

Monitoring unintended consequences of changes in antibiotic policy

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Background

In 2008 the Scottish Antimicrobial Prescribing Group (SAPG) issued advice to NHS boards to restrict the use of antibiotics associated with a higher risk of *Clostridium difficile* infection (CDI) as one of a series of measures to reduce CDI rates in Scotland¹. SAPG developed a programme to monitor both intended and unintended consequences of widespread change in antibiotic policy. This programme included evaluating any changes in 30-day mortality in patients admitted to hospital with sepsis.

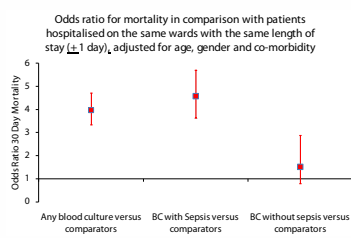
Aim

To monitor 30-day mortality in patients with sepsis admitted through acute medical admissions units in NHS Tayside following the introduction of a restricted antibiotic policy.

Method

Interrupted time series analysis with a segmented regression autoregressive error model was used to look at changes to antibiotic use, CDI rate and 30-day mortality immediately following the introduction of a restricted antibiotic policy and over time in NHS Tayside. A new outcome indicator for monitoring mortality in patients with sepsis was identified and an observational study was used to validate the new outcome indicator comparing 30-day mortality in 2157 cases with blood cultures prospectively collected from 2008-2010 vs. 5839 comparators who were in the same wards for the same length of stay (+/- 1 day) but did not have blood cultures taken. Sepsis was present in 1342 (62.2%, 95%CI 60.2% - 64.3%) of 2157 blood culture cases. After adjustment for age, gender and co-morbidity the odds ratio for 30-day mortality in blood culture cases vs. comparators was 3.97 (95% CI: 3.34 - 4.72). Most of the increased risk was attributable to cases with sepsis (OR 4.57, 95% CI 3.64-5.71), whereas risk of mortality was not increased in patients who had blood cultures taken but did not have sepsis (OR 1.51, 95%CI 0.79-2.88, p=0.217). Blood culture sampling was used as a proxy marker to identify patients with sepsis (see Figure 1).

Figure 1: Odds ratio comparing 30-day mortality in patients with a blood culture vs. comparator



Results

There was a 16% increase (95% CI: -1%, 33%) in the use of recommended antibiotics and a 49% decrease (95% CI: -69%, -28%) in use of restricted antibiotics six months after the new policy was introduced (see Figure 2) which contributed to a 28% decrease (95% CI: -49%, -6%) in CDI (see Figure 3). No other significant interventions were implemented in the acute medical admissions unit during this time period and a temporal relationship between antibiotic use and CDI was established.

There was a non-significant decrease of 25% (95% CI: -49%, -1%) in 30-day mortality in patients with a blood culture taken (see Figure 4). Subgroups analyses by age and Charlson Co-morbidity Index Score showed non-significant decreases in 30-day mortality.

Figure 2: Use of restricted antibiotics (cephalosporins, quinolones, co-amoxiclav, clindamycin) in Acute Medicine

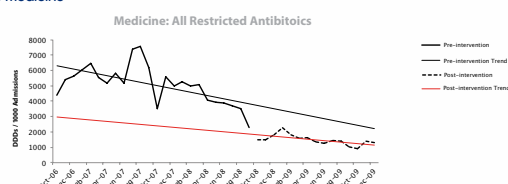


Figure 3: *Clostridium difficile* infection rate in Acute Medicine

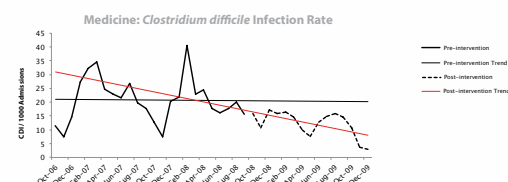
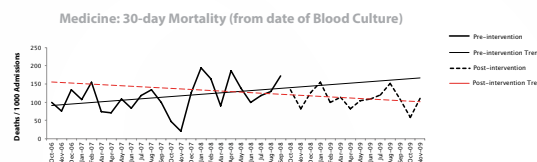


Figure 4: 30-day mortality in medical patients with blood cultures (proxy for sepsis)



Conclusion

The results provide assurance that restricting agents associated with a higher risk of CDI had no unintended adverse consequences on 30-day mortality in patients with sepsis. The methodology will be used to evaluate effects of policy change in other NHS boards in Scotland.

¹Chief Executive letter 30 (2008) www.sehd.scot.nhs.uk/mels/CEL2008_30.pdf