Comment

New tools for antibiotic stewardship: a lesson for prescribers, researchers, or policy makers?

Evidence from the past 20 years has made us confident that antibiotic stewardship interventions should be considered the gold standard for patient care, being safe and effective in improving the quality of antibiotic prescribing.¹ However, how to successfully translate evidence for antibiotic stewardship interventions to implementation into practice still requires research.²

In *The Lancet Infectious Diseases*, Martin J Llewelyn and colleagues report the results of a stepped-wedge cluster-randomised trial evaluating the efficacy of the antibiotic review kit for hospitals (ARK-Hospital) programme in safely reducing antibiotic consumption.³ The intervention targeted the medical wards of 39 UK facilities over a 4-year period. The antibiotic review kit (ARK) intervention was primarily based on categorising diagnostic uncertainty relative to the infection status, followed by a systematic re-evaluation of prescription at 48–72 h. The intervention reached a reduction in total antibiotic consumption of 4.8% defined daily doses per acute medical admission per year, with no relevant effect on length of hospital stay and an inconsistent effect on mortality.³

We read the Article with great interest and praise the authors for conducting such a well designed and logistically complex trial. We believe that the study not only substantially adds to the evidence on antibiotic stewardship interventions but also has great potential to trigger discussion on implementation of ARK in real life from three different point of views: prescribers, researchers, and policy makers.

Notably for a prescriber, a mean of 52% of prescriptions were categorised using the decision tool 12 weeks from the start of the intervention, and some decline in the proportion of revised prescriptions was noted over time. Although those figures might suggest a small intervention uptake, it is important to emphasise that embedding the tool in the electronic system was not possible for most of the facilities, leaving the use of the tool to the willingness of single prescribers in the study. A prescriber might then use the results of the study to request a more robust integration of clinical and prescription data with information technology at the hospital level than is currently available in their own practice, if available at all, to promote a more capillary uptake (ie, consistent and involving all prescribing staff) of antibiotic stewardship intervention and sustain the efficacy over time. The second point that the prescriber would notice is that the study results suggest that hospitals with higher adherence to the educational, audit, and feedback activities had a greater decrease in antibiotic consumption than did hospitals with lower adherence to these activities. From the point of view of the prescriber, the most important message is, therefore, the importance of behavior change as a crucial element for improving the quality of antibiotic prescribing.⁴⁵

From the researcher standpoint, Llewelyn and colleagues' Article raises several fundamental questions about how we could improve the adequacy of the outcomes and the study design that researchers use for capturing the efficacy of antibiotic stewardship interventions. After reading the Article conclusion, we feel that the relatively small effect on the primary outcome (ie, a reduction of 4.8% compared with the expected 15% used for the power calculation) does not do justice to all the potentially relevant intervention components. Conversely, visiting the online webpages dedicated to ARK and the ARK research programme gave us an increased sense of the potential effects of the intervention in promoting organisational change, creating engagement among prescribers, and favouring peer collaboration among stewardship champions. The researcher could then suggest using the study results to design new studies with an explicit focus on behavioural aspects. They might also notice that important clinically relevant outcomes (eq, antibiotic resistance rates or treatment durations) could not be captured due to data collection issues. Additionally, facilities had different levels and trends of baseline antibiotic consumption, and the choice of performing an overall analysis might have diluted or emphasised the actual effect of the intervention. Researchers should consider how to solve the dilemma on the benefits of patient-level versus aggregated data and whether a multicentre national study, supported by a standardised data-collection platform, could answer the clinical question in terms





Lancet Infect Dis 2022

Published **Online** October 4, 2022 https://doi.org/10.1016/ S1473-3099(22)00546-1

See Online/Articles https://doi.org/10.1016/ S1473-3099(22)00508-4

For more on ARK see https:// www.antibioticreviewkit.org.uk For more on the ARK research programme see https:// arkstudy.ox.ac.uk of appropriateness of prescribing (ie, matching the prescribed antibiotic with the infection that prompted its use and the national recommendations for choosing antibiotics).

From the perspective of the policy maker, there are important lessons to learn. Notably, the essential element of the implementation process was creating a local team led by a representative who would champion the intervention and engage local prescribers in each hospital. Importantly, if such an intervention is to be transferred to low-resource settings with few infection specialists or advanced information technology systems, the fact that neither the functional role of the champion nor whether prescribing systems were electronic or paper based made a difference to the success of the intervention is imperative. To our understanding, no further structural or economic resources were needed from the hospital to join the trial. So, once again, dedicated time and personnel for conducting antibiotic stewardship is the core step for starting a successful programme. Additionally, the inclusion of differentsized facilities with various degrees of infrastructure for data collection proved, on the one hand, that the intervention was feasible in many settings. On the other hand, this choice limited the collection of data to what sites could provide, resulting in missing key variables. With no access to individual prescription or microbiology data, the researchers were left only with the information available from bulk antibiotic consumption from the pharmacy and national registries for anagraphic data. Given the large volume of data included, it would have been unfeasible to perform data collection manually or ask for individual patient consent, thus considerably limiting the study's potential. We shared a similar dilemma within a large multicentre cohort study in patients with SARS-CoV-2 infection across Europe. We noted that the absence of adequate infrastructure for data sharing across hospitals and the, sometimes too, strict data protection regulations are severely undermining the success of adequately designed (and funded) trials. We believe that data collection and harmonisation across trials targeting rapidly evolving diseases with high burden on public health, such as COVID-19 or antimicrobial resistance, should be supported by innovative infrastructures and regulations to inform relevant public health decisions in a timely manner.⁶

The efficacy of stewardship interventions is once again shown in this high-quality study. It would be interesting to send these results to relevant national policy makers and ask if the new evidence will have an effect on their antibiotic strategic plans for the next year. We expect that most policy makers would definitively say yes, however, we are pessimistic that, come next year, few would have acted on their promises. We cannot have it both ways: on the one hand bemoan the scarcity of high-quality studies on hospital antibiotic stewardship interventions and, on the other hand, fail to implement the findings of excellent studies when they show a positive effect.

We declare no competing interests.

*Evelina Tacconelli, Marc Mendelson, Elena Carrara evelina.tacconelli@univr.it

Infectious Disease, Department of Diagnostics and Public Health, University of Verona, Verona, Italy (ET, EC); Groote Schuur Hospital, University of Cape Town, Cape Town, South Africa (MM)

- Davey P, Marwick CA, Scott CL, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2017; 2: CD003543.
- Morris AM, Calderwood MS, Fridkin SK, et al. Research needs in antibiotic stewardship. Infect Control Hosp Epidemiol 2019; 40: 1334–43.
- Llewelyn MJ, Budgell EP, Laskawiec-Szkonter M, et al. Antibiotic review kit for hospitals (ARK-Hospital): a stepped-wedge cluster-randomised controlled trial. Lancet Infect Dis 2022; published online Oct 4. https://doi. org/10.1016/S1473-3099(22)00508-4.
- 4 Rodríguez-Baño J, Pérez-Moreno MA, Peñalva G, et al. Outcomes of the PIRASOA programme, an antimicrobial stewardship programme implemented in hospitals of the Public Health System of Andalusia, Spain: an ecologic study of time-trend analysis. *Clin Microbiol Infect* 2020; 26: 358–65.
- Donisi V, Sibani M, Carrara E, et al. Emotional, cognitive and social factors of antimicrobial prescribing: can antimicrobial stewardship intervention be effective without addressing psycho-social factors? J Antimicrob Chemother 2019; **74:** 2844–47.
- Tacconelli E, Gorska A, Carrara E, et al. Challenges of data sharing in European COVID-19 projects: a learning opportunity for advancing pandemic preparedness and response. *Lancet Reg Health Eur* 2022; 21: 100467.

For more on the **large** multicentre cohort study see https://www.orchestra-cohort.eu