisher's exact test (PTT2)

This example illustrates the relationship between the three sample size tables for comparison of two independent proportions. Suppose an investigator thinks that one group will have almost all successes and another group almost all failures, and he enters the values shown into PTT0.

nQuery Advisor - [PTT0-1]

File Edit View Options Assistants Plot Window Help

Two group χ^2 test of equal proportions (odds ratio = 1) (equal n's)

	1	2	3	4	
Test significance level, α	0.050				
1 or 2 sided test?	2				
Group 1 proportion, π_1	0.025				
Group 2 proportion, π_2	0.975				
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	1521.000				
Power (%)					
n per group					

When the investigator now wants to solve for the sample size per group giving 80% power, the warning box titled **Sample Size Too Small** will appear.

Sample Size Too Small

The calculated value for n per group using normal approximation formulas is 2.7. However, with this sample size, the minimum expected cell size for your study would be smaller than 3.8 and the normal approximation might not be valid. You should examine the computed sample size to make sure it is large enough to provide reasonable numbers of successes and failures for your planned analysis.

If the minimum expected cell size seems unnecessarily conservative, you may alter the minimum size requirement by choosing the item "Change Minimum Cell Size" in the Options menu.

OK

When you click on **OK**, PTT0 shows a required sample size of 3 per group.

Two group χ^2 test of equal proportions (odds ratio = 1) (equal n's)					
	1	2	3	4	
Test significance level, α	0.050				
1 or 2 sided test?	2				
Group 1 proportion, π_1	0.025				
Group 2 proportion, π_2	0.975				
Odds ratio, $\psi = \pi_2(1 - \pi_1) / [\pi_1(1 - \pi_2)]$	1521.000				
Power (%)	80				
n per group	3				

However, when the sample size is 3 in each group, the expected values in each cell under the null hypothesis are 1.5 successes and 1.5 failures in each group. Under the alternative hypothesis, the expected values of successes and failures in group 1 are 0.075, and 2.925, respectively. In group 2 these expected values are 2.925 and 0.075.

Note: A common rule of thumb in computing a χ^2 test is that the minimum expected value in a cell is at least 5. Clearly, neither under the null hypothesis nor under the alternative can such a large cell size be expected.

The minimum cell size computed by nQuery Advisor depends on the significance level chosen for the test. For a 5% two-sided test, the minimum cell size is 3.8, as shown in the warning box. When you see this warning box, you should evaluate whether the sample size computed is large enough to be adequate.

For this example, the Fisher's exact test cannot reject the null hypothesis at the two-sided 5% level for any possible outcome if the sample sizes are as small as 3, so the computed sample size is far too small. In some other instances, however, you may see the warning box when the computed sample size is, in fact, adequate.

The table PTT1 is designed to provide the sample size which would be required for the continuity corrected Chi-square test which serves as an approximation for the sample size required for Fisher's exact test.

Filling in the PTT1 table with the same numbers, we obtain the following results.



Two groups continuity corrected χ^2 test of equal proportions (odds ratio = 1) (equal n's)				
	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Group 1 proportion, π_1	0.025			
Group 2 proportion, π_2	0.975			
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	1521.000			
Power (%)	80			
n per group	5			

The same **Sample Size Too Small** warning box is seen, and the required sample size is shown as 5 per group.

Let us now turn to the table (PTT2) which makes exact calculations of power for Fisher's exact test. We enter the same information but now instead of entering power and solving for sample size, we enter values 3, 4, and 5 for sample size and have nQuery compute the actual power for Fisher's exact test. Results are shown in the following table.

Two group Fisher's-exact test of equal proportions (odds ratio = 1) (equal n's)					
	1	2	3	4	5
Test significance level, α	0.050	0.050	0.050		
1 or 2 sided test?	2	2	2		
Group 1 proportion, π_1	0.025	0.025	0.025		
Group 2 proportion, π_2	0.975	0.975	0.975		
Power (%)	1	81	97		
n per group	3	4	5		

When n is 3 in each group, it is impossible to reject the null hypothesis at the two-sided 5% level and nQuery returns a power of 1%. For a sample size of 4 in each group the power is 81%, and for a sample size of 5 in each group, the power is 97%. Exact results will frequently lie between results from the PTT0 and PTT1 tables.

In the following example, the **Sample Size Too Small** warning box is seen, but the sample size obtained using PTT0 is, in fact, adequate. The tables below are obtained by using **Print Table to Clipboard** from the **File** menu.

The **Print Table to Clipboard** option uses RTF format to preserve the table structure. This means that you can use your own font choice for the text and numbers, along with the symbol font for the Greek symbols. For details, see Chapter 4, *The Edit Menu*.

Two group χ^2 test of equal proportions (odds ratio = 1) (equal n's)

	1
Test significance level, α	0.025
1 or 2 sided test?	1
Group 1 proportion, π_1	0.025
Group 2 proportion, π_2	0.500
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	39.000
Power (%)	90
n per group	16

Two group continuity corrected χ^2 test of equal proportions (odds ratio = 1) (equal n's)

	1
Test significance level, α	0.025
1 or 2 sided test?	1
Group 1 proportion, π_1	0.025
Group 2 proportion, π_2	0.500
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	39.000
Power (%)	90
n per group	20

Two group Fisher's-exact test of equal proportions (equal n's)

	1	2	3	4	5
Test significance level, α	0.025	0.025	0.025	0.025	0.025
1 or 2 sided test?	1	1	1	1	1
Group 1 proportion, π_1	0.025	0.025	0.025	0.025	0.025
Group 2 proportion, π_2	0.500	0.500	0.500	0.500	0.500
Power (%)	87	90	92	94	95
n per group	16	17	18	19	20

Note that the power cannot be expected to increase monotonically for all parameter choices.

For this example, the sample size given by PTT0 is adequate and gives almost the desired power, while the sample size given by PTT1 is larger than necessary.

Under the null hypothesis, the expected value in each cell is 8, perfectly adequate for a two-sided 5% level test. Under the alternative hypothesis, the expected values for group 1 are 8 and 8, and for group 2 are 0.4 and 15.6. However, the expected values per cell which are relevant to the validity of Type I error are the expected values conditioned on the margins of the observed table. Those expected values are expected to be 4.2 in the smallest cells, a value which should be adequate for validity of the χ^2 test.



Example 5

Confidence interval for $\ln(\text{PTC2})$

In many epidemiologic applications, the investigator wishes to estimate the odds ratio and a confidence interval for it.

In this example, the investigators plan to evaluate an educational program for expectant mothers. The educational program attempts to reduce the risk of preterm birth among expectant mothers who are seen in county prenatal clinics.


Previous studies have found preterm birth rates of 7-9% in similar populations. The intervention would be of interest if it reduced the rate of preterm births enough to produce an odds ratio of 0.5.

The investigator tentatively plans to assign 500 pregnant women to a control group and 500 to an educational intervention group. The question is: how wide is the 95% two-sided confidence interval for the odds ratio likely to be?

The appropriate table for this design is **Confidence interval for $\ln(\text{odds ratio})$.**

To bring up the PTC2 sample size table:



Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions, Two, Confidence**.

Select the third analysis method from the list of analysis methods.

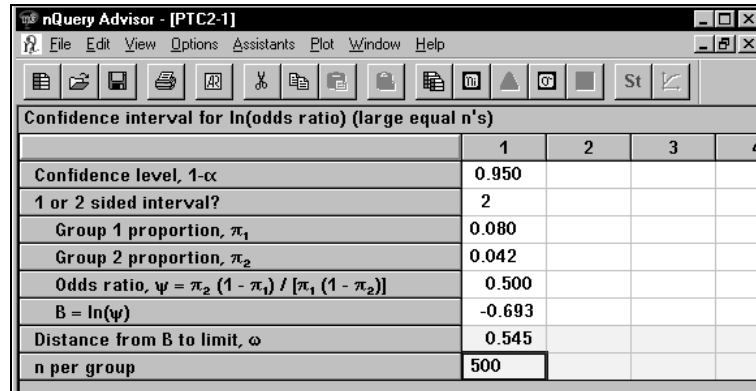
Click **OK**. The Confidence interval for $\ln(\text{odds ratio})$ table will appear with no values entered. The following table shows the table with values for confidence level and 2-sided interval already filled in.

Confidence interval for $\ln(\text{odds ratio})$ (large equal n's)				
	1	2	3	
Confidence level, $1-\alpha$	0.950			
1 or 2 sided interval?	2			
Group 1 proportion, π_1				
Group 2 proportion, π_2				
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$				
$B = \ln(\psi)$				
Distance from B to limit, ω				
n per group				

To complete the table using one proportion and the odds ratio:

Enter **.08** for the proportion of preterm births expected in the **Control** group.

Type **0.5** for the **Odds ratio** and **500** for the **n per group** to get the following completed column. nQuery Advisor will calculate the proportion expected in the Education group, the natural log of the odds ratio and the expected distance from the log odds ratio to the upper or lower limit of the confidence interval.



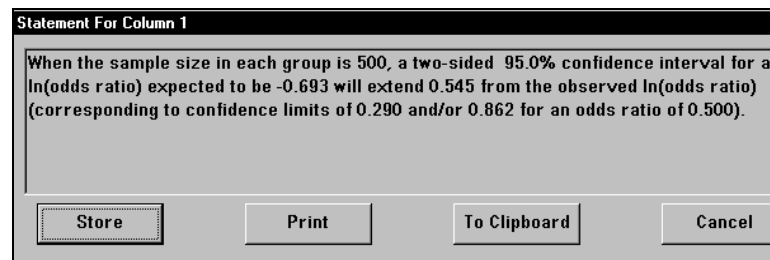
The screenshot shows the nQuery Advisor window with a menu bar (File, Edit, View, Options, Assistants, Plot, Window, Help) and a toolbar. Below the toolbar is a table titled "Confidence interval for ln(odds ratio) (large equal n's)". The table has 5 columns labeled 1, 2, 3, and 4. The first column contains labels for various statistical parameters, and the second column contains their calculated values. The other columns are empty.

	1	2	3	4
Confidence level, $1-\alpha$	0.950			
1 or 2 sided interval?	2			
Group 1 proportion, π_1	0.080			
Group 2 proportion, π_2	0.042			
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	0.500			
$B = \ln(\psi)$	-0.693			
Distance from B to limit, ω	0.545			
n per group	500			

To get the statement for this column:

Click on any cell in the calculated column.

Click on the **Create Statement** button. The statement will appear.



The screenshot shows a dialog box titled "Statement For Column 1". It contains a text area with a statement about the confidence interval. Below the text area are four buttons: Store, Print, To Clipboard, and Cancel.

Statement For Column 1

When the sample size in each group is 500, a two-sided 95.0% confidence interval for a ln(odds ratio) expected to be -0.693 will extend 0.545 from the observed ln(odds ratio) (corresponding to confidence limits of 0.290 and/or 0.862 for an odds ratio of 0.500).

Store Print To Clipboard Cancel

The statement gives the actual lower and upper confidence limits expected for an odds ratio of 0.5 when 500 patients are studied in each group; here, they are 0.290 and 0.862.



Example 6


Two-group Chi-square test comparing proportions in C categories (PTT3)

Investigators want to evaluate whether the combination of two genetic markers has a relationship to the type of inflammatory bowel disease. Two groups of patients will be studied, those with Crohn's disease and those with Ulcerative Colitis.

The proportions who have both markers, only marker A, only marker B, or neither marker will be compared using a Chi-square test. The same number of patients will be recruited from each of the two diagnostic groups, so we will use a two-group Chi-square test with equal n's.

(Please note that there is no unequal n's version of this table. If you have unequal n's, you must use a different table to find sample size or power for a two-group design with C response categories and unequal n's in the two groups. In the Study Goal and Design box, select **Proportion**, **>Two groups**, **Test**, and select the third item in the list, **G group Chi-square test comparing proportions in C categories**, and mark the box for Unequal n's. When the table appears, enter 2 for the number of groups.)

To bring up the sample size table for a 2 x C Chi-square:

Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **Two group**, **Test**.

Select the fourth entry in the list, **Two-group Chi-square test comparing proportions in C categories**.

Click **OK**. The sample size table will appear.

The following table shows the significance level, and the number of response categories already filled in.

nQuery Advisor - [PTT3-1]

File Edit View Options Assistants Plot Window Help

Two-group Chi-square test comparing proportions in C categories

	1	2	3	4
Test significance level, α	0.050			
Number of categories, C	4			
Effect size, $\Delta^2 = \Sigma(\pi_{2i} - \pi_{1i})^2 / [2(\pi_{2i} + \pi_{1i})]$				
Power (%)				
n per group				

To obtain a side table to allow you to enter the expected proportions in each category in each of the two groups, select the **Assistants** menu **Compute Effect Size** option or click on the δ button in the toolbar.

You will see the following side table:

PTT3-1: Aid for col 1 -- Comparison of proportions in C categories

Compute Transfer Close Restore Clear Cut Copy Paste Print

Group	Cat. 1	Cat. 2	Cat. 3	Cat. 4	$\Sigma_i \pi_{ii}$
1					
2					
$\Delta^2 = \Sigma(\pi_{2i} - \pi_{1i})^2 / [2(\pi_{2i} + \pi_{1i})]$					

For Group 1, enter the proportions of subjects expected in each of the four categories:

- Cat. 1 - both markers
- Cat. 2 - marker A only
- Cat. 3 - marker B only
- Cat. 4 - neither marker

For Group 2, enter the proportions expected in the four categories.

When you have finished entering the proportions into the category cells, the Compute button will activate. Click on the **Compute** button. nQuery will fill in the rest of the table, and the Transfer button will activate.

PTT3-1: Aid for col 1 -- Comparison of proportions in C categories

Compute Transfer Close Restore Clear Cut Copy Paste Print

Group	Cat. 1	Cat. 2	Cat. 3	Cat. 4	$\Sigma_i \pi_{ii}$
1	0.040	0.200	0.200	0.560	1.000
2	0.400	0.100	0.100	0.400	1.000
$\Delta^2 = \Sigma(\pi_{2i} - \pi_{1i})^2 / [2(\pi_{2i} + \pi_{1i})]$	0.194				



Click on **Transfer** to transfer the effect size back to the main table.

PTT3-1: Main		
Two-group Chi-square test comparing proportions in C categories		
	1	2
Test significance level, α	0.050	
Number of categories, C	4	
Effect size, $\Delta^2 = \sum(\pi_{2i} - \pi_{1i})^2 / [2(\pi_{2i} + \pi_{1i})]$	0.1939	
Power (%)		
n per group		

The investigator hopes that 40 subjects in each group will provide reasonable power. So enter **40** in the bottom row for **n per group**. nQuery calculates the power as 92%, so the planned study size is adequate.

PTT3-1: Main		
Two-group Chi-square test comparing proportions in C categories		
	1	2
Test significance level, α	0.050	
Number of categories, C	4	
Effect size, $\Delta^2 = \sum(\pi_{2i} - \pi_{1i})^2 / [2(\pi_{2i} + \pi_{1i})]$	0.1939	
Power (%)	92	
n per group	40	

You can print out the table and side table, or you can save the tables.


Example 7

Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata (PTT4)

Investigators plan a clinical trial in which a new drug for prevention of nighttime heartburn will be compared to a placebo. It is felt that body mass index may influence the response rates, so patients will be assigned to three strata based on BMI. In the target population, it is expected that 35% will have a BMI less than 25, 45% will have a BMI from 25 to less than 30, and 20% a BMI of 30 or greater.

Investigators wish to test whether the odds ratio for comparing the success rate in the treated group to that in the placebo group differs from 1.0, assuming that it is not affected by the BMI stratum. The data will be analyzed using the Cochran test (closely related to the Mantel-Haenszel test).

To bring up the sample size table for Mantel-Haenszel (Cochran) test:

Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

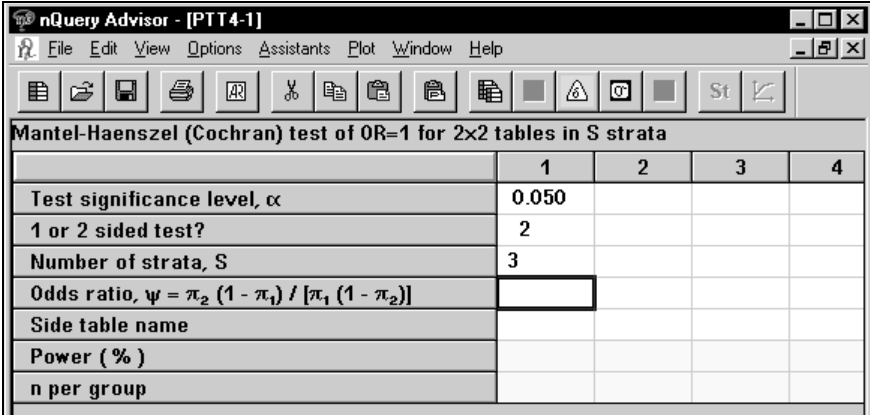
Select **Proportions**, **Two group**, **Test**.

Double click on the entry **Mantel-Haenszel (Cochran) test**, or click on the + sign to the left of this entry.

Then select the top one of the two choices, **Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata**.

Click **OK**. The sample size table for **Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata** will appear.

The following table shows the significance level, one or two-sided test, and the number of strata filled in.



The screenshot shows the 'nQuery Advisor - [PTT4-1]' window. The title bar includes standard window controls. The menu bar contains: File, Edit, View, Options, Assistants, Plot, Window, Help. The toolbar has icons for various functions, including a 'St' button. Below the toolbar, the window displays the title 'Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata'. Below this title is a table with 5 columns and 8 rows. The first column contains labels for various parameters, and the subsequent four columns are numbered 1, 2, 3, and 4. The table is as follows:

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Number of strata, S	3			
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$				
Side table name				
Power (%)				
n per group				

A side table will allow you to enter the expected proportions of each group in each stratum, the OR, and the response rates expected in each stratum for the placebo group. To obtain a side table, select the **Assistants** menu **Compute Effect Size** option or click on the δ button in the toolbar.

You will see the following side table:



PTT4-1: Aid table E1 -- Mantel-Haenzel (Cochran) test								
Compute	Transfer	Close	Restore	Clear	Cut	Copy	Paste	Print
		f_s	OR	Controls, π_{1s}	Cases, π_{2s}			
Odds ratio, $OR = \pi_{2s}(1-\pi_{1s}) / [\pi_{1s}(1-\pi_{2s})]$								
Stratum 1								
Stratum 2								
Stratum 3								
Σf_s								
$D_1 = \Sigma f_s(\pi_{2s} - \pi_{1s})$								
$V_0 = \Sigma f_s \pi_{1s}(1-\pi_{1s})$								
$V_1 = (1/2) \Sigma f_s [(\pi_{1s}(1-\pi_{1s}) + \pi_{2s}(1-\pi_{2s}))]$								

Proportion of subjects expected in each stratum, f_s

In the column headed f_s enter the proportion of subjects expected in each of the three BMI strata.

Proportion responding in each stratum among Controls, π_{1s}

In the column headed Controls, π_{1s} , enter the proportions of placebo-treated patients expected to report successful prevention of nighttime heartburn for each of the three strata. In this example, we expect that the prevention rates will decrease as BMI increases.

Odds Ratio, OR

Enter the expected odds ratio and press <Enter>. Here we are looking for the odds ratio of 1.6 or greater. nQuery will automatically calculate the resulting proportions reporting successful prevention of heartburn expected for the active treatment group in each of the strata.

After you have entered all necessary values, the Compute button will be activated. Click on the button marked **Compute**. The nQuery program will fill in the rest of the table, and the Transfer button will be activated.

PTT4-1: Aid table E1 -- Mantel-Haenzel (Cochran) test									
Compute	Transfer	Close	Restore	Clear	Cut	Copy	Paste	Print	
			f_s	OR	Controls, π_{1s}		Cases, π_{2s}		
Odds ratio, $OR=\pi_2(1-\pi_1)/[\pi_1(1-\pi_2)]$				1.600					
Stratum 1			0.350		0.500		0.615		
Stratum 2			0.450		0.400		0.516		
Stratum 3			0.200		0.300		0.407		
Σf_s			1.000000						
$D_1=\Sigma f_s(\pi_{2s}-\pi_{1s})$			0.113999						
$V_0=\Sigma f_s\pi_s(1-\pi_s)$			0.243745						
$V_1=(1/2)\Sigma f_s[(\pi_{1s}(1-\pi_{1s})+\pi_{2s}(1-\pi_{2s}))]$			0.240493						

Click on **Transfer** to transfer these values back to the main table. For this sample size table, the values of the three parameters necessary for computing sample size will not be displayed in the main table. However, the name of the side table will appear, and you can copy and paste that name to other columns.

PTT4-1: Main				
Mantel-Haenszel (Cochran) test of $OR=1$ for 2x2 tables in S strata				
	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Number of strata, S	3			
Odds ratio, $\psi = \pi_2(1 - \pi_1) / [\pi_1(1 - \pi_2)]$	1.600			
Side table name	E1			
Power (%)				
n per group				

Note: Changing the values in this side table will affect all columns in which its name appears.

Since the investigator wants 90% power, enter **90** as the required power and press the <Enter> key. nQuery reports that 90% power requires **393** assigned to the placebo group and the same number to the active treatment group, for a total of almost 800 subjects needed for the clinical trial.



PTT4-1: Main				
Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata				
	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Number of strata, S	3			
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	1.600			
Side table name	E1			
Power (%)	90			
n per group	393			

To get the statement for this column:

Click on any cell in the calculated column.

Click on the **Create Statement** button. The statement will appear and can be saved to clipboard, printed directly, or stored in the Stored Statements panel of your screen

A Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in 3 strata will have 90% power to detect an odds ratio of 1.600 using a two-sided 0.050 level test, when the sample size is 393 and the stratum and response proportions are those displayed in the side-table for this column.


Example 8

Test for linear trend in G x 2 table (logistic model)(PGT1)

nQuery Advisor provides sample size computations for a logistic model when the response variable is yes/no and the covariate is a discrete ordered variable such as fixed dose levels. Suppose the investigator wants to demonstrate a dose response to 5 doses of a new drug to prevent transplant rejection. The response variable is survival to a fixed time post transplant.

To bring up the PGT1 sample size table:

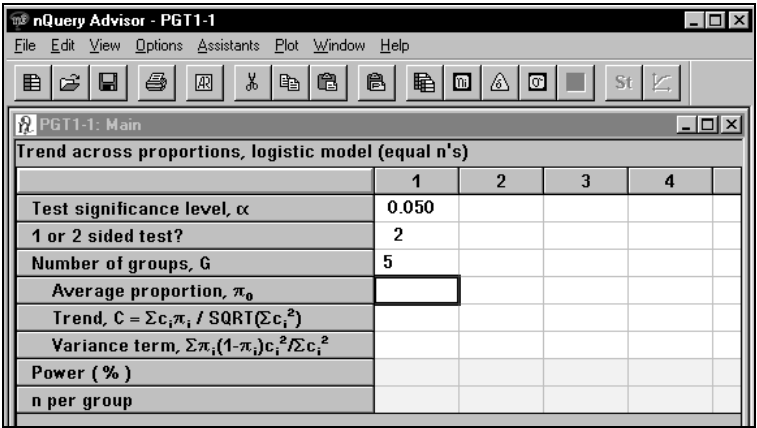


Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions, >Two, Test**.

Select the second analysis method from the list of analysis methods.

Click **OK**. The **Trend across proportions, logistic model** table will appear with no values entered. The following table shows the table with values for significance level, 2-sided test, and 5 groups entered.



The screenshot shows the nQuery Advisor - PGT1-1 window. The title bar reads 'nQuery Advisor - PGT1-1'. The menu bar includes 'File', 'Edit', 'View', 'Options', 'Assistants', 'Plot', 'Window', and 'Help'. The toolbar contains various icons for file operations and calculations. The main window displays a table titled 'Trend across proportions, logistic model (equal n's)'. The table has columns for parameters and four dose levels (1, 2, 3, 4). The following table represents the data entered in the screenshot:

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Number of groups, G	5			
Average proportion, π_0				
Trend, $C = \sum c_i \pi_i / \text{SQRT}(\sum c_i^2)$				
Variance term, $\sum \pi_i (1 - \pi_i) c_i^2 / \sum c_i^2$				
Power (%)				
n per group				

To obtain a side table to allow you to enter the proportions expected to survive at each dose level, select **Compute Effect Size** from the **Assistants** menu or click on the **δ** button.

Enter the proportions expected at each dose level. The coefficients necessary to test for linear trend for equally spaced doses have already been entered in the table. If your doses are unequally spaced, replace these with the appropriate set of coefficients.

When all values have been entered, click on **Compute** to see the summary values shown.



nQuery Advisor - PGT1-1					
File Edit View Options Assistants Window Help					
PGT1-1: Main					
Trend across proportions, logistic model (equal n's)					
	1	2	3	4	
Test significance level, α	0.050				
1 or 2 sided test?	2				
Number of groups, G	5				
PGT1-1: Aid for col 1 - Test for trend across proportions-logistic model (equ...					
Compute	Transfer	Close	Clear	Cut	Copy Paste Print
Group	Proportion	Coefficient			
1	0.200	-2.000			
2	0.300	-1.000			
3	0.400	0.000			
4	0.500	1.000			
5	0.600	2.000			
Trend, $C = \sum c_i \mu_i / \text{SQRT}(\sum c_i^2)$	0.316	$\sum C_i = 0.000$			
Average proportion, π_0	0.400				
Variance term, $\sum \pi_i (1-\pi_i) c_i^2 / \sum c_i^2$	0.206				

After computing, click on **Transfer** to transfer these values back to the main table. For this study, the investigator wants to have 80% power. At least 19 animals would be required per dose group.

nQuery Advisor - PGT1-1					
File Edit View Options Assistants Plot Window Help					
PGT1-1: Main					
Trend across proportions, logistic model (equal n's)					
	1	2	3	4	
Test significance level, α	0.050				
1 or 2 sided test?	2				
Number of groups, G	5				
Average proportion, π_0	0.400				
Trend, $C = \sum c_i \pi_i / \text{SQRT}(\sum c_i^2)$	0.31623				
Variance term, $\sum \pi_i (1-\pi_i) c_i^2 / \sum c_i^2$	0.206000				
Power (%)	80				
n per group	19				

Note that the side table can be printed to Clipboard for inclusion in other documents, printed directly, and/or saved with the main table.

Example 9

Equivalence and Bioequivalence for Paired Proportions

Paired test of equivalence in proportions (n large) (POE0)

Paired test of equivalence in proportions: Lower confidence limit for difference in paired proportions (simulation), Upper confidence limit for difference in paired proportions (simulation), Two-sided confidence limits for difference in paired proportions (simulation) (POE1abc)


An investigator wishes to demonstrate that sensitivity for a new cheaper diagnostic test is as least as high as that of the standard diagnostic test, about 85%. If the investigator wants to demonstrate that sensitivity with the new test is no more than 5% lower than the older test, how big a sample of patients with the disease must be evaluated using both tests?

She wants to demonstrate non-inferiority for the new diagnostic test. The null hypothesis to be tested is $H_0: \pi_T - \pi_S \leq -.05$ (i.e. sensitivity is not equivalent and is inferior) versus the alternative hypothesis that $H_1: \pi_T - \pi_S > -.05$ (sensitivity is not inferior).

The investigator wants a power of 85% when the two tests have equal sensitivity. The data will be analyzed using the Blackwelder approach to testing equivalence of paired proportions.

To get a preliminary idea of the required sample size, we use the table **Paired test of equivalence in proportions (n large) (POE0)**. To bring up this sample size table:



Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **One group**, **Equivalence**.

Select the first entry **Paired responses: Equivalence of Proportions**.

Click **OK**. The sample size table for **Paired test of equivalence in proportions (n large)** will appear.

The following table shows the significance level already filled in.



nQuery Advisor - [POE0-1]

File Edit View Options Assistants Plot Window Help

Paired test of equivalence in proportions (n large)

	1	2	3	4	5
Test significance level, α (one-sided)	0.050				
Equivalence limit difference, Δ_0					
Expected difference, Δ_1					
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$					
Power (%)					
n (number of pairs)					

The specified equivalence limit difference is **-.05** (the null hypothesis of inferiority.) The expected difference is **0.0** (the alternative hypothesis of equivalence or non-inferiority). We enter those values in their respective rows.

We must now specify the expected proportion discordant, that is, the proportion of patients in whom the two diagnostic tests will disagree under the alternative hypothesis. Since both margins of the 2x2 table are assumed to be .85 for the probability of a positive test, if the results on the two tests were independent, we would expect:

- both to be positive in 72.35% of patients
- standard to be positive and test negative in 12.75% of cases
- standard to be negative and test positive in 12.75% of patients
- both to be negative in 2.25% of patients.

For this scenario, the proportion of discordant results would be .255. However, we would expect a positive correlation between test results; that is that the outcomes “both positive” and “both negative” would be more likely than under the independence scenario. So, let us postulate that the values in the four cells are 80%, 5%, 5%, and 10% respectively, with a total of 10% discordant. So, we enter **0.10** for the proportion discordant. We then enter **85** for the requested power. nQuery reports that a sample size of **288** patients with the disease will be required.

nQuery Advisor - [POE0-1]						
File Edit View Options Assistants Plot Window Help						
<div> </div>						
Paired test of equivalence in proportions (n large)						
	1	2	3	4	5	
Test significance level, α (one-sided)	0.050					
Equivalence limit difference, Δ_0	-0.050					
Expected difference, Δ_1	0.000					
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$	0.100					
Power (%)	85					
n (number of pairs)	288					

Now we want to compare the number of pairs required for 85% power versus 90% power. To calculate 90% power, we use the **Edit** menu **Copy** option to copy the entries in the first four rows of column 1. We use the **Edit** menu **Paste** option to paste those entries into the first four rows of column 2.

Type 90 in the Power row for column 2, and nQuery computes 343 pairs for 90% power.

nQuery Advisor - [POE0-1]						
File Edit View Options Assistants Plot Window Help						
<div> </div>						
Paired test of equivalence in proportions (n large)						
	1	2	3	4	5	
Test significance level, α (one-sided)	0.050	0.050				
Equivalence limit difference, Δ_0	-0.050	-0.050				
Expected difference, Δ_1	0.000	0.000				
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$	0.100	0.100				
Power (%)	85	90				
n (number of pairs)	288	343				


Results for this sample size table are based on a normal approximation.

Since the equivalence test is essentially based only on the number of patients in which there is discordance (expected to be about 34 when 343 are enrolled), we want to check that the 343 cases will really be enough. To do this, we use another sample size table in nQuery which computes power for a test of non-equivalence based on the observed lower limit of the confidence interval for the difference in proportions.



To bring up the sample size table for Lower confidence limit for difference in paired proportions:



Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **One** group, **Equivalence**.

Double click on the entry **Paired responses: Equivalence of proportions (using Confidence Interval)**, or click on the + sign to the left of that entry.

Then select the top of the three choices, **Lower limit for confidence interval for $\pi_T - \pi_S$ (paired responses)**.

Click **OK**. The sample size table for **Lower confidence limit for difference in paired proportions (simulation)** will appear.

The following table shows the confidence level, and the expected difference filled in.

POE1a-1				
Lower confidence limit for difference in paired proportions (simulation)				
	1	2	3	4
Confidence level, $1-\alpha$ (one-sided)	0.950			
Expected difference, $\pi_T - \pi_S, \Delta_1$	0.000			
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$				
Proportion both yes, π_{11}				
Lower limit for $\pi_T - \pi_S$, LL				
Number of simulations				
Random seed for simulations				
Power (%)				
n (number of pairs)				

This table has a side table to help you fill in the expected proportions.

To obtain a side table to allow you to enter the expected proportions of patients in each cell of the 2x2 table, select the **Assistants** menu **Compute Effect Size** option, or click on the δ button in the toolbar.

You will see the following table. We have already filled in the postulated proportions described above.

POE1a-1: Aid for col 4 -- 2 x 2 probabilities for paired proportions			
Compute	Transfer	Close	Restore
Proportions		Standard yes	Standard no
Test yes		0.800	0.050
Test no		0.050	
Column Proportion, π_S			
Difference, $\Delta_1 = \pi_T - \pi_S$			
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$			
Odds ratio, $\psi_{M1} = \pi_{10} / \pi_{01}$			
Proportion, π_{01} (in blue cell)			
$P = 0.5 + 0.5 \Delta_1 / \eta$			
Product-moment correlation, ϕ			

Click on the Compute button, and nQuery computes the summary values.

POE1a-1: Aid for col 4 -- 2 x 2 probabilities for paired proportions			
Compute	Transfer	Close	Restore
Proportions		Standard yes	Standard no
Test yes		0.800	0.050
Test no		0.050	0.100
Column Proportion, π_S		0.850	
Difference, $\Delta_1 = \pi_T - \pi_S$		0.000	
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$		0.100	
Odds ratio, $\psi_{M1} = \pi_{10} / \pi_{01}$		1.000	
Proportion, π_{01} (in blue cell)		0.050	
$P = 0.5 + 0.5 \Delta_1 / \eta$		0.500	
Product-moment correlation, ϕ		0.608	

Note that the values we have postulated correspond to an assumed correlation of .608 between the results of the two tests, see bottom row of the side table. Click on the **Transfer** button, and nQuery will transfer the necessary summary values back to the main table.



POE1a-1: Main				
Lower confidence limit for difference in paired proportions (simulation)				
	4	5	6	7
Confidence level, $1-\alpha$ (one-sided)	0.950			
Expected difference, $\pi_T - \pi_S, \Delta_1$	0.000			
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$	0.100			
Proportion both yes, π_{11}	0.800			
Lower limit for $\pi_T - \pi_S, LL$				
Number of simulations				
Random seed for simulations				
Power (%)				
n (number of pairs)				

Enter the value **-.05** for the lower limit of the confidence interval for $\pi_T - \pi_S$.

At this point, you must select a number of simulated experiments. Here we enter **3600** to get an estimate of power accurate to within about $\pm 1\%$ for powers near 90%. Next you specify a random seed for the simulation (any integer greater than or equal to 0), along with n , number of pairs, then nQuery Advisor will provide an estimate of the power. We enter **12** for the random seed for the simulations, enter the sample size **343** and press the **<Enter>** key.

nQuery Advisor will first give an estimate of how long the calculations will take on your computer; you can choose to cancel, or run minimized. If you do not run minimized, when nQuery starts the 3600 simulations to calculate the Power, you can watch the progress of the calculation or cancel the process.

Progress of simulations	
<div><div></div><div></div></div>	
Simulations completed:	280 / 3600
Time elapsed:	4.7
Estimated power:	89.64
95% confidence interval for power, normal approximation	
Lower limit:	86.07
Upper limit:	93.21
<div>CancelMinimize</div>	

If you click on the **Cancel** button, you will see a dialog box outlining the calculations performed so far.

Confirm cancellation of survival simulation

Simulations completed:

544 / 3600

Estimated power:

89.89

95% confidence interval for power, normal approximation

Lower limit:

87.36

Upper limit:

92.42

You may wish to write down the above information before choosing the "Confirm cancellation" button, as this information will not be saved. You may return to the calculation by choosing the "Continue simulations" button.

Confirm cancellation

Continue simulations

Using this dialog box, you can continue the simulations or confirm the cancellation. (This simulation takes about 20 seconds on a 600 MHz computer.)

For details on the simulation method used, see *Methods of Computation for Each Table in Section 1 of the Appendix*.

POE1a-1: Main				
Lower confidence limit for difference in paired proportions (simulation)				
	4	5	6	
Confidence level, 1- α (one-sided)	0.950			
Expected difference, $\pi_T - \pi_S, \Delta_1$	0.000			
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$	0.100			
Proportion both yes, π_{11}	0.800			
Lower limit for $\pi_T - \pi_S, LL$	-0.050			
Number of simulations	3600			
Random seed for simulations	12			
Power (%)	88			
n (number of pairs)	343			

The computed power is a little less than 90%, so in the next column we re-compute power with an n of 355.



POE1a-1: Main				
Lower confidence limit for difference in paired proportions (simulation)				
	4	5	6	
Confidence level, $1-\alpha$ (one-sided)	0.950	0.950		
Expected difference, $\pi_T - \pi_S, \Delta_1$	0.000	0.000		
Proportion discordant, $\eta = \pi_{10} + \pi_{01}$	0.100	0.100		
Proportion both yes, π_{11}	0.800	0.800		
Lower limit for $\pi_T - \pi_S, LL$	-0.050	-0.050		
Number of simulations	3600	3600		
Random seed for simulations	12	13		
Power (%)	88	90		
n (number of pairs)	343	355		

To get the statement for the second column:

Click on any cell in the calculated column.

Click on the **Create Statement** button. The statement will appear, and you can save the statement to clipboard, print it out directly, or store the statement in the Stored Statements panel of your screen. Note that you can select the font to be used for your statement, see Chapter 4, *The Edit Menu* for details.

With 355 subjects, the lower limit of the observed one-sided 95.0% confidence interval will be expected to exceed -0.050 with 90% power when the Expected difference, $\pi_T - \pi_S, \Delta_1$, is 0.000 and the Proportion discordant, $\eta = \pi_{10} + \pi_{01}$, is 0.100 and the Proportion both yes, π_{11} , is 0.800; results are based on 3600 simulations using the Newcombe-Wilson score method to construct the confidence interval. (Newcombe RG (1988) Improved confidence intervals for the difference between binomial proportions based on paired data. *Statistics in Medicine* 17:2635-2650.)

If the investigator wanted to demonstrate that sensitivity for the new test was neither higher nor lower than that for the standard, she could use the table **Two-sided confidence limits for difference in paired proportions (simulation) (POE1c)**.

Example 11 shows how to use the two one-sided test (TOST) approach to demonstrating equivalence in the context of independent proportions.

Example 10

Equivalence and Bioequivalence for Independent Proportions

Two group test of equivalence in proportions (PTE0)

Two group test of equivalence in proportions:

Lower confidence limit for difference in proportions (simulation),

Upper confidence limit for difference in proportions (simulation),

Two-sided confidence limits for difference in proportions (simulation) (PTE1abc)


What sample size is required for a study comparing a new type of dental implant to a reference standard? Outcome variables are five-year implant success rate, pocket depth, gingival health scores and rate of bone loss. Previous results with the standard implant show success rates varying from 90% to 95%.

We pose the question as one of demonstrating non-inferiority. The null hypothesis to be tested is $H_0: \pi_T - \pi_S \leq -.05$ (i.e. five-year success rate with the new implant is not equivalent and is inferior to that with the standard) versus the alternative hypothesis that $H_1: \pi_T - \pi_S > -.05$ (success rate is not inferior).

The investigator wants a power of 85% when the two types of implants have the same success rate. The data will be analyzed using the Blackwelder approach to testing equivalence of independent proportions.

To get a preliminary idea of the required sample size, we use the table **Two group test of equivalence in proportions (PTE0)**. To bring up this sample size table:



Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **Two group**, **Equivalence**.

Select the first entry **Two group test of equivalence in proportions**.

Click **OK**. The sample size table for **Two group test of equivalence in proportions (large equal n's)** will appear.

The following table shows the significance level already filled in.



nQuery Advisor - [PTE0-1]

File Edit View Options Assistants Plot Window Help

Two group test of equivalence in proportions (large equal n's)

	1	2	3	4
Test significance level, α (one-sided)	0.050			
Standard proportion, π_S				
Equivalence limit difference, $\pi_T - \pi_S, \Delta_0$				
Test expected proportion, π_T				
Expected difference, $\pi_T - \pi_S, \Delta_1$				
Power (%)				
n per group				

In the first column, we will compute sample size assuming that the success rate for the standard implant is 90%, so enter **0.90** in the Standard proportion row of the table. The specified equivalence limit difference is **-0.05** (the null hypothesis of inferiority), and the expected value for the proportion of successes for the new implant is **0.90**, so the difference is **0.0** (the alternative hypothesis of equivalence or non-inferiority).

The investigator wants 85% power, so enter **85** for the requested power and press <Enter>. nQuery reports that a sample size of **518** patients must be studied with the new implant type, and the same number with the reference implant, for a total of 1036 patients needed in the trial.

nQuery Advisor - [PTE0-1]

File Edit View Options Assistants Plot Window Help

Two group test of equivalence in proportions (large equal n's)

	1	2	3	4
Test significance level, α (one-sided)	0.050			
Standard proportion, π_S	0.900			
Equivalence limit difference, $\pi_T - \pi_S, \Delta_0$	-0.050			
Test expected proportion, π_T	0.900			
Expected difference, $\pi_T - \pi_S, \Delta_1$	0.000			
Power (%)	85			
n per group	518			

We will use the second column to see what sample size will be needed if both standard and test success rates are 95%.


Two group test of equivalence in proportions (large equal n's)				
	1	2	3	4
Test significance level, α (one-sided)	0.050	0.050		
Standard proportion, π_S	0.900	0.950		
Equivalence limit difference, $\pi_T - \pi_S, \Delta_0$	-0.050	-0.050		
Test expected proportion, π_T	0.900	0.950		
Expected difference, $\pi_T - \pi_S, \Delta_1$	0.000	0.000		
Power (%)	85	85		
n per group	518	274		

We see that the assumptions made about the expected success rates have a large influence on the required sample size.

Results for this sample size table are based on a normal approximation.

Since the expected proportions are 90% and 95%, we want to check that these sample sizes are adequate. To do this, we use another sample size table in nQuery, the table which computes power for a test of non-equivalence based on the observed lower limit of the confidence interval for the difference in proportions.

To bring up the sample size table for Lower confidence limit for difference in proportions (simulation):

Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions, Two group, Equivalence**.

Double click on the second entry **Two group test of equivalence in proportions (using Confidence Interval)**, or click on the + sign to the left of this entry.

Then select the upper of the three choices, **Lower limit of confidence interval for $\pi_T - \pi_S$** .

Click **OK**. The sample size table for **PTE1a** will appear.

The following table shows the confidence level, and the expected proportions for standard and test already filled in.



nQuery Advisor - [PTE1a-1]

File Edit View Options Assistants Plot Window Help

Lower confidence limit for difference in proportions (simulation)

	1	2	3	4	5
Confidence level, $1-\alpha$ (one-sided)	0.950				
Standard proportion, π_S	0.900				
Test expected proportion, π_T	0.900				
Lower limit for $\pi_T - \pi_S$, LL					
Number of simulations					
Random seed for simulations					
Power (%)					
n per group					

Enter the value **-.05** for the lower limit of the confidence interval for $\pi_T - \pi_S$.

At this point, you must select a number of simulated experiments. Here we enter **5100** to get an estimate of power accurate to within about $\pm 1\%$ for powers near 85%.

(The confidence interval for a proportion, p , extends about $\pm 2\sqrt{p(1-p)/n}$ using the normal approximation to the binomial, so when $p=.85$ and $n=5100$, this value is $\pm .01$.)

Next you specify a random seed for the simulation (any integer greater than or equal to 0), along with n , number of pairs, then nQuery Advisor will provide an estimate of the power. We enter **35** for the random seed for the simulations, enter the sample size **518** obtained using the previous table PTE0 and press the **<Enter>** key. You will see dialog boxes showing the progress of the simulation, see Example 9 for details. (The simulation for this example takes about 40 seconds on a 266 MHz computer.)

For details on the simulation method used, see *Methods of Computation for Each Table* in Section 1 of the Appendix.

Lower confidence limit for difference in proportions (simulation)					
	1	2	3	4	5
Confidence level, $1-\alpha$ (one-sided)	0.950				
Standard proportion, π_S	0.900				
Test expected proportion, π_T	0.900				
Lower limit for $\pi_T - \pi_S$, LL	-0.050				
Number of simulations	5100				
Random seed for simulations	35				
Power (%)	84				
n per group	518				

The computed power is a little less than 85%; in the second column we compute power under the assumption that the success rates are higher, using an n of 274 per group, the sample size obtained using the previous table, PTE0.

Lower confidence limit for difference in proportions (simulation)					
	1	2	3	4	
Confidence level, $1-\alpha$ (one-sided)	0.950	0.950			
Standard proportion, π_S	0.900	0.950			
Test expected proportion, π_T	0.900	0.950			
Lower limit for $\pi_T - \pi_S$, LL	-0.050	-0.050			
Number of simulations	5100	5100			
Random seed for simulations	35	35			
Power (%)	84	82			
n per group	518	274			

To get a statement for the second column:

Click on any cell in the calculated column.

Click on the **Create Statement** button. The statement will appear and can be saved to clipboard, printed directly, or stored in the Stored Statements panel of your screen. Note that you can select the font to be used for your statement. See Chapter 4, *The Edit Menu for details*.

With 274 subjects in each group, the lower limit of the observed one-sided 95.0% confidence interval will be expected to exceed -0.050 with



82% power when the Standard proportion, π_s , is 0.950 and the Test expected proportion, π_T , is 0.950; results are based on 5100 simulations using the Newcombe-Wilson score method to construct the confidence interval. (Newcombe RG (1988) Interval estimation for the difference between independent proportions: comparison of eleven methods. Statistics in Medicine 17:873-890.)

Unequal n's


If the investigator wanted to study fewer patients in the group receiving the standard implants, sample size could be determined for unequal n's. The PTE1 tables are available for unequal n's.

You can access the unequal n's version of a table in two ways:

- Request unequal n's version of the current table
- Use Study Goal and Design box to request new table for unequal n's

To get the Unequal n's version of the current table:

Click on the **Unequal n's** button, .

Or, click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **Two group**, **Equivalence**.

Double click on the second entry **Two group test of equivalence in proportions (using Confidence Interval)**, or click on the + sign to the left of that entry.

Then select the top one of the three choices, **Lower limit of confidence interval for $\pi_T - \pi_s$** .

Check the **Unequal n's** field in the lower left of the Study Goal and Design box.

Click **OK**. The sample size table for **PTE1aU** will appear.

Lower confidence limit for difference in proportions (simulation) (unequal n's)					
	1	2	3	4	5
Confidence level, $1-\alpha$ (one-sided)					
Standard proportion, π_S					
Test expected proportion, π_T					
Lower limit for $\pi_T - \pi_S$, LL					
Number of simulations					
Random seed for simulations					
Power (%)					
n_S					
n_T					

You work with this table in the same way as the previous, equal n's table, except that now you must enter the sample sizes for each group.

Bioequivalence – Test results are neither higher nor lower

For studies in which you want to demonstrate that results for the new test are neither higher nor lower than the results for the standard, you could use the table **Two-sided confidence limits for difference in proportions (simulation) (PTE1c)**. For an example of finding the sample size for a two one-sided test (TOST) approach to demonstrating equivalence, see Example 11, the next example in this chapter.

Example 11

Equivalence and Bioequivalence for Independent Proportions (TOST procedure)

Two group test of equivalence in proportions (PTE0))

Lower confidence limit for difference in proportions (simulation), Upper confidence limit for difference in proportions (simulation), Two-sided confidence limits for difference in proportions (simulation) (PTE1)abc)

What sample size is required for a study to demonstrate that the proposed ED50 of a new drug is comparable to the ED50 of the standard? Rats will be randomly assigned to either the new or the standard drug, and the proportion of rats showing the required response will be recorded.




The ED50 of the new drug should be neither more nor less potent than that of the standard; that is both should produce a 50% response rate. The two doses will be considered equivalent if we can reject both:

- the null hypothesis that $H_{0L}: \pi_T - \pi_S \leq -.10$
- and
- the null hypothesis that $H_{0U}: \pi_T - \pi_S \geq +.10$ each at a one-sided 5% level.

Alternatively, one requires that a 90% confidence interval for $\pi_T - \pi_S$ has lower limit above -0.10 and upper limit below +0.10. The investigator wants a power of 90% when the ED50 does have the same 50% response rate. The data will be analyzed using the Newcombe-Wilson score method to construct the confidence interval.

To get a preliminary idea of the required sample size, we use the table **Two group test of equivalence in proportions (PTE0)**.

To bring up the PTE0 sample size table:

Click on the **File** menu **New** option or , the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions**, **Two group**, **Equivalence**.

Select the first entry **Two group test of equivalence in proportions**.

Click **OK**. The sample size table for **Two group test of equivalence in proportions (large equal n's)** will appear.

The following table shows the significance level already filled in.

Two group test of equivalence in proportions (large equal n's)				
	1	2	3	4
Test significance level, α (one-sided)	0.050			
Standard proportion, π_S				
Equivalence limit difference, $\pi_T - \pi_S, \Delta_0$				
Test expected proportion, π_T				
Expected difference, $\pi_T - \pi_S, \Delta_1$				
Power (%)				
n per group				

We compute sample size for a test of the single null hypothesis H_{0L} by assuming that the response rate for the standard drug is 50%, so enter **0.50** in the second


row of the table. The specified equivalence limit difference is **-0.10** (the null hypothesis of less effectiveness.)

The expected value for the proportion of successes for the new drug is **0.50**, so the difference is **0.0** (the alternative hypothesis of equivalence). The investigator wants 90% power for the two tests, so enter **95** for the requested power for this single test. Power for the combined tests is obtained as 100 times $(1-2\beta)$ where β is the probability of a Type II error for a single test under the alternative of equality of the two proportions. nQuery reports that a sample size of 542 rats must be studied with each drug, for a total of 1084 rats needed in the study.

Two group test of equivalence in proportions (large equal n's)				
	1	2	3	
Test significance level, α (one-sided)	0.050			
Standard proportion, π_S	0.500			
Equivalence limit difference, $\pi_T - \pi_S, \Delta_0$	-0.100			
Test expected proportion, π_T	0.500			
Expected difference, $\pi_T - \pi_S, \Delta_1$	0.000			
Power (%)	95			
n per group	542			

Although we expect that a sample size sufficient for 95% power for each of the single tests will provide 90% power for both when the two drugs are, in fact equivalent, we can check this by using another sample size table in nQuery. This table computes power for a test of non-equivalence based on the observed upper and lower limits of the confidence interval for the difference in proportions.

To bring up the sample size table for Two-sided confidence limit for difference in proportions (simulation):

Click on the **File** menu **New** option or  the **New** icon. The Study Goal and Design dialog box will appear.

Select **Proportions, Two group, Equivalence**.

Double click on the second entry **Two group test of equivalence in proportions (using Confidence Interval)**, or click on the + sign to the left of the entry.



Then select the third of the three choices:

Two sided confidence interval for $\pi_T - \pi_S$.

Click **OK**. The sample size table for **Two-sided confidence interval for difference in proportions (simulation)** will appear.

The following table shows the confidence level, and the expected proportions for standard and test already filled in.

Two-sided confidence limits for difference in proportions (simulation)					
	1	2	3	4	
Confidence level, $1-\alpha$	0.900				
Standard proportion, π_S	0.500				
Test expected proportion, π_T	0.500				
Lower limit for $\pi_T - \pi_S$, LL					
Upper limit for $\pi_T - \pi_S$, UL					
Number of simulations					
Random seed for simulations					
Power (%)					
n per group					

Enter the value **-.10** for the lower limit of the confidence interval for $\pi_T - \pi_S$ and **+0.10** for the upper limit. Request the desired number of simulations; here we enter **3600** to get an estimate of power accurate to within about $\pm 1\%$ for powers near 90%. We also enter a value for the random seed for the simulations, and enter the sample size **542**.

As discussed in Example 9 in this chapter, nQuery Advisor will first give an estimate of how long the calculations will take on your computer; you can choose to cancel, or run minimized. If you do not run minimized, when nQuery starts the 3600 simulations to calculate the Power, the Progress of Simulations dialog box appears. You can use that dialog box to watch the progress of the calculation or cancel the process.

Progress of simulations

Simulations completed: 193 / 3600

Time elapsed: 2.5

Estimated power: 90.67

95% confidence interval for power, normal approximation

Lower limit: 86.50

Upper limit: 94.75

Cancel Minimize

The computed power is 90% as expected.

Two-sided confidence limits for difference in proportions (simulation)					
	1	2	3	4	
Confidence level, $1-\alpha$	0.900				
Standard proportion, π_S	0.500				
Test expected proportion, π_T	0.500				
Lower limit for $\pi_T - \pi_S$, LL	-0.100				
Upper limit for $\pi_T - \pi_S$, UL	0.100				
Number of simulations	3600				
Random seed for simulations	101				
Power (%)	90				
n per group	542				

To get a statement for this result:

Click on any cell in the calculated column.

Click on the **Create Statement** button. The statement will appear and can be saved to clipboard, printed directly, or stored in the Stored Statements panel of your screen. Note that you can select the font to be used for your statement, while preserving Greek symbols. For details, see Chapter 4, *The Edit Menu*.


With 542 subjects in each group, the observed two-sided 90.0% confidence interval will be expected to lie between -0.100 and 0.100 with 90% power when the Standard proportion, π_S , is 0.500 and the Test expected



proportion, π_T , is 0.500; results are based on 3600 simulations using the Newcombe-Wilson score method to construct the confidence interval. (Newcombe RG (1988) Interval estimation for the difference between independent proportions: comparison of eleven methods. *Statistics in Medicine* 17:873-890.)

Unequal n's

If the investigator wanted to study fewer patients in the group receiving the standard drug, sample size could be determined for unequal n's. You can access the unequal n's version of a table in two ways:

- Request unequal n's version of the current table by clicking on , the Unequal n's button.
- Use the Study Goal and Design box to request a new table for unequal n's.

16. Survival Analysis Tables

Survival analysis methods are designed for studies in which patients are entered into a trial and followed until a specified event occurs, they are lost to followup, or the study ends. For example, researchers might follow patients until death, hospital discharge, cancer recurrence, or heart attack.

The essential difference between survival analysis methods and the methods appropriate for comparing means or proportions has to do with the outcome measure. For some patients in a survival study, the outcome measure, time to the event of interest, is known only to be larger than some followup interval.

For example, in a five year study, one patient who entered the trial 18 months before its termination is known not to have had a heart attack during the 18 months before the study ended. Another patient was followed only 3 months before he left the state and could not be contacted further. In the first case, time to heart attack is known to be longer than 18 months. In the second case, time to heart attack is known to be longer than 3 months. This type of data is called right censored.


If all patients are followed for the same fixed time period, say 3 years, we could simply analyze the proportion of patients surviving (not having the event of interest) during that time. We could use sample size methods based on comparison of proportions. However, even when the data are not censored at different time points, we may lose information by ignoring the time to the event. For example, survival under two treatment regimens might look much the same by three years when most of the patients have suffered a recurrence, but might differ considerably during the first year.

If the researchers followed all patients until the event of interest occurred, recording time to the event, we could analyze these continuous measurements of time to event by comparing groups on mean time to event. Thus, we could determine sample sizes by using methods for comparisons of means, although time to event data typically have distributions which are skewed to the right. For example, length of hospital stay is generally only 3-5 days, but some patients are hospitalized for weeks. In addition, following all subjects until the event of interest occurs is often not feasible.

We can base sample size computations for survival studies on:

- an estimate of the surviving proportions at some fixed time
- a model for the entire survival curve.

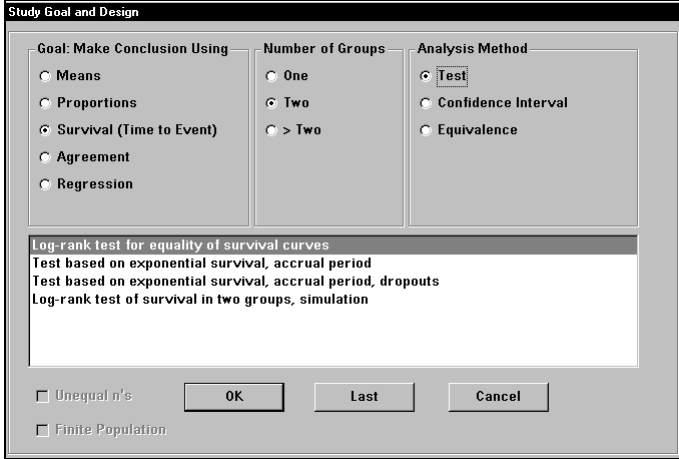
To open a survival sample size table:

Select **File menu New** option or click on the **New** button . In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Survival**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.



Study Goal and Design

Goal: Make Conclusion Using

- ☐ Means
- ☐ Proportions
- ☒ Survival (Time to Event)
- ☐ Agreement
- ☐ Regression

Number of Groups

- ☐ One
- ☒ Two
- ☐ > Two

Analysis Method

- ☒ Test
- ☐ Confidence Interval
- ☐ Equivalence

Log-rank test for equality of survival curves
Test based on exponential survival, accrual period
Test based on exponential survival, accrual period, dropouts
Log-rank test of survival in two groups, simulation

☐ Unequal n's ☐ Finite Population

OK Last Cancel

These selections bring up the four sample size tables for survival analysis. From each of the survival sample size tables, you can access a table which helps you to convert between different parameters characterizing expected survival times. See Example 2 in this chapter for details on using the parameter conversion table.

Log-rank test for equality of survival curves

This sample size table provides sample size estimates for an analysis based on the nonparametric log-rank test. It is assumed that all patients are followed for a fixed length of time, and that the hazard ratio is constant over time.



Test based on exponential survival, accrual period STT0

This sample size table provides sample size estimates for an analysis based on the assumption that the survival curves are exponential in shape. This restrictive assumption may lead to smaller sample size estimates than given by the sample size table based on the log-rank test.

Test based on exponential survival, accrual period, dropouts STT2

This sample size table is the same as the preceding one, except that it provides for dropouts which follow an exponential model.

Log-rank test with user specified survival, hazard, accrual, dropout rates, simulation STT3

This table allows user specification of survival curves which are not exponential in shape, or hazard ratios which are not constant throughout, and more complex patterns of accrual or dropout. The table provides a simulation solution for power given sample size. There are two versions of this table, one requiring equal sample sizes in the two groups and one which allows unequal sample sizes in the two groups.

See references for these sample size methods in Section 1 of the Appendix or in the Help menu under Methods of Computation for each table.


Example 1

Computing Sample Size Based on the Log-rank Test (STT0)

To illustrate this procedure, we use an example involving the study question: Does TIPS surgery for bleeding esophageal varices prolong life over shunt surgery? The study design calls for randomization to one of two parallel groups; in group 1 patients will receive shunt surgery, and in group 2 patients will receive the TIPS procedure.

The primary outcome measure is time to death due to any cause. All patients will be followed for a minimum of one year; in prior studies no patients were lost to followup. Data will be analyzed using the survival analysis log-rank test with a two-sided 5% significance level. Based on results in previous studies, it is expected that 65% of patients will survive one year following shunt surgery. TIPS surgery would be considered to be markedly worse if only 45% of patients survived one year; the investigator wants 85% power for this alternative.

To calculate n for this example based on log-rank test, open the survival sample size table for log-rank:

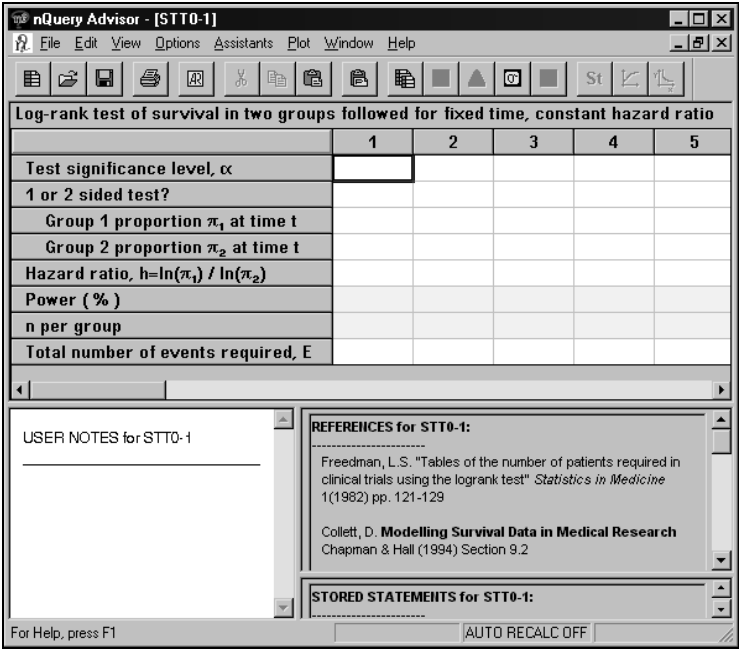
Select **File menu New** option or click on the **New** button . In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Survival**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.

Choose the first option, **Log-rank test for equality of survival curves**. You will see the following table.



The screenshot shows the nQuery Advisor - [STT0-1] window. The main table is titled "Log-rank test of survival in two groups followed for fixed time, constant hazard ratio". The table has 6 columns: a label column and five data columns numbered 1 to 5. The rows are as follows:

	1	2	3	4	5
Test significance level, α					
1 or 2 sided test?					
Group 1 proportion π_1 at time t					
Group 2 proportion π_2 at time t					
Hazard ratio, $h = \ln(\pi_1) / \ln(\pi_2)$					
Power (%)					
n per group					
Total number of events required, E					

Below the table, there are three sections: "USER NOTES for STT0-1", "REFERENCES for STT0-1:", and "STORED STATEMENTS for STT0-1:". The REFERENCES section lists two references: Freedman, L.S. "Tables of the number of patients required in clinical trials using the logrank test" *Statistics in Medicine* 1(1982) pp. 121-129, and Collett, D. *Modelling Survival Data in Medical Research* Chapman & Hall (1994) Section 9.2. At the bottom, there is a status bar with "For Help, press F1" and "AUTO RECALC OFF".

In the **Test significance level** row, enter **.05** and press <Enter>.



In the **1 or 2 sided test** row, enter **2** and press <Enter>.

In the **Group 1 proportion** row, enter **.65** and press <Enter>.

In the **Group 2 proportion** row, enter **.45** and press <Enter>. The program will calculate the Hazard ratio.

	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Group 1 proportion π_1 at time t	0.650				
Group 2 proportion π_2 at time t	0.450				
Hazard ratio, $h = \ln(\pi_1) / \ln(\pi_2)$	0.539				
Power (%)					
n per group					
Total number of events required, E					

In the **Power** row, enter **85** and press <Enter>. The program will calculate the n per group, and the total number of required events.

	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Group 1 proportion π_1 at time t	0.650				
Group 2 proportion π_2 at time t	0.450				
Hazard ratio, $h = \ln(\pi_1) / \ln(\pi_2)$	0.539				
Power (%)	85				
n per group	112				
Total number of events required, E	94				

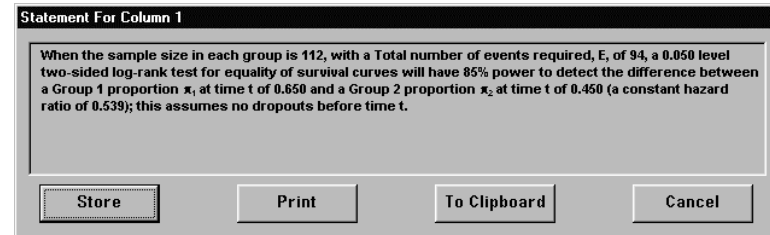
In the context of this example, the total number of required events would be the number of deaths that must be observed (in the two groups combined) to achieve the specified power.

Total number of events required

The total number of events required, E, is the number of events that must be observed in the two groups combined to achieve the specified power for the test comparing survival in the two groups. Note that this does not depend on accrual or dropout rates but only on specified significance level, power, and the natural log of

the hazard ratio; see Help or Appendix for formula. The derivation of the number of required events includes an approximation, so the calculated number of required events may be an underestimate. To compensate for this, some rounding up of the calculated value is suggested.

Now that you have the required n per group, click on the **Create Statement** button to create the statement which fully describes the results in this column.



Example 2

Conversion Between Parameters Assistants table to obtain Alternate Rates for Exponential Survival Curves

When any of the four survival tables are active, you can access the conversion table. The conversion table lets you convert between:

- survival rates expressed as median survival (time by which half of the patients entering the trial at time 0 have died and half still survive)
- proportion surviving at specified time t
- parameter of exponential survival curve.

These conversions are based on the assumption that the survival curve is exponential in shape.

To get the conversion to alternate rates table:

Retaining the sample size table from Example 1, select the **Assistants** menu.

Select the **Conversion Between Parameters** option. The conversion table will appear.



nQuery Advisor - [STT00-1]

File Edit View Options Assistants Plot Window Help

Conversion to alternate rates for exponential survival curves

	1	2	3
Time t			
Group 1 proportion π_1 at time t			
median survival			
exponential parameter, λ_1			
Group 2 proportion π_2 at time t			
median survival			
exponential parameter, λ_2			
Hazard ratio, $h = \ln(\pi_1)/\ln(\pi_2) = \text{med}_2/\text{med}_1 = \lambda_1/\lambda_2$			

Enter the **time t** in the first column of the first row; here we are interested in survival at one year, so enter **1.0** for time t with the time units understood to be years.

For **Group 1**, make an entry in the proportion row, median survival row, or exponential parameter row. Press <Enter>. The program will calculate the other two values for Group 1.

nQuery Advisor - [STT00-1]

File Edit View Options Assistants Plot Window Help

Conversion to alternate rates for exponential survival curves

	1	2	3
Time t	1.0		
Group 1 proportion π_1 at time t	0.650		
median survival	1.609		
exponential parameter, λ_1	0.4308		
Group 2 proportion π_2 at time t			
median survival			
exponential parameter, λ_2			
Hazard ratio, $h = \ln(\pi_1)/\ln(\pi_2) = \text{med}_2/\text{med}_1 = \lambda_1/\lambda_2$			

For Group 2, make an entry in the proportion row, median survival row, or exponential parameter row. Press <Enter>. The program will calculate the other two values for Group 2.

The program will calculate the hazard ratio. Here we have entered the proportions expected to survive to one year from Example 1. nQuery calculates the median survival, exponential parameter, and hazard ratio.

Conversion to alternate rates for exponential survival curves			
	1	2	3
Time t	1.0		
Group 1 proportion π_1 at time t	0.650		
median survival	1.609		
exponential parameter, λ_1	0.4308		
Group 2 proportion π_2 at time t	0.450		
median survival	0.868		
exponential parameter, λ_2	0.7985		
Hazard ratio, $h = \ln(\pi_1)/\ln(\pi_2) = \text{med}_2/\text{med}_1 = \lambda_1/\lambda_2$	0.539		

You can then copy required values to the survival sample size table you are using. See Example 3 for details of how to copy these values to the main survival analysis sample size table or side table you are using.

Note that the values obtained for the exponential parameters depend on the time scale used. If we enter time as 12 months instead of 1 year, we get different values for the exponential parameters. Even though the scale has changed, the hazard ratio remains constant.

Conversion to alternate rates for exponential survival curves			
	1	2	3
Time t	1.0	12.0	
Group 1 proportion π_1 at time t	0.650	0.650	
median survival	1.609	19.308	
exponential parameter, λ_1	0.4308	0.0359	
Group 2 proportion π_2 at time t	0.450	0.450	
median survival	0.868	10.417	
exponential parameter, λ_2	0.7985	0.0665	
Hazard ratio, $h = \ln(\pi_1)/\ln(\pi_2) = \text{med}_2/\text{med}_1 = \lambda_1/\lambda_2$	0.539	0.539	




Example 3

Test based on exponential survival, accrual period, dropouts (STT2)

Now let us reconsider Example 1 under different possible design scenarios. First, we'll evaluate the effect of continuing accrual on the sample size required for the study.

To get the table for the two-group test of equal exponential survival:

Select **File menu New** option or click on the **New** button . In the Study Goal and Design Box, you will see three columns of options.

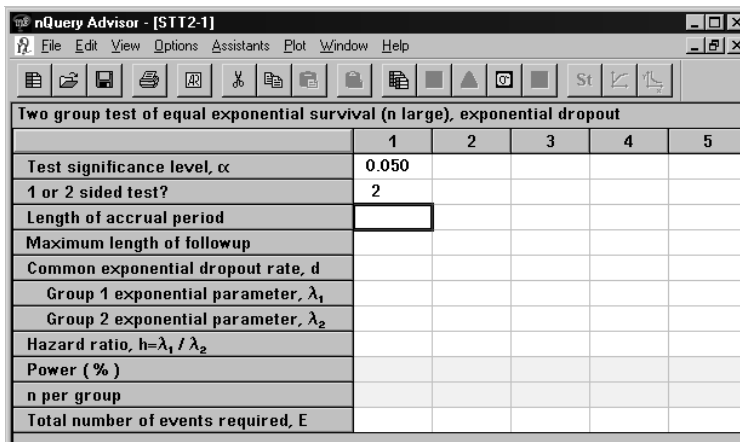
Under **Goal: Make conclusion using**, select **Survival**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.

Select the third option, **Test based on exponential survival, accrual period, dropouts**.

Fill in the significance level and 1 or 2 sided test as before. You will see the following table.



	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Length of accrual period					
Maximum length of followup					
Common exponential dropout rate, d					
Group 1 exponential parameter, λ_1					
Group 2 exponential parameter, λ_2					
Hazard ratio, $h = \lambda_1 / \lambda_2$					
Power (%)					
n per group					
Total number of events required, E					

It will be easier to specify varying lengths of accrual if we change to a time scale of 12 months for the study. In the first column let us specify that the total followup period will be 12 months as in our first example.

Enter **1** in the **Length of accrual period** row.

Enter **12** in the **Maximum length of followup** row.

Then we will consider the difference in sample size required for the study if:

- all patients are accrued in the first month (enter 1 month for length of accrual period)

versus

- accrual is continued throughout the study period (enter 12 months for length of accrual period.)

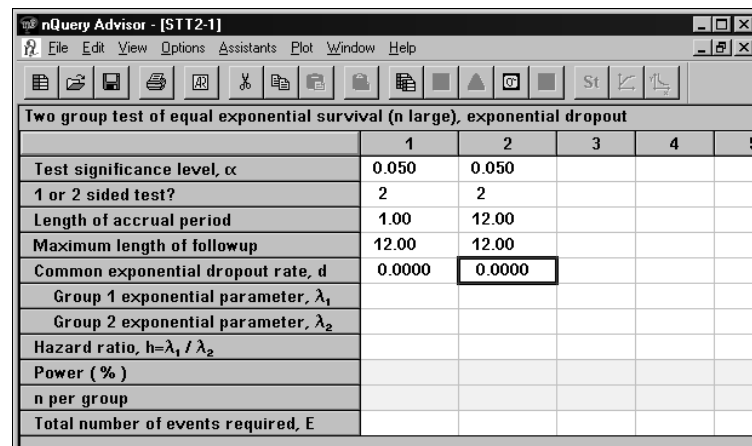
Copy the contents of the first two rows of column 1. Paste them into column 2.

In the second column, enter **12** in the **Length of accrual period** row.

Enter **12** in the **Maximum length of followup** row.

For the time being, we assume that there are no dropouts, so the exponential dropout rate is 0.

Enter **0** in the **Common exponential dropout rate** row for both columns.



The screenshot shows the nQuery Advisor software window titled "nQuery Advisor - [STT2-1]". The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. Below the menu bar is a toolbar with various icons. The main window displays a table titled "Two group test of equal exponential survival (n large), exponential dropout". The table has columns for parameters and two groups (1 and 2). The parameters listed are: Test significance level, α ; 1 or 2 sided test?; Length of accrual period; Maximum length of followup; Common exponential dropout rate, d ; Group 1 exponential parameter, λ_1 ; Group 2 exponential parameter, λ_2 ; Hazard ratio, $h = \lambda_1 / \lambda_2$; Power (%); n per group; and Total number of events required, E. The values entered in the table are: Test significance level, α (0.050); 1 or 2 sided test? (2); Length of accrual period (1.00); Maximum length of followup (12.00); Common exponential dropout rate, d (0.0000); Group 1 exponential parameter, λ_1 (0.0000); Group 2 exponential parameter, λ_2 (0.0000); Hazard ratio, $h = \lambda_1 / \lambda_2$ (0.0000); Power (%) (0.0000); n per group (0.0000); and Total number of events required, E (0.0000).

	1	2	3	4	5
Test significance level, α	0.050	0.050			
1 or 2 sided test?	2	2			
Length of accrual period	1.00	12.00			
Maximum length of followup	12.00	12.00			
Common exponential dropout rate, d	0.0000	0.0000			
Group 1 exponential parameter, λ_1					
Group 2 exponential parameter, λ_2					
Hazard ratio, $h = \lambda_1 / \lambda_2$					
Power (%)					
n per group					
Total number of events required, E					

Now we need the exponential parameters for the 12 month survival percentages.

Choose the **Assistants** menu **Conversions Between Parameters** option. The Conversion between parameters window will appear.


Enter 12 in the Time row.

Enter **.65** in the Group 1 proportion and **.45** in the Group 2 proportion. nQuery will calculate the exponential parameters for the proportions.




Conversion to alternate rates for exponential survival curves			
	1	2	3
Time t	12.0		
Group 1 proportion π_1 at time t	0.650		
median survival	19.308		
exponential parameter, λ_1	0.0359		
Group 2 proportion π_2 at time t	0.450		
median survival	10.417		
exponential parameter, λ_2	0.0665		
Hazard ratio, $h = \ln(\pi_1)/\ln(\pi_2) = \text{med}_2/\text{med}_1 = \lambda_1/\lambda_2$	0.539		



Use the **Edit** menu **Copy** or Copy button, , or <Ctrl><C> to copy the exponential parameter corresponding to 12 month survival of 65%.

Use the Window menu to return to the main table **Two-group test of equal exponential survival**.

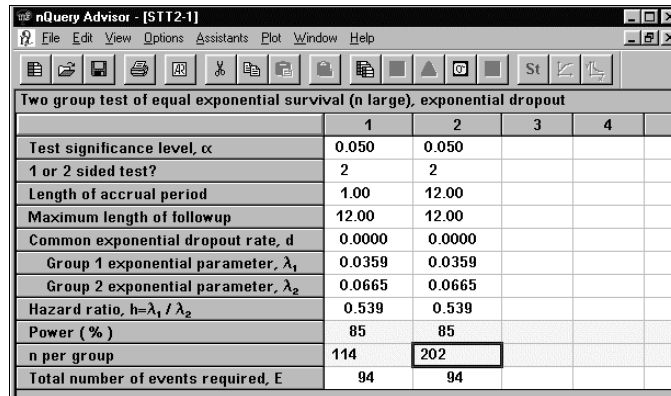


Use the **Edit** menu **Paste Unformatted** or , the Paste Unformatted button, to paste the value into the **Group 1 exponential parameter** row in the main table.

Repeat the copy and paste steps above to copy the exponential parameter corresponding to 12 month survival of 45% to the Two-group table.

Request **85%** power and find a required sample size of 114 per group when all patients are accrued within the first month. Remember that 112 was the answer given by sample size table STT0 when all accrual was prior to the 12 month study period.

You get a required sample size of 202 when accrual will be continuous throughout the 12 month study.



	1	2	3	4
Test significance level, α	0.050	0.050		
1 or 2 sided test?	2	2		
Length of accrual period	1.00	12.00		
Maximum length of followup	12.00	12.00		
Common exponential dropout rate, d	0.0000	0.0000		
Group 1 exponential parameter, λ_1	0.0359	0.0359		
Group 2 exponential parameter, λ_2	0.0665	0.0665		
Hazard ratio, $h = \lambda_1 / \lambda_2$	0.539	0.539		
Power (%)	85	85		
n per group	114	202		
Total number of events required, E	94	94		

Total number of events required

The total number of events required, E, is the number of events that must be observed in the two groups combined to achieve the specified power for the test comparing survival in the two groups. Note that this does not depend on accrual or dropout rates but only on specified significance level, power, and the natural log of the hazard ratio; see Help or Appendix for formula. The derivation of the number of required events includes an approximation, so the calculated number of required events may be an underestimate. To compensate for this, some rounding up of the calculated value is suggested.

Returning to the example, suppose we expect that about 5% of subjects entering the trial will drop out within 6 months of their entry.

To use columns 3 and 4 to determine the n per group for 1 and 12 month accrual periods when we expect 5% to drop out:

Select the first 4 rows of columns 1 and 2.

Use the **Edit** menu **Copy** option to copy the contents of the rows.

Place the cursor in column 3.

Use the **Edit** menu **Paste**, Paste icon, or **<Ctrl><V>** to paste the values into columns 3 and 4.

Use Windows menu to return to the **Conversion to alternate rates** table, STT00.

This time, we will use the table to compute the exponential dropout rate. Enter **6** months and proportion **95%** (remaining in the study without dropping out) to obtain the exponential dropout parameter, .0085.




nQuery Advisor - [STT00-1]				
File Edit View Options Assistants Plot Window Help				
Conversion to alternate rates for exponential survival curves				
	1	2	3	
Time t	12.0	6.0		
Group 1 proportion π_1 at time t	0.650	0.950		
median survival	19.308	81.080		
exponential parameter, λ_1	0.0359	0.0085		
Group 2 proportion π_2 at time t	0.450			
median survival	10.417			
exponential parameter, λ_2	0.0665			
Hazard ratio, $h = \ln(\pi_1)/\ln(\pi_2) = \text{med}_2/\text{med}_1 = \lambda_1/\lambda_2$	0.539			

Use the **Edit** menu **Copy** option to copy **.0085**.

Use the **Windows** menu to return to the **Two-group test of exponential survival** table, STT2.



Use the **Edit** menu **Paste Unformatted** option or , the Paste Unformatted icon, to paste the exponential parameter into the **Common exponential dropout rate** row in columns 3 and 4.

Use the **Edit** menu **Copy** option to copy the Group 1 and 2 exponential parameters from columns 1 and 2. Use the **Edit** menu **Paste** option to paste into columns 3 and 4.

Enter 85 into the Power row for columns 3 and 4. The nQuery program calculates the n per group.

Although the required total number of events is unchanged, we see that accounting for dropouts will require about 5-6 more patients per group.


Two group test of equal exponential survival (n large), exponential dropout					
	1	2	3	4	5
Test significance level, α	0.050	0.050	0.050	0.050	
1 or 2 sided test?	2	2	2	2	
Length of accrual period	1.00	12.00	1.00	12.00	
Maximum length of followup	12.00	12.00	12.00	12.00	
Common exponential dropout rate, d	0.0000	0.0000	0.0085	0.0085	
Group 1 exponential parameter, λ_1	0.0359	0.0359	0.0359	0.0359	
Group 2 exponential parameter, λ_2	0.0665	0.0665	0.0665	0.0665	
Hazard ratio, $h=\lambda_1 / \lambda_2$	0.539	0.539	0.539	0.539	
Power (%)	85	85	85	85	
n per group	114	202	119	208	
Total number of events required, E	94	94	94	94	

Example 4

Log-rank test with user specified survival, hazard, accrual, dropout rates (simulation) (STT3)

Sample size tables STT1 and STT2 allow evaluation of the effect of early versus continuous accrual, and constant dropout rates. However, these sample size tables don't allow specification of survival curves which are not exponential in shape, or hazard ratios which are not constant throughout, or of more complex patterns of accrual or dropout. For these purposes, we have provided a simulation solution for power given sample size which allows considerable flexibility in specification of survival, accrual, and dropout parameters. We will demonstrate the use of this table for the examples evaluated above. Later, we discuss an example concerning survival curves which are not exponential in shape.

To use the log-rank test for survival in two groups, simulation:

Select **File menu** **New** option or click on the **New** button . In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Survival**.

Under **Number of groups**, select **Two** groups.

Under **Analysis method**, select **Test**.

Select the fourth option, **Log-rank test, user-specified survival rates, accrual, dropouts (simulation)**.



Fill in the significance level and 1 or 2 sided test as before, and you will see the following table.

Log-rank test of survival in two groups, simulation with specified rates					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Number of periods					
Side table name					
Number of simulations					
Random seed for simulations					
Power (%)					
n per group					

We then choose to specify the survival curve in each of 12 one month periods, so enter **12** in the **Number of periods** row.

Select **Compute effect size** from the **Assistants** menu or click on the Compute effect size button marked [δ] to bring up a special side table.

Time-dependent hazard info for log-rank survival test				
	1	2	3	4
End of period, time t	0.000			
Accrual (% of total)	100.000			
Group 1 exponential hazard rate, λ_1	0.0000			
Group 2 exponential hazard rate, λ_2	0.0000			
Group 1 expected % surviving time t	100.000			
Group 2 expected % surviving time t	100.000			
Common exponential dropout rate, d	0.0000			

Note that the first column has already been filled in. If you wanted to specify that all accrual takes place before the start of the study, you would simply fill in zeros for the rest of the accrual row. None of the values in this first column can be edited, although they will change as you enter values for the other columns.

Enter the time at the end of each period. In this case, each period specified in the side table is one month (they need not be the same length.)

In the **End of period, time t** row, enter **1** in the second column, **2** in the third column, etc., until you have entered all 12 periods.

For the first example, 100% of the accrual will take place in the period ending at one month. The percent of total accrual entered in the first column with end of period at time 0, will contain a value equal to 100 minus the sum of percent accrual specified in the rest of the time periods.

Enter **100** in the **Accrual** row of the second column.

Enter **0** in the **Accrual** row of the remaining columns.

Copy the **ameters** from Example 3 and paste them into the **exponential hazard rate** rows. Be sure to use the **Paste Unformatted** option, so that you can simply copy the exponential parameters from one sample size table and paste them into another type of sample size table.

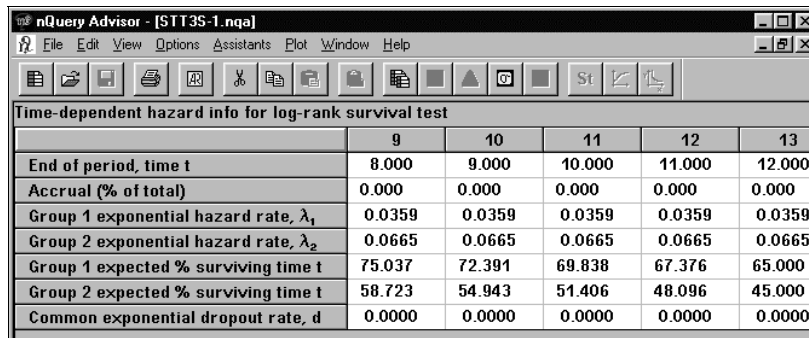
Select the filled **exponential hazard rate** cells, and use the **Edit** menu **Fill Right** option to repeat those values across the table. nQuery Advisor fills in the expected survival at the end of each period. Or you can enter the expected survival at the end of each period and nQuery Advisor will fill in the exponential parameters.

For the first example, no dropouts are expected, so we enter **0** in the **Common exponential dropout rate** row.

Select the filled **Common exponential dropout rate** row and use the **Edit, Fill Right** option to complete the row.

Note that this table will have 13 columns, one for each period specified in the main table and one for the period ending at time 0. In these views of the screen, we can see only 4 columns at a time. The first four and last five columns of the filled-in side table are shown in the next two figures.

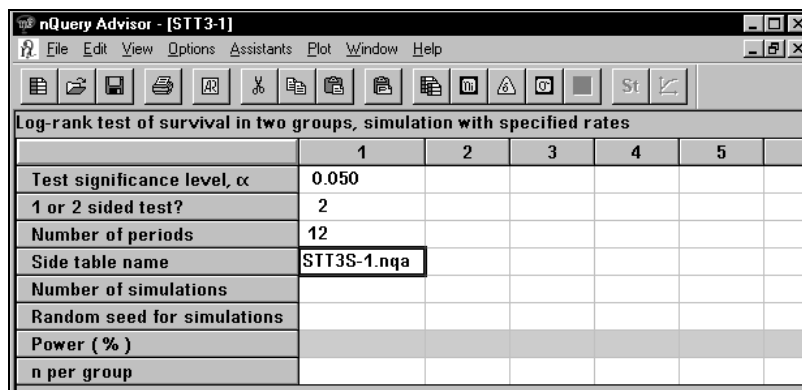
	1	2	3	4	5
End of period, time t	0.000	1.000	2.000	3.000	4.000
Accrual (% of total)	0.000	100.000	0.000	0.000	0.000
Group 1 exponential hazard rate, λ_1	0.0000	0.0359	0.0359	0.0359	0.0359
Group 2 exponential hazard rate, λ_2	0.0000	0.0665	0.0665	0.0665	0.0665
Group 1 expected % surviving time t	100.000	96.474	93.072	89.790	86.624
Group 2 expected % surviving time t	100.000	93.562	87.539	81.904	76.631
Common exponential dropout rate, d	0.0000	0.0000	0.0000	0.0000	0.0000



	9	10	11	12	13
End of period, time t	8.000	9.000	10.000	11.000	12.000
Accrual (% of total)	0.000	0.000	0.000	0.000	0.000
Group 1 exponential hazard rate, λ_1	0.0359	0.0359	0.0359	0.0359	0.0359
Group 2 exponential hazard rate, λ_2	0.0665	0.0665	0.0665	0.0665	0.0665
Group 1 expected % surviving time t	75.037	72.391	69.838	67.376	65.000
Group 2 expected % surviving time t	58.723	54.943	51.406	48.096	45.000
Common exponential dropout rate, d	0.0000	0.0000	0.0000	0.0000	0.0000

Save the side table. See Example 7 for instructions on how to obtain a plot of these survival curves and how to use this plot to change the specified survival proportions and within period exponential rates to obtain the survival curves you want.

When the side table is completed and saved, we return to the main table using **<Ctrl><Tab>** or the **Window** menu. The name under which we saved the side table will appear in black in the row titled Side table name. If the side table is still incomplete, the name will appear in blue, and you should complete the side table.



	1	2	3	4	5	6
Test significance level, α	0.050					
1 or 2 sided test?	2					
Number of periods	12					
Side table name	STT3S-1.nqa					
Number of simulations						
Random seed for simulations						
Power (%)						
n per group						

At this point, you must choose how many simulated experiments to request, specify a random seed for the simulation (any integer greater than or equal to 0) and a preliminary choice of the sample size planned for each group, then nQuery Advisor will provide an estimate of the power.

If your computer is slow, we suggest that you begin by requesting 100 simulations for each choice of sample size in order to settle on a sample size giving you close to the power you want. Simulations with 100 samples should provide an estimate of power to within $\pm 10\%$. Otherwise, simulations with 1000 samples should provide an estimate of power to within $\pm 2\%$ for powers near 90%, simulations with 1600

samples, should provide an estimate of power to within $\pm 2\%$ for powers near 80%, and simulations with 10,000 samples will provide estimates for power to within $\pm 1\%$.

Note: These figures are based on a 95% confidence interval for an estimated proportion.

If you want to plot power versus sample size, be sure to request at least 1000 samples to stabilize the estimates of power. Plots may take some time, as they are based on simulations for seven points; you will see the time estimate and progress of simulations boxes for each point.

For this example, we specify 100 simulations and a random seed of 25. Based on the sample sizes computed using STT2, we specify a sample size of 114.

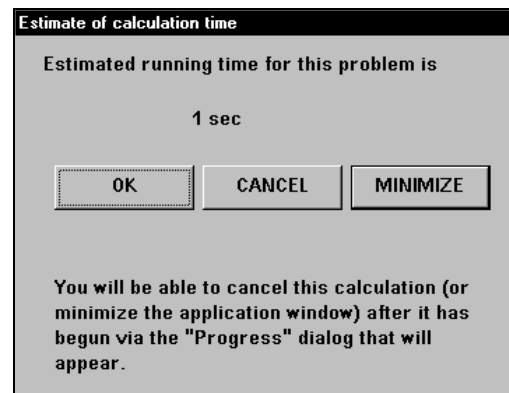
Enter **100** in the **Number of simulations** row.

Enter **25** in the **Random seed for simulations** row.

Enter **114** in the **n per group** row.

When everything in the column except power is filled in, nQuery Advisor will make an estimate of the time required to complete the simulations you have requested on your computer. (This estimate is based on making a small number of preliminary simulations.)

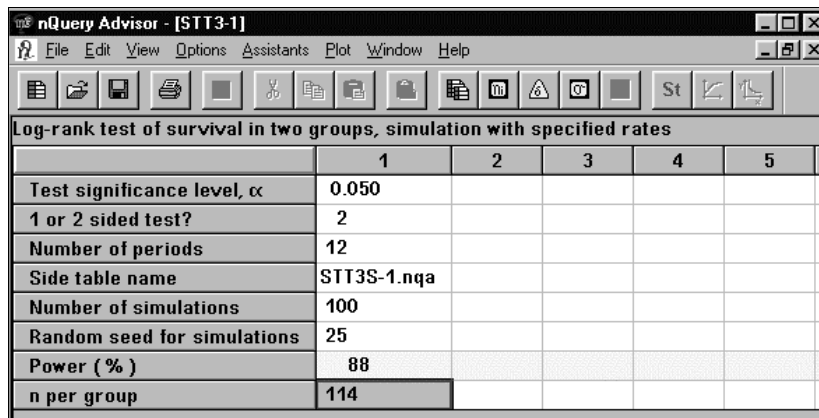
You will see a box like the following. At that point, you can choose to cancel the simulation, run nQuery Advisor minimized during computation of the simulations, or take a brief break while you wait. The following example took only 1 second to compute on this particular computer, but when we specify more simulations, the computation takes longer.



If you want to cancel the calculation of power after it has begun, click on the Cancel button within the Progress of Survival Simulations dialog box.



If you prefer to minimize the window for the calculation of power after it has begun, click on the **Minimize** button within the **Progress of Survival Simulations** dialog box.



Log-rank test of survival in two groups, simulation with specified rates					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Number of periods	12				
Side table name	STT3S-1.nqa				
Number of simulations	100				
Random seed for simulations	25				
Power (%)	88				
n per group	114				

We show the results of two estimates of power based on 100 simulations each with different random seeds, and an estimate of power based on 1600 simulations.

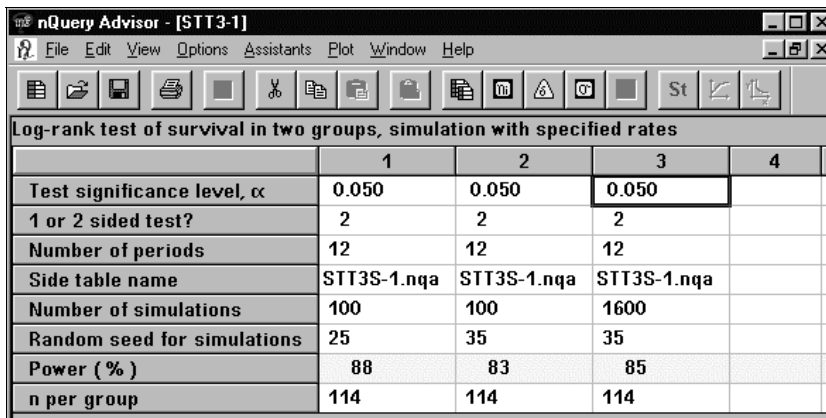
When preparing the sample size table below:



Use the **Edit** menu **Copy** option or the Copy icon, or the Copy keyboard shortcut, **<Ctrl><C>**, to copy the Side table name from the first column.

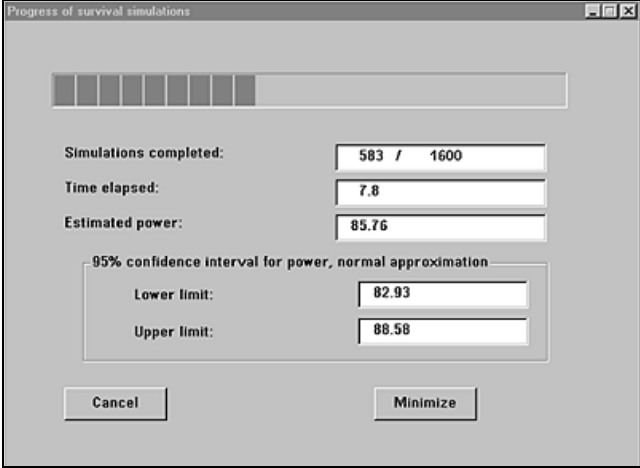


Use the **Edit** menu **Paste unformatted** option or the Paste unformatted icon, to paste the side table name into columns 2 and 3.



Log-rank test of survival in two groups, simulation with specified rates				
	1	2	3	4
Test significance level, α	0.050	0.050	0.050	
1 or 2 sided test?	2	2	2	
Number of periods	12	12	12	
Side table name	STT3S-1.nqa	STT3S-1.nqa	STT3S-1.nqa	
Number of simulations	100	100	1600	
Random seed for simulations	25	35	35	
Power (%)	88	83	85	
n per group	114	114	114	

When nQuery Advisor starts the 1600 simulations to calculate the Power, you can watch the progress of the calculation or cancel the process.



Progress of survival simulations

Simulations completed: 583 / 1600

Time elapsed: 7.8

Estimated power: 85.76

95% confidence interval for power, normal approximation

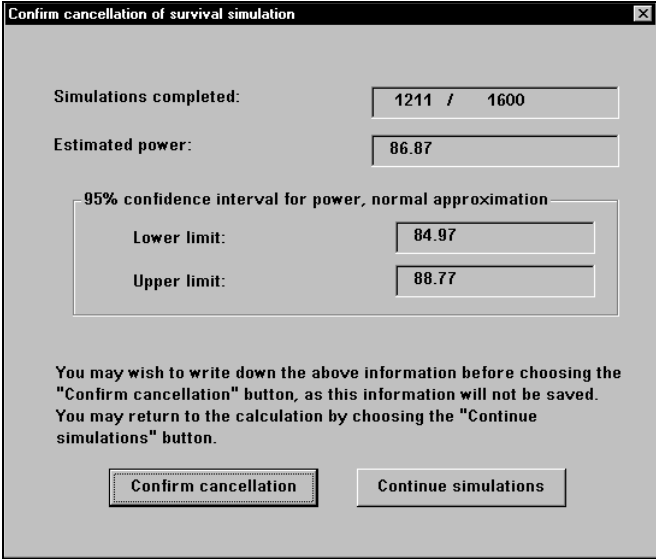
Lower limit: 82.93

Upper limit: 88.58

Cancel Minimize

This dialog box shows the progress of survival simulations. It includes a progress bar at the top, followed by fields for 'Simulations completed' (583 / 1600), 'Time elapsed' (7.8), and 'Estimated power' (85.76). Below these is a section for the '95% confidence interval for power, normal approximation', with 'Lower limit' (82.93) and 'Upper limit' (88.58). At the bottom are 'Cancel' and 'Minimize' buttons.

If you click on the **Cancel** button, you will see a dialog box outlining the calculations performed so far.



Confirm cancellation of survival simulation

Simulations completed: 1211 / 1600

Estimated power: 86.87

95% confidence interval for power, normal approximation

Lower limit: 84.97

Upper limit: 88.77

You may wish to write down the above information before choosing the "Confirm cancellation" button, as this information will not be saved. You may return to the calculation by choosing the "Continue simulations" button.

Confirm cancellation Continue simulations

This dialog box is titled 'Confirm cancellation of survival simulation'. It displays the current state of the simulation: 'Simulations completed: 1211 / 1600', 'Estimated power: 86.87', and the '95% confidence interval for power, normal approximation' with a 'Lower limit: 84.97' and 'Upper limit: 88.77'. A message at the bottom states: 'You may wish to write down the above information before choosing the "Confirm cancellation" button, as this information will not be saved. You may return to the calculation by choosing the "Continue simulations" button.' At the bottom are two buttons: 'Confirm cancellation' and 'Continue simulations'.

Using this dialog box, you can continue the simulations or confirm the cancellation.



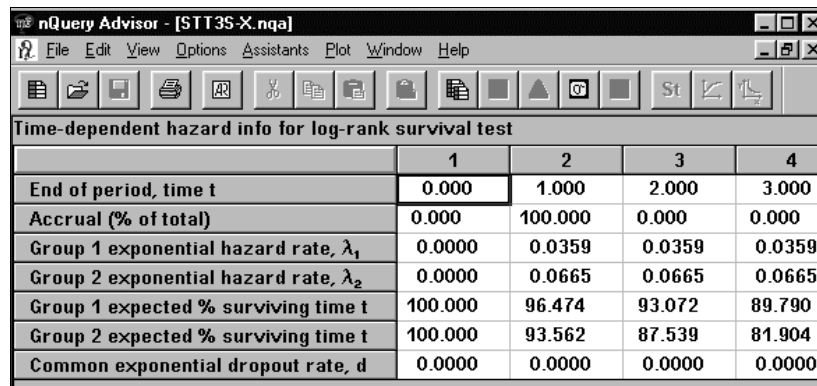
Example 5

Log-rank test for survival in two groups (simulation)(STT3)

In this example, we repeat sample size computations for the study in example 4, using the same survival patterns, but considering the case where accrual is uniform across the 12 months of the study.

To repeat the computations of power for Example 4 with 1/12 of the accrual during each month of the study and retain both the current side table and a new edited table:

Start with the current side table. Use the File menu Save as option to change its name to STT3S-X.nqa.



The screenshot shows the nQuery Advisor window with the title bar 'nQuery Advisor - [STT3S-X.nqa]'. The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons for file operations and analysis. The main window displays a table titled 'Time-dependent hazard info for log-rank survival test'.

	1	2	3	4
End of period, time t	0.000	1.000	2.000	3.000
Accrual (% of total)	0.000	100.000	0.000	0.000
Group 1 exponential hazard rate, λ_1	0.0000	0.0359	0.0359	0.0359
Group 2 exponential hazard rate, λ_2	0.0000	0.0665	0.0665	0.0665
Group 1 expected % surviving time t	100.000	96.474	93.072	89.790
Group 2 expected % surviving time t	100.000	93.562	87.539	81.904
Common exponential dropout rate, d	0.0000	0.0000	0.0000	0.0000

Select the **Accrual** row in columns 2 through 13 and use the **Edit** menu **Cut** option or **<Ctrl><X>** to remove the cell contents.

Edit the side table to specify 1/12 of the accrual in each period: 8.33% in periods 2-12 and 8.37% in period ending at month 1. Remember, we are editing starting at column 2, time period 1. We cannot edit column 1 directly, but the contents of column 1 change as we edit the succeeding columns. We show only the first four columns of the table below.

Time-dependent hazard info for log-rank survival test				
	1	2	3	4
End of period, time t	0.000	1.000	2.000	3.000
Accrual (% of total)	0.000	8.330	8.330	8.330
Group 1 exponential hazard rate, λ_1	0.0000	0.0359	0.0359	0.0359
Group 2 exponential hazard rate, λ_2	0.0000	0.0665	0.0665	0.0665
Group 1 expected % surviving time t	100.000	96.474	93.072	89.790
Group 2 expected % surviving time t	100.000	93.562	87.539	81.904
Common exponential dropout rate, d	0.0000	0.0000	0.0000	0.0000

Use <Ctrl><Tab> or the **Window** menu to move back to the main Log rank test of survival table, STT3.

The nQuery program will automatically calculate the Power for each column in the sample size table.

To change the sample sizes, use the **Edit** menu **Cut** option or <Ctrl><X> to cut the Power and n per group.

Enter the **n per group**.

The program computes the power for each column.

Log-rank test of survival in two groups, simulation with specified rates

	1	2	3
Test significance level, α	0.050	0.050	0.050
1 or 2 sided test?	2	2	2
Number of periods	12	12	12
Side table name	STT3S-X.nqa	STT3S-X.nqa	STT3S-X.nqa
Number of simulations	100	100	1600
Random seed for simulations	25	35	35
Power (%)	71	68	62
n per group	114	114	114

With the sample size of 114 per group, and accrual stretched over the 12 months, the power is now too low. Referring back to Example 3 earlier in this chapter, we see that to obtain 85% power, survival table STT2 showed that a sample size of 202 per group would be necessary. We copy rows 1-6 to column 4 and enter a sample size of 202.



Log-rank test of survival in two groups, simulation with specified rates

	1	2	3	4
Test significance level, α	0.050	0.050	0.050	0.050
1 or 2 sided test?	2	2	2	2
Number of periods	12	12	12	12
Side table name	STT3S-X.nqa	STT3S-X.nqa	STT3S-X.nqa	STT3S-X.nqa
Number of simulations	100	100	1600	1600
Random seed for simulations	25	35	35	35
Power (%)	71	68	62	85
n per group	114	114	114	202

We see essentially the same results as were obtained using the survival table STT2 in Example 3 earlier in this chapter.

Note: To copy and paste a side table name from one column of the sample size table to another, the side table name must appear in black. Then you can **Copy** the side table name using the **Edit** menu **Copy** option or



, the Copy icon, or the Copy keyboard shortcut, <Ctrl><C>.

You can paste the side table name to another column by using the **Edit**



menu **Paste** option or , the Paste icon, or the Paste keyboard shortcut, <Ctrl><V>.

Example 6

Log-rank test for survival in two groups, simulation, unequal n's

We return to the study discussed in Example 5 and now ask what happens to power if we study 130 patients in Group 1, the shunt group, and 260 patients in Group 2, the TIPS group.



If you have the main survival table open, click on , the unequal n's icon. If you do not, follow the procedure below.

To use the log-rank test for survival in two groups, simulation, unequal n's:



Select **File** menu **New** option or click on the **New** button . In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Survival**.

Under **Number of groups**, select **Two** groups.

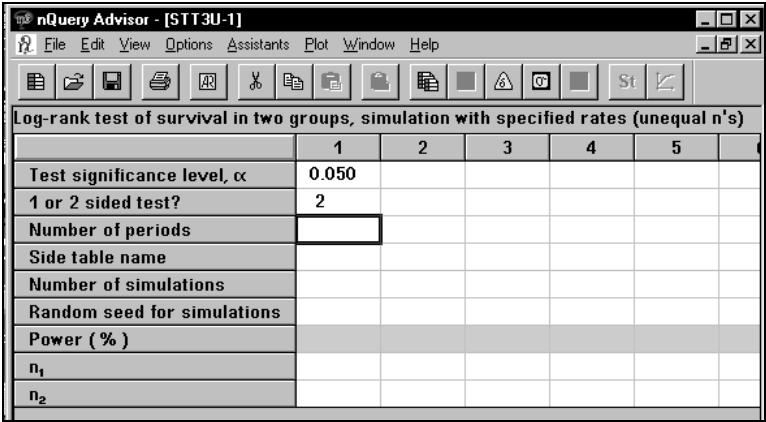
Under **Analysis method**, select **Test**.

Select the fourth option, **Log-rank test, user-specified survival rates, accrual, dropouts (simulation)**

Check the **Unequal n's** box in the lower left corner of the Study Goal and Design Dialog box.

Click **OK**.

In the sample size table, fill in the significance level and 1 or 2 sided test as before. You will see the following table.



The screenshot shows the 'nQuery Advisor - [STT3U-1]' window. The title bar includes 'File', 'Edit', 'View', 'Options', 'Assistants', 'Plot', 'Window', and 'Help'. The menu bar contains icons for file operations (New, Open, Save, Print, Copy, Paste, Find, Replace, Undo, Redo) and a 'St' icon. The main area is titled 'Log-rank test of survival in two groups, simulation with specified rates (unequal n's)'. It contains a table with the following rows and columns:

	1	2	3	4	5	6
Test significance level, α	0.050					
1 or 2 sided test?	2					
Number of periods						
Side table name						
Number of simulations						
Random seed for simulations						
Power (%)						
n_1						
n_2						

We then choose to specify the survival curve in each of 12 one month periods, so enter **12** in the **Number of periods** row.

Open the side-table used in Example 5, STT3S-X.nqa, and enter the name of the side-table, STT3S-X.nqa.

Note: To avoid having to retype long side table names in the main table, open the side table, and select the name by double clicking on the side table name in the **Notes** pane. Click on **Copy** or use **<Ctl><C>** to copy the name to clipboard. Then return to the main table, and select the appropriate cell in the Side table name row. Click on **Paste** or **<Ctrl><V>** to paste the side table name into the appropriate row.



Log-rank test of survival in two groups, simulation with specified rates (unequal n's)						
	1	2	3	4	5	
Test significance level, α	0.050					
1 or 2 sided test?	2					
Number of periods	12					
Side table name	STT3S-X.nqa					
Number of simulations						
Random seed for simulations						
Power (%)						
n_1						
n_2						

Entering the sample sizes we obtained in Example 5 and a different random seed, we find an estimated power of 86%.

Log-rank test of survival in two groups, simulation with specified rates (unequal n's)

	1
Test significance level, α	0.050
1 or 2 sided test?	2
Number of periods	12
Side table name	STT3S-X.nqa
Number of simulations	1600
Random seed for simulations	30
Power (%)	86
n_1	200
n_2	200

Entering the sample sizes 130 and 260, we find an estimated power of only 79%.

Log-rank test of survival in two groups, simulation with specified rates (unequal n's)

	1	2
Test significance level, α	0.050	0.050
1 or 2 sided test?	2	2
Number of periods	12	12
Side table name	STT3S-X.nqa	STT3S-X.nqa
Number of simulations	1600	1600
Random seed for simulations	30	30
Power (%)	86	79
n_1	200	130
n_2	200	260

Noting that for the two-sample t in large samples, the total sample size required when n's are unequal is $(1+r)^2/4r$ times the total sample size required for equal n's ($r = n_2/n_1$), we would expect that it would take about $(9/8)400 = 450$ cases total to get the same power when $r=2$ as we got with 400 cases with $r=1$. Trying sample sizes of 150 and 300, we get an estimated power of 84%.

Note that to change both n's in a column, you need to highlight power and both n's and use the **Edit** menu **Cut** or the toolbar button for cut or the Cut keyboard shortcut, <Ctrl><X>, to remove these values. Then enter the new sample sizes.

Log-rank test of survival in two groups, simulation with specified rates (unequal n's)

	1	2	3
Test significance level, α	0.050	0.050	0.050
1 or 2 sided test?	2	2	2
Number of periods	12	12	12
Side table name	STT3S-X.nga	STT3S-X.nga	STT3S-X.nga
Number of simulations	1600	1600	1600
Random seed for simulations	30	30	30
Power (%)	86	79	84
n_1	200	130	150
n_2	200	260	300

Example 7

Plotting Survival Curves

We specify the survival rates observed in a previous trial of shunt surgery instead of using the exponential model, but for this example we consider a three year trial and specify survival at only 5 time points.

We open a new table STT3, enter 5 for the number of periods and select the Assistants menu Compute effect size option. The group 1 survival is that seen in the previous trial for shunt surgery, a little over 79% at 2 months, 69% at 12 months, 60% at 24 months, 59% at 30 months, and 57% at 36 months, and the group 2 exponential parameters are computed as 1.5 times the group 1 exponential parameters. We then save this table with a new name TIPS.nga to avoid confusion with previous examples. The next two screen shots show the first three and last three columns of this table

Time-dependent hazard info for log-rank survival test			
	1	2	3
End of period, time t	0.000	2.000	12.000
Accrual (% of total)	100.000	6.000	28.000
Group 1 exponential hazard rate, λ_1	0.0000	0.1116	0.0134
Group 2 exponential hazard rate, λ_2	0.0000	0.1674	0.0201
Group 1 expected % surviving time t	100.000	80.000	69.967
Group 2 expected % surviving time t	100.000	71.548	58.520
Common exponential dropout rate, d	0.0000	0.0000	0.0000



Time-dependent hazard info for log-rank survival test			
	4	5	6
End of period, time t	24.000	30.000	36.000
Accrual (% of total)	33.000	17.000	16.000
Group 1 exponential hazard rate, λ_1	0.0110	0.0055	0.0055
Group 2 exponential hazard rate, λ_2	0.0165	0.0083	0.0083
Group 1 expected % surviving time t	61.315	59.325	57.399
Group 2 expected % surviving time t	48.008	45.676	43.457
Common exponential dropout rate, d	0.0000	0.0000	0.0000

To edit the row names for the expected % surviving rows:

Choose the **Edit** menu **Edit row names** option. The Edit row names dialog box appears, displaying the two rows to be changed.

Click on row to edit

Group 1 expected % surviving time t

Group 2 expected % surviving time t

Accept Edit Row

Update Table Row Name

Cancel

Click on the **Group 1 row**. Group 1 will appear in the white editing field in the middle of the dialog box. Click on **Group 1** in the editing field and enter **Shunt**. Click on the **Accept Edit Row** button.

Click on the **Group 2 row**. The dialog box will show the edited Shunt row, and Group 2 will appear in the editing field.

Click on row to edit

Shunt expected % surviving time t

Group 2 expected % surviving time t

Accept Edit Row

Update Table Row Name

Cancel

Click on Group 2 in the editing field and enter TIPS. Click on the Accept Edit Row button.

Click on the **Update Table Row Names** button to update the table.

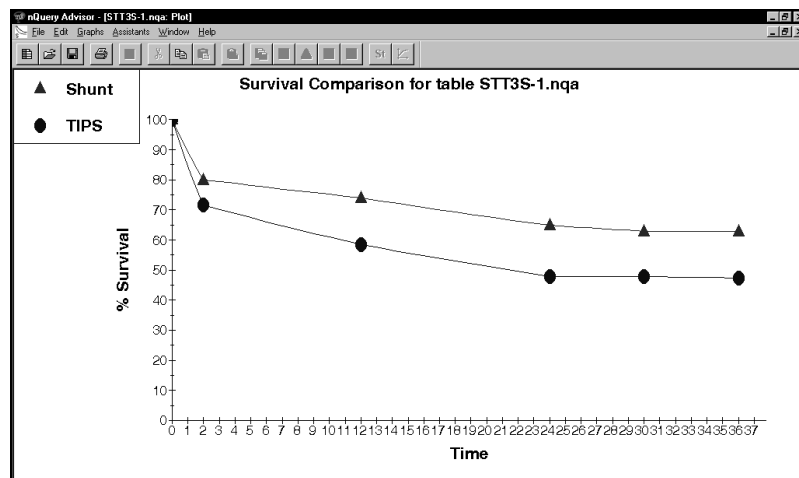
Time-dependent hazard info for log-rank survival test			
	1	2	3
End of period, time t	0.000	2.000	12.000
Accrual (% of total)	100.000	6.000	28.000
Group 1 exponential hazard rate, λ_1	0.0000	0.1116	0.0134
Group 2 exponential hazard rate, λ_2	0.0000	0.1674	0.0201
Shunt expected % surviving time t	100.000	80.000	69.967
TIPS expected % surviving time t	100.000	71.548	58.520
Common exponential dropout rate, d	0.0000	0.0000	0.0000

To see the plot of these survival curves:

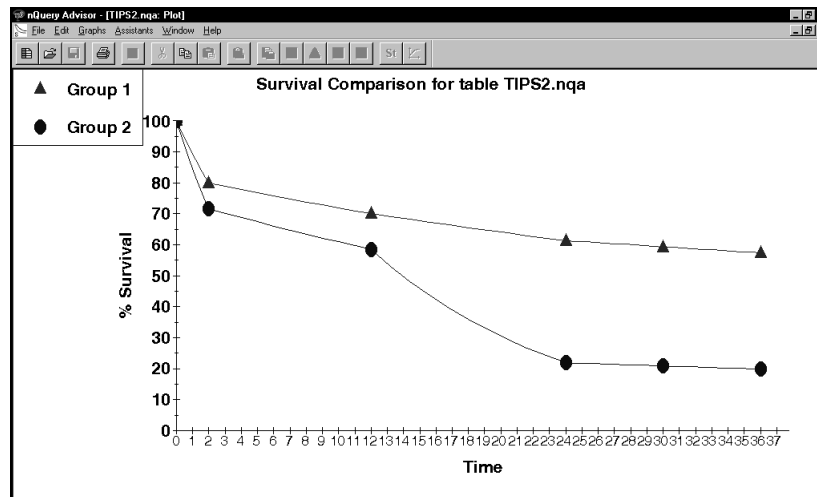
In the side table, select all six columns.

Select **Plot** menu **Plot survival vs time** option.

The plot will appear. Neither of the Plot buttons on the toolbar can be used to produce this plot.



You can adjust the values for survival at the ends of each period. Click and hold on the plot symbol. After a rectangle appears and disappears, drag the plotted point to the new position. In the following plot, we have lowered the three circles on the right in the lower curve.

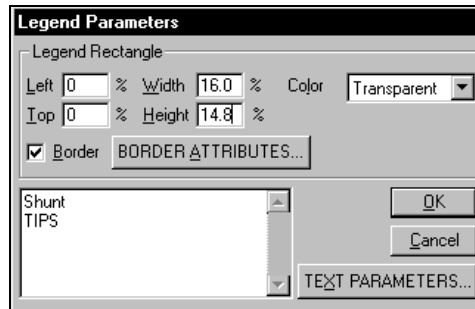


These changes will be reflected in the side table. You can change values in the side table, and they will be reflected in the plot, or change values in the plot, and they will be reflected in the side table. The altered side table has been resaved as TIPS2.nqa.

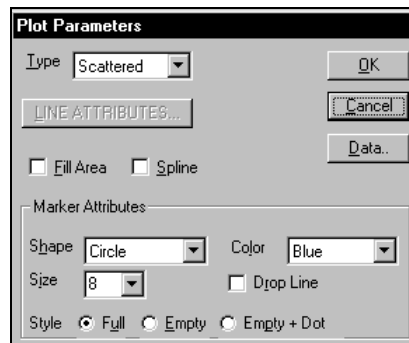
Time-dependent hazard info for log-rank survival test			
	4	5	6
End of period, time t	24.000	30.000	36.000
Accrual (% of total)	33.000	17.000	16.000
Group 1 exponential hazard rate, λ_1	0.0110	0.0055	0.0055
Group 2 exponential hazard rate, λ_2	0.0819	0.0083	0.0083
Group 1 expected % surviving time t	61.315	59.325	57.399
Group 2 expected % surviving time t	21.904	20.840	19.827
Common exponential dropout rate, d	0.0000	0.0000	0.0000

Note the changes in the Group 2 hazard rates and survival values for the last 3 columns.

You can double click on the legend to move or edit the legend. The Legend Parameters dialog box appears, and you can enter new values.




For each curve, you can change the plot type, along with the point marker shape, color and size. To edit the curve, double click on one point in the curve to bring up the Plot Parameters dialog box.



Using the Multi-period Side Tables with Simulation Survival Table (STT3)

While you are using a survival table, as soon as you have entered a number of

periods, you can click on the  button to get an almost blank side table. Only the first column is filled in, and you cannot edit that column of values. However, the accrual value in the first column will change as you make entries in the accrual row in other columns.

When you return to the main table, the main table will display the name of the attached side table in black letters. When you start from the survival table and use the delta button or the Assistants menu Compute Effect size option, your side table will be automatically attached and its contents used in further calculations. There will be no need to manually enter the side table name.



Opening a Survival Table and its Side Table

When you open a survival table and its side table at a later time, the side table may not be attached to the main table. To force the survival table to recognize its previously-attached side table, open the side table first. Then open the survival table.

If the related side table is not open when viewing the main table, the side table name will appear in red. You must then double click on the side table name in the survival table and type the side table name to attach the table. nQuery will decide whether to recalculate power for the column.

Colors for Side Table Names

The color of the side table name signals the attachment status of the side table.

Name in Red

The side table is not attached, so its contents cannot contribute to any calculations.

- If the side table is open, simply double click on the side table name in the survival table and type the side table name again.
- If the side table is not open, open it. Then double click on the side table name in the survival table and type the side table name again.

Name in Blue

When the side table is still incomplete, the name will appear in blue. You should complete the side table and save it.

Name in Black

The side table is attached, and its values will contribute to the survival table calculations.

Changing a Side Table Name

Double click on the existing Side table name and type the side table name. If you change the side table name in a completed column in a survival table, nQuery will decide whether to recalculate power. Of course, there will be no recalculation if you have reattached the side table used to compute the current values.

17. Agreement Tables

Measures of agreement are designed to assess how closely two different measurement methods or two different raters agree on the values for an outcome measure. Often, one method is the “gold standard,” and an investigator wants to study whether a new, cheaper method of measurement agrees well enough with the gold standard to warrant its use. The nQuery Advisor program provides sample size tables for tests or confidence intervals for three methods of measuring agreement. These are all one-sample problems.

Dichotomous outcome methods using Intraclass Kappa

AOT0 Agreement between two dichotomous ratings (intraclass kappa)

AOC0 Confidence interval for intraclass kappa (n large)

These sample size tables are applicable when two conditions hold:

- both the proposed version of the outcome/response variable and the gold standard version have only two possible categories (yes/no, success/failure, normal/abnormal)
- the intraclass version of the measure of agreement κ is to be used.

This version of κ is an index of the degree to which we can simply substitute one measure for the other. To assist you in computing values of kappa from proportions entered into a two-way table, nQuery Advisor provides a side table accessible from the Assistants menu Compute Effect Size option or from the Compute Effect Size icon; see example later in this chapter.

Continuous outcome methods using Pearson r

AOT1 Correlation test that $\rho = \rho_0$ for x and y bivariate normal

AOC1 One-sided confidence interval for ρ for x and y bivariate normal

These sample size tables are applicable when two conditions hold:

- both the proposed version of the outcome/response variable and the gold standard version are continuous measurements
- we can assume that their distributions are bivariate normal.

When those two assumptions are true, the Pearson correlation coefficient provides an index of the degree to which a linear relationship fits the data. Note that, even if the correlation coefficient is very close to 1.0, a scale change might be necessary before substituting one measure for the other.

Continuous outcome methods using Lin's concordance coefficient

- AOT2** Large sample test that Lin's concordance coefficient = K_0
- AOC2** One-sided large sample confidence interval for concordance coefficient

Lin's concordance coefficient is a modification of the Pearson correlation coefficient. Lin's concordance coefficient indexes the degree to which the proposed version of the outcome/response variable and the gold standard can be substituted for each other. Thus, it indexes how well the bivariate measurements fall on the line of identity.

The nQuery Advisor program provides a side table accessible from the Assistants menu Compute Effect Size option or from the Compute Effect Size icon. The side table computes values of the concordance coefficient from values for the Pearson correlation coefficient, the scaled difference in means, and the ratio of standard deviations.

Example

Confidence Interval for Intraclass kappa (AOC0)

This example pertains to a study planned to assess regional wall motion in the heart using a new test. Researchers want to validate the new test with measurements made using a test called echocardiography. Patients will undergo both tests and each test will be scored as 0=abnormal or 1=normal.

The goal of the study is to estimate the agreement as measured by κ between the two methods of classifying heart studies as normal or abnormal. We want to estimate the value of κ to within a value of ± 0.1 . The researcher plans to compute a two-sided 95% confidence interval.

Prior small studies comparing another measurement method to echocardiography found that the proportion of patients assessed as abnormal was between 0.65 and 0.70. The estimated values of κ were between 0.70 and 0.80.



To bring up the AOC0 sample size table:

Click on the **File** menu **New** option or the **New** icon. The Study Goal and Design dialog box will appear.

Select Agreement, **One**, Confidence interval.


Select the first analysis from the list of analyses.

Click **OK**. The Confidence interval for intraclass kappa (n large) table will appear.

The following table shows the significance level, 2-sided test, and desired distance, ω , to the confidence limit already filled in.

	1	2	3	4	5
Confidence level, $1-\alpha$	0.950				
1 or 2 sided interval?	2				
Proportion successes, π					
Agreement, κ					
Distance from κ to limit, ω	0.100				
n					

To compute the expected value of from proportions in a 2x2 table:

Select the **Assistants** menu **Compute Effect Size** option, or click on , the Compute Effect Size icon, to get the side table.

The blank side table for the intraclass kappa Confidence interval will appear.
For details concerning the side table buttons, see Chapter 12.

Proportions	Rater2 (+)	Rater2 (-)	Row proportion
Rater1 (+)			
Rater1 (-)			
Column Proportion			
Proportion successes, π			
Agreement, κ			

We expect the proportion of patients with abnormal wall motion to be about 65%.

To use this side table to calculate κ :

Enter **0.6** in the cell representing **Rater 1 (+)** and **Rater 2 (+)**. Both of these measurements are abnormal.

To represent the expected variation in raters, enter **0.05** for **Rater 1 (-)** and **Rater 2 (+)** or for **Rater 1 (+)** and **Rater 2 (-)**. Under the model for intraclass kappa, the two discordant cells are expected to have equal proportions; see reference for this table in the Appendix or Help.

Click on the **Compute** button.

ADC0-1: Aid for col 1 -- Confidence interval for intraclass kappa			
Compute	Transfer	Close	
	Clear	Cut	Copy
	Paste	Print	
Proportions	Rater2 (+)	Rater2 (-)	Row proportion
Rater1 (+)	0.600	0.050	0.650
Rater1 (-)	0.050	0.300	0.000
Column Proportion	0.650	0.000	0.000
Proportion successes, π	0.650		
Agreement, κ	0.780		

The program calculates the rest of the values for the table. These values give 0.65 as the proportion of patients with abnormal wall motion. The value of κ is 0.78 which is close to the value we expect based on other studies. We decide to use these values.

To send the new values to the sample size table:

Click on the **Transfer** button.

The computed values appear in the sample size table.


The sample size table automatically solves for **n**.

ADC0-1: Main					
Confidence interval for intraclass kappa (n large)					
	1	2	3	4	5
Confidence level, $1-\alpha$	0.950				
1 or 2 sided interval?	2				
Proportion successes, π	0.650				
Agreement, κ	0.780				
Distance from κ to limit, ω	0.100				
n	167				

To get the statement for this solution:

Click on any cell in the computed column.



Click on the **Create Statement** icon, . The statement will appear, and you may copy it to clipboard for pasting in another document, print it, or store it in the store statements panel on your screen.

Statement For Column 1

When the sample size is 167, a two-sided 95.0% confidence interval for the intraclass kappa will extend 0.100 from the observed value of kappa, assuming that the true value of the intraclass kappa is 0.780 and the proportion of successes is 0.650.

Store

Print

To Clipboard

Cancel

18. Regression Tables

nQuery Advisor can help determine the required sample size for research studies involving correlation or regression analyses of the relationship between x variables (predictor variables, covariates, independent variables) and a y variable or dependent variable.

Choosing a Regression Table

Your choice of sample size table depends on:

- the nature of the y variable — whether it is a yes/no (dichotomous or two-level variable) or a continuous variable, such as cholesterol level
- the number and characteristics of the x variables — whether you have one or multiple x variables, and whether they are dichotomous, ordered, or continuous.

Dichotomous y (Logistic Regression)

When the y variable, the variable you wish to predict, has only two levels, success versus failure, alive versus dead, yes versus no, a logistic regression model is often used to assess the predictive value of covariates. nQuery Advisor provides several options for computing sample size for studies where logistic regression will be used.

For a single dichotomous covariate use:

PTT0U Two-group χ^2 test of equal proportions (odds ratio = 1)
(unequal n's)
See Example 1a in this chapter.

For a single dichotomous covariate adjusted for p multiple covariates already in the model use:

PTT0U Two-group χ^2 test of equal proportions (odds ratio = 1)
(unequal n's) and apply the variance inflation factor.
See Example 1b in this chapter.

For a single ordered covariate, that is for studies in which the predictor variable has several ordered levels (as for three dose levels), use:

PGT1 **Trend across proportions (logistic model)**
See Example 8 in Chapter 15, *Sample Size Tables for Proportions*.

For a single continuous covariate, use:

ROT0 **Logistic regression test that $\beta = 0$ for one normally distributed covariate, x**
See Example 2 in this chapter.

MTT0U **Two group t test of equal means (unequal n 's)**
See Example 3 in this chapter

For a single continuous covariate adjusted for p multiple covariates already in the model use:

ROT1 or use MTT0U and apply the variance inflation factor.

ROT1 **Logistic regression test that $\beta = 0$ for one normal covariate x , adjusting for prior covariates**
See Example 3 in this chapter.

or

MTT0U **Two group t test of equal means (unequal n 's)**
See Example 4 in this chapter.

Continuous y

When the variable to be predicted is continuous, and its relationship to the continuous predictor variable is expected to be linear, use linear regression models to determine the sample size necessary to assess the predictive value of continuous covariates.



For a single continuous covariate, use:

ROT2 **Linear regression test that $\rho = 0$ for one normally distributed covariate, x**

This table provides sample size or power for the t test of the null hypothesis that the Pearson correlation coefficient, ρ , equals 0. That is, the t test tests a null hypothesis that there is no linear relationship between x and y.

To obtain the sample size required for a test of the null hypothesis that ρ is some value other than 0, or for a confidence interval of specified width for ρ , see sample size tables listed under **Agreement**:

AOT1 **Correlation test that $\rho = \rho_0$ for x and y bivariate normal**

AOC1 **One-sided confidence interval for ρ for x and y bivariate normal**

nQuery Advisor also provides sample size tables for tests and confidence intervals for regression slopes in one and two sample designs.

ROT5 **Linear regression test that $\beta = \beta_0$ for one x**

See Example 4 in this chapter. .

ROC0 **Linear regression confidence interval for β**

RTT0 **Linear regression test that $\beta_1 = \beta_2$ for one x**

See Example 5 in this chapter.

RTC0 **Linear regression confidence interval for $\beta_1 - \beta_2$**

For multiple covariates, use:

ROT3 **Multiple linear regression test that $R^2 = 0$ for k normally distributed covariates.**

This table provides sample size or power for the F-test which tests the null hypothesis that a set of k predictor variables have no linear predictive relationship with y. That is, the F-test tests the null hypothesis that the squared multiple correlation between y and the x variables is 0.

For two sets of covariates, use:

ROT4 **Multiple regression, test 0 increase in R^2 for B covariates adjusted for A covariates.**

This table provides sample size or power for the F-test of the null hypothesis that a set of B predictor variables have no linear predictive relationship with y, after y has been adjusted for A prior covariates. That is, the F-test will test the null hypothesis

that the squared multiple correlation between y and the combined sets of A and B predictor variables is no larger than the squared multiple correlation between y and the initial set of A covariates.

Logistic Regression

The model for logistic regression with one covariate is

$$\beta_0 + \beta_1 x = \ln \left(\frac{P}{1 + P} \right)$$
$$P = \text{Pr } ob(Y = 1)$$

The null hypothesis to be tested is that

$$H_0: \beta_1 = 0$$

Example 1

Logistic regression with a dichotomous covariate (PTT0U)


Hsieh, Bloch, Larsen (1998) Statistics in Medicine 17:1623-1634 recommend using the following method to obtain sample sizes for logistic regression with a dichotomous covariate. Let the covariate X define two groups; group 1 contains cases in which $x = 1$ and the probability that $y=1$ is π_1 while group 2 contains cases in which $x = 0$ and the probability that $y=1$ is π_2 .

Example 1a

Single covariate

As an example, we suppose that about 1% of the population is expected to have a particular adverse reaction to a certain drug used to treat a severe illness. It is thought that those with a specific pre-existing condition (expected to be about 20% of the population) will be much more likely to have such a reaction; it will be important to detect an odds ratio of four for the likelihood of a reaction in this group using a 5% two-sided logistic regression test.

To select the PTT0U table for this logistic regression example:

Choose the **File** menu **New** option or click on the **New** icon button . The Study Goal and Design dialog box will appear.

Select **Proportions, Two, Test**.

Five choices will appear in the list box in the lower part of the dialog box.

Select the first analysis type and click on **Unequal n's**.



Study Goal and Design

Goal: Make Conclusion Using <ul style="list-style-type: none"><input type="radio"/> Means<input checked="" type="radio"/> Proportions<input type="radio"/> Survival (Time to Event)<input type="radio"/> Agreement<input type="radio"/> Regression	Number of Groups <ul style="list-style-type: none"><input type="radio"/> One<input checked="" type="radio"/> Two<input type="radio"/> > Two	Analysis Method <ul style="list-style-type: none"><input checked="" type="radio"/> Test<input type="radio"/> Confidence Interval<input type="radio"/> Equivalence
-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

☒ Chi-square test to compare two proportions
☒ Chi-square test (continuity corrected)
 ☒ Compute power or sample size
 ☐ Compute one of two proportions
 ☐ Fisher's exact test
 ☐ Two-group Chi-square test comparing proportions in C categories
☒ Mantel-Haenszel(Cochran) test

☒ Unequal n's ☐ Finite Population

OK Cancel

Double click on the first choice , select Compute Power or sample size and select Unequal n's. Then press **OK**, and the sample size table appears. Note that we have already turned off the guide cards.

Two group χ^2 test of equal proportions (odds ratio = 1) (unequal n's)					
	1	2	3	4	5
Test significance level, α					
1 or 2 sided test?					
Group 1 proportion, π_1					
Group 2 proportion, π_2					
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$					
Power (%)					
n_1					
n_2					
Ratio: n_2 / n_1					
$N = n_1 + n_2$					

Use the Edit menu Edit Row Names option to change the Group 1 and Group 2 row names to **No condition** and **Pre-existing condition**, respectively.

Two group χ^2 test of equal proportions (odds ratio = 1) (unequal n's)					
	1	2	3	4	5
Test significance level, α					
1 or 2 sided test?					
No condition proportion, π_1					
Pre-existing condition proportion, π_2					
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$					
Power (%)					
n_1					
n_2					
Ratio: n_2 / n_1					
$N = n_1 + n_2$					

Enter **.05** in the Test significance level row.

Enter **2** in the **1 or 2 sided test** row.

Enter **.01** in the No condition proportion.

Enter **4** in the Odds ratio row, and the Pre-existing proportion row value will be calculated.

Enter **90** in the Power row for a power of 90%.

Enter **.25** in the Ratio n_2/n_1 row. This is a ratio of 20/80=.25.

The remaining row values will be calculated.

Two group χ^2 test of equal proportions (odds ratio = 1) (unequal n's)					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
No condition proportion, π_1	0.010				
Pre-existing condition proportion, π_2	0.039				
Odds ratio, $\psi = \pi_2 (1 - \pi_1) / [\pi_1 (1 - \pi_2)]$	4.000				
Power (%)	90				
n_1	1345				
n_2	337				
Ratio: n_2 / n_1	0.250				
$N = n_1 + n_2$	1681				

This study would require a total sample size of almost 1700 patients.



Example 1b

Variance inflation factor for p prior covariates

For example 1a, the total sample size was computed as N for testing the significance of one dichotomous covariate. The sample size, N_p required to test for the significance of this dichotomous covariate after prior inclusion of p other covariates in the model, is given by

$$N_p = N \left(\frac{1}{1 - \rho^2} \right)$$

where the factor $1/(1 - \rho^2)$ is called the “variance inflation factor”,

$$VIF = \left(\frac{1}{1 - \rho^2} \right)$$

and ρ^2 is the squared multiple correlation of the covariate of interest with the covariates already included in the model.

For example 1a above, if four patient demographic variables will be entered into the logistic regression model prior to testing the covariate indicating presence or absence of the pre-existing condition (x_1 say), and these demographic variables have a squared multiple correlation with x_1 of 0.2, then a total sample size of at least 2,100 patients would be required.

$$N_p = 1681 \left(\frac{1}{1 - 0.2} \right) = 2101$$

Example 2

Logistic regression with a continuous covariate (ROT0)


Patients with blocked or narrowed coronary arteries may undergo interventions designed to increase blood flow. Typically, about 30% of patients followed for a year will have renewed blockage, or restenosis, of the artery.

A study is to be planned to use logistic regression to assess factors related to the likelihood of restenosis. One such factor is serum cholesterol level. Based on the results of a large screening trial, mean serum cholesterol in middle-aged males is about 210 mg/dL; one standard deviation above the mean (which corresponds to about the 85th percentile) is about 250 mg/dL.

In the screening study, the odds ratio for six-year death rate for these two cholesterol levels was about 1.5. Consider that you want to design a study large enough to

detect an effect of serum cholesterol on arterial restenosis of a size similar to that seen for death rate.

To select the ROT0 logistic regression table:

Choose the **File** menu **New** option or click on the **New** icon, .

In the Study Goal and Design dialog box, click on the radio buttons for **Regression**, **One**, and **Test**. The list box will display the six regression analysis choices.

Study Goal and Design

Goal: Make Conclusion Using

☐ Means

☐ Proportions

☐ Survival (Time to Event)

☐ Agreement

☒ Regression

Number of Groups

☒ One

☐ Two

☐ > Two

Analysis Method

☒ Test

☐ Confidence Interval

☐ Equivalence

Logistic regression, one normal covariate

Logistic regression, one normal covariate adjusted for others

Linear regression, one covariate

Linear regression, multiple covariates

Linear regression, multiple covariates adjusted for others

Linear regression, test of coefficient

☐ Unequal n's

☐ Finite Population

OK

Cancel

Click on **Logistic regression one normal covariate**, then click on **OK**. The following table will appear.

Logistic regression, test that $\beta = 0$ for one normally distributed covariate, x					
	1	2	3	4	5
Test significance level, α					
1 or 2 sided test?					
Proportion, p_M , at mean μ of covariate x					
At $x_T = \mu + \sigma$, Proportion, p_T					
Odds ratio = $p_T (1 - p_M) / [p_M (1 - p_T)]$					
Coefficient, $B = \ln(\text{odds ratio})$					
Power (%)					
n					



Since you plan to use a logistic regression test at the two-sided 5% level:

Enter **.05** in the **Test significance level** row.

Enter **2** in the **1 or 2 sided test** row.

You must now specify the response rate at the mean of the covariate; for this example, we don't know the response rate at the mean of the covariate and so we use the overall restenosis rate of 30% as an initial guess.

Enter **.3** in the **Proportion** row.

When you enter a value in any one of the next three rows, the nQuery Advisor program will compute the values for the other two rows. In this case, we do not know what response proportion to expect for cholesterol levels one standard deviation above the mean. However, we would be interested in detecting an odds ratio of 1.5.

Enter **1.5** in the **Odds ratio** row, and nQuery Advisor will compute the Proportion, $p_T = .391$, and Coefficient, $B = .405$.

You want 90% power, so enter **90** in the **Power** row. The nQuery Advisor program solves for a sample size of 360 cases. The next screen shows the filled-in table.

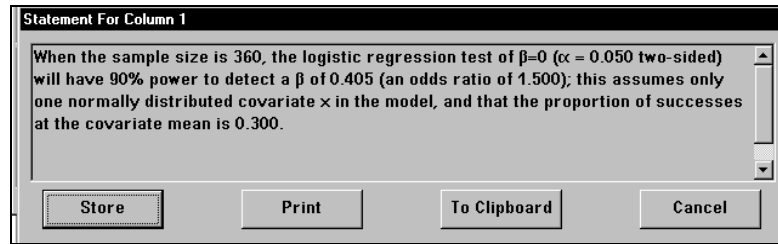
Logistic regression, test that $\beta = 0$ for one normally distributed covariate, x					
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Proportion, p_M , at mean μ of covariate x	0.300				
At $x_T = \mu + \sigma$, Proportion, p_T	0.391				
Odds ratio = $p_T (1 - p_M) / [p_M (1 - p_T)]$	1.500				
Coefficient, $B = \ln(\text{odds ratio})$	0.405				
Power (%)	90				
n	360				

Note that for this sample size table for logistic regression, the odds ratio must be between 0.40 and 2.50 (and not equal to 1.0.) This is because the approximate method on which computations are based (Hsieh, F.Y. (1989) Sample size tables for logistic regression. *Statistics in Medicine* 8:795-802) is derived using the assumption that the odds ratio is small. For studies designed to detect a more extreme odds ratio, see Example 3.

To get the statement for the completed column:

Select one or more rows in the column.

Click on the **Create Statement** button. The full statement will appear.



At this point, you can click on the **Store** button to store the statement with the sample size table. You can click on the **Print** button to print the statement directly, or click on the **To Clipboard** button to copy the statement to the clipboard using the font of your choice.

The sample size required to evaluate the significance of cholesterol level in predicting the likelihood of restenosis is 360.

Adjusting for Prior Covariates (ROT1 or Variance Inflation Factor)

If two other covariates whose squared multiple correlation with cholesterol is .15 are to be entered into the logistic regression first, you have two choices. First, you can multiply the sample size obtained for a single covariate by the variance inflation factor, $1/(1-\rho^2)$, to increase the required sample size to 424. The alternative is to use table ROT1, the sample size table for logistic regression for one covariate after adjustment for prior covariates.



Study Goal and Design

Goal: Make Conclusion Using <input type="radio"/> Means <input type="radio"/> Proportions <input type="radio"/> Survival (Time to Event) <input type="radio"/> Agreement <input checked="" type="radio"/> Regression	Number of Groups <input checked="" type="radio"/> One <input type="radio"/> Two <input type="radio"/> > Two	Analysis Method <input checked="" type="radio"/> Test <input type="radio"/> Confidence Interval <input type="radio"/> Equivalence
--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------	---------------------------------------------------------------------------------------------------------------------------------------------------

Logistic regression, one normal covariate
Logistic regression, one normal covariate adjusted for others
 Linear regression, one covariate
 Linear regression, multiple covariates
 Linear regression, multiple covariates adjusted for others
 Linear regression, test of coefficient

☐ Unequal n's
☐ Finite Population

OK Cancel

ROT1, the sample size table for logistic regression for one covariate after adjustment for prior covariates, requires the same input as the logistic regression sample size table for a single covariate.

Enter **.05** in the **Test significance level** row.

Enter **2** in the **1 or 2 sided test** row.

Enter **.3** in the **Proportion** row.

Enter **1.5** in the **Odds ratio** row, and nQuery Advisor will compute the Proportion, $p_T = .391$.

Enter **Coefficient, B = .405**.

You want 90% power, so enter **90** in the **Power** row. The nQuery Advisor program solves for a sample size of 360 cases. The next screen shows the filled-in table.

Logistic regression, test that $\beta = 0$ for one normal covariate, x , adjusting for prior covariates					
	1	2	3	4	
Test significance level, α	0.050				
1 or 2 sided test?	2				
Proportion, p_M , at mean μ of covariate x	0.300				
At $x_T = \mu + \sigma$, Proportion, p_T	0.391				
Odds ratio = $p_T (1 - p_M) / [p_M (1 - p_T)]$	1.500				
Coefficient, $B = \ln(\text{odds ratio})$	0.405				
$p^2 = \text{squared corr. of } x \text{ with included covariates}$	0.150				
Power (%)	90				
n	424				

The only difference is that we must provide an estimate of the squared multiple correlation of x with the covariates already in the model.

Example 3

Logistic regression with a continuous covariate (MTT0U)

Hsieh, Bloch, Larsen (1998) *Statistics in Medicine* 17:1623-1634 recommend using the following method to obtain sample sizes for logistic regression with a continuous covariate. Let the response Y define two groups; group 1 contains cases in which $Y = 1$ with $N\pi_1$ cases expected, while group 2 contains cases in which $Y = 0$ with $N(1-\pi_1)$ cases expected. (The probability π_1 is labeled p_M in the sample size tables ROT0 and ROT1.) The ratio of the expected sample size in group 2 to the expected sample size in group 1, r , is $(1-\pi_1)/\pi_1$. The natural log of the odds ratio, the coefficient B of the covariate, x , is equal to the difference between the mean of the covariate in group 1 and the mean of the covariate in group 2 divided by the within-group standard deviation of x . Therefore, a sample size table for the two group t test with unequal n 's can be used to estimate sample size for logistic regression with one continuous covariate.

To select the table MTT0U to use for logistic regression:

Choose the **File** menu **New** option or click on the **New** icon,



In the Study Goal and Design dialog box, click on the radio buttons for **Means**, **Two**, and **Test**. The list box will display four main means test choices. Under the first choice Two-sample t -test, select the highlighted choice, Student's t test, and click on **Unequal n 's**.



Study Goal and Design

Goal: Make Conclusion Using <ul style="list-style-type: none"><input checked="" type="radio"/> Means<input type="radio"/> Proportions<input type="radio"/> Survival (Time to Event)<input type="radio"/> Agreement<input type="radio"/> Regression	Number of Groups <ul style="list-style-type: none"><input type="radio"/> One<input checked="" type="radio"/> Two<input type="radio"/> > Two	Analysis Method <ul style="list-style-type: none"><input checked="" type="radio"/> Test<input type="radio"/> Confidence Interval<input type="radio"/> Equivalence
-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

☒ **Two-sample t test**

- ☒ Student's t test (equal variances)
- ☐ Satterthwaite's t test (unequal variances)
- ☐ Two group t-test for fold change assuming log-normal distribution (equal n's)
- ☐ Two group t-test of equal fold change with fold change threshold (equal n's)
- ☐ Wilcoxon/Mann-Whitney rank-sum test (continuous outcome)
- ☐ Wilcoxon/Mann-Whitney rank-sum test (ordered categories)
- ☐ Two-group univariate repeated measures ANOVA (Greenhouse-Geisser correction)

☒ Unequal n's ☐ Finite Population

Click on **OK** to bring up the sample size table.

Two group t-test of equal means (unequal n's)						
	1	2	3	4	5	6
Test significance level, α						
1 or 2 sided test?						
Group 1 mean, μ_1						
Group 2 mean, μ_2						
Difference in means, $\mu_1 - \mu_2$						
Common standard deviation, σ						
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$						
Power (%)						
n_1						
n_2						
Ratio: n_2 / n_1						
$N = n_1 + n_2$						

Referring back to Example 2 in which the predictive effect of cholesterol level on the probability of restenosis is to be studied, we enter **.05** for significance level, **2** for a two-sided test.

The sample size necessary to detect an odds ratio of 1.5 for values of cholesterol of 250 mg/dL versus 210 mg/DL with 90% was requested. We enter the value of the natural log of the odds ratio of 1.5, **0.405**, into the effect size row. The ratio of sample sizes expected to be in the no-restenosis and the restenosis groups, r , equals $.7/.3 = 2.333$

Enter **90** in the **Power** row.

To obtain a power of 90%, we find that a total sample size of 310 is required. Hsieh, Bloch, and Larsen (1998) demonstrate that the approximate formula recommended earlier by Hsieh (1989) and used in ROT0 and ROT1 gives larger than required sample sizes.

Two group t-test of equal means (unequal n's)						
	1	2	3	4	5	6
Test significance level, α	0.050					
1 or 2 sided test?	2					
Group 1 mean, μ_1						
Group 2 mean, μ_2						
Difference in means, $\mu_1 - \mu_2$						
Common standard deviation, σ						
Effect size, $\delta = \mu_1 - \mu_2 / \sigma$	0.405					
Power (%)	90					
n_1	93					
n_2	217					
Ratio: n_2 / n_1	2.333					
$N = n_1 + n_2$	310					

If two other covariates with a squared multiple correlation with cholesterol of .15 are to be entered into the logistic regression first, multiply the sample size obtained for a single covariate by the variance inflation factor, $1/(1-\rho^2)$, to increase the required sample size to 365.

Linear Regression

Example 4


Linear regression test that $\beta = \beta_0$ for one x (ROT5) .

A quick test for measuring cholesterol is to be assessed in comparison with the current gold standard. To ensure that the new test is calibrated properly and agrees well with the gold standard in one of the target populations, 300 middle-aged males will be tested using both methods.

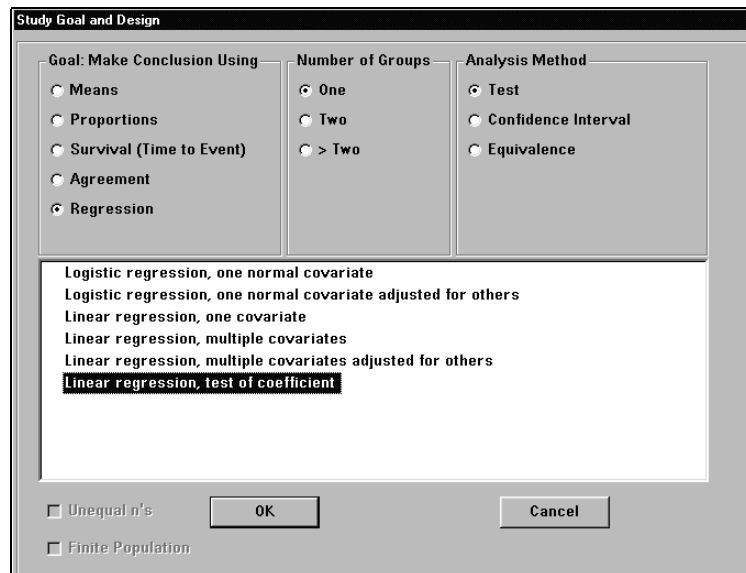
To ensure that there is no bias in the new test, the researcher will fit a regression line and run tests to see whether the slope differs from its expected value of 1 and whether the intercept differs from its expected value of 0. To make sure that sample size will be adequate for the test on slope, the investigator wants to know the expected power for deviations of 10% from a slope of 1.0. The standard deviation of cholesterol values for this population is expected to be 40 mg/dL and previous results suggest that the correlation between new test and gold standard results will be 0.90.



To select the ROT5 table for a test of the regression slope:

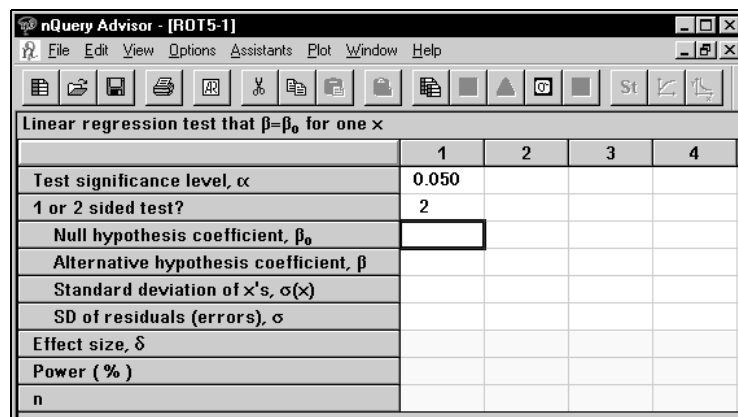
Choose the **File** menu **New** option or click on the **New** icon, .

In the Study Goal and Design dialog box, click on the radio buttons for **Regression**, **One**, and **Test**. The list box will display the six regression analysis choices.



The 'Study Goal and Design' dialog box has three sections: 'Goal: Make Conclusion Using', 'Number of Groups', and 'Analysis Method'. In 'Goal', 'Regression' is selected. In 'Number of Groups', 'One' is selected. In 'Analysis Method', 'Test' is selected. Below these sections is a list box containing six options: 'Logistic regression, one normal covariate', 'Logistic regression, one normal covariate adjusted for others', 'Linear regression, one covariate', 'Linear regression, multiple covariates', 'Linear regression, multiple covariates adjusted for others', and 'Linear regression, test of coefficient'. The last option is highlighted. At the bottom are checkboxes for 'Unequal n's' and 'Finite Population', and 'OK' and 'Cancel' buttons.

Click on **Linear regression, test of coefficient**, then click on **OK**. The following table will appear; we have already filled in .05 for test significance level, and 2 for a two-sided test.



The 'nQuery Advisor - [ROT5-1]' window shows a table for a linear regression test. The title bar says 'nQuery Advisor - [ROT5-1]'. The menu bar includes File, Edit, View, Options, Assistants, Plot, Window, and Help. The toolbar contains various icons. The table is titled 'Linear regression test that $\beta = \beta_0$ for one x'. It has 5 columns: the first column lists parameters, and the next four columns are numbered 1, 2, 3, and 4. The first row is a header. The second row has 'Test significance level, α ' in the first column and '0.050' in the second column. The third row has '1 or 2 sided test?' in the first column and '2' in the second column. The fourth row has 'Null hypothesis coefficient, β_0 ' in the first column and an empty cell in the second column. The fifth row has 'Alternative hypothesis coefficient, β ' in the first column and an empty cell in the second column. The sixth row has 'Standard deviation of x's, $\sigma(x)$ ' in the first column and an empty cell in the second column. The seventh row has 'SD of residuals (errors), σ ' in the first column and an empty cell in the second column. The eighth row has 'Effect size, δ ' in the first column and an empty cell in the second column. The ninth row has 'Power (%)' in the first column and an empty cell in the second column. The tenth row has 'n' in the first column and an empty cell in the second column.

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Null hypothesis coefficient, β_0				
Alternative hypothesis coefficient, β				
Standard deviation of x's, $\sigma(x)$				
SD of residuals (errors), σ				
Effect size, δ				
Power (%)				
n				

Enter **40** for **Standard deviation of x's**, and **300** for **n**, the planned sample size.

nQuery Advisor - [R0T5-1]

File Edit View Options Assistants Plot Window Help

Linear regression test that $\beta = \beta_0$ for one x

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Null hypothesis coefficient, β_0	1.000			
Alternative hypothesis coefficient, β	1.100			
Standard deviation of x 's, $\sigma(x)$	40.000			
SD of residuals (errors), σ				
Effect size, δ				
Power (%)				
n	300			

The investigator does not know what to enter for the standard deviation of the residuals. To estimate the standard deviation of the residuals from the information already available, use a side-table available by selecting the **Assistants** menu **Estimate SD** option or the toolbar icon marked σ .

Estimate Standard Deviation

- ☒ From Standard Error
- ☐ From SD1 and SD2 (pooled SD)
- ☐ From Range
- ☐ From Percentile
- ☐ From Coefficient of Variation
- ☐ From Upper Confidence Limit
- ☐ From SD1, SD2, Correlation
- ☐ For Cluster Sampling
- ☐ For specified x values
- ☐ Of residuals (errors)

OK Cancel

Select the last entry **Of residuals (errors)**. You will see the following table.



nQuery Advisor - [MOT18-1]

File Edit View Options Assistants Plot Window Help

Residual (error) standard deviation around the line for one predictor x

	1	2	3	4	5
Regression coefficient, β					
Correlation coefficient, ρ					
Standard deviation of x , $\sigma(x)$					
Standard deviation of y , $\sigma(y)$					
SD of residuals (errors), σ					

Enter the values for the regression coefficient (the slope), the expected correlation coefficient, and the expected standard deviation of the x 's, and nQuery will compute the expected standard deviation of the residuals.

nQuery Advisor - [MOT18-1]

File Edit View Options Assistants Plot Window Help

Residual (error) standard deviation around the line for one predictor x

	1	2	3	4	5
Regression coefficient, β	1.000				
Correlation coefficient, ρ	0.900				
Standard deviation of x , $\sigma(x)$	40.000				
Standard deviation of y , $\sigma(y)$	44.444				
SD of residuals (errors), σ	19.373				

Copy the value **19.373** and paste it into the main table in the SD of residuals row. Then nQuery will compute the power.

nQuery Advisor - [ROT5-1]

File Edit View Options Assistants Plot Window Help

Linear regression test that $\beta = \beta_0$ for one x

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
Null hypothesis coefficient, β_0	1.000			
Alternative hypothesis coefficient, β	1.100			
Standard deviation of x 's, $\sigma(x)$	40.000			
SD of residuals (errors), σ	19.373			
Effect size, δ	0.206			
Power (%)	94			
n	300			

The power is computed as 94%, so the planned sample size is adequate for this aspect of the assessment of the calibration of the new test.

To get the statement for the completed column:

Select one or more rows in the column.

Click on the **Create Statement** button. The full statement will appear.

At this point, you can click on the **Store** button to store the statement with the sample size table. You can click on the **Print** button to print the statement directly, or click on the **To Clipboard** button to copy the statement to the clipboard. The statement, as it appears below, can be pasted into your document.

A sample size of 300 will have 94% power to detect a difference between a null hypothesis regression slope of 1.000 and an alternative regression slope of 1.100, assuming that the standard deviation of the predictor variable, x , is 40.000 and the standard deviation of the residuals is 19.373 using a t-test with a 0.050 two-sided significance level.


Example 5

Linear regression test that $\beta_1 = \beta_2$ for one x (RTT0)

To evaluate whether drug A has a synergistic effect on the dose response to drug B, an investigator plans a trial in which 10 rats will be assigned at random to each of 6 doses of drug B. Half of the 10 animals receiving each dose of drug B will also receive drug A, and half will receive a control substance.

The investigator has evaluated the dose response under control conditions in the past. When the doses of drug B were 2, 4, 8, 16, 32, 64, the slope of the regression of the response variable on the log to the base 10 of the dose was 6.9 with a residual mean squared error of 25. The researcher wants to know whether the power will be adequate to detect a doubling in the slope of the regression line?

To select the RTT0 table for a test of equality of the regression slopes:

Choose the **File** menu **New** option or click on the **New** icon, .

In the Study Goal and Design dialog box, click on the radio buttons for **Regression**, **Two**, and **Test**. The list box will display a single analysis choice.

Click on **Test of equality for equality of slopes for one x** , then click on **OK**. The following table will appear; we have already filled in **.05** for **Test significance level**, and **2** for a **2 sided test**.



nQuery Advisor - [RTT0-1]

File Edit View Options Assistants Plot Window Help

Linear regression test that $\beta_1 = \beta_2$ for one x

	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Group 1 coefficient, β_1					
Group 2 coefficient, β_2					
Standard deviation of x's, $\sigma(x)$					
SD of residuals (errors), σ					
Effect size, δ					
Power (%)					
n per group					

The investigator wishes to test the null hypothesis that the slopes are equal versus the alternative hypothesis that the slope under control conditions is **6.9** and that under drug A is **13.8**. Thus, in the **Group 1 coefficient** row, enter **6.9**; in **Group 2**, enter **13.8**.

In the **SD of residuals** row, enter **5**, the square root of the residual mean square error. (To get the table with customized row names shown below, we used the **Edit** menu **Edit row names** option.)

nQuery Advisor - [RTT0-1]

File Edit View Options Assistants Plot Window Help

Linear regression test that $\beta_1 = \beta_2$ for one x

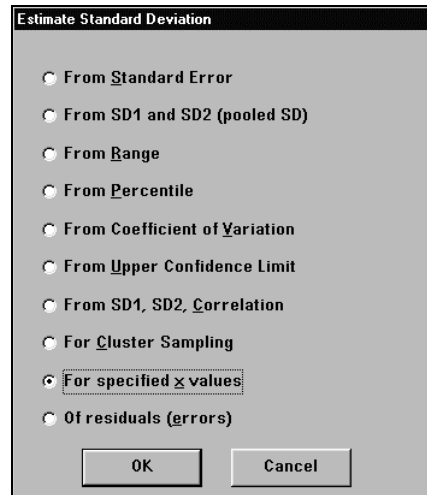
	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Control coefficient, β_1	6.900				
Drug A coefficient, β_2	13.800				
Standard deviation of x's, $\sigma(x)$					
SD of residuals (errors), σ	5.000				
Effect size, δ					
Power (%)					
n per group					

Now the investigator still needs to provide the standard deviation of the x's. To compute this from the doses of drug B, we use a table from the Assistants menu.

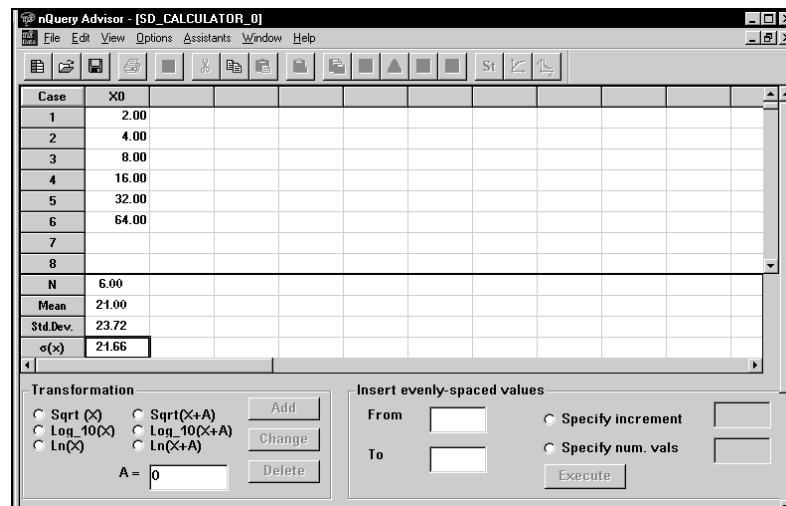
To compute the standard deviation for specified x values:

Select the **Assistants** menu **Estimate SD** option, or click on the toolbar icon marked σ .

The Estimate Standard Deviation dialog box will appear. This dialog box is explained in detail in Chapter 9.



Select the next to last entry **For specified x values**. You will see the following table.



We have already entered six dose levels in the side table. To get the log dose values, we click on the radio button beside **log₁₀(x)**, then click on the **Add** button. The nQuery program calculates the log values and enters those values in the adjacent column.



nQuery Advisor - [SD_CALCULATOR 0]

File Edit View Options Assistants Window Help

Case	X0	Log X0								
1	2.00	0.30								
2	4.00	0.60								
3	8.00	0.90								
4	16.00	1.20								
5	32.00	1.51								
6	64.00	1.81								
7										
8										
N	6.00	6.00								
Mean	21.00	1.05								
Std.Dev.	23.72	0.56								
$\sigma(x)$	21.66	0.51								

Transformation

☐ Sqrt(X) ☐ Sqrt(X+A) ☐ Log_10(X) ☐ Log_10(X+A) ☐ Ln(X) ☐ Ln(X+A)

A = 0

Insert evenly-spaced values

From To ☐ Specify increment ☐ Specify num. vals

Execute

Select the population standard deviation of the logs of the doses in the row labeled $\sigma(x)$. (This standard deviation divides the sum of squared deviations about the mean by n instead of $n-1$.)

Use the **Edit** menu **Copy** option to copy that value.

Use the Windows menu to select **RTT0** again.

Use the **Edit** menu **Paste** option to paste the standard deviation of the log doses into the row labeled Standard deviation of x 's, $\sigma(x)$. Note that more digits are now visible.

Then nQuery will calculate the **Effect size**.

Enter **30** for the **n per group**, because the study will have five rats at each of six doses.

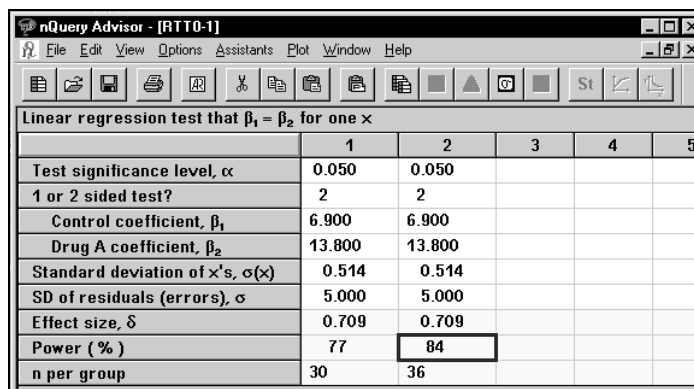
nQuery Advisor - [RTT0-1]

File Edit View Options Assistants Plot Window Help

Linear regression test that $\beta_1 = \beta_2$ for one x

	1	2	3	4	5
Test significance level, α	0.050				
1 or 2 sided test?	2				
Control coefficient, β_1	6.900				
Drug A coefficient, β_2	13.800				
Standard deviation of x 's, $\sigma(x)$	0.514				
SD of residuals (errors), σ	5.000				
Effect size, δ	0.709				
Power (%)	77				
n per group	30				

nQuery computes the power as 77%, so the planned sample size is not adequate for detection of the effects of drug A.



Linear regression test that $\beta_1 = \beta_2$ for one x					
	1	2	3	4	5
Test significance level, α	0.050	0.050			
1 or 2 sided test?	2	2			
Control coefficient, β_1	6.900	6.900			
Drug A coefficient, β_2	13.800	13.800			
Standard deviation of x's, $\sigma(x)$	0.514	0.514			
SD of residuals (errors), σ	5.000	5.000			
Effect size, δ	0.709	0.709			
Power (%)	77	84			
n per group	30	36			

In the next column we have recalculated power using 6 rats per dose for each of the six doses of drug B in the control group and the same number in the drug A group (36 per group). Using 72 rats total will provide 84% power, which the investigator considers to be adequate.

To get the statement for the completed column:

Select one or more rows in the column.

Click on the **Create Statement** button. The full statement will appear.

At this point, you can click on the **Store** button to store the statement with the sample size table. You can click on the **Print** button to print the statement directly, or click on the **To Clipboard** button to copy the statement to the clipboard.

A sample size of 36 per group will have 84% power to detect a difference between a Group 1 coefficient, β_1 regression slope of 6.900 and a Group 2 coefficient, β_2 slope of 13.800, assuming that the standard deviation of the predictor variable, x, is 0.514 and the standard deviation of the residuals is 5.000 using a t-test with a 0.050 two-sided significance level.

19. Sampling from Finite Populations

Most nQuery Advisor sample size tables are based on the assumption that inferences will be made to a very large population. Consider samples selected from a finite population—of 1000 subjects, for example. Inferences will be made only about those 1000 subjects. In such a situation, you can use nQuery Advisor tables designed for finite populations to select the required sample size.

Define the required sample size for sampling from a finite population of size N as n_A ; the sampling fraction is then n_A/N . In the context of estimating a single mean from a finite population, the variance of the sample mean is reduced from

$$\frac{\sigma^2}{n} \text{ to } \left(\frac{N - n_A}{N} \right) \frac{\sigma^2}{n_A}.$$

Thus, a sample from a finite population can be somewhat smaller than a sample from a very large population.

nQuery Advisor provides sample size tables with a finite population correction for the following situations.

Means, One group, Test

- MOT0F** One group t test that a mean equals a user-specified value
- MOT1F** Paired t test of mean difference equal to zero

Means, One group, Confidence Interval

- MOC0F** Confidence interval for mean based on z (n large)
- MOC1F** Confidence interval for mean based on t (with coverage probability)
- MOC2F** Confidence interval for interval in paired means based on z (n large)
- MOC3F** Confidence interval for difference in paired means based on t (coverage probability)

Proportions, One Group, Test

POT0F One group χ^2 test that proportion equals user-specified value (normal approximation)

Proportions, One Group, Confidence Interval

POC0 Confidence interval for proportions using normal approximation (n large)

Example


Proportions, One Group, Test (POC0F)

These adjustments to the required sample size won't result in a large reduction in the required sample size unless the sampling fraction is greater than about 5%. We must remember that the normality assumption underlying the tests and confidence intervals for means cannot literally hold for finite populations. In addition, these nQuery Advisor tables are intended for finite populations which are reasonably large so that the sampling fraction is not near 100%.

If the outcome measure is a proportion, and the population size is small and/or the sampling fraction larger than 50%, exact or simulation methods should be used to establish the required sample size.

In a survey sampling setting, one may wish to estimate a mean or a proportion from a finite population of size N . For example, one might wish to estimate the proportion of students who would return the following year if a proposed increase in student tuition and fees takes place. In the past three years, retention rates have been close to 60%. There would be considerable concern if the retention rates could be expected to drop markedly as a result of the fee increases. If there are 8,534 students who would be eligible to return the following year, how many must be surveyed to assess the retention rate to be expected to within $\pm 5\%$ if fees increase?

To bring up the correct sample size table:

Choose the **File** menu **New** option or click on , the New icon button.

In the Study Goal and Design Box, you will see three columns of options.

Under **Goal: Make conclusion using**, select **Proportions**.

Under **Number of groups**, select **One** group.



Under Analysis method, select Confidence Interval.

Select **Confidence interval for proportion**.

Select **Finite Population** box at the bottom of the Study Goal and Design Box.

Click on **OK**.

You will see the following table. It looks like the standard table for a confidence interval for a proportion, except that there is an additional row for population size.

nQuery Advisor - [POC0F-1]

File Edit View Options Assistants Plot Window Help

Confidence interval for proportion (normal approx.) (n large) adjusted for finite pop

	1	2	3	4	
Confidence level, $1-\alpha$					
1 or 2 sided interval?					
Expected proportion, π					
Distance from proportion to limit, ω					
Population size, N					
n_A					

Fill in the table as shown below.

nQuery Advisor - [POC0F-1]

File Edit View Options Assistants Plot Window Help

Confidence interval for proportion (normal approx.) (n large) adjusted for finite population

	1	2	3	4	5	
Confidence level, $1-\alpha$	0.950	0.950				
1 or 2 sided interval?	2	2				
Expected proportion, π	0.600	0.600				
Distance from proportion to limit, ω	0.050	0.050				
Population size, N	1000000	8534				
n_A	369	354				

After filling in the table, we see in the first column that the sample size required when the population was very large is 369. The second column uses the number of returning students as the Population size. For a population of 8534 returning students, it would be necessary to survey only 354 students for the same precision of estimate, a sampling fraction of 3.6%.

If the investigator wanted to estimate retention rate with the same precision for the 2010 students who are currently freshman, it would be necessary to survey 312 students (a sampling fraction of 15.5%).

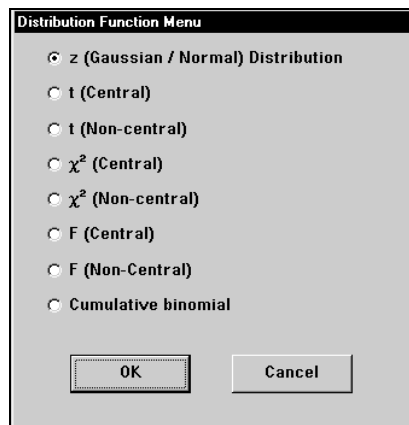
20. Distribution Function Tables

For the advanced user who wants to make sample size calculations for formulas not included in nQuery Advisor, the program provides access to central and non-central distribution functions

To access the distribution functions:

- ◆ Select **Distribution Functions** from the **Assistants** menu.

The Distribution Function Menu provides the following choices:



Example

The Non-central t Distribution

This example uses the non-central t distribution to compute power for the paired t test. We want to know the power for a two-sided 5% level paired t test, for which the expected difference in means is 5.0, the standard deviation of differences is 10.0, and the planned sample size is 25.

In this case, we can answer the question directly.

To calculate the power using the paired t-test sample size table:

Click on the **File** menu **New** option or the **New** icon. The Study Goal and Design dialog box will appear.

Select **Means, One, Test**.

Select the second analysis.

Click **OK**. The Paired t-test for differences in means table will appear.

Enter .05 for significance level, 2 for a two-sided test, 5.0 for expected difference in means, 10.0 for standard deviation of differences, and 25 for sample size. The nQuery Advisor program will calculate the power.

	1	2	3	4
Test significance level, α	0.050			
1 or 2 sided test?	2			
First condition mean, μ_1				
Second condition mean, μ_2				
Mean difference, $\mu_d = \mu_1 - \mu_2$	5.000			
Standard deviation of differences, σ_d	10.000			
Effect size, $\delta = \mu_d / \sigma_d$	0.500			
Power (%)	66			
n	25			

For Help, press F1 66.97077 AUTO RECALC OFF

This table gives the answer 66%. Note that the status bar gives a more exact value, 66.97.

To calculate the power using the Distribution Function Menu option:

Select **Distribution Functions** from the **Assistants** menu.

Distribution Function Menu

- ☒ z (Gaussian / Normal) Distribution
- ☐ t (Central)
- ☐ t (Non-central)
- ☐ χ^2 (Central)
- ☐ χ^2 (Non-central)
- ☐ F (Central)
- ☐ F (Non-Central)
- ☐ Cumulative binomial

OK Cancel



Select **t (Non-central)** to obtain the following table.

t (Non-central) Distribution						
Degrees of freedom						
Non-centrality parameter						
Probability, Prob(t < t_p)						
t_p						
+						

In this example, the paired t-test which has n-1 degrees of freedom will have 24 degrees of freedom. The formula for the non-centrality parameter for the non-central t distribution in the case of the paired t-test is

$$\delta\sqrt{n} = [(\mu_1 - \mu_2)/\sigma]\sqrt{n}.$$

Thus, for our example, the non-centrality parameter is $0.5(5) = 2.5$.

With a sample size of 25, the critical value of t will be 2.064 for a two-sided 5% level t-test (obtained either from a table or by using t (Central)).

To calculate the probability, Prob(t < t_p):

Enter **24** in the **Degrees of freedom** row.

Enter **2.5** in the **Non-centrality parameter** row.

Enter **2.064** in the **t_p** row. The program will calculate the Probability.

t (Non-central) Distribution						
Degrees of freedom	24					
Non-centrality parameter	2.500					
Probability, Prob(t < t_p)	0.330					
t_p	2.064					
+						

The probability that $t < t_p$ is given as .330. Thus, the probability that $t > t_p$, the power of the t-test, is $1 - .33 = .67$. This value is the same as that achieved with the sample size table for the paired t-test (MOT1).

21. Appendix — References and Formulas

Every nQuery Advisor sample size table, distribution function table, standard deviation table, and table-specific side table has been tested for computational accuracy across table-specific ranges of parameters. Also, each table has been tested for full functionality of editing options and menu items (side tables, plots, statements) for one or more table-specific parameter sets.

You can review the methods used for testing. See the descriptions on the Statistical Solutions Ltd. Internet site, <http://www.statsol.ie/valid.htm>.

The first section of this appendix provides a brief description of the method used for computations in each table. These descriptions specify degrees of freedom and non-centrality parameters for each test based on non-central t, F, or χ^2 . Definitions of the non-centrality parameters use the values for δ , Δ , or Δ^2 shown in the relevant row title of the specific table. Tables grouped together are tables for which nQuery uses the same computational method.

The second section provides details on methods used for computing statistical distribution functions.

Section 1

The nQuery program provides an inquiry table for more than 100 different types of analyses. To simplify table identification, nQuery uses abbreviations for each table name. These abbreviations create a unique abbreviation or code for each table without spelling out the table name in detail.

The first letter of the code represents the selection in the first column of the Study Goal and Design Box:

Means, **P**roportions, **S**urvival, **A**greement, or **R**egression

The second letter of the code represents the selection in the second column of the Goal and Design Box, denoting the number of groups in the design:

One, **T**wo, or **G** (>2 groups)

The third letter of the code represents the selected type of analysis from the third column:

Test, **C**onfidence Interval, or **E**quivalence

The fourth character in the code represents the number of the selection in the list box. The numbers start with 0 at the top of the list box.

For unequal n's tables, the code ends with the letter U. For example, the code for Two-sample t test with unequal n's is MTT0U.

Methods of computation for each table

Note: s=1 for a one-sided test and s=2 for a two-sided test. We define $z_{1-\alpha}$ as the 100(1- α) percentile of the normal (Gaussian) distribution.

MOT0 One-sample t test

MOT1 Paired t test for difference in means

Power, sample size, or effect size are computed using central and non-central t where the non-centrality parameter is $\sqrt{n} \delta$ and δ is defined in the table row title. See, for example, O'Brien, R.G., Muller, K.E. (1993) "Unified Power Analysis for t-tests through Multivariate Hypotheses", in Edwards, L.K. (Ed.), *Applied Analysis of Variance in Behavioral Science*, Marcel Dekker, New York. Chapter 8 (pp 297-344).

MOE0 Paired t test for equivalence of means

Power, sample size, or effect size are computed using central and non-central t where the non-centrality parameter is $\sqrt{n} \delta$ and δ is defined in the table row title. See, for example, Machin, D., Campbell, M.J. (1987) *Statistical Tables for Design of Clinical Trials*, Blackwell Scientific Publications, Oxford.

MOT2 Univariate one-way repeated measures analysis of variance

MOT3 One-way repeated measures contrast

Power, sample size, or effect size are computed using central and non-central F. For MOT2, the numerator and denominator degrees of freedom are (M-1) and (M-1)(n-1), and the non-centrality parameter is nM times the effect size. For MOT3, the numerator and denominator degrees of freedom are 1 and (M-1)(n-1), and the non-centrality parameter is n times the square of the effect size. The effect sizes are defined in the row titles in the respective tables. For MOT2, see Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill. Chapter 14. For MOT3, see Overall, J.E., Doyle, S.R. (1994) Estimating Sample Sizes for Repeated Measures Designs, *Controlled Clinical Trials* 15:100-123.

MOT4 Univariate one-way repeated measures analysis of variance (Greenhouse-Geisser)

Power, sample size, or effect size are computed using methods taken from Muller, KE, Barton CN (1989) Approximate Power for Repeated-Measures ANOVA lacking Sphericity, *Journal of the American Statistical Association* 84:549-555.



- MOC0** **Confidence interval for mean based on z (n large)**
MOC2 **Confidence interval for difference in paired means (n large)**
for
MOC4 **Confidence interval for repeated measures contrast for**

Sample size or confidence interval width are computed using the large sample normal approximation, where the equations for interval width are given in the guide cards for the interval width row. See Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill. Pages 80-85. For MOC4 see also Overall, J.E., Doyle, S.R. (1994) Estimating Sample Sizes for Repeated Measures Designs, *Controlled Clinical Trials* 15:100-123.

For MOC0 and MOC2, the formula for n is $n = \frac{z_{1-\alpha/2}^2 \sigma^2}{\omega^2}$.

For MOC4, the formula for n is $n = \frac{z_{1-\alpha/2}^2 \sigma^2 (1 - \rho) D^2}{\omega^2}$.

- MOC1** **Confidence interval for mean based on t (with coverage probability) for**
MOC3 **Confidence interval for difference in paired means (coverage probability) for**

Sample size or confidence interval width are computed using iterative tolerance interval routines requiring central and non-central t and chi-square. See Kupper, L.L. and Hafner, K.B. (1989) How appropriate are popular sample size formulas? *The American Statistician* 43:101-105.

- MOC5** **Confidence interval for percentile of a normal distribution for**

Sample size or confidence interval width are computed based on section 4.4 in Hahn GJ, Meeker WQ (1991) *Statistical Intervals. A guide for practitioners*. John Wiley & Sons, Inc. New York. The P^{th} percentile of a normal distribution is estimated as the sample mean + k (sd) where sd is the sample standard deviation of the distribution and k is chosen to satisfy $\text{Prob}(z < k) = P$. The distance from the estimated percentile to the lower limit of the confidence interval is given by $-t_{1,\alpha} \sigma / \sqrt{n} + k\sigma$ where $t_{1,\alpha}$ is non-central t with $n-1$ degrees of freedom and non-centrality parameter $k \sqrt{n}$. The distance from the estimated percentile to the upper limit of the confidence interval is given by

$+ t_{1,\alpha} \sigma / \sqrt{n} - k\sigma$.

MOT0F	One group t-test that a mean equals user-specified value in finite population
MOT1F	Paired t-test of mean difference equal to zero in finite population
MOC0F	Confidence interval for mean based on z (n large) adjusted for finite population for
MOC1F	Confidence interval for mean based on t (with coverage probability) finite population for
MOC2F	Confidence interval for difference in paired means based on z (n large) adjusted for finite population for
MOC3F	Confidence interval for difference in paired means based on t (with coverage probability) finite population for

Computations for these tables are made in the same way as for the corresponding tables without the finite population correction except that the standard deviation is multiplied by the square root of one minus the sampling fraction. For explanation of the effects of finite sampling see Cochran, G. (1977) *Sampling Techniques* 3rd Edition. John Wiley & Sons Inc. New York. Pages 23-28.

MTT0	Two-sample t-test
MTE0	Equivalence of two means

Power, sample size, or effect size are computed using central and non-central t where the non-centrality parameter is $\sqrt{n} \delta / \sqrt{2}$ and δ is defined in the table row title. See Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill or O'Brien, R.G., Muller, K.E. (1993) "Unified Power Analysis for t-tests through Multivariate Hypotheses", in Edwards, L.K. (Ed.), *Applied Analysis of Variance in Behavioral Science*, Marcel Dekker, New York. Chapter 8 (pp 297-344).

MTT0cv	Two group t-test for fold change assuming log-normal distribution
---------------	--------------------------------------------------------------------------

After taking $\ln(FC)$ as the difference in means and setting $\sigma = \sqrt{\ln(1 + CV^2)}$,

the methods used for computing power and sample size are the same as for MTT0. See also Diletti, E., Hauschke D., Steinijans, V.W. "Sample size determination for bioequivalence assessment by means of confidence intervals" *Int. Journal of Clinical Pharmacology* 29(1991) p. 7.

**MTT0fct Two group t-test of equal fold change with fold change threshold**

After taking $\ln(FC)$ as the difference in means and setting $\sigma = \sqrt{\ln(1 + CV^2)}$,

nQuery uses simulation methods based on the assumption of normally distributed independent samples to estimate the probability of detection. The probability of detection is the percent of simulations in which two conditions are both satisfied: the result is significant at the specified alpha level and the observed fold change exceeds the fold change threshold. It is assumed that the original distributions are log-normal and that the two groups have equal variances in the log scale (that is the CV is constant across groups). Michael Elashoff, personal communication. See also Diletti, E., Hauschke D., Steinijans, V.W. "Sample size determination for bioequivalence assessment by means of confidence intervals" *Int. Journal of Clinical Pharmacology* 29(1991) p. 7.

MTT0uv Two group Satterthwaite t-test of equal means (unequal variances)

Power and sample are computed using numerical integration methods based on the formulas from Moser, B.K., Stevens, G.R., Watts, C.L. "The two-sample t test versus Satterthwaite's approximate F test" *Commun. Statist.-Theory Meth.* 18(1989) pp. 3963-3975.

MTE1tg Two one-sided equivalence tests (TOST) for two-group design

Power or sample size are computed based on the bivariate non-central t-distribution with degrees of freedom $2(n-1)$ and non-centrality parameters

$$\delta_L = \frac{(\mu_T - \mu_S - \Delta_L)\sqrt{n}}{\sigma\sqrt{2}} \quad \delta_U = \frac{(\mu_T - \mu_S - \Delta_U)\sqrt{n}}{\sigma\sqrt{2}}$$

using an algorithm due to Owen. When n per group > 5000, a large sample normal approximation is used. See Chow, S.C, Liu, J.P. *Design and Analysis of Bioavailability and Bioequivalence Studies*, Marcel Dekker, Inc. (1992), Schuirmann DJ (1987) A comparison of the two one-sided tests procedure and the power approach for assessing the equivalence of average bioavailability, *J. Pharmacokinet Biopharm* 15:657-680, Phillips KE (1990) Power of the two one-sided tests procedure in bioequivalence, *J. Pharmacokinet Biopharm* 18:137-143 and Owen DB (1965) A special case of a bivariate non-central t-distribution. *Biometrika* 52:437- 446.

MTE1co Two one-sided equivalence tests (TOST) for crossover design

After defining $\sigma = \sigma_d/2 = \sqrt{\text{MSE}/2}$, the same methods are used as for MTE1tg.

MTE2tg TOST for ratio of means (log scale) for two-group design

Power or sample size are computed using the same methods as for MTE1 except that the entered values for the ratio of means and the upper and lower limits are replaced by their natural logs, and the value

$$\sqrt{[\ln(1 + CV^2)]}$$

is substituted for σ before computing the non-centrality parameters.

MTE2co TOST for ratio of means (log scale) for crossover design

After defining $\sigma = \sigma_d/2 = \sqrt{\text{MSE}/2}$, the same methods are used as for MTE1tg.

MTE3 TOST for ratio of means for two-group design (original scale)

Power or sample size are computed using the same methods as for MTE1 with non-centrality parameters

$$\delta_L = \frac{(\mu_T / \mu_S - \Delta_L)\sqrt{n}}{\sigma / \mu_S \sqrt{1 + \Delta_L^2}} \quad \delta_U = \frac{(\mu_T / \mu_S - \Delta_U)\sqrt{n}}{\sigma / \mu_S \sqrt{1 + \Delta_U^2}}$$

In this case however this involves an approximation since the value 1 is substituted for the actual correlation between the two tests

$$\rho_{LU} = \frac{2}{\sqrt{1 + \Delta_L^2} \sqrt{1 + \Delta_U^2}}$$

See Hauschke D, Kieser M, Diletti E, Burke M (1999) Sample size determination for proving equivalence based on the ratio of two means for normally distributed data. *Statistics in Medicine* 18: 93-105.

MTE4 TOST for ratio of means for crossover design (original scale)

The exact methods for power and sample size computation are given in Hauschke D, Kieser M, Diletti E, Burke M (1999) Sample size determination for proving equivalence based on the ratio of two means for normally distributed data. *Statistics in Medicine* 18: 93-105. Here, we compute power or sample size using the same methods as for MTE1 with non-centrality parameters:



$$\delta_L = \frac{(\mu_T/\mu_S - \Delta_L)\sqrt{2n}}{\sqrt{CV_B^2(1 - \Delta_L)^2 + CV_I^2(1 + \Delta_L^2)}} \quad \delta_U = \frac{(\mu_T/\mu_S - \Delta_U)\sqrt{2n}}{\sqrt{CV_B^2(1 - \Delta_U)^2 + CV_I^2(1 + \Delta_U^2)}}$$

In this case, however, this involves an approximation, since the value 1.0 is substituted for the actual correlation between the two tests.

**MTT1 Wilcoxon (Mann-Whitney) rank-sum test that $P(X < Y) = .5$
(continuous outcome)**

Power, sample size, or p_1 are computed using a normal approximation formula from Noether GE (1987) Sample size determination for some common nonparametric statistics. *J. Am Stat. Assn* 82:645-647.

**MTT2 Wilcoxon (Mann-Whitney) rank-sum test that $P(X < Y) = .5$
(ordered categories)**

Power is computed based on approximating the unconditional distribution of the test statistic under the null and alternative hypotheses using the first four moments of the distribution; these approximation methods were developed by Kolassa J (1995) A comparison of size and power calculations for the Wilcoxon statistic for ordered categorical data. *Statistics in Medicine* 14: 1577-1581. A Cornish-Fisher approximation is used to approximate the critical value for a test of size alpha (equation 5 in Kolassa 1995); a continuity correction is made to this critical value—integer part of computed value +0.5 (or -0.5 if the critical value is negative) (Kolassa personal communication). An Edgeworth series approximation is used to approximate the power under the alternative distribution (equation 6 in Kolassa 1995).

**MTT3 Two-group univariate repeated measures analysis of
variance (Greenhouse-Geisser)**

Power and sample size are computed using methods taken from Muller, KE, Barton CN (1989) Approximate Power for Repeated-Measures ANOVA lacking Sphericity. *Journal of the American Statistical Association* 84:549-555.

MTC0 Confidence interval for difference of two means (N large)

MGC0 Confidence interval width for one-way contrast

Sample size or confidence interval width are computed using the large sample normal approximation, where the equations for interval width are given in the guide cards for the interval width row. See Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill. Pages 80-85 and 130-131.

For MTC0 and MTC0U, the formula for the total sample size, $N = n_1 + n_2$, is

$$N = \frac{z_{1-\alpha/2}^2 \sigma^2 (1+r)^2}{\omega^2 r}$$

where $r = n_2/n_1$ is the ratio of the sample sizes in the two groups. For MGC0,

the total sample size is
$$N = \frac{z_{1-\alpha/2}^2 \sigma^2 \sum \frac{c_i^2}{r_i} \sum r_i}{\omega^2}$$

where $r_i = n_i/n_1$ and the c_i are the contrast coefficients.

MTC1 Confidence interval for difference of two means (coverage probability)

Sample size or confidence interval width are computed using central and non-central t and chi-square with coverage probability constraints, see Kupper, L.L. and Hafner, K.B. (1989) How appropriate are popular sample size formulas? *The American Statistician*, 43:101-105.

MGT0 One-way analysis of variance

MGT1 Single one-way contrast

Power, sample size, or effect size are computed using central and non-central F. For MGT0, the numerator and denominator degrees of freedom are (G-1) and (N-G), and the non-centrality parameter is N times the effect size (for equal n's $N=nG$). For MGT1, the numerator and denominator degrees of freedom are 1 and (N-G), and the non-centrality parameter is the number of cases in group 1 times the square of the effect size. The effect sizes are defined in the row titles in the respective tables. See O'Brien, R.G., Muller, K.E. (1993) "Unified Power Analysis for t-tests through Multivariate Hypotheses", in Edwards, L.K. (Ed.), *Applied Analysis of Variance in Behavioral Science*, Marcel Dekker, New York. Pages 297-344.

MGT2 Two-way analysis of variance

Power and sample size for the two main effects and the interaction effect are computed using central and non-central F. The numerator degrees of freedom are (a-1), (b-1), and (a-1)(b-1), respectively, and the denominator degrees of freedom are ab(n-1). The non-centrality parameters are nab times the respective effect sizes for factor A, factor B, and the interaction. The formulas for the effect sizes are defined in the guide cards for the table. See O'Brien, R.G., Muller, K.E. (1993) "Unified Power Analysis for t-tests through Multivariate Hypotheses", in Edwards, L.K. (Ed.), *Applied Analysis of Variance in Behavioral Science*, Marcel Dekker, New York. Pages 297-344.

**MGC1 Confidence interval for one-way contrast (with coverage probability)**

Sample size or confidence interval width are computed using central and non-central t and Chi-square with coverage probability constraints, see Kupper, L.L. and Hafner, K.B. (1989) How appropriate are popular sample size formulas? *The American Statistician*, 43:101-105.

POT0 One sample Chi-square (normal approximation)

Power or sample size are computed using the normal approximation to the binomial, see Dixon, WJ and Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th edition. McGraw-Hill. The sample size is given by

$$n = \frac{\left[z_{1-\alpha/s} \sqrt{\pi_0(1-\pi_0)} + z_{1-\beta} \sqrt{\pi_1(1-\pi_1)} \right]^2}{(\pi_0 - \pi_1)^2}$$

POT0x Exact test for single proportion

Power is computed using the cumulative binomial distribution. The cut-point for rejection is computed as the largest k for which the probability of observing k or fewer successes is $\leq \alpha$ when $\pi = \pi_0$ for a one-sided test in which $\pi_A < \pi_0$. For a one-sided test in which $\pi_A > \pi_0$, we choose the smallest k for which the probability of observing k or more successes is $\leq \alpha$. For a two-sided test we require both probabilities to be $\leq \alpha/2$. Power is computed for the rejection regions for $\pi = \pi_A$. See Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill. Pages 281-284 and Chernick, M.R., Liu, C. Y. "The saw-toothed behavior of power versus sample size and software solutions: single binomial proportion using exact methods." *The American Statistician* 56(2002) pp 149-155.

POT1 McNemar's test of equality of paired proportions

Power or sample size are computed using equation (5.6) from Miettinen, O.S. (1968). On the matched-pairs design in the case of all-or-none responses. *Biometrics*, 24: 339-352. For POT1, the formula for n is

$$n = \frac{\left[z_{1-\alpha/s} \sqrt{\eta} + z_{1-\beta} \sqrt{\eta - \frac{\delta^2(3+\eta)}{4\eta}} \right]^2}{\delta^2}$$

where δ and η are defined in the row titles and the effect size side table.

POT1x Exact sign test of equality of paired proportions

For each sample size n , we generate the distribution of m , the number of discordant pairs, using the binomial distribution with parameters n , and proportion $\eta = \pi_{10} + \pi_{01}$. For each value of m the rejection region is computed for a test of the null hypothesis that the probability of a success = 0.50 (see paragraph on methods for POT0x). Then the power of the test is computed based on the binomial for a sample size of m and a probability of success of $(1/2)(1+\delta/\eta)$. The powers are added up over the possible values of m weighting by their probabilities, except that we do not consider values of m less than m_0 or greater than m_1 , where m_0 is such that $P(m < m_0) \leq 10^{-7}$ and m_1 is such that $P(m > m_1) \geq 10^{-7}$. See Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill. Pages 388-389 and Chernick, M.R., Liu, C. Y. "The saw-toothed behavior of power versus sample size and software solutions: single binomial proportion using exact methods." *The American Statistician* 56(2002) pp 149-155.

POT2 Chi-square test of specified proportions in C categories

Power, sample size, or effect size are computed based on central and non-central chi-square, see Lachin, J. M. (1977). Sample size determinations for $r \times c$ comparative trials. *Biometrics*, 33: 315-324. The non-centrality parameter is $n\Delta^2$ where the effect size Δ^2 is defined in the side table and row title.

POC0 Confidence interval for proportions (n large)

Interval width or sample size are computed using the normal approximation to the binomial where the equation for interval width is given in the guide card for the interval width row. See Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill. Pages 105-107. For POC0, the formula for n is

$$n = \left(\frac{z_{1-\alpha/2}}{\omega} \right)^2 [\pi(1 - \pi)]$$

POC1 Confidence interval for odds ratio for paired proportions (n large)

Confidence limit or sample size computed based on normal approximation from Smith, J., Connett, J., McHugh, R. (1985). Planning the size of a matched case-control study for estimation of the odds ratio. *American Journal of Epidemiology* 122:345-347 where the equation for interval width is given in the guide card for the interval width row. For POC1, the sample size is given by



$n = \frac{z_{1-\alpha/s}^2 (\Psi_M + 1)}{\omega^2 \pi_{01} \Psi_M}$ where the terms are defined in the row titles and the effect size side table.

POC2 Confidence interval for probability of observing a rare event for

The relationship between probability of an event, π , sample size, and the probability of observing one or more events, P , is given by

$$P = 1 - (1 - \pi)^n$$

See Machin, D., Campbell, M.J. (1987) *Statistical Tables for Design of Clinical Trials*, Blackwell Scientific Publications, Oxford. Section 6.2

POT0F One group test for proportion (normal approximation) adjusted for finite population

POC0F Confidence interval for proportion using normal approximation (n large) adjusted for finite population

Computations for these tables are made in the same way as for the corresponding tables without the finite population correction except that the adjusted sample size is $nN/(n+N)$ where n is the unadjusted sample size. For explanation of the effects of finite sampling see Cochran, G. (1977) *Sampling Techniques* 3rd Edition. John Wiley & Sons Inc. New York. Pages 23-28.

POE0 Paired responses: equivalence of π_0 and π_1

Power or sample size are computed using the normal approximation given in the guide card for the first row in the table. This is obtained by noting that the maximum value of the variance of the difference in proportions under the null or alternative hypotheses is η . For POE0, the formula for n is

$$n = \frac{\eta [z_{1-\alpha/s} + z_{1-\beta}]^2}{(\Delta_0 - \Delta_1)^2}$$
 where the terms are defined in the row titles and the

effect size side table. These methods were developed based on personal communication with Gary G. Koch. See also Tango, T. (1998): Equivalence test and confidence interval for the difference in proportions for the paired-sample design. *Statistics in Medicine* 17:891-908.

POE1 Paired test of equivalence in proportions using confidence interval

The power is calculated as the percentage of randomly-generated 2x2 tables for which the null hypothesis is rejected. The cells of the 2x2 table are filled in using the specified probabilities π_{11} (control yes, case yes), π_{10} (control yes, case no), π_{01} (control no, case yes), π_{00} (control no, case no). For each simulation the 2x2 table is generated using a number of trials equal to the sample size (to give the sum of the "control yes" entries) and choosing a random binomial variate with probability $\pi_{11} + \pi_{10}$. The sum of the "control no" entries is obtained by subtracting this value from the total sample size. The "yes, yes" cell is obtained as a random binomial variate with number of trials equal to the previously-computed sum of the first row and probability equal to $\pi_{11} / (\pi_{11} + \pi_{10})$. The "no, yes" cell is obtained similarly, and the other two cells are obtained by subtracting from the known row sums.

The Newcombe-Wilson score method (continuity corrected Method 10) is used for the confidence interval limits. (Newcombe RG (1988) Improved confidence intervals for the difference between binomial proportions based on paired data. *Statistics in Medicine* 17:2635-2650.) The power is computed as the proportion of simulations in which the observed confidence limits are within the specified equivalence range.

PTT0 Two group χ^2 test of equal proportions (odds ratio = 1)

PTT0p Two group χ^2 test of equal proportions

Power or sample size are computed using the normal approximation, see for example Machin, D, and Campbell M.J. (1987) *Statistical Tables for the Design of Clinical Trials*, Blackwell Scientific Publications, Oxford, or Fleiss, J.L., Tytun, A., and Ury, S.H.K. (1980) A simple approximation for calculating sample sizes for comparing independent proportions. *Biometrics* 36:343-346. For PTT0, the formula for n is

$$n = \frac{\left[z_{1-\alpha/2} \sqrt{2\pi(1-\pi)} + z_{1-\beta} \sqrt{\pi_1(1-\pi_1) + \pi_2(1-\pi_2)} \right]^2}{(\pi_1 - \pi_2)^2}.$$

PTT1 Two group continuity corrected χ^2 test of equal proportions (odds ratio = 1)

PTT1p Two group continuity corrected χ^2 test of equal proportions

Power or sample size are computed starting with the answer from PTT0 and modifying n as shown in Fleiss, J.L., Tytun, A., and Ury, S.H.K. (1980) A simple approximation for calculating sample sizes for comparing independent



proportions. *Biometrics*, 36:343-346. For PTT1, the sample size is given by

$$n' = \frac{n}{4} \left[1 + \sqrt{1 + \frac{4}{n|\pi_1 - \pi_2|}} \right]^2$$

PTT2 Fisher's Exact Test

The computed power is the expected power, obtained by summing the products of the conditional power given a particular first-column sum times the probability of that sum. The conditional powers are obtained by summing the bivariate binomial probability density over the critical region, where, to speed computation, all terms less than one-millionth of the estimated maximum term are dropped. See Fleiss, J.L. (1981) *Statistical Methods for Rates and Proportions*. 2nd Edition. Wiley, New York. Pages 24-26 and Chernick, M.R., Liu, C. Y. "The saw-toothed behavior of power versus sample size and software solutions: single binomial proportion using exact methods." *The American Statistician*, 56(2002) pp 149-155.

PTT3 Two-group Chi-square test comparing proportions in C categories

Power, sample size, or effect size are computed based on central and non-central chi-square, see Lachin, J. M. (1977) Sample size determinations for rxc comparative trials. *Biometrics*, 33: 315-324. The non-centrality parameter is $2n\Delta^2$ where the effect size Δ^2 is defined in the side-table and row title.

PTT4 Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata

PTT4cc Mantel-Haenszel (Cochran) test of OR=1 for 2x2 tables in S strata (continuity corrected) (Cochran)

Power and sample size are computed using approximate formulas from Nam, Jun-Mo (1992) Sample size determination for case-control studies and the comparison of stratified and unstratified analyses. *Biometrics*, 38: 389-395. The terms used in the formulas are defined in the side-table row names.

PTC0 Confidence interval for $\pi_1 - \pi_2$ (n large) for

Interval width or sample size are computed based on the normal approximation where the equations for interval width are given in the guide cards for the interval width rows. For PTC0, the formula for n is

$$n = \frac{z_{1-\alpha/2}^2 [\pi_1(1 - \pi_1) + \pi_2(1 - \pi_2)]}{\omega^2}$$

See Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill. Pages 286-288.

PTC1 Confidence interval for $\pi_1 - \pi_2$ (continuity corrected) for

Interval width or sample size are computed based on the normal approximation for a continuity corrected interval given in Fleiss, J.L. (1981) *Statistical Methods for Rates and Proportions* 2nd edition. Wiley, New York .

PTC2 Confidence interval for ln(odds ratio) (n large) for

Interval width or sample size are computed based on the normal approximation from O'Neill, R.T. (1984) Sample size for estimation of the odds ratio in unmatched case-control studies. *American Journal of Epidemiology* 120:145-153. For PTC2, the formula for n is

$$n = \frac{z_{1-\alpha/2}^2 \left[\frac{1}{\pi_1(1-\pi_1)} + \frac{1}{\pi_2(1-\pi_2)} \right]}{\omega^2}.$$

PTE0 Two-sample Chi-square test for equivalence

Power or sample size are computed based on the normal approximation. See for example Machin, D., Campbell, M.J. (1987) *Statistical Tables for the Design of Clinical Trials*, Blackwell Scientific Publications, Oxford, for the equal n case, and Farrington & Manning (1990) Test statistics and sample size formulae for comparative binomial trials with null hypotheses of non-zero risk difference for non-unity relative risk. *Statistics in Medicine* 9: 1447-1454 for the unequal n case. For PTE0, the formula for n is

$$n = \frac{(z_{1-\alpha} + z_{1-\beta})^2 [\pi_S(1-\pi_S) + \pi_T(1-\pi_T)]}{(\Delta_1 - \Delta_0)^2}$$

where the terms are defined in the row titles.

PTE1 Two-group test of equivalence in proportions using confidence interval

The binomial results are simulated separately for each group. The Newcombe-Wilson score method (uncorrected) is used for the confidence interval limits. (Newcombe RG (1988) Interval estimation for the difference between independent proportions: comparison of eleven methods. *Statistics in Medicine* 17:873-890.) The power is computed as the proportion of simulations in which the observed confidence limits are within the specified equivalence range.

**PGT0 Chi-square for Gx2 table**

Power or sample size are computed based on central and non-central chi-square using the formulation given as Case 2 in Lachin, J. M. (1977). Sample size determinations for rxc comparative trials. *Biometrics*, 33: 315-324.

PGT1 Test for linear trend in Gx2 table (logistic model)

Power or sample size are computed using the equation from Nam, J. (1987). A simple approximation for calculating sample sizes for detecting linear trend in proportions. *Biometrics*, 43: 701-705. For PGT1, the formula for n_1 , the sample size in group 1 is

$$n_1 = \left[\frac{z_{1-\alpha/s} \sqrt{\bar{\pi}(1-\bar{\pi}) \sum r_i (x_i - \bar{x})^2} + z_{1-\beta} \sqrt{\sum r_i \pi_i (1-\pi_i) (x_i - \bar{x})^2}}{\sum r_i \pi_i (x_i - \bar{x})^2} \right]^2 \text{ and}$$

the other terms are defined in the table and the compute effect size side table

$$\text{and } \bar{\pi} = \sum \frac{n_i \pi_i}{N}.$$

PGT2 G group Chi-square test comparing proportions in C categories

Power, sample size, or effect size are computed based on central and non-central chi-square, see Lachin, J. M. (1977) Sample size determinations for rxc comparative trials. *Biometrics*, 33: 315-324. The non-centrality parameter is $N \Delta^2$ where the effect size Δ^2 is defined in the side-table and row title and N is the total sample size (Gn for the equal n's case).

STT0 Log-rank test for equality of survival curves in two groups

Power or sample size are computed based on approximation from Freedman, L.S. (1982). Tables of the number of patients required in clinical trials using the logrank test. *Statistics in Medicine*, 1:121-129. For STT0, the sample size formula is

$$n = \frac{(z_{1-\alpha/s} + z_{1-\beta})^2 (h+1)^2}{(2 - \pi_1 - \pi_2)(h-1)^2} \text{ where the terms are defined in the row titles.}$$

STT1 Test based on exponential survival, accrual period
STT2 Test based on exponential survival, accrual period, dropouts

Power or sample size are computed based on equations from Lakatos, E. and Lan, K.K.G.1992. A comparison of sample size methods for the logrank statistic. *Statistics in Medicine*, 11: 179-91. For STT1 and STT2, the sample size is

$$n = \left(\frac{z_{1-\alpha/2} + z_{1-\beta}}{\ln(\lambda_E) - \ln(\lambda_C)} \right)^2 \left(\frac{1}{E(P_E)} + \frac{1}{E(P_C)} \right)$$

where $E(P_i) = \frac{\lambda_i}{\lambda_i + d} \left[1 - \frac{e^{-(\lambda_i + d)(T - T_0)} - e^{-(\lambda_i + d)T}}{(\lambda_i + d)T_0} \right]$, T_0 is the length of the accrual period and T the total length of followup, and the other terms are defined in the row titles.

For STT0, STT1, and STT2, The required number of events, E , can be obtained approximately from the equation

$$E = \frac{4(z_{\alpha/2} + z_{\beta})^2}{[\ln(h)]^2}$$

where $z_{\alpha/2}$ and z_{β} are the upper $\alpha/2$ and upper β points, respectively, of the standard normal distribution and h is the hazard ratio. See Collett, D. (1994) *Modelling Survival Data in Medical Research*, Chapman & Hall, Formula 9.2

STT3 Log-rank test of survival in two groups, simulation with specified rates

Power is computed by simulating two groups of individuals following the course of the experiment and subject to accrual, hazard, and dropout rates specified in the corresponding side table. In each simulation, the fate of each individual is controlled by the output of the random number generator. The test statistic is computed according to the method specified in Chapter 5, pages 127-128, of Lee, E.T. (1980) *Statistical Methods for Survival Data Analysis*. Lifetime Learning Publications. Belmont, California. The number of simulations in which the test statistic indicated a significant outcome is divided by the total number of simulations, and the quotient is reported as the power. If a one-sided test is specified, the program tracks separately the simulations that are significant in the positive direction and in the negative direction and reports the quotient that gives the greater power. As long as the power is reasonably



high, the number of simulations that appear significant in the “wrong” direction should be very small.

The data for each individual are simulated using a deterministic pseudo-random number generator, so for the same inputs and the same seed, the computed power will always be the same. The particular generator used is called r250 and is described in *Journal of Computational Physics* v. 40, pp. 517-526 (1981). The random number generator r250 is a Tausworthe-style shift-register random number generator, based on a primitive trinomial in which the state is initialized using some other random number generator, and a trick is then used to make certain that the columns are linearly independent. The cited paper describes various statistical tests to validate the output.

The present implementation differs from that of the authors cited in that we initialize the state of r250 using the default random number generator in Microsoft Visual C++, which is a mixed linear congruential random number generator. In contrast, the authors use GGL, which is a multiplicative congruential random number generator. Our approach has the advantage that pure-multiplicative random number generators perform very poorly with regard to the independence of sequences generated by different seeds. To test our implementation of this generator, we compared the results of simulations done with r250 to those done with the default Microsoft generator, and also to the Wichmann-Hill generator (*Applied Statistics*, v. 31, pp. 188-190). For several examples with 10,000 simulations, all three generators produced values for power agreeing to within .005.

AOT0 Agreement between two dichotomous ratings (intraclass kappa)

AOC0 Confidence interval for intraclass kappa (n large)

Power or confidence interval width, or sample size are computed using the large sample standard error of estimated kappa from Block, D.A. and Kraemer, H.C. (1989). 2x2 kappa coefficients: measures of agreement or association. *Biometrics*. 45:269-287.

AOT1 Test for value of correlation coefficient

AOC1 Confidence interval for correlation coefficient

Power or confidence interval width, or sample size are computed based on the large sample normal approximation using Fisher’s z transformation; see Dixon, W.J., Massey, F.J. *Introduction to Statistical Analysis*. 4th Edition McGraw-Hill (1983) p. 224. The sample size for AOT1 is given by

$$n = \frac{(z_{1-\alpha/s} + z_{1-\beta})^2}{[\text{FZ}(\rho_1) - \text{FZ}(\rho_0)]^2} + 3 \quad \text{where FZ denotes the Fisher's z transform, } \text{FZ}(\rho) = \frac{1}{2} \ln \left[\frac{1+\rho}{1-\rho} \right].$$

AOT2 **Lin's concordance coefficient (continuous outcome)**

AOC2 **Confidence interval for Lin's concordance coefficient (continuous outcome)**

Power or interval width, or sample size are computed using normal approximation formulas given in Lin, L.I. (1992). Assay validation using the concordance correlation coefficient. *Biometrics* 48:599-604.

ROT0 **Logistic regression (binary outcome), single x**

ROT1 **Logistic regression, x_i adjusted for p X's (binary outcome),**

Power or sample size are computed using normal approximation formulas given in Hsieh, F.Y. (1989). Sample size tables for logistic regression. *Statistics in Medicine* 8:795-802.

The sample size for ROT0 is:

$$n = \frac{\left[z_{1-\alpha/s} + z_{1-\beta} \exp\left(\frac{-\beta^2}{4}\right) \right]^2}{p_M \beta^2} [1 + 2p_M \Delta]$$

where

$$\Delta = \frac{\left[1 + (1 + \beta^2) \exp\left(\frac{5\beta^2}{4}\right) \right]}{1 + \exp\left(\frac{-\beta^2}{4}\right)}$$

$$\text{For ROT1, } n = \frac{n_1}{1 - \rho^2}$$

where n_1 is the sample size obtained in the case of a single covariate.

ROT2 **Linear regression (continuous outcome), single x**

ROT3 **Multiple linear regression with k covariates,**

ROT4 **Multiple linear regression, x_i adjusted for A covariates**



Power, sample size, and detectable correlation coefficient are computed using central and non-central F with numerator and denominator degrees of freedom 1 and n-2 for ROT2, k and (n-k-1) for ROT3, and b and (n-a-b-1) for ROT4 based on a conditional power viewpoint. Non-centrality parameters are nf^2 where $f^2 = \rho^2 / (1 - \rho^2)$ for ROT2, $f^2 = R^2 / (1 - R^2)$ for ROT3, and

$f^2 = (R_{AB}^2 - R_A^2) / (1 - R_{AB}^2)$ for ROT4. See Gatsonis, C., Sampson, A.R. (1989) Multiple Correlation: Exact Power and Sample Size Calculations. *Psychological Bulletin* 106:516-524.

ROT5 Linear regression test that $\beta = \beta_0$ for one x

Power, sample size, or effect size are computed based on central and non-central t, with n-2 degrees of freedom. The non-centrality parameter is the effect size, δ , times \sqrt{n} , where δ is defined in the guide card for the effect size row. See Dupont, W., Plummer, W. (1998) Power and sample size calculations for studies involving linear regression. *Controlled Clinical Trials* 19:589-601.

ROC0 Linear regression confidence interval for $\beta = \beta_0$ for

Interval width and sample size are computed using the large sample normal approximation; the formula for the interval width is shown in the guide card for that row. See Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill. Pages 214-219.

RTT0 Linear regression test that $\beta_1 = \beta_2$ for one x

Power, sample size, or effect size are computed based on central and non-central t with 2n-4 degrees of freedom. The non-centrality parameter is the effect size, δ , times $\sqrt{n/2}$, where δ is defined in the guide card for the effect size row. See Dupont, W., Plummer, W. (1998) Power and sample size calculations for studies involving linear regression. *Controlled Clinical Trials* 19:589-601.

RTC0 Linear regression confidence interval for $\beta_1 - \beta_2$ for two groups

Interval width and sample size are computed using the large sample normal approximation; the formula for the interval width is shown in the guide card for that row. See Dixon, W.J., Massey, F.J. (1983) *Introduction to Statistical Analysis*. 4th Edition. McGraw-Hill. Pages 227-229.

Section 2

Central functions (computing cumulative distribution function)

Normal distribution z

The method used to compute the cumulative value of the normal distribution up to x will differ, depending on the value of x . Specifically:

1. If x is between -1.5 and 3.0, the c.d.f. is computed via the Taylor series centered at 0.
2. If x is between 3.0 and 10.0 or between -10.0 and -1.5, the program uses a continued fraction given by A. G. Adams in his 1969 communication in *CACM* vol. 12 pp. 565-566.
3. If x is less than -10.0 or greater than 10.0, the value of the c.d.f. is set as 0.0 or 1.0, respectively.

F distribution

The cumulative value of the F distribution up to x with m numerator degrees of freedom and n denominator degrees of freedom is usually calculated by a call to the function that computes the incomplete beta function with a equal to $m/2$ and b equal to $n/2$, integrating up to $n/(n + mx)$, and subtracting the result from 1.

However, if either n or m is particularly large, the value may be calculated from the cumulative χ^2 distribution function. This will occur when $\lgamma(m+n) - \lgamma(m+1) - \lgamma(n) + m*\log(y) + n*\log(1-y)$ is greater than or equal to 500, where \lgamma is the logarithm of the gamma function and y equals $n/(n + mx)$, or when the value calculated in the paragraph above is equal to zero and at least one of m, n is greater than 100.

t distribution

There is no separate computation for the c.d.f of the central t distribution. Instead, it is computed from the F distribution with 1 numerator degree of freedom, using the square of the t value and distinguishing between positive and negative values of t.

χ^2 distribution

If the degrees of freedom exceed 150, the c.d.f of the χ^2 distribution up to x is computed via the Wilson-Hilferty approximation (see N.C. Severo and M.



Zelen, *Biometrika* vol. 47 pp. 411-416, 1960); that is, one computes the cumulative normal distribution up to:

$$\left[(x/\nu)^{\frac{1}{3}} - (1 - 2/(9\nu)) \right] \sqrt{2/(9\nu)}.$$

Otherwise use is made of a recurrence relation that reduces degrees of freedom by 2 (see Abramowitz and Stegun, 1970, equation 26.4.8); this reduces the problem to calculating the χ^2 distribution with 1 or 2 degrees of freedom (according to whether the original degrees of freedom are odd or even); this is easily done exactly in terms of the normal distribution function or the exponential function.

Incomplete beta function $I_x(a,b)$

The incomplete beta function may be computed either by a power series or by a continued fraction derived from the power series. The power series is described in *Numerical Recipes in C* 2nd Edition, equation 6.4.4. Equation 6.4.5 describes the continued fraction

nQuery Advisor makes several tests to see if for the given values of x , a and b , the value of $I_x(a,b)$ is negligibly close to zero or one; if so, the program returns zero or one as appropriate. If not, then nQuery checks to see if the power series can be predicted to converge rapidly; if so, nQuery uses the power series. Otherwise, nQuery uses the continued fraction.

Cumulative binomial

If π is the probability of success on a single trial, then the probability that the number of successes is less than or equal to k , given n independent trials, is calculated as $1 - I_{\pi}(k+1, n-k)$, see definition of the incomplete beta function above. If $k=n$, however, the probability is taken to be 1.

Non-Central functions (computing cumulative distribution function)

Non-central F

In the usual case the c.d.f. of the non-central F distribution is computed via a call to the non-central beta function, which is a Poisson mixture of incomplete beta values in the same way that non-central F is a Poisson mixture of values of the c.d.f for the central F distribution.

Just as in the central F case, there are approximations for use for large degrees of freedom. When numerator degrees of freedom are large, we compute the desired value from the c.d.f for central X^2 . When the denominator degrees of freedom are large, we use the non-central X^2 .

Non-central beta

The non-central beta function $I_x(a, b, \delta)$ is defined as the sum as i ranges from 0 to infinity of

$$P_i(\delta) I_x(a + i, b),$$

where $P_i(\delta)$ is the Poisson probability for i with Poisson parameter δ , and

$$I_x(a + i, b)$$

is the incomplete beta function as before. This sum is computed from a minimum value of i to a maximum value, where the contribution of terms outside this range is considered negligible. For this purpose the incomplete beta distribution is considered negligible past 100 standard deviations from the mean, and the Poisson distribution is considered negligible past 10 standard deviations to the left, or 100 standard deviations to the right, of the mean. Also the summation is terminated if the value of $I_x(a + i, b)$ falls below 10^{-12} .

Non-central t

Following exercise 23.24 of Stuart and Ord, *Advanced Theory of Statistics*, vol. 2, p. 904, it is possible to compute the c.d.f. of the non-central t in a manner quite analogous to the computation of non-central beta detailed above. That is, you can use a generalized Poisson mixture of values of incomplete beta, where for successive terms the value of one of the parameters for incomplete beta changes by $1/2$ rather than by 1. Similarly for the Poisson factor, the Poisson distribution is generalized to non-integer values. We sum until the integer Poisson values sum to within $5 * 10^{-13}$ of 1. Since the half-odd-integer Poisson



values should be about the same, this should be within about 10^{-12} of the right answer.

The x value for the values of incomplete beta going into the series is the reciprocal of

$$1 + t^2/v,$$

where t is the upper value of the c.d.f. and v is degrees of freedom. If this value is too small, i.e. less than 10^{-8} , we risk losing information due to roundoff error. Therefore, we approximate our result as the normal c.d.f up to $t - \delta$, and add a correction term linear in t . Note that the quadratic term is correct already.

Non-central χ^2

The c.d.f. of the “non-central χ^2 distribution” is a Poisson mixture of central χ^2 c.d.f’s, and much the same considerations apply as for non-central beta.

Percentage points and non-centrality parameters

Percentage points of normal distribution

For probability $p < 0.5$, one computes $y = \sqrt{(\log(1/p^2))}$. Then the percentage point z is computed as $y + P(y) / Q(y)$ where P and Q are fourth-degree polynomials in y with appropriate coefficients. For $p > 0.5$, the situation is symmetrical. This method is due to Odeh and Evans, *Applied Statistics* v. 23(1974), pp. 96-97.

Percentage points of central F distribution

An initial estimate of the percentage point is obtained via an approximate formula. The code then searches for another value that falls on the opposite side of the true percentage point from the estimate already obtained (i.e. the two estimates bracket the true value).

Then the Illinois method (more fully described below) is used to find a value of F such that the c.d.f. up to F differs from the desired value by at most 0.01.

Finally, Halley’s method (See Huh, *Communications in Statistics--Simulation and Computation* v. 15(1986).pp.1191-1198) is used until two criteria are met:

- a) The c.d.f. up to F differs from the desired value by at most 0.0001.

-
- b) Successive estimates of F differ from one another by at most 0.0001 proportionally, that is to say, by at most 0.0001 times the absolute value of the more recent estimate. (In the F case, of course, all estimates are nonnegative.)

It is also worth noting that if numerator degrees of freedom are greater than denominator degrees of freedom, we reverse the degrees of freedom and take the reciprocal of the percentage point.

Percentage points of central t distribution

Again there is no separate computation. We take the square root of the F percentage point, first doubling the probability and using 1 numerator degree of freedom, and assigning the sign as appropriate.

Percentage points of central χ^2 distribution

First, an initial estimate is obtained via the Wilson-Hilferty approximation referenced above. If degrees of freedom exceed 150, this is used as the answer.

Otherwise, a modification is used of Halley's method (referenced above). Again the iteration is continued until the c.d.f. up to the estimate differs from the desired value by at most 0.0001 and two successive estimates differ proportionally by at most 0.0001.

Percentage points of non-central F distribution

The Illinois method (see Kennedy and Gentle, *Statistical Computing*, Marcel Dekker: New York(1980)) is used. That is, two initial estimates are chosen. Those estimates ideally should bracket the true solution, but this is usually not critical. We then find successive estimates by linear interpolation, splitting the interval as appropriate so that our two estimates continue to bracket the true solution. The only exception is that if the older of the two estimates remains fixed, its corresponding ordinate is adjusted (halved, if we think of ourselves as looking for the zero of a function). That is, if we're looking for the value of the monotonic function f , we choose x_0 and x_1 such that $f(x_0)$ and $f(x_1)$ have opposite sign, then compute x_2 as

$$[x_0 f(x_1) - x_1 f(x_0)] / [f(x_1) - f(x_0)]$$

Then if $f(x_1)$ and $f(x_2)$ have opposite sign we replace x_0 by x_1 and x_1 by x_2 and continue. If on the other hand they have the same sign we again replace x_1 by x_2 but we leave x_0 as it is. However on the next round, we shall use a value half as large for $f(x_0)$.



The iteration continues until both $f(x_i)$ has absolute value less than 0.0001 and x_0 and x_i differ proportionally by at most 0.0001 (i.e. they differ by less than 0.0001 times the arithmetic mean of their absolute values).

In the case of percentage points of non-central F there seems to be no need for subtlety in choosing the initial estimates; they are chosen to be 0.0 and 100000.0.

Percentage points of non-central t distribution

The Illinois method is used as described above. If δ is the non-centrality parameter, then the bracketing values are chosen to be $\delta-100$ and $\delta+100$, except in the one-degree-of-freedom-case, when they are chosen to be $\delta-1000$ and $\delta+1000$.

Percentage points of non-central χ^2 distribution

The Illinois method is used as described above. The initial bracketing values are chosen to be 0.0 and 100000.0.

Non-centrality parameter of the non-central F distribution (given both the probability and the percentage point)

The Illinois method is used as described above. The bracketing values are obtained as follows: The program first tries the upper limit 5000. If this value is not large enough, an error message is produced. (An error message is also generated if the probability given by central F is larger than the desired value, since that indicates the value zero for the non-centrality parameter to be too large.)

Otherwise we start with $\lambda_0 = 0.0$ and $\lambda_1 = 1.0$. If the true value is between these, we continue with the Illinois method; otherwise we replace λ_0 by λ_1 and double λ_1 , and repeat.

Non-centrality parameter of the non-central t distribution

The Illinois method is used. The initial estimates are chosen as -100.0 and 100.0.

Non-centrality parameter of the non-central χ^2 distribution

The Illinois method is used. The initial values are chosen as for the non-centrality parameter of non-central F and the same error checking is performed.

Use of distribution functions in computing power, sample size, and effect size, or interval width and sample size

Power

We are given the desired significance level of the test, an “effect size” or values from which it may be calculated, and the sample size. We wish to determine the power of the study to reject the null hypothesis.

First one determines the appropriate percentage point of the central t, F, or χ^2 distribution, depending on the problem at hand, where the degrees of freedom depend on the sample size in a manner that depends on the test being considered (see Methods of Computation for each table). The “appropriate” percentage point means the $100(1-\alpha)\%$ point, in a one-sided test, or the $100(1-\alpha/2)\%$ point in a two-sided test. Then the non-centrality parameter of the distribution of the test statistic under the alternative hypothesis is calculated from the effect size in a manner depending on the test being considered (see Methods of Computation for each table). Finally the power is computed as the c.d.f. of non-central distribution with the degrees of freedom and non-centrality parameter as in Methods of Computation for each table.

Sample sizes for tests

The section above describes how power is computed from effect size and sample size. When given power and effect size, one can compute the required sample size by searching for the minimum integer value required to produce (at least) the requested power. This is done, essentially, via the Illinois method. The initial values are obtained by trying the values 100, 10 and 2 in that order. If two values are found that bracket the desired value they are used; otherwise (i.e. if a sample size of 100 is too small) linear extrapolation is used to find an upper bound.

Another feature to note is that the iteration will terminate under two conditions:

1. If the calculated power is within 0.0001 of the requested value.
2. If we have two estimates within 1 of each other (since we’re only looking for the least integer that is large enough).



Effect sizes for tests

To calculate effect size from power and sample size, one simply reverses the procedure given above for computing power. That is, one calculates as before the central percentage point corresponding to significance, then the non-centrality parameter of the t , F , or χ^2 that gives a c.d.f. equal to one minus the specified power at the calculated percentage point. Then one solves for the effect size from the non-centrality parameter in a manner depending on the particular test being considered (see Methods of Computation for each table).

Interval width for means confidence intervals with tolerance probability

We obtain the half-width of a confidence interval for a mean (or difference between means, or means contrast) by multiplying a t -percentage point (corresponding to a confidence level) by an estimate for the standard deviation. (Also there may be a scaling factor for the difference or contrast case.)

Since the estimate for the variance is distributed as χ^2 , the tolerance probability is the c.d.f. of the χ^2 distribution. Note that the tolerance probability is the chance that the confidence interval obtained from the study will be no wider than the specified value.

Therefore, we multiply the relevant t -percentage point by the square root of the relevant χ^2 -percentage point, and multiply by the standard deviation, the scaling factor, and other factors depending on sample size (corresponding to the factors necessary to make the distribution of estimated standard deviation be χ^2).

Sample size for means confidence intervals with tolerance probability

As in the case of the means t -tests, we have a quantity that increases with sample size, and that we want to be at least a certain value. This quantity is not power, but tolerance probability. The same variation on the Illinois method is used to determine the minimum necessary sample size.

Index

- in Study Goal and Design, 7-7
- agreement tables, 17-1
- abbreviation codes for sample size tables, 7-8
- acceptable entries
 - for rows in sample size table, 7-2
- adjusting for prior covariates, 18-7
- Adobe Acrobat pdf
 - printing plot to, 6-19
- advice
 - at startup, 3-16
- agreement
 - between two dichotomous ratings
 - intraclass kappa, 21-17
 - confidence interval for correlation
 - coefficient, 21-17
 - confidence interval for intraclass kappa, 21-17
 - confidence interval for Lin's concordance
 - coefficient (continuous outcome), 21-18
 - continuous outcome tables, 17-1
 - dichotomous outcome tables, 17-1
 - Lin's concordance coefficient (continuous outcome), 21-18
 - test for value of correlation coefficient, 21-17
- analyses
 - by abbreviation codes, 7-8
- analysis method
 - specifying, 2-2, 3-2
 - choosing in Study Goal and Design, 7-7
- analysis of variance, 13-3
 - example, single one-way contrast MGT1, 12-14
 - example, one-way contrast, MGT1, 12-19
 - example, one-way MGT0, 12-1
 - example, one-way MGT1, 12-14, 12-16
 - example, one-way repeated measures
 - MOT2, 13-16
 - example, two group repeated measures
 - MTT3, 13-20
- MSE, 9-18
- one-way, 8-4, 21-8
- one-way repeated measures contrast, 21-2
- one-way, example, 8-9
- repeated measures, 8-3
 - tables for, 13-3
 - two-way, 8-4, 21-8
- univariate one-way repeated measures,
 - MOT4, 21-2
- univariate two-group repeated measures
 - (Greenhouse Geisser), MTT3, 21-7
- AOC0
 - example, confidence interval for intraclass
 - kappa, 17-2
- AOC0, 7-11, 21-17
- AOC1, 7-11, 21-17
- AOC2, 7-11, 21-18
- AOT0, 7-11, 21-17
- AOT1, 7-11, 21-17
- AOT2, 7-11, 21-18
- appendix, 21-1
- arrange icons, 7-6
- Assistants menu, 5-1
 - compute effect size, 5-4
 - conversion between parameters, 5-9
 - data entry, 5-4
 - distribution functions, 5-13
 - estimate SD, 5-11
 - finite population adjustment, 5-3
 - specify covariance matrix, 5-12
 - unequal n's, 5-1
 - Windows calculator, 5-14
- auto recalculation, 2-7, 3-13, 3-14
 - and unequal n's, 3-15
 - green when On, 3-15
 - On, 3-14, 3-15
- axis labels, 6-6
 - editing in plot, 6-26
 - using Greek letters in, 6-8
- beta
 - incomplete, 21-21
 - non-central, 21-22
- binomial distribution, 20-1
- bio-equivalence testing
 - tables for, 11-1, 11-2, 15-3, 15-4
 - two-sided, 11-6, 11-15
 - two-sided "neither better nor worse", 11-22
- border attributes, 6-24, 6-29
- calculator
 - for Windows, 5-14

- cancel, 4-11
- cascade, 7-6
- case-control studies, 13-1, 15-1
- cell count
 - change minimum expected, 3-12
- cell size
 - changing minimum, 3-13
- central Chi-square distribution
 - percentage points of, 21-24
- central F distribution
 - percentage points of, 21-23
- central functions, 21-20
- central t distribution
 - percentage points of, 21-24
- change minimum expected cell count, 3-13
- characters
 - Greek, 4-14
 - special, 4-14
- Chi-square distribution, 21-20
 - (central), 5-13, 20-1, 21-24
 - (non-central), 5-13, 20-1, 21-23, 21-25
- Chi-square test, 15-2
 - See also* examples for proportions, 15-2
 - comparing proportions in C categories, 21-13
 - example, two-group continuity corrected PTT1, 15-17
 - example, two group test PTT0, 15-17
 - for equivalence, 21-14
 - for G groups in C categories, 21-15
 - for Gx2 table, 21-15
 - of equal proportions, 21-12
 - of equal proportions (continuity corrected), 21-12
 - of specified proportions in C categories, 21-10
 - one sample (normal approximation), 21-9
 - tables for, 15-2, 15-3, 15-4
 - two group test of equal proportions, 21-12
 - two group test of equal proportions (odds ratio =1), 21-12
- clear, 2-20, 4-1
- existing table, 2-20
- clipboard
 - copy guide cards to, 3-7, 4-2
 - copy references to, 3-7, 4-2
 - copy side table to, 3-7, 4-2
 - copy statements to, 3-7, 4-2
 - copy table to, 3-7, 4-2
 - clipboard contents
 - pasting, 4-10
- close, 3-5
 - program, 3-4
 - table, 3-5
- cluster randomization, 9-19
- cluster sampling
 - estimate SD from, 5-11, 9-19
- Cochran test, 15-3
 - example PTT4, 15-25
 - test of OR=1 for 2x2 tables in S strata, 21-13
 - test of OR=1 for 2x2 tables in S strata (continuity corrected), 21-13
- codes used by nQuery Advisor for tables, 21-1
- coefficient of variation
 - estimate SD from, 5-11, 9-13, 9-23, 9-26
 - tables using, 8-15, 8-18, 11-18, 11-23, 11-24
- Cohen's effect size, 14-2
- color in the sample size table, 2-7, 6-25, 6-27
 - for side table names, 16-31
- column names
 - copying and pasting, 4-12, 4-13
 - editing, 2-17, 4-12
 - editing for use in plot legend, 6-2
- column numbers, 2-5
- column values
 - editing, 2-16
- common standard deviation
 - specifying, 2-13
- computational methods
 - for sample size tables, 21-1
- compute button
 - in side table, 5-6
- compute effect size, 5-4, 12-1, 13-9, 13-10, 13-12, 13-19, 14-5, 15-6, 15-23, 15-25, 15-29, 15-32, 17-3
- concordance coefficient, 17-2
 - Lin's, 21-18
- confidence interval, 2-16, 15-2
 - See also* agreement tables, 17-1
 - See also* means, sample size tables, 8-1
 - See also* proportions tables, 15-4
 - See also* regression, choosing table, 18-1
 - contrast between means, 8-4
 - difference of two means, 8-3, 8-9
 - example, for intraclass kappa AOC0, 17-2
 - estimation, 11-4
 - example for MTC1, 8-9
 - for correlation coefficient, 21-17



- for difference in paired means, 8-3, 21-3
- for difference in paired means (coverage probability), 21-3
- for difference in paired means based on t (with coverage probability) finite population, 21-4
- for difference in paired means based on z(n large) adjusted for finite population, 21-4
- for difference in two means, 11-28
 - example for MTC1, 8-9
- for difference of two means (coverage probability), 21-8
- for difference of two means (n large), 21-7
- for equivalence testing, 11-1, 11-2
- for intraclass kappa, 21-17
- for linear regression (one group), 21-19
- for linear regression (two groups), 21-19
- for Lin's concordance coefficient, 21-18
- for ln(odds ratio), 21-14
 - example PTC2, 15-21
- for mean based on t, 21-3
 - (with coverage probability) finite population, 21-4
- for mean based on z, 21-3
 - (n large) adjusted for finite population, 21-4
- for odds ratio for paired proportions (n large), 21-10
- for one-way contrast, 8-4
 - (with coverage probability), 21-9
- for one-way repeated measures contrast, 8-3, 13-3
- for paired designs, 13-2
- for percentile of a normal distribution, 8-2, 21-3
 - example for MOC5, 8-11
- for probability of observing a rare event, 21-11
- for proportion using normal approximation (n large) adjusted for finite population, 21-11
- for proportions, tables for, 15-2, 15-3, 15-4
- for proportions (n large), 21-10
 - (continuity corrected), 21-14
 - based on normal distribution, 21-13
- for repeated measures contrast, 21-3
- for simulated probability, 8-20
 - for two groups, 8-9
 - interval widths, 11-29
 - tables for means, 8-2, 8-3, 8-4
 - width for one-way contrast, 21-7
- continuity corrected, 15-1
- continuous y
 - in regression, 18-2
- contrast, 8-3
 - one-way (with coverage probability),
 - confidence interval for, 21-9
 - single one-way, 21-8
- conversion
 - between parameters, 5-9
 - to alternate rates for exponential parameters, 16-6
- copy, 4-2
 - choosing font, 4-3
 - guide card contents, 7-3
 - guide card to clipboard, 4-15
 - in right-click menu, 4-15
 - notes to clipboard, 4-15
 - on plot Edit menu, 6-23
 - references to clipboard, 4-15
 - rows, 10-3
 - statement to clipboard, 2-26, 4-10, 4-15
 - table to clipboard, 4-15
- correlation
 - coefficient, estimate SD from, 5-11
 - Kappa, 17-1, 17-4
 - methods of computation, 21-17
 - Pearson's r, 17-1
 - specify for covariance matrix, 9-1, 9-26
 - tables for, 18-3
- covariance matrix, 13-22
 - specify, 5-12, 9-1, 9-27
 - specify correlations for, 9-31
 - specify standard deviations for, 9-30
- create statement, 2-23, 3-10, 4-8, 8-7, 12-12
 - in right-click menu, 4-15
- crossover designs, 13-1, 13-2, 13-3, 13-4
 - carryover effects, 13-4
 - covariance matrix
 - within-subject, 13-4
 - error variance, 13-4
 - example M period MOT3, 13-12
 - example, M period MOT1, 13-14

-
- example, M period, M treatment MOT2, 13-8
 - example, two-period, two-treatment MTT0, 13-4
 - Latin square, 13-8
 - means, 8-4
 - repeated measures contrasts, 13-12
 - period effects, 13-4
 - residual effects, 13-4
 - cumulative binomial distribution, 5-13, 20-1, 21-20, 21-21
 - customize regional settings, 1-7
 - cut, 4-2
 - in right-click menu, 4-15
 - CV
 - See also* coefficient of variation
 - estimating SD from, 9-14, 9-23, 9-26
 - data entry, 5-4
 - equally spaced values, 9-24
 - SD calculator, 9-2
 - transformation in, 9-4
 - design
 - choosing study design, 2-1
 - dichotomous outcome, 15-1
 - in regression, 18-1
 - display font choice reminder upon copy, 3-17
 - distribution function menu, 5-13
 - Chi-square (central) distribution, 5-13
 - Chi-square (non-central) distribution, 5-13
 - cumulative binomial distribution, 5-13
 - F (central) distribution, 5-13
 - F (non-central) distribution, 5-13
 - t (central) distribution, 5-13
 - t (non-central) distribution, 5-13
 - z (gaussian/Normal) distribution, 5-13
 - distribution function tables, 20-1
 - dropouts, 16-13
 - edit
 - See also* fill right
 - See also* specify multi-factor table
 - column names, 4-12, 6-3, 8-23
 - plot axis, 6-26
 - plot legend, 6-29
 - plot parameters, 6-28
 - plot text, 6-25
 - row names, 2-5, 4-11
 - values in a column, 2-16
 - Edit menu, 4-1
 - in right-click menu, 4-15
 - effect size
 - See also* compute effect size
 - computational methods for, 21-26
 - computing, 5-4, 5-5, 14-2, 14-5
 - specifying, 2-11
 - equality of two means
 - equivalence tests for, 11-1, 11-2
 - equivalence
 - See also* examples for equivalence testing
 - See also* examples for proportions
 - Chi-square test for, 21-14
 - example for two groups, 11-4
 - for two groups, 11-8, 11-11
 - in proportions, 15-2, 15-3, 15-4
 - methods of computation, 21-12
 - two group test using confidence interval, 21-14
 - of paired responses, 21-11
 - of two means, 21-4
 - t test for equivalence of means, 21-2
 - tables for, 11-1, 11-2
 - tests, one-sided, 11-3
 - tests, two-sided, 11-6
 - estimate SD, 5-11, 9-1 to 9-26
 - events
 - number of, 16-5, 16-12
 - exact tests, 13-2
 - See also* proportions, tables
 - caveat for, 15-11
 - exact sign test, 13-2
 - example POT1, 15-6
 - for single proportion, 21-9
 - of equality of paired proportions, 21-10
 - exact size of plot, 6-22
 - examples for agreement
 - confidence interval for intraclass kappa AOC0, 17-2
 - examples for equivalence testing
 - See also* examples for proportions
 - non-inferiority for difference in means MTE0, 11-4
 - TOST for difference of means two-group MTE1tg, 11-8
 - TOST for difference of means in crossover MTE1co, 11-11
 - TOST for ratio of means in crossover (log scale) MTE2co, 11-20
 - TOST for ratio of means in crossover MTE4, 11-24



- TOST for ratio of means two group (log scale) MTE2tg, 11-18
- TOST for ratio of means two group MTE3, 11-23
- TOST for ratio of means, two group, using logs, MTE1tg, 11-16
- examples for means
 - See also examples for equivalence testing confidence interval for percentile of normal distribution, MOC5, 8-11
 - M period crossover MOT1, 13-14
 - M period crossover MOT3, 13-12
 - M period M treatment crossover MOT2, 13-8
 - MTT0 tutorial, 2-1
 - one way ANOVA MGT0, 12-1
 - one-way ANOVA contrast MGT1, 12-19
 - one-way ANOVA MGT1, 12-14, 12-16
 - one-way repeated measures ANOVA MOT2, 13-16
 - one-way repeated measures contrast MOT3, 13-18
 - paired t-test for MOT1, 8-5
 - two-group repeated measures ANOVA Greenhouse-Geisser MTT3, 13-20
 - two-group Satterthwaite t-test of equal means MTT0uv, 8-13
 - two-group t-test for fold change MTT0cv, 8-15
 - two-group t-test of equal fold change MTT0fct, 8-18
 - two-sample confidence interval MTC1, 8-9
 - unequal n's MTT0, 10-2
- examples for proportions
 - Chi-square test, comparing, PTT3, 15-23
 - Chi-square test, PTT0, 15-17
 - confidence interval for, ln PTC2, 15-21
 - confidence interval for, POC0, 15-4
 - exact sign test, POT1x, 15-6
 - linear trend in Gx2 table, PGT1, 15-29
 - Mantel-Haenszel test, PTT4, 15-25
 - McNemar's test, POT1, 15-6
 - paired test for non-inferiority for proportions, POE1a, 15-32
 - paired test of equivalence in, POE0, 15-32
 - proportions one-group test, POC0F, 19-2
 - two group test of non-inferiority for, PTE0, 15-40
 - two-group Chi-Square test (solve for proportion) PTT0, 15-12
 - two-group Fisher's exact test, PTT2, 15-17
 - two-group TOST test of equivalence in, PTE0, 15-46
 - two-sided confidence limits for non-inferiority for, PTE1a, 15-40
 - two-sided TOST confidence limits for difference in , PTE1c, 15-46
- examples for regression
 - linear regression for one x, ROT5, 18-14
 - linear trend in Gx2 table, logistic model, PGT1, 15-29
 - logistic regression with continuous covariate, MTT0U, 18-12
 - logistic regression with continuous covariate, ROT0, 18-7
 - logistic regression with dichotomous covariate, PTT0U, 18-4
- examples for survival analysis
 - conversion between parameters assistants table to obtain alternate rates, 16-6
 - exponential survival, STT2, 16-9
 - log-rank test for survival in two groups, 16-23
 - log-rank test, fixed followup, STT0, 16-3
 - log rank test, simulation, STT3, 16-14, 16-21
 - log-rank test, simulation, survival plots, 16-26
 - test based on exponential survival, STT2, 16-9
 - using side tables with survival, STT3, 16-30
- examples for non-parametric tests
 - Wilcoxon/Mann-Whitney rank sum, MTT1, 14-1
 - Wilcoxon/Mann-Whitney rank sum, MTT2, 14-4
- examples of plot
 - plot power vs. n for MOT1, 6-1
 - plot user-selected rows
 - for MOT1, 6-6
 - for MTC1, 6-17
 - for MTT0, 6-10
 - for PTT0, 6-14

-
- Excel
 - pasting into, 4-10
 - exit, 3-4, 3-11
 - from statement dialog box, 2-27
 - expected cell count
 - changing, 3-13
 - effect of, 15-18
 - exponential parameters, 16-6, 16-8, 16-10, 16-11, 16-13, 16-16, 16-26
 - See also* conversion
 - exponential survival
 - See also* survival analysis
 - example, STT2, 16-9
 - export side table to Word, 12-6
 - F distribution, 21-20, 21-25
 - central, 5-13, 20-1, 21-23
 - non-central, 5-13, 20-1, 21-22, 21-24
 - features of nQuery Advisor
 - new in Version 5.0, 1-4
 - File menu
 - from a sample size table, 3-4
 - initial, 3-1
 - fill right, 2-20, 2-21, 4-6
 - finite population
 - adjustment, 5-3, 19-1
 - checkbox, 3-3
 - in Study Goal and Design, 7-8
 - sampling from, 19-1
 - size of, 19-2
 - Fisher's Exact test, 15-3, 21-13
 - See also* exact tests, caveat for
 - example, two-group PTT2, 15-17
 - fold change
 - example, two-group t-test for, MTT0cv, 8-15
 - two-group t-test for, 8-2
 - fold change threshold
 - example in MTT0fct, 8-18
 - two-group t-test of equal fold change, 8-3
 - font, 6-27
 - choosing for pasting table contents, 4-4
 - editing in plot axis labels, 6-26
 - editing in plot legend, 6-30
 - editing in plot text, 6-26
 - for external pasting, 3-16
 - selecting, 3-8
 - format plot, 6-6, 6-27
 - formulas used in nQuery Advisor, 21-1
 - fresh table, 2-20, 3-5
 - give advice when program starts, 3-16
 - goal, 2-2, 3-2
 - choosing in Study Goal and Design, 7-7
 - Greek letters and symbols, 3-7
 - appearance in Windows application documents, 4-4
 - using in column names, 6-2
 - using in notes, 4-14
 - green row
 - in sample size table, 3-15
 - Greenhouse-Geisser, 8-3, 13-3, 13-20
 - guide card, 1-3, 2-7, 2-9, 7-2
 - copy to clipboard, 3-9, 7-3
 - font for pasting, 3-7
 - On by default, 3-16
 - option on View menu, 7-2
 - paste, 3-9
 - print, 3-9, 7-5
 - turn Off or On, 2-7, 2-8
 - help for nQuery Advisor, 1-3
 - from guide cards, 2-7, 2-9, 7-3
 - hotkey
 - copy from table, 4-2, 4-5
 - cut from table, 4-2
 - paste within table, 4-4
 - icon
 - bar, 2-4
 - yellow tags on, 1-3
 - incomplete beta function, 21-21
 - interval width, 21-27
 - computing using distribution functions, 21-26
 - intraclass correlation
 - cluster SD for, 9-21
 - intraclass kappa, 17-1, 17-3
 - methods of computation, 21-17
 - introduction to nQuery Advisor, 1-1
 - kappa, 17-1, 17-2, 17-3
 - intraclass
 - methods of computation, 21-17
 - labels
 - position in plot, 6-6, 6-27
 - last label in plot, 6-6, 6-27
 - legend in plot
 - editing, 6-29
 - editing column names for, 6-2
 - Lin's concordance coefficient, 17-2, 21-18
 - line parameters in plot, 6-24, 6-29
 - editing, 6-25



- linear regression, 18-3
 - See also* examples for regression
 - confidence interval for, 21-19
 - confidence interval for (two groups), 21-19
 - continuous outcome, single x, 21-18
 - example, for one x, ROT5, 18-14
 - for one x, 21-19
 - model for, 18-14
 - one-group, ROT5, 18-14
 - one group, RTT0, 18-18
 - tables for, 18-3
- linear trend
 - in Gx2 table, 15-29, 21-15
 - example, PGT1, 15-29
- log transform, 9-2
 - See also* log-normal data
 - See also* log-normal distribution
- logistic regression
 - See also* regression, choosing table
 - See also* proportions, tables
 - adjusting for prior covariates, 18-10
 - example, linear trend in Gx2 table, logistic model, PGT1, 15-29
 - example, with continuous covariate, MTT0U, 18-12
 - example, with continuous covariate, ROT0, 18-7
 - example, with dichotomous covariate, PTT0U, 18-4
- log-normal data
 - CV, 9-14, 9-22, 9-25
- log-normal distribution
 - equivalence tables for, MTE2co, tg, 8-4
 - tables for fold change, MTT0cv, 8-2, 8-15
 - tables for fold change, MTT0fct, 8-3, 8-18
 - unequal variance,s MTT0uv, 8-2, 8-13
- log-rank test, 21-15
 - example, computing sample size, STT0, 16-3
 - for equality of survival curves, 21-15
 - of survival in two groups, simulation with specified rates, 21-16
- maintain aspect ratio, 6-22
- Mann-Whitney, 8-3, 14-1
 - rank-sum test (continuous outcome), 21-7
 - rank-sum test (ordered categories), 21-7
- Mantel-Haenszel, 15-3
 - example, PTT4, 15-25
 - test of OR=1 for 2x2 tables in S strata, 21-13
 - test of OR=1 for 2x2 tables in S strata (continuity corrected), 21-13
- maximize first table, 3-16
- McNemar's test, 13-2
 - example, POT1, 15-6
 - of equality of paired proportions, 21-9
- means
 - See also* examples for equivalence testing, 11-1
 - See also* examples for means, 8-1
 - entering, 2-12
 - sample size tables, 8-1
 - tests for equivalence of, 11-1
 - tests for non-inferiority of, 11-1
- menu bar, 3-1, 2-4
- menus
 - right-click, 2-11
 - specific to panes, 2-11
- metafile
 - save plot as, 6-20
- MGC0, 21-7
- MGC1, 21-9
- MGT0, 21-8
 - example, one way ANOVA, 12-1
- MGT1, 21-8
 - example, one-way ANOVA, 12-14
 - example, one-way ANOVA, 12-16
 - example, one-way ANOVA contrast, 12-19
- MGT2, 21-8
- Microsoft Word
 - pasting from nQuery, 3-7
- MOC0, 21-3
- MOC0F, 21-4
- MOC1, 21-3
- MOC1F, 21-4
- MOC2, 21-3
- MOC2F, 21-4
- MOC3, 21-3
- MOC3F, 21-4
- MOC4, 21-3
- MOC5, 21-3
 - example, 8-11
- MOE0, 21-2
- MOT0, 21-2
- MOT0F, 21-4

MOT1, 21-2
 example, 8-5
 example, M period crossover, 13-14
 plot power vs. n example, 6-1
 plot user-selected rows example, 6-6
 MOT1F, 21-4
 MOT2, 21-2
 example, M period M treatment crossover,
 13-8
 example, one-way repeated measures
 ANOVA, 13-16
 MOT3, 21-2
 example, M period crossover, 13-12
 example, one-way repeated measures
 contrast, 13-18
 MOT4, 21-2
 mouse buttons in data entry, 2-10
 MTC0, 21-7
 MTC1, 21-8
 example, 8-9
 plot user-selected rows example, 6-17
 MTE0, 21-4
 MTE1co, 21-6
 example TOST for difference of means in
 crossover, 11-11
 MTE1tg, 21-5
 example TOST for difference of means
 two-group, 11-8
 TOST for ratio of means, two group, using
 logs, 11-16
 MTE2co, 21-6
 example, TOST for ratio of means
 crossover (log scale), 11-20
 MTE2tg, 21-6
 example, TOST for ratio of means two-
 group (log scale), 11-18
 MTE3, 21-6
 example, TOST for ratio of means two
 group, 11-23
 MTE4, 21-6
 example, TOST for ratio of means
 crossover, 11-24
 MTT0, 21-4
 example, two-period crossover, 13-4
 example, unequal n's, 10-2
 plot user-selected rows example, 6-10
 MTT0cv, 21-4
 example, 8-15
 MTT0fct, 21-5
 example, 8-18
 MTT0U
 example, logistic regression with
 continuous covariate, 18-12
 MTT0uv, 21-5
 example, 8-13
 MTT1, 21-7
 example, Wilcoxon/Mann-Whitney rank
 sum, 14-1
 MTT2, 21-7
 example, Wilcoxon/Mann-Whitney rank
 sum, ordered categories, 14-4
 MTT3, 21-7
 example, two-group repeated measures
 ANOVA, 13-20
 multi-factor table
 specifying, 2-20, 2-21, 4-6
 multiple correlation
 tables for, 18-3
 multiple linear regression, 18-3
 adjusted for A covariates, 21-18
 with k covariates, 21-18
 n per group
 recalculating, 2-16
 new
 features in Version 5.0, 1-4
 new table, 2-2, 2-20, 3-1
 new window, 7-6
 non-central
 beta, 21-22
 Chi-square, 21-23
 non-centrality parameter, 21-25
 F distribution, 21-22
 non-centrality parameter, 21-25
 percentage points of, 21-24
 functions, 21-22
 t distribution, 21-22
 non-centrality parameter, 21-25
 percentage points of, 21-25
 non-centrality parameter, 20-3, 21-23
 non-inferiority
 tests for, 11-1, 11-2
 nonparametric tests, 8-3, 14-1
 normal distribution, 5-13, 21-20, 21-23
 percentage points of, 21-23
 normality assumption, 19-2
 and finite populations, 19-2



- notes, 2-9
 - adding to table, 2-14
 - pasting statement into, 12-12
 - printing, 3-6
- number of groups, 2-2, 3-2
 - choosing in Study Goal and Design, 7-7
- odds ratio, 15-2
 - estimation, example, PTC2, 15-21
- one-way analysis of variance, 8-1, 12-1
- one-way repeated measures contrast, 8-1, 13-3, 13-15
- open a new table, 2-20, 3-3, 6-20
- Options menu, 3-12
 - autorecalculation, 3-13
 - change minimum expected cell count, 3-12
 - preferences, 3-15
- paired designs, 13-2
 - See also* means, sample size tables, 8-1
 - See also* proportions, tables, 15-1
- paired t test for MOT1, 13-2
 - example, 8-5
- parameters
 - specifying, 2-9
- parameters in plot
 - editing, 6-24
- paste, 4-4
 - choosing font for, 4-10
 - from clipboard, 4-5
 - in right-click menu, 4-15
 - into Windows applications, 3-7, 3-8
- paste unformatted, 4-5
 - in right-click menu, 4-15
- pdf
 - printing plot to, 6-19
- Pearson's r
 - confidence interval, AOC1, 17-1
 - tables for, 18-3
 - test, AOT1, 17-1
- percentage points, 21-23
- percentiles
 - estimate P^{th} from data, 8-11
 - estimate SD from, 5-11, 9-1, 9-11
- PGT0, 21-15
- PGT1, 21-15
 - example, linear trend in Gx2 table, 15-29
- PGT2, 21-15
- plot, 2-19, 6-1
 - border attributes, 6-24
 - edit, 6-25, 6-26, 6-27
 - axis label text or font, 6-6, 6-8, 6-26
 - line in, 6-12, 6-29
 - legend, 6-18, 6-29
 - legend text, 6-30
 - parameters, 6-28
 - text, 6-27
 - title text or font, 6-5
 - expected fold change example, 8-24
 - line parameters, 6-24
 - paste into Windows application, 6-19
 - print, 6-15, 6-23
 - parameters, 6-16
 - to pdf, 6-19
 - using Greek letters in axis label, 6-8
- plot menus, 6-1
 - Assistants, 6-25
 - Edit menu, 6-23
 - File menu, 6-20
 - Graphs menu, 6-23
 - parameters on, 6-24
- plot legend
 - editing, 6-29
 - text editing, 6-30
- plot power vs n, 2-19
 - example for MOT1, 6-1
- plot user-selected rows
 - example for MOT1, 6-6
 - example for MTC1, 6-17
 - example for MTT0, 6-10
 - example for PTT0, 6-14
- plotting
 - a column, 2-19
 - area background, 6-22
 - survival curves
 - example, 16-26
- POC0, 21-10
 - example, confidence interval for proportion, 15-4
- POC0F, 21-11
 - example, proportions, one-group test, 19-2
- POC1, 21-10
- POC2, 21-11

POE0, 21-11
 example, paired test of equivalence in proportions, 15-32
 POE1, 21-12
 example, paired test of equivalence in proportions, 15-32
 pooled SD
 estimate from SD1, SD2, 9-1, 9-8
 population size, 19-1, 19-2, 19-3
 POT0, 21-9
 POT0F, 21-11
 POT1, 21-9
 example, McNemar's test, 15-6
 POT1x, 21-10
 example, exact sign test, 15-6
 POT2, 21-10
 power, 21-26
 computing, 2-14
 computing using distribution functions, 21-26
 entering a value, 2-15
 evaluating, 2-1
 rounded down, 8-22
 vs. sample size plot, 6-4, 6-12
 Preferences menu, 3-15
 display font choice reminder upon copy, 3-17
 font for external pasting, 3-16
 give advice when program starts, 3-16
 guide on by default, 3-16
 maximize first table, 3-16
 respect regional settings, 3-16
 print, 3-6, 3-7, 3-8, 3-9, 3-10, 3-11
 active view, 3-7
 current page, 6-21, 6-22
 dialog box, 3-6
 from right-click menu, 3-9
 guide card contents, 7-5
 in right-click menu, 3-9
 notes, 3-7
 options, 6-21
 parameters dialog box, 6-22
 plot, 6-23
 references, 3-7
 sample size justification statement, 3-10
 sample size table, 2-25
 setup, 3-4, 6-21, 6-22
 side tables, 3-7
 statement, 2-25, 3-7, 4-10
 stored statement, 3-10, 3-11
 tables, 3-7, 3-9
 print table to clipboard, 3-7
 prior covariates
 adjustment for, 18-11
 probability of detection
 MTT0fct example, 8-18
 precision of estimate, 8-20
 proportions
 Chi-square test of specified proportions in C categories, 21-10
 confidence interval for (n large), 21-10
 confidence interval for odds ratio for paired, 21-10
 equivalence tests for, 11-2
 exact sign test for equality of paired, 21-10
 exact test for single, 21-9
 example, confidence interval for, POC0, 15-4
 example, confidence limits for difference in PTE1, 15-46
 example, Exact sign test, POT1x, 15-6
 example, Fisher's exact test, PTT2, 15-17
 example, Mantel-Haenszel, PTT4, 15-25
 example, McNemar's test, POT1, 15-6
 example, one-group test, POC0F, 19-2
 example, paired test of equivalence in, POE0, 15-32
 example, paired test of equivalence in, POE1, 15-32
 example, test for linear trend in G x 2 table, PGT1, 15-29
 example, test of equivalence in, POE0, 15-32
 example, test of equivalence in, POE1, 15-32
 example, two-group Chi-square test comparing proportions in C categories, PTT3, 15-23
 example, two-group Chi-square test, PTT0, 15-12
 example, two-group continuity-corrected Chi-square test, PTT1, 15-17
 example, two-group test of equivalence of, PTE0, 15-40
 example, two-group TOST test of equivalence in, PTE0, 15-46
 example, two-sided confidence limits for difference in proportions, PTE1, 15-40
 example, confidence interval for ln, PTC2, 15-21



- in one group, 15-2
- McNemar's test of equality of paired, 21-9
- non-inferiority tests for, 11-2
- one-group test for, (normal approximation)
 - adjusted for finite population, 21-11
- sample size tables for, 15-1
- tables, 15-1
- PTC0, 21-13
- PTC1, 21-14
- PTC2, 21-14
 - example, confidence interval for OR ln, 15-21
- PTE0, 21-14
 - example, two group test of non-inferiority in proportions, 15-40
 - example, two-group TOST test of equivalence in proportions, 15-46
- PTE1, 21-14
 - example, confidence limits for equivalence of proportions PTE1, 15-46
 - example, confidence limits for non-inferiority for proportions, 15-40
- Pth percentile
 - estimating from the data, 8-11
- PTT0, 21-12
 - example, Chi-square test, 15-17
 - example, two-group Chi-square test (small n), 15-12
 - plot user-selected rows example, 6-14
- PTT0U
 - example, logistic regression with dichotomous covariate, 18-4
- PTT1, 21-12
 - example, two-group continuity-corrected Chi-square test PTT1, 15-17
- PTT1p, 21-12
- PTT2, 21-13
 - example, Fisher's exact test, 15-17
- PTT3, 21-13
 - example, Chi-square test comparing C proportions, 15-23
- PTT4, 21-13
 - example, Mantel-Haenszel test, 15-25
- PTT4cc, 21-13
- range
 - estimate SD from, 5-11, 9-1, 9-10
- rank-sum test, 8-3, 14-1
- ratio of means, 8-3, 8-4.
 - See also* examples for equivalence testing
 - equivalence tests for, 11-1
 - example, MTT0cv, 8-15
 - example, MTT0fct, 8-18
 - t-test for, 8-4
- recalculation, 2-17
 - automatic, 3-13, 3-14
- recent file, 3-4
- references, 2-9, 21-1
 - copying to clipboard, 3-7
 - pasting, 3-7
 - printing, 3-6
- regional settings, 1-7, 3-16
- register product, 1-2
- regression
 - See also* examples for regression
 - choosing table, 18-1
 - linear tables for, 18-3
 - linear, confidence interval for, 21-19
 - linear, confidence interval for (two groups), 21-19
 - linear, continuous outcome, single x, 21-18
 - linear, for one x, 21-19
 - logistic, adjusted for p X's, 21-18
 - logistic, binary outcome, 21-18
 - multiple linear, adjusted for A covariates, 21-18
 - multiple linear, with k covariates, 21-18
 - multiple tables for, 18-3
- repeated measures, 13-1, 13-3, 13-15
 - ANOVA
 - example, one-way, MOT2, 13-16
 - example, two group Greenhouse-Geisser, MTT3, 13-20
 - one-way contrast, 21-2
 - two-group (Greenhouse-Geisser), 21-7
 - univariate one-way, 21-2
 - example, M period, M treatment crossover, MOT2, 13-8
 - Greenhouse-Geisser, 13-16
 - tables for, 13-1, 13-2, 13-3
- repeated measures contrast, 8-3
 - example, one-way, MOT3, 13-12, 13-18
- Rich Text Format, 4-4
- right-click menu, 2-11
 - for guide cards, 4-15

- for notes, 4-15
- for references, 4-15
- for sample size table, 4-15
- for side tables, 12-6
- for statements, 4-15
- ROC0, 21-19
- ROT0, 21-18
 - example, logistic regression with continuous covariate, 18-7
- ROT1, 21-18
- ROT2, 21-18
- ROT3, 21-18
- ROT4, 21-18
- ROT5, 21-19
 - example, linear regression for one group, 18-14
- row names, 2-5
 - editing, 2-5, 4-11, 8-23
- row values
 - duplicate with fill right, 4-6
 - fill with specify multi-factor table, 4-6
- RTC0, 21-19
- RTT0, 21-19
 - example, linear regression for one x, 18-18
- running nQuery Advisor, 1-1
- sample size
 - computing, 2-14
 - computing using distribution functions, 21-26
 - for means confidence intervals, 21-27
 - for tests, 21-26
 - justification statement, 2-23
 - creating, 4-8
 - printing, 3-10, 4-10
 - storing, 4-9
 - to clipboard, 4-10
- sample size methods
 - relationships between, 11-26
- sample size tables, 2-4
 - closing, 3-5
 - colors in, 2-7
 - computational methods for, 21-1
 - finite population adjustment in, 5-4
 - for agreement, 17-1
 - for means, 8-1
 - for proportions, 15-1
 - for regression, 18-1
 - for survival analysis, 16-1
 - how to open, 3-3
 - how to select, 3-2
 - new in Version 5.0, 1-5
 - pasting from clipboard, 3-7
 - printing to clipboard, 3-7
 - printing, 3-6
 - right-click menu, 3-9
 - save as, 3-5
 - saving, 3-5
 - testing methods for, 21-1
- sample size too small warning, 15-17
- sampling fraction, 19-1
- Satterthwaite t test, 8-2
 - of equal means (unequal variances), 21-5
- save, 3-5
- save as, 3-5
- save plot as
 - metafile, 6-20, 6-23
 - old-style metafile, 6-21
- saved table
 - how to open, 3-3
- SD button, 9-1, 9-2, 9-6
- SD for specified equally spaced x's, 18-20
- SD of residuals, 18-16
- SD1 and SD2
 - calculate SD from, 5-11
- SD1, SD2, Correlation
 - estimating SD from, 9-17
- sensitivity analysis, 2-16
- set automatic recalculation, 2-16, 3-14
- side tables, 5-8, 12-1
 - buttons, 12-4
 - changing names, 16-31
 - colors for names, 16-31
 - compute effect size, 5-4, 5-5, 5-8
 - copying to clipboard, 4-3, 12-6
 - font for copying, 3-17
 - for survival analysis, STT3, 16-15, 16-21, 16-26
 - MTT2, 14-4, 14-6
 - printing, 3-6
 - right-click menu, 12-6
 - sample size tables using, 5-8
- sigma, 9-1, 13-22
- sign test, 13-2, 15-6
- significance test, 2-9
- significant digits, 2-6
- simulations, 15-37, 15-49
 - progress of, 8-21, 16-18
- single one-way contrast table, 12-14



- single proportions
 - confidence intervals for, 15-2
 - tests for, 15-2
- size of plot, 6-27
- special characters, 4-14
- specify correlations
 - for covariance matrix, 9-31
- specify covariance matrix, 5-12, 9-27, 9-28
- specify multi-factor table, 2-20, 2-21, 4-6
- specify SIGMA, 5-12
- specify standard deviations
 - for covariance matrix, 9-30
- split-plot designs, 13-1
- spreadsheet like Excel
 - pasting table contents into, 3-9
- standard deviation
 - and mean response, 9-14
 - calculating, 9-1, 9-3
 - conservative estimate, 9-15
 - estimate for cluster sampling, 9-19
 - estimate from coefficient of variation, 9-23, 9-26
 - estimate from CV, 9-13, 9-22, 9-24
 - estimate from percentile, 9-11
 - estimate from pooled SD, 9-8
 - estimate from range, 9-10
 - estimate from s.e., 9-6
 - estimate from SD1, SD2, correlation, 9-17
 - estimate from upper confidence interval, 9-15
 - estimate from coefficient of variation, 9-14
 - estimating, 5-11, 9-1
 - for specified x-values, 9-23
 - of differences, 9-18
 - of residuals, 9-26
 - precision, 9-15
 - pre-treatment, post-treatment, 9-17
 - using the data entry table, 9-1
- standard error
 - calculate SD from, 5-11, 9-7
- starting nQuery Advisor, 1-1, 1-3
- statement, 2-9, 2-23, 17-4
 - copying, 3-7
 - copy to clipboard, 3-7, 4-10
 - creating, 3-10, 4-8, 8-7, 12-12
 - customizing, 12-12
 - pasting, 3-7
 - pasting into notes, 8-8, 12-12
 - pasting to Windows applications, 8-8
 - printing, 3-6, 4-10
 - storing, 4-9, 12-12
- status bar, 1-3, 2-6, 2-10, 7-1
- store statement, 2-24, 4-9
 - printing, 4-9
- STT0
 - example for survival analysis, conversion between parameters assistants table to obtain alternate rates, 16-6
- STT0, 16-3, 21-15
 - example, log-rank test of survival, 16-3
- STT1, 21-16
- STT2, 16-3, 21-16
 - example, test based on exponential survival, 16-9
- STT3, 16-3, 21-16
 - example, log rank test for survival in two groups, 16-21
 - example, log rank test with user-specified survival, 16-14
 - example, using side tables with survival, 16-30
- study design
 - specify, 2-1
- Study Goal and Design dialog box, 2-2, 3-1, 7-6
 - codes, 21-1
 - finite population in, 5-3
 - unequal n's in, 5-2
- successes in outcome, 15-1
- survey sampling, 19-2
- survival analysis, 16-1, 16-2, 16-3
 - example, log rank test for survival in two groups, STT3, 16-21
 - example, log rank test with user specified survival, STT3, 16-14
 - example, log-rank test for survival in two groups, 16-23
 - example, using side tables, STT3, 16-30
 - exponential survival, accrual period, 16-3, 21-16
 - exponential survival, accrual period, dropouts, 16-3, 21-16
 - log-rank test for equality of survival curves, 16-2, 21-15

-
- log-rank test, two groups, simulation with specified rates, 21-16
 - simulation, 16-14
 - versus proportions, 16-1
 - survival curves
 - example, plotting, 16-26
 - exponential, conversion to alternate rates, 5-9
 - symbols, 3-7
 - t (central) distribution, 5-13, 20-1, 21-24
 - t (non-central) distribution, 5-1, 20-1, 21-23, 21-25
 - t distribution, 21-20
 - t test, 11-26, 13-2
 - See also* examples for equivalence testing.
 - See also* examples for means
 - example, equal means, unequal variances, MTT0uv, 8-13
 - example for equal fold change, MTT0fct, 8-18
 - example for fold change, MTT0cv, 8-15
 - examples for equivalence testing, two-group TOST for ratio of means, MTE1tg, 11-16
 - example, TOST for ratio of means, two group, MTE2tg, 11-18
 - for difference in means (paired), 21-2
 - for difference in means equal to 0 (paired), 21-4
 - for equivalence, 11-1
 - for equivalence of means (paired), 21-2
 - for mean equal specified value (one group), 21-4
 - for non-inferiority testing, 11-1
 - for two-samples, 21-4
 - list of means tables, 8-2
 - of equal fold change with fold change threshold, 21-5
 - of equivalence of means, 8-4
 - one sample, 21-2
 - one-group, 8-2
 - paired, 8-1, 8-3, 8-5
 - example, 8-5
 - Satterthwaite for two groups, equal means (unequal variances), 21-5
 - two group for fold change, assuming log-normal distribution, 21-4
 - two-group, 8-1, 8-2, 8-4, 11-1, 11-15, 13-2
 - table
 - closing, 3-5
 - copy to clipboard, 3-7
 - how to select, 3-2
 - name abbreviation, 21-1
 - opening, 3-3
 - pasting from clipboard, 3-7
 - printing, 3-6
 - right-click menu, 3-7
 - save as, 3-5
 - saving, 3-5
 - title, 2-5
 - tests
 - for agreement, 17-1
 - for crossover, 13-2
 - for equivalence, 11-1
 - for means, 8-1
 - for paired designs, 13-2
 - for proportions, 15-1
 - for regression, 18-1
 - for repeated measures, 13-3
 - for survival, 16-1
 - specify effect size for, 2-11
 - text in plot
 - editing, 6-26, 6-27
 - tile, 7-6
 - title bar, 2-4
 - title for table, 2-5
 - to clipboard
 - statement, 2-24, 2-26, 4-10
 - toolbar, 7-1
 - TOST
 - bioequivalence testing, two-sided, 11-6
 - example, difference of means in crossover, MTE1co, 11-11
 - example, ratio of means crossover, MTE4, 11-24
 - example, ratio of means crossover (log scale), MTE2co, 11-20
 - example, ratio of means two group (log scale), MTE2tg, 11-18
 - example, ratio of means two group, MTE3, 11-23
 - example, ratio of means, two group, using logs, MTE1tg, 11-16
 - ratio of means, 11-15
 - ratio of means for crossover design (log scale), 21-6



- ratio of means for crossover design (original scale), 21-6
- ratio of means for two-group design (log scale), 21-6
- ratio of means for two-group design (original scale), 21-6
- t-test for, 8-4, 11-1
- two one-sided equivalence tests for crossover design, 21-6
- two one-sided equivalence tests, 21-5
- TOST tests for proportions
 - example, equivalence for independent proportions, PTE0, PTE1a, 15-40
 - example, equivalence for independent proportions, PTE0, PTE1c, 15-46
 - example, equivalence for paired proportions, POE0, POE1a, 15-32
- transfer, 13-10
 - button in side table, 5-6
- transformation
 - in data entry, 9-4
- troubleshooting, 1-8
- tutorial, 2-1
- two group
 - See also* examples for means
 - See also* examples for proportions
 - See also* examples for survival analysis
 - See also* examples for regression
 - Satterthwaite t-test of equal means, MTT0uv example, 8-13
 - t-test example, MTT0, 2-2
 - t-test for fold change, MTT0cv example, 8-15
 - t-test of equal fold change, MTT0fct example, 8-18
- undo, 4-1
 - in right-click menu, 4-15
- unequal n's, 5-1, 10-1, 15-51
 - caveat, 3-15, 10-5
 - example, MTT0, 10-2
 - from sample size table, 5-2
 - from Study Goal and Design, 3-3, 7-8, 10-1
 - from the icon, 10-1
 - proportions, 15-45
- unequal variances, 8-2
- uninstalling nQuery Advisor, 1-2
- univariate one-way repeated measures
 - analysis of variance, 13-3
- update table row name, 2-6
- upper confidence level
 - estimating SD from, 5-11, 9-15
- values
 - acceptable entries for, 7-2
 - changing, caveat, 10-5
- variance
 - in means, compute effect size, 12-3
 - inflation factor, 18-7, 18-10
 - of means, computing, 13-9
- View menu
 - from sample size menu, 7-2
 - initial, 7-1
- white rows, 2-7
- width of plot, 6-25
- Wilcoxon/Mann-Whitney, 8-3, 14-1
 - example, ordered categories, MTT2, 14-4
 - example, rank sum test, MTT1, 14-1
 - rank-sum test (continuous outcome), 21-7
 - rank-sum test (ordered categories), 21-7
- Window menu, 7-5
- Windows application
 - pasting plot into, 6-19
 - pasting from nQuery Advisor, 3-7
- Windows calculator, 5-14
- wmf, 6-21
- Word
 - exporting side table to, 12-6
 - pasting from nQuery Advisor, 3-7
- x variables, 18-1
- yellow rows, 2-7
- z (Gaussian/normal) distribution, 5-13
- z distribution, 20-1
