BMJ Open

Improving antibiotic prescribing by general practitioners: a protocol for a systematic review of interventions involving pharmacists

Sajal K Saha, Lesley Hawes, Danielle Mazza

To cite: Saha SK, Hawes L, Mazza D. Improving antibiotic prescribing by general practitioners: a protocol for a systematic review of interventions involving pharmacists. *BMJ Open* 2018;**8**:e020583. doi:10.1136/bmjopen-2017-020583

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2017-020583).

Received 13 November 2017
Revised 12 February 2018
Accepted 22 February 2018

Check for updates

Department of General Practice, School of Primary Health Care, Monash University, Building 1, 270 Ferntree Gully Road, Notting Hill, Melbourne, Victoria 3168, Australia

Correspondence to
Sajal K Saha;
sajal.saha@monash.edu

ABSTRACT

Introduction Effective antibiotic options in general practice for patients with infections are declining significantly due to antibiotic over-prescribing and emerging antibiotic resistance. To better improve antibiotic prescribing by general practitioner (GP), pharmacist–GP collaborations have been promoted under antibiotic stewardship programmes. However, there is insufficient information about whether and how pharmacists help GPs to more appropriately prescribe antibiotics. This systematic review aims to determine whether pharmacist-led or pharmacist-involved interventions are effective at improving antibiotic prescribing by GPs.

Methods and analysis A systematic review of English language randomised controlled trials (RCTs), cluster RCTs, controlled before-and-after studies and interrupted time series studies cited in MEDLINE, EMBASE, EMCARE, CINAHL Plus, PubMed, PsycINFO, Cochrane Central Register of Controlled Trials and Web of Science databases will be conducted. Studies will be included if a pharmacist is involved as the intervention provider and GPs are the intervention recipients in general practice setting. Data extraction and management will be conducted using Effective Practice and Organisation of Care data abstraction tools and a template for intervention description and replication. The Cochrane and ROBINS-I risk of bias assessment tools will be used to assess the methodological quality of studies. Primary outcome measures include changes (overall, broad spectrum and guidelines concordance) of GP-prescribed antibiotics. Secondary outcomes include quality of antibiotic prescribing, delayed antibiotic use, acceptability and feasibility of interventions. Meta-analysis for combined effect and forest plots, χ^2 test and I^2 statistics for detailed heterogeneity and sensitivity analysis will be performed if data permit. Grading of Recommendations Assessment, Development and Evaluation and Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols guidance will be used to report findings.

Ethics and dissemination No ethics approval is required as no primary, personal or confidential data are being collected in this study. The findings will be disseminated to national and international scientific sessions and published in a peer-reviewed journal.

PROSPERO registration number CRD42017078478.

Strengths and limitations of this study

- To the best of our knowledge, this will be the first systematic review assessing pharmacist-led or pharmacist-involved interventions to improve antibiotic prescribing by general practitioners (GPs).
- This review is solely focused on general practice or family practice which may increase applicability of the findings.
- An expected heterogeneity in design and varying methodological quality across study may hinder meta-analysis and interpretation of findings.
- Searches of this review will be limited to English language studies.

INTRODUCTION

Growing antibiotic resistance (AR) and a shortage of new effective antibiotics have become an urgent global threat to public health[1 2] with a risk of a significant rise in morbidity, mortality and healthcare costs.[2 3] AR annually causes 23 000 death in America, 25 000 deaths in the European Union and 700 000 deaths in worldwide.[4] By 2050, it is predicted that there will be 10 million deaths annually and US$100 trillion in global economic loss caused by drug-resistant bacterial infections if AR continues to rise at the same pace as in the last decades.[5] Overprescribing and inappropriate prescribing of antibiotics are the principal and the modifiable driver of AR.[6–8]

Primary care is where the majority antibiotics are prescribed and dispensed[8–10] as evidenced by 85%–95% antibiotics in Europe and nearly 70% of antibiotics in the USA are supplied in primary care. The major primary care antibiotic prescribers are general practitioners (GPs) or family practitioners (FPs) and ambulatory clinic physicians.[11] It has been reported that in respiratory tract infections (RTIs), urinary tract infections and in skin infections, guideline incongruent antibiotic prescription

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rates in primary care were 50%–90%,[10 12–14]80% and 46%,[15] respectively. Inappropriate antibiotic prescribing leads to adverse effects, resource wasting, reconsultations, rising treatment costs, ineffective antibiotics and bacterial resistance.[6 16] Inappropriate prescribing of antibiotics are influenced by individual, interpersonal, social, organisational and national-level barriers. Mostly, these factors are behavioural and health system oriented.[17] More specifically, knowledge deficits among prescribers, the practice environment and prior experience of the practitioner, peer pressure, patient pressure, patients expectation, time constraints, diagnostic uncertainties, lack and/or ineffective communication between prescriber, pharmacist and patients[18] have been implicated in inappropriate antibiotic prescribing practices.

There is a major body of literature documenting many interventions to cut the established barriers and behaviours of clinicians related to antibiotic prescribing. Over the last 15 years, systematic reviews[19–25] have explored the effectiveness of clinician-targeted interventions to improve their antibiotic prescribing in inpatient and outpatient settings. However, no reviews were solely focused on general practices.[26] Multifaceted interventions involving physicians, pharmacists and patients are more likely to produce a greater effect size in reducing antibiotic prescribing and increasing guideline recommended antibiotic prescribing.[27 28] Although another review concluded that single but focused interventions are more effective than multidimensional interventions at improving antibiotic choice by clinicians.[23] According to WHO global strategies against antimicrobial resistance (AMR), isolated interventions have little effect on improving the quality of antibiotic prescribing.[29]

Pharmacists play an active role in improving the appropriateness of antibiotic prescribing practice by GPs through the provision of expert advice, education and training, liaison with regards to formulary, the provision of resistance data, raising awareness of guideline-adherence and policy-guided antibiotic prescribing.[30 31] In many countries, these interventions are being increasingly integrated at the healthcare system or practice level with the aim of achieving more collaborative care by physicians, pharmacists and other health professionals to optimise antibiotic use.[32] Practitioner–pharmacist collaboration model[33] is such an example. Such collaboration is more firmly established in hospitals than in primary care. Burdet *et al*'s 2015 review outlined four specific workable models of collaboration in primary care focused on relationship, conceptual and attitudinal models among GPs and pharmacists, but their effectiveness and acceptability was inconclusive and under-researched.[34] As GPs and pharmacists are being increasingly engaged in antibiotic stewardship programmes, a workable intervention model is required to improve GPs' antibiotic prescribing in community setting.[35 36] Vervloet *et al's* 2016 showed that family practitioners (FPs) and pharmacists collaborative pharmacotherapy audit meeting to reduce antibiotic prescriptions in RTI was effective.[37] In the UK, utilisation of antimicrobial pharmacists, infectious disease pharmacists and community pharmacists are emerging to support GPs in right decision-making about antibiotic prescribing.[38] AMR Pacesetter project[39] which was implemented to support GPs in adopting good antimicrobial stewardship in primary care through auditing antimicrobial prescribing, developing an action plan in collaboration with GPs and delivering patient education to reduce 'patient pressure' on prescribing antibiotics by GPs. The achievement of a 16.09% reduction of antimicrobials prescribing from the project in 2015 highlighted the contribution of antimicrobial pharmacists to the effective collaboration with GPs .[39] The evidences of other intervention studies support the important role of pharmacists to GPs as a therapeutic adviser[40], a trainer[30 41], an academic detailer[42 43], a reviewer of medication prescription and feedback provider[23] to improve their antibiotic prescribing norms and culture. This evidence clearly shows the importance of pharmacists in supporting GPs to foster appropriate prescribing practice of antibiotics. Therefore, it is crucial to explore the evidences of effective interventions where pharmacists play a role as an interventionist to GPs to improve quality of antibiotic prescribing.

Understanding such interventions which are more likely to improve engagement between GPs and pharmacists and optimising antibiotic prescribing in general practices is a priority. However, no systematic review has yet explored which interventions involving pharmacists are effective at improving GPs' antibiotic prescribing. Hence, there is insufficient information to design future GP–pharmacist collaborative models to optimise antibiotic use in the community. This systematic review, therefore, aims to find pharmacist-led or pharmacist-involved interventions to improve antibiotic prescribing by GPs and to assess their effectiveness. The second objective of this review is to explore the feasibility and acceptability of the interventions if data permit. It is very difficult to make the definitive conclusions regarding the effectiveness of interventions unless interventions are focused and very specific to a practice area.[44] This review will explore studies specific to general practice settings where the intervention is either pharmacist led or pharmacist involved and the intervention recipients are GPs.

METHODS

Guidance regarding the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols (PRISMA-P) was used to develop this systematic review protocol. The planned period of this review study is from 1 June 2017 to 30 January 2018.

Study design

The selected studies will be either randomised controlled trials (RCTs) (including cluster parallel group and factorial), controlled before-and-after studies (CBAs) or interrupted time series analyses (ITS). The guidance on study

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design as recommended by the Effective Practice and Organisation of Care group (EPOC) that all RCTs must have at least two intervention and control sites and that interrupted time series studies must have a minimum of three time points both before and after the intervention will be followed. The EPOC study design algorithm will be used to determine the study design and to avoid ambiguous terminology.

Review question

The research question is: What pharmacist-led or pharmacist-involved interventions are effective to improve antibiotic prescribing by GPs in primary care?

Eligibility criteria

Types of participants

We will include studies that examine interventions targeted at GPs or FPs within primary care. Intervention providers include either a pharmacist alone or as part of a team consisting of pharmacist/others (eg, GPs/clinicians/microbiologists/infectious disease experts) in a general practice environment. No restrictions will be made on age, gender, ethnicity and residence of participants. Intervention recipients include GPs or FPs. Physicians, nurses or dentist practitioners working in aged care facilities, long-term care facilities, nursing homes or dental care facilities will be excluded. We will exclude any studies targeting health professionals working in inpatient settings, hospital settings or residential settings as well.

Types of interventions and comparators

Studies will be included if they meet following conditions:

- Conduct interventions by either a pharmacist(s) alone or a pharmacist(s) engaged in a multidisciplinary team to improve antibiotic prescribing by GPs.
- Investigate a single or multicomponent or multifaceted intervention with the primary objective of reducing quantity or improving quality (selection/appropriateness) of antibiotic prescribing.
- Evaluate the effect of interventions based on changes in GPs' antibiotic prescribing.
- Evaluate any type of intervention (eg, educational, clinical, managerial or regulatory).
- Where GPs or FPs receive the interventions.
- Apply any mode of intervention delivery techniques.
- Conduct the intervention at any time.

Studies will be excluded when the:

- Intervention is delivered in an inpatient/hospital setting/secondary care/tertiary care, long-term care, residential care, ambulatory care, aged care facility, nursing home or dental care facility.
- Intervention does not include pharmacist(s).
- Study evaluates no outcome measures related to GP's antibiotics prescribing.

We will include intervention studies that aim to improve antibiotic prescribing compared with control or usual care.

Settings

Only studies in general practice/family practice will be included. General practice or family practice for this review will be defined as 'the first point of care where individuals and families in their communities are provided person centred, continuing, comprehensive and coordinated whole person healthcare'.[45]

Language

Only English language articles will be included.

Time

There will be no restrictions on study publishing date. The inception of databases until the date of search will be the time limit for the search strategy. Studies will be included regardless of intervention follow-up time.

STUDY OUTCOME MEASURES

Effectiveness

Primary outcomes

The effect of interventions to reduce the quantity and improve quality of antibiotic prescribing will be measured by:

- Change in total antibiotics prescribed by GPs or FPs.
- Change in broad-spectrum antibiotic prescribing.
- Change in antibiotic prescribing congruent with published antibiotic guidelines or therapeutic guidelines or WHO listed alert antibiotic guides.

Secondary outcomes

- Change in antibiotic dose and/or dose regimen on antibiotic prescriptions in response to any intervention.
- Changes in consultation rates including reconsultation of patients with infections.
- Change in antibiotic dispensing Rx/1000 patients where antibiotic prescribing data are not available.
- Change of cases/visits where antibiotics were prescribed in response to deterioration of condition or adverse effect of antibiotics.
- Clinician knowledge about antibiotic use and/or AR.
- Cases of adverse effects of antibiotics.
- Types of interventions.
- Intervention components (eg, types, formats, mode of delivery, providers).

The measurement unit of antibiotic prescribing will be a number or per cent or proportion of prescribed antibiotics. Antibiotic prescribing rate will be defined as number of patients with antibiotic prescription divided by total number of patient visits during a designated interval. The rate of antibiotic prescribing adherence with guidelines will be defined as the number of patients with recommended antibiotic prescription divided by total number of patient visits with antibiotic prescription during a designated period.

Feasibility and acceptability

Secondary outcomes

These outcomes will be assessed as secondary outcomes by assessing ease of implementation, required resources,

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acceptability and satisfaction of the targeted clinicians after the intervention.

Data sources and search methods

Electronic databases

We will conduct this systematic review and meta-analysis in accordance with the PRISMA-P guidelines.[46] A uniform search strategy will be developed and applied to the following databases: MEDLINE, EMBASE, EMCARE, PubMed, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL plus and Web of Sciences. We will also manually search reference lists of retrieved articles and relevant articles. The databases will be searched from:

- MEDLINE and Ovid (1946 to searched date).
- EMBASE and Ovid (1974 to searched date).
- EMCARE (1995 to searched date).
- PubMed (1974 to searched date).
- PsycINFO (1806 to searched date).
- Cochrane CENTRAL (1889 to searched date).
- CINAHL PLUS (1982 to searched date).
- Science Citation Index and Social Sciences Citation Index, ISI Web of Science (1975 to searched date).

Search terms and strategy

The search strategy will capture studies that include each of three groups of terms within PICO format: populations (pharmacists, GPs), intervention (any) and outcomes (antibiotics, prescribing practice changes and settings). Matched terms under each group against possible medical subject headings or keywords as follows will be used in a systematic search through eight databases.

A. Population terms:
   Pharmacist: Pharmacists/OR Pharmacist* OR (pharmacy or pharmacies) OR (retail pharmacist or community pharmacist or clinical pharmacist or antimicrobial pharmacist or infectious disease pharmacist)
   Physician: Family Physicians/OR General Practitioners/OR (GP* or family practitioner* general practitioner* or clinician* or doctor* or rural practitioner or family medicine practitioner)

B. Intervention terms
   Intervention: intervention* or program* or health promotion* or education* or educational outreach* or training* or academic detailing* or educational meeting* or workshop or communication skill* or audit* or guideline* or group meeting* or decision support* or poster* or leaflet* or flyer* or incentive* or regulation or reminder* or consultation* or web based training* or electronic prescribing* or medication review* or medication reconciliation* or drug review or stewardship or multi-prong* or strategy or single or multicomponent* or multi-component or multiple or multifaceted or multidisciplinary or multi-disciplinary or physician aid or physician-aid or collaborative or collaboration or counselling or pharmacist supported or pharmacist-led or pharmacist led or team based or team-based or shared

C. Outcome terms
   Antibiotics: Anti-Bacterial Agents/OR (antibacterial or anti-bacterial or antibiotic or anti-biotic or antimicrobial or anti-microbial or antibiotic* or antimicrob* or antibacteria* or antibacterial agent) OR Anti-infective agents/or (broad spectrum or short spectrum or narrow spectrum or narrow-spectrum)
   Practice changes: Drug Prescriptions/OR Inappropriate prescribing/OR Appropriate prescribing/OR practice pattern, Physicians/OR (prescribe or prescription* or practice or practising or dispense or dispensing or stewardship or antibiotic therapy or antibiotic treatment or antibiotic prescribing or pattern* or behaviour or behaviour or reduce or reduced or reduction or reducing or increase or increasing or increased or change or changing or changed or optimize or optimise or optimizing or optimization or optimising optimisation or effect* or effective or effectiveness or influence or influenced or influencing or impact.
   Settings: GP/primary healthcare/OR (primary care or primary healthcare or primary healthcare).

Hand searching

We will manually search key journals (eg, The LANCET Infectious Diseases, Journal of Antimicrobial Chemotherapy, Journal of Antimicrobial Agents, BioMed Central (http://www.biomedcentral.com/), British Medical Journal, Annals of pharmacotherapy, International Journal of Pharmacy Practice, JAMA, WHO's Library Databases. If required, direct contact with authors will be undertaken to obtain other relevant articles. Cited original articles in relevant systematic reviews will also be retrieved and analysed. We will update our literature search using the auto alert system in individual databases before publication of this review to avoid missing of any potential articles.

Study selection

All electronically and manually searched records will be merged to remove duplicate citations. Two reviewers will independently screen titles and abstracts to identify eligible articles using the inclusion and exclusion criteria. Where there is uncertainty regarding whether an article meets eligibility criteria, the full text of the article will be reviewed to determine final inclusion. Discrepancies between the reviewers will be resolved through discussion until a consensus is reached. If necessary, a third reviewer will be consulted to resolve the disagreement. If there is an information gap in a paper and/or a need for further clarification, the author will be contacted to clarify the issue by email. A PRISMA flow diagram will be used to maintain transparency in the article selection process and to record remaining studies in each stage of selection with a valid explanation regarding reasons of studies' exclusion.

Data extraction and management

A tailored version of EPOC's data abstraction tool[47] and the EPOC data collection checklist forms will be used as

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a guide to developing a data extraction form. This form will be adapted to answer the research question of this review and identify confounding factors. Additionally, recommendations for improving the consideration and description of interventions in a systematic review and a template for intervention description and replication (TIDieR) checklist[48 49] will be followed. The developed data extraction form will be pilot tested by the data extractors (SKS, LH) to ensure that it has captured all the relevant information.[50] Feedback from the extractors will be used to modify the data extraction form to ensure its usability and completeness. Data extraction in duplicate will be accomplished independently. Any disagreements between two parties will be resolved through discussion. The third reviewer will arbitrate if a consensus is unreachable.

We will extract data on (1) general information (title, author, year, study ID), (2) aims and rationale, (3) study design (includes brief description of method limitation), (4) study period, (5) study participants and settings, (6) intervention characteristics in details (eg, component, types, format, delivery strategy, timing, provider and recipient characteristics, effect, feasibility, acceptability, sustainability), (7) intervention outcomes (eg, control and intervention group results, effect, effect size, confidence interval (CI), odds ratio (OR), and (8) recommendations and conclusions. The intervention results will be carefully extracted to make them statistically meta-analysable. If data presentation is problematic, unclear, missing or presented in an unextractable form, the respective authors will be contacted for clarification by email with a response time limit of 2 weeks. If the author is unresponsive, then they will be classified as uncontactable. We will group interventions based on disease cases, intervention types, effect size, country, provider population and sources of variation (eg, seasonal and regional).

Assessment of risk of bias

Two reviewers (SKS and LH) will independently evaluate quality features of included articles using established guidelines and criteria tools.[51–54] Internal validity of RCTs will be assessed using Cochrane risk of bias tools.[52] The domains of this tool will be selection bias (random sequence generation, allocation concealment), reporting bias (selective reporting), performance bias (blinding of participant and personnel), detection bias (blinding of outcome assessment) and attrition bias (incomplete outcome data). We will avoid scoring the quality of the trials because of debates regarding scoring methods.[55] Each study will be categorised as high risk, low risk and unclear risk of bias under each of the criteria based on guidelines.[52] A study will be deemed as being at low risk of bias if it meets greater than or equal to four criteria out of six criteria with low risk of bias and the other two criteria must not be attrition or reporting bias. Studies will be considered as at unclear risk of bias if at least one domain has an unclear risk of bias and at most three domains have a low risk of bias. Studies with three domains with low risk of bias excluding attrition or reporting bias will be treated as studies with medium risk of bias. In studies where there are at least four domains at risk of bias or having random sequence generation bias, they will be considered as studies with high risk of bias. Based on this criteria, each study will be given an overall assessment of the low, moderate or high risk of bias. The quality assessment tool will be piloted on a small sample of included studies (5). The quality assessment criteria for non-randomised studies (CBA and ITS) will be based on Risk of bias In Non-randomised Studies- of Interventions risk assessment tools[53] and methodological quality criteria and guidance[55 56] from the Cochrane Collaborations.[51] We will also evaluate reporting criteria (eg, outcome definition, sample size calculation, sources of funding) for each of the included studies. The findings of each trial's risk of bias assessment will be recorded in a summary table.

Data synthesis and analysis

The findings of the included studies will be summarised in a table format for outcome measures including key information features regarding study types, design, number, participant characteristics, interventions, outputs and outcome measures. All the categorical variables of RCT, CBA and ITS trials (eg, antibiotic prescribing rate) will be reported with the same unit with 95% CIs and continuous variables with the mean difference and 95% CI. As primary outcomes, we will assess the proportion or volume or rate of (1) overall changes of antibiotic prescribing, (2) changes in broad spectrum and (3) changes in antibiotic prescribing adherence with a therapeutic guideline indicating appropriateness of GPs' antibiotic prescribing. We will calculate the effect size of each study by subtracting preintervention differences (intervention group–control groups) and postintervention differences. Absolute risk may be determined to express clinical significance. Summary statistics with 95% CIs and exact p value will be reported if studies have sufficient data for calculations. The combined analyses will represent the real percentage change in the rate of antibiotic prescribing or appropriateness of prescribing that is intervention attributed.

Where appropriate, outcome data will be combined for meta-analysis using Rev Man Review Manager 5.3, Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2014 . The pooled effect estimates will be generated using random-effects modelling to calculate interstudy heterogeneity in the intervention effect size. Fixed-effect modelling will be used if no substantial interstudy heterogeneity exists. For substantial interstudy heterogeneity, Forest plots,[54] χ^2 test and I^2 statistic[52] will be used to compare the effect size of trials with and without characteristics (eg, study features, context or intervention variation) of interest. The scale of heterogeneity will be low (<25%), moderate (50%), severe (up to 75%) and very severe (>75%). A meta-regression analysis will be performed to measure potential sources of heterogeneity if there are a substantial number of studies. A statistician

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will be approached if standardisation is required across studies for meta-analysis of continuous outcomes.

We will explain our data within an analytical stratum using the median and interquartile ranges (IQR) of effect sizes of trials. We will evaluate the association between type of intervention strategies and effect size, using the methods described above. In addition, we will assess other characteristics of studies as important confounders of the observed association. Assessment of confounders will be undertaken if the study characteristic meets two criteria: (1) if there is an independent association with the effect size and (2) where trials with that characteristic across the intervention types (eg, clinician education only, or combined with audit and feedback) have an uneven distribution. We will use Wilcoxon rank-sum tests to evaluate the association between each intervention trial characteristic and effect size, and Fisher's exact test or Mann Whitney U test to evaluate uneven distributions of study characteristics over intervention types. We will specify $p<0.05$ as statistically significant for this association. All analyses will be performed using STATA V.13. Where quantitative analysis is not possible, evidence will be presented as a descriptive synthesis.

Unit of analysis errors

In case of a potential unit of analysis error of RCT and CBAs, methods for reanalysis as guided by EPOC, 2015, will be used. Incorrect analysis of cluster RCTs due to the absence of accounting for clustering will be handled with reanalysis if possible. If correction is not possible, we will report the effect size without a SE and CI as they are unlikely to be accurate.

Reanalysis methods for inappropriate analysis

If appropriate, segmented time-series regression will be applied according to EPOC guidance to reanalyse the data of studied trials followed by a method described in Ramsay *et al*.[57]

Dealing with missing data

If any missing data exist within working trials, the respective authors will be contacted to avoid the inappropriate description of study results and to minimise the risk of bias in meta-analysis.[58] A guidance[52] will be followed to handle missing data.

Assessment of publication bias

The assessment of publication bias will be conducted by extrapolating the study trials effect estimate with inversion of trials SE through the usage of a funnel plot. The assessment of the plots will be both visually and by Egger's test with a $p<0.1$ considered as significant publication bias.[59]

Quality assessment of evidence

The evidence summaries (intervention profiles and table of findings) will be formulated based on the guidance recommended by Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group[60] and the TIDieR checklist.[48 49]

Sensitivity analysis

A sensitivity analysis will be conducted to estimate the effect of study quality and effect of missing data on the meta-analysis of outcome measures. Two meta-analyses (one including all eligible studies and the second including only those studies defined by EPOC criteria as being high quality for quality assessment) will be performed to determine the effect of study quality. In case of unobtainable data, we will conduct complete case analysis and perform sensitivity analysis of outcomes (continuous and dichotomous) to address the potential impact of missing data on meta-analysis using a method discussed by Akl *et al*.[61]

Subgroup analysis

Should enough data be available, this review will conduct subgroup analysis for primary outcomes. Important varieties of exploratory subgroup analysis may be performed by (1) provider population, (2) country settings (eg, developed vs middle income vs low income), (3) study design, (4) disease cases (among RTIs or RTI vs skin), (5) risk of bias (high risk vs low risk of bias) (6) antibiotic classes (7) intervention types, (8) mode of delivery of intervention (9) follow-up timing of intervention studies.

Ethics and dissemination

No formal ethical approval is required as no primary, personal and confidential data are being collected in this study. We will present our findings including GRADE evidence and descriptive evidence tables in Australia and at international scientific meetings, seminars, workshops and conferences in addition to publishing in a peer-reviewed journal.

DISCUSSION

To the best of our knowledge, this is the first systematic review assessing pharmacist-led or pharmacist-involved interventions to improve GPs' antibiotic prescribing in primary care. This review is solely focused on family practice or general practice settings. The findings may be reproducible to general practices due to less contextual variation led by different settings of care. This review will cover a large number of databases and other journal sources as well. Use of English language articles is a limitation of the review. Poor quality studies and heterogeneity in results may lead to difficulty in interpreting findings.

It is anticipated that the findings of this systematic review will be relevant to many stakeholders. First, the review will present a comprehensive overview of pharmacy intervention features for primary care researchers and will additionally highlight any potential gaps in the current literature on this topic. Second, it will highlight international evidence from peer-reviewed literature on the effectiveness, feasibility and acceptability of interventions

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with the assessment of methodological quality of relevant studies thereby increasing the applicability of the findings. Third, the review could provide information regarding valuable interventions which may increase GP–pharmacist collaboration and more judicious antibiotic prescribing in general practices. Fourth, the review may be useful for funders to better understand interventions which could be prioritised for future funding. This will be informed by ranking outcomes in an innovative approach. Finally, the findings may support GPs, pharmacist, researchers and health policy-makers to design future interventions to improve antibiotic prescribing by GPs in primary care.

Registration and publishing

This systematic review protocol is registered on the International Prospective Register of Systematic Reviews (PROSPERO) with a trial number, CRD42017078478 (https://www.crd.york.ac.uk/prospero/#myprospero) dated 8 November 2017. A PRISMA-P checklist[46] will be used to report the review. The findings of the review will be published in international peer-reviewed journals.

Acknowledgements The authors would like to express thanks to Anne Young, subject librarian for Faculty of Medicine, Nursing and Health Sciences for her contribution to the development of the search strategy. The special appreciation of the authors goes to research team members of the Department of General Practice (DGP) for their valuable feedback on the draft of review protocol and manuscript.

Contributors Review concept was designed by DM and SKS. SKS and LH developed the study design and literature search strategies. Screening of literature was conducted by SKS and LH. Design of study quality risk assessment tools, data extraction tools, data synthesis and meta-analysis and statistical tests were developed by SKS, LH and DM. SKS wrote this manuscript and also drafted the whole protocol according to PRISMA-P. Revision of the draft manuscript was undertaken by all authors.

Funding SKS as a PhD student is supported by a Faculty of Medicine, Nursing and Health Sciences and Monash International Post Graduate Scholarship (MIPRS) from Monash University in Australia.

Competing interests None declared.

Patient consent Not required.

Ethics approval Not required

Provenance and peer review Not commissioned; externally peer reviewed.

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