

Targeting Treatment to the Patients: The 2022 Antimicrobial Playlist

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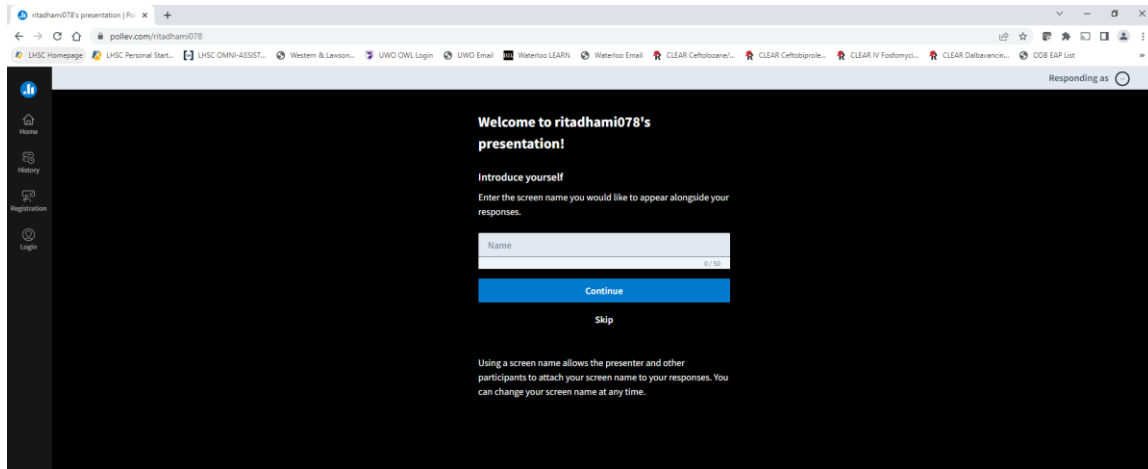
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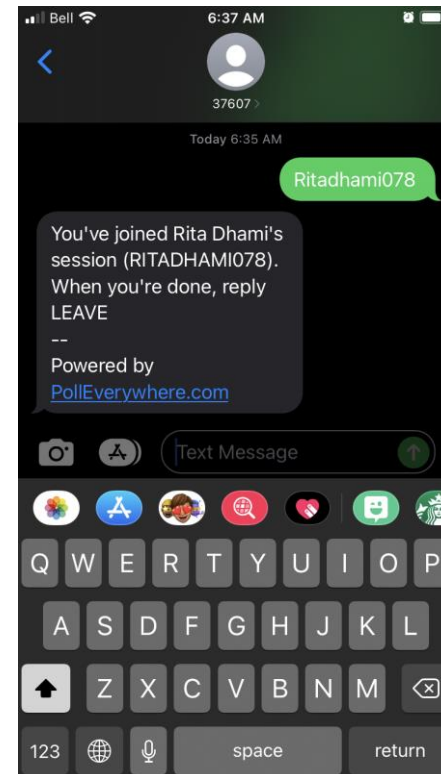
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Objectives

- Describe today's infectious disease patient
- Describe landscape of Canadian antimicrobial use today
 - “CLASSICS”
- Describe the newer antimicrobial agent and unique characteristics
 - “UP & COMING”
- Identify potential roles of these new agents in the management of your patients with infectious diseases
- Discuss strategies for treating infectious disease in challenging patients

Speaker Disclosure

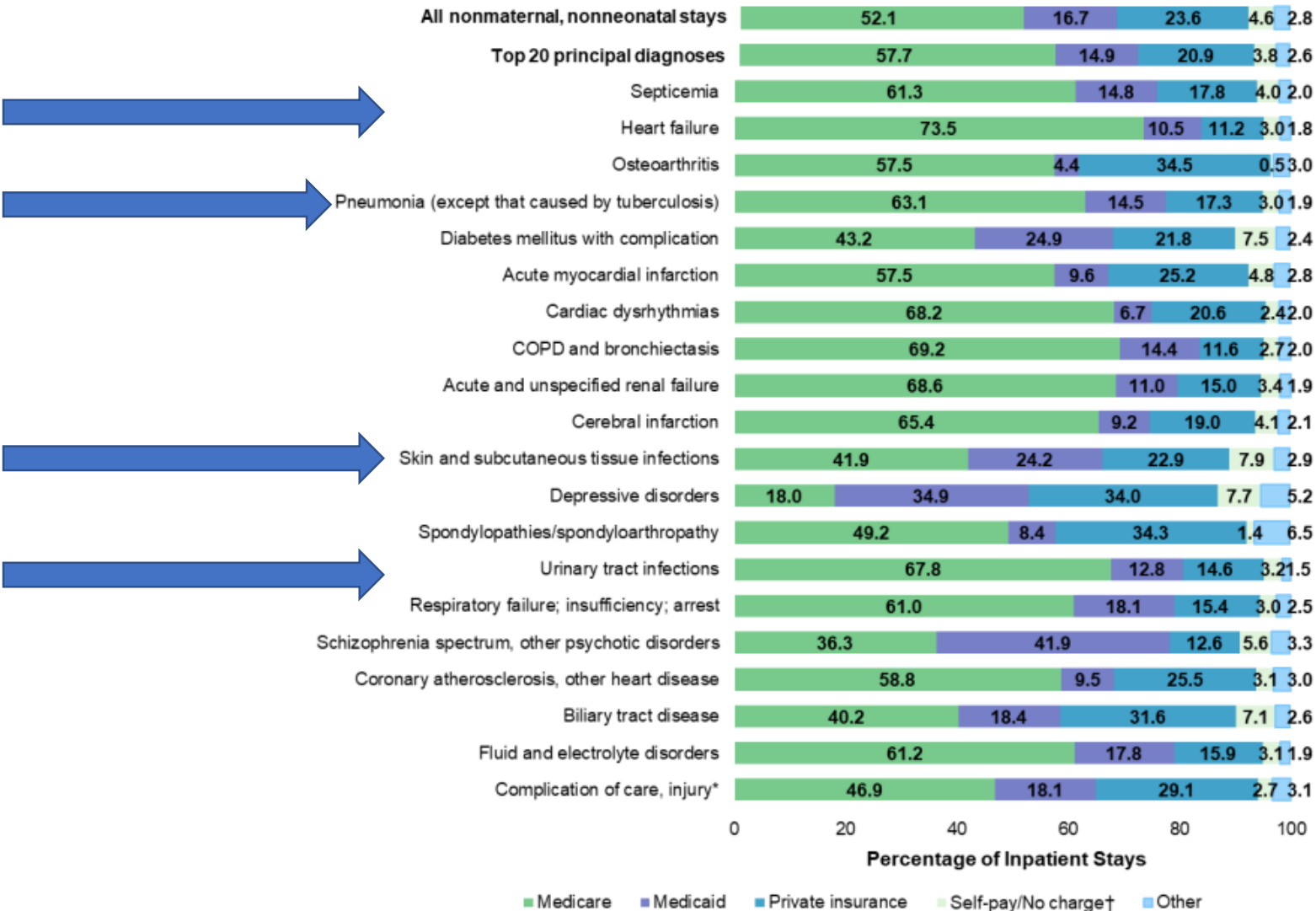
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- Relationships with financial sponsors:
 - Grants/Research Support: N/A
 - Speakers Bureau/Honoraria: Pfizer, Paladin Labs
 - Consulting Fees: N/A
 - Patents: N/A
 - Other: N/A

Disclosure

- This event is sponsored by Paladin Labs Inc.
- The speaker has full editorial control over the presentation and will present off-label data.
- Paladin Labs does not support claims that are not consistent with the Health Canada-approved product monograph (off-label).

Infectious diseases in 2022...

Reasons for hospital admissions now



Interactive Map: In-Hospital Sepsis (per 1,000), undefined

Data Export

Hover over data points for additional information or select data points to access health region, hospital and long-term care organization results, when available. Contextual information is displayed below the map, based on your selection. More information can be found on the [Resources Page](#) of the Indicator Library.

undefined results are for 2020–2021 except for Quebec; these results are for 2019–2020.

- Above average performance
- Same as average performance
- Below average perform
- No assessment



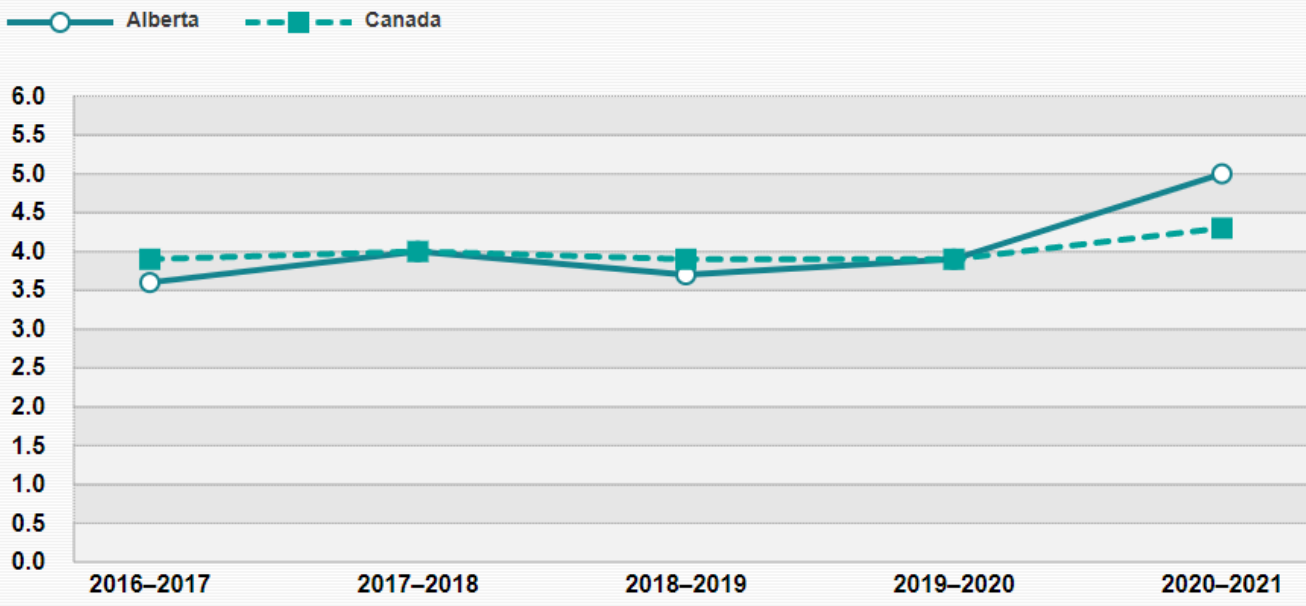
Information (CIHI)

Trend Over Time: In-Hospital Sepsis (per 1,000)

ADD a province, territory, health region, long-term care organization or hospital using the search boxes below. You can also ADD a city to find results for the corresponding health region. At least 3 years of data must be available for trend results to appear on the graph.

The graph will refresh when a filter is selected. The filtered data will be reflected in the downloadable Excel file, available by selecting Data Export following the graph.

[Methodology \(PDF\)](#)



Error Bar Add Comparator

Please enter 2 or more characters... Add

Why are infections so problematic

Drug Related

- Poor penetration
- Insufficient dose or route
- PK/PD not optimized

Pathogen Related

- Wrong pathogen
- Multidrug resistant organism
- Inoculum effect

Patient Related

- Comorbidities
- Adherence
- Inappropriate administrations of route

Canadian Landscape of Antimicrobial Use

Canadian Nosocomial Infection Surveillance Program: Antimicrobial Use



Quantitative Antimicrobial Usage Surveillance Amongst Adult and Paediatric Inpatients at CNISP Hospital Sites across Canada

CNISP AMU Working Group 2022

John Conly (adult), Michelle Science (paediatrics), Daniel Thirion (pharmacy)
CNISP epidemiologists: Kelly Choi, Joelle Cayen, Linda Pelude, Wallis Rudnick
CNISP MPH student: Janine Xu

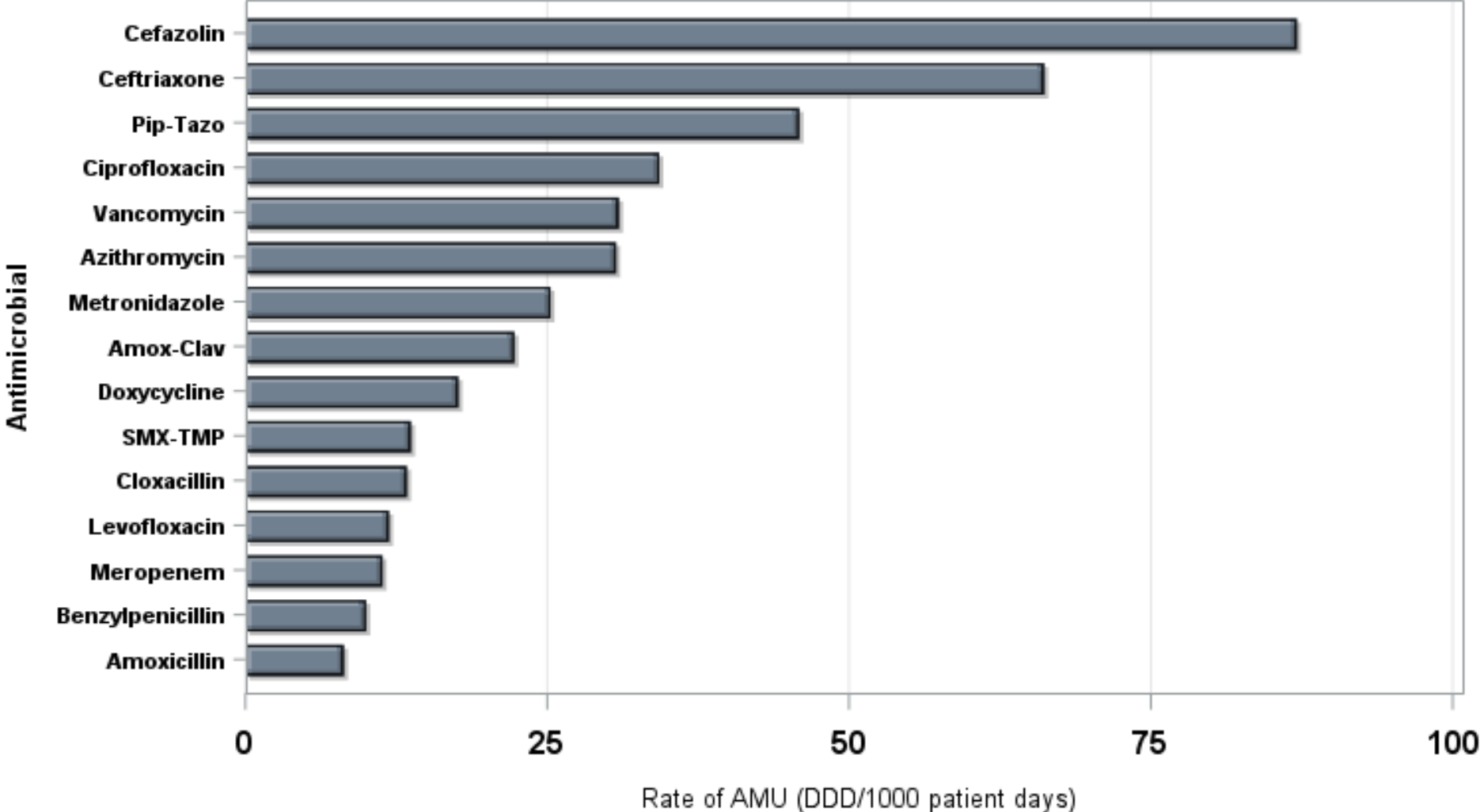
Preliminary data – please do not share

PROTECTING AND EMPOWERING CANADIANS
TO IMPROVE THEIR HEALTH



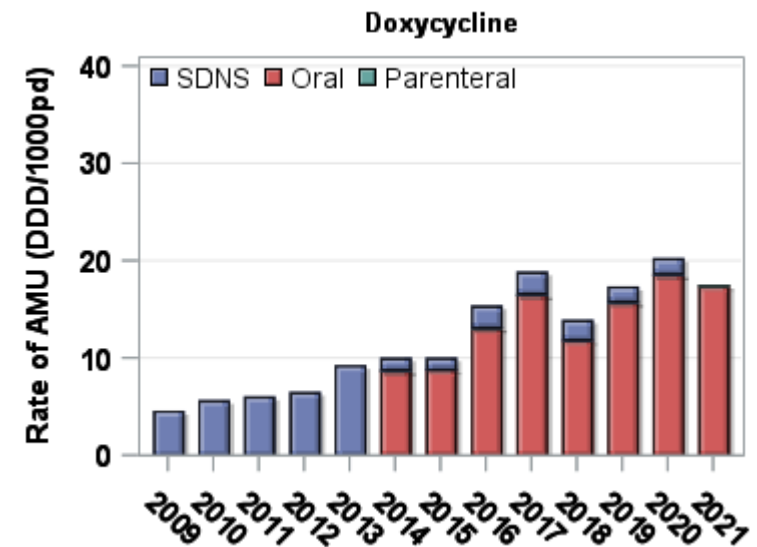
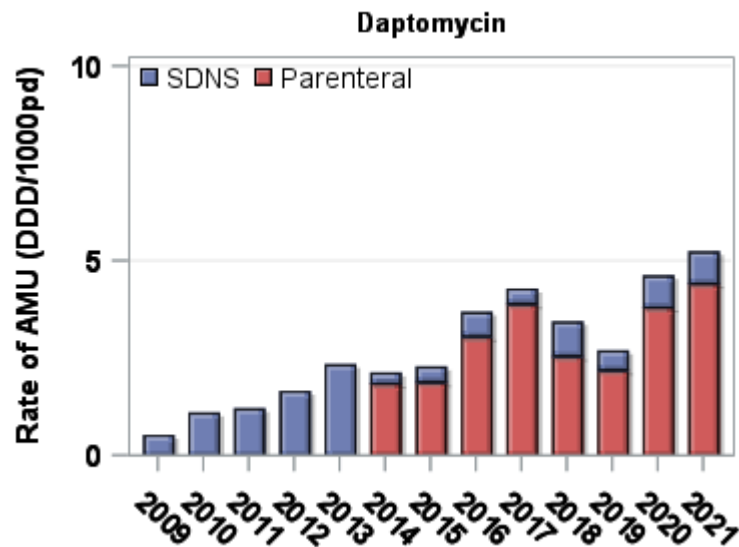
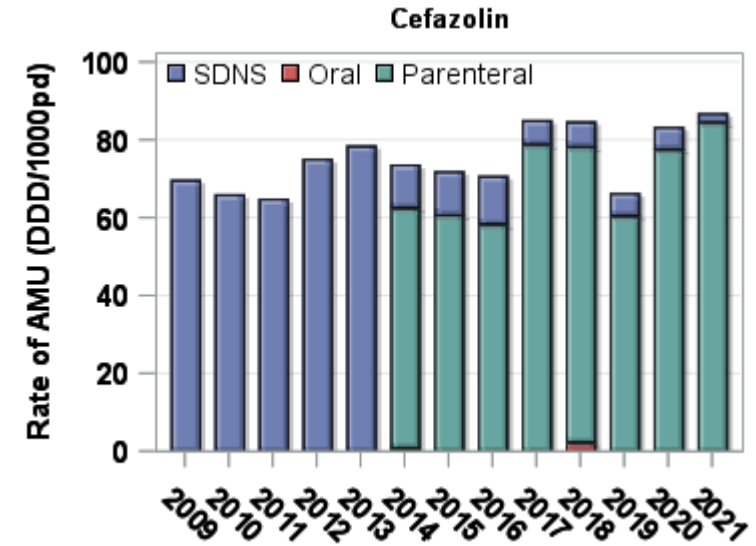
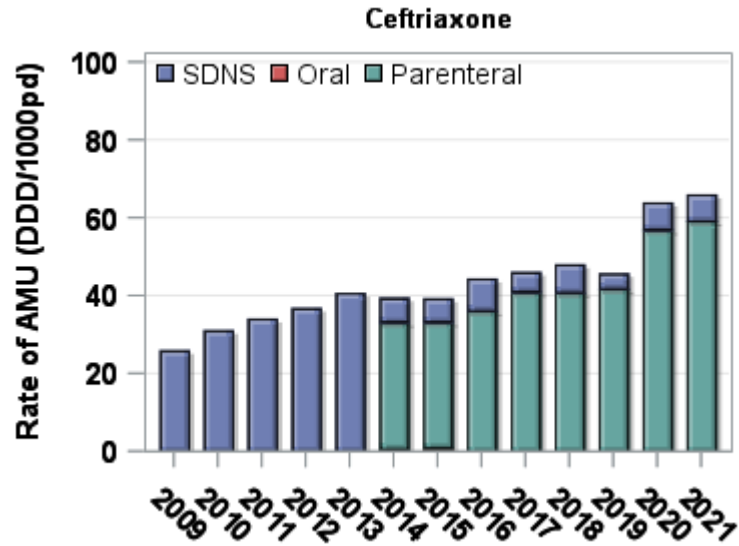
Most frequent antimicrobials in 2021

(n=103 hospitals)



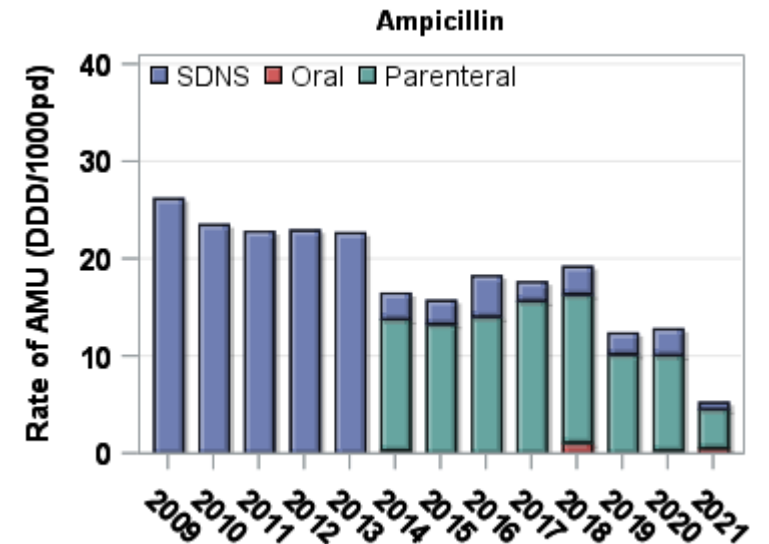
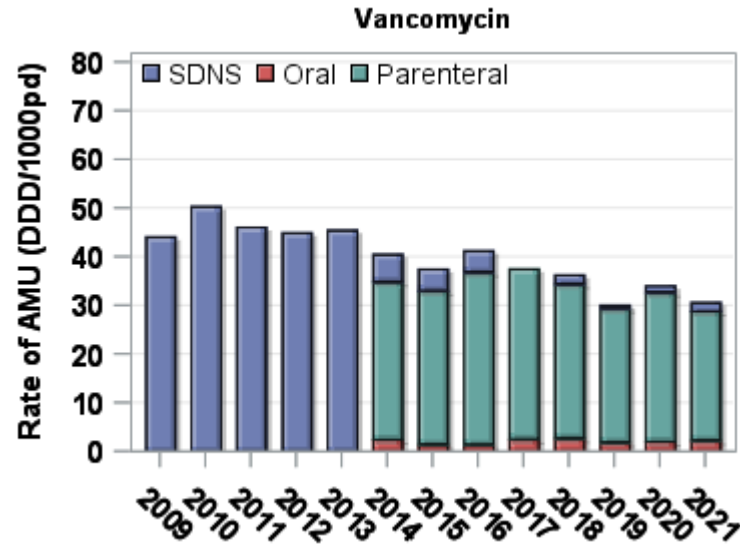
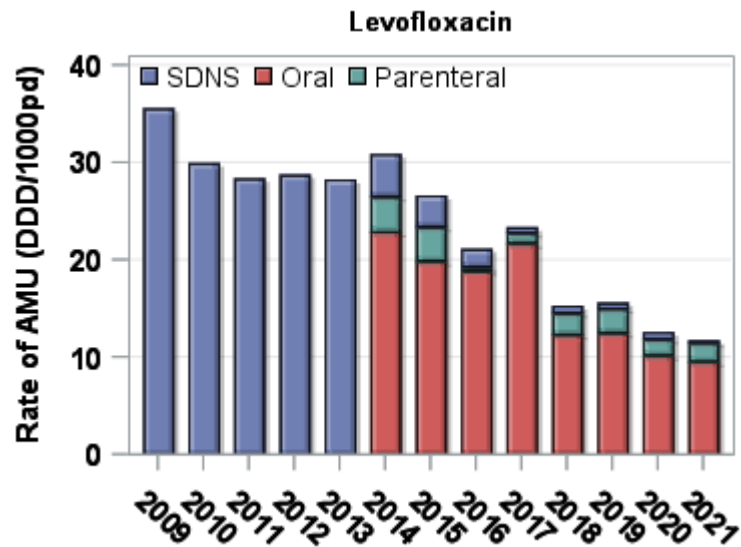
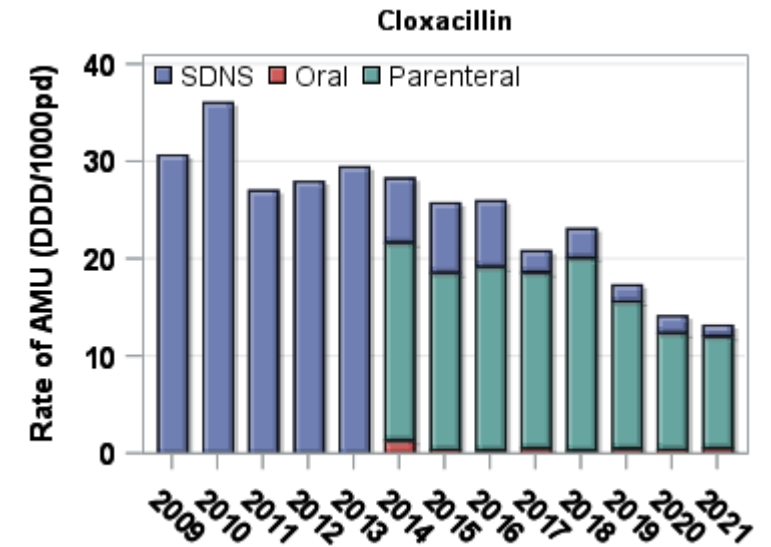
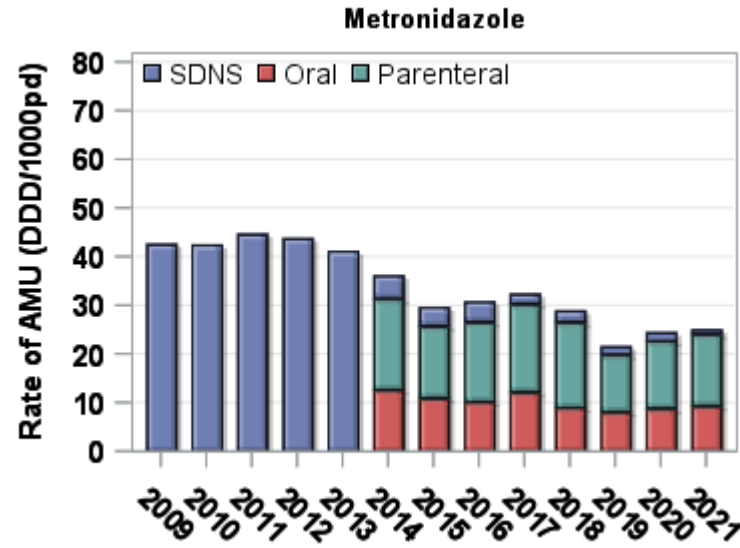
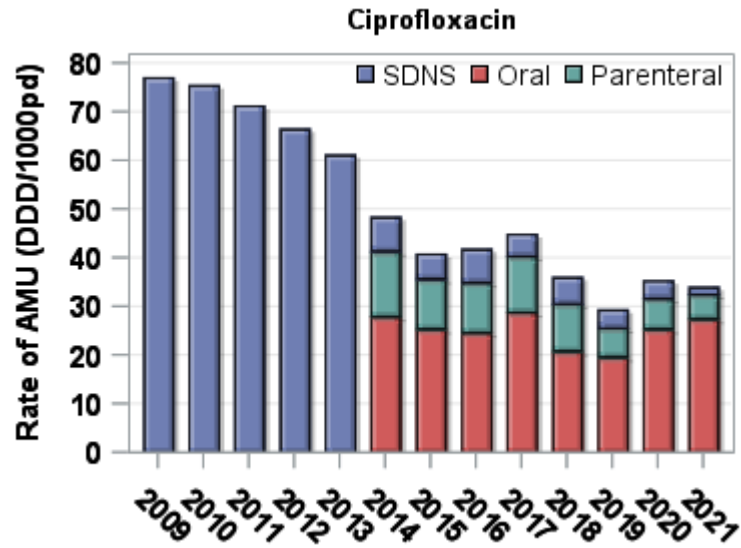
Antibiotics with the greatest absolute increases

2009–2014 to 2016–2021 (all sites); SDNS = Site not specify administration route



Antibiotics with the greatest absolute decreases

2009–2014 to 2016–2021 (all sites) ; SDNS = 'Site did not specify route of administration'



CLASSIC  **HITS**

THE GREATEST ANTIMICROBIALS ON EARTH

“CLASSICS”



BEST NEW ARTIST
NOMINEES

64th Annual Grammy Awards

“UP & COMING”

Strategy for dealing with the ‘challenging’ patient infections

Amoxicillin-clavulanate

- Dose:
 - 5:1 1000 mg/200 mg every 6-8 hours
 - 10:1 2000 mg/200 mg every 8-12 hours
- Spectrum:
 - *Staphylococcus spp*, *Streptococcus spp*,
Enterococcal spp
 - *H.influenzae*, *H.parainfluenzae*, *M.catarrhalis**
P.multocida, *P.mirabilis*
 - *Clostridium spp*. *Peptostreptococcus spp*.
- Indications.... Endless!



Fosfomycin IV (Ivozfo[®])

- Spectrum:
 - Gram positive bacteria such as *S. aureus* (incl. MRSA) and *Enterococcal spp.* (incl. VRE)
 - Gram negative bacteria *N.gonorrhoeae*, *ESBL* & Carbapenemase Enterobacteriaceae
 - Anaerobic bacteria such as *Peptococcus* species

- Dose

Table 1: General dosage guidelines for adults by indication

Indication	Daily dose
Osteomyelitis	12–24 g* in 2–3 divided doses
Complicated urinary tract infection	12–16 g in 2–3 divided doses
Nosocomial lower respiratory tract infection	12–24 g* in 2–3 divided doses
Bacterial meningitis	16–24 g* in 3–4 divided doses

*The high-dose regimen (> 16 g/day in 3 divided doses) should be used in severe infections expected or known to be caused by less susceptible bacteria (see **MICROBIOLOGY**).

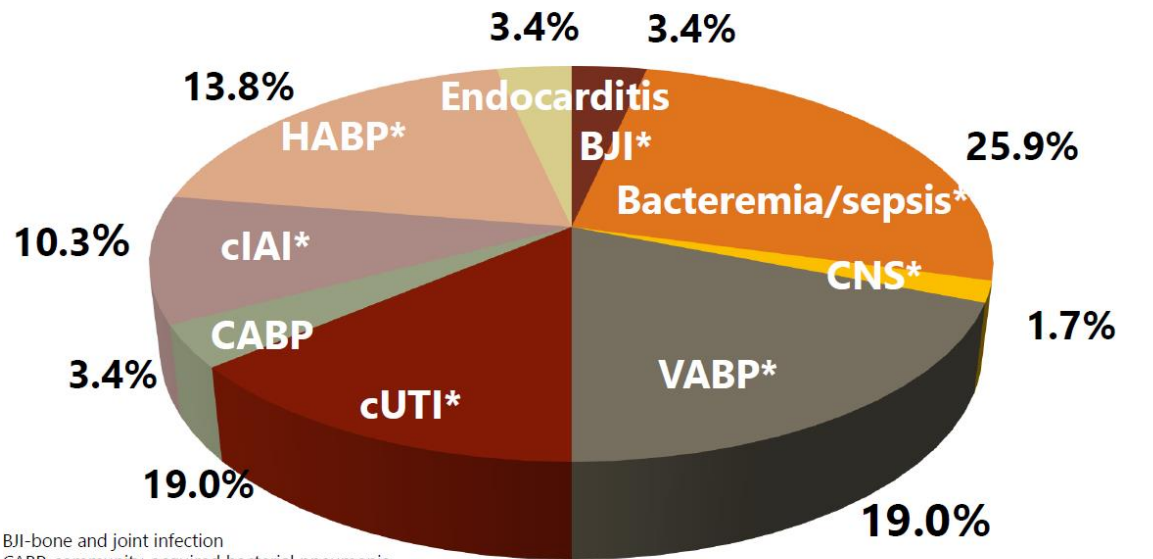
Individual doses must not exceed 8 g.

- Watch sodium load



CLEAR* Registry

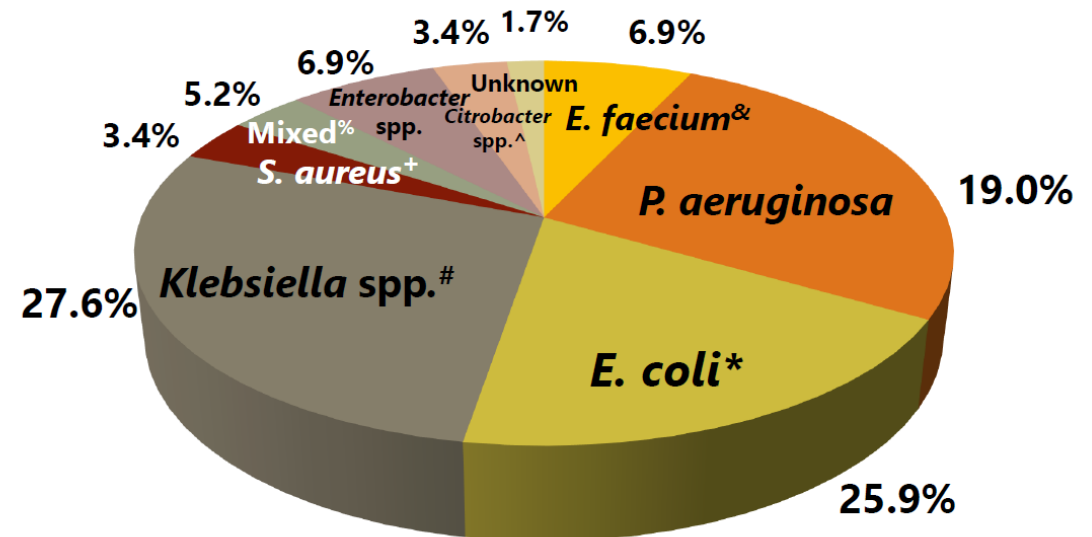
CLEAR (n=58): IV Fosfomycin Infections Treated



* On label

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE **CARA**

CLEAR (n=58): IV Fosfomycin Pathogens Treated



* 1 ESBL-extended spectrum β -lactamase producing and 13 CRE-carbapenem resistant Enterobacterales

3 ESBL-extended spectrum β -lactamase producing and 13 CRE-carbapenem resistant Enterobacterales

& 3 of 4 isolates were vancomycin-resistant *Enterococcus faecium*-VRE

+ 1 MRSA

^ KPC producing

% Mixed (*E. coli*/*Klebsiella* spp and *Klebsiella* spp/*P. aeruginosa*)

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE **CARA**

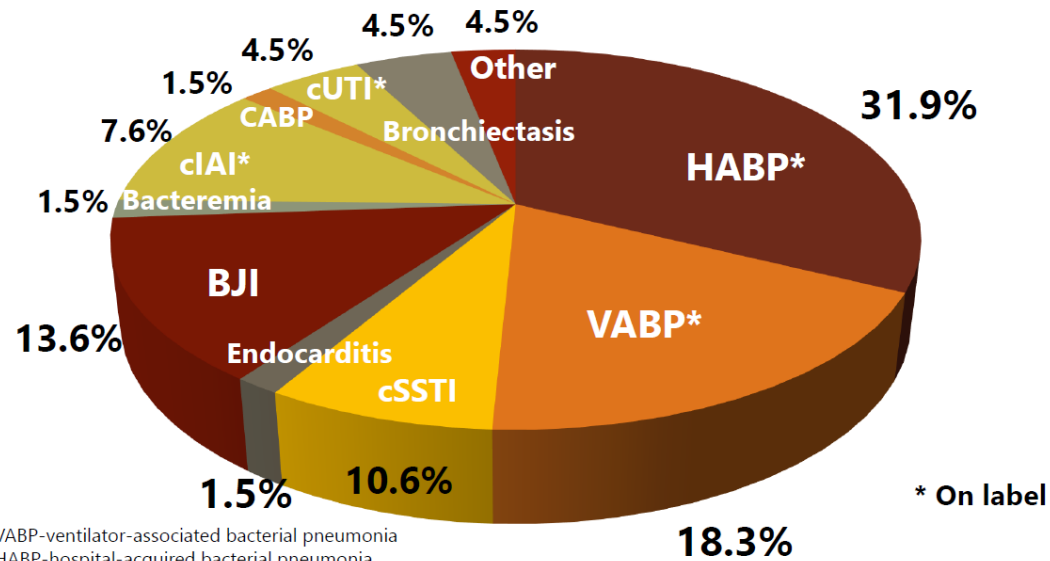
Ceftolozane-tazobactam (Zerbaxa®)

- Dose: 1.5-3g IV Q8H
- Spectrum: *E.cloacae*, *E.coli*, *K.oxytoca*, *K.pneumoniae*, *P.mirabilis*, *P.aeruginosa*, *B.fragilis*, *S.anginosus*, *S.salivarius*.
- Indicated for cIAI, cUTI, Nosocomial Pneumonia, CAP



CLEAR Registry

CLEAR (n=66): Ceftolozane/tazobactam Infections Treated

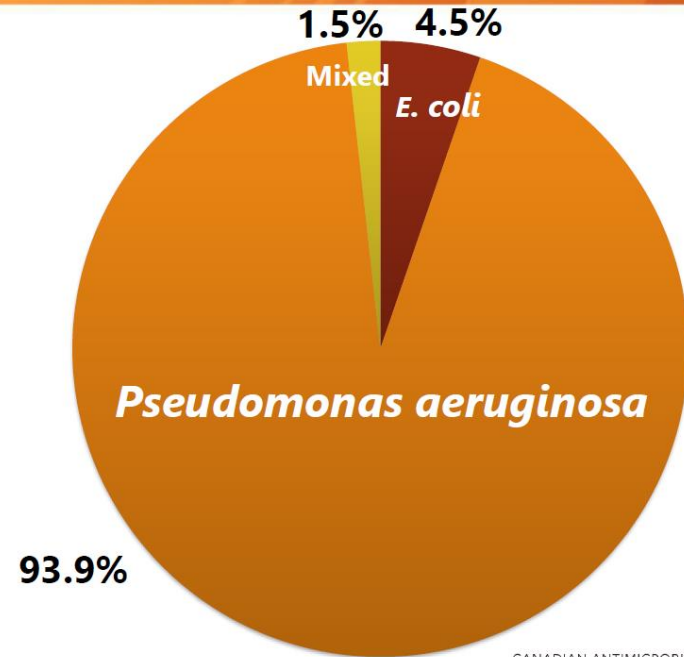


* On label

VABP-ventilator-associated bacterial pneumonia
 HABP-hospital-acquired bacterial pneumonia
 cIAI-complicated intra-abdominal infection
 cUTI-complicated urinary tract infection
 cSSTI-complicated skin/skin structure infection
 BJI-bone/joint infection
 CABP-community-acquired bacterial pneumonia

Other-1 patient each; exacerbation of chronic bronchitis, exacerbation of cystic fibrosis, necrotizing otitis and device related infection

CLEAR (n=66): Ceftolozane/tazobactam Pathogens Treated



Mixed- *Pseudomonas aeruginosa* and *Enterococcus faecium*

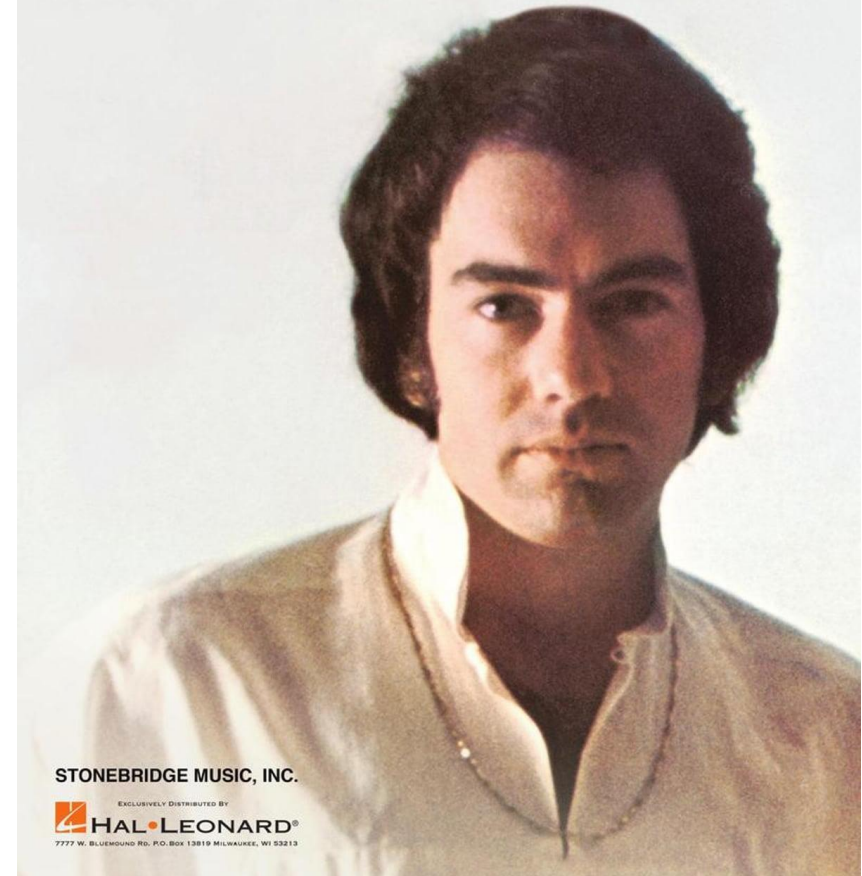
CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE **CARA**

Ceftaroline (Teflaro®)

- Available through Health Canada SAP
- *Covers S.pneumoniae, S.aureus (including MRSA), H.influenzae, E.coli, K.pneumonia*
- Indication for CAP; Evidence for MRSA salvage therapy
- Dose: 600mg IV q12h
 - Doses q8h for IE
 - Renal dose adjustment required

“Ceftaroline”

A **NEIL DIAMOND** CLASSIC



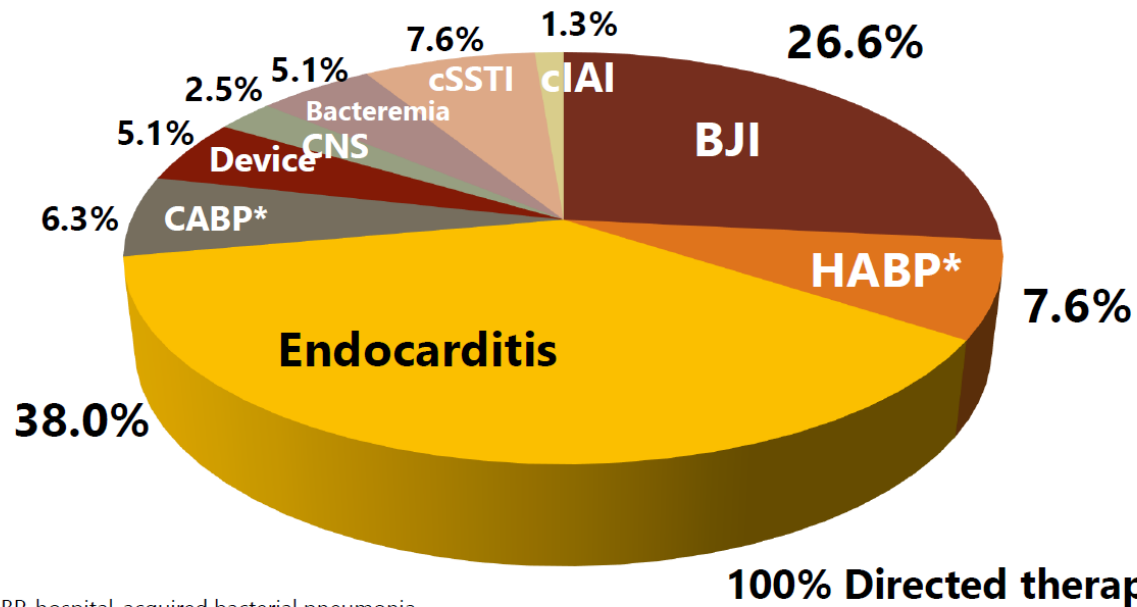
Ceftobiprole (Zevtera[®])

- Spectrum: *S.aureus* (including MRSA), *S.pneumoniae*, *E.coli* K. pneumoniae, *H.influenzae*
- Role: Indication is CAP/HAP, Previously on market for SSTI
- Dose: 500mg IV q8h



CLEAR Registry

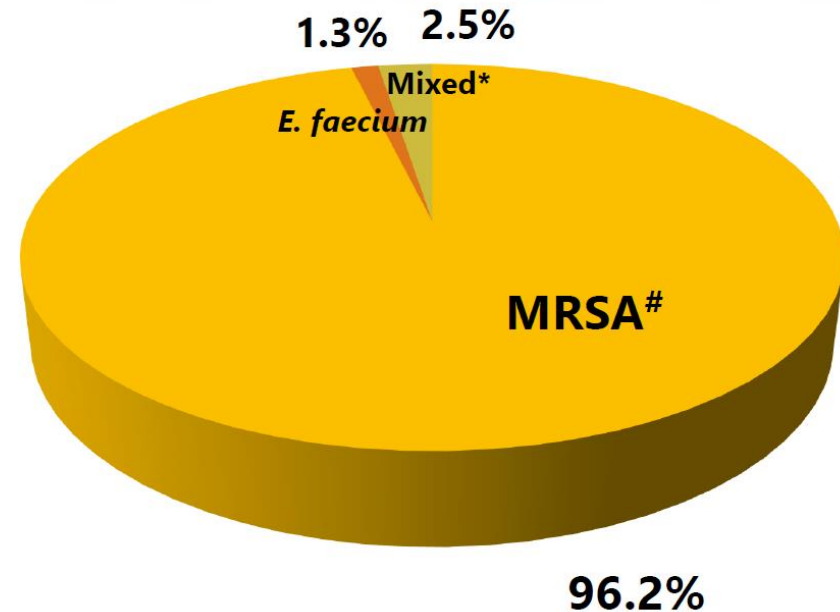
CLEAR (n=79): Ceftobiprole Infections Treated



HABP-hospital-acquired bacterial pneumonia
 CABP-community-associated bacterial pneumonia
 BJI-bone/joint infection
 cSSTI-complicated skin and skin structure infection

CNS-central nervous system infection
 Device-device related infection
 cIAI-complicated intraabdominal infection

CLEAR (n=79): Ceftobiprole Pathogen Treated



- * Mixed-*Pseudomonas aeruginosa* and *Staphylococcus aureus*; *Klebsiella oxytoca* and *Staphylococcus aureus*
- # 1 VISA

Dalbavancin

- Spectrum: *Staphylococcus spp*, *Streptococcus pyogenes*, *Enterococcus spp* (vancomycin-susceptible isolates only)
- Role: SSTI
- Dosing regimens: 1500mg IV once
1000mg x 1, 500mg 1 week later



CLEAR Registry



Novel Beta lactamase inhibitor combinations

- Not in Canada
 - Ceftazidime-avibactam (Avycaz[®])
 - Meropenem-vaborbactam (Vabomere[®])
 - Tebipenem (Orapenem[®])
 - Imipenem-cilistatin-relebactam* (Recarbrio[®])

Transitions to Outpatient

Strategy for dealing with the 'challenging' patient discharges

Transition to Outpatient IV to PO

- Clinical data supports efficacy for given indication, including adequate penetration to the site of infection
- Excellent bioavailability,
- No significant food-drug or drug-drug absorption issues
- Few adverse events when taken orally
- Ensure not barriers to administration (*easy to swallow pills, taste of oral solution, Infrequent dosing schedule, Cost, not on back-order*)

Oral vs. IV Abx for Bacteremia

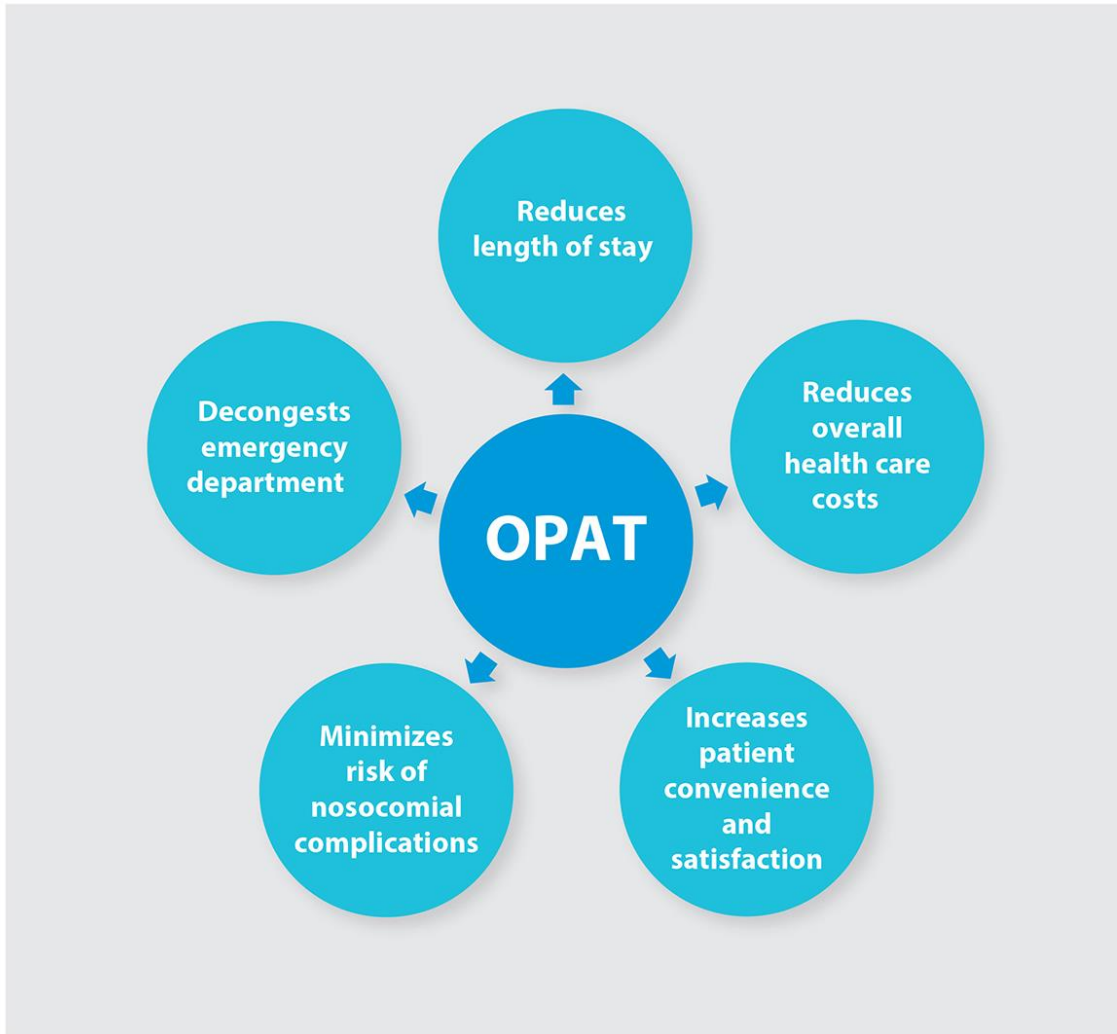
Author	Yr	N	Regimen (Oral vs. IV)	Success
Amodio-Groton	'96	50	Ciprofloxacin oral vs. IV—GNB	83% (20/24) v 77% (20/26)
San Pedro	'02	51	Linezolid vs. ceph— <i>S. pneumo</i>	93% (27/29) v 68% (15/22)
Deville	'03	36	Linezolid vs. vanco—GPC (peds)	80% (20/25) v 64% (7/11)
Jantusch	'03	103	Linezolid vs. vanco—GPC (peds)	72% (54/75) v 64% (18/28)
Kaplan	'03	80	Linezolid vs. vanco—GPC (peds)	82% (47/57) v 74% (17/23)
Schrenzel	'04	67	FQ + rif vs. βL/vanco— <i>Staph</i>	87% (34/39) v 89% (25/28)
Wilcox	'04	56	Linezolid vs. teicoplanin—GPC	89% (23/26) v 57% (17/30)
Wilcox	'09	166	Linezolid vs. vancomycin—GPC	75% (70/93) v 81% (59/73)
Monmaturopaj*	'12	17	Cefditoren vs. ceftriaxone—GNB	100% (6/6) v 91% (10/11)
Park	'14	59	Ciprofloxacin vs. std IV—GNB	93% (27/29) v 93% (28/30)
Total (N=10 RCTs)		685		81% (328/403) v 77% (216/282)

*N = 82 pts with pyelonephritis of whom 17 were bacteremic with *E. coli*, patients were randomized to continue ceftriaxone or switch to oral cefditoren at day 3. Refs at <https://www.bradspellberg.com/oral-antibiotics>

(+ 1 quasi-expl') (004)

18% (317/404) v 68% (281/411)

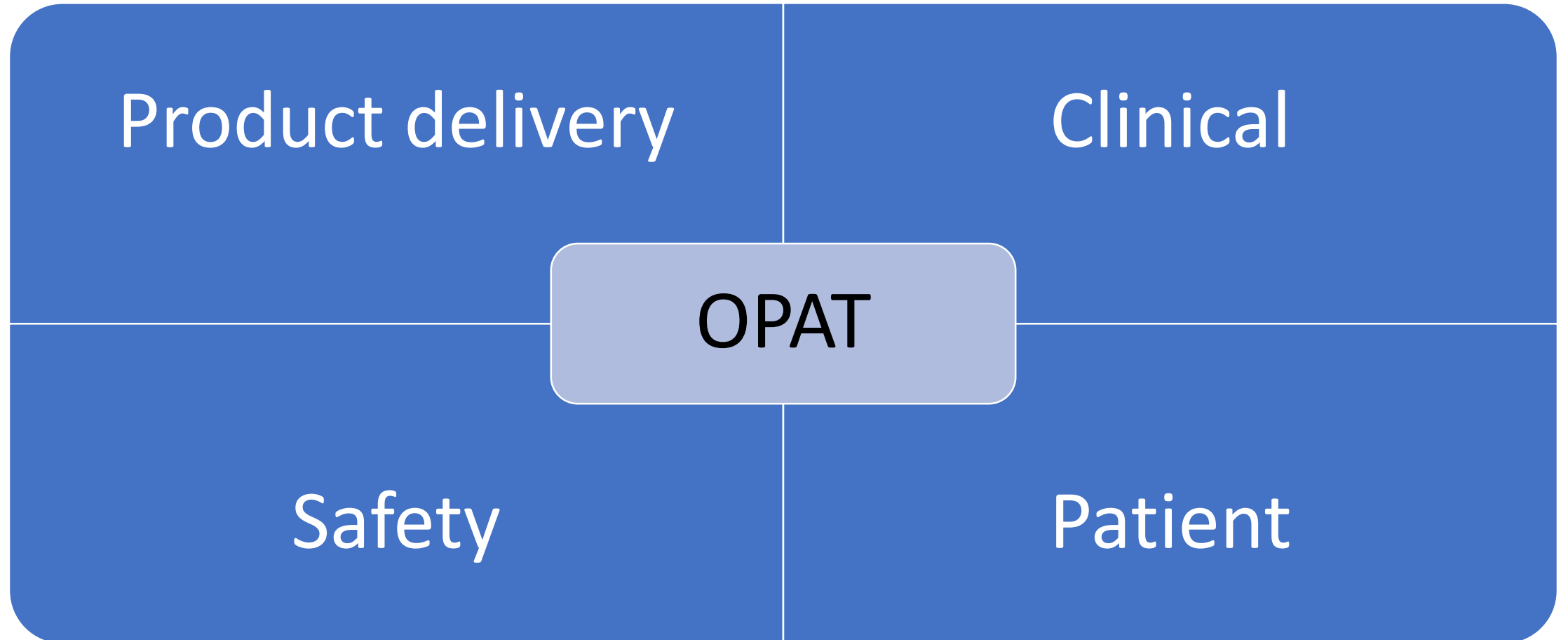
Transition to Outpatient Antimicrobial Therapy (OPAT)



- Models include:
 - Traditional home infusion models
 - Home self-administration
 - OPAT infusion clinics
- Alleviate patient beds in acute care
- Empowers patients & caregiver engagement patient in care

FIGURE 1. Outpatient parenteral antimicrobial therapy (OPAT) model for treating infections.

Considerations for Outpatient Parenteral Antimicrobial Therapy



Criteria for Receiving Home IV therapy

For any Parenteral drug

- Informed consent/Willingness of both the patient and family/caregivers
- Availability of optimal communication by phone;
- Residence within the region of the healthcare system range
- Ideal hygienic and sociofamiliar conditions;
- Clinical and hemodynamic stability of the patient.

For Antimicrobial Therapy

- Requirement for intravenous administration;
- Public formulary coverage
- Administration of the first dose in a hospital setting

Challenges with OPAT

- Low funding for OPAT implementation from healthcare institutions
 - Resource intensive for nursing and pharmacy
- Difficulties in tracking OPAT patients through the medical record system.
- Gaps in communication with other OPAT service providers
- Turnaround time in obtaining laboratory results

OPAT Monitoring in London

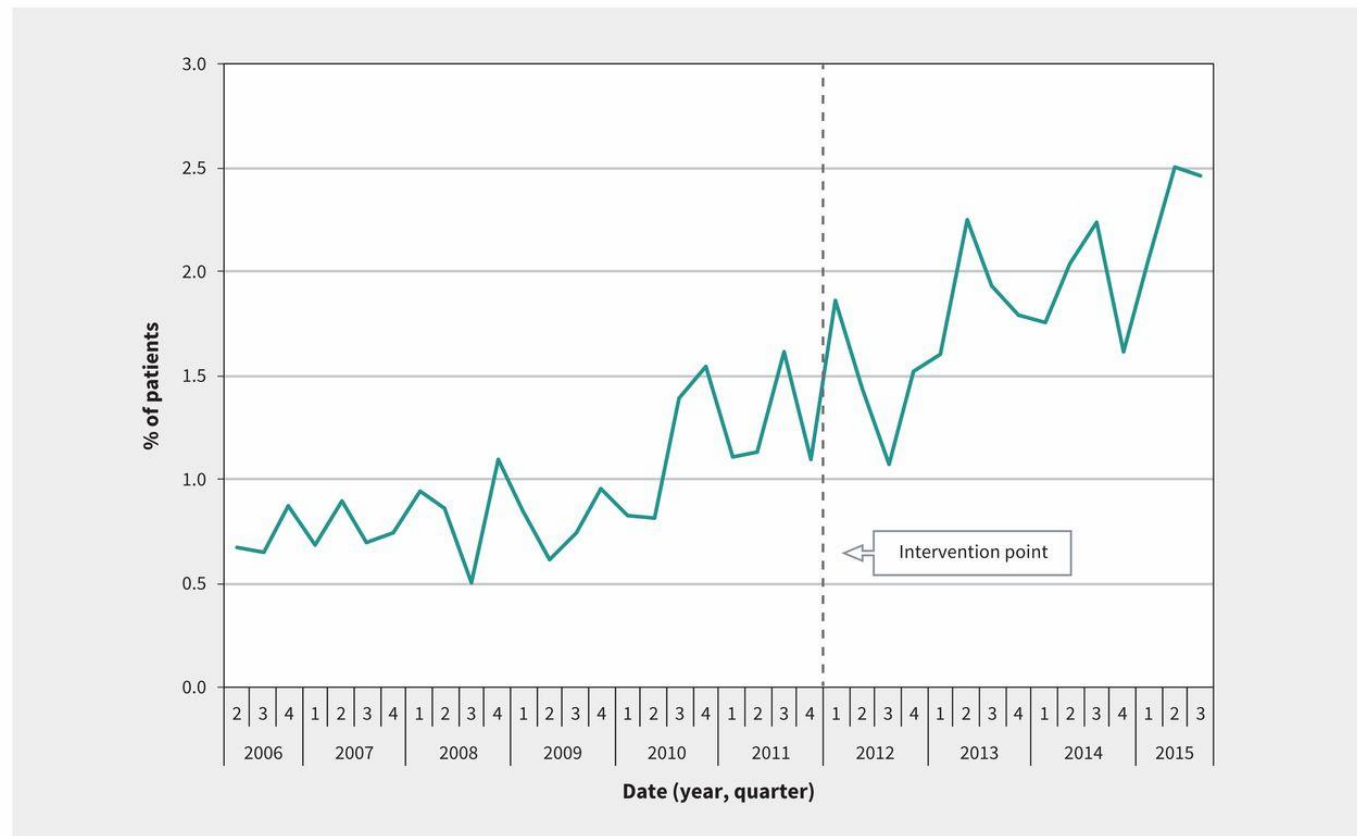
- Virtual Vancomycin Monitoring Clinic
 - Nurse-led clinic 7 days a week
 - In-patient Hospital ID Pharmacist
 - completes assessment of discharge dosing, teaching for the patient, documents progress / transfer note, sends referral form

Treat beyond the infection...

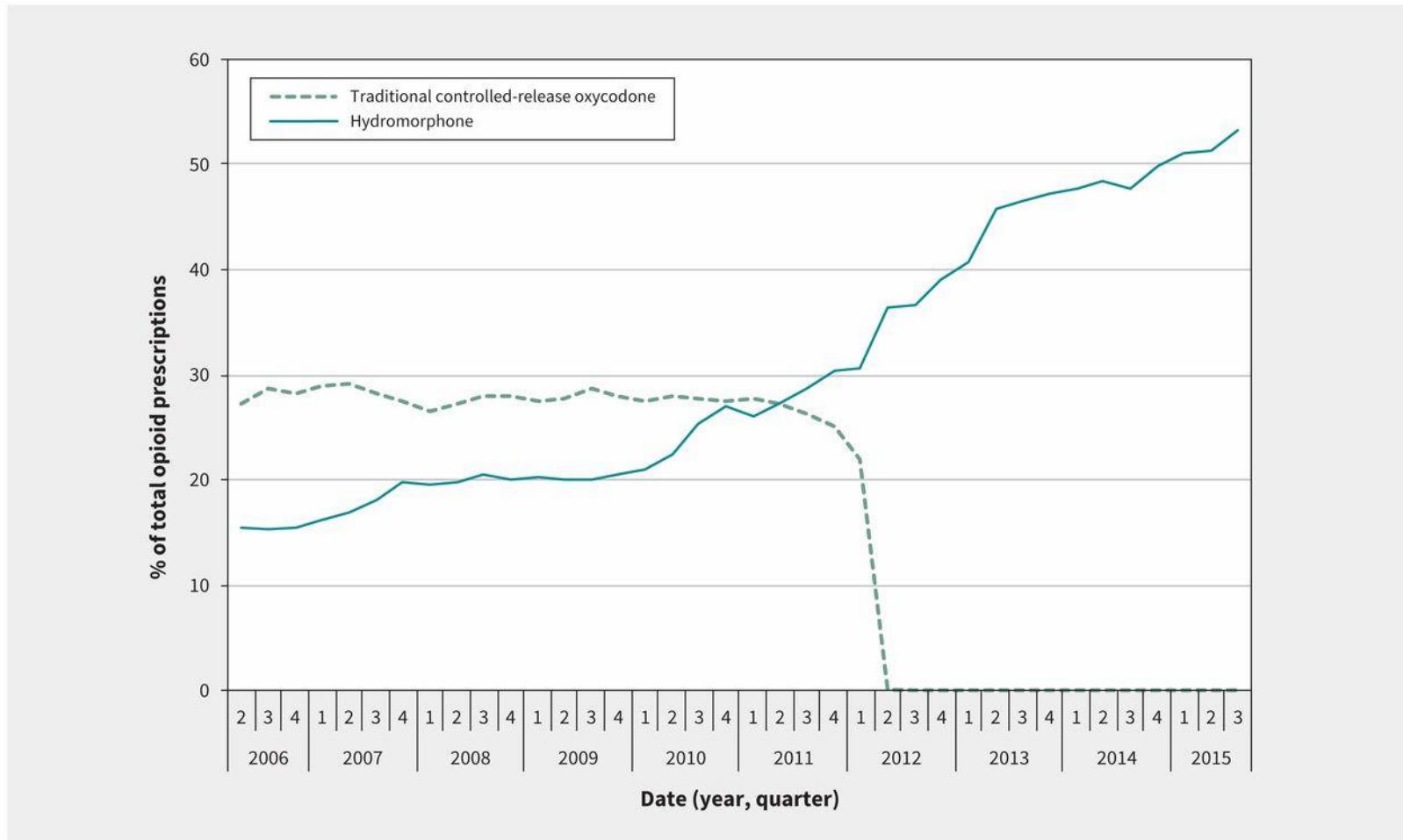
Strategy for dealing with the 'challenging' patients

Beyond the Infection: The London Experience

Quarterly percentage of patients with evidence of injection drug use admitted with infective endocarditis.

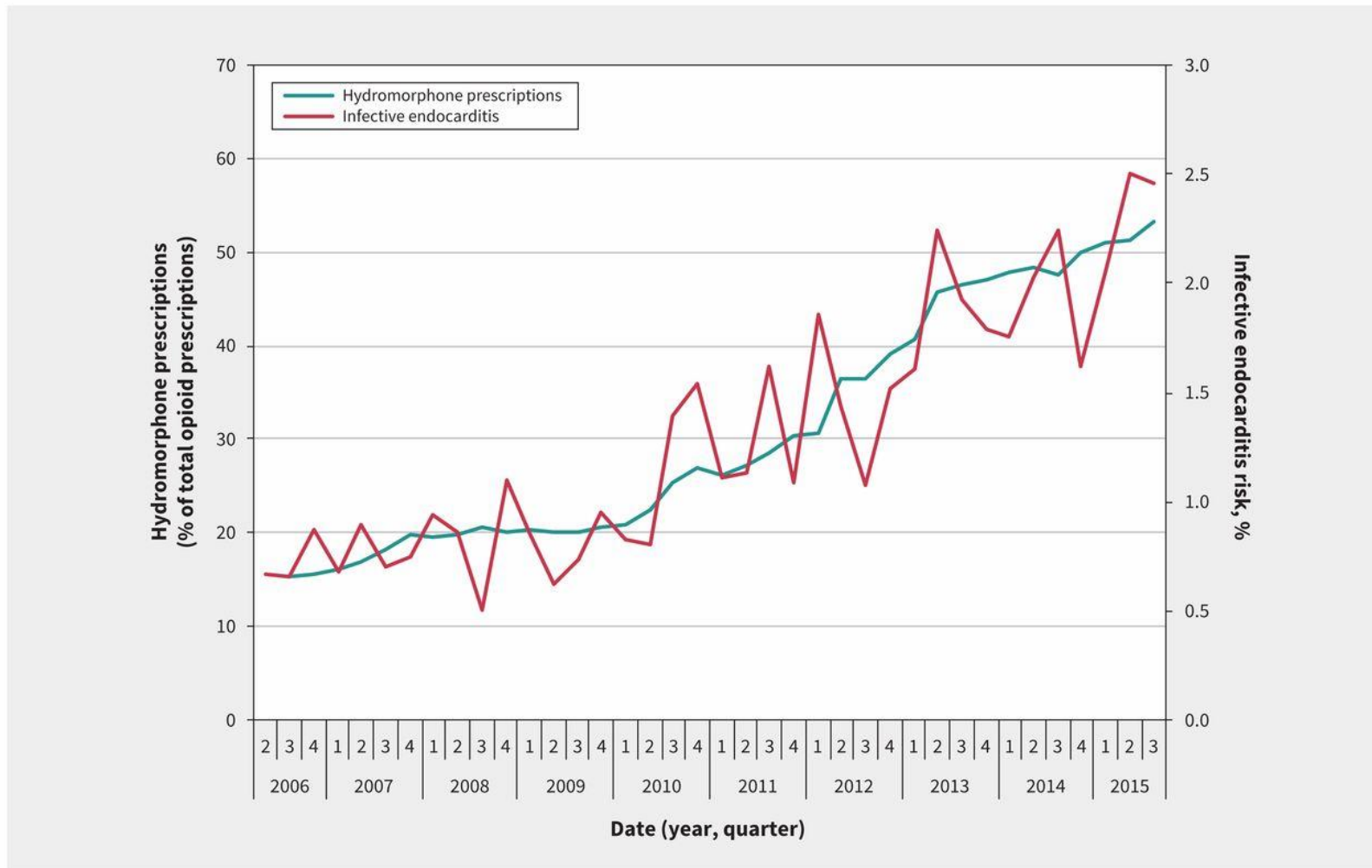


Quarterly prescriptions for traditional controlled-release oxycodone and hydromorphone as percentages of total opioid prescriptions.



Matthew A. Weir et al. CMAJ 2019;191:E93-E99

Quarterly prescriptions for hydromorphone as a percentage of total opioid prescriptions and the risk of infective endocarditis related to injection drug use.



Matthew A. Weir et al. CMAJ 2019;191:E93-E99

The key to addressing challenging patients

Infection



Patient characteristics
Optimal dosing strategies
Local antibiograms
Early appropriate empiric therapy

Substance use Disorder

Diabetes

Smoking

Mental health

Hygiene

Malnutrition

Obesity

Skin integrity

**TREAT BEYOND
THE
INFECTION**

SUMMARY

SUMMARY

- Today's infectious diseases are influenced by patient, pathogen and drug related factors
- Canadian antimicrobial use monitoring data is skewed by "CLASSICS"
- "UP & COMING" antimicrobial agents offer unique characteristics and potential roles
- Multifaceted solutions are needed for treating infectious disease in challenging patients