The Use of Plasma Next-Generation Sequencing Test in the Management of Immunocompetent and Immunocompromised Patients – A Single Center Retrospective Study

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Abstract

BACKGROUND

Microbiological culture data is a longstanding gold standard in diagnostics. Unfortunately, yield from cultures have been inconsistent and slow, prompting the need for newer tests including the plasma-based next generation sequencing (NGS) tool.

This study aims to describe the use of NGS and the corresponding change in management.

METHODS

A descriptive retrospective study was done on hospitalized adults at CHI-Baylor St. Luke's in Houston, Texas with NGS tests from Jan 1, 2017 to Dec 31, 2018.

RESULTS

There were 167 NGS tests performed. Most patients were non-Hispanic (n=129) Caucasian (n=106) males (n=116) with a mean age of 52. Furthermore, 61 were immunocompromised patients [solid organ transplant (n=30), HIV-AIDS (n=14) and rheumatology patients on immunosuppression (n=12)].

During the study, the hospital staff prepared a list of indications for NGS testing including: systemic or deep seated infection where a biopsy or other workup is negative or not possible (n=50), fever of unknown origin (n=26), culture negative endocarditis (n=15), HIV/AIDS with fever (n=10), transplant patient with fever (n=5). There were 60 cases where the indications were not on this list (36%).

Results showed that 118/167 (71%) were positive. The most common organisms identified were gram negative bacteria (54/118; 46%) followed by viruses (49/118; 42%), gram-positive bacteria (48/118; 41%), fungi (16/118; 14%), atypical bacteria (9/118; 8%), mycobacterium (4/118; 3%), and parasites (4/118; 3%). Blood cultures were concurrently obtained in 148/167 (89%) of the cases and returned negative in 137/148 (93%) of cases.

In terms of change of management, the largest change was found in glycopeptide use (36 fewer patients after NGS results). Next was on anti-mycobacterial drugs where 27 were added among 8 instances. Only 36 patients were taken off antibiotics, even though 49 patients had negative results. In total, 120 out of 160 cases had antibiotic changes.

CONCLUSION

We observed a large decrease in glycopeptide use after NGS results which suggests physicians' comfort in withdrawing MRSA coverage. In addition, anti-mycobacterial coverage increased corresponding to early mycobacterial detection with NGS. This study highlights the importance of clinical judgement in the age of rapid diagnostics.
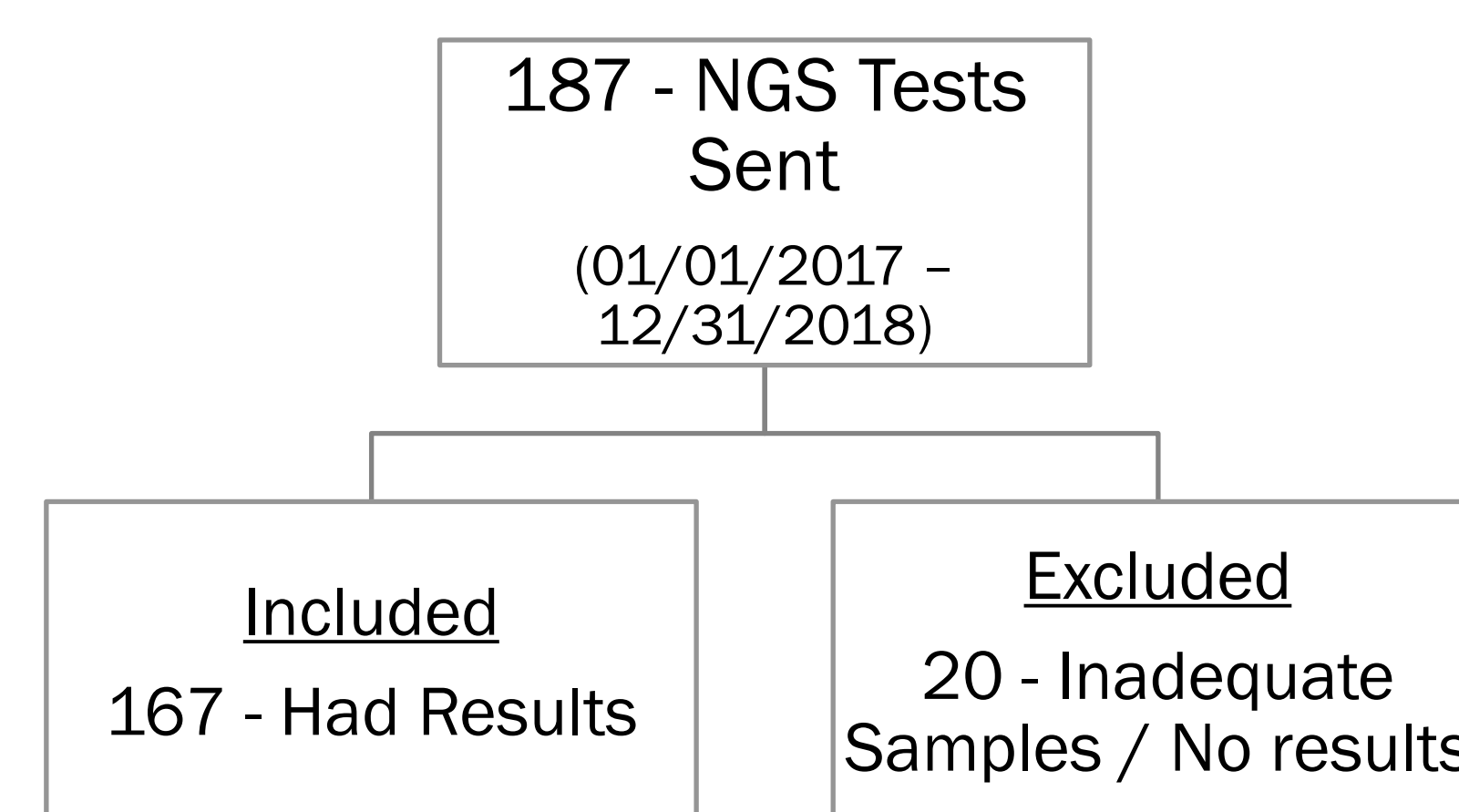
Aims and Methods

AIM:
- To describe change in management in antibiotic choice *before* and after a NGS test
  - Number of antibiotics used
  - Change in treatment (based on pathogen coverage)

Exclusion:
- Less than 18 years old
- NGS tests that did not have a result due to inadequate/inappropriate sample

Figure 1. Next Generation Sequencing Test Breakdown

187 - NGS Tests Sent (01/01/2017 – 12/31/2018)

Included 167 - Had Results

Excluded 20 - Inadequate Samples / No results

Results

Table 1. Demographic and Laboratory Characteristics

Variable	Total N (%/SD) N=167	NGS + (%/SD) N=118	NGS - (%/SD) N=49	P-Value
Age (mean, SD)	52 (16)	51 (16)	54 (15)	0.26
Gender				
Male	116 (69%)	83 (70%)	33 (67%)	0.70
Female	51 (31%)	35 (30%)	16 (33%)	
Race				
Caucasian or White	106 (63%)	75 (64%)	31 (63%)	0.87
Black or African American	38 (23%)	28 (24%)	10 (20%)	
Asian	13 (8%)	9 (8%)	4 (8%)	
Others	10 (6%)	6 (5%)	4 (8%)	
Ethnicity				
Hispanic	36 (22%)	27 (23%)	9 (18%)	0.44
Not Hispanic	129 (77%)	89 (75%)	40 (82%)	
Unable to Determine	2 (1%)	2 (2%)	0 (0%)	
Charlson's Comorbidity Index (mean, SD)	3.70 (2.79)	3.74 (2.76)	3.61 (2.87)	0.79
Immune System Status				
Immunocompetent	106 (64%)	75 (64%)	31 (63%)	0.97
Immunosuppressed	61 (36%)	43 (36%)	18 (37%)	
HIV-AIDS	14 (23%)	13 (30%)	1 (6%)	
Neutropenic	3 (5%)	2 (5%)	0 (0%)	
Solid Organ Transplant	30 (49%)	21 (49%)	9 (50%)	
Hematopoietic Stem Cell Transplant	1 (2%)	0 (0%)	1 (6%)	
Rheumatological	12 (20%)	7 (16%)	5 (28%)	
Others	1 (2%)	0 (0%)	1 (6%)	
Approved Indications for Testing	107 (64%)	79 (67%)	28 (57%)	0.23
Culture Negative Endocarditis	15 (9%)	10 (8%)	5 (10%)	
Fever of Unknown Origin	26 (16%)	20 (17%)	6 (12%)	
HIV/AIDS with Fever	10 (6%)	9 (8%)	1 (2%)	
Transplant with Fever	5 (3%)	4 (3%)	1 (2%)	
Systemic/Deep Seated Infection Where Biopsy or Other Workup is Negative or Not Possible	50 (30%)	35 (29%)	15 (31%)	
Others	60 (36%)	39 (33%)	21 (43%)	
Waiting Period (mean, SD)				
Days between Collected and Received	2 (1)	2 (1)	2 (1)	
Days between Collected and Reported	3 (1)	3 (1)	3 (1)	

Results

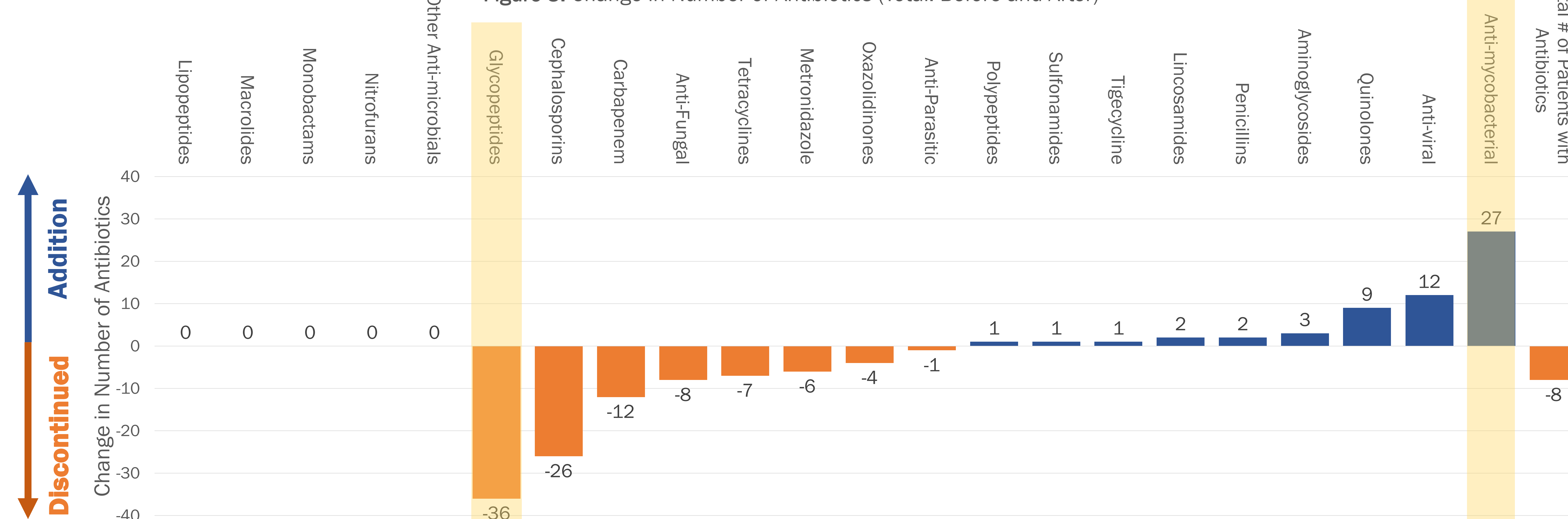Figure 3: Change in Number of Antibiotics (Total: Before and After)

Figure 4. Indications for Testing and Change in Number of Antibiotics (p=0.148)

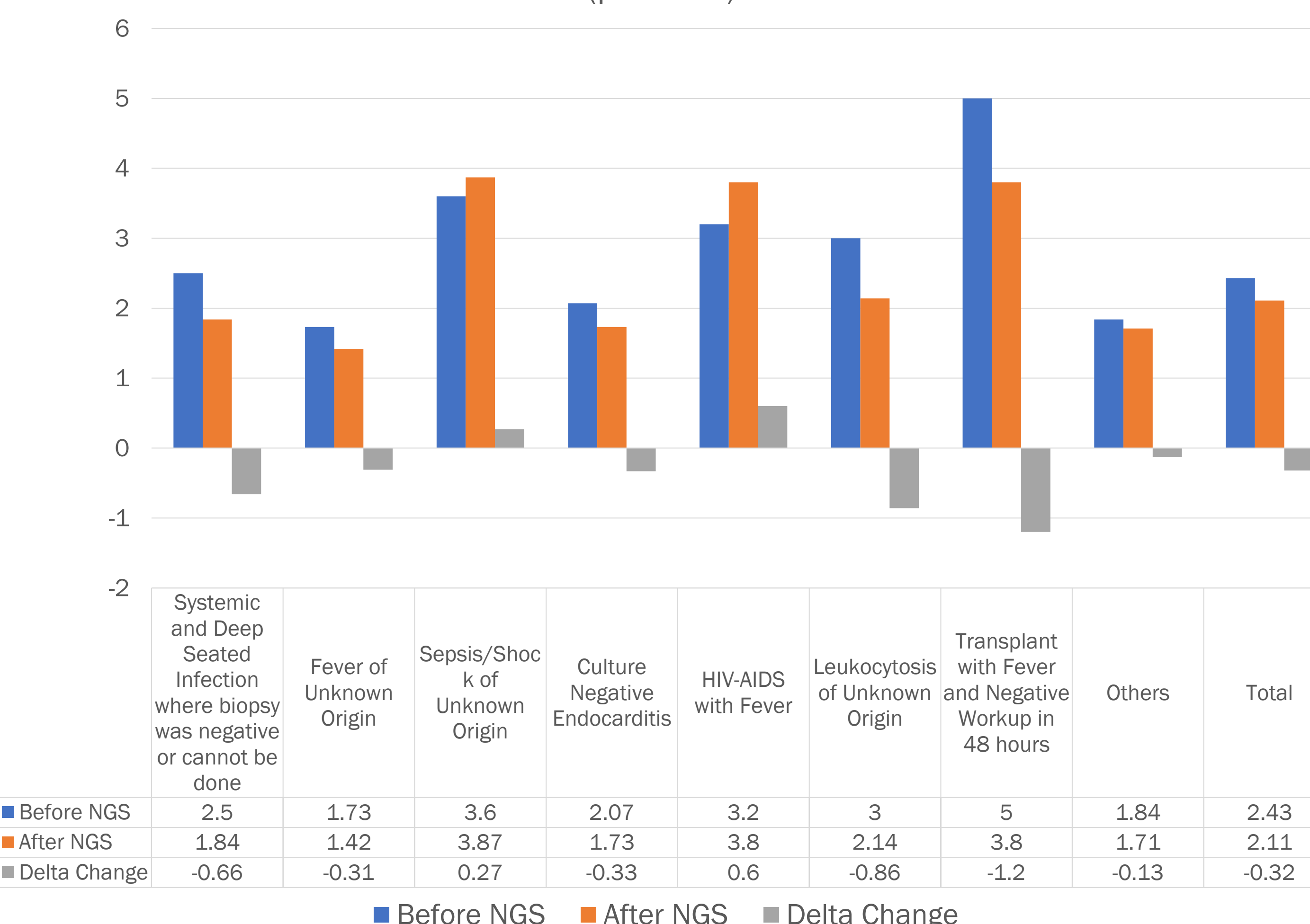|	Systemic and Deep Seated Infection where biopsy was negative or cannot be done	Fever of Unknown Origin	Sepsis/Shock of Unknown Origin	Culture Negative Endocarditis	HIV-AIDS with Fever	Leukocytosis of Unknown Origin	Transplant with Fever and Negative Workup in 48 hours	Others	Total
Before NGS	2.5	1.73	3.6	2.07	3.2	3	5	1.84	2.43
After NGS	1.84	1.42	3.87	1.73	3.8	2.14	3.8	1.71	2.11
Delta Change	-0.66	-0.31	0.27	-0.33	0.6	-0.86	-1.2	-0.13	-0.32

Figure 5. Indications for Testing and Change in Antimicrobial Coverage (p=0.546)
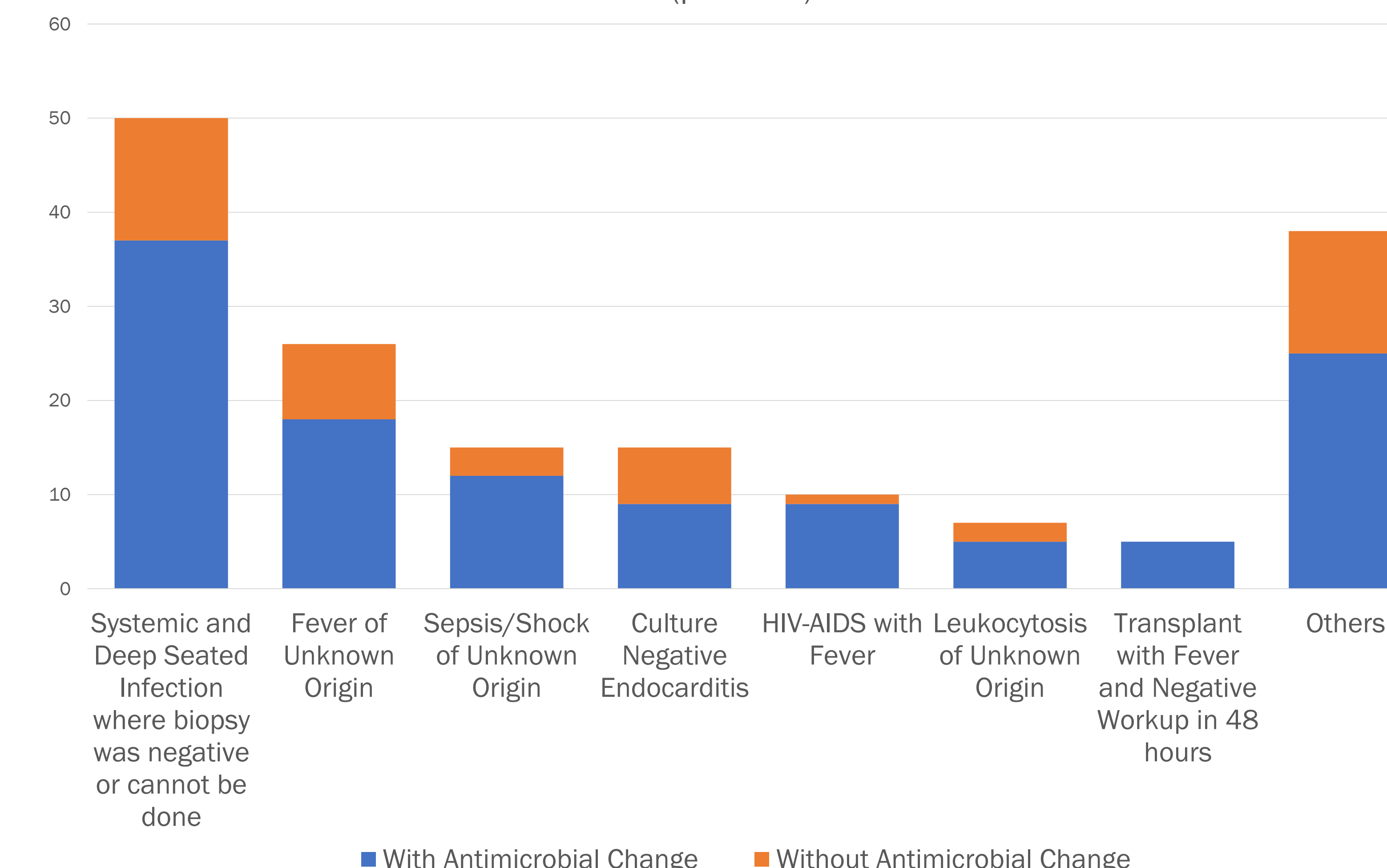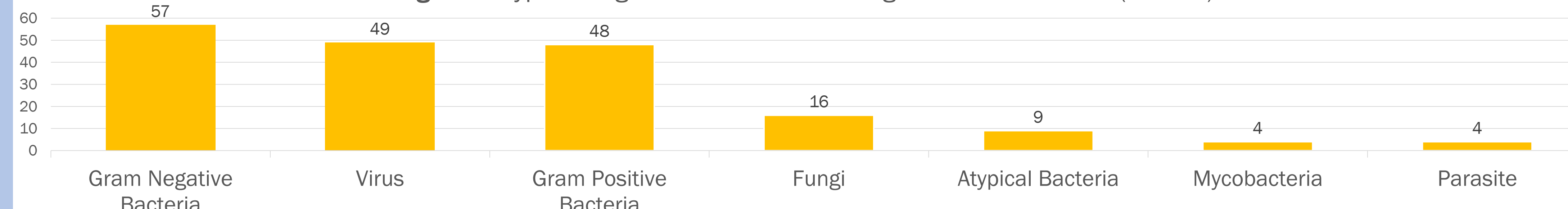

Figure 2: Type of Organism Identified Among Positive NGS Tests (N=118)

References

Blauwkamp TA, Thair S, Rosen MJ, et al. Analytical and clinical validation of a microbial cell-free DNA sequencing test for infectious disease. Nature Microbiology. 2019;4(4):663-674. doi:10.1038/s41564-018-0349-6

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