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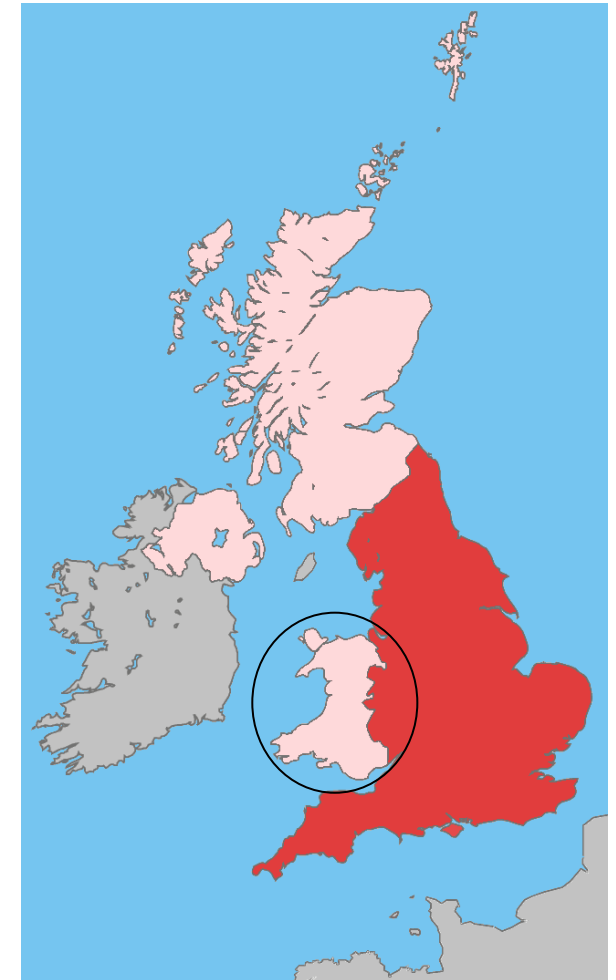
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Cymru  
Public Health  
Wales

# Luminex GPP xPERIENCE within Public Health Wales

Michael Perry – Clinical Scientist  
Rotterdam – 19<sup>th</sup> June 2013

# Public Health Wales

- Provides an expert public health resource as part of the NHS in Wales.
- Ambition to achieve a healthier, happier and fairer Wales.



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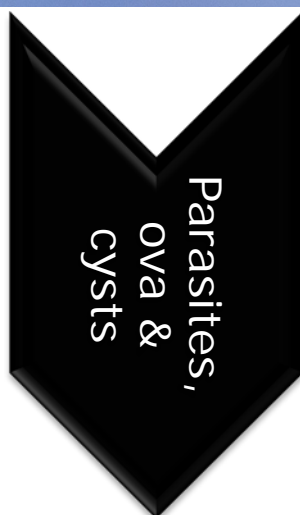
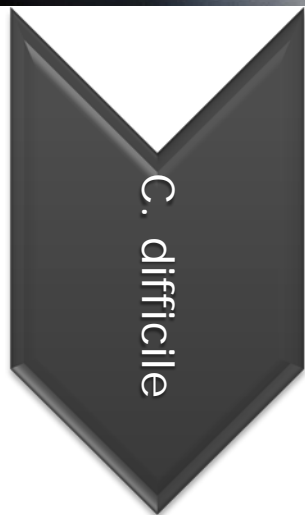
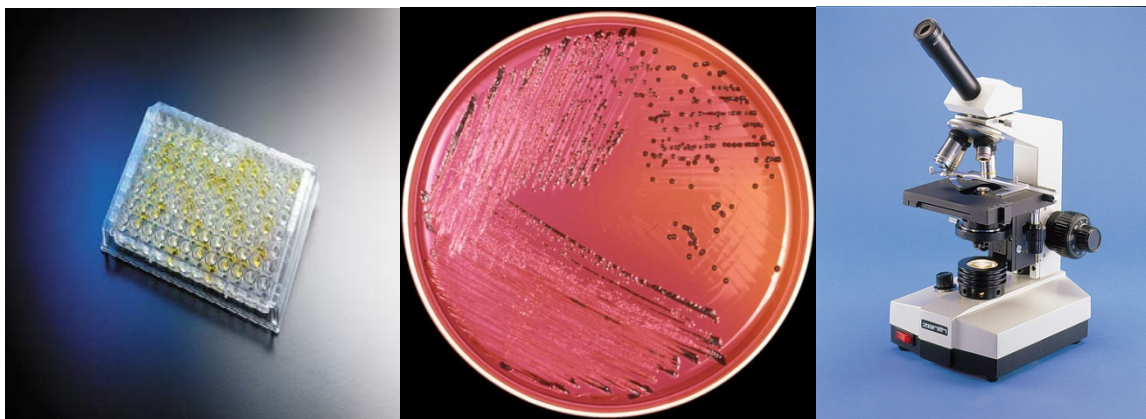
# Public Health Wales

- Includes a network of microbiology laboratory services that provide services relating to the diagnosis, surveillance, prevention and control of communicable diseases for hospitalised patients and the community.

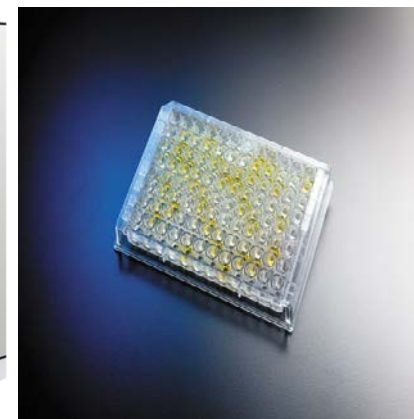
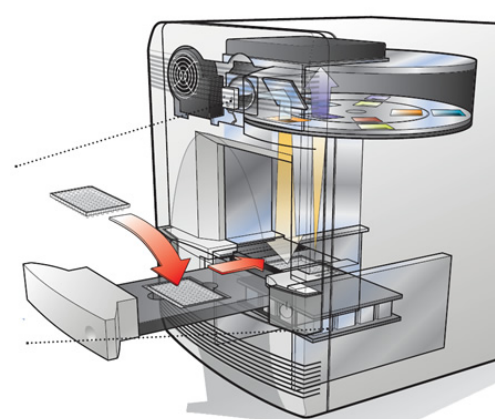
# Microbiology Cardiff

- University Hospital of Wales - 1000 bed hospital in Cardiff
- Serves C&V NHS trust and the larger population of Wales
- Process c.1M tests/year

# Current strategy



Bacteriology Laboratory (90%)



Virology Laboratory (10%)

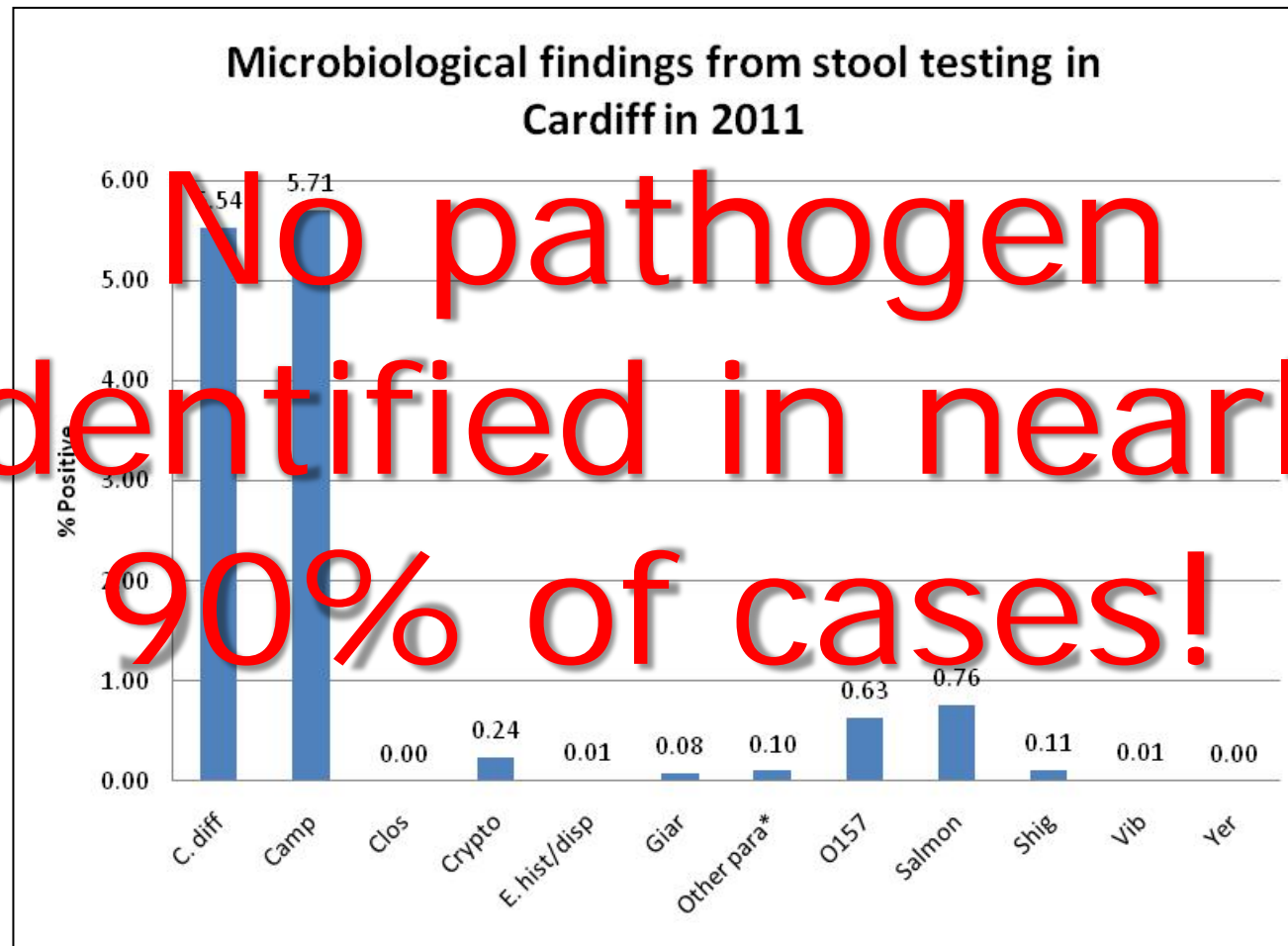
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# Faecal Pathogen Detection



# Poor diagnostic yield

- Insufficient testing – STEC/ETEC, viruses etc
- Low sensitivity (microscopy/ELISA)
- Non-viable/non-culturable – time & selective processes

# Current strategy

- Labour intensive
- Subjective
- Low yield
- Confusing
- Inefficient



# Syndromic approach

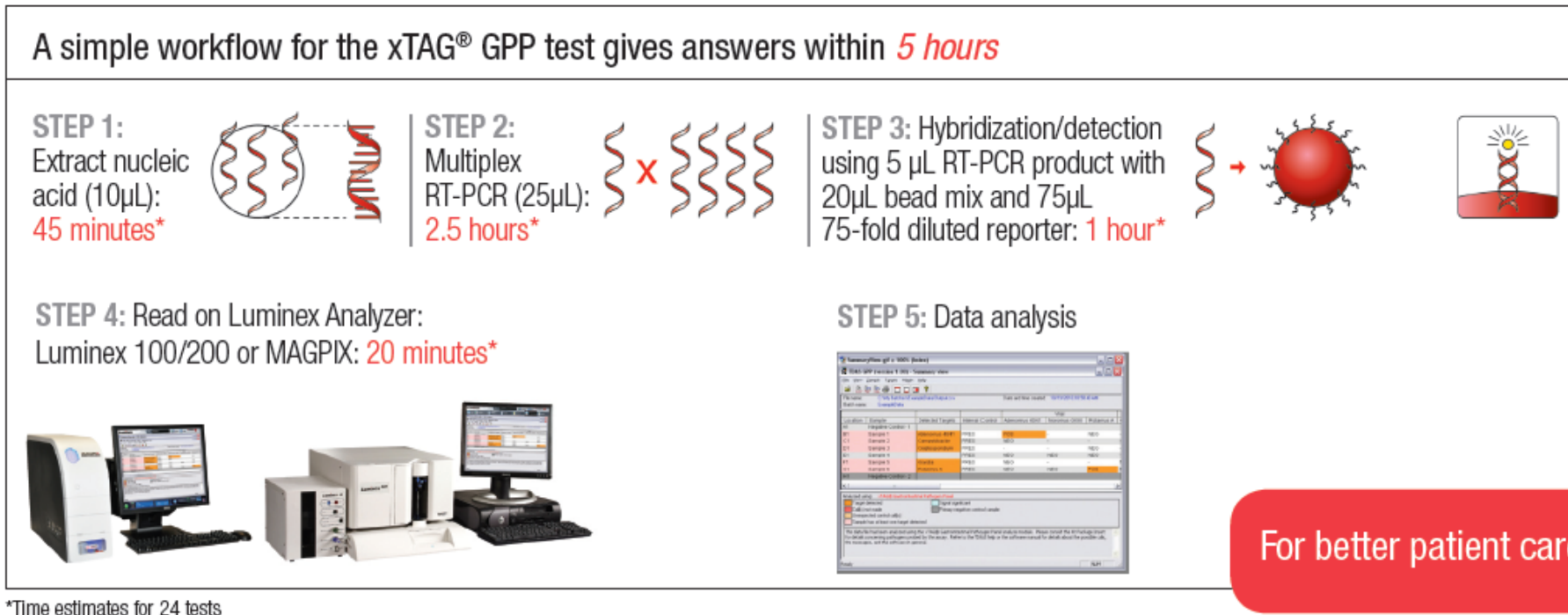
- One sample
- One laboratory
- Increased laboratory efficiency
- Increased yield?
- Improved clinical outcome?
- Costs?

# Luminex xTAG GPP

- 15 'targets':
  - 9 bacterial
  - 3 viral
  - 3 parasite
- 1 tube/test!

Target (Analyte)
<i>Salmonella</i>
<i>Shigella</i>
<i>Campylobacter</i>
<i>Yersinia enterocolitica</i>
Enterotoxigenic <i>E. coli</i> (ETEC) LT/ST
<i>Escherichia coli</i> O157
Shiga-like Toxin producing <i>E. coli</i> (STEC) stx 1/stx 2
<i>Clostridium difficile</i> Toxin A/B
<i>Vibrio cholerae</i>
Adenovirus 40/41
Rotavirus A
Norovirus GI/GII
<i>Giardia lamblia</i>
<i>Cryptosporidium</i>
<i>Entamoeba histolytica</i>

# Luminex xTAG Gastrointestinal Pathogen Panel (GPP)



Product is region specific and may not be approved in your country of residence.  
For a complete list of warnings and precautions, consult the package insert.

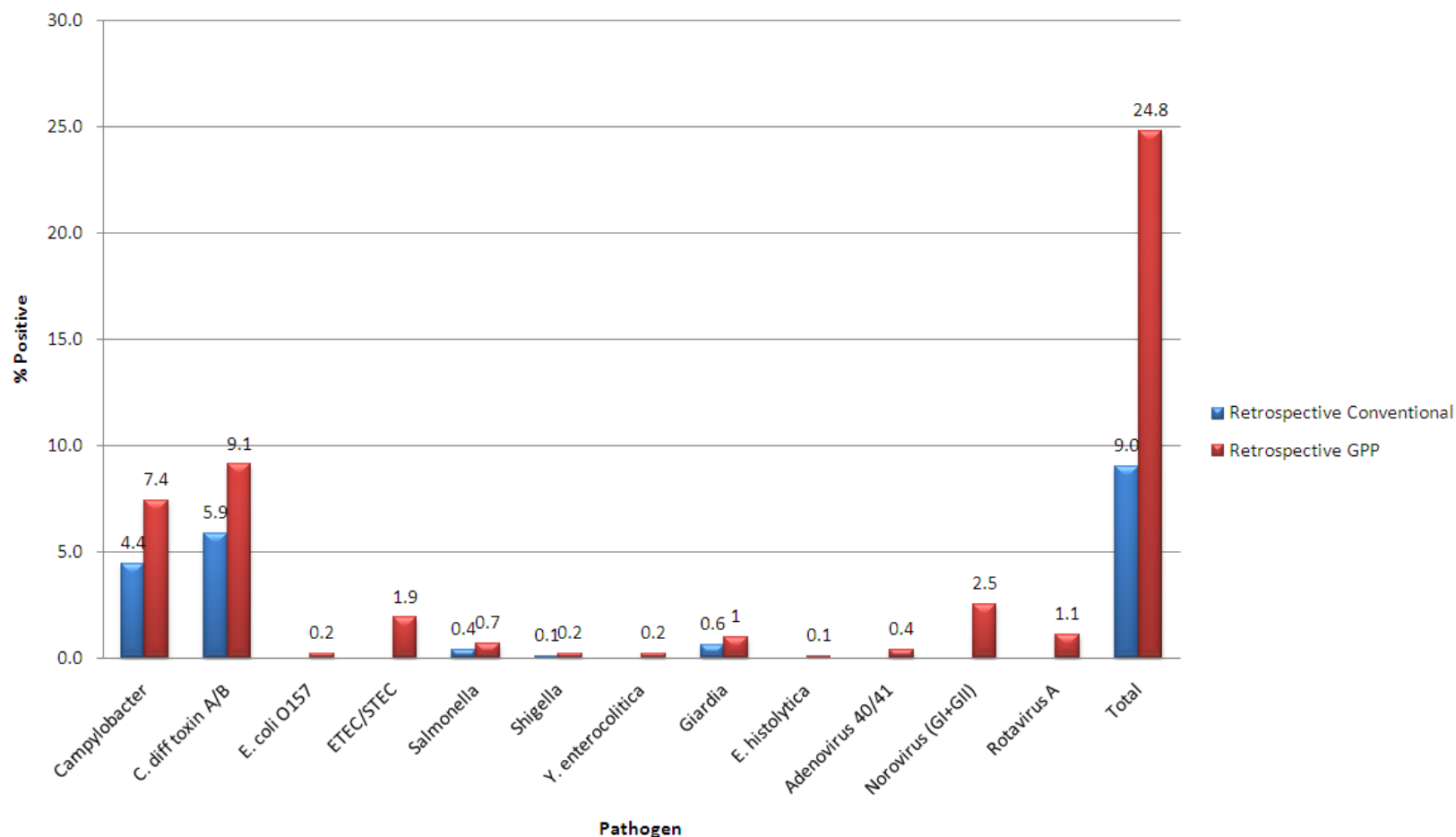
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# Luminex GPP vs. conventional approach

- 1000 clinical samples
- Conventional testing:
  - Ova, cysts & parasites (n=995)
  - *Campylobacter*, *E. coli* O157, *Salmonella* and *Shigella* (n=991)
  - *C. difficile* ('vulnerable' patients only n=597)

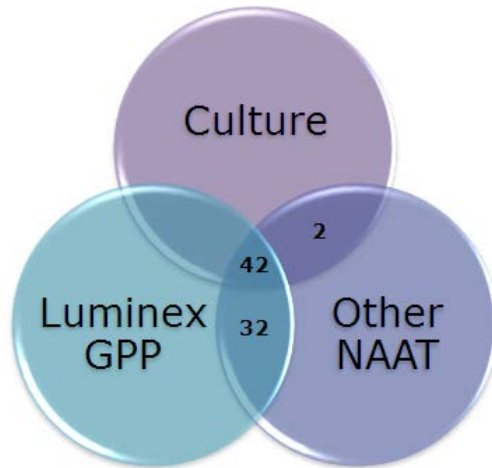
# Retrospective test results

Gastrointestinal pathogen detection by conventional methods and the  
Luminex GPP assay (n=1000)

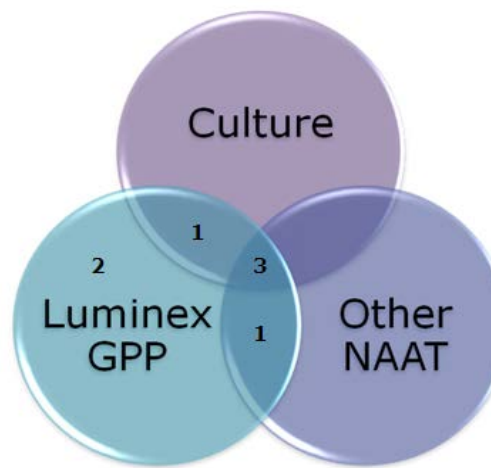


# GPP analytical validity - 1

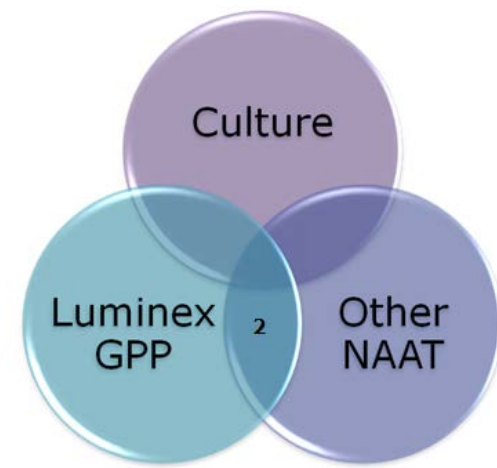
*Campylobacter*



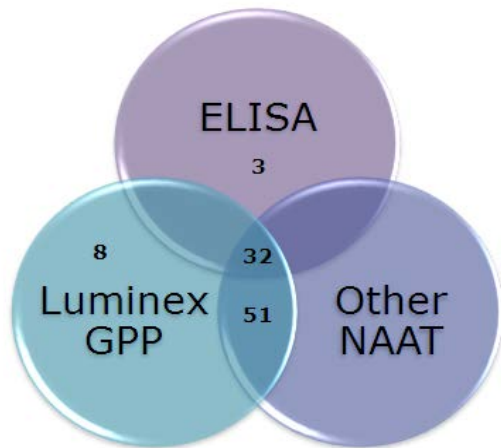
*Salmonella*



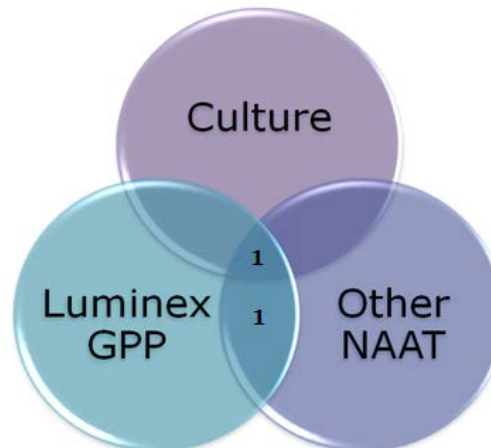
*E. coli* O157



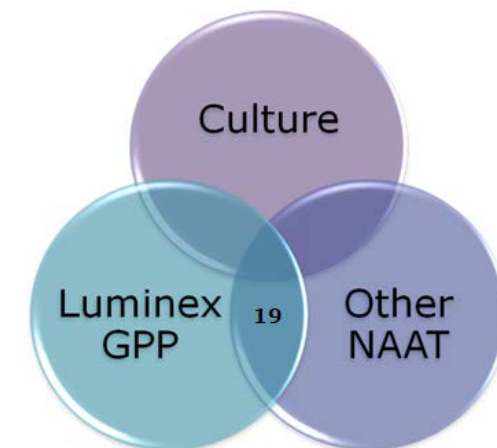
*C. difficile* toxin A/B



*Shigella*



Other STEC/ETEC



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# Results - In detail

- *Campylobacter*:
  - 44 culture detections
  - 74 GPP detections
- Positivity difference = 3% (1.9-4.3)
- z-test: 5.14,  $P < 0.001$
- Culture 59.5% sensitive
  - Tam *et al.* 2012: 58%; Bessède *et al.* 2011: ~60%

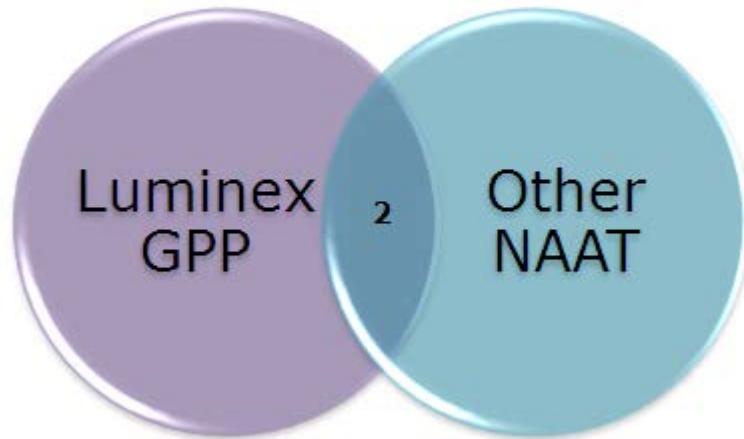
# Results - In detail

- *C. difficile*:
  - 35/80 GDH toxin A/B EIA detections
  - 57/80 GDH GPP toxin detections
  - Additional 34 GDH neg GPP detections
- Positivity difference = 27.5% (15.3-38.3)
- z-test:
  - Toxin EIA vs. GPP: 44  $P < 0.001$

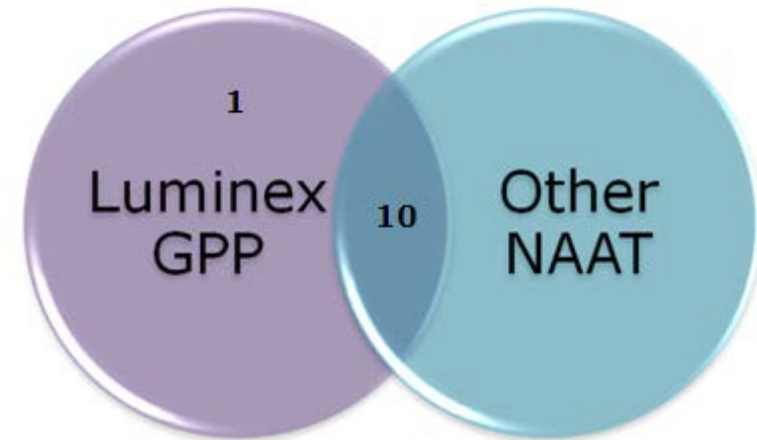


# GPP analytical validity - 2

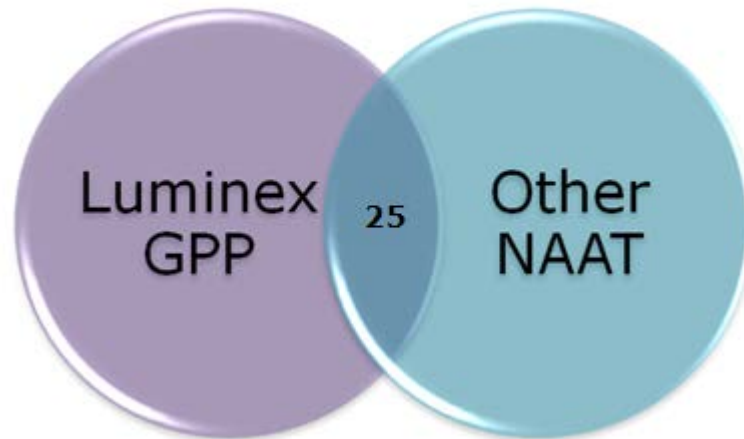
*Y. enterocolitica*



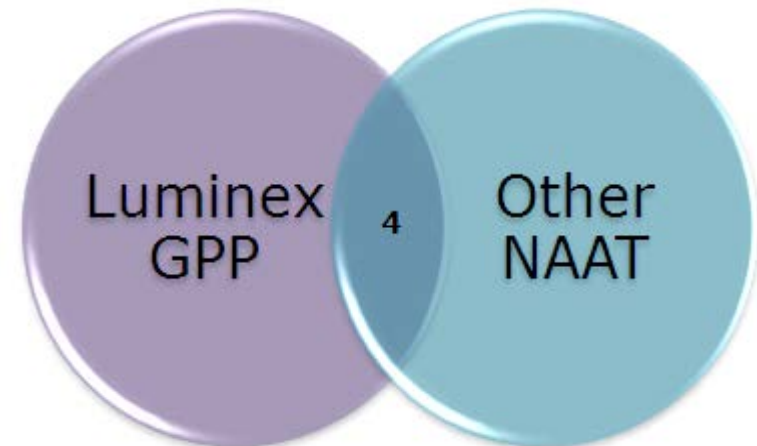
Rotavirus A



Norovirus GI&II

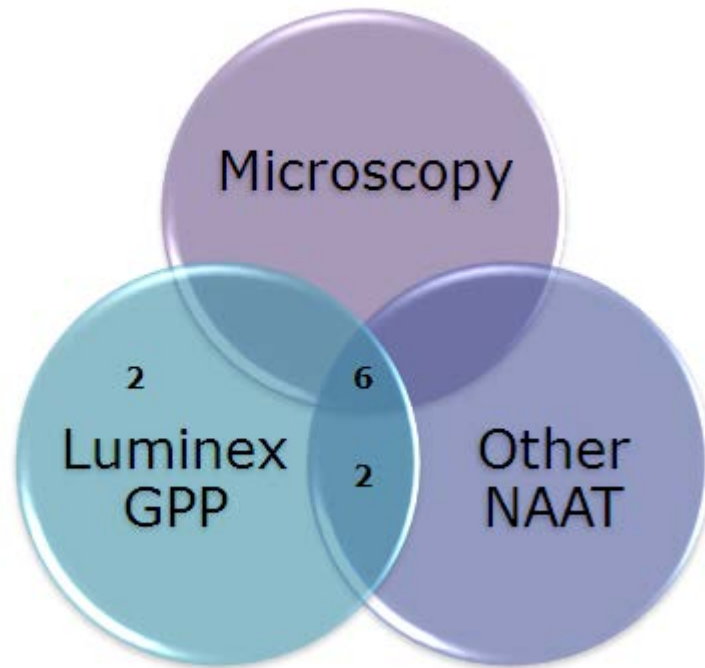


Adenovirus 40/41

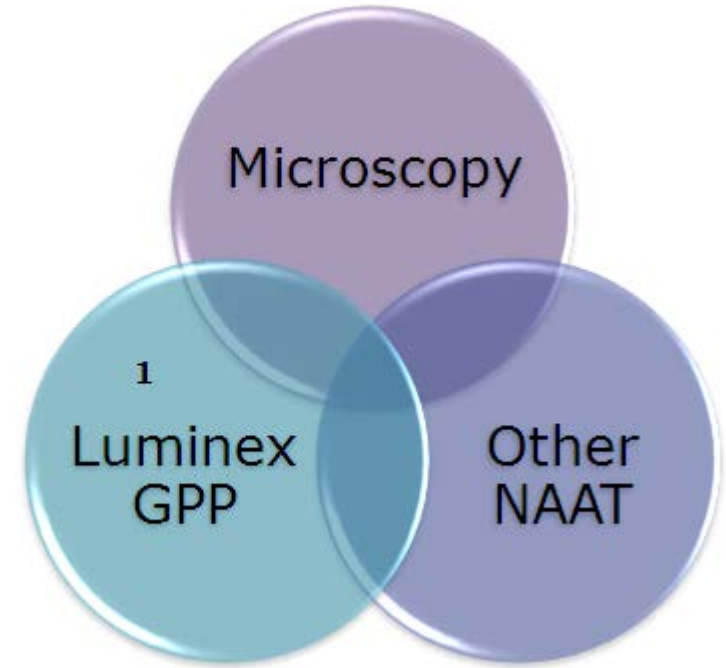


# GPP analytical validity - 3

*Giardia*



*E. histolytica*



- No *Cryptosporidium* detections

# UK Cryptosporidium Reference unit

- All samples correctly identified.
- Included:
  - 2 low-level
  - 5 potential cross reactive samples

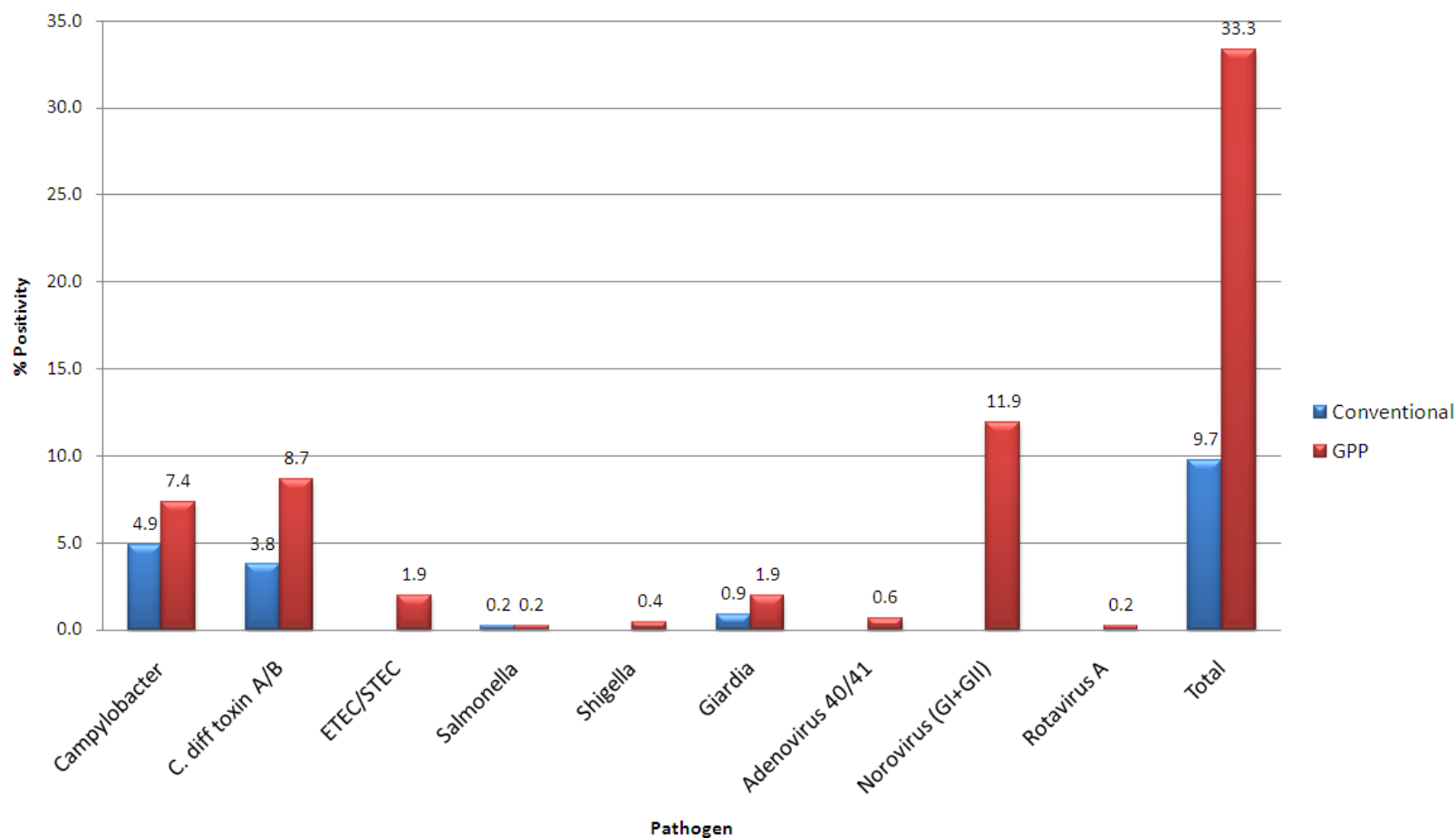
Sample ID	Sample type	Species or genotype	Cryptosporidium spp. (real time PCR)	Luminex GPP result
1	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
2	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
3	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
4	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
5	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
6	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
7	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
8	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
9	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
10	Human sample	<i>Giardia duodenalis</i>	Not done	Giardia
11	Human sample	<i>C. hominis</i>	<i>C. hominis</i>	<i>Cryptosporidium</i>
12	Human sample	<i>C. hominis</i>	<i>C. hominis</i>	<i>Cryptosporidium</i>
13	Human sample	<i>C. hominis</i>	<i>C. hominis</i>	<i>Cryptosporidium</i>
14	Human sample	<i>C. hominis</i>	<i>C. hominis</i>	<i>Cryptosporidium</i>
15	Human sample	<i>C. hominis</i>	<i>C. hominis</i>	<i>Cryptosporidium</i>
16	Human sample	<i>C. hominis</i>	<i>C. hominis</i>	<i>Cryptosporidium</i>
17	Human sample	<i>C. hominis</i>	<i>C. hominis</i>	<i>Cryptosporidium</i>
18	Human sample	<i>C. parvum</i>	<i>C. parvum</i>	<i>Cryptosporidium</i>
19	Human sample	<i>C. parvum</i>	<i>C. parvum</i>	<i>Cryptosporidium</i>
20	Human sample	<i>C. parvum</i>	<i>C. parvum</i>	<i>Cryptosporidium</i>
21	Human sample	<i>C. parvum</i>	<i>C. parvum</i>	<i>Cryptosporidium</i>
22	Human sample	<i>C. parvum</i>	<i>C. parvum</i>	<i>Cryptosporidium</i>
23	Human sample	<i>C. parvum</i>	<i>C. parvum</i>	<i>Cryptosporidium</i>
24	Human sample	<i>C. parvum</i>	<i>C. parvum</i>	<i>Cryptosporidium</i>
25	Human sample	<i>C. parvum</i>	<i>C. parvum</i>	<i>Cryptosporidium</i>
W23736	DNA extract	Not Cryptosporidium	Challenging sample	ND
126	DNA extract	Not Cryptosporidium	Challenging sample	ND
204	DNA extract	Not Cryptosporidium	Challenging sample	ND
W28023	DNA extract	Not Cryptosporidium	Challenging sample	<i>E. histolytica</i>
W28029	DNA extract	Not Cryptosporidium	Challenging sample	<i>E. histolytica</i>

# Retrospective co-pathogens

Co-pathogen type	GSTS	Cardiff
Viral/Viral	4	2
Viral / Bacterial	0	6
Viral / Parasitic	3	0
Bacterial / Bacterial	2	2
Parasitic/parasitic	1	0
Bacterial / Parasitic	2	0
Viral / Bacterial / Parasitic	0	0
<b>TOTAL</b>	<b>12</b>	<b>10</b>

# Prospective test results

Gastrointestinal pathogen detection by conventional methods and the  
Luminex GPP assay (n=472)



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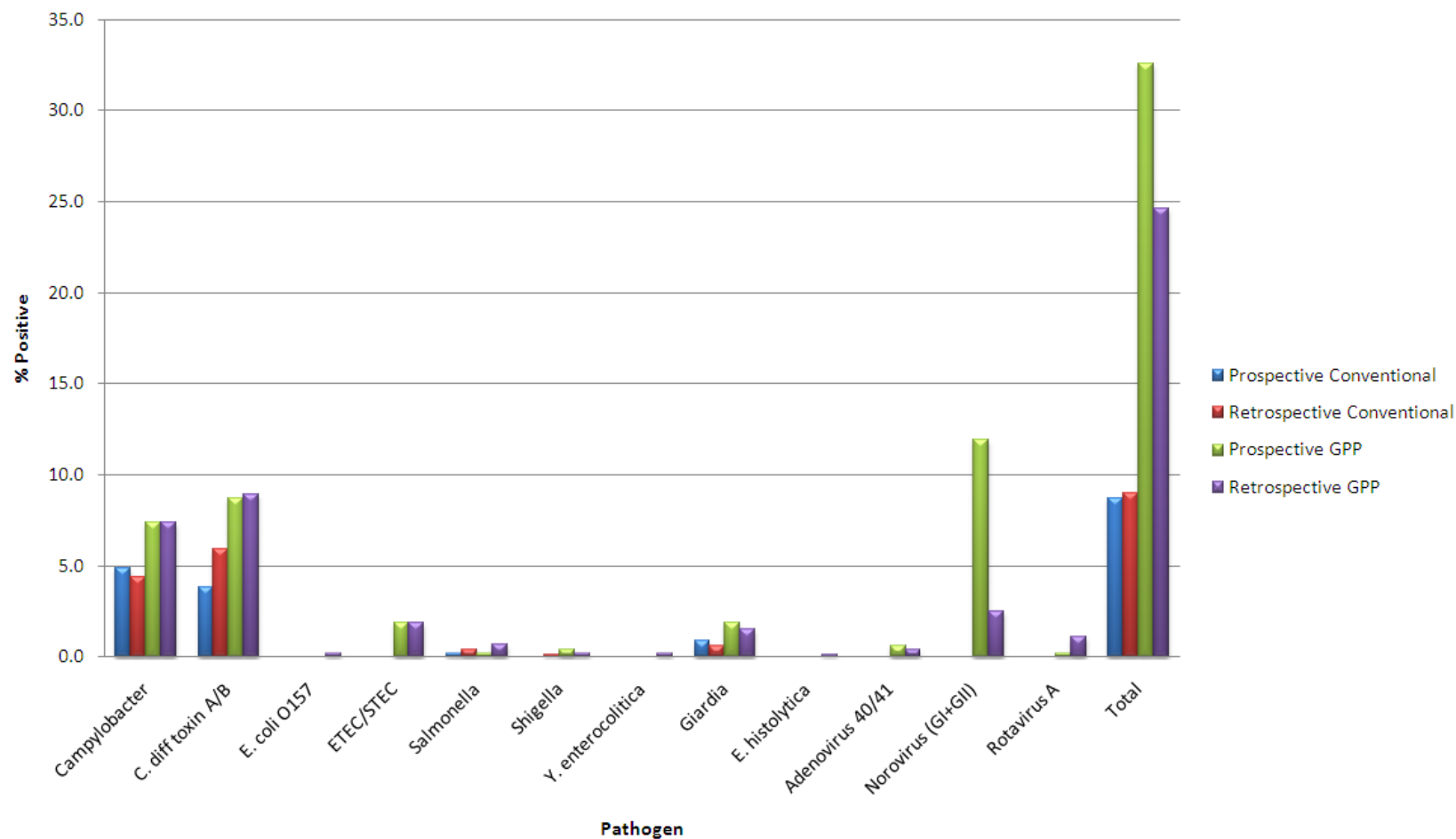


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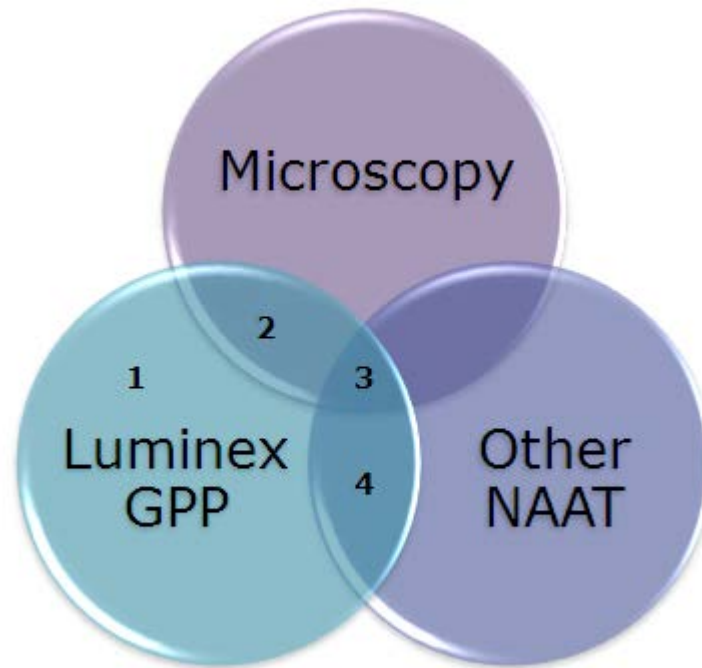
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# Prospective vs. retrospective

Gastrointestinal pathogen detection by conventional methods and the Luminex GPP assay in prospective and retrospective testing



# Prospective Giardia accuracy



# Prospective co-pathogens

Co-pathogen type	Cardiff
Viral / Bacterial	5
Bacterial x 2 / Parasitic	1
<b><i>TOTAL</i></b>	<b>6</b>



# Prospective vs. retrospective

- Summer vs. winter
- Non-selective vs. selective
- Inhibition rate similar

# Infection control

- *C. difficile*:
  - 40 GPP
  - 14 tox ELISA
  - 32 toxigenic culture
    - 5 culture neg
    - 1 toxin neg
- 81% of patients - toxigenic *C. diff*

# Infection control

- Concerns over increased reporting
- Positive anecdotes

# Workflow

- Only 2 lab technicians required
  - Less skilled than current staff
  - Results reported from 6-24 hours depending on when samples arrive in laboratory

# Conclusion

- **FASTER**: turn-around-times
  - 24-72hrs to 6-24hrs
- **HIGHER**: efficiency & yield
  - 5 'tests'/2 samples to 1 'test'/1 sample
  - 9% to 25-33% yield
- **STRONGER**: compared to conventional testing strategies – positive & negative results

# Further work/bottlenecks

- Clinical impact & healthcare economics
- Process automation
- Other syndromes

# Acknowledgements & References

- Public Health Wales colleagues
- UK Cryptosporidium Reference Unit colleagues
- GSTS colleagues
- Luminex
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