



INTRODUCTION

- Critically ill patients with pneumonia are frequently placed on broad-spectrum antibiotics even if they have few or no risk factors for antibiotic resistance
- Physicians feel uncomfortable not covering for the most resistant organisms in patients requiring intubation
- In general, these patients are changed from a typical community-acquired pneumonia regimen such as ceftriaxone and azithromycin to a broad-spectrum regimen to cover MRSA and *Pseudomonas aeruginosa*.
- Frequently the azithromycin which gives coverage for atypical organisms is removed at the same time.
- Unfortunately, guidance based on CAP vs HCAP vs HAP has not shown particular success in separating out who actually needs broad spectrum antibiotics and who does not.
- The DRIP score (Drug Resistance in Pneumonia) is an attempt to segregate patients based on clinical history (Table 1) into those who are more likely to need broad-spectrum antibiotics and those who are unlikely to need broad-spectrum antibiotics.
- Several hospitals who have implemented the DRIP score report significantly lower use of broad-spectrum antibiotics without negative consequences.

Characteristic	# of points
Major risk factors:	
Antibiotic use within previous 60 days	2
Residence in a long-term-care facility	2
Tube feeding	2
Prior infection with a DRP (1 yr)	2
Minor risk factors:	
Hospitalization within previous 60 days	1
Chronic pulmonary disease	1
Poor functional status	1
Gastric acid suppression	1
Wound care	1
MRSA colonization (1 yr)	1

Table 1: DRIP Score Contributing Factors

Organism	Resistance	Gene
Acinetobacter spp.	Carbapenem	kpc
Chlamydia pneumoniae		ndm
Citrobacter freundii		oxa-23
Enterobacter cloacae complex		oxa-24
Escherichia coli		oxa-48
Haemophilus influenzae		oxa-58
Klebsiella oxytoca		vim
Klebsiella pneumoniae		
Klebsiella variicola	3rd generation cephalosporins	ctx-M
Legionella pneumophila		
Moraxella catarrhalis		
Mycoplasma pneumoniae		
Mycobacterium abscessus		
Pseudomonas aeruginosa	Oxacillin/cefepime	mecA
Proteus spp.		
Pseudomonas aeruginosa		
Serratia marcescens		
Staphylococcus aureus	Penicillin	tem
Stenotrophomonas maltophilia		
Streptococcus pneumoniae		

Table 2: Unyvero LRTI Targets

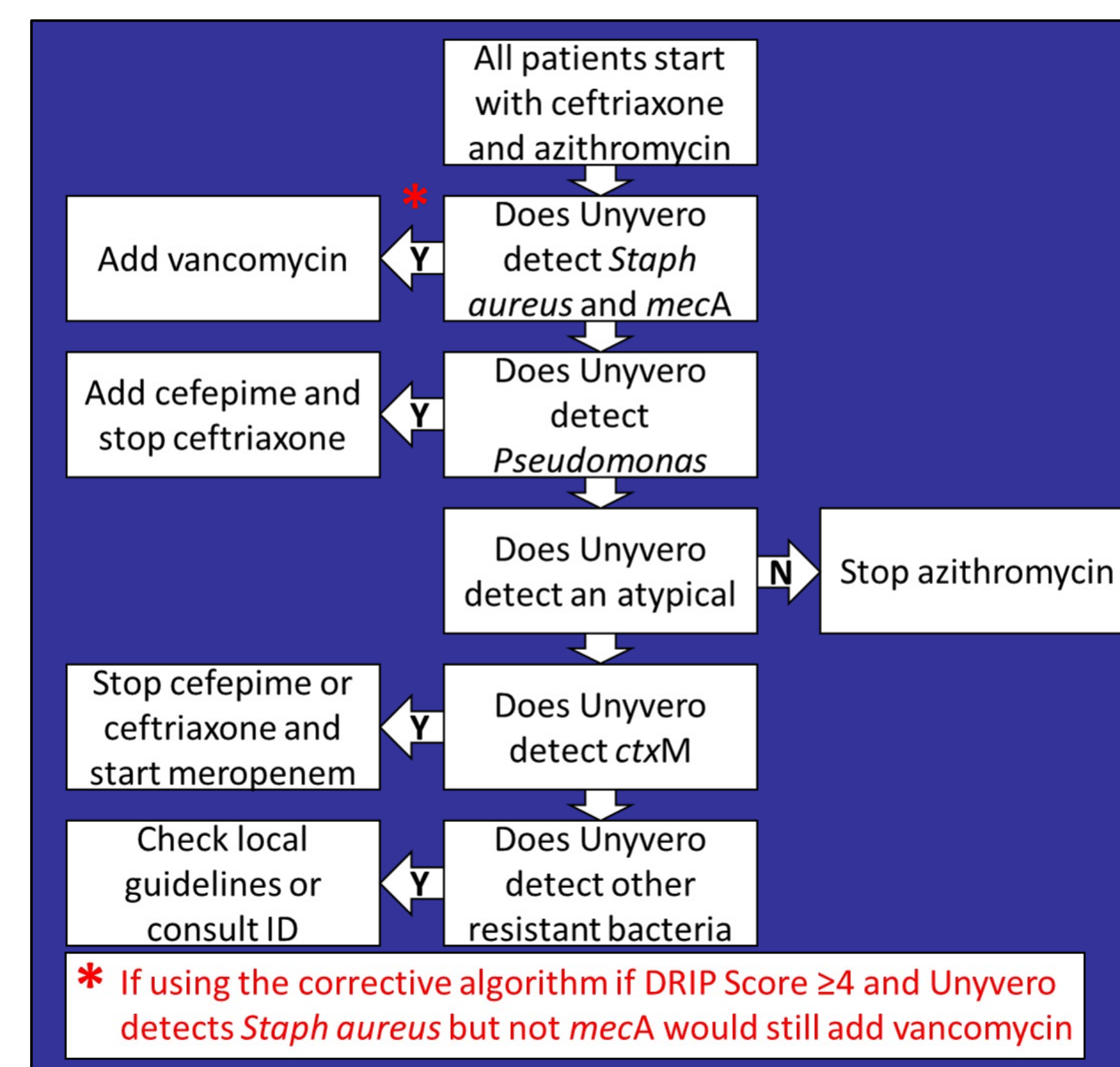


Figure 1: Unyvero Interpretive Algorithm + *Staph aureus* Correction Algorithm

DRIP Score	Additional Resistant Organisms Detected	Count
DRIP ≥4	ESBL Producer	15
	Acinetobacter	13
	Carbapenem Resistant Acinetobacter	9
	KPC Producer	2
	Legionella	2
	Mycoplasma	1
DRIP <4	ESBL Producer	1
	Acinetobacter	1
	Carbapenem Resistant Acinetobacter	0
	KPC Producer	0
	Legionella	0
	Mycoplasma	1
Stenotrophomonas maltophilia	7	
Total		80

Table 3: Other Antibiotic Resistant Organisms Detected by Unyvero In Cohort

RESULTS

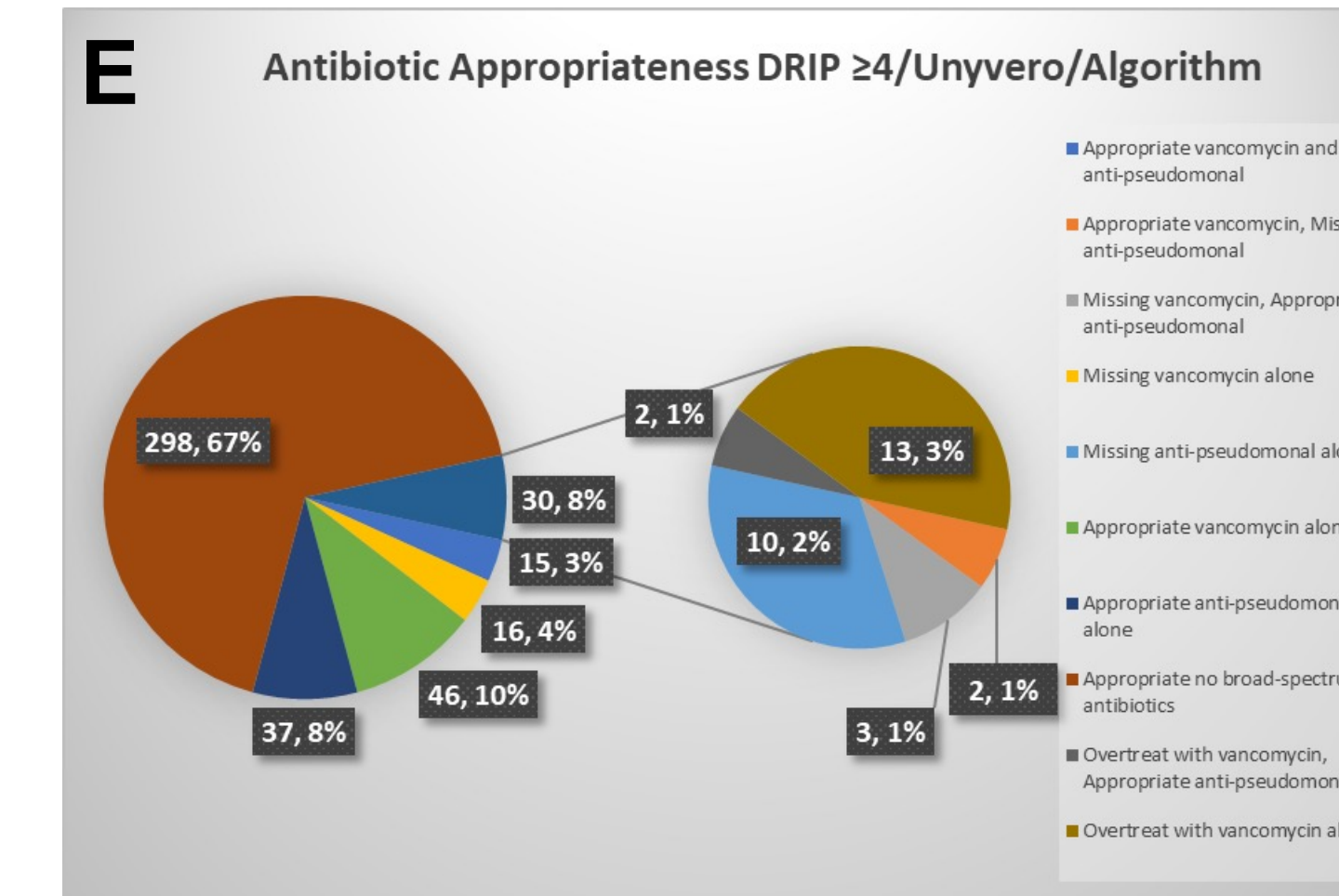
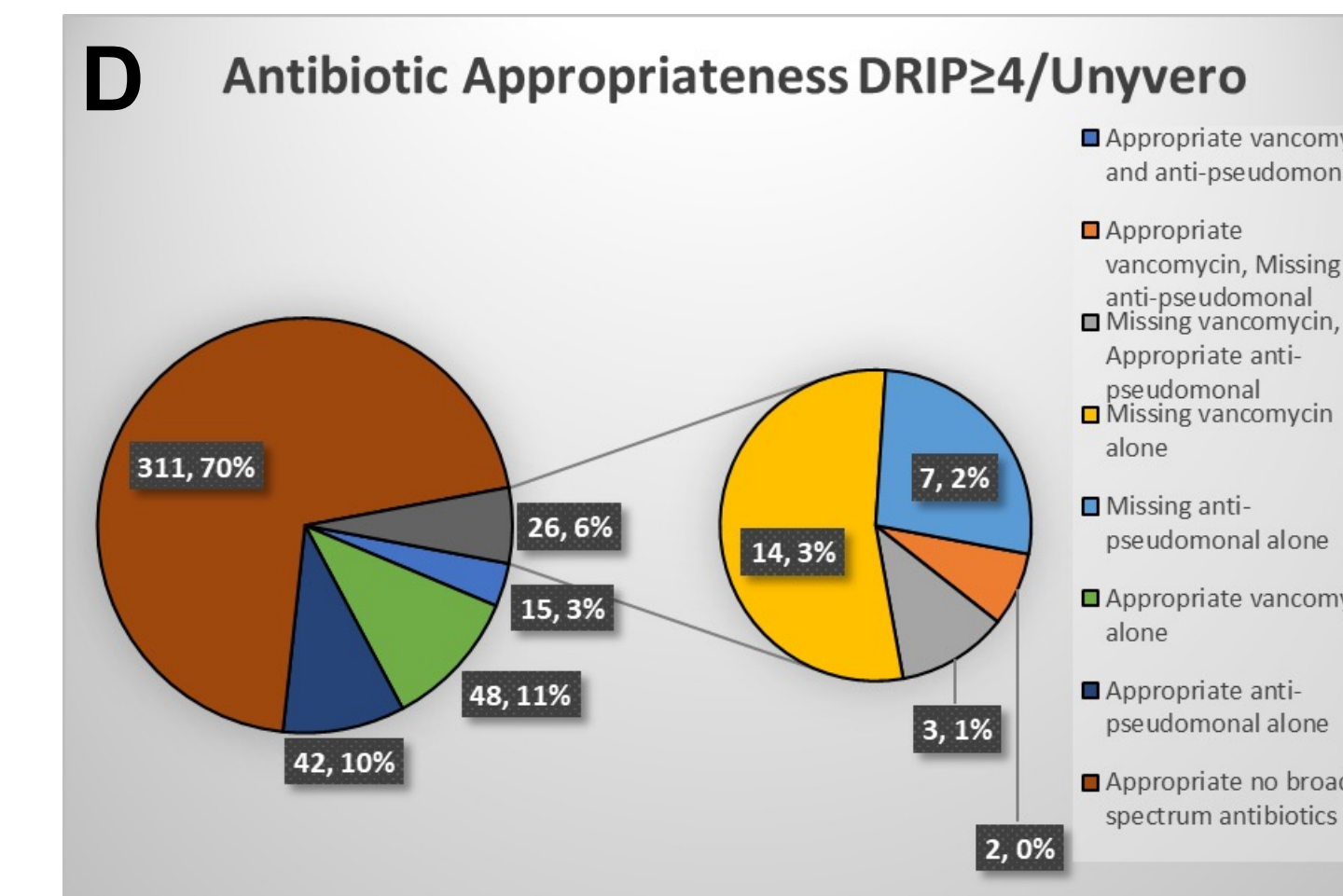
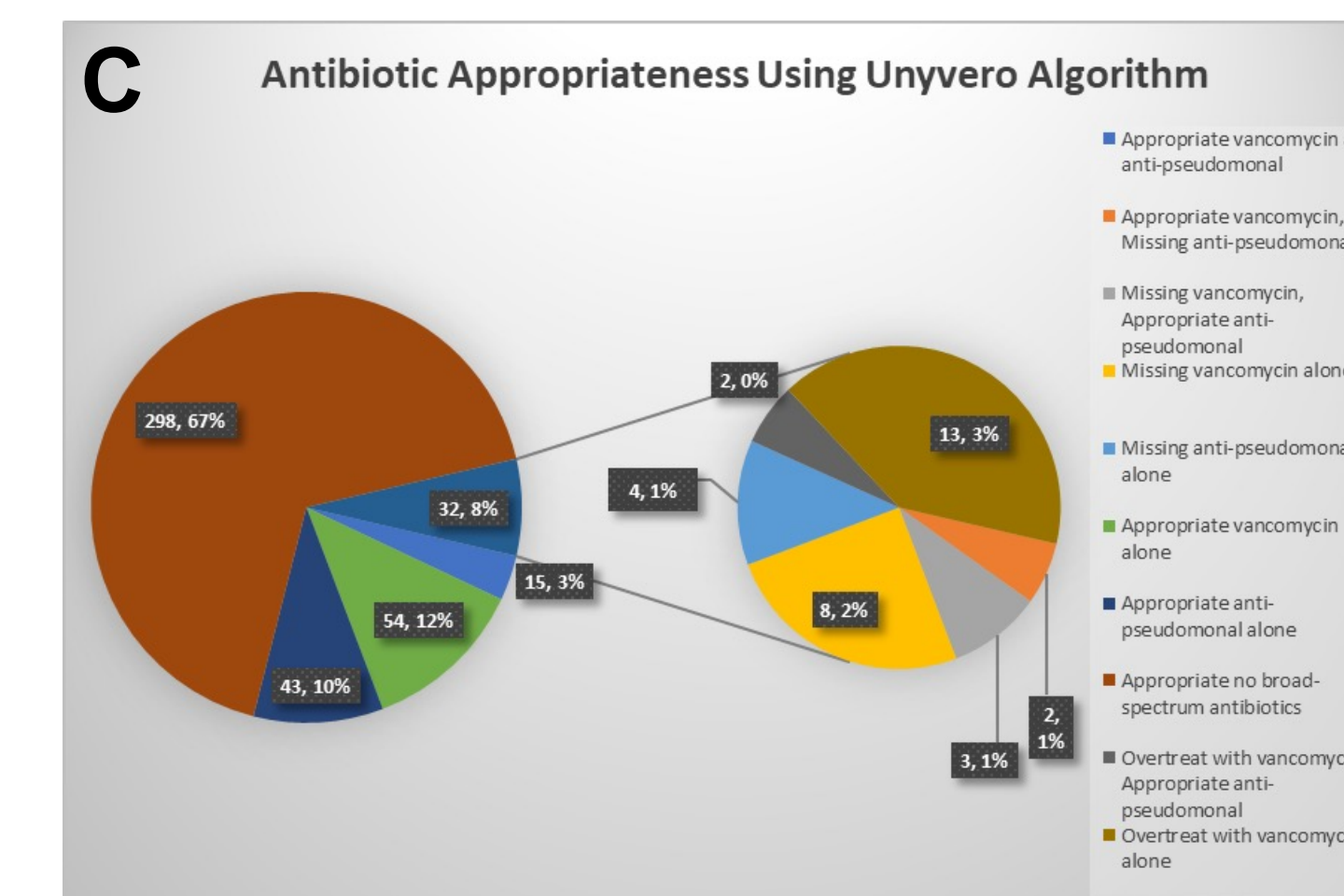
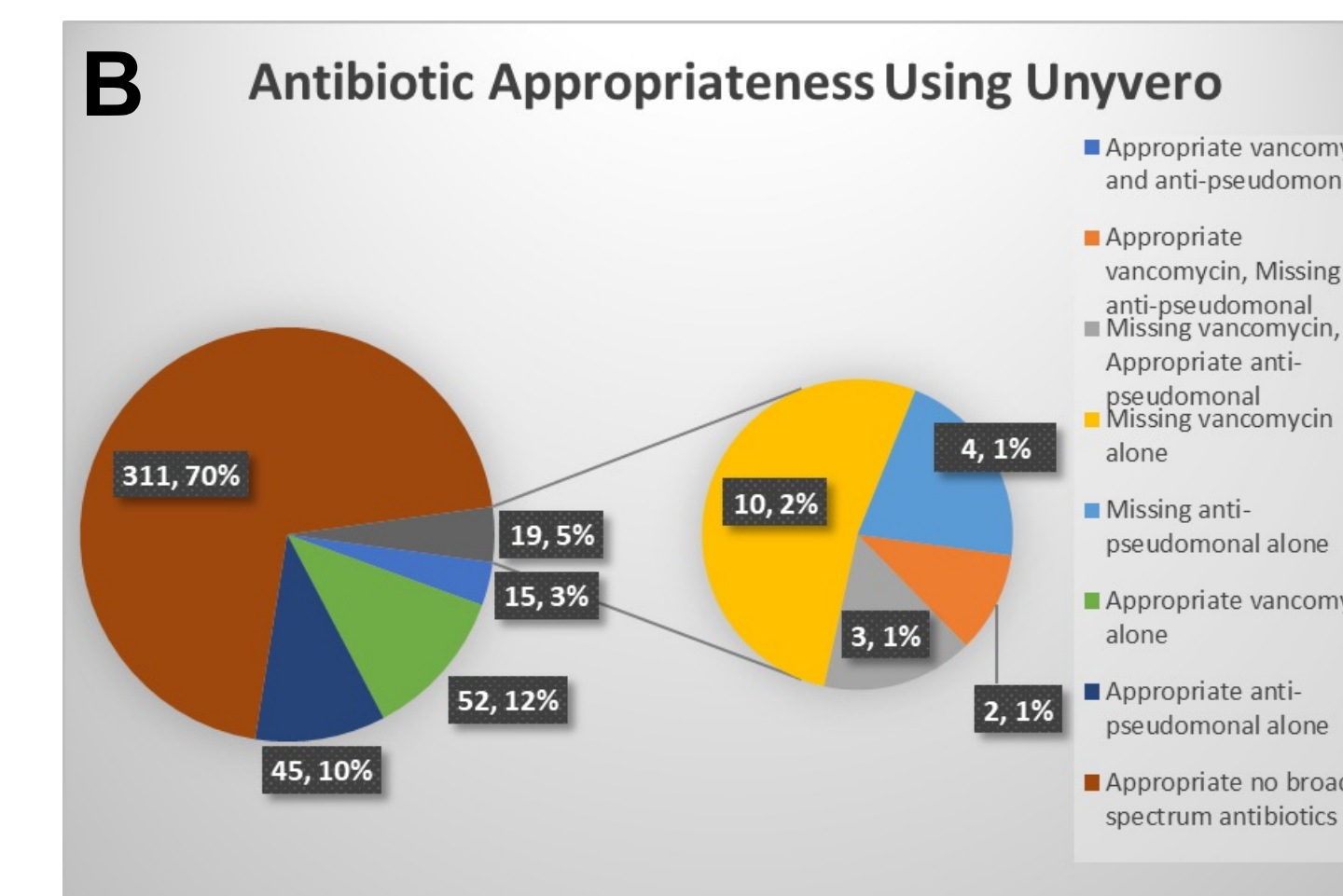
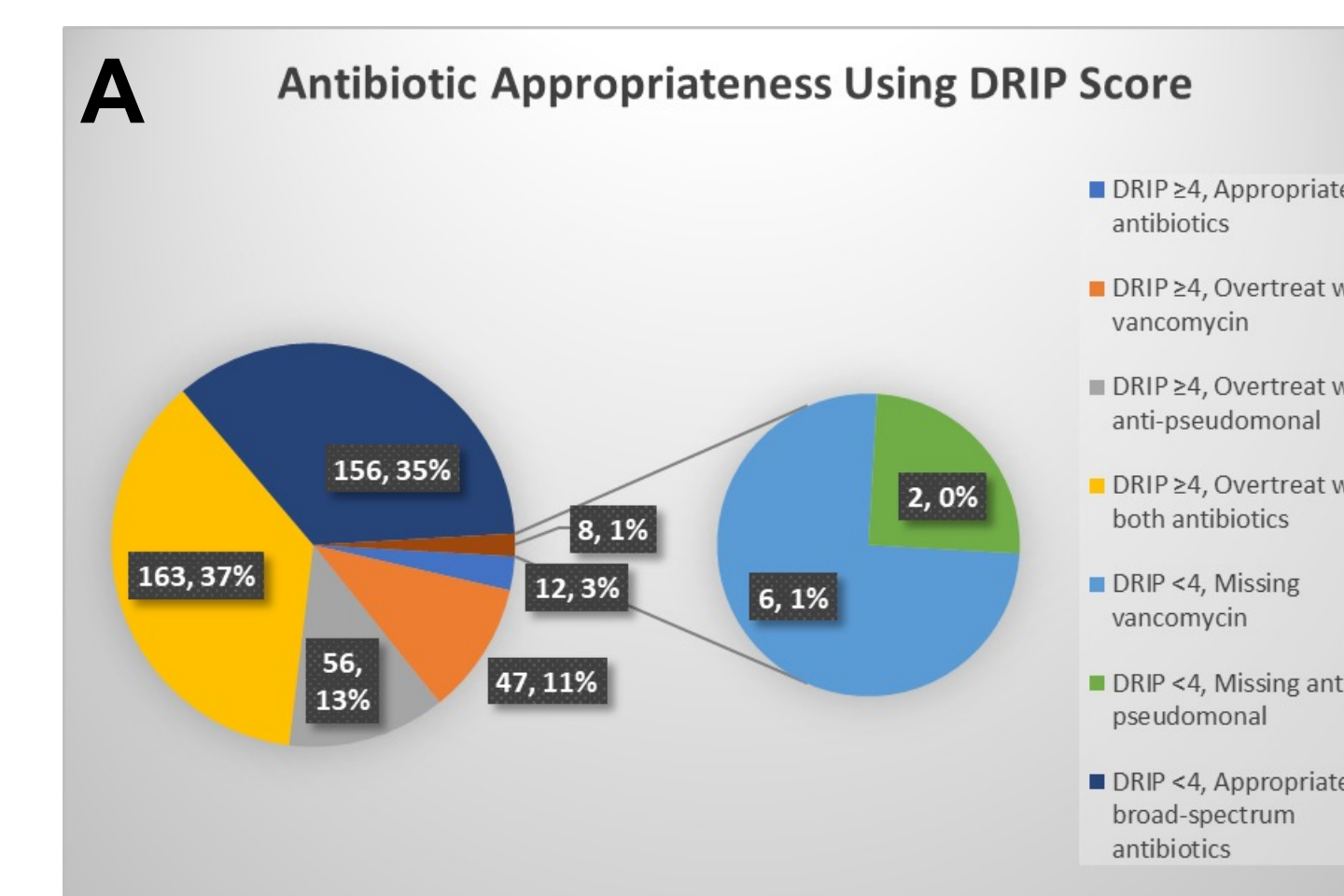


Figure 2: Antibiotic Appropriateness DRIP vs Unyvero

DRIP Complete		Sens	Spec	PPV	NPV	MCC
DRIP Alone	MRSA or Pseudomonas	0.91	0.58	0.45	0.94	0.44
	MRSA	0.88	0.50	0.25	0.96	0.28
Unyvero Alone	MRSA or Pseudomonas	0.95	0.51	0.24	0.99	0.32
	MRSA	0.87	1.00	1.00	0.95	0.91
Unyvero and Algorithm	MRSA or Pseudomonas	0.83	1.00	1.00	0.97	0.90
	MRSA	0.94	1.00	1.00	0.99	0.96
DRIP ≥4, Unyvero	MRSA or Pseudomonas	0.89	0.98	0.94	0.96	0.88
	MRSA	0.87	0.98	0.90	0.97	0.86
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.94	1.00	1.00	0.99	0.96
	MRSA	0.79	1.00	1.00	0.92	0.85
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.76	1.00	1.00	0.95	0.85
	MRSA	0.87	1.00	1.00	0.98	0.92
DRIP Max	MRSA or Pseudomonas	0.81	0.98	0.93	0.93	0.82
	MRSA	0.80	0.98	0.90	0.96	0.81
DRIP Min	MRSA or Pseudomonas	0.87	1.00	1.00	0.98	0.92
	MRSA	0.93	0.49	0.41	0.95	0.39
Unyvero Alone	MRSA or Pseudomonas	0.92	0.43	0.24	0.96	0.27
	MRSA	0.97	0.43	0.21	0.99	0.28
Unyvero and Algorithm	MRSA or Pseudomonas	0.85	1.00	1.00	0.94	0.90
	MRSA	0.84	1.00	1.00	0.97	0.90
DRIP ≥4, Unyvero	MRSA or Pseudomonas	0.87	0.95	0.88	0.95	0.82
	MRSA	0.87	0.96	0.83	0.97	0.81
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.91	1.00	1.00	0.98	0.95
	MRSA	0.80	1.00	1.00	0.92	0.86
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.79	1.00	1.00	0.95	0.87
	MRSA	0.87	1.00	1.00	0.98	0.92
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.81	0.95	0.88	0.93	0.78
	MRSA	0.82	0.96	0.82	0.96	0.78
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.87	1.00	1.00	0.98	0.92
	MRSA	0.85	1.00	1.00	0.94	0.90
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.84	1.00	1.00	0.97	0.90
	MRSA	0.87	0.98	0.92	0.97	0.87
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.87	0.98	0.92	0.97	0.87
	MRSA	0.91	1.00	1.00	0.98	0.95
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.74	1.00	1.00	0.90	0.82
	MRSA	0.73	1.00	1.00	0.94	0.83
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.81	1.00	1.00	0.97	0.89
	MRSA	0.75	0.98	0.94	0.91	0.79
DRIP ≥4, Unyvero and Algorithm	MRSA or Pseudomonas	0.76	0.98	0.91	0.95	0.80
	MRSA	0.81	1.00	1.00	0.97	0.89

Table 4: Performance of Predictive Diagnostics and Algorithms

CONCLUSIONS

- While the DRIP score allows for a significant reduction in overuse of broad-spectrum antibiotics it is non-specific and still leads to overuse of the combination of vancomycin and an anti-pseudomonal.
- Using the Unyvero LRTI allows for a specific reduction in overuse of broad-spectrum antibiotics where only vancomycin or an anti-pseudomonal antibiotic is used as needed.
- The Unyvero LRTI also finds specific pathogens and specific resistances which require antibiotics outside of just vancomycin and anti-pseudomonals.
- The combination of DRIP score and Unyvero LRTI increases the sensitivity for MRSA but with a loss of specificity and an increase in the inappropriate use of vancomycin to cover a few missed MRSA's.
- There is a significant cost to applying the Unyvero LRTI to every potentially eligible patient. Since the DRIP score has a very high negative predictive value, running the Unyvero LRTI only patients who have a DRIP or DRIP_{Max} ≥4 will catch nearly all the patients with resistant bacteria.

DISCUSSION

- The National Action Plan for Combating Antibiotic-Resistant Bacteria 2020-2025 (NAP) is to "advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria.
- The NAP also notes that "one major impediment to introducing new diagnostics is a lack of research on their appropriate use in clinical and veterinary care"
- Multiple studies have shown that use of the DRIP score can decrease empiric broad-spectrum antibiotic use in patients admitted with pneumonia.
- The best way to utilize DRIP score is unclear when data is missing. In this study we imputed either the highest or lowest points for patients with missing data and found that imputing the highest value increased sensitivity, decreased specificity, and increased negative predictive value and led to fewer missed pathogens.
- Using the Unyvero LRTI rapid diagnostic is more targeted as it identifies specific pathogens including MRSA and *Pseudomonas*.
- Using DRIP score in our cohort of 442 patients would have led to 6 cases where MRSA was missed, 2 cases where *Pseudomonas* was missed, but 210 cases of overtreatment with vancomycin and 219 cases of overtreatment with an anti-pseudomonal
- Using Unyvero in our cohort of 442 patients would have led to 13 cases where MRSA was missed and 6 cases where *Pseudomonas* was missed but no overtreatment. It also picked up 8 cases of MRSA and 8 cases of *Pseudomonas* missed by culture and 90 additional pathogens that would modify treatment further.
- Using our algorithm to try to adjust for missed cases picked up 2 extra cases of MRSA but led to 15 cases of overtreatment with vancomycin.
- Restricting use of the Unyvero to only those patients with a DRIP score ≥4 led to 17 missed cases of MRSA and 9 missed cases of *Pseudomonas* but reduced the number of Unyvero runs by 164.
- Unyvero is excellent for Antibiotic Stewardship while restricting it to DRIP score ≥4 is excellent for Diagnostic Stewardship.

REFERENCES

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