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Reducing fluoroquinolone usage is a key step in controlling the burden of *Clostridium difficile* infection

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Dingle KE, Didelot X, Quan TP, et al. Effects of control interventions on Clostridium difficile infection in England: an observational study. The Lancet Infectious Diseases 2017; 17(4): 411–421

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Summary Title: Reducing fluoroquinolone usage is a key step in controlling the burden of *Clostridium difficile* infection

Summary:

Controlling the costly burden of *Clostridium difficile* infection (CDI) is a critical priority in healthcare. A recent study from England demonstrates that government regulated reduction in antibiotics, and fluoroquinolones in particular, played a key role in reducing CDI in their country.[1] Following the implementation of national control policies in England in 2007, which included recommendations on improving infection control as well as limiting antibiotics, there was an 80% decline in the incidence of CDI. Dingle et al now report on an observational study, including genetic analysis of CDI specimens, that was undertaken to determine which of the control measures was responsible for the marked decline.

Antimicrobial prescribing data were obtained from the UK and combined with UK CDI incidence reporting data. In addition, a large cohort of 4045 CDI cases and C. difficile isolates from the Oxford University Hospitals NHS Trust (Oxfordshire) from 2006 to 2013 was analyzed in greater detail. Genome sequencing was used to determine both C. difficile genotype and fluoroquinolone susceptibility. Using univariable comparisons with bivariate cross-correlations, the authors compared antimicrobial prescribing with incidence of CDI. They then used negative-binomial regression to estimate the incidence of infection in fluoroquinolone-resistant vs fluoroquinolone susceptible isolates both overall and per genotype. Phylogenetic trees were constructed to analyze transmission of resistant versus susceptible strains.

The authors demonstrated a high correlation between CDI and the use of cephalosporins (CC=0.97) and fluoroquinolones (CC=1.00) in the UK. This was also shown in the Oxfordshire cohort (CC=0.73) where the proportion of fluoroquinolone-resistant isolates declined from 67% in 2006 to 3% in 2013 over four distinct genotypes. The incidence of infection due to fluoroquinolone susceptible isolates of the same cohort remained unchanged. Phylogenetic analysis revealed that the decline in transmissible CDI was attributable to a decline in fluoroquinolone-resistant isolates (aIRR 0.21) rather than fluoroquinolone-susceptible isolates (aIRR 0.87).

The authors initially hypothesized that if the decline in CDI was driven by improved infection control, then the incidence of infection both overall and in transmissible cases would decline regardless of fluoroquinolone susceptibility. However, their results demonstrated that the decline was driven by a reduction in fluoroquinolone-resistant strains. This led them to conclude that restricting fluoroquinolone prescribing was a more important factor in the decline of CDI above other measures (i.e. infection control).

Comment