Antibiotics: Bugs and Drugs

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What we'll cover

- Bad bugs, really bad bugs… are they in Oregon?
- Can your lab look for these really bad bugs?
- Pretty bad bugs in common places… they're definitely in Oregon
- New drugs for pretty bad bugs in common places
- An old friend with a new spin?

CDC Report Finds Sharp Rise in Dangerous Drug-Resistant Bacteria

RELEASE

For immediate release: September 23, 2025

CDC Media Relations
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https://www.cdc.gov/media/

https://www.cdc.gov/media/releases/2025/2025-cdc-report-finds-sharp-rise-in-dangerous-drug-resistant-bacteria.html

Annals of Internal Medicine

OBSERVATIONS: BRIEF RESEARCH REPORTS

Changes in Carbapenemase-Producing Carbapenem-Resistant Enterobacterales, 2019 to 2023

Table. Unadjusted and Age-Adjusted CP-CRE Incidence Rates per 100 000 Persons Across Open Cohort of U.S. States With Required CRE Isolate Submission, 2019–2023*

Year	States Included, *n*	Unadjusted Population, *n*	CP-CRE† Cases, *n*	Unadjusted‡ Incidence per 100 000 Persons (95% CI), *n*	Age-Adjusted§ Incidence per 100 000 Persons (95% CI), *n*
2019	24	102 253 036	2267	2.22 (2.13–2.31)	1.98 (1.90–2.07)
2020	28	115 487 153	1903	1.65 (1.58–1.72)	1.48 (1.41–1.54)
2021	29	117 033 977	2534	2.17 (2.08–2.25)	1.91 (1.84–1.99)
2022	29	117 566 458	3137	2.67 (2.58–2.76)	2.35 (2.27–2.44)
2023	29	118 211 191	4341	3.67 (3.56–3.78)	3.16 (3.07–3.26)

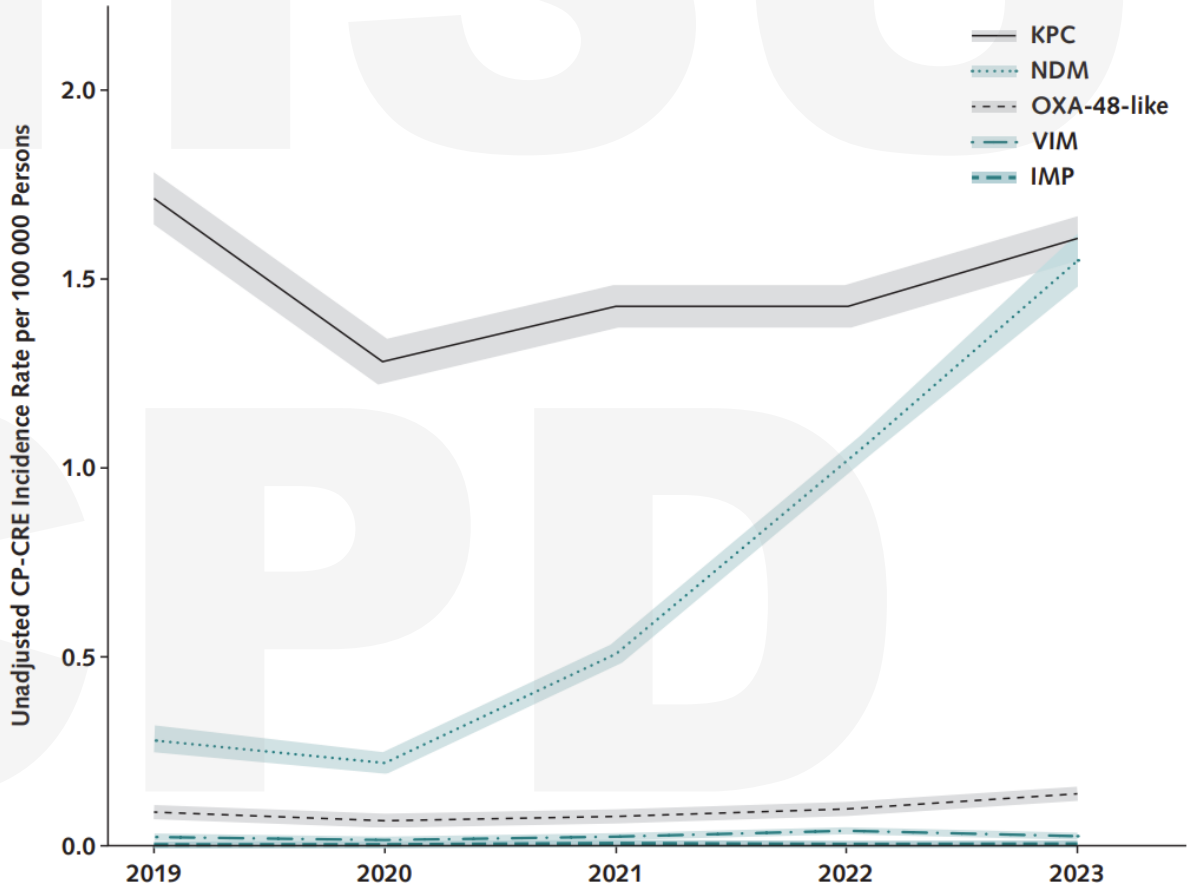
Rankin DA, et al. *Ann Intern Med* 2025. https://doi.org/10.7326/ANNALS-25-02404

Annals of Internal Medicine

Observations: Brief Research Reports

Changes in Carbapenemase-Producing Carbapenem-Resistant Enterobacterales, 2019 to 2023

Figure. Unadjusted CP-CRE incidence rates per 100 000 persons across an open cohort of U.S. states with required CRE isolate submission, by carbapenemase gene (*top*) and by organism grouping and carbapenemase gene (*bottom*), 2019–2023.



Rankin DA, et al. *Ann Intern Med* 2025. https://doi.org/10.7326/ANNALS-25-02404

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Observations: Brief Research Reports

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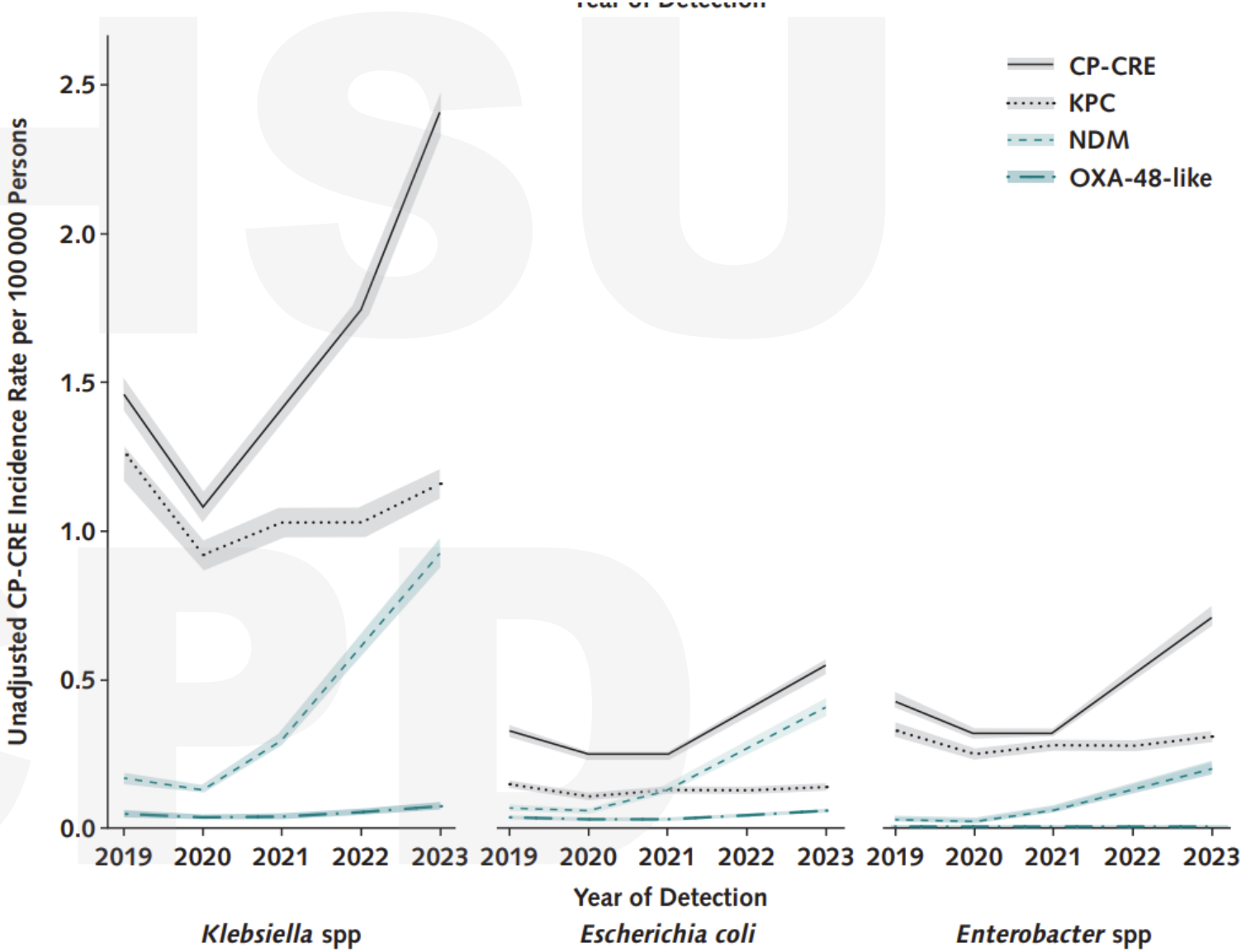
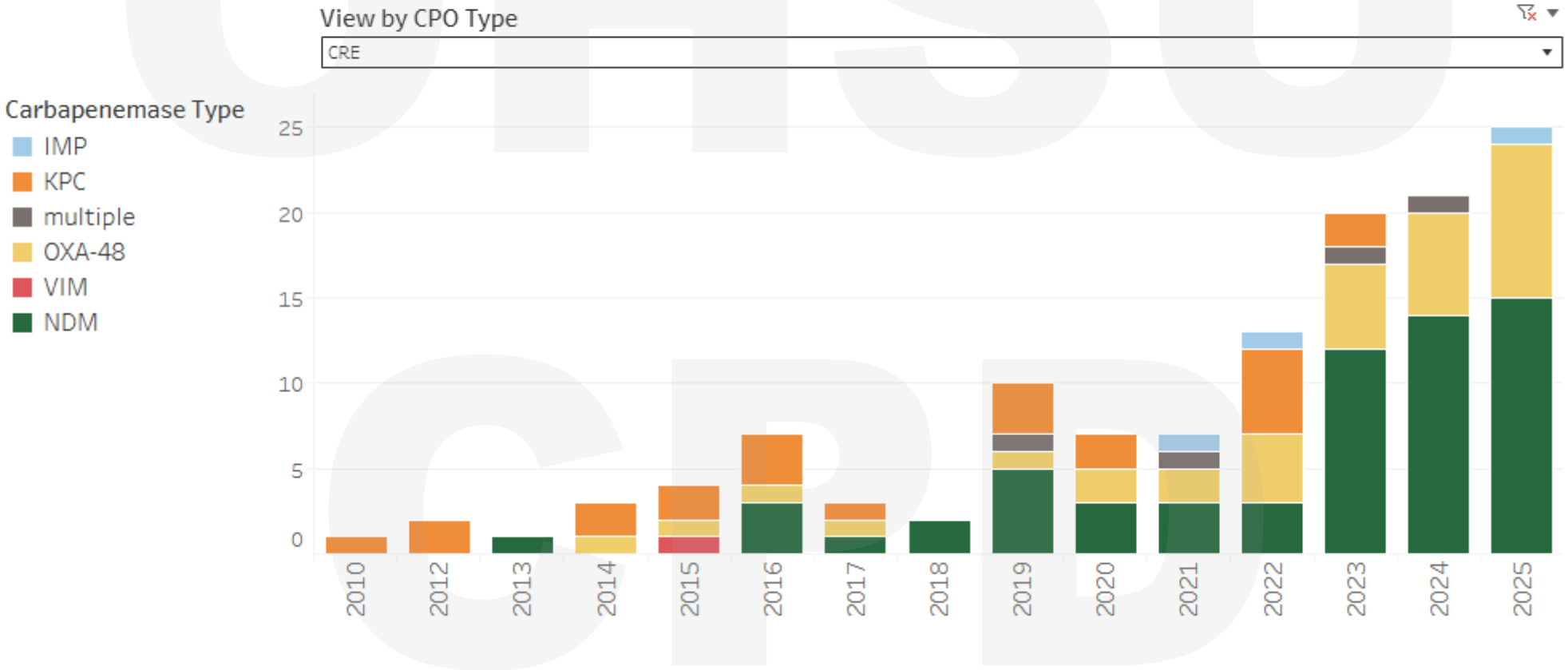


Rankin DA, et al. *Ann Intern Med* 2025. https://doi.org/10.7326/ANNALS-25-02404

Carbapenemase Type identified by Oregon laboratories by Year[1]

CPOs are not endemic in Oregon, but cases are increasing. The most commonly identified carbapenemase in recent years has been NDM. Use the filter below to filter by organism type: carbapenem-resistant Enterobacterales (CRE), carbapenem-resistant *Acinetobacter* (CRA), carbapenem-resistant *Pseudomonas aeruginosa* (CRPA). CRA became reportable in 2023 and CRPA is not mandatory to report.



https://public.tableau.com/app/profile/oregon.public.health.division.acute.and.communicable.disease.pre/viz/MDRODashboard/CPODashboard#1 – Accessed 4/2026

Words of wisdom from the IDSA GN guidelines

- “Treatment decisions should be refined based on the species and the AST profile of the pathogen, as well as on the identification of any prominent ß-lactamase genes that have been identified.”

- “Clinical microbiology laboratories are strongly encouraged to implement either nucleic acid or antigen testing to identify the presence of the specific carbapenemases produced by clinical CRE isolates.”

Tamma PD, et al. *Clin Infect Dis* 2024. https://doi.org/10.1093/cid/ciae403

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A simple and efficient test for carbapenemase detection in *Enterobacteriaceae* and *Pseudomonas aeruginosa*

New FDA 510(k) cleared test detects carbapenemase-

Summary of new(er) antibiotics for MDR gram negative infections

	ESBL	AmpC	KPC	Metallo (NDM/IMP/VIM)	Class D (eg OXA-48)	DTR *P.aeruginosa*	Carbapenem R Acinetobacter
Ceftol-Tazo							
Ceftaz-Avi							
Mero-Vabor							
Imi-Rel							
Cefiderocol							
Ceftaz-Avi+Aztreo							
Aztreo-Avi							
Sulbactam-Durlobactam							

Macesic N, et al. *Lancet* 2025;405:257

Recurrent UTIs: Causative pathogens

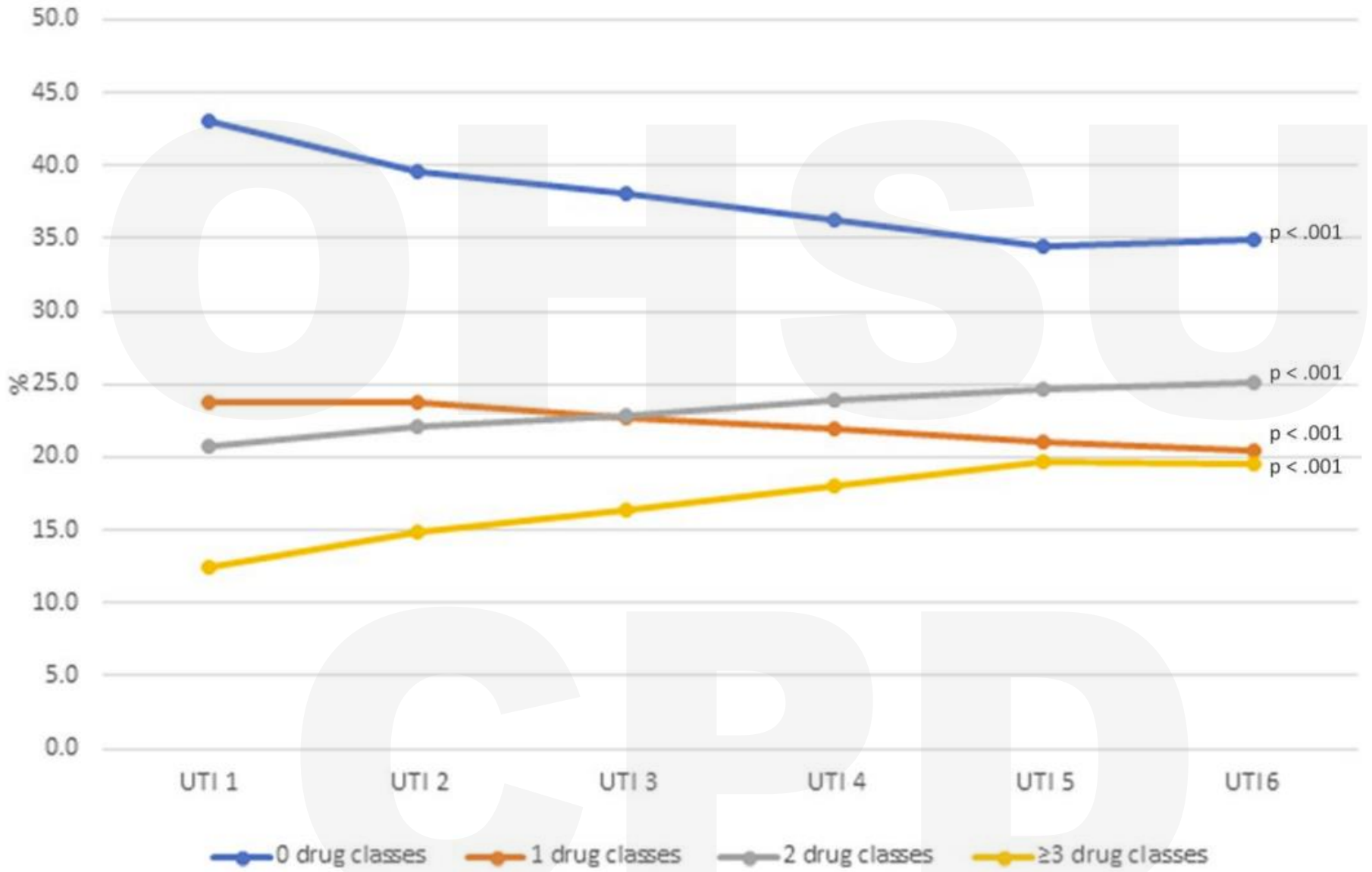
Table 2. Distribution of Pathogens Identified in Urinary Tract Infections, 2016–2021

	UTI, No. (%)						
Pathogen	UTI 1 (Index uUTI)	UTI 2	UTI 3	UTI 4	UTI 5	UTI 6	*P* for Trend
Escherichia coli	117 955 (79.2)	21 416 (76.5)	10 140 (75.0)	5435 (73.0)	3099 (72.0)	1895 (72.7)	<.001
Klebsiella	10 192 (6.8)	2436 (8.7)	1324 (9.8)	780 (10.5)	482 (11.2)	282 (10.8)	<.001
Proteus mirabilis	6305 (4.2)	1339 (4.8)	596 (4.4)	332 (4.5)	165 (3.8)	100 (3.8)	.63
Multiple	2963 (2.0)	745 (2.7)	415 (3.1)	281 (3.8)	179 (4.2)	98 (3.8)	<.001
Others[a]	11 579 (7.8)	2033 (7.3)	1035 (7.7)	607 (8.2)	381 (8.8)	232 (8.9)	.03
Total	148 994	27 969	13 510	7435	4306	2607	NA

Abbreviations: NA, not applicable; UTI, urinary tract infection; uUTI, uncomplicated urinary tract infection.

[a]Does not include contaminants.

Ku JH, et al. *J Infect Dis* 2024;230:e1344-54



Proportion of nonsusceptible isolates, by the number of nonsusceptible antibiotic classes by urinary tract infection (UTI) event (all pathogens combined), 2016–2020.

Ku JH, et al. *J Infect Dis* 2024;230:e1344-54

E. Coli vs common UTI drugs

2025 Oregon Antibiogram, Gram-Negative Organisms

Facility Org ID(s): All

Viewing Region: All, Specimen Type: All, Age Group: All, Hospital Type: All

Antibiotic Class(es): Fluoroquinolones & Others

	Fluoroquinolones		Others	
Pathogen	Ciprofloxacin	Levofloxacin	Nitrofurant..	Sulfamethoxazole with Trimet..
Acinetobacter baumannii & calcoaceticus-baumannii com..	89% n=161	92% n=114		91% n=150
Acinetobacter spp.	91% n=276	95% n=172		92% n=263
Citrobacter spp.	88% n=1,456	90% n=906	87% n=1,281	92% n=936
Enterobacter spp.	91% n=1,583	95% n=1,198	37% n=1,245	89% n=1,830
Escherichia coli	77% n=33,172	77% n=21,915	97% n=31,038	78% n=35,125

https://public.tableau.com/app/profile/oregon.public.health.division.acute.and.communicable.disease.pre/viz/OregonHospitalAntibiogram2025forReview/ORAntibiogram#1 – Accessed 4/26

2025 Oregon Antibiogram, Gram-Negative Organisms

Facility Org ID(s): All

Viewing Region: All, Specimen Type: All, Age Group: All, Hospital Type: All

Antibiotic Class(es): Penicillins, Cephalosporins, Monobactams and 6 more

						Cephalosporins				
Pathogen	Cefazolin	Cefepime	Cefotaxime	Cefotetan	Cefoxitin	Ceftazidime	Ceftazidime/ Avibactam	Ceftolozane/ Tazobactam	Ceftriaxone
Acinetobacter baumannii & calcoaceticus-baumannii com..		88% n=189	81% n=32			87% n=182			46% n=95
Acinetobacter spp.		91% n=315	71% n=48			86% n=327			50% n=174
Citrobacter spp.	20% n=776	98% n=1,374	76% n=168		34% n=805	79% n=625	99% n=90		78% n=1,164
Enterobacter spp.	0% n=1,068	91% n=1,736	64% n=209		0% n=1,071	70% n=828			66% n=926
Escherichia coli	80% n=32,008	94% n=30,219	85% n=3,373	100% n=253	93% n=18,157	92% n=13,035	100% n=1,540	99% n=1,484	91% n=33,671
Klebsiella aerogenes	1% n=465	98% n=828	73% n=99		0% n=501	72% n=375	100% n=62		72% n=624
Klebsiella spp.	76% n=6,998	92% n=7,609	83% n=977	100% n=63	95% n=4,835	89% n=3,504	100% n=495	98% n=472	89% n=8,335
Morganella morganii	1% n=370	99% n=353	83% n=60		54% n=361	84% n=169	100% n=36	73% n=30	87% n=370
Proteus spp.	57% n=3,799	98% n=3,641	94% n=454		96% n=2,497	98% n=1,690	100% n=155	99% n=155	96% n=4,016
Pseudomonas aeruginosa		93% n=3,858				90% n=2,786	99% n=699	98% n=710	
Serratia marcescens	0% n=484	98% n=683	78% n=102		0% n=502	90% n=331	97% n=74	97% n=71	88% n=678

https://public.tableau.com/app/profile/oregon.public.health.division.acute.and.communicable.disease.pre/viz/OregonHospitalAntibiogram2025forReview/ORAntibiogram#1 – Accessed 4/26

Table 2. Treatment Guidelines for Acute UTI and Recurrent UTI in Women

	EAU 2025 [8]	NICE 2018 And 2024 [32, 33]	AUA/CUA/SUFU 2022 And IDSA 2010[a] [24, 34]
Acute uUTI in women			
First choice	Fosfomycin single dose or nitrofurantoin 5 d or pivmecillinam 3–5 d	Nitrofurantoin 3 d or trimethoprim 3 d (if low risk of resistance) If pregnant: Nitrofurantoin 7 d	Nitrofurantoin 5 d or pivmecillinam 5 d or trimethoprim 3 d (avoid if prevalence of resistance exceeds 20% or if used in previous 3 m) or fosfomycin single dose
Second choice	Cephalosporins (eg cefadroxil) 3 d If local resistance pattern for *E. coli* is <20%: Trimethoprim 5 d or co-trimoxazole 3 d	Pivmecillinam 3 d or fosfomycin single dose If pregnant: Amoxicillin 7 d or cephalexin 7 d	
Recurrent uUTI in women (prophylaxis)			
First choice	Nitrofurantoin once daily or fosfomycin once a week or trimethoprim once daily	Methenamine twice a day or trimethoprim once daily or nitrofurantoin once daily	Trimethoprim once daily or nitrofurantoin once daily or cephalexin once daily or fosfomycin every 10 d
Second choice	*If pregnant:* Cephalexin once daily or cefaclor once daily	Amoxicillin once daily or cephalexin once daily	
Duration	Usually from 3–12 m (no consensus)	Review at least every 6 m	

Abbreviations: AUA, American Urological Association; CUA, Canadian Urological Association; cUTI, complicated urinary tract infection; EAU, European Association of Urology; IDSA, Infectious Diseases Society of America; NICE, National Institute for Health and Care Excellence; SUFU, Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction; UTI, urinary tract infection; uUTI, uncomplicated urinary tract infection.

[a]IDSA 2010 guidelines refer to acute uUTI [24]. IDSA 2025 guidelines outline treatment and management recommendations for cUTI only and therefore are not summarized here [9].

Canton R, et al. *Clin Infect Dis* 2026;epub 2/25/26 - https://doi.org/10.1093/cid/ciaf705

Pivmecillinam (Pivya)

- Cost: around $100/tablet
- Oral prodrug of mecillinam
- FDA approved indication: uUTI in females 18yo & older caused by susceptible *E. coli*, *Proteus mirabilis*, & *S. saprophyticus*.
- Dose: 185 mg tablet orally 3x/d for 3 to 7 days (so +/-$300/d)
- Common side effects: Nausea (4.3%), Diarrhea (2.1%), VVC (1.8%)

https://pivya.com/assets/pdf/pivya-prescribing-information.pdf?1

Pivmecillinam: Why is this cool?...Or is it?

- Beta-lactam antibacterial drug with a targeted spectrum of activity. Mainly active against gram-negative bacteria.
- Most beta-lactam agents, bind gram-negative PBP-1A, -1B or -3, mecillinam acts on PBP-2 in the gram-negative cell wall.
- **In-vitro activity against Enterobacterales with beta-lactamases including extended-spectrum beta-lactamases (ESBL) of the following groups: CTX-M, SHV, TEM and AmpC.**

https://pivya.com/assets/pdf/pivya-prescribing-information.pdf?1

Pivmecillinm:
So where are you going to use this?

- Problems
  - 1: Susceptibility testing not routinely available
  - 2: $$$
  - 3: Can you say pivmecillinam?
  - 4: Only indicated for uUTI
  - 5: No data for complicated UTI/pyelo

- Strengths
  - 1: Tons of clinical and safety data
  - 2: Already in guidelines and breakpoints are established
  - 3: Consistently active against ESBL *E. coli* – *However*…

Hawkins BK, et al. *Antimicrob Agents Chemother* 2025; https://doi.org/10.1128/aac.01824-24

Gepotidacin (Blujepa)

- **Cost**: +/- $100/tablet
- **Mechanism**: non-fluoroquinolone topoisomerase II inhibitor
- **FDA approved indications**:

  1: **uUTI in females** 12yo & older at least 40kg caused by susceptible *E. coli*, *K. pneumoniae*, *C. freundii*, *E. faecalis*, & *S. saprophyticus*.

  2: **Uncomplicated urogenital gonorrhea (UUG)** in patients >12yo weighing at least 45kg with no or limited alternative options. Indication based on limited safety data.

- **Dose:**
  - uUTI:1500mg (two 750mg tablets) twice daily for 5 days (+/-$400/d)
  - UUG: 3000mg (four 750mg tablets) once and repeated once 12h later. (+/-$800)
- **Note:** Take after a meal to reduce GI side effects

https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Blujepa/pdf/BLUJEPA-PI-MG.PDF

Gepotidacin: Why is this cool?...Or is it?

- Non-FQ topoisomerase II and topoisomerase IV inhibitor which inhibits DNA replication. – **Like a quinolone but different binding**
- In studies of certain amino acid substitutions in GyrA and ParC of *E.coli* and *N. gonorrhoeae*, a direct relationship between gepotidacin and fluoroquinolone susceptibility was not established. - **Not like a quinolone**
- **Consistent in-vitro activity against quinolone resistant Enterobacterales, particularly E. coli.**

https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Blujepa/pdf/BLUJEPA-PI-MG.PDF

Gepotidacin: What's not cool

- **QT prolongation** – avoid in patients with prolonged QTc, relevant pre-existing cardiac disease, on antiarrhythmics, or other QTc prolonging meds
- **Avoid with:** Strong CYP3A4 inhibitors, CrCl <30, Child-Pugh Class C hepatic impairment. Warnings get stronger for UUG patients
- **Adverse drug reactions**
  - Diarrhea: 16% gepo vs 3% nitro
  - Nausea: 9% gepo vs 4% nitro
  - Abd pain: 4% gepo vs 2% nitro

Gepotidacin:
So where are you going to use this?

- Problems
  - 1: Susceptibility testing not routinely available
  - 2: $$$
  - 3: Can you say gepotidacin?
  - 4: Only indicated for uUTI, no data for complicated UTI/pyelo
  - 5: Only indicated for UUG when no other options available

- Strengths
  - 1: Dual targeting of both topo II and topo IV hopefully reduce resistance risks
  - 2: Familiar mechanism of action
  - 3: Consistently active against ESBL *E. coli* – *However…*

https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Blujepa/pdf/BLUJEPA-PI-MG.PDF

Sulopenem-probenecid (Orlynvah)

- **Cost**: +/- $300/tablet
- **Mechanism**: sulopenem etzadroxil, a penem antibacterial, and probenecid, a renal tubular transport inhibitor
- **FDA approved indications**:

  uUTI due to *E. coli*, *K. pneumoniae*, or *P. mirabilis* in adult women who have limited or no alternative oral antibacterial treatment options.

- **Dose:** One 500mg sulopenem/500mg probenecid tablet twice daily for 5 days (+/-$600/d)
- **Note:** Take with food to improve absorption of sulopenem

https://www.orlynvah.com/pdf/prescribing-information.pdf

Sulopenem-probenecid : Why is this cool?...Or is it?

- An oral penem antibiotic: spectrum similar to ertapenem BUT pharmacokinetics are very different.
- Resistance to sulopenem is caused by certain extended spectrum beta-lactamases (ESBLs) including carbapenemases, alteration of PBPs, over expression of efflux pumps and loss of outer membrane porins.
- Sulopenem demonstrated activity against Enterobacterales in the presence of certain beta-lactamases and ESBLs, e.g., AmpC, CTX-M, TEM, SHV.

https://www.orlynvah.com/pdf/prescribing-information.pdf

Sulopenem-probenecid : What's not cool

- **It's an oral penem… not quite a carbapenem, but really close.**
- **Contraindicated** in patients with known uric acid kidney stones.
- In patients with a history of **gout**, implement measures to reduce the risk of uric acid kidney stone development should be instituted, such as increased fluid intake and alkalization of the urine.
- May cause exacerbation of **gout**. In patients with a known history of gout, ensure appropriate therapy of gout is instituted
- **Adverse drug reactions**
  - Diarrhea: 10% sulo vs 4% comparator

https://www.orlynvah.com/pdf/prescribing-information.pdf

Another significant issue…

- Probenecid (a component of ORLYNVAH) is an inhibitor of organic anion transporters 1 and 3 (OAT1/3) and may increase plasma concentrations of drugs that are dependent on OAT1/3 for elimination.
  - Including:
    - NSAIDS
    - Methotrexate
    - Rifampin
    - Lorazepam
    - Oral sulfonylureas

https://www.orlynvah.com/pdf/prescribing-information.pdf

Sulopenem-probenecid :
So where are you going to use this?

- Problems
  - 1: Susceptibility testing not routinely available, ertapenem a possible surrogate
  - 2: $$$
  - 3: Diarrhea worse than amox-clav in trial
  - 4: Only indicated for uUTI – failed stepdown pyelo trials
  - 5: Do we really want oral penems in the community?

- Strengths
  - 1: A penem
  - 2: Familiar mechanism of action
  - 3: Consistently active against ESBL *E. coli* – *However:* **NO PSEUDOMONAS!!!**

https://www.orlynvah.com/pdf/prescribing-information.pdf

NEJM Evidence

Published June 24, 2025
NEJM Evid 2025;4(7)
DOI: 10.1056/EVIDoa2400414

ORIGINAL ARTICLE

Sulopenem versus Amoxicillin/Clavulanate for the Treatment of Uncomplicated Urinary Tract Infection

Sailaja Puttagunta, M.D.,[1] Steven I. Aronin, M.D.,[2] Jayanti Gupta, Ph.D.,[3] Anita F. Das, Ph.D.,[4] Kalpana Gupta, M.D., M.P.H.,[5] and Michael W. Dunne, M.D.[1]

Table 2. Overall Response, Clinical Response, and Microbiologic Response at Day 12 — Microbiologic-Modified Intent-to-Treat Population.*

Outcome	Sulopenem, n (%) (N=522)	Amoxicillin/Clavulanate, n (%) (N=468)	Difference, Percentage Points (95% CI)	P Value
Overall response at day 12				
Success	318 (60.9)	260 (55.6)	5.4 (−0.8 to 11.5)	0.0437
Failure	177 (33.9)	185 (39.5)		
Indeterminate	27 (5.2)	23 (4.9)		
Clinical success at day 12	397 (76.1)	358 (76.5)	−0.4 (−5.7 to 4.9)	
Microbiologic success at day 12	390 (74.7)	315 (67.3)	7.4 (1.8 to 13.1)	

- Treatment-emergent adverse events: Sulopenem vs amoxicillin/clavulanate, including diarrhea (8.1% vs. 4.1%), nausea (4.3% vs. 2.9%), and headache (2.2% vs. 1.5%).

Conclusions

- Carbapenem resistance in Enterobacterales is spreading
- It is present in Oregon
- Your lab is a huge resource and the drugs get complicated
- ESBLs are increasingly common in Oregon
- New drugs provide new options in the urine, but come with problems