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Effect of changes in national antimicrobial use on Gram-negative resistance

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Background: Associations between rates of antimicrobial use and resistance (AMR) are well documented but there are few studies investigating the effect on AMR of reductions in antimicrobial use. Since 2008, broad spectrum antimicrobials associated with increased risk of *Clostridium difficile* infection (CDI) have been targeted for reduction across Scotland. The aim was to investigate associations between total population use of specific antimicrobials and AMR among Gram negative bacteraemia, over time

Material/methods: Using the NHS Scotland Infection Intelligence Platform (IIP), data on antimicrobial use for the whole of Scotland from 2009 to 2014 were extracted from the Hospital Medicines Utilisation Database (HMUD) and from the Prescribing Information System (PIS) which holds information on all prescriptions dispensed in primary care. Combined WHO Collaborating Centre defined daily doses (DDD) per 1000 Scottish population per month were calculated for co-amoxiclav, fluoroquinolones and 3rd generation cephalosporins. Over the same time period, data on all *E.coli* and *Klebsiella*

bacteraemias with drug susceptibility were extracted from ECROSS (Electronic Communication of Surveillance in Scotland). For patients with multiple eligible samples, the first per calendar quarter was included. Binomial general linear regression models incorporating time, NHS Health Board region and antimicrobial use, with proportion resistant bacteraemia as the outcome, quantified associations between use and resistance for each bacteria/antimicrobial combination. Lag terms at 3, 6 and 12 months were tested for any impact on each model.

Results: Use of fluoroquinolones and co-amoxiclav was 35% lower, and cephalosporins 41% lower, in 2014 than in 2009, all with significant trends over time. Eligible bacteraemia cases increased between 2009 and 2014; *E.coli* from 4185 to 5059 and *Klebsiella* from 1654 to 1732. Resistance to cephalosporins and fluoroquinolones decreased among *E.coli* (relative reductions of 24% and 17% respectively), but not to co-amoxiclav and there were no changes in *Klebsiella* resistance. In regression models there were significant associations between antimicrobial use and *E.coli* resistance for cephalosporins (odds ratio, OR (95% confidence interval), 1.07 (1.02–1.13); interpreted as 7% (2–13%) increase in resistance with each additional DDD/1000 pop), fluoroquinolones (OR 1.02 (1.01–1.03)) and co-amoxiclav (OR 1.01 (1.01–1.01)). There were no significant associations between use of these antimicrobials and *Klebsiella* resistance. Health Board region was a significant factor in most models but the addition of lag terms made no difference in any.

Conclusions: Reductions in use of antimicrobials with high CDI risk in Scotland has been associated with reduced resistance among *E.coli* but not *Klebsiella* bacteraemia. The Infection Intelligence Platform (IIP) enabled this analysis across the whole population.

