Antibiotic stewardship interventions in hospitals: effect on clinical outcomes

A systematic review and meta-analysis looked at the effects of antimicrobial stewardship interventions on clinical outcomes. The review found that giving empirical therapy based on guidelines and de-escalating therapy reduced risk of mortality in hospital, but a lack of high quality data meant the effect of other interventions was less clear. Healthcare professionals should follow the NICE guideline on antimicrobial stewardship.

Overview and current advice

The NICE guidance on antimicrobial stewardship states that antimicrobial stewardship is ‘an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness’. The guideline recommends organisations establish an antimicrobial stewardship programme, taking account of the resources needed to support antimicrobial stewardship across all care settings. The guideline considers a number of antimicrobial interventions, including the review of prescribing by antimicrobial stewardship teams, promotion of antimicrobials recommended in local or national guidelines, IT or decision support systems and education-based programmes.

The impact of antimicrobial interventions on patient care has been examined in a number of studies, including a Cochrane review, last updated in 2013, that looked at interventions to improve antibiotic prescribing practices in hospitals. The authors concluded that interventions to reduce excessive antibiotic prescribing to hospital inpatients can reduce antimicrobial resistance or hospital-acquired infections, and interventions to increase effective prescribing can improve clinical outcome. This Medicines Evidence Commentary article summarises a recently published systematic review that focused on antimicrobial stewardship interventions.

The NICE Pathway on antimicrobial stewardship brings together all related NICE guidance and associated products on this condition in a set of interactive topic-based diagrams.

New evidence

A systematic review and meta-analysis assessed whether antimicrobial stewardship interventions improved patient outcomes in hospitals, examining 14 interventions, using 4 main outcomes: clinical outcomes, adverse events, cost and bacterial resistance. The review included randomised controlled trials (RCTs), non-RCTs, interrupted time series and observational studies. The analysis included 145
studies and found evidence for 9 of the 14 hospital antimicrobial stewardship interventions. The NICE guideline on antimicrobial stewardship, published in August 2015, included studies up to October 2014, some of which are likely to be included in this analysis.

**Empirical therapy (given before culture results) according to the local or national guidelines** was the most common AMS intervention, reported in 40 observational studies; all studies had a high risk of bias. The majority of studies included people with respiratory infections, mainly community acquired pneumonia. Effect on mortality was reported in 37 studies with a relative risk reduction for mortality across all studies of 35% (relative risk [RR] 0.65, 95% confidence interval [CI] 0.54 to 0.80, p<0.0001). Four studies reported on treatment failure rates, showing a significant benefit with adherence to guidelines. Twenty-four studies assessed the effect of length of hospital stay, although a statistically significant reduction in stay was only observed in 8 studies. Data from 4 studies suggested that adherence to guidelines resulted in cost savings².

**De-escalation of therapy based on culture**, defined as changing to narrow-spectrum antibiotic or stopping antibiotics as soon as culture results are available, was assessed in 25 studies; 1 good quality RCT and 24 observational studies with a high risk of bias. Nineteen observational studies reported an effect on mortality, with a relative risk reduction of 66% (RR 0.44, 95% CI 0.30 to 0.66, p<0.0001)*. Length of hospital stay was assessed in 10 studies, of which only 2 observational studies reported statistically significant reductions in length of stay. Cost of treatment was reported in 13 studies, with 5 reporting statistically significantly lower costs for de-escalation therapy compared with unmodified therapy. Two studies reported increased costs associated with de-escalation, caused by culturing samples or higher daily antimicrobial costs.

Evidence of the effect of other antimicrobial stewardship interventions was less clear. Five observational studies reported on dose adjustment for renal function, all studies had a high risk of bias, were considered of poor quality and the results were inconclusive. **Switching from intravenous to oral therapy** was assessed in 18 studies (13 RCTs and 5 observational studies of low quality due to high risk of bias and small sample sizes), with most studies showing no statistically significant benefit in clinical outcomes, although 7 studies reported a statistically significant reduction in length of stay and 3 studies reporting a statistically significant reduction in cost. **Therapeutic drug monitoring** was reported in 16 studies, with 13 studies reporting on the rate of nephrotoxicity, finding a relative risk reduction of 50% for people who received monitoring (RR 0.50, 95% CI 0.29 to 0.88, p=0.02). A statistically significant reduction in length of hospital stay was reported in 2 studies. Three studies reported on discontinuation of therapy based on no evidence of infection; the studies were considered to be of low or moderate quality, and clinical end points were similar irrespective of whether treatment was discontinued. One observational study reported on the use of local antibiotic guidance, finding mortality was reduced in people with community-acquired infections, hospital-acquired infections and post-operative intra-abdominal infections if local guidance was available. The observational nature of the study meant the quality of evidence was low for this intervention. The use of restricted antibiotic lists was investigated in 30 studies; 1 non-blinded RCT and 29 observational studies, most with a high risk of bias meaning the general quality of the evidence was low. In general resistance rates for restricted antibiotics were significantly decreased for a wide variety of antibiotics and drug combinations. A few studies reported increased resistance rates for non-restricted antibiotics. The effect of bedside consultations was reported in 7 observational studies; most studies had a high risk of bias. Three studies found a statistically significant reduction in mortality with bedside consultation by an infectious disease specialist, although the overall effect on mortality was not significant. A sensitivity analysis found statistically significant reductions in mortality for people with *Staphylococcus aureus* bacteraemia (RR 0.34, 95% CI 0.15 to 0.75, p=0.008)².
The authors did not find any studies that evaluated the other 5 antimicrobial stewardship interventions, which were: blood cultures, cultures from infection site, documented antibiotic plan, assessment of patients’ adherence and local antibiotic guide in agreement with national antibiotic guidelines.

**Commentary**

**Commentary provided by Philip Howard, Consultant Antimicrobial Pharmacist, Leeds Teaching Hospitals NHS Trust**

The study by Schuts et al. reinforces current hospital antimicrobial stewardship (AMS) practice within England by providing further evidence of what interventions impact on improving patient survival and other outcomes. It will help AMS teams to prioritise their core services to have the biggest impact, especially where resources are limited.

The study demonstrates that ensuring that empiric prescribing for infections that follow guidelines improves patient survival. It further supports the drive to improve review and refine empiric therapy within 72 hours (day 3) based on culture results, and that IV to oral switch strategies do no harm. Review of empiric therapy against guidelines should be embedded as a key function of ward pharmacy teams alongside medicines reconciliation. Regular audit and feedback is pivotal to improvement. The current hospital improvement incentives (Commissioning for Quality and Innovation [CQUIN] framework) for sepsis and antimicrobial resistance aims to ensure that review of empiric therapy becomes routine. Patient safety will be further improved with therapeutic drug monitoring for nephrotoxic drugs thus supporting the acute kidney injury work streams within hospitals. In addition, a restricted antibiotic system will reduce costs and consumption of those antibiotics that we wish to protect. We should use the term "protected" antibiotics to promote the importance of these systems. Finally, the study provides evidence that formal consultation by an infectious disease specialist for patients with *S. aureus* bacteraemia can improve survival.

Overall, this is a useful study that supports current practice.

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**References**


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