1. The Problem

- Betsi Cadwaladr University Health Board had a major outbreak of *Clostridium difficile* (CD) in 2013 resulting in multiple deaths and continues to be high outlier in UK CD rates\(^1\)
- The Health Board is large covering 6 counties across North Wales
- Need to better understand epidemiology to help target actions to reduce CD rates

2. Study Aim

- To improve the management of *Clostridium difficile* by combining phylogenetic analysis of whole genome sequences of CD isolates with epidemiological data to inform the Health Board response

3. Study Design

- Prospective cohort study February -July 2015 of all *Clostridium difficile* GDH positive adult patients across N Wales (toxin positive and toxin negative cases)
- Whole genome sequencing of isolates \(^2\)
- Risk exposure data collected on cases
- Data on organisational factors collected (staffing, cleanliness, antimicrobial prescribing)
- Two single nucleotide polymorphisms were used as a cut off for distinguishing related and unrelated isolates, within previous 6 months

4. Study Population Sampled

- 6 CHILDREN (0-6 YEARS OF AGE) excluded from study
- Nested case control on hospital acquired toxin positives 1:1

5. Key Findings

- 75.7% of cases were not related to another case, if the first case in a cluster is assumed not to be due to cross-infection, the percentage of unrelated cases rises to 84%
- Cluster timelines showed intra-ward, within hospital and between-hospitals transmission events
- Antibiotic use in the 12 weeks prior to onset was high (Figure 1)
- Cases were detected up to 3 months apart, with no intermediate case identified during that time (Figure 2)
- Fluoroquinolone resistance was apparent within sampled isolates. Published indicators of antibiotic use showed inadequate stewardship across the Health Board
- Comparing whole genome sequence data to ribotyping confirmed that cases are unlinked when from different ribotypes, however single ribotypes contain highly divergent strains meaning a common ribotype is not confirmation of cross-infection
- Further analysis of study data is planned, including more detailed risk factor analysis

5. Conclusions and Implications

- The data points to causes other than case to case transmission behind the majority of observed cases; antibiotic use is likely to be key. Antibiotic stewardship should thus be improved across the Health Board
- The long gap between transmission events has implications for monitoring and definitions used in surveillance programmes
- Infection prevention to reduce hospital based transmission requires sustained vigilance
- The evidence for long-term survival of CD in the environment should inform cleaning practices

References

1. Duerden B. Review of governance arrangements, structures and systems for the prevention and control of healthcare-associated infections in the Betsi Cadwaladr University Health Board. Dr Noel Craine, Trefor Morris, Dr Phil Mannion, Kim Bowden, Dr Mari Morgan: Public Health Wales
2. Eyre DW et al. Diverse sources of *C.difficile* infection identified on whole-genome sequencing. NEJM 2013; 369:1195-1205.