

INTRODUCTION



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Saphetor SA
Head of Business Development

Saphetor SA

- **Precision medicine & Bioinformatics**
- Creator of VarSome suite
- Founded 2014
- Switzerland, Lausanne
- EPFL Innovation Park
- Several offices around Europe



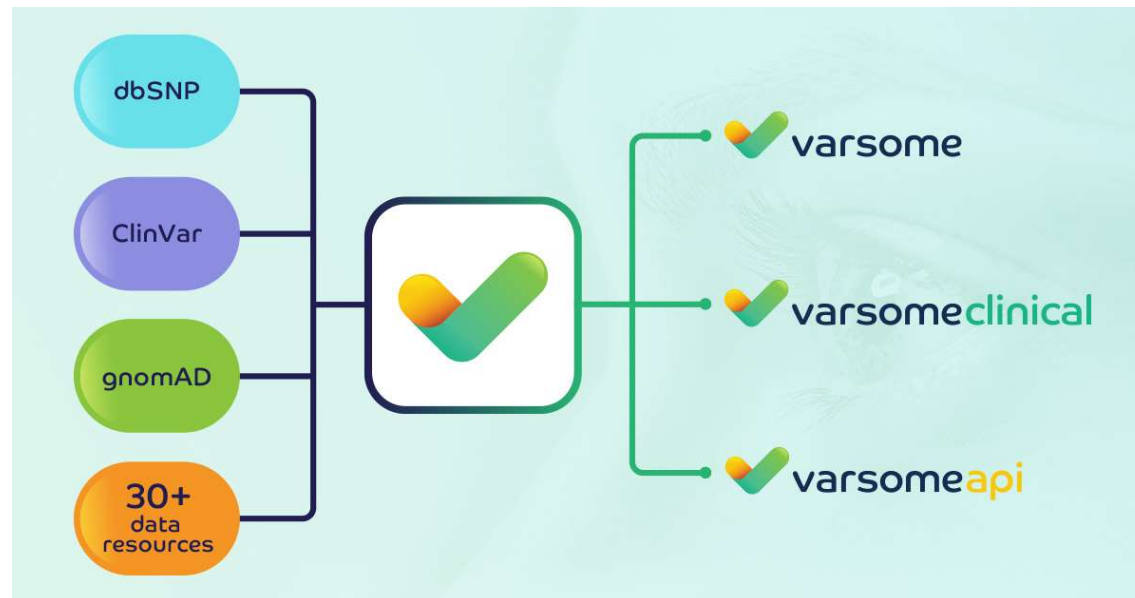
Challenges in bringing NGS to a clinical practice

1. Annotation data fragmented and spread over many websites
2. New findings and publications generated 'every day'
3. Little standardization & consistency

→ **Assessing pathogenicity for a variant very time consuming**



Genomics Knowledge Base and Human Genomics Community





Challenge #1 – Annotation data fragmented and spread over many websites

→ **Data Integration: 50+ Data Resources, and growing!**

Literature

- PubMed (article title, abstracts & authors)
- VarSome community contributions
- Links from other data sources such as ClinVar, PMKB, UniProt, many databases contain PubMed references.

Clinical

- ClinVar
- UniProt - protein domains & functions
- Cosmic (currently disabled due to licensing)
- GDC (Genomic Data Commons)

Cancer

- ICGC
- PMKB
- CIViC

Population Studies

- GWAS

Transcripts

- RefSeq
- Ensembl

Expression

- GTEX (coming soon)
- dbNSFP genes

Pharmaceutical

- DrugBank
- AACT
- FDA approved drugs

CNVs

- ExAC
- DGV
- Decifer
- ClinVar

In-Silico Tools

- DANN
- Mutation Taster
- Mutation Assessor
- FATHMM
- FATHMM-MKL
- FATHMM-XL
- LRT
- DEOGEN
- EIGEN
- SIFT
- Provean
- Revel
- PrimateAI
- Polyphen (only in VarSome clinical)
- scSNV (splice-site prediction)

Conservation

- GERP
- Phylo P17, P30, P100
- Phast Cons 30 & 100
- FitCons
- MPC
- bStatistic

Frequencies

- GnomAD exomes, genomes, coverage
- Kaviar

Genes

- dbNSFP
- GHR (Genetics Home Reference)
- HPO (Human Phenotype Ontology)
- ClinVar Structural Variants
- PanelApp (Genomics England)
- CGD (Clinical Genomics Database)
- Domino (predicts mode of inheritance)
- PubMed (article title, abstracts & authors)



Challenge #2 – New findings coming every day

→ On VarSome we keep the annotation data always up to date!



Challenge #3 – Little standardization & consistency

→ *Guidelines for standardization*


- **ACMG**
 - Robust (35+ data resources + contributions)
 - Transparent (review each rule)
 - Flexible (adjust the verdict)
- **Coming in Q1 2020**
 - AMP
 - NCCN
 - ASCO



200.000 users globally! Sharing the knowledge with each other.

- Publication links
- Variant classifications
- Comments and discussions
- Cross-border collaborations - Connecting users & laboratories

Recent linked publications


 [Roger_Colobran](#) [Vall d'Hebron Hospital] linked the publication '*Expanding the Clinical and Genetic Spectra of Primary Immunodeficiency-Related Disorders With Clinical Exome Sequencing: Expected and Unexpected Findings.*'

Recent classifications

 [isabelle_STRUBI](#) [Centre Hospitalier Régional Universitaire de Lille] classified [NM_001447.2\(FAT2\):c.742C>T](#) as **Likely Benign**
20-Nov-2019

Do it Yourself versus Do it Right

- Bioinformatician solves the primary and secondary analysis
- However, he or she usually struggles with the tertiary analysis (i.e. interpretation)
 - To do it right, you need to evaluate as much annotation data as possible
 - Challenge #1 – Fragmentation of annotation data

	DIY	DIR  varsome
Bioinformaticians	1+	10%
Software Engineers	0	80%

The challenge lies in the interpretation part of the pipeline, which requires engineering skills rather than bioinformatics ones

- However, having an *in house* bioinformatics expertise is an advantage.
- We develop tools, not a replacement for a bioinformatician in your team.
- Our tools allow your bioinformatician to be more productive and systematic, and thus increase the diagnostic yield for your patients.



Watch VarSome Video!

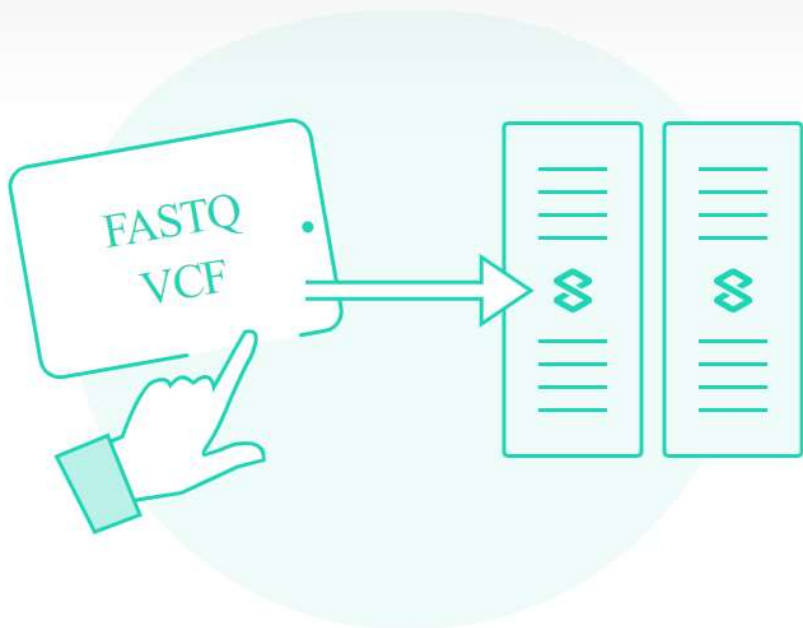
<https://www.youtube.com/watch?v=5FB0PogqgCU>





VarSome Clinical is a clinically-certified platform allowing fast and accurate variant discovery, annotation, and interpretation of NGS data for whole genomes, exomes, and gene panels.





1 Upload FASTQ or VCF

VarSome Clinical accepts FASTQ and VCF files. You can upload the data easily and securely through its web interface or you can harness *VarSome*'s powerful API for an automated and secure data transfer. Once the data are uploaded, you can start the analysis!

✓ ANNOTATE FASTQ

✓ ANNOTATE VCF

✓ JOINT CALLING

✓ MULTI-SAMPLE ANALYSIS



2 Annotation & Classification

VarSome Clinical's robust pipeline is capable of analyzing whole genomes, exomes, and gene panels, for individual samples, trios, families, and cohorts in minutes. *VarSome Clinical* leverages the massive cross-referenced knowledge base of the free *VarSome* and offers also access to licensed databases.

✓ OVER 30 DATA RESOURCES

✓ ACMG CLASSIFICATION

✓ PROPRIETARY DATA RESOURCES

✓ QUALITY CONTROL REPORTS



Launching an analysis



Samples Filter sets Gene lists Upload / view files Launch analysis Support & Manual

Tags Audit Trail Dr Tomas Kucera ▾

New sample analysis from FASTQ files

Dashboard / New sample analysis (FastQ files)

Sample Information

Sample #1



Select the file(s) to use

Select the UMI file to use



Sample Identifier

Sample Identifier - We do not accept names or other personally identifying information ⓘ

Description

Description

Phenotypes

Fill in a phenotype

Launch

- ☒ Analysis of Single sample
- ☐ Analysis of several, independent single samples with the same settings
- ☐ Family Trio
- ☐ Couple (for carrier risk analysis)
- ☐ Generic multi-sample analysis combining several samples (e.g. extended family)

Sample type

- ☒ Germline
- ☐ Tumor

Assay

swi



Swift 62G 171215

Swift Amplicon CP182

Swift Amplicon CP225

Swift Accel Amplicon CFTR

Swift Inherited Diseases Panel

Swift Accel Amplicon BRCA1 BRCA2

Ethnicity (for GnomAD annotation)

Sequencer



3 Intuitive Web Portal

VarSome Clinical's feature-rich and intuitive web interface allows filtering variants according to pathogenicity, ACMG classification, allele frequency, gene list or phenotype, to name a few! Dynamic and algorithmic filters allow you to perform simple or advanced filtering, like segregation analysis, identification of *de novo* variants or variants in imprinted genes, and much more!

✓ DYNAMIC FILTERS


✓ ALGORITHMIC FILTERS

✓ SAMPLE CROSS-REFERENCING

✓ VARIANT SHARING



Browsing the results









SamplesFilter setsGene listsUpload / view filesLaunch analysisSupport & Manual

TagsAudit TrailDr Tomas Kucera






NA12878.wgs.12152019 (hg19)

Analysis actionsFiltered Variants















Filters







50Search.



Fre...Clini...Tra...GenesCG...# S...Nea...Aud...

Variant	Variant type		Class
<input type="checkbox"/> chr11:6638385 C⇒T	SNV	 	Pathogenic
<input type="checkbox"/> chr7:142458531 C⇒T	SNV		Pathogenic
<input type="checkbox"/> chr12:42499814 delGTA	Deletion (3)		Pathogenic
<input type="checkbox"/> chr12:42499692 A⇒T	SNV		Pathogenic
<input type="checkbox"/> chr12:103234252 T⇒C	SNV	  	Likely pathogenic
<input type="checkbox"/> chr7:142458526 A⇒G	SNV		Likely pathogenic
<input type="checkbox"/> chr7:142458451 A⇒T	SNV		Likely pathogenic
<input type="checkbox"/> chr16:15696480_1 insAG...AG (23)	Insertion (23)		Likely pathogenic
<input type="checkbox"/> chrX:152858048 delG	Deletion (1)		Likely pathogenic
<input type="checkbox"/> chr12:42499817_8 insTT	Insertion (2)		Likely pathogenic
<input type="checkbox"/> chr14:104845825 delCT	Deletion (2)		Likely pathogenic

Showing 1 to 50 of 5389392 entries

**1**


☐ All manually classified


☐ All except common artefacts


☐ All manually classified except common artefacts


☐ Clear filter


Global classifications


 Benign


 Likely Benign


 Uncertain Significance


 Likely Pathogenic


 Pathogenic


 Common Artefact

 Drug Response


 Disease Association


 Risk Factor


 Protective


 Phenotype Association


Your classifications


 community


 discuss

 laura

 linked samples

 pharmacogenomics

 to review later

 to show the lab director

population)

Variant

This variant

chr11:6638385 C⇒G

population)

Variant

chr11:6638385 C⇒G

Filtering the variants

The screenshot displays the varsomeclinical web application interface. The top navigation bar includes the logo, a menu with 'Samples', 'Filter sets', 'Gene lists', 'Upload / view files', 'Launch analysis', and 'Support & Manual', and a user profile section with 'Tags', 'Audit Trail', and 'Dr Tomas Kucera'. A 'Filters' sidebar on the left allows for filtering by 'monday 2' (Total Variants: 5389392), 'Allele Frequencies' (Frequency: 0.01, variants 4768478 and 620914), 'Pathogenicity class' (Class: 5, 4, variants 620904 and 10), and 'ACMG Rules' (PP5, variants 7 and 3). The main table shows variant details with columns for variant type, class (Pathogenic, Likely pathogenic), and ACMG Rules (PVS1, PM2, PP3, PP5, PM1, PM5, PP2, PP3, PS1, PM1, PP2, PP5). A right-hand panel provides 'Analysis actions' such as 'Filtered Variants', 'SNVs & Indels', 'Phenotype - Disease information (Sample)', 'Sample/Analysis information', 'Reuse sample files', 'View QC report', 'Download QC report (PDF)', 'Download QC report (docx)', 'Download VCF', 'Downloads', 'New Gene-List Analysis', and 'New Algorithmic Filter Analysis'. Below these actions, a table shows 'GnomAD Exomes (full population)' and 'GnomAD Genomes (full population)' with 'Frequency' columns and specific variant details like 'chr11:6638385 C⇒G'.

varsomeclinical Samples Filter sets Gene lists Upload / view files Launch analysis Support & Manual Tags Audit Trail Dr Tomas Kucera

Filters

monday 2 **Apply** **Create** Total Variants: 5389392

monday 2

Allele Frequencies Frequency: 0.01 4768478 620914

Pathogenicity class Class: 5, 4 620904 10

ACMG Rules PP5 7 3

Filters

50 Search.

Variant type	Class	ACMG Rules
	Pathogenic	PVS1 PM2 PP3 PP5
	Likely pathogenic	PM1 PM5 PP2 PP3 P
	Likely pathogenic	PS1 PM1 PP2 PP5 B

Analysis actions **Filtered Variants**

SNVs & Indels

Phenotype - Disease information (Sample)

Sample/Analysis information

Reuse sample files

View QC report

Download QC report (PDF)

Download QC report (docx)

Download VCF

Downloads

New Gene-List Analysis

New Algorithmic Filter Analysis

variant

Frequency

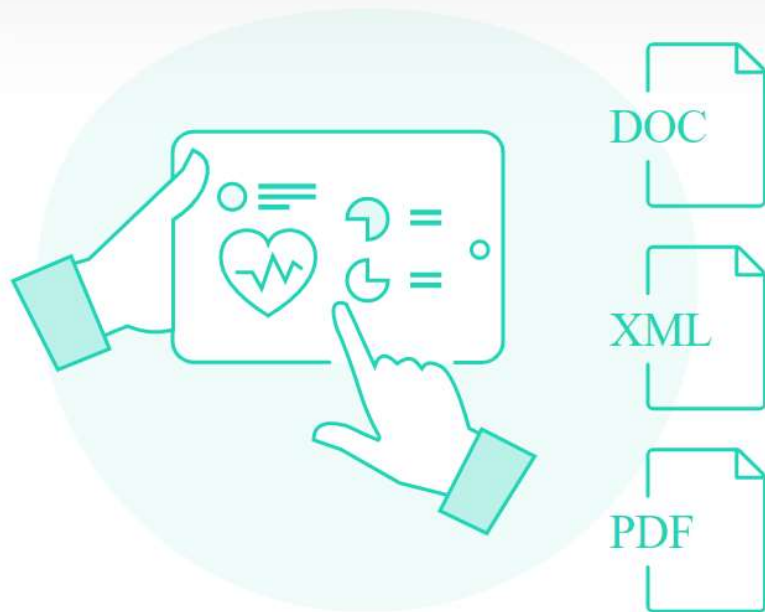
0.0000119

0.000402

GnomAD Genomes (full population)

Frequency

0.000383 chr11:6638385 C⇒G



4 Clinical Report Generation

Once you have narrowed down the list of variants of interest, you can proceed with the generation of the clinical report, which includes all the details of your variants, including literature references and your custom comments. The layout of the report can be fully customized according to your unique branding policy.

✓ CUSTOMIZABLE REPORTS

✓ CE-IVD CERTIFICATION

✓ AUDIT TRAIL

[illegible]

s)	Exon	Variant Type	RS ID	Zygosity	Frequency	Coverage
	intron 5 of 12 <u>position</u> 147 of 147	SNV	rs56144125	Heterozygous	0.00001193	35



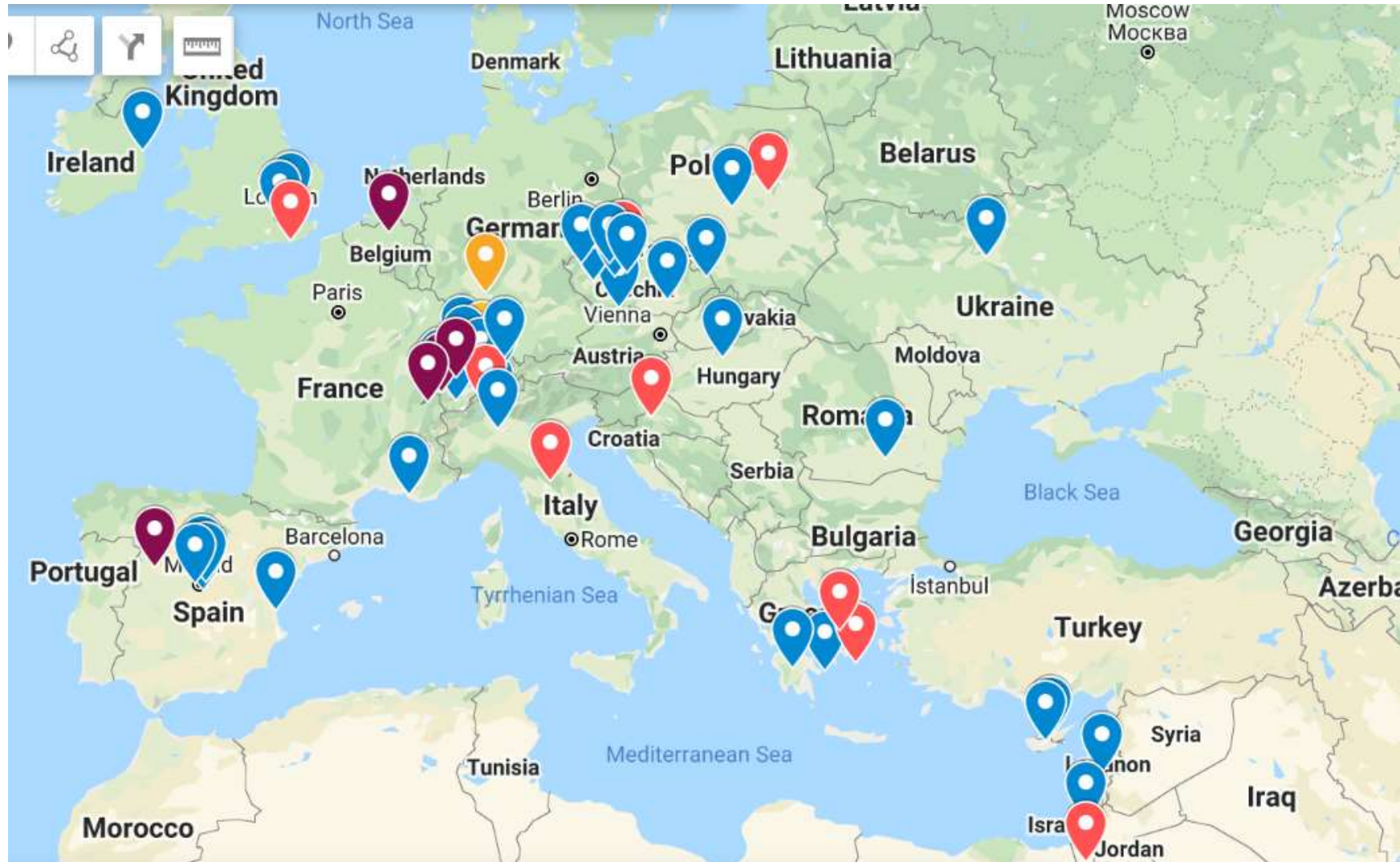
Watch VarSome Clinical Video!

<https://www.youtube.com/watch?v=5EWB74kxMaM>





varsomeclinical





varsomeclinical



General Pricing Guidelines

1. NO License Fee

2. Sample Fee

- FASTQ – Number of megabases in reads
- VCF – Number of variants

Price by megabases in reads per sample
(1 megabase = 1 million bases)

Up to 250 megabases
250 to 500 megabases
500 to 1,000 megabases
1,000 to 2,000 megabases
2,000 to 4,000 megabases
4,000 to 8,000 megabases
8,000 to 20,000 megabases
20,000 to 40,000 megabases
40,000 to 80,000 megabases
80,000 to 150,000 megabases

Per sample



Price by number of variants per sample

1 to 100
101 to 400
401 to 1,000
1,001 to 2,000
2,001 to 4,000
4,001 to 10,000
10,001 to 20,000
20,001 to 40,000
40,001 to 80,000

Per sample



3. Volume Discounts

4. Small User Fee

Modes of use



1. Stand-alone Solution – Pay as you go

- VarSome Clinical open for any kind of NGS sample
 - Be it gene panel, exome, genome
 - Invoicing on a monthly basis depending on the platform use
 - No License Fee
 - Just Sample Fee
 - Plus Small User Fee + Small Storage Fee
-
- **Credit:** You may prepay a credit and then use it towards the use of the platform, as opposed to monthly invoicing

Modes of use



2. Bundled Solution – Pre-payment

- Assay bundled with VarSome Clinical for data analysis and reporting
- Pre-payment of a certain number of analysis
- An analysis token – price depends on the number and type of samples



TK1

Partners in the pipeline:



Slide 25

TK1

add agilent logo

Tomas Kucera, 27-Jan-20

Modes of use

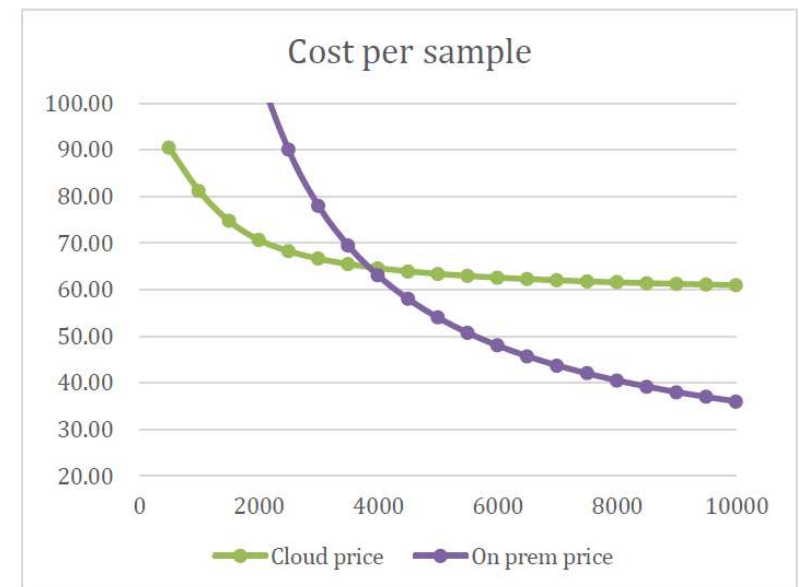


3. On Prem Installation

- For partners, labs and hospitals with large volume (aggregated) of samples
- Fixed Yearly/Monthly License Fee
- Plus 80% discounted sample fee
- Becomes economical since a certain number of samples (4000 exomes, for example)

Model situation

- In line with Part 1, assuming the sample fee: list price 90 € per single sample (average exome, starting from FASTQ)



Working together with distributors

- **Distributor may provide you with a better quotation than us directly**
- **Distributor to be your primary point of contact**
- **Distributor to provide 1st level of support**
- **VarSome to provide:**
 - Customizations – We like to work very closely with our clients.
 - Trainings
 - Documentation
 - 2nd level of support – We back you up!

Contact

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