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Position paper

Prioritizing research areas for antibiotic stewardship programmes in hospitals: a behavioural perspective consensus paper

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ABSTRACT

Scope: Antibiotic stewardship programmes (ASPs) are necessary in hospitals to improve the judicious use of antibiotics. While ASPs require complex change of key behaviours on individual, team organization and policy levels, evidence from the behavioural sciences is underutilized in antibiotic stewardship studies across the world, including high-income countries (HICs). A consensus procedure was performed to propose research priority areas for optimizing effective implementation of ASPs in hospital settings using a behavioural perspective.

Methods: A workgroup for behavioural approaches to ASPs was convened in response to the fourth call for leading expert network proposals by the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR). Eighteen clinical and academic specialists in antibiotic stewardship, implementation science and behaviour change from four HICs with publicly funded healthcare systems (e.g. Canada, Germany, Norway and the UK) met face-to-face to agree on broad research priority areas using a structured consensus method.

Question addressed and recommendations: The consensus process assessing the ten identified research priority areas resulted in recommendations that need urgent scientific interest and funding to optimize effective implementation of ASPs for hospital inpatients in HICs with publicly funded healthcare systems. We suggest and detail behavioural science evidence–guided research efforts in the following areas: (a) comprehensively identifying barriers and facilitators to implementing ASPs and clinical recommendations intended to optimize antibiotic prescribing; (b) identifying actors ('who') and actions ('what needs to be done') of ASPs and clinical teams; (c) synthesizing available evidence to support future research and planning for ASPs; (d) specifying the activities in current ASPs with the purpose of defining a control

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group for comparison with new initiatives; (e) defining a balanced set of outcomes and measures to evaluate the effects of interventions focused on reducing unnecessary exposure to antibiotics; (f) conducting robust evaluations of ASPs with built-in process evaluations and fidelity assessments; (g) defining and designing ASPs; (h) establishing the evidence base for impact of ASPs on resistance; (i) investigating the role and impact of government and policy contexts on ASPs; and (j) understanding what matters to patients in ASPs in hospitals.

Conclusions: Assessment, revisions and updates of our priority-setting exercise should be considered at intervals of 2 years. To propose research priority areas in low- and middle-income countries, the methodology reported here could be applied. **M. Rzewuska, Clin Microbiol Infect 2019;25:163**

Introduction

Scope

The proposed overarching priority research areas are intended for researchers, representatives from funding agencies and policy makers. These priorities provide suggestions on what needs urgent scientific interest and funding to optimize effective implementation of antibiotic stewardship programmes (ASPs) for hospital inpatients using theoretical and empirical evidence from behavioural sciences. We based these suggestions on experiences from HICs with publicly funded healthcare systems, where most evidence on antibiotic stewardship come from.

Context

Antibiotic resistance is a globally important problem associated with excess mortality and morbidity, prolonged hospital stays and increased healthcare costs [1]. Overuse or inappropriate use of antibiotics drives the development of antibiotic resistance [2]. Most human consumption of antibiotics occurs in primary-care settings and nursing homes [3], but antibiotic resistance has predominantly been a clinical problem in hospitals, which are particularly susceptible to harbouring multidrug-resistant organisms [4]. Therefore, antibiotic stewardship is essential to improve the judicious use of antibiotics in hospitals by providing practitioners with tools to prescribe effective therapy while reducing antibiotic-related adverse events, such as antibiotic resistance [1,4].

An antibiotic stewardship programme (ASP) is a coherent set of collective daily actions that promotes using antibiotic agents responsibly, where 'action' is defined as a strategy (i.e. a specific set of coherent interventions) [5]. In practice, ASPs involve a heterogeneous group of system- and organization-based actions, so understandably there is not only substantial transnational variability in the development and implementation of ASPs [6] but even organization-level variability in HICs [7–10]. This suggests a global need to optimize and standardize the implementation of ASPs. Coordinated transnational response efforts are underway to enhance the implementation (i.e. uptake into practice and policy) of effective ASPs [4]. The planning of such large-scale quality improvement initiatives first requires optimizing the use of existing research resource management [11]. The growing number of research projects on ASPs being conducted and submitted for publication demonstrates that it is a priority area [12], but a number of important research gaps still need to be addressed [4]. Addressing high-importance questions (i.e. research priorities) will reduce avoidable research waste [11]. Core elements and checklist items for global ASPs, including in low- and middle-income countries (LMICs), where most of antibiotics are prescribed, have been developed [13], but without a behavioural lens. More robust qualitative research investigating contextual influences on ASPs is needed from LMICs to propose research priorities for those countries using a behavioural lens.

An ASP requires complex behaviour change; multiple healthcare providers are required to change multiple behaviours at different time points in the patient care pathway. Moreover, change is required at the individual, team organization and policy levels to change key behaviours. It has been widely recognized that evidence from behavioural science can be used to inform that change [3,4,14,15]. The underlying principle of this need is understanding the difference between recommendations for appropriate antibiotic use (the 'what') and behaviour change interventions (the 'how') [3]. To inform the development of a more effective health behaviour change intervention (i.e. a systematic interference designed to modify how an individual acts), researchers have started to specify the active ingredients of interventions in terms of their component behaviour change techniques (BCTs) [16]. BCTs are the observable, replicable components of behaviour change interventions. We know from a Cochrane review that interventions to improve the translation of antibiotic use recommendations into practice are effective in increasing compliance with antibiotic policy and reducing duration of antibiotic treatment in acute care hospital settings [14]. However, the review suggests that few of those interventions used effective BCTs (e.g. action planning or feedback), the role of a key stakeholder (i.e. junior doctors) is mostly overlooked, and interventions are developed at the local level on an *ad hoc* basis [14]. One of the main recommendations from the review included a need to bring together world experts in antibiotic stewardship in partnership with experts in implementation and social sciences to develop a research agenda to guide future research efforts to optimize effective implementation of ASPs in hospital settings [14].

Question addressed

What are the research priority areas to optimize effective implementation of ASPs in hospital settings in HICs with publicly funded healthcare systems?

Methods

Description of development group

A transnational multidisciplinary workgroup on behavioural approaches to ASPs was convened in response to the fourth call for leading experts' network proposals of the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR). The steering committee (CR, JMG, PGD) identified 16 members (all the other coauthors) through a process of peer knowledge sharing and consultation through existing research networks and contacts.

Members were invited on the basis of their recognized expertise in antibiotic stewardship, behavioural and implementation science, including clinical leads, senior academic staff or experts for health authorities or policy makers, with at least 10 years of experience in their subject area; or being frontline clinical staff, clinical-academic or nonclinical academic staff with extensive experience in the above three areas; and coming from a HICs with publicly funded healthcare systems. In total, the group included 19 members from the United Kingdom ($n = 11$), Germany ($n = 2$), Norway ($n = 2$) and Canada ($n = 4$). The members had different backgrounds, including infectious disease physicians, nurses and researchers; implementation scientists; health psychologists; intervention design methodologists; and healthcare service scientists (Supplementary Materials S1).

Consensus procedure

The workgroup met face-to-face on 27–28 April 2017 in Birmingham, UK, and 30–31 October 2017 in Aberdeen, UK. Meetings were audiorecorded and summarized, and notes were taken. To ensure that the priority-setting team had necessary information about the context [17], each meeting was guided by an agenda for activities, including practical group work and presentations of knowledge synthesis undertaken by the workgroup. The latter included a nonsystematic review and knowledge synthesis of existing evidence on ASP implementation efforts worldwide; a systematic review of multicountry studies on barriers and facilitators to ASPs in hospitals (PROSPERO registration CRD42017076425); and the Cochrane review of interventions to improve antibiotic prescribing to hospital inpatients [14].

The stages of the priority setting process were informed by existing literature [18] and are summarized in Fig. 1. We used the nominal group technique, a commonly used formal consensus development method involving a highly structured face-to-face group interaction. Practical benefits for which we chose the nominal group technique included: immediate dissemination of results to the group [19], giving equal voice to each participant by encouraging individual input [19], reduction of personality effects (e.g. influences of a power structure) and creating an environment conducive to initiation of change [20]. In our experience, research needs within the area of behavioural approaches to ASPs are vast and intertwined. Also, in practice, specific research questions are likely to vary across systems and specific settings [8]. Therefore, similar to Healy *et al.* [21], we used a modified James Lind Alliance (JLA) process [22], which led to suggesting unique broad general prioritization research areas rather than specific research questions.

The process protocol is presented in Supplementary Materials S1. The session began with the workgroup coordinator (CR) providing an introduction to the whole group and explaining the purpose of the activity. Participating members then split into two equal-size groups. Each group was allocated one consensus decision-making process facilitator (KG and EMD). Both have been previously involve in a consensus process, and one facilitator (KG) also had previous experience with the JLA process. We selected facilitators with the skills to unite differing perspectives and spheres of expertise and to enable interaction [23]. To capture experiential differences in people with similar background, thereby giving rise to new perspectives, participants with similar areas of expertise were grouped together (e.g. experts in infectious diseases, and health psychology and implementation). At the same time, to stimulate discussion, each group included subgroups with at least three different areas of expertise, and we also included a clinical-academic in each group. Participants were asked to generate specific research ideas in these groups. For this purpose, in silence, participants wrote down research ideas on provided sticky notes. They were instructed to write one idea per note and were encouraged to use as many notes as needed. Each participant presented and brought their research ideas forward for discussion in their groups by reading them aloud and explaining their choices. All ideas were collected, numbered and displayed on a flipchart board by a group facilitator. All participants were then asked to read the ideas generated by the other group.

Participants were brought together through discussion and inductively collated overlapping research ideas into topics. In the JLA process of priority setting—a well-established framework—typically the main focus is to agree the list of the top ten priorities for future research [22]. However, to avoid artificial consensus, the group was not informed about this specific number. Instead, we planned to offer the group an option to decide how many research priority topics would be carried forward for ranking, and we prepared *a priori* a strategy to reduce the number of generated topics if necessary (Supplementary Materials S1).

After a short break, each participant was provided with a printed copy of the prioritized research topics and asked to rank these priorities from most to least important. An e-polling system that collects and summarizes responses was used to collate the ranking of the priority ideas. Responses were submitted using personal electronic devices. After an interval for another activity, the results were presented to the group on a large projection screen. A facilitator then guided the participants through listening to each idea, opinion and concern, and initiated discussion to reach consensus (i.e. a solution that everyone actively supports or at least can accept).

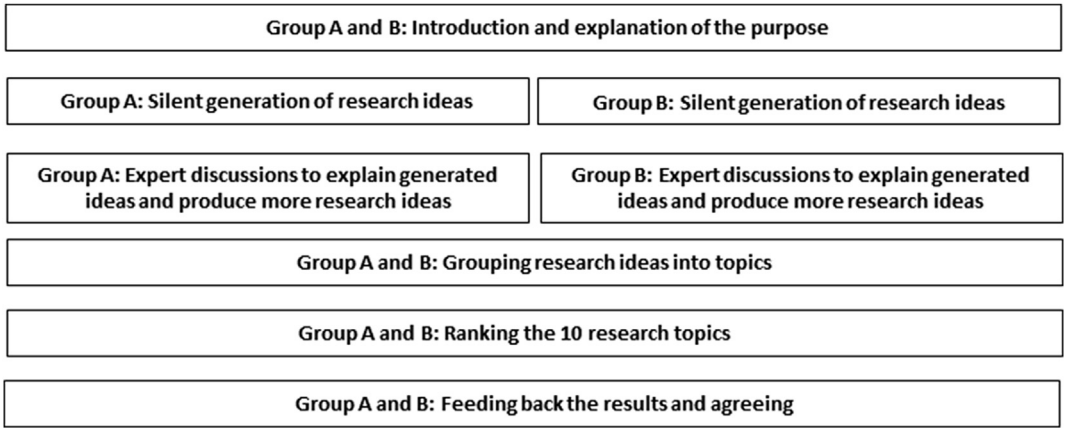

Fig. 1. Stages of research priorities setting process for antibiotic stewardship programmes in hospital settings.

Results

Consensus process

The consensus process for research priority setting took place in Aberdeen in October 2017 and lasted 2.5 hours. Sixteen members generated and collated research ideas into topics, of whom 15 (one person had to leave an activity early) ranked the prioritized research topics. After discussion, the group spontaneously collated individually generated overlapping research ideas into ten research topics, so there was no need to consider reducing the numbers of generated topics. During the discussion of the results of ranking of the prioritized research topics, the group concluded that the top five research priorities received similar ranking scores; priority research areas are interdependent, and so research is much needed across all ten areas.

The dynamic of each group was different because of different personalities, experiences, expertise, backgrounds, communication styles and levels of confidence. The discussions were vigorous, however, and each participant took strong ownership of his or her own proposed ideas. The presence of a facilitator, with experience in both behavioural and implementation science, to moderate those discussions ensured mutual understanding. Placing individuals with similar background and prior presentations and group activities also facilitated shared understanding. In the next step, pragmatism was required to collate individual research ideas to reach acceptable compromises and revision of opinions in the search for consensus. At this point the group required the assistance of the second facilitator and an administrator for record keeping, to ensure full, fair, respectful and equal participation.

Recommendations

Table 1 lists the priorities and ranked research topics grouped into three main descriptive themes. Individual research ideas are presented in Supplementary Materials S2. We would anticipate research teams to select the broad research areas prioritized and develop a specific research project from them. For example, one research objective for the top research priority would be developing a core outcome set which reflected clinicians' and patients' views to enable evaluation of effectiveness of an intervention to support behaviour change, which was specified in terms of target, action, context, time, actor (TACTA), focusing on reducing unnecessary exposure to antibiotics in hospital patients. Within the second top research priority topic, a specific research objective could be developing and piloting a multicentre, transnational, cluster-randomized controlled trial to compare short- and long-term effects of two ASPs with different BCT-specified antibiotic stewardship interventions in hospital inpatient settings. An example research objective within the third research topic might be: Estimating short- and long-term effects of TACTA-specified ASP behaviours on Gram-negative and Gram-positive bacteria using a controlled interventional study design and data reporting.

Implications

The main implication of this consensus work is potentially reducing avoidable waste and inefficiency in research by directing future research to address the proposed uncertainties of importance [23]. To facilitate this process, participation of a priority-setting team in discussion with the community of interest, to share findings and experiences, is recommended [17]. Research teams are encouraged to identify opportunities for building robust proposals focused on comprehensively addressing research objectives within these priorities. Robust proposals could be informed by recommendations for avoiding research waste [11] as well as by guidance on designing and reporting of ASP intervention studies [24,25], implementation studies [26] and behaviour change interventions [27,28]. ASPs are a global concern and are thus best addressed by engaging existing research teams to collaborate internationally and contribute evidence to answer the prioritized research topics.

The JPIAMR Virtual Research Institute has offered to provide a platform to achieve this by increasing coordination, improving visibility and facilitating knowledge exchange globally (https://www.jpiamr.eu/activities/jpiamr-virtual-research-institute/). A promising innovative solution for contributing generalizable evidence is implementation laboratories [29], such as the one proposed for audit and feedback (http://www.ohri.ca/auditfeedback/). For ASPs, this would involve a research team integrated into healthcare systems undertaking research projects directly relevant to the healthcare systems' priorities for ASPs. This could offer a much-needed platform for moving forward from small-scale studies developed on an *ad hoc* basis towards coordinated large-scale initiatives focusing on applied research to develop, implement and evaluate theoretically informed ASPs in different

Table 1
Prioritized ten research topics—an overarching aspiration: more impactful hospital ASPs

Theme	Research priority area	Overall ranking
Theme 1. Establishing the evidence base and understanding current practice in ASPs	Comprehensively identifying barriers and facilitators to implementing ASPs and clinical recommendations intended to optimize antibiotic prescribing (i.e. good clinical practice for antibiotic use).	4
	Identifying actors ('who') and actions ('what needs to be done') of ASPs and clinical teams.	6
	Synthesizing available evidence to support future research and planning for ASPs.	7
	Specifying the activities in current ASPs with the purpose of defining a 'control group' for comparison with new initiatives.	8
Theme 2. Design and evaluation of ASPs	Defining a balanced set of outcomes and measures to evaluate the effects of interventions focused on reducing unnecessary exposure to antibiotics.	1
	Conducting robust evaluations of ASPs with built-in process evaluations and fidelity assessments.	2
	Defining and designing ASPs.	5
Theme III. Research priority topics crosscutting to themes 1 and 2	Establishing the evidence base for impact of ASPs on resistance.	3
	Investigating the role and impact of government and policy contexts on ASPs.	9
	Understanding what matters to patients in ASPs in hospitals.[a]	10

ASP, antibiotic stewardship programme.
[a] The involvement of patients in hospital antibiotic stewardship research has been traditionally limited and hence was ranked as No. 10. This is because patients treated with antimicrobials in hospital settings are typically more ill than patients treated in primary care settings, so they may have less capacity to make their own decisions about their care.

contexts. Sufficient and sustainable resources to support further research efforts are needed to take this agenda forwards. According to Chalmers *et al.* [23], 'Research funders have primary responsibility for reduction in waste resulting from decisions about what research to do,' and hence they should be encouraged to integrate set research priorities into their organizational plans, research strategies and funding calls.

Our aim was to further optimize ASPs for hospital inpatients, based on experiences of research partners from HICs. Globally, the majority of prescribing takes place in LMICs [3]. We fully agree with proposals to advance antibiotic stewardship research in those countries [4,24], as evidenced by the fact that most of our group members collaborate with research partners in LMICs. However, the health research capacity strengthening research field with a focus on implementation science is emerging, and currently evidence bases are not yet sufficiently advanced to effectively inform health research capacity strengthening research programme planning [30]. On the basis of our best knowledge and experiences, we recognized that implementation of ASPs varies greatly across types of healthcare systems, let alone LMICs, so inviting a limited number partners from LMICs was likely to unfairly prioritize specific research needs in their countries. We expect a similar consensus procedure to be conducted with a range of frontline clinicians and academics from LMICs with extensive experience with antibiotic prescribing in partnership with experts in implementation, intervention design and behavioural sciences from HICs and LMICs. More robust qualitative research investigating contextual influences on ASPs is needed from LMICs to inform such a consensus procedure.

We did not include patients whose role in hospital antibiotic stewardship was traditionally limited but is now starting to increase [31]. We anticipated that a major practical challenge to include patients would be a need to overcome patient-reported doubts on their ability to understand antibiotic use–related medical information [31]. We expect that including patients would affect the completeness of the prioritized areas; hence, this is needed. As recommended by Nasser et al. [17], improving and refining the proposed research priorities should be continued, so we encourage assessment, revisions and updates of our consensus process at intervals of 2 years, including involvement of other stakeholders (e.g. patients). Single systematic literature reviews around each priority topic could be conducted, where numbers and types of scientific publications could serve as a proxy to quantitatively assess the impact of our research priority areas.

Conclusions

We propose ten research priorities areas—shared by clinicians as well as clinical and nonclinical academics from HICs with publicly funded healthcare systems—for future research on hospital ASPs. For this we focused on a behavioural science perspective, a mode currently underutilized in antibiotic stewardship studies [3,14,15,32]. This way, we addressed a recognized important gap in knowledge [14]. We specified how optimizing implementation of ASPs will depend on using theoretical and empirical evidence from behavioural science for knowledge synthesis; investigating implementation failures; and informing the research community of the improved design and evaluation of effectiveness, sustainability and scalability of ASPs as quality improvement initiatives.

Transparency declaration

Funding received from the Research Council of Norway (RCN) through the JPIAMR under the fourth call (2016). Costs included travel costs, running face-to-face meetings and dissemination of results. The Health Services Research Unit is core funded by the Chief Scientist Office of the Scottish Government Health and Social Care Directorates. JMG holds a Canada research chair in Health Knowledge Transfer and Uptake. EC is funded by National Institute of Health Research Imperial Biomedical Research Centre and the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Healthcare Associated Infections and Antimicrobial Resistance at Imperial College London and the Economic and Social Research Council. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the report. All authors report no conflicts of interest relevant to this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2018.08.020.

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