Who's to Blame? Environment versus the Patient

A review of the literature attempting to ascertain the truth about where HAIs most likely come from.

Why is this an important topic?

If it's the Environment

- More focus on cleaning and testing of the environment
- The ROI for expensive cleaning devices becomes greater
- HAIs are viewed as more preventable
- Patient's with HAIs have a lot more reasons to be angry

If it's the patient

- More focus on preventing translocation of the patient's own flora
- Different interventions (cleaning the room versus antibiotic stewardship)
- HAIs are fundamentally harder to prevent

Our Efforts and Resource Expenditure Look Different

Our sides

Arguing for the Environment:
Kim Delahanty, BSN, PHN, MBA/HCM, CIC, FAPIC

- 1.6 meters tall
- 56.5 kilograms

Arguing for the patient:
Frank Edward Myers III, BA, MA, CIC, FAPIC

- 1.85 meters tall
- 94 kilograms

It's Us, Clean the Room and Wash your Hands Dummy!

- 3 well done papers show that rooms are risk factors for getting an HAI even after adjusting in different ways for patient acuity
- Shaughnessy MK et al Evaluation of Hospital Room Assignment and Acquisition of Clostridium difficile Infection INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY MARCH 2011, VOL. 32, NO. 3
  - Shows that occupying a room previously occupied by a patient with C diff increases your hazard ratio by 2.35 (1.21-4.54 95% CI p=0.01) AFTER adjusting for patient's age, APACHE III score, exposure to proton pump inhibitors, and antibiotic use!

Study 2

- Drees M et al. Prior Environmental Contamination Increases the Risk of Acquisition of Vancomycin-Resistant Enterococci CID 2008:46 (1 March)

Risk	Hazard Ratio	95% CI	P value
Room with prior VRE pt	3.8	2.0-7.4	P<0.001
Room with VRE pt in last 2 weeks	2.7	1.4-5.3	P=0.01
Room with positive VRE cx prior to VRE aquisition	4.4	1.49-12.75	P=0.007

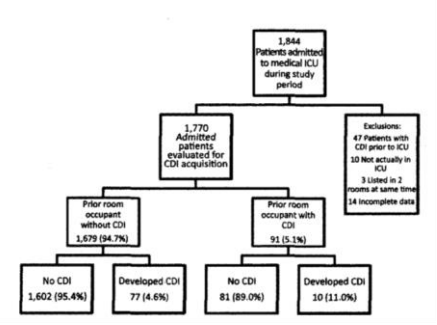
Study 3

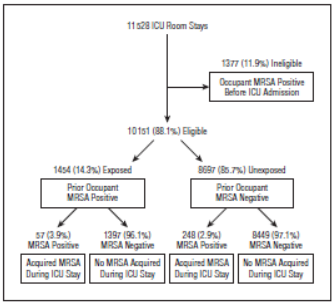
- Huang S et al. Risk of Acquiring Antibiotic-Resistant Bacteria From Prior Room Occupants ARCH INTERN MED/VOL 166, OCT 9, 2006
- "Among patients whose prior room occupant was MRSA positive, 3.9% acquired MRSA, compared with 2.9% of patients whose prior room occupant was MRSA negative (adjusted odds ratio, 1.4; *P*=.04)."

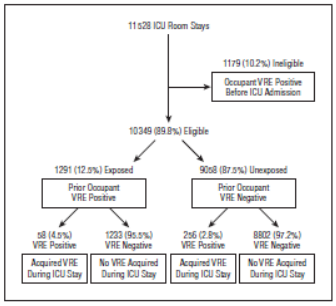
" VRE, Among patients whose prior room occupant was VRE positive, these values were 4.5% and 2.8% respectively (adjusted odds ratio, 1.4; *P*=.02)"

Do you believe everything you read?

- Taking these three studies at face value These charts are problematic.







The environment in these pro environment studies are showing it as a small % of the issue

- From Huang: “These excess risks accounted for 5.1% of all incident MRSA cases and 6.8% of all incident VRE cases, with a population attributable risk among exposed patients of less than 2% for either organism. Acquisition was significantly associated with longer post–intensive care unit length of stay.”

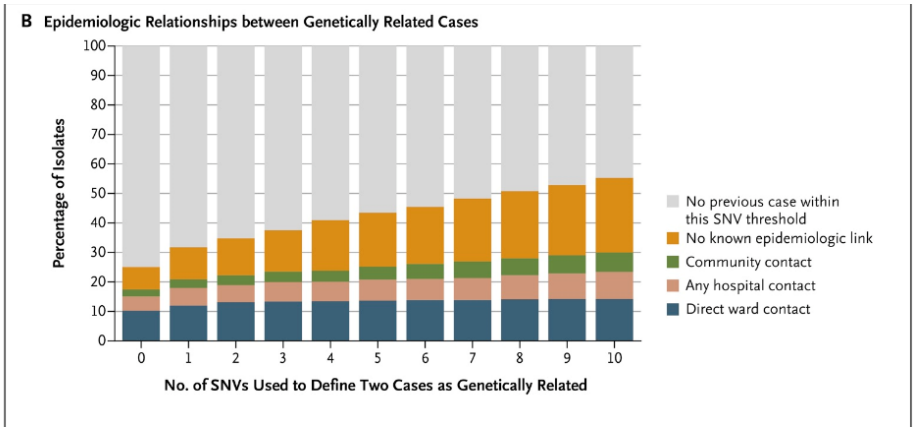
Let's go to a far bigger *C difficile* study that is far more specific using whole genome sequencing

- But first a brief moment to explain terms in in whole genome sequencing:
- Single-nucleotide variants (SNVs) are differences between two bacteria.
- 0-1 SNV differences–Definitive transmission as the two organisms are functionally identical
- 2 SNV differences- Overwhelmingly likely transmission
- 3-10 SNV differences- With each SNV difference less likely the organisms are closely related
- 11 + SNV differences- Transmission did not occur, they are clearly different bacteria

UK health system looks at C. difficile relatedness

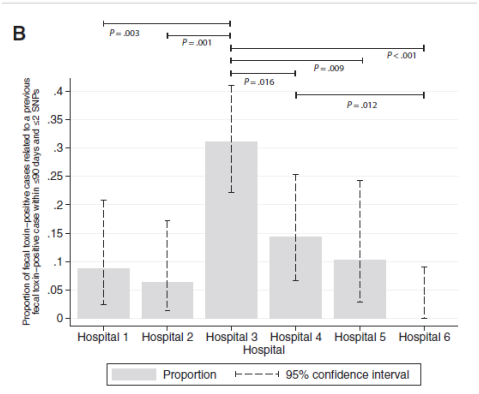
- Eyre DW et al. Diverse Sources of C. difficile Infection Identified on Whole-Genome Sequencing NEJM September 26, 2013 vol. 369 no. 13
- 1250 C. difficile cases that were evaluated, 1223 (98%) were successfully sequenced.
- In a comparison of 957 samples obtained from April 2008 through March 2011 with those obtained from September 2007 onward, a total of 333 isolates (35%) had no more than 2 SNVs from at least 1 earlier case (definitive transmission), and 428 isolates (45%) had more than 10 SNVs from all previous cases (clearly unrelated).
- Of the 333 patients with no more than 2 SNVs (consistent with transmission), 126 patients (38%) had close hospital contact with another patient, and 120 patients (36%) had no hospital or community contact with another patient. So of 1223 CDI cases sequences only 126 patients had some spatial relationship with another patient and a clear genetic link (10.3% of all cases)

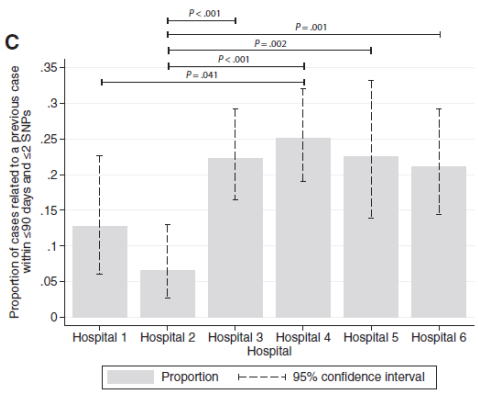
It ain't me!!
While transmission is occurring it is not the majority of cases



Wait A Minute!

DW Eyre et al. Comparison of Control of Clostridium difficile Infection in Six English Hospitals Using Whole-Genome Sequencing CID 2017:65 (1 August)





Strain transmission rates vary (but could be due to local dominance of certain strains)

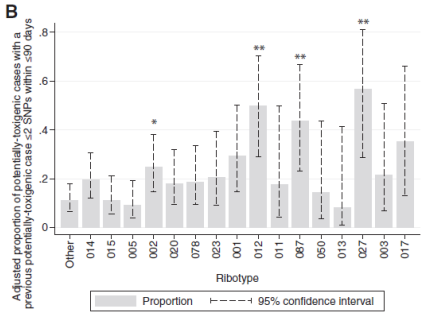


Figure 4. Proportion of cases linked to a previous case by hospital, adjusted for ribotype (*A*), and by ribotype, adjusted for hospital (*B*). In panel *B*, * indicates $P < .05$ compared to the "Other" ribotype category, and ** $P < .01$. Abbreviation: SNP, single-nucleotide polymorphism.

Not so Fast!

- Hongbing J Nosocomial transmission of Clostridium difficile ribotype 027 in a Chinese hospital, 2012–2014, traced by whole genome sequencing BMC Genomics (2016) 17:405

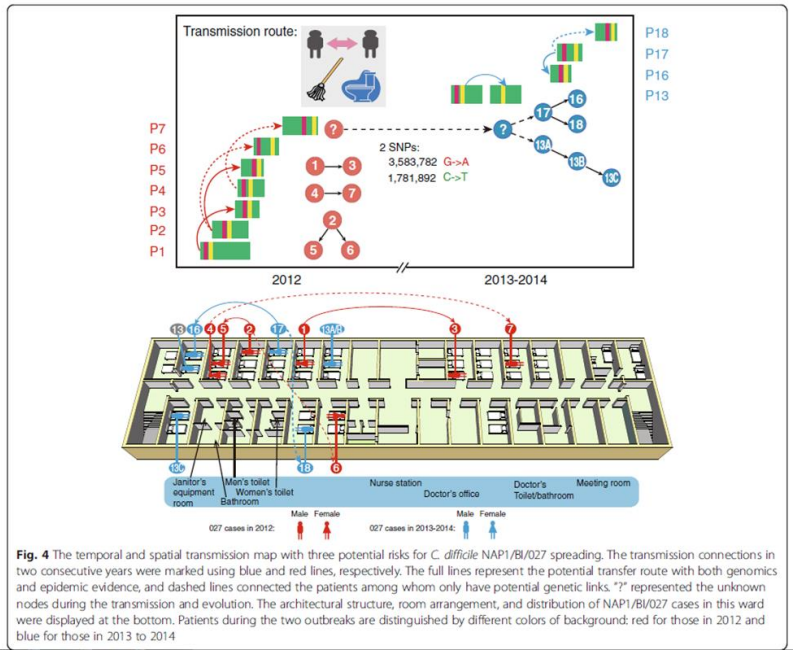


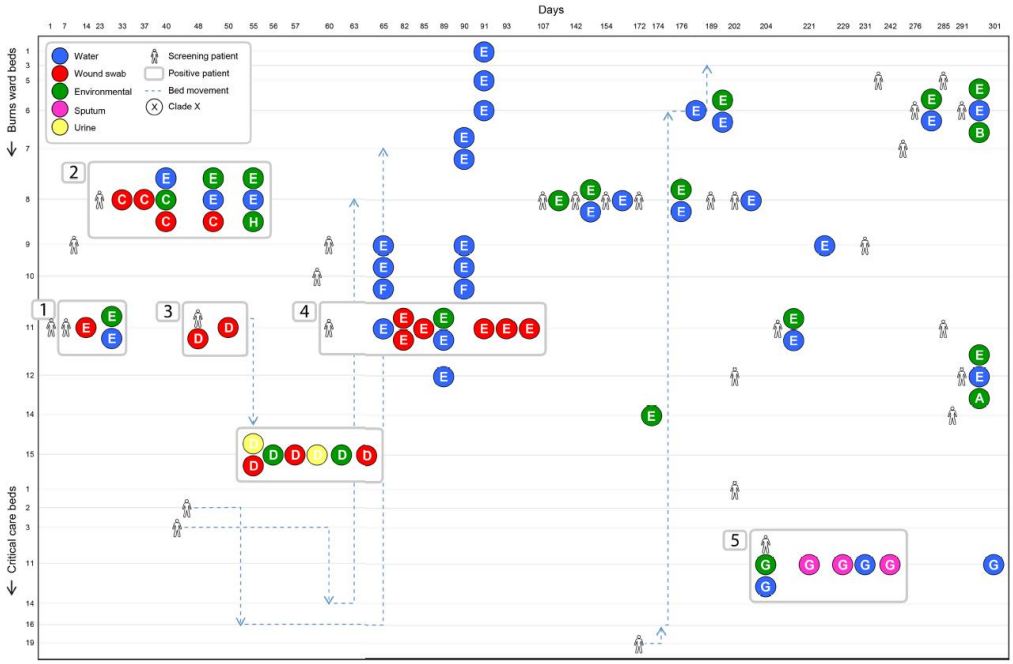
Fig. 4 The temporal and spatial transmission map with three potential risks for *C. difficile* NAP1/BI/027 spreading. The transmission connections in two consecutive years were marked using blue and red lines, respectively. The full lines represent the potential transfer route with both genomics and epidemic evidence, and dashed lines connected the patients among whom only have potential genetic links. "?" represented the unknown nodes during the transmission and evolution. The architectural structure, room arrangement, and distribution of NAP1/BI/027 cases in this ward were displayed at the bottom. Patients during the two outbreaks are distinguished by different colors of background: red for those in 2012 and blue for those in 2013 to 2014

Think of other organisms!

- Lewis T, High-throughput whole-genome sequencing to dissect the epidemiology of *Acinetobacter baumannii* isolates from a hospital outbreak JHI 75 (2010)
- 6 patient outbreak in a hospital
- "Our analyses support transmission of MDR-Aci from the wound of a military patient M2 to the respiratory tract of a civilian patient C2. As MDR-Aci was not isolated from C2 until several weeks after M2 left the adjacent bed, however, we cannot determine when and how transmission occurred. One possibility is that C2 became colonised when the two patients were nursed together, but that colonisation did not reach detectable levels in the sputum until much later. Another possibility is that M2 contaminated the local environment and C2 acquired the organism from the environmentonly (sic) after M2 had left the ward. This latter option would be consistent with a significant role of the environment in transmission of MDR-Aci, as suggested by others."

Quick, J Seeking the source of Pseudomonas aeruginosa infections in a recently opened hospital: an observational study using whole-genome sequencing BMJ Open 2014;4:e006278. doi:10.1136/bmjopen-2014-006278

- Results: "WGS (Whole genome sequencing) for 141 P. aeruginosa isolates were obtained from patients, hospital water and the ward environment. Phylogenetic analysis revealed eight distinct clades, with a single clade representing the majority of environmental isolates in the burns unit. Isolates from three patients had identical genotypes compared with water isolates from the same room. There was clear clustering of water isolates by room and outlet, allowing the source of acquisitions to be unambiguously identified. Whole-genome shotgun sequencing of biofilm DNA extracted from a thermostatic mixer valve revealed this was the source of a P. aeruginosa subpopulation previously detected in water. In the remaining two cases there was no clear link to the hospital environment."
- Conclusions: That acquisition of PSA can be traced to a specific source within a hospital ward.



Let's talk about what we care about

- Price JR Transmission of Staphylococcus aureus between health-care workers, the environment, and patients in an intensive care unit: a longitudinal cohort study based on whole-genome sequencing
- **Sampled 198 health-care workers, 40 environmental locations, and 1854 patients (386 were positive, 357 of those on admission); 1819 isolates were sequenced. Median nasal carriage rate of *S aureus* in health-care workers at 4-weekly time points was 36.9% and 115 (58%) health-care workers had *S aureus* detected at least once during the study. *S aureus* was identified in 8–50% of environmental samples. 605 genetically distinct subtypes were identified at a rate of 38 (IQR 34–42) per 4-weekly cycle. Only 25 instances of transmission to patients (seven from health-care workers, two from the environment, and 16 from other patients) were detected. So only 8% of HAI cases were from the environment, 92% weren't**

That Means…..

- **"In the presence of standard infection control measures, health-care workers were infrequently sources of transmission to patients. *S aureus* epidemiology in the ICU and HDU is characterised by continuous ingress of distinct subtypes rather than transmission of genetically related strains."**
- **"Many acquisitions might be attributable to recrudescence of cryptic carriage and should not be routinely ascribed to transmission and breached infection control."**

Replication of Findings

- **SW Long Absence of Patient-to-Patient Intrahospital Transmission of *Staphylococcus aureus* as Determined by Whole-Genome Sequencing**
- **398 *S. aureus* isolates from sterile-site infections. The *S. aureus* strains were collected from four hospitals over a 6-month period. No evidence of transmission of *S. aureus* between patients with sterile-site infections. "The lack of intrahospital transmission may reflect a fundamental difference between day-to-day transmission events in the hospital setting and the more frequently studied outbreak scenarios."**

Lastly Bloodstream Infections

- Tamburini, FB Precision Identification of Diverse Bloodstream Pathogens in the Gut Microbiome Nat Med. 2018 Dec; 24(12): 1809–1814
- Population BMT patients, "We find that patients with *Escherichia coli* and *Klebsiella pneumoniae* bloodstream infections have concomitant gut colonization with these organisms, suggesting that the gut may be a source of these infections. We also find cases where classically non-enteric pathogens, such as *Pseudomonas aeruginosa* and *Staphylococcus epidermidis*, are found in the gut microbiome, thereby challenging existing informal dogma of these infections originating from environmental or skin sources."

Review of the Evidence

- 1) WGS is a valid tool of identifying relatedness of strains and is much more specific than old technologies of PFGE or traditional descriptive epidemiology
- 2) In outbreaks WGS has confirmed that there are true outbreaks where the environment plays a role
- 3) Studies using standard epidemiologic approaches have shown rooms (the environment presumably) are a risk factor for acquisition of bacteria
- 4) WGS Studies over time have shown that transmission of microbes from patient to patient or from the environment in many cases are rare

Evidence part II

- 5) For some organisms like PSA the environment may play a larger role
- 6) In an outbreak, the environment may play an important role
- 7) For most of the organisms studied, environmental interventions will only reduce rates by 8-40%