CHI Memorial

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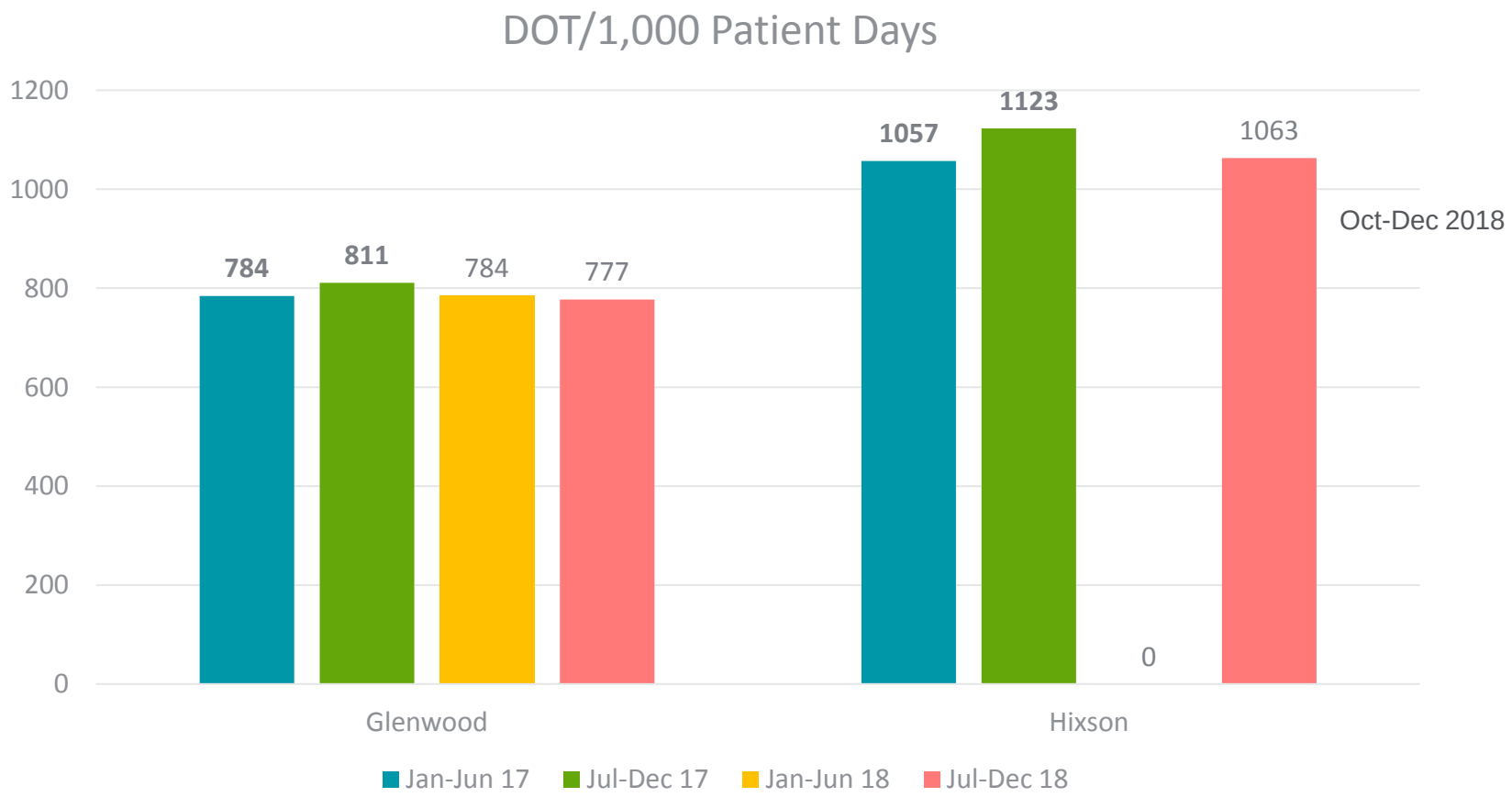
What's new in ASP?

May 28, 2019

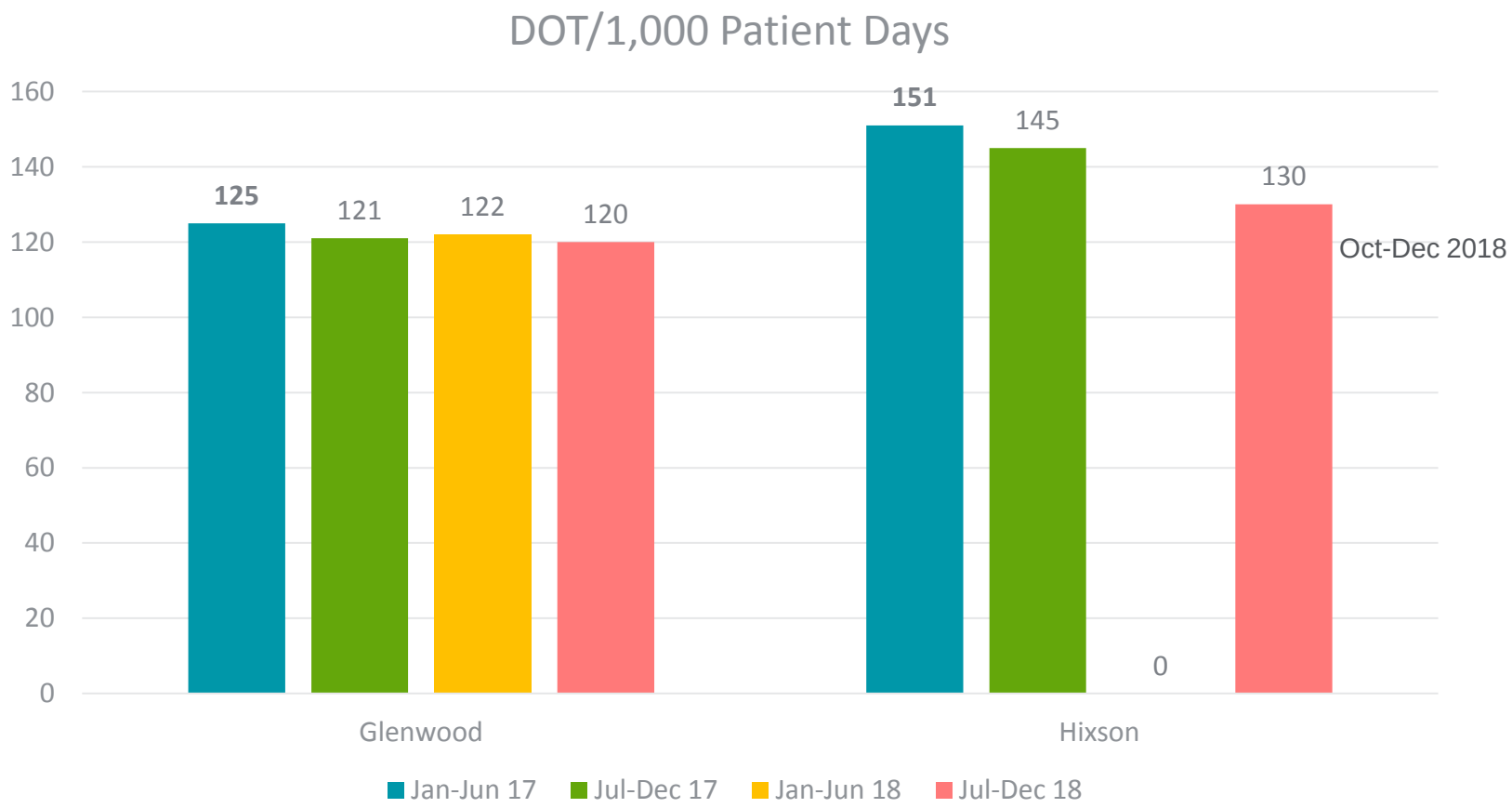
Topics for Discussion

- Metrics
- Antibiogram
  - Hospital
  - Combination antibiogram
- *Clostridioides Difficile* updates
- Asymptomatic bacteriuria vs. UTI
- Vabomere (meropenem/vaborbactam)
- Interesting clinical trials
  - MERINO trial
  - 7 vs. 14 days for uncomplicated gram negative bacteremia

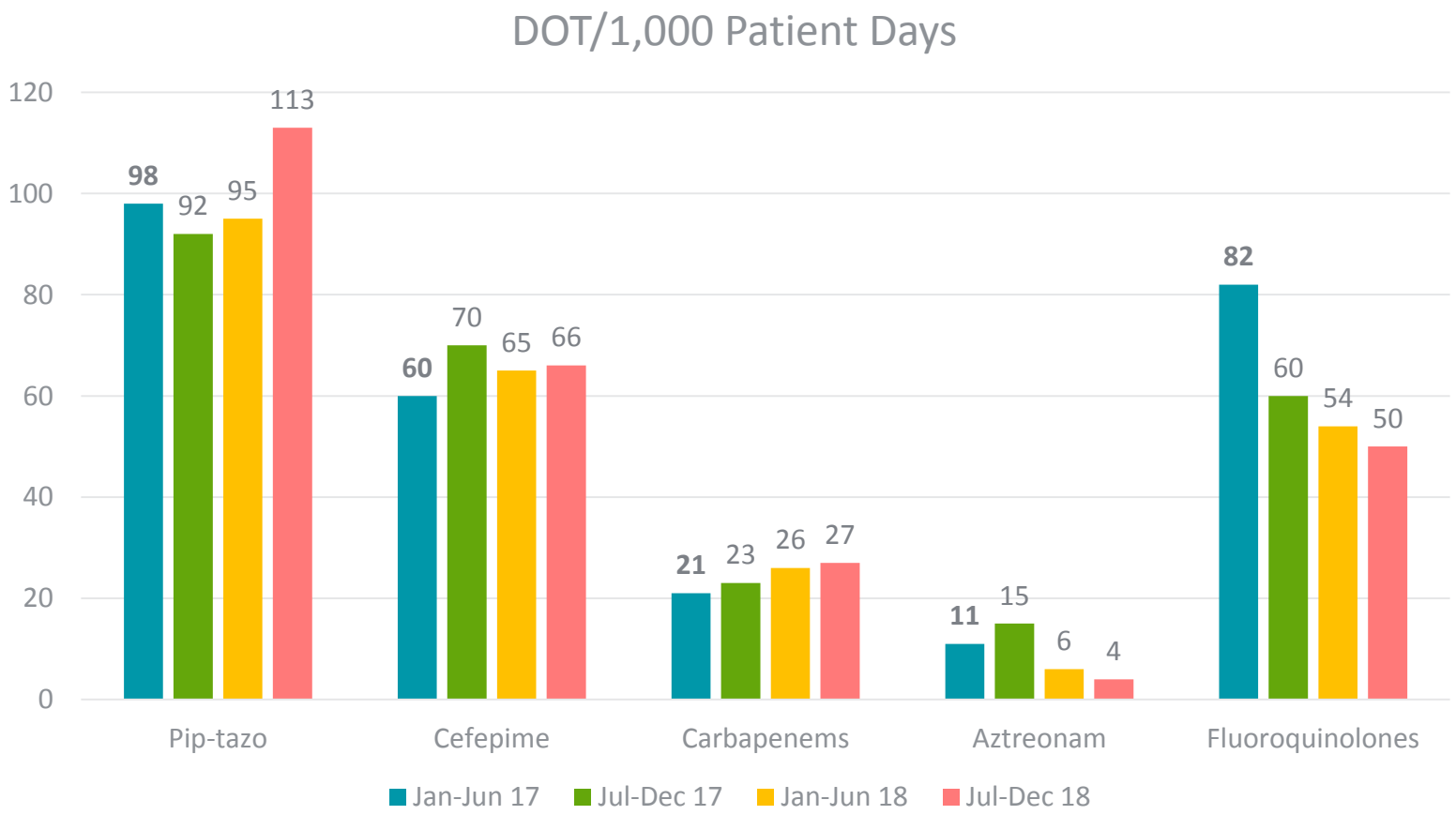
DOT/1,000 Patient Days: All antibiotics



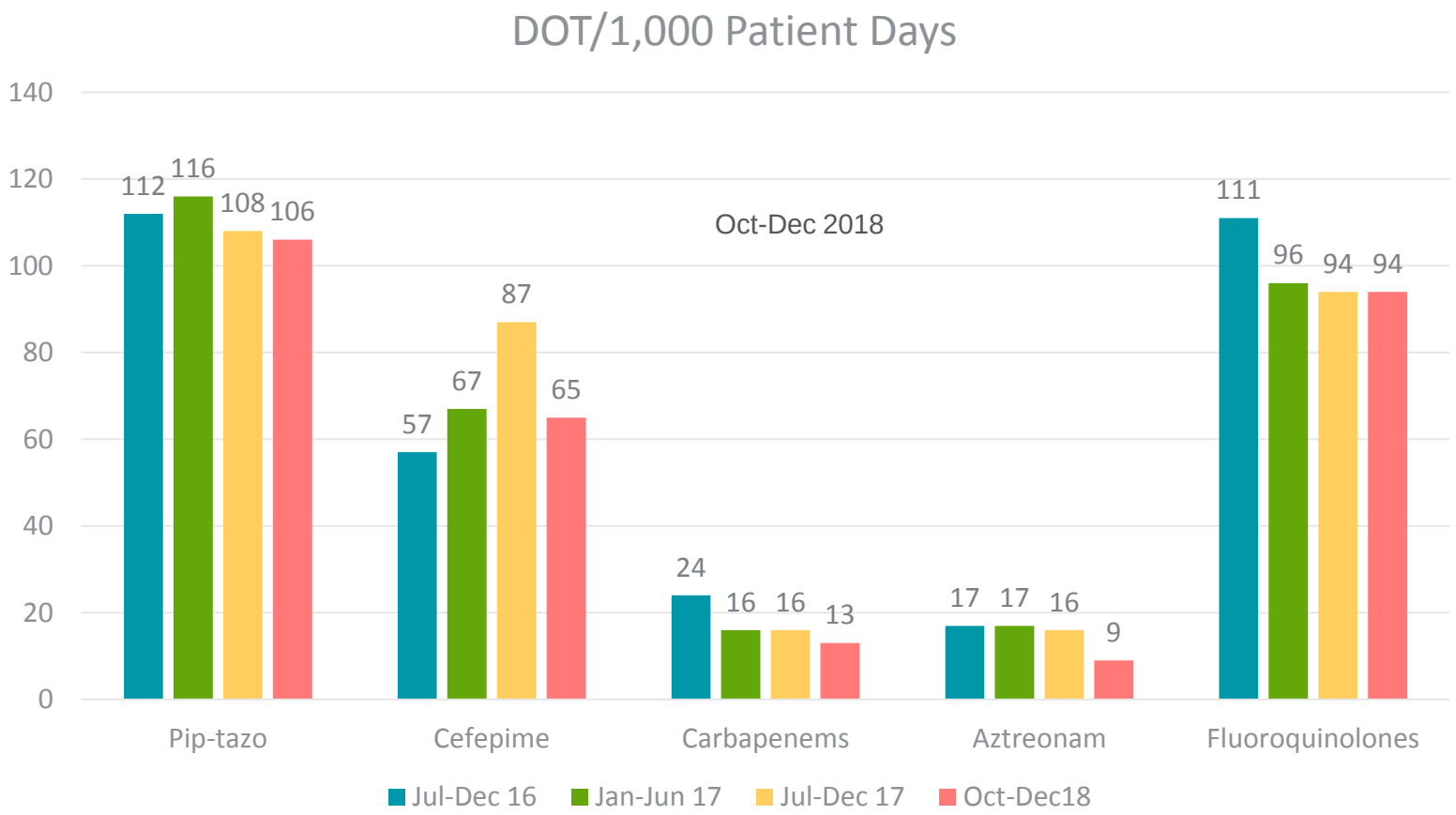
DOT/1,000 Patient Days: Vancomycin



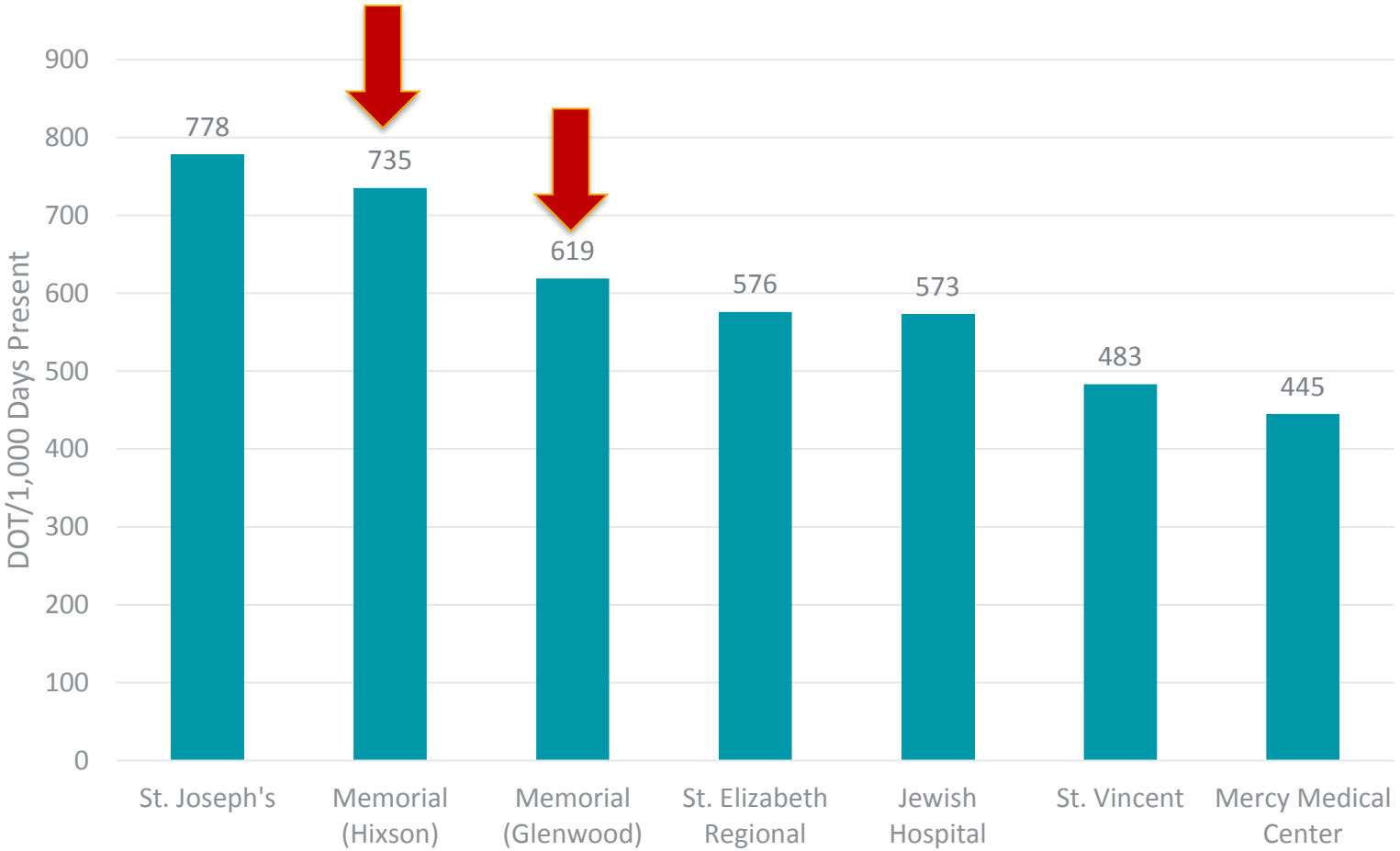
DOT/1,000 Patient Days: Glenwood



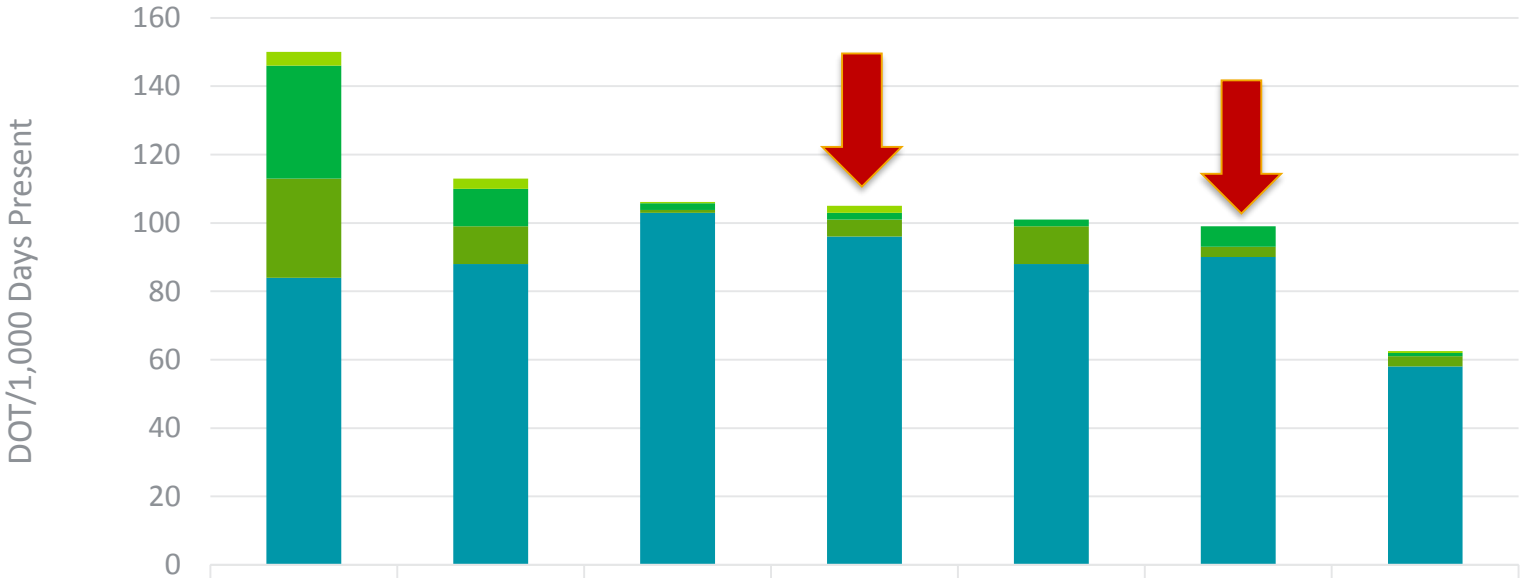
DOT/1,000 Patient Days: Hixson



All systemic antibiotics: Jul-Dec 2018

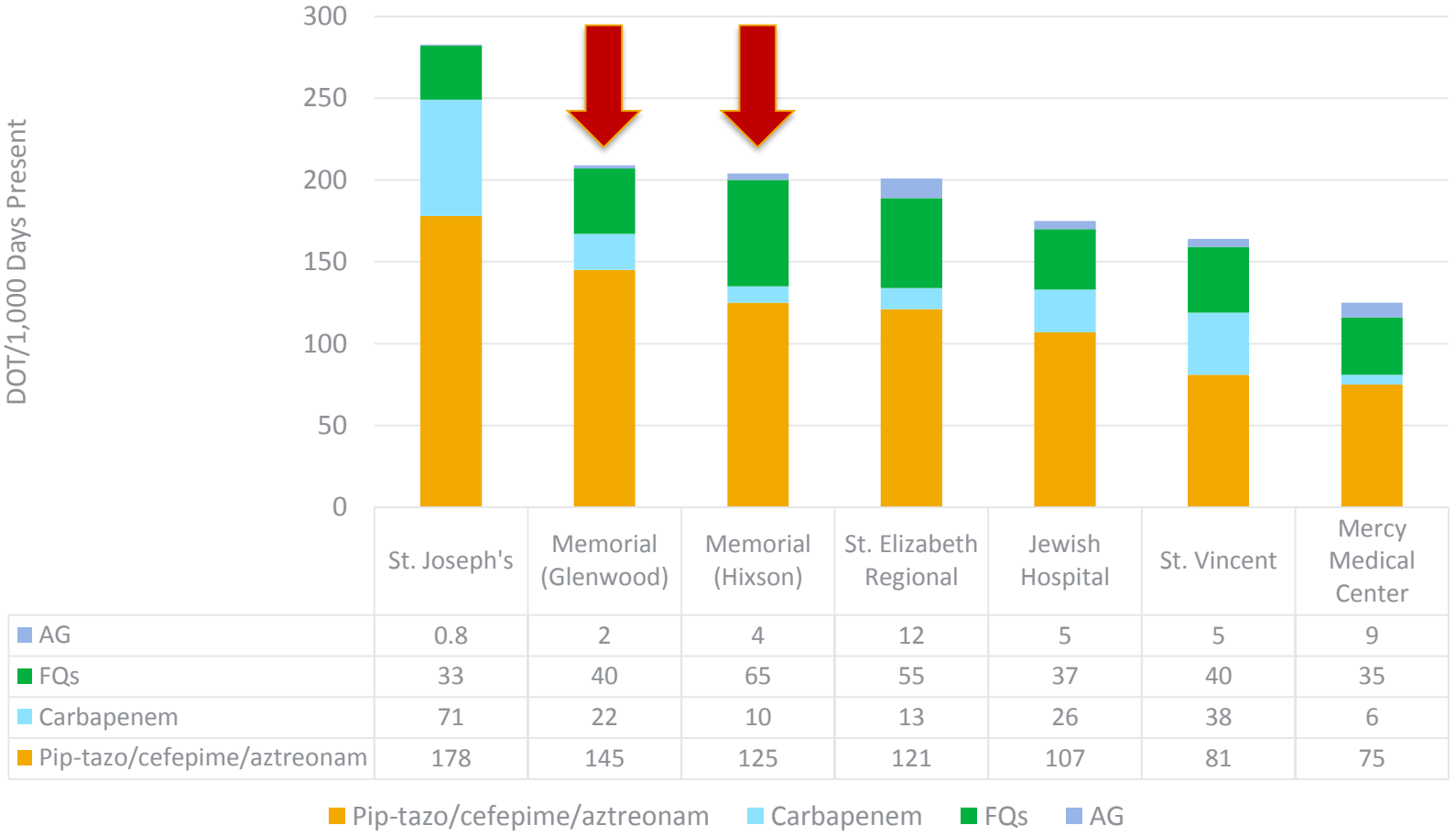


Anti-MRSA Agents: Jul-Dec 2018



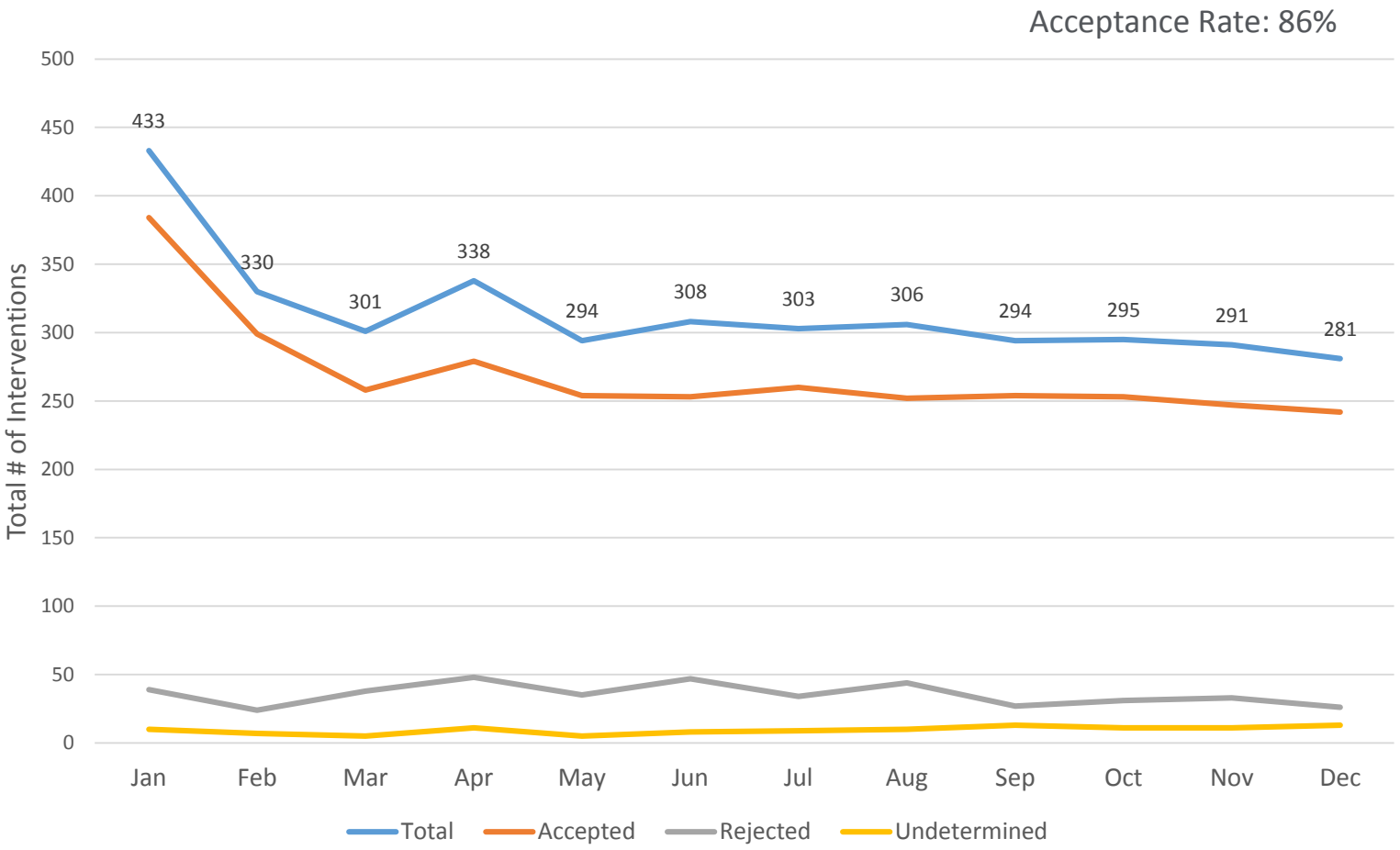
	St. Joseph's	Jewish Hospital	St. Vincent	Memorial (Glenwood)	St. Elizabeth Regional	Memorial (Hixson)	Mercy Medical Center
Ceftaroline	4	3	0.3	2	0	0	0.5
Linezolid	33	11	2	2	2	6	1
Daptomycin	29	11	0.8	5	11	3	3
Vancomycin	84	88	103	96	88	90	58

Anti-Pseudomonal Agents: Jul-Dec 2018



	St. Joseph's	Memorial (Glenwood)	Memorial (Hixson)	St. Elizabeth Regional	Jewish Hospital	St. Vincent	Mercy Medical Center
AG	0.8	2	4	12	5	5	9
FQs	33	40	65	55	37	40	35
Carbapenem	71	22	10	13	26	38	6
Pip-tazo/cefepime/aztreonam	178	145	125	121	107	81	75

ASP Interventions



Antibiogram: *Gram-negative*

Organism	Total Isolates	A/S	CZOL	CXM	CTRX	CFPM	P/T	MER	AZT	CIP	GEN	TOB	T/S	NIT
Acinetobacter baumannii	*62	72			38	56		66		54	56	59	59	
Enterobacter aerogenes	50					100	84	100	74	98	98	98	98	19
Enterobacter cloacae	134					96	82	100	75	89	95	94	87	14
Escherichia coli	1082	54	76	78	82	83	96	100	83	63	88	87	71	71
Klebsiella oxytoca	92	62	38	83	88	90	93	100	88	95	100	94	95	35
Klebsiella pneumoniae	470	80	85	84	87	89	95	99	88	92	94	94	86	33
Morganella morganii	42				74	98	98	100	88	64	88	93	69	
Proteus mirabilis	211	78	74	83	87	90	100	100	89	64	91	92	71	
Pseudomonas aeruginosa	379					86	89	87	75	74	75	89		
CVICU, CCU, MICU	91					75	83	84	64	66	72	88		
Non-ICU	288					89	90	88	78	76	76	90		
Serratia marcescens	64				78	98	84	98	84	95	100	88	98	
* 2017 and 2018 combined														

A/S-ampicillin-sulbactam, **CZOL**- cefazolin, **CXM**-cefuroxime, **CTRX**-ceftriaxone, **CFPM**-cefepime, **P/T**-piperacillin-tazobactam, **MER** –meropenem, **AZT**-aztreonam, **CIP**-ciprofloxacin, **GEN**-gentamicin, **TOB**-tobramycin, **T/S**-trimethoprim/sulfamethoxazole, **NIT**-nitrofurantoin

Antibiogram: *Gram-negative comparative*

Pseudomonas aeruginosa	Total Isolates	CFPM	P/T	MER	AZT	CIP	GEN	TOB
2018	379	86	89	87	75	74	75	89
2017	367	86	88	92	76	78	84	94
2016	288	83	86	80	71	75	77	95
2015	268	79	85	90	68	76	79	92
2014	279	81	94	89	69	67	72	88

Acinetobacter baumanii	Total Isolates	CFPM	A/S	MER	T/S	CIP	GEN	TOB
2018 (2 years)	62	56	72	66	59	54	56	59
2017	33	48	66	60	48	48	51	54
2016	37	53	26	37	43	40	43	40
2015 (2 years)	29	52	80	69	52	51	69	42
2014	19	42	74	58	53	47	58	53

Enterobacteriaceae:

- Carbapenems: overall high susceptibility (≥98%)
- P/T: stable susceptibilities for most organisms except known ampC producers
- CFPM: stable to slightly improved sensitivities
- FQ: Remains similar to last year

Escherichia coli	Total Isolates	CXM	CTRX	MER	GEN	TOB	T/S	CIP	NIT
2018	1082	78	82	100	88	87	71	63	96
2017	1067	76	79	100	86	85	65	58	95
2016	946	70	81	100	86	85	66	60	93
2015	754	80	86	100	88	88	67	58	96
2014	848	77	82	100	88	88	64	66	96

Antibiogram: *Gram-positive*

Organism	Total isolates	PCN	OXA	ERY	CLIN	DOX	T/S	VANC	LIN	DAP
Staphylococcus aureus	753		40	28	62	92	96	99	100	100
MRSA	450				56	92	93	99	100	100
MSSA	303	27	100	53	71	93	100	100	100	100
Enterococcus faecalis	344	100				27		99	100	100
Enterococcus faecium	49	38				53		48	100	100

PCN-penicillin**, OXA-**oxacillin, **ERY**-erythromycin, **CLIN-**clindamycin, **DOX-**doxycycline, **T/S-**trimethoprim/sulfamethoxazole
VANC-vancomycin, **LIN**-linezolid, **DAP**-daptomycin

- **Streptococcus pneumoniae** — Of 48 isolates in 2018, 93% were ceftriaxone susceptible and 98% levofloxacin susceptible.
- **Enterococcus species** — Of 36 enterococcal bacteremias in 2018, 28 were due to Enterococcus faecalis and 8 were due to Enterococcus faecium. 100% of the Enterococcus faecalis isolates were sensitive to ampicillin. 75% of the Enterococcus faecium isolates were vancomycin resistant (VRE). Of the VRE isolates, none were linezolid or daptomycin resistant.

Antibiogram: *Gram-positive comparative*

MRSA	Total Isolates	OXA	CLIN	DOX	T/S	VANC	LIN	DAP
2018	450		56	92	93	99	100	100
2017	396		56	90	94	100	100	100
2016	381		60	93	91	99	100	100
2015	320		55	93	92	100	100	100
2014	416		49	96	93	99	100	100
2013	502		48	94	92	100	100	100
MSSA	**Total Isolates**	**OXA**	**CLIN**	**DOX**	**T/S**	**VANC**	**LIN**	**DAP**
2018	303	100	71	93	100	100	100	100
2017	301	100	77	94	99	100	100	100
2016	254	100	80	91	99	100	100	100
2015	223	100	81	96	99	100	100	100
2014	170	100	76	96	100	100	99	100
2013	254	100	75	93	98	100	100	100

MRSA rates: 72% (2011), 68, 66, 71, 59, 60, 56, 60%

***Staphylococcus aureus*:**

- MRSA rate ~ 60%
- Clinda-S differs among MRSA (56%) & MSSA (71%)
- Stable susceptibilities to DOX, T/S

***Enterococcus faecium*:**

- 52% VRE (60% in 2017); all were linezolid and daptomycin sensitive

Combination Antibiogram – All gram (-)

- Included:
  - All gram-negative cultures except stool
  - 1st isolate of each organism per patient per year

Population	CTX → CTX + FQ*	AZT → AZT + FQ	AZT → AZT + TOB	P/T → P/T + FQ	P/T → P/T + TOB
All adult inpatients	84 → 91%	83 → 90%	83 → 94%	92 → 97%	92 → 97%
ICU	82 → 90%	76 → 88%	76 → 91%	88 → 95%	86 → 94%
Floor	85 → 91%	84 → 91%	84 → 95%	93 → 98%	93 → 98%
	CPM → CPM + FQ	**CPM → CPM + TOB**	**MER → MER + FQ**	**MER → MER + TOB**	
All adult inpatients	88 → 92%	88 → 95%	97 → 98%	97 → 98%	
ICU	82 → 89%	82 → 91%	94 → 96%	94 → 95%	
Floor	89 → 92%	89 → 95%	97 → 99%	97 → 98%	

- CTX excludes *Pseudomonas, Acinetobacter, Stenotrophomonas spp*

Combination Antibiogram – Pseudomonas

- Included:
  - All Pseudomonas cultures except stool
  - 1st isolate per patient per year

	P/T→ P/T + FQ	P/T→ P/T + TOB	CPM → CPM + FQ	CPM → CPM + TOB	MER→ MER + FQ	MER→ MER + TOB
All Patients	92 → 96%	92 → 98%	90 → 95%	90 → 97%	91 → 94%	91 → 96%
ICU	86 → 94%	86 → 95%	83 → 89%	83 → 94%	89 → 91%	89 → 95%
Floor	93 → 97%	93 → 99%	93 → 97%	93 → 98%	92 → 95%	92 → 97%

	AZT→ AZT+FQ	AZT→ AZT+TOB
All Patients	78 → 91%	78 → 95%
ICU	69 → 85%	69 → 94%
Floor	81 → 93%	81 → 96%

Syndromic Antibiogram – PNA

- Included:
  - Sputum, tracheal aspirate, bronch specimens, and pleural fluid
  - 1st isolate per patient per year

- Excluded:
  - *Stenotrophomonas maltophilia*
  - < 5 isolates of an organism

Regimens	Sensitive (%)
CPM	68
CPM + VANC	90
CPM + VANC + FQ	94
CPM + VANC + TOB	96

Regimens	Sensitive (%)
AZT	44
AZT + VANC	85
AZT + VANC + FQ	93
AZT + VANC + TOB	95

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Assessment of the management of asymptomatic bacteriuria and urinary tract infections at a community hospital

Antimicrobial Stewardship Initiative

To Improve Diagnosis & Management of ASBs & UTIs

- Urinalysis with reflex to culture: only if > trace LE or >20 WBCs
- Cascade susceptibility reporting
- Development of inpatient and ED UTI guidelines
  - Physician education

Methods

Study Design

- Single center, retrospective cohort analysis
- IRB approved study

- Inclusion Criteria:
  - ≥ 18 years of age
  - Pre-period: June 1st – June 30th 2015 (ICD-9 codes for UTI)
  - Post-period: June 1st – June 30th 2016 (ICD-10 codes for UTI)

- Exclusion Criteria:
  - Patient discharge prior to culture finalization
  - Treatment of a concomitant infection
  - Antibiotics prior to admission
  - Urine culture that was not significant (i.e. no growth, contaminant, <100,000 CFUs if clean catch etc.)

Methods

Objectives

Primary Objective

- To assess guideline based:
  - Identification and decision to treat ASB vs UTI
  - Antibiotic selection (empiric and final)
  - Duration of therapy

Secondary Objective

- *Clostridioides difficile* infection rates
- 90 day hospital readmission
- Overall mortality

Methods

Definitions- Classification

- Positive urine culture: ≥100,000 CFUs of an organism or ≥1,000 CFUs if culture obtained from catheter
- Urinary symptoms: dysuria, urgency, frequency, cause, suprapubic pain, CVA tenderness, flank pain, altered mental status (without secondary cause)

UTI

- Positive urine culture
- Urinary symptoms
- Meets SIRS criteria

ASB

- Positive urine culture
- **No** urinary symptoms
- Does not meet SIRS criteria

Methods

Definitions- Antibiotic Selection

Empiric Selection

- 2nd-3rd Generation Cephalosporin
- Nitrofurantoin (if cystitis, good renal function)

Exceptions

- Beta-lactam allergy: aztreonam, aminoglycoside
- History ESBL producing organisms: carbapenem
- History of *Pseudomonas aeruginosa*: cefepime, piperacillin/tazobactam, aminoglycoside, fluoroquinolone

Final Antibiotic Selection

- Antibiotics adjusted based on organism identified
  - De-escalated to more narrow spectrum agent
  - Escalated to cover drug-resistant organism
  - Stopped antibiotic if ASB

Methods

Definitions- Duration

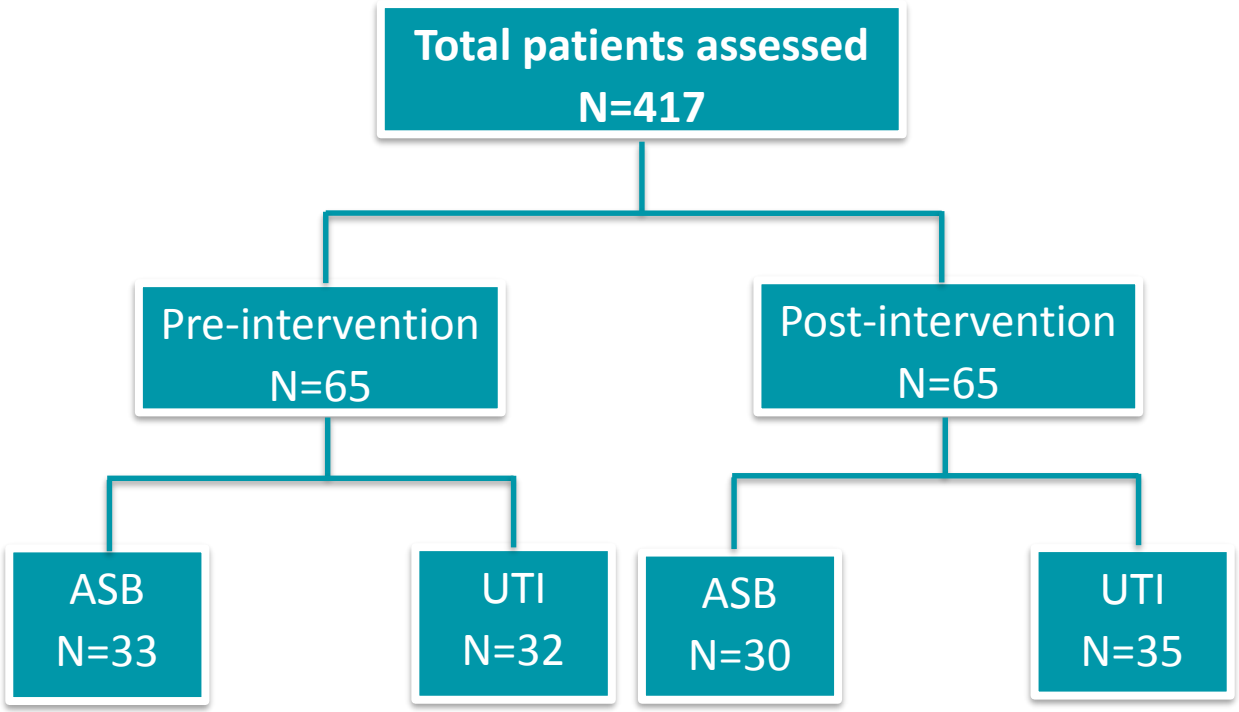
Appropriate duration of therapy:

- Uncomplicated Cystitis:
  - Fosfomycin x 1 day
  - TMP-SMX x 3 days
  - Nitrofurantoin x 5 days
  - Beta-lactam x 7 days

Complicated Cystitis	CA-UTI	Pyelonephritis
7 – 14 days	**7 – 14 days**	**10 – 14 days**

Results

Study Design



Results

Baseline Demographics

	Pre-intervention (n=65)	Post-intervention (n=65)	p-value
Age > 65, n (%)	54 (83.1)	47 (72.3)	0.20
Male, n (%)	23 (35.4)	18 (27.7)	0.45
LTC, n (%)	15 (23.1)	4 (6.2)	0.01
Urologic abnormality, n (%)	21 (32.3)	14 (21.5)	0.24
ICU Admission, n (%)	11 (16.9)	6 (9.2)	0.30

Results

Appropriately Classified & Treated Patients

	Pre-intervention (n=65)	Post-intervention (n=65)	p-value
UTI	32/32 (100%)	35/35 (100%)	1.0
ASB	11/33 (33.3%)	11/30 (36.7%)	0.80
Total	42 (64.6%)	46 (70.8%)	0.57

- Pre-intervention appropriately managed ASB:
  - **5 were not treated**
  - **Of the 28 who were treated**
    - **4** – Planned urologic procedure during visit
    - **1** – History of renal transplant
    - **1** – Stopped antibiotic within 48 hours of starting

- Post-intervention appropriately managed ASB:
  - **4 were not treated**
  - **Of the 26 who were treated**
    - **7** – Stopped antibiotic within 48 hours of starting
      3 – pharmacist interventions
      1 – ID consult

Results

Appropriate Antibiotic Selection in Treated Patients

	Pre-intervention (n=60)	Post-intervention (n=61)	p-value
Empiric, n (%)	57 (95)	52 (85)	0.13
Final, n (%)	41 (68.3)	49 (80)	0.15
Most narrow	19/41 (46.3)	41/49 (83.6)	0.0003
Rx Intervention, n (%)	18 (40)	12 (24)	0.07

- Post-period:
  - Most narrow agent was selected more often despite fewer pharmacist interventions (cascade susceptibility report)
    - Most narrow penicillin, cephalosporin, TMP-SMX, nitrofurantoin, an aminoglycoside, or fluoroquinolone (if *Pseudomonas aeruginosa*, an ESBL producer, or pyelonephritis for discharge purposes)

Results

Appropriate Durations of Therapy in UTI Patients

	Pre-intervention (n=31)	Post-intervention (n=34)	p-value
Uncomplicated cystitis	5/12 (41.7%)	14/19 (73.7%)	0.13
Complicated cystitis	6/7 (85.7%)	3/3 (100%)	1.0
CA-UTI	9/11* (82%)	5/5 (100%)	1.0
Pyelonephritis	1/1 (100%)	6/7* (85.7%)	1.0

* Antibiotic duration was unknown for one patient

- Pre-intervention duration of therapy, median (IQR): 8 (6-10)
- Post-intervention duration of therapy, median (IQR): 6.5 (6-9)

Results

Secondary Endpoints

	Pre-intervention (n=65)	Post-intervention (n=65)	p-value
***Clostridioides difficile* Infection, n (%)**	1 (1.5)	3 (4.6)	0.61
Readmission within 90 days, n (%)	25 (38.4)	22 (33.8)	0.72
Mortality, n (%)	0	0	1.0

- Pre-intervention: ASB patient
  - Patient receiving ceftriaxone
- Post-intervention: 2 ASB patients; 1 uncomplicated cystitis
  - All patients were receiving levofloxacin

Limitations

- Retrospective design
- Small sample size
- Many excluded patients
- ICD-9 & 10 codes for UTI, not ASB
- Not able to measure the effect of UA w/ reflex to culture as all patients w/o a significant culture were excluded

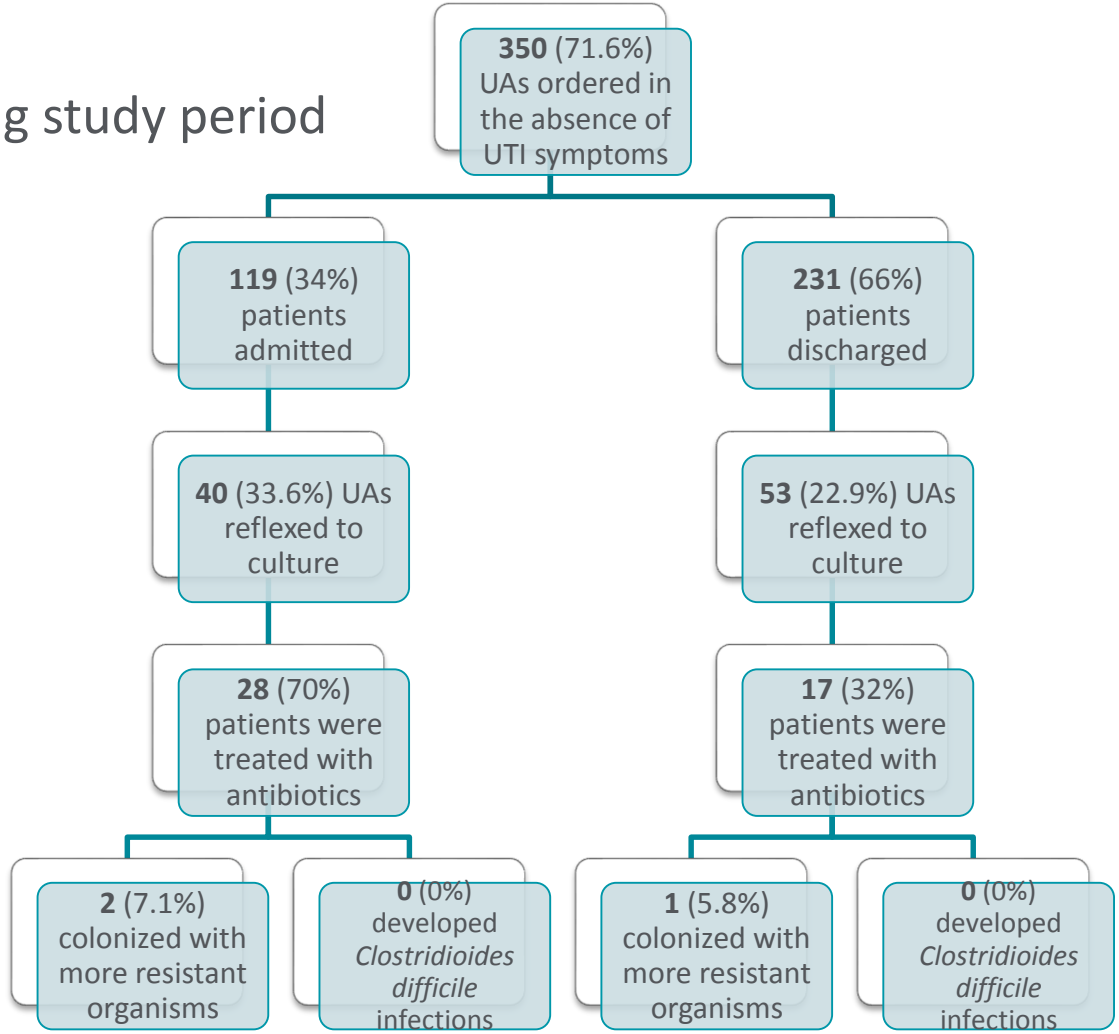
Conclusion
Endpoints

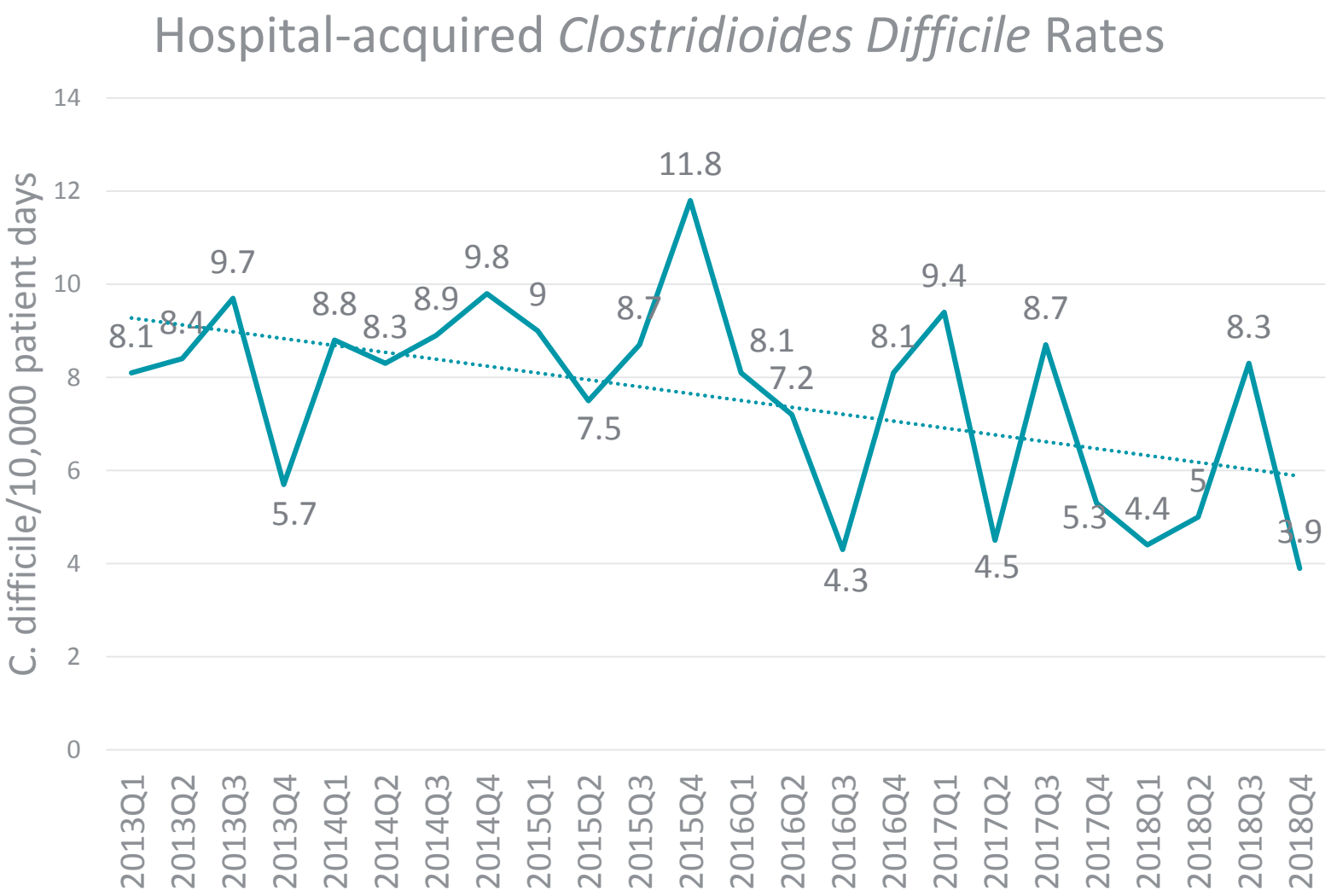
- Primary Endpoint
  - Asymptomatic bacteriuria (ASB)
    - Over treated
  - Cystitis
    - Empiric coverage broader in the post-period
    - De-escalation and duration of treatment more appropriate in the post-period

- Secondary Endpoint
  - Most patients with *C. difficile* super-infections should not have received antibiotics

Evaluation of urinalysis in the ED

1 week:
489 orders for UAs during study period




Hospital-acquired *Clostridioides Difficile* Rates
C. difficile/10,000 patient days
0
2
4
6
8
10
12
14
8.1
8.4
9.7
5.7
8.8
8.3
8.9
9.8
9
7.5
8.7
11.8
8.1
7.2
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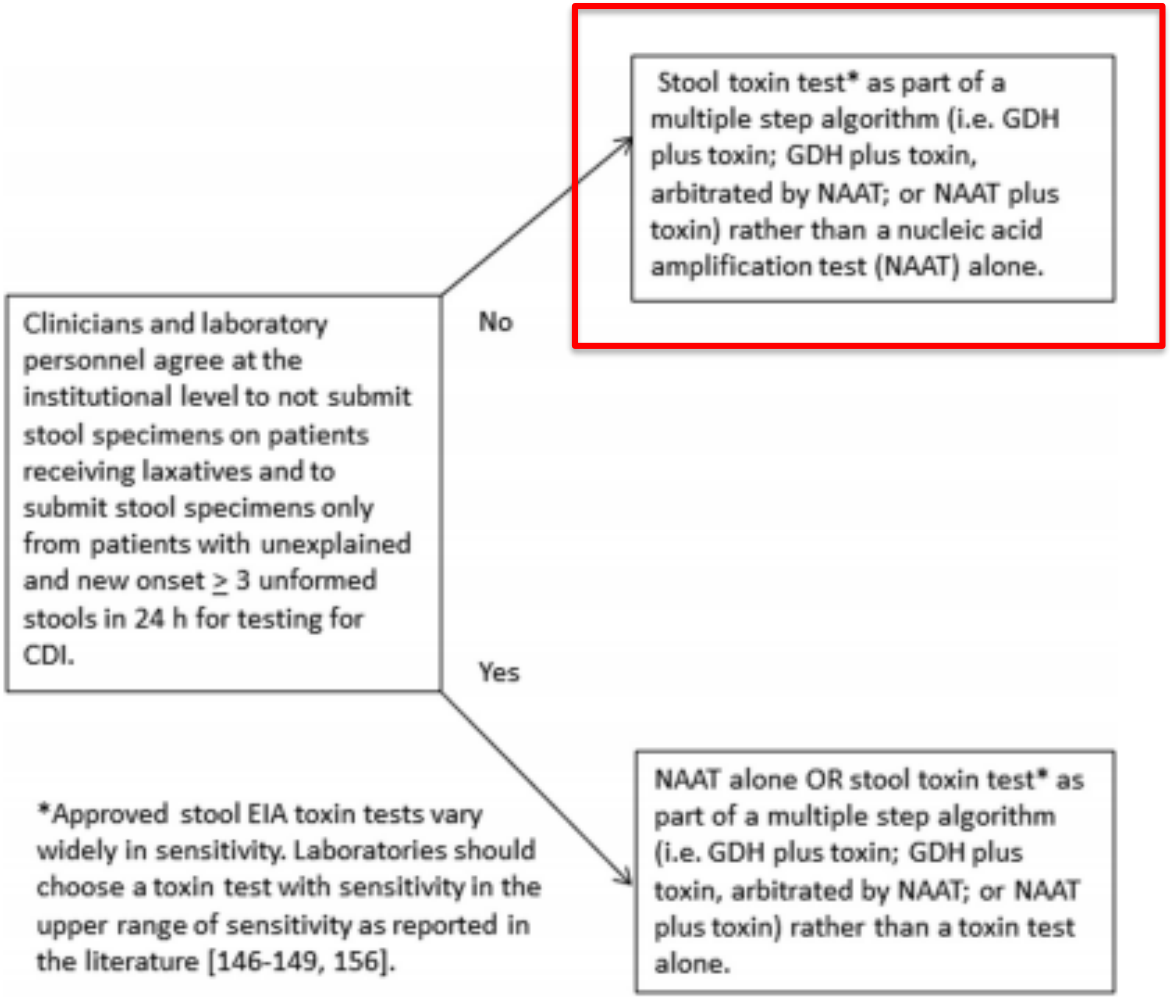
2016Q2
2016Q3
2016Q4
2017Q1
2017Q2
2017Q3
2017Q4
2018Q1
2018Q2
2018Q3
2018Q4

Clostridioides difficile treatment

Table 1. Recommendations for the Treatment of *Clostridium difficile* Infection in Adults

Clinical Definition	Supportive Clinical Data	Recommended Treatment[a]	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	Leukocytosis with a white blood cell count of ≤15 000 cells/mL and a serum creatinine level <1.5 mg/dL	• VAN 125 mg given 4 times daily for 10 days, OR	Strong/High
		• FDX 200 mg given twice daily for 10 days	Strong/High
		• Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days	Weak/High
Initial episode, severe[b]	Leukocytosis with a white blood cell count of ≥15 000 cells/mL or a serum creatinine level >1.5 mg/dL	• VAN, 125 mg 4 times per day by mouth for 10 days, OR	Strong/High
		• FDX 200 mg given twice daily for 10 days	Strong/High
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	• VAN, 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present.	Strong/Moderate (oral VAN); Weak/Low (rectal VAN); Strong/Moderate (intravenous metronidazole)
First recurrence	…	• VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR	Weak/Low
		• Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR	Weak/Low
		• FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode	Weak/Moderate
Second or subsequent recurrence	…	• VAN in a tapered and pulsed regimen, OR	Weak/Low
		• VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR	Weak/Low
		• FDX 200 mg given twice daily for 10 days, OR	Weak/Low
		• Fecal microbiota transplantation[c]	Strong/Moderate

Clostridioides Difficile testing



Clostridioides Difficile testing

- PCR, followed by toxin if PCR positive
  - If PCR (-): C. difficile negative
  - If PCR (+) & Toxin (+): Initiate C. difficile treatment. Stop acid suppressive medications & antimicrobials if possible.
  - If PCR (+) & Toxin (-): Patient has a lower level of C. difficile colonization and may not need therapy. Treatment should be individualized and considered in patients with severe, non-resolving, or unexplained diarrhea strongly suggestive of C. difficile infection
- All PCR (+) patients will be placed on contact isolation

Meropenem-vaborbactam: Overview

- Brand name: Vabomere™
- Manufacturer: The Medicines Company
- FDA approval date: 8/29/17
- Indication: Complicated UTI, including pyelonephritis
- Vaborbactam:
- Class: cyclic boronate
  - Active against: Class A & C serine beta-lactamase (particularly KPC carbapenemase)
  - Not-active against: metallo-beta lactamases, oxacillinases

A	B	C	D
Serine-based	Metallo-based	Serine-based	Serine-based
KPC, CTX-M, TEM	IMP, VIM, NDM	AmpC	Oxa
Enterobacteriaceae (K. pneumoniae, E. coli)	Pseudomonas, Enterobacteriaceae	CAPES	Acinetobacter, Klebsiella

Meropenem-vaborbactam: Dosing

- Renal Dose adjustments:
  - eGFR 50mL/min/1.73m^2: 4g IV q8h
  - eGFR 30-49mL/min/1.73m^2: 2g IV q8h
  - eGFR 15-29mL/min/1.73m^2: 2g IV q12
  - eGFR <15mL/min/1.73m^2 & hemodialysis: 1g IV q12

- Hepatic impairment: no dose adjustment necessary

Meropenem-vaborbactam: Microbiology

	Meropenem		Meropenem-vaborbactam	
Organisms	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}
Enterobacteriaceae	0.03	0.06	≤ 0.015	0.06
KPC-producing Enterobacteriaceae	32	> 32	0.12	1
Non-KPC producing CRE	8	> 32	4	> 32
Lactose non-fermenting GNR				
P. aeruginosa	0.5	8	0.5	8
A. baumannii	8	32	4	32
S. maltophilia	> 32	> 32	> 32	> 32

Meropenem-vaborbactam: Pharmacokinetics

Intermittent infusion – steady state

	Meropenem (Mean)	Vaborbactam (Mean)
C_{max} (mg/L)	46.0	50.7
CL (L/hr)	14.6	12.3
AUC (mg*h/L)	414	588
$T_{1/2}$	1.5	1.99

- *Protein Binding:* meropenem (2%); vaborbactam (33%)
- *Excretion:* Primarily kidneys – meropenem (40-60%), vaborbactam (75-95%)

Extended infusion – steady state

	Meropenem (Mean)	Vaborbactam (Mean)
C_{max} (mg/L)	57.3	71.3
CL (L/hr)	10.5	7.95
AUC (mg*h/L)	650	835
$T_{1/2}$	2.3	2.25

Meropenem-vaborbactam: Efficacy

	Tango I	Tango II
Features	Site/Indication focus	Pathogen focused (CRE)
Sites of Infection	Complicated UTI & AP	cUTI/AP, HABP, VABP, bacteremia
Design	Randomized 1:1 Double-blind	Randomized 2:1 Open-label
No. of patients	550	72
Comparator	Piperacillin-tazobactam	"Best available therapy" (aminoglycoside, tigecycline, polymyxin, carbapenem alone or combo); or cefazidime-avibactam as monotherapy
Result	NI shown	Study stopped after interim analysis showed advantage for meropenem-vaborbactam

Meropenem-vaborbactam: Safety

- Drug-interactions:
  - Valproic acid
  - Probenecid

- Adverse reactions:

	Meropenem-vaborbactam N=295	Comparators N=289
Any ADEs	43%	38%
Headache	9%	4%
Diarrhea	4%	5%
Infusion site reactions	4%	1%
N/V	2%	2%
ALT increase	2%	1%
AST increase	1%	1%

Meropenem-vaborbactam: Cost

Drug	Cost/day	Cost (x 7 days)	Cost (x 14 days)
Avycaz	$ 998.31	$ 6,988.17	$ 13,976.34
Vabomere	$ 808.38	$ 5,658.66	$ 11,317.32

- Switch from avycaz to vabomere: restricted to ID for the treatment of CRE

MERINO Trial

- Prospective, randomized, open-label, non-inferiority trial
  - Adult patients w/ at least 1 positive blood culture with *E. coli* or *Klebsiella* spp. nonsusceptible to ceftriaxone but susceptible to pip-tazo
  - Pip-tazo 4.5 g IV q6h (n=188) vs. meropenem 1g IV q8h (n=191) for min of 4 days, max 14 days (median treatment time 13 days)
  - Median time to randomization ~53 hrs after blood cxs obtained
  - Demographics: Well balanced; most common organism - E.coli; most common source - urinary tract

MERINO Trial

- Primary outcome: all cause mortality at 30 days – favored mero vs. pip-tazo (3.7% vs 12.3%). Pip-tazo could not be classified as non-inferior
  - Difference maintained across all pre-specified subgroups

Table 2. Primary Analysis and Subgroup Analyses

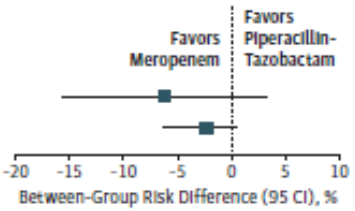
	30-d Mortality, No./Total No. (%)		Risk Difference, % (1-Sided 97.5% CI)[a]	*P* Value for Noninferiority
	Piperacillin-Tazobactam	Meropenem		
Primary analysis	23/187 (12.3)	7/191 (3.7)	8.6 (−∞ to 14.5)	.90
Per-protocol analysis	18/170 (10.6)	7/186 (3.8)	6.8 (−∞ to 12.8)	.76
Subgroup analyses[b]				*P* Value for Interaction
OECD country income				
Middle income	8/37 (21.6)	1/35 (2.9)	18.8 (−∞ to 35.0)	.31
High income	15/150 (10.0)	6/156 (3.9)	6.2 (−∞ to 12.5)	
Pitt score				
≥4	5/18 (27.8)	0/9	27.8 (−∞ to 51.3)	.99
<4	18/169 (10.7)	7/182 (3.9)	6.8 (−∞ to 12.8)	
Infecting species				
E coli	17/161 (10.6)	7/166 (4.2)	6.3 (−∞ to 12.6)	.99
K pneumoniae	6/26 (23.1)	0/25	23.1 (−∞ to 42.3)	
Infection				
HAI	18/107 (16.8)	4/107 (3.7)	13.1 (−∞ to 21.8)	.26
Non-HAI	5/80 (6.3)	3/84 (3.6)	2.7 (−∞ to 10.7)	
Appropriate empirical antibiotic therapy				
Appropriate	18/126 (14.3)	5/127 (3.9)	10.3 (−∞ to 18.0)	.70
Inappropriate	5/61 (8.2)	2/64 (3.1)	5.1 (−∞ to 15.2)	
UT vs non-UT source				
UT	7/102 (6.9)	4/128 (3.1)	3.7 (−∞ to 10.7)	.44
Non-UT	16/85 (18.8)	3/63 (4.8)	14.1 (−∞ to 24.5)	
Immune compromise[c]				
Present	10/51 (19.6)	1/40 (2.5)	17.1 (−∞ to 30.5)	.27
Absent	13/136 (9.6)	6/151 (4.0)	5.6 (−∞ to 12.2)	

CHI Memorial

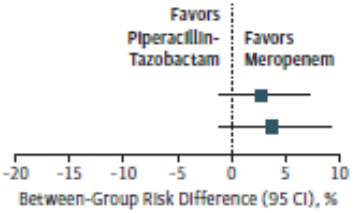
MERINO Trial

- Secondary endpoint:
  - Early assessment of response (day 4) tended to favor mero over pip-tazo (consistent with primary outcome)
  - Relapse and acquisition of a new MDR organism tended to occur more frequently among those patients in the pip-tazo arm

Measure of Success	Patients Meeting End Point, No./Total No. (%)		Between-Group Difference (95% CI)
	Piperacillin-Tazobactam	Meropenem	
Clinical and microbiological success at day 4[a]	121/177 (68.4)	138/185 (74.6)	-6.2 (-15.5 to 3.1)
Microbiological success at day 4	169/174 (97.1)	184/185 (99.5)	-2.3 (-6.1 to 0.4)



Measure of Failure	Patients Meeting End Point, No./Total No. (%)		Between-Group Difference (95% CI)
	Piperacillin-Tazobactam	Meropenem	
Microbiological relapse	9/187 (4.8)	4/191 (2.1)	2.7 (-1.1 to 7.1)
Secondary infection with multiresistant organism or *Clostridium difficile*	15/187 (8.0)[b]	8/191 (4.2)[c]	3.8 (-1.1 to 9.1)



[a] Clinical and microbiological success defined as survival, negative blood cultures, temperature of 38°C or less, and peripheral white blood cell count of less than or equal to 12 000/μL (to convert to $\times 10^9$/L, multiply by 0.001).

[b] Twelve patients with meropenem- or piperacillin-tazobactam–resistant organism and 3 with *Clostridium difficile* infection.

[c] Six patients with meropenem- or piperacillin-tazobactam–resistant organism and 2 with *Clostridium difficile* infection.

CHI Men

7 vs. 14 days for uncomplicated GNR bacteremia

- Randomized, multicenter, open-label, NI trial

- Inclusion: Inpatients with GNR bacteremia, afebrile & hemodynamically stable for 48h
- Exclusion: Uncontrolled source of infection, polymicrobial infection, Brucella or Salmonella bacteremia, immunosuppression (HIV, neutropenia, recent stem cell transplant)
  - N=604 (306, short course & 298, long course)

- Primary endpoint: Cumulative all-cause mortality, clinical failure (relapse or complications), re-admission or extended hosp. stay

- Secondary endpoints: Individual primary endpoints, new infection, functional capacity, total hospital & antibiotic days, resistance, adverse effects

7 vs. 14 days for uncomplicated GNR bacteremia

Characteristic	Short duration (n=306)	Long duration (n=298)
Hospital-acquired	81 (26.5%)	95 (31.9%)
SOFA at presentation	2 (1-3)	2 (1-3)
Appropriate empirical therapy within 48 hours	260 (85%)	242 (81.2%)
Bacteria type		
E. coli	186 (60.8%)	72 (24.2%)
Klebsiella spp.	47 (15.3%)	19 (6.4%)
Other Enterobacteriaceae	40 (13.1%)	8 (2.7%)
Acinetobacter spp.	2 (0.7%)	13 (4.4%)
Pseudmonas spp.	28 (9.2%)	20 (6.7%)
Other	3 (1%)	4 (1.3%)
Multi-drug resistant gram-negative organism	58 (18.9%)	51 (17.1%)
Source of bacteremia		
Urinary tract	212 (69.3%)	199 (66.8%)
Primary bacteremia	23 (7.5%)	28 (9.4%)
Abdominal	37 (12.1%)	34 (11.4%)
Respiratory	14 (4.6%)	10 (3.4%)
Central venous catheter	15 (4.9%)	23 (7.7%)
Skin and soft tissue	5 (1.6%)	4 (1.3%)

7 vs. 14 days for uncomplicated GNR bacteremia

- Primary Outcome
  - Short duration: 140/306 (45.8%)
  - Long duration: 144/298 (48.3%)
  - Risk difference: -2.6 (-10.5% to 5.3%); p=0.527

- Secondary Outcomes:
  - 90 day all-cause mortality: 11.8% vs 10.7%; p=0.702
  - Relapse of bacteremia: 2.6% vs 2.7%; p=0.957
  - Readmissions: 38.9% vs 42.6%; p=0.363
  - Extended hospitalization (beyond 14d): 4.9% vs 6.4%; p=0.483
  - Time to return to baseline: 2 wks (0-8.3) vs 3 wks (1-12); p=0.01
  - C. diff/ resistance/ ADEs: no difference

Thank You!