

Every silver lining has a cloud: Point prevalence survey of multidrug-resistant organisms reveals no carbapenemase-producing Enterobacteriaceae (CPE), but high rates of vancomycin-resistant *Enterococcus faecium* (VRE) within a University hospital

Hayley J. Wilson (Brodrick)¹, Fahad Khokhar¹, David A Enoch^{2,3}, Nicholas M. Brown^{2,3}, Jag Ahluwalia², Gordon Dougan^{1,4}, M. Estée Török^{1,2,3}

¹Department of Medicine, University of Cambridge; ²Cambridge University NHS Foundation Trust, Cambridge; ³Public Health England, Clinical Microbiology & Public Health Laboratory, Cambridge; ⁴Wellcome Trust Sanger Institute, Hinxton; United Kingdom

Introduction

Multidrug-resistant (MDR) bacteria are a major cause of morbidity and mortality in hospital in patients. In 2017 The World Health Organization (WHO) published a list of priority MDR organisms to focus and advance research into new antimicrobial development. Carbapenemase-producing Enterobacteriaceae (CPE) were named in the critical section of this list due to high levels of antimicrobial resistance, increasing prevalence and a propensity to spread antimicrobial resistance to other species. During a previous prospective surveillance study for MDRO, conducted between June and December 2016, we identified 2 unsuspected outbreaks of carbapenem-resistant *Klebsiella pneumoniae*. We also detected high rates of carriage of vancomycin-resistant *Enterococcus faecium* (VRE), another WHO priority pathogen. We therefore decided to conduct a point prevalence study of all adult inpatients at Addenbrooke's hospital in order determine the prevalence of CPE and VRE, identify potential reservoirs of infection, and target future infection control interventions.

Methods

All adult inpatients (aged 18 years or older) were eligible for inclusion in the study. Under the guidance of the infection control team, ward nurses approached inpatients, explained the survey to them, and obtained verbal consent. A single rectal swab or stool sample was collected. Sigma Transwabs (MWE, Wiltshire, England) were used to maximise uptake of faecal matter. Samples were plated onto selective chromogenic media - CHROMID® CARBA SMART (bioMérieux, Marcy l'Etoile, France) and Brilliance VRE (Oxoid, Basingstoke, UK) – and incubated at 37° C for 24 hours. Suspect colonies were identified using matrix-assisted laser desorption-ionisation time-of-flight mass spectrometry (MALDI-ToF). Samples identified as CPE or VRE underwent antimicrobial susceptibility testing, using the Vitek-2 platform (bioMérieux, Marcy l'Etoile, France). Carbapenem-resistant isolates were tested for carbapenemase genes, using the Cepheid Xpert Carba-R assay.

Results

The study was conducted between 5 and 9 June 2017. Thirty-nine wards were included in the study, and the total capacity of the participating wards was 917 patients. 781 / 917 (85%) patients were approached and invited to participate. Of these, 558 (71.4%) consented to participation, 132 patients (16.9%) declined to take part, 57 patients (7.3%) were deemed unable to consent for themselves, and 11 patients (1.4%) were unavailable at the time of sampling. In 4 patients (0.5%) it was unclear if they were approached or not. Nineteen patients were excluded from the study as they were less than 18 years of age, or because of duplicate samples. The breakdown of recruitment by ward is shown in Figure 1.

We examined the antimicrobial susceptibility patterns of each VRE isolate. These patterns (antibiograms) have been used previously to infer transmission of a pathogen between patients. Each different antibiogram is shown in the heatmap in Figure 3A.

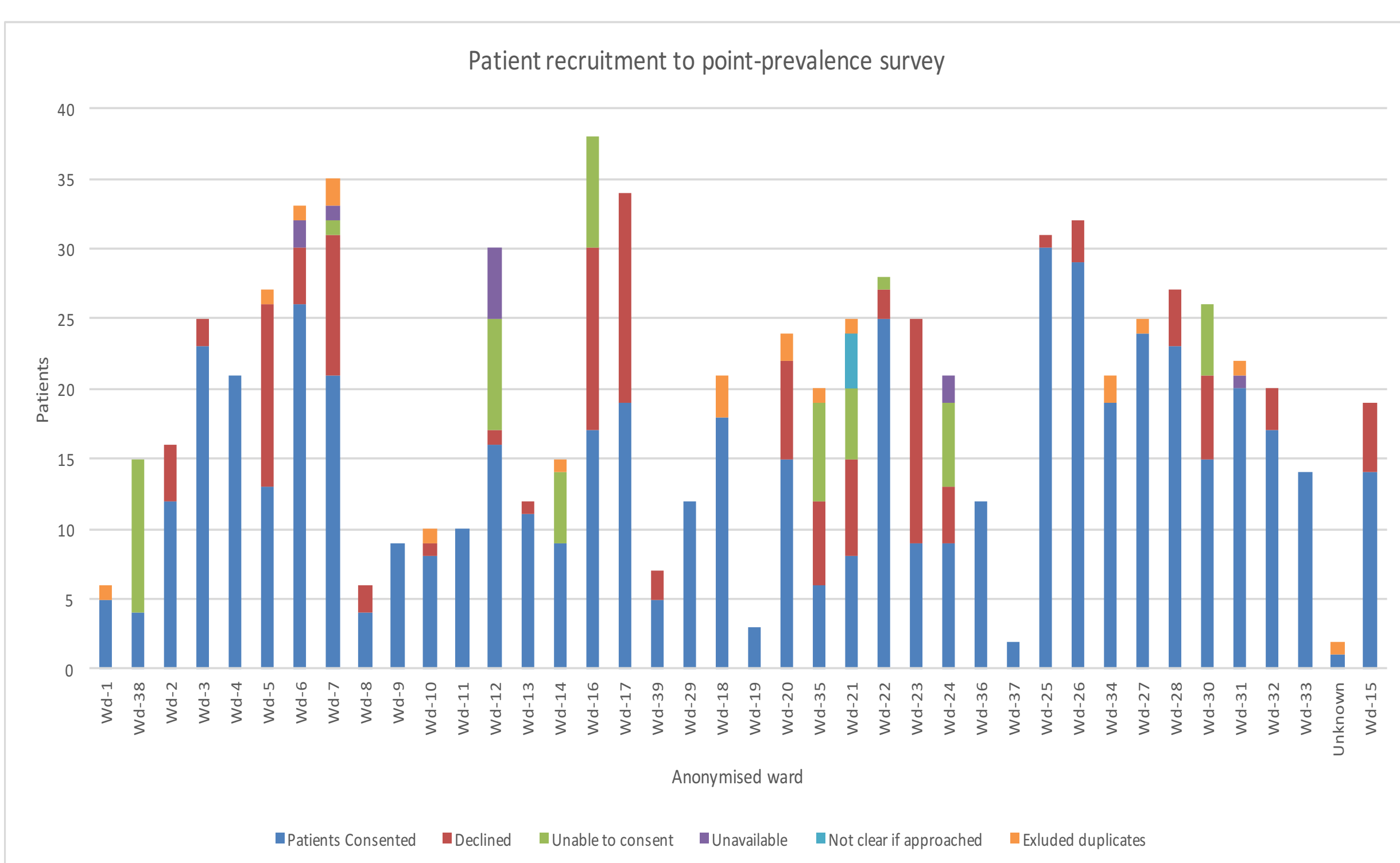


Figure 1: Patient recruitment into the point-prevalence survey

Following de-duplication, 558 samples were available for analysis. No samples were positive for CRE, and 140 (26.1%) of the samples were positive for VRE (Figure 2).

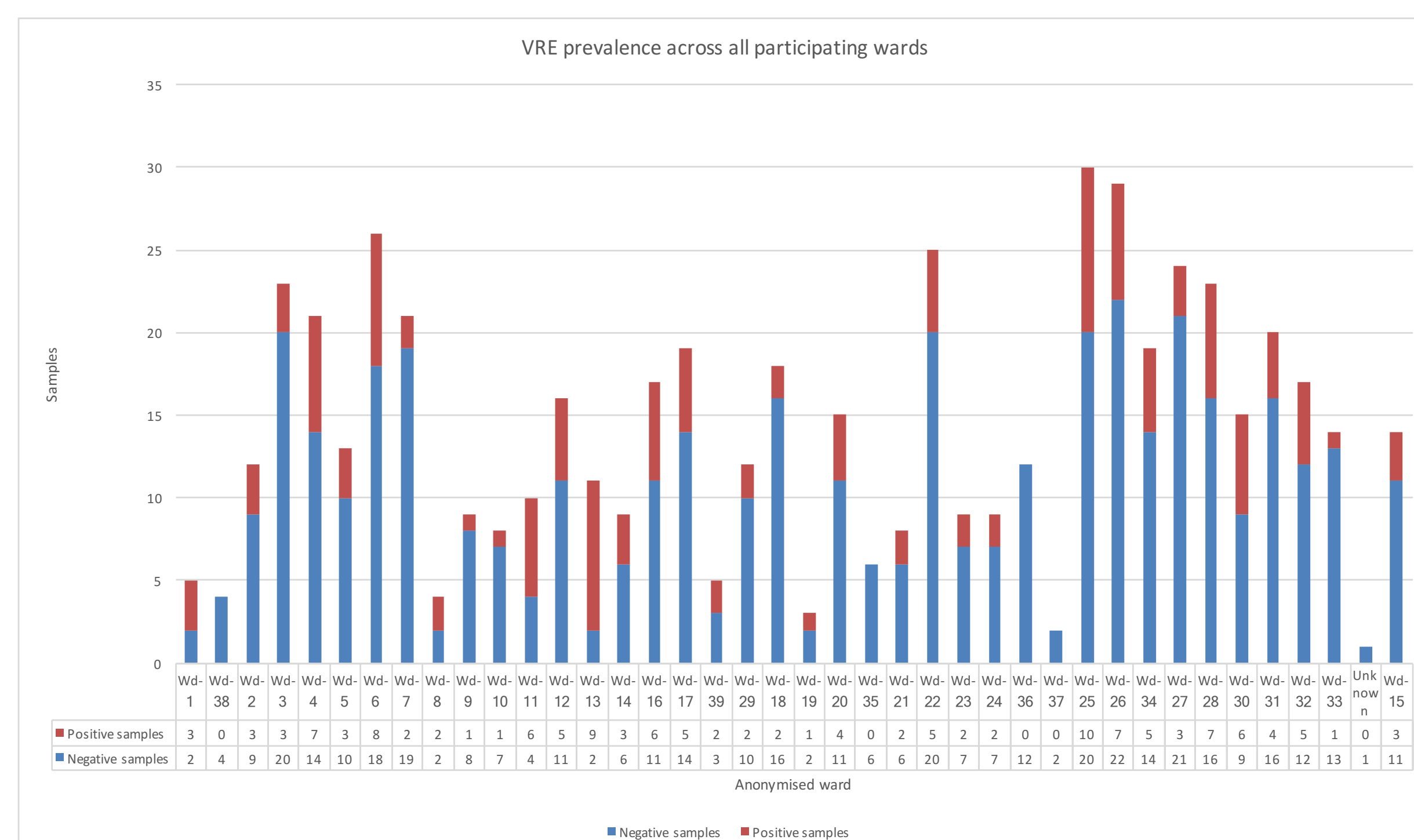


Figure 2: VRE prevalence in patients sampled

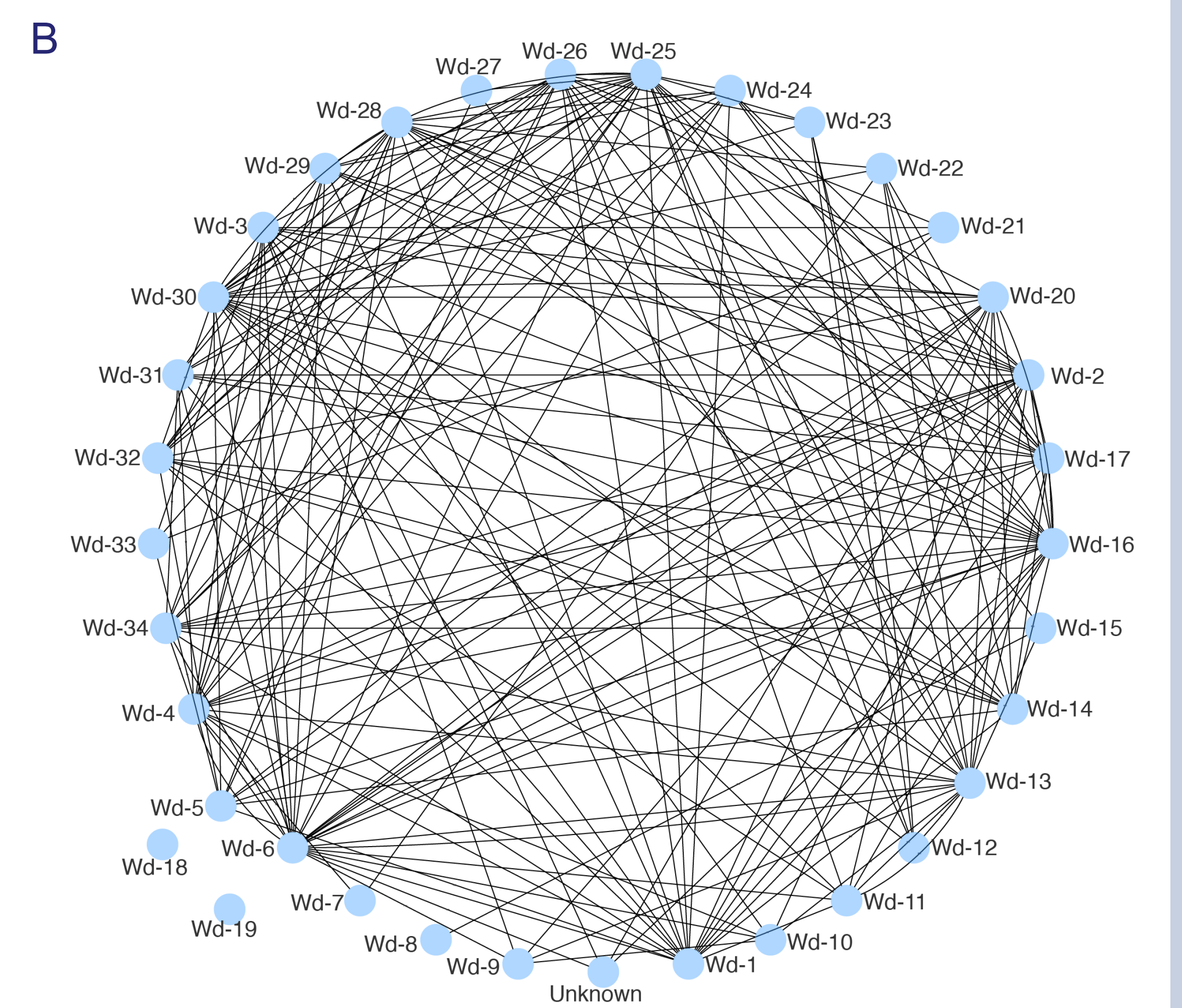
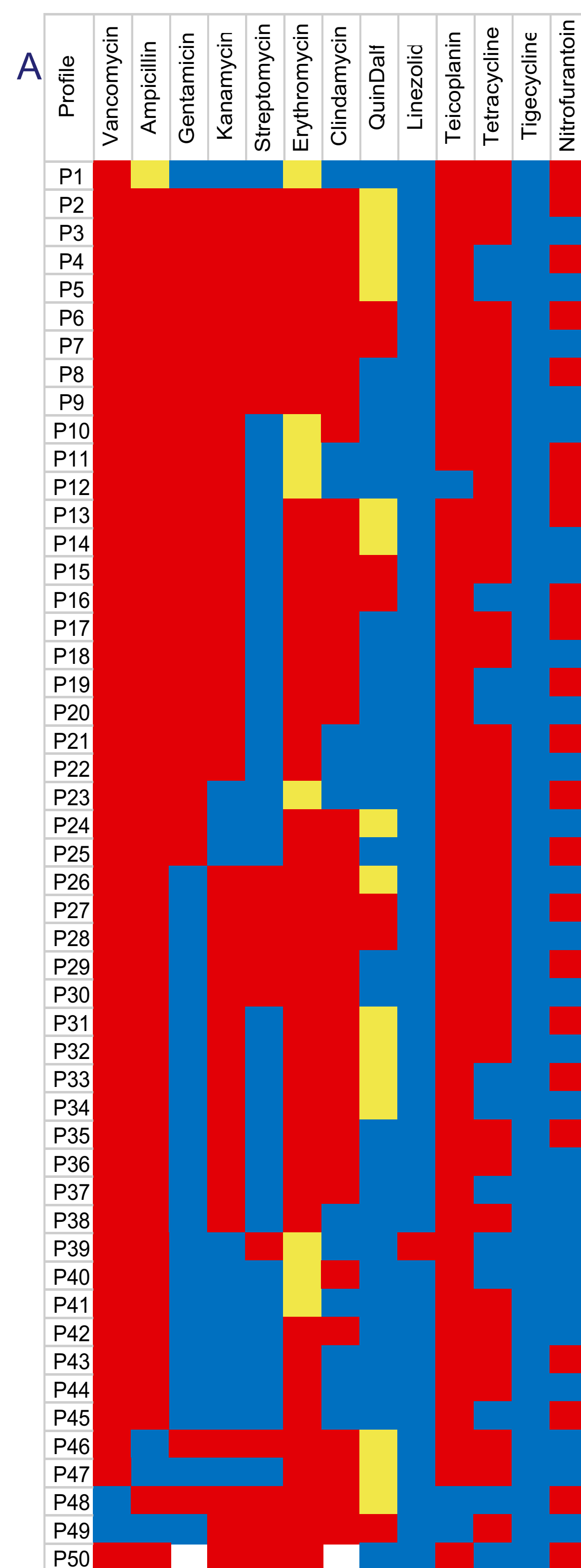


Figure 3: A: Heatmap demonstrating antibiograms identified in isolates collected during the point-prevalence survey. Red: resistant to antibiotic tested, blue: susceptible, yellow: intermediate susceptibility, white: no result produced. Antibiotics are shown in the columns with each profile (P) being shown in a separate row. B: A visualization of antibiograms shared between wards. Each circle represents a ward with black lines linking wards which share the same antibiogram. Wards external to the main plot do not share antibiograms with other wards.

Fifty different antibiograms were present in 140 positive samples, with 27 profiles (54%) being seen in one patient only. One profile in particular, P4, suggested a number of transmission events may have occurred, as it was identified in 19 different patients, from 13 different wards. Cytoscape was used to visualize the relationships between each profile and the ward(s) that it was detected on. Figure 3B demonstrates how this links physically separate wards within the hospital. Antibigrams were not ward specific, but were distributed throughout the hospital, although P4 was identified in 50% of Ward 6 and Ward 25 samples.

Conclusions

- Reassuringly, we did not detect CPE carriage in adult inpatients during the study period
- However, 26.1% of adult inpatients were found to be carrying VRE
- VRE carriage was found in all adult wards throughout the hospital, and not just in high-risk populations, as previously thought
- VRE antibiograms demonstrated high levels of variability, and suggesting transmission between patients and wards

Funding This study was funded by the Academy of Medical Sciences, Health Foundation, NIHR Cambridge Biomedical Research Centre, and Cambridge University Hospitals NHS Foundation Trust