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Tackling antimicrobial resistance in the community

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Introduction

This chapter provides an overview of why and how antimicrobial resistance (AMR) is being tackled through antimicrobial stewardship (AMS) activities in the community. We discuss the relevance of AMR to antibiotic prescribing in primary care services and for the health professionals who need to engage with AMS activities in order to help tackle AMR. We provide an overview of types of community-level interventions which have been trialled to help promote more prudent use of antibiotics and the evidence behind these. We highlight interventions which currently look to have the most potential and consider how to assess the cost-effectiveness of such interventions. Lastly we assess the challenges to implementing policy on AMS activities at the community-level.

Background

To avoid the increasing burden of AMR, all countries need to implement effective AMS strategies in order to tackle the overuse and misuse of antibiotics. Within the European Union (EU), all antibiotics for systemic use are only available through a prescription written by a qualified health professional. The vast majority of these prescriptions are issued in primary care, rather than secondary or tertiary settings. Across England three quarters of all antibiotics prescribed in 2015 through the National Health Service (NHS) were prescribed for patients seen in a general practice (74%) (Public Health England, 2016). This was followed by hospital inpatients (11%), hospital outpatients (7%), patients seen in dental practices (5%), and patients in other community settings (3%). Therefore, it is important that AMS strategies focus on community settings and target the relevant stakeholders providing and accessing community-based care.

Primary care doctors, or general practitioners (GPs), are the focus of the primary care literature since they are the most frequent prescribers of antibiotics. Nurse practitioners and pharmacists working in community settings also have an important role. In the past 10 years, the role of nurses has expanded to include prescribing in a number of countries and is on the policy agenda in many more (Ball et al., 2009; Hurlock-Chorostecki et al., 2014). Nurse prescribing has been introduced to better utilize the skills and knowledge of health professionals, allow more efficient access to medications and to help reduce the workload of doctors (Courtenay et al., 2014). In the UK, the numbers of nurses qualified to prescribe has steadily increased over the last 5 years and around 31 000 nurses now have the same prescribing capability as doctors (Courtenay et al., 2014). Pharmacists in the UK are also able to register as independent prescribers, usually specializing in prescribing for a particular health condition; for example, diabetes. It is more common for pharmacists to work in secondary care settings, rather than primary. Lastly, dentists are overlooked as prescribers of antibiotics due to the relatively small number of antibiotics prescriptions they give relative to their general practice colleagues. More recently, attention has been paid to dentistry with efforts to promote AMS strategies that encourage more prudent prescribing (Faculty of General Dental Practice, 2016).

Patients presenting in primary care with respiratory, urinary, skin, or tooth infections account for the majority of antibiotic prescriptions. Of these, most antibiotics are prescribed for acute respiratory tract infections (RTIs) (Goossens et al., 2005; Gulliford et al., 2014a; Shapiro et al., 2014). While antibiotics are effective for some RTIs (e.g. community-acquired bacterial pneumonia), the bulk of acute RTIs are self-limiting, as most are of viral origin. Empirical studies have shown that infections such as RTIs and sore throats benefit very little from antibiotics, which often reduce the duration of the symptomatic phase by only a few hours (Smith et al., 2014; Spinks et al., 2013). As such, there is a need to reduce the number of prescriptions for these types of, often viral, infections and empower patients to self-manage their symptoms. For other infections, such as urinary tract infections (UTIs) or skin infections, antibiotics may offer more benefit for patients (Albert et al., 2004; Yue et al., 2016). With these presentations, the aim of AMS strategies may not be to reduce antibiotic prescriptions but rather to encourage narrow-spectrum over broad-spectrum antibiotic use and first-line use where appropriate (Vellinga et al., 2016).

When considering how best to implement AMS, it is important to identify the specific behaviours being carried out by stakeholders in order to target them and encourage change. Health professional behaviour is most often focused on the act of prescribing an antibiotic. Within primary care, this behaviour usually involves a single health professional who assesses the patient and issues the prescription. This is opposed to secondary care, where a team of health professionals may provide a prescription with various actors undertaking different parts of a longer process (Charani et al., 2013). As mentioned before, changing prescribing behaviour can prevent prescription as a whole or involve a change in the prescription type, dose, or duration of treatment.

Once a patient has been given a prescription, they then have to use the prescription, collect the antibiotic, and take the antibiotic. Collecting the prescription and consuming the antibiotic can be seen as two distinct behaviours. However, the latter cannot occur without the former. The (self-reported) consumption of antibiotics is the most common behaviour measured in patients within randomized trials of AMS interventions (Spurling et al., 2017). Alongside antibiotic consumption, it is also important to consider patient behaviour prior to accessing health services. This help-seeking behaviour is potentially more influential on antibiotic prescribing because, if patients do not attend primary care services, they are very unlikely to be able to access antibiotics, ultimately decreasing consumption. Many public campaigns have focused on help-seeking behaviour by the public when implementing AMS strategies (Huttner et al., 2010; Earnshaw et al., 2009; Goossens et al., 2006).

Types of community interventions to tackle AMR and evidence for their effectiveness

Interventions to promote AMS may be identified by the stakeholder groups they target, such as clinicians, patients, or the public. Several multifaceted interventions may target more than one of these groups. The following sections discuss interventions with their main target group(s) in mind when considering the behaviour change of interest. Trials of different interventions are cited as examples of interventions which have worked to change antibiotic prescribing behaviour or consumption behaviour. A description of intervention types, their likely behavioural mechanisms, and evidence for each is presented in Table 3.1.

Table 3.1 *Community behaviour change interventions to target antimicrobial resistance*

Intervention type	Description ^a	Behavioural mechanisms	Example trials or reviews
Clinician-focused interventions			
Clinician education	<p>To include:</p> <ol style="list-style-type: none"> 1. Educational materials for clinicians: printed, electronic, or audiovisual materials that target the health care professional. 2. Educational meetings: health care professionals attending conferences, lectures, training courses, or workshops. 3. Educational outreach visits: health care professionals receiving information from a trained professional in their practice setting. 	<p>Increases clinician knowledge about appropriate antibiotic prescribing.</p> <p>Interactive sessions can increase motivation to change prescribing and increase self-efficacy in prescribing only when indicated.</p>	Van der Velden et al. (2012)
Audit and feedback	Any summary of clinical performance of health care over a specified time period provided to the health care professional.	Allows clinicians to self-monitor prescribing behaviour and to evaluate how well their prescribing matches guidelines and/or their peers. Provides motivation and opportunity to change by highlighting discrepancy in actual and desired behaviour.	Ivers et al. (2012)
Reminders	Verbal, written, or electronic information intended to prompt a health care professional to recall information, to include (computer) decision support systems.	An environmental cue, present at the time of a prescribing decision, designed to interrupt habitual or unconscious processes in clinician prescribing decisions and encourage alternative action.	Garg et al. (2005) Gulliford et al. (2014b)

Financial interventions	Targeting the health care professional (as an individual or a team) to include financial incentives (e.g. fee-for-service) and financial penalties (e.g. direct or indirect financial penalty for inappropriate behaviour).	Increasing clinician motivation to change their prescribing behaviour by incentivizing desired behaviour and/or punishing undesirable behaviour.	Greene et al. (2004) Martens et al. (2006)
Point-of-care tests	Equipment for use by health care professionals in their practice setting, to be used at the time and place of patient care, to provide rapid diagnostic information.	Provides additional clinical information which may decrease clinician uncertainty about diagnosis and/or appropriate management for a specific patient. May also be used as a communication technique to reassure patients that antibiotics are not needed.	Cals et al. (2009) Little et al. (2013) Andreeva & Melbye, 2013)

Clinician- and patient-focused interventions

Enhanced communication training	Any resource targeted at the health care professional and/or patient that encourages discussion about management options to include: <ol style="list-style-type: none"> 1. clinician-delivered patient educational interventions; 2. improved communication interventions (for clinician–patient interaction); 3. shared decision-making. 	Encourages explicit discussion about patient needs and expectations and the benefits and risks of taking antibiotics for the individual in order for the clinician to provide patient-centred care. May increase clinician self-efficacy in discussing management options with patients and may increase patient self-efficacy in self-managing symptoms.	Altiner et al. (2007) Cals et al. (2009) Little et al. (2013) Butler et al. (2012)
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Table 3.1 (cont.)

Intervention type	Description^a	Behavioural mechanisms	Example trials or reviews
Patient education materials	Educational materials for patients, or parents of child patients, designed to give new information in printed, electronic, or audiovisual form.	Increases patient or parent knowledge about the illness, symptoms and appropriate management. Likely to provide information about risks and benefits of antibiotics for specific conditions. May increase self-efficacy in self-management of illness.	Francis et al. (2009) Macfarlane Holmes & Macfarlane (1997)
Delayed prescribing strategies	Any resource targeted at the health care professional and/or patient that encourages giving a prescription for a patient to collect or use later than the initial consultation if symptoms do not improve.	Encourages additional explanation from the clinician to increase patient or parent knowledge about the illness and appropriate management. Can increase patient self-efficacy to self-care for their illness and empower patients to decide how to manage their symptoms.	Little et al. (2005) Spiro et al. (2006) De la Poza Abad et al. (2016)
Public-focused interventions			
National Campaigns	Any resource targeted at the health care professional, patient and/or member of the public at the population level employing varied use of communication.	Increases knowledge and awareness of appropriate antibiotic use and antibiotic resistance across several stakeholder groups and may decrease motivation to prescribe or consume antibiotics for self-limiting infections. May increase opportunities for people to discuss the use of antibiotics and/or provide patients with suggesting of questions to ask health care providers.	Huttner et al. (2010) Goossens et al. (2006)

^aDescriptions of interventions taken from Tonkin-Crine et al., 2017

Clinician-focused interventions

There are many types of intervention that have been designed to influence the antibiotic prescribing behaviour of clinicians. Interventions can take the form of a single component (e.g. a guideline) or can be multifaceted, combining a number of components which are complementary (e.g. an intervention utilizing guidelines, reminders, and audit and feedback).

The provision of clinician education is the basis for the majority of interventions. The success of clinical practice guidelines is dependent on their implementation (Carlsen et al., 2007). Guidelines are designed to improve the standard and consistency of health care and assume a knowledge deficit. However, guidelines that improve knowledge alone are unlikely to be enough to encourage significant behaviour change (NICE, 2007). Outreach visits can support guideline implementation by offering clinicians the opportunity to discuss the relevance of guidelines to their own patient population and to learn about the experiences of their peers. Such interaction can increase clinician motivation to change, and increase their confidence in changing their prescribing behaviour, which thereby increases self-efficacy. Research has shown that interventions containing educational meetings can be effective at changing clinician prescribing behaviour (van der Velden et al., 2012).

Audit and feedback involves monitoring clinicians' prescribing practices and then reporting back to the individual about their prescribing patterns. This can be helpful when clinicians underestimate the number or type of prescriptions given and can also enable comparisons between peers to demonstrate how prescribing could be improved safely. Audit and feedback interventions work by increasing motivation to change and by allowing clinicians to self-monitor their own prescribing, providing information which can be used to set clear prescribing goals. A Cochrane review found audit and feedback generally led to small but potentially important improvements in professional practice. However, the effectiveness of audit and feedback appeared to depend on baseline performance and how feedback was provided (Ivers et al., 2012).

Interventions may also involve the use of reminders for clinicians, often incorporated into computer software used within consultations. These systems commonly advise on the recommended treatment for a particular patient based on the information that has been entered. Such reminders can serve as a cue that interrupts habitual behaviour and makes clinicians more conscious of their decision-making process when

prescribing. Studies have indicated that computerized decision support systems can improve practitioner performance. Specifically, interventions using such a system have led to decreases in antibiotic prescriptions for RTIs (Garg et al., 2005; Gulliford et al., 2014b; Meeker et al., 2016).

Financial incentives are commonly used to influence clinical practice in areas identified as high priority by health organizations. Previous trials indicate that financial incentives can reduce antibiotic prescribing; however, changes may only be short-term (Greene et al., 2004; Martens et al., 2006). In UK general practice, prudent antibiotic prescribing practices have been endorsed through the introduction of the Quality and Outcomes Framework in 2004 and the Quality Premium in 2015. These initiatives enable general practices to obtain additional funding by meeting pre-set targets, often reducing all antibiotic prescribing by a specific percentage or decreasing the proportion of broad-spectrum antibiotic prescribing. Incentives increase motivation to change behaviour and may also present opportunities to change when supported with other initiatives. The Quality Premium 2015/16 contributed to two million fewer antibiotic prescriptions between April and December 2015 in England, down 7.9% from the previous year (NHS Commissioning Board, 2017).

Interventions may also focus on training clinicians to learn or develop their existing skills to encourage evidence-based prescribing decisions. The use of point-of-care tests (POCTs) in the community aims to provide additional clinical information by which a prescribing decision can be made more easily. These tests can make a clinician more confident in making a diagnosis or prescribing decision which increases their self-efficacy in not providing an antibiotic when it is not indicated. Commonly, trials have focused on testing C-reactive protein (CRP) POCTs and trials have suggested that these are effective in reducing antibiotic prescriptions for RTIs (Cals et al., 2009; Little et al., 2013; Andreeva & Melbye, 2014). Other studies have included the use of procalcitonin and rapid viral diagnostics to help clinicians distinguish between minor and more severe infections, although these have commonly been trialled in emergency departments (Schuetz et al., 2012; Doan et al., 2014). The use of POCTs in community health services varies across Europe, depending on the availability and reimbursement of these tests by health organizations, with tests commonly being used in Scandinavian countries where their costs are reimbursed (Dahler-Eriksen et al., 1997).

Clinician- and patient-focused interventions

Other skill-based interventions have focused on enhanced communication training for clinicians. These interventions also consider the patient role in the consultation and can include intervention components targeted at the patient. Communication training strategies have developed through the understanding that clinicians can overestimate patient expectations for antibiotics, which can contribute to unnecessary prescribing (Butler et al., 1998a; 1998b). Through specific communication techniques, eliciting patient expectations for treatment and concerns about their illness can help a clinician to provide reassurance and information about self-care rather than an unnecessary prescription. Trials testing interventions that contain communication skills training for clinicians, have shown effectiveness in reducing the number of antibiotic prescriptions for the treatment of RTIs (Cals et al., 2009; Little et al., 2013; Altiner et al., 2007; Butler et al., 2012).

Shared decision-making (SDM) is defined as the process of enabling a health professional and patient to make a joint decision about management based on the best available evidence and the patient's values and preferences (Coxeter et al., 2015). SDM, by definition, is specifically designed to target both the clinician and patient. It can involve a variety of techniques including discussing options, communicating benefits and risks, and checking or clarifying understanding (Makoul & Clayman, 2006). SDM is a relatively new term in the literature that also applies to older interventions using the same or similar techniques.

Similar to clinician educational materials, patient educational materials are also used to promote prudent antibiotic prescribing. Such materials may be used within communication-based interventions or alone. Patient educational materials are usually provided at the time of the consultation and may or may not be discussed by the clinician (Francis et al., 2009). In addition, materials may be focused on one type of infection (e.g. sore throats), a patient group (e.g. parents of young children), or on a range of infections across age groups. One large trial testing parent information booklets in UK general practice for children with RTIs showed a reduction in antibiotic prescribing (Francis et al., 2009). However, a previous trial with adult patients presenting with RTIs showed no difference in the trial arm using a patient booklet (Macfarlane, Holmes & Macfarlane, 1997). Patient information booklets have been used as a component of effective communication interventions, which

may suggest that patient materials need to be used interactively in the consultation in order to reduce prescribing practices (Little et al., 2013; Francis et al., 2009).

Delayed prescribing (DP) strategies target both clinicians and patients. DP can be implemented in two ways: patients are given the prescription immediately and get specific advice on when to use it or the prescription may be kept “on hold” for the patient to collect after a few days (Little et al., 2005). Interventions promoting DP look to encourage clinicians to issue delayed antibiotic prescriptions rather than immediate antibiotic prescriptions and to change the way the antibiotic prescription is discussed in the consultation. DP is considered appropriate for infections that are associated with self-limiting symptoms (e.g. sore throat, nasal discharge) or infections appearing to be more than a simple viral illness but with no established evidence of a bacterial infection that requires immediate treatment. When given a delayed prescription, a patient is given information about the likely duration of symptoms and is encouraged to only take antibiotics if symptoms continue for longer than expected or if symptoms worsen (Thompson et al., 2013). Following the consultation, DP strategies seek to change patient behaviour by allowing infections to resolve in their own time. This enables patients to learn that symptoms are self-limiting and increases their self-efficacy in management of their symptoms. Trials of DP strategies indicate significantly reduced consumption of antibiotics by patients compared to trial arms providing “immediate prescriptions” (Little et al., 2005; Spiro et al., 2006; De la Poza Abad et al., 2016).

Public-focused interventions

Public-focused interventions most often take the form of national campaigns, which are promoted during winter periods when infections are more prevalent. Most contain messages targeted at the public but may also include components that are tailored to clinicians and specific patient groups. In the UK, campaigns have been running regularly since 1999; however, many more European countries have been encouraged to conduct similar campaigns since the first European Awareness Day on 18 November 2008 (Earnshaw et al., 2009). Evaluations of campaigns in high-income countries, including Belgium and France, suggest that they may help to reduce antibiotic prescribing and consumption,

although these studies emphasize that benefits are likely to be seen in countries that are considered high prescribers and only if campaigns use specific behavioural and social marketing techniques to target specific populations (Huttner et al., 2010; Goossens et al., 2006).

Community-level interventions with most potential

As noted above, there have been numerous clinical trials of behaviour change interventions targeted at clinicians, patients, and the public testing their effectiveness in changing antibiotic prescribing or consumption behaviour. To date, certain types of interventions have been trialled more often than others due to initial interest from clinicians and policy-makers, the accessibility and cost of interventions, and the success of previous trials. This section will summarize the evidence to date, for three types of interventions that appear to show promise in tackling AMR in community settings (Table 3.2).

Enhanced communication strategies and shared decision-making

Shared decision-making (SDM) has been identified as a promising approach to tackling AMR since it involves both the clinician and the patient. This strategy can potentially be adapted for any community setting with minimal resources. A Cochrane review of nine randomized controlled trials (RCT) concluded that interventions that facilitated SDM reduced overall antibiotic use (prescription, dispensing, or consumption of antibiotics) for RTI consultations in primary care at time of consultation and up to six weeks after (Coxeter et al., 2015). The authors found that SDM interventions helped reduce antibiotic prescribing without increasing re-consultation for the same illness or affecting patient satisfaction. Seven of the trials were carried out in European general practice and two were carried out in Canadian primary care. Trials included adults and/or children. Another review focused on interventions that reduce antibiotic prescribing for RTIs in children and also identified that interventions which supported clinician–parent interaction in the consultation increased effectiveness in reducing prescribing (Vodicka et al., 2013).

Table 3.2 *A summary of systematic review evidence for three types of community-based antimicrobial stewardship interventions*

Intervention	Review of the evidence	Outcomes	Quality of evidence (GRADE ^a)	Summary
CRP point-of-care test versus usual care	Aabenhus, Costa & Vaz-Carneiro (2014)	Change in antibiotic prescription for RTI at consultation: RR 0.78 (0.66 to 0.92)	Moderate	Use of CRP testing probably reduces antibiotic prescribing in general practice and results in little or no difference in patient satisfaction or re-consultation.
		Patient satisfaction: RR 0.79 (0.57 to 1.08)	Moderate	
		Re-consultation: RR 1.08 (0.93 to 1.27)	Moderate	
Shared decision-making versus usual care	Coxeter et al. (2015)	Change in antibiotics prescribed or dispensed within 6 weeks of consultation: RR 0.61 (0.55 to 0.68)	Moderate	Use of shared decision-making probably reduces antibiotic use in general practice and results in little or no difference in patient satisfaction or re-consultation.
		Patient satisfaction: RR 0.86 (0.57 to 1.30)	Low	
		Re-consultation: RR 0.87 (0.74 to 1.03)	Moderate	
Delayed prescribing strategies versus immediate prescribing	Spurling et al. (2017)	Change in antibiotic use – delayed versus immediate antibiotic prescription: OR 0.04 (0.03 to 0.05)	Moderate	Use of delayed prescriptions probably reduces antibiotic use compared to immediate prescriptions in primary care settings and results in little or no difference in patient satisfaction or re-consultation.
		Patient satisfaction – delayed versus immediate antibiotic prescription: OR 0.65 (0.39 to 1.10)	Moderate	
		Re-consultation – delayed versus immediate antibiotic prescription: OR 1.04 (0.55 to 1.98)	Moderate	

^a GRADE: Grading of Recommendations, Assessment, Development and Evaluation (see <https://training.cochrane.org/resource/grade-handbook>)

Notes: CRP: C-reactive protein; RTI: respiratory tract infection; RR: relative risk; OR: odds ratio.

Point-of-care tests

C-reactive protein is the most common POCT that is assessed for its effectiveness in reducing antibiotic prescribing in community settings. Such experiments are typically conducted through control trials with comparison groups. A Cochrane review concluded that CRP testing is an effective way to reduce antibiotic prescribing for RTIs in primary care (Aabenhus, Costa & Vaz-Carneiro, 2014). Studies included in the reviews were carried out most often in European general practices and included adult patients with RTI symptoms. Additional Cochrane reviews have looked at the evidence for the use of procalcitonin and rapid viral diagnostics, indicating the effectiveness of the former but not the latter in decreasing antibiotic prescribing. However, these studies have mainly been conducted in emergency departments (Schuetz et al., 2012; Doan et al., 2014). Recent studies exploring diagnostic POCTs for respiratory viruses indicate that tests could positively influence the prescription of antibiotics by GPs, but that diagnostic accuracy needs to be improved and the influence on clinician decision-making should be further assessed (Bruning et al., 2017). Studies have also explored the implementation of such tests in community pharmacists and identified that offering such a test can improve access to care outside normal clinic hours (Klepser et al., 2017).

Delayed prescribing strategies

In a recent update of a Cochrane review, 11 studies that test DP strategies were identified. The result of DP was compared to both immediate prescribing and no-prescribing strategies for clinical outcomes, antibiotic use, and patient satisfaction (Spurling et al., 2017). Interventions encouraging clinicians to use DP resulted in lower antibiotic use than when an immediate use prescription was given. However, there was no difference between delayed and no-antibiotic prescribing in symptom control or disease complications. Patient satisfaction was greatest when either type of prescription was given. Authors recommended that clinicians should favour no-antibiotic prescribing when they feel confident an antibiotic is not required and encourage patients to re-consult if symptoms do not resolve. However, when clinicians are not confident in using a no-prescribing strategy, DP may help to reduce antibiotic consumption while maintaining patient satisfaction.

Examples of community-level interventions

It is useful to highlight some examples of successful primary care interventions that have been effective in reducing antibiotic prescribing and/or consumption in the community. This section describes three interventions, in detail, to identify the intervention components and mechanisms of behaviour change that contributed to the reduction in antibiotic use.

GRACE INTRO

The Genomics to combat Resistance against Antibiotics for Community-acquired LRTI (lower respiratory tract infection) in Europe/INternet Training for Reducing antibiOtic use (GRACE INTRO) project was an international programme of research carried out across several European countries. A component of GRACE INTRO involved the design and development of a multifaceted intervention to reduce antibiotic prescribing in general practice for acute cough in adults (Little et al., 2013).

The intervention, aimed to train GPs in 1) the use of a CRP POCT during the consultation to inform management decisions and 2) enhanced communication skills, with interactive use of a patient booklet in the consultation, to explain to patients when antibiotics were unlikely to benefit them (Anthierens et al., 2012). CRP training was proposed to help reduce clinician uncertainty about whether a patient would benefit from antibiotics. Clinicians received online tutorials on using the test and interpreting the results, and a visit from a representative of the test manufacturer. A desk reminder was provided to clinicians, giving CRP cut-off values and recommendations for treatment. When an antibiotic is not indicated for patient treatment, communication skills training and interactive use of a booklet was proposed to help clinicians identify patients' needs and concerns which could be addressed with self-management advice and reassurance.

The intervention was tested through a 2×2 factorial RCT across six countries and was shown to be effective at reducing antibiotic prescriptions compared to usual care (Little et al., 2013). Intervention practices received either one or both interventions, with use of both interventions resulting in the greatest decrease in the number of antibiotic prescriptions.

A process evaluation indicated that GPs felt reducing antibiotic prescribing was more important and less risky after taking part in the

study. It also found that GPs trained in communication skills were more confident in not prescribing antibiotics for an acute cough (Yardley et al., 2013; Anthierens et al., 2015). Patients in the intervention arms with the interactive booklet reported higher levels of enablement and satisfaction following their consultation compared to other trial arms (Yardley et al., 2013; Tonkin-Crine et al., 2014). Within the CRP intervention arms, there is some evidence that GPs used the tests to convince patients of a no-antibiotic decision rather than as a way to obtain additional clinical information (Tonkin-Crine et al., 2014).

EQUIP

The Enhancing the Quality of Information-sharing in Primary care (EQUIP) project focused on general practice consultations for children with RTIs. The project set out to evaluate whether training clinicians in the use of an interactive parent booklet could influence antibiotic use and rates of re-consultation for the same illness (Francis et al., 2008a).

The intervention used a booklet that was designed for clinicians to discuss with the parents of their patient during a consultation. The booklet went through a vigorous design and development process and included contributions from both parents and GPs. This enhanced its readability and enabled it to meet the required needs of both groups (Francis et al., 2008b). The booklet sought to inform parents about when antibiotics were required and to provide self-care advice for minor infections. It also included safety-netting advice for when parents should consult in primary care. The intervention also included online training for clinicians on how to use the booklet during consultations. This training encouraged clinicians to 1) identify the parents' main concerns and expectations and 2) explicitly discuss prognosis and treatment options. The intervention was tested through a cluster RCT and showed to be effective at reducing antibiotic prescribing by GPs and reducing parents' intention to re-consult without affecting parental satisfaction with care (Francis et al., 2009).

A process evaluation indicated that both clinicians and parents found intervention materials acceptable for use in daily practice (Francis et al., 2013). Intervention materials were thought to increase clinician confidence in discussing a no-prescribing decision and to increase parent confidence in self-caring for their child's RTI. Clinicians reported some barriers to using the booklet interactively in the consultation including

lack of familiarity with the booklet, lack of time, and difficulty modifying their consultation style.

Antibiotic Guardian

The UK's "Antibiotic Guardian Campaign", launched in September 2014, aimed to increase awareness and engagement with AMR by health professionals and the public (Ashiru-Oredope & Hopkins, 2015; Chaintarli et al., 2016). The campaign differed from previous UK campaigns in that it was available all year round rather than being seasonal only.

The campaign included a website where people could make online pledges to act to reduce AMR (<http://www.antibioticguardian.com>). A list of pledges relevant to health professionals or the public was available, and people could choose which pledge they wanted to make. Making an online pledge was hypothesized to bridge the intention-behaviour gap, identified in psychological literature as a barrier to behaviour change. This was accomplished by supporting people when making implementation intentions. These implementation intentions, presented as "if-when plans", help people to identify how they will act in a given situation. Examples for patients include: "If I'm prescribed antibiotics, I will take them exactly as prescribed and never share them with others", and for clinicians: "I will ensure all prescribers in my practice including locums have easy access to the local antibiotic guidance".

The impact of the campaign was assessed via an online survey sent to 9 016 self-selected "Antibiotic Guardians" to assess changes in self-reported knowledge and behaviour (Chaintarli et al., 2016). Two thirds of respondents reported that they had always acted on the pledge they made, around half of participants indicated that their knowledge of AMR had increased due to the campaign, and 70% reported that they felt some personal responsibility for AMR (compared to 58% at baseline).

Results indicated that the Antibiotic Guardian campaigns led to increases in self-reported knowledge of AMR and self-reported behaviour change in line with pledges. A process evaluation of the campaign indicated that people signed up out of personal concern about AMR (Kesten et al., 2018). Pledges encouraged reflection on AMR-related behaviours and keeping to pledges reflected new behaviour change and maintenance of existing behaviours. Responding collectively to a campaign was thought to have a greater impact than individual

action. However, respondents felt that the campaign needed greater visibility, especially to engage groups who are less familiar with AMR. Respondents were mostly health care professionals or people who were connected to the health care system and less than a third of respondents pledged as members of the public.

Assessing cost–effectiveness of community interventions

Uptake of AMS interventions in practice relies on a compelling health-economic justification. Health care budgets are limited, so investment in new interventions will inevitably come at the expense of other treatments. Health-economic analysis provides information on how the new intervention compares to what it will replace in terms of costs and benefits, thereby helping health providers align their investment decisions with their overall aims to provide the best possible health outcomes (Drummond, 2005).

There are four components to consider in assessing the cost–effectiveness of AMS strategies. First is effectiveness in reducing antibiotic prescribing. Second is effectiveness in terms of health outcomes. This is important because if a reduction in prescribing results in inferior health outcomes, this will need to be weighed against the value of reducing the health consequences of future AMR as well as against that of alternative interventions that may have improved health outcomes. The third component is cost. Many new interventions, such as POCTs, will cost more than the antibiotics they replace. For example, amoxicillin costs £1.02 for a three-week course while a CRP test costs £5.53, and if additional appointments are required the cost of those extra resources will quickly add up (Joint Formulary Committee, 2018; Hunter, 2015).

Cost–effectiveness studies that assess AMS strategies in terms of the above three components are increasingly common. However, most cost–effectiveness analyses continue to ignore the potential impact on AMR as an outcome or consequence entirely. For example, one study of UTI management evaluated the cost–effectiveness of strategies only in terms of reduction in symptom duration, despite UTI being a strong driver of antibiotic prescribing (Little et al., 2009).

The final component of AMR cost–effectiveness is the value of AMR itself. In economic terms, there is an opportunity cost to preventing AMR in terms of benefits foregone now, such as current health and cost savings. There is considerable uncertainty around both how much society

is willing to give up to avoid future AMR, and how much would be necessary to avoid it (Coast et al., 1996). Assuming that not all strategies simultaneously save costs, improve current health, and reduce AMR, these values are required to make a transparent judgement on whether AMS interventions are truly cost-effective.

There have been a small number of studies attempting to consider these outcomes in cost-effectiveness analysis. One study evaluated the proportion of societal costs attributable to AMR from a single prescription of antibiotics, based on global estimates of AMR costs found in three large analyses including the UK AMR review (O'Neill, 2016). They then applied this single cost to each prescription to give some idea of the opportunity cost of antibiotic prescriptions in RTI (Oppong et al., 2016). However, as yet studies are unable to provide valid results on the cost-effectiveness of AMS strategies and considerable methodological work in this area is still required.

Challenges to implementing policy

To date the majority of clinical trials have tested the effectiveness of community interventions which are targeted at general practice settings and focused on reducing antibiotic prescribing for RTIs. The vast majority of these trials have been carried out in high-income countries, with some conducted in middle-income countries such as China (Tonkin-Crine et al., 2017).

Previous trials carried out across Europe have indicated minimal differences in how interventions are accepted and implemented by health professionals and patients (Little et al., 2013). This is encouraging, as interventions have shown to be effective in different health care organizations and in health systems with different financial structures (e.g. services free at the point of care or insurance-based health care). However, the influence of culture and context on antibiotic use is currently underexplored and other studies have highlighted that such factors may be a barrier in transferring effective interventions from one context/country to another (Touboul-Lundgren et al., 2015). The current evidence in this area is limited in how readily it can apply to other low- and middle-income countries (Tonkin-Crine et al., 2017). Interpreting evidence for these settings is a barrier to policy-makers as there is a limited understanding of the contextual factors that influence antibiotic prescribing behaviour and antibiotic consumption behaviour.

Policy-makers should be cautious about assuming that an effective intervention in one context will be effective in another given differences in health care organization, culture, and/or country.

The evidence base is also limited for the long-term impact of interventions. Many trials have focused on short-term outcomes, either a few weeks or months post-intervention. Although these results are positive, it is difficult to establish whether interventions lead to long-term behaviour change or whether clinicians and patients eventually return to habitual pre-trial behaviours. Larger trials have observed interventions applied in clinical practice from 1 to 3 years to explore the subsequent long-term effect on prescribing rates (Little et al., 2005; Cals et al., 2013). These trials suggest that particular types of intervention are potentially more likely to support long-term behaviour change than other types. For example, the use of enhanced communication strategies is more likely to have an effect long-term than the use of CRP tests when reducing antibiotic prescribing for RTIs (Little et al., 2005; Cals et al., 2013). This suggests that interventions based on enhancing the skills of health professionals may be implemented more easily than use of novel technologies as there is potentially less disruption to clinical practice, and skills can be rehearsed and learnt more easily. The impact of the long-term effects of interventions needs to be researched more thoroughly and again may differ depending on the context of interest.

Conclusions

Interventions aimed at tackling AMR can target a number of behaviours carried out by different stakeholders, including in the course of consulting, prescribing, dispensing and consumption of antibiotics. Policy-makers wanting to tackle AMR should identify the specific behaviours that are going to have the greatest impact. To date, the literature has focused on RTIs in general practice, which account for the vast majority of antibiotic prescribing in Europe. However, for different contexts and countries, the target behaviour may be very different.

There are a number of influences on antibiotic prescribing and consumption behaviours. The clinical factors at patient presentation can be very similar between contexts; however, the social, cultural and environmental factors may be significantly different. Interventions need to address all of these influences to be effective at changing behaviour. As such, interventions being trialled in new contexts must take into account

the cultural and social preferences of the groups whose behaviour they are trying to change.

Community interventions that tackle AMR require further testing in primary care contexts outside general practice and in low- and middle-income countries where little is known about the influences on antibiotic-related behaviours.

References

- Aabenhus R, Jensen JU, Jørgensen KJ et al. (2014). Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. *Cochrane Database Syst Rev.* 11:CD010130.
- Albert X, Huertas I, Pereiró II et al. (2004). Antibiotics for preventing recurrent urinary tract infection in non-pregnant women. *Cochrane Database Syst Rev.* 4:CD001209.
- Altiner A, Brockmann S, Sielk et al. (2007). Reducing antibiotic prescriptions for acute cough by motivating GPs to change their attitudes to communication and empowering patients: a cluster-randomized intervention study. *J Antimicrob Chemother.* 60(3):638–644.
- Andreeva E, Melbye H (2014). Usefulness of C-reactive protein testing in acute cough/respiratory tract infection: an open cluster-randomised clinical trial with CRP testing in the intervention group. *BMC Family Pract.* 15:80.
- Anthierens S, Tonkin-Crine S, Douglas E et al. (2012). General practitioners' views on the acceptability and applicability of a web-based intervention to reduce antibiotic prescribing for acute cough in multiple European countries: a qualitative study prior to a randomised trial. *BMC Family Pract.* 13:101.
- Anthierens S, Tonkin-Crine S, Cals JW et al. (2015). Clinicians' views and experiences of interventions to enhance the quality of antibiotic prescribing for acute respiratory tract infections. *J Gen Int Med.* 30(4):408–416.
- Ashiru-Oredope D, Hopkins S (2015). Antimicrobial resistance: moving from professional engagement to public action. *J Antimicrob Chemother.* 70(11):2927–2930.
- Ball J, Barker G, Buchanan J (2009). Implementing nurse prescribing: an updated review of current practice internationally. Geneva: International Council of Nurses.
- Bruning AH, de Kruijf WB, van Weert HCPM et al. (2017). Diagnostic performance and clinical feasibility of a point-of-care test for respiratory viral infections in primary health care. *Fam Pract.* 34(5):558–563.

- Butler CC, Rollnick S, Kinnersley P et al. (1998a). Reducing antibiotics for respiratory tract symptoms in primary care: consolidating “why” and considering “how”. *Br J Gen Pract.* 48(437):1865–1870.
- Butler CC, Rollnick S, Pill R et al. (1998b). Understanding the culture of prescribing: qualitative study of general practitioners’ and patients’ perceptions of antibiotics for sore throats. *BMJ.* 317:637–642.
- Butler CC, Simpson SA, Dunstan F et al. (2012). Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial. *BMJ.* 344:d8173.
- Cals JW, Butler CC, Hopstaken RM et al. (2009). Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial. *BMJ.* 338:b1374.
- Cals JWL, de Bock L, Beckers PJ et al. (2013). Enhanced communication skills and C-reactive protein point-of-care testing for respiratory tract infection: 3.5-year follow-up of a cluster randomized trial. *Ann Fam Med.* 11(2):157–164.
- Carlsen B, Glenton C, Pope C (2007). “Thou shalt versus thou shalt not”: a meta-synthesis of GPs’ attitudes to clinical practice guidelines. *Br J Gen Pract.* 57(545):971–978.
- Chaintarli K, Ingle SM, Bhattacharya A et al. (2016). Impact of a United Kingdom-wide campaign to tackle antimicrobial resistance on self-reported knowledge and behaviour change. *BMC Pub Health.* 16:393.
- Charani E, Castro-Sanchez E, Sevdalis N et al. (2013). Understanding the determinants of antimicrobial prescribing within hospitals: The role of “prescribing etiquette”. *Clin Infect Dis.* 57(2):188–196.
- Coast J, Smith RD, Millar MR (1996). Superbugs: Should antimicrobial resistance be included as a cost in economic evaluation? *Health Econom.* 5(3):217–226.
- Courtenay M, Gillespie D, Lim R (2017). Patterns of dispensed non-medical prescriber prescriptions for antibiotics in primary care across England: a retrospective analysis. *J Antimicrob Chemother.* 72(10):2915–2920.
- Coxeter P, Del Mar CB, McGregor L et al. (2015). Interventions to facilitate shared decision making to address antibiotic use for acute respiratory infections in primary care. *Cochrane Database Syst Rev.* 11:CD010907.
- Dahler-Eriksen BS, Lassen JF, Lund ED et al. (1997). C-reactive protein in general practice – how commonly is it used and why? *Scand J Prim Health Care.* 15(1):35–38.

- De la Poza Abad M, Mas Dalmau G, Moreno Bakedano M et al. (2016). Prescription strategies in acute uncomplicated respiratory infections. *JAMA*. 176(1):21–29.
- Doan Q, Enarson P, Kissoon N et al. (2014). Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department. *Cochrane Database Syst Rev*. 9:CD006452.
- Drummond MF (2005). *Methods for the economic evaluation of health care programmes*, 3rd edn. Oxford: Oxford University Press.
- Earnshaw S, Monnet DL, Duncan B et al. (2009). European Antibiotic Awareness Day, 2008 – the first Europe-wide public information campaign on prudent antibiotic use: methods and survey of activities in participating countries. *Euro Surveill*. 14(30):19280.
- Faculty of General Dental Practice (2016). *Antimicrobial prescribing for GPs*. London: Faculty of General Dental Practice. (<https://www.fgdp.org.uk/guidance-standards/antimicrobial-prescribing-gdps> accessed 05 December 2019).
- Francis NA, Hood K, Simpson S et al. (2008a). The effect of using an interactive booklet on childhood respiratory tract infections in consultations: Study protocol for a cluster randomised controlled trial in primary care. *BMC Family Pract*. 9(1):23.
- Francis NA, Wood F, Simpson S et al. (2008b). Developing an “interactive” booklet on respiratory tract infections in children for use in primary care consultations. *Patient Educ Couns*. 73(2):286–293.
- Francis NA, Butler CC, Hood K et al. (2009). Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on re-consulting and antibiotic prescribing: a cluster randomised controlled trial. *BMJ*. 339:374–376.
- Francis NA, Phillips R, Wood F et al. (2013). Parents’ and clinicians’ views of an interactive booklet about respiratory tract infections in children: a qualitative process evaluation of the EQUIP randomised controlled trial. *BMC Family Pract*. 14:182.
- Garg AX, Adhikari NK, McDonald H et al. (2005). Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. *JAMA*. 293:1223–1238.
- Goossens H, Ferech M, Vander Stichele R et al. (2005). Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet*. 365(9459):579–587.
- Goossens H, Guillemot D, Ferech M et al. (2006). National campaigns to improve antibiotic use. *Eur J Clin Pharmacol*. 62(5):373–379.

- Greene RA, Beckman H, Chamberlain J et al. (2004). Increasing adherence to a community-based guideline for acute sinusitis through education, physician profiling, and financial incentives. *Am J Manag Care*. 10:670–678.
- Gulliford MC, Dregan A, Moore MV et al. (2014a). Continued high rates of antibiotic prescribing to adults with respiratory tract infection: survey of 568 UK general practices. *BMJ Open* 4:e006245.
- Gulliford MC, van Staa T, Dregan A et al. (2014b). Electronic health records for intervention research: A cluster randomized trial to reduce antibiotic prescribing in primary care (eCRT Study). *Ann Fam Med*. 12(4):344–351.
- Hunter R (2015). Cost-effectiveness of point-of-care C-reactive protein tests for respiratory tract infection in primary care in England. *Adv Ther*. 32(1):69–85.
- Hurlock-Chorostecki C, Forchuk C, Orchard C et al. (2014). Labour saver or building a cohesive interprofessional team? The role of the nurse practitioner within hospitals. *J Interprof Care*. 28:260–266.
- Huttner B, Goossens H, Verheij T et al. (2010). Characteristics and outcomes of public campaigns aimed at improving the use of antibiotics in outpatients in high-income countries. *Lancet Infect Dis*. 10(1): 17–31.
- Ivers N, Jamtvedt G, Flottorp S et al. (2012). Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev*. 6:CD000259.
- Joint Formulary Committee (2018). British National Formulary (online). London: BMJ Group and Pharmaceutical Press. (<http://www.medicinescomplete.com>, accessed 06 September 2018).
- Kesten JM, Bhattacharya A, Ashiru-Oredope D et al. (2018). The Antibiotic Guardian campaign: a qualitative evaluation of an online pledge-based system focused on making better use of antibiotics. *BMC Pub Health*. 18:5.
- Klepser DG, Klepser ME, Smith JK et al. (2017). Utilization of influenza and streptococcal pharyngitis point-of-care testing in the community pharmacy practice setting. *Res Social Adm Pharm*. 14(4):356–359.
- Little P, Rumsby K, Kelly J et al. (2005). Information leaflet and antibiotic prescribing strategies for acute lower respiratory infection. *JAMA*. 293(24):3029–3035.
- Little P, Turner S, Rumsby K et al. (2009). Dipsticks and diagnostic algorithms in urinary tract infection: development and validation, randomised trial, economic analysis, observational cohort and qualitative study. *Health Tech Assess*. 13(19):1–73.
- Little P, Stuart B, Francis N et al. (2013). Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a

- multinational, cluster, randomised, factorial, controlled trial. *Lancet*. 382(9899):1175–1182.
- Little P, Stuart B, Francis N (2017). Antibiotic prescribing for acute respiratory tract infections 12 months after internet-based training in communication skills and an interactive patient booklet, and in the use of a CRP point-of-care test: a multi-national cluster-randomised controlled trial. *Personal communication*.
- Macfarlane JT, Holmes WF, Macfarlane RM (1997). Reducing consultations for acute lower respiratory tract illness with an information leaflet: a randomized controlled study of patients in primary care. *Br J Gen Pract*. 47:719–722.
- Makoul G, Clayman ML (2006). An integrative model of shared decision making in medical encounters. *Patient Educ Couns*. 60:301–312.
- Martens JD, Werkhoven MJ, Severens JL et al. (2006). Effects of a behaviour independent financial incentive on prescribing behaviour of general practitioners. *J Eval Clin Pract*. 13:369–373.
- Meeker D, Linder JA, Fox CR et al. (2016). Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: A randomized clinical trial. *JAMA*. 315(6):562–570.
- National Institute for Health and Care Excellence (NICE) (2007). Behaviour change: general approaches. NICE public health guidance 6. London: NICE. (<https://www.nice.org.uk/guidance/PH6>, accessed 06 September 2018).
- NHS Commissioning Board (2017). Antibiotic prescribing quality premium 2016/17. London: NHS Commissioning Board. (<http://medicines.necu.nhs.uk/antibiotic-prescribing-quality-premium-201617/>, accessed 06 September 2018).
- O'Neill J (2016). Tackling drug-resistant infections globally: final report and recommendations. The Review on Antimicrobial Resistance. London: Wellcome Trust and Government of the United Kingdom. (<https://amr-review.org/Publications.html>, accessed 06 September 2018).
- Oppong R, Smith RD, Little P et al. (2016). Cost effectiveness of amoxicillin for lower respiratory tract infections in primary care: an economic evaluation accounting for the cost of antimicrobial resistance. *Br J Gen Pract*. 66(650):e633–e639.
- Public Health England (PHE) (2016). English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) 2010–2015: report 2016. London: Public Health England. (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/575626/ESPAUR_Report_2016.pdf, accessed 06 September 2018).

- Schuetz P, Müller B, Christ-Crain M et al. (2012). Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. *Cochrane Database Syst Rev.* 9:CD007498.
- Shapiro DJ, Hicks LA, Pavia AT et al. (2014). Antibiotic prescribing for adults in ambulatory care in the USA, 2007–09. *J Antimicrob Chemother.* 69(1):234–240.
- Smith SM, Fahey T, Smucny J et al. (2014). Antibiotics for acute bronchitis. *Cochrane Database Syst Rev.* 3:CD000245.
- Spinks A, Galsziou PP, Del Mar CB (2013). Antibiotics for sore throat. *Cochrane Database Syst Rev.* 11:CD000023.
- Spiro DM, Tay KY, Arnold DH et al. (2006). Wait-and-see prescription for the treatment of acute otitis media: a randomized controlled trial. *JAMA.* 296(10):1235.
- Spurling GKP, Del Mar CB, Dooley L et al. (2017). Delayed antibiotic prescriptions for respiratory infections. *Cochrane Database Syst Rev.* 9:CD004417.
- Thompson M, Vodicka TA, Blair PS et al. (2013). Duration of symptoms of respiratory tract infections in children: systematic review. *BMJ.* 347:f7027.
- Tonkin-Crine S, Anthierens S, Francis NA et al. (2014). Exploring patients' views of primary care consultations with contrasting interventions for acute cough: a six-country European qualitative study. *Prim Care Resp Med.* 24:14026.
- Tonkin-Crine S, Anthierens S, Hood K et al. (2016). Discrepancies between qualitative and quantitative evaluation of randomised controlled trial results: achieving clarity through mixed methods triangulation. *Implement Sci.* 11:66.
- Tonkin-Crine S, Tan PS, van Hecke O et al. (2017). Clinician-targeted interventions to influence antibiotic prescribing behaviour for acute respiratory infections in primary care: an overview of systematic reviews. *Cochrane Database Syst Rev.* 9:CD012252.
- Touboul-Lundgren P, Jensen S, Draai J et al. (2015). Identification of cultural determinants of antibiotic use cited in primary care in Europe: A mixed research synthesis study of integrated design “culture is all around us”. *Health behavior, health promotion and society.* BMC Pub Health. 15(1):908.
- van der Velden AW, Pijpers EJ, Kuyvenhoven MM et al. (2012). Effectiveness of physician-targeted interventions to improve antibiotic use for respiratory tract infections. *Br J Gen Pract.* 62(605):e801–e807.
- Vellinga A, Galvin S, Duane S et al. (2016). Intervention to improve the quality of antimicrobial prescribing for urinary tract infection: a cluster randomized trial. *CMAJ.* 188(2):108–115.

- Vodicka TA, Thompson M, Lucas P et al. (2013). Reducing antibiotic prescribing for children with respiratory tract infections in primary care: a systematic review. *Br J Gen Pract.* 63(612):e445– e454.
- Yardley L, Douglas E, Anthierens S et al. (2013). Evaluation of a web-based intervention to reduce antibiotic prescribing in six European countries: quantitative process analysis of the GRACE/INTRO randomised controlled trial. *Implement Sci.* 8:134.
- Yue J, Dong BR, Yang M et al. (2016). Linezolid versus vancomycin for skin and soft tissue infections. *Cochrane Database Syst Rev.* 1:CD008056.