

# Evaluation of A Rapid Highly Multiplexed Molecular Diagnostic Lower Respiratory Tract Panel for Clinical Impact and Antibiotic Stewardship



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## INTRODUCTION

- Currently diagnosis of an lower respiratory tract infection (LRTI) is based on a combination of clinical and radiological evidence and initial treatment of these patients is generally with empiric antibiotics.
- Specific antibiotic treatment is based on culture results which can take several days to obtain results and may still not be sufficient to determine the pathogen causing the LRTI.
- The Unyvero platform is a rapid molecular diagnostics platform which obtained FDA approval on April 3, 2018
- The platform uses cartridges in order to perform highly multiplexed analyses of various types of infections.
- Currently in the United States, the only approved cartridge is for lower respiratory tract infections.
- While there are clear benefits to a rapid and sensitive diagnostic system, there is debate as to whether such a system would lead to overuse of broad spectrum antibiotics versus improving stewardship.

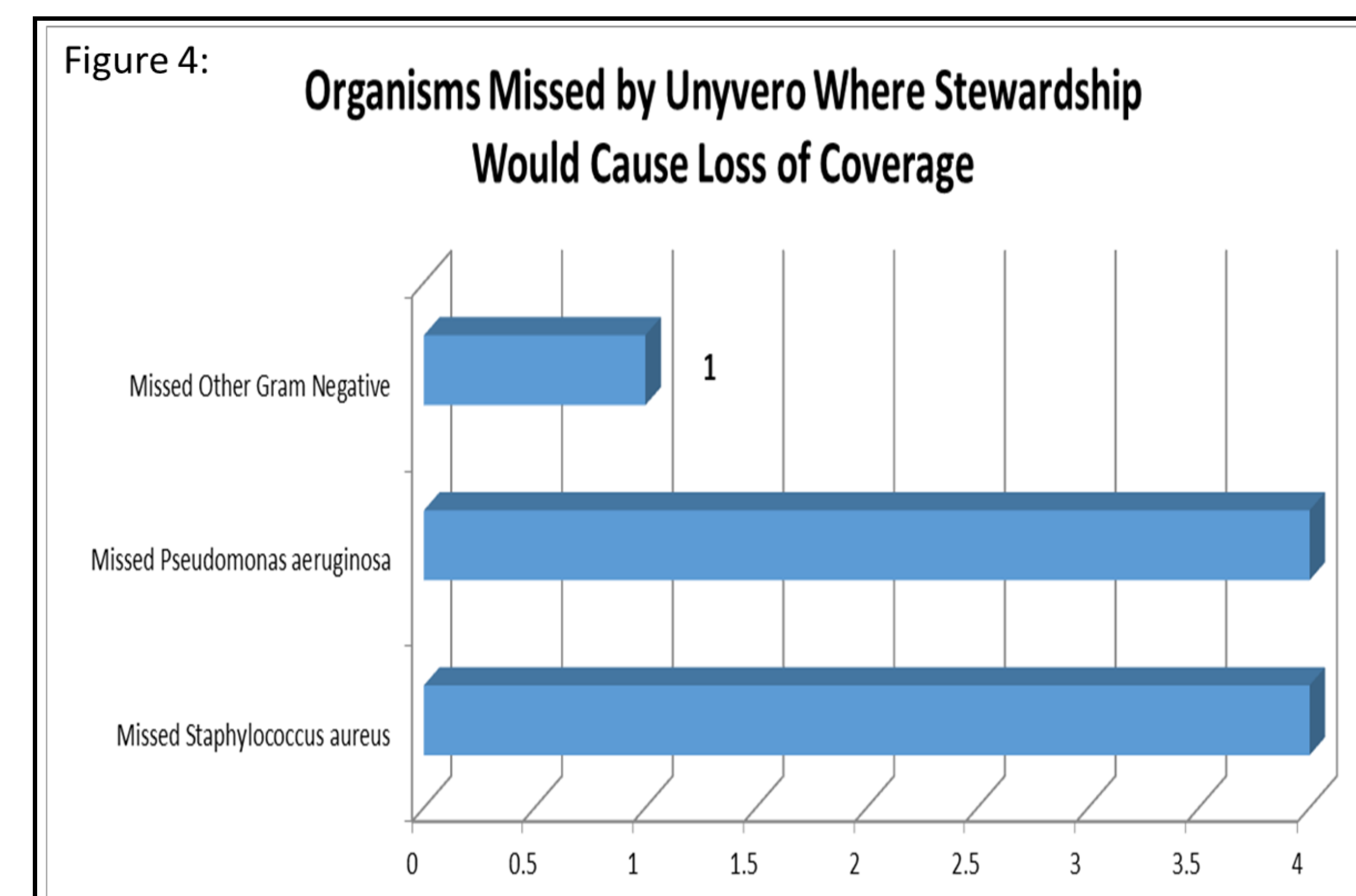
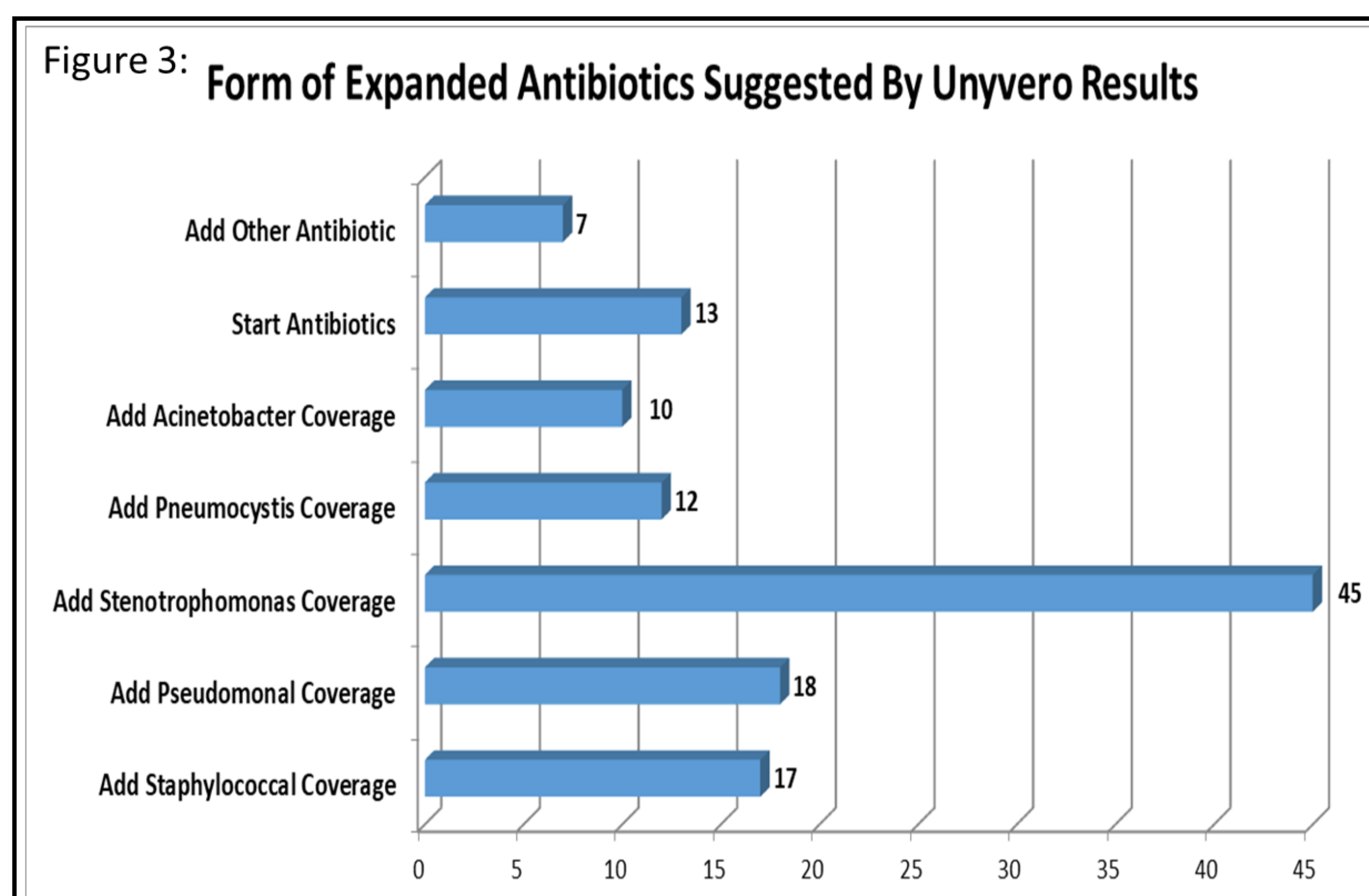
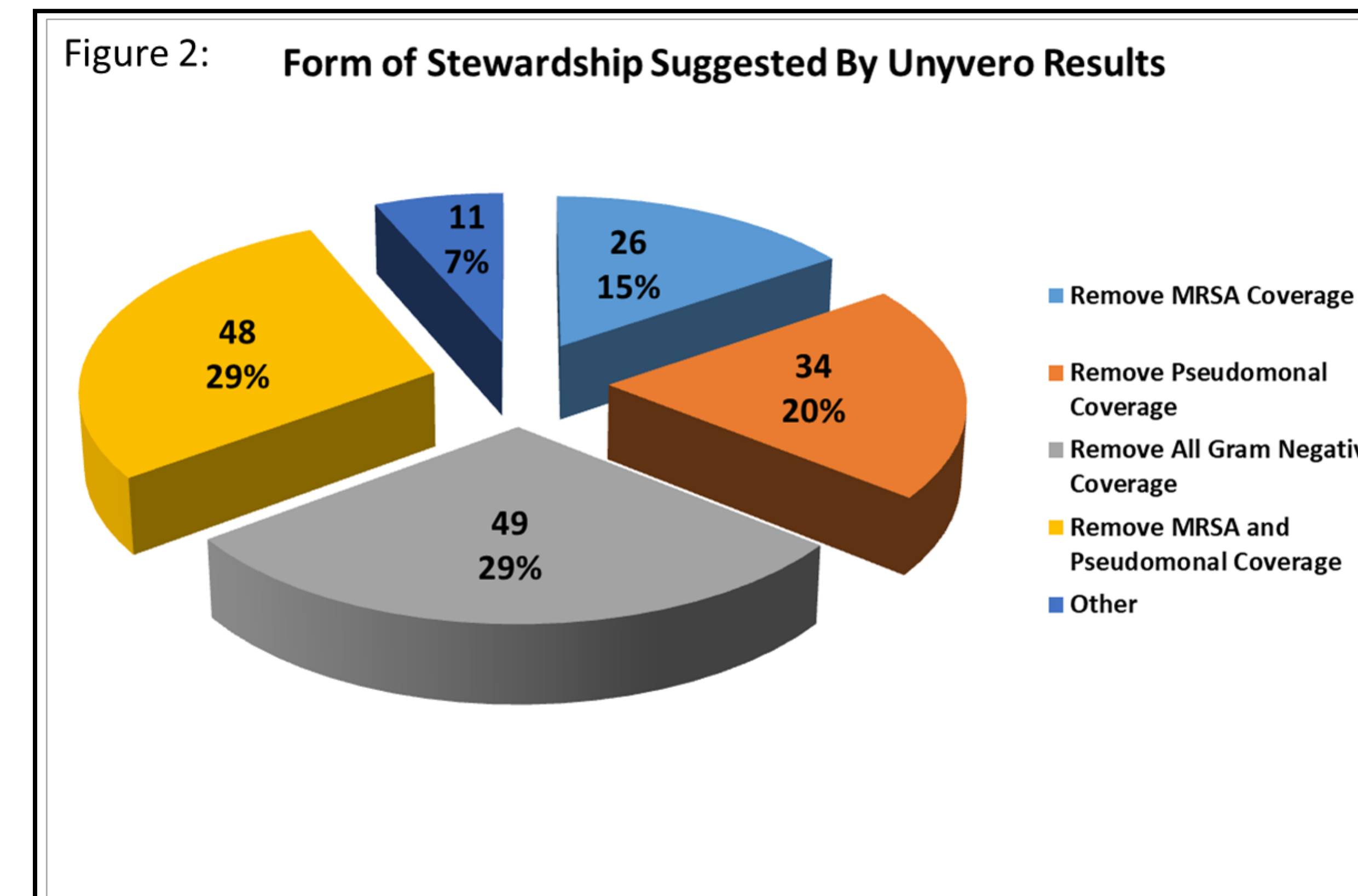
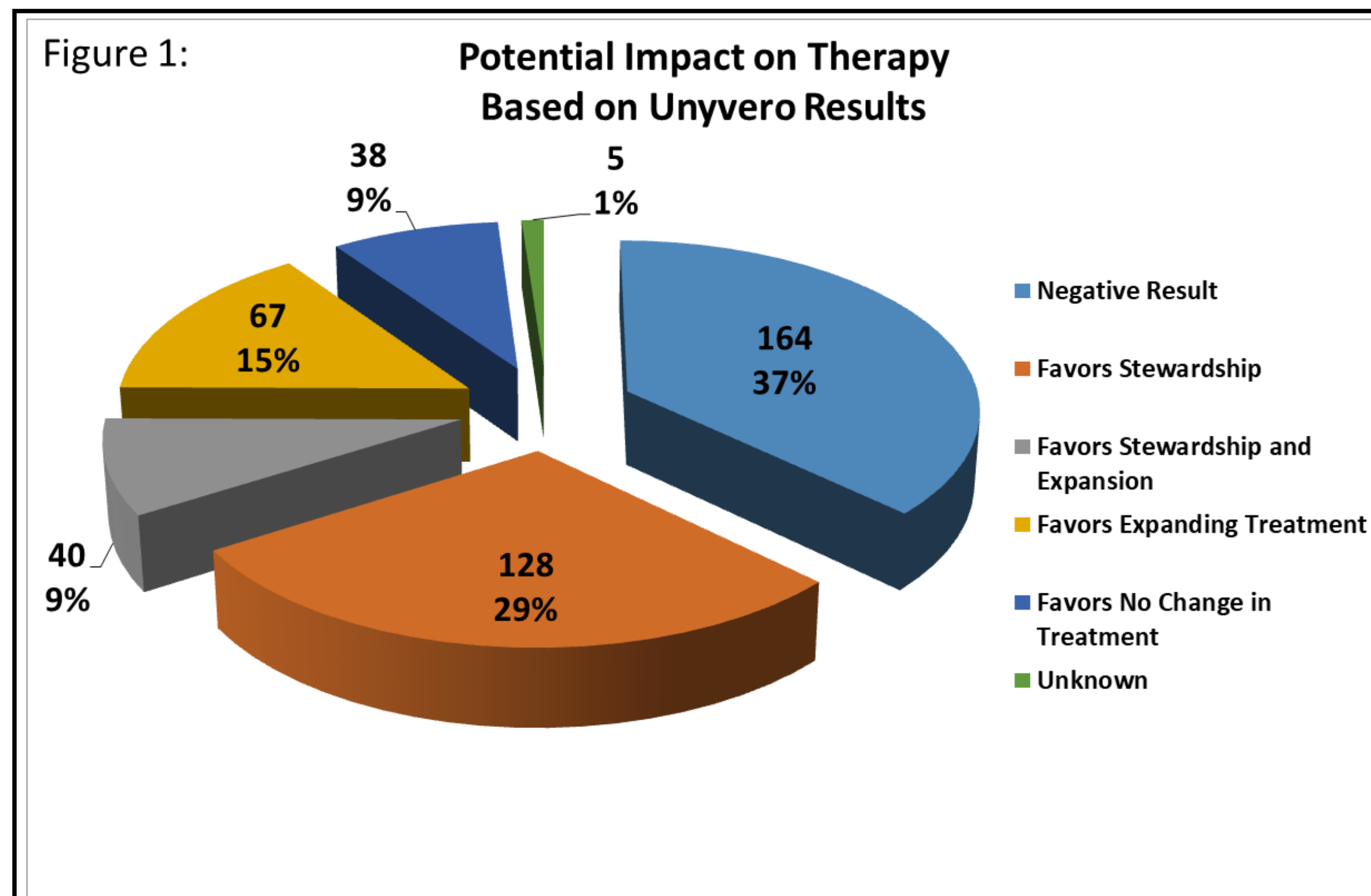
## METHODOLOGY

- In the seminal trial of the Unyvero LRTI cartridge (NCT01922024), we enrolled 442 samples at Beaumont Health.
- A retrospective chart review was performed for all enrolled patients at Beaumont Health.
- Culture results, antibiotic treatment given, and outcomes were analyzed and a determination was made as to how knowing the results of the Unyvero test, which detects 20 pathogens and 16 antibiotic resistance genes, would have altered antibiotic use.
- Cases were defined as follows:
  - No Change – Antibiotics were completely appropriate for the pathogens detected
  - Negative – No pathogens were found and thus no statement could be made regarding antibiotic use
  - Favors stewardship – An obvious change could be made to narrow the antibiotics by knowing the pathogen
  - Favors expansion – An obvious change could be made to the antibiotics to cover a pathogen which was not being covered
  - Favors both – A change toward both stewardship and expansion was favored based on the identified pathogens
- It should be noted that the panel tested here is not 100% identical to the panel that was approved by the FDA.

## RESULTS

20 Microorganisms		16 Resistance Markers	
Acinetobacter baumannii complex	Moraxella catarrhalis	bla <sub>TEM</sub>	mecA
Chlamydia pneumoniae	Morganella morganii	bla <sub>SHV</sub>	sul1
Citrobacter freundii	Mycoplasma pneumoniae	bla <sub>TEM</sub>	gyrA83 mutation (of E. coli)
Enterobacter cloacae complex	Pneumocystis jirovecii	bla <sub>NDM</sub>	gyrA87 mutation (of E. coli)
Escherichia coli	Proteus spp.	bla <sub>KPC</sub>	gyrA83 mutation (of P. aeruginosa)
Haemophilus influenzae	Pseudomonas aeruginosa	bla <sub>CTX-M</sub>	gyrA87 mutation (of P. aeruginosa)
Klebsiella oxytoca	Serratia marcescens	bla <sub>OXA-23</sub>	
Klebsiella pneumoniae	Staphylococcus aureus	bla <sub>OXA-24</sub>	
Klebsiella variicola	Stenotrophomonas maltophilia	bla <sub>OXA-48</sub>	
Legionella pneumophila	Streptococcus pneumoniae	bla <sub>OXA-58</sub>	

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	positive LRT result	negative LRT result	PPA [%]	95% CI range
Acinetobacter baumannii complex	14	0	100	78.5 - 100.0
Enterobacter cloacae complex	22	2	91.7	74.2 - 97.7
Escherichia coli	27	1	96.4	82.3 - 99.4
Haemophilus influenzae	5	1	83.3	43.7 - 97.0
Klebsiella oxytoca	9	1	90	59.6 - 98.2
Klebsiella pneumoniae	26	3	89.7	73.6 - 96.4
Klebsiella variicola	3	0	100	43.9 - 100.0
Moraxella catarrhalis	5	0	100	56.6 - 100.0
Morganella morganii	1	0	100	20.7 - 100.0
Proteus spp.	17	2	89.5	68.6 - 97.1
Pseudomonas aeruginosa	51	3	94.4	84.9 - 98.1
Serratia marcescens	7	0	100	64.6 - 100.0
Staphylococcus aureus	83	8	91.2	83.6 - 95.5
Stenotrophomonas maltophilia	29	0	100	88.3 - 100.0
Streptococcus pneumoniae	5	0	100	56.6 - 100.0
<b>total</b>	<b>304</b>	<b>21</b>	<b>93.5</b>	<b>90.3 - 95.7</b>



## CONCLUSIONS

- The Unyvero platform along with the LRTI cartridge allows for a rapid and accurate determination of the organisms which are found within samples from the lung (Tracheal aspirate and BAL).
- Despite concerns that such a system would lead to overuse of broad spectrum antibiotics, our analysis shows that it favors narrowing antibiotics over expanding antibiotics nearly two-fold (29% vs 15%).
- There are concerns over the possibility of missing potential pathogens using a PCR-based system. In our study, when compared to culture, this only occurred in 9 out of 442 samples (2%) where potentially needed antibiotics would have been removed due to stewardship.
- The number of times additional potential pathogens were found by the Unyvero was 89 of 442 (20%).
- When expansion of antibiotics was favored, the most common pathogen was Stenotrophomonas which is generally not covered by empiric antibiotics and is commonly found in the ICU setting due to frequent use of broad spectrum antibiotics.
- Expanding coverage to cover common organisms such as Staphylococcus aureus or Pseudomonas was less common as they are generally covered in empiric antibiotic regimens.

## DISCUSSION

- As with any diagnostic test, the use of the Unyvero platform must be tempered with good clinical judgement.
- A result indicating the presence of an unexpected organism should not automatically trigger addition of new antibiotics in a stable or improving patient.
- The ability to distinguish potential pathogens earlier and in the presence of multiple organisms where the Unyvero platform has great potential for clinical utility in the unstable or worsening patient.
- A clinical trial to determine actual benefit to patients when using an algorithm-based treatment plan guided by the Unyvero platform and the LRTI cartridge would be of great benefit.

## Acknowledgements

We would like to thank everyone at Curetis for all of their support in the original trial as well as allowing us to continue to work on our internal data.