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Nudge interventions to reduce unnecessary antibiotic prescribing in primary care: a systematic review

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ABSTRACT

Objectives

Antibiotic prescribing in primary care contributes significantly to antibiotic overuse. Nudge interventions alter the decision-making environment to achieve behaviour change without restricting options. Our objectives were to conduct a systematic review to examine the types of nudge interventions used to reduce unnecessary antibiotic prescribing in primary care, and their effects on prescribing.

Methods

Medline, Embase and grey literature were searched for randomised trials or regression discontinuity studies. Risk of bias was assessed independently by two researchers. Vote counting was applied to synthesise effects on overall antibiotic prescribing. Effects of social norm nudges were examined for features that may enhance effectiveness.

Results

Nineteen studies were included, testing 23 nudge interventions. Four studies were rated as having a high risk of bias, nine as moderate risk of bias, and six as at low risk. Overall, 78.3% (n=23, 95% CI: 58.1, 90.3) of the nudges evaluated reported a reduction in overall antibiotic prescribing rates. Social norm feedback was the most frequently applied nudge (n=17), with 76.5% (n=13; 95% CI: 52.7, 90.4) of these studies reporting a reduction in antibiotic prescribing. Other nudge strategies applied were changing option consequences (n=3; with 2 reporting a reduction), providing reminders (n=2; 1 reporting a reduction), and facilitating commitment (n=1; reporting a reduction). Social norm nudges considered features such as who to target, use of a respected authority for messaging, and the frequency of feedback, to increase effectiveness. Physicians with the lowest rates of antibiotic prescribing were used as the comparison point in effective social norm nudges.

Conclusions

Nudge interventions are effective for improving antibiotic prescribing in primary care. Expanding the use of nudge interventions beyond social norm nudges could reap further improvements in antibiotic prescribing practices. Policy makers and managers need to be mindful how social norm nudges are implemented to enhance intervention effects.

STRENGTHS AND LIMITATIONS

- Nudges are potentially useful interventions to influence clinical decisions so that they align with guidelines; however their effects can vary.
- This systematic review describes the types of nudges evaluated and their reported effects on antibiotic prescribing in primary care.
- A strength of the study is the broad search strategy with the assessment of whether an intervention was a nudge at the full-text stage.
- We were not able to synthesise results with meta-analysis due to the differences in outcome measures reported.

KEYWORDS

Antimicrobial Stewardship; Primary Health Care; General Practice; Clinical Decision-Making; Quality of Health Care; Economics, Behavioural; Psychology; Systematic Review;

INTRODUCTION

Antimicrobial resistance is one of the most pressing challenges to global health [1]. Overuse and inappropriate use of antibiotics is a major contributor to the rise of antimicrobial resistance, and yet, between 2000 and 2010 global antibiotic consumption rose by 35% [2]. Concerningly, global per-capita consumption of antibiotics flagged by the World Health Organization (WHO) as having high resistance potential (Watch category) [3] rose by 90.9% between 2000 and 2015 [4]. Primary care accounts for the majority of antibiotic use, and rates of inappropriate use are estimated to be high [5-7]. For example, the majority of upper respiratory tract infections do not benefit from antibiotic treatment, particularly when weighed against the rates of adverse effects, however, antibiotics continue to be prescribed [5, 8, 9].

Efforts to reduce antibiotic prescribing in primary care have predominantly focused on the use of point-of-care testing, shared decision-making, and education strategies aimed at physicians and patients [10-12]. While some of these intervention strategies have been successful in improving antibiotic prescribing, they can be resource intensive, and in some cases only provide marginal reductions in antibiotic prescribing [10-12]. Furthermore, these intervention strategies rarely take account of how cues in the environment, unrelated to clinician knowledge or access to resources such as information or tests, can influence decision-making.

The field of behavioural economics has generated a collection of approaches, called 'nudges', that involve subtle changes in the decision-making environment, or choice architecture, to guide people towards a specific decision or behaviour. Nudge interventions are typically simple and low-cost interventions, and thus are attractive to healthcare managers and policy makers. Furthermore, they do not restrict choices or penalise 'unfavourable' choices, thus preserving an individual's autonomy in the decision-making process.

Nudge interventions have similarities to traditional behaviour change techniques applied in health services and public health.[13, 14] For example, audit and feedback has long been applied in health service interventions and has similarities to social norm feedback nudges. However, audit and feedback may not necessarily include a comparison to the performance of peers, the essential component that would make it a nudge.[15, 16] Furthermore, social norm feedback nudges tend to target 'underperformers', as evidence from psychology has demonstrated a 'boomerang' effect; i.e. that high performers drop their performance toward the group mean (beyond that expected due to regression toward the mean). However, audit and feedback interventions used in health services may not take performance into account when deciding on who should receive feedback. Thus, there can be nuanced differences in the techniques from each of these paradigms.

Nudge interventions have been successfully implemented in fields other than health [17], and the evidence base for their use in influencing consumers' health-related behaviours is growing [18, 19]. However, while the use of nudge interventions in specific areas of health services and to influence clinical decision making is increasing,[17, 20] there is emerging evidence that the effect of nudges can vary depending on the context in which they are applied, as well as the type of nudge implemented. Against this background, our aim was to explore the use of nudge interventions and their effectiveness to improve antibiotic prescribing in primary care, and to draw out lessons to inform future directions for nudge intervention design and testing in healthcare. Our specific objectives were to describe the types of nudge interventions trialled to date, their key features, and their effects on the rates of antibiotic prescribing overall.

METHODS

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Supplementary file 1) [21].

Information sources and search strategy

The databases MEDLINE (via Ovid and PubMed) and Embase were searched for original research articles reporting on randomised trials or regression discontinuity studies of interventions to improve antibiotic prescribing in primary care, published in English in the last 20 years. Though the behavioural economics term 'nudge' was proposed in 2008, many of the interventions now termed 'nudges' have been applied to influence behaviour prior to the emergence of this term. Therefore, we did not exclude articles published before 2008 if the interventions met the criteria for a nudge intervention, and our search strategy did not include 'nudges' as a theme. Instead, our search strategy covered three themes: antibiotics AND primary care AND intervention study designs. The reference lists of included studies were hand searched for relevant citations. Websites of government nudge units and other organisations working to apply and test nudge theory were also searched for grey literature of relevance. Searches were carried out in April 2021. The full search strategy is presented in Supplementary file 2.

Eligibility criteria

Studies conducted in primary care facilities, general and family practices were included. Studies in hospital wards or in long-term care were excluded. The intervention tested had to fall under the broad definition of a nudge proposed by Thaler and Sunstein: "*A nudge… is any aspect of the choice architecture that alters people's behaviour in a predictable way without forbidding any options or significantly changing their economic incentives. To count as a mere nudge, the intervention must be easy and cheap to avoid*" [22]. For further guidance on whether the intervention used qualified as a nudge, we used a taxonomy of choice architecture techniques which focuses on interventions rather than the underlying cognitive processes of the interventions [23]. Interventions involving education, providing physicians with access to guidelines, passive decision support tools the clinician had to actively decide to use, and audit and feedback interventions with no social norm comparison were excluded. Studies evaluating multifaceted interventions that included a nudge strategy were also excluded as they did not allow evaluation of the impact of the nudge intervention alone. Studies had to evaluate the impact of the intervention on antibiotic prescribing rates or rates of appropriate antibiotic prescribing to be eligible. Randomised controlled trials and regression discontinuity studies were included. Interrupted time-series, controlled before-after, cross-sectional, and before-after studies were excluded as they are at higher risk of bias.

Study selection

Titles and abstracts of citations returned from the searches were independently reviewed by at least two reviewers. At this stage, the reviewers assessed study setting, study design and outcomes for eligibility. The full-text of all selected citations were then reviewed independently by two of three authors against all eligibility criteria, including an assessment of whether the intervention qualified as a nudge using the definitions outlined above. Discrepancies between reviewers were resolved through discussions until consensus was reached.

Data collection and data items

Data extraction and categorisation of interventions was carried out independently by two reviewers for each study. We extracted data on study characteristics (country, study years, sample size), nudge intervention description, types of infections targeted (e.g. all, respiratory tract infections [RTIs], urinary tract infections [UTIs]), outcomes, and study results. When studies reported more than one outcome, we extracted results for the outcome measuring changes in overall antibiotic use, appropriate antibiotic use, and any outcome defined as the primary outcome of the study. When a study trialled more than one nudge intervention, or the same nudge was implemented with differing features, we extracted intervention data for all nudges.

Nudge interventions were classified using a taxonomy of choice architecture techniques (Table 1) [23], and we refer to these as nudge intervention categories. Since social norm feedback nudge interventions are a frequent behaviour change technique in healthcare, often termed audit and feedback, but are implemented with varying features, we extracted details of the implementation. We recorded whether a social norm feedback nudge targeted high antibiotic prescribers or all physicians; the frequency of feedback; whether feedback was based on prescribing data for practices or individual physicians; the mode of intervention delivery (e.g. letter, email); whether a graphic representation of data was included; and the types of supporting information provided in addition to the social norm feedback.

Table 1: Taxonomy of choice architecture techniques with implementation examples[23]

Category	Technique	Technique examples
A. Decision information	A1. Translate information	• Reframe information • Simplify information
	A2. Make information visible	• Provide real-time feedback • Make external information visible
	A3. Provide social reference point	• Refer to descriptive norm (social norm feedback) • Refer to opinion leader
B. Decision structure	B1. Change choice defaults	• Set no-action default • Use prompted choice
	B2. Change option-related effort	• Increase/decrease physical effort • Increase/decrease financial effort
	B3. Change range or composition of options	• Change categories of options • Change grouping of options
	B4. Change option consequences	• Connect decision to benefit or cost • Change social consequences
C. Decision assistance	C1. Provide reminders	• Make information more or less salient
	C2. Facilitate commitment	• Support self-commitment/public commitment

Assessment of risk of bias in included studies

The risk of bias of each study was assessed using the Cochrane Effective Practice and Organisation of Care group's tool for studies with a separate control group [24]. Each study was independently assessed by two authors against each of the nine criteria assigning a score of either low risk, high risk, or unclear risk of bias. Discrepancies were resolved through discussion. A summary assessment of the overall risk of bias was allocated to each study as follows: *low risk of bias* when all criteria were scored 'low', *medium risk of bias* when one or two criteria were scored 'unclear' or 'high' risk, and *high risk* when more than two criteria scored 'unclear' or 'high' [25].

Synthesis of results

Inconsistencies in the outcomes and data reported in the studies precluded meta-analysis. Thus, we applied vote counting to summarise results for each category of nudge intervention and for features of social norm feedback nudges.[26] Vote counting allows a comparison of the number of effects reporting a benefit to the number that showed no benefit. It is the recommended method by Cochrane for summarising studies when meta-analysis or other quantitative methods are not able to be applied.[26] For each nudge intervention, we recorded whether the study demonstrated a reduction or no change in overall antibiotic prescribing compared to controls. As per the Cochrane Handbook, the statistical significance of the effect was not taken into account, so as not to erroneously conclude that underpowered studies had no effect. For studies with multiple study outcomes, we only considered the effect on overall antibiotic prescribing. The percentage of interventions with a reduction in overall antibiotic prescribing was calculated for all nudge interventions and social norm feedback nudges. Sensitivity analyses were conducted removing studies with a high risk of bias. Confidence intervals for proportions were calculated using the Wilson method. Effect sizes from studies were summarised narratively by reporting the range of change for overall antibiotic prescribing outcomes.

We used harvest plots to graphically summarise the vote counting results.[27] In a harvest plot, each mark represents a study or intervention. We used the position of the mark to indicate whether the intervention effect (reduction or no change in overall antibiotic prescribing) and the size of the mark to indicate the risk of bias of the study (low risk studies having a larger mark). Harvest plots were created for all nudge interventions by nudge category, and for social norm nudges by whether the intervention targeted high antibiotic prescribers or all prescribers, the frequency of feedback (once or more than once) and whether the comparison group was the average or above average performers. The stratification of the social norm nudge interventions by these features aimed to examine if there was evidence supporting one implementation strategy over another. Lastly, results from studies which directly compared different nudge interventions or implementation strategies or examined intervention effects over time or on different sub-groups were described narratively.

Public and Patient Involvement

Patients or the public were not involved.

RESULTS

Nineteen studies were assessed as eligible for inclusion (Figure 1) [28-43]. Table 2 presents study characteristics. The majority of studies were conducted in Europe (n=8) [30, 32-35, 41, 42], six in the United States [31, 36-38, 40], two in Australia [29, 39], two in China [43], and one in Sudan [28]. Seventeen studies were randomised controlled trials and two were regression discontinuity studies [30, 41]. Interventions were aimed at improving antibiotic use for all types of infections in nine studies [28-30, 32, 33, 39, 41], RTIs in eight studies [31, 36-38, 40, 42, 43], UTIs in one study [35], and both RTIs and UTIs in one study [34].

Risk of bias in included studies

Four studies were rated as having a high overall risk of bias [28, 31, 35, 40], nine as moderate risk of bias [29, 30, 34, 37-39, 41, 42], and six as at low risk of bias (Table 2) [32, 33, 36, 43]. Overall scores of meeting risk of bias criteria ranged from 4/9 to 9/9 across studies. No single criterion was more frequently at high or unclear risk of bias across studies. Supplementary file 3 shows the risk of bias assessment against each of the criteria for each study.

Description of nudge interventions

Seventeen studies evaluated one type of nudge intervention and two evaluated three types of nudge interventions each [37, 38], with a total of 23 nudge interventions evaluated. Three studies compared different implementation strategies of social norm nudges[29, 36].

Social norm feedback nudges ('Decision information' category of nudge interventions; Table 2) were the most common intervention (n=17) evaluated [28-36, 38-42]. Implementation of social norm feedback varied between studies (Table 3). Social norm feedback was most commonly: based on prescribing data for individual physicians (n=12) [29, 31, 33, 35, 36, 38-42]; provided more than once (n=11) [28, 31, 33-35, 38-40]; sent to all prescribers (n=11) [28, 31, 34-36, 39, 40, 42] as opposed to the highest prescribers only; and distributed via letters (n=11) [28-30, 32-34, 36, 39, 41, 42]. Studies also cited application of other behavioural techniques or considerations in the design of their social norm feedback, such as the inclusion of actionable advice, addressing the feedback letter from a high profile or respected individuals, providing positive feedback to high performers (i.e. low prescribers), and comparison to the mean of the top performers as opposed to the group mean.

Three interventions used nudge techniques from the 'Decision structure' category involving changing option consequences (Table 4) [38, 40, 43]. Three interventions used techniques from the 'Decision assistance' category (Table 4) involving providing reminders via suggested alternatives to antibiotic use (n=2) [38, 40] and a statement of public commitment to reducing antibiotic use in RTIs (n=1) [37].

Table 4: Description of nudge and direction of effect on overall antibiotic prescribing in primary care (other than social norm feedback)

Nudge category/ Author, year	Type of nudge	Mode	Description	Intervention effect*
Decision structure – change option consequences				
Meeker, 2016	Accountable justification	Electronic health record	At time of prescribing an antibiotic, physicians were asked to justify their treatment decision in a mandatory free text field. The prompt informed physicians the justification would be visible in the patient's record.	Reduction
Persell, 2016	Accountable justification	Electronic health record	At time of prescribing an antibiotic, physicians were asked to justify their treatment decision in a mandatory free text field. The prompt informed physicians the justification would be visible in the patient's record.	No change
Yang, 2014	Public reporting	Posters and reports	Posters with antibiotic prescribing data were publicly displayed in the primary care clinics and reports with the data were sent to clinic managers and local health authorities.	Reduction
Decision assistance – provide reminders				
Meeker, 2016	Suggested alternatives	Electronic health record	At time of prescribing an antibiotic, a pop-up screen stated antibiotics are generally not indicated for the diagnosis and showed a list of alternative treatments.	Reduction
Persell, 2016	Suggested alternatives	Electronic health record	At time of prescribing an antibiotic, a computerised order set appeared with treatment alternatives and education materials for the patient.	Reduction
Decision assistance – facilitate commitment				
Meeker, 2014	Public commitment	Poster	A poster-sized letter signed by physicians and posted in examination rooms indicating commitment to reducing antibiotics for RTIs.	Reduction

*Results of vote counting assessment based on nudge effect on overall antibiotic prescribing

Effect of nudge interventions on overall antibiotic prescribing rates

Of the 23 nudge interventions evaluated, 78.3% (n=17, 95% CI: 58.1, 90.3) showed a reduction in overall antibiotic prescribing rates. Removing studies with a high risk of bias, the percentage of studies showing a reduction in overall antibiotic prescribing was 76.5% (n=12, 95% CI: 52.7, 90.4). Figure 2 shows the distribution of intervention effects by the type of nudge strategy evaluated.

Of the seventeen studies evaluating social norm feedback nudges, 76.5% (n=13, 95% CI: 52.7, 90.4) reported a reduction in overall antibiotic prescribing (Figure 2). Removing studies with a high risk of bias, this percentage was 69.2% (n=9, 95% CI: 42.4, 87.3). Figure 3 shows social norm nudges stratified by the frequency of feedback, whether they targeted only high prescribers or all prescribers, and the comparison group. More studies showed a reduction than no change in overall antibiotic prescribing irrespective of the frequency of feedback and who was targeted by the intervention. However, only half of the studies that used the mean antibiotic prescribing of the group as the comparison reported a reduction in antibiotic prescribing, with the other half reporting no change.

Effect size of nudge interventions on antibiotic prescribing rates

The effect sizes of social norm feedback interventions on the number of antibiotics/1000 consultations (n=3) ranged from no change [39] to a reduction of 13.6% (95% CI: 16.6, 10.6) at 6-months post-intervention [29]; and the number of antibiotic prescriptions/1000 registered population (n=5) from no change [44] to an approximate 5% reduction (-58.7/1000 population [95% CI: 116.7, 0.7]) 12-months post intervention [30].

Studies measuring antibiotic prescribing for specific infection types reported absolute difference effect sizes of -1.2% (95% CI: -10.5, 8.2) [34], -1.7% (p=0.93) [31], and -5.2% (95% CI: -6.9, -1.6) [38] in the proportion of upper RTI treated with an antibiotic; a relative decrease of 9.6% (p=0.0004) [35] in inappropriate antibiotic for UTIs, and lower odds of antibiotic prescribing for RTI (OR: 0.73 (95% CI: 0.53, 0.995)) [40].

The effect sizes of the two studies of accountable justification interventions ranged from no change [40] to a reduction of 7.0 percentage points (95% CI: 9.1, 2.9) [38] in the number of antibiotics/100 antibiotic inappropriate infections. One study of public reporting showed a 1.93 percentage point reduction (95% CI: -6.61, 2.75) in the percentage of RTI consultations with an antibiotic, and a 6.97 percentage point (95% CI: -13.9, 0.00) reduction in the percentage of RTI consultations with >1 antibiotic.

Supplementary file 4 provides details of the effects of interventions on outcomes.

Studies comparing the effects of different nudge interventions

Two studies compared the impact of three different types of nudge interventions on antibiotic prescribing for RTIs [38, 40]. One study (with a moderate risk of bias) examined the impact of nudges on RTI where an antibiotic was not indicated, i.e. antibiotic inappropriate RTIs.[38] This study reported a reduction in the prescribing of antibiotics for antibiotic inappropriate RTIs in the physician groups receiving social norm feedback and accountable justification nudges, and a non-significant reduction in the physician group receiving a suggested alternatives nudge intervention [38]. The second study (high risk of bias) compared the same three nudge interventions, and reported a reduction in antibiotic prescribing for all RTIs for the social norm feedback and suggested alternative nudges, but not in the groups receiving the accountable justification nudges.[40]

Supplementary file 4 provides details of the impact of interventions on outcomes and their vote counting results.

Social norm nudge effects over time and following repeat messaging

Two studies examined the effect of a single social norm nudge letter sent to high antibiotic prescribing physicians over time and both reported a diminishing effect on prescribing rates compared to controls over time [29, 30]. In one study, the effect of the intervention was examined over 12-months after the letter was sent [30]. While there was a significant reduction in antibiotic prescribing compared to controls in the 12 months after the intervention, the effect diminished over time, such that the reductions in antibiotic prescribing rates in the second, third and fourth quarters after the intervention were not statistically significant. The second study also reported a diminishing effect of the social norm nudge letter over a 12-month period, but the reduction continued to remain significant at 12-months after the intervention [29, 45].

Two studies examined the impact of repeat social norm feedback interventions over time [33, 41]. In the first study, the effect of quarterly social norm feedback sent to the top 50% of antibiotic prescribers was assessed for 2 years [33]. While there was no difference in overall antibiotic prescribing rates in the first and second years of the intervention, there was a significant reduction in the antibiotic prescribing for children and adolescents in the first year (-8.6%) and young to middle-aged adults in the second year of the intervention (-4.6%). In the second study, a social norm nudge was first used in 2014 targeting the top 20% antibiotic prescribers, and due to its success was repeated annually since [41]. The study evaluated whether the intervention reduced antibiotic prescribing by physicians who had previously received the letter and those that had not. The top 10% of prescribers did not reduce their prescribing whether or not they had previously been sent a letter. However, the top 11-20% antibiotic prescribers reduced their antibiotic prescribing even when they had previously been sent a letter. The authors speculated that the failure of the top 10% to reduce antibiotic prescribing may have been due to the more forceful message in the communication they received (i.e. that the great majority (90%) of practices prescribed fewer antibiotics), resulting in negative attitudes to the message and a lower behavioural intention to reduce prescribing.

DISCUSSION

In this systematic review we have compiled the evidence on the effectiveness of nudge interventions in reducing antibiotic prescribing in primary care. Overall, 78.3% of studies reported a reduction in antibiotic prescribing. Social norm feedback was the most frequently evaluated nudge, and the evidence suggests that performance should be compared to high performers, rather than the average, to enhance intervention effects. Only four studies examined nudge strategies other than social norm nudges, such as changing option consequences, providing reminders and facilitating commitment. Thus, while the evidence base supports the effectiveness of social norm nudges in this context, further research is needed to evaluate other nudge strategies despite promising results thus far of their effectiveness.

The studies included in this review trialled five different nudges (social norm feedback, accountable justification, public reporting, suggested alternatives and public commitment) from four of the nine subcategories of choice architecture techniques described by Munscher.[23]. Two other broad reviews of nudges targeting health providers reported identifying a similar number of nudges employed in their included studies, but the types of nudges applied differed to those that we identified.[20, 46] For example, changing choice defaults is a frequently applied nudge to guide health care provider behaviour, but was not used to influence antibiotic prescribing in our review.[20, 46] Another example of a nudge not applied in studies in our review, but used in other contexts targeting health providers is changing the framing of information.[20, 46] Thus, there is scope for implementing and evaluating other nudge techniques in the primary care setting to improve antibiotic use. This is important since it is currently not clear whether the same nudge applied over more than one year will continue to have sustained impact.

We attempted to elucidate whether features of social norm feedback nudges have a role in their effectiveness. For example, the behavioural economics literature suggests that social norm nudges should only be provided to poor performers (i.e. high antibiotic prescribers in our case).[22] This is because of the 'boomerang effect' that may occur in individuals performing above average when they are provided social norm feedback confirming their above average performance, i.e. they reduce their performance. The studies in our review most frequently provided the social norm feedback to all prescribers (not only high prescribers) and all but one of these studies showed a reduction in overall antibiotic prescribing. However, the studies providing feedback to all prescribers also predominantly provided feedback more than once, which may have played a role in the reduction in antibiotic prescribing. Other factors that may have played a role in the prevention of a 'boomerang' effect in low prescribers, was the way the message was delivered and the comparison group used in the feedback. For example, one study informed the physicians with the lowest prescribing that they were a 'top performer', whereas the remaining physicians were informed they were 'not a top performer'.[38] The psychology literature supports the use of an injunctive when providing feedback i.e. conveying social approval or disapproval, as a way to eliminate the 'boomerang' effect.[47] The study also compared physicians' performance to the mean of the lowest decile prescribers, rather than the group mean. In fact, our results showed that comparison of performance to the group mean was the only feature of social norm feedback nudges that produced results that were evenly distributed between a reduction and no change in antibiotic prescribing. However, the studies that used comparisons to the lowest prescribers or ranked the prescriber against their peers all reported reductions in antibiotic prescribing.

The frequency of feedback may also play a role in social norm nudge effects. In the study described above that informed prescribers they were a 'top performer' or 'not a top performer', feedback was provided on a monthly basis, which allowed physicians to assess the degree to which they had changed their antibiotic prescribing.[38] This is a different approach to studies that targeted only the high prescribers, i.e. poor performers. These studies tended to provide the feedback once, informing the physicians that they prescribed at a higher rate than e.g. 80% of their peers.[29, 30, 32, 41, 45] The other behavioural feature included in the studies targeting high prescribers was that the letter was addressed from a high-profile figure to increase the credibility of the message.[29, 30, 32, 41, 45]

It has been suggested that we can also learn from nudges that fail.[14, 48] There were four studies that implemented a social norm feedback nudge that had no effect on overall antibiotic prescribing.[33, 34, 39, 44] All four studies had two intervention features in common. Firstly, the peer comparison used was the mean prescribing rate of the group or in the case of one study the interquartile range of the group. For those prescribers that were at the mean prescribing level or marginally below it, this may not have provided enough motivation to change their behaviour. Furthermore, as mentioned above, the 'boomerang effect' may occur in individuals performing above average. Secondly, the feedback in the four evaluations of social norm nudges that did not reduce overall prescribing was not provided from a high-profile or respected figure, which may have reduced the salience of the message.

The literature on audit and feedback interventions in healthcare provides insights into what features make these interventions more effective, and complement those from the behavioural economics and psychology literature.[16] A Cochrane review found that feedback is more likely to be effective when: baseline performance is low; the source is a supervisor or colleague; the frequency is more than once; it is delivered both verbally and in written formats; and when feedback includes both targets and an action plan.[15] Many of these features were included in the social norm nudges we identified in this review. For example, most of the social norm nudges included information on appropriate antibiotic prescribing in primary care. Thus, synthesising such evidence from behavioural economics and psychology is likely to enhance the effectiveness of these interventions.

This systematic review has a number of strengths. Firstly, our search strategy was inclusive of all studies evaluating interventions to improve antibiotic prescribing in primary care. The selection of studies based on the type of intervention occurred at the full-text screening stage to ensure that studies not explicitly stating they used nudge techniques were included. Secondly, we used a comprehensive taxonomy of behavioural architecture techniques,[23] rather than attempting to ascertain whether the underlying cognitive processes addressed by the intervention had the features of a nudge. However, we were unable to perform a meta-analysis or summarise the results quantitatively due to the heterogenous reporting of study outcomes. Nonetheless, this review has provided practical insights into the use of nudge interventions to reduce antibiotic use in primary care, and highlighted areas for further research.

CONCLUSIONS

Health systems worldwide continue to struggle to deliver evidence-based care.[49] Nudges can be used in lieu of, or to augment, more traditional efforts such as education (targeting clinicians, as well as the public), financial incentives, promotion of guidelines, and changing models of care. Evaluation of nudges applied in healthcare will play a key role in identifying interventions suitable for use in different contexts, including primary care, and in further developing applications of nudge strategies to improve the delivery of effective healthcare services.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

MZR conceived the study with JW and BN. MZR and GG designed the search strategy and GG ran the searches. MZR, GG and AN screened articles for inclusion with input from BN. MZR, GG and AN conducted data extraction and quality assessments. LL and KS provided support for the compilation of results. MZR compiled results and wrote the initial manuscript draft. All authors contributed to the editorial process of the manuscript and approved the final manuscript.

DATA SHARING STATEMENT

All data is available in the manuscript or Supplementary files.

ETHICS APPROVAL

This study does not involve human participants.

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FIGURE LEGENDS

Figure 1: PRISMA flow chart of search and screening results
*One study had two publications.

Figure 2: Harvest plot of effects of nudge interventions targeting antibiotic prescribing in primary care on overall antibiotic prescribing. Each mark or column represents one nudge

intervention. Column height represents the risk of bias in the study: tallest columns are studies with low risk of bias; medium columns are moderate risk of bias; short columns are high risk of bias.

Figure 3: Harvest plot of effects of social norm feedback nudge interventions on overall antibiotic prescribing by intervention features. Each mark or column represents one nudge intervention. Column height represents the risk of bias of the study: tallest columns are studies with low risk of bias; medium columns are moderate risk of bias; short columns are high risk of bias.

TABLES

Table 2: Characteristics of studies evaluating nudge interventions to improve antibiotic prescribing in primary care

Author, Year	Country	Sample size	Infections targeted	Nudge intervention/s	Outcomes of interest	Overall risk of bias[a]
Awad, 2006	Sudan	20 practices	All	Social norm feedback	No. of consultations with AB; No. of consultations with an inappropriate AB[b]	High
BETA, 2018 & 2020	Australia	6608 physicians	All	Social norm feedback	No. of ABs per 1000 consultations	Moderate
Bradley, 2019	Northern Ireland	331 practices	All	Social norm feedback	No. of ABs per 1000 registered population	Moderate
Chang, 2020	China	163 physicians	All	Social norm feedback	No. of AB prescriptions per 100 prescriptions	Moderate
Curtis, 2021	England	1401 practices	All	Social norm feedback	% broad spectrum AB of all AB	Low
Gerber, 2013	USA	162 physicians	RTI	Social norm feedback	% broad spectrum ABs among children with AB prescription; ABs for viral RTI	High
Hallsworth, 2016	England	1581 practices	All	Social norm feedback	No. of ABs per 1000 registered population	Low
Hemkens, 2017	Switzerland	2900 physicians	All	Social norm feedback	Antibiotic DDD per 1000 consultations	Low
Hurlimann, 2016	Switzerland	136 practices	RTI; UTI	Social norm feedback	% AB prescriptions for upper RTIs; % penicillins for RTI; % trimethoprim/sulfamethoxazole for UTI	Moderate
Kronman, 2020	US	57 physicians	RTI	Social norm feedback	% of RTI with AB prescribed	Low
Lagerlov, 2000	Norway	199 physicians	UTI	Social norm feedback	% inappropriate ABs for UTI	High
Mainous, 2000	USA	216 physicians	RTI	Social norm feedback	% inappropriate AB treatments	Low

Meeker, 2014	USA	14 physicians	RTI	Public commitment	No. of ABs per 100 AB inappropriate RTIs	Moderate
Meeker, 2016	USA	244 physicians	RTI	Social norm feedback, accountable justification, suggested alternatives	No. of ABs per 100 AB inappropriate RTIs	Moderate
O'Connell, 1999	Australia	2440 physicians	All	Social norm feedback	No. of ABs per 100 consultations	Moderate
Persell, 2016	USA	28 physicians	RTI	Social norm feedback, accountable justification, suggested alternatives	No. of ABs per 100 RTIs; No. of ABs per 100 AB inappropriate RTIs	High
Ratajczak, 2019	England	6995 practices	All	Social norm feedback	No. of ABs per 1000 registered population	Moderate
Sondergaard, 2003	Denmark	299 physicians	RTI	Social norm feedback	No. of ABs per 1000 registered population	Moderate
Yang, 2014	China	20 practices (54 physicians)	RTI	Public reporting	% of RTI consultations with AB; % of RTI consultations with >1 AB	Low

RTI is respiratory tract infections; UTI is urinary tract infections. AB is antibiotic. No. is number. DDD is defined daily doses.
[a]Risk of bias assessed using the Cochrane Effective Practice and Organisation of Care group's tool for studies with a control group. Overall rating assigned 'low' when all criteria were 'low' risk; 'medium' when 1-2 criteria were scored 'unclear' or 'high' risk; and 'high' when >2 criteria were scored 'unclear' or 'high' risk.
[b]Inappropriate with respect to antibiotic, doses and/or duration.

Table 3: Characteristics and promise rating of social norm feedback nudge interventions to improve antibiotic prescribing in primary care

Author, Year	Based on individual physician or practice data?	Frequency of feedback	Targeting high prescribers or all prescribers?	Prescribing compared to which peers?	Mode	Graphic display of prescribing?	Supporting information provided in intervention group	Effect on overall antibiotic prescribing
Awad, 2006	Practice	Twice, one month apart	All	Average of region	Letter	No	Recommendations for improvement; 2 personal visits	Reduction
BETA, 2018 & 2020	Physician	Once	Top 30% highest prescribers	Prescribing at a higher rate than e.g. 70% of physicians	Letter	Group 1: No Group 2: No Group 3: Yes	Group 1: education material Group 2: delayed prescribing Group 3: none	Reduction
Bradley, 2019	Practice	Once	Top 20% highest prescribing practices	Prescribing at higher rate than 80% of practices	Letter	No	None	Reduction
Chang, 2020	Physician	Every 10 days	All	Ranking within department	Electronic	No	Precautions for antibiotics being used	Reduction
Curtis, 2021	Practice	Thrice, 5 weekly	Top 20% highest broad-spectrum prescribing	All other practices	Letter, fax & email	Yes	Group 1: none Group 2: contact for more details, cost savings data	No change
Gerber, 2013	Physician	Quarterly for 1 year	All	Mean of practice and region	Email	Yes	1 hour presentation	Reduction
Hallsworth, 2016	Practice	Once	Top 20% highest prescribing practices	Prescribing at higher rate than 80% of practices	Letter	No	Patient focused education material	Reduction
Hemkens, 2017	Physician	Quarterly for 2 years	Top 50% highest prescribers	Mean of all physicians	Letter	Yes	Link to guidelines	No change

Hurlimann, 2016	Practice	Twice yearly for 2 years	All	Mean of intervention group	Letter	No	Guidelines	No change
Kronman, 2020	Physician	Four times, over 11 months	All	Mean of 20% lowest prescribers	Unclear	Yes	Online tutorials and videos	Reduction
Lagerlov, 2000	Physician	Twice, one week apart	All[a]	Mean of group	Meeting	Unclear	2 x educational meetings	Reduction
Mainous, 2000	Physician	Once	All	Percentile rank compared to peers	Letter	Unclear	Group 1: none Group 2: patient education	Reduction for group 2
Meeker, 2016	Physician	Monthly for 18 months	All[b]	Mean of top 10% lowest prescribers	Email	No	Link to guidelines	Reduction
O'Connell, 1999	Physician	Twice, six months apart	All	Interquartile range (25th-75th percentile)	Letter	Yes	Educational newsletter	No change
Persell, 2016	Physician	Monthly	All[b]	Mean of top 10% lowest prescribers	Email	No	Link to guidelines	Reduction
Ratajczak, 2019	Physician	Once	Top 20% highest prescribers	Prescribing at higher rate than 80%/90% of practices	Letter	No	Patient focused education material	Reduction
Sondergaad, 2003	Physician	Once	All	Mean of region	Letter	Unclear	Guidelines	Reduction

[a]Antibiotic prescribing rates for individual physicians were compared to that of 4-8 other physicians in their group based on geographical area.
[b]The prescribers with the lowest prescribing (bottom 10%) were notified they were 'Top performers'

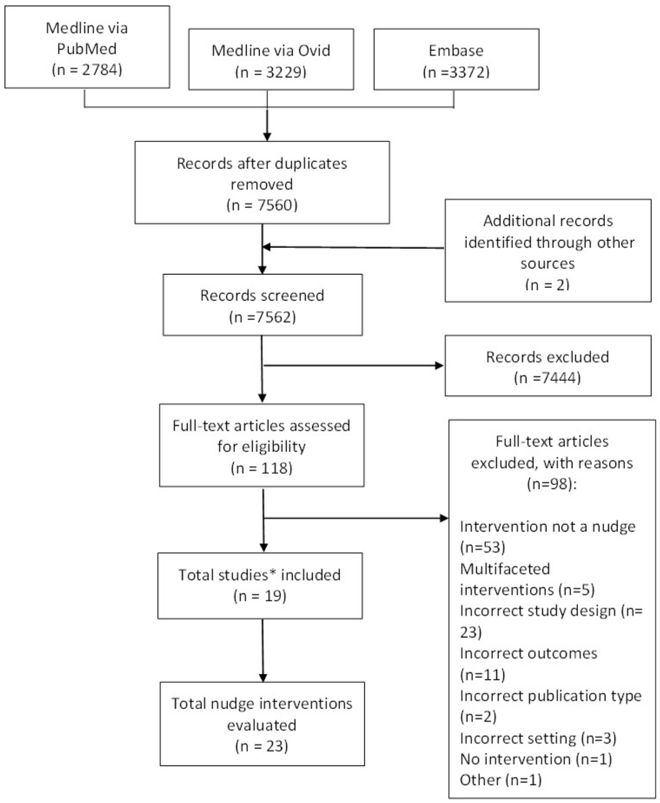

Figure 1: PRISMA flow chart of search and screening results
*One study had two publications.

243x193mm (120 x 120 DPI)

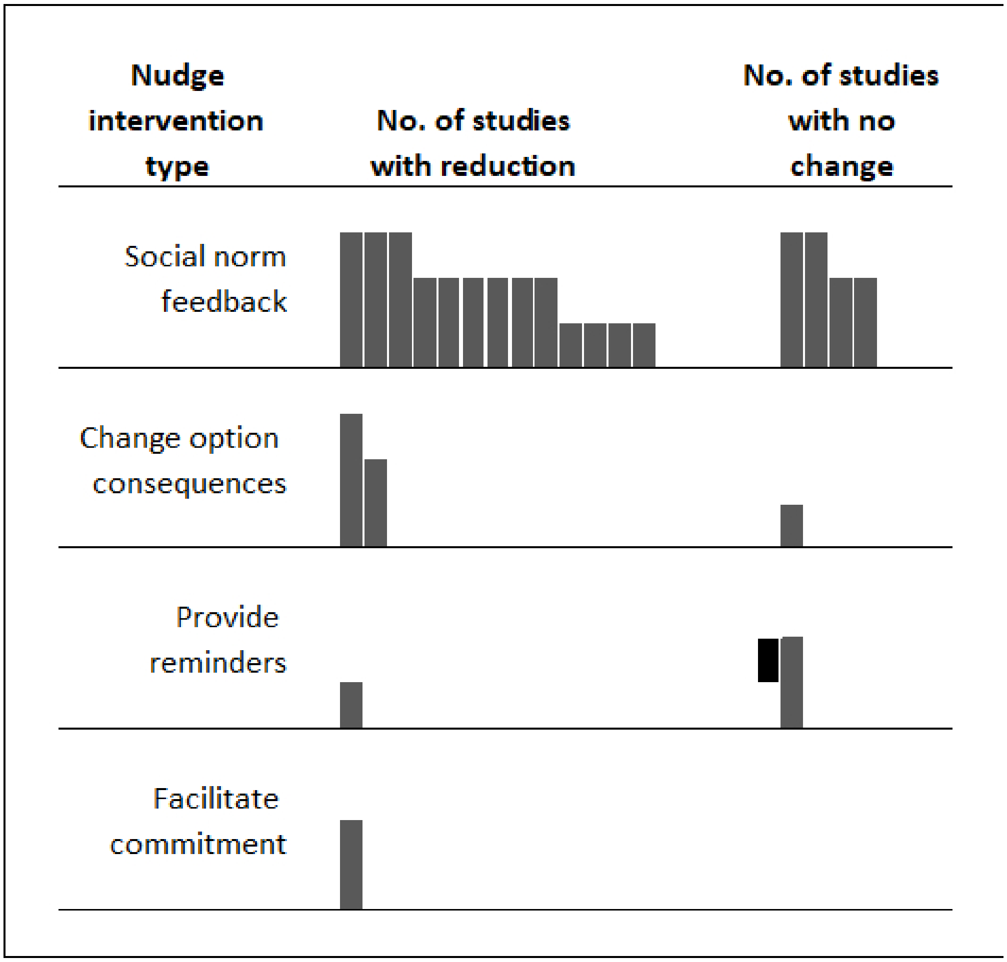

Figure 2: Harvest plot of effects of nudge interventions targeting antibiotic prescribing in primary care on overall antibiotic prescribing. Each mark or column represents one nudge intervention. Column height represents the risk of bias in the study: tallest columns are studies with low risk of bias; medium columns are moderate risk of bias; short columns are high risk of bias.

285x272mm (47 x 47 DPI)

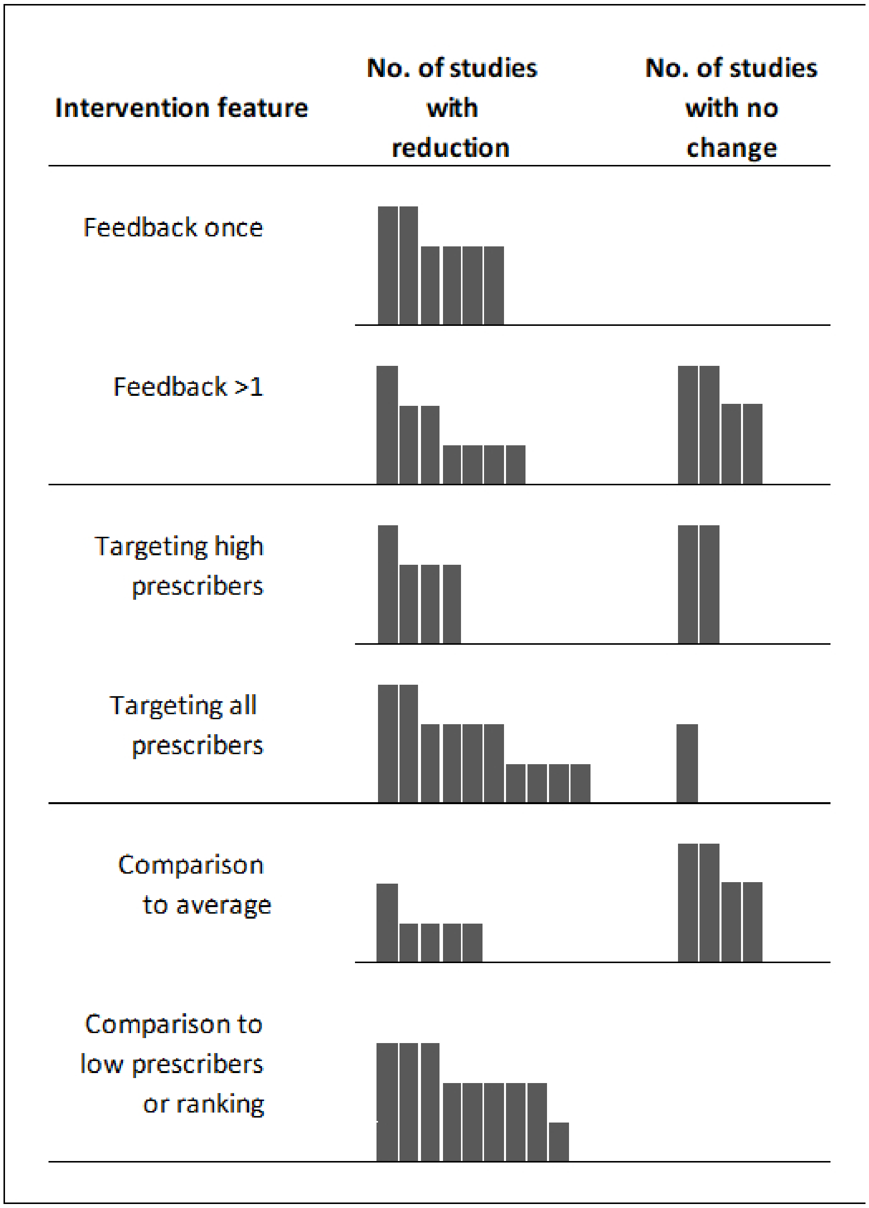

Figure 3: Harvest plot of effects of social norm feedback nudge interventions on overall antibiotic prescribing by intervention features. Each mark or column represents one nudge intervention. Column height represents the risk of bias of the study: tallest columns are studies with low risk of bias; medium columns are moderate risk of bias; short columns are high risk of bias.

281x390mm (47 x 47 DPI)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5-6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	n/a
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8-9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	10-11

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	n/a
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10-11
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	12
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12 & Supp file 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Tables 3 & 4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	14-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	12 & Supp file 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	17-18
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	22
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	22-23
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	24

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PRISMA 2009 Checklist

For more information, visit: www.prisma-statement.org.

Page 2 of 2

Raban et al. Nudge interventions to reduce unnecessary antibiotic prescribing in primary care: a systematic review

SEARCH STRATEGY

MEDLINE (via Ovid and PubMed)

Date searched: 23 April 2021

Search ID#	Search Terms
1	exp Ambulatory Care/
2	exp Community Medicine/
3	exp General Practice/
4	exp General Practitioners/
5	exp Primary Health Care/
6	exp Physicians, Family/
7	exp Physicians, Primary Care/
8	"general practice".ti,ab.
9	"general practitioner*".ti,ab.
10	"family physician*".ti,ab.
11	"family practice".ti,ab.
12	"primary care".ti,ab.
13	"primary health care".ti,ab.
14	"primary healthcare".ti,ab.
15	exp *anti-bacterial agents/tu or exp *anti-infective agents, urinary/tu
16	antibiot*.ti,ab.
17	anti-biot*.ti,ab.
18	anti-microb*.ti,ab.
19	antimicrob*.ti,ab.
20	anti-infective*.ti,ab.
21	antiinfective*.ti,ab.
22	anti-bacterial*.ti,ab.
23	antibacterial*.ti,ab.
24	randomized controlled trial.pt
25	controlled clinical trial.pt
26	pragmatic clinical trial.pt
27	multicenter study.pt
28	exp non-randomized controlled trials as topic/
29	exp controlled before-after studies/
30	(randomis* or randomiz* or randomly).ti,ab.
31	groups.ab.
32	(trial or multicenter or multi center or multicentre or multi centre).ti.
33	(intervention? or effect? or impact? or controlled or control group? or (before adj5 after) or (pre adj5 post) or ((pretest or pre test) and (posttest or post test)) or quasiexperiment* or quasi experiment* or evaluat*).ti,ab.
35	or/1-14
36	or/15-23
37	or/24-34

38	35 and 36 and 37
39	limit 38 to yr="1997 -Current"
40	limit 39 to english language
41	limit 40 to journal article
42	limit 41 to humans

Embase (via Ovid)

Date searched: 23 April 2021

Search ID#	Search Terms
1	exp Ambulatory Care/
2	exp Community Medicine/
3	exp General Practice/
4	exp General Practitioners/
5	exp Primary Health Care/
6	exp Family Medicine/
7	exp Primary Medical Care/
8	"general practice".ti,ab.
9	"general practitioner*".ti,ab.
10	"family physician*".ti,ab.
11	"family practice".ti,ab.
12	"primary care".ti,ab.
13	"primary health care".ti,ab.
14	"primary healthcare".ti,ab.
15	exp *anti-infective agents/
16	exp *anti-infective therapy/ or exp *antimicrobial therapy/
17	exp *antibiotic agent/
18	antibiot*.ti,ab.
19	anti-biot*.ti,ab.
20	anti-microb*.ti,ab.
21	antimicrob*.ti,ab.
22	anti-infective*.ti,ab.
23	antiinfective*.ti,ab.
24	anti-bacterial*.ti,ab.
25	antibacterial*.ti,ab.
26	exp "controlled clinical trial (topic)"/
27	exp epidemiology/
28	(randomis* or randomiz* or randomly).ti,ab.
29	groups.ab.
30	(trial or multicenter or multi center or multicentre or multi centre).ti.
31	(intervention? or effect? or impact? or controlled or control group? or (before adj5 after) or (pre adj5 post) or ((pretest or pre test) and (posttest or post test)) or quasiexperiment* or quasi experiment* or evaluat*).ti,ab.
32	or/1-14

Raban et al. Nudge interventions to reduce unnecessary antibiotic prescribing in primary care: a systematic review

33	or/15-25
34	or/26-31
35	32 and 33 and 34
36	limit 35 to english language
37	limit 36 to human
38	limit 37 to yr="1997 -Current"
39	limit 38 to (conference abstract or "conference review" or editorial or erratum or letter or note or "review")
40	38 not 39
41	remove duplicates from 40
42	limit 41 to embase

Websites searched

Date searched: 23 April 2021

Organisation name	**URL**
Behavioural Economics Team of the Australian Government	https://behaviouraleconomics.pmc.gov.au/
Behavioural Insights Team	https://www.bi.team
Danish Nudging Network	https://www.danishnudgingnetwork.dk/
iNudgeyou	https://inudgeyou.com/en/
Nudge France	http://www.nudgefrance.org/
Nudge-it	https://www.nudge-it.eu/
Nudge Italia	http://www.nudgeitalia.it/
Norwegian Nudging Network	https://sites.google.com/view/norsknudgenet/home
Penn Medicine Nudge Unit	https://nudgeunit.upenn.edu
The European Nudging Network	http://tenudge.eu/
The Swedish Nudging Network	https://theswedishnudgingnetwork.com/

Raban et al. Nudge interventions to reduce unnecessary antibiotic prescribing in primary care: a systematic review

SUPPLEMENTARY FILE 3

Table S3: Assessment of risk of bias* against each criterion for individual studies

Study	Random sequence generation	Allocation concealment	Baseline outcome measurements similar	Baseline characteristics similar	Incomplete outcome data	Blinding of outcome measurement assessment	Protections against contamination	Selective reporting	Other bias	TOTAL number of criteria with low risk of bias
Awad, 2006	✓	?	✓	?	?	?	✓	X	✓	4/9
BETA, 2018 & 2020	✓	✓	✓	✓	?	✓	✓	✓	✓	8/9
Bradley, 2019	X	X	✓	✓	✓	✓	✓	✓	✓	7/9
Chang, 2020	✓	X	✓	✓	✓	✓	✓	✓	✓	8/9
Curtis, 2021	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Gerber, 2013	✓	✓	✓	✓	?	X	?	✓	✓	6/9
Hallsworth, 2016	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Hemkens, 2017	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Hurlimann, 2016	✓	✓	✓	✓	✓	X	✓	✓	✓	8/9
Kronman, 2020	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Lagerlov, 2000	✓	✓	✓	✓	X	?	✓	?	X	6/9
Mainous, 2000	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Meeker, 2014	✓	✓	✓	✓	✓	✓	?	✓	✓	8/9
Meeker, 2016	✓	✓	?	?	✓	✓	✓	✓	X	6/9
O'Connell, 1999	?	✓	✓	✓	✓	✓	✓	✓	✓	8/9
Persell, 2016	✓	✓	✓	?	✓	✓	?	✓	X	7/9
Ratajczak, 2019	X	X	✓	✓	✓	✓	✓	✓	✓	7/9
Sondergaard, 2003	?	✓	✓	✓	✓	✓	✓	✓	✓	8/9
Yang, 2014	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Number of studies with high risk of bias	2	3	0	0	1	2	0	1	3	
Number of studies with unclear bias	2	1	1	3	3	2	3	1	0	
Number of studies with	15	15	15	16	15	15	16	17	16	

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low risk of bias										

'X' denotes high risk of bias for this criterion; '?' denotes unclear risk of bias; '✓' denotes low risk of bias.
*Risk of bias assessed using the Cochrane Effective Practice and Organisation of Care group's tool (https://epoc.cochrane.org/sites/epoc.cochrane.org/files/public/uploads/Resources-for-authors2017/suggested_risk_of_bias_criteria_for_epoc_reviews.pdf)

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SUPPLEMENTARY FILE 4

Table S4: Effects of nudge interventions to improve antibiotic use in primary care

Study	Design	Interventions	Control	Outcome/s	Follow-up period	Reported statistics	95% CI, p-value	Vote counting assessment
Decision information – provide social reference point								
Awad, 2006	Cluster randomised trial	Social norm feedback	Usual care	No. of consultations with AB prescribed	3-months post	Mean difference: -2.8	(-1.1, -4.6), p=0.004	Reduction
				No. of consultations with an inappropriate AB[a]	3-months post	Mean difference: -1.9	(-0.1, -3.7), p=0.040	n/a
BETA, 2018 & 2020	Cluster randomised trial	Social norm feedback with graph	Usual care	No. of ABs per 1000 consultations	6 & 12months post	Mean difference (6-months): -13.6 (~12% reduction) (12-months): -9.3 (~9.4% reduction)	6-months: (-16.6, -10.6), p<0.00001 12-months: (-12.3, -6.2); p<0.001	Reduction
		Social norm feedback with education material	Usual care	No. of ABs per 1000 consultations	6 & 12-months post	Mean difference (6-months): -10.3 (~9.3% reduction) (12-months):	6-months: (-13.8, -6.8), p<0.001 12-months: (-11, -5.6); p<0.001	n/a

						-8.3 (~8.4% reduction)		
		Social norm feedback with delayed prescribing	Usual	No. ABs per 1000 consultation	6 & 12-months post	Mean difference (6-months): -11.8 (~10.7% reduction) (12-months): -8.8 (~8.9% reduction)	6 months: (-14.7, -8.9); p<0.001 12-months: (-11.6, -6.0); p<0.001	n/a
Bradley, 2019	Regression discontinuity study	Social norm feedback	Usual care	No. of ABs per 1000 registered population	3-months post	Mean difference: -25.7	(-42.5, -8.8), p=0.0028	Reduction
					12-months post	Mean difference: -58.7 (~5% reduction)	(-116.7, -0.7), p=0.047	n/a
Chang, 2020	Cluster randomised crossover-controlled trial	Social norm feedback	Usual care	No. of AB prescriptions per total prescriptions	3-month intervention period	Relative reduction in intervention arm: 35.2%; in control arm: 30.8%	p<0.001	Reduction
					3-month intervention period (after crossover)	Relative reduction in intervention arm: 14.2%; in control arm: 4.6%	p<0.001	n/a

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Curtis, 2021	Randomised trial	Social norm feedback (standard)	Usual care	AB prescriptions per 1000 population	6-months post	No change	NS	No change
				Proportion of antibiotics which were broad spectrum	6-months post	2.1% reduction compared to controls	p=0.104	n/a
		Social norm feedback (optimised)	Usual care	AB prescriptions per 1000 population	6-months post	No change	NS	No change
				Proportion of antibiotics which were broad spectrum	6-months post	2.1% reduction compared to controls	P=0.046	n/a
Gerber, 2013	Cluster randomised trial	Social norm feedback	Usual care	ABs for viral RTI	12-month intervention period	DID: -1.7%	NR, p=0.93	Reduction
				Percent of broad spectrum ABs among children with AB prescription	12-month intervention period	DID: -6.7%	NR, p=0.01	n/a
Hallsworth, 2016	Randomised trial	Social norm feedback	Usual care	No. of ABs per 1000 registered population	6-months post	IRR: 0.967[b] (~3.3% reduction)	(0.957, 0.977), p<0.0001	Reduction
Hemkens, 2017	Randomised trial	Social norm feedback	Usual care	DDD per 1000 consultations	First 1-year intervention period	Between group difference: 0.81%	(-2.56, 4.30), NR	No change
					Second 1-year intervention period	Between group difference: -1.73%	(-5.07, 1.72%), p=0.32	

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Hurlimann, 2016	Cluster randomised trial	Social norm feedback	Usual care	Percentage of AB prescriptions for upper RTIs	24-month intervention period	Difference in proportion: -1.2	(-10.5, -8.2), p=0.66	No change
				Percentage of penicillins for RTI	24-month intervention period	OR: 1.42	(1.08-1.89), p=0.01	n/a
				Percentage of trimethoprim/sulfamethoxazole for UTI	24-month intervention period	OR: 2.16	(1.19-3.91), p=0.01	n/a
Kronman, 2020	Stepped wedge cluster randomised trial	Social norm feeback	Usual care	Percentage of RTI with antibiotic prescription	12-months	OR: 0.93	(0.90, 0.96), NR	Reduction
Lagerlov, 2000	Randomised trial	Social norm feedback	Intervention for asthma care	Percentage of inappropriate ABs for UTI	12-months post	Relative decrease: -9.6%	NR, p=0.0004	Reduction
Mainous, 2000	Randomised trial	Social norm feedback	Usual care	Mean proportion of inappropriate AB treatments	5-months post	NR	Not significant	-
		Social norm feedback with patient education material	Usual care	Mean proportion of inappropriate AB treatments	5-months post	Dunnett's T: 2.374	NR, p<0.05	Reduction
Meeker, 2016	Cluster randomised trial	Social norm feedback	Usual care	No. of ABs per 100 AB inappropriate RTIs	18-month intervention period	DID: -5.2%	(-6.9, -1.6), p<0.01	Reduction
O'Connell, 1999	Randomised trial	Social norm feedback	Interventions for other medication use	No. of AB prescriptions per 100 consultations	4-months post	Median: no difference between intervention and controls	NR	No change

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Persell, 2016	Randomised trial	Social norm feedback	Usual care	No. of ABs per 100 RTIs	12-month intervention period	OR: 0.73	(0.53, 0.995), p<0.05	Reduction
				No. of ABs per 100 AB inappropriate RTIs	12-month intervention period	OR: 0.45	(0.18, 1.11), NR	n/a
Ratajczak, 2019	Regression discontinuity study	Social norm feedback	Usual care	No. of ABs per 1000 registered population	6-months post	Percent change in intervention group: -3.69%	(-5.10,-2.29), p<0.001	Reduction
Sondergaad, 2003	Randomised trial	Social norm feedback	Guidelines	No. of ABs per 1000 registered patients	3-months post	Mean difference: -0.6	(-2.8, 1.6), NR	Reduction
				Percent of prescriptions for narrow-spectrum penicillins	3-months post	Mean difference: 0.7	(-0.41, 1.7), NR	n/a
Decision structure – change option consequences								
Meeker, 2016	Cluster randomised trial	Accountable justification	Usual care	No. of ABs per 100 AB inappropriate RTIs	18-month intervention period	DID: -7.0%	(-9.1, -2.9), p<0.001	Reduction
Persell, 2016	Randomised trial	Accountable justification	Usual care	No. of ABs per 100 RTIs	12-month intervention period	OR: 1.05	(0.80, 1.39), NR	No change
				No. of ABs per 100 AB inappropriate RTIs	12-month intervention period	OR: 0.98	(0.42, 2.29), NR	n/a
Yang, 2014	Cluster randomised trial	Public reporting	Education	Percentage of RTI consultations with AB	5-8 months post	DID: -1.93	(-6.61, 2.75), p=0.419	Reduction
				Percentage of RTI consultations with >1 AB	5-8 months post	DID: -6.97	(-13.94, 0.00), p=0.049	n/a

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Decision assistance – provide reminders								
Meeker, 2016	Cluster randomised trial	Suggested alternatives	Usual care	No. of ABs per 100 AB inappropriate RTIs	18-month intervention period	DID: -5.0%	(-7.8, 0.1%), p=0.66	Reduction
Persell, 2016	Randomised trial	Suggested alternatives	Usual care	No. of ABs per 100 RTIs	12-month intervention period	OR: 0.72	(0.54, 0.96), p<0.01	Reduction
				No. of ABs per 100 AB inappropriate RTIs	12-month intervention period	OR: 0.68	(0.29, 1.58), NR	n/a
Decision assistance – facilitate commitment								
Meeker, 2014	Randomised trial	Public commitment		No. of ABs per 100 AB inappropriate RTIs	12-week intervention period	DID: -19.7%	(-5.8, -33.04), p=0.02	Reduction

No. is 'number'. AB is 'antibiotic'. CI is 'confidence interval'. IRR is 'incidence rate ratio'. DDD is 'defined daily doses'. OR is odds ratio. RTI is 'respiratory tract infection'. UTI is 'urinary tract infection'. DID is 'difference in differences analysis'. NR is not reported. NS is 'not significant'.

*The intervention promise was assessed based on all antibiotic outcomes reported in each study.

[a]Inappropriate with respect to antibiotic, doses and/or duration.

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Nudge interventions to reduce unnecessary antibiotic prescribing in primary care: a systematic review

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ABSTRACT

Objectives

Antibiotic prescribing in primary care contributes significantly to antibiotic overuse. Nudge interventions alter the decision-making environment to achieve behaviour change without restricting options. Our objectives were to conduct a systematic review to describe the types of nudge interventions used to reduce unnecessary antibiotic prescribing in primary care, their key features, and their effects on antibiotic prescribing overall.

Methods

Medline, Embase and grey literature were searched for randomised trials or regression discontinuity studies in April 2021. Risk of bias was assessed independently by two researchers using the Cochrane Effective Practice and Organisation of Care group's tool.

Results were synthesised to report the percentage of studies demonstrating a reduction in overall antibiotic prescribing for different types of nudges. Effects of social norm nudges were examined for features that may enhance effectiveness.

Results

Nineteen studies were included, testing 23 nudge interventions. Four studies were rated as having a high risk of bias, nine as moderate risk of bias, and six as at low risk. Overall, 78.3% (n=23, 95% CI: 58.1, 90.3) of the nudges evaluated resulted in a reduction in overall antibiotic prescribing. Social norm feedback was the most frequently applied nudge (n=17), with 76.5% (n=13; 95% CI: 52.7, 90.4) of these studies reporting a reduction. Other nudges applied were changing option consequences (n=3; with 2 reporting a reduction), providing

reminders (n=2; 1 reporting a reduction), and facilitating commitment (n=1; reporting a reduction). Successful social norm nudges typically either included an injunctive norm, compared prescribing to physicians with the lowest prescribers or targeted high prescribers. .

Conclusions

Nudge interventions are effective for improving antibiotic prescribing in primary care. Expanding the use of nudge interventions beyond social norm nudges could reap further improvements in antibiotic prescribing practices. Policy-makers and managers need to be mindful how social norm nudges are implemented to enhance intervention effects.

STRENGTHS AND LIMITATIONS

- This study employed a broad search strategy and the assessment of whether an intervention was a nudge was conducted at the full-text stage.
- Implementation features of social norm nudges were extracted from the studies.
- We were not able to synthesise results with meta-analysis due to the differences in outcome measures reported.

KEYWORDS

Antimicrobial Stewardship; Primary Health Care; General Practice; Clinical Decision-Making; Quality of Health Care; Economics, Behavioural; Psychology; Systematic Review;

INTRODUCTION

Antimicrobial resistance is one of the most pressing challenges to global health [1]. Overuse and inappropriate use of antibiotics is a major contributor to the rise of antimicrobial resistance, and yet, between 2000 and 2010 global antibiotic consumption rose by 35% [2]. Concerningly, global per-capita consumption of antibiotics flagged by the World Health Organization (WHO) as having high resistance potential (Watch category) [3] rose by 90.9% between 2000 and 2015 [4]. Primary care accounts for the majority of antibiotic use, and rates of inappropriate use are estimated to be high [5-7]. For example, the majority of upper respiratory tract infections do not benefit from antibiotic treatment, particularly when weighed against the rates of adverse effects, however, antibiotics continue to be prescribed [5, 8, 9].

Efforts to reduce antibiotic prescribing in primary care have predominantly focused on the use of point-of-care testing, shared decision-making, and education strategies aimed at physicians and patients [10-12]. While some of these intervention strategies have been successful in improving antibiotic prescribing, they can be resource intensive, and in some cases only provide marginal reductions in antibiotic prescribing [10-12]. Furthermore, these intervention strategies rarely take account of how cues in the environment, unrelated to clinician knowledge or access to resources such as information or tests, can influence decision-making.

The field of behavioural economics has generated a collection of approaches, called 'nudges', that involve subtle changes in the decision-making environment, or choice architecture, to guide people towards a specific decision or behaviour. Nudge interventions are typically simple and low-cost interventions, and thus are attractive to healthcare managers and policy makers. Furthermore, they do not restrict choices or penalise 'unfavourable' choices, thus preserving an individual's autonomy in the decision-making process. Examples of nudge interventions include changing default settings, changing option consequences, and providing reminders during the decision-making process.

Nudge interventions have similarities to traditional behaviour change techniques applied in health services and public health.[13, 14] For example, audit and feedback has long been applied in health service interventions and has similarities to social norm feedback nudges. However, audit and feedback may not necessarily include a comparison to the performance of peers, the essential component that would make it a nudge.[15, 16] Furthermore, social norm feedback nudges tend to target 'underperformers', as evidence from psychology has demonstrated a 'boomerang' effect; i.e. that high performers drop their performance toward the group mean (beyond that expected due to regression toward the mean).[17] However, audit and feedback interventions used in health services may not take performance into account when deciding on who should receive feedback. Thus, there can be nuanced differences in the techniques from each of these paradigms.

Nudge interventions have been successfully implemented in fields other than health [18], and the evidence base for their use in influencing consumers' health-related behaviours is growing [19, 20]. However, while the use of nudge interventions in specific areas of health services and to influence clinical decision making is increasing,[18, 21] there is emerging evidence that the effect of nudges can vary depending on the context in which they are applied, as well as the type of nudge implemented [22, 23]. Against this background, our aim was to explore the use of nudge interventions and their effectiveness to improve antibiotic prescribing in primary care, and to draw out lessons to inform future directions for nudge intervention design and testing in healthcare. Our specific objectives were to describe the types of nudge interventions trialled to date, their key features, and their effects on the rates of antibiotic prescribing overall, in order to elucidate "what kind of nudges work best in this … setting?"[22].

METHODS

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Supplementary file 1) [24].

Information sources and search strategy

The databases MEDLINE (via Ovid and PubMed) and Embase were searched for original research articles reporting on randomised trials or regression discontinuity studies of interventions to improve antibiotic prescribing in primary care, published in English in the last 20 years. Though the behavioural economics term 'nudge' was proposed in 2008, many of the interventions now termed 'nudges' have been applied to influence behaviour prior to the emergence of this term. Therefore, we did not exclude articles published before 2008 if the interventions met the criteria for a nudge intervention, and our search strategy did not include 'nudges' as a theme. Instead, our search strategy covered three themes: antibiotics AND primary care AND intervention study designs. The reference lists of included studies were hand searched for relevant citations. Websites of government nudge units and other organisations working to apply and test nudge theory were also searched for grey literature of relevance. Searches were carried out in April 2021. The full search strategy is presented in Supplementary file 2.

Eligibility criteria

Studies conducted in primary care facilities, general and family practices were included. Studies in hospital wards or in long-term care were excluded. The intervention tested had to fall under the broad definition of a nudge proposed by Thaler and Sunstein: "*A nudge… is any aspect of the choice architecture that alters people's behaviour in a predictable way without forbidding any options or significantly changing their economic incentives. To count as a mere nudge, the intervention must be easy and cheap to avoid*" [25]. For further guidance on whether the intervention used qualified as a nudge, we used a taxonomy of choice architecture techniques which focuses on interventions rather than the underlying cognitive processes of the interventions [26]. Interventions involving education, providing physicians with access to guidelines, passive decision support tools the clinician had to actively decide to use, and audit and feedback interventions with no social norm comparison were excluded. Studies evaluating multifaceted interventions that included a nudge strategy were also excluded as they did not allow evaluation of the impact of the nudge intervention alone. Studies had to evaluate the impact of the intervention on antibiotic prescribing rates or rates of appropriate antibiotic prescribing to be eligible. Randomised controlled trials and regression discontinuity studies were included. Regression discontinuity studies allow assessment of causality in studies where a cut-off point is used to allocate an intervention. This is of particular relevance to social norm nudges, where, e.g. the bottom 10% performers are targeted by an intervention. Studies have shown that regression discontinuity studies have similar effect estimates to randomised trials, though they require a large sample size.[27, 28] Interrupted time-series, controlled before-after, cross-sectional, and before-after studies were excluded as they are at higher risk of bias.

Study selection

Titles and abstracts of citations returned from the searches were independently reviewed by at least two reviewers. At this stage, the reviewers assessed study setting, study design and outcomes for eligibility. The full-text of all selected citations were then reviewed independently by two of three authors against all eligibility criteria, including an assessment of whether the intervention qualified as a nudge using the definitions outlined above. Discrepancies between reviewers were resolved through discussions until consensus was reached.

Data collection and data items

Data extraction and categorisation of interventions was carried out independently by two reviewers for each study. We extracted data on study characteristics (country, study years, sample size), nudge intervention description, types of infections targeted (e.g. all, respiratory tract infections [RTIs], urinary tract infections [UTIs]), outcomes, and study results. When studies reported more than one outcome, we extracted results for the outcome measuring changes in overall antibiotic use, appropriate antibiotic use, and any outcome defined as the primary outcome of the study. When a study trialled more than one nudge intervention, we extracted intervention data on the impact of each nudge individually.

Nudge interventions were classified using a taxonomy of choice architecture techniques (Table 1) [26], and we refer to these as nudge intervention categories.

Table 1: Taxonomy of choice architecture techniques with implementation examples[26]

Category	Technique	Technique examples
A. Decision information	A1. Translate information	• Reframe information • Simplify information
	A2. Make information visible	• Provide real-time feedback • Make external information visible
	A3. Provide social reference point	• Refer to descriptive norm (social norm feedback) • Refer to opinion leader
B. Decision structure	B1. Change choice defaults	• Set no-action default • Use prompted choice
	B2. Change option-related effort	• Increase/decrease physical effort • Increase/decrease financial effort
	B3. Change range or composition of options	• Change categories of options • Change grouping of options
	B4. Change option consequences	• Connect decision to benefit or cost • Change social consequences
C. Decision assistance	C1. Provide reminders	• Make information more or less salient
	C2. Facilitate commitment	• Support self-commitment/public commitment

Social norm feedback nudge interventions are a frequent behaviour change technique in healthcare, often termed audit and feedback. Social norm feedback involves providing people with feedback on their performance relative to their peers. However, this can be implemented in a variety of way. For example, the comparison can be descriptive or injunctive, i.e. associating a judgement to the performance. Psychology and health research has shown that certain features may enhance social norm feedback interventions,[15-17, 29] and thus, we extracted details of how social norm nudges were implemented (Box 1), with the aim that this may further elucidate the important features of effective social norm nudges to reduce antibiotic prescribing in primary care.

Box 1: Social norm feedback nudge features extracted from studies

- Target of intervention: high antibiotic prescribers or all physicians
- The comparison group (average of group, top performers or rank within peers)
- Use of injunctive or descriptive norm
- Frequency of feedback
- For studies with more than one round of feedback: whether the norm for comparison was static or dynamic (i.e. did it change as the outcome change?)
- Use of a static norm or dynamic norm (i.e. one that changes with group performance)
- Whether feedback was based on prescribing data for practices or individual physicians
- Whether the reported performance was relative or absolute
- Was the antibiotic use reported on for all antibiotics or for diagnoses where antibiotic use is inappropriate
- The mode of intervention delivery (e.g. letter, email, meeting)
- Whether a graphic representation of data was included
- Whether supporting information was provided to aid behaviour change

Assessment of risk of bias in included studies

The risk of bias of each study was assessed using the Cochrane Effective Practice and Organisation of Care group's tool for studies with a separate control group [30]. Each study was independently assessed by two authors against each of the nine criteria assigning a score of either low risk, high risk, or unclear risk of bias. Discrepancies were resolved through discussion. A summary assessment of the overall risk of bias was allocated to each study as follows: *low risk of bias* when all criteria were scored 'low', *medium risk of bias* when one or two criteria were scored 'unclear' or 'high' risk, and *high risk* when more than two criteria scored 'unclear' or 'high' [31].

Synthesis of results

Inconsistencies in the outcomes and data reported in the studies precluded meta-analysis. Thus, we applied vote counting to summarise results for each category of nudge intervention and for features of social norm feedback nudges [32]. Vote counting allows a comparison of the number of effects reporting a benefit to the number that showed no benefit. It is the recommended method by Cochrane for summarising studies when meta-analysis or other quantitative methods are not able to be applied [32]. For each nudge intervention, we recorded whether the study demonstrated a reduction or no change in overall antibiotic prescribing compared to controls. As per the Cochrane Handbook, the statistical significance of the effect was not taken into account, so as not to erroneously conclude that underpowered studies had no effect. For studies with multiple study outcomes, we only considered the effect on overall antibiotic prescribing. The percentage of interventions with a reduction in overall antibiotic prescribing was calculated for all nudge interventions and social norm feedback nudges. Sensitivity analyses were conducted removing studies with a high risk of bias. Confidence intervals for proportions were calculated using the Wilson method. Effect sizes from studies were summarised narratively by reporting the range of change for overall antibiotic prescribing outcomes.

We used harvest plots to graphically summarise the vote counting results [33]. In a harvest plot, each mark represents a study or intervention. We used the position of the mark to indicate whether the intervention effect (reduction or no change in overall antibiotic prescribing) and the size of the mark to indicate the risk of bias of the study (low risk studies having a larger mark). Harvest plots were created for all nudge interventions by nudge category, and for social norm nudges by whether the intervention targeted high antibiotic prescribers or all prescribers, whether the comparison group was the average or above average performers, and whether the feedback was a descriptive or injunctive norm. These features were chosen as there is evidence from the psychology literature that they play an important role in intervention effects and avoid possible negative impacts, such as the boomerang effect. Thus, the stratification of the social norm nudge interventions by these features aimed to examine if there was evidence these features were important for intervention effects in the context of antibiotic prescribing in primary care. Lastly, results from studies that directly compared different nudge interventions, social norm nudge implementation strategies, or examined intervention effects over time or on different sub-groups, were described narratively.

Public and patient involvement

Patients or the public were not involved.

RESULTS

Nineteen studies were assessed as eligible for inclusion (Figure 1) [34-49]. Table 2 presents study characteristics. One study was a pilot study [46] of a larger trial [44], but was included as a separate study as it was conducted in a different population. The majority of studies were conducted in Europe (n=8) [36, 38-41, 47, 48], six in the United States [37, 42-44, 46], two in Australia [35, 45], two in China [49], and one in Sudan [34]. Seventeen studies were randomised controlled trials and two were regression discontinuity studies [36, 47]. Interventions were aimed at improving antibiotic use for all types of infections in nine studies [34-36, 38, 39, 45, 47], RTIs in eight studies [37, 42-44, 46, 48, 49], UTIs in one study [41], and both RTIs and UTIs in one study [40].

Risk of bias in included studies

Four studies were rated as having a high overall risk of bias [34, 37, 41, 46], nine as moderate risk of bias [35, 36, 40, 43-45, 47, 48], and six as at low risk of bias (Table 2) [38, 39, 42, 49]. Overall scores of meeting risk of bias criteria ranged from 4/9 to 9/9 across studies. No single criterion was more frequently at high or unclear risk of bias across studies. Supplementary file 3 shows the risk of bias assessment against each of the criteria for each study.

Description of nudge interventions

Seventeen studies evaluated one type of nudge intervention and two evaluated three types of nudge interventions each [43, 44], with a total of 23 nudge interventions evaluated. Three studies compared different features of social norm nudges[35, 42].

Social norm feedback nudges ('Decision information' category of nudge interventions) were the most common intervention (n=17) evaluated [34-42, 44-48]. Implementation of social norm feedback varied between studies (Figure 2). Social norm feedback was most commonly: sent to all prescribers (n=11) [34, 37, 40-42, 45, 46, 48] as opposed to the highest prescribers only [35, 36, 38, 39, 47, 50, 51]; and compared prescribing to the group average (n=12) [34-36, 38, 40, 41, 45, 47, 48, 50]. Only four studies used an injunctive norm, which also provided a positive reinforcement to those performing well.[41, 44, 46, 52] Feedback was typically provided more than once (n=11) [34, 37, 39-41, 44-46]; based on prescribing data for individual physicians (n=12) [35, 37, 39, 41, 42, 44-48]; and distributed via letters (n=11) [34-36, 38-40, 42, 45, 47, 48]. Studies also cited application of other behavioural techniques or considerations in the design of their social norm feedback, such as the inclusion of actionable advice, and addressing the feedback letter from a high profile or respected individuals.

Three interventions used nudge techniques from the 'Decision structure' category involving changing option consequences (Table 3) [44, 46, 49]. Three interventions used techniques from the 'Decision assistance' category (Table 3) involving providing reminders via suggested alternatives to antibiotic use (n=2) [44, 46] and a statement of public commitment to reducing antibiotic use in RTIs (n=1) [43].

Table 3: Description of nudge and direction of effect on overall antibiotic prescribing in primary care (other than social norm feedback)

Nudge category/ Author, year	**Type of nudge**	**Mode**	**Description**	**Intervention effect***
Decision structure – change option consequences				
Meeker, 2016	Accountable justification	Electronic health record	At time of prescribing an antibiotic, physicians were asked to justify their treatment decision in a mandatory free text field. The prompt informed physicians the justification would be visible in the patient's record.	Reduction
Persell, 2016	Accountable justification	Electronic health record	At time of prescribing an antibiotic, physicians were asked to justify their treatment decision in a mandatory free text field. The prompt informed physicians the justification would be visible in the patient's record.	No change
Yang, 2014	Public reporting	Posters and reports	Posters with antibiotic prescribing data were publicly displayed in the primary care clinics and reports with the data were sent to clinic managers and local health authorities.	Reduction
Decision assistance – provide reminders				
Meeker, 2016	Suggested alternatives	Electronic health record	At time of prescribing an antibiotic, a pop-up screen stated antibiotics are generally not indicated for the diagnosis and showed a list of alternative treatments.	Reduction
Persell, 2016	Suggested alternatives	Electronic health record	At time of prescribing an antibiotic, a computerised order set appeared with treatment alternatives and education materials for the patient.	Reduction

Decision assistance – facilitate commitment				
Meeker, 2014	Public commitment	Poster	A poster-sized letter signed by physicians and posted in examination rooms indicating commitment to reducing antibiotics for RTIs.	Reduction

*Results of vote counting assessment based on nudge effect on overall antibiotic prescribing

Effect of nudge interventions on overall antibiotic prescribing rates

Of the 23 nudge interventions evaluated, 78.3% (n=17, 95% CI: 58.1, 90.3) showed a reduction in overall antibiotic prescribing rates. Removing studies with a high risk of bias, the percentage of studies showing a reduction in overall antibiotic prescribing was 76.5% (n=12, 95% CI: 52.7, 90.4). Figure 3 shows the distribution of intervention effects by the type of nudge strategy evaluated.

Of the seventeen studies evaluating social norm feedback nudges, 76.5% (n=13, 95% CI: 52.7, 90.4) reported a reduction in overall antibiotic prescribing (Figure 3). Removing studies with a high risk of bias, this percentage was 69.2% (n=9, 95% CI: 42.4, 87.3). Figure 4 shows social norm nudges stratified by whether they targeted only high prescribers or all prescribers, the comparison group and the use of an injunctive or descriptive norm. All but two (83%) studies targeting high prescribers or using an injunctive norm or a comparison to low prescribers reported a reduction in overall prescribing. Whereas 60% of studies without these features reported a reduction in antibiotic prescribing.

Effect size of nudge interventions on antibiotic prescribing rates

The effect sizes of social norm feedback interventions on the number of antibiotics/1000 consultations (n=3) ranged from no change [45] to a reduction of 13.6% (95% CI: 16.6, 10.6) at 6-months post-intervention [35]; and the number of antibiotic prescriptions/1000 registered population (n=5) from no change [51] to an approximate 5% reduction (-58.7/1000 population [95% CI: 116.7, 0.7]) 12-months post intervention [36].

Studies measuring antibiotic prescribing for specific infection types reported absolute difference effect sizes of -1.2% (95% CI: -10.5, 8.2) [40], -1.7% (p=0.93) [37], and -5.2% (95% CI: -6.9, -1.6) [44] in the proportion of upper RTI treated with an antibiotic; a relative decrease of 9.6% (p=0.0004) [41] in inappropriate antibiotic for UTIs, and lower odds of antibiotic prescribing for RTI (OR: 0.73 (95% CI: 0.53, 0.995)) [46].

The effect sizes of the two studies of accountable justification interventions ranged from no change [46] to a reduction of 7.0 percentage points (95% CI: 9.1, 2.9) [44] in the number of antibiotics/100 antibiotic inappropriate infections. One study of public reporting showed a 1.93 percentage point reduction (95% CI: -6.61, 2.75) in the percentage of RTI consultations with an antibiotic, and a 6.97 percentage point (95% CI: -13.9, 0.00) reduction in the percentage of RTI consultations with >1 antibiotic.

Supplementary file 4 provides details of the effects of interventions on outcomes.

Studies comparing the effects of different nudge interventions

Two studies compared the impact of three different types of nudge interventions on antibiotic prescribing for RTIs [44, 46]. One study (with a moderate risk of bias) examined the impact of nudges on RTI where an antibiotic was not indicated, i.e. antibiotic inappropriate RTIs [44]. This study reported a reduction in the prescribing of antibiotics for antibiotic inappropriate RTIs in the physician groups receiving social norm feedback and accountable justification nudges, and a non-significant reduction in the physician group receiving a suggested alternatives nudge intervention [44]. The second study (high risk of bias) compared the same three nudge interventions, and reported a reduction in antibiotic prescribing for all

RTIs for the social norm feedback and suggested alternative nudges, but not in the groups receiving the accountable justification nudges [46].

Supplementary file 4 provides details of the impact of interventions on outcomes and their vote counting results.

Social norm nudge effects over time and following repeat messaging

Two studies examined the effect of a single social norm nudge letter sent to high antibiotic prescribing physicians over time and both reported a diminishing effect on prescribing rates compared to controls over time [35, 36]. In one study, the effect of the intervention was examined over 12-months after the letter was sent [36]. While there was a significant reduction in antibiotic prescribing compared to controls in the 12 months after the intervention, the effect diminished over time, such that the reductions in antibiotic prescribing rates in the second, third and fourth quarters after the intervention were not statistically significant. The second study also reported a diminishing effect of the social norm nudge letter over a 12-month period, but the reduction continued to remain significant at 12-months after the intervention [35, 50].

Two studies examined the impact of repeat social norm feedback interventions over time [39, 47]. In the first study, the effect of quarterly social norm feedback sent to the top 50% of antibiotic prescribers was assessed for 2 years [39]. While there was no difference in overall antibiotic prescribing rates in the first and second years of the intervention, there was a significant reduction in the antibiotic prescribing for children and adolescents in the first year (-8.6%) and young to middle-aged adults in the second year of the intervention (-4.6%). In the second study, a social norm nudge was first used in 2014 targeting the top 20% antibiotic prescribers, and due to its success was repeated annually since [47]. The study evaluated whether the intervention reduced antibiotic prescribing by physicians who had previously received the letter and those that had not. The top 10% of prescribers did not reduce their prescribing whether or not they had previously been sent a letter. However, the top 11-20% antibiotic prescribers reduced their antibiotic prescribing even when they had previously been sent a letter. The authors speculated that the failure of the top 10% to reduce antibiotic prescribing may have been due to the more forceful message in the communication they received (i.e. that the great majority (90%) of practices prescribed fewer antibiotics), resulting in negative attitudes to the message and a lower behavioural intention to reduce prescribing.

DISCUSSION

In this systematic review we have compiled the evidence on the effectiveness of nudge interventions in reducing antibiotic prescribing in primary care. Overall, 78.3% of studies reported a reduction in antibiotic prescribing. Social norm feedback was the most frequently evaluated nudge, and the evidence suggests that comparisons should include an aspirational target, injunctive norm or target high prescribers to enhance intervention effects. However, future research should explore the types of features that will further enhance social norm feedback nudges in this context. Only four studies examined nudge strategies other than social norm nudges, such as changing option consequences, providing reminders and facilitating commitment, thus further research is also needed to evaluate other nudge strategies despite promising results thus far of their effectiveness.

The studies included in this review trialled five different nudges (social norm feedback, accountable justification, public reporting, suggested alternatives and public commitment) from four of the nine subcategories of choice architecture techniques described by Munscher [26]. Two other broad reviews of nudges targeting health providers reported identifying a similar number of nudges employed in their included studies, but the types of nudges applied differed to those that we identified.[21, 53] For example, changing choice defaults is a frequently applied nudge to guide health care provider behaviour, but was not used to influence antibiotic prescribing in our review.[21, 53] Another example of a nudge not applied in studies in our review, but used in other contexts targeting health providers is changing the framing of information.[21, 53] Thus, there is scope for implementing and evaluating other nudge techniques in the primary care setting to improve antibiotic use. This is important since it is currently not clear whether the same nudge applied over more than one year will continue to have sustained impact.

We attempted to elucidate whether features of social norm feedback nudges have a role in their effectiveness. For example, the behavioural economics literature suggests that social norm nudges should only be provided to poor performers (i.e. high antibiotic prescribers in our case).[25] This is because of the 'boomerang effect' that may occur in individuals performing above average when they are provided social norm feedback confirming their above average performance, i.e. they reduce their performance. The studies in our review most frequently provided the social norm feedback to all prescribers (not only high prescribers) and all but one of these studies showed a reduction in overall antibiotic prescribing. However, the studies providing feedback to all prescribers also predominantly provided feedback more than once, which may have played a role in the reduction in antibiotic prescribing. Other factors that may have played a role in the prevention of a 'boomerang' effect in low prescribers, was the way the use of an injunctive norm and the comparison group used in the feedback. For example, one study informed the physicians with the lowest prescribing that they were a 'top performer', whereas the remaining physicians were informed they were 'not a top performer' [44]. The psychology literature supports the use of an injunctive norm when providing feedback i.e. conveying social approval or disapproval, as a way to eliminate the 'boomerang' effect [17]. The study also compared physicians' performance to the mean of the lowest decile prescribers, rather than the group mean [44]. Our results showed that comparison of performance to the group mean, use of a descriptive norm and targeting all prescribers produced mixed results with three of five studies reporting a reduction in antibiotic prescribing. Thus, our results support the use of injunctive norms, comparisons to the lowest prescribers or targeting the highest prescribers.

The frequency of feedback may also play a role in social norm nudge effects. In the study described above that informed prescribers they were a ‘top performer’ or ‘not a top performer’, feedback was provided on a monthly basis, which allowed physicians to assess the degree to which they had changed their antibiotic prescribing [44]. This is a different approach to studies that targeted only the high prescribers, i.e. poor performers. These studies tended to provide the feedback once, informing the physicians that they prescribed at a higher rate than e.g. 80% of their peers [35, 36, 38, 47, 50]. However, care should be taken when deciding on the comparison group, as if becoming a ‘top performer’ is perceived as unattainable, this can be demotivating. This can occur when the comparison norm is dynamic, i.e. changes according the group’s behaviour, which was the case in all our studies that provided feedback more than once (Figure 2). For example, if the comparison group is consistently the top 10%, 90% of people will never reach the target. One study included in our review reported that the top 10% of prescribers did not change their prescribing behaviour following the social norm nudge, despite an overall reduction following the intervention [47]. The authors speculated this may be due to the message not motivating behaviour change. Furthermore, individuals need to trust the data being presented is an accurate representation of their performance, and in the case of antibiotic prescribing, adequately accounts for the clinical features of the populations they treat. Thus, it is crucial for there to be an understanding of factors that may affect the intervention during intervention design so as to maximise impact [23].

It has been suggested that we can also learn from nudges that fail [14, 54]. There were four studies that implemented a social norm feedback nudge that had no effect on overall antibiotic prescribing [39, 40, 45, 51]. All four studies had two intervention features in common. Firstly, the peer comparison used was the mean prescribing rate of the group or in the case of one study the interquartile range of the group. For those prescribers that were at the mean prescribing level or marginally below it, this may not have provided enough motivation to change their behaviour. Furthermore, as mentioned above, the 'boomerang effect' may occur in individuals performing above average. Secondly, the feedback in the four evaluations of social norm nudges that did not reduce overall prescribing was not provided from a high-profile or respected figure, which may have reduced the salience of the message.

The literature on audit and feedback interventions in healthcare provides insights into what features make these interventions more effective, and complement those from the behavioural economics and psychology literature [16]. A Cochrane review found that feedback is more likely to be effective when: baseline performance is low; the source is a supervisor or colleague; the frequency is more than once; it is delivered both verbally and in written formats; and when feedback includes both targets and an action plan [15]. Many of these features were included in the social norm nudges we identified in this review. For example, most of the social norm nudges included information on appropriate antibiotic prescribing in primary care. Thus, synthesising such evidence from behavioural economics and psychology is likely to enhance the effectiveness of these interventions.

This systematic review has a number of strengths. Firstly, our search strategy was inclusive of all studies evaluating interventions to improve antibiotic prescribing in primary care. The selection of studies based on the type of intervention occurred at the full-text screening stage to ensure that studies not explicitly stating they used nudge techniques were included. Secondly, we used a comprehensive taxonomy of behavioural architecture techniques,[26] rather than attempting to ascertain whether the underlying cognitive processes addressed by the intervention had the features of a nudge. However, there are a number of limitations. We were unable to perform a meta-analysis or summarise the results quantitatively due to the heterogenous reporting of study outcomes. Furthermore, though we aimed to examine the features of social norm nudges that may enhance their effectiveness, the variation with which these nudges were implemented across a small number of studies prevented firm conclusions being drawn. The need for further research to improve the effectiveness of social norm nudges, also sometimes called audit and feedback interventions, in healthcare is recognised. Nonetheless, this review has provided practical insights into the use of nudge interventions to reduce antibiotic use in primary care, and highlighted areas for further research.

CONCLUSIONS

Health systems worldwide continue to struggle to consistently deliver evidence-based care [55]. Nudges can be used in lieu of, or to augment, more traditional efforts such as education (targeting clinicians, as well as the public), financial incentives, promotion of guidelines, and changing models of care. Evaluation of nudges applied in healthcare will play a key role in identifying interventions suitable for use in different contexts, including primary care, and in further developing applications of nudge strategies to improve the delivery of effective healthcare services.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

MZR conceived the study with JW and BN. MZR and GG designed the search strategy and GG ran the searches. MZR, GG and AN screened articles for inclusion with input from BN. MZR, GG and AN conducted data extraction and quality assessments. LL and KS provided support for the compilation of results. MZR compiled results and wrote the initial manuscript draft. All authors contributed to the editorial process of the manuscript and approved the final manuscript.

DATA SHARING STATEMENT

All data is available in the manuscript or Supplementary files.

ETHICS APPROVAL

This study does not involve human participants.

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FIGURE LEGENDS

Figure 1: PRISMA flow chart of search and screening results
*One study had two publications.

Figure 2: Implementation features of social norm feedback nudge interventions

Figure 3: Harvest plot of effects of nudge interventions targeting antibiotic prescribing in primary care on overall antibiotic prescribing. Each mark or column represents one nudge intervention. Column height represents the risk of bias in the study: tallest columns are studies with low risk of bias; medium columns are moderate risk of bias; short columns are high risk of bias.

Figure 4: Harvest plot of effects of social norm feedback nudge interventions on overall antibiotic prescribing by implementation features. Each mark or column represents one nudge intervention. Column height represents the risk of bias of the study: tallest columns are studies with low risk of bias; medium columns are moderate risk of bias; short columns are high risk of bias.

TABLES

Table 2: Characteristics of studies evaluating nudge interventions to improve antibiotic prescribing in primary care

Author, Year	**Country**	**Sample size**	**Infections targeted**	**Nudge intervention/s**	**Outcomes of interest**	**Overall risk of bias[a]**
Awad, 2006	Sudan	20 practices	All	Social norm feedback	No. of consultations with AB; No. of consultations with an inappropriate AB[b]	High
BETA, 2018 & 2020	Australia	6608 physicians	All	Social norm feedback	No. of ABs per 1000 consultations	Moderate
Bradley, 2019	Northern Ireland	331 practices	All	Social norm feedback	No. of ABs per 1000 registered population	Moderate
Chang, 2020	China	163 physicians	All	Social norm feedback	No. of AB prescriptions per 100 prescriptions	Moderate
Curtis, 2021	England	1401 practices	All	Social norm feedback	% broad spectrum AB of all AB	Low
Gerber, 2013	USA	162 physicians	RTI	Social norm feedback	% broad spectrum ABs among children with AB prescription; ABs for viral RTI	High
Hallsworth, 2016	England	1581 practices	All	Social norm feedback	No. of ABs per 1000 registered population	Low
Hemkens, 2017	Switzerland	2900 physicians	All	Social norm feedback	Antibiotic DDD per 1000 consultations	Low
Hurlimann, 2016	Switzerland	136 practices	RTI; UTI	Social norm feedback	% AB prescriptions for upper RTIs; % penicillins for RTI; % trimethoprim/sulfamethoxazole for UTI	Moderate
Kronman, 2020	US	57 physicians	RTI	Social norm feedback	% of RTI with AB prescribed	Low
Lagerlov, 2000	Norway	199 physicians	UTI	Social norm feedback	% inappropriate ABs for UTI	High
Mainous, 2000	USA	216 physicians	RTI	Social norm feedback	% inappropriate AB treatments	Low

Meeker, 2014	USA	14 physicians	RTI	Public commitment	No. of ABs per 100 AB inappropriate RTIs	Moderate
Meeker, 2016	USA	244 physicians	RTI	Social norm feedback, accountable justification, suggested alternatives	No. of ABs per 100 AB inappropriate RTIs	Moderate
O'Connell, 1999	Australia	2440 physicians	All	Social norm feedback	No. of ABs per 100 consultations	Moderate
Persell, 2016	USA	28 physicians	RTI	Social norm feedback, accountable justification, suggested alternatives	No. of ABs per 100 RTIs; No. of ABs per 100 AB inappropriate RTIs	High
Ratajczak, 2019	England	6995 practices	All	Social norm feedback	No. of ABs per 1000 registered population	Moderate
Sondergaard, 2003	Denmark	299 physicians	RTI	Social norm feedback	No. of ABs per 1000 registered population	Moderate
Yang, 2014	China	20 practices (54 physicians)	RTI	Public reporting	% of RTI consultations with AB; % of RTI consultations with >1 AB	Low

RTI is respiratory tract infections; UTI is urinary tract infections. AB is antibiotic. No. is number. DDD is defined daily doses.

[a]Risk of bias assessed using the Cochrane Effective Practice and Organisation of Care group's tool for studies with a control group. Overall rating assigned 'low' when all criteria were 'low' risk; 'medium' when 1-2 criteria were scored 'unclear' or 'high' risk; and 'high' when >2 criteria were scored 'unclear' or 'high' risk.

[b]Inappropriate with respect to antibiotic, doses and/or duration.

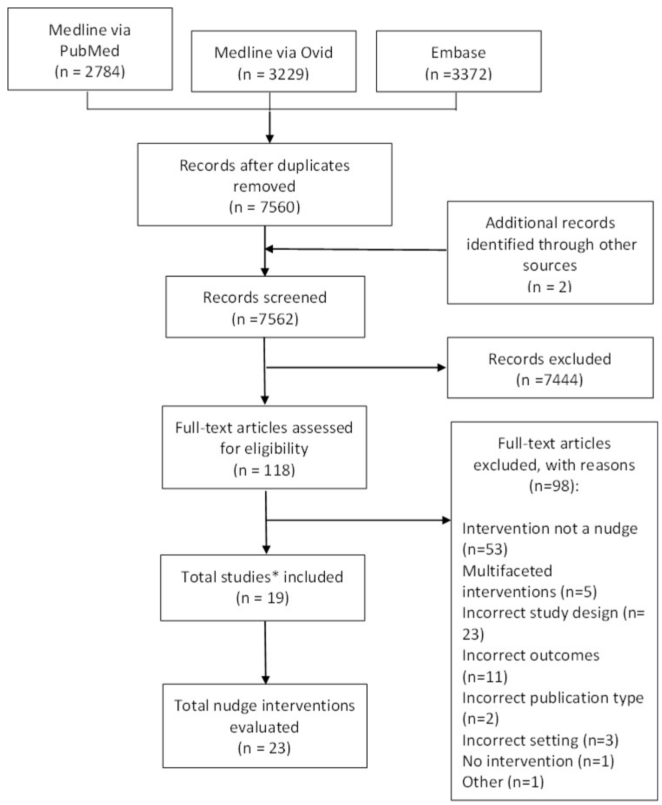

Figure 1: PRISMA flow chart of search and screening results
*One study had two publications.

243x193mm (120 x 120 DPI)

	Targeting high prescribers or all prescribers?		Prescribing compared to which peers?			Injunctive or descriptive norm		Targeting high prescribers or comparison to top performers/rank or injunctive norm		Relative or absolute performance to peers			Based on individual physician or practice data?		Frequency of feedback		Static vs dynamic norms		Private vs public reporting		All or diagnosis-specific antibiotics		Mode of feedback			Graphic display of prescribing?		Supporting information provided in intervention group	
	All	High	Average/median	Top performers	Rank with all peers	Injunctive	Descriptive	Yes	No	Absolute	Relative	Both	Physician	Practice	Once	>1	Static	Dynamic	Private	Public	All	Inappropriate	Letter	Electronic	Meeting	Yes	No	Yes	No
Studies reporting a reduction																													
Awad, 2006	●		●				●		●	●				●		●	unclear		●		unclear		●				●	●	
BETA, 2018 & 2020		●	●				●	●				●	●		●		na		●		●		●			●		●	
Bradley, 2019		●	●				●	●			●			●	●		na		●		●		●				●		●
Chang, 2020	●				●		●	●			●		●			●		●	●		●			●			●	●	
Gerber, 2013	●		●				●		●	●			●			●		●	●			●a		●		●		●	
Hallsworth, 2016		●	●				●	●			●			●	●		na		●		●		●				●	●	
Kronman, 2020	●			●		●		●		●			●			●	unclear		●			●a	unclear			●		●	
Lagerlov, 2000	●		●			●		●		●			●			●		●		●b	●				●	●		●	
Mainous, 2000	●				●		●	●		●			●		●		na		●			●	●			unclear		●	
Meeker, 2016	●			●		●		●		●			●			●		●	●			●		●			●	●	
Persell, 2016	●			●		●		●		●			●			●		●	●			●		●			●	●	
Ratajczak, 2019		●	●				●	●			●		●			●		●	●		●		●				●	●	
Sondergaad, 2003	●		●				●		●	●			●		●		na		●		●		●			unclear		●	
Total number of studies (%)	9 (64)	5 (36)	8 (62)	3 (23)	2 (15)	4 (31)	9 (69)	10 (77)	3 (23)	8 (62)	4 (31)	1 (8)	10 (77)	3 (23)	5 (38)	8 (62)	0	6 (100)	12 (92)	1 (8)	7 (58)	5 (42)	7 (58)	4 (33)	1 (8)	4 (36)	7 (64)	12 (92)	1 (8)
Studies reporting no change																													
Curtis, 2021		●	●				●	●		●				●		●		●	●		●		●			●		●	
Hemkens, 2017		●	●				●	●		●			●			●		●	●		●		●			●		●	
Hurlimann, 2016	●		●				●		●	●				●		●		●	●		●		●				●	●	
O'Connell, 1999	●		●c				●		●	●			●			●	na		●		●		●			●		●	
Total number of studies (%)	2 (50)	2 (50)	4 (100)	0	0	0	4 (100)	2 (50)	2 (50)	4 (100)	0	0	2 (50)	2 (50)	0	4 (100)	0	3 (100)	4 (100)	0	4 (100)	0	4 (100)	0	0	3 (75)	1 (25)	4 (100)	0

na is not applicable. ● indicates the feature was pesent in the study
a All antibiotics for respiratory tract infection
b Individual performance discussed within the group of physicians
c Interquartile range for all other physicians

Figure 2: Implementation features of social norm feedback nudge interventions

869x610mm (47 x 47 DPI)

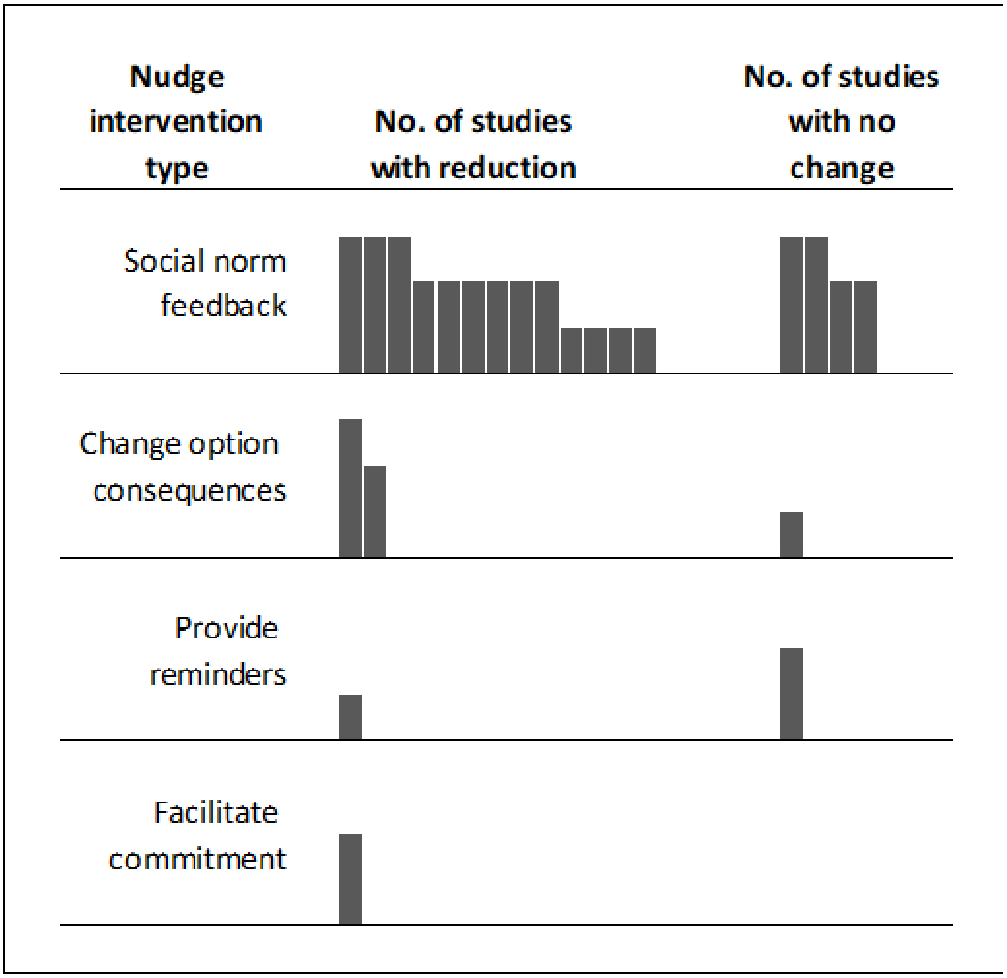

Figure 3: Harvest plot of effects of nudge interventions targeting antibiotic prescribing in primary care on overall antibiotic prescribing.
Each mark or column represents one nudge intervention. Column height represents the risk of bias in the study: tallest columns are studies with low risk of bias; medium columns are moderate risk of bias; short columns are high risk of bias.

278x270mm (47 x 47 DPI)

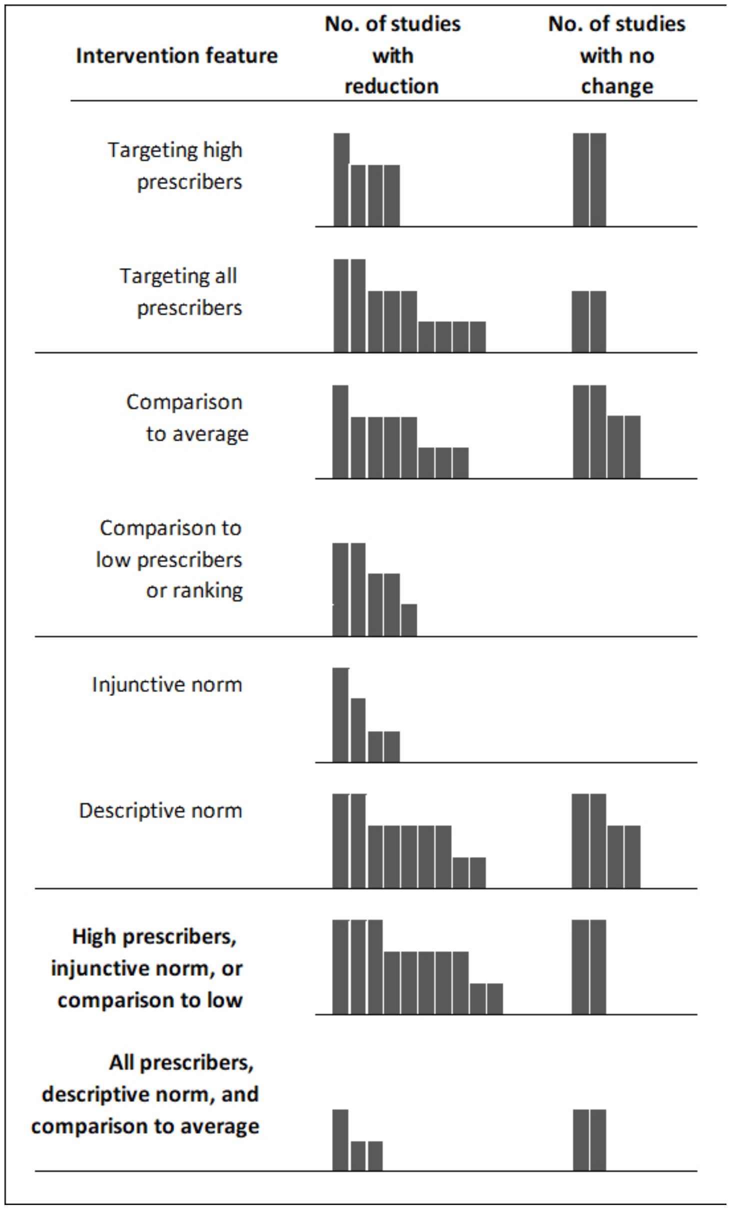

Figure 4: Harvest plot of effects of social norm feedback nudge interventions on overall antibiotic prescribing by implementation features.
Each mark or column represents one nudge intervention. Column height represents the risk of bias of the study: tallest columns are studies with low risk of bias; medium columns are moderate risk of bias; short columns are high risk of bias.

295x489mm (47 x 47 DPI)

PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	In main text
Registration	12	Provide the register name and registration number.	N/A

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	See previous page
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	6
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	7
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	8
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	8
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	9
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	10
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	11
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	11-12
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	11
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	12
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	12
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	12
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	12
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	10
Certainty	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
assessment			
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	12
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	12
Study characteristics	17	Cite each included study and present its characteristics.	12
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	13
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary file 4
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	13-18
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	13-18
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	19-22
	23b	Discuss any limitations of the evidence included in the review.	23
	23c	Discuss any limitations of the review processes used.	23
	23d	Discuss implications of the results for practice, policy, and future research.	22
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Not registered
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	24
Competing interests	26	Declare any competing interests of review authors.	24
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Supplementary files

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

PRISMA 2020 Checklist

For more information, visit: http://www.prisma-statement.org/

Raban et al. Nudge interventions to reduce unnecessary antibiotic prescribing in primary care: a systematic review

SEARCH STRATEGY

MEDLINE (via Ovid and PubMed)

Date searched: 23 April 2021

Search ID#	Search Terms
1	exp Ambulatory Care/
2	exp Community Medicine/
3	exp General Practice/
4	exp General Practitioners/
5	exp Primary Health Care/
6	exp Physicians, Family/
7	exp Physicians, Primary Care/
8	"general practice".ti,ab.
9	"general practitioner*".ti,ab.
10	"family physician*".ti,ab.
11	"family practice".ti,ab.
12	"primary care".ti,ab.
13	"primary health care".ti,ab.
14	"primary healthcare".ti,ab.
15	exp *anti-bacterial agents/tu or exp *anti-infective agents, urinary/tu
16	antibiot*.ti,ab.
17	anti-biot*.ti,ab.
18	anti-microb*.ti,ab.
19	antimicrob*.ti,ab.
20	anti-infective*.ti,ab.
21	antiinfective*.ti,ab.
22	anti-bacterial*.ti,ab.
23	antibacterial*.ti,ab.
24	randomized controlled trial.pt
25	controlled clinical trial.pt
26	pragmatic clinical trial.pt
27	multicenter study.pt
28	exp non-randomized controlled trials as topic/
29	exp controlled before-after studies/
30	(randomis* or randomiz* or randomly).ti,ab.
31	groups.ab.
32	(trial or multicenter or multi center or multicentre or multi centre).ti.
33	(intervention? or effect? or impact? or controlled or control group? or (before adj5 after) or (pre adj5 post) or ((pretest or pre test) and (posttest or post test)) or quasiexperiment* or quasi experiment* or evaluat*).ti,ab.
35	or/1-14
36	or/15-23
37	or/24-34

Raban et al. Nudge interventions to reduce unnecessary antibiotic prescribing in primary care: a systematic review

38	35 and 36 and 37
39	limit 38 to yr="1997 -Current"
40	limit 39 to english language
41	limit 40 to journal article
42	limit 41 to humans

Embase (via Ovid)

Date searched: 23 April 2021

Search ID#	Search Terms
1	exp Ambulatory Care/
2	exp Community Medicine/
3	exp General Practice/
4	exp General Practitioners/
5	exp Primary Health Care/
6	exp Family Medicine/
7	exp Primary Medical Care/
8	"general practice".ti,ab.
9	"general practitioner*".ti,ab.
10	"family physician*".ti,ab.
11	"family practice".ti,ab.
12	"primary care".ti,ab.
13	"primary health care".ti,ab.
14	"primary healthcare".ti,ab.
15	exp *anti-infective agents/
16	exp *anti-infective therapy/ or exp *antimicrobial therapy/
17	exp *antibiotic agent/
18	antibiot*.ti,ab.
19	anti-biot*.ti,ab.
20	anti-microb*.ti,ab.
21	antimicrob*.ti,ab.
22	anti-infective*.ti,ab.
23	antiinfective*.ti,ab.
24	anti-bacterial*.ti,ab.
25	antibacterial*.ti,ab.
26	exp "controlled clinical trial (topic)"/
27	exp epidemiology/
28	(randomis* or randomiz* or randomly).ti,ab.
29	groups.ab.
30	(trial or multicenter or multi center or multicentre or multi centre).ti.
31	(intervention? or effect? or impact? or controlled or control group? or (before adj5 after) or (pre adj5 post) or ((pretest or pre test) and (posttest or post test)) or quasiexperiment* or quasi experiment* or evaluat*).ti,ab.
32	or/1-14

Raban et al. Nudge interventions to reduce unnecessary antibiotic prescribing in primary care: a systematic review

33	or/15-25
34	or/26-31
35	32 and 33 and 34
36	limit 35 to english language
37	limit 36 to human
38	limit 37 to yr="1997 -Current"
39	limit 38 to (conference abstract or "conference review" or editorial or erratum or letter or note or "review")
40	38 not 39
41	remove duplicates from 40
42	limit 41 to embase

Websites searched

Date searched: 23 April 2021

Organisation name	**URL**
Behavioural Economics Team of the Australian Government	https://behaviouraleconomics.pmc.gov.au/
Behavioural Insights Team	https://www.bi.team
Danish Nudging Network	https://www.danishnudgingnetwork.dk/
iNudgeyou	https://inudgeyou.com/en/
Nudge France	http://www.nudgefrance.org/
Nudge-it	https://www.nudge-it.eu/
Nudge Italia	http://www.nudgeitalia.it/
Norwegian Nudging Network	https://sites.google.com/view/norsknudgenet/home
Penn Medicine Nudge Unit	https://nudgeunit.upenn.edu
The European Nudging Network	http://tenudge.eu/
The Swedish Nudging Network	https://theswedishnudgingnetwork.com/

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SUPPLEMENTARY FILE 3

Table S3: Assessment of risk of bias* against each criterion for individual studies

Study	Random sequence generation	Allocation concealment	Baseline outcome measurements similar	Baseline characteristics similar	Incomplete outcome data	Blinding of outcome measurement assessment	Protections against contamination	Selective reporting	Other bias	TOTAL number of criteria with low risk of bias
Awad, 2006	✓	?	✓	?	?	?	✓	X	✓	4/9
BETA, 2018 & 2020	✓	✓	✓	✓	?	✓	✓	✓	✓	8/9
Bradley, 2019	X	X	✓	✓	✓	✓	✓	✓	✓	7/9
Chang, 2020	✓	X	✓	✓	✓	✓	✓	✓	✓	8/9
Curtis, 2021	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Gerber, 2013	✓	✓	✓	✓	?	X	?	✓	✓	6/9
Hallsworth, 2016	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Hemkens, 2017	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Hurlimann, 2016	✓	✓	✓	✓	✓	X	✓	✓	✓	8/9
Kronman, 2020	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Lagerlov, 2000	✓	✓	✓	✓	X	?	✓	?	X	6/9
Mainous, 2000	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Meeker, 2014	✓	✓	✓	✓	✓	✓	?	✓	✓	8/9
Meeker, 2016	✓	✓	?	?	✓	✓	✓	✓	X	6/9
O'Connell, 1999	?	✓	✓	✓	✓	✓	✓	✓	✓	8/9
Persell, 2016	✓	✓	✓	?	✓	✓	?	✓	X	7/9
Ratajczak, 2019	X	X	✓	✓	✓	✓	✓	✓	✓	7/9
Sondergaard, 2003	?	✓	✓	✓	✓	✓	✓	✓	✓	8/9
Yang, 2014	✓	✓	✓	✓	✓	✓	✓	✓	✓	9/9
Number of studies with high risk of bias	2	3	0	0	1	2	0	1	3	
Number of studies with unclear bias	2	1	1	3	3	2	3	1	0	
Number of studies with	15	15	15	16	15	15	16	17	16	

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low risk of bias										

'X' denotes high risk of bias for this criterion; '?' denotes unclear risk of bias; '✓' denotes low risk of bias.
*Risk of bias assessed using the Cochrane Effective Practice and Organisation of Care group's tool (https://epoc.cochrane.org/sites/epoc.cochrane.org/files/public/uploads/Resources-for-authors2017/suggested_risk_of_bias_criteria_for_epoc_reviews.pdf)

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SUPPLEMENTARY FILE 4

Table S4: Effects of nudge interventions to improve antibiotic use in primary care

Study	Design	Interventions	Control	Outcome/s	Follow-up period	Reported statistics	95% CI, p-value	Vote counting assessment
Decision information – provide social reference point								
Awad, 2006	Cluster randomised trial	Social norm feedback	Usual care	No. of consultations with AB prescribed	3-months post	Mean difference: -2.8	(-1.1, -4.6), p=0.004	Reduction
				No. of consultations with an inappropriate AB[a]	3-months post	Mean difference: -1.9	(-0.1, -3.7), p=0.040	n/a
BETA, 2018 & 2020	Cluster randomised trial	Social norm feedback with graph	Usual care	No. of ABs per 1000 consultations	6 & 12months post	Mean difference (6-months): -13.6 (~12% reduction) (12-months): -9.3 (~9.4% reduction)	6-months: (-16.6, -10.6), p<0.00001 12-months: (-12.3, -6.2); p<0.001	Reduction
		Social norm feedback with education material	Usual care	No. of ABs per 1000 consultations	6 & 12-months post	Mean difference (6-months): -10.3 (~9.3% reduction) (12-months):	6-months: (-13.8, -6.8), p<0.001 12-months: (-11, -5.6); p<0.001	n/a

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						-8.3 (~8.4% reduction)		
		Social norm feedback with delayed prescribing	Usual	No. ABs per 1000 consultation	6 & 12-months post	Mean difference (6-months): -11.8 (~10.7% reduction) (12-months): -8.8 (~8.9% reduction)	6 months: (-14.7, -8.9); p<0.001 12-months: (-11.6, -6.0); p<0.001	n/a
Bradley, 2019	Regression discontinuity study	Social norm feedback	Usual care	No. of ABs per 1000 registered population	3-months post	Mean difference: -25.7	(-42.5, -8.8), p=0.0028	Reduction
					12-months post	Mean difference: -58.7 (~5% reduction)	(-116.7, -0.7), p=0.047	n/a
Chang, 2020	Cluster randomised crossover-controlled trial	Social norm feedback	Usual care	No. of AB prescriptions per total prescriptions	3-month intervention period	Relative reduction in intervention arm: 35.2%; in control arm: 30.8%	p<0.001	Reduction
					3-month intervention period (after crossover)	Relative reduction in intervention arm: 14.2%; in control arm: 4.6%	p<0.001	n/a

Curtis, 2021	Randomised trial	Social norm feedback (standard)	Usual care	AB prescriptions per 1000 population	6-months post	No change	NS	No change
				Proportion of antibiotics which were broad spectrum	6-months post	2.1% reduction compared to controls	p=0.104	n/a
		Social norm feedback (optimised)	Usual care	AB prescriptions per 1000 population	6-months post	No change	NS	No change
				Proportion of antibiotics which were broad spectrum	6-months post	2.1% reduction compared to controls	P=0.046	n/a
Gerber, 2013	Cluster randomised trial	Social norm feedback	Usual care	ABs for viral RTI	12-month intervention period	DID: -1.7%	NR, p=0.93	Reduction
				Percent of broad spectrum ABs among children with AB prescription	12-month intervention period	DID: -6.7%	NR, p=0.01	n/a
Hallsworth, 2016	Randomised trial	Social norm feedback	Usual care	No. of ABs per 1000 registered population	6-months post	IRR: 0.967[b] (~3.3% reduction)	(0.957, 0.977), p<0.0001	Reduction
Hemkens, 2017	Randomised trial	Social norm feedback	Usual care	DDD per 1000 consultations	First 1-year intervention period	Between group difference: 0.81%	(-2.56, 4.30), NR	No change
					Second 1-year intervention period	Between group difference: -1.73%	(-5.07, 1.72%), p=0.32	

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Hurlimann, 2016	Cluster randomised trial	Social norm feedback	Usual care	Percentage of AB prescriptions for upper RTIs	24-month intervention period	Difference in proportion: -1.2	(-10.5, -8.2), p=0.66	No change
				Percentage of penicillins for RTI	24-month intervention period	OR: 1.42	(1.08-1.89), p=0.01	n/a
				Percentage of trimethoprim/sulfamethoxazole for UTI	24-month intervention period	OR: 2.16	(1.19-3.91), p=0.01	n/a
Kronman, 2020	Stepped wedge cluster randomised trial	Social norm feeback	Usual care	Percentage of RTI with antibiotic prescription	12-months	OR: 0.93	(0.90, 0.96), NR	Reduction
Lagerlov, 2000	Randomised trial	Social norm feedback	Intervention for asthma care	Percentage of inappropriate ABs for UTI	12-months post	Relative decrease: -9.6%	NR, p=0.0004	Reduction
Mainous, 2000	Randomised trial	Social norm feedback	Usual care	Mean proportion of inappropriate AB treatments	5-months post	NR	Not significant	-
		Social norm feedback with patient education material	Usual care	Mean proportion of inappropriate AB treatments	5-months post	Dunnett's T: 2.374	NR, p<0.05	Reduction
Meeker, 2016	Cluster randomised trial	Social norm feedback	Usual care	No. of ABs per 100 AB inappropriate RTIs	18-month intervention period	DID: -5.2%	(-6.9, -1.6), p<0.01	Reduction
O'Connell, 1999	Randomised trial	Social norm feedback	Interventions for other medication use	No. of AB prescriptions per 100 consultations	4-months post	Median: no difference between intervention and controls	NR	No change

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Persell, 2016	Randomised trial	Social norm feedback	Usual care	No. of ABs per 100 RTIs	12-month intervention period	OR: 0.73	(0.53, 0.995), p<0.05	Reduction
				No. of ABs per 100 AB inappropriate RTIs	12-month intervention period	OR: 0.45	(0.18, 1.11), NR	n/a
Ratajczak, 2019	Regression discontinuity study	Social norm feedback	Usual care	No. of ABs per 1000 registered population	6-months post	Percent change in intervention group: -3.69%	(-5.10,-2.29), p<0.001	Reduction
Sondergaad, 2003	Randomised trial	Social norm feedback	Guidelines	No. of ABs per 1000 registered patients	3-months post	Mean difference: -0.6	(-2.8, 1.6), NR	Reduction
				Percent of prescriptions for narrow-spectrum penicillins	3-months post	Mean difference: 0.7	(-0.41, 1.7), NR	n/a
Decision structure – change option consequences								
Meeker, 2016	Cluster randomised trial	Accountable justification	Usual care	No. of ABs per 100 AB inappropriate RTIs	18-month intervention period	DID: -7.0%	(-9.1, -2.9), p<0.001	Reduction
Persell, 2016	Randomised trial	Accountable justification	Usual care	No. of ABs per 100 RTIs	12-month intervention period	OR: 1.05	(0.80, 1.39), NR	No change
				No. of ABs per 100 AB inappropriate RTIs	12-month intervention period	OR: 0.98	(0.42, 2.29), NR	n/a
Yang, 2014	Cluster randomised trial	Public reporting	Education	Percentage of RTI consultations with AB	5-8 months post	DID: -1.93	(-6.61, 2.75), p=0.419	Reduction
				Percentage of RTI consultations with >1 AB	5-8 months post	DID: -6.97	(-13.94, 0.00), p=0.049	n/a

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Decision assistance – provide reminders								
Meeker, 2016	Cluster randomised trial	Suggested alternatives	Usual care	No. of ABs per 100 AB inappropriate RTIs	18-month intervention period	DID: -5.0%	(-7.8, 0.1%), p=0.66	Reduction
Persell, 2016	Randomised trial	Suggested alternatives	Usual care	No. of ABs per 100 RTIs	12-month intervention period	OR: 0.72	(0.54, 0.96), p<0.01	Reduction
				No. of ABs per 100 AB inappropriate RTIs	12-month intervention period	OR: 0.68	(0.29, 1.58), NR	n/a
Decision assistance – facilitate commitment								
Meeker, 2014	Randomised trial	Public commitment		No. of ABs per 100 AB inappropriate RTIs	12-week intervention period	DID: -19.7%	(-5.8, -33.04), p=0.02	Reduction

No. is ‘number’. AB is ‘antibiotic’. CI is ‘confidence interval’. IRR is ‘incidence rate ratio’. DDD is ‘defined daily doses’. OR is odds ratio. RTI is ‘respiratory tract infection’. UTI is ‘urinary tract infection’. DID is ‘difference in differences analysis’. NR is not reported. NS is ‘not significant’.

*The intervention promise was assessed based on all antibiotic outcomes reported in each study.

[a]Inappropriate with respect to antibiotic, doses and/or duration.