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Optimising antimicrobial stewardship interventions in English primary care: a behavioural analysis of qualitative and intervention studies

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ABSTRACT

Objective While various interventions have helped reduce antibiotic prescribing, further gains can be made. This study aimed to identify ways to optimise antimicrobial stewardship (AMS) interventions by assessing the extent to which important influences on antibiotic prescribing are addressed (or not) by behavioural content of AMS interventions.

Settings English primary care.

Interventions AMS interventions targeting healthcare professionals' antibiotic prescribing for respiratory tract infections.

Methods We conducted two rapid reviews. The first included qualitative studies with healthcare professionals on self-reported influences on antibiotic prescribing. The influences were inductively coded and categorised using the Theoretical Domains Framework (TDF). Prespecified criteria were used to identify key TDF domains. The second review included studies of AMS interventions. Data on effectiveness were extracted. Components of effective interventions were extracted and coded using the TDF, Behaviour Change Wheel and Behaviour Change Techniques (BCTs) taxonomy. Using prespecified matrices, we assessed the extent to which BCTs and intervention functions addressed the key TDF domains of influences on prescribing.

Results We identified 13 qualitative studies, 41 types of influences on antibiotic prescribing and 6 key TDF domains of influences: 'beliefs about consequences', 'social influences', 'skills', 'environmental context and resources', 'intentions' and 'emotions'. We identified 17 research-tested AMS interventions; nine of them effective and four nationally implemented. Interventions addressed all six key TDF domains of influences. Four of these six key TDF domains were addressed by 50%–67% BCTs that were theoretically congruent with these domains, whereas TDF domain 'skills' was addressed by 24% of congruent BCTs and 'emotions' by none.

Conclusions Further improvement of antibiotic prescribing could be facilitated by: (1) national implementation of effective research-tested AMS interventions (eg, electronic decision support tools, training in interactive use of leaflets, point-of-care testing); (2) targeting important, less-addressed TDF domains (eg, 'skills', 'emotions'); (3) using relevant, under-used BCTs to target key TDF domains (eg, 'forming/reversing habits', 'reducing negative emotions', 'social support'). These could be incorporated into existing, or developed as new, AMS interventions.

Strengths and limitations of this study

- The study combined systematic reviewing and behavioural analysis methods to assess qualitative and intervention studies. This novel approach allowed us to identify how well existing interventions address influences on antibiotic prescribing and potential improvements.
- We focused on developing recommendations for English primary care so generalisability of findings to other contexts may be limited.
- Behavioural analysis relies on the quality and completeness of available reports and does not account for potential differences in delivery, contexts or engagement with and receipt of interventions.

BACKGROUND

Optimising the use of antimicrobial medicines to control the spread of antimicrobial resistance (AMR) is a global and English public health priority.[1 2] Despite antibiotic prescribing in England slowly decreasing since 2014, the majority of antibiotics continue to be prescribed in primary care (72% in general practice in 2018),[3] with up to 23% estimated to be prescribed inappropriately, that is for self-limiting respiratory tract infections (RTIs) when antibiotics are not indicated or by using a suboptimal type of antibiotics (eg, broad instead of narrow spectrum).[4] While not all antibiotic prescribing is inappropriate, further optimising antibiotic prescribing behaviours (eg, by reducing

unnecessary antibiotics for self-limiting infections) in primary care remains important.

Many antimicrobial stewardship (AMS) strategies have targeted healthcare professionals' (HCPs) behaviours to optimise antibiotic prescribing. For example, an overview of systematic reviews identified 44 trials evaluating interventions targeted at antibiotic prescribing in primary care and found that the average effect size from these interventions tends to be small, with most interventions achieving about a quarter or less reduction in total antibiotic prescribing.[5] Recently, 39 nationally implemented interventions (with 22 targeted at prescribers) were identified that aimed at reducing antibiotic prescribing and use for RTIs in England alone.[6] Considering the large number of interventions and the typically modest effects, it would be informative to identify how well the interventions address influences on antibiotic prescribing and whether interventions have 'gaps' which could highlight areas for improvement.

Behavioural analysis offers one possible approach to assessing behaviour change interventions. It involves categorising determinants of (influences on) behaviour(s) and intervention components to link them to behavioural mechanisms of action. This can be done by using existing behavioural sciences frameworks that synthesise behaviour change theories and mechanisms. The Theoretical Domains Framework (TDF) is a synthesis of determinants of behaviour from existing behaviour change theories; it includes 14 domains of determinants of behaviour (box 1).[7] The Behaviour Change Wheel (BCW) is a synthesis of behaviour change theories with the COM-B model (capability, opportunity, motivation—behaviour) at the centre, and integrating it with nine intervention functions and seven policy categories (box 1).[8 9] The third helpful framework is the Behaviour Change Techniques (BCTs) Taxonomy (V.1) that includes 93 types of techniques ('active ingredients') to change behaviours.[10] These frameworks allow moving from focusing on specific intervention components to more general, abstract categories so that different types of interventions can be linked with behaviour change mechanisms and compared. For example, an AMS intervention may include the following component: explaining the link between antibiotic prescribing, AMR and future ineffective antibiotic treatment. We can identify a behaviour change mechanism that this component aims to facilitate by expressing it as a BCT 'providing information about health consequences' that works through 'education' (intervention function) by targeting change in 'beliefs about consequences' (TDF domain).

There is a risk that despite numerous AMS interventions, they may overlap in their content and target the same determinants of behaviour (TDF domains) using the same mechanisms (BCTs/intervention functions). Behavioural analysis allows recognising any overlap to help avoid potential duplication and identifying potential gaps: any influences which are not targeted or any BCTs and intervention functions that are underused.

Box 1 Summary of components of the behavioural sciences frameworks

Theoretical Domains Framework[7]—domains of determinants of behaviours

1. Knowledge
2. Skills
3. Social/professional role and identity
4. Beliefs about capabilities
5. Optimism
6. Beliefs about consequences
7. Reinforcement
8. Intentions
9. Goals
10. Memory, attention and decision processes
11. Environmental context and resources
12. Social influences
13. Emotion
14. Behavioural regulation

Behaviour Change Wheel[89] - Sources of behaviour (COM-B):

1. Capability (physical, psychological)
2. Opportunity (physical, social)
3. Motivation (automatic, reflective)

Behaviour Change Wheel[89] - Intervention functions:

1. Training
2. Restriction
3. Persuasion
4. Incentivisation
5. Environmental restructuring
6. Education
7. Coercion
8. Enablement
9. Modelling

Behaviour Change Wheel[8 9]-Policy categories:

1. Guidelines
2. Environmental/social planning
3. Communication/marketing
4. Legislation
5. Service provision
6. Regulation
7. Fiscal measures

Such behavioural analysis methods have been used, for example, to assess interventions to prevent sepsis,[11] catheter-associated urinary tract infections,[12] AMS interventions targeted at public[13] and national AMS interventions.[6]

Building on a recent study that assessed the behavioural content of national AMS interventions in England,[6] the overall aim of this study was to identify possible ways to optimise AMS interventions in English primary care. To achieve this we aimed to assess the extent to which current national and research interventions addressed influences on antibiotic prescribing (and identify any potential gaps) by addressing the following objectives:

1. Identify the influences on appropriate antibiotic prescribing.
2. Identify research interventions that are effective at reducing antibiotic prescribing.

3. Assess the extent to which national and effective, research-tested AMS interventions address key influences on antibiotic prescribing.

We focused on interventions targeting HCPs' antibiotic prescribing for RTIs in primary care (including general practices, out-of-hours (OOH), walk-in/urgent care centres and community pharmacies).

METHODS

The study was conducted in three stages. First, we conducted a rapid review of qualitative studies to identify perceived key influences on antibiotic prescribing. Second, we conducted a rapid review of intervention studies to identify research evidence on effective AMS interventions. We then compared these research interventions with previously identified national AMS interventions[6] to see which effective interventions have been already nationally implemented. Third, we conducted a behavioural analysis, using behaviour sciences frameworks and matrices, to compare the extent to which national and research AMS interventions (stage 2) address the key influences on antibiotic prescribing (stage 1). Discrepancies between the national and research interventions (stage 2), and between the key influences and behavioural content of interventions (stage 3) were used to develop recommendations for potential avenues for improving AMS interventions in England. We then consulted stakeholders about feasibility of different ways of improving AMS interventions (reported separately[14]). In stages 1 and 2, we used rapid review methods (ie, without full double screening and assessing study quality) because relevant and recent systematic reviews already exist; we used these reviews to identify individual studies and then searched for more recent studies (that were not included in previous reviews).

Stage 1: Rapid review of qualitative studies to identify influences on antibiotic prescribing

Search and study selection

Five electronic databases (Medline, Embase, PsycINFO, Cochrane Library and Cumulative Index to Nursing and Allied Health Literature (CINAHL)) were searched on 5 November 2018 (updated on 18 June 2020) using a detailed search strategy informed by previous research (online supplemental document 1).[15] Two searches were conducted: one to identify systematic reviews and one for primary qualitative studies.

We included systematic reviews of qualitative studies and primary qualitative studies of HCPs' self-reported views about antibiotic prescribing for RTIs in relevant settings (ie, general practice, OOH, walk-in/urgent care, community pharmacy). Conference abstracts, dissertations/theses, reviews without eligible studies and not in English were excluded. Due to time constraints and to identify studies most relevant to current practice in England, we included only studies published since January 2000 and conducted in the UK (studies conducted across the UK did not report findings for England alone). To further focus on influences on appropriate prescribing (rather than influences on the use of particular interventions), we excluded papers reporting process evaluations of and focused on specific interventions.

Titles and abstracts, and then full texts, were screened by AJB, with 20% independently double-screened by MW. Differences were discussed and resolved with ST-C. Primary qualitative studies were initially identified from the included systematic reviews. Since the most up-to-date systematic review searched for studies up to June 2016,[16] qualitative studies identified in our database search published since 2016 were screened to identify more recent studies. All electronic search results were also searched specifically for studies conducted in OOH, walk-in/urgent care centres and community pharmacies.

Data extraction and analysis

We extracted data on study characteristics, aims and key findings, study design, methods, setting and participants. Included papers were uploaded to NVivo software (V.11). All data within each paper relevant to the research questions were included in the analysis, including authors' interpretations and direct participants' quotes. Three papers were independently coded by AJB, MW and ST-C using an inductive approach. After discussion, a coding framework was agreed and then used to code remaining papers. The codes were reviewed, discussed and arranged into higher level categories describing types of influences on antibiotic prescribing. The coded data were reviewed to identify whether each influence was described as a barrier or facilitator to appropriate antibiotic prescribing, or both.

We used the TDF[7] to categorise each barrier and facilitator to enable a comparison between the types of influences reported by HCPs and the types of influences targeted by AMS interventions. TDF domains were ranked based on: frequency (number of studies reporting influences within the domain); elaboration (number of types of influences identified within the domain); and evidence of 'bi-directionality' (when influences within the domain could act as either barriers or facilitators). The six highest ranked domains were considered to be the 'key TDF domains', following previous research.[12]

Stage 2: Rapid review of research studies to identify effective AMS interventions

Search and study selection

The same five electronic databases were searched on 5 November 2018 (updated on 25 June 2020) using a search strategy informed by previous research (online supplemental document 2).[15] Two searches were conducted: one to identify systematic reviews and one for primary studies.

We included systematic reviews and primary studies of AMS interventions targeting antibiotic prescribing or use for RTIs in relevant settings (ie, general practice, OOH, walk-in centres, community pharmacy). Any study design

was included, but papers had to report impact of interventions on changing antibiotic prescribing or use. As above, only studies published in English since January 2000 and conducted in the UK were included.

Titles and abstracts, and then full texts, were screened by AJB, with 20% independently double-screened by MW. Differences were discussed and resolved with ST-C. Individual studies were initially identified from the included systematic reviews. Since the most up-to-date systematic review searched for studies up to January 2018,[17] studies published in 2018 retrieved from our database search were screened to identify more recent studies. All electronic search results were also searched specifically for studies conducted in OOH, walk-in/urgent care centres and community pharmacy.

Data extraction and analysis

We extracted data on study characteristics, aims, study design, interventions and comparators, setting, participants and effectiveness of interventions on antibiotic prescribing/use. The data were summarised descriptively.

The identified research interventions were compared with the nationally implemented AMS interventions in England (identified previously[6]) to see which national interventions were evaluated and had evidence of effectiveness, and which effective research interventions have not been yet nationally implemented.

Stage 3: Analysis of behavioural content of AMS interventions (stage 2) to assess the extent to which they address the key influences on antibiotic prescribing (stage 1)

From the interventions included in the rapid review, we selected interventions that were shown effective (ie, with statistically significant effect of the intervention on reducing antibiotic prescribing). Studies of delayed antibiotic prescriptions were excluded as they targeted change in patient's antibiotic use and did not include behavioural strategies to influence HCPs' prescribing behaviour beyond the context of the trials (ie, in the identified studies, HCPs' randomly assigned eligible patients to different trial arms rather than choosing their prescribing strategy).

Intervention components were extracted into an Excel spreadsheet from the included papers and, where available, from published protocols and intervention development papers. Each component was retrospectively categorised using the TDF,[7] the BCW (intervention functions)[8 9] and BCTs taxonomy.[10] Data were extracted and coded by AJB and, where uncertain, checked by and discussed with MW, ST-C and LA. Behavioural content of the national AMS interventions was similarly extracted and categorised as part of the previous study.[6]

The TDF domains, intervention functions and BCTs in effective research interventions were summarised descriptively, and the numbers were compared between research and national AMS interventions. The TDF domains in effective research and national interventions were compared with the six key TDF domains to explore the extent to which interventions address influences on antibiotic prescribing (from stage 1).

A prespecified matrix[12] was used to link BCTs with theoretically congruent TDF domains. The six key TDF domains were listed with all potential BCTs theoretically congruent with each TDF domain based on the matrix.[12] The numbers of national and effective research interventions using each BCT within each TDF domain were identified. The percentages of BCTs used at least once out of all theoretically congruent BCTs in that domain were calculated. Following previous research,[12] high theoretical congruence between BCTs and TDF domains was defined as a BCT being paired with two or more of the theoretically matching key TDF domains (or with one key TDF domain if, according to the matrix, *only one* domain was theoretically linked to that BCT); medium congruence was defined as a BCT being paired with one key TDF domain (out of more than one domains theoretically linked in the matrix); low congruence was defined as a BCT not being paired with any key TDF domains.

Another prespecified matrix[8] was used to link intervention functions with TDF domains to compare the extent to which intervention functions of national and research interventions addressed the theoretically congruent key TDF domains.

RESULTS

Influences on antibiotic prescribing

Three relevant systematic reviews[16 18 19] and 10 studies (published after the most up-to-date review) were identified, resulting in 65 potentially eligible qualitative studies being screened. After full-text screening, 13 qualitative studies were included,[20–32] published between 2003 and 2017. Eleven studies were conducted in general practice, one in OOH,[31] and one in a walk-in centre.[26] Eleven studies involved general practitioners and five nurse and/or pharmacist prescribers. The update search in June 2020 identified 105 references, with one study matching the inclusion criteria (although it was not included in the analysis).[33] Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart is available in online supplemental document 3 and study characteristics in online supplemental document 4.

Forty-one types of self-reported influences on antibiotic prescribing were identified and organised into 14 categories (table 1). Within these influences, 49 barriers and 45 facilitators to appropriate prescribing were identified. Table 2 reports the six highest ranked TDF domains. There were no self-reported influences categorised with TDF domains 'optimism', 'goals' and 'behavioural regulation'.

Effective AMS interventions

Eighteen relevant systematic reviews[5 15 17 34–48] and 26 individual studies (published after the most up-to-date review) were identified, resulting in 48 potentially eligible studies being screened. After full-text screening, 17 studies were

Table 1 Influences on antibiotic prescribing

Types of influences	Influences on antibiotic prescribing
(1) Evidenceandeducation	1. Evidenceandguidelines 2. Peer discussionandlearning 3. GP training on antibiotic prescribing 4. Advice fromandinfluence of relevant experts
(2) Clinical experienceandconfidence	5. Clinical experienceandconfidence 6. Experience of and concern about adverse events resulting from prescribing decisions 7. GP's preference for certain antibiotics
(3) Clinical assessment	8. Clinical assessment of signsandsymptomsandmaking a diagnosis 9. Clinical uncertainty about illness aetiology, severity and/or progression 10. Patient's risk of complications or poor outcomes 11. Patient's perceptionandpresentation of illness 12. Access to patient's medical records or history 13. 'Gut feeling' (intuition) about patientandillness 14. Additional diagnostic information from testing
(4) Knowledgeandperceptions of the patient	15. Prior knowledge ofandfamiliarity with the patient 16. Perceptions of the patient 17. Ability to reassess or follow-up the patient (or lack of it) 18. Patient's social factors
(5) Perceptions of patient's expectationsandsatisfaction	19. Perceptions of patient's expectations of antibiotics 20. Preserving a good relationship with patient, patient satisfactionandavoiding conflict 21. Patient's preference for certain antibiotics
(6) Communication skillsandstrategies	22. Ability to elicitandmanage patient's concernsandexpectations 23. Ability to reassureandsafety-net 24. Perceived importance of shared decision making 25. Abilityandmotivation to educate patients in consultations
(7) Timeandworkload	26. Timing of consultationandaccess to GP/medical services 27. Time pressureandworkload (eg, wanting to save timeandprevent future consultations by educating patients; prescribing as a quicker way to close consultations than educating patients) 28. Consultation length
(8) Professional roleandethos	29. Perceptions of professional roleandethos
(9) Awarenessandperceptions of responsibility for AMS	30. Prioritising immediate pressures vs long-term consequences of inappropriate prescribing 31. Awareness/knowledge ofandattitude to AMS
(10) Monitoring, feedbackandaccountability	32. Use of monitoringandaudit 33. Receiving feedback on prescribing 34. Accountability for own prescribing (or its lack)
(11) Perceptions of ownandothers' prescribing	35. Perceptions of own prescribing as compared with others 36. Consistent approach to antibiotic prescribing between HCPs or organisations (or lack of it)
(12) Costs associated with prescribing	37. Perception of costs related to antibiotic prescribing
(13) Legal issues	38. Concern with legal issues (or patient complaints) resulting from not prescribing antibiotics

Continued

Table 1 Continued

Types of influences	Influences on antibiotic prescribing
(14) Attitudes toanduse of AMS strategies	39. Views onanduse of delayed antibiotic prescriptions 40. Access toanduse of patient leaflets 41. Use of financial incentives

AMS, antimicrobial stewardship ; GP, general practitioner; HCP, healthcare professional.

included,[49–65] published between 2000 and 2018. Thirteen were (cluster) randomised controlled trials,[49 52–57 61–66] two were pre–post studies,[51 58] and two were service evaluations without control groups.[59 60] Fifteen were conducted in general practice, one in an urgent care centre (evaluating C reactive protein point-of-care testing

Table 2 Ranking of Theoretical Domains Framework (TDF) domains

TDF domain (in ranking order)	Frequency * (max n=13 studies)	Elaboration † (number of influences)	Bidirectionality ‡	Types of influences on antibiotic prescribing
1. Beliefs about consequences	13	33	Yes	▶ Evidence and education ▶ Clinical experience ▶ Clinical assessment ▶ Knowledge and perceptions of patient ▶ Perceptions of patient expectations and satisfaction ▶ Time and workload ▶ Awareness and perception of responsibility for AMR ▶ Costs associated with prescribing ▶ Legal issues ▶ Attitudes to and use of AMS strategies
2. Social influences	12	13	Yes	▶ Knowledge and perceptions of patient ▶ Perceptions of patient expectations and satisfaction ▶ Communication skills and strategies ▶ Monitoring, auditing, feedback and accountability ▶ Perceptions of own and others' prescribing
3. Skills	11	8	Yes	▶ Communication skills and strategies ▶ Perceptions of patient expectations and satisfaction
4. Environmental context and resources	10	12	Yes	▶ Time and workload ▶ Perceptions of own and others' prescribing ▶ Attitudes to and use of AMS strategies
5. Intentions §	10	7	Yes	▶ Evidence and education ▶ Perceptions of patient expectations and satisfaction ▶ Communication skills and strategies ▶ Attitudes to and use of AMS strategies
6. Emotions ¶	10	3	Yes	▶ Clinical experience (eg, concern related to it) ▶ Legal issues (eg, concern with it)
7. Social / professional role and identity	8	10	Yes	▶ Perception of professional role and ethos ▶ Communication skills and strategies ▶ Monitoring, auditing, feedback and accountability **
8. Knowledge	7	6	Yes	▶ Evidence and education ▶ Awareness and perception of responsibility for AMR ▶ Monitoring, auditing, feedback and accountability**
9. Beliefs about capabilities	5	4	Yes	▶ Clinical experience and confidence
10. Memory, attention, decision processes	1	2	Yes	▶ Awareness and perceptions of responsibility for AMR (responding to immediate pressures over long-term consequences or vice versa) ††
11. Reinforcement	2	1	No	▶ Attitudes to and use of AMS strategies (use of financial incentives)

*Number of studies in which the TDF domain was identified.
†Number of influences identified in studies in each TDF domain.
‡Bidirectionality was when the influence could be either a barrier or a facilitator to appropriate prescribing (eg, the influence 'knowledge of evidence or guidelines' could be a barrier (ie, a lack of knowledge of evidence or guidelines) or a facilitator (ie, having knowledge of evidence and guidelines).
§TDF domain 'intentions' was double-coded with TDF domains 'skills' and 'beliefs about consequences'.
¶TDF domain 'emotions' was double-coded with TDF domain 'beliefs about consequences'.
**Some influences included in the theme 'Monitoring, auditing, feedback and accountability' were also double-coded with TDF domain 'social influences'.
††Some influences included in the theme 'Awareness & perceptions of responsibility for AMR' were also double-coded with TDF domain 'beliefs about consequences'.
AMR, antimicrobial resistance ; AMS, antimicrobial stewardship.

(CRP POCT)),[60] and one in a community pharmacy (evaluating sore throat test-and-treat service).[59] The update search in June 2020 identified 336 references, with none matching the inclusion criteria. PRISMA flow chart is available in online supplemental document 5 and study characteristics in online supplemental document 6.

Nine of these 17 interventions were effective in changing antibiotic prescribing.[50–58] They included: the 'STAR (Stemming the Tide of Antibiotic Resistance)' online communication skills training with a practice seminar[50]; online communication skills training and CRP POCT (together and separately, with biggest effect when combined)[56]; workshops about antibiotic prescribing, guidelines and 'TARGET' resources[57 58]; letters from the Chief Medical Officer (CMO) to the highest prescribing practices with feedback and suggested strategies to reduce prescribing[54]; electronic decision support tools[53]; FeverPAIN Clinical Score with and without rapid antigen detection testing[55]; use of interactive booklet for parents/carers of children presenting with RTIs[52]; and an evidence-based practice protocol for managing sore throats.[51] These nine effective interventions were included for behavioural analysis.

Comparison of national and research interventions

Twenty-six nationally implemented interventions targeting prescribers and community pharmacists in England were identified in previous research.[6] Four effective research interventions have been nationally implemented (table 3).

Behavioural content of AMS interventions

Table 4 summarises the behavioural content (TDF domains, intervention functions and BCTs) of the 26 national interventions (identified and analysed previously,[6] including the four effective research interventions), and of the five effective research-only interventions (31 in total). The content of each effective research intervention is reported in online supplemental document 7.

TDF domains

Interventions addressed all 14 TDF domains. The majority (81%) of interventions addressed 'knowledge', which was not a key influence (based on the ranking of self-reported influences identified in qualitative studies). Four of the six key TDF domains were addressed by several interventions. For example, 'skills' (55% of interventions) was addressed by providing training on communication and consultation skills and instructions related to antibiotic prescribing; 'environmental context and resources' (48%)—by adding objects (eg, leaflets, clinical scores) to practice environment; 'beliefs about consequences' (45%)—by providing information about benefits and harms of antibiotics, and impact on future consultations; 'social influences' (36%)—by using trusted (credible) sources to promote AMS and prudent prescribing, comparing prescribing rates between practices, providing support and encouragement (including peer discussions and sharing). The key domain 'intentions' was addressed by seven nationally implemented (23% of all) interventions (eg, by encouraging HCPs' intentions to review prescribing or make a pledge on the Antibiotic Guardian website), three of which were also effective research-tested interventions (ie, TARGET resources, CMO letters and STAR training). The key domain 'emotions' was addressed in only one intervention (ie, the nationally available Health Education England video comparing AMR to a terrorist attack).

Intervention functions

Interventions used eight (out of nine) intervention functions. 'Training' was used in 87% of interventions, for example, by providing training, instructions and demonstrations of relevant behaviours. 'Enablement' was used in 77% of interventions, for example, by providing support (eg, via meetings or forums to reflect on own practice and share good practice), patient leaflets (used as substitute for prescriptions) and facilitating action planning and monitoring of antibiotic prescribing. 'Education' was used in 74% of interventions, for example, by providing information about antibiotic prescribing, prescribing guidelines and AMR. 'Persuasion' was used in 12 nationally implemented interventions, three of which were also effective research-tested interventions (ie, TARGET resources, CMO letters and STAR training). 'Modelling' was used in three national interventions, two of which were also effective research interventions (ie, TARGET resources and STAR training). 'Coercion' was used in two national interventions (ie, via BCT 'future punishment' in the UK five-year AMR strategy and 'managing acute respiratory tract infection' e-module), but neither were research-tested. 'Restriction' was the only intervention function not used in any intervention.

Behaviour change techniques

Thirty-four BCTs were used in interventions; between 1 and 15 (mean 5) in national interventions, and 3–15 (mean 8) BCTs in research interventions. The majority (94%) of interventions included the BCT 'instruction on how to perform the behaviour'. In research interventions it was delivered, for example, by providing prescribing guidelines and instructions related to consultation skills, use of leaflets, CRP POC testing and use of other resources (eg, TARGET toolkit). BCT 'information about health consequences' was used in 55% of interventions, for example, by providing information about links between antibiotic prescribing and AMR or providing evidence about health-related outcomes of using or not using antibiotics for RTIs. Other commonly used BCTs (in over 25% of interventions) were: 'adding objects to the environment' (eg, patient leaflets, decision support tools, computer prompts, clinical scores), 'feedback on behaviour' (eg, feedback on antibiotic prescribing rates) and 'credible source' (eg, CMO or other trusted HCPs to communicate information about antibiotics). Only one BCT 'verbal persuasion about capabilities' was used in a

Table 3 Comparison of national and effective research antimicrobial stewardship (AMS) interventions

AMS interventions (national interventions identified in Ref. 6, effective research interventions identified in stage 2 rapid review)	Targeted at prescribers	Targeted at community pharmacy staff
National and effective research interventions		
1. CMO letters to high prescribing practices[54]	✓	
2. FeverPAIN (clinical score) (with/without rapid antigen detection test)[55]	✓	
3. TARGET online toolkit (the study involved workshops in general practices promoting TARGET toolkit)[57]	✓	
4. STAR online communications skills training (the study involved also a practice seminar; nationally available training is online only)[50]	✓	
National interventions (without research evidence of effectiveness)		
5. AMS Competencies	✓	
6. UK 5-year AMR strategy	✓	
7. NG15 (guideline)	✓	✓
8. NG63 (guideline)	✓	✓
9. NG79 (guideline)	✓	
10. NG84 (guideline)	✓	
11. NICE QS61 (quality standards)	✓	
12. NICE QS121 (quality standards)	✓	
13. NICE CG69 (guideline)	✓	
14. PHE managing infections (guideline)	✓	
15. Royal Pharmaceutical Society (RPS) AMS quick reference guide (guideline summary)		✓
16. PHE Fingertips (website with prescribing data)	✓	
17. PrescQIPP (website with prescribing data)	✓	
18. Centor (clinical score)	✓	
19. Managing Acute Respiratory Tract Infections e-module (online training)	✓	
20. Health Education England video for GPs (online training)	✓	
21. Centre for Pharmacy Postgraduate Education Antimicrobial stewardship e-module (online training)	✓	✓
22. The Learning Pharmacy (online training)		✓
23. UK Clinical Pharmacy Association/RPS professional practice curriculum (online training)	✓	
24. Antibiotic Guardian (campaign)	✓	✓
25. Antibiotic Action (campaign)	✓	
26. Treat Yourself Better with Pharmacist Advice (campaign)		✓
Effective research-only interventions (not nationally implemented)		
27. Electronic decision support tools[53]	✓	
28. CRP POCT (with/without communication skills training)[56]	✓	
29. Training and using interactive booklet ('When Should I Worry') with parents/cares of children with RTIs[52]	✓	
30. Evidence-based practice protocol for management of sore throats[51]	✓	
31. Workshops on antibiotic prescribing[58]	✓	

CMO, chief medical officer; CRP POCT, C reactive protein point-of-care testing; GP, general practitioner; NICE, National Institute for Health and Care Excellence; PHE, Public Health England
; RPS, Royal Pharmaceutical Society; RTI, respiratory tract infection.

Table 4 Summary of intervention content in national and research interventions

	National interventions (n=26) *	Research interventions (n=5) †	All interventions (n=31)
TDF domains (bold=key six TDF domains with a rank number)			
Knowledge	21	4	25
Skills (3)	12	5	17
Environmental context and resources (4)	12	3	15
Beliefs about consequences (1)	12	2	14
Behavioural regulation	13	0	13
Social influences (2)	7	4	11
Social/professional role and identity	6	1	7
Intentions (5)	7	0	7
Memory, attention, decision making	3	2	5
Reinforcement	4	0	4
Goals	2	1	3
Optimism	2	0	2
Beliefs about capabilities	1	0	1
Emotions (6)	1	0	1
Intervention functions			
Training	24	3	27
Enablement	19	5	24
Education	19	4	23
Persuasion	12	0	12
Incentivisation	5	4	9
Environmental restructuring	3	3	6
Modelling	3	0	3
Coercion	2	0	2
BCTs			
Instruction on how to perform the behaviour	24	5	29
Information about health consequences	14	3	17
Adding objects to the environment	9	3	12
Feedback on behaviour	7	2	9
Credible source	7	1	8
Action planning	6	1	7
Demonstrating the behaviour	4	3	7
Information about social, environmental consequences	5	2	7
Social comparisons	6	1	7
Social support (practical)	6	1	7
Identification of self as a role model	6	0	6
Self-monitoring of behaviour	6	0	6
Social support (unspecified)	2	4	6
Behavioural substitution	2	3	5
Feedback on outcome(s) of behaviour	5	0	5
Behavioural practice/rehearsal	3	0	3
Self-monitoring of outcomes	3	0	3
Prompts/cues	1	2	3

Continued

Table 4 Continued

	National interventions (n=26) *	Research interventions (n=5) †	All interventions (n=31)
Future punishment	2	0	2
Non-specific reward	2	0	2
Salience of consequences	2	0	2
Social/non-material reward	2	0	2
Commitment	1	0	1
Focus on past success	1	0	1
Framing/reframing	1	0	1
Goal setting	1	0	1
Material reward	1	0	1
Pharmacological support	1	0	1
Problem solving	1	0	1
Pros and cons	1	0	1
Restructuring the physical environment	1	0	1
Incentive	1	0	1
Monitoring of the behaviour by others	1	0	1
Verbal persuasion about capabilities	0	1	1

*Twenty-six national interventions identified in the previous project,[6] including four effective research interventions.
†Five effective research interventions identified in this project, without the four effective research interventions that were also nationally implemented.
BCT, behaviour change technique; TDF, Theoretical Domains Framework.

research intervention and not in any national intervention—all other BCTs used in research interventions were also already used in national interventions.

Theoretical congruence with key TDF domains

Based on a predefined matrix,[12] all six key TDF domains (identified on the basis of self-reported influences on antibiotic prescribing) were targeted by at least one congruent intervention function (online supplemental document 8). However, theoretical congruence was lacking between intervention function 'restriction' and linked key TDF domains 'social influences' and 'environmental context and resources' as the function was not used in any intervention.

Interventions contained most theoretically congruent BCTs within the TDF domains 'environmental context and resources' (67% of theoretically congruent BCTs), 'beliefs about consequences' (60%) and 'social influences' (60%) (table 5). There was a low proportion of potential, theoretically congruent BCTs used in the domain 'skills' (24%), with most interventions using one BCT 'instruction on how to perform the behaviour'. No theoretically congruent BCTs addressed the domain 'emotions'. Of the 34 BCTs identified in interventions, 16 BCTs had high and 14 medium theoretical congruence with key TDF domains, whereas 4 BCTs ('behavioural substitution', 'focus on past success', 'problem solving' and 'verbal persuasion about capabilities') had low congruence, meaning they were not linked with theoretically congruent key TDF domains (online supplemental document 9).

DISCUSSION

We identified 41 types of self-reported influences on antibiotic prescribing and six key TDF domains representing these influences. We next identified nine research-tested interventions effective at reducing antibiotic prescribing, with four already nationally implemented. All research interventions contained multiple behavioural components. Lastly, we compared the behavioural content of 31 (national and effective research) interventions with the six key TDF domains of influences. This behavioural analysis showed that interventions address all 14 TDF domains, 8/9 intervention functions and 34 BCTs (with 30 theoretically congruent with the key TDF domains). All BCTs except 'verbal persuasion about capabilities' used in effective research interventions were also used in national interventions. Interventions used most (50%–67%) theoretically congruent BCTs within the TDF domains 'environmental context and resources', 'beliefs about consequences' and 'social influences'.

Implications

We found that five effective research interventions have not been implemented nationally in England, with three

Table 5 Frequency of theoretically congruent behaviour change techniques (BCTs) within the key Theoretical Domains Framework (TDF) domains

BCTs theoretically congruent with the key TDF domains (based on a predefined matrix[12] †)	BCT frequency		% Potentially relevant BCTs used ¶
	National interventions (n=26) ‡	Research interventions (n=5) §	
TDF domain 1: beliefs about consequences			
Information about health consequences	14	3	60% (9/15)
Information about social and environmental consequences	5	2	
Salience of consequences	2	0	
Pros and cons	1	0	
Credible source	7	1	
Information about emotional consequences	0	0	
Covert sensitisation	0	0	
Anticipated regret	0	0	
Vicarious reinforcement	0	0	
Threat	0	0	
Comparative imagining of future outcomes	0	0	
Self-monitoring of behaviour	6	0	
Self-monitoring of outcome(s) of behaviour	3	0	
Feedback on behaviour	7	2	
Feedback on outcome(s) of behaviour	5	0	
TDF domain 2: social influences			
Social comparisons	6	1	60% (6/10)
Social support (practical)	6	1	
Social support (unspecified)	2	4	
Demonstration of the behaviour	4	3	
Social support (emotional)	0	0	
Information about others' approval	0	0	
Vicarious consequences	0	0	
Restructuring the social environment	0	0	
Identification of self as role model	6	0	
Social reward	2	0	
TDF domain 3: skills			
Instruction on how to perform the behaviour*	12	5	24% (4/17)
Demonstration of the behaviour	4	3	
Behavioural practice / rehearsal	3	0	
Pharmacological support*	1	0	
Graded tasks	0	0	
Habit reversal	0	0	
Habit formation	0	0	
Goal setting (outcome)	0	0	
Goal setting (behaviour)	1	0	
Monitoring by others without feedback	1	0	
Self-monitoring	6	0	
Reward (outcome)	0	0	
Self-reward	0	0	
Incentive	1	0	
Material reward	1	0	
Non-specific reward	2	0	
Generalisation of target behaviour	0	0	
TDF domain 4: environmental context and resources			

Continued

Table 5 Continued

BCTs theoretically congruent with the key TDF domains (based on a predefined matrix[12] †)	BCT frequency: National interventions (n=26) ‡	BCT frequency: Research interventions (n=5) §	% Potentially relevant BCTs used ¶
Adding objects to the environment	9	3	67% (4/6)
Restructuring the physical environment	1	0	
Discriminative cue	0	0	
Prompts/cues	1	2	
Avoidance/reducing exposure to cues for the behaviour	0	0	
Restructuring the social environment	0	0	
TDF domain 5: intentions			
Commitment	1	0	50% (1/2)
Behavioural contract	0	0	
TDF domain 6: emotions			
Reduce negative emotions	0	0	0% (0/5)
Information about emotional consequences	0	0	
Self-assessment of affective consequences	0	0	
Social support (emotional)	0	0	
Conserving mental resources	0	0	

*BCTs that were not included in the matrix,[12] but corresponded with that TDF domain in the coded intervention components.
†The BCTs were matched with theoretically congruent TDF domains based on the matrix developed previously and available elsewhere (p93,[12]). BCT 'biofeedback' was removed from the TDF domain 'beliefs about consequences' and BCT 'body changes' was removed from TDF domain 'skills' (despite being listed in the matrix) as they are considered not relevant to antimicrobial stewardship interventions, and therefore not 'possible' BCTs.
‡Twenty-six national interventions identified in the previous project,[6] including four effective research interventions.
§Five effective research interventions identified in this project, without the four effective research interventions that were also nationally implemented.
¶Proportion of all possible BCTs theoretically congruent with each TDF domain (according to the matrix[12]) that were used at least once in interventions.

of them also supported by international evidence from systematic reviews. Thus, wider implementation of these interventions may be route to improvement. These interventions include:

- Electronic decision support tools (accessed during consultations),[53] which are also supported by international evidence from systematic reviews.[17 42] The update search identified another study that evaluated a multifaceted intervention of electronically delivered prescribing feedback and decision support and showed safe and moderate reductions of antibiotic prescribing for adults with RTIs in UK general practices.[67]
- Training in the interactive use of 'When Should I Worry' booklets for parents/carers of children with RTIs[52]; the use of written information is supported by systematic reviews.[41 43]
- CRP POCT (with and without communication skills training and interactive use of a patient booklets),[56] which is supported by evidence from systematic reviews[5 17 42]; however, national implementation would need to consider specific barriers to adoption[14] and longer-term sustainability.[68] The update search identified a 12-month follow-up of the included intervention,[56] and showed that the initial improvement in antibiotic prescribing when using CRP POCT decreased, while the initially lesser effects of communication skills training were more sustainable.[68]
- Implementing evidence-based practice protocols for management of RTIs (although the evidence is from a pre–post study in one general practice).[51]
- Workshops on antibiotic prescribing, guidelines and promoting of online TARGET resources[58]; these are currently being rolled out more widely through training of TARGET trainers.[69]

While these interventions have not been nationally implemented in England, some (eg, CRP POCT) may have been implemented locally, depending on local priorities and resources. Some interventions (eg, developing and implementing specific practice-based protocols) may be more suited for local, tailored implementation. As antibiotic prescribing varies, specific, tailored interventions may be needed locally (and not necessarily nationally) to address particular issues in areas/practices with high prescribing. Implementation of interventions may also need to be tested locally before a national roll-out.

The behavioural analysis showed that current AMS interventions include a wide range of TDF domains, intervention functions and BCTs. However, the key TDF domains that are currently under-represented in AMS interventions could be addressed by a wider range of theoretically congruent BCTs; for example:

- The top TDF domain 'beliefs about consequences' is currently mainly addressed by BCT 'information about health consequences'; other congruent BCTs could be used, such as 'information about emotional consequences' (eg, resulting from providing good

care and educating patients by prescribing only when necessary) or 'comparative imagining of future outcomes'.

- Key TDF domain 'skills' is primarily addressed by BCT 'providing instructions'; other BCTs could also be used, for example, 'reversing and forming habits'.
- Key TDF domain 'intentions' could be addressed in more interventions by theoretically congruent BCTs, for example, 'commitment' or 'behavioural contract'.
- Key TDF domain 'emotions' is currently not addressed by theoretically congruent BCTs; interventions could include BCTs, such as 'reducing negative emotions' (eg, those related to not prescribing or concerns with medico-legal consequences) or 'social support (emotional)' (eg, providing encouragement or reassurance).
- Intervention function 'restriction' is currently not addressed in interventions, despite being congruent with the key TDF domains 'social influences' and 'environmental context and resources'; it could be addressed, for example, by making access to antibiotics more restricted than to alternative strategies for managing self-limiting illness (eg, leaflets) or adding barriers to immediate use of antibiotics (eg, using delayed/back-up prescriptions by post-dating or asking patients to collect them at a later date if needed).

Current, or new, interventions could also facilitate under-used behavioural mechanisms (ie, TDF domains and BCTs that are less commonly addressed/used); for example:

- TDF domain 'social/professional role and identity' could be facilitated, for example, by BCTs providing emotional 'social support' (eg, encourage perceiving self-care advice and patient education as central to HCPs' roles and address concerns perceived as undermining professional roles/expertise).
- TDF domain 'beliefs about capabilities', for example, by BCTs 'verbal persuasion about capabilities' (used in research but not in national interventions), 'focus on past success' or 'problem solving'.
- TDF domain 'memory, attention, decision making', for example, by BCTs 'prompts and cues' (eg, prompting self-care advice or delayed prescription instead of immediate antibiotics).
- TDF domain 'reinforcement', for example, by BCTs (material and non-material) 'incentives' or 'rewards'.

These suggestions should be considered carefully as there is currently no evidence on whether addressing more or fewer, and which, TDF domains, intervention functions and BCTs contribute to effectiveness of AMS interventions. Future research may test effectiveness of specific mechanisms and BCTs in changing behaviours related to AMS. Qualitative research suggests that multifaceted interventions (ie, combining multiple interventions within one approach) may be more attractive and helpful to clinicians, especially with components that help reflect on own prescribing, decrease clinical uncertainty, educate about appropriate prescribing and promote patient-centred care.[19] Such multifaceted interventions may provide better results, but more primary research evidence is needed.[5]

In addition to optimising the content of AMS interventions, it is important to increase engagement with these interventions. Consulting relevant stakeholders may help identify factors specific to implementation and engagement.[14 70] For example, high workloads, competing priorities and insufficient time were reported by HCPs as barriers to appropriate antibiotic prescribing,[27 29 31] and by stakeholders as barriers to engaging with current AMS interventions in England.[14] Thus, specifically targeting such barriers may improve both engagement and prescribing. More in-depth analysis focused on specific interventions (eg, involving both behavioural analysis and consultations with intervention users) may help identify implementation-specific opportunities for optimisation.[11 70]

It may also be informative to explore why interventions may be less or not effective. In our behavioural analysis of intervention content, we did not include interventions that were not shown effective (ie, with statistically significant reduction of antibiotic prescribing). However, most showed promising results. Two studies were small service evaluations of diagnostic testing without pre–post measures or comparators, but showing that a minority of patients tested required antibiotics.[59 60] One multifaceted intervention (web-based tool and printouts for carers) for children with RTIs showed higher rates of antibiotic prescribing in the intervention than control arm, but the authors considered this to be due to a differential recruitment (with more children with severe illness in the intervention arm).[49] Despite sometimes non-significant differences between trial arms testing delayed prescriptions (particularly those comparing different formats), studies showed that delayed prescriptions can safely reduce patients' use of antibiotics.[61–65] Further behaviour change interventions are also needed aimed at promoting prescribers' *choice* to use delayed prescriptions.

Finally, we found that the majority of the UK-based qualitative and intervention studies have been conducted in general practice. Only one identified intervention study was conducted in urgent care/walk-in centre, evaluating CRP POCT and showing promising results.[60] In community pharmacy, a sore throat test-and-treat service (using the Centor criteria and a throat swab) showed that only 9.8% patients tested were given antibiotics.[59] The update search identified two recent studies in community pharmacies. One piloted CRP POCT for RTIs and showed that the majority of tested patients were recommended to 'watch and wait' or self-care, rather than antibiotics.[71] The other evaluated a multifaceted intervention including AMS webinar and patient leaflets, and showed more frequent self-care advice and fewer referrals to general practice in the intervention arm.[72] Future research should focus more on understanding influences on antibiotic prescribing/use, and developing, testing and optimising

AMS interventions in primary care settings other than general practice.

Strengths and limitations

By using systematic methods for identifying and reviewing relevant literature, including evidence on effectiveness of interventions, we have extended the previous research on AMS interventions implemented in English primary care.[6] The study combined systematic reviewing with behavioural analysis methods, using a novel approach and established theoretical frameworks.[7–10] These were also supplemented by feedback from stakeholders and experts, reported previously.[14]

As up-to-date evidence from systematic reviews is available, we used rapid review methods (eg, studies' quality was not assessed). We aimed to develop suggestions for AMS interventions in England so we only included UK-based studies. The majority of studies identified were conducted in general practice. Thus, generalisability of findings and implications for other settings are limited. Influences on prescribing were identified only from qualitative studies of self-reports—it is possible that some influences on antibiotic prescribing were missed (eg, subconscious) or some were over-reported (eg, those most salient to participants). Conducting and reviewing other types of studies (eg, analyses of actual prescribing, predictors of prescribing or patients' perspectives) might lead to different influences being identified and ranked. We used prespecified criteria[12] to identify the key domains of influences—other domains of influences might also be important to address. Coding behavioural content of interventions depended (and was limited by) the reporting quality and did not account for differences in delivery, contexts or engagement with and receipt of interventions or BCTs. The relevance, importance and effectiveness of different BCTs or intervention functions may vary between types of interventions, behaviours and contexts. Links between constructs may also evolve as the frameworks, definitions and matrices develop.[73 74] Finally, we used the behavioural analysis tools retrospectively to assess the content of interventions that (except[54]) were not developed or reported using these frameworks (many published before the frameworks), so the coding relied on our interpretation of intervention components in behavioural terms. Such retrospective use of behavioural frameworks is common but it will be more precise and reliable as more researchers use these tools/frameworks to develop and describe behavioural interventions.

CONCLUSIONS

National and effective research AMS interventions in England address a relatively wide range of TDF domains, intervention functions and BCTs, and target the key types of influences on antibiotic prescribing. AMS in England may be further optimised by nationally implementing other effective interventions (eg, electronic decision support tools, training in interactive use of leaflets, point-of-care CRP testing) and by using additional theoretically congruent BCTs to target the less commonly addressed influences (eg, BCTs reversing and forming habits, reducing negative emotions or providing social support). Where appropriate, effective AMS interventions could also be adapted to, tested and implemented in other primary care settings (ie, OOH, urgent care, community pharmacies) where little research has been conducted.

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Online Supplemental Documents

Borek A, Wanat M, Atkins L, et al. **Optimising antimicrobial stewardship interventions in English primary care: a behavioural analysis of qualitative and intervention studies**. BMJ Open 2020. doi:10.1136/bmjopen-2020-039284

Contents

Supplemental Document 1. Search strategy to identify qualitative studies

The search strategy was performed in Medline database and adapted for other databases as necessary (with the same search terms).

1	exp Respiratory Tract Infections/
2	((respiratory or chest) adj3 (infect* or inflam*)).ti,ab.
3	(ARI or ARTI or URTI or LRT).ti,ab.
4	(pharyngit* or nasopharyngit* or naso-pharyngit* or rhinopharyngit* or rhino-pharyngit* or sinusit* or nasosinusit* or naso-sinusit* or rhinosinusit* or rhino-sinosit* or rhinit* or rhinorrhoea or rhinorrhea or ((runny or running or discharg* or congest* or blocked or stuff* or dripping or runn*) adj2 (nose* or nasal))).ti,ab.
5	((throat* adj3 (sore or pain or inflam* or infect*)) or tonsillit* or laryngit* or rhinolaryngit* or rhino-laryngit* or nasolaryngit* or naso-laryngit* or sinonasal* or sino-nasal*).ti,ab.
6	(croup or pseudocroup or tracheitis or tracheobronchit* or laryngotracheobronchit* or bronchit* or bronchiolit* or pneumon* or pleuropneumon* or bronchopneumon* or pleurisy).ti,ab.
7	(cough or sneez* or common cold).ti,ab.
8	(influenza or flu).ti,ab.
9	(otitis media or aom or ome or earache*).ti,ab.
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11	exp Anti-Bacterial Agents/
12	(antibiotic* or anti-biotic* or antibacterial* or anti-bacterial* or antimicrobial* or anti-microbial* or macrolide* or beta-lactam* or penicillin or methicillin or ampicillin or azithromycin or cephalexin).ti,ab.
13	11 or 12
14	Inappropriate Prescribing/
15	exp Prescriptions/
16	Practice Patterns, Physicians'/
17	(prescribing or prescription?).ti,ab.
18	((antibiotic* or anti-biotic* or antibacterial* or anti-bacterial* or antimicrobial* or anti-microbial* or macrolide* or beta-lactam* or penicillin or methicillin or ampicillin or azithromycin or cephalexin) adj3 ("use" or overuse or overprescri* or usage or consum* or uptake or delay* or demand? or reduc* or discontinu* or stop*)).ti,ab.
19	stewardship.ti,ab.
20	14 or 15 or 16 or 17 or 18 or 19

21 Ambulatory Care/ or exp Ambulatory Care Facilities/

22 exp general practice/ or exp general practitioners/ or exp physicians, family/ or exp physicians, primary care/ or exp Primary Health Care/ or exp Office Visits/

23 COMMUNITY PHARMACY SERVICES/ or PHARMACY/

24 Pharmacists/

25 (ambulatory adj3 (care or setting? or facilit* or ward? or department? or service?)).ti,ab.

26 ((general or family) adj2 (practi* or physician? or doctor?)).ti,ab.

27 (primary care or primary health care or primary healthcare).ti,ab.

28 (after hour? or afterhour? or "out of hour?" or ooh).ti,ab.

29 ((health* or medical) adj2 (center? or centre?)).ti,ab.

30 (clinic? or visit?).ti,ab.

31 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30

32 attitude/ or exp "attitude of health personnel"/ or exp attitude to health/

33 (attitude? or knowledge or view? or opinion? or experience?).ti,ab.

34 (barrier? or challeng* or obstacle? or facilitat* or enab* or opportunit* or implement*).ti,ab.

35 32 or 33 or 34

36 10 and 13 and 20 and 31

37 10 and 13 and 20 and 31 and 35

38 (Qualitative systematic review* or (systematic review and qualitative)).ti,ab.

39 (evidence synthesis or realist synthesis or realist review).ti,ab.

40 (Qualitative and synthesis).ti,ab.

41 (meta-synthesis* or meta synthesis* or metasynthesis).ti,ab.

42 (meta-ethnograph* or metaethnograph* or meta ethnograph*).ti,ab.

43 (meta-study or metastudy or meta study).ti,ab.

44 systematic review*.ti,ab. and qualitative research/

45 38 or 39 or 40 or 41 or 42 or 43 or 44

46 36 and 45

47 limit 46 to (english language and yr="2000 -Current")

48 qualitative research/

49 *interviews as topic/ or focus groups/ or narration/

50	observation.ti.
51	interview?.ti,ab.
52	(qualitative adj2 (interview* or study or research)).ti,ab.
53	qualitative.ti.
54	(focus group? or story or stories or narration or narrative* or discourse or discursive or grounded theory or ethnogra* or phenomenolog*).ti,ab.
55	"Surveys and Questionnaires"/
56	(questionnaire? or survey?).ti,ab.
57	48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56
58	37 and 57
59	limit 58 to (english language and yr="2000 -Current")
60	47 or 59

Note: Results of the search in line 47 were used to identify systematic reviews of qualitative studies, whereas results of the search in line 60 were used to identify individual qualitative studies.

Supplemental Document 2. Search strategy to identify research interventions

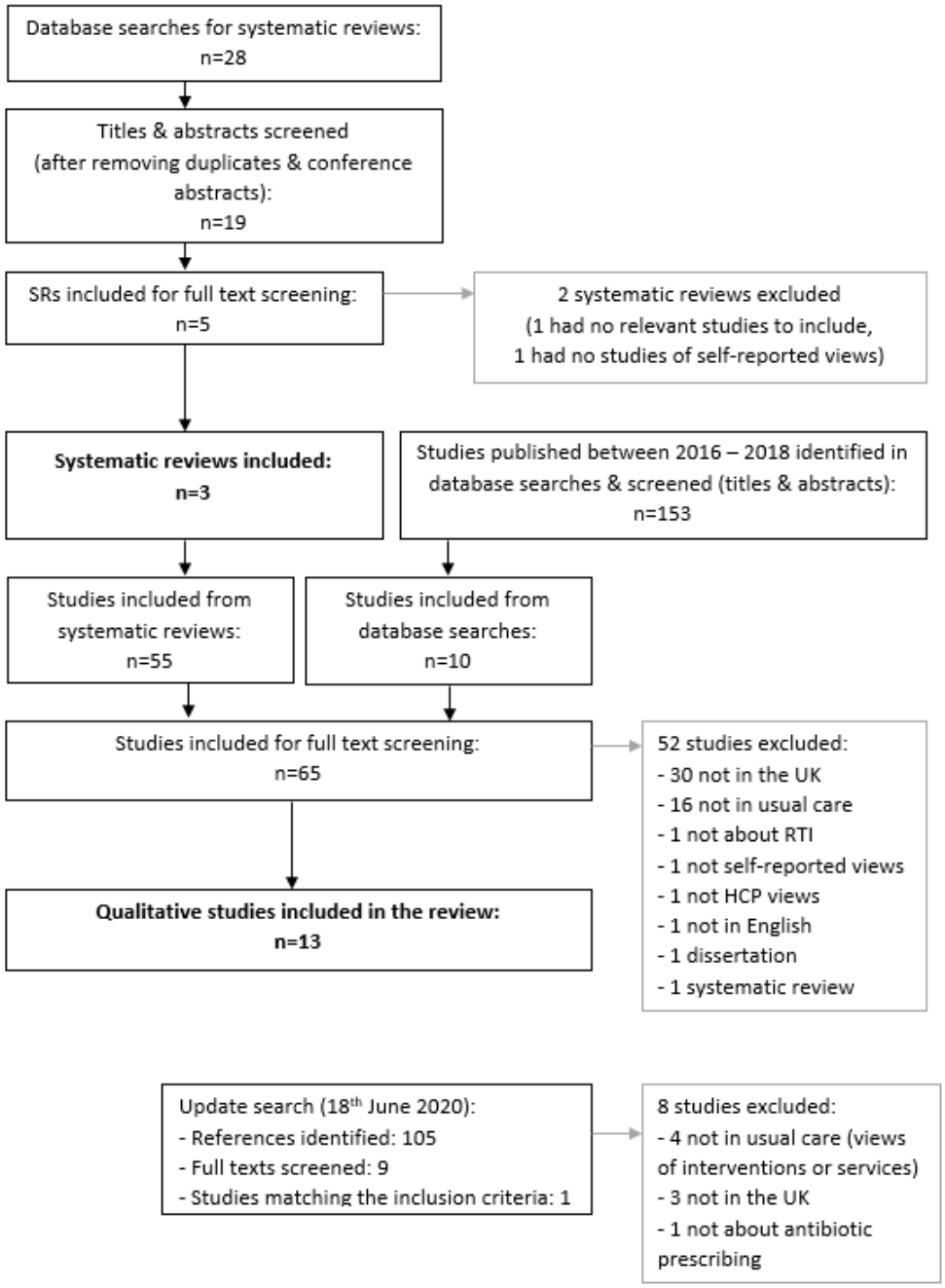
The search strategy was performed in Medline database and adapted for other databases as necessary (with the same search terms).

1	exp Respiratory Tract Infections/
2	((respiratory or chest) adj3 (infect* or inflam*)).ti,ab.
3	(ARI or ARTI or URTI or LRT).ti,ab.
4	(pharyngit* or nasopharyngit* or naso-pharyngit* or rhinopharyngit* or rhino-pharyngit* or sinusit* or nasosinusit* or naso-sinusit* or rhinosinusit* or rhino-sinosit* or rhinit* or rhinorrhoea or rhinorrhea or ((runny or running or discharg* or congest* or blocked or stuff* or dripping or runn*) adj2 (nose* or nasal))).ti,ab.
5	((throat* adj3 (sore or pain or inflam* or infect*)) or tonsillit* or laryngit* or rhinolaryngit* or rhino-laryngit* or nasolaryngit* or naso-laryngit* or sinonasal* or sino-nasal*).ti,ab.
6	(croup or pseudocroup or tracheitis or tracheobronchit* or laryngotracheobronchit* or bronchit* or bronchiolit* or pneumon* or pleuropneumon* or bronchopneumon* or pleurisy).ti,ab.
7	(cough or sneez* or common cold).ti,ab.
8	(influenza or flu).ti,ab.
9	(otitis media or aom or ome or earache*).ti,ab.
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11	exp Anti-Bacterial Agents/
12	(antibiotic* or anti-biotic* or antibacterial* or anti-bacterial* or antimicrobial* or anti-microbial* or macrolide* or beta-lactam* or penicillin or methicillin or ampicillin or azithromycin or cephalexin).ti,ab.
13	11 or 12
14	Inappropriate Prescribing/
15	exp Prescriptions/
16	Practice Patterns, Physicians'/
17	(prescribing or prescription?).ti,ab.
18	((antibiotic* or anti-biotic* or antibacterial* or anti-bacterial* or antimicrobial* or anti-microbial* or macrolide* or beta-lactam* or penicillin or methicillin or ampicillin or azithromycin or cephalexin) adj3 ("use" or overuse or overprescri* or usage or consum* or uptake or delay* or demand? or reduc* or discontinu* or stop*)).ti,ab.
19	stewardship.ti,ab.
20	14 or 15 or 16 or 17 or 18 or 19

21	Ambulatory Care/ or exp Ambulatory Care Facilities/
22	exp general practice/ or exp general practitioners/ or exp physicians, family/ or exp physicians, primary care/ or exp Primary Health Care/ or exp Office Visits/
23	COMMUNITY PHARMACY SERVICES/ or PHARMACY/
24	Pharmacists/
25	(ambulatory adj3 (care or setting? or facilit* or ward? or department? or service?)).ti,ab.
26	((general or family) adj2 (practi* or physician? or doctor?)).ti,ab.
27	(primary care or primary health care or primary healthcare).ti,ab.
28	(after hour? or afterhour? or "out of hour?" or ooh or walk-in or walkin).ti,ab.
29	((health* or medical) adj2 (center? or centre?)).ti,ab.
30	(clinic? or visit?).ti,ab.
31	21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32	10 and 13 and 20 and 31
33	limit 32 to "reviews (maximizes specificity)"
34	limit 33 to (english language and yr="2000 -Current")
35	randomized controlled trial.pt.
36	controlled clinical trial.pt.
37	randomized.ab.
38	placebo.ab.
39	clinical trials as topic.sh.
40	randomly.ab.
41	trial.ti.
42	35 or 36 or 37 or 38 or 39 or 40 or 41
43	exp animals/ not humans.sh.
44	42 not 43
45	32 and 44
46	limit 45 to (english language and yr="2000 -Current")

Note: Results of the search in line 34 were used to identify systematic reviews of research studies, whereas results of the search in line 46 were used to identify individual research studies.

Supplemental Document 3. Flow chart of selection process of qualitative studies



Supplemental Document 4. Characteristics of included qualitative studies

First author, year, title (reference)	Study aim	Design / Methods	Setting & Participants	Key findings (related to HCP views, based on paper abstracts)
Ashdown 2016, Prescribing antibiotics to 'at-risk' children with influenza-like illness in primary care: qualitative study (1)	To investigate GPs' accounts of factors influencing their decision-making about antibiotic prescribing in the management of at-risk children with influenza-like illness.	Semi-structured telephone interviews (with a case vignette); maximum variation sampling; thematic analysis	General practice: 41 GPs: 40 in England, 1 in Northern Ireland	There was considerable uncertainty and variation in the way GPs responded to the case and difference of opinion about how long-term comorbidities should affect their antibiotic prescribing pattern. Factors influencing their decision included the child's case history and clinical examination; the GP's view of the parent's ability to self-manage; the GP's own confidence and experiences of managing sick children and assessment of individual versus abstract risk. GPs rarely mentioned potential influenza infection or asked about immunisation status. All said that they would want to see the child; views about delayed prescribing varied in relation to local health service provision including options for follow-up and paediatric services.
Brookes-Howell 2012a, Clinical influences on antibiotic prescribing decisions for lower respiratory tract infection: a nine country qualitative study of variation in care (2)	To investigate clinicians' accounts of clinical influences on antibiotic prescribing decisions for LRTI to better understand variation and identify opportunities for improvement.	Semi-structured interviews (with a scenario to reflect); randomly selected sample; 5-stage (thematic) analytic framework approach	General practice: 80 GPs from the UK and 6 other countries, including: 6 GPs in	Four main individual clinical factors guided clinicians' antibiotic prescribing decision: auscultation, fever, discoloured sputum and breathlessness. These were considered alongside a general impression of the patient derived from building a picture of the illness course, using intuition and familiarity with the patient. Comorbidity and older age were considered main risk factors for poor outcomes. Clinical factors were similar across networks, apart from C reactive protein near patient testing in Tromsø. Clinicians developed ways to handle diagnostic and management uncertainty through their own clinical routines.

			England, and 8 GPs in Wales	
Brookes-Howell 2012b, Understanding variation in primary medical care: a nine-country qualitative study of clinicians' accounts of the nonclinical factors that shape antibiotic prescribing decisions for lower respiratory tract infection (3)	To investigate clinicians' accounts of non-clinical factors that influence their antibiotic prescribing decision for patients with LRTI, to understand variation and identify opportunities for addressing possible unhelpful variation.	Semi-structured interviews (with a scenario to reflect); randomly selected sample; 5-stage (thematic) analytic framework approach	General practice: 80 GPs from the UK and 6 other countries, including: 6 GPs in England and 8 GPs in Wales	Non-clinical factors imposed by the healthcare system operating within specific regional primary care research networks: patient access to antibiotics before consulting a doctor (Barcelona and Milan), systems to reduce patient expectations for antibiotics (Southampton and Antwerp) and lack of consistent treatment guidelines (Balatonfüred and Lódz). Secondly, accounts revealed factors related to specific characteristics of clinicians regardless of network (professional ethos, self-belief in decision-making and commitment to shared decision-making).
Cabral 2015, 'It's safer to ...' parent consulting and clinician antibiotic prescribing decisions for children with respiratory tract infections: an analysis across four qualitative studies (4)	To understand the drivers of parental consulting and clinician prescribing behaviour when children under 12 years consult primary care with acute RTI.	Cross-study analysis of 4 studies: A. focus groups with parents; (B. interviews with parents; C. interviews with clinicians on experiences of RTI consultations with children (ref. to conference paper);	General practice: Study C: 28 professionals, including 22 GPs and 6 nurses in England	Four overarching themes were identified: the perceived vulnerability of children; seeking safety in the face of uncertainty; seeking safety from social disapproval; and experience and perception of safety. The social construction of children as vulnerable and normative beliefs about the roles of parents and clinicians were reflected in parents' and clinicians' beliefs and decision making when a child had an RTI. Consulting and prescribing antibiotics were both perceived as the safer course of action. Therefore perception of a threat or uncertainty about that threat tended to lead to parental consulting and clinician antibiotic prescribing. Clinician and parent experience could influence the perception of safety in either direction, depending on

		D. systematic review synthesising parent and clinician views of prescribing for children with acute illness. Themes and common patterns identified across dataset through iterative approach, translating common themes across studies and re-organising themes into conceptual groups.		whether previous action had resulted in perceived increases or decreases in safety.
Cabral 2016, Influence of clinical communication on parents' antibiotic expectations for children with respiratory tract infections (5)	To understand clinicians' and parents' perceptions of communication within consultations for RTI in children and what influence clinician communication had	Video recordings of 60 consultations for children with RTIs and cough in 6 general practices; purposive sampling of 27 parents and 13	General practice: 13 clinicians, including 9 GPs, 3 nurse prescribers and 1 physician	While clinicians commonly told parents that antibiotics are not effective against viruses, this did not have much impact on parents' beliefs about the need to consult or on their expectations concerning antibiotics. Parents believed that antibiotics were needed to treat more severe illnesses, a belief that was supported by the way clinicians accompanied viral diagnoses with problem minimizing language and antibiotic prescriptions with more problem-oriented language. Antibiotic prescriptions tended to confirm parents'

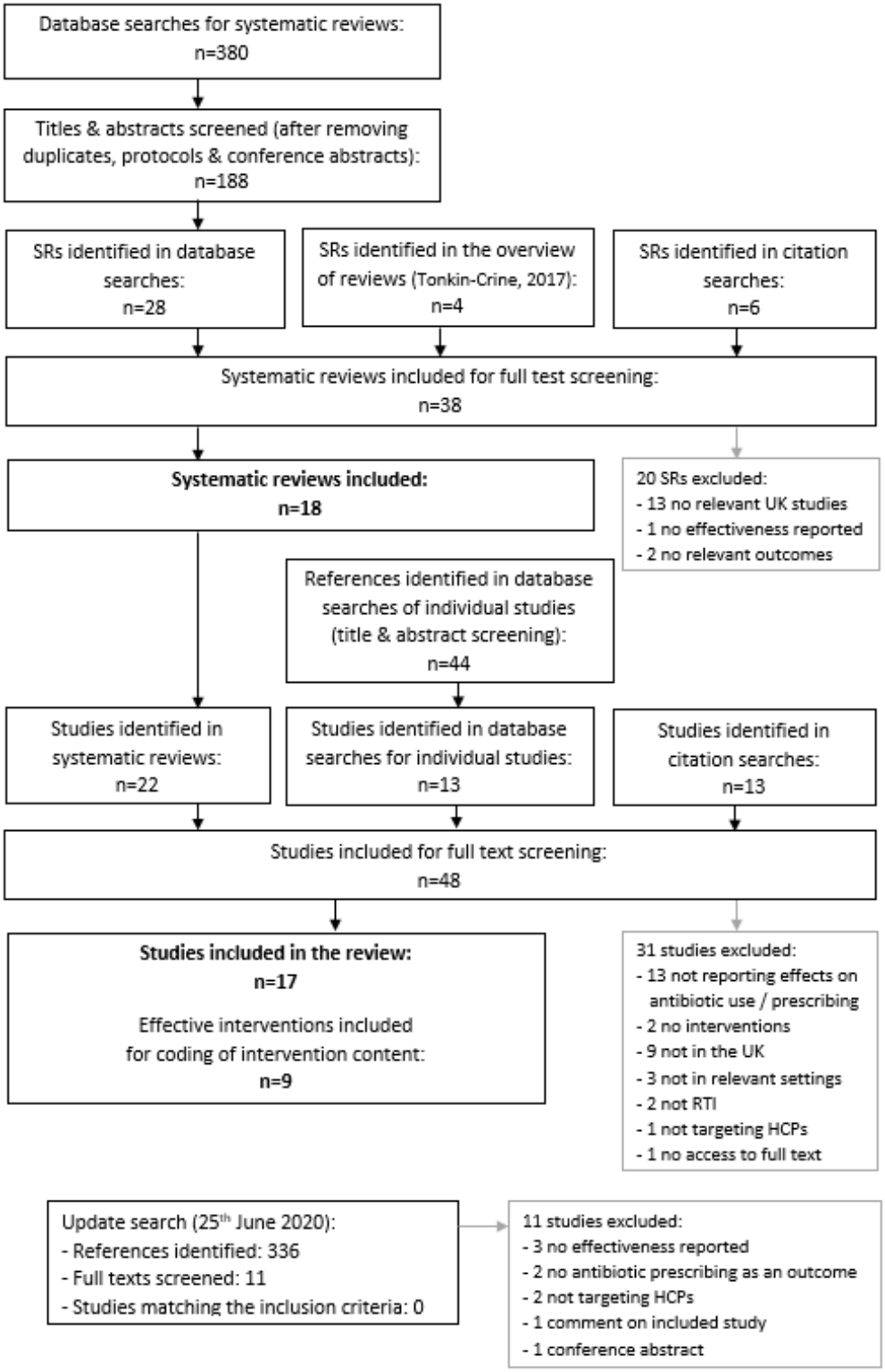
	on parents' understanding of antibiotic treatment.	clinicians for semi-structured video-elicited interviews; thematic analysis	assistant in England	beliefs about what indicated illness severity, which often took into account the wider impact on a child's life.
Courtenay 2017, Antibiotics for acute respiratory tract infections: a mixed-methods study of patient experiences of non-medical prescriber management (6)	To (1) explore patients' expectations and experiences of nurse and pharmacist non-medical prescriber-led management of RTIs, (2) examine whether patient expectations for antibiotics affect the likelihood of receiving them and (3) understand factors influencing patient satisfaction with RTI consultations.	Mixed methods: (i) questionnaires with 120 patients, (ii) interviews with 22 patients, (iii) interviews with 16 nurse and pharmacist non-medical prescribers; qualitative analysis informed by quantitative findings, inductive thematic analysis	General practice: 16 nurse and pharmacist non-medical prescribers: 7 in England, 5 in Scotland and 4 in Wales	There was alignment between self-reported patient expectations and those perceived by non-medical prescribers. 'Patient-centred' management strategies (including reassurance and providing information) were received by 86.7% of patients. Regardless of patients' expectations or the management strategy employed, high levels of satisfaction were reported for all aspects of the consultation. Taking concerns seriously, conducting a physical examination, communicating the treatment plan, explaining treatment decisions and lack of time restrictions were each reported to contribute to patient satisfaction.
Horwood 2016, Primary care clinician antibiotic prescribing decisions in consultations for children with RTIs: a	To investigate healthcare professional (HCP) diagnostic and antibiotic prescribing	Semi-structured interviews; purposive maximum-variation	General practice & walk-in centre:	HCPs varied in the symptom and clinical examination findings used to identify children they thought might benefit from antibiotics. Their diagnostic reasoning and assessment of perceived clinical need for antibiotics used a dual process, combining an initial rapid assessment with subsequent detailed deductive reasoning. HCPs reported confidence

qualitative interview study (7)	decisions for children with RTIs.	sampling; thematic analysis	22 GPs and 6 nurses from 6 general practices and one walk-in centre (unclear if they were in England or across the UK)	diagnosing and managing most minor and severe RTIs. However, residual prognostic uncertainty, particularly for the intermediate illness severity group, frequently led to antibiotic prescribing to mitigate the perceived risk of subsequent illness deterioration. Some HCPs perceived a need for more paediatrics training to aid treatment decisions. The study also identified a number of non-clinical factors influencing prescribing.
Kumar 2003, Why do general practitioners prescribe antibiotics for sore throat? Grounded theory interview study (8)	To understand why GPs prescribe antibiotics for some cases of sore throat and to explore the factors that influence their prescribing.	Open-ended interviews using an interview guide; purposive and theoretical sampling; grounded theory, constant comparative analysis	General practice: 40 GPs (unclear if they were in England or across the UK)	GPs are uncertain which patients will benefit from antibiotics but prescribe for sicker patients and for patients from socioeconomically deprived backgrounds because of concerns about complications. They are also more likely to prescribe in pressured clinical contexts. Doctors are mostly comfortable with their prescribing decisions and are not prescribing to maintain the doctor-patient relationship.
Mustafa 2014, Managing expectations of antibiotics for upper respiratory tract infections: a qualitative study (9)	To explore the views and experiences of GPs about asking patients directly whether they expect to receive antibiotics & focusing on the problem of eliciting	Semi-structured interviews; convenience sampling (all GPs in the area invited, interviewed those	General practice: 20 GPs in Wales	Physicians assumed most patients or parents wanted antibiotics, as well as wanting to be “checked out” to make sure the illness was “nothing serious.” Physicians said they did not ask direct questions about expectations, as that might lead to confrontation. They preferred to elicit expectations for antibiotics in an indirect manner, before performing a physical examination. The majority described reporting their findings of the

	expectations of antibiotics as a possible treatment for URTIs.	who responded); thematic analysis		examination as a "running commentary" so as to influence expectations and help avoid generating resistance to a soon-to-be-made-explicit plan not to prescribe antibiotics. The physicians used the running commentary to preserve and enhance the physician-patient relationship.
Rowbotham 2012, Challenges to nurse prescribers of a no-antibiotic prescribing strategy for managing self-limiting respiratory tract infections (10)	To explore the experiences of nurse prescribers in managing patients with self-limiting RTIs.	Semi-structured interviews and focus groups; purposive maximum-variation sampling; qualitative approach to develop conceptual categories and themes	General practice: Interviews: 15 nurses; 3 focus groups with 21 nurses (5, 4 and 12 in each) (unclear if they were in England or across the UK)	Although participants reported experiencing numerous challenges within these consultations, they believed that they possessed some of the communication skills to deal effectively with patients without prescribing antibiotics. Participants reported that protocols supported their decision-making and welcomed the benefits of peer support in dealing with 'demanding' patients. However, the newness of nurses and other non-medical prescribers to the prescribing role meant that some were cautious in dealing with patients with respiratory tract infections.
Tonkin-Crine 2011, GPs' views in five European countries of interventions to promote prudent antibiotic use (11)	To explore GPs' views and experiences of strategies to promote a more prudent use of antibiotics.	Semi-structured, telephone (in UK) interviews; purposive sampling from high and low-prescribing practices; thematic and	General practice: 52 GPs from the UK and 4 other countries, including 11 GPs in the UK	Themes were remarkably consistent across the countries. GPs had a preference for interventions that allowed discussion and comparison with local colleagues, which helped them to identify how their practice could improve. Other popular components of interventions included the use of near-patient tests to reduce diagnostic uncertainty, and the involvement of other health professionals to increase their responsibility for prescribing.

		framework analysis	(unclear if they were in England or across the UK)	
Williams 2017, General practitioner and nurse prescriber experiences of prescribing antibiotics for respiratory tract infections in UK primary care out-of-hours services (the UNITE study) (12)	To explore GP and nurse prescriber (NP) views on and experiences of prescribing antibiotics for RTIs in primary care OOH services.	Semi-structured interviews; purposive maximum-variation sampling supported by snowball/chain sampling; inductive thematic analysis	Out-of-hours: 30: 15 GPs and 15 nurse prescribers in England	The research shows that factors particular to OOH influence antibiotic prescribing, including a lack of patient follow-up, access to patient GP records, consultation time, working contracts and implementation of feedback, audit and supervision. Nurse prescribers reported perceptions of greater accountability for their prescribing compared with GPs and reported they had longer consultations during which they were able to discuss decisions with patients. Participants agreed that more complex cases should be seen by GPs and highlighted the importance of consistency of decision making, illness explanations to patients as well as a perception that differences in clinical training influence communication with patients and antibiotic prescribing decisions.
Wood 2007, Socially responsible antibiotic choices in primary care: a qualitative study of GPs' decisions to prescribe broad-spectrum and fluoroquinolone antibiotics (13)	To explore the reasons for GPs' choice of prescribed antibiotic, in particular their decision to prescribe fluoroquinolones.	Interviews; purposive and theoretical sampling; grounded theory approach, data indexed into analytical categories	General practice: 40 GPs in Wales	Choosing to prescribe a broad-spectrum antibiotic such as a fluoroquinolone, rather than a narrow-spectrum antibiotic, related to a number of clinical considerations, perceptions of patient expectations and organizational influences. GPs from high fluoroquinolone prescribing practices were more likely to prioritize patients' immediate needs, whereas GPs from average prescribing practices were more likely to consider longer term issues. GPs from both high and average fluoroquinolone prescribing practices justified their antibiotic choices on the basis of a desire to do their best for their patients and society.

Supplemental Document 5. Flow chart of selection process of intervention studies



Supplemental Document 6. Characteristics of included studies

First author, year, title (study name, reference)	Study design	Setting & participants	Interventions & comparators	Outcomes measured	Key results (on effectiveness of interventions on antibiotic prescribing/use; green shading indicates effective interventions)
McNulty 2018, Effects of primary care antimicrobial stewardship outreach on antibiotic use by general practice staff: pragmatic randomized controlled trial of the TARGET antibiotics workshop (14)	McNulty-Zelen RCT (a form of cluster-RCT where practices were not aware that they were taking part in a trial)	General practice: 152 practices England	1) **TARGET workshop** (1 hour workshop facilitated by existing NHS healthcare staff with promotion of the TARGET website resources) **2) Control** (no workshop offered)	Antibiotics dispensed per 1000 practice patients; workshop uptake; dispending of antibiotics typically prescribed for RTIs, UTIs and broad-spectrum antibiotics	Antibiotics dispensing was 2.7% lower in intervention practices (95% CI -5.5% to 1%, P = 0.06) compared with controls. Dispensing in intervention practices was 4.4% lower for amoxicillin / ampicillin (95% CI 0.6%–8%, **P=0.02**); 5.6% lower for trimethoprim (95% CI 0.7%–10.2%, **P=0.03**); and a non-significant 7.1% higher for nitrofurantoin (95% CI 0.03 to 15%, P=0.06).
Ward 2018, Point-of-care C-reactive protein testing to optimise antibiotic use in a primary care urgent care centre setting (15)	Service evaluation	Urgent care centre / walk-in service: Prescribers England	**CRP POCT** (Alere Afinion) (no comparator group)	Use of CRP POCT; type of antibiotics prescription (immediate, delayed or no prescription)	Pre-test decision (i.e. the decision that would have been made if no test was available): 72/141 (51.1%) patients would have been given an immediate antibiotic prescription, 6 (4.2%) would have been given a delayed prescription and 63 (44.1%) would not have received an antibiotic. Decision after doing CRP tests: 32 (22.7%) patients received an immediate antibiotic, 22 (15.6%)

					received a delayed prescription and 87 (61.7%) received no antibiotic.
Blair 2017, Feasibility cluster randomised controlled trial of a within-consultation intervention to reduce antibiotic prescribing for children presenting to primary care with acute respiratory tract infection and cough (CHICO) (16)	Cluster RCT (feasibility study)	General practice: 32 practices, including: 501 children (3 months – 11 years) with acute cough and RTI England	1) **Within-consultation complex intervention** (interactive web-based tool, including: recording symptoms and signs, elicitation and recording of carers' concerns, guidelines on antibiotics associated with risk strata, personalised printout for carers) 2) **Control** (Usual care)	Feasibility and acceptability; use of intervention; RTI-related antibiotic prescriptions; re-consultations; RTI-related hospitalisations	The overall antibiotic prescribing rates for children's RTIs were 25% (19.9% immediate and 5.1% delayed) in intervention group and 15.8% (**p=0.018**) in control group. *(In the Discussion, the authors suggest that this result might be due to a post-randomisation differential recruitment (with intervention arm having more children with more severe baseline characteristics) that might have biased the estimated intervention effect.)*
Hallsworth 2016, Provision of social norm feedback to high prescribers of antibiotics in general practice: a pragmatic national randomised controlled trial (17)	RCT	General practice: 1581 practices with antibiotic prescribing rates in the top 20% of the NHS Local Area England	1) **Prescribing feedback** (a letter from England's Chief Medical Officer stating that the practice was at a higher rate of antibiotic prescribing than 80% of practices in its area + a patient leaflet), 2) **patient-focused information** (promoting reduced use of antibiotics), 3) **Control** (no intervention)	Antibiotic items dispensed per 1000 weighted population, controlling for past prescribing	1) Feedback intervention: difference of 4.27 (3.3%; incidence rate ratio 0.967 [95% CI 0.957–0·977]; **p<0.0001**), representing an estimated 73 406 fewer antibiotic items dispensed. 2) Patient-focused intervention: incidence rate ratio for difference between groups 1.01, 95% CI 1.00–1.02; p=0.105.
Thornley 2016, A feasibility service evaluation of screening	Service evaluation	Community pharmacy:	**Sore throat test-and-treat service** (assessing patient's condition using the Centor score and patients meeting	Uptake of the throat swab testing;	Following screening by pharmacy staff, 149/367 (40.6%) patients were eligible for throat swab testing. Of these, only 36/149 (24.2%) were

and treatment of group A streptococcal pharyngitis in community pharmacies (18)		35 pharmacies, including 367 patients England	3 or all 4 Centor criteria were offered a throat swab test) (no comparator group)	antibiotic provision by the pharmacist	positive for group A streptococci. Antibiotics were supplied to 9.8% (n=36/367) of all patients accessing the service.
Gulliford 2014, Electronic health records for intervention research: a cluster randomized trial to reduce antibiotic prescribing in primary care (eCRT study) (19)	Cluster RCT	General practice: 100 practices, including 603,409 patients (aged 18-59) with RTIs England (50 practices), Scotland (50 practices)	1) **Decision support tools** (electronically delivered & remotely installed, accessed during the consultations), 2) **Control** (usual care)	Proportion of consultations for RTIs with antibiotic prescriptions	Reduction in proportion of consultations with antibiotic prescriptions of 1.85% (95% CI, 0.10%-3.59%, **P = 0.038**) and in the rate of antibiotic prescriptions for RTIs (9.69%; 95% CI, 0.75%-18.63%, fewer prescriptions per 1,000 patient-years, **P = 0.034**).
Little 2014, Delayed antibiotic prescribing strategies for respiratory tract infections in primary care: pragmatic, factorial, randomised controlled trial (20)	RCT	General practice: 25 practices, 889 patients (aged 3+) with RTIs UK	**4 delayed prescribing strategies**: 1) Re-contact for antibiotics, 2) Post-dated prescription, 3) Collection of prescription, 4) Antibiotic prescription given to patient, 5) No antibiotic prescription	Symptom severity; antibiotic use; patients' beliefs in effectiveness of antibiotic use; secondary: comparison of delayed prescription strategies with immediate antibiotics	Modest and non-significant difference between the randomised delayed prescribing groups in antibiotic use (26%, 37%, 37%, 33%, 39%; 4.96, P = 0.292). 97% of patients given immediate antibiotics used them but with no benefit for symptom severity or duration.
Little 2013a, Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a	Cluster RCT	General practice: 246 practices, 4264 patients with RTIs	1) Training in the use of **CRP POCT**, 2) Training in **enhanced communication skills**,	Antibiotic prescriptions; secondary: re-consultations; new signs; hospital	Antibiotic prescribing was lower with CRP POCT training than without (33% vs 48%, adjusted risk ratio 0.54, 95% CI 0.42–0.69) and with enhanced communication skills training than without (36% vs 45%, 0.69, 0.54–

multinational, cluster, randomised, factorial, controlled trial (GRACE INTRO) (21)		England and Wales	3) **Combined** training in the use of CRP and in enhanced communication skills, 4) **Control** (usual care)	admission; symptom severity and duration	0.87). The combined intervention (CRP POCT + communication skills training) was associated with the greatest reduction in prescribing rate (CRP risk ratio 0.53, 95% CI 0.36–0.74, **p<0.0001**; enhanced communication 0.68, 0.50–0.89, **p=0.003**; combined 0.38, 0.25–0.55, **p<0.0001**).
Little 2013b, Clinical score and rapid antigen detection test to guide antibiotic use for sore throats: randomised controlled trial of PRISM (primary care streptococcal management) (22)	Cluster RCT	General practice: 21 practices, 631 patients (aged 3+) with a sore throat England	1) **Delayed prescription** to be collected after 3-5 days if symptoms are not better or get worse, 2) **Clinical score** (FeverPAIN), 3) **Rapid antigen test** (RADT; rapid streptococcal antigen detection test) used **with clinical score** (FeverPAIN)	Patient-reported symptom severity; duration of symptoms; patient-reported antibiotic use	1) In delayed prescription group, 75/164 (46%) patients used antibiotics. 2) In the clinical score group antibiotic use (60/161) was 29% lower (adjusted risk ratio 0.71, 95% CI 0.50-0.95; **p=0.02**). 3) In the RADT + clinical score group antibiotic use (58/164) was 27% lower (0.73, 0.52-0.98; **p=0.03**).
Butler 2012, Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial (STAR) (23)	Cluster RCT	General practice: 68 practices, 263 GPs Wales	1) **Communication skills training** (including a practice seminar, online training and practising consulting skills), 2) **Control** (usual care)	Antibiotic items dispensed per 1000 practice patients in the year after the intervention, adjusted for the previous year's dispensing; secondary: re-consultations; hospital admissions; costs.	Antibiotics dispensed decreased by 14.1 in the intervention group but increased by 12.1 in the control group, a net difference of 26.1. After adjustment for baseline dispensing rate, this amounted to a 4.2% (95% CI 0.6%-7.7%) reduction in total oral antibiotic dispensing for the year in the intervention group relative to the control group (**p=0.02**).

Francis 2009, Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: a cluster randomised controlled trial (24)	Cluster RCT	General practice: 61 practices, 558 children (6 months - 14 years) with RTIs England (25 practices), Wales (36 practices)	1) Training in the use of **interactive booklet** on RTIs & use of the booklet in consultations, 2) **Control** (usual care)	Proportion of children re-consulting during 2 week follow-up; secondary: antibiotic use; future consulting intentions; parental satisfaction; reassurance; enablement.	Antibiotics were prescribed at index consultation to 19.5% of children in the intervention group and 40.8% of children in the control group (absolute risk reduction 21.3%, 95% CI 13.7-28.9), **p<0.001**). A significant difference was still present after adjusting for clustering (odds ratio 0.29; 0.14 to 0.60).
Little 2005, Information leaflet and antibiotic prescribing strategies for acute lower respiratory tract infection: a randomized controlled trial (25)	RCT	General practice: 37 GPs, 807 patients (aged 3+) with cough as the main symptom England	1) **Patient leaflet** (information on natural history of lower RTI addressing patient concerns) 2) **No patient leaflet** 3) **Immediate antibiotic prescription** 4) **No antibiotic prescription** 5) **Delayed prescription** (on request if symptoms don't resolve after 14 days)	Symptom severity and duration; patient-reported antibiotic use.	Fewer patients in the delayed prescribing and no antibiotic prescription groups used antibiotics compared with the immediate antibiotics group (20%, 16%, 96%, respectively; **p=0.001**). 57% patients used antibiotics in the no leaflet group compared with 55% in the leaflet group (p=0.58).
Macfarlane 2002, Reducing antibiotic use for acute bronchitis in primary care: blinded, randomised controlled	RCT	General practice: 3 practices, 259 adults (aged 16+) with acute bronchitis England	Patients judged to not need antibiotics: 1) **Delayed prescription + verbal reassurance** (prescription given to	Antibiotic use in the next two weeks; re-consultation for the same symptoms in the next month.	Fewer patients who received leaflet took antibiotics compared with those who did not receive the leaflet: 49 (23.1%) v 63 (29.7%) out of 212, risk ratio 0.76, 95% CI 0.59 to 0.97, **p=0.04**.

trial of patient information leaflet (26)			patients with advice to use it if they got worse), 2) **Delayed prescription + verbal reassurance + leaflet** (on natural course of lower RTI symptoms, pros and cons of antibiotic use), 3) Patients judged to need antibiotics and given **immediate AP**		44/47 (93.6%) patients judged to need antibiotics and given immediate antibiotic prescription took antibiotics.
Cox 2001, Is it possible to decrease antibiotic prescribing in primary care? An analysis of outcomes in the management of patients with sore throats (27)	Observational (pre-post)	General practice: 1 practice, 785 patients (aged 2+) with a sore throat as the main complaint England	1) **Old protocol** for management of sore throats in practice, 2) **Revised evidence-based protocol** for management of uncomplicated sore throats (focused on low antibiotic use)	Antibiotic prescriptions; patient acceptability; recovery; consultation rates.	Antibiotic prescriptions decreased from 56% to 19% during the study (**p<0.0001**).
Dowell 2001, A randomised controlled trial of delayed antibiotic prescribing as a strategy for managing uncomplicated respiratory tract infection in primary care (28)	RCT	General practice: 22 practices, 191 adults (aged 16+) with cough Scotland	1) **Immediate antibiotic prescription** 2) **Delayed prescription** (patients asked to wait a week before deciding whether to collect the prescription from reception)	Symptom duration; prescription uptake; patient satisfaction; patient enablement; subsequent consultation rates.	In delayed prescription group, 45% (43/95) patients picked up their prescription; 35% (12/34) waited 7 days as asked.
Little 2001, Pragmatic randomised controlled trial of two	RCT	General practice: 65 practices,	1) **Immediate antibiotic prescription + advice sheet**,	Symptom resolution; absence from school or nursery; paracetamol	132/134 (98.5%) participants who were given an immediate antibiotic prescription reported using antibiotics

prescribing strategies for childhood acute otitis media (29)		315 children (6 months - 10 years) presenting with otitis media England	2) **Delayed prescription + advice sheets** (patients asked to collect the prescription after 72 hours if no improvement)	consumption; collection of prescription; reported antibiotic use.	at some stage during the illness compared to 36/150 (24%) participants in the delayed prescription group.
McNulty 2000, Primary care workshops can reduce and rationalize antibiotic prescribing (30)	Pre-post	General practice: 84 practices England	1) **Workshops** on antibiotic prescribing (1.5-2 hour, including presentation of a poster, discussion of new antibiotic prescribing guidelines, key messages), 2) **Microbiology tutorials** in practices, 3) **Control** (no intervention)	Dispensed antibiotics.	51 practices offered workshops decreased antibiotic prescribing by 3.4%, compared with 2.2% decrease in 33 practices not offered workshops (p=0.09). Broad-spectrum antibiotic prescriptions declined by 15.4% in practices receiving workshops, compared with a 6.5% increase in practices with tutorials (**p=0.002**). Use of narrow-spectrum antibiotics (encouraged) did not change in workshop practices, but decreased by 12% in tutorials practices (p=0.003).

Abbreviations used in the table: CI – confidence intervals, CRP – C-reactive protein, POCT – point-of-care test(ing), RAD – Rapid antigen detection test(ing).

Supplemental Document 7. Behavioural content of effective research interventions

First author, year, title (reference)	Setting: targeted HCPs	Intervention	BCTs	TDF domain	Intervention function
McNulty 2018, Effects of primary care antimicrobial stewardship outreach on antibiotic use by general practice staff: pragmatic randomized controlled trial of the TARGET antibiotics workshop (14)	General practice: all staff	**TARGET workshop** - 1 hour workshop facilitated by existing NHS healthcare staff with promotion of TARGET website resources	- Credible source - Information about health consequences - Information about social, environmental consequences - Instruction on how to perform behaviour - Feedback on behaviour - Social comparisons - Adding objects to the environment - Behavioural substitution - Action planning - Self-monitoring of behaviour - Monitoring of behaviour by others - Social support (practical) - Social support (unspecified) - Demonstrating behaviour - Incentive	- Social influences - Beliefs about consequences - Environmental context and resources - Skills - Knowledge - Behavioural regulation	- Environmental restructuring - Enablement - Incentivisation - Persuasion - Education - Training
Hallsworth 2016, Provision of social norm feedback to high prescribers of antibiotics in general practice: a pragmatic national randomised controlled trial (17)	General practice: prescribers	**Feedback intervention** - Letter from England's Chief Medical Officer stating that the practice was at a higher rate of	- Feedback on behaviour - Social comparisons - Credible source - Instruction on how to perform the behaviour - Adding objects to the environment - Behavioural substitution - Information about health consequences	- Knowledge - Social influences - Skills - Environmental context and resources - Behavioural regulation - Optimism	- Education - Persuasion - Training - Environmental restructuring - Enablement

		antibiotic prescribing than 80% of local practices), and including suggestions to address it (e.g. a patient leaflet)		- Beliefs about consequences	
Gulliford 2014, Electronic health records for intervention research: a cluster randomized trial to reduce antibiotic prescribing in primary care (eCRT study) (19)	General practice: prescribers	**Decision support tools**, electronically delivered & remotely installed, accessed during consultations *[Reported issues: low utilization in some practices, perhaps as some GPs enter read codes after consultation; unable to ensure all prescribers saw the training materials and video]*	- Adding objects to the environment - Prompts, cues - Behaviour substitution - Instruction on how to perform behaviour - Demonstrating the behaviour - Information about health consequences - Information about social, environmental consequences - Verbal persuasion about capability - Social support (unspecified)	- Environmental context and resources - Memory, attention, decision making - Behavioural regulation - Skills - Knowledge - Beliefs about consequences - Social influences	- Environmental restructuring - Enablement - Training - Education - Persuasion
Little 2013a, Effects of internet-based training on antibiotic prescribing rates for acute	General practice: prescribers	1) **CRP POCT** - provision of testing equipment and training incl. instructions on when	- Adding object to the environment - Behaviour substitution - Instruction on how to perform behaviour - Demonstrating the behaviour - Social support (unspecified)	- Environmental context and resources - Behavioural regulation - Skills	- Environmental restructuring - Enablement - Training - Persuasion - Education

respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial (GRACE INTRO) (21)		and how to use the tests 2) **Training in enhanced communication skills** - how to negotiate management decisions with patients	- Social support (practical) - Information about health consequences - Information about social, environmental consequences - Credible source	- Social influences - Beliefs about consequences	
Little 2013b, Clinical score and rapid antigen detection test to guide antibiotic use for sore throats: randomised controlled trial of PRISM (primary care streptococcal management) (22)	General practice: prescribers	1) **Delayed prescription** to be collected after 3-5 days if symptoms are not better or get worse 2) **Clinical score** (FeverPAIN), 3) **Rapid antigen test** used **with clinical score** (FeverPAIN)	- Adding object to the environment - Instruction on how to perform behaviour - Information about health consequences	- Environmental context and resources - Skills - Beliefs about consequences	- Environmental restructuring - Training - Education
Butler 2012, Effectiveness of multifaceted educational programme to reduce	General practice: prescribers	**Educational programme** (STAR) including a practice seminar, online	- Self-monitoring of behaviour - Information about health consequences - Information about social and environmental consequences	- Behavioural regulation - Beliefs about consequences - Skills	- Enablement - Education - Training - Persuasion - Incentivisation

antibiotic dispensing in primary care: practice based randomised controlled trial (STAR) (23)		training and practice of consulting skills	- Instruction on how to perform behaviour - Demonstrating the behaviour - Credible source - Behavioural practice / rehearsal - Social support (unspecified) - Social support (practical) - Feedback on behaviour - Feedback on outcome - Social comparisons - Non-specific reward	- Social influences - Knowledge - Reinforcement	
Francis 2009, Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: a cluster randomised controlled trial (24)	General practice: prescribers	Training in the use of **interactive booklet** on RTIs & use of the booklet in consultations	- Adding object to the environment - Behavioural substitution - Instruction on how to perform the behaviour - Social support (unspecified) - Prompts, cues - Demonstrating the behaviour	- Environmental context and resources - Behavioural regulation - Skills - Social influences - Memory, attention, decision making	- Environmental restructuring - Enablement - Training - Persuasion
Cox 2001, Is it possible to decrease antibiotic prescribing in primary care? An analysis of outcomes in the management of	General practice: prescribers	**Revised evidence-based protocol** for management of uncomplicated sore throats (focused on low antibiotic use)	- Feedback on behaviour - Information about health consequences - Action planning - Instruction on how to perform the behaviour	- Knowledge - Beliefs about consequences - Behavioural regulation - Skills	- Education - Enablement

patients with sore throats (27)					
McNulty 2000, Primary care workshops can reduce and rationalize antibiotic prescribing (30)	General practice: prescribers	**Workshops** on antibiotic prescribing - 1.5-2 hours, presentation of a poster, discussion of new antibiotic prescribing guidelines, key messages [compared to no workshops or tutorials by a microbiologist]	- Feedback on behaviour - Social comparisons - Instruction on how to perform the behaviour - Social support (unspecified)	- Knowledge - Social influences - Skills	- Education - Persuasion - Enablement

Supplemental Document 8. Theoretical congruence between intervention functions and key TDF domains

Key six TDF domains	**Intervention functions** (Number of interventions with components addressing each function; 26 national & 5 research interventions, max N=31)								
	Education (n=23)	Persuasion (n=12)	Incentivisation (n=9)	Coercion (n=2)	Training (n=27)	Restriction (n=0)	Environmental restructuring (n=6)	Modelling (n=3)	Enablement (n=24)
Beliefs about consequences									
Social influences									
Skills									
Environmental context & resources									
Intentions									
Emotion									

Note: Green indicates where there is congruence between TDF domains and intervention functions addressed in interventions; red indicates lack of congruence, i.e. where there is a theoretical congruence between the domain and intervention function, but the function was not addressed in any interventions.

Supplemental Document 9. Theoretical congruence between BCTs and TDF domains

BCTs [a]	**National interventions** (n=26)	**Research interventions** (n=5)	**Linked TDF domains** (according to matrix; key domains in bold)	**TDF domain ranking**	**Theoretical congruence between BCT & TDF domain** [b]
Instruction on how to perform a behaviour*	24	5	**Skills**	3	High
Information about health consequences	14	3	**Beliefs about consequences** Knowledge	1 8	Medium
Adding objects to the environment	9	3	**Environmental context & resources**	4	High
Feedback on behaviour	7	2	**Beliefs about consequences** Knowledge Beliefs about capabilities Goals	1 8 9 0	Medium
Credible source	7	1	**Beliefs about consequences** **Intentions** Goals	1 5 0	High
Action planning	6	1	**Intentions** Goals Memory, attention, decision making Behavioural regulation	5 0 10 0	Medium
Demonstrating the behaviour	4	3	**Social Influences** **Skills**	2 3	High
Information about social, environmental consequences	5	2	**Beliefs about consequences** Knowledge	1 8	Medium
Social comparisons	6	1	**Social influences**	2	High
Social support (practical)	6	1	**Social influences** **Intentions** Beliefs about capabilities Social/professional role & identity Goals	2 5 9 7 0	High

Identification of self as a role model	6	0	**Social influences**	2	High
Self-monitoring of behaviour	6	0	**Beliefs about consequences** **Skills** Memory, attention, decision making Behavioural regulation Beliefs about capabilities	1 3 10 9 0	High
Social support (unspecified)	2	4	**Social influences** Social/professional role & identity	2 7	Medium
Behavioural substitution	2	3	Behavioural regulation	0	Low
Feedback on outcome of behaviour	5	0	**Beliefs about consequences** Knowledge Beliefs about capabilities Goals	1 8 9 0	Medium
Behavioural practice / rehearsal	3	0	**Skills** Beliefs about capabilities	3 9	Medium
Self-monitoring of outcomes	3	0	**Beliefs about consequences** Beliefs about capabilities Memory, attention, decision making	1 9 10	Medium
Prompts / cues	1	2	**Environmental context & resources** Memory, attention, decision making Behavioural regulation	4 10 0	Medium
Future punishment*	2	0	**Intentions** **Emotions** Goals Reinforcement	5 6 0 11	High
Non-specific reward	2	0	**Skills** Goals Reinforcement	3 0 11	Medium
Salience of consequences	2	0	**Beliefs about consequences** Knowledge	1 8	Medium
Social / non-material reward	2	0	**Social Influences**	2	High
Commitment	1	0	**Intentions** Goals	5 0	Medium

Focus on past success	1	0	Beliefs about capabilities	9	Low
Framing / reframing*	1	0	**Beliefs about consequences** Optimism	1 0	Medium
Goal setting	1	0	**Skills** **Intentions** Behavioural regulation Beliefs about capabilities Goals	3 5 0 9 0	High
Material reward	1	0	**Skills** Reinforcement	3 11	Medium
Pharmacological support*	1	0	**Skills**	3	High
Problem solving	1	0	Goals Beliefs about capabilities	0 9	Low
Pros and cons	1	0	**Beliefs about consequences**	1	High
Restructuring the physical environment	1	0	**Environmental context & resources**	4	High
Incentive	1	0	**Skills**	3	High
Monitoring of behaviour by others	1	0	**Skills**	3	High
Verbal persuasion about capabilities	0	1	Beliefs about capabilities Optimism Goals	9 0 0	Low

Notes:

[a] BCTs marked with asterisk (*) were not included in the previously developed matrix (31) and were matched with theoretically congruent TDF domains based on a discussion with LA.

[b] Following previously developed methods and matrix (31), 'high theoretical congruence' (green cells) between BCTs and TDF domains was defined as a BCT being paired with two or more of the theoretically-matching key TDF domains (or with one key TDF domain *if only one* domain was theoretically linked to that BCT); 'medium congruence' (orange cells) was defined as a BCT being paired with one key TDF domain (out of more than one domains theoretically linked in the matrix); 'low congruence' (red cells) was defined as a BCT not being paired with any of the key TDF domains.

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