

## EDITORIAL

# Antimicrobial stewardship: we know it works; time to make sure it is in place everywhere

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The first antimicrobial stewardship programmes were introduced in hospitals more than 30 years ago to address inappropriate antibiotic prescribing and increasing antibiotic resistance.[1][2] Since then a large body of evidence on the effectiveness and safety of this approach has accumulated, and a new Cochrane Review updates the evidence on interventions and delivery methods to improve antibiotic prescribing.[3] The purpose of antimicrobial stewardship is to promote the prudent use of antibiotics in order to optimize patient outcomes while at the same time minimizing the probability of adverse effects, including toxicity and the selection of pathogenic organisms, and the emergence and spread of antibiotic resistance.[4] Key evidence-based stewardship interventions (e.g. empirical treatment according to local or national guidelines, de-escalation of treatment, parenteral-to-oral switch, therapeutic drug monitoring, restricted antimicrobial lists) demonstrate benefits in terms of clinical outcome, adverse events, treatment costs, and antibiotic resistance rates.[5]

The previous Cochrane Review by the same group demonstrated that interventions to reduce excessive antibiotic prescribing were successful, with persuasive and restrictive interventions being equally effective in reducing prescribing after six months.[6] The recent update demonstrates that enabling and restrictive interventions are associated with a 15% increase in compliance with desired practice, a 1.95-day decrease in duration of antibiotic treatment, and a 1.12-day decrease in inpatient length of stay, without compromising patient safety.[3]

Antimicrobial stewardship can incorporate various types of interventions. The Cochrane Review authors compared interventions based on whether they included enabling measures that facilitate appropriate antibiotic treatment or restrictive measures that reduce the opportunity for undesirable antibiotic decisions. Both enabling and restricting interventions were shown to be effective in reducing antibiotic use. It is not surprising that enabling interventions were associated with better acceptance and, when combined with restricting measures, enhanced sustainability of the latter. There were concerns that restrictive interventions could be detrimental to the communication between the clinical and stewardship teams. Moreover, potential delays in initiating antibiotic treatment were observed with some restricting interventions, which would need further refinement before widespread implementation. While these results are encouraging and the impact of the interventions

increased compliance with prescribing recommendations from 43% to 58%, they suggest that further improvement could be achieved with additional behaviour change intervention functions, particularly explicit goal setting and action planning. Nevertheless, information on behaviour change intervention functions is difficult to obtain. In a previous systematic review on the effectiveness of behaviour change techniques to improving hospital antibiotic prescribing, only 25% of authors responded to requests for further information on their studies.[7] Frequently it was difficult to assess which intervention functions were delivered as part of the study. This highlights the importance of both researchers and journal editors using the TIDieR criteria,[8] to state explicitly which behavioural change methodologies and interventions are under study, thereby increasing the impact of research and the translation of evidence to practice.

Initiatives for implementing or strengthening antimicrobial stewardship were primarily developed as a response to increasing antibiotic resistance. Increasing antibiotic use results in increasing antibiotic resistance rates. But does improving antibiotic prescribing reverse antibiotic resistance rates? The updated Cochrane Review does not provide an answer; only 9% of the randomized controlled trials and 19% of the interrupted time series studies reported microbial outcome data. The small number of studies with large heterogeneity in study design and microbial outcome endpoints did not allow conclusions related to changes in antibiotic resistance in gram-negative or gram-positive bacteria. On the other hand, a reduction in the rate of *Clostridium difficile* infections – a short-term outcome and primary target of antimicrobial stewardship – was consistently demonstrated in the studied interventions. The impact on antibiotic resistance requires longer-term studies to assess the outcome of the initial stewardship intervention on subsequent infections and to distinguish the impact of antimicrobial stewardship from the effects of other concurrent interventions (e.g. infection control) and long-term trends in antibiotic resistance.

The armamentarium of antimicrobial stewardship interventions is broad. Judiciously harnessing the potential of novel diagnostics, electronic prescribing, and decision support systems is promising, but at the same time challenging and demanding for the healthcare systems, especially in low-resource settings. Effective and sustained improvement in antibiotic prescribing will require multifaceted quality improvement approaches using behaviour change techniques and methodologies, so that effective

interventions are implemented knowing the target audience, the reasons for the intervention, and the contexts in which to deliver them.

What remains to be done? Despite the extensive evidence base, antimicrobial stewardship programmes are not a requirement in all hospitals.[9] Antimicrobial resistance requires global action. The available evidence base suggests that antimicrobial stewardship programmes should be introduced, with sufficient trained staff and funding, as widely as possible. This requires political commitment and resources, suggesting a role for continued advocacy by public health and specialist professionals and organizations. The implementation of antimicrobial stewardship programmes is included in the Global Action Plan on Antimicrobial Resistance.[10] The importance of antimicrobial stewardship has also been highlighted by other international initiatives, such as the Transatlantic Taskforce on Antimicrobial Resistance.[11] One significant characteristic of the evidence base is that 183 of the 221 studies in the updated Cochrane Review were performed in Europe or North America.[3] Tailored approaches are required, especially defining organizational and cultural determinants, to ensure that antimicrobial stewardship is effectively implemented everywhere.

Antimicrobial stewardship is effective and safe. We need to ensure that it is implemented, and this Cochrane Review highlights two key delivery methods. Political commitment and adequate funding will be essential if antimicrobial stewardship is to be implemented in every healthcare setting.

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