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Antibiograms Cannot Be Used Interchangeably Between Acute Care Medical Centers and Affiliated Nursing Homes

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Title: Antibiograms Cannot be Used Interchangeably between Acute-Care Medical Centers and Affiliated Nursing Homes

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Brief Summary: We found that antibiograms did not agree between nursing homes and medical centers across the Veterans Health Administration. This suggests that acute-care antibiograms should not be used in affiliated nursing homes.

Abstract

Objective: To determine whether antibiograms for Veterans Affairs (VA) nursing homes (NHs), termed Community Living Centers, are similar to their affiliated acute-care medical centers.

Design: Descriptive study.

Setting and Participants: We compared the 2017 antibiograms for VA NHs to their affiliated VA medical centers (VAMCs). Antibiograms included antibiotic susceptibility rates for commonly observed bacteria in this setting (*Staphylococcus aureus*, *Enterococcus spp.*, *Escherichia coli*, *Klebsiella spp.*, *Proteus mirabilis*, and *Pseudomonas aeruginosa).*

Methods: Antibiograms were considered to be in complete agreement when the overall susceptibility rate between the NH and affiliated VAMC was either at or above 80% or below 80% across all bacteria and antibiotics. Average percent of bacteria-antibiotic comparisons in disagreement per facility pair, and number of facilities with agreement for specific bacteria-antibiotic comparisons were also assessed. The Chi-square test was used to compare disagreement between NH-VAMC facilities based on geographic proximity of the NH to the VAMC, culture source, and bed size.

Results: A total of 119 NH-VAMC affiliate pairs were included in this analysis, with 71% (84/119) on the same campus and 29% (35/119) on geographically distinct campuses. None of the NH-VAMC pairs demonstrated complete agreement (all bacteria versus all antibiotics) between their antibiograms. On average, 20% of the bacteria-antibiotic comparisons from the antibiogram disagreed clinically per NH-VAMC pair, and almost twice as often it was the nursing home that had the lower susceptibility (higher

resistance) than the acute-care facility. Some bacteria-antibiotic comparisons agreed in all facilities (e.g. *E. coli*-imipenem; *S. aureus*-linezolid; *S. aureus*-vancomycin), while others showed greater disagreement (e.g. *Klebsiella spp.*-cefazolin; *Klebsiella spp.*-ampicillin/sulbactam; *P. aeruginosa*-ciprofloxacin). Rates of clinical disagreement were similar by geographic proximity of the NH to the VAMC, culture source, and bed size. Conclusions and Implications: Overall, this study showed a moderate lack of agreement between VA NH antibiograms and their affiliate VAMC antibiograms. Our data suggest that antibiograms of acute-care facilities are often not accurate approximations of the nursing home resistance patterns and therefore should be used with caution if at all in guiding empiric antibiotic therapy.

Introduction

Antibiograms are profile reports of antibiotic susceptibility rates of bacteria from a single facility over a duration of one calendar year.[1] These reports are used to guide empiric antibiotic prescribing and to track emerging bacterial resistance within the facility. They are especially informative for antimicrobial stewardship practices that help guide appropriate empiric prescribing when waiting for culture results.[2-5] Unfortunately, due to a lack of resources and a low number of clinical cultures, the creation of antibiograms in nursing home (NH) settings can often be challenging.[6,7] To overcome these barriers, some NHs may use antibiograms from nearby or affiliated acute-care facilties.[8]

The rationale for NH use of acute-care facility antibiograms is that NH residents are often admitted to nearby acute-care facilities, and there are high rates of bidirectional patient movement and pathogen transmission between the two settings.[9-11] The same rationale supports the use of regional antibiograms when facility-specific antibiograms are unavailable.[1,12] Despite this convention, there are no studies that assess whether antibiograms from acute-care settings can be applied to NHs. Specifically, it is largely unknown if the susceptibly profiles amongst NHs and their affiliated acute-care facilities are similar enough to produce the same empiric antibiotic treatment recommendations and if providers can use acute-care antibiograms to make decisions about empiric antibiotic therapy in NHs. To address this question, we evaluated culture results from a national cohort from the Veterans Health Administration to develop antibiograms for individual Veterans Affairs (VA) Community Living Centers, herein termed VA NHs, and

compared them to the antibiograms for their affiliated acute-care VA medical centers (VAMCs).

Methods

VA NHs and VAMC pairs. Culture and susceptibility results from Veterans admitted to VA NHs and their affiliated VAMCs from January 1st, 2017 through December 31st, 2017 were included (n= 119 NH-VAMC pairs). NH campuses were classified by the project coordinator of this study as either being geographically similar or distinct from their affiliate VAMC based on an email and/or telephone query of medical directors, or chiefs of service. VA NHs that were reported to be on the same building or in a separate building contiguous with the affiliated VAMC were classified as "same" campus NH-VAMC pairs; all others were classified as "remote" campus NH-VAMC pairs.

Culture and Susceptibility Data. We evaluated the following pathogens: *Staphylococcus aureus*, *Enterococcus spp.*, *Escherichia coli*, *Klebsiella spp.*, *Proteus mirabilis*, and *Pseudomonas aeruginosa.* For each bacterial species, susceptibility rates to several commonly used antibiotics were assessed including nine antibiotics for the Gram-negative bacteria and nine antibiotics for the Gram-positive bacteria.

Antibiograms. Antibiograms were created for all individual VA NHs and VAMCs for the calendar year of 2017 according to Clinical and Laboratory Standards Institute (CLSI) recommendations of using the first clinical isolate cultured per patient per bacterial species (regardless of specimen source) for percent susceptibility calculations.[1] The

percent susceptibility was calculated by dividing the number of susceptible isolates by the total number of isolates tested against that antibiotic multiplied by 100. All isolates of the aforementioned bacterial species were included, regardless if there were <30 isolates per year, which are typically removed from antibiogram reports in clinical use as recommended by CLSI.[1]

Weighted national antibiograms were created for all VA NHs and VAMCs for 2017 and VA NH-VAMC differences in weighted percent susceptibilities, as well as carbapenem resistance and multi-drug resistance rates, were compared using Chi-square tests. *E. coli*, *Klebsiella spp.*, and *P. mirabilis* carbapenem-resistant isolates were defined as resistant to ≥1 carbapenem (doripenem, ertapenem, imipenem, or meropenem), with the same definition used for *P. aeruginosa* with the exception of ertapenem, which is not an anti-pseudomonal carbapenem. *E. coli*, *Klebsiella spp.*, and *P. mirabilis* multidrug-resistant isolates were defined as resistant to at least one drug in at least three of the following categories: 1) extended-spectrum cephalosporins (cefepime, cefotaxime, ceftazidime, ceftriaxone), 2) fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin), 3) aminoglycosides (amikacin gentamicin, tobramycin), 4) carbapenems (imipenem, meropenem, doripenem, ertapenem), or 5) piperacillin group (piperacillin, piperacillin/tazobactam), with the same definition used for *P. aeruginosa* with the exception of the antibiotics that do not have anti-pseudomonal activity (cefotaxime, ceftriaxone, moxifloxacin, doripenem).[13]

Analyses of Clinical Agreement between Antibiograms. VA NH antibiograms were compared to each affiliate VAMC antibiogram for clinical agreement for each bacteria-antibiotic combination. Clinical practice guidelines from the Infectious Diseases Society of America (IDSA) suggest that an antibiotic is appropriate for empiric treatment if the percent susceptibility on an antibiogram is ≥ 80%.[14,15] Therefore, NH-VAMC pairs were defined as agreeing clinically if the percent susceptibility for the bacteria-antibiotic combination was ≥80% in both the NH and VAMC, or <80% in both the NH and VAMC. Complete agreement was defined as agreement for all bacteria-antibiotic comparisons per NH-VAMC pair.

Disagreement was defined as differences in the percent susceptibility between the NH and VAMC for the bacteria-antibiotic combination, where the percent susceptibility was ≥80% in one facility and <80% in the other facility. Average percent of bacteria-antibiotic comparisons which clinically disagreed per facility were calculated. Clinical disagreement was assessed by type of disagreement (NH susceptibility ≥80% and VAMC susceptibility <80%, or NH susceptibility <80% and VAMC susceptibility ≥80%), geographic proximity of the NH to the VAMC, culture source, and bed size. Number of facilities with agreement for specific bacteria-antibiotic comparisons were also assessed.

The Chi-square test was used to compare the proportion of agreement between NH-VAMC facilities that were on the same campus versus those on geographically distinct campuses. Bonferroni corrections were performed to correct for multiple comparisons

(e.g. comparison of 9 antibiotic susceptibilities for *E. coli*, p-value (α) = 0.05/9 = 0.006). To determine whether agreement was greater for certain antibiotics, Kappa statistics were calculated for the percent of agreement between facilities by antibiotic.

Results

A total of 119 NH-VAMC affiliate pairs were included in this analysis, with 71% (84/119) on the same campus and 29% (35/119) on geographically distinct campuses. None of the NH-VAMC pairs demonstrated complete agreement in their antibiograms. On average, 20% of the bacteria-antibiotic comparisons from the antibiogram disagreed clinically per NH-VAMC pair (**Table 1**). Disagreement, where NH susceptibility was <80% and VAMC susceptibility was ≥80%, accounted for 13% of the disagreement versus 7% where the resistance was higher in the VAMC. Rates of clinical disagreement were similar by geographic proximity of the NH to the VAMC, culture source, and bed size.

Some bacteria-antibiotic comparisons agreed in all facilities (*E. coli*-imipenem; *S. aureus*-linezolid; *S. aureus*-vancomycin), while others showed greater disagreement (*Klebsiella spp.*-cefazolin; *Klebsiella spp.*-ampicillin/sulbactam; *P. aeruginosa*-ciprofloxacin). **Figures 1a-1f** show the agreement rate for each antibiotic-bacteria combination assessed. Since not every NH or VAMC had a culture for each of the 6 organisms or 18 antibiotics assessed, the maximum number of NH-VAMC pairs available for inclusion for a specific bacteria-antibiotic combination in the comparisons was 114 and the minimum was 29. Greater clinical agreement was observed between

VA NHs and VAMCs for imipenem (Kappa statistic 0.73) and nitrofurantoin (0.71) among the Gram-Negatives, and linezolid (0.66) among the Gram-Positives. For the remaining antibiotics antibiotic-specific clinical agreement was lower (Kappa less than 0.50; Figure 1).

Statistically significant differences were observed in weighted percent susceptibilities between VA NHs and VAMCs, all in which the VA NHs had lower susceptibilities than the VAMCs (**Table 2a and 2b**). With the exception *of P. aeruginosa*-ciprofloxacin, both the VA NH and VAMC susceptibilities either fell below the 80% susceptibility threshold or above the threshold and therefore would not have indicated different clinical decisions in most scenarios. Multidrug-resistant and carbapenem-resistant rates of the included Gram-negative bacteria were found to be similar between VA NHs and VAMCs (**Table 2a**).

Discussion

We found none of the VA NH antibiograms and their affiliate VAMC antibiograms had complete clinical agreement, suggesting that antibiograms of acute-care facilities, should not be used to guide therapy in affiliated nursing homes. Our study demonstrated that clinical similarities and differences exist between annual antibiograms in NHs and affiliate medical centers. The average percent clinical disagreement rate between the NH and affiliate medical center antibiograms was 20% and the agreement rate varied greatly from 55-100% among the specific bacteria-antibiotic combination assessed. These results suggest that NHs may have similar rates

of susceptibility to their affiliate medical center that will result in similar empiric prescribing decisions in certain scenarios, but not all of the time. Moreover, higher rates of clinical agreement (82%-100%) were observed for most broad-spectrum intravenous antibiotics such as cefepime, linezolid, and daptomycin. These antibiotics are often reserved for treatment of severe acute infections that require inpatient hospitalization and are not commonly used in NHs.[16] Lower rates of agreement (56-83%) were observed for orally available antibiotics such as ciprofloxacin and sulfamethoxazole-trimethoprim. Since these agents tend to be commonly prescribed in the NH setting, this further suggests that antibiograms of acute-care facilities should not be used to guide therapy in affiliated nursing homes.[16-18]

Describing the similarities helps to determine if utilizing affiliate medical center antibiograms is an appropriate practice within NHs that either cannot make antibiograms of their own or have few bacteria isolated. Studies have shown that antibiotic-resistant bacteria are more prevalent in NH populations than other populations, but it has been unclear if such differences would be large enough to change empiric prescribing recommendations.[19] For example, one study found that when compared to the general community patients, those ≥65 years of age who resided in a single nursing home were found to have more methicillin-resistant *Staphylococcus aureus* (MRSA) from all culture sites and more resistant Enterobacteriaceae from urine cultures over a 5 year period.[20] Additionally, other studies have argued the importance of creating antibiograms specific to special populations and facilities due to differences in susceptibility rates of specific bacteria to antibiotics.[21-24] For example, community-

acquired compared to nosocomial-acquired *E. coli* infections in an 860-bed tertiary hospital in Zurich, Switzerland were found to be less susceptible to sulfamethoxazole/trimethoprim (susceptibility rate of 70% vs. 67%, p=0.006).[25] Although the susceptibility rates differed statistically, the rates of both 70% and 67% would make sulfamethoxazole/trimethoprim a poor empiric therapy option for *E. coli* coverage. Therefore, our study interprets the differences in NH and affiliate medical center antibiograms that would likely correlate with different empiric prescribing recommendations.

As use of the affiliate hospital antibiogram is unreliable for commonly used antibiotics within the NH, potential other solutions to decide appropriate treatment may include extending the time period of the antibiogram data collection beyond one year, collapsed antibiograms specific to specimen site/infection type, and NH antibiograms including bacteria species regardless of low isolate numbers.[8] Although some of the approaches would help circumvent the issue of low isolate numbers, they still may not be representative of the bacteria acquired within the NH, and it is not yet elucidated which of these approaches best informs empiric prescribing. Additionally, several other patient-specific considerations aside from just the antibiogram data, such as prior infection history, need to be considered when empirically prescribing an antibiotic.[26,27] Exactly how to integrate the use of the antibiogram into clinical practice within a NH is also currently unknown.

This work is limited in that this is a Veteran population which may differ from other NH populations considering many facilities were on the same campus as their affiliate

medical center, and it is a unique closed healthcare system. Additionally, only culture data that was entered into the VA microbiology system were included, and as such cultures obtained from facilities outside the VA may not be completely captured if they were not manually entered into that resident's electronic medical record. While some NH-VAMC pairs use the same microbiology laboratory, others use different laboratories. Culture practices are not standardized throughout the VA, therefore some may have implemented the 2010 CLSI updated breakpoints for Enterobacteriaceae and *P. aeruginosa* while others may not have.[28] Tested antibiotics and bacteria combinations also may have differed, and overall the susceptibility interpretations of the testing microbiology laboratories were relied on. Another limitation is that an 80% susceptibility cut-off was used in this study and other clinicians may use different cut-offs to guide empiric antibiotic choices within their institutions. Further, positive cultures of any source (e.g. skin/soft tissue, urine, and respiratory cultures) could represent colonization and/or contamination rather than infection. Lastly, many of the nursing homes had few cultures to assess, depending on the organism, which affects the accuracy of the susceptibility estimate.

Conclusions and Implications

Overall, this study showed a lack of complete agreement between VA NH antibiograms and their affiliate VAMC antibiograms and a wide range of agreement among the specific bacteria-antibiotic combination assessed. Although this work was limited to the Veteran population, we demonstrated that even in a closed health-care system, where the majority of NH patients may come from a single acute-care facility, the extent of

disagreement limits the use of susceptibility data from acute-care hospitals. This may result from differences in the patient populations, culture practices, length of stay, and antibiotic use between NHs and hospitals. Other nursing homes outside the VA system, even those which receive the majority of their patients from a single acute-care facility, should reconsider using that acute-care hospital's susceptibility data. Our data suggests that antibiograms of acute-care facilities should be used with caution if at all in guiding empiric antibiotic therapy within nursing homes.

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Figure caption:

Figures 1a-1f: Percent of Nursing Homes and Affiliated Medical Centers with Clinical Agreement in Bacteria-Specific Antimicrobial Susceptibility

The above figures indicate the percent of nursing homes and affiliated medical center pairs with clinical agreement for specific bacteria-antibiotic combinations. Agreement between NH-VAMC pairs was defined as NH and VAMC susceptibilities both ≥80% or both NH and VAMC susceptibilities <80%. Antibiotic-specific Kappa statistics for Gram-Negative organisms in NHs versus VAMCs were: ampicillin/sulbactam 0.38, cefazolin 0.29, cefepime 0.22, ceftriaxone 0.27, ciprofloxacin 0.48, imipenem 0.73, nitrofurantoin 0.71, piperacillin/tazobactam 0.07, and sulfamethoxazole/trimethoprim 0.43. Antibiotic-specific Kappa statistics for Gram-Positive organisms in NHs versus VAMCs were: ampicillin 0.22, clindamycin 0.12, gentamicin 0.50, linezolid 0.66, oxacillin 0.23, tetracycline 0.01, vancomycin 0.24.

Antibiotic abbreviations: amp/sulb=ampicillin/sulbactam; pip/tazo=piperacillin/tazobactam; sulfa/trimeth=sulfamethoxazole/trimethoprim.

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Table 1: Percent of bacteria-specific antimicrobial susceptibilities with clinical disagreement between the nursing home and affiliated medical center

	Number of nursing home and affiliated medical center pairs	Mean	Standard deviation	Median	Interquartile range
All NH-VAMC pairs	119	20%	8%	19%	14-24%
NH susceptibility ≥80%, VAMC susceptibility <80%	119	7%	5%	5%	3-10%
NH susceptibility <80%, VAMC susceptibility ≥80%	119	13%	8%	12%	6-17%
Campus					
Remote campus	35	19%	8%	20%	13-24%
Same campus	84	20%	8%	19%	15-24%
Culture source					
Urine	117	21%	9%	20%	15-27%
Skin/Soft Tissue	114	23%	14%	21%	14-30%
Respiratory	57	24%	17%	25%	13-33%
Blood	73	26%	20%	25%	13-38%
Nursing home bed size					
<50 beds	32	21%	9%	21%	17-24%
50-99 beds	35	18%	7%	17%	13-22%
100-199 beds	45	20%	7%	19%	15-24%
>199 beds	7	18%	9%	17%	12-27%

NH = nursing home; VAMC = Veterans Affairs Medical Center.

Table 2a: Weighted Antibiotic Resistance and Susceptibility Rates for Gram-Negative Bacteria in VA NHs and VAMCs

Gram-Negative Organisms		%MDR	% Carbapenem resistance	Percent Susceptible								
				Ampicillin/ sulbactam	Cefazolin	Cefepime	Ceftriaxone	Ciprofloxacin	Imipenem	Nitrofurantoin	Piperacillin/ tazobactam	Trimethoprim-sulfamethoxazole
Escherichia coli	NH	8.4%	1.2%	46	66	89	80	53	100	94	92	67
	VAMC	6.7%	0.4%	52	73	92	84	65	100	96	95	71
	Diff. in %	1.7%	0.8%	-6*	-7*	-3	-4	-12*	0	-2	-3*	-4
Klebsiella spp.	NH	8.8%	1.9%	69	74	92	84	86	98	40	90	82
	VAMC	5.2%	1.1%	73	76	92	86	90	98	47	91	86
	Diff. in %	3.6%	0.8%	-4	-2	0	-2	-4*	0	-7*	-1	-4
Proteus mirabilis	NH	4.5%	19.0%	83	68	97	92	39	40	--	99	58
	VAMC	5.1%	18.6%	83	65	96	90	59	35	--	99	66
	Diff. in %	-0.6%	0.4%	0	3	1	2	-20*	5	--	0	-8*
Pseudomonas aeruginosa	NH	12.3%	15.2%	--	--	87	--	73	82	--	85	--
	VAMC	9.1%	13.4%	--	--	89	--	80	83	--	88	--
	Diff. in %	3.2%	1.8%	--	--	-2	--	-7*	-1	--	-3	--

MDR = multi-drug resistant; Diff. = difference.
*Statistically significant difference using Bonferroni correction for multiple comparisons.
Note: The percent of multi-drug resistant and carbapenem-resistant isolates are indicated in the corresponding columns. Otherwise the columns indicate percent susceptibility.

Table 2b: Weighted Antibiotic Susceptibility Rates for Gram-Positive Bacteria in VA NHs and VAMCs

Gram-Positive Organisms		Ampicillin	Clindamycin	Daptomycin	Gentamicin	Linezolid	Oxacillin	Tetracycline	Trimethoprim-sulfamethoxazole	Vancomycin
Staphylococcus aureus	NH	--	58	99	93	100	39	86	93	100
	VAMC	--	73	100	97	100	54	92	96	100
	Diff. in %	--	-15*	-1	-4*	0	-15*	-6*	-3	0
Enterococcus spp.	NH	88	--	99	58	99	--	--	--	84
	VAMC	88	--	100	70	99	--	--	--	87
	Diff. in %	0	--	-1	-12*	0	--	--	--	-3

Diff. = difference.
*Statistically significant difference using Bonferroni correction for multiple comparisons.

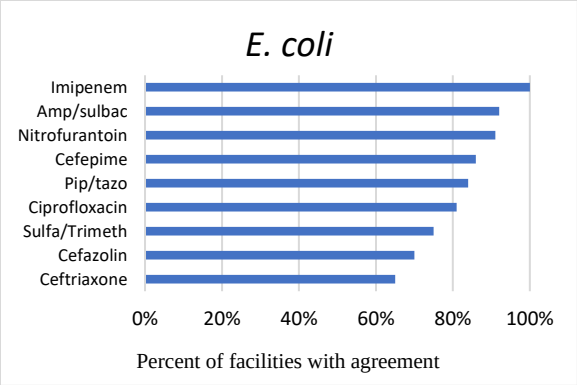

Figure 1a.

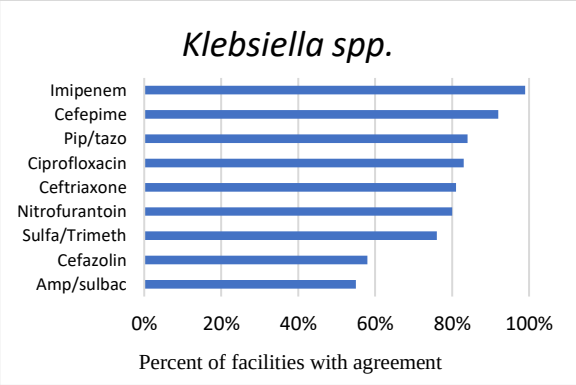

Figure 1b.

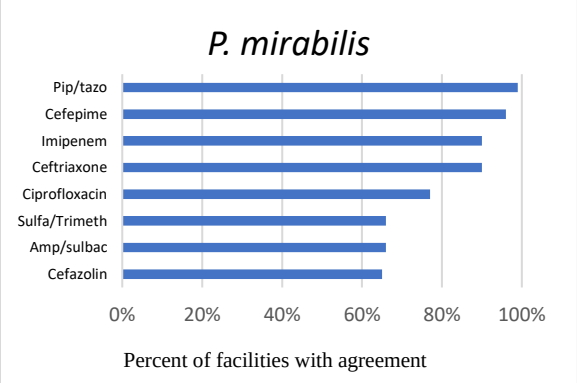

Figure 1c.

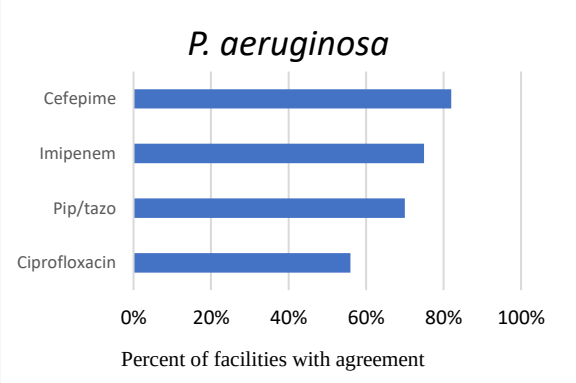

Figure 1d.

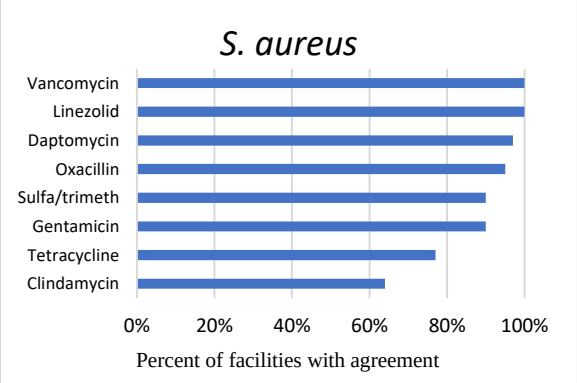

Figure 1e.

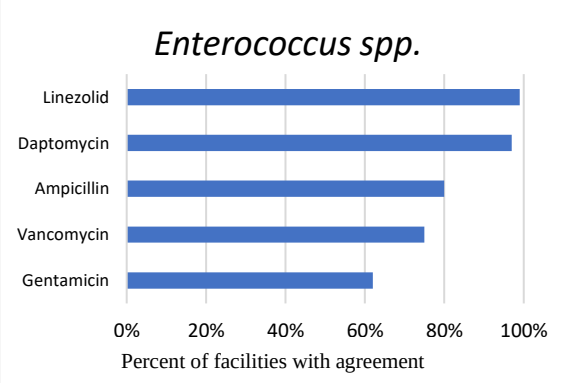

Figure 1f.