AMS AND THE PEADIATRIC SETTING

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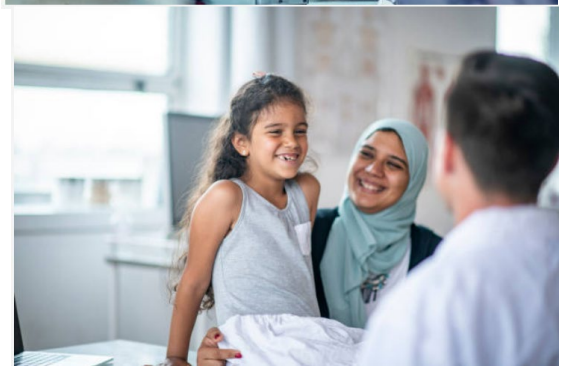
BRITISH SOCIETY FOR ANTIMICROBIAL CHEMOTHERAPY

GULF/MIDDLE EAST/AFRICA COLLABORATIVE CONFERENCE



Antimicrobial Stewardship in the Pediatric Setting

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Disclosures

None

Abbreviations

AMS = Antimicrobial Stewardship

AMR = Antimicrobial Resistance

ABx = Antibiotics

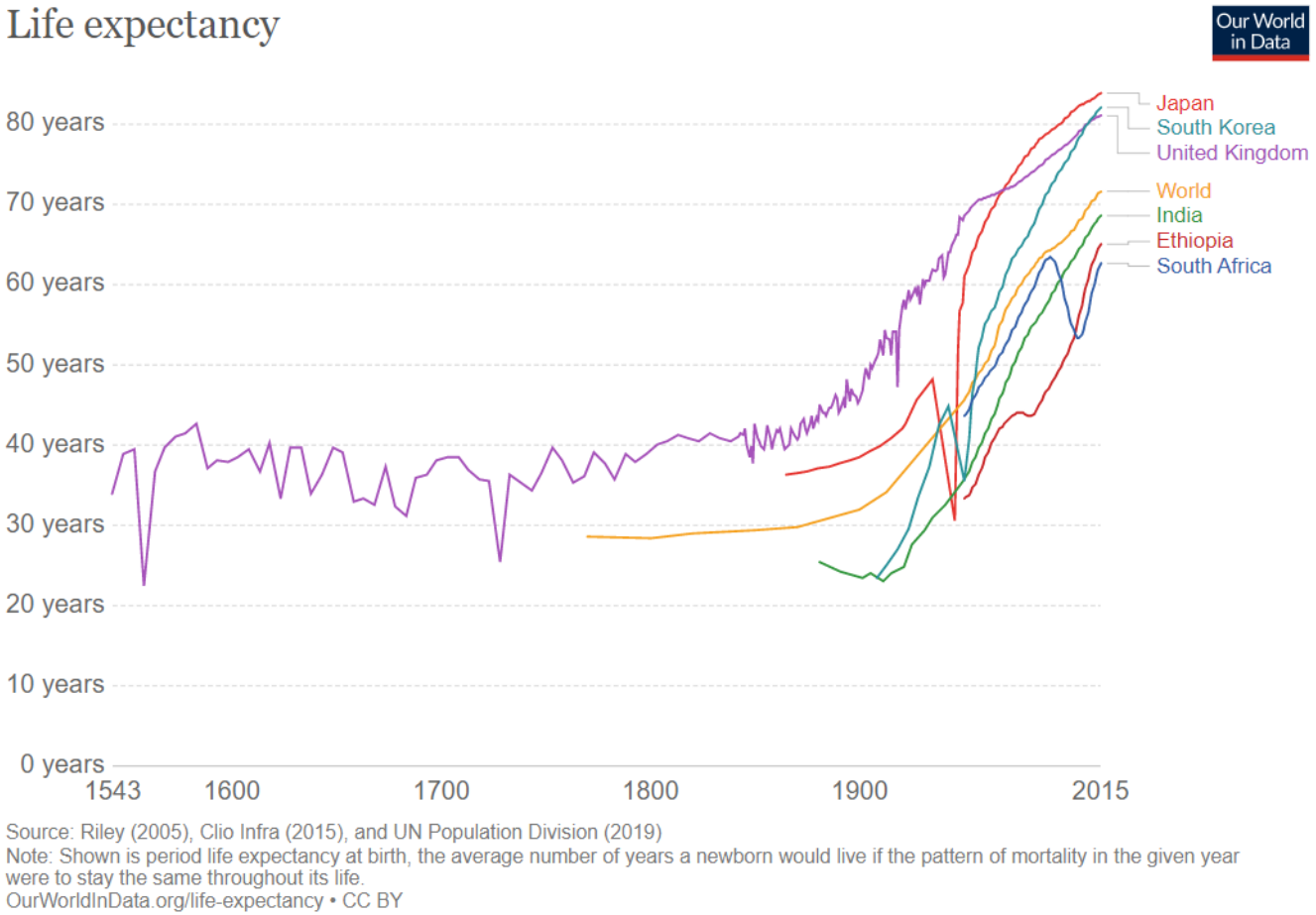
PPx = Prophylaxis

Session Outline

- Historical view on antibiotics and AMR
- Antibiotic utilization in children
  - Community setting
  - Hospital setting
- AMS strategies in pediatrics
  - Community setting
  - Hospital setting
- AMS metrics in pediatrics – what to measure?

Major Victories in Public Health

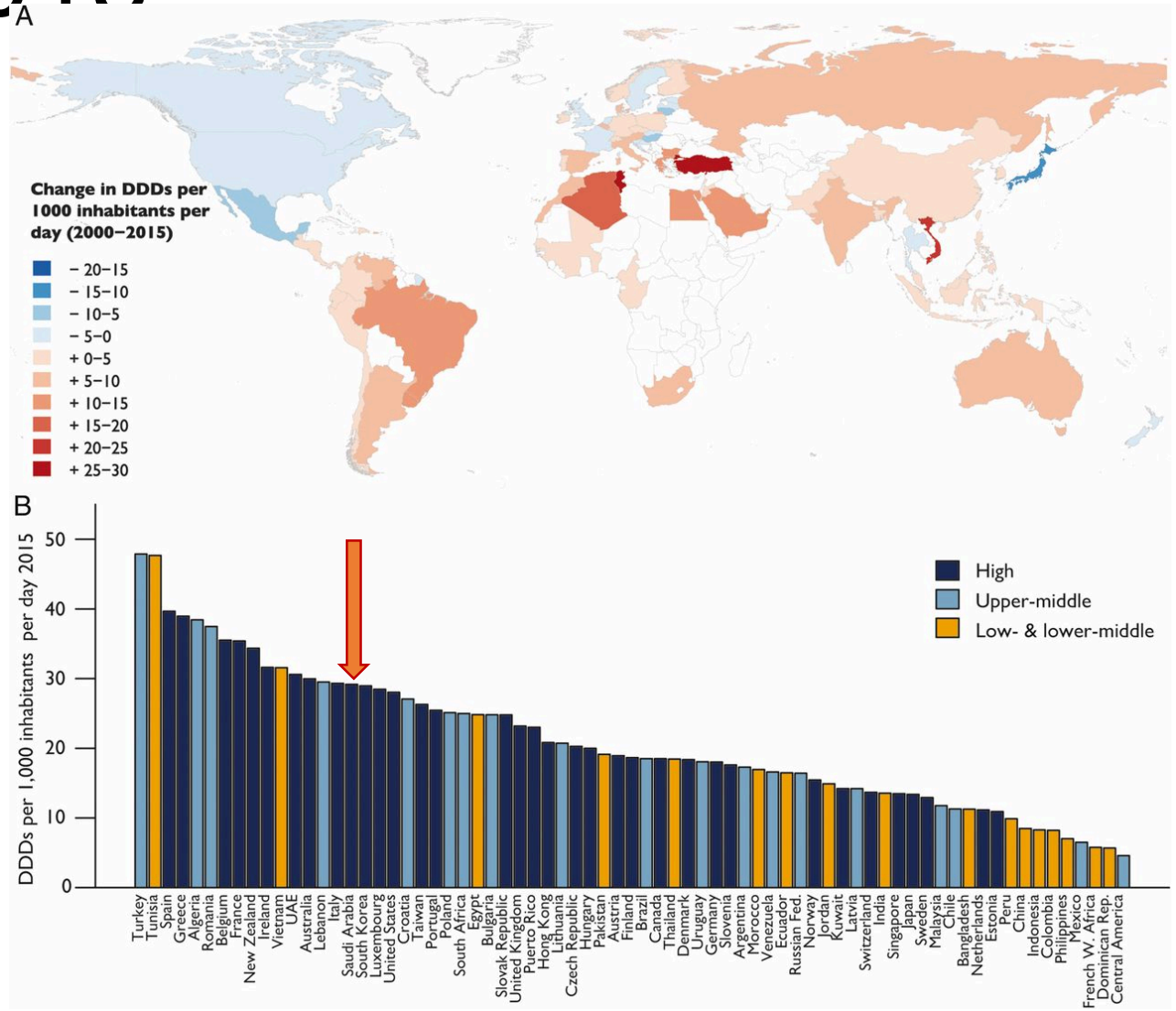
- Clean water
- Sanitation
- Antibiotics
- Vaccinations



Modern Medicine Era

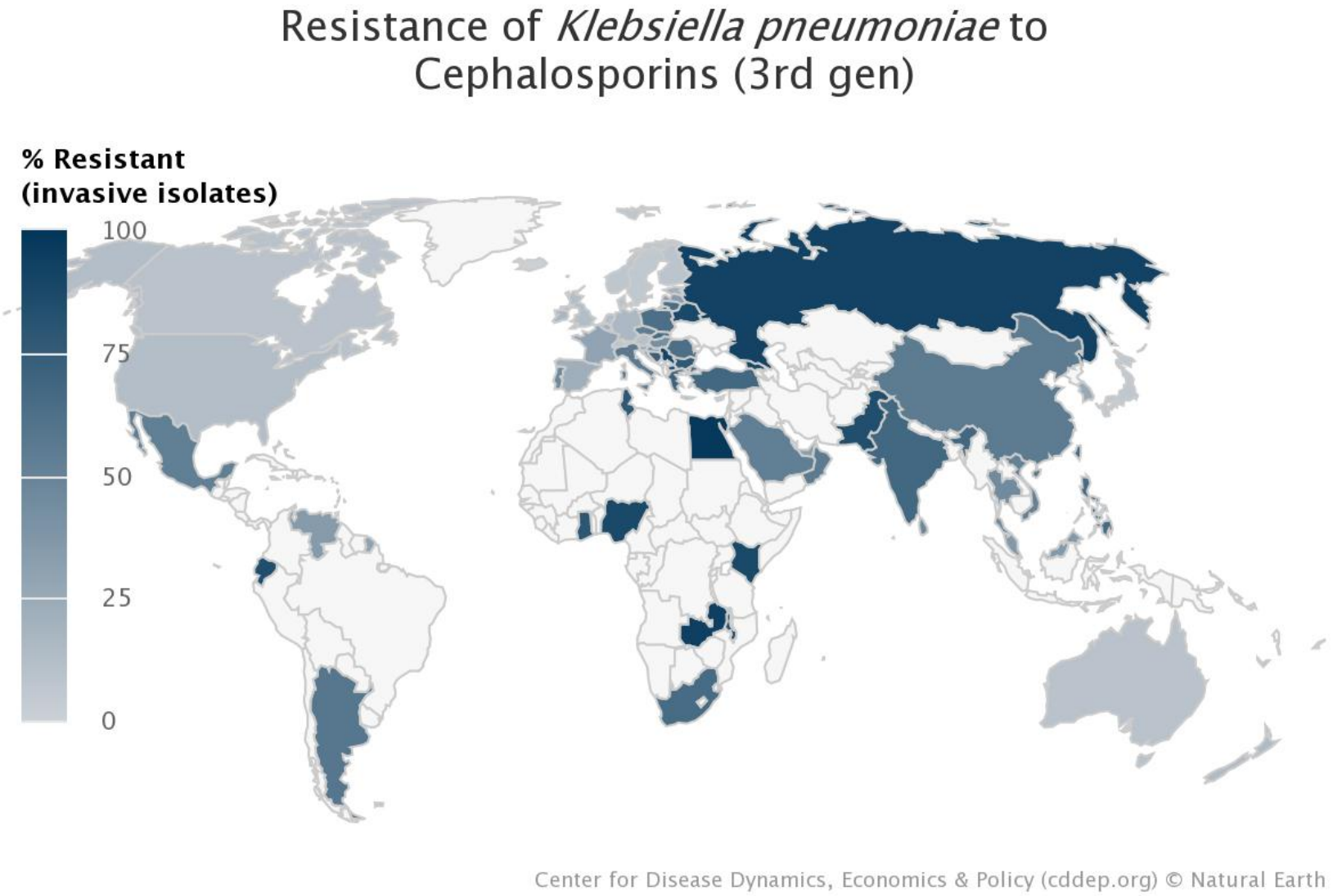
- Intensive care
- Safe surgeries
- Cancer care
- Neonatal care
- Organ Transplantation

Global antibiotic consumption by country: 2000–2015



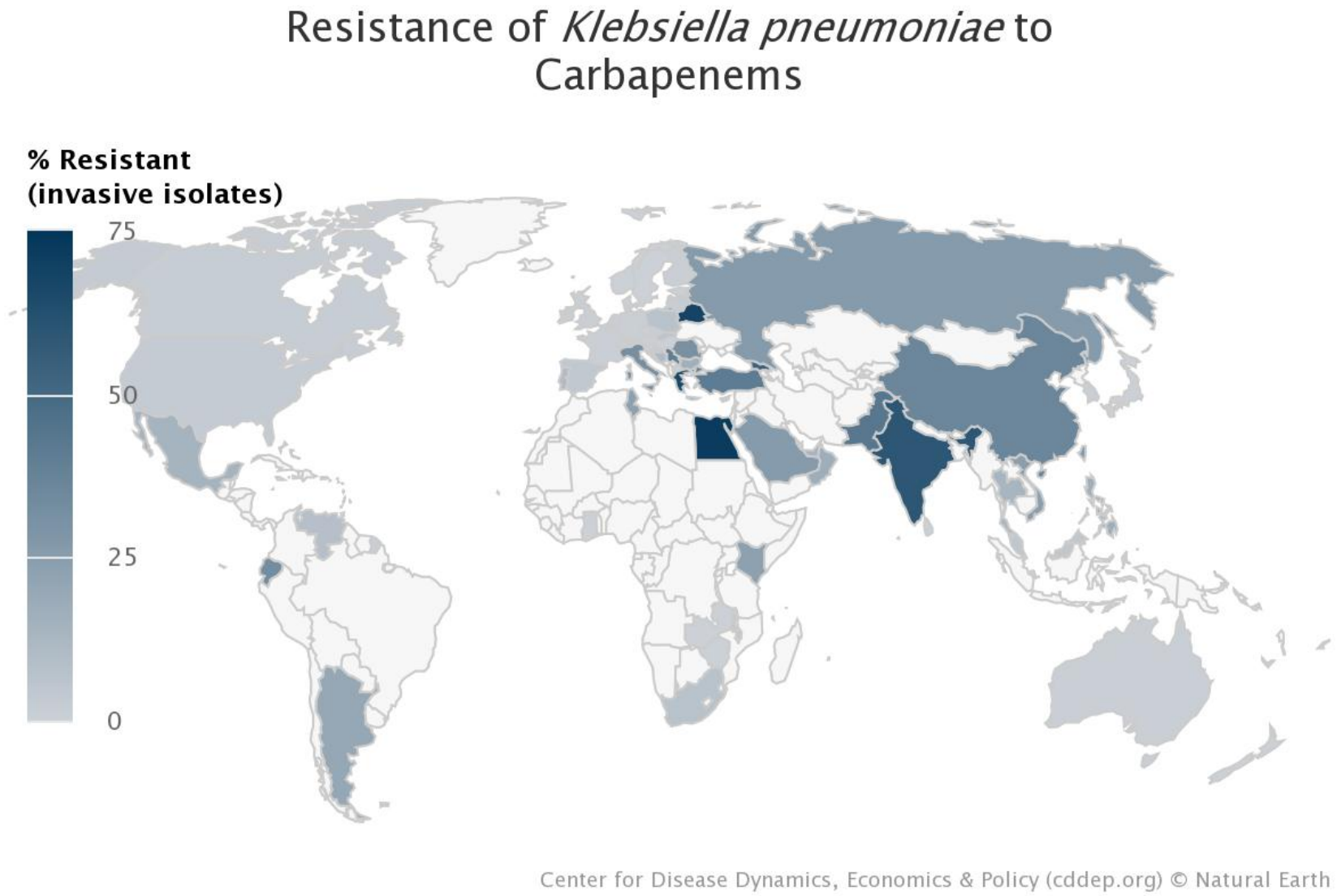
Eili Y. Klein et al. PNAS 2018;115:15:E3463-E3470

AMR - Where do we stand?



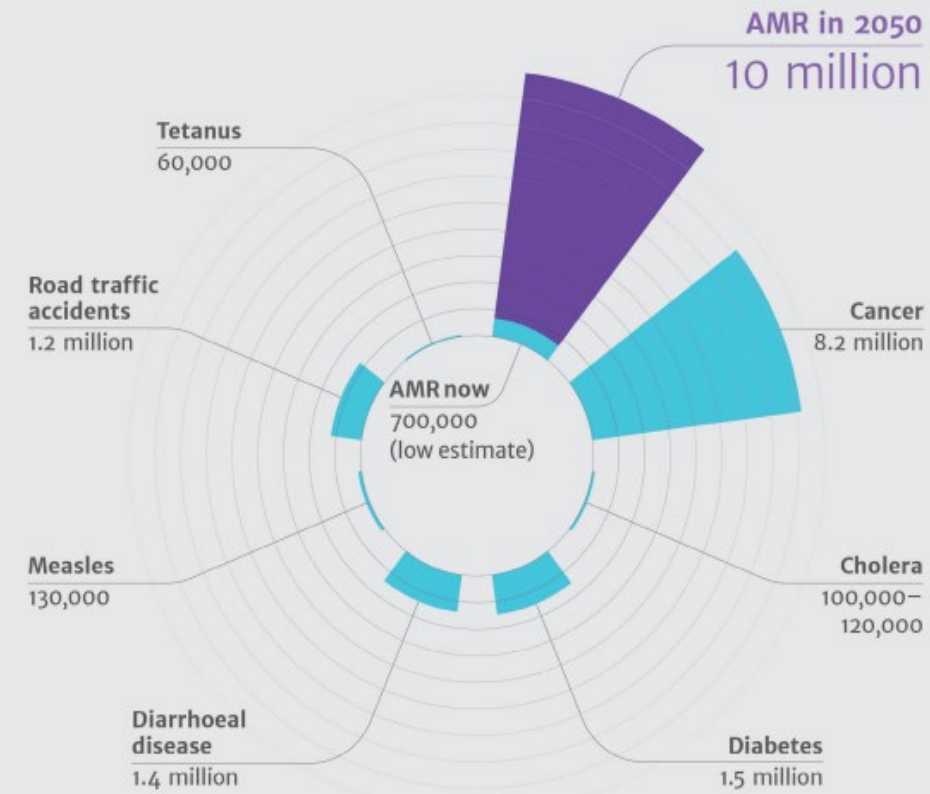
https://resistancemap.cddep.org/

AMR - Where do we stand?

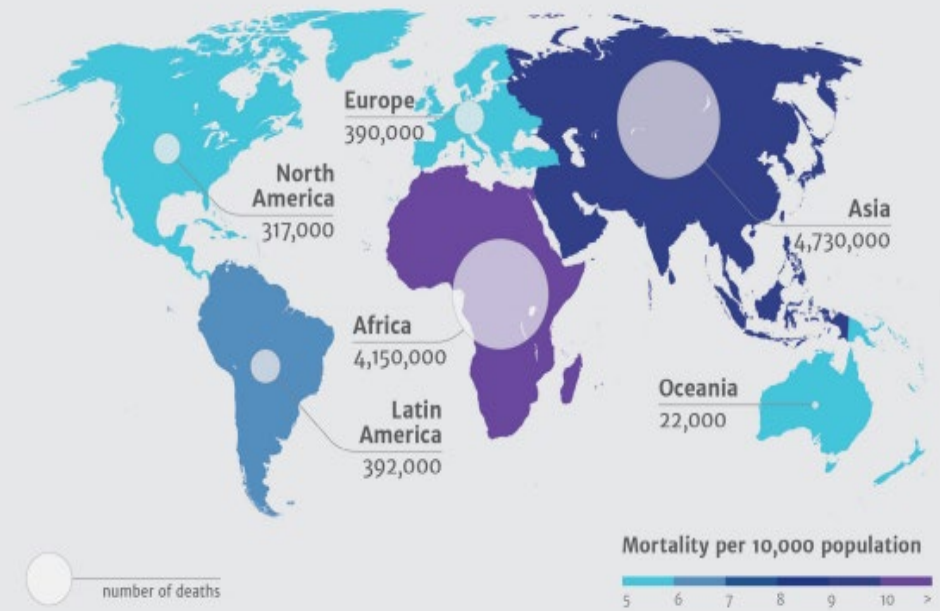


https://resistancemap.cddep.org/

Deaths attributable to AMR every year compared to other major causes of death



Deaths attributable to AMR every year by 2050



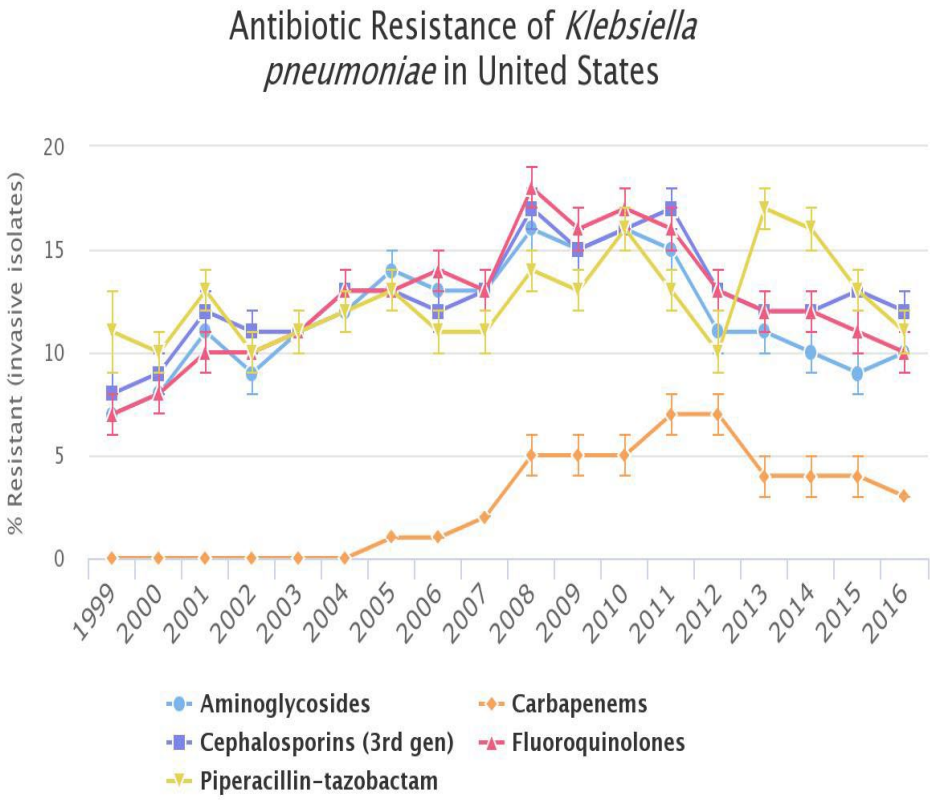
THE REVIEW ON ANTIMICROBIAL RESISTANCE – 2016

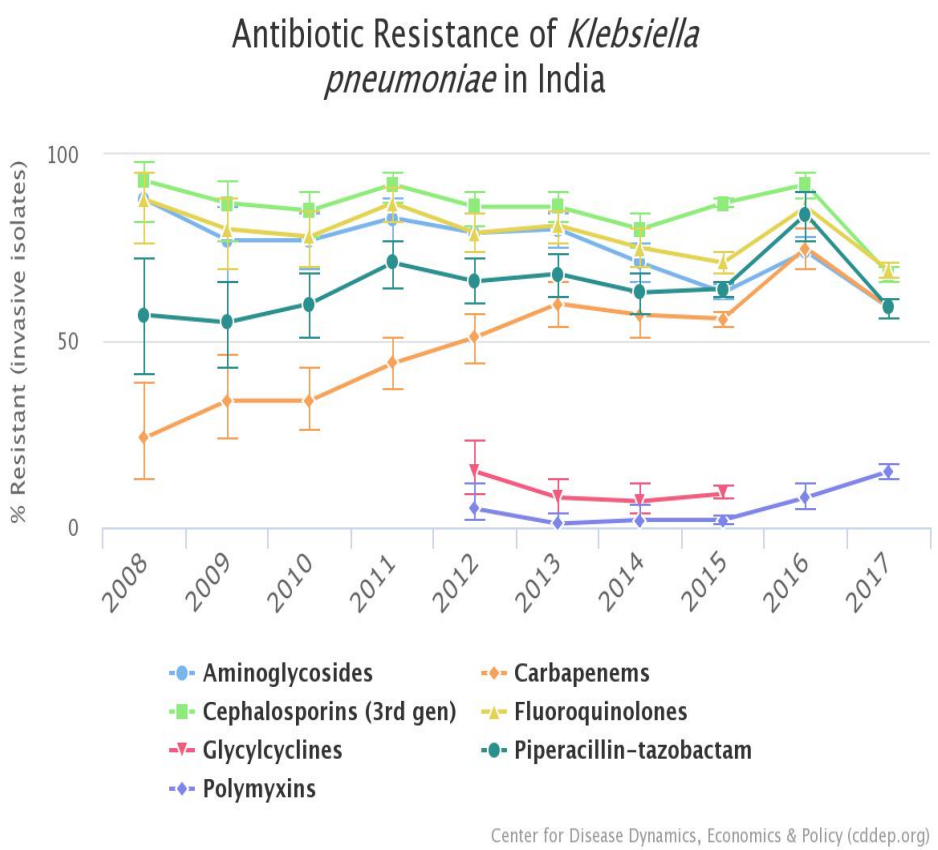
Fighting Back Against Antibiotic Resistance

1. Preventing infections, preventing the spread of resistance
2. Tracking
3. Improving antibiotic prescribing/Stewardship
4. Developing new drugs and diagnostic tests

www.cdc.gov

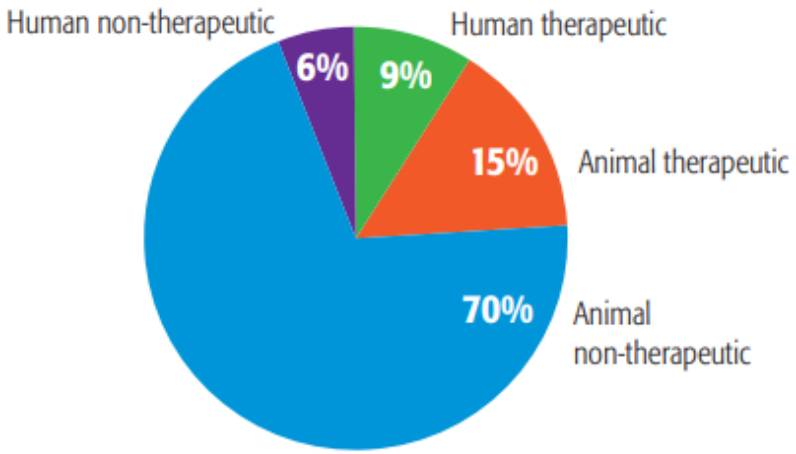
A Global Issue = A Global Action

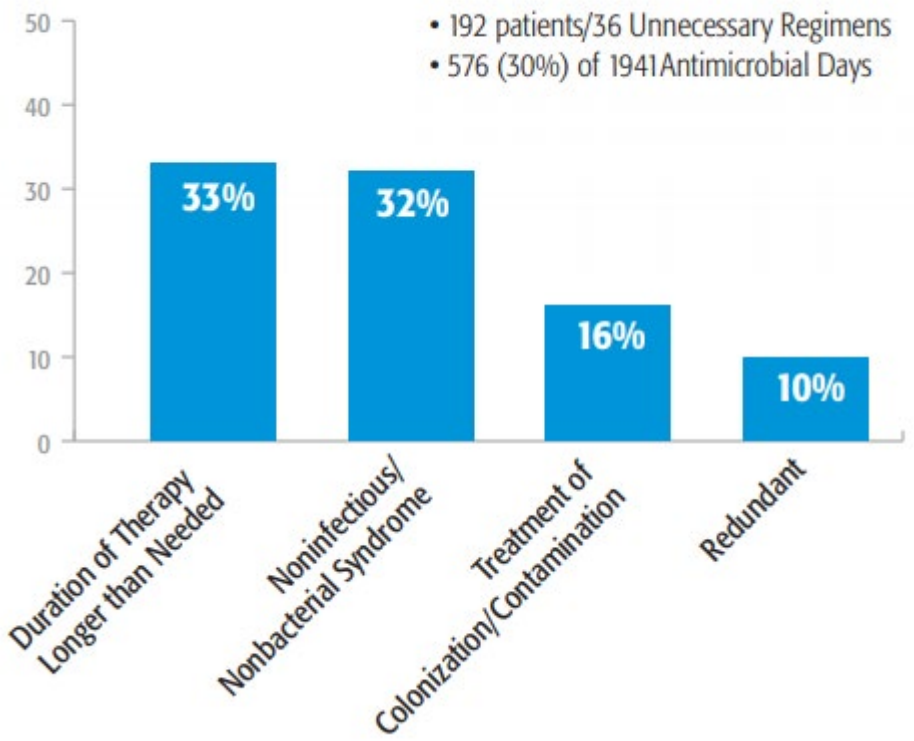




https://resistancemap.cddep.org/

Antibiotic Misuse





Hecker MT. et al. Arch Intern Med. 2003;162:972-978
Hoffman et al., 2007; Wise et al., 1999; John et al., 1997
www.pewhealth.org

Antibiotic Prescribing in Children

- Who is prescribing?
  - 74% general practices (community-based setting)
  - 11% hospital inpatient
  - 7% hospital outpatient
  - 5% dental practices
  - 3% other community setting

English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) Report 2017

Antibiotic Prescribing in Children

Top 10 Indications in Children (%)		Top 10 Indications in Neonates (%)	
Bacterial lower respiratory tract infection	18.7	Sepsis	36.4
Prophylaxis for medical problems	15.1	Prophylaxis for maternal risk factor	12.2
Prophylaxis for surgical disease	9.9	Prophylaxis for newborn risk factor	11.3
Sepsis	9.0	Lower respiratory tract infection	8.7
Treatment for surgical disease	6.1	Prophylaxis for surgical disease	5.4
Urinary tract infection	5.6	Prophylaxis for medical problems	5.1
Febrile neutropenia in oncologic patient	4.8	Catheter-related blood stream infection	3.4
Upper respiratory tract infection	4.6	CNS infection	3.2
Skin/soft tissue infection	4.4	Treatment for surgical disease	2.6
Viral lower respiratory tract infection	3.7	Skin/soft tissue infections	2.6

Abx Prescription in Community Setting in Children Under 5 Years of Age

Table 1. GP diagnosis and association with antibiotic prescription

GP working diagnosis	Children with diagnosis, *n* (%)	Proportion prescribed oral antibiotics (%)	Proportion of antibiotic prescriptions, %
Tonsillitis/sore throat	58 (5.8)	54/58 (93.1)	20.7
Ear infection	51 (5.1)	42/51 (82.4)	16.1
LRTI	90 (9.0)	63/90 (70.0)	24.1
UTI	54 (5.4)	26/54 (48.1)	10.0
URTI	297 (29.7)	43/297 (14.5)	16.5
Other	167 (16.7)	18/167 (10.8)	6.9
No diagnosis given	68 (6.8)	5/68 (7.4)	1.9
Viral illness	145 (14.5)	9/145 (6.2)	3.4
Gastroenteritis	42 (4.2)	1/42 (2.4)	0.4
Conjunctivitis	27 (2.7)	0/27 (0)	0
Total	**999**	**261 (26.1)**	**100**

LRTI = lower respiratory tract infection. URTI = upper respiratory tract infection. UTI = urinary tract infection.

O'Brien et al. Br J Gen Pract 2015; DOI: 10.3399/bjgp15X686497

Abx Use in Children in Hospital Setting

- Retrospective cohort at 40 Children Hospitals in the US in 2008
  - 60% of all admitted children received at least one antibiotic during their hospitalization

- Cross Sectional PPS at 226 pediatric hospitals in 41 countries in 2012 included 17,693 pediatric patients
  - 37% received antibiotics
  - 33% received at least 1 antimicrobial for prophylaxis use
  - 80-87% of all surgical ppx continue > 1 day

Gerber et al. *Pediatrics*. 2010; 126(6): 1067–1073
Hufnagel et al. *JPIDS*. 2019; 8(2): 143-151

Abx Use in Children in Hospital Setting

- Retrospective cohort in pediatric/neonatal intensive care units in 6 major medical centers in the US (2008-2013)
  - 73% of labeled pediatric ventilator-associated condition who received > 4 days of antibiotics had no associated positive respiratory or non-respiratory diagnostic test
  - The mean duration of new antimicrobial use is 8.8 days ± 11.5 days in PICUs

[1]Karandikar et al. *Infect Control Hosp Epidemiol*. 2019; 50: 32-39

Abx Use in Saudi Arabia

Cross sectional point prevalence survey of all inpatients in 26 MOH hospitals – 2016

- 47% were receiving antibiotics
- 23.4% administered for surgical ppx (**78% > 24 hours**)

- Adherence to antibiotic guidelines was 48%
- Indication of antibiotic was not documented in 51% of prescriptions

Al Matar et al. / *Journal of Infection and Public Health. 2019 ;12:* 77–82

What Drives the Extensive Use of Antibiotics in Children

- Infections have been and remain the most common cause of death in children under 5 globally
- Abx are cheap
- Abx generally are well tolerated

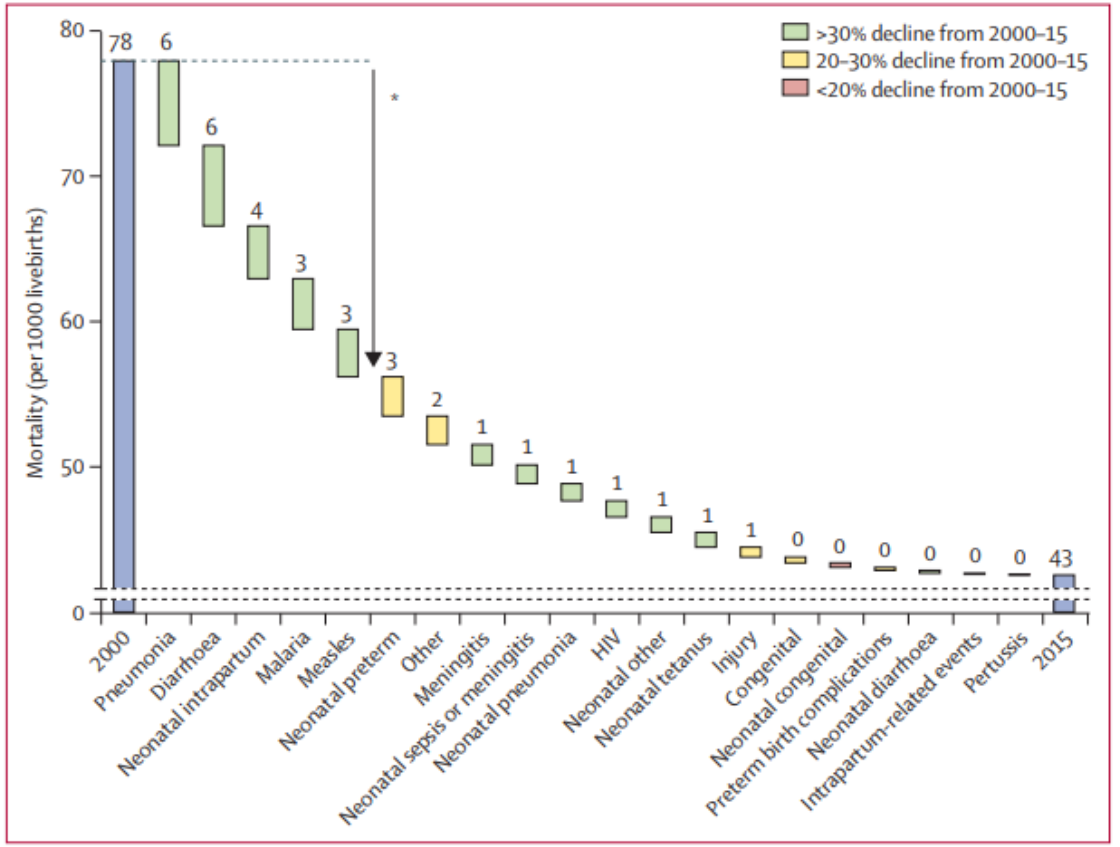
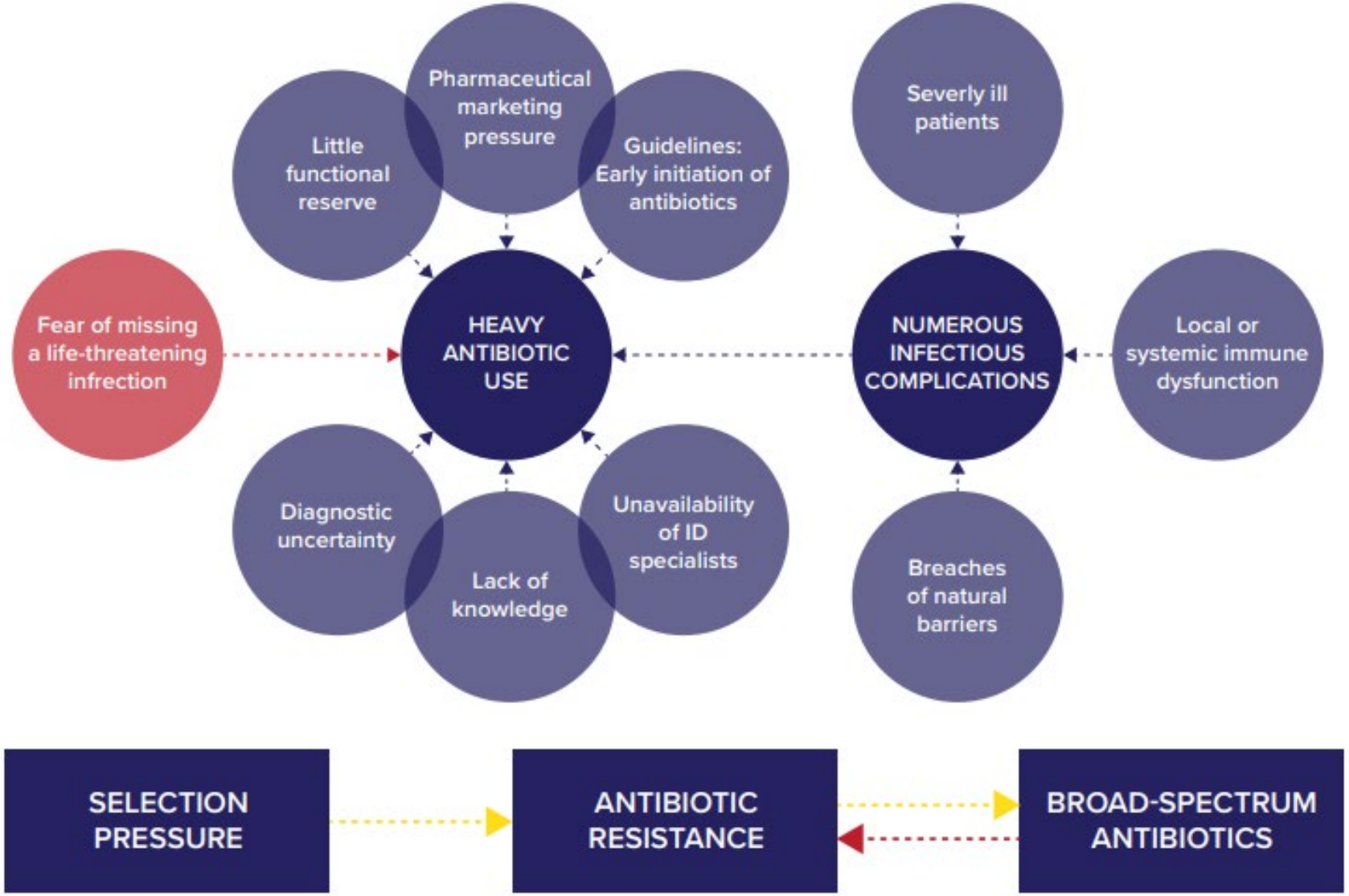


Figure 2: **Global trends in cause-specific mortality rates in neonates and children aged 1–59 months, 2000–15**
*About 61% of the reduction comes from pneumonia, diarrhoea, malaria, and measles among 1-59-month olds and neonatal intrapartum related events.

Liu et al. Lancet 2016; 388: 3027–35
Patel & Vergnano. Curr Opin Infect Dis 2018, 31:216–223

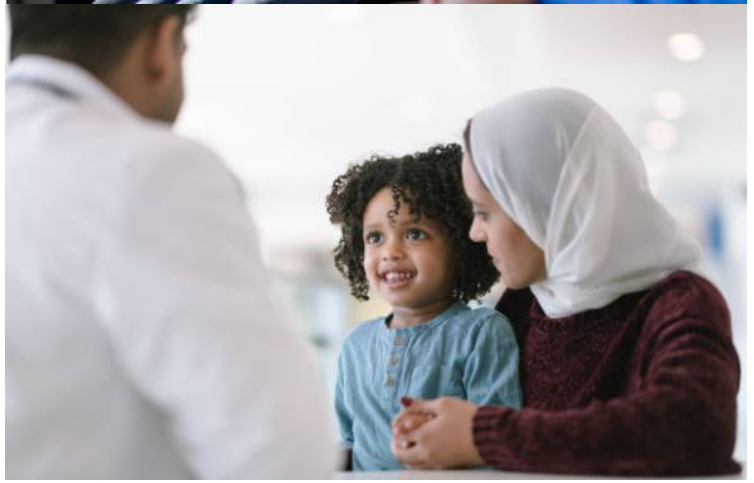
The Complicated Decisions Around Antibiotic Prescription



Albrich & Harbarth. Intensive Care Med (2015) 41: 1739

Factors Influencing Antibiotic-Prescribing Decisions

- Factors influencing parent health-seeking behavior for children with RTI
  - To eliminate the risk of a potential health threat
  - Experience during previous illnesses (previously Abx prescription or test)
  - Cannot afford to visit the doctor again
  - Low tolerance to fever



Cabral et al. Social Science & Medicine 136-137 (2015) 156-164
Horwood et al. Br J Gen Pract 2016;66(644):e207-13.
Patel & Vergnano. Curr Opin Infect Dis 2018, 31:216–223

Factors Influencing Clinician Antibiotic-Prescribing Decisions

- Factors influencing clinician's antibiotic prescribing decision for children with RTI
  - Perceived vulnerability of children (a bit more careful with children as they change quickly and cant tell you..)
  - Clinical assessment and diagnostic process (how the child appears at the moment or if there is any abnormal clinical sign in ear/throat/chest)

Cabral et al. Social Science & Medicine 136-137 (2015) 156-164
Horwood et al. Br J Gen Pract 2016;66(644):e207-13.
Patel & Vergnano. Curr Opin Infect Dis 2018, 31:216–223

Factors influencing clinician antibiotic-prescribing decisions

- Factors influencing clinician's antibiotic prescribing decision for children with RTI
  - Uncertainty in diagnosis, prognosis (one can't tell if viral vs. bacterial – can't risk leaving a developing serious RTI)
  - Repercussions of "missing something" in a child (fear of litigation or risk to professional status)
  - Nonclinical influences (multiple consultations during the same illness)

Cabral et al. Social Science & Medicine 136-137 (2015) 156-164
Horwood et al. Br J Gen Pract 2016;66(644):e207-13.
Patel & Vergnano. Curr Opin Infect Dis 2018, 31:216–223

Why Does it Matter?
Abx Use Consequences in Children

- Patients <21 years of age in four free standing children hospitals in the US:

Exposure to **ANY** antibiotic (**regardless of the spectrum and duration**)

RR of having an extended-spectrum-beta-lactamase-producing (ESBL) *Escherichia coli* or *Klebsiella pneumoniae* isolate within 30 days was 2.2 times higher than those without Abx exposure

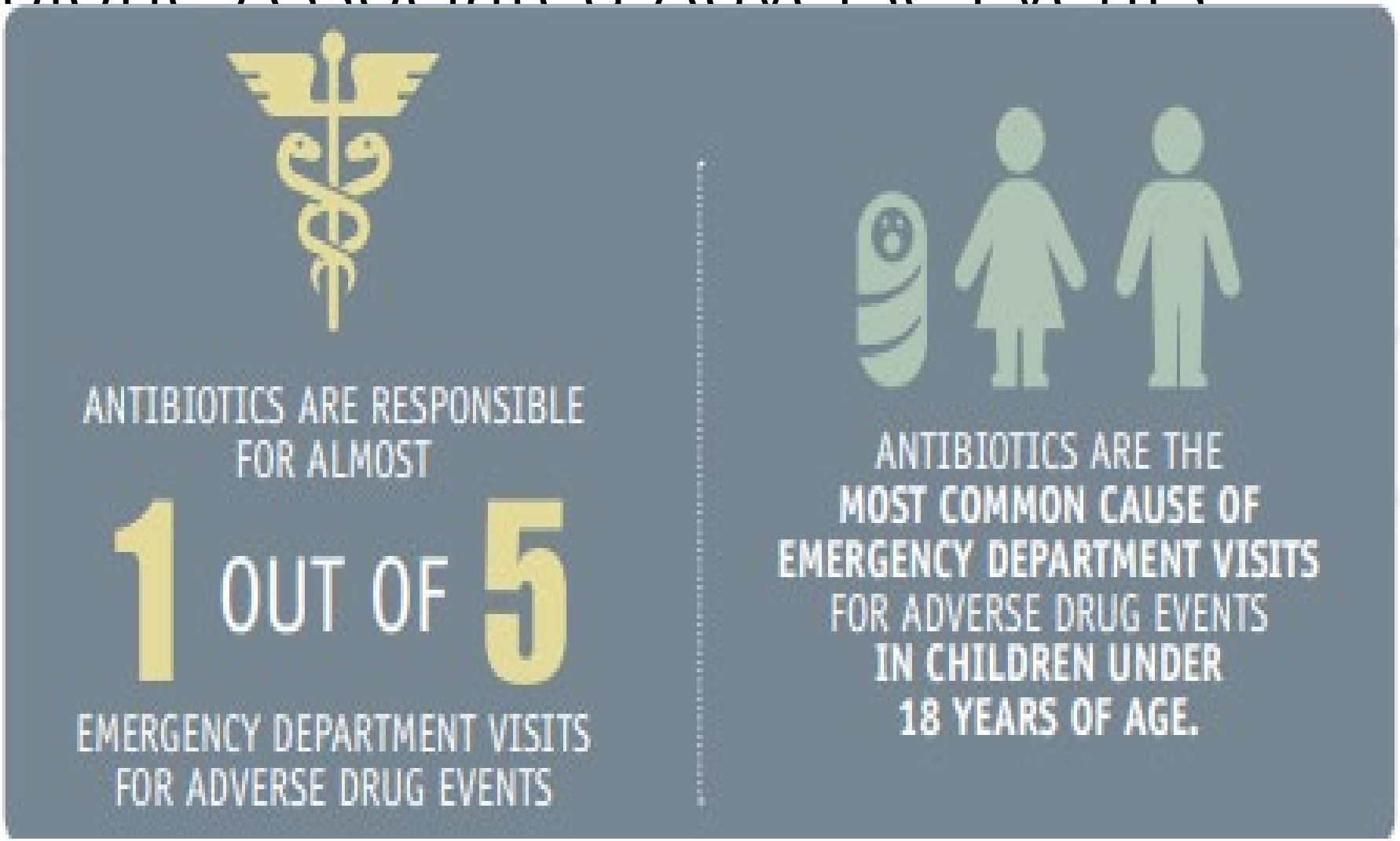
Zerr et al. Antimicrob Agents Chemother. 2016; 60:4237–4243.
Das et al. Antimicrob Agents Chemother. 2017; 61:e02656-16.

Why Does it Matter?
Abx Use Consequences in Children

- Children infected with CRE *in 3 major free-standing children hospitals in US:*
  - More often hospitalized in the ICU (61% vs. 40% in CSE)
  - More often had health-care associated infections (71% vs 38% in CSE)
  - Higher 30-day mortality = 8.3% in CRE patients (infection-related mortality was 6.5% in CRE and 0% in CSE)

Chiogos et al. Open Forum Infect Dis. 2018;5(10):ofy222

Apart from AMR - Why Does It Matter? Antibiotic-Associated Adverse Events



Apart from AMR - Why Does It Matter? Antibiotic-Associated Adverse Events

- During a one-year period in a major medical center in the US 375 children visited the emergency department or urgent care clinic for antibiotic adverse drug reactions (2013-2014)
  - Total cost for these visits was $170,893.20
  - Of these ADRs, 17% were likely avoidable
- *Clostridioides difficile* infection (Hospital-Onset)
  - Increased risk of mortality OR 6.73 (3.77-12.02)
  - Increased length of stay-5.5 days (4.5-6.5 days)
  - Increased hospital costs-$93K (80-107,200)

Beck et al. JPIDS. 2019;8(1):66–8
Sammons J et al. Clin Infec Dis 2013: 57:1-8

A Word about AMS in Neonatal Units

- Age-specific considerations:
  - Have greater susceptibility to infections compared with any other age group
  - Microbiologically proven infections are difficult to prove (volume challenge)

- Overuse of antimicrobials is associated with a number of factors unique to this population
  - Increased risk of necrotizing enterocolitis
  - Increased risk of candidemia
  - Long-term sequalae such as asthma, obesity and inflammatory bowel disease
  - Prolonged antimicrobial courses drive multi resistant Gram-negative colonization
  - Infections with multi resistant Gram-negative bacteria are associated with adverse neurodevelopmental outcomes, increased length of stay and mortality

Kuppala et al. J Pedatrics. 2011: 159 (5): 720-725, Saari et al. Pediatrics. 2015: 135(4): 617-626
Clock et al. J Ped Inf Dis Soc. 2017: 6(3): 219-226. Tsai et al. Pediatrics. 2014: 133(2): e3220329
Giuffre et al. Medicine (Balt). 2016: 95(10): e3016

AMS Strategies in Pediatrics

- Community setting
- Hospital setting

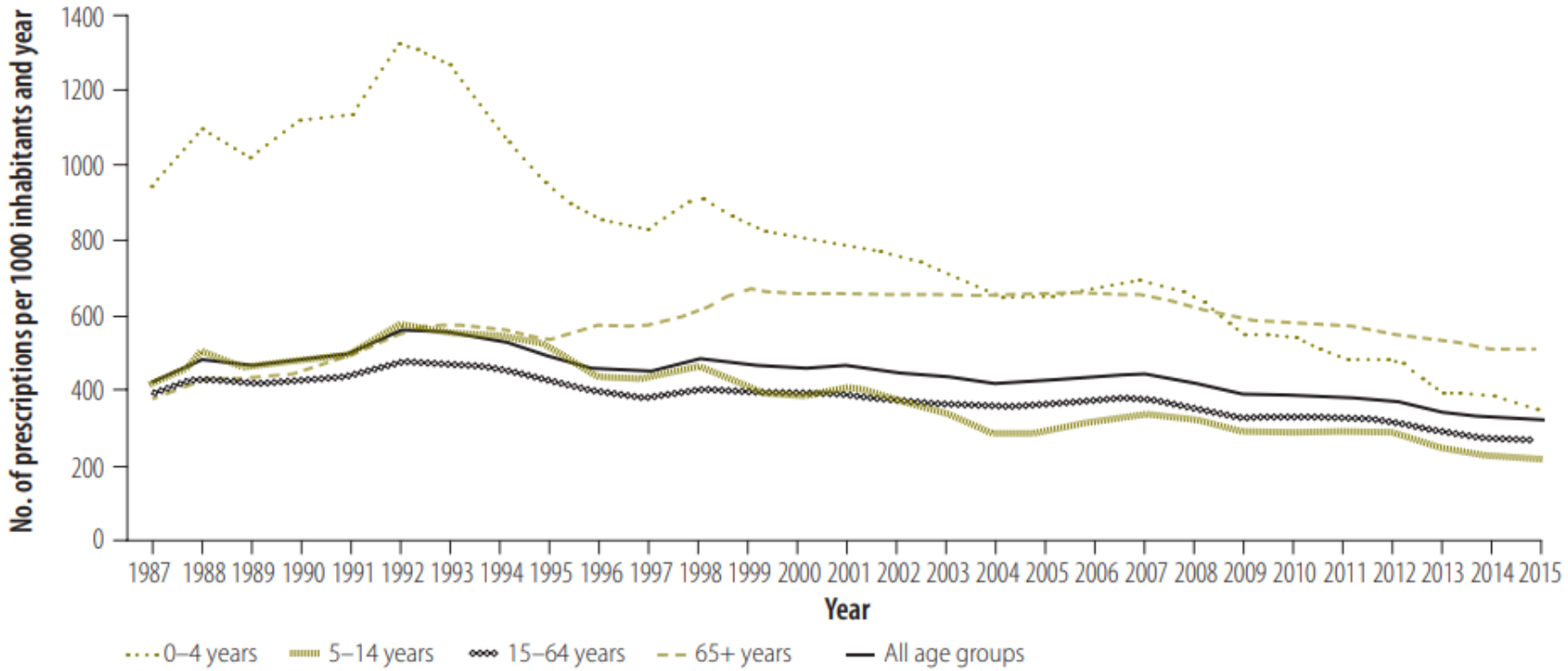
Pediatric AMS in Community-Based Settings

- Issue with access to care
- Issue with access to antibiotics

- Some employed strategies to decrease inappropriate antibiotic prescribing:
  - Nation-wide approach– variable results
    - Sweden vs. UK
  - Antibiotic shared decision approach
  - Immediate vs. delayed prescription

Pediatric AMS in Community-Based Settings

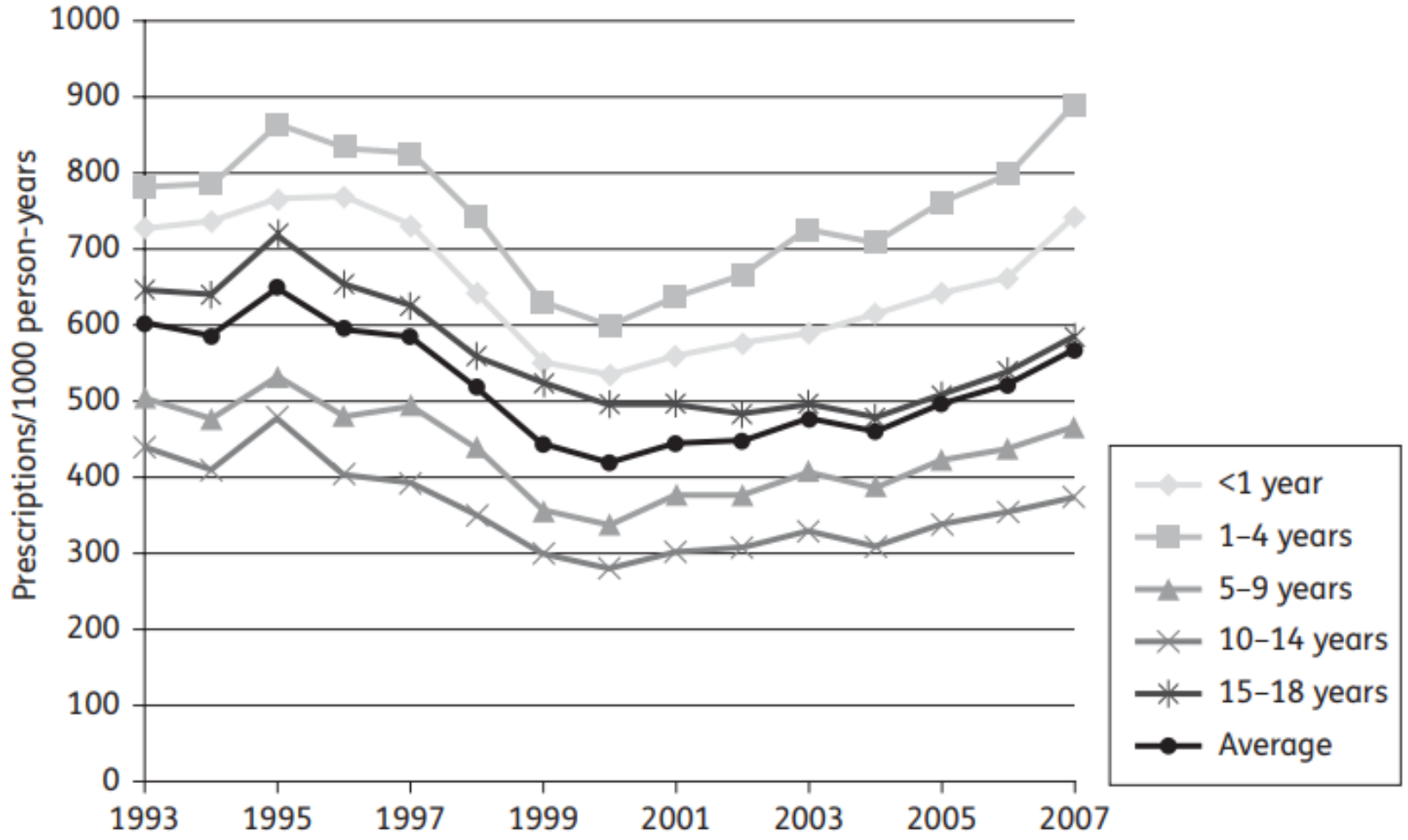
Fig. 1. **Sales of antibiotics for systemic use in outpatient care, Sweden, 1987–2015**



Notes: Includes all antibiotic sales on prescriptions, presented as prescriptions per 1000 inhabitants and year for both sexes by different age groups.
Source: Public Health Agency of Sweden, 2016.[9]

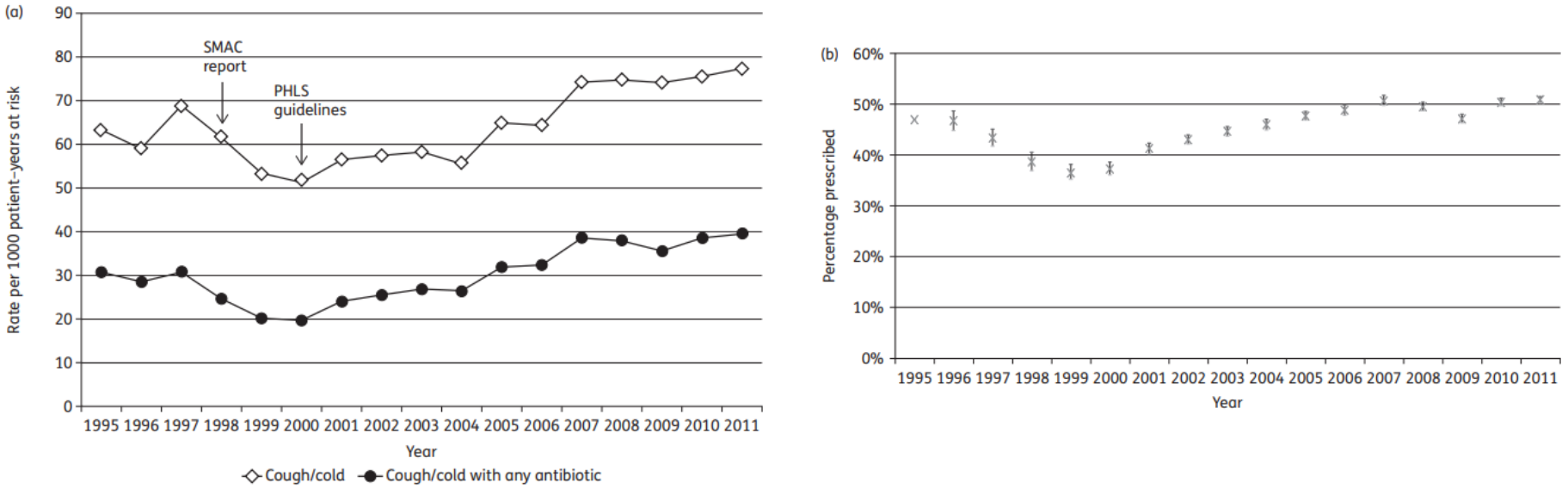
Mölstad et al. Bull World Health Organ 2017;95:764–773

Pediatric AMS in Community-Based Settings



Schneider-Lindner et al. J Antimicrob Chemother 2011; 66: 424–433

Trends in Antibiotic Prescribing in Primary Care – UK 1995-2011



(a) Incidence of selected cough/cold diagnoses and of episodes with antibiotic prescribed, 1995–2011. (b) Percentage of cough/cold episodes prescribed an antibiotic, 1995–2011 (with 95% CIs for within-practice year-on-year variation).

Hawker et al. J Antimicrob Chemother 2014; 69: 3423–3430

Strategies for Reducing Antibiotic Prescribing in Community Settings

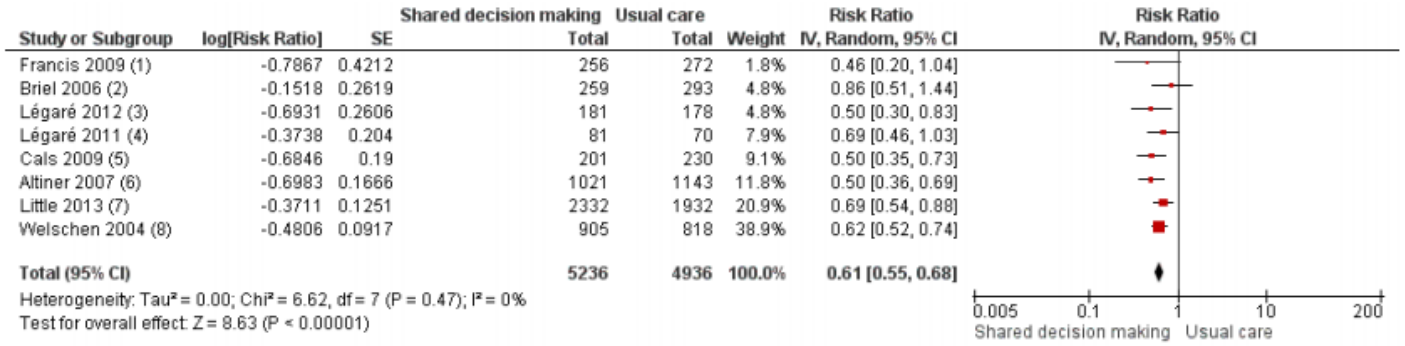
- Shared decision-making during office visits
  - Telling parents that antibiotics are not effective against viruses did not have an impact on parents' beliefs about the need to consult or their expectations concerning antibiotics
  - Parents believed that antibiotics were needed to treat more severe illnesses
  - Antibiotic prescriptions tended to confirm parents' beliefs about what indicated illness severity, which often took into account the wider impact on a child's life
  - Most parents poorly understand the risk of antimicrobial resistance

Cabral et al. Ann Fam Med 2016;14:141-147
Coxeter et al. Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD010907

Strategies for Reducing Antibiotic Prescribing in Community Settings

- Shared decision-making during office visits
  - Reduce antibiotic use for ARIs in primary care (immediately after or within six weeks of the consultation), compared with usual care, from 47% to 29%
  - Reduction in antibiotic prescribing occurred without an increase in patient-initiated re-consultations or a decrease in patient satisfaction with the consultation

Figure 4. Forest plot of comparison: 1 Shared decision making versus usual care (control), outcome: 1.1 Antibiotics prescribed, dispensed or decision to use (short-term, index consultation to ≤ 6 weeks).



Study or Subgroup	log[Risk Ratio]	SE	Shared decision making Total	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Francis 2009 (1)	-0.7867	0.4212	256	272	1.8%	0.46 [0.20, 1.04]
Briel 2006 (2)	-0.1518	0.2619	259	293	4.8%	0.86 [0.51, 1.44]
Légaré 2012 (3)	-0.6931	0.2606	181	178	4.8%	0.50 [0.30, 0.83]
Légaré 2011 (4)	-0.3738	0.204	81	70	7.9%	0.69 [0.46, 1.03]
Cals 2009 (5)	-0.6846	0.19	201	230	9.1%	0.50 [0.35, 0.73]
Altiner 2007 (6)	-0.6983	0.1666	1021	1143	11.8%	0.50 [0.36, 0.69]
Little 2013 (7)	-0.3711	0.1251	2332	1932	20.9%	0.69 [0.54, 0.88]
Welschen 2004 (8)	-0.4806	0.0917	905	818	38.9%	0.62 [0.52, 0.74]
Total (95% CI)			**5236**	**4936**	**100.0%**	**0.61 [0.55, 0.68]**

Heterogeneity: Tau² = 0.00; Chi² = 6.62, df = 7 (P = 0.47); I² = 0%
Test for overall effect: Z = 8.63 (P < 0.00001)

Coxeter et al. Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD010907

Strategies for Reducing Antibiotic Prescribing in Community Settings

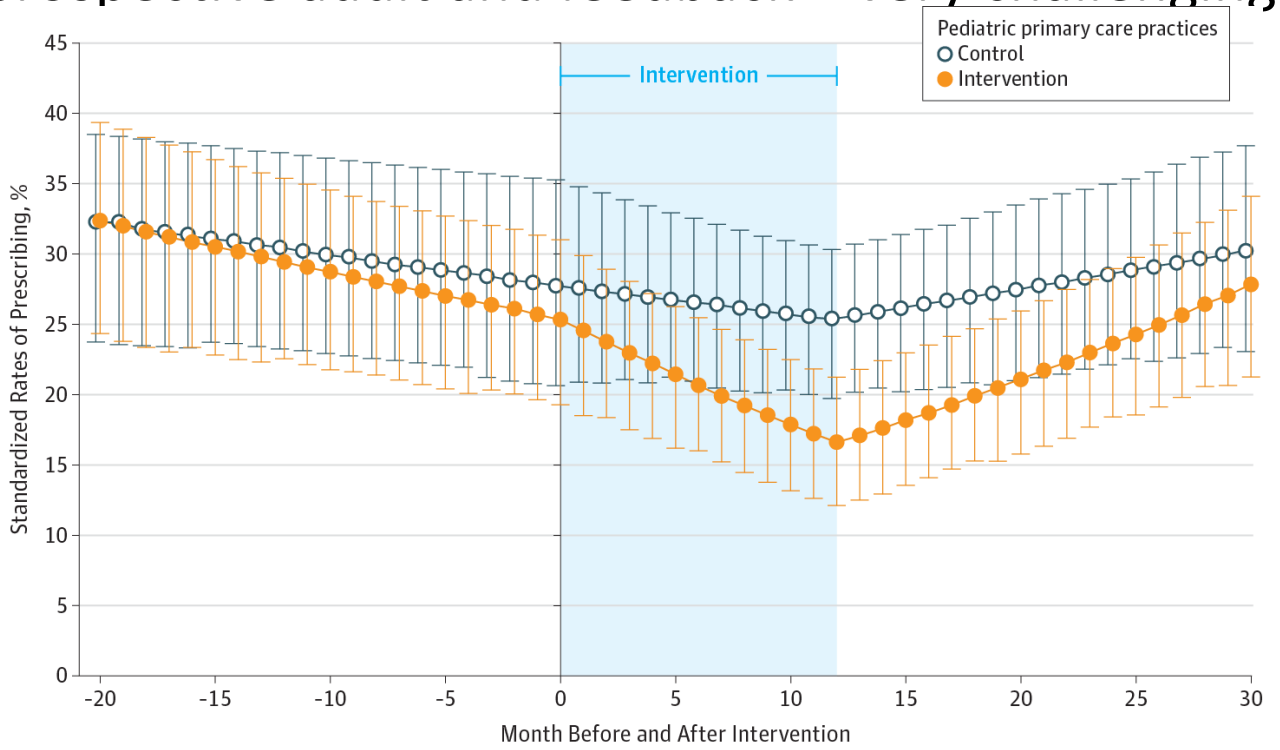
- Shared decision-making during office visits
  - Safety netting significantly reduce the rate of antibiotic prescribing in children
    - A cluster randomized controlled trial using an interactive booklet on RTI in children used by clinicians to give parents clear information about symptoms suggestive of severe illness and the action required reduced Abx prescribing from 40.8 to 19.5%

- Delayed prescribing
  - Antibiotic prescription can be collected at the parents' discretion after 72 hours if they feel that their child is not improving
  - Parents are extremely reassured
  - Overall use of antibiotics reduced by 80% in some studies

Dekker et al. J Antimicrob Chemother 2018; 73: 1416–1422
Little et al. *BMJ* 2001;322:336

Strategies for Reducing Antibiotic Prescribing in Community Settings

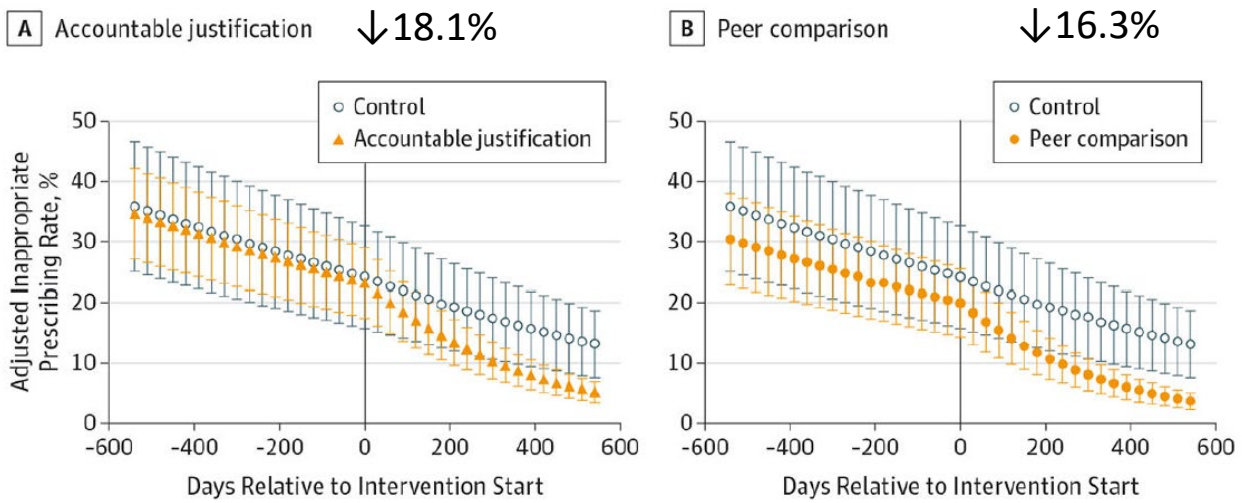
- Outpatient antibiotic stewardship
  - Real-time prospective audit and feedback – very challenging



Gerber et al. JAMA. 2014;312(23):2569-2570

Strategies for Reducing Antibiotic Prescribing in Community Settings

- Outpatient antibiotic stewardship
  - Timely review of microbiology results to decide whether antibiotics need to be continued
    - Implementation of a protocol to routinely follow up pediatric urine culture results within a community based setting → increased discontinuation rate of antibiotics from 4 to 84% and avoiding 40% of antibiotic days prescribed
  - Peer-comparison has significant impact on antimicrobial prescribing rates



Saha et al. Pediatrics 2017; 139: pii: e20162103
Meeker et al. JAMA. 2016; 315(6): 562–570

Pediatric AMS in the Inpatient Setting

- Elements of pediatric inpatient AMS include a variable mix of the following:

Strategy	Pros	Cons
1- Antibiotic restriction and preauthorization	• Immediate effect on prescribing rate • Easy to implement	• Perception of autonomy loss • Potential delays in appropriate antibiotic administration • Increase use of other antibiotics • Lack of education about AMS principles

Ambroggio et al. Pediatrics 2013;131:e1623–e1631
Patel & Vergnano. Curr Opin Infect Dis 2018, 31:216–223

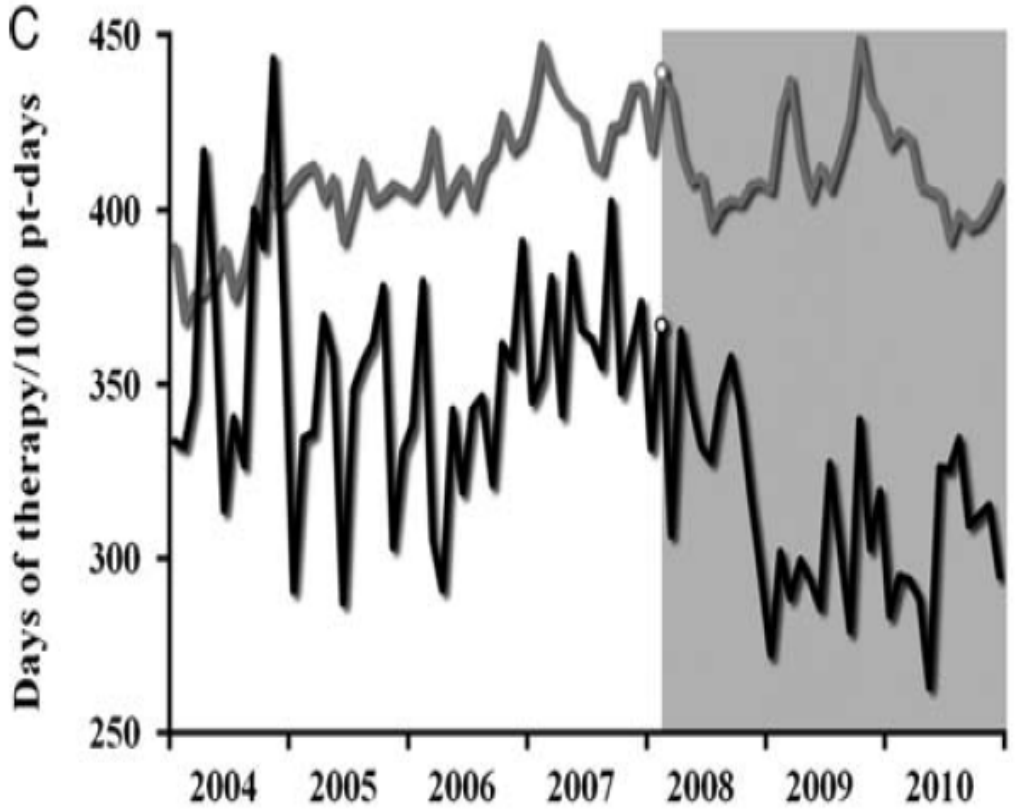
Pediatric AMS in the Inpatient Setting

- Elements of pediatric inpatient AMS include a variable mix of the following:

Strategy	Pros	Cons
2- Prospective audit and feedback	• Very effective • Improves patient safety • Increase ID consultations • Safe net for potential medication error or bug-drug mismatch • Allows education and facilitate behavior change	• Labor intensive • Personnel dependent • Requires training • Leadership acceptance • Need a reliable system in real-time identification of patients on antibiotics • Depends on prescribers to accept the recommendation of the AMS team • Documentation

Ambroggio et al. Pediatrics 2013;131:e1623–e1631
Patel & Vergnano. Curr Opin Infect Dis 2018, 31:216–223

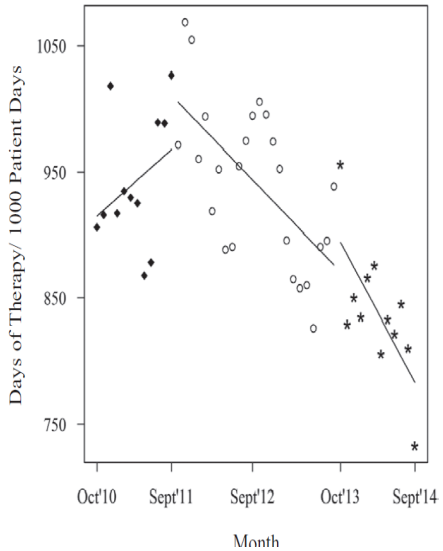
Impact of Prospective Audit and Feedback

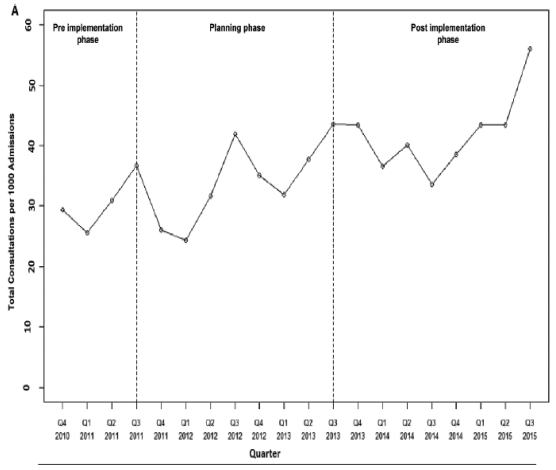


Newland et al. JPIDS. 2012; 1 (3); 179-86

Stewardship Rounds – Handshake Rounds

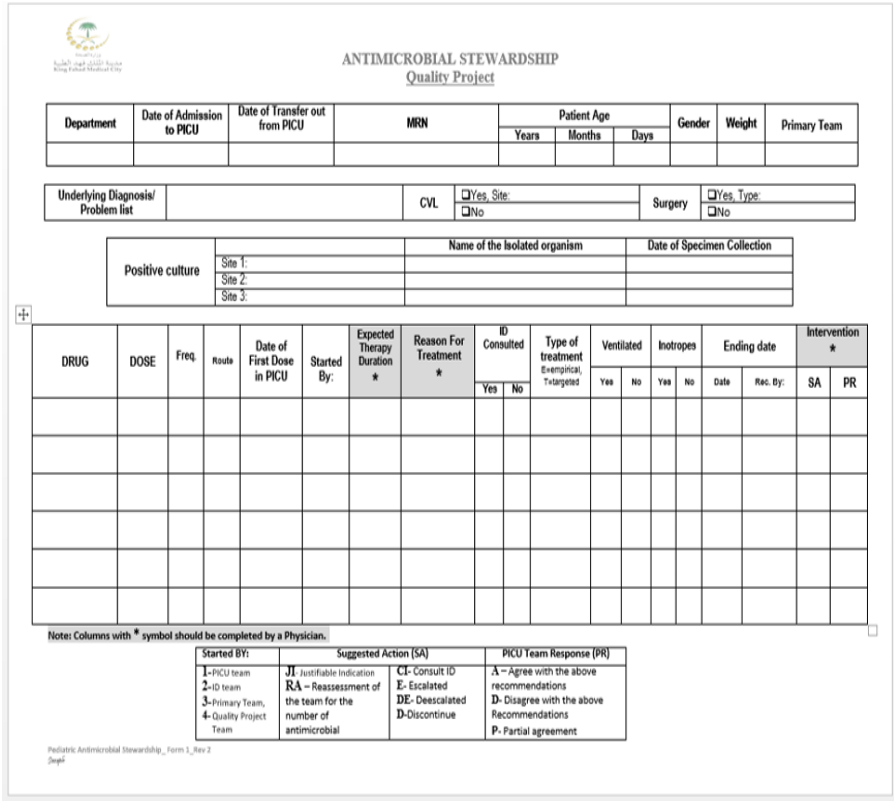
- Children's Hospital Colorado 2013
- Review of ***all prescribed*** antimicrobials and perform a rounding-based, in-person approach to feedback by a pharmacist–physician team
- Significant drop in antimicrobial days of therapy
- Significant increase in ID consultation from all studied units
- High acceptance rate – up to 86%
- Widely accepted and adopted model in US children's hospitals





Hurst et al. *Pediatr Infect Dis J* 2016;35:1104–1110)
Massacar et al. CID. 2017;64(10):1449–52

Antimicrobial Stewardship Program in a Pediatric Intensive Care Unit of a Tertiary Care Children's Hospital in Saudi Arabia–a Pilot Study



ANTIMICROBIAL STEWARDSHIP
Quality Project

Department	Date of Admission to PICU	Date of Transfer out from PICU	MRN	Patient Age			Gender	Weight	Primary Team
				Years	Months	Days			

Underlying Diagnosis/ Problem list		CVL	☐Yes, Site: ☐No	Surgery	☐Yes, Type: ☐No

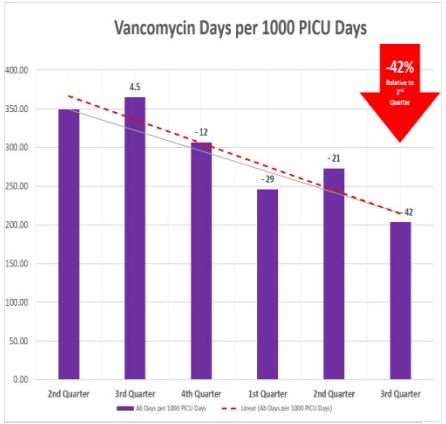
Positive culture		Name of the Isolated organism	Date of Specimen Collection
	Site 1:		
	Site 2:		
	Site 3:		

DRUG	DOSE	Freq.	Route	Date of First Dose in PICU	Started By:	Expected Therapy Duration *	Reason For Treatment *	ID Consulted		Type of treatment E=empirical, T=targeted	Ventilated		Inotropes		Ending date		Intervention *	
								Yes	No		Yes	No	Yes	No	Date	Rec. By:	SA	PR

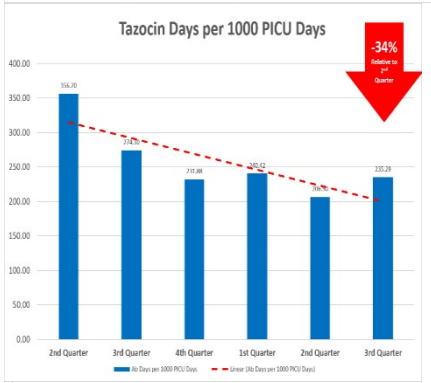
Note: Columns with * symbol should be completed by a Physician.

Started BY:	Suggested Action (SA)		PICU Team Response (PR)
1-PICU team 2-ID team 3-Primary Team, 4-Quality Project Team	JI- Justifiable Indication RA – Reassessment of the team for the number of antimicrobial	CI- Consult ID E- Escalated DE- Deescalated D-Discontinue	A – Agree with the above recommendations D- Disagree with the above Recommendations P- Partial agreement

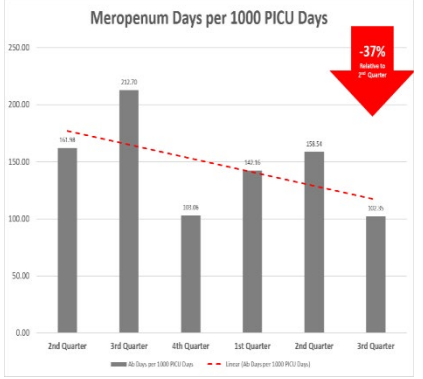
Pediatric Antimicrobial Stewardship_ Form 1_Rev 2



Vancomycin
- 42%



Pip-Tazo
- 34%



Meropenem
- 37%

Alawdah et al. *Antimicrobial resistance and infection control*. 2015 1;4(S1):P173.

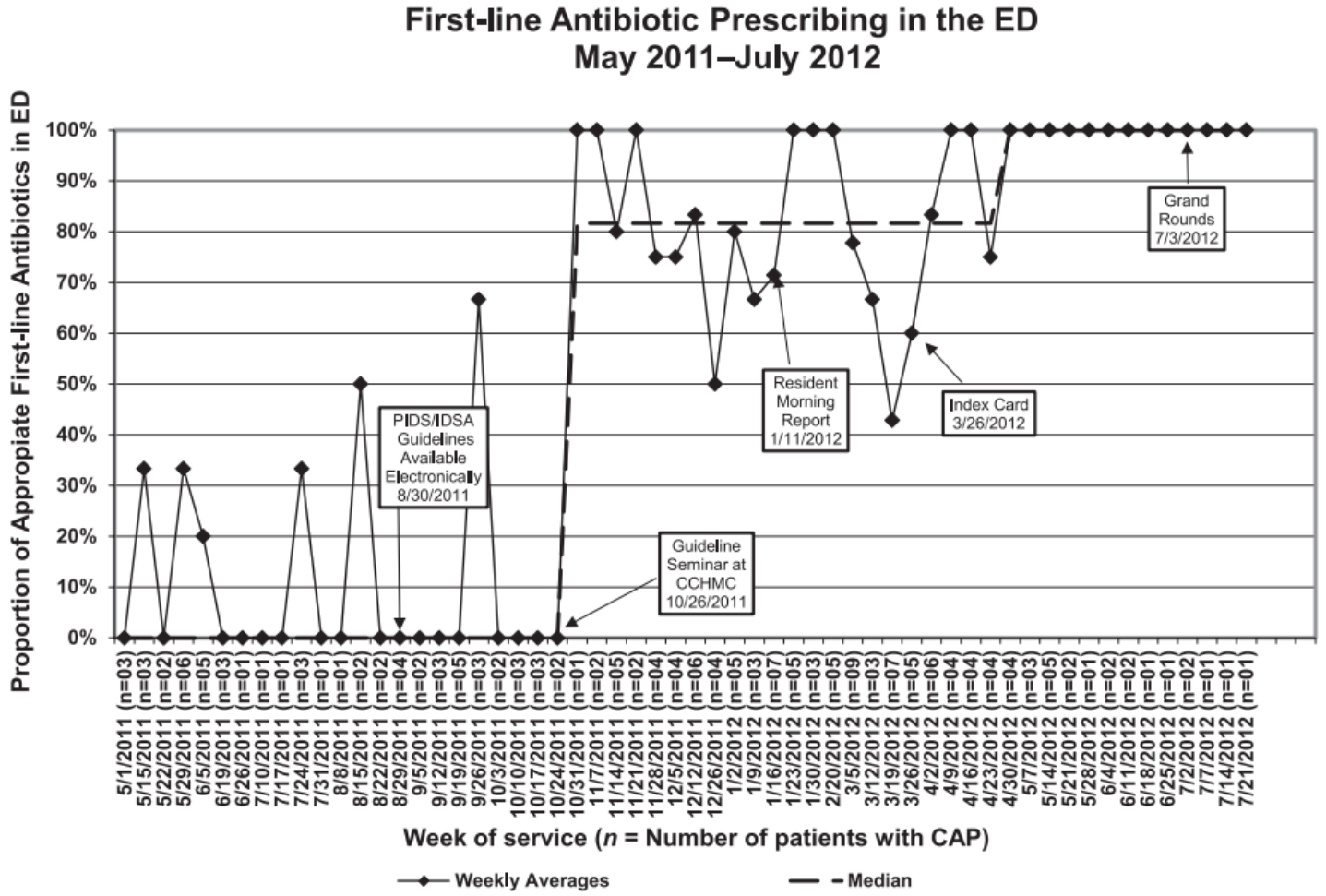
Pediatric AMS in the Inpatient Setting

- Elements of pediatric inpatient AMS include a variable mix of the following:

Strategy	Pros	Cons
3- Implementation of institution-specific guidelines for common syndromes (e.g. CAP or Surgical prophylaxis)	• Effective if widely accessible and associated with monitoring and feedback • Utilization of digital apps and decision support software	• Requires periodic update and education • Depends on physician's documentation of indication

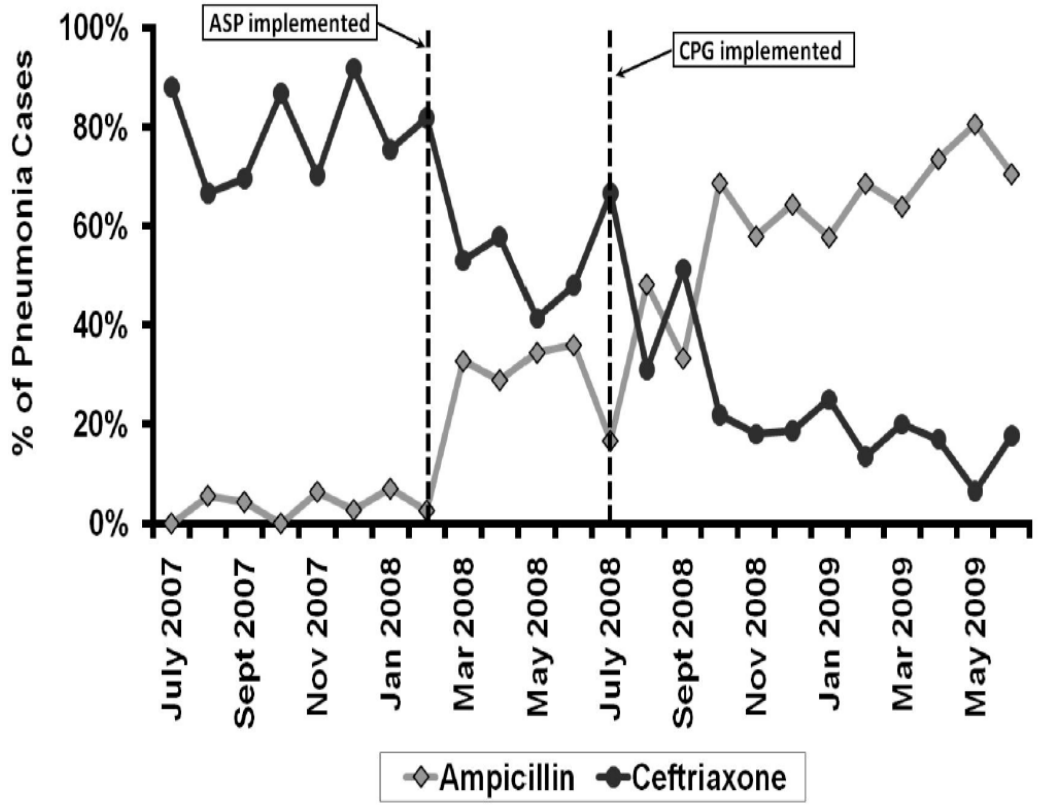
Ambroggio et al. Pediatrics 2013;131:e1623–e1631
Patel & Vergnano. Curr Opin Infect Dis 2018, 31:216–223

Example: Guideline Implementation and Adherence Monitoring



Ambroggio et al. Pediatrics 2013;131:e1623–e1631

Impact of Guidelines on Practice in One US Hospital



Newman R et al. Pediatrics 2012 129:e597-04

Kingdom of Saudi Arabia
Ministry of Health
King Fahad Medical City

المملكة العربية السعودية
وزارة الصحة
مدينه الملك فهد الطبية

Guidelines for Empirical Antimicrobial Therapy In Children

CENTRAL NERVOUS SYSTEM

Indication	Suspected Pathogens	Antimicrobial of Choice	Alternative Therapy/Comments
Meningitis			
Neonate (up to 4 weeks)	Gr B Streptococcus, Gram negative Enteric Bacilli, Listeria	IV Ampicillin + IV Cefotaxime	
4 weeks – 3 months	Same as Neonates and Older Children	IV Ampicillin + IV Cefotaxime	Add Vancomycin in sick patients
Older Children	S. pneumoniae, N. meningitidis, H. influenzae	IV Ceftriaxone + IV Vancomycin	Deescalate antibiotic according to sensitivity
Encephalitis	Herpes Simplex Virus	IV Acyclovir	If meningoencephalitis is suspected, refer to empiric antibiotics for Meningitis. Ensure sending HSV and other viruses PCR from CSF Samples
V-P Shunt Related Infection	Coagulase-negative Staphylococci, Enteric gram-negative bacili	IV Vancomycin + IV Ceftazidime	Review previous shunt infection episodes and cover previously isolated pathogens if documented sensitivity is available or consult ID

SEPTICEMIA/BACTEREMIA (Excluding Meningitis)

Indication	Suspected Pathogens	Antimicrobial of Choice	Alternative Therapy/Comments
Septicemia or Bacteremia			
Neonates	Gr B Streptococcus, Gram negative Enteric Bacilli, Listeria, Enterococcus	IV Ampicillin + IV Gentamycin	
1-3 months	Same as Neonates and Older Children	IV Ampicilin + IV Cefotaxime	Add Vancomycin in severely ill patient
> 3 months	S. pneumoniae, Meningococcus, S. aureus, H. influenza, E. coli	IV Ceftriaxone	Add Vancomycin in severely ill patient.
> 48 hours of Hospitalization	Hospital acquired Pathogens including P. aeruginosa, klebsiella pneumoniae and E. coli, staph aureus	IV Piperacillin-Tazobactam ± IV Vancomycin	Consider Aminoglycocide in severely ill patient
Sickle Cell Disease with sepsis	S. pneumoniae, H. influenzae, Salmonella	IV Ceftriaxone ± IV Vancomycin	β-Lactam Allergy: Clindamycin+Ciprofloxacin

RESPIRATORY SYSTEM

Indication	Suspected Pathogens	Antimicrobial of Choice	Alternative Therapy/Comments
Pneumonia			
Neonates	Group B Streptococcus, Gram negative Enteric Bacilli, Listeria	IV Ampicillin + IV Gentamycin	
Community-acquired			
1-3 months	S. pneumoniae, C. trachonatis, B. pertussis, S. aureus, H. influenzae	IV Cefotaxime + Macrolides	Obtain a viral NPA especially if <2 years and consider Adding Oseltimavir.
3 months – 12 years			
Immunized	Strept. Pneumo, mycoplasma , staph aureus	IV Ampicillin ± Macrolides	IV Augmentin
Non-immunized	Strept. Pneumo, H. influenza, M.P. S. Aureus,	IV Cefturoxime ± Macrolides	
Aspiration pneumonia	Anaerobes, enteric gram negative	IV Augmentin	IV Clindamycin
Complicated pneumonia			
**Necrotizing pneumonia, para pneumonic effusion, empyema, pneumatocele & lung abscess.	S. pneumoniae, S. aureus, H. influenzae, S. pyogenes, C. pneumoniae, M. pneumoniae	IV Ceftriaxone + IV Clindamycin ± Macrolides	
Healthcare associated Pneumonia			
Ventilated	Gram negative bacilli including P. aeruginosa anaerobes, staph aureus	IV Pipracilin/Tazobactam +IV Vancomycin + IV **Aminoglycocides	Cefepime+Clindamycin. **Add aminoglycocide if patient colonized with MDR organisms.
Non ventilated	Gram neg. bacilli, Staph aureus	IV Pipracilin/Tazobactam	

URINARY SYSTEM

Indication	Suspected Pathogens	Antimicrobial of Choice	Alternative Therapy/Comments
UTI	E. coli, Proteus spp.	IV Ceftriaxone	Amikacin if ESBL is suspected

OTHER SYSTEMS

Indication	Suspected Pathogens	Antimicrobial of Choice	Alternative Therapy/Comments
Febrile Neutropenic Child	Gram negative bacili including P. aeruginosa	IV Pipracillin-Tazobactam + IV Amikacin ± IV Vancomycin	Refer to Pediatric Febrile Neutropenia Guidelines
Catheter-Related BSI	S. aureus, CONS, enteric gram-negative bacilli, Plus P. Aeruginosa and MDR Gram negative bacteria in immunocompromised patient.	Ceftazidime + Vancomycin	IV Cefepime +IV Vancomycin. Add aminoglycocides in severely ill patients and/or immunocompromised patients.
Brucellosis	B. melitensis B. abortus		
< 8 years		Rifampicin + TMP/SMX	Add IV Gentamycin for hospitalized patient
> 8 years		Rifampicin + Doxycycline	

SKIN & SOFT TISSUE INFECTIONS

Indication	Suspected Pathogens	Antimicrobial of Choice	Alternative Therapy/Comments
Cellulitis	S. aureus, Gr A Streptococcus	IV Cloxacillin or Cefazolin	IV Clindamycin
Necrotizing Fasciitis	Gr A streptococcus, S. aureus, Polymicrobial, Clostridium spp.	IV Clindamycin + IV Cloxacillin	Consult ID on all cases Consult Pediatric Surgery
Periorbital cellulitis	Strept. Pneumo, staph aurues, GAS, H. Influenzae	Cefturoxime or Augmentin	Clindamycin if MRSA is suspected
Orbital cellulitis	Strept. Pneumo, moraxella, GAS, anaerobes	Clindamycin + Ceftriaxone	IV Vancomycin + Ceftriaxone ± Metronidazole

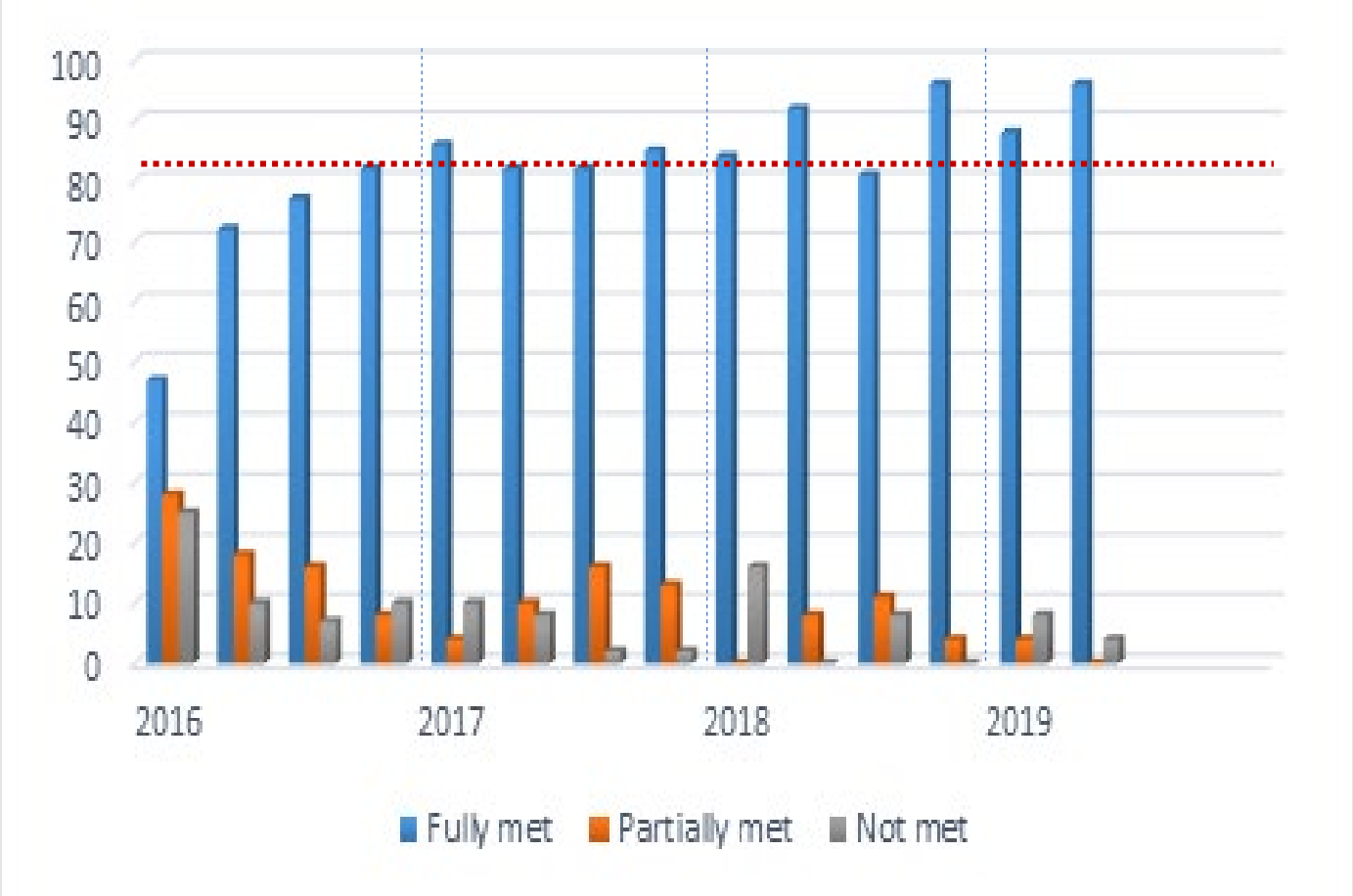
OSTEOARTICULAR

Indication	Suspected Pathogens	Antimicrobial of Choice	Alternative Therapy/Comments
Neonate	Staph aureus, GBS-enteric gram negative bacilli	IV Cefotaxime + IV Vancomycin	
All other age group	Staph aureus, strep. Pneumo, strep. Pyogenes,	IV Clindamycin	IV Vancomycin **Add ceftriaxone for non-immunized patients.
Sickle cell anemia	Strept. Pneumonae salmonella, Staph aureus	Clindamycin + Ceftriaxone	

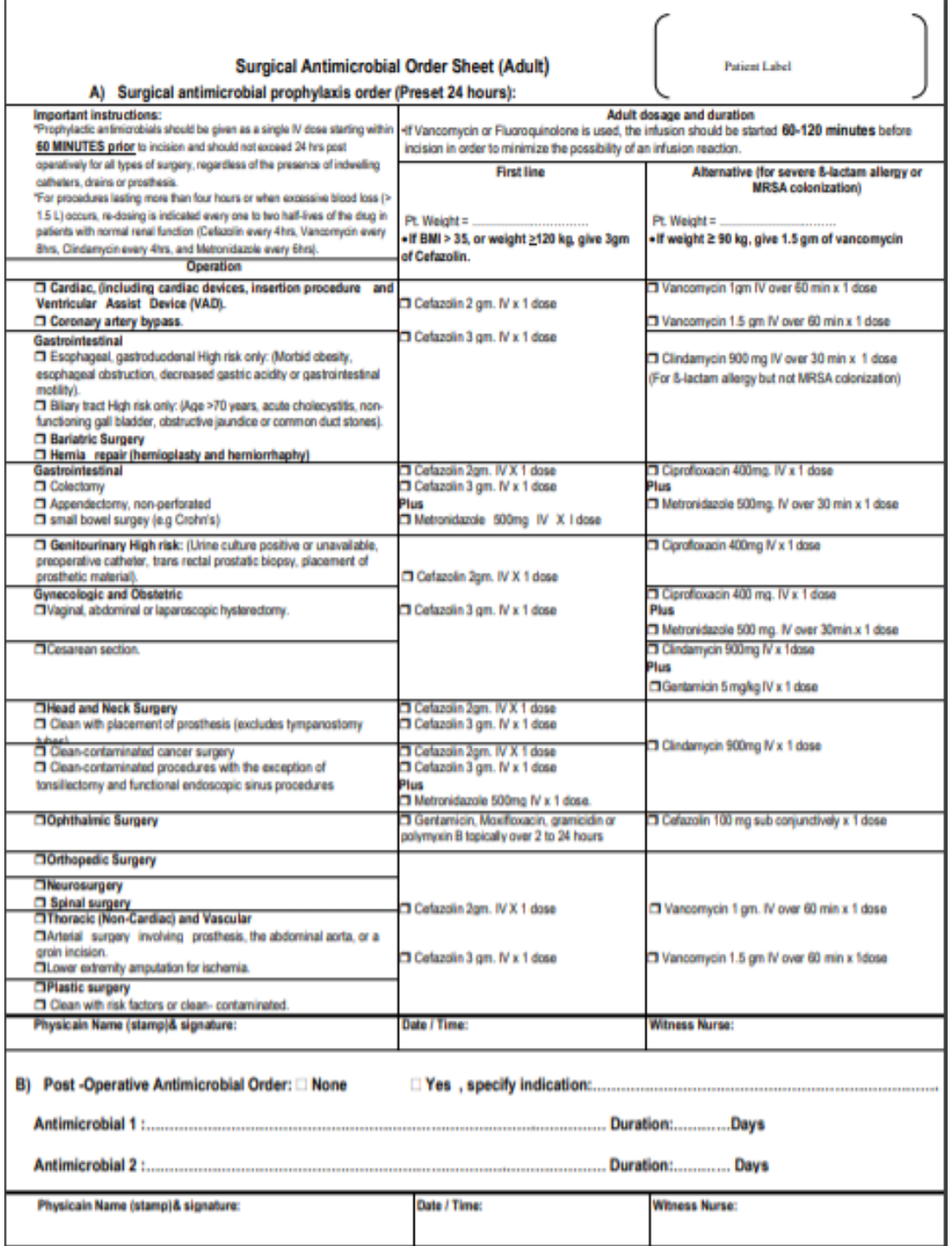
GASTROINTESTINAL SYSTEM

Indication	Suspected Pathogens	Antimicrobial of Choice	Alternative Therapy/Comments
Enterocolitis			
Neonates (NEC)	Enteric gram negative bacilli, Enterococcus spp., anaerobes	IV Ampicillin + IVGentamycin ± Metronidazole	
C. Difficile-Associated	C. Difficile	Stop offending antibiotic + PO Metronidazole	Alternative therapy: PO Vancomycin
Peritonitis			
Primary (spontaneous)	Strept. Pneumo, gram negative bacilli	IV Ceftriaxone	
Secondary (i.e., post perforation)	Gram negative bacilli, anaerobes	IV Ampicillin + Gentamycin + Metronidazole	Consult ID

Percentage of Compliance to Empiric Antibiotic Guidelines at CSH-KFMC at Hospital Admission



Surgical Prophylaxis Manual Order Set



Surgical Antimicrobial Order Sheet (Adult)

Patient Label

A) Surgical antimicrobial prophylaxis order (Preset 24 hours):

Important instructions:
*Prophylactic antimicrobials should be given as a single IV dose starting within **60 MINUTES prior** to incision and should not exceed 24 hrs post operatively for all types of surgery, regardless of the presence of indwelling catheters, drains or prosthesis.
*For procedures lasting more than four hours or when excessive blood loss (> 1.5 L) occurs, re-dosing is indicated every one to two half-lives of the drug in patients with normal renal function (Cefazolin every 4hrs, Vancomycin every 8hrs, Clindamycin every 4hrs, and Metronidazole every 6hrs).

Adult dosage and duration
•If Vancomycin or Fluoroquinolone is used, the infusion should be started **60-120 minutes** before incision in order to minimize the possibility of an infusion reaction.

Operation	First line Pt. Weight = ... **• If BMI > 35, or weight ≥120 kg, give 3gm of Cefazolin.**	Alternative (for severe ß-lactam allergy or MRSA colonization) Pt. Weight = ... **• If weight ≥ 90 kg, give 1.5 gm of vancomycin**
❒ **Cardiac, (including cardiac devices, insertion procedure and Ventricular Assist Device (VAD).** ❒ **Coronary artery bypass.**	❒ Cefazolin 2 gm. IV x 1 dose ❒ Cefazolin 3 gm. IV x 1 dose	❒ Vancomycin 1gm IV over 60 min x 1 dose ❒ Vancomycin 1.5 gm IV over 60 min x 1 dose
Gastrointestinal ❒ Esophageal, gastroduodenal High risk only: (Morbid obesity, esophageal obstruction, decreased gastric acidity or gastrointestinal motility). ❒ Biliary tract High risk only: (Age >70 years, acute cholecystitis, non-functioning gall bladder, obstructive jaundice or common duct stones). ❒ **Bariatric Surgery** ❒ **Hernia repair (hernioplasty and herniorrhaphy)**		❒ Clindamycin 900 mg IV over 30 min x 1 dose (For ß-lactam allergy but not MRSA colonization)
Gastrointestinal ❒ Colectomy ❒ Appendectomy, non-perforated ❒ small bowel surgey (e.g Crohn's)	❒ Cefazolin 2gm. IV X 1 dose ❒ Cefazolin 3 gm. IV x 1 dose **Plus** ❒ Metronidazole 500mg IV X I dose	❒ Ciprofloxacin 400mg. IV x 1 dose **Plus** ❒ Metronidazole 500mg. IV over 30 min x 1 dose
❒ **Genitourinary High risk:** (Urine culture positive or unavailable, preoperative catheter, trans rectal prostatic biopsy, placement of prosthetic material).	❒ Cefazolin 2gm. IV X 1 dose	❒ Ciprofloxacin 400mg IV x 1 dose
Gynecologic and Obstetric ❒Vaginal, abdominal or laparoscopic hysterectomy.	❒ Cefazolin 3 gm. IV x 1 dose	❒ Ciprofloxacin 400 mg. IV x 1 dose **Plus** ❒ Metronidazole 500 mg. IV over 30min.x 1 dose
❒Cesarean section.		❒ Clindamycin 900mg IV x 1dose **Plus** ❒Gentamicin 5 mg/kg IV x 1 dose
❒**Head and Neck Surgery** ❒ Clean with placement of prosthesis (excludes tympanostomy tubes)	❒ Cefazolin 2gm. IV X 1 dose ❒ Cefazolin 3 gm. IV x 1 dose	❒ Clindamycin 900mg IV x 1 dose
❒ Clean-contaminated cancer surgery ❒ Clean-contaminated procedures with the exception of tonsillectomy and functional endoscopic sinus procedures	❒ Cefazolin 2gm. IV X 1 dose ❒ Cefazolin 3 gm. IV x 1 dose **Plus** ❒ Metronidazole 500mg IV x 1 dose.	
❒**Ophthalmic Surgery**	❒ Gentamicin, Moxifloxacin, gramicidin or polymyxin B topically over 2 to 24 hours	❒ Cefazolin 100 mg sub conjunctively x 1 dose
❒**Orthopedic Surgery** ❒**Neurosurgery** ❒ **Spinal surgery**	❒ Cefazolin 2gm. IV X 1 dose	❒ Vancomycin 1 gm. IV over 60 min x 1 dose
❒**Thoracic (Non-Cardiac) and Vascular** ❒Arterial surgery involving prosthesis, the abdominal aorta, or a groin incision. ❒Lower extremity amputation for ischemia.	❒ Cefazolin 3 gm. IV x 1 dose	❒ Vancomycin 1.5 gm IV over 60 min x 1dose
❒**Plastic surgery** ❒ Clean with risk factors or clean- contaminated.		
Physicain Name (stamp)& signature:	**Date / Time:**	**Witness Nurse:**

B) Post -Operative Antimicrobial Order: ☐ **None** ☐ **Yes , specify indication:**.....

Antimicrobial 1 :..... **Duration:**.....**Days**

Antimicrobial 2 :..... **Duration:**..... **Days**

Physicain Name (stamp)& signature:	Date / Time:	Witness Nurse:

Pediatric-Specific Cumulative Antibiogram

ANTIMICROBIAL SUSCEPTIBILITY OF CLINICAL ISOLATES AT KFMC
DEPARTMENT OF MICROBIOLOGY
KING FAHAD MEDICAL CITY

LOCATION	PEDIATRIC	YEAR	JANUARY – DECEMBER 2018	TABLE	GRAM NEGATIVE NON-FERMENTING BACTERIA

NO ISOLATES NAME	ISOLATE TESTED	CAZ	CPE	CIP	TZP	GM	AN	IMP	MER	SXT	CL	LEVO
Pseudomonas aeruginosa	323	85%	80%	78%	74%	83%	90%	64%	70%		100%	74%
Acinetobacter baumannii	67	51%	51%	45%	45%	43%	51%	43%	40%		97%	46%
Stenotrophomonas maltophilia	50	50%								94%		40%

ABBREVIATIONS FOR ANTIBIOTICS

AMP	Ampicillin	AUG	Augmentin	CF	Cephalothin	CXM	Cefuroxime	CAZ	Ceftazidime	FOX	Cefoxitin
CPE	Cefepime	CIP	Ciprofloxacin	GM	Gentamicin	AN	Amikacin	SXT	Trimethoprim - Sulfamethoxazole	TZP	Piperacillin - Tazobactam
IMP	Imipenem	MER	Meropenem	NIT	Nitrofurantoin	ERY	Erythromycin	CL	Colistin	SM	Streptomycin
TC	Tetracycline	RA	Rifampin	TGC	Tigecycline	LEVO	Levofloxacin	CTX	Cefotaxime	DOXY	Doxycycline

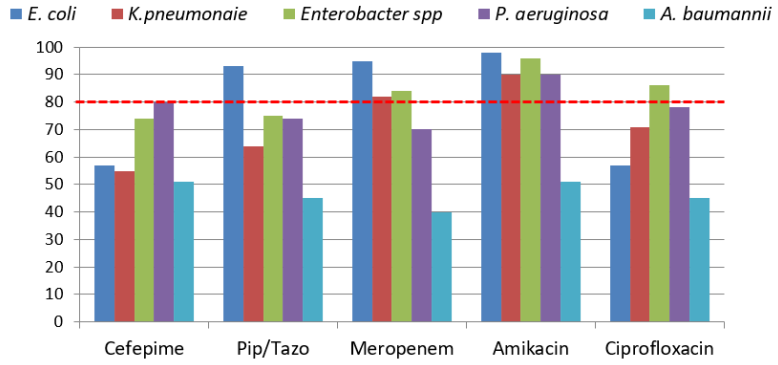
** Tested on urinary tract isolates only*

<= 69 %	Caution in selecting this antibiotic is advised, discussion with Microbiologist or ID is recommended.	70 % - 79 %	recommended for empiric therapy if no other choice	>=80 %	reasonably good susceptibility, recommended as first line empiric therapy for the suspected organism

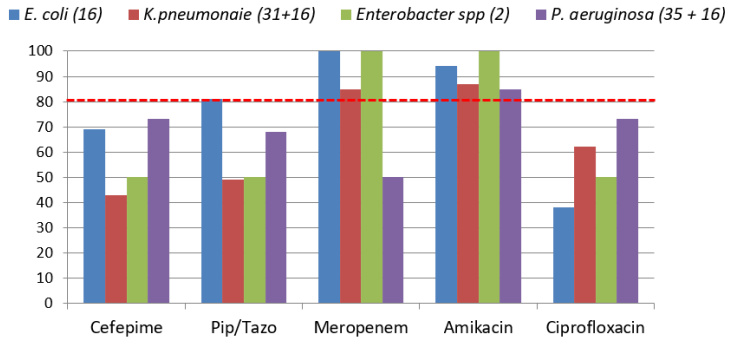
Local Fever & Neutropenia in Children with Cancer Protocol

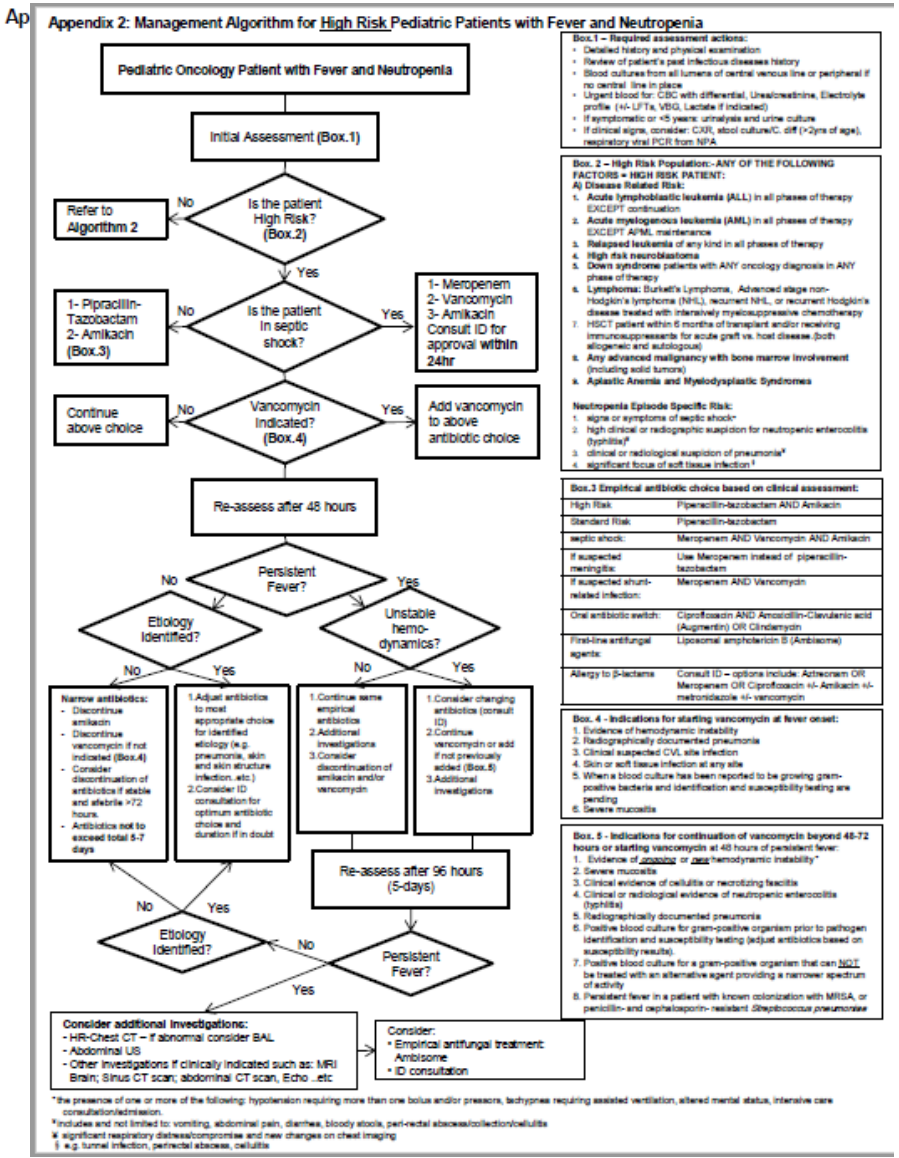
Empiric Gram Negative Coverage Choice

2018 CSH Antibiogram for clinically important gram-negative bacteria



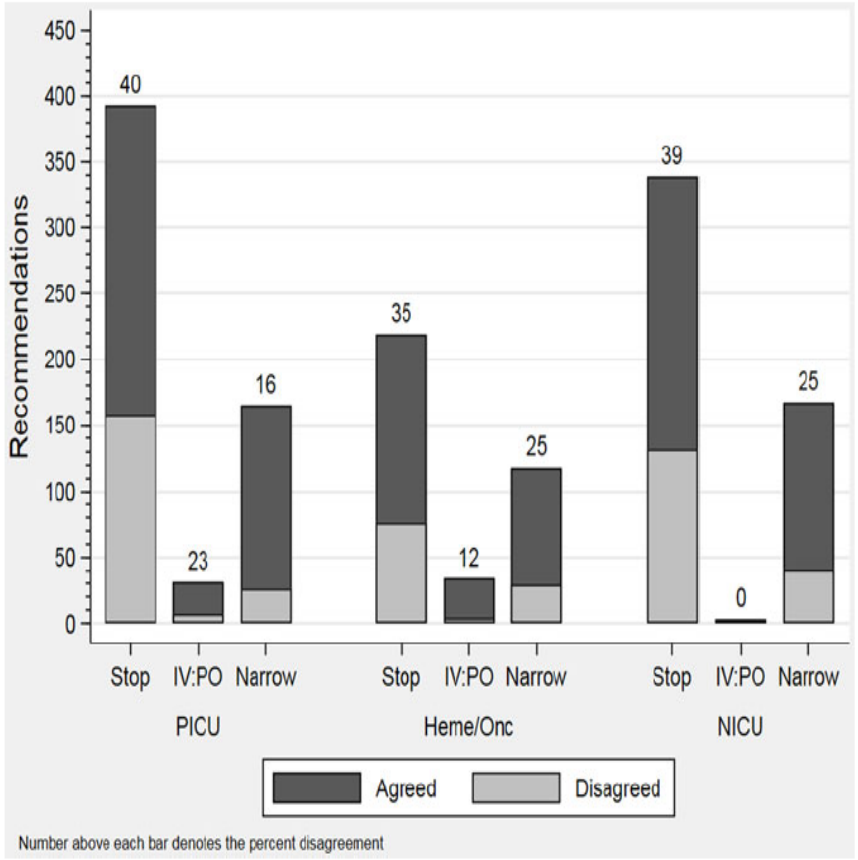
2017 + 2018 CSH Pediatric Oncology Antibiogram (manually combined)





Safety of ASP on High Risk Pediatric Patients

- In patients for whom an ASP recommendation was given, the odds of mortality was significantly lower (adjusted odds ratio [aOR], 0.72; 95% CI 0.54–0.96; *P = 0.023*)
- A stop recommendation was not associated with increased odds of 30-day readmission (aOR, 0.98; 95% CI, 0.82–1.17; *P = 0.842*)
- The LOS for agreement with ASP recommendations was significantly shorter compared to cases in which disagreement occurred (10.2 days vs 12.5 days; *P = 0.021*)



Goldman et al. Infection Control & Hospital Epidemiology. 2019. 40: 968–973

Tracking & Reporting

- Collect baseline data
- Process measures
  - Recommendation acceptance rate
  - Dose optimization
  - Route optimization
  - Discontinuation of inappropriate antibiotics
- Outcome measures
  - Total antibiotic expenditures (cost, DOT/1000 patient days)
  - Impact assessment (C. difficile and MDRO rates) – will take time
  - 30-day readmission rates on cases that ASP intervened in

AMS Metrics

- Days of Therapy (DOT)/ 1000 patient days (based on the hospital census)

- Antibiotic Use and Resistance (AUR) Module
  - Days of therapy (DOT)/ 1000 days present
  - More nuanced Assessment
  - Allows for benchmarking antibiotic use inter-and intra-facilities
  - National Healthcare Safety Network (NHSN)/CDC require reporting this metric

- Defined Daily Doses (DDD)/ 1000 patient days

- Antibiotic spectrum index

- Other
    - DOT/Length of therapy (LOT)
    - Time to optimal therapy in invasive infections
    - Time of conversion from IV to PO for highly bioavailable antimicrobials

Barlam et al. CID. 2016;62(10):e51-e77.
https://www.cdc.gov/nhsn/
Gerber et al. Infect Control Hosp Epidemiol 2017;38:993–997.
Kronman et al. JPIDS. 2018;7(3):241–8

AMS Metrics in Pediatrics

- DDD is not ideal – large weight range
- Prescribed daily dose (mg/kg/day/100 bed days)
- Neonatal DDD for 8 most commonly used antimicrobials considering an average body weight of 2 kg – not validated or widely used
- Days of therapy per 100 or 1000 patient-day – widely used especially in the US.
- Antibiotic spectrum index
- Other metrics of antimicrobial consumption:
  - Proportion of hospitalized children on antimicrobials
    - Specific cohort (healthcare associated vs. community acquired infections)
    - Specific antimicrobial benchmarking (e.g. piperacillin-tazobactam or meropenem)

Petal & Vergnano. Curr Opin Infect Dis 2018, 31:216–223

Antibiotic Spectrum Index

Antibiotic	AbSI Score
Dicloxacillin Sodium	1
Oxacillin	1
Amoxicillin	2
Ampicillin	2
Cephalexin	2
Erythromycin	2
Erythromycin-Sulfisoxazole	2
Metronidazole	2
Penicillin G Benzathine	2
Penicillin G Sodium	2
Penicillin V Potassium	2
Aztreonam	3
Cefazolin	3
Cefdinir	3
Cefixime	3
Cefpodoxime	3
Rifampin	3
Azithromycin	4
Cefprozil	4
Ceftazidime	4
Cefuroxime	4
Chloramphenicol	4
Clarithromycin	4
Clindamycin	4
Piperacillin	4
Sulfamethoxazole-Trimethoprim	4
Cefotaxime	5
Cefoxitin	5
Ceftriaxone	5
Colistimethate Sodium	5
Daptomycin	5
Doxycycline Hyclate	5
Gentamicin	5
Minocycline HCl	5
Telavancin	5
Tobramycin	5
Vancomycin	5
Amikacin Sulfate	6
Amoxicillin-Pot Clavulanate	6
Ampicillin-Sulbactam	6
Cefepime	6
Linezolid	6
Ticarcillin-Clavulanate	6
Ceftaroline	8
Ciprofloxacin	8
Piperacillin-Tazobactam	8
Ertapenem	9
Levofloxacin	9
Meropenem	10
Moxifloxacin HCl	10
Imipenem-Cilastatin	11
Tigecycline	13

Gerber et al. *Infect Control Hosp Epidemiol* 2017;38:993–997

Antimicrobial Quality Metrics for Hospitalized Neonates and Children

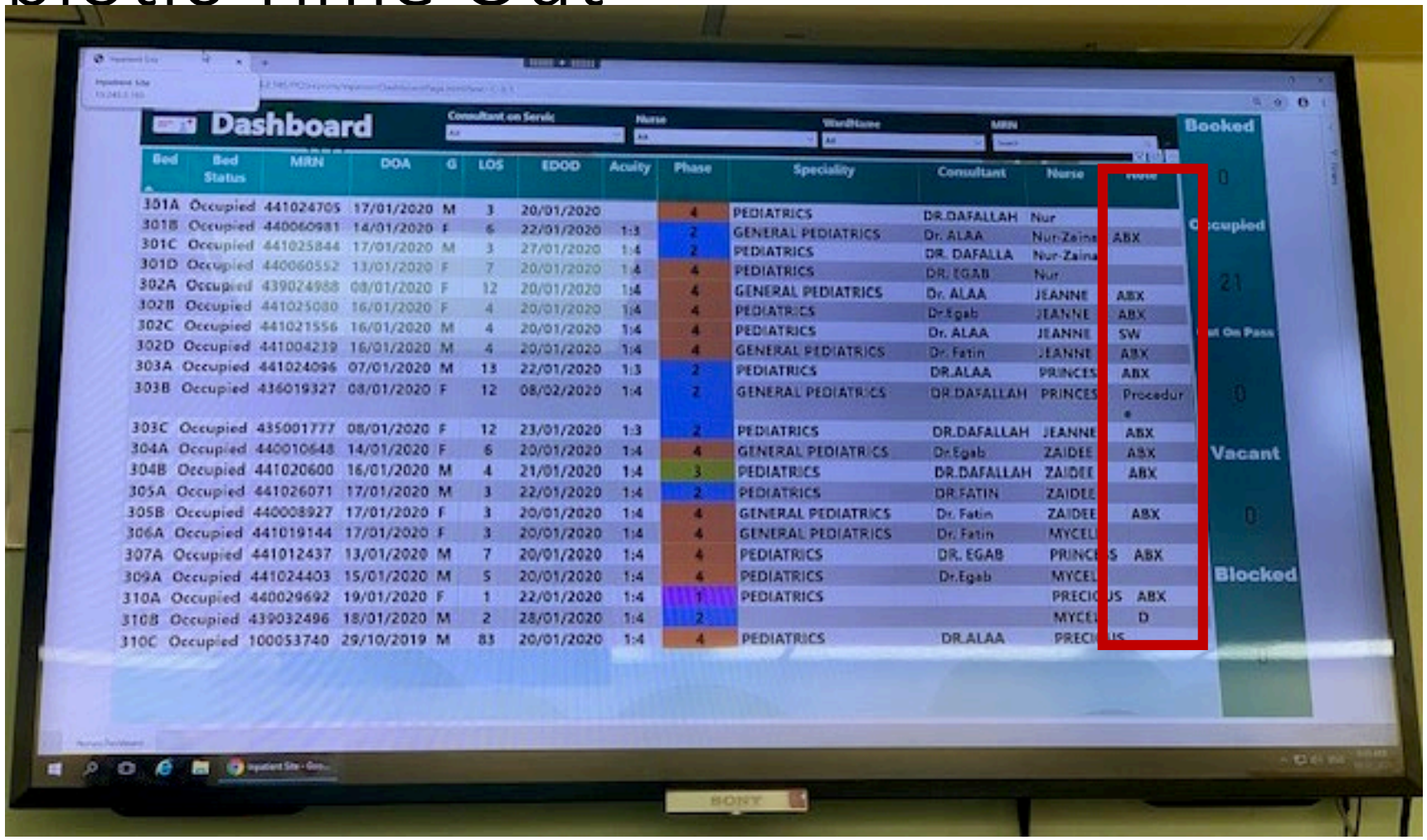
1. Documentation of the reason for antimicrobial prescribing in the notes
2. Targeted therapeutic antibiotic prescribing
3. Parenteral administration of antibiotics
4. Number of antibiotic combination therapies
5. Broad-spectrum antibiotic prescribing
6. Antibiotic prevalence rates for hospital-acquired infections
7. Targeted broad-spectrum antibiotic prescribing for hospital-acquired infections
8. Empirical broad-spectrum antibiotic prescribing for community-acquired infections
9. Broad-spectrum antibiotic prescribing for surgical prophylaxis
10. Prolonged antibiotic prescribing for surgical prophylaxis

Versporten et al. J Antimicrob Chemother 2016; 71: 1106–1117

Barriers to Implementing AMS in our Clinical Setting

- Lack of ASP expertise – relatively new concept
- Limited pediatric pharmacist time and number
- No protected time for physician ASP activities
- Lack of true accountability/structure for ASP
- Limited IT support
- Incomplete medical records/documentation
- Manual data collection – prone to error/human factors

AMS @ CSH in 2020
“Antibiotic Time Out”



Antibiotic Time Out

Who: Primary team including nurses

When: at 72 hours of antibiotic initiation

Supported by prospective audit and feedback rounds by ID + clinical pharmacist two days a week on cases non-consulted by ID team

Goals:

1. Improve documentation of indication and duration of therapy
2. Reduction of aminoglycosides and vancomycin days

Pediatric AMS in Resource Limited Setting

- Assess your local antibiotic use
- Identify the most feasible strategy
- Identify a way to embed AMS in the regular workflow
- Enforce the importance role of accurate diagnostics
- Educate providers
- Obtain leadership buy-in
- Start with simple strategies:
  - Advocating against over the counter antibiotic access
  - Physician and parent education
  - Institution specific guidelines
  - Antibiotic time-out culture (indication and duration documentation)
  - Antibiotic restriction and preauthorization
- Collaborate with microbiology, clinical pharmacy, and infection prevention and control services

Some Advices

- Assess your hospital readiness and gaps
- Build on what you currently have and keep improvement initiatives going
- Have good relationship with everyone – especially your ID colleagues
- Start small but aim big
- Talk to related stakeholders/services before implementing any new policy
- Start with antimicrobial restriction and empiric guidelines
- Then focus on appropriateness, de-escalation, and time-outs
- Don’t be threatening to teams
- Don’t get offended if they did not accept your recommendations
- Measure, measure, measure – ALL what you do
  - Be data driven – analytics are not the destination but part of the journey
- Education is your role!
- It’s a global problem **= we ALL need to participate in taking an action Today**

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