The Hemodialysis Patient with a Multidrug Resistant Organism

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Disclosures

None

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Outline

- Overview of MDRO infections

- Risk factors for MDRO colonization and infection
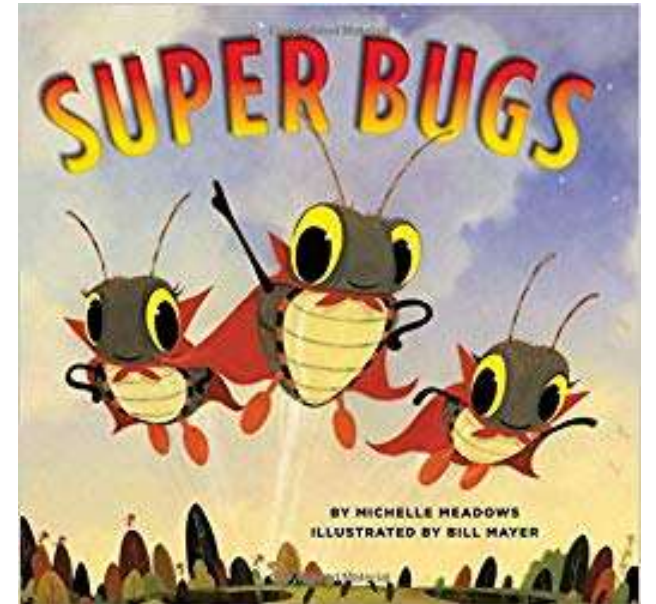
- MDRO prevention and control

Case

- 65yrs old, Chinese, Male
- End stage renal disease secondary to diabetic kidney disease
- Past history of diabetes, hypertension, ischemic heart disease and peripheral vascular disease with a previous ray amputation
- Declined pre-emptive AVF creation
- Hemodialysis via tunneled dialysis catheter

Case

- Catheter Related Blood Stream Infections (CRBSI) episodes
  - MSSA bacteremia – treated with Cloxacillin followed by cefazolin
  - MRSA bacteremia – treated with Vancomycin

  Hemodialysis patient with multidrug resistant organism
  .
  - MRI foot - Osteomyelitis
  - Septic shock, vegetation on tricuspid valve
  - Demise in Intensive care unit

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Multidrug resistant organisms (MDRO)

- Defined as microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents

  IOM (1998), eds. Harrison, P.F. Lederberg, J. (National academy press, Washington, DC), pp. 8-74

- Inconsistency in the definitions of MDRO
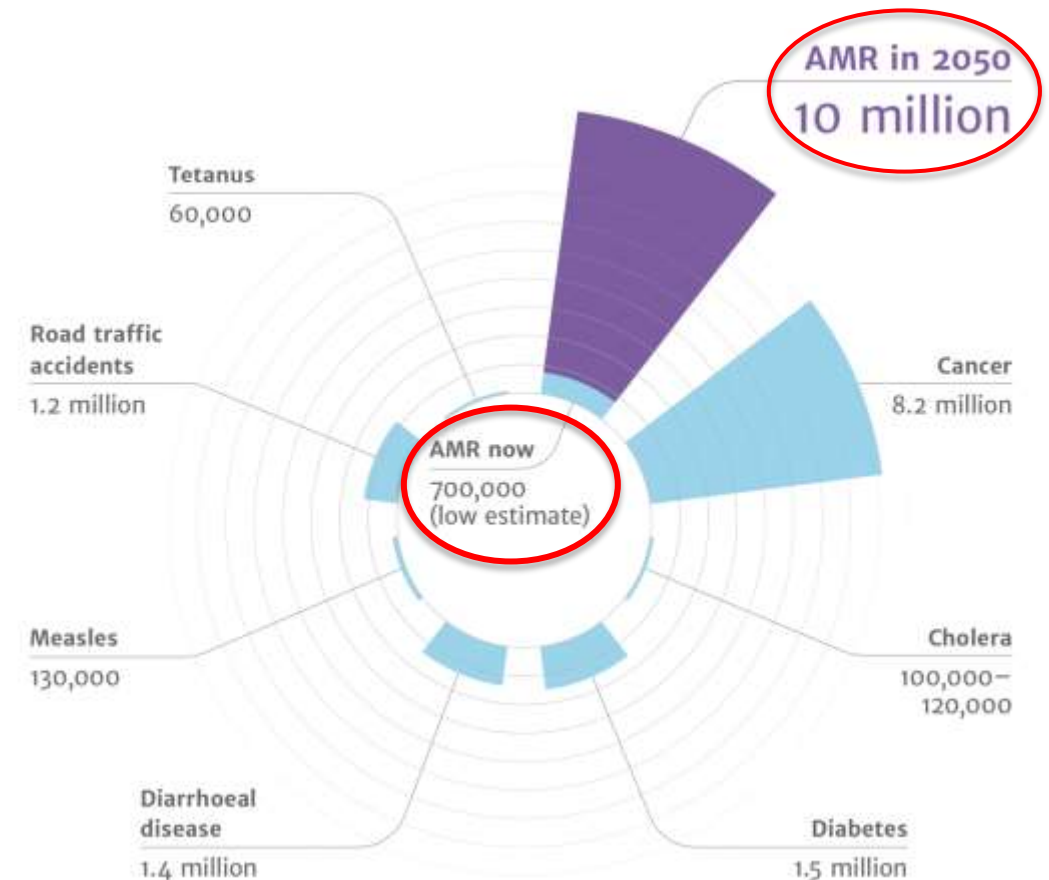
AMR in 2050
10 million

Tetanus
60,000

Road traffic accidents
1.2 million

AMR now
700,000
(low estimate)

Cancer
8.2 million

Measles
130,000

Cholera
100,000–120,000

Diarrhoeal disease
1.4 million

Diabetes
1.5 million

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Antibiotic resistance trends across OECD countries
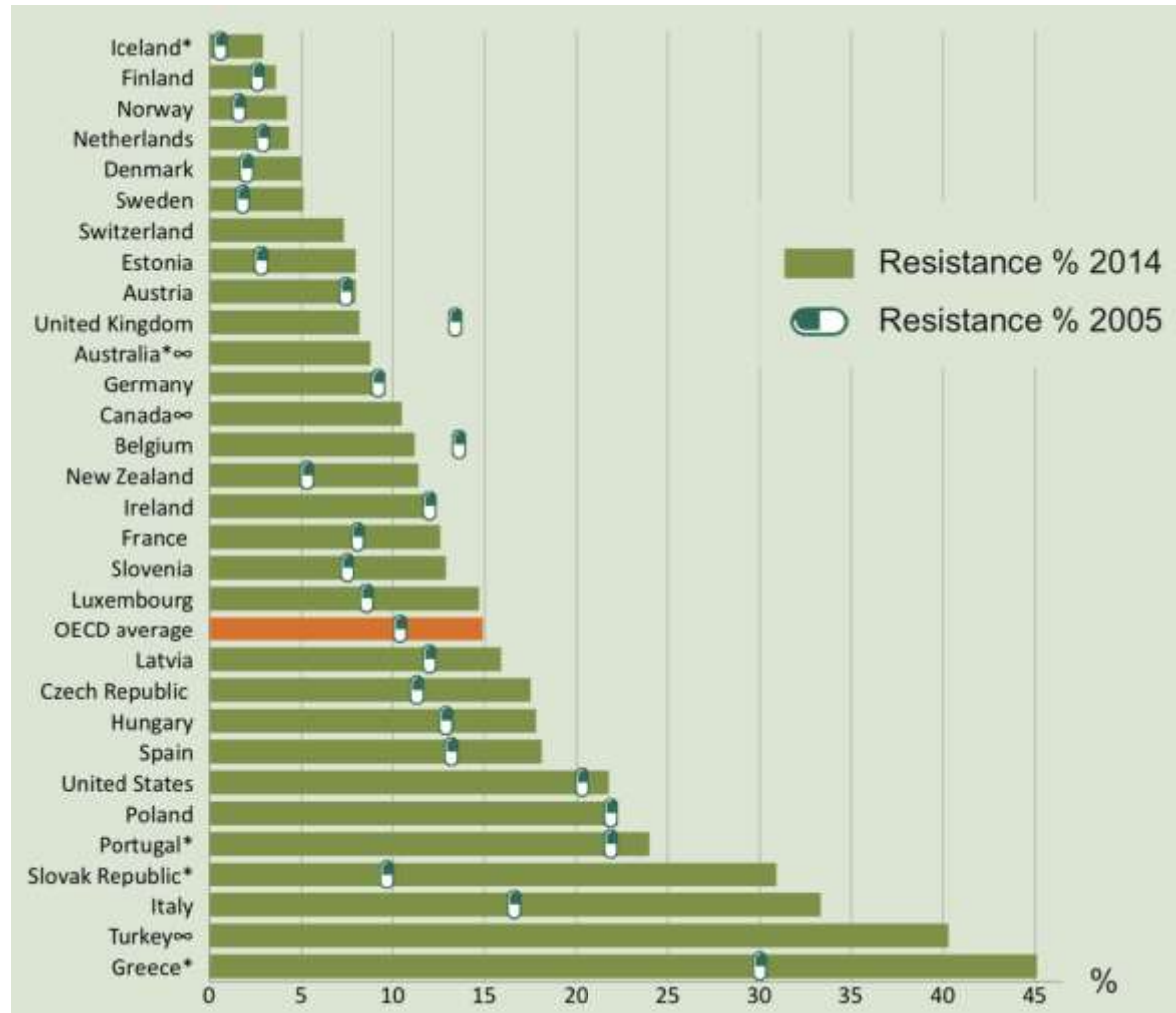
ESAC-Net Database and CDDEP

Timeline of antimicrobial development and resistance
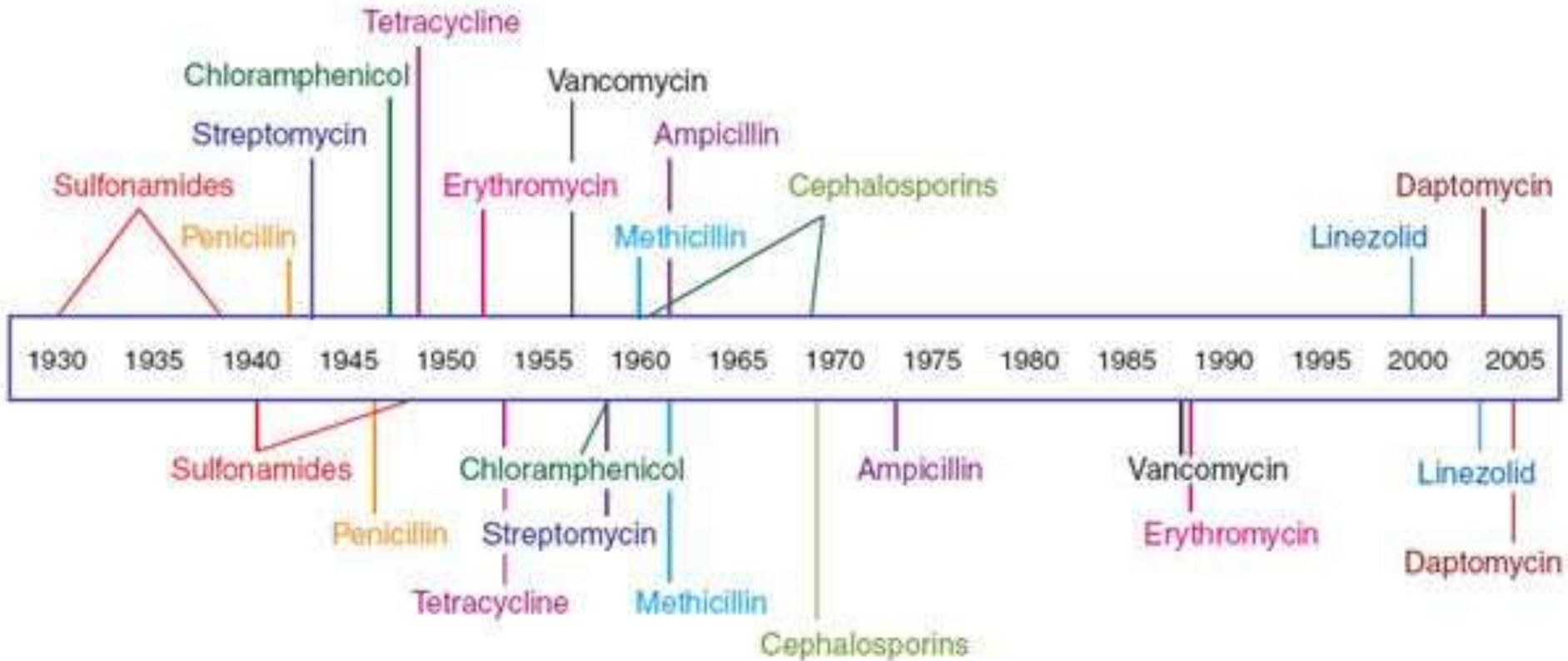
Clatworthy et al. Nature Chemical Biology:2007;3:54 1-8

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Time From Antibiotic Approval or Introduction to Detection of Resistance in Clinical Samples
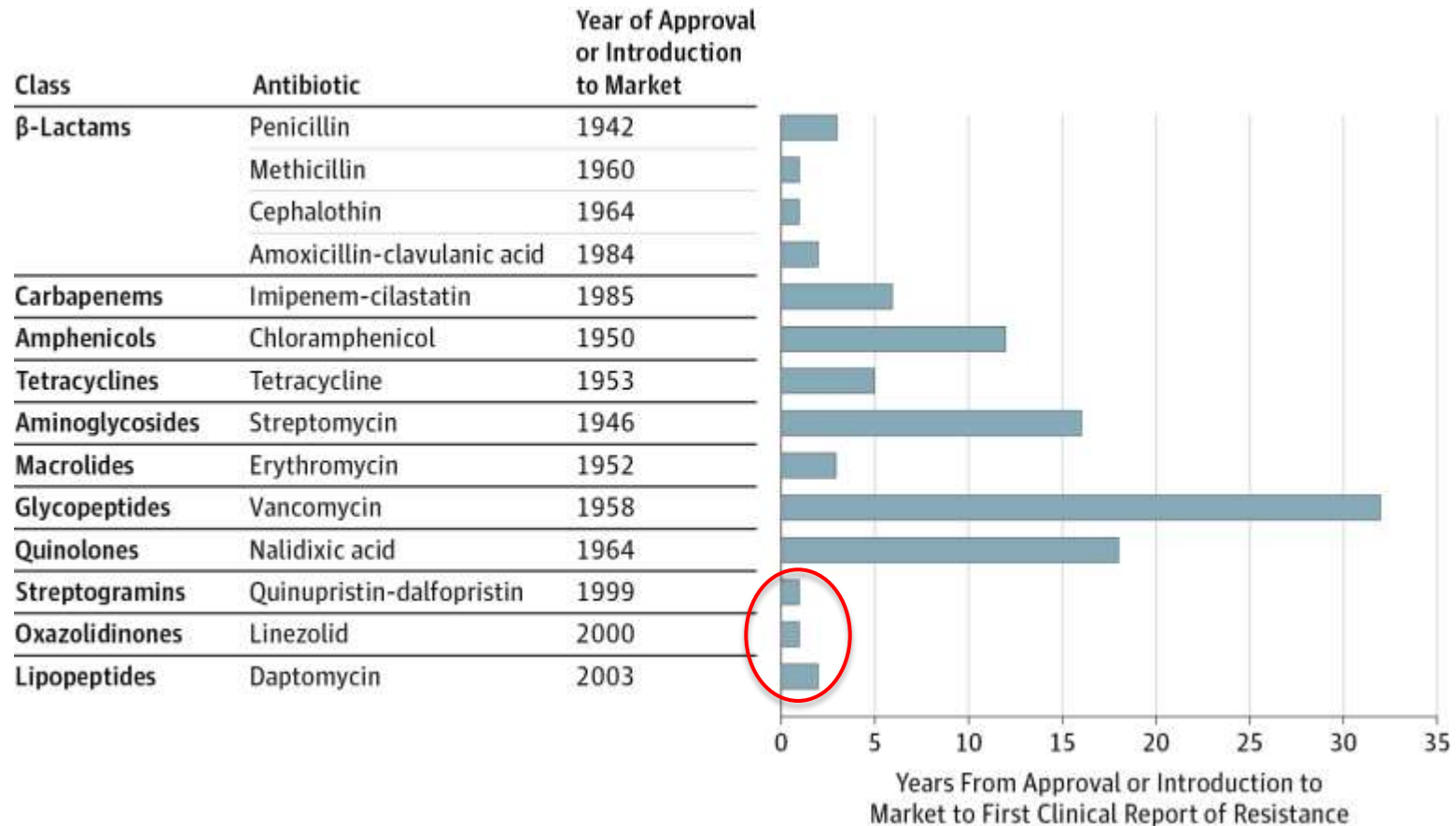
Marston HD et al JAMA. 2016;316(11):1193–1204

Number of new antimicrobials approved by the United States Food and Drug Administration since 1983

No. of new antibiotics

| Year | 1983-1987 | 1988-1992 | 1993-1997 | 1992-2002 | 2003-2007 | 2008-2012 |
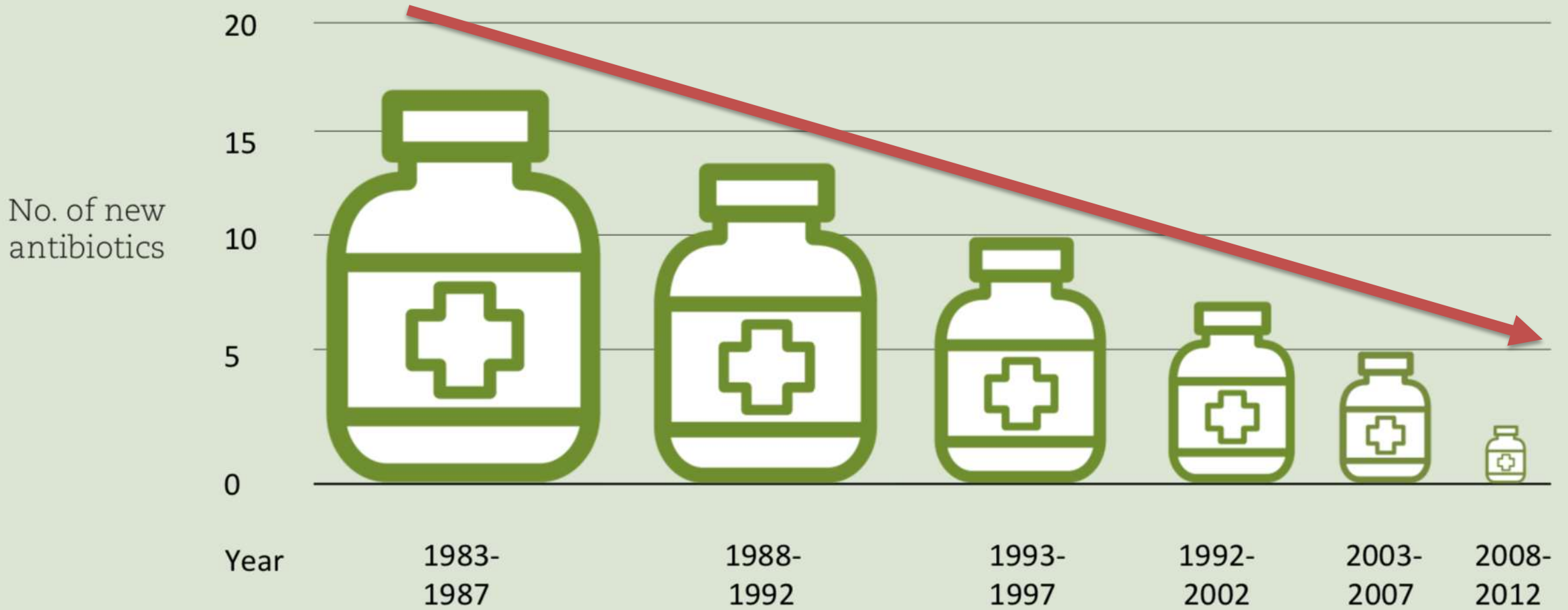
Source: OECD (2015). Antimicrobial resistance in G7 countries and beyond: economic issues, policies and options for action.

Development of new antibiotics

TABLE 4-4. OVERVIEW OF FDA DRUG DEVELOPMENT PROCESS

Phase	Timeline	Overall probability of success
Preclinical	1–6 years	
Clinical	6–11 years	
Investigational new drug application		
Phase 1	21.6 months	30%
Phase 2	25.7 months	14%
Phase 3	30.5 months	9%
Approval of new drug application	0.6–2 years	8%
Phase 4, post-market surveillance	11–14 years	

Source: http://www.fdareview.org/approval_process.shtml

Rate of success

- Preclinical
- Phase I — 9.3%
- Phase II — 33%
- Phase III — 75%
- Approval — 85.7%
- 75%

1.5% of antibiotic compounds make it to the market
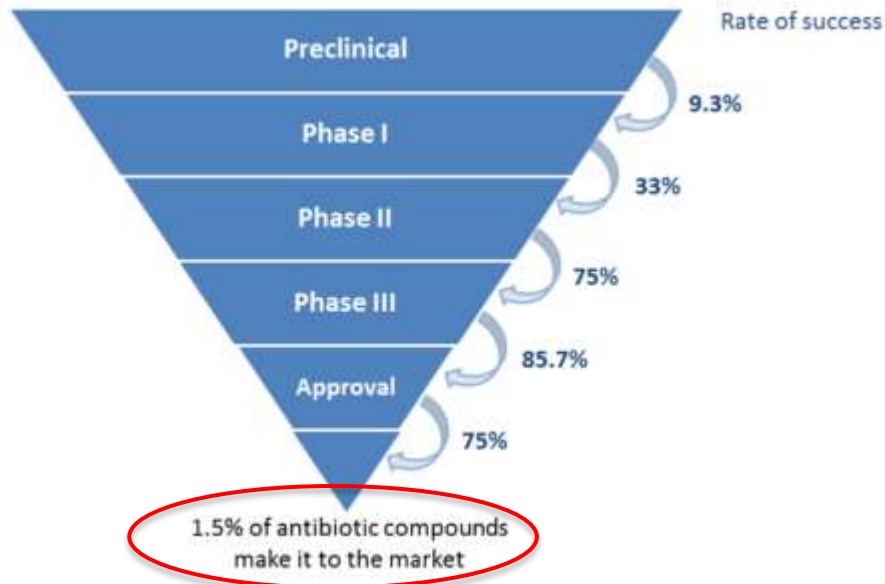
Breaking even

Cumulative profits from antibiotic research*, $m

PRE-CLINICAL RESEARCH | CLINICAL RESEARCH | ON-PATENT SALES | OFF-PATENT SALES

Years since beginning research
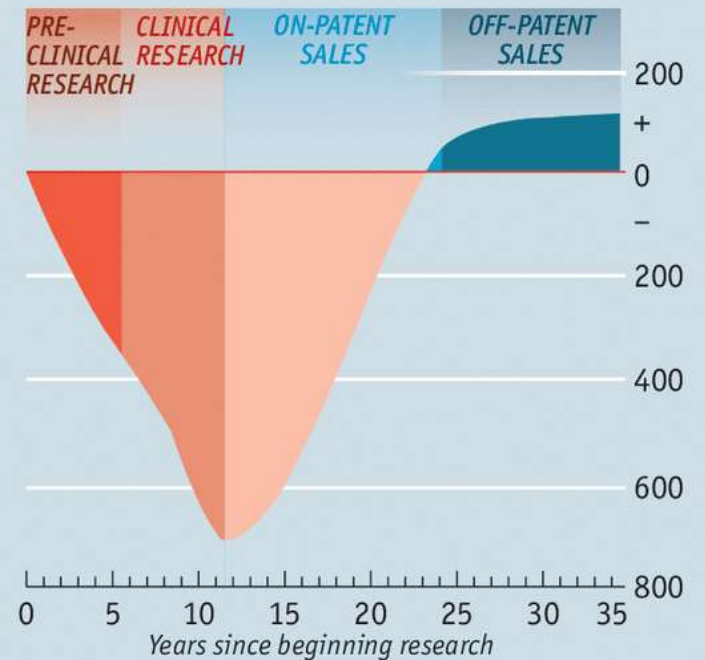
Source: Review on Antimicrobial Resistance

*Based on average of representative sample of R&D processes

Economist.com

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Cause of death in prevalent dialysis population
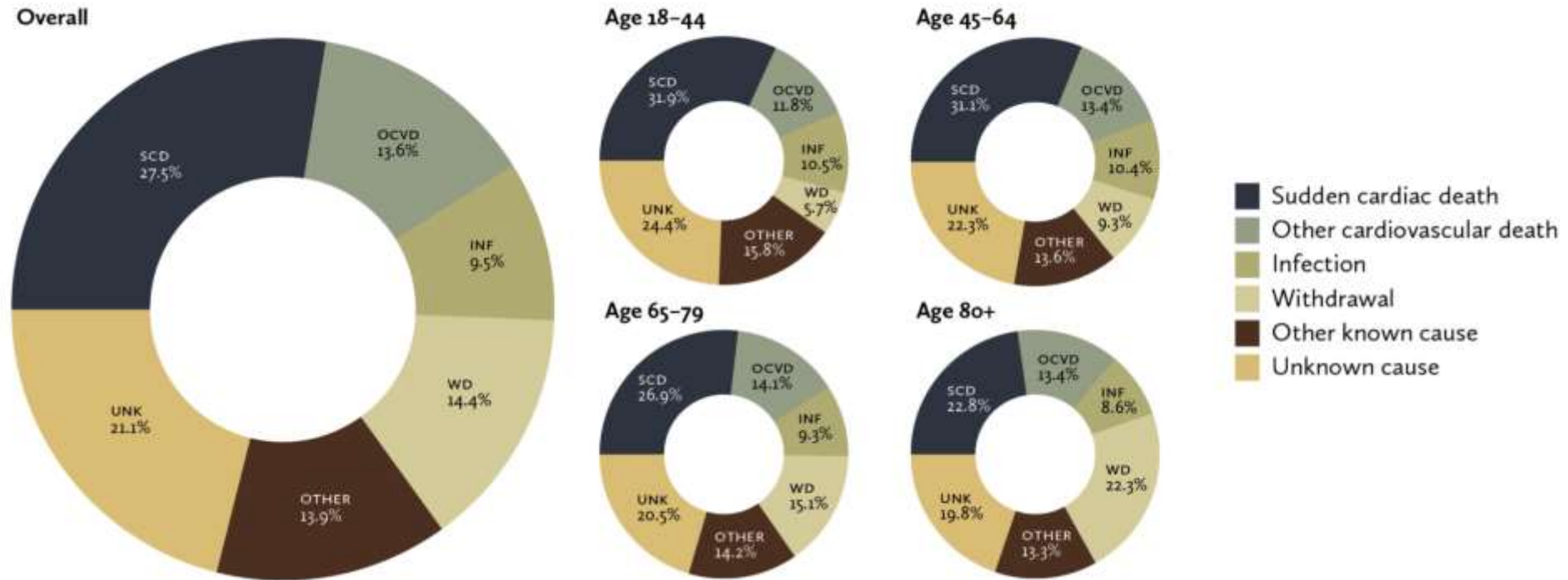
PEER Report: Dialysis Care & Outcomes in the U.S., 2014 |Hospitalization |

MDRO in dialysis population

- Disproportionately affected by MDROs compared to general population
- Mortality rates due to infections caused by MDRO are 2-5 fold higher

Mortality with VRE bacteremia vs Vancomycin sensitive enterococcus bacteremia
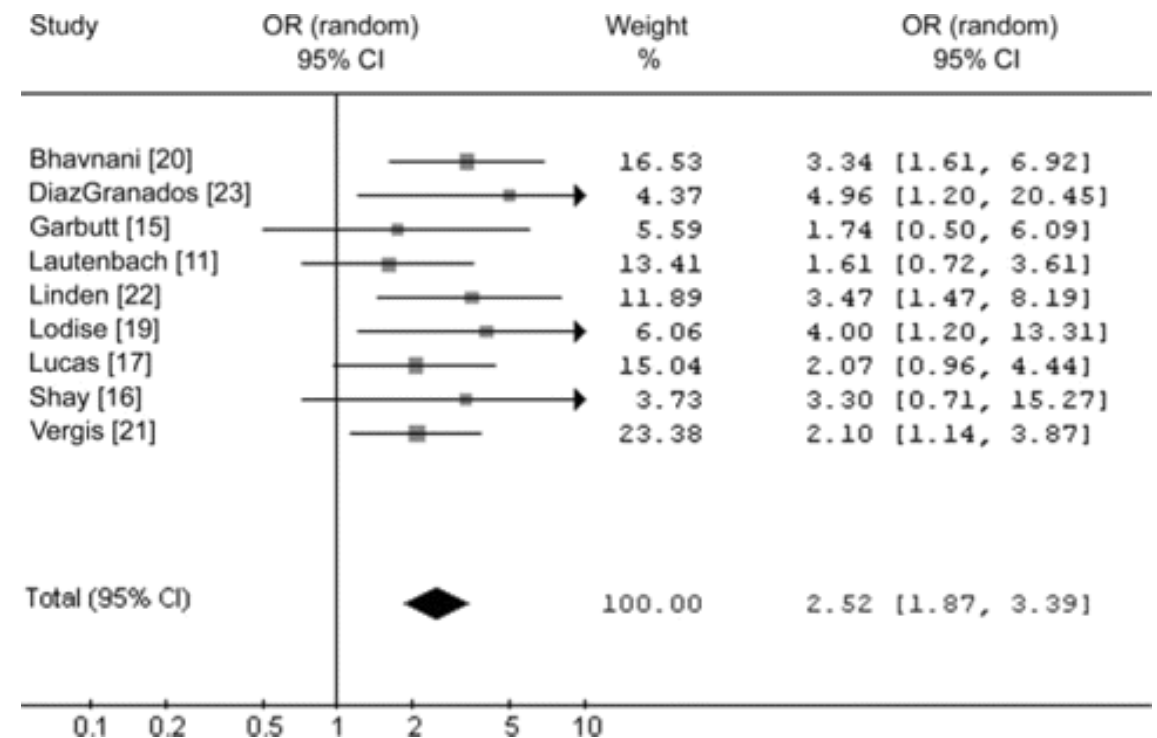
Study	OR (random) 95% CI	Weight %	OR (random) 95% CI
Bhavnani [20]		16.53	3.34 [1.61, 6.92]
DiazGranados [23]		4.37	4.96 [1.20, 20.45]
Garbutt [15]		5.59	1.74 [0.50, 6.09]
Lautenbach [11]		13.41	1.61 [0.72, 3.61]
Linden [22]		11.89	3.47 [1.47, 8.19]
Lodise [19]		6.06	4.00 [1.20, 13.31]
Lucas [17]		15.04	2.07 [0.96, 4.44]
Shay [16]		3.73	3.30 [0.71, 15.27]
Vergis [21]		23.38	2.10 [1.14, 3.87]
Total (95% CI)		100.00	2.52 [1.87, 3.39]

0.1 0.2 0.5 1 2 5 10

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Multidrug resistant organisms (MDRO)

- Methicillin-resistant Staphylococcus aureus
- Vancomycin-resistant enterococci
- Multidrug-resistant gram negative bacteria
    - Extended-spectrum beta-lactamase producing gram-negative bacteria (ESBL)
        - Resistant to cephalosporins and most other antimicrobials
    - Carbapenemase producing gram-negative bacteria
        - Only suspectable to Colistins

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Multidrug resistant organisms (MDRO)

	MRSA	VRE	MDR – Gram negative
Infective rates – CRBSI Dialysis Surveillance Report: National Healthcare Safety Network (NHSN)—Data Summary for 2006	20% were due to Staph aureus, out of which 51% were MRSA	8.5% were due to Enterococcus species, out of which 22.5% were VRE	25% of BSI are due to gram-negative bacteria 9.7% ESBL isolates and 3.4% CPCRE isolates
Colonization rates	1.4 to 27% David P Calfee Seminars in Dialysis. Vol 26, No 4 2103, 447-456	2.8 -10.8%	Fewer studies One study showed rates of 16%
Colonization to infection	17-35% of MRSA colonized dialysis patients develop subsequent MRSA infection within one year of detection of carriage Lu P et al Nephrol Dial Transplant 23:1659-1665, 2008	23% of VRE-colonized dialysis patients, compared to only 1% of noncolonized dialysis patients, went on to develop VRE infection	No studies

Risk factors for exposure to MDROs

- Hospital exposure

- Dialysis facility exposure
  - Direct patient to patient transmission
  - Environmental transmission
    - Following a 4hr outpatient HD session of fecally-continent VRE positive patients - VRE was detected on dialysis chairs in 54%, on HCW gown in 25% and BP cuff on 8% of the dialysis sessions (Grabsch et al 2006)
  - Health care worker to patient transmission
    - HCW nasal MRSA carriage 2.8-11.6%

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Prevalence and acquisition of MRSA, VRE and MDR-GNB in an out-patient hemodialysis facility
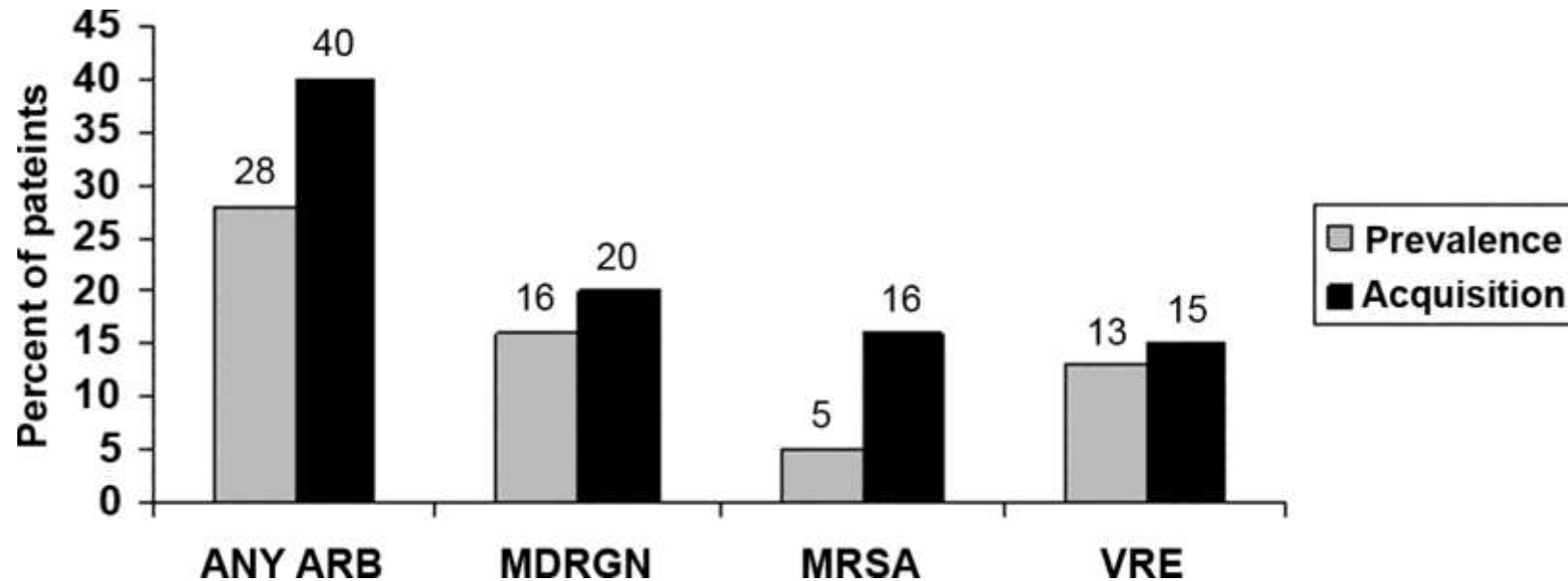
Aurora Pop-Vicas et al. CJASN 2008;3:752-758

Spread of MDRO from dialysis patients

- USRDS data 2009
  - 2 admissions per year
  - Average length of stay of 12 days
  - 36% has readmission with in 30days
- Higher prevalence of MDRO colonization in the family members of dialysis patients

Adjusted hospital admission rates & days, by modality

Admissions per patient year

Hemodialysis
Peritoneal dialysis
All dialysis
Transplant

Hospital days per patient year

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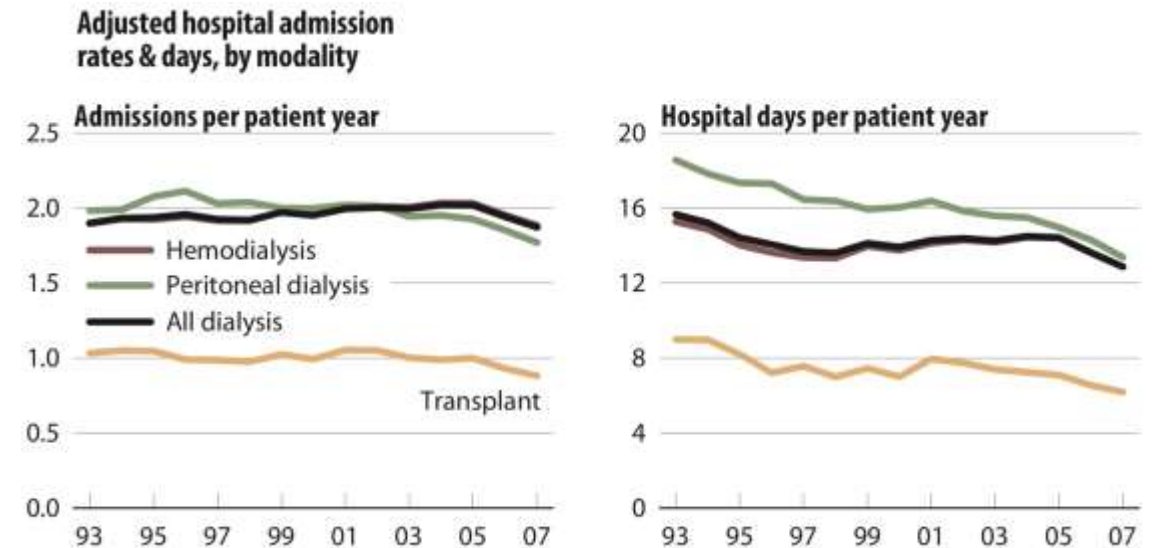
Risk factors for colonization and infection

- Antibiotic exposure
- Type of vascular access

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Percentage of antibiotics prescribed according to antibiotic classes for adult ambulatory visits, 2007–09

- 10% of the visits resulted in antibiotic prescription (101million)

- 61% broad spectrum antibiotics

- 40million for presumed respiratory infections (2/3 no indication for antibiotics)

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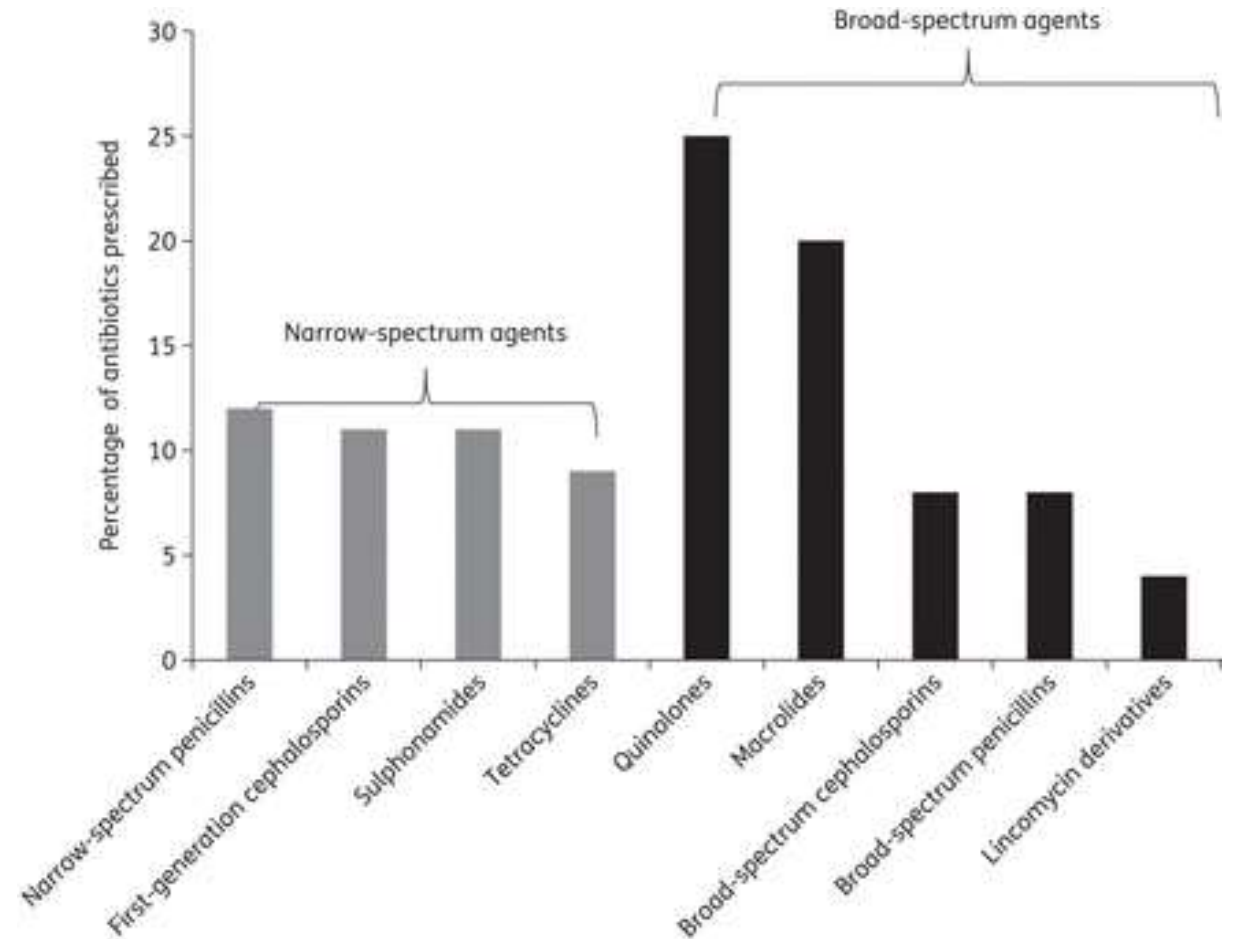
Vancomycin Use Among Chronic Haemodialysis Patients

Appropriate	
Empiric therapy for a febrile patient on haemodialysis pending culture/susceptibility data	73(45)
Treatment of β-lactam–resistant organisms	51(31
β-Lactam allergy	5(3)
Surgical prophylaxis in patient with a prosthesis	2(1)
Total	131(80)
Inappropriate	
Continued therapy despite negative cultures for β-lactam–resistant organisms	23(14)
Routine surgical prophylaxis	4(2)
Single positive blood culture for coagulase-negative staphylococci	1(1)
Prophylaxis for indwelling or peripheral intravascular catheters	5(3)
Total	33(20)

Green K, D'Agata E, Am J Kidney Dis 2000

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Type of vascular access

Patients dialyzing with a tunneled or non- tunneled dialysis catheter have a 12-57 times higher rates of vascular access infections, respectively, than those who dialyze with AVF

Access-associated bloodstream infection		
Fistula	26	0.2
Graft	31	0.4
Perm. central line	272	3.1
Temp. central line	21	17.8

Klevens RM et al NHSN data summary for 2006. Semin Dial 21: :24-28, 2008

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MDRO prevention and control

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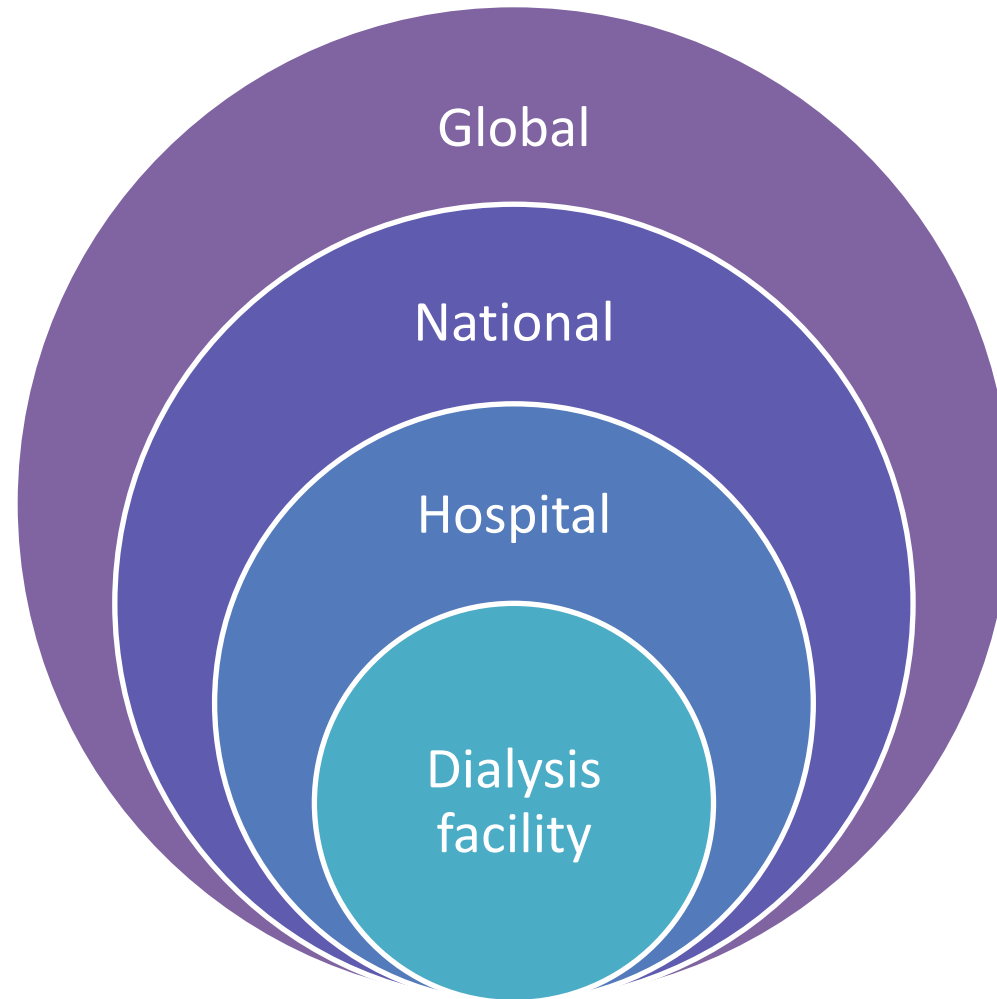
HD unit - Horizontal Interventions

BEFORE touching a patient ▸ BEFORE clean / aseptic procedure ▸ AFTER body fluid exposure ▸ AFTER touching a patient ▸ AFTER touching a patient's surroundings

- "Horizontal" intervention
  - Infection control practices for all patients due to all pathogens
    - Hand hygiene
    - Wear gloves during all patient contact
    - Clean and disinfect environmental surfaces around the dialysis machine
    - Aseptic technique during care of vascular access devices
    - Preparation of medications away from the patient's machine and only one patient's medications should be administered at a time
  - Current guidelines doesn't mandate segregation of patients in a dialysis facility, as per their carrier status

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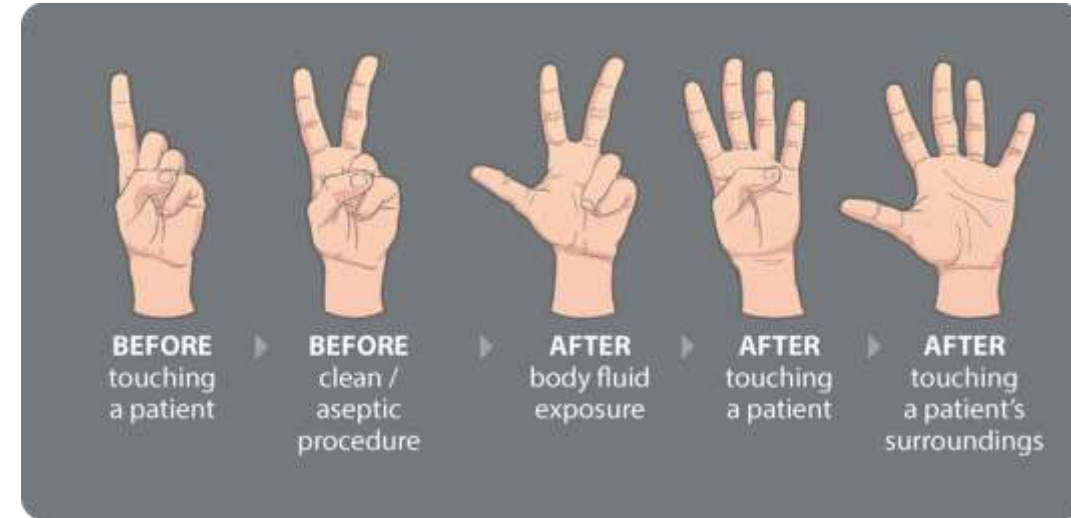
Checklist: Hemodialysis catheter connection

- [ ] Wear mask (if required)
- [ ] Perform hand hygiene
- [ ] Put on new, clean gloves
- [ ] Clamp the catheter and remove caps
- [ ] Scrub catheter hub with antiseptic
- [ ] Allow hub antiseptic to dry
- [ ] Connect catheter to blood lines aseptically
- [ ] Remove gloves
- [ ] Perform hand hygiene

Checklist: Hemodialysis catheter exit site care

- [ ] Wear mask (if required) and remove dressing
- [ ] Perform hand hygiene
- [ ] Put on new, clean gloves
- [ ] Apply skin antiseptic
- [ ] Allow skin antiseptic to dry
- [ ] Do not contact exit site (after antisepsis)
- [ ] Apply antimicrobial ointment*
- [ ] Apply dressing aseptically
- [ ] Remove gloves
- [ ] Perform hand hygiene

* Use an ointment that does not interact with catheter material

Checklist: Dialysis Station Routine Disinfection

This list can be used if there is no visible soil on surfaces at the dialysis station. If visible blood or other soil is present, surfaces must be cleaned prior to disinfection. The proper steps for cleaning and disinfecting surfaces that have visible soil on them are not described herein. Additional or different steps might be warranted in an outbreak situation. Consider gathering necessary supplies[1] prior to Part A.

Part A: Before Beginning Routine Disinfection of the Dialysis Station

- [ ] Disconnect and takedown used blood tubing and dialyzer from the dialysis machine.
- [ ] Discard tubing and dialyzers in a leak-proof container[2].
- [ ] Check that there is no visible soil or blood on surfaces.
- [ ] Ensure that the priming bucket has been emptied[3].
- [ ] Ensure that the patient has left the dialysis station[4].
- [ ] Discard all single-use supplies. Move any reusable supplies to an area where they will be cleaned and disinfected before being stored or returned to a dialysis station[5].
- [ ] Remove gloves and perform hand hygiene.

PART B: Routine Disinfection of the Dialysis Station – AFTER patient has left station

- [ ] Wear clean gloves.
- [ ] Apply disinfectant[6] to all surfaces[7] in the dialysis station using a wiping motion (with friction).
- [ ] Ensure surfaces are visibly wet with disinfectant. Allow surfaces to air-dry[8].
- [ ] Disinfect all surfaces of the emptied priming bucket[3]. Allow the bucket to air-dry before reconnection or reuse.
- [ ] Keep used or potentially contaminated items away from the disinfected surfaces.
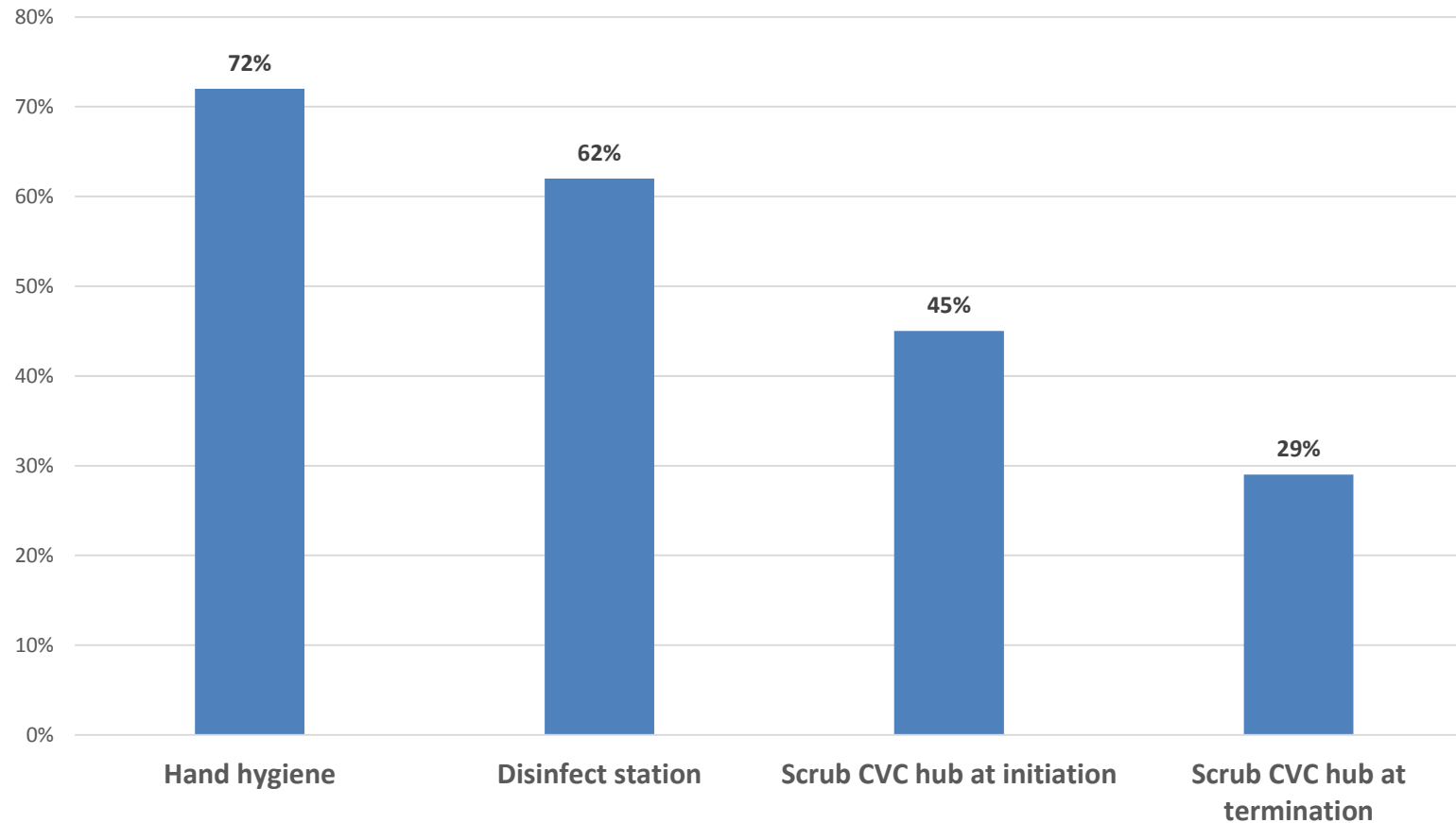- [ ] Remove gloves and perform hand hygiene.

Do not bring patient or clean supplies to station until these steps have been completed.

https://www.cdc.gov/dialysis/prevention-tools/audit-tools.html

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Infection control practices in 34 US hemodialysis facilities

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Vascular access

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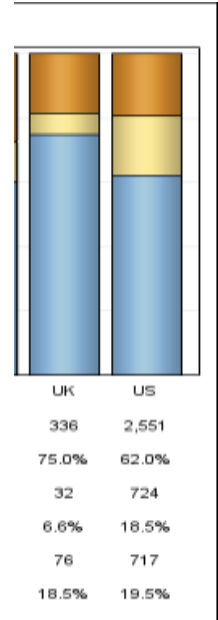
HD Unit - Vertical interventions

- "Vertical" intervention – focus on prevention of transmission of one or more specific pathogens

- MRSA decolonization
  - Old studies included MSSA rather than MRSA
  - Topical as well as systemic therapy
  - Reduction in nasal carriage and invasive staphylococcal infections
  - Routine use of Mupirocin and chlorhexidine resulted in development of resistant strains
 - Unresolved issue

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Vaccination in Hemodialysis patients
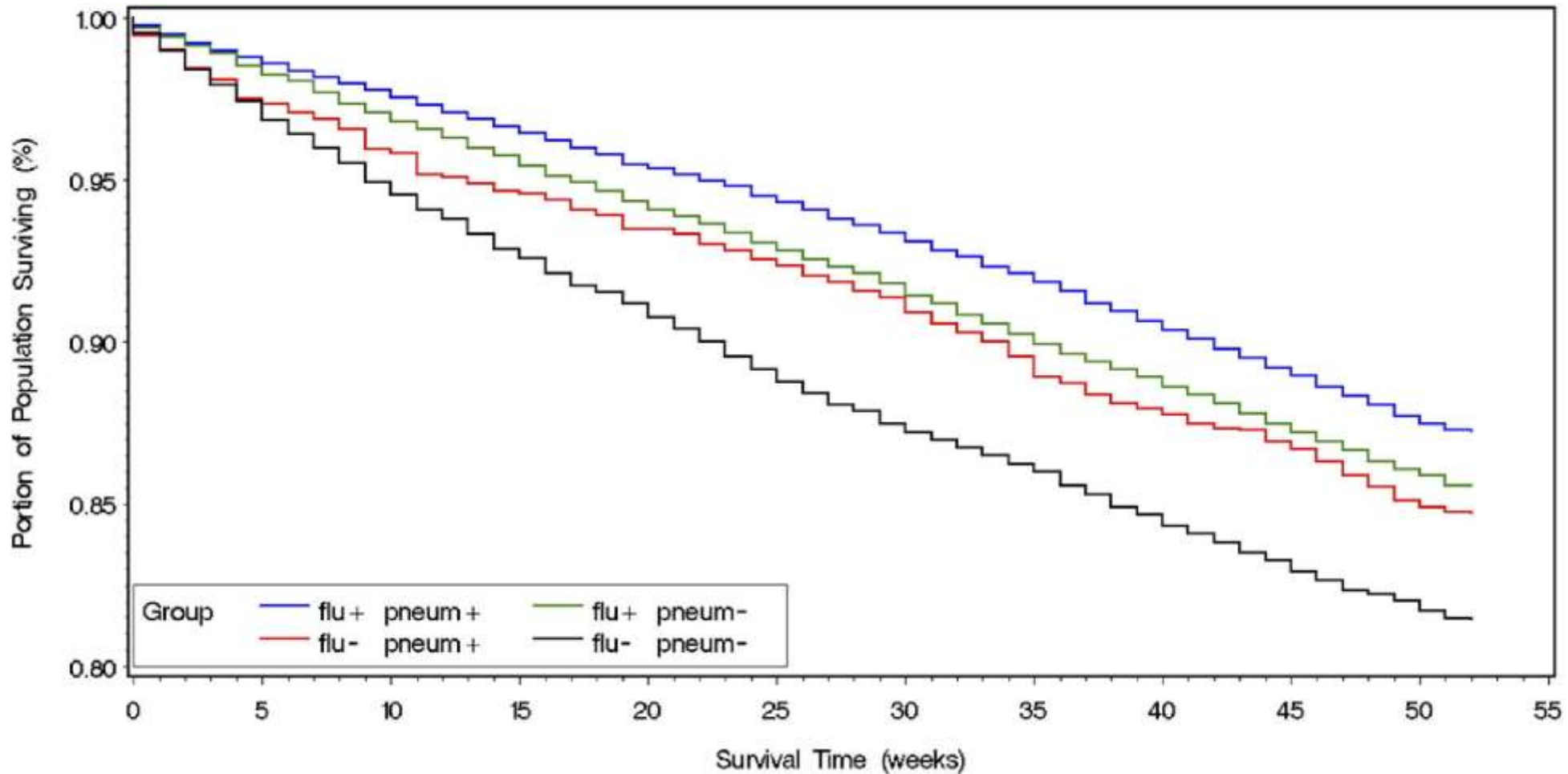
Christopher Bond et al, AJKD, Volume 60, Issue 6, 2012, Pages 959-965

Further interventions in dialysis unit

- Education to the staff and patients

- Root cause analysis of all the MDRO bacteremias

- Quality initiatives in the renal unit to reduce infections
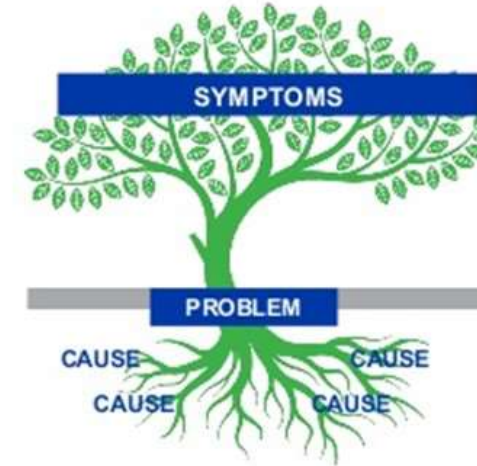
QI project to reduce dialysis catheter related BSI – CGH experience

List of PDSAs

PDSA #1 (March 2016) : Educate patients & ward nurses during handing over

PDSA #2 (March 2016): Conducted training for NC on dressing change

PDSA #3 (April 2016): 100% dressing change for newly inserted catheter

PDSA #4 (Jun 2016): Quarterly staff competency audit in Renal and Radiography unit

PDSA #5 (Jun 2016): Pilot wards to change dressing at exit site if required

PDSA #6 (Nov 2016): Ordering of Mupirocin nasal cream and Chlorhexidine body wash

PDSA #7 (Dec 2016): Ask 5 Take 5 conducted in Renal & Radiology for doctors and nurses on catheter insertion process

PDSA #8 (Jan2017): Use of Chlorhexidine wipes to reduce bacteremia load on patients

PDSA #9 (Jan2017): Hospital-wide wet dressing change in wards

PDSA #10 (Jul 2017): Renal patients to wear mask when catheter is being manipulated

PDSA #11 (Aug 2017): Use CHG dressing for all renal patients
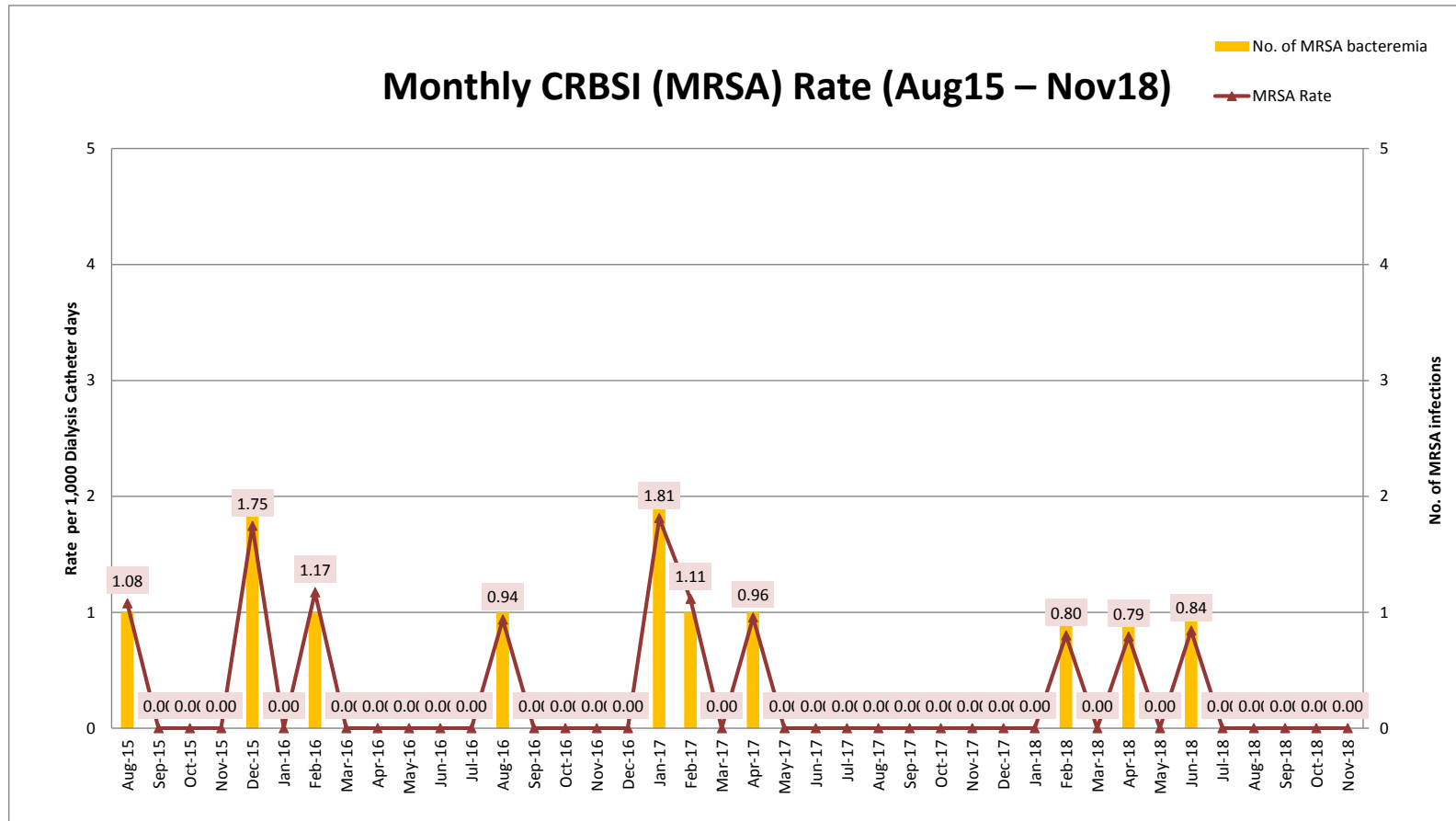
PDSA #12 (Nov 2017): Standardize guidelines on prevention of Intravascular device related infection
Standardize guidelines for guidewire exchange of temporary central venous catheters

Plan-Do-Study-Act Cycle

Achieved CRBSI (MRSA) target rate since Jul 17

**Baseline: 0.56 per 1,000 catheter days | Target: 0.28 per 1,000 catheter days |
Current: 0.14 per 1,000 catheter days (Jul 17 to Nov 18)**

Monthly CRBSI (MRSA) Rate (Aug15 – Nov18)

Hospital – Infection control practices

- **Vertical approaches**
  - Active surveillance testing to identify asymptomatic carriers
  - Contact precautions for patients colonized or infected with specific organisms
  - ?Decolonization of patients colonized or infected with specific organisms
- **Horizontal approaches**
  - Standard precautions (eg. hand hygiene)
  - Universal use of gloves or gloves and gowns
  - Environmental cleaning and disinfection
  - Antimicrobial stewardship

Hospital: Antibiotic stewardship program

Core elements of antibiotic stewardship. Global Alliance for Infections in Surgery

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FIGURE 5-1: Six strategies needed in national antibiotic policies

International

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