Adaptation and implementation of the ARK (Antibiotic Review Kit) intervention to safely and substantially reduce antibiotic use in hospitals: a feasibility study☆

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SUMMARY

Background: Antimicrobial stewardship initiatives in secondary care depend on clinicians undertaking antibiotic prescription reviews but decisions to limit antibiotic treatment at review are complex.
Aim: To assess the feasibility and acceptability of implementing ARK (Antibiotic Review Kit), a behaviour change intervention made up of four components (brief online tool, prescribing decision aid, regular data collection and feedback process, and patient leaflet) to support stopping antibiotic treatment when it is safe to do so among hospitalized patients; before definitive evaluation through a stepped-wedge cluster-randomized controlled trial.
Methods: Acceptability of the different intervention elements was assessed for a period of 12 weeks by uptake of the online tool, adoption of the decision aid into prescribing practice, and rates of decisions to stop antibiotics at review (assessed through repeated point-prevalence surveys). Patient perceptions of the information leaflet were assessed through a brief questionnaire.
Findings: All elements of the intervention were successfully introduced into practice. A total of 132 staff encompassing a broad range of prescribers and non-prescribers completed the online tool (19.4 per 100 acute beds), including 97% (32/33) of the pre-specified essential clinical staff. Among 588 prescription charts evaluated in seven point-prevalence surveys over the 12-week implementation period, 82% overall (76—90% at each survey) used the decision aid. The median antibiotic stop rate post implementation was 36% (range: 29—40% at each survey) compared with 9% pre implementation ($P < 0.001$).

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Conclusion: ARK provides a feasible and acceptable mechanism to support stopping antibiotics safely at post-prescription reviews in an acute hospital setting.

Introduction

Hospital prescribing accounts for a minority of human antibiotic consumption but is where the great majority of broad-spectrum antibiotics are prescribed [1]. Reducing antibiotic overuse in hospitals is challenging because patients who present acutely unwell or who are critically ill require prompt and adequate initial antibiotic therapy [2,3]. Controlling antibiotic overuse relies on regular review and revision of antibiotic prescribing decisions; in the UK National Health Service (NHS) 'Start Smart then Focus' guides that the continued need for antibiotics is assessed at 24–72 h when more diagnostic information is available and treatment response can be assessed [4]. Similarly, recommendations from the US Centers for Disease Control and Prevention (CDC) include antibiotic 'time-outs' to prompt reassessment of the continued need for and choice of antibiotic treatment [5].

Wide-ranging educational and practice resources exist to support hospital antibiotic stewardship but significant improvements in hospital antibiotic overprescribing have not been achieved [1,6,7]. Knowledge, system, and behavioural factors combine to make it very hard for doctors to take active decisions to stop antibiotics, and less than 10% of antibiotic prescriptions are discontinued at review in the NHS [8,9]. For these reasons, the Antibiotic Review Kit (ARK) intervention was designed and carefully optimized using an integrated person-based approach to address the barriers to behaviour change [10]. ARK aims to support prescribing and non-prescribing healthcare professionals to apply the 'review and revise' approach to antibiotic prescriptions for acute and general medical inpatients, and specifically to stop antibiotic treatment more often when it is safe to do so.

The clinical impact of many research programmes evaluating novel antimicrobial prescribing interventions is hampered by design and reporting limitations [11]. In particular all stages of evaluation should be reported, allowing clinicians to understand how potential barriers and facilitators have been considered. Ahead of the definitive evaluation of ARK in a multi-centre, stepped-wedge, cluster-randomized trial we undertook a single-site feasibility study. Here we report the practicalities of implementing the ARK hospital intervention in a single acute hospital. We investigated the feasibility of adapting the intervention according to local needs while maintaining fidelity to the core elements and acceptability of the intervention to front-line staff.

Methods

Ethics

Approvals were obtained from the South Central — Oxford C Research Ethics Committee (17/SC/0034) and Confidentiality Advisory Group (17/CAG/0015). The trial is registered with Current Controlled Trials (ISRCTN:12674243). This study has been reported in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)-AMS tool (Supplementary Table S1) [12].

Intervention description

ARK has four components: an online tool; prescribing decision aid (Supplementary Figure S1); data collection and feedback process; and a patient leaflet (summarized in Table I). ARK implementation is led by an ARK Champion and Core Team, involving an AMS team member, and clinical staff considered essential to the local implementation of ARK. The implementation guidance sets out the main activities needed to establish ARK in seven phases, beginning three months before kick-off, covering three months of implementation and then addressing sustainability (Supplementary Figure S2).

Design

This single-site study focused on three key aspects: (a) feasibility of adapting ARK to local needs, (b) feasibility of key intervention components, and (c) acceptability of ARK to the implementation team and the wider clinical team. The site for the feasibility study was selected from Trusts represented by the healthcare professionals involved in stakeholder consultations during the intervention development [10].

Setting

Brighton and Sussex University Hospitals NHS Trust (BSUHT) is an acute, medium-sized teaching hospital delivering secondary and tertiary services across two main sites. ARK was implemented on the larger 680-bed site, where ~75% of medical admissions come through a 32-bed acute medical unit (AMU). Medical patients are referred from primary care or from the emergency department. Patients who have an anticipated length of stay of >72 h are transferred to an inpatient ward managed by an appropriate general or specialist team, e.g. respiratory, elderly care, endocrine, or gastroenterology.

Before implementation, the Trust's total antibiotic prescribing (4711 defined daily doses per 1000 admissions) reflected national statistics (median in England: 4868 (range: 1619–10,475) in the fourth quarter of 2016/17). The Trust used paper-drug charts including an antibiotic prescription page on which treatment duration was limited to five calendar days. The Trust had an AMS lead (0.2 whole-time equivalent consultant microbiologist) and two full-time antimicrobial pharmacists working through an AMS committee, who met monthly with representation from infection control, service commissioners, and trainees in infection medicine. The AMS committee reported upwards to the Trust's Drugs and Therapeutics Committee (DTC) and the Infection Control Committee. In terms of education and training, the Trust used the Micro-Guide™ platform as a mobile resource containing antibiotic prescribing guidelines and other AMS-related educational content. Prescribing practice was monitored through Trust-

Table I
The four components of the ARK (Antibiotic Review Kit) intervention

Component	Description
Online tool	A brief (7–10 min) online tool on the University of Southampton LifeGuide platform (https://www.lifeguideonline.org) that promotes motivation and confidence to implement 'review and revise', by discussing the risks and benefits associated with antibiotic treatment duration decisions and introducing the Decision Aid.
Decision Aid[a]	Allows prescriber to acknowledge and record the degree of certainty around an initial antibiotic prescription and link this to the review decision, using two key antibiotic prescribing moments.
	1. Initial prescription, at which point prescriptions are categorized as based on either:
	— 'possible' risk from infection (infection less likely but antibiotics are being prescribed until serious infection can be excluded) or
	— 'probable' risk of infection (infection is likely but more information is required before finalizing the diagnosis/treatment).
	2. Review, at which point prescriptions can either be stopped (where there is not a clear justification for continued treatment) or finalized (where a senior/specialist decides on agent, route, and duration).
Data collection and feedback process	Uses point-prevalence data gathered with a Microsoft Excel workbook (Microsoft Corporation, Redmond, CA, USA) to inform brief, frequent and supportive discussions with clinical teams about Decision Aid use and rates of stopping antibiotics, reinforcing learning about antibiotic prescribing decisions.
Patient leaflet	Explains the 'review and revise' process, why antibiotics may be stopped, then potentially restarted, and gives safety-netting advice.

[a] See Supplementary Figure S1 for further explanation.

wide audits, based on the NHS Safety Thermometer (NHS-ST) tool, whereby ward pharmacists collect data on antibiotic prescriptions for up to five patients per ward on a monthly basis [13]. Antimicrobial consumption was monitored regularly and reported externally to Public Health England.

Data collection

Quantitative data on use of the online training module was collected automatically through LifeGuide. Point-prevalence data on use of the Decision Aid categories and antibiotic prescribing were collected from paper drug charts using the ARK data collection workbook, prior to implementation and at weeks 1, 2, 3, 4, 6, 8, and 12. Data were collected from all patients on the AMU, respiratory, elderly care, endocrine, and gastroenterology wards who had received antibiotics during their current inpatient stay. Data were gathered for each antibiotic indication rather than individual agent. Indications were assumed to reflect infection as diagnosed by the prescriber and not defined further. Patient views on the patient leaflet were elicited through a brief questionnaire (Supplementary Appendix) scored on a 1–7 Likert scale in a small sample of AMU patients who had been prescribed antibiotics and who had agreed to take part in a telephone interview (F. Mowbray *et al.*, unpublished data).

Outcomes

Details of how the Core Team locally adapted and implemented each of the four ARK intervention components are reported alongside the relevant outcome measures. The champion identified key essential staff members who they felt would facilitate their clinical colleagues' engagement with ARK. These included consultants and training-grade doctors from each relevant medical specialty, senior nurses and pharmacists working in the clinical areas where ARK was imple-

mented, and infection specialist doctors. The primary outcome was the proportion of pre-identified key essential staff who completed the online training.

Other usage data for the online tool included the overall number of staff who completed it per 100 acute-beds, to reflect levels of staff engagement. Other outcomes reflected the process of implementation, specifically the proportion of initial prescriptions that: used the Decision Aid categories; were reviewed within 72 h; had been stopped at review. These were all pre-specified in the protocol as secondary outcomes for the main trial. Other actions taken at review, i.e. switch agent (narrow/broaden), move from intravenous to oral route, or outpatient parenteral antimicrobial therapy, were also considered in secondary analyses. Targets for ARK to be considered feasible and progress to the main trial were that >70% of staff identified by the champion as essential for ARK to be implemented should complete the online tool, and that >50% of prescriptions audited should have used the Decision Aid. These thresholds were chosen because, with no evidence base for estimating the level of engagement necessary to achieve changes in prescribing behaviour, >70% engagement of key opinion leaders in the hospital and >50% use of the Decision Aid were thought to be required to impact intervention outcomes.

Analysis

Binary outcomes were assessed using univariable and multivariable logistic regression (or Fisher's exact test if the outcome was identical for all prescriptions in one group), and other actions at review using multinomial regression. Evidence for variation across the implementation period (weeks 1–12) was assessed using Wald tests, and combined models comparing baseline versus post implementation were used where there was no evidence of variation over time. Statistical analysis was performed using Stata version 14 (StataCorp, College Station, TX, USA).

Results

Core Team and essential clinical staff

At the feasibility site the Core Team included: the Champion (consultant in infectious diseases), the Trust's AMS lead, two acute medicine consultants, two antimicrobial pharmacists, two acute medicine charge nurses and three training-grade doctors. The Core Team received access to the intervention materials in February 2017 to begin planning towards implementation on April 18th, 2017. The team met four times over the 10 weeks to work through the guidance, assign, and deliver key tasks. The Champion identified 33 key essential staff to promote the wider clinical teams' involvement with ARK. These included 21 consultants (nine acute medicine, four microbiology and infection, two elderly care, two endocrine, two critical care, one each in respiratory and gastroenterology), four training-grade doctors in acute and general medicine including the 'chief' medical registrar, four pharmacists working in acute and infection medicine, and two acute medicine and two infection control nurses. All clinical staff were invited to a Grand Round, covering the background and practicalities, four weeks before implementation. Twelve separate 'kick-off' meetings were also held with individual clinical teams, nursing staff, pharmacy staff, and junior doctors. The details of how the Core Team locally adapted and implemented each of the four ARK intervention components are shown in Table II.

Online tool

In terms of the primary outcome, the proportion of key essential staff who completed the online tool was 97% (32/33), exceeding the target of >70%. Including essential clinical staff, a total of 175 healthcare professionals registered to use the online tool and 132 completed it (19.4 per 100 acute beds). Of those completing the tool, 34% (45/132) were consultants, 26% (34/132) were training-grade doctors, 19% (25/132) were nurses, 11% (14/132) were pharmacists or pharmacy technicians, 4% (5/132) were other healthcare professionals, and 7% (9/132) did not disclose their profession. Staff who completed the online tool logged into the website version a mean of 1.65 times (SD: 1.4; median 1; interquartile range (IQR): 1–2; maximum: 12) and spent a median of 14.3 min (IQR: 10.1–28.2) on it. Although most users logged in only once (61%, 80/132), just under one-third logged in twice (30%; 40/175), and 9% (12/132) logged in three times or more.

Decision aid

Throughout the 12-week implementation, >75% of audited antibiotic prescriptions had applied the Decision Aid categories (Figure 1), exceeding the 50% target, with no evidence of variation over time post implementation (heterogeneity $P = 0.61$). More prescriptions using the Decision Aid were categorized as 'probable' rather than 'possible', but the proportion categorized as 'possible' increased over the 12-week implementation period (heterogeneity $P = 0.008$) (Figure 1).

Table II
Description of the local adaptation and implementation of the ARK (Antibiotic Review Kit) intervention components

| Component	Local adaptation and implementation
Online tool	— Approved by The Department of Medical Education to be available on the Trust's e-learning platform. — Approximately 1 month before implementation, the ARK Champion invited the 33 members of essential staff to complete the tool. — On implementation, the Medical Director sent a Trust-wide email inviting all medical staff to complete the tool. — Further e-mail invitations and publicity within the 12-week implementation period also contained a link to the online tool.

Decision Aid	— A new antibiotic prescription section of the paper drug chart was designed to incorporate the Decision Aid and containing an:
	   — initial prescription section with 'possible' and 'probable' categories, allowing a maximum of 3 calendar days of antibiotics;
	   — finalized prescription section, allowing 6 calendar days to be administered.
	 — In the 2 months prior to implementation it was piloted across a range of medical specialties and approval for the final design (Supplementary Figure S3) was gained from the Trust's Drugs and Therapeutics Committee (DTC) before implementation.
	 — During the study it was administered as an A4-size sticker placed over the existing antibiotic page of all drug charts in emergency department and acute medical unit but post implementation the DTC decided to incorporate the design permanently into the paper drug chart.

Data collection and feedback process	— Forums used included handover meetings, multi-disciplinary team meetings, governance meetings, teaching sessions and informally on the wards. — To reinforce understanding of the Decision Aid, a number of brief case vignettes based on current or recent inpatients were also discussed (Supplementary Figure S4).
Patient leaflet	— Approved by the Trust's DTC with the addition of local contact details and the Trust's logo. — Printed copies available in the acute medical unit's doctors' office, ward bays, and clinical room. — Healthcare professionals were encouraged through the online tool, posters, e-mail and feedback sessions, to give the leaflet to all patients who were prescribed antibiotics.
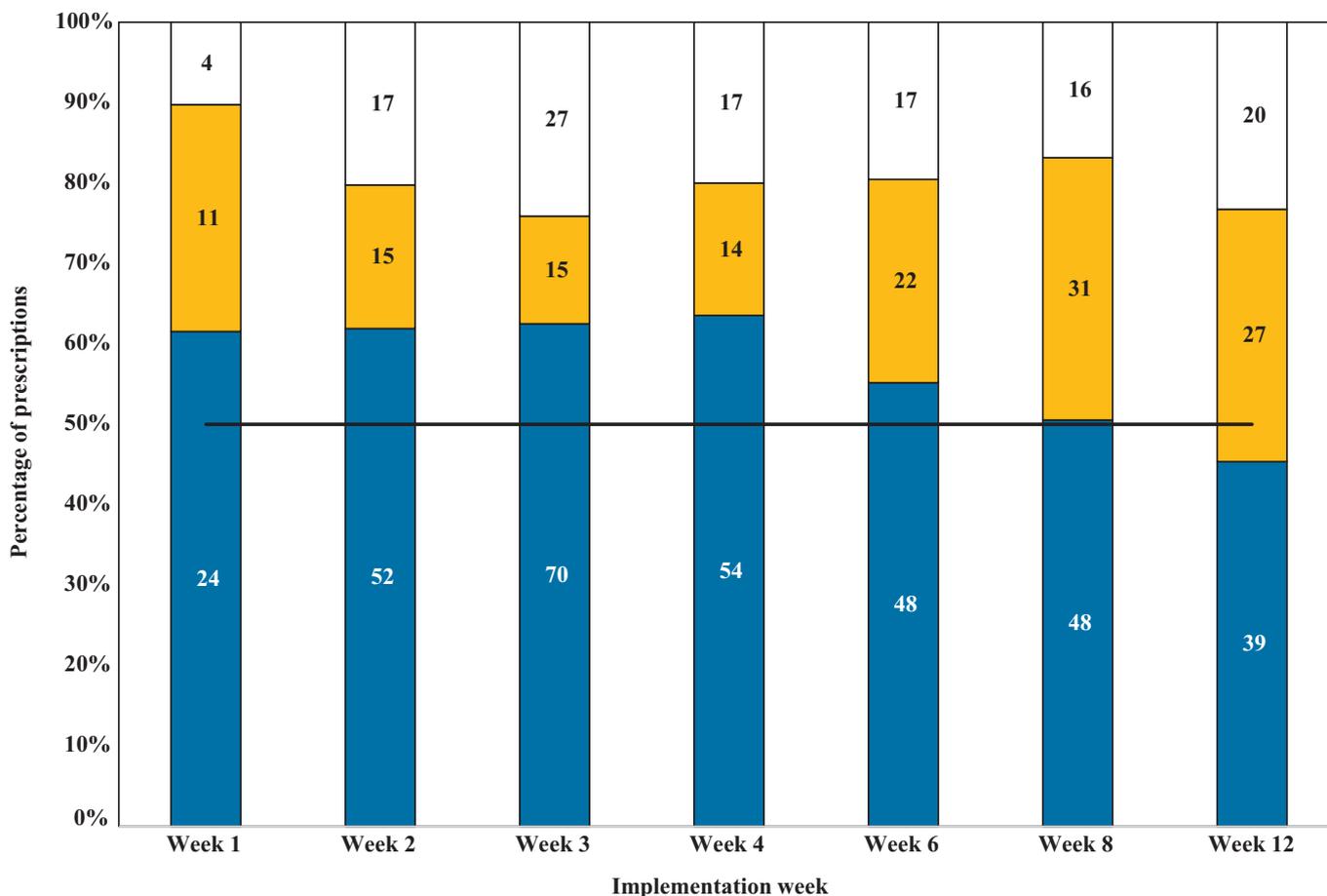
Figure 1. Categorization of initial antibiotic prescriptions following incorporation of the ARK (Antibiotic Review Kit) Decision Aid into the antibiotic prescription chart. White bars: no category; yellow bars: possible; blue bars: probable; black line: stop—go criteria for applying Decision Aid categories.

Data collection and feedback

During the 12-week implementation, the Core Team undertook 32 point-prevalence audits of antibiotic prescriptions using the ARK data collection tool, covering 107 prescriptions pre implementation (baseline) and 588 post implementation. Pre-implementation wards audited included acute medicine (27%; 29/107), respiratory (26%; 28/107), elderly care (32%; 34/107), endocrine (10%; 11/107), and haematology (5%; 5/107). Post-implementation prescriptions were audited on wards implementing ARK, namely elderly care (42%; 246/588), acute medicine (25%; 146/588), respiratory (16%; 92/588), endocrine (12%; 70/588), and gastroenterology (6%; 34/588). The Core Team delivered a total of 20 sessions to feed back antibiotic prescribing data across these four clinical teams.

Patient leaflet

All patients (N = 15) rated the leaflet highly on providing all the information they needed (mean score (maximum 7): 6.5; SD: 0.52), being helpful (6.4; SD: 0.63), trustworthy (6.5; SD: 0.64), and something they would recommend to others (6.2; SD: 0.86), with 13/15 (87%) stating that they would be likely or extremely likely to recommend the leaflet to friends and family taking antibiotics in hospital. The commonest method of dis-

tribution was in discharge medication bags, meaning that most patients only received the leaflet on discharge.

Impact on antibiotic review and decision-making

Review within 72 h of initial prescription

Throughout the 12-week implementation, >96% of prescriptions were reviewed within 72 h (Figure 2), remaining approximately stable over time (Fisher's exact P = 0.80). Overall review rates increased from 91% (69/76) at baseline to 99% (450/457) post implementation (odds ratio (OR) post vs pre implementation: 6.52 (95% CI: 2.22—19.16); P = 0.001).

Stopping antibiotics

The median antibiotic stop rate across audits post implementation was 36% (range: 29—40%) (Figure 2) remaining relatively stable over time (heterogeneity P = 0.87). Overall, the percentage stopping antibiotics by 72 h increased from 9% (6/69) at baseline to 35% (156/450) post implementation (OR: 5.57; 95% CI: 2.36—13.16; P < 0.001). Post implementation, antibiotic stop rates varied significantly according to the Decision Aid category, with 48% (51/106) of prescriptions categorized as 'possible' stopped by 72 h versus 29% (75/260)
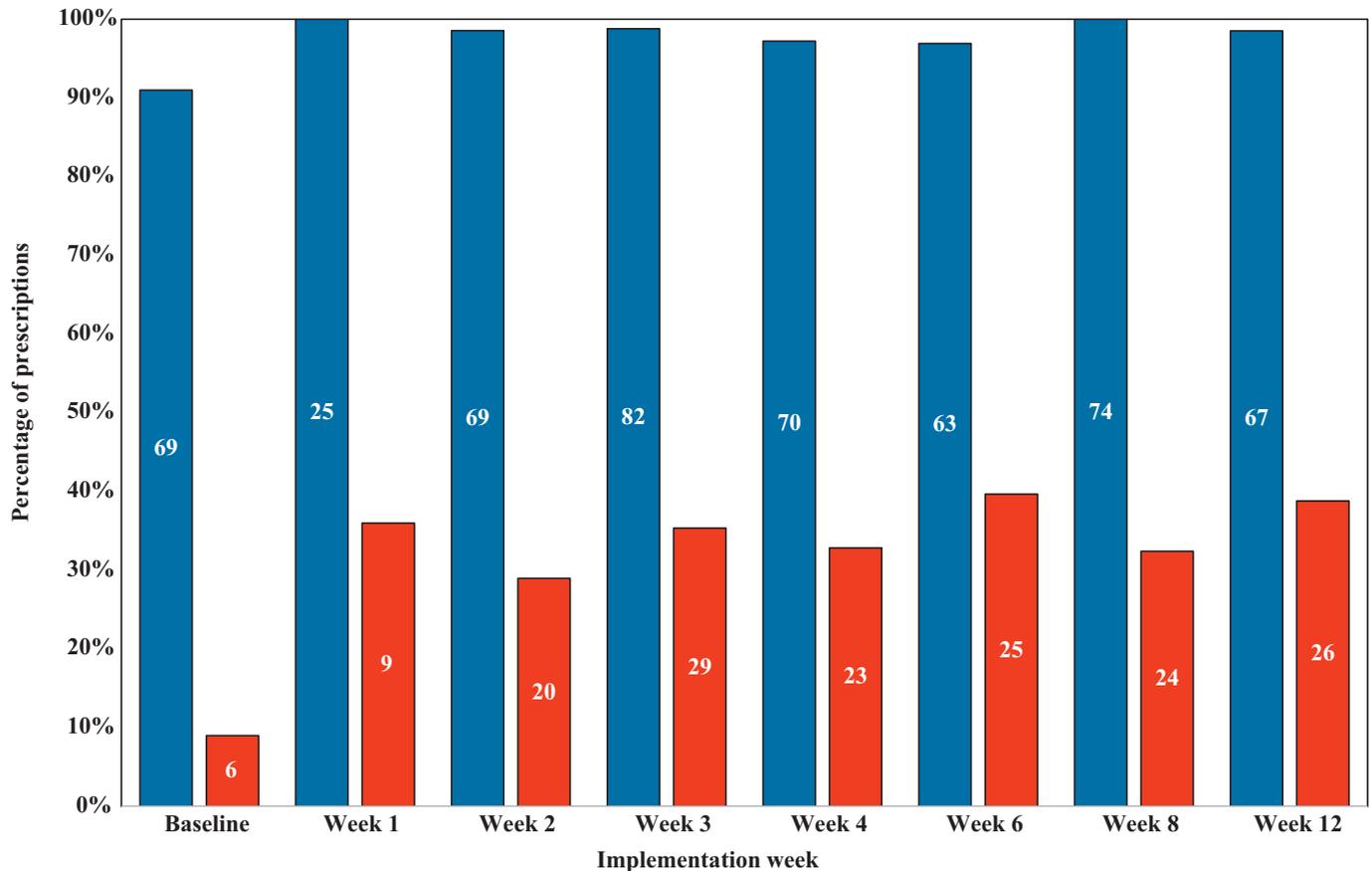
Figure 2. Rates of antibiotic prescription review (blue bars) and decisions to stop (red bars) within 72 h prior to and following implementation of ARK (Antibiotic Review Kit)-Hospital.

'probable' (OR (possible:probable): 2.29; 95% CI: 1.44—3.64; $P = 0.001$), compared with 36% (30/84) of prescriptions where the Decision Aid was not used.

Other actions taken at review

Over the 12-week implementation, the proportion of antibiotic prescriptions where no change was made declined (150/450 (33%) vs 37/69 (54%) baseline), as did the proportion switched to other agents (69/450 (15%) vs 15/69 (22%) baseline, $P = 0.71$ vs 'no change') (Figure 3). The proportion of antibiotics changed from intravenous to oral remained stable (75/450 (17%) vs 11/69 (15%) baseline; $P = 0.16$ vs 'no change'). There was no evidence that other actions depended on the Decision Aid category used ($P > 0.15$). No patient started outpatient parenteral antimicrobial therapy during the study.

Discussion

This study assessed the feasibility of implementing the novel, multi-faceted ARK intervention which has been developed to address overprescribing of antibiotics to hospitalized patients. The four elements of the intervention were successfully introduced into AMS practice at a medium-sized acute NHS hospital, facing typical pressures of under-staffing and patient burden [14]. The percentage of pre-specified essential staff who completed the online tool greatly exceeded the target

level for progression to full trial evaluation. The tool was also completed by a substantial number of front-line healthcare workers encompassing the main professional groups involved in antimicrobial treatment. The proportion of initial prescriptions using the Decision Aid also substantially exceeded the target threshold at all time-points. Implementation of ARK was associated with a substantial and sustained increase in antibiotic stop rates over the 12-week study period. The sustained use of the Decision Aid and the Trust's decision to adopt it into the antibiotic prescribing process, both long-term and Trust-wide, attest to the acceptability of the intervention. The increase in the proportion of prescriptions categorized as 'possible' over time may be related to an improved understanding of the Decision Aid categories over the course of the intervention; the importance of the 'possible' category in enabling prescribers to change antibiotic prescriptions at review was repeatedly emphasized during feedback sessions. Patient questionnaire responses indicated that patients received the leaflet very positively; this was also confirmed by qualitative interviews with patients (F. Mowbray *et al.*, unpublished data). The AMS structures and processes were typical of acute NHS Trusts and remained so after the implementation of ARK, incorporating most core recommended elements [15].

Our study has important limitations. Most notably, as a feasibility study we were not seeking to establish whether the ARK intervention is effective in reducing antibiotic consumption itself. Antibiotic consumption across acute medical
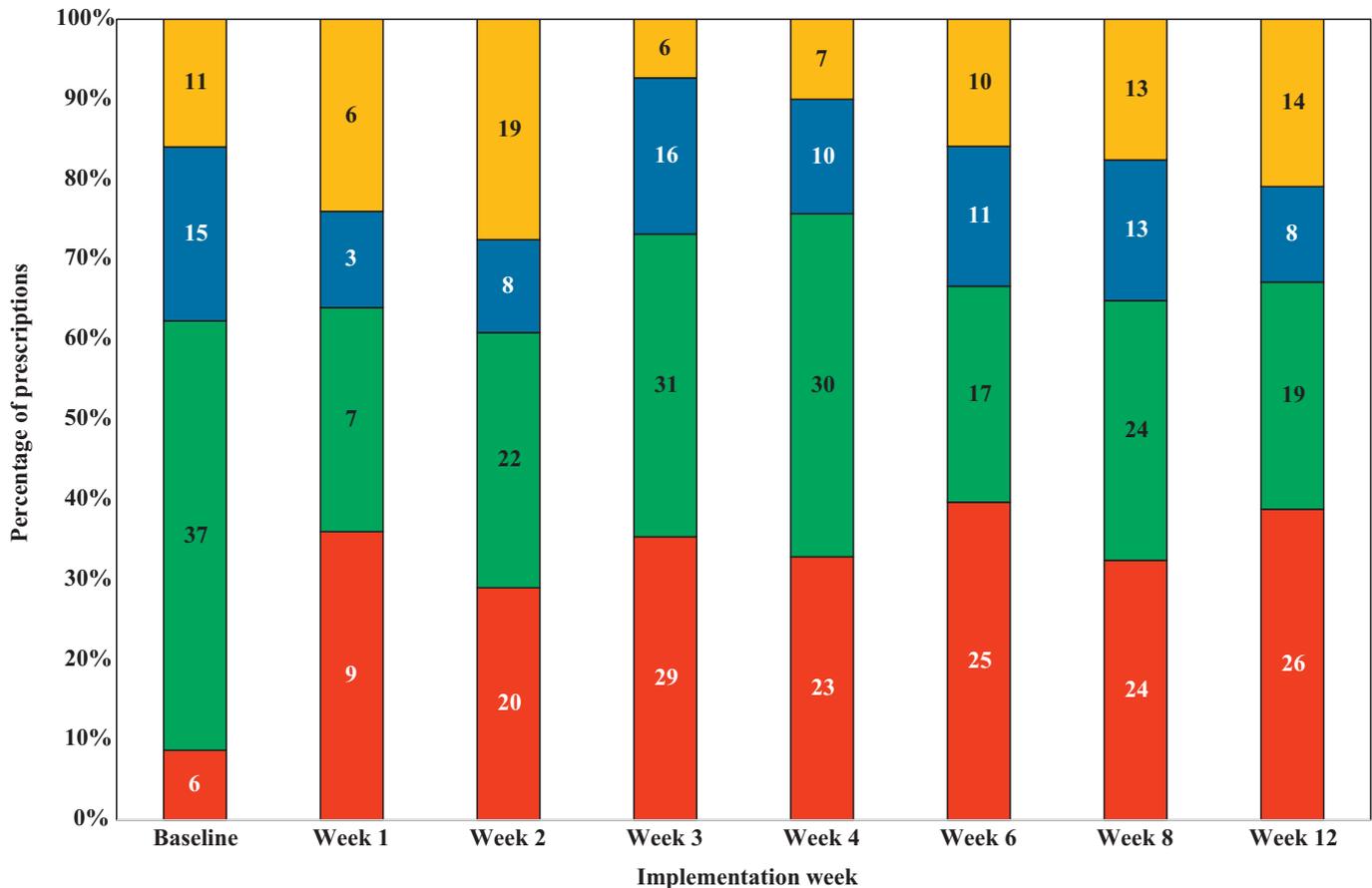
Figure 3. Percentage of audited antibiotic prescriptions stopped (red bars), unchanged (green bars), switched (blue bars), moved from intravenous to oral formulations (yellow bars). No patients started outpatient parenteral antibiotic therapy during the study.

patients at a hospital varies markedly month by month and over time, with strong seasonality. Assessment of ARK's impact on consumption requires thorough experimental evaluation, which will be achieved through a nationwide stepped-wedge cluster-randomized trial with prolonged follow-up to account for secular trends and to assess sustainability. For these reasons, we have not investigated patient-level outcomes. Robust assessment of safety in terms of preserving good clinical treatment outcomes while reducing antibiotic exposure is a key part of assessing a stewardship intervention and this will also be assessed in the full trial. Of note, the ARK intervention aims to support clinicians' 'review and revise' antibiotic decision-making in line with 'Start Smart then Focus' recommendations, rather than demonstrate whether this is, of itself, a safe and effective strategy to mitigate risks of antimicrobial overuse [4]. This approach closely follows recommendations followed in other healthcare systems, for example the CDC's Core Elements of Hospital AMS Programmes which include 'antibiotic time outs' to review prescribing decisions. Time-limiting initial antibiotic prescriptions has not, as far as we know, been evaluated in the NHS previously but has been found in the USA to reduce the total consumption of antibiotics and the use of inappropriate agents without negatively impacting mortality [16,17]. As a measure of acceptability of the online learning, we could have reported the proportion of staff who completed it using either the number of staff who work in the areas where ARK was implemented or of staff invited to do the

online learning. However, the way the learning was made available to healthcare workers involved in acute medicine and general medicine meant that neither of these denominators could be obtained. Using the proportion of key essential staff gives a reliable but restricted measure. We cannot discount the possibility that other staff members who could have been key influencers were not identified by the ARK Champion. However, this did not appear to have a negative impact on other study outcomes. The number of 19.4 staff trained per 100 acute beds is hard to interpret but the fact that 132 staff found time to do the online learning in a busy Trust indicates it is not overly burdensome. As this study was conducted at a single acute hospital site, the results cannot be generalized to non-hospital settings and may be less applicable to hospitals with different infrastructures, which may be the case in other countries.

Nonetheless, an important strength of our study is that we have been able to characterize the delivery and uptake of a novel multi-faceted intervention in a setting typical of the wider NHS environment in which its definitive evaluation will be undertaken. This study shows that the ARK intervention is adaptable and can be applied to other acute hospitals within the UK. It has informed how these sites can prepare for implementing ARK and has led to multiple additions to the implementation guidance, e.g. more emphasis on how to incorporate the patient leaflet component. All materials developed in this feasibility study (such as slide sets, e-mail and letter templates, poster and drug chart templates) form

the basis of a resources set that is available to sites implementing ARK during the full trial. Another product has been the establishment of a national network involving champions and their colleagues at sites involved in the full trial evaluation, a forum where they can communicate, and a repository where they can share resources.

In conclusion, we have established the feasibility and acceptability of a complex behaviour change intervention aimed at increasing the rate of antibiotic stop decisions among acute medical admissions at a single acute NHS Trust. There is promising evidence that the ARK intervention may be able to motivate and support better adherence to existing guidance to stop antibiotics at review. A nationwide stepped-wedge randomized controlled trial is currently underway to establish the impact of this intervention on antibiotic consumption and patient outcome.

Conflict of interest statement
None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2019.07.017.

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