Thorny topics related to CRE control

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  - Illinois Department of Public Health

Thorny questions

1. Where does CRE live on a patient?
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Bad bug, no drugs

BLOOD CULTURE (PERIPHERAL) (Abnormal):
PROCEDURE: BLOOD CULTURE (PERIPHERAL)
SOURCE: BLOOD
COLLECTED:

---------- FINAL REPORT ----------

FINAL REPORT
GROWTH OF GRAM NEGATIVE RODS
FINAL IDENTIFICATION: KLEBSIELLA PNEUMONIAE
This isolate demonstrates carbapenemase production.
Carbapenems, cephalosporins, and penicillins are unlikely to be effective in treatment of serious infections. Contact precautions required.

---------- SUSCEPTIBILITY TESTING ----------

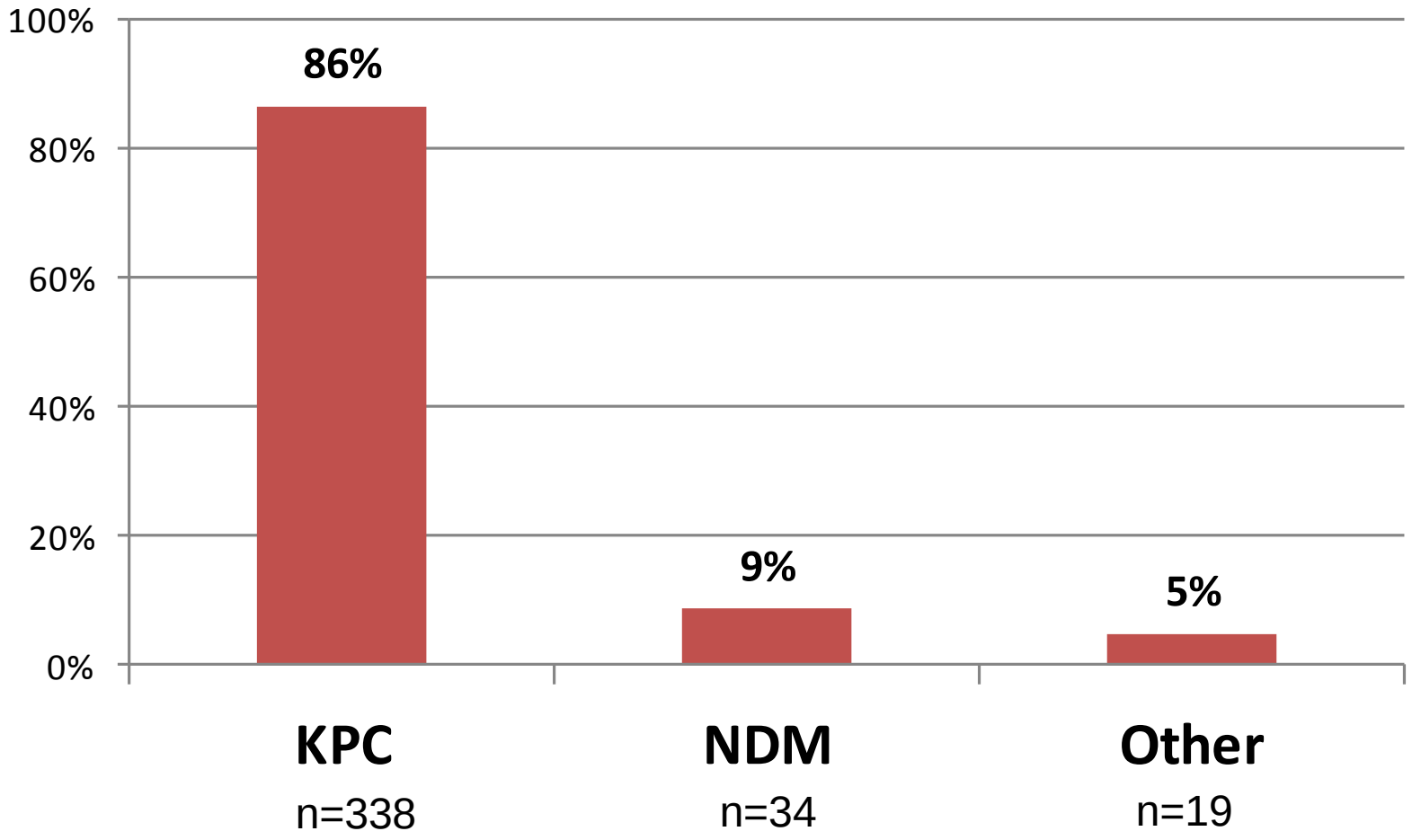
K PNEUMO

	MIC mcg/ml	MIC INTERP	MIC mcg/ml	ET INTERP
TRIMETH/SULFA	>2/38	RESISTNT		
CEFAZOLIN	>16	RESISTNT		
TIGECYCLINE			1.00	SUSCEPT
LEVOFLOXACIN	>4	RESISTNT		
CEFOXITIN	16	INTERMED		
PIP/TAZOBACTAM	>64	RESISTNT		
TICARCIL/K CLAV	>64	RESISTNT		
CEFTRIAXONE	>32	RESISTNT		
GENTAMICIN	<=4	SUSCEPT		
TOBRAMYCIN	>8	RESISTNT		
AMIKACIN	16	SUSCEPT		
IMIPENEM	8	RESISTNT		
MEROPENEM	>8	RESISTNT		
CEFEPIME	16	RESISTNT		
COLISTIN			.38	SUSCEPT
A ERTAPENEM	>4	RESISTNT		

Illinois CRE trend (unique pts)

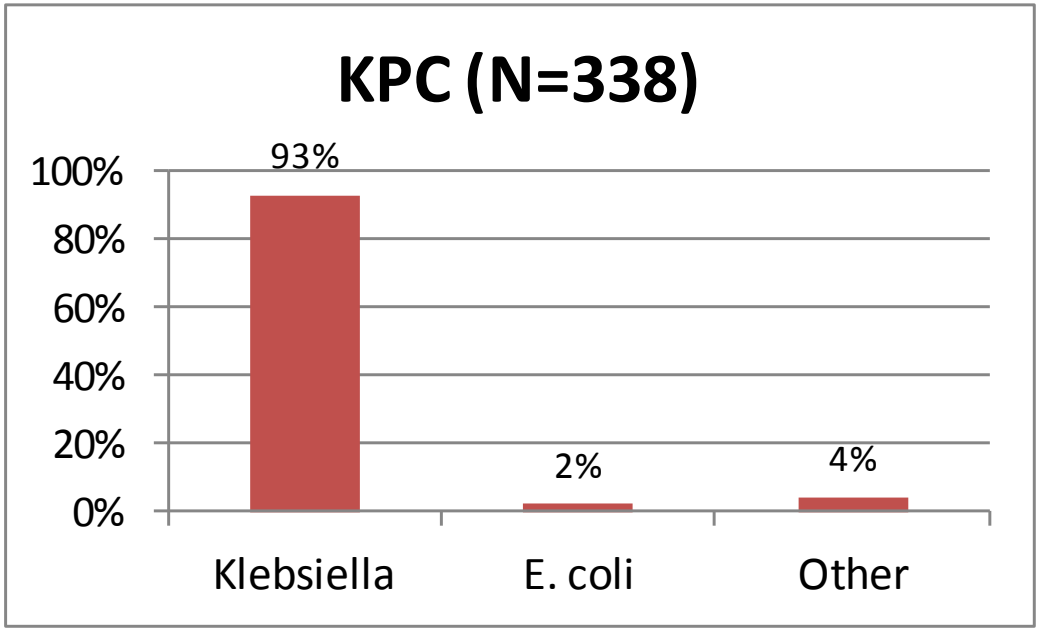
618 total patients reported; **471** pts since Nov. 2013 (average 2 to 3 patients reported per day)

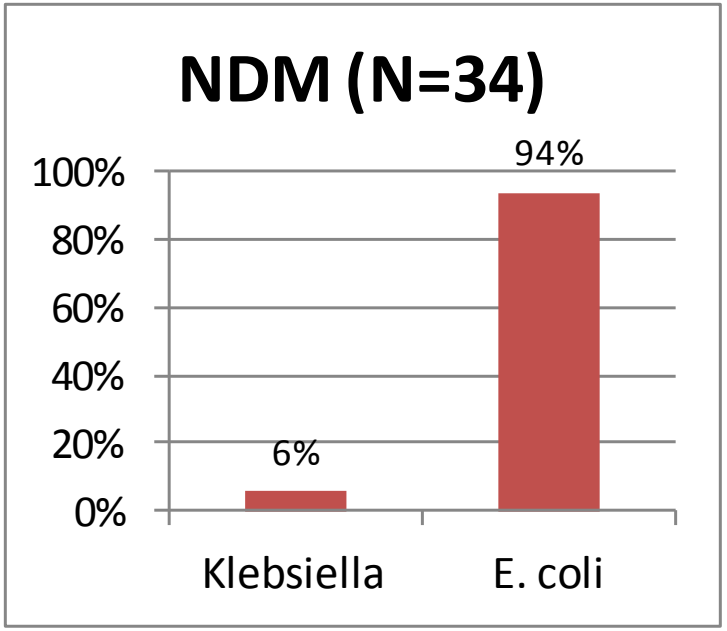
Resistance mechanisms reported to XDRO registry



Data through May 5, 2014; from pts with reported mechanism data, 63% of total

Organism distribution





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Specimen sources of reported CRE

	%
Urine	49
Wound	14
Sputum	13
Rectal (screening)	12
Blood	7
Body fluid, tissue, other	5

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Skin colonization common

TABLE 2. Sensitivity of Culture of Different Anatomic Sites for *Klebsiella pneumoniae* Carbapenemase–Producing Enterobacteriaceae

	No. of positive cultures ($N = 24$)	Sensitivity, % (95% CI)
Skin sites		
Inguinal	19	79 (58–93)
Axillary	18	75 (53–90)
Upper back	6	25 (10–47)
Antecubital fossae	6	25 (10–47)
Nonskin sites		
Rectal[a]	21	88 (68–97)
Urine ($N = 19$)[b]	10	53 (29–76)
Oropharyngeal/tracheal secretions	10	42 (22–63)
Combined sites		
Rectal and inguinal	24	100 (86–100)
Rectal and axillary	23	96 (79–100)
Axillary and inguinal	22	92 (73–99)

NOTE. CI, confidence interval.

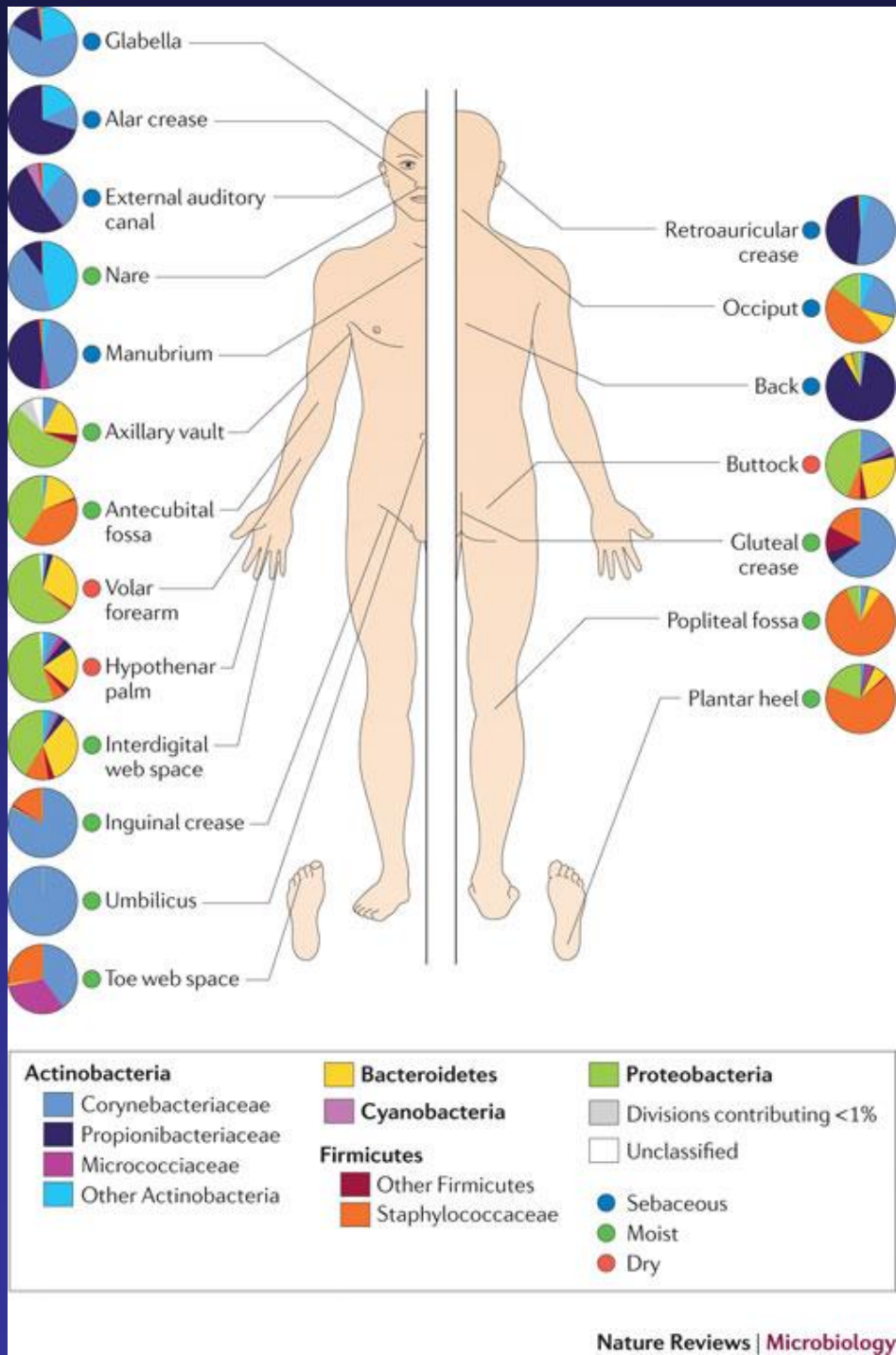
[a] Three patients had negative rectal swab cultures but positive cultures of inguinal skin.

[b] Five patients were anuric, so urine was not collected for culture.

Thurlow et al. ICHE 2013. 34(1): 56-61

The skin microbiome varies by site

- Variation due to differences in skin characteristics, type of sweat gland
- In chronically ill patients, skin microbiome shifts towards more gram negatives



Grice and Segre. "The skin microbiome." *Nature Reviews Microbiology* 2011; 9(4) 244-253.

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CHG minimum inhibitory concentrations

Organism	MIC (µg/mL)
Staphylococcus aureus	≤ 4
Coagulase-negative Staphylococcus	≤ 4
Enterococcus spp.	≤ 4
Klebsiella pneumoniae (ST258)	32 to 256

CRE skin colonization common. Daily CHG bathing can help.

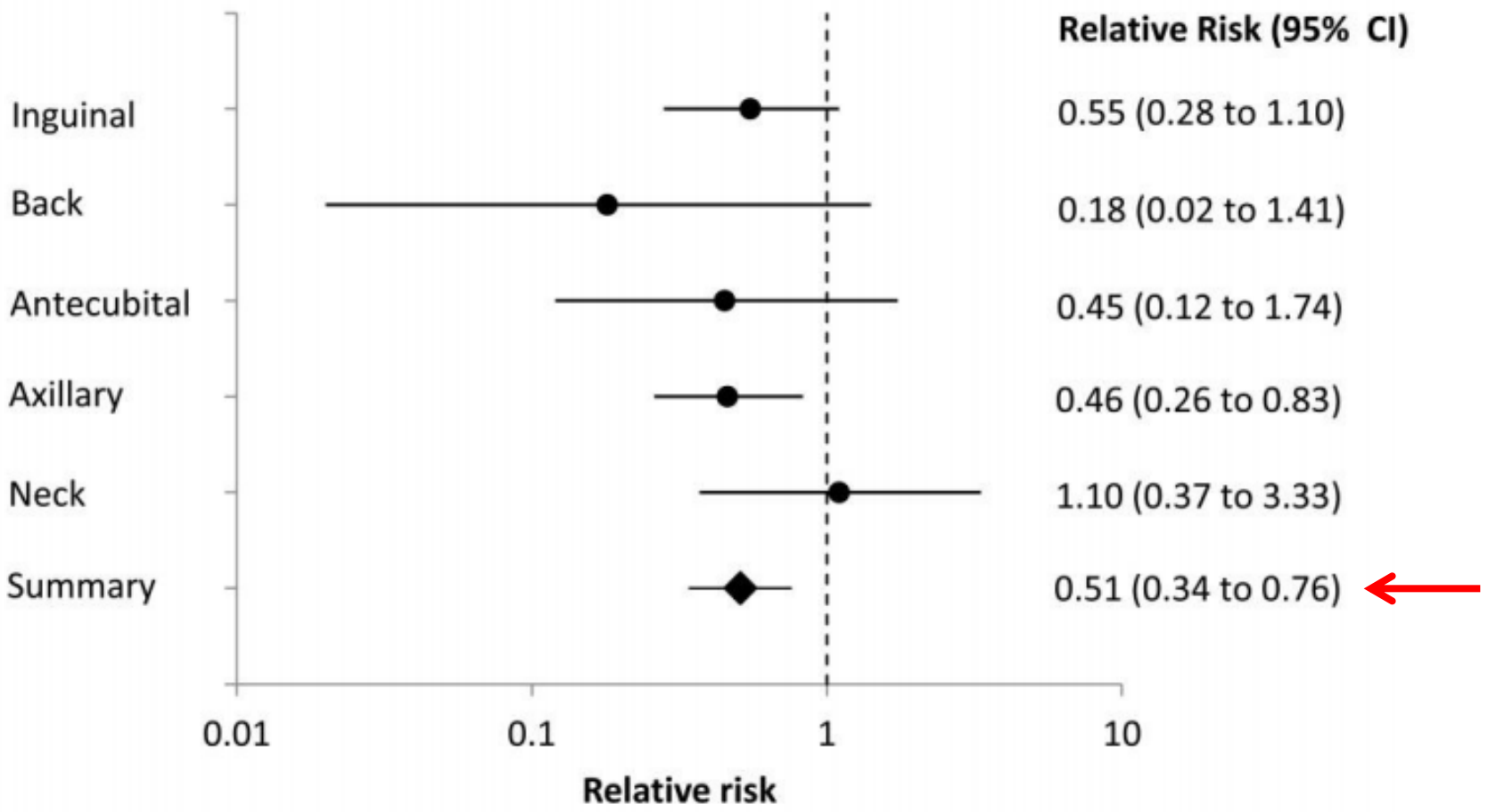
TABLE 1. *Klebsiella pneumoniae* Carbapenemase–Producing Enterobacteriaceae (KPC) Culture Positivity and Chlorhexidine Gluconate (CHG) Concentrations, by Skin Site

Variable	Inguinal	Back	Antecubital	Axilla	Neck	*P*
KPC positive, %						
Before bath	37	8	10	39	8	<.001
After bath	15	5	5	11	15	.16
CHG concentration, median μg/mL						
Before bath	312.5	19.5	58.6	156.3	14.7	<.001
After bath	1,250.0	234.4	312.5	625.0	78.1	<.001
CHG concentration ≥128 μg/mL, %						
Before bath	81	23	27	61	6	<.001
After bath	97	66	77	84	47	<.001

NOTE. *P* value tests the null hypothesis that all body sites have the same proportion or value.

Lin et al. ICHE 2014; 35(4): 440-442.

CHG bathing reduces CRE skin colonization by about 50%



Relative risk of recovering KPC when comparing higher CHG skin concentration (≥128 µg/mL) versus lower concentration. Relative risk <1 is protective.

Lin et al. ICHE 2014; 35(4): 440-442.

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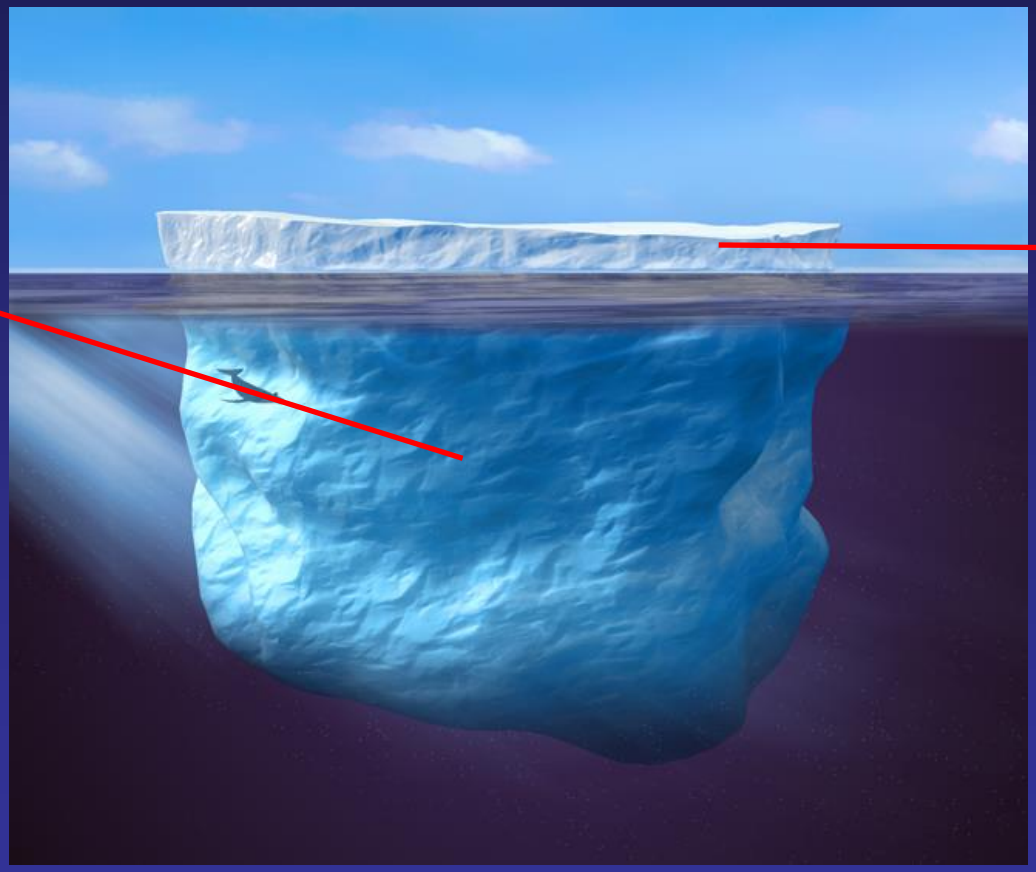
CRE resistance iceberg

Most CRE patients are asymptomatic carriers (“colonized”)



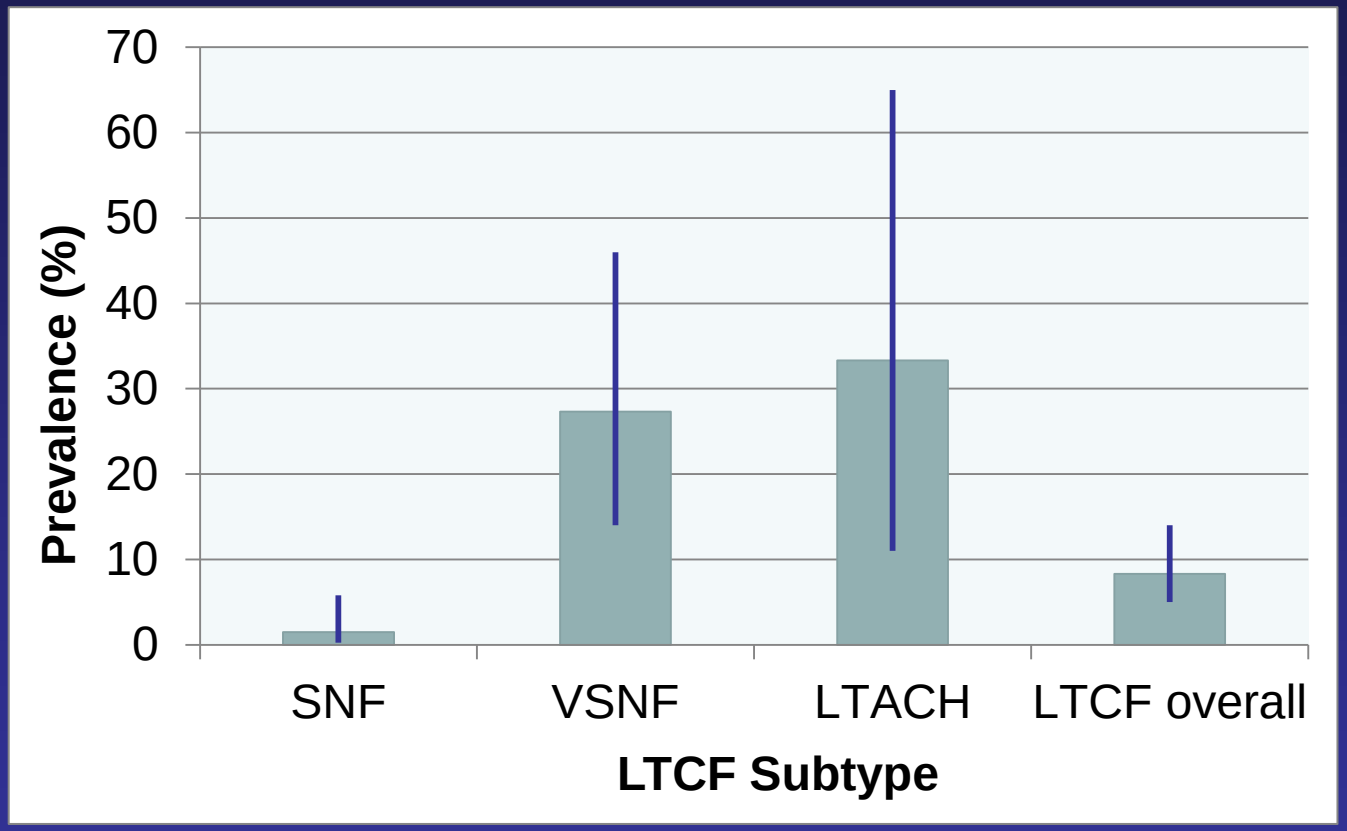
Some patients have positive clinical cultures (~30% in 1 small study)

Wiener-Well et al. *Journal of Hospital Infection* 2010; 74(4): 344-349.

Active surveillance

- Data are mixed for MRSA and VRE
- In 2 randomized controlled trials:
  - STAR*ICU trial (NEJM 2011): no benefit for MRSA and VRE
  - REDUCE MRSA trial (NEJM 2013): MRSA active surveillance out-performed by universal decolonization (CHG + mupirocin)
- For CRE, no trials, just observational studies
  - Active surveillance included in most outbreak control bundles

KPC admission prevalence differed by type of long term care facility



Patients from SNFs with ventilator care (VSNFs) had KPC prevalence rates comparable to LTACH patients

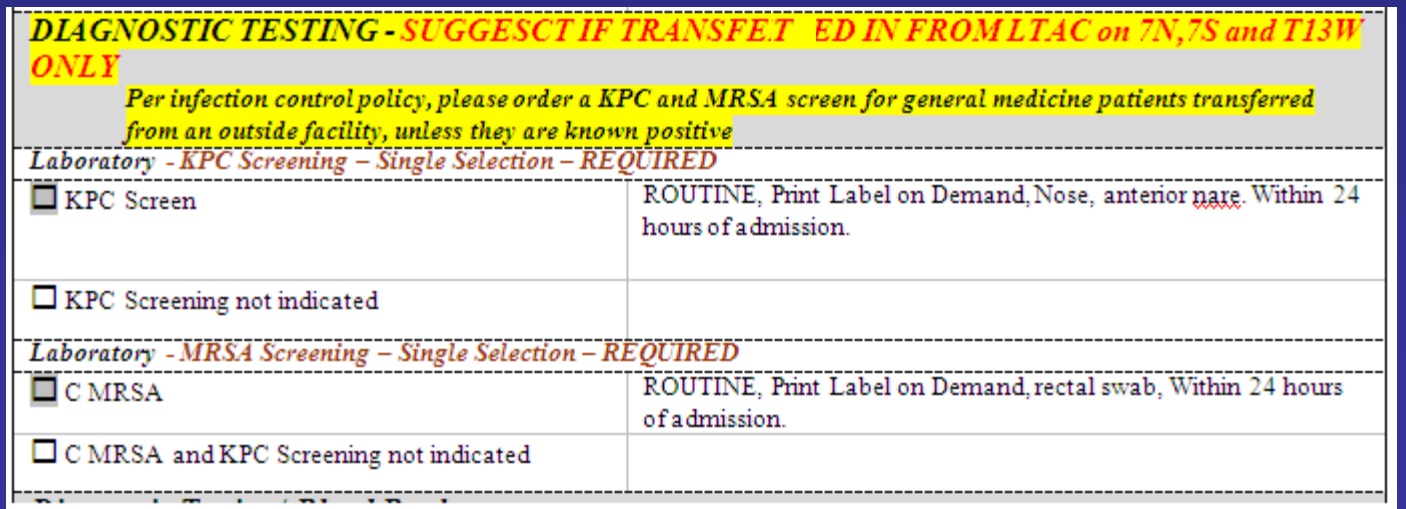
Prabaker K et al. Infect Control Hosp Epidemiol 2012, 33(12)

CRE active surveillance

- Considered a “supplemental measure” in the CDC CRE Toolkit
- Depends on local CRE epidemiology
- In Chicagoland region, consider CRE admission screening if you admit high-risk patients (to/from LTACH, “vSNFs”)

Active surveillance example

- At Rush, any adult patient transferred from an outside facility (ACH, LTACH, SNF) to our ICUs or medical wards undergoes CRE screening
  - We use a universal billing code ('Point of origin') to identify transfer patients electronically
  - For transfer patients, the admission form will automatically display "Smartset" for ordering provider



DIAGNOSTIC TESTING - SUGGESCT IF TRANSFE.T ED IN FROM LTAC on 7N,7S and T13W ONLY ***Per infection control policy, please order a KPC and MRSA screen for general medicine patients transferred from an outside facility, unless they are known positive***	
Laboratory - KPC Screening – Single Selection – REQUIRED	
☐ KPC Screen	ROUTINE, Print Label on Demand, Nose, anterior nare. Within 24 hours of admission.
☐ KPC Screening not indicated	
Laboratory - MRSA Screening – Single Selection – REQUIRED	
☐ C MRSA	ROUTINE, Print Label on Demand, rectal swab, Within 24 hours of admission.
☐ C MRSA and KPC Screening not indicated	

Active surveillance: which body site?

- Rectal culture (can substitute stool)
- Supplemental sites (less common)
  - Peri-rectal
  - Inguinal/axillary sites
  - Urine (if readily available)

CRE active surveillance, lab issues

- What is the capability of your lab?
  1) CDC has published a screening method (See Toolkit; but it is time intensive)
  2) Culture-based method (modified Hodge test)
  3) Molecular (PCR) method
  4) Carba NP method

- Who pays?

Surveillance of epidemiologically linked patients (aka “Ring surveillance”)

- This is standard part of CRE Toolkit
- What is the threshold for screening?
  - Every CRE patient?
  - Having one CRE patient who is not in contact precautions?
- Benefit uncertain
  - Northwestern’s published experience: 2011-2013, 14 ring surveillance efforts performed, involving 174 pts and identifying 3 asymptomatic CRE carriers (but no transmissions found)

» Fitpatrick et al. ICHE 2014; 35(4)

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Duration of CRE carriage study

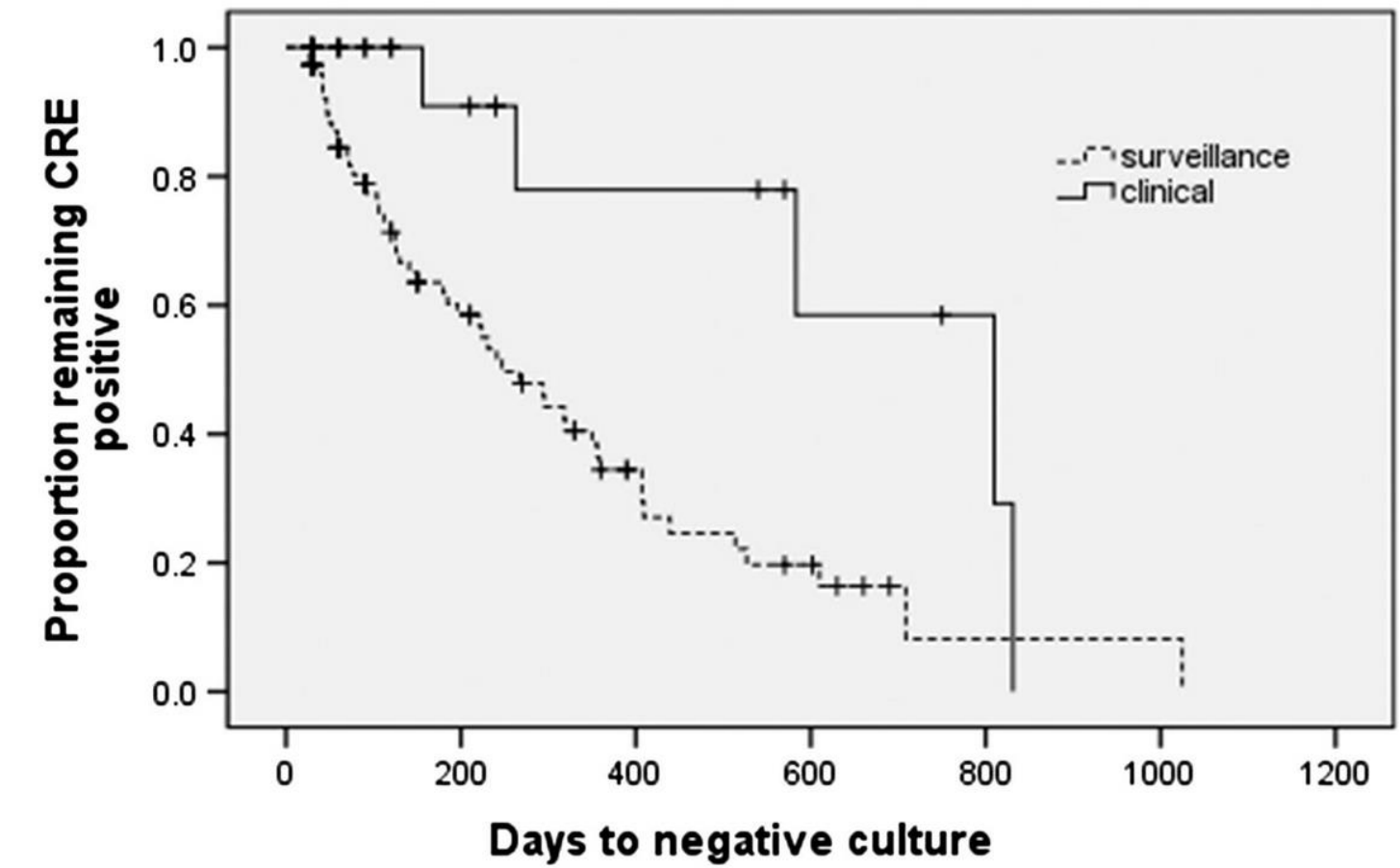
- 137 patients with CRE-positive culture
  - Mean time to CRE negativity was 387 days

Time lag from first CRE+ culture	CRE positive (%)
3 months	78
6 months	65
1 year	39

  - Risk factors with prolonged CRE carriage
    - Repeat hospitalization
    - CRE identified by clinical culture (versus surveillance culture)

Zimmerman et al. Am J Infect Control 2013; 41(3):190-4

CRE carriage is prolonged



Number at risk						
clinical	18	11	7	4	2	2
surveillance	79	64	27	13	4	1

Zimmerman et al. Am J Infect Control 2013; 41(3):190-4

Probably need more than 1 negative rectal culture to clear a patient

- 125 CRE-positive pts followed for 6 months with monthly rectal cultures

Number of negative screens (performed monthly)	True negative (%)
1	67
2	85
3	90

- Overall, 52% of patients cleared their CRE
  - Patients who had a remote CRE positive result, were high functioning, free of medical devices (eg, catheters), and discharged to home (vs long term care) were more likely to lose CRE carriage

Feldman et al. Clin Microbiol Infect 2013; 19(4):E190-6

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CRE can survive on dry surfaces

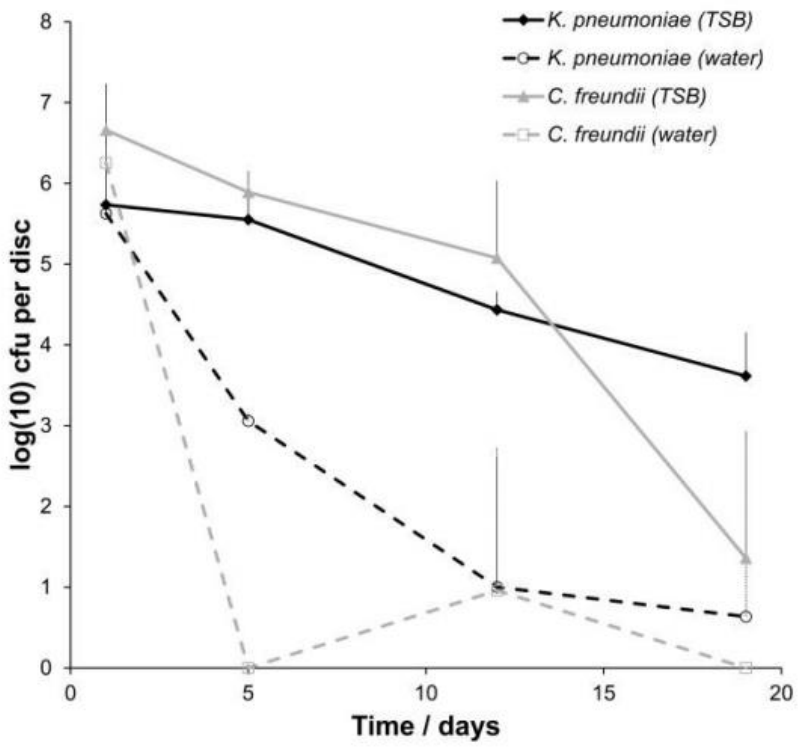

FIGURE 1. Survival of carbapenem-resistant Enterobacteriaceae dried onto metal discs. Each point represents a mean of 3 samples; error bars represent +1 standard deviation from the mean. cfu, colony-forming units.

- Klebsiella can persist on experimental surfaces for 20 days

Havill et al. ICHE 2014; 35(4):445-7

However, CRE are not commonly found in the hospital environment

- In 6 LTACH environments (with overall CRE prevalence ranging from 10 – 53%):
  - Only 2 of 371 environmental sites were positive for CRE (0.5%: 1 bedrail, 1 call button)
  - 15% of the sites grew other carbapenem-resistant gram negative bacteria (majority were *Acinetobacter baumannii*)

CRE and environment

- CDC CRE Toolkit: enhanced environmental disinfection is not a core intervention
- Klebsiella less viable on surfaces compared to other gram negatives (Acinetobacter)
- If enhanced cleaning performed, focus on high touch surfaces near patient

Take home points

1. CRE commonly found on skin (axillae, inguinal) in addition to GI tract
2. CHG can decrease CRE skin burden (preventing transmission to other pts as well as BSIs)
3. Targeted active surveillance can be considered for high risk patients (LTACH, vSNF pts)
4. Contact precautions – CRE carriage is prolonged. Unclear if/when to stop precautions.
5. CRE in the environment: probably not important. My opinion: for outbreaks, focus on reducing CRE skin burden (CHG bathing), active surveillance (on admission and periodically), and consider cohorting patients.