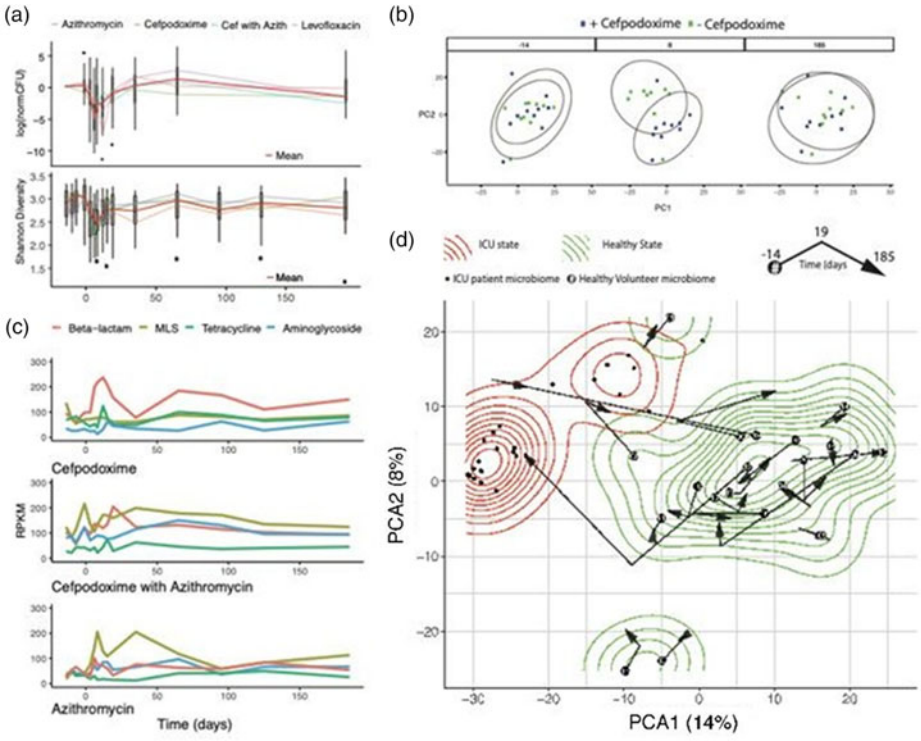

Figure 2. A. Healthy volunteers exhibit acute perturbation of the log-relative CFUs, and in community diversity (Shannon's index). B. Antibiotic-specific changes in PCA dimensions of taxonomic profiles form clusters 3 days after antibiotic administration, but these differences disappear by 185, suggesting resolution of perturbations to community diversity. Variance explained by both axes is shown on subplot D. C. Antibiotic-specific changes to resistance burden after antibiotic administration demonstrate healthy microbiomes are primed to respond to antibiotics, and burden remains elevated for much of the study. D. Antibiotic perturbation moves healthy volunteer microbiomes towards a state similar to the ICU patients, defined as the density gradient estimated from ICU taxonomic profiles. The healthy state is defined as a density gradient estimated from the taxonomic profiles of healthy volunteers before antibiotics. Arrows track the longitudinal change in healthy volunteer microbiomes over time.

Fig. 2.

The HV microbial metabolic profiles were significantly enriched for important biosynthesis pathways producing chorismate and polysaccharides. MICU patient gut microbiomes were enriched for fatty acid regulation and quinolone biosynthesis, and for many degradation pathways important for different aspects of antibiotic resistance such as membrane integrity, alternative respiration, and antibiotic inactivation. **Conclusions:** Short courses of antibiotics can cause acute and chronic microbiome disruptions in HVs, as evidenced by decreased microbiome diversity and increases in specific innate resistance elements. These data support the need for antimicrobial stewardship to support rationale antibiotic use to prevent gut microbiome disruptions.

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Distinguished Oral

A Ten-Year Review of Carbapenemase Producing Enterobacterales (CPE) in London, United Kingdom

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Background: To determine the pattern of CPE observed in a single region in the United Kingdom. **Methods:** From 2009 to 2018, clinical laboratories in England were requested to send suspected CPE from all sites to the national reference laboratory for confirmation and investigation of carbapenem resistance mechanism(s). Isolates of Enterobacterales from London laboratories and confirmed to have 1 or more carbapenemase genes were included in the analysis. **Result:** Between 2009 and 2018, 5,133 isolates were confirmed to produce a carbapenemase; at least 1 CPE was identified in every London Laboratory and hospital. Confirmations increased from 28 isolates in 2009 to 1857 in 2018 and with a sharp rise after the introduction of the 'PHE toolkit' in 2013 (Fig. 1). Most CPE (2655, 51.7%) were from rectal screens (the 3 most frequently identified carbapenemase families were OXA-48–like in 1,263 isolates, NDM in 971 and IMP in 128), 631 (12.3%) were from urine samples, 180 (3.5%) from blood cultures, 103 (2.0%) from sputum specimens and the remainder (1564, 30.5%) were swabs, fluids and tissues from various body sites. Moreover, 51 CPE (1%) were identified from environmental swabs. Isolates were predominantly *Klebsiella* spp (2,525, 49%; 2,088 were *K. pneumoniae*), followed by *Escherichia coli* (1,434, 27.9%), *Enterobacter* spp (746, 14.5%; 605 were *E. cloacae* complex), and *Citrobacter* spp (349, 6.8%); 10 other species contributed smaller numbers. Within the carbapenemase families, OXA-48-like enzymes predominated overall (2303,

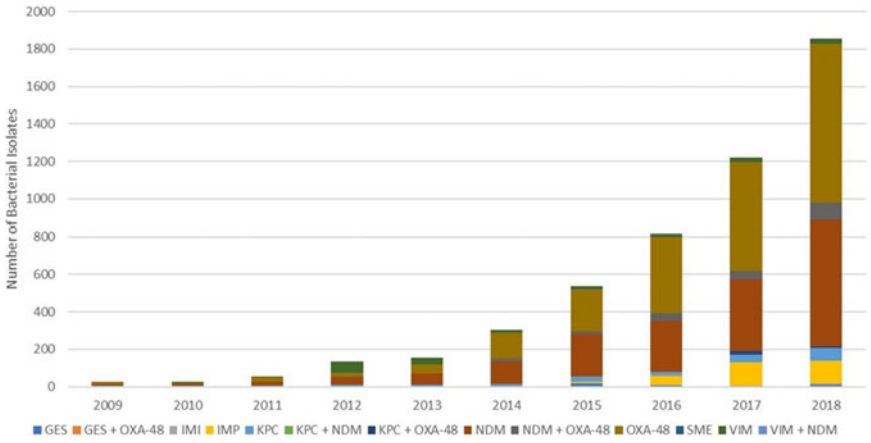

Fig. 1

44.9%), followed by NDM (1822, 35.5%), IMP (313, 6.1%), VIM (207, 4.0%), NDM+OXA-48-like (205, 4.0%), and KPC (196, 3.8%). The first detection of a CPE with 2 distinct enzymes occurred in 2012 (OXA-48-like and NDM) and since then 235 co-detections have been identified; 233 related to OXA-48-like with another gene. **Conclusion:** The first CPE isolate in London was identified in 2003, a *Klebsiella* spp with a VIM enzyme. The number of isolates submitted to the national reference laboratory has continued to increase year on year. VIM and NDM carbapenemases predominated in the early years, because of their association with several outbreaks; these have now been overwhelmed by OXA-48-like detections and outbreaks. The increasing numbers of CPE with a combination of a metallo- and a non-metallo carbapenemase increases the therapeutic challenges to treat infected patients. Bacteremia caused by CPE remains rare, suggesting that infection prevention and control efforts are having some impact. However, as colonization prevalence increases, the number of clinical infections will rise in the future unless control measures to limit transmission and spread are improved.

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Clinical Metrics for a Large Healthcare System's Antimicrobial Management Program

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Background: Clinical metrics and outcomes for evaluation of antimicrobial management programs (AMP) are challenging and inconsistent throughout the United States. Here, we present the results of the development of clinical metrics to measure and trend AMP outcomes within 161 acute-care facilities affiliated with a large healthcare system. **Methods:** Key AMP metrics were implemented in 2018 using 2017 as baseline: use of fluoroquinolones in UTIs, dosing of vancomycin, de-escalation, and intravenous (IV)-to-oral conversion of targeted drugs. Fluoroquinolone (FQ) and UTI metric evaluated all inpatients who received at least 1 dose of a FQ based on barcoded medication administration (BCMA) data and urinary tract infections were based on cystitis ICD-10 coding. Vancomycin dosing metric evaluated inpatient vancomycin troughs within therapeutic range during the admission. De-escalation metric evaluated for patients on a broad-spectrum antibiotic with a positive culture and sensitivity to narrower antibiotics. The IV-to-oral ratio was used to monitor targeted medications. Nonantimicrobial medications appropriate for IV-to- oral conversion were included in the ratio. Goals were established for each metric using the 75th percentile and ranges for "at goal," "close to goal," and "not at goal" were established using green–yellow–red color coding. Metrics were monitored via a systemwide dashboard that included all affiliated facilities. Data were shared monthly to key stakeholders including physicians, pharmacists, and senior leadership. **Results:** From 2017 to the third quarter of 2019, the FQ and UTI metric decreased 55%. This reduction in the FQ usage in UTI metric correlated with a reduction of 26.7 days of therapy (DOT) per 1,000 days present for FQ and a 50% reduction in FQ DOT for all affiliated facilities. The vancomycin dosing metric improved 2.9% from 75.2% of patients to 78.1% of patients with at least 1 vancomycin trough within range during the admission, which represents ~2,000 more patients with dosing in the target range over baseline. The de-escalation metric improved by 7% overall from 2018 to the third quarter of 2019, which translates to ~1,600 more patients with therapy de-escalated. The IV-to-oral ratio metric improved 5.5%, which means that ~180,000 more oral dosages were administered. **Conclusions:** Implementing AMP program clinical metrics in a large health system positively influenced antimicrobial medication therapy management for patients. Monitoring of process metrics should be considered for all AMP programs to advance antibiotic stewardship.

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Decreased Hospitalizations and Costs From Infection in Sixteen Nursing Homes in the SHIELD OC Regional Decolonization Initiative

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