



Germeni, E. , Frost, J., Garside, R., Rogers, M., Valderas, J. M. and Britten, N. (2018) Antibiotic prescribing for acute respiratory tract infections in primary care: an updated and expanded meta-ethnography. *British Journal of General Practice*, 68(674), e633-e645. (doi:[10.3399/bjgp18X697889](https://doi.org/10.3399/bjgp18X697889)).

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Deposited on: 23 July 2018

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**Antibiotic prescribing for acute respiratory tract infections in primary care:
an updated and expanded meta-ethnography**

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ABSTRACT

Background: Reducing unnecessary prescribing remains a key priority for tackling the global rise of antibiotic-resistant infections.

Aim: We sought to update a 2011 qualitative synthesis of GPs' experiences of antibiotic prescribing for acute respiratory tract infections (ARTIs), including their views of interventions aimed at more prudent prescribing. We expanded the original scope to encompass all primary care professionals (PCPs) who can prescribe or dispense antibiotics for ARTIs (e.g. nurses, pharmacists).

Design and setting: Systematic review and meta-ethnography of qualitative studies.

Methods: A systematic search was conducted on MEDLINE, EMBASE, PsycINFO, CINAHL, ASSIA, and Web of Science. No date or language restrictions were used. Identified studies were grouped according to their thematic focus (usual care vs. intervention) and two separate syntheses were performed.

Results: Fifty-three articles reporting the experiences of over 1200 PCPs were included. Analysis of usual care studies showed that PCPs tend to assume multiple roles in the context of ARTI consultations (the Expert Self; the Benevolent Self; the Practical Self), depending on the range of intrapersonal, interpersonal, and contextual situations in which they find themselves. Analysis of intervention studies identified four possible ways in which PCPs may experience quality improvement interventions (Compromise; "Supportive aids"; Source of distress; Unnecessary).

Conclusion: Contrary to the original review, our results suggest that the use of the same intervention is experienced in a totally different way by different PCPs and that the same elements that are perceived as benefits by some, could be viewed as drawbacks by others. Acceptability of interventions is likely to increase if these are context-sensitive and take into account PCPs' varying roles and changing priorities.

Key words: respiratory tract infections; anti-bacterial agents; primary health care; inappropriate prescribing; qualitative research; interventions

How this fits in

A 2011 systematic review and qualitative synthesis of GPs' views and experiences of antibiotic prescribing for acute respiratory tract infections (ARTIs) concluded that, to maximize acceptability, interventions aimed at more prudent prescribing should incorporate five aspects: allow GPs to reflect on their own prescribing; help decrease uncertainty about appropriate ARTI management; educate GPs about appropriate prescribing; facilitate more patient-centred care; and be beneficial to implement in practice. Yet, several new studies have been published since then and the continued relevance of these findings cannot be assumed. We performed an update of this work, while expanding the initial focus to encompass all primary care professionals (PCPs) who can prescribe or dispense antibiotics for ARTIs. Our study produced an up-to-date conceptual model of antibiotic prescribing in primary care, as well as a typology of ARTI intervention acceptance, which could serve as valuable tools for current policy and practice.

INTRODUCTION

Antimicrobial resistance has been characterised as "one of the world's most pressing public health problems".¹ Over the last decade, a number of national and international organizations have called for action, but often with a limited impact due to lack of coordination or failure to recognize the global dimensions of the problem.² On January 21, 2016, the joint Declaration on Combating Antimicrobial Resistance³ -signed by more than 80 leading pharmaceutical, diagnostics and biotechnology companies- fuelled a new momentum in the global response to these challenges. A few months later, the publication of two high profile reports^{4, 5} -the first commissioned by the UK government and the second authored by the World Bank Group- attracted both scientific and media attention, as they provided estimates of the immense global burden and financial impact of drug-resistant infections if urgent action is not taken.

Excessive prescribing of antibiotics remains an important driver of antimicrobial resistance. The bulk of antibiotic prescribing occurs in primary care, with acute respiratory tract infections (ARTIs) representing the most common indication.⁶ Although ARTIs are often self-limiting and seldom require antibiotics for treatment,⁷ primary care clinicians have been found to overprescribe for a variety of clinical and, predominantly, non-clinical factors (e.g. prior negative experience of non-antibiotic management, perceived patient pressure).⁸⁻¹⁰ Qualitative research, focusing on the meanings that people attach to their experiences, is uniquely situated to explain this "non-pharmacological" basis of prescribing, and primary qualitative studies have offered, to date, valuable insights into the reasons why clinicians may choose not to follow evidence-based guideline recommendations. Synthesizing the findings from diverse and often small-scale qualitative studies has the potential, not only to situate them in a larger interpretative context, but also to make them more "ready-to-use" for healthcare practice and policy-making.¹¹

Similar to statistical meta-analyses, however, qualitative syntheses may also become out-of-date, as beliefs, experiences, health care contexts and social phenomena are bound to change.¹² Thus, the goal of this study was to update a 2011 qualitative synthesis of general practitioners' (GPs') experiences of antibiotic prescribing for ARTIs, including their views of interventions aimed at more prudent prescribing.¹³ Tonkin-Crine et al. were the first to review and synthesize published qualitative literature on processes involved in management decisions for ARTIs. Yet, most studies included in their review came from the UK and Scandinavia, limiting the transferability of findings to countries with different healthcare systems and antibiotic consumption rates.¹³ In an effort to address the global aspects of the problem (i.e. several disciplines are involved in the delivery of primary care and their involvement/role/tasks varies widely across countries),¹⁴ we expanded the original focus to encompass all primary care professionals (PCPs) who can prescribe or dispense antibiotics for ARTIs (e.g. nurses, pharmacists).

METHOD

The reporting of this review is in accordance with the ENTREQ statement (Table S1).¹⁵ The review protocol was registered with PROSPERO (CRD42016042861).

Search strategy and selection criteria

An information specialist (MR) revised the original search strategy to fit the purpose of the updated review (Table S2). We performed a systematic, all-language search of the following databases from inception to June 29, 2016: MEDLINE, EMBASE, PsycINFO, CINAHL, ASSIA and Web of Science. We also hand searched reference lists of included papers and used Web of Science to do forward citation tracking. Studies were eligible for inclusion if they: (a) were published as original research articles in peer-reviewed journals; (b) used both qualitative data collection and analysis methods; and (c) reported findings about PCPs' attitudes and experiences of antibiotic prescribing/dispensing for ARTIs or their views of interventions aimed at reducing inappropriate prescribing/dispensing. Mixed methods studies were also eligible for inclusion, provided that the qualitative findings were adequately reported and discussed separately from the quantitative findings. Studies that did not provide participant quotations (raw data) to illustrate main themes/findings were excluded. We also excluded studies involving mixed participant groups (e.g. patients and PCPs) that did not present separately or in detail findings from PCPs.

Data screening and quality assessment

Titles and abstracts of identified references were uploaded into EndNote and screened independently by two reviewers: EG served as Reviewer 1, whereas JF, RG, and NB served as Reviewer 2, each screening one-third of the articles. Full-texts of potentially eligible articles were retrieved and assessed independently by the same reviewers, as previously described. In both stages, disagreements were resolved by consensus. Key study details (e.g. country, sample) were extracted into a Microsoft Excel spreadsheet. Recognizing the

tension between reporting quality and potential contribution of a paper to the synthesis,^{16, 17} we eventually opted for not using a formal appraisal checklist (e.g. CASP) to exclude papers on the basis of their reporting quality. Instead, drawing on the categorization of Dixon-Woods et al.,¹⁸ we classified studies as follows: (a) key (i.e. papers that were likely to make an important contribution to the synthesis due to their high analytic/explanatory power and high relevance); (b) satisfactory (i.e. papers with high analytic/explanatory power but sufficient relevance, or papers with high relevance but sufficient analytic/explanatory power); (c) unsure (i.e. papers that we were unsure of their potential contribution to the synthesis due to either limited analytic/explanatory power or borderline relevance); (d) fatally-flawed (i.e. papers that either presented their findings in a numerical way or did not provide participant quotations); and (e) irrelevant (i.e. papers that were not relevant to the review question). Papers judged as “irrelevant” and “fatally-flawed” were excluded during full-text screening, whereas for the remainder we followed an all-inclusive strategy.

Data analysis

In line with the original synthesis, we used the technique of meta-ethnography to synthesize available findings. Meta-ethnography is the qualitative equivalent to meta-analysis; yet, rather than aggregating findings, it focuses on the translation of individual studies into one other and the development of new interpretations.¹⁹ Given the large amount of identified papers, we began by organizing them into groups according to their thematic focus (usual care vs. intervention) and then, within each group, by date of publication. To allow for the exploration of potential intervention-specific differences, we further classified intervention studies based on type of intervention (clinical, educational, system-level, or multifaceted), using McDonagh et al.’s framework²⁰, and use of intervention (naturalistic, controlled trial, or hypothetical). Starting from the usual care group, we repeatedly read all studies, noting first-order (PCPs’ quotations) and second-order (authors’ interpretations of PCPs’ experiences) constructs. To understand how the studies related to each other, we created a grid and

juxtaposed all identified second-order constructs. This enabled us to determine which type of synthesis was most appropriate –a reciprocal (where concepts from one study can easily encompass another) or refutational translation (where concepts are contested across papers) or line-of-argument synthesis, which involves first translating the studies into each other and then constructing an overarching argument about the whole set of studies. Considering the different thematic focus of the two groups of papers, we conducted two separate line-of-argument syntheses.

RESULTS

Of 507 unique citations found, 67 were eligible for full-text review and 53 were included in the synthesis (Figure 1). The 53 included papers^{10, 21-72} corresponded to 45 different studies and reported the experiences of more than 1200 PCPs (i.e. 1113 GPs/family physicians; 74 nurses; 41 pediatricians; 33 pharmacists; 1 physiotherapist; 1 physician assistant) practicing in 21 countries (Table 1). The earliest paper was published in 1998; yet, more than half (28) were published after the publication of the original synthesis. Twenty-five papers discussed PCPs' experiences of antibiotic prescribing/dispensing in usual care, 22 focused on their views of an intervention (or combination of interventions), and 6 reported mixed information. Those 6 papers contributed to both syntheses.

Among the 28 intervention/mixed studies, 13 focused on a clinical intervention (e.g. point-of-care testing, delayed prescribing, clinical scoring tools), 7 described a system-level intervention (e.g. electronic decision support, antimicrobial stewardship programs), 4 were about an educational intervention (e.g. communication skills training), and another 4 discussed a multi-faceted intervention (e.g. point-of-care testing in combination with communication skills training). Moreover, in the same group of papers, 12 focused on an intervention implemented in naturalistic (real-life) settings, another 12 on an intervention implemented in controlled trial settings, and the remaining 4 discussed participants' views about the hypothetical introduction of an intervention (either in naturalistic or in controlled trial settings).

Synthesis of Group 1 (usual care) studies

Table 2 presents a list of all second-order constructs that we identified from the 31 usual care studies, along with a narrative translation of each construct (i.e. a description that encompasses all the papers from which it was drawn). By re-ordering, re-linking and re-analyzing identified second-order constructs, we were able to generate 6 third-order

constructs, which constitute our own interpretations of included studies. Based on these, we created a conceptual model showing how PCPs may choose to present themselves differently in the context of ARTI consultations (the Expert Self; the Benevolent Self; and the Practical Self), depending on the range of intrapersonal, interpersonal, and contextual situations in which they find themselves and according to the function that a certain identity serves at a given moment (Figure 2).

In particular, the Expert Self corresponds to the self who holds the expertise and is constructed through formal (i.e. history taking and physical examination) and non-formal (i.e. overall impression of how the patient looks on the day and “gut feeling”) methods of clinical assessment. Antibiotic decisions were, to a large extent, guided by and communicated (or justified) in reference to: problematic or potentially worsening signs and symptoms (e.g. discolored sputum, high or persistent fever), clinical findings (e.g. chest sounds on auscultation), or “expert” assessments (e.g. the patient looked “toxic” or “miserable”). Several PCPs reported recognizing “*the sick patient in among the just unwell as they walked through the door*”,²⁴ whereas others described the development of individual “guidelines” or “rules-of-thumb” as a mark of expertise.^{51, 67}

The Benevolent Self corresponds to the self who wants to please and “help”. It is constructed through the interaction with the patients and validated by prevailing social norms and role expectations associated with what constitutes a “good” PCP. In this context, building and maintaining a good relationship with the patient was viewed as a top priority for most PCPs and some admitted that they were not willing to jeopardise this “*for the sake of a prescription for penicillin V*”.⁷² Concerns about being perceived as “*having done nothing*”³⁰ for the patient or not being “*proper doctors*”,¹⁰ if they did not prescribe antibiotics, were also common among GPs and several expressed dissatisfaction when not being able to offer a tangible solution. Furthermore, PCPs’ desire to “*do their best for the patient in front of*

*them*⁶⁰ seemed, in many cases, to override expert judgment: pharmacists admitted giving out antibiotics to patients who could not afford to pay fees or private medical consultations, whereas clinicians described how the circumstances in an individual's life (ranging from the environment in which he/she lived to plans for leisure activities) often led to unnecessary prescribing.

Last, the Practical Self corresponds to the self who thinks practically (e.g. avoiding a lawsuit in case of a mistake), but also to the self who has to cope with specific system demands and practical considerations (e.g. patient retention and financial considerations): *"You shouldn't be treating all respiratory infections with antibiotics? Certainly. Is it practical? Probably not. I probably wouldn't have as good of a collection rate. I truly think that part of what you're doing is consumer-based medicine"*.⁶¹ Legitimized by broader system factors, prescribing, in this context, was seen as the "safest" or "easiest" choice. GPs in Lithuania, for example, reported occasionally giving in to patient pressure for antibiotics, as they felt "unsafe" and threatened by current legislation on patients' rights,⁴⁴ whereas GPs in Iceland described themselves as "slaves of the green forms",⁶⁷ since their salary consisted of a mixture of wages and a fee-for-service part, collected by means of green forms.

Although the Expert Self constitutes the "default" identity of PCPs, how they choose to present themselves in the context of ARTI consultations is dependent on a mixture of intrapersonal, interpersonal and contextual factors. Specifically, PCPs' prior experience of ARTI management and their level of self-confidence were found to have a considerable impact on their current prescribing practices: in general, experience in ARTI management increased self-confidence and reinforced the expert identity, whereas a previous negative case of non-antibiotic management challenged clinical expertise and often led to overprescribing *"to be on the safe side"*.²⁷ Likewise, both characteristics of the PCP-patient interaction (i.e. actual or perceived patient pressure, mutual trust and confidence with the

patient) and contextual factors (i.e. degree of diagnostic uncertainty accompanying each patient case, presence or lack of continuous care, work pressure and fatigue, timing of consultation, system factors) influenced the identity that PCPs chose to articulate.

While this shifting of identities may allow for flexibility in decision-making, it is not always voluntary. In such cases, PCPs may feel pressured to assume a role that they do not wish to assume and experience ambivalence, or even frustration, regarding their management decisions. As a study participant put it: *"I'm Dr. Jekyll and Mr. Hyde"*.⁴⁰

Synthesis of Group 2 (intervention) studies

Similarly, our synthesis of intervention studies identified 13 second-order constructs, which were further abstracted to generate 4 third-order constructs (Table 3). Such analysis led to the development of a typology of ARTI intervention acceptance in primary care that depicts four possible ways in which PCPs may experience interventions (Figure 3).

In the first cell of our typology, *interventions as a compromise*, PCPs tend to view interventions solely as a compromise and use them selectively, that is, only in cases of a perceived deadlock (either clinical or interpersonal). This was commonly the case with clinical interventions, such as near-patient tests and delayed prescribing, which were used by many PCPs either in cases of clinical doubt, as a means of managing diagnostic uncertainty and safety netting against the condition worsening, or in cases of potentially confrontational encounters with patients who had strong expectations for antibiotics: *"I have used [wait-and-see prescriptions] for several years, but to a small extent only... It is for those who want medication, though you argue that they don't need it, but then they win at the end and I say: 'Can you at least wait for a couple of days and see how it develops?' You become somewhat pragmatic with the years"*.⁵⁴

In the second cell, *interventions as “supportive aids”*, PCPs choose to integrate interventions into their routine practice, as they perceive them mostly as tools that can support clinical decision-making and enhance the encounter with the patient. Although some concerns could still be present, interventions here were typically seen as feasible to implement in practice, and their use was thought to: augment clinical authority and enhance both practitioners’ and patients’ confidence in prescribing decisions; provide an opportunity for educating and empowering the patient; help practitioners gain greater insight into patients’ perspectives and provide more patient-centered care; as well as contribute to more effective targeted treatment, prevention of unnecessary prescribing and reduced re-consultation rates.

All of the above perceived benefits of interventions are viewed from the exact opposite angle by PCPs representing the third cell, *interventions as a source of distress*. For them, interventions appeared to constitute a source of distress, as they were considered to: convey mixed messages to patients about the competence of the physician or the efficacy of antibiotics for ARTIs; diminish provider-patient trust and result in a paternalistic approach; lead to possible disconnect with clinical assessment and intuition, as well as to potentially inappropriate management of ARTIs. Moreover, PCPs belonging in this group typically saw interventions as too costly or too time-consuming to fit into usual practice: *“In an ideal world yes... I have seen 17 patients [so far] today. And each is given 10 minutes of appointment. If you end up admitting one, or end up doing some examinations, it takes longer... So in an ideal world, yes, I could test urines. I could test various things. H. pylori and various other things”*.⁵⁸

In the last cell, *interventions as unnecessary*, PCPs choose not to integrate interventions into their own practice, but accept their utility for other, mostly inexperienced, groups of prescribers. Specifically, this was the case with certain PCPs who reported that, although interventions were unnecessary for them, they did have *“a place within primary care”*,³⁸ as

they could prove a useful tool for inexperienced practitioners (e.g. newly qualified GPs) or new prescribers (e.g. nurses).

The proposed typology, however, is neither static nor decontextualized. PCPs continuously evaluate both the added value and the feasibility of a specific intervention, meaning that the proposed types are rather dynamic and may change over time or depending on the characteristics of the encounter. The same practitioner, for instance, who on one occasion, may view the implementation of an intervention as particularly distressing (e.g. issuing a wait-and-see prescription in the after-hours care setting, where they do not know the patients and the scope for follow-up is limited), could, on another, see it as a "supportive aid" (e.g. issuing a wait-and-see prescription in their regular list patient practice, where they know their patients and can start a discussion about the necessity or effectiveness of antibiotics).

DISCUSSION

Summary

This work constitutes one of the very few updates of qualitative syntheses currently available^{12, 73-75} and, to our knowledge, the first conducted by a different team of reviewers. Our updated review incorporated findings from 53 papers (i.e. 41 more than the original review), published over the span of two decades and reporting the experiences of more than 1200 PCPs practicing in 21 countries around the world. By expanding our search beyond GPs, we were able to incorporate in our analysis a range of perspectives, while capturing more of a global context, given international differences in the involvement of various disciplines in the delivery of primary care. Most of the factors identified in the original review as responsible for inappropriate prescribing were found to be still pertinent. Yet, identification of more studies added depth to these concepts and led to a better understanding of the phenomenon. Specifically, we were able to show how PCPs manage their professional identity in the context of ARTI consultations (the Expert Self; the Benevolent Self; and the Practical Self), depending on the range of intrapersonal, interpersonal, and contextual situations in which they find themselves. Furthermore, inclusion of recent evidence on PCPs' experiences of interventions (used not only as part of randomized controlled trials, but also in real-life settings) allowed us to draw important conclusions about the possible ways that these may be employed. Contrary to Tonkin-Crine et al.,¹³ we found that the use of the same intervention might be experienced in a totally different way by different PCPs and that the same elements that are perceived as benefits by some, could be viewed as drawbacks by others. Most importantly, we created a typology of ARTI intervention acceptance, which could serve as a valuable tool for current policy and practice. Our typology presents four different stances towards the use of interventions (Compromise; "Supportive aids"; Source of distress; Unnecessary), which are however dynamic and mutable, as PCPs seem to continuously evaluate both their feasibility and their added value.

Comparison with existing literature

The need to approach antibiotic prescribing as a simultaneously medical, social, and cultural practice has already been stressed by Ackerman and Gonzales,⁷⁶ who argued that the case of antibiotic overuse powerfully illustrates the importance of “context” for clinical practice. Indeed, our synthesis of usual care studies unveils the complex interplay of clinical experience, social norms and expectations, cultural trends, as well as broader system factors (e.g. organization and financing of primary care). Most importantly, it offers an in-depth understanding of how PCPs perceive their role in such a “context”, while accounting for the wide variation that exists in the acceptability of interventions (see Table S3 for an indicative -yet, far from exhaustive- list of possible scenarios). Although the notion of multiple identities as a result of expectations and negotiations goes back several years, the recent shift towards consumerism seems to have sparked a renewed interest in how the emerging model of the patient as “reflexive consumer” has impacted on physicians’ professional identity.⁷⁷ Our results suggest that, in the highly uncertain context of ARTI consultations, the traditional role of the PCP as the “expert” whose job is to “treat infections” is expanded to include a benevolent identity that wants to satisfy and “help” the patient, as well as a practical identity that has to cope with system demands and real-life considerations.

The practice of benevolence constitutes the implicit basis upon which all healthcare professionals operate. How benevolence may interfere with antibiotic decision-making and what the practical consequences of this might be, however, is a topic that necessitates further investigation. Broom et al.⁷⁸ found that benevolence constitutes a core principle of action among medical doctors, justifying suboptimal prescribing practices in the hospital. Yet, it could be argued that in primary care, where the duty of the professional is to serve as the patient’s first contact with the healthcare system, expectations around the performance of benevolence may become even more salient. In this context, for instance, the act of issuing an unnecessary prescription as a way of demonstrating concern and consideration

for the patient's life circumstances (regardless of whether these involve living under insanitary conditions in poor areas of India⁵⁵ or having to attend an important meeting the following day⁶²) might not only be legitimate, but also valued and encouraged by social and professional norms around what constitutes a "good" PCP.

Another topic that has been remarkably overlooked in current efforts to optimize prescribing patterns is the role of "gut feelings" in PCPs' diagnostic reasoning. A growing body of evidence indicates that "gut feelings" are common among PCPs and constitute an integral part of clinical decision-making.⁷⁹⁻⁸¹ Our results resonate with prior findings, while also emphasizing the symbolic effect that intuition may have in reinforcing PCPs' expert identity. Considering that problems presenting in primary care are often early in their natural history, with vague symptoms and a broad range of diagnostic possibilities, being able to "recognize the sick patient as they walk through the door"²⁴ may be crucial in allowing PCPs to re-establish themselves as the competent technical experts in a shifting context of power relations. This also relates to our finding that fear of possible disconnect with clinical intuition was a major barrier to the routine use of clinical interventions.

Strengths and limitations

The development and spread of antibiotic-resistant infections has predominantly been a clinical problem in hospital settings and much of available social science research has focused on investigating norms of practice among hospital-based professionals.^{78, 82} Yet, resistance to primary care prescribed antibiotics is also common and the transmission potential of these infections across healthcare settings could be substantial. Our study offers a comprehensive, up-to-date overview of available qualitative literature on PCPs' management decisions for ARTIs, while highlighting the complexity of the problem in primary care. Nevertheless, certain limitations need to be acknowledged. First, although we expanded the original review question to encompass all PCPs who can prescribe or

dispense antibiotics, our search located only one study focusing on pharmacists' dispensing practices. We cannot, therefore, be confident that our findings hold relevance for understanding antibiotic dispensing in primary care. Likewise, although we included evidence from a wide range of countries and were able to identify themes that were consistent across different healthcare systems and prescribing contexts, our synthesis of intervention studies relied solely on findings from high-income countries, meaning that we are unaware of whether our typology of ARTI intervention acceptance can be extrapolated to low- or middle-income countries. Finally, we recognize that the process of synthesizing qualitative research is essentially interpretative. Therefore, it could be argued that differences in conclusions reached might be due to differences in interpretations between the original and the new team. In an effort to check our interpretations, we contacted the original team and asked them to clarify previously emergent concepts, as well as to provide feedback on draft versions of updated models.

Implications for research and practice

Updating of quantitative systematic reviews and statistical meta-analyses is now mainstream practice. The same, however, does not apply for systematic reviews and syntheses of qualitative evidence, for which to date the process of updating has remained largely unexplored. Our work provides empirical evidence for the necessity of regularly updating qualitative syntheses, and shows that, in the same way that updated meta-analyses can inform about whether healthcare interventions continue to be safe and effective, updated qualitative syntheses can provide evidence on whether these continue to remain relevant to target audiences' changing needs, preferences, and experiences. Moreover, identifying and incorporating new evidence into a previously completed qualitative synthesis may lead to new conceptual insights and a more nuanced understanding of the phenomenon under study, which is not something that an updated meta-analysis is able (or aims) to achieve.

The original meta-ethnography concluded that, to maximize acceptability, interventions aimed at more prudent prescribing for ARTIs should incorporate five aspects: allow GPs to reflect on their own prescribing; help decrease uncertainty about appropriate ARTI management; educate GPs about appropriate prescribing; facilitate more patient-centred care; and be beneficial to implement in practice.¹³ Seven years later, our updated synthesis suggests that one-size-fits-all approaches are doomed to result in variable uptake, as different professionals experience the same elements in a very different way. We argue that acceptability of interventions is likely to increase if these are context-sensitive and take into account PCPs' varying roles and changing priorities. Similar to Ackerman and Gonzales,⁷⁶ we embrace a wider definition of "context" that can account for both specific situational factors (e.g. setting and timing of consultation) and broader socio-economic, cultural, and system influences.

Several context-specific differences that link (either directly or indirectly) to the acceptability of interventions were apparent in our work. First, PCPs practicing in countries with fee-for-service payment systems often reported feeling pressured to over-prescribe due to business concerns.^{41, 61, 67} Similarly, PCPs practicing in countries where antibiotic use still remains largely unregulated, extensively discussed how patients' direct access to antibiotics and self-medication restricted their management options and led to unnecessary prescribing.^{25, 37, 43, 44, 46, 55} By comparison, PCPs from Belgium, Iceland and the UK emphasized how systems to reduce patient expectations, such as public information campaigns, had made their work easier over the last few years.^{43, 51} Of note, in the only study that included a follow-up (i.e. the same Icelandic GPs were interviewed in 1995 and, again, in 2006), Bjornsdottir et al.⁵¹ found increased use of point-of-care tests and the perception by GPs that patients were more willing to "wait and see".

In conclusion, our results suggest that, to work towards achieving more impactful outcomes, pragmatically tailoring interventions to better fit them to specific PCP groups and local conditions might be a necessary first step. In countries, for example, where over-the-counter sales of antibiotics is allowed, it might be rather difficult to implement clinical interventions; instead, promoting tailored educational interventions, such as physician communication skills training and public campaigns, might be more efficient. Likewise, building flexibility into the design of interventions, so that these can be adjusted according to different circumstances and priorities (e.g. time-pressured settings), could eliminate situational barriers and ensure a more consistent use of interventions. The solution of a global problem might not lie on the development of a universal, multi-faceted approach, but on addressing deep-rooted, local *modus operandi*.

Funding

Evi Germeni was supported by an Advanced Postdoc Mobility grant from the Swiss National Science Foundation (P300P1_164574). Ruth Garside, Morwenna Rogers, and Nicky Britten were partially supported by the UK National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care South West Peninsula. The content is solely the responsibility of the authors and does not necessarily represent the views of the Swiss National Science Foundation, the UK National Institute for Health Research, the UK National Health Service, or the UK Department of Health.

Ethical approval

Not required.

Competing interests

The authors have no conflicts of interest to declare.

REFERENCES

1. Centers for Disease Control and Prevention. Get smart: Know when antibiotics work in doctor's offices. <https://www.cdc.gov/getsmart/community/about/fast-facts.html> (accessed July 31, 2017).
2. Carlet J, Jarlier V, Harbarth S, Voss A, Goossens H, Pittet D. Ready for a world without antibiotics? The Penalties Antibiotic Resistance Call to Action. *Antimicrob Resist Infect Control* 2012; 1(1): 11.
3. International Federation of Pharmaceutical Manufacturers & Associations. Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance. <https://www.ifpma.org/partners-2/declaration-by-the-pharmaceutical-biotechnology-and-diagnostics-industries-on-combating-antimicrobial-resistance-amr/> (accessed July 31, 2017).
4. The Review On Antimicrobial Resistance. Tackling Drug-Resistant Infections Globally: Final Report and Recommendations. http://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf (accessed July 31, 2017).
5. World Bank Group. Drug-Resistant Infections: A Threat to Our Economic Future. <http://documents.worldbank.org/curated/en/323311493396993758/pdf/114679-REVISED-v2-Drug-Resistant-Infections-Final-Report.pdf> (accessed July 31, 2017).
6. Goossens H, Ferech M, Vander Stichele R, Elseviers M. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 2005; 365(9459): 579-87.
7. Huang Y, Chen R, Wu T, Wei X, Guo A. Association between point-of-care CRP testing and antibiotic prescribing in respiratory tract infections: a systematic review and meta-analysis of primary care studies. *Br J Gen Pract* 2013; 63(616): e787-94.

8. Strumilo J, Chlabicz S, Pytel-Krolczuk B, Marcinowicz L, Rogowska-Szadkowska D, Milewska AJ. Combined assessment of clinical and patient factors on doctors' decisions to prescribe antibiotics. *BMC Fam Pract* 2016; 17: 63.
9. Akkerman AE, Kuyvenhoven MM, van der Wouden JC, Verheij TJ. Determinants of antibiotic overprescribing in respiratory tract infections in general practice. *J Antimicrob Chemother* 2005; 56(5): 930-6.
10. Petursson P. GPs' reasons for "non-pharmacological" prescribing of antibiotics. A phenomenological study. *Scand J Prim Health Care* 2005; 23(2): 120-5.
11. Sandelowski M, Docherty S, Emden C. Focus on qualitative methods. Qualitative metasynthesis: issues and techniques. *Res Nurs Health* 1997; 20(4): 365-71.
12. France EF, Wells M, Lang H, Williams B. Why, when and how to update a meta-ethnography qualitative synthesis. *Syst Rev* 2016; 5: 44.
13. Tonkin-Crine S, Yardley L, Little P. Antibiotic prescribing for acute respiratory tract infections in primary care: a systematic review and meta-ethnography. *J Antimicrob Chemother* 2011; 66(10): 2215-23.
14. Freund T, Everett C, Griffiths P, Hudon C, Naccarella L, Laurant M. Skill mix, roles and remuneration in the primary care workforce: Who are the healthcare professionals in the primary care teams across the world? *Int J Nurs Stud* 2015; 52(3): 727-43.
15. Tong A, Flemming K, McInnes E, Oliver S, Craig J. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. *BMC Med Res Methodol* 2012; 12: 181.
16. Smith LK, Pope C, Botha JL. Patients' help-seeking experiences and delay in cancer presentation: a qualitative synthesis. *Lancet* 2005; 366(9488): 825-31.
17. Malpass A, Shaw A, Sharp D, et al. 'Medication career' or 'Moral career'? Two sides of managing antidepressants: A meta-ethnography of patient's experience of antidepressants. *Soc Sci Med* 2009; 68(1): 154-68.

18. Dixon-Woods M, Sutton A, Shaw R, et al. Appraising qualitative research for inclusion in systematic reviews: a quantitative and qualitative comparison of three methods. *J Health Serv Res Policy* 2007; 12(1): 42-7.
19. Britten N, Campbell R, Pope C, Donovan J, Morgan M, Pill R. Using meta ethnography to synthesise qualitative research: a worked example. *J Health Serv Res Policy* 2002; 7(4): 209-15.
20. McDonagh M, Peterson K, Winthrop K, Cantor A, Holzhammer B, Buckley DI. Improving Antibiotic Prescribing for Uncomplicated Acute Respiratory Tract Infections. Comparative Effectiveness Review No. 163. AHRQ Publication No. 15(16)-EHC033-EF. Rockville, MD: Agency for Healthcare Research and Quality, 2016.
21. Andre M, Grondal H, Strandberg EL, Brorsson A, Hedin K. Uncertainty in clinical practice - an interview study with Swedish GPs on patients with sore throat. *BMC Fam Pract* 2016; 17: 56.
22. Ashdown HF, Raisanen U, Wang K, Ziebland S, Harnden A. Prescribing antibiotics to 'at-risk' children with influenza-like illness in primary care: qualitative study. *BMJ Open* 2016; 6(6): e011497.
23. Cabral C, Ingram J, Lucas PJ, et al. Influence of Clinical Communication on Parents' Antibiotic Expectations for Children With Respiratory Tract Infections. *Ann Fam Med* 2016; 14(2): 141-7.
24. Horwood J, Cabral C, Hay AD, Ingram J. Primary care clinician antibiotic prescribing decisions in consultations for children with RTIs: a qualitative interview study. *Br J Gen Pract* 2016; 66(644): e207-13.
25. Zhang Z, Zhan X, Zhou H, et al. Antibiotic prescribing of village doctors for children under 15 years with upper respiratory tract infections in rural China: A qualitative study. *Medicine (Baltimore)* 2016; 95(23): e3803.

26. Anthierens S, Tonkin-Crine S, Cals JW, et al. Clinicians' views and experiences of interventions to enhance the quality of antibiotic prescribing for acute respiratory tract infections. *J Gen Intern Med* 2015; 30(4): 408-16.
27. Cabral C, Lucas PJ, Ingram J, Hay AD, Horwood J. "It's safer to ..." parent consulting and clinician antibiotic prescribing decisions for children with respiratory tract infections: An analysis across four qualitative studies. *Soc Sci Med* 2015; 136-137: 156-64.
28. Grondal H, Hedin K, Strandberg EL, Andre M, Brorsson A. Near-patient tests and the clinical gaze in decision-making of Swedish GPs not following current guidelines for sore throat - a qualitative interview study. *BMC Fam Pract* 2015; 16: 81.
29. Dallas A, van Driel M, van de Mortel T, Magin P. Antibiotic prescribing for the future: exploring the attitudes of trainees in general practice. *Br J Gen Pract* 2014; 64(626): e561-7.
30. Dempsey PP, Businger AC, Whaley LE, Gagne JJ, Linder JA. Primary care clinicians' perceptions about antibiotic prescribing for acute bronchitis: a qualitative study. *BMC Fam Pract* 2014; 15: 194.
31. Hedin K, Strandberg EL, Grondal H, Brorsson A, Thulesius H, Andre M. Management of patients with sore throats in relation to guidelines: an interview study in Sweden. *Scand J Prim Health Care* 2014; 32(4): 193-9.
32. McDermott L, Yardley L, Little P, et al. Process evaluation of a point-of-care cluster randomised trial using a computer-delivered intervention to reduce antibiotic prescribing in primary care. *BMC Health Serv Res* 2014; 14: 594.
33. Mustafa M, Wood F, Butler CC, Elwyn G. Managing expectations of antibiotics for upper respiratory tract infections: a qualitative study. *Ann Fam Med* 2014; 12(1): 29-36.
34. Szymczak JE, Feemster KA, Zaoutis TE, Gerber JS. Pediatrician perceptions of an outpatient antimicrobial stewardship intervention. *Infect Control Hosp Epidemiol* 2014; 35 Suppl 3: S69-78.

35. Cals JW, van Leeuwen ME, Chappin FH, de Bont EG, Dinant GJ, Butler CC. "How Do You Feel about Antibiotics for This?" A Qualitative Study of Physician Attitudes towards a Context-Rich Communication Skills Method. *Antibiotics (Basel)* 2013; 2(3): 439-49.
36. Francis NA, Phillips R, Wood F, Hood K, Simpson S, Butler CC. Parents' and clinicians' views of an interactive booklet about respiratory tract infections in children: a qualitative process evaluation of the EQUIP randomised controlled trial. *BMC Fam Pract* 2013; 14: 182.
37. Jaruseviciene L, Radzeviciene Jurgute R, Bjerrum L, Jurgutis A, Jarusevicius G, Lazarus JV. Enabling factors for antibiotic prescribing for upper respiratory tract infections: perspectives of Lithuanian and Russian general practitioners. *Ups J Med Sci* 2013; 118(2): 98-104.
38. Leydon GM, McDermott L, Moore M, et al. A qualitative study of GP, NP and patient views about the use of rapid streptococcal antigen detection tests (RADTs) in primary care: 'swamped with sore throats?'. *BMJ Open* 2013; 3(4).
39. Roque F, Soares S, Breitenfeld L, Lopez-Duran A, Figueiras A, Herdeiro MT. Attitudes of community pharmacists to antibiotic dispensing and microbial resistance: a qualitative study in Portugal. *Int J Clin Pharm* 2013; 35(3): 417-24.
40. Strandberg EL, Brorsson A, Hagstam C, Troein M, Hedin K. "I'm Dr Jekyll and Mr Hyde": are GPs' antibiotic prescribing patterns contextually dependent? A qualitative focus group study. *Scand J Prim Health Care* 2013; 31(3): 158-65.
41. Anthierens S, Tonkin-Crine S, Douglas E, et al. General practitioners' views on the acceptability and applicability of a web-based intervention to reduce antibiotic prescribing for acute cough in multiple European countries: a qualitative study prior to a randomised trial. *BMC Fam Pract* 2012; 13: 101.
42. Brookes-Howell L, Hood K, Cooper L, et al. Clinical influences on antibiotic prescribing decisions for lower respiratory tract infection: a nine country qualitative study of variation in care. *BMJ Open* 2012; 2(3).

43. Brookes-Howell L, Hood K, Cooper L, et al. Understanding variation in primary medical care: a nine-country qualitative study of clinicians' accounts of the non-clinical factors that shape antibiotic prescribing decisions for lower respiratory tract infection. *BMJ Open* 2012; 2(4).
44. Jaruseviciene L, Radzeviciene-Jurgute R, Lazarus JV, et al. A study of antibiotic prescribing: The experience of Lithuanian and Russian GPs. *Cent Eur J Med* 2012; 7: 790-9.
45. Rowbotham S, Chisholm A, Moschogianis S, et al. Challenges to nurse prescribers of a no-antibiotic prescribing strategy for managing self-limiting respiratory tract infections. *J Adv Nurs* 2012; 68(12): 2622-32.
46. Vazquez-Lago JM, Lopez-Vazquez P, Lopez-Duran A, Taracido-Trunk M, Figueiras A. Attitudes of primary care physicians to the prescribing of antibiotics and antimicrobial resistance: a qualitative study from Spain. *Fam Pract* 2012; 29(3): 352-60.
47. Peters S, Rowbotham S, Chisholm A, et al. Managing self-limiting respiratory tract infections: a qualitative study of the usefulness of the delayed prescribing strategy. *Br J Gen Pract* 2011; 61(590): e579-89.
48. Tonkin-Crine S, Yardley L, Coenen S, et al. GPs' views in five European countries of interventions to promote prudent antibiotic use. *Br J Gen Pract* 2011; 61(586): e252-61.
49. Wood F, Brookes-Howell L, Hood K, et al. A multi-country qualitative study of clinicians' and patients' views on point of care tests for lower respiratory tract infection. *Fam Pract* 2011; 28(6): 661-9.
50. Bekkers MJ, Simpson SA, Dunstan F, et al. Enhancing the quality of antibiotic prescribing in primary care: qualitative evaluation of a blended learning intervention. *BMC Fam Pract* 2010; 11: 34.
51. Bjornsdottir I, Kristinsson KG, Hansen EH. Diagnosing infections: a qualitative view on prescription decisions in general practice over time. *Pharm World Sci* 2010; 32(6): 805-14.

52. Cals JW, Chappin FH, Hopstaken RM, et al. C-reactive protein point-of-care testing for lower respiratory tract infections: a qualitative evaluation of experiences by GPs. *Fam Pract* 2010; 27(2): 212-8.
53. Frich JC, Hoye S, Lindbaek M, Straand J. General practitioners and tutors' experiences with peer group academic detailing: a qualitative study. *BMC Fam Pract* 2010; 11: 12.
54. Hoye S, Frich J, Lindboek M. Delayed prescribing for upper respiratory tract infections: a qualitative study of GPs' views and experiences. *Br J Gen Pract* 2010; 60(581): 907-12.
55. Kotwani A, Wattal C, Katewa S, Joshi PC, Holloway K. Factors influencing primary care physicians to prescribe antibiotics in Delhi India. *Fam Pract* 2010; 27(6): 684-90.
56. McDermott L, Yardley L, Little P, Ashworth M, Gulliford M. Developing a computer delivered, theory based intervention for guideline implementation in general practice. *BMC Fam Pract* 2010; 11: 90.
57. Cals JW, Butler CC, Dinant GJ. 'Experience talks': physician prioritisation of contrasting interventions to optimise management of acute cough in general practice. *Implement Sci* 2009; 4: 57.
58. Butler CC, Simpson S, Wood F. General practitioners' perceptions of introducing near-patient testing for common infections into routine primary care: a qualitative study. *Scand J Prim Health Care* 2008; 26(1): 17-21.
59. Stock K, Wollny A, Brockmann S, Abholz H-H, Altiner A. Qualitativer Blick in die Blackbox: Edukative Intervention zur Senkung unnötiger Antibiotikaverordnungen (CHANGE) - A Qualitative Glance into the Blackbox: Educational Intervention to Reduce Unnecessary Antibiotic Prescriptions. *Z Allg Med* 2008; 84: 444-50.
60. Wood F, Simpson S, Butler CC. Socially responsible antibiotic choices in primary care: a qualitative study of GPs' decisions to prescribe broad-spectrum and fluoroquinolone antibiotics. *Fam Pract* 2007; 24(5): 427-34.

61. Hart AM, Pepper GA, Gonzales R. Balancing acts: deciding for or against antibiotics in acute respiratory infections. *J Fam Pract* 2006; 55(4): 320-5.
62. Altiner A, Knauf A, Moebes J, Sielk M, Wilm S. Acute cough: a qualitative analysis of how GPs manage the consultation when patients explicitly or implicitly expect antibiotic prescriptions. *Fam Pract* 2004; 21(5): 500-6.
63. Varonen H, Sainio S. Patients' and physicians' views on the management of acute maxillary sinusitis. *Scand J Prim Health Care* 2004; 22(1): 22-6.
64. Kumar S, Little P, Britten N. Why do general practitioners prescribe antibiotics for sore throat? Grounded theory interview study. *BMJ* 2003; 326(7381): 138.
65. Arroll B, Goodyear-Smith F, Thomas DR, Kerse N. Delayed antibiotic prescriptions: what are the experiences and attitudes of physicians and patients? *J Fam Pract* 2002; 51(11): 954-9.
66. Bjornsdottir I, Hansen EH. Intentions, strategies and uncertainty inherent in antibiotic prescribing. *Eur J Gen Pract* 2002; 8:18–24.
67. Bjornsdottir I, Hansen EH. Ethical dilemmas in antibiotic prescribing: analysis of everyday practice. *J Clin Pharm Ther* 2002; 27(6): 431-40.
68. Rollnick S, Seale C, Rees M, Butler C, Kinnersley P, Anderson L. Inside the routine general practice consultation: an observational study of consultations for sore throats. *Fam Pract* 2001; 18(5): 506-10.
69. Coenen S, Van Royen P, Vermeire E, Hermann I, Denekens J. Antibiotics for coughing in general practice: a qualitative decision analysis. *Fam Pract* 2000; 17(5): 380-5.
70. Elwyn G, Gwyn R, Edwards A, Grol R. Is 'shared decision-making' feasible in consultations for upper respiratory tract infections? Assessing the influence of antibiotic expectations using discourse analysis. *Health Expect* 1999; 2(2): 105-17.
71. Barden LS, Dowell SF, Schwartz B, Lackey C. Current attitudes regarding use of antimicrobial agents: results from physician's and parents' focus group discussions. *Clin Pediatr (Phila)* 1998; 37(11): 665-71.

72. Butler CC, Rollnick S, Pill R, Maggs-Rapport F, Stott N. Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats. *BMJ* 1998; 317(7159): 637-42.
73. Daker-White G, Donovan J, Campbell R. Redefined by illness: meta-ethnography of qualitative studies on the experience of rheumatoid arthritis. *Disabil Rehabil* 2014; 36(13): 1061-71.
74. McCann S, Campbell M, Entwistle V. Recruitment to clinical trials: a meta-ethnographic synthesis of studies of reasons for participation. *J Health Serv Res Policy* 2013; 18(4): 233-41.
75. Britten N, Riley R, Morgan M. Resisting psychotropic medicines: A synthesis of qualitative studies of medicine-taking. *Adv Psychiatr Treat* 2010; 16: 207-18.
76. Ackerman S, Gonzales R. The context of antibiotic overuse. *Ann Intern Med* 2012; 157(3): 211-2.
77. Yagil D, Medler-Liraz H. Clinical Expert or Service Provider? Physicians' Identity Work in the Context of Counterprofessional Patient Requests. *Qual Health Res* 2015; 25(9): 1199-211.
78. Broom A, Broom J, Kirby E. Cultures of resistance? A Bourdieusian analysis of doctors' antibiotic prescribing. *Soc Sci Med* 2014; 110: 81-8.
79. Stolper E, Van de Wiel M, Van Royen P, Van Bokhoven M, Van der Weijden T, Dinant GJ. Gut feelings as a third track in general practitioners' diagnostic reasoning. *J Gen Intern Med* 2011; 26(2): 197-203.
80. Stolper E, van Royen P, Dinant GJ. The 'sense of alarm' ('gut feeling') in clinical practice. A survey among European general practitioners on recognition and expression. *Eur J Gen Pract* 2010; 16(2): 72-4.
81. McCutcheon HH, Pincombe J. Intuition: an important tool in the practice of nursing. *J Adv Nurs* 2001; 35(3): 342-8.

82. Charani E, Castro-Sanchez E, Sevdalis N, et al. Understanding the determinants of antimicrobial prescribing within hospitals: the role of "prescribing etiquette". *Clin Infect Dis* 2013; 57(2): 188-96.

Figure 1. Flow diagram of study selection

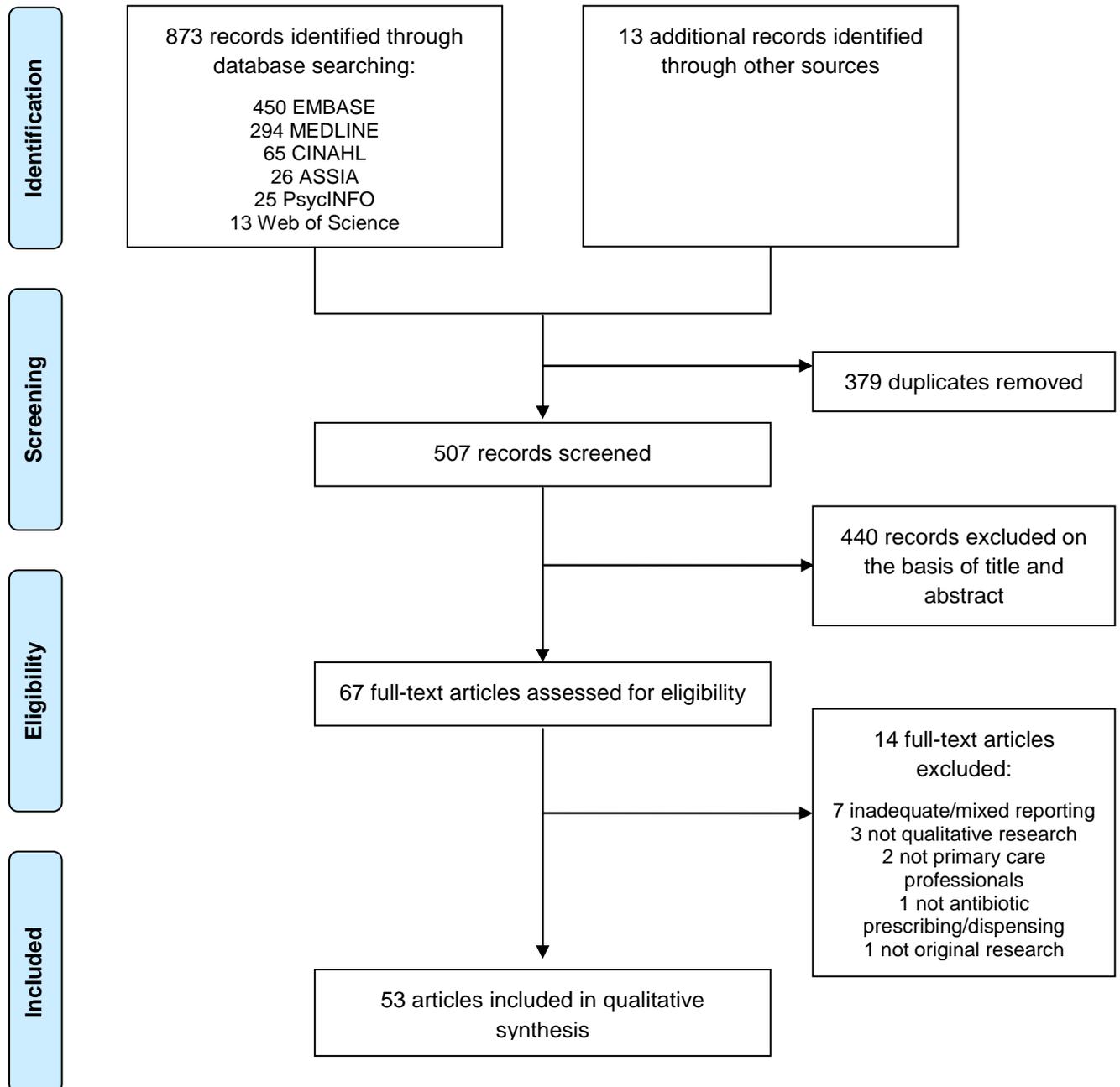


Figure 2. Line-of-argument synthesis of Group 1 (usual care) studies: A model of antibiotic prescribing and dispensing for ARTIs in primary care

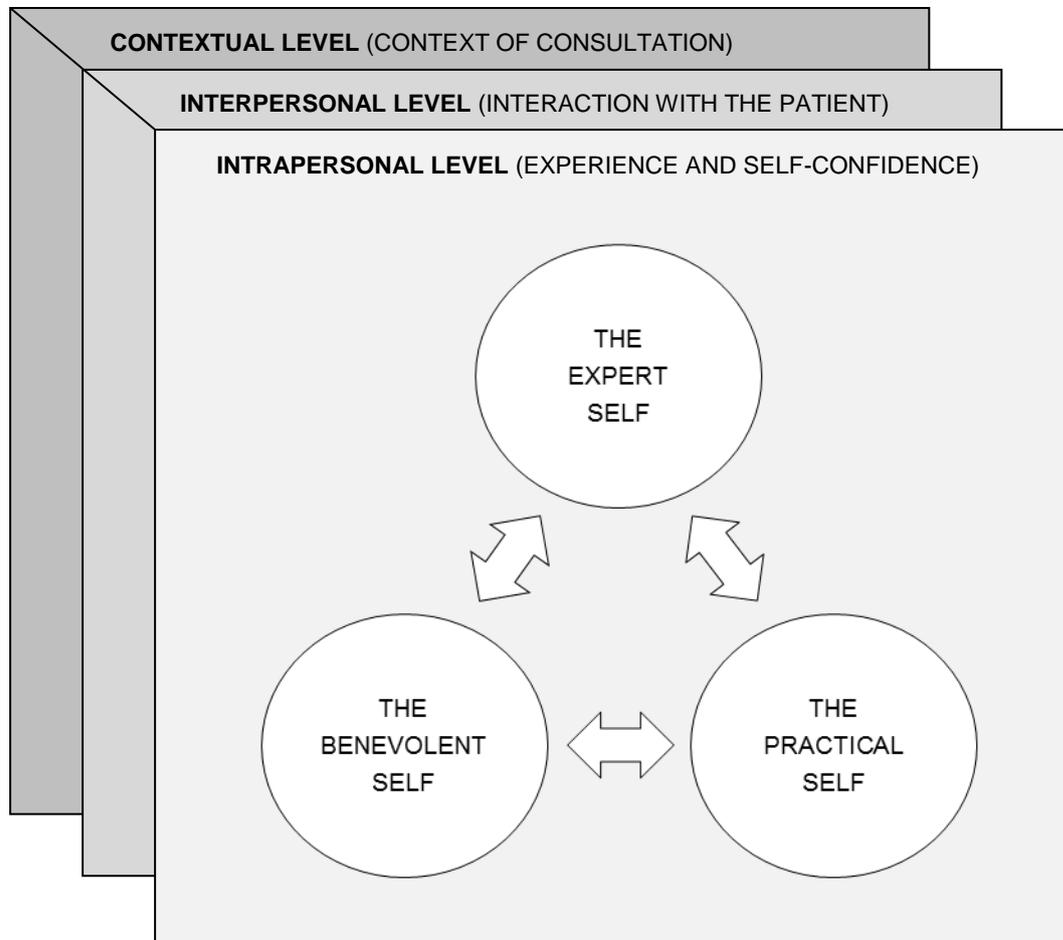


Figure 3. Line-of-argument synthesis of Group 2 (intervention) studies: A typology of ARTI intervention acceptance in primary care

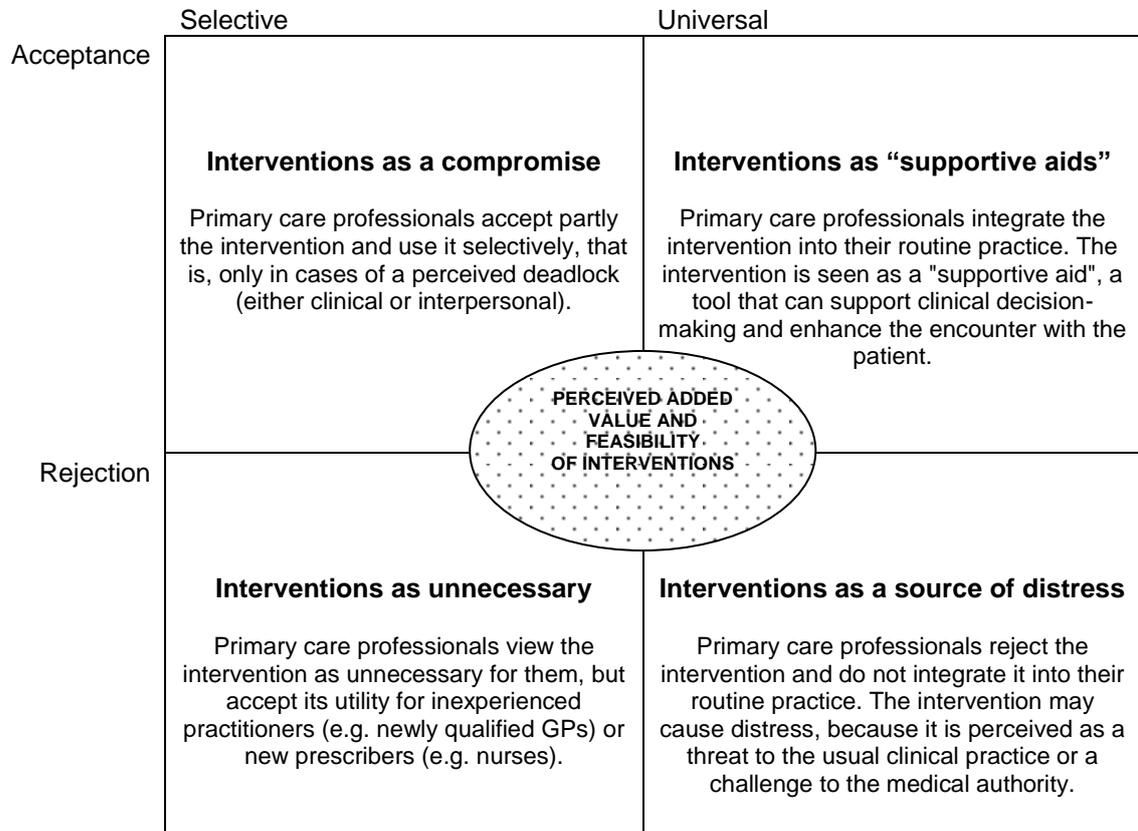


Table 1. Characteristics of included studies

Citation	Country	Type of study	Aim	Participants	Data collection	Analysis
Andre et al. (2016) ²¹	Sweden	Intervention	To describe strategies for coping with uncertainty in patients with pharyngotonsillitis in relation to guidelines	25 GPs	Semi-structured face-to-face interviews	Qualitative content analysis
*Ashdown et al. (2016) ²²	UK	Non-intervention	To investigate GPs' accounts of factors influencing their decision-making about antibiotic prescribing in the management of at-risk children with influenza-like illness	41 GPs	Semi-structured telephone interviews	Thematic analysis
Cabral et al. (2016) ²³	UK	Non-intervention	To understand clinicians' perceptions of communication within consultations for RTI in children	13 primary care clinicians	Semi-structured video-elicitation interviews	Thematic analysis
*Horwood et al. (2016) ²⁴	UK	Mixed	To investigate healthcare professionals' diagnostic and antibiotic prescribing decisions for children with RTIs	28 healthcare professionals (22 GPs and 6 nurses)	Semi-structured face-to-face interviews	Thematic analysis
Zhang et al. (2016) ²⁵	China	Non-intervention	To explore the knowledge, attitudes, and practices of village doctors regarding the prescribing of antibiotics for children under 15 years with upper respiratory tract infections in rural China	35 village doctors	Focus groups	Thematic analysis
*Anthierens et al. (2015) ²⁶	Belgium, Spain, UK, Poland, and the Netherlands	Intervention	To explore clinicians' experiences of training in communication skills and use of a patient booklet and/or a C-reactive protein point-of-care test to reduce antibiotic prescribing for ARTIs	66 primary care clinicians	Semi-structured face-to-face and telephone interviews	Thematic and framework analysis
*Cabral et al. (2015) ²⁷	UK	Non-intervention	To understand the drivers of clinician prescribing behaviour when children under 12 years consult primary care with ARTIs	28 healthcare professionals (22 GPs and 6 nurses)	Semi-structured face-to-face interviews	Thematic analysis
*Grondal et al. (2015) ²⁸	Sweden	Intervention	To deepen the understanding of what role the near-patient tests play in the decision-making of these GPs who do not follow guidelines in their management of patients with sore throat	16 GPs	Semi-structured face-to-face interviews	Qualitative content analysis
*Dallas et al. (2014) ²⁹	Australia	Mixed	To explore the attitudes of trainees in general practice towards antibiotic use and resistance, and the perceived influences on their prescribing	17 GP registrars	Semi-structured interviews and focus group	Thematic analysis

Citation	Country	Type of study	Aim	Participants	Data collection	Analysis
*Dempsey et al. (2014) ³⁰	USA	Mixed	To identify and understand primary care clinician perceptions about antibiotic prescribing for acute bronchitis	13 primary care clinicians (12 medical doctors and 1 nurse practitioner)	Semi-structured telephone interviews	Thematic content analysis
*Hedin et al. (2014) ³¹	Sweden	Intervention	To explore how Swedish GPs manage patients with a sore throat in relation to current guidelines	25 GPs	Semi-structured face-to-face interviews	Qualitative content analysis
*McDermott et al. (2014) ³²	UK	Intervention	To conduct a process evaluation for the trial of a computer-delivered intervention to reduce antibiotic prescribing in primary care	20 GPs	Semi-structured telephone interviews	Thematic analysis
Mustafa et al. (2014) ³³	UK	Non-intervention	To explore how and why family physicians elicit and address patients' or parents' expectations for antibiotics	20 family physicians	Semi-structured face-to-face interviews	Thematic analysis
*Szymczak et al. (2014) ³⁴	USA	Intervention	To explore the perceptions of an outpatient antimicrobial stewardship intervention and antibiotic overuse among participating clinicians	24 pediatricians	Semi-structured face-to-face and telephone interviews	Modified grounded theory
*Cals et al. (2013) ³⁵	Netherlands	Intervention	To explore experiences and views of GPs on a communication skills training program for managing LRTIs, and its applicability and implementation in daily practice	17 GPs	Semi-structured face-to-face interviews	Thematic content analysis
*Francis et al. (2013) ³⁶	UK	Intervention	To understand how acceptable an interactive booklet about RTIs was to clinicians, how it was implemented, the mechanisms for any observed effects, and contextual factors that could have influenced its effects	13 primary care clinicians	Semi-structured telephone interviews	Framework analysis
*Jaruseviciene et al. (2013) ³⁷	Lithuania and Russia	Non-intervention	To explore experiences of GPs in Lithuania and the Russian Federation with regard to antibiotic prescription for upper respiratory tract infections	51 GPs	Focus groups	Thematic analysis
*Leydon et al. (2013) ³⁸	UK	Intervention	To explore healthcare practitioners' views of clinical scores and rapid antigen detection tests	42 healthcare practitioners (29 GPs and 13 nurses)	Semi-structured face-to-face and telephone interviews	Thematic analysis

Citation	Country	Type of study	Aim	Participants	Data collection	Analysis
Roque et al. (2013) ³⁹	Portugal	Non-intervention	To explore pharmacists' knowledge, attitudes, perceptions and dispensing habits with respect to antibiotics and microbial resistance	32 pharmacists	Focus groups	Not stated
*Strandberg et al. (2013) ⁴⁰	Sweden	Non-intervention	To explore factors and circumstances contributing to prudent antibiotic prescribing for respiratory tract infections in primary care	13 GPs	Focus groups	Editing analysis
*Anthierens et al. (2012) ⁴¹	Belgium, Spain, UK, Poland, and the Netherlands	Intervention	To explore GPs' views on the initial version of a web-based intervention, to test acceptability and potentially increase applicability for use in multiple countries before the start of a randomised trial	30 GPs	Semi-structured face-to-face interviews using a "think-aloud" approach	Thematic analysis
*Brookes-Howell et al. (2012) ⁴²	Belgium, Hungary, Spain, UK, Poland, Italy, Norway, and the Netherlands	Mixed	To explore primary care clinicians' accounts of the <i>clinical processes</i> that inform their management of patients with symptoms of LRTI, particularly in relation to antibiotic prescribing	80 primary care clinicians	Semi-structured face-to-face interviews	Framework analysis
*Brookes-Howell et al. (2012) ⁴³	Belgium, Hungary, Spain, UK, Poland, Italy, Norway, and the Netherlands	Non-intervention	To investigate primary care clinicians' accounts of <i>non-clinical factors</i> that influence their antibiotic prescribing decision for patients with LRTI, to understand variation and identify opportunities for addressing possible unhelpful variation	80 primary care clinicians	Semi-structured face-to-face interviews	Framework analysis
*Jaruseviciene et al. (2012) ⁴⁴	Lithuania and Russia	Non-intervention	To examine the experiences of Lithuanian and Russian GPs with regard to antibiotic prescription for upper respiratory tract infections, including their perceptions of when it is not prudent or indicated clinically or pharmacologically	51 GPs	Focus groups	Thematic analysis
*Rowbotham et al. (2012) ⁴⁵	UK	Non-intervention	To explore how nurse prescribers and other non-medical prescribers experience RTI consultations, and the challenges they face in trying to implement a no-prescribing strategy	33 nurse and other non-medical prescribers (31 nurses, 1 pharmacist and 1 physiotherapist)	Semi-structured face-to-face interviews and focus groups	Not stated
Vazquez-Lago et al. (2012) ⁴⁶	Spain	Non-intervention	To ascertain the opinions and attitudes of GPs in Spain with respect to antibiotics and resistance	33 primary care physicians	Focus groups	Not stated

Citation	Country	Type of study	Aim	Participants	Data collection	Analysis
*Peters et al. (2011) ⁴⁷	UK	Intervention	To investigate how delayed prescribing is used within UK primary care, and the benefits and challenges associated with this strategy	82 primary care prescribers (GPs, trainee GPs and nurses)	Semi-structured face-to-face and telephone interviews and focus groups	Grounded theory
*Tonkin-Crine et al. (2011) ⁴⁸	Belgium, France, Poland, Spain, and the UK	Intervention	To explore GPs' views and experiences of strategies to promote a more prudent use of antibiotics across five countries	52 GPs	Semi-structured face-to-face and telephone interviews	Thematic and framework analysis
*Wood et al. (2011) ⁴⁹	Belgium, Hungary, Spain, UK, Poland, Italy, Norway, and the Netherlands	Intervention	To explore clinician views about point of care tests to assist with the diagnosis and management of LRTI in primary care	80 primary care clinicians	Semi-structured face-to-face interviews	Framework analysis
*Bekkers et al. (2010) ⁵⁰	UK	Intervention	To conduct a process evaluation of the Stemming the Tide of Antibiotic Resistance (STAR) trial	31 primary care prescribers (30 GPs and 1 nurse practitioner)	Semi-structured telephone interviews	Thematic content analysis
Bjornsdottir et al. (2010) ⁵¹	Iceland	Mixed	To understand the use of evidence by GPs in the diagnostic process preceding antibiotic prescribing, and explore changes over time in the diagnostic process	8 GPs	Re-interviewing (telephone/email) of participants recruited 11 years ago	Grounded theory
*Cals et al. (2010) ⁵²	Netherlands	Intervention	To explore GPs' attitudes and experiences of introducing C-reactive protein point-of-care testing for LRTIs in primary care	20 GPs	Semi-structured face-to-face interviews	Thematic content analysis
Frich et al. (2010) ⁵³	Norway	Intervention	To explore GPs' experiences of peer group academic detailing, as well as reasons for deviating from recommended prescribing practice	39 GPs	Focus groups	Thematic content analysis
*Hoye et al. (2010) ⁵⁴	Norway	Intervention	To explore GPs' views on and experiences with delayed prescribing in patients with acute upper respiratory tract infections	33 GPs	Focus groups	Content analysis
*Kotwani et al. (2010) ⁵⁵	India	Non-intervention	To explore the factors that influence primary care physicians to prescribe antibiotics and to investigate possible interventions	36 primary care physicians	Focus groups	Grounded theory

Citation	Country	Type of study	Aim	Participants	Data collection	Analysis
McDermott et al. (2010) ⁵⁶	UK	Intervention	To identify factors and characteristics likely to influence adherence to guidelines for antibiotic prescribing in respiratory tract infections, in order to inform development and refinement of computer-delivered prompts	33 GPs	Semi-structured face-to-face and 'think-aloud' interviews	Thematic analysis
*Cals et al. (2009) ⁵⁷	Netherlands	Intervention	To study the role of experience with interventions in influencing clinician prioritising of intervention uptake	20 GPs	Semi-structured face-to-face interviews	Thematic analysis
*Butler et al. (2008) ⁵⁸	UK	Intervention	To explore GPs' perspectives on the possible introduction of near-patient tests for the management of common infections	40 GPs	Semi-structured face-to-face interviews	Thematic content analysis
Stock et al. (2008) ⁵⁹	Germany	Intervention	To gain insight into the experiences, motivations and views of GPs participating in an intervention aiming to reduce antibiotic prescriptions	23 GPs	Semi-structured telephone interviews	Qualitative content analysis
*Wood et al. (2007) ⁶⁰	UK	Non-intervention	To understand GPs' 'choice' of antibiotic class, in particular the decision to prescribe fluoroquinolones	40 GPs	Semi-structured face-to-face interviews	Grounded theory
*Hart et al. (2006) ⁶¹	USA	Non-intervention	To describe how clinicians make decisions to prescribe antibiotics for ARTIs	21 primary health care clinicians (17 MDs and 4 nurse practitioners)	Semi-structured face-to-face interviews	Grounded theory
*Petursson (2005) ¹⁰	Iceland	Non-intervention	To study the reasons cited by Icelandic GPs for their "non-pharmacological" prescribing of antibiotics	16 GPs	Face-to-face, open-ended interviews	Vancouver school of doing phenomenology
Altiner et al. (2004) ⁶²	Germany	Non-intervention	To analyse how GPs manage the consultations for acute cough when patients explicitly or implicitly expect antibiotic prescriptions	8 GPs	Analysis of audiotaped consultations	Not stated
Varonen & Sainio (2004) ⁶³	Finland	Non-intervention	To study the views of physicians on the management of suspected acute maxillary sinusitis and on suggested changes in practice	20 primary care physicians	Focus groups	Not stated
*Kumar et al. (2003) ⁶⁴	UK	Mixed	To understand why GPs prescribe antibiotics for some cases of sore throat and to explore the factors that influence their prescribing	40 GPs	Face-to-face, open-ended interviews	Grounded theory

Citation	Country	Type of study	Aim	Participants	Data collection	Analysis
*Arroll et al. (2002) ⁶⁵	New Zealand	Intervention	To explore physicians' experiences of delayed antibiotic prescriptions for URTIs	13 family physicians	Semi-structured telephone interviews	Grounded theory
*Bjornsdottir & Hansen (2002) ⁶⁶	Iceland	Non-intervention	To explore physicians' perceived reasons for deciding to prescribe antibiotics	10 GPs	Open-ended, semi-structured interviews and observations of doctor-patient contacts	Grounded theory
*Bjornsdottir & Hansen (2002) ⁶⁷	Iceland	Non-intervention	To explore GPs' views on their obligations with respect to diagnosing infections and prescribing antibiotics	10 GPs	Open-ended, semi-structured interviews and observations of doctor-patient contacts	Grounded theory
Rollnick et al. (2001) ⁶⁸	UK	Non-intervention	To examine how GPs manage the consultation for URTIs and the prescribing of antibiotics, to understand what skills and strategies are used in managing URTIs without antibiotics, and to note evidence of pressure on doctors to prescribe and whether there are signs of overt disagreement about prescribing in the consultation	5 GPs	Analysis of audiotaped consultations	Conversation analysis
Coenen et al. (2000) ⁶⁹	Belgium	Non-intervention	To explicate GPs diagnostic and therapeutic decisions regarding adult patients who consult them with complaints about coughing, and to investigate what determines decision-making	24 GPs	Focus groups	Qualitative content analysis
Elwyn et al. (1999) ⁷⁰	UK	Non-intervention	To examine the discourse of consultations in which conflict occurs between parents and clinicians about the necessity of antibiotics to treat an URTI, and to appraise the feasibility of shared decision-making in such consultations	1 GP	Analysis of audiotaped consultations	Discourse analysis
Barden et al. (1998) ⁷¹	USA	Non-intervention	To explore physicians' attitudes regarding the use of antibiotics	22 physicians (17 pediatricians and 5 family physicians)	Focus groups	Not stated
*Butler et al. (1998) ⁷²	UK	Non-intervention	To better understand reasons for antibiotics being prescribed for sore throats	21 GPs	Semi-structured face-to-face interviews	Grounded theory

* Indicates paper evaluated as "key" (i.e. likely to make an important contribution to the synthesis)

Table 2. Group 1 (usual care) studies: Translation of second-order constructs and third-order constructs

Third-order constructs	Second-order constructs	Summary definition (translation) of second-order construct	Papers that include the second-order construct
The expert self	Patient history and physical examination	Antibiotic prescribing decisions are, to a large extent, guided by (and justified in reference to) history taking and physical examination. Sometimes, patient complaints or the medical history of the patient might form the 'diagnostic basis'. In other cases, decisions are guided by clinical signs and presenting symptoms, such as fever and discoloured sputum, which are interpreted in light of relevant risk factors (e.g. older age) and comorbidities.	22, 23, 24, 25, 29, 42, 46, 51, 60, 64, 68, 69, 72
	General impression and 'gut feeling'	Many primary care professionals admit that, apart from the structured examination, the overall assessment of how the patient seems on the day plays a major role in their decision-making. Assessments such as 'very ill', 'weakened' and 'miserable' are common, whereas primary care professionals' 'gut feeling' can, in many cases, override a decision based purely on clinical factors.	22, 24, 42, 62, 64, 72
The benevolent self	Dissatisfaction in not meeting patient expectations	Many primary care professionals feel that once a patient makes the effort to come into the clinic, it is unsatisfying not to be able to offer a solution. Concerns of being perceived as 'having done nothing' for the patients or not being 'proper doctors' if they do not prescribe antibiotics are common.	10, 29, 30, 43, 72
	Desire to avoid conflict and maintain a good relationship with patients	Building and maintaining a good relationship with their patients is viewed as a priority for healthcare professionals working in primary care and several admit that they would not jeopardise this "for the sake of a prescription for penicillin V".	10, 24, 25, 33, 43, 64, 71, 72
	Beneficence/non-maleficence	Primary care professionals justify their prescribing decisions on the basis of a desire to do their best for the patients. Although some report prioritizing potential resistance problems and longer term issues, the majority feels that their priority should be 'the patient in front of them' and his/her immediate needs. The desire to 'help' the patient is not restricted to treating a patient that is ill, but involves a broader consideration of the circumstances in an individual's life, such as the environment in which he/she lives, his/her socio-economic status or vulnerability on the job market, as well as plans for leisure activities.	10, 55, 60, 61, 62, 64, 66, 67, 71, 72
The practical self	Patient retention and financial considerations	Many primary care professionals fear that their patients will not be satisfied if they do not receive a prescription and, as a consequence, they will not return to the clinic again. In this way, prescribing is seen as a means of ensuring self-preservation, especially in the case of professionals who collect on a fee-for-service basis.	10, 25, 30, 39, 46, 55, 61, 67, 69

Third-order constructs	Second-order constructs	Summary definition (translation) of second-order construct	Papers that include the second-order construct
	Medicolegal concerns	The possibility of 'missing something' in a patient is seen as a potential threat to primary care professionals' expertise or standing and many express fear of overlooking something, making a mistake, and being sued. Patients' increasing power in medical encounters and knowledge of the opportunity for legal action are commented as important factors influencing prescribing decisions.	10, 24, 27, 44, 71, 72
Confidence and experience	Confidence and experience	Primary care professionals report increased confidence in more accurately differentiating between patients who need treatment and those who can be safely monitored, as they see more patients over time with similar symptoms. On the other hand, they admit that previous bad experience of non-antibiotic management can have substantial impact on current prescribing practices.	22, 23, 24, 27, 29, 43, 45, 46, 61, 69
Interaction with the patient	Mutual trust and confidence with the patient	The degree of confidence and trust that primary care professionals have with their patients shapes prescribing decisions. The more insecure they feel about patients' ability to recognise a worsening illness and re-consult, the more inclined they become to an antibiotic prescription.	22, 24, 27, 40
	Patient pressure	Pressure in the form of a clear demand or gesture, or of a patient's obvious fear (e.g. anxiety, repeated consultations for the same episode), is regarded as a main reason for unnecessary antibiotic prescribing. Although explicit requests for antibiotics seem to be less frequent in developed, as compared to developing, countries, most healthcare professionals report 'giving in' occasionally to (actual or perceived) patient pressure, either for their own and the patient's reassurance or because they feel they cannot do anything else.	10, 24, 27, 30, 39, 55, 62, 66, 67, 68, 70, 71
Context of consultation	Diagnostic uncertainty	The lack of conclusive evidence to support diagnosis and management of ARTIs in primary care creates uncertainty and many prescribers report difficulties in differentiating between viral and bacterial infections on clinical grounds alone. This might often lead to a tendency to 'play it safe', namely adopt a defensive practice and prescribe antibiotics, as they fear the possibility of missing a serious diagnosis (especially for children or people with co-morbidities).	10, 22, 24, 25, 27, 29, 30, 42, 43, 45, 46, 51, 55, 61, 63, 66, 67, 69, 72

Third-order constructs	Second-order constructs	Summary definition (translation) of second-order construct	Papers that include the second-order construct
	Continuity of care	Continuity of care promotes diagnostic accuracy and confidence in prescribing decisions through personal knowledge. Through familiarity with what is normal for the patient, primary care professionals are able to make a more informed evaluation of usual health status. On the other hand, lack of continuous care creates insecurity and often leads to unnecessary 'just-in-case' prescribing.	10, 22, 24, 40, 42, 45
	Work pressure and fatigue	Primary care professionals acknowledge the impact of work pressure and fatigue on their prescribing habits and several report changing their prescribing practices according to different contexts (e.g. prescribing more when on call or at the emergency centre). It is primarily lack of time that makes them lower their threshold of tolerance. An antibiotic prescription is seen, in such cases, as 'the easiest way out', a tool to conclude the consultation as quickly as possible without endangering a good doctor-patient relationship.	10, 24, 29, 30, 40, 55, 60, 64, 66, 69, 71, 72
	Timing of consultations	Primary care professionals report feeling more pressure to prescribe if patients consult on the eve of a weekend ("Friday prescriptions") or holiday. It is important for them to help their patients so that they will not have to seek after-hours care or medical care abroad, in case their condition deteriorates.	10, 22, 24, 43
	System factors	Non-clinical factors imposed by healthcare systems, such as over-the-counter sales of antibiotics or lack of formal, consistently available national guidelines on antibiotic prescribing, are regarded by primary care professionals as important in prescribing decision-making. Equally important are considered by many the incentives from the pharmaceutical industry, which influence prescribing practices both directly (through visits to medical practitioners) and indirectly (through support of continuing medical education).	25, 30, 37, 43, 44, 46, 55, 61, 71

Table 3. Group 2 (intervention) studies: Translation of second-order constructs and third-order constructs

Third-order constructs	Second-order constructs	Summary definition (translation) of the second-order construct	Papers that include the second-order construct
Interventions as a compromise	Managing clinical uncertainty	Clinical interventions can decrease uncertainty related to the diagnosis and treatment of ARTIs, while minimizing PCPs' fear of bad outcomes. Although the usefulness of having additional diagnostic tools is valued, most practitioners prefer to rely on clinical findings when deciding about antibiotic treatment and use interventions only in cases of clinical doubt ('when unsure'). In such cases, interventions are perceived as providing a safety net for both the practitioner and the patient.	21, 26, 28, 29, 47, 48, 51, 52, 58, 64
	Coping with potentially confrontational encounters	Interventions can help practitioners cope with the pressure they experience from patients expecting antibiotics. They are often viewed as a negotiation tool within the practitioner-patient encounter, a compromise needed to avoid or limit conflict, as well as a way for managing patient expectations for antibiotics and demonstrating that their illness is being taken seriously.	24, 47, 54, 58, 59, 65
Interventions as "supportive aids"	Enhancing confidence in clinical decision-making	Interventions can augment clinical assessment and authority and enhance both practitioners' and patients' confidence in clinical decision-making. Confirming prescribing decisions from several angles can be reassuring both for the practitioner and for the patient, whereas it can lead to improved satisfaction with care, as well as increased patient compliance with the treatment disposal.	26, 29, 30, 31, 32, 35, 36, 38, 41, 48, 49, 50, 52, 56, 57, 58
	Educating and empowering the patient	Interventions are viewed as 'golden moments' for patient education. They can provide a stimulus for opening a discussion about the necessity or effectiveness of antibiotics and empower patients to become more involved in their own health care management.	26, 38, 48, 49, 52, 54, 59, 65
	Provision of more patient-centred care	Interventions can help primary care professionals gain greater insight into patients' perspectives, needs and expectations and work together to achieve shared antibiotic prescribing decisions.	35, 36, 50, 57, 64, 65
	Improved management/treatment	Interventions can provide more effective targeted treatment, prevent unnecessary prescription of antibiotics and reduce the likelihood of re-consultation.	26, 32, 35, 36, 38, 41, 42, 49, 50, 52, 53, 64, 65
	Perceived ease of use and feasibility of interventions	Perceived ease of use and feasibility of incorporating an intervention into clinical practice increases its actual use.	29, 32, 38, 52, 56
Interventions as unnecessary	Useful for inexperienced practitioners/ Unnecessary for experienced practitioners	Interventions are viewed as useful for inexperienced practitioners (e.g. newly qualified GPs) or new prescribers (e.g. nurses), but are considered unnecessary for experienced practitioners.	32, 38, 56

Third-order constructs	Second-order constructs	Summary definition (translation) of the second-order construct	Papers that include the second-order construct
Interventions as a source of distress	Giving mixed messages to patients	Certain interventions, such as delayed prescribing, may convey contradictory messages to patients about the competence of the physician or the efficacy of antibiotics for ARTIs. On the other hand, the increased availability of clinical interventions, such as near-patient tests, might lead patients to consider ARTIs more serious than they actually are.	26, 38, 47, 64, 65
	Resulting in a paternalistic approach	Interventions might diminish the trust between the patient and the clinician, disrupt the usual quality of rapport, and lead to the use of a paternalistic (rather than shared decision-making) approach.	36, 41, 64
	Fear of inappropriate management/treatment	The reliability of interventions is often questioned and many primary care professionals express concerns related to inappropriate management/treatment of ARTIs, such as missing the diagnosis of a serious infection or prescribing unnecessary antibiotics due to a false positive test result.	38, 48, 49, 51, 58, 65
	Tension and possible disconnect with clinical assessment and intuition	Interventions are perceived as a threat to the clinical assessment and intuition (especially in cases that there is a conflict between what the prescriber thinks as clinically best and what the intervention indicates as clinically best) and many primary care professionals express the fear of "treating test results rather than patients".	34, 38, 42, 48, 49, 52, 53
	Time and cost concerns	Interventions are perceived as too costly or too time-consuming to fit into usual practice.	26, 32, 35, 36, 38, 49, 51, 53, 57, 58