

# **Reducing unnecessary antibiotic use for upper respiratory infections by focusing on patients**

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Thesis submitted to the University of Ottawa  
in partial Fulfillment of the requirements for the  
Master's degree in Epidemiology

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## **Abstract**

**Background:** Antibiotics are prescribed frequently for upper respiratory tract infections (URTIs) despite the fact that most of them do not require antibiotics. This over-prescription contributes to antibiotic resistance which is a major health problem. Physicians perceive that patients' expectations influence their antibiotic prescribing practice.

**Methods:** As the first phase of the thesis, we conducted a systematic review to determine the effectiveness of patient-oriented interventions to reduce unnecessary use of antibiotics for URTIs. As the second phase, we conducted a qualitative descriptive study to explore patients' views about URTIs and identify ways they manage them by using semi-structured interviews based on Common Sense-Self-Regulation Model (CS-SRM).

**Results:** Our systematic review included 14 studies which based on their interventions were classified into two major categories: delayed prescriptions and patient/public information and education interventions. Our meta-analysis revealed that almost all studies with delayed prescription significantly reduced use of antibiotics for URTIs. Our subgroup analysis showed that prescriptions that were given at a later time and prescriptions that were given at the index consultation had similar effects regarding antibiotic use. The small number of included studies in the patient/public information and education group did not allow us to make a definite conclusion on their effectiveness. For the qualitative study, 15 individuals were interviewed. almost all participants mentioned that they only visited their doctor if their symptoms got progressively worse and they could no longer self-manage URTI symptoms. When visiting a doctor, most participants reported that they expected to receive an examination and an explanation for their symptoms.

**Discussion:** Patient-oriented interventions (especially delayed prescriptions) may be effective in reducing antibiotic use or prescription for URTIs in patients. Further research is needed to investigate the costs and feasibilities of implementing these interventions as part of routine clinical practice. Our participants reported good knowledge regarding the likely lack of benefit from antibiotics for URTIs. The results suggest a discrepancy between our participants' reported reasons for visiting doctors and doctors' perceptions about patients' reason for their visit identified in previous studies. Focusing on interventions that facilitate the communication between patients and doctors, instead of providing more education to public may help in reducing the use of unnecessary antibiotics.

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## **Acknowledgments**

I would like to thank my thesis supervisor Dr Jeremy M. Grimshaw for his unwavering support and encouragement, as well as sharing his expertise and knowledge throughout the process.

I would like to thank my thesis advisory committee, Dr Dawn Stacey and Dr Sacha Bhatia, for their valuable comments and guidance from the very early stages.

A special thanks to Dr Andrea Patey for being so generous in sharing her knowledge and experience with me.

Thanks to Dr Alykhan Abdulla for being so accommodating for allowing me to access his health center for the interviews. Without his support this study could not be possible.

Thanks to Stefanie Linklater, for helping me to navigate the necessary administrative processes to get me to where I am today.

Finally, I would like to thank my husband, Stephen Healey, for his emotional support and encouragement during the most difficult moments of my thesis.

## List of abbreviations

**AA:** Alykhan Abdulla

**AOM:** Acute otitis media

**AP:** Andrea Patey

**ARI:** Acute respiratory infections

**AY:** Ashley M. Yu

**BH:** Brien Younho Hong

**CBA:** Controlled before after

**CC&CRG:** Cochrane Consumers and Communication Review Group

**CCCG:** Cochrane Consumers and Communication Group

**CCNet:** Cochrane Consumers Network

**CENTRAL:** Cochrane Central Register of Controlled Trials

**CI:** Confidence interval

**CMA:** Canadian Medical Association

**COPD:** Chronic obstructive pulmonary disease

**CWC:** Choosing Wisely Canada

**EPOC:** Effective Practice and Organization of Care

**GDP:** Gross domestic product

**GP:** General practitioner

**ICTRP:** International Clinical Trials Registry Platform

**ITS:** Interrupted time series

**ITT:** Intention To Treat

**JG:** Jeremy M. Grimshaw

**LRTI:** Lower respiratory tract infection

**MD:** Mean difference

**OR:** Odds ratio

**OTC:** Over the counter

**PH:** Patrick Jiho Hong

**PRISMA:** Preferred items for systematic reviews and meta-analyses

**RCT:** Randomised controlled trial

**SM:** Sameh Mortazhejri

**CS-SRM:** Common Sense-Self regulation model

**UK:** The United Kingdom

**URTI:** Upper respiratory tract infections

**USA:** The United States of America

**WHO:** World Health Organization

# **Chapter 1**

## **Introduction**

# **Introduction**

## **Antibiotic use for upper respiratory tract infections**

Between 2010 and 2014, more than 60% of antibiotic prescriptions that were dispensed by community pharmacists in Canada were prescribed by general practitioners (GPs), of which about 20% were for Upper respiratory tract infections (URTIs) in 2014 (1). URTIs include infections of nasopharynx, ears, tonsils and sinuses and are characterized by symptoms such as malaise, fever, headache, cough, sore throat, nasal discharge or congestion and pain in sinuses (2). Most URTIs are non-bacterial and self-limiting (3). In addition, the results of several recent systematic reviews show that there are no or small benefit from the antibiotics for most URTIs (4, 5, 6). However, GPs in many parts of the world, including Canada, still prescribe antibiotics to treat URTIs (7, 8, 9, 10, 11, 12, 13, 14). A primary care study in Ontario revealed that antibiotics were prescribed for 46% of elderly patients with non-bacterial URTIs (15). A 2006 study on GPs in Ontario showed that more than 85% of patients with acute sinusitis and 90% of patients with acute otitis media (AOM) received antibiotics against guidelines recommendations (16).

Antibiotics are the only class of drugs whose prescription to individuals has a large-scale influence on bacterial ecology (17, 18, 19). Antibiotic resistance is a result of both their excessive and inappropriate prescription (20, 21), and is a main reason for the increase in the cost of outpatient infection management, as well as the increase in the length of hospital stay and inpatient mortality (17, 18, 19). Furthermore, with prescription of unnecessary antibiotics, more people are exposed to the potential risk of adverse effects and drug interactions related to treatments that are not justified, and this adds to further healthcare costs (22, 23).

## **Choosing Wisely Canada**

“Choosing Wisely” is a campaign that began in 2012 in United States with the aim of reducing low value care (24). A similar initiative for Canada, “Choosing Wisely Canada” (CWC), was established in 2014 by a team of physicians in partnership with the Canadian Medical Association (CMA). CWC aims to optimize cost-effective and evidence-based care, and to encourage more meaningful use of healthcare resources. CWC defines low value care as tests and treatments that are commonly used in each specialty but are not supported by evidence and/or could expose patients to unnecessary harm (25). For each clinical speciality, CWC provides lists of items that are considered as low-value. The Canadian College of Family Practitioners and the Forum on General and Family Practice Issues of the Canadian Medical Association published 13 evidence-based recommendations regarding low value care in family practice (26). One of the recommendations suggests avoiding antibiotic use for URTIs that are likely viral in origin, such as influenza-like illness, or self-limiting, such as sinus infections of less than seven days of duration (26). The CWC recommendation on antibiotic use for URTIs is important for the promotion of antibiotic stewardship to reduce the risk of developing antibiotic-resistant bacteria (27), which is an expanding menace to people all over the world (28, 29).

It is clear that the identification of low value practices is necessary; however, this alone does not lead to optimal care. Additional implementation and dissemination strategies are required for evidence-based recommendations to be applied in clinical practice (30). To ensure effective and long standing changes within the healthcare system, it is essential to engage all relevant stakeholders including patients, physicians, the general public, and regulatory bodies to affect change in clinical practice (31).

## **Patients as important stakeholders**

Although most implementation intervention studies focus on changing healthcare providers' behaviour, many physicians believe that patient demands and expectations are important barriers to reducing low value care (32, 33). Increasing public awareness about low value care through different interventions could empower patients to be actively involved in more informative and constructive discussions with their doctors (32). There is evidence that providing patients with information can motivate health professionals to successfully decrease the prescription of low value prescriptions of some classes of drugs (34). Several studies have shown that physicians believe that patients' demand for antibiotics for URTIs drives their prescription (35, 36). Therefore, interventions that are directed at patients may be helpful in decreasing the unnecessary use of antibiotics.

## **Relevance**

Reducing use of antibiotics for URTIs will contribute to the reduction in antimicrobial resistance (37). It also has the potential to address some of the waste in healthcare expenditures. Between 2000 and 2013, mean worldwide healthcare expenditures have risen from 7.7% to 9.3% of gross domestic product (GDP) (38). It is believed that almost 20%-30% of healthcare is unnecessary and even sometimes harmful (39), and there is evidence that Canada deals with the same problem (40).

## **Thesis objectives and work**

My thesis aimed to explore the potential of addressing patients to reduce unnecessary antibiotic use. There were two specific objectives.

The **first objective** was to identify the most effective patient-oriented interventions to reduce unnecessary use of antibiotics for URTIs. To meet this objective, we conducted a systematic review of current studies that had applied patient-oriented interventions to improve antibiotic use for URTIs and assessed their effectiveness (Chapter 2). Building on this systematic review, we studied a group of patients to understand which one of those interventions may work better considering patients' current way of dealing with URTIs. Hence, the **second objective** was to explore patients' knowledge, beliefs and attitude about URTIs (including the role of self management, primary care consultation and antibiotics) and the way they manage their URTIs (including attendance in primary care and taking antibiotics). To meet this objective, we conducted a qualitative descriptive study by using semi-structured interviews with patients based on common sense-self-regulation model (CS-SRM) (41) (Chapter 3). Finally, the last chapter provides a discussion in which we consider how the findings of chapter 2 and 3 can be integrated and used in practice and research (chapter 4).

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## **Chapter 2**

# **Systematic review of patient-oriented interventions to reduce unnecessary use of antibiotics for upper respiratory tract infections**

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## **Authors' contribution**

**Sameh Mortazhejri (SM)** developed the research protocol and the search strategy, conducted the research, screening and data extraction, evaluated risk of bias in included studies, analysed the data, and prepared the manuscript.

**Jeremy M. Grimshaw (JG)** provided guidance on planning the research, supervised all parts of the project and reviewed drafts of the manuscript.

**Ashley M. Yu (AY)** conducted the screening and data extraction, evaluated risk of bias in included studies and reviewed drafts of the manuscript.

**Patrick Jiho Hong (PH)** conducted the screening and data extraction, evaluated risk of bias in included studies and reviewed drafts of the manuscript.

**Brian Younho Hong (BH)** conducted the screening and data extraction, evaluated risk of bias in included studies and reviewed drafts of the manuscript.

**Dawn Stacey** helped with the development of the proposal, provided comments and guidance on conducting the project and data analysis and reviewed drafts of the manuscript.

**Sacha Bhatia** helped with the development of the proposal, provided comments and guidance on conducting the project and data analysis and reviewed drafts of the manuscript.

All the authors approved the final version.

## **Acknowledgements**

I would like to thank Dr Monica Taljaard for her assistance and advice on the methodology of interrupted time series.

Thanks to Madison Foster and Katrina Sullivan, for helping with screening of abstracts.

Thanks to Michael Boutet, for his advice and assistance with developing the search strategy.

## **Abstract**

**Background:** Antibiotics are prescribed frequently for upper respiratory tract infections (URTIs) despite the fact that most of them do not require antibiotics. This over-prescription contributes to antibiotic resistance which is a major health problem. As doctors' prescribing behaviour is influenced by patients' expectations, there may be some opportunities to reduce antibiotic prescribing using patient-oriented interventions.

**Objectives:** To determine the effectiveness of patient-oriented interventions to reduce unnecessary use of antibiotics for URTIs.

**Methods:** We conducted a systematic review. We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, CINAHL and the Web of Science. We searched for ongoing studies on ClinicalTrials.gov and the World Health Organization ICTRP. We also searched the bibliographies of retrieved full texts of relevant studies. We included English language randomized controlled trials (RCTs), quasi-RCTs, controlled before and after studies (CBA), and interrupted time series (ITS) studies. Two review authors screened the abstract/titles and full-texts according to the inclusion criteria. Two review authors extracted data and assessed study risk of bias. If pooling was appropriate, Review Manager 5 software was used to meta-analyse the studies using a random-effects model. Where pooling the data was not possible, a narrative synthesis of results was conducted.

**Results:** We included 14 studies (one ITS, two cluster RCTs and eleven RCTs). Most studies were conducted in Europe, with a few other studies from USA, Canada, Asia and New Zealand. All interventions could be classified into two major categories: delayed prescriptions (seven studies) and patient/public information and education interventions (seven studies). Our meta-analysis

revealed that almost all studies with delayed prescription significantly reduced use of antibiotics for URTIs (OR=0.09, CI: 0.03 to 0.23; six studies). Our subgroup analysis showed that prescriptions that were given at a later time (requiring either a return visit to pick up a prescription from a family practice or a new family practice appointment) (three studies) and prescriptions that were given at the index consultation (to be filled at a later date) (four studies) had similar effects regarding antibiotic use. The studies in the patient/public information and education group varied according to their methods of delivery. Since only one or two studies were included for each method, we could not make a definite conclusion on their effectiveness. However, their effect was generally much smaller compared to the effect of delayed prescriptions. In general, applying booklets or pamphlets demonstrated promising effects on antibiotic prescription, if discussed by a practitioner.

**Conclusion:** Patient-oriented interventions (especially delayed prescriptions) may be effective in reducing antibiotic use or prescription for URTIs in patients. Further research is needed to investigate the costs and feasibilities of implementing these interventions as part of routine clinical practice.

## **Background**

One third of visits to general practitioners are because of infectious diseases, and half of these cases are for respiratory tract infections (1). Antibiotics are prescribed frequently for upper respiratory tract infections (URTIs) by family physicians in Canada (2) and other parts of the world (3, 4, 5) despite the fact that most URTIs are viral, self-limiting and commonly resolve without further complications (6). Recent systematic reviews reveal small or no benefit from the antibiotics for most of the URTIs (7, 8, 9).

Resistance to antibiotics is a result of both their excessive and inappropriate prescription (10, 11). Antibiotic resistance is a main reason for the increase in outpatient infection management costs and the length of hospital stay and mortality of inpatients (12, 13, 14). Furthermore, with prescription of unnecessary antibiotics, more people are exposed to the risk of adverse effects and drug interactions related to treatments that are not justified (15, 16).

As patients are the end consumers of antibiotics, there may be opportunities in considering patients' role in the reduction of antibiotic use. Studies have shown that physicians' prescribing behavior can be affected by patients' (real or perceived) expectations about medications (17). Interventions that influence patients' behaviors, attitudes and/or knowledge may be helpful in decreasing the unnecessary use of antibiotics.

To identify the interventions directed at patients to reduce unnecessary use of antibiotics and to better understand the ones that are more effective, we conducted a systematic review of all current literature.

## **Methods**

We conducted a systematic review of existing studies. Prior to undertaking the review, we registered the protocol in PROSPERO (ID= CRD42016048007). The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) checklist was applied as a reporting guideline (18).

## **Criteria for considering studies for this review (Appendix 1)**

### **Types of studies**

We included randomized controlled trials (RCTs), quasi-RCTs, controlled before and after studies (CBA), and interrupted time series (ITS) studies (Appendix 1). We used Cochrane Consumers and Communication Review Group (CC&CRG) eligibility guidance for CBA and ITS studies (19).

### **Types of participants**

Participants were public, healthy individuals or patients of all age groups with URTIs (e.g. sinusitis, pharyngitis, sore throat, otitis media, common cold and acute cough) who sought treatment in any general practice setting. Patients with lower respiratory tract infections (LRTIs) and those with chronic lung conditions (such as chronic obstructive pulmonary disease (COPD)) were excluded.

### **Types of interventions**

Patient oriented interventions (i.e. any intervention that was directed to patients, parents of patients (in the case of paediatric patients), public or healthy individuals) to reduce unnecessary use of antibiotics for URTIs in primary care setting were included. Interventions that were directed to healthcare providers or clinical staff were excluded. The interventions that targeted patients

indirectly (the primary and main effect of the intervention were directed to healthcare providers and patients benefited secondarily from that effect) were excluded.

## **Types of comparisons**

We compared (19):

- Interventions directed at patients/public versus no intervention.
- Interventions directed at patients/public versus standard or usual care.
- One form of intervention directed at patients/public versus another.

## **Types of outcome measures**

### **Primary outcomes**

Our primary outcome was prescription of antibiotics by doctors or use of antibiotics by patients for URTIs in the primary care setting. Studies that did not report the primary outcome were excluded.

### **Secondary outcomes**

- Public/patients' satisfaction with the treatment or consultation.
- Public/patients' beliefs that antibiotics were effective for URTIs.
- Re-consultation with a physician for the same illness.

## **Type of language**

We only included studies that were published in English.

## **Search methods for identification of studies**

We developed a search strategy combining terms for patient-oriented interventions, antibiotics, respiratory tract infections and primary care settings in Medline (Appendix 2) with the help of a librarian and adapted it to search other databases. Both MeSH terms and keywords were applied.

The following databases were searched:

- Medline: 1946 to 2016/11/11
- Embase: 1974 to 2016/11/11
- Cochrane Central Register of Controlled Trials (CENTRAL) including the Cochrane Effective Practice and Organisation of Care (EPOC) and Cochrane Consumer Network (CCNet): inception to 2016/10/23
- CINAHL: 1981 to 2016/10/24
- Web of Science: 1900 to 2016/10/28

World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) and [www.clinicaltrials.gov](http://www.clinicaltrials.gov) were also searched to detect completed and ongoing trials.

## **Data collection and analysis**

### **Selection of studies**

Two review authors (SM and either AY, PH or BH) independently screened all title and abstracts to determine study eligibility. They screened the full-texts independently and in duplicate following title and abstract screening. In case of uncertainty, complete manuscripts were reviewed, discussed, and resolved through consensus or discussion with a third party (JG). All potentially

relevant papers that were excluded at this stage were listed as excluded studies. The references of all included studies were screened to identify potentially relevant articles.

## **Data extraction and management**

Two review authors (SM and either AY, PH or BH) independently extracted the data from included studies. Any discrepancies were resolved by discussion until consensus was reached. The data extraction form (Appendix 3) was developed based upon EPOC and Cochrane Consumers and Communication group (CCCG) guides (20, 21).

The following key characteristics of included studies were extracted:

- Methods (study design, unit of randomization, number of arms or groups, inclusion/exclusion criteria for participation in study, methods used to analyse data)
- Participants (age, gender, setting, number of persons allocated to each intervention arm, number of missing persons in each arm, number of participants in each arm)
- Interventions (intervention name and description, target of the intervention, content of the intervention, methods of delivery, location of delivery, frequency of delivery, co-interventions, modification or adaptation of the intervention during the study, assessment of fidelity, description of control group)
- Outcomes (primary and secondary outcomes, method of assessing outcome measures, measurement time-points)
- Results (type of the outcome, number of participants in control group, number of participants in intervention(s) group, baseline data in control and intervention groups, post-intervention data in control and intervention groups and post-intervention comparison between control and intervention groups)

- Risk of bias

Study authors were contacted for additional information whenever there was an ambiguity in methods or data.

### **Risk of bias assessments**

Two reviewers (SM and either AY, PH or BH) independently assessed the risk of bias of included studies in accordance with the risk of bias assessment guide of EPOC (Appendix 4) (22). The items that were considered for RCT and CBA studies included: allocation sequence generation, allocation concealment, similarity of baseline outcome measurements, similarity of the baseline characteristics, addressing of incomplete outcome data, prevention of knowledge of the allocated interventions during the study, contamination and selective outcome reporting. The items that were examined for ITS studies included: intervention independency of other changes, pre-specification of the shape of the intervention effect, likelihood of the intervention affecting data collection, prevention of knowledge of the allocated interventions during the study, addressing incomplete outcome data and selective outcome reporting.

### **Measures of intervention effect**

For dichotomous outcomes, data were analysed based on the number of events and the number of people assessed in the intervention and comparison groups. These data were used to calculate the odds ratio (OR) and 95% confidence interval (CI). For continuous measures, data were used to calculate mean differences (the absolute difference between the mean value in two groups) (MD) and 95% CI. For studies with more than one intervention group, we split the data in the control group to provide multiple two-arm comparisons (23).

## **Dealing with common methodological issues**

### **Unit of analysis issues in cluster allocated studies**

Studies that allocate at the cluster level (cluster RCTs and CBA studies) and analyse at the cluster member level need to account for the clustered nature of the data during analysis. Failure to do this, results in over-precise results (i.e. small P-values) but not biased effect sizes (23). Therefore, we checked whether the analysis of such studies had taken account of clustering. If not, we made a note in the limitations of the study and only reported the pointed effect estimate without mentioning the CI or P-values.

### **Inappropriate analysis of ITS studies**

We evaluated the method of analysis in ITS studies to check if they compared time trends before and after the intervention. If an appropriate analysis was not provided in the original paper, we re-analysed the data by extracting data points from the graphs (24). We performed a segmented time series regression model to estimate the effect of the intervention by taking into account time trends and autocorrelation.

### **Dealing with missing data**

There were no missing data but there was some incompatibility between data presented in tables and data presented in the text of the articles, where we contacted the authors to seek clarification. Where we did not hear back from the authors within 6 months, raw numbers were used in the analysis.

## **Data synthesis**

We categorized the studies according to the type of their interventions. Afterwards, we inspected the studies within categories of similar interventions to see if there was sufficient similarity to consider pooling. If pooling was possible, Review Manager 5 software (25) was used to meta-analyse the studies using a random-effects model. Where pooling the data using meta-analysis was not possible, a narrative synthesis of results was conducted. The similarities and differences between the findings of studies were investigated, as well as the exploration of patterns in the data (26). We conducted subgroup analysis based on subtypes of the intervention. We presumed different subtypes of the intervention would influence the effect size and explain heterogeneity.

### **Assessment of heterogeneity**

We assessed heterogeneity among studies by visual inspection of forest plots and by examining the  $I^2$  statistic.  $I^2$  statistic describes the percentage of variation across studies that is due to heterogeneity rather than chance (27). Bigger percentages suggest more heterogeneity.

### **Assessment of reporting biases**

We planned to assess the risk of publication bias by using a funnel plot. However, because less than 10 studies were suitable for pooling, we could not use this method to assess the publication bias (28).

### **Sensitivity analysis**

We conducted sensitivity analysis by investigating the effect of omitting studies that were outliers compared to other studies in the forest plot.

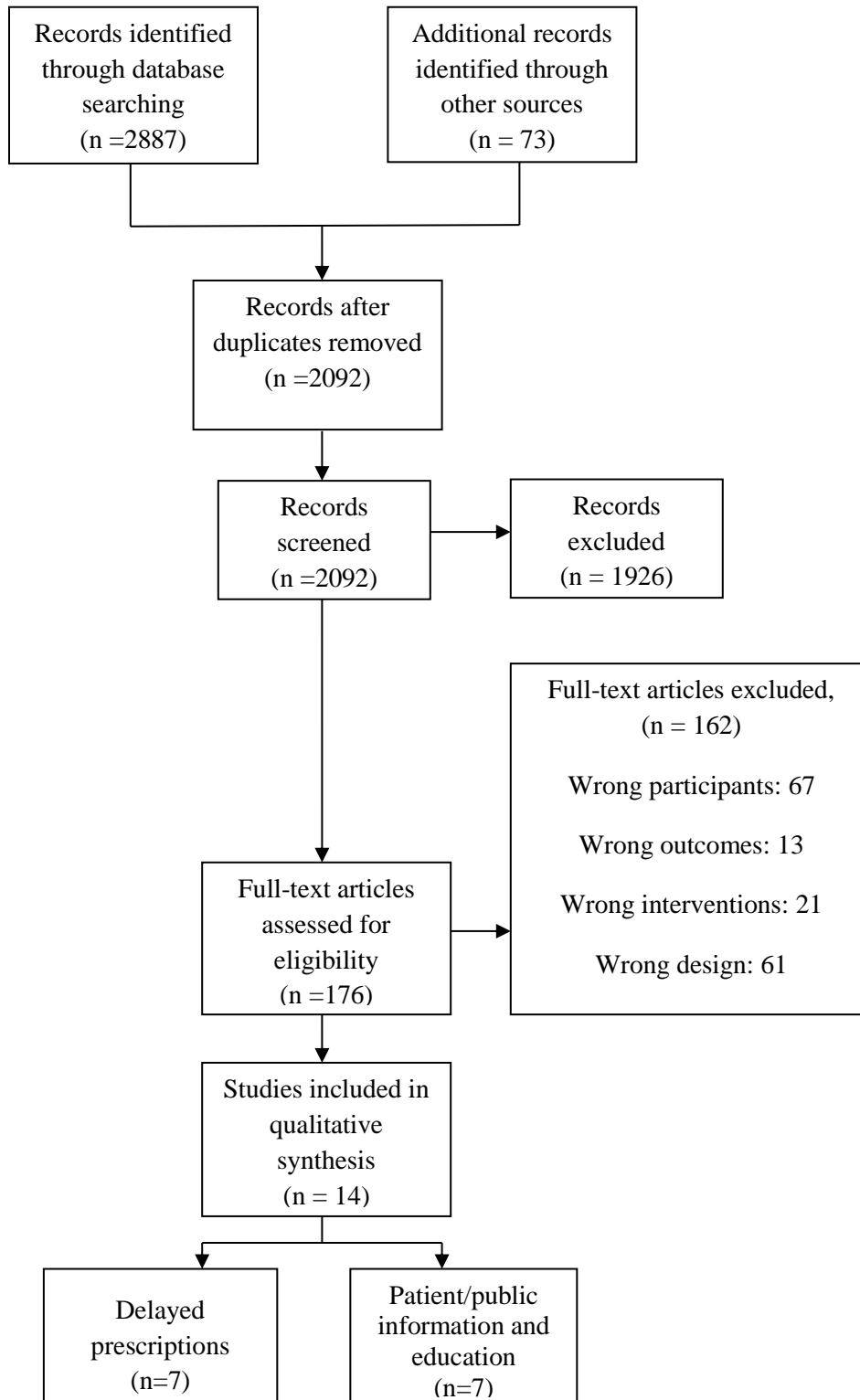
# **Results**

## **Description of studies**

### **Results of the search**

The literature search resulted in 2092 unique records after de-duplication. After title and abstract screening, 176 studies were included for full text evaluation. Following full-text screening, a total of 14 studies were selected for inclusion in the review (see Appendix 6 for details of excluded studies). The study flow diagram is presented in Figure 1.

**Figure 1) Study Flow diagram**



## **Included studies**

Full details of the included studies are available in the “characteristics of included studies” table (Table 1 and Appendix 5). We included 11 RCTs, two cluster RCTs, and one study that we re-analysed as ITS (details below) (Table 1). Most studies were conducted in Europe (nine studies) with a few other studies from USA (two studies), Canada (one study), Asia (two studies) and New Zealand (one study). Studies were completed between 1997 and 2016.

One study (29) used a retrospective CBA study to evaluate the effects on prescribing of antibiotics for the populations covered by two cycles of mass media campaigns. The authors used a repeated measures analysis of variance to analyze monthly prescribing data in the intervention and control populations. The model was used to make 36 pair-wise comparisons between the intervention and control populations at each month before and after the intervention. Their analysis did not control for baseline differences or secular trends, nor for multiple testing. The authors admitted that it was difficult to draw causal conclusions from their analysis, but reported a significant mean difference of 21.7 items per 1000 population in the intervention population versus the control population, aggregated over 5 post-hoc selected months, with the months identified based on statistical significance. Given the limited conclusions which could be drawn from their analysis, Plot Digitizer software was used to extract data for the intervention series over the 36 month observation period and data were reanalyzed using an ITS approach.

## **Interventions**

All interventions could be classified into two major categories: 1) delayed prescriptions (30, 31, 32, 33, 34, 35, 36), and 2) patient/public information and education interventions (29, 37, 38, 39, 40, 41, 42). Two studies compared different types of delayed prescription (34, 35). Patient

education was provided through pamphlets, booklets or videotapes in four studies (37, 38, 39, 40) through educational sessions in one study (41) and via online educational program in one study (42). One study (29) used mass media as an educational tool.

### **Outcomes**

Included studies reported a wide range of outcomes; the most common were: use of antibiotics, prescription of antibiotics, collection or filling of prescriptions by patients, satisfaction with the treatment, satisfaction with the consultation, patients' beliefs about the effectiveness of antibiotics and re-consultation with a physician for the same or similar episodes of URIs.

### **Funding sources**

Ten studies reported being funded by government or research foundation funds; two studies reported no funding; two studies did not declare the sources of their funding.

**Table 1) Summary of characteristics of included studies**

<b>Alexandrino 2016</b>	
Methods	RCT, 2 arms. Settings: Portugal, 10 private daycare centers.
Participants	Caregivers, Number of participants: 177
Interventions	Health Education Session (HES).
Outcomes	Primary: Impact of HES on the indicators of individual health and health care utilization.
<b>Arroll 2002</b>	
Methods	RCT, 2 arms. Settings: New Zealand, one family practice (15 physicians)
Participants	Patients presenting with the common cold, Number of participants: 129
Interventions	Delayed antibiotic prescription
Outcomes	Primary: Antibiotic use.
<b>Francis 2009</b>	
Methods	Cluster RCT, 61 clusters, 2 arms. Settings: UK, general practices.
Participants	Children with a respiratory tract infection, Number of participants: 558
Interventions	Interactive booklet.
Outcomes	Primary: The proportion of children who attended a face-to-face consultation about the same illness during the two week follow-up period.
<b>Lambert 2007</b>	
Methods	ITS. Settings: UK, a single geographical population in the North East of England.
Participants	People of the community
Interventions	Mass media education.
Outcomes	Primary: Prescribing rates for all microbial agents.
<b>Lee 2017</b>	
Methods	RCT, 2 arms. Settings: Singapore, primary care setting.
Participants	Patients presenting RTI symptoms, Number of participants: 914
Interventions	Education through pamphlets and counselling scripts.
Outcomes	Primary: Antibiotic prescription.
<b>Little 1997</b>	
Methods	RCT, 3 arms. Settings: UK, general practices.
Participants	Patients with sore throat, Number of participants: 716
Interventions	2 Intervention groups: delayed prescription of antibiotics, no antibiotics.
Outcomes	Primary: Antibiotic use.
<b>Little 2001</b>	
Methods	RCT, 2 arms. Settings: UK, general practices.
Participants	Children with acute otalgia, Number of participants: 315
Interventions	Delayed prescription of antibiotics.
Outcomes	Primary: Use and collection of antibiotic prescriptions.
<b>Little 2014</b>	
Methods	RCT, 5 arms. Settings: UK, primary care setting.
Participants	Patients with a respiratory tract infection, Number of participants: 556
Interventions	Intervention groups: Delayed patient led, post-dated prescription, delayed-collection, delayed-re-contact, no prescription.
Outcomes	Primary: Symptom severity.
<b>Little 2016</b>	
Methods	RCT, 2 arms. Settings: UK, primary care setting.
Participants	Adult patients, Number of participants: 2923
Interventions	Interactive website
Outcomes	Primary: General practitioner consultation.
<b>Mainous 2000</b>	
Methods	Cluster RCT, 4 clusters, 4 arms. Settings: USA, primary care setting.
Participants	Patients with respiratory tract infections, Number of participants: 269 physicians.

Interventions	3 intervention groups: performance feedback about antibiotic prescribing, patient education materials about antibiotic use, and both feedback and education materials.
Outcomes	Primary: Change in antibiotic prescribing.
<b>Pshetizky 2003</b>	
Methods	RCT, 2 arms. Settings: Israel, primary care setting.
Participants	Parents of children with acute otitis media, Number of participants: 81
Interventions	Delayed prescription of antibiotics
Outcomes	Primary: Antibiotic use
<b>Poza Abad 2016</b>	
Methods	RCT, 4 arms. Settings: Spain, primary care setting.
Participants	Patients with uncomplicated respiratory infections, Number of participants: 398
Interventions	3 intervention groups: delayed patient-led, delayed collection, no antibiotic.
Outcomes	Primary: Duration and severity of symptoms.
<b>Taylor 2005</b>	
Methods	RCT, 2 arms. Settings: USA, primary care setting.
Participants	Healthy children, Number of participants: 499
Interventions	Parental education through pamphlets and videos.
Outcomes	Primary: Number of diagnoses of otitis media and sinusitis per study child, number of visits per child for which antibiotics (oral or intramuscular) were prescribed.
<b>Worrall 2010</b>	
Methods	RCT, 2 arms. Settings: Canada, primary care setting.
Participants	Adult patients with acute URTIs, Number of participants: 149.
Interventions	Post-dated delayed antibiotic prescription.
Outcomes	Primary: Filling the prescription by the patients.

## **Risk of bias in included studies**

RCT/ Cluster RCT: Regarding random sequence generation and allocation concealment, all studies were of low or unclear risk of bias (see Figure 2). Only one study (37) was considered high risk regarding similarity of baseline characteristics because there was imbalance regarding these characteristics between the study groups. All studies were judged to be low or unclear risk for addressing incomplete outcome data, protection against contamination and selective outcome reporting. Four studies (33, 34, 35, 36) were assigned high risk of bias regarding prevention of knowledge of allocated interventions because the participants were not blinded to the interventions. One study (37) was considered high risk regarding other sources of bias. There was no information in this study on cluster size or adjustments for the effect of clustering. Furthermore, the outcome (antibiotic prescription) was reported for episodes of care, defined as one patient-physician consultation. Individuals could have more than one episode of care per disease and it made it difficult to judge if the post intervention difference between control and intervention groups was merely due to difference in antibiotic prescription or was a result of difference both in antibiotic prescription and number of episodes.

ITS: The main source of bias in the ITS study (29) was that the intervention was not independent of other changes and the authors mentioned that they were unable to control or document the complementary interventions. Also, the method of analysis of the data did not take into account the time trends before and after the interventions.

**Figure 2) Risk of bias summary**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Similarity of baseline outcome measurements	Similarity of baseline characteristics	Incomplete outcome data (attrition bias)	Prevention of knowledge of the allocated interventions during the study	Protection against contamination	Selective reporting (reporting bias)	Other bias	Intervention independent (ITS)?	Shape of effect pre-specified (ITS)?	Unlikely to affect data collection (ITS)?	Prevention of knowledge of the allocated interventions during the study (ITS)	Incomplete outcome data (attrition bias) (ITS)	Selective reporting (reporting bias) (ITS)	Other bias (ITS)
Alexandrino 2016	+	+	?	+	?	?	?	+	?							
Arroll 2002	+	+	?	+	+	?	?	+	?							
Francis 2009	?	?	?	+	+	+	+	+	+							
Lambert 2007										-	+	+	+	?	+	-
Lee 2017	?	+	?	+	+	+	?	+	?							
Little 1997	?	+	?	+	+	-	?	+	?							
Little 2001	?	+	?	+	+	-	?	+	+							
Little 2014	+	+	+	+	+	-	?	+	?							
Little 2016	+	+	+	+	+	+	?	?	?							
Mainous 2000	?	?	+	-	?	?	+	+	-							
Poza abad 2016	+	+	?	+	?	-	?	+	+							
Pshetizky 2003	?	+	?	+	?	+	?	?	?							
Taylor 2005	+	+	+	+	+	?	?	+	+							
Worrall 2010	?	?	?	?	?	?	?	+	?							

## Effects of interventions

### Primary outcome

#### 1) Delayed prescription (seven studies)

Most studies in this category compared immediate prescription of antibiotics with delayed prescription in a two-arm RCT design (30, 31, 32, 33). Three studies (34, 35, 36) used multi-arm RCTs to evaluate different types of delayed prescriptions. The types of delayed prescriptions evaluated were:

Delayed patient-led: the delayed prescription was given to the patients at the time of the initial visit, and patients were given instructions to fill the prescription after a given time period (two to three days, depending on the study) (30, 31, 34, 35).

Post-dated prescription: the delayed prescription was given at the time of the visit; however, it was post-dated (32, 35).

Delayed collection: the delayed prescription was not provided to patients at the time of the visit, but rather was lodged at the practice's reception or pharmacy, and patients were invited to collect or fill their prescription if their symptoms had not improved or worsened after a few days (two to seven days, depending on the study) (33, 34, 35, 36).

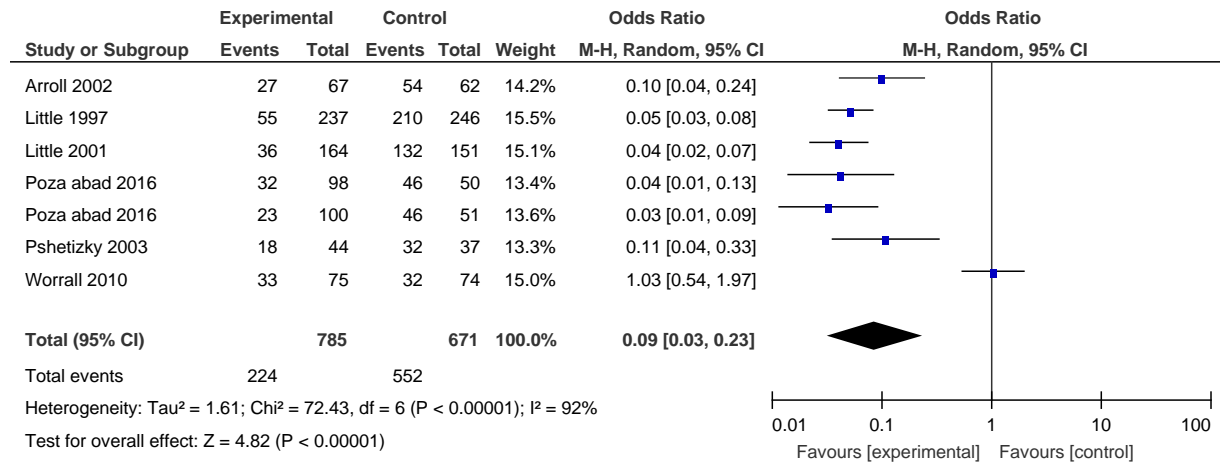
Delayed re-contact: patients were asked to contact or phone and leave a message to request antibiotics (35).

A few studies (34, 35, 36) included a group of no antibiotic prescription along with other intervention groups. We did not use the data from this group in our analysis.

### **1.1) Analysis of data comparing delayed prescription with immediate prescription**

We performed a meta-analysis of six RCTs studies involving a total of 1,788 participants that compared delayed prescription (30, 31, 32, 33, 34, 36) with an immediate prescription control group. The study by Little et al. 2014 could not be included because there was no immediate prescription control group within this study (35). Most studies reported antibiotic use as one of their outcomes while one study (32) only reported the filling of the prescriptions by patients. We assumed that filling the prescription from the pharmacy will lead to antibiotic use, so data from all these studies were pooled. We used an intention-to-treat (ITT) approach to analyse the data by using the original number of participants that were randomized to intervention and control groups in each study. Overall, the participants in the delayed prescription group were less likely than participants in the immediate prescription group to use antibiotics (OR=0.09, CI: 0.03 to 0.23). There was considerable heterogeneity in the estimate of effect size among studies ( $I^2=92\%$ ) (Figure 3); we performed subgroup analysis to investigate the heterogeneity.

**Figure 3) Forest plot of comparing antibiotic use between intervention and control groups in all studies in the delayed prescription group.**

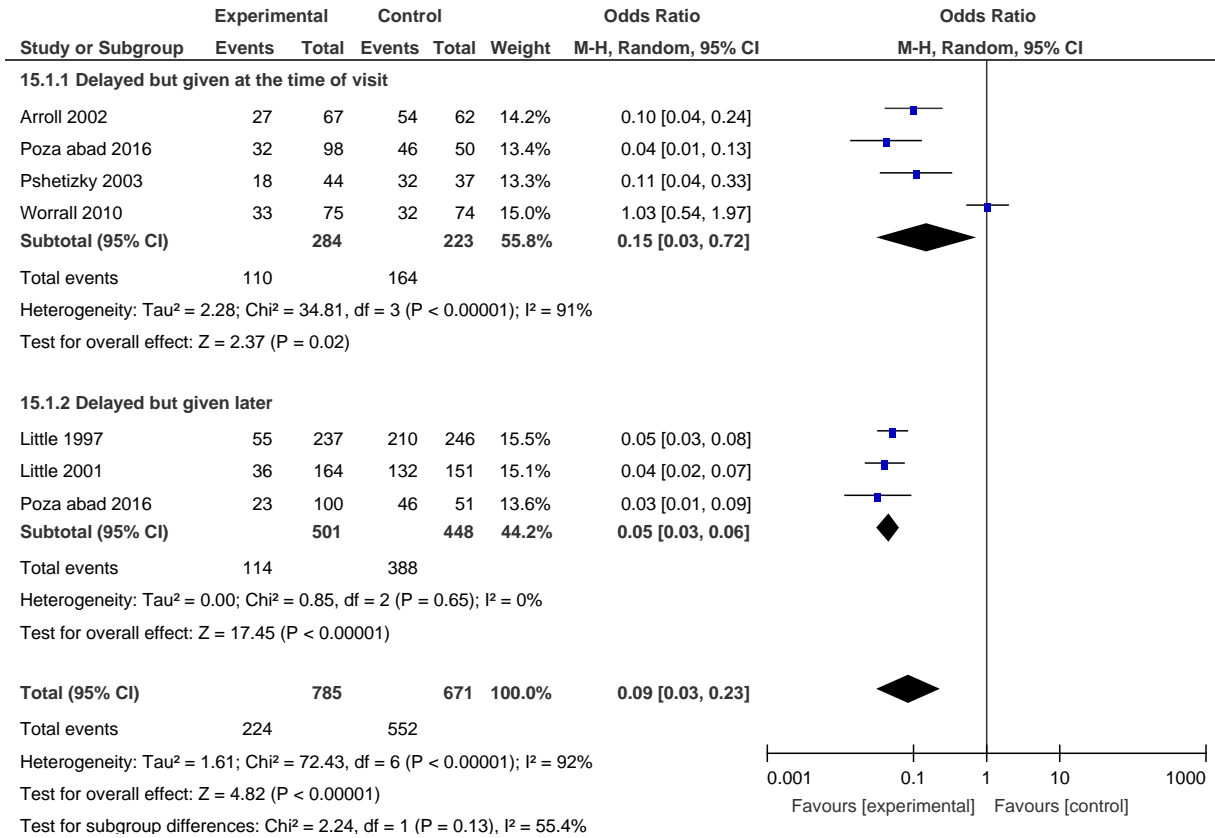


### **1.1.a) Exploring the heterogeneity by subgroup analysis according to the time of prescription delivery**

To explore the source of heterogeneity, we divided the studies in the delayed prescription group into two subgroups: subgroup 1) studies in which the prescription was given at the time of visit with some instructions to wait for a few days before filling it (delayed patient-led and post-dated prescription), and subgroup 2) studies in which the prescription was not given at the time of the visit, and patients were asked to return to collect the prescription after a period of time (delayed collection).

Subgroup 1 consisted of Arroll et al., Pshetizky et al., Worrall et al. and part of Poza Abad et al. (30, 31, 32, 34). The OR of antibiotic use in this group was 0.15 (CI: 0.03 to 0.72) and the calculated heterogeneity ( $I^2$ ) was 91% (Figure 4). Subgroup 2 consisted of Little et al. 1997, Little et al. 2001 and part of Poza Abad et al. (33, 34, 36). The OR of antibiotic use in this group was 0.05 (CI: 0.03 to 0.06) with no heterogeneity (Figure 4).

**Figure 4) Forest plot of comparing antibiotic use between intervention and control groups, sub-grouped according to the time of prescription delivery**



### **1.1.b) Sensitivity analysis of data comparing delayed prescription with immediate prescription**

Even after sub-grouping the studies, there was a considerable amount of heterogeneity in subgroup 1. Worrall et al. was the only study that showed almost no difference in antibiotic use between intervention and control groups (OR=1.03, CI: 0.54 to 1.97) (Figure 4) (32). In this study, patients in both the intervention and control groups were informed verbally that it was better not to use antibiotics until after a few days. Furthermore, patients in the intervention group (post-dated prescription) were able to fill the prescriptions earlier than the assigned date. These issues could cause similar antibiotic use in the intervention and control groups. To determine the robustness of the results, we re-analysed the data by omitting the Worrall et al. study (Appendix 7). After deleting the Worrall et al. Study, subgroups 1 (delayed given at the index consultation) and 2 (delayed, but given later) showed similar ORs of antibiotic use (OR=0.08, CI: 0.04 to 0.14 and OR=0.05, CI: 0.03 to 0.06, respectively). Furthermore, omitting the Worrall et al. study resulted in an overall OR of 0.05 (CI: 0.04 to 0.07) and total heterogeneity ( $I^2$ ) of 6% (Appendix 7). Since the direction and magnitude of the effect of the intervention did not change dramatically after omitting the Worrall et al. study, we kept it along with the other remaining studies.

### **1.2) Analysis of data comparing different types of delayed prescription**

Little et al. 2014 studied five intervention groups: delayed-patient led, delayed collection, post-dated prescription, delayed re-contact and no antibiotic prescription. Their study showed no significant difference in antibiotic use between these groups. This analysis did not compare antibiotic use between delayed prescription methods with immediate prescription, but only

demonstrated that different methods of delayed prescription seem to be the same in terms of their effect on antibiotic use (likelihood ratio test=4.96, P-value=0.292) (35).

## **2) Patient/public information and education methods**

Studies in this group differed based on their educational material and their methods in providing the education. Education was offered through pamphlets, booklets, videotapes, educational teaching sessions, online educational program or mass media.

### **2.1) Pamphlets/booklets/videotapes (four studies)**

There were four studies that used booklets or pamphlets to educate patients. Due to heterogeneity in reporting the outcomes, it was not possible to perform a meta-analysis.

Mainous et al was a cluster RCT, but there was no adjustment for the effect of clustering in the study. There were two kinds of interventions, one directed at doctors and one directed at patients, we only extracted the data from the latter group. The intervention directed at patients included “your child and antibiotics” pamphlets (more details in Appendix 5) and was delivered to patients by doctors. The study results showed that despite the increase in mean percentage of episodes receiving antibiotics after the intervention in both the control and intervention group, the mean was still less in the intervention group compared to the control group (MD= -9.87 in mean percentage of episodes receiving antibiotics) (37).

Parents of healthy children younger than 24 months old seen in the offices of participating clinics in the Taylor et al. study received “your child and antibiotics” pamphlet (as described above), as well as a video that emphasized the main points of the pamphlet. Additional copies of the pamphlets were mailed to the parents at six weeks and six months after enrolment. The authors

reported no significant differences in the total number of prescriptions for antibiotics per patient in the intervention and control groups during the 12-month observation period (MD=-0.3, P-value=0.23) (39).

The pamphlets that were used in the Lee et al. study covered the causes of URTIs and the role of antibiotics and were designed to address the major misconceptions about URTIs that were recognized in previous local studies. The researcher verbally educated participants via the educational pamphlets. Participants were patients aged 21 years and above, presenting with URTI symptoms at participating clinics. The results of the study demonstrated no significant difference in antibiotic prescription between the intervention and control groups (OR=1.20, CI: 0.84 to 1.72) (38).

In a cluster RCT, Francis et al. used booklets on RTIs in children (six months to 14 years) consulting with a respiratory tract infection and their parents. The booklets included information on the effectiveness of antibiotic treatment, potential adverse effects from antibiotics, other treatment suggestions, and symptoms that should prompt re-consultation and were used within the consultations by doctors, as well as a resource to be taken home by participants. The authors mentioned proper adjustments for the effect of clustering. The OR of antibiotic prescription at the index consultation was 0.29 in the favor of intervention (CI: 0.14 to 0.60). The authors also reported the OR taking antibiotics within the first two weeks as 0.35 (CI: 0.18 to 0.66) (40).

## **2.2) Educational sessions plus booklet (one study)**

One study used educational sessions to inform parents or legal tutors of paediatric patients (children under three years old in day-care centers). Alexandrino et al. used “Health Education Sessions” (HES) (more details in Appendix 5) of mean duration of 90 minutes delivered by a

respiratory physiotherapist in small groups of 10 to 15 caregivers (parents or legal tutors). The sessions included information on prevention of acute respiratory infections (ARIs), signs and symptoms of ARIs, signs of worsening, medications and nasal clearance techniques. The participants were also provided with a booklet with a summary of the information at the end of the sessions. The results showed less antibiotic use in the intervention group compared to the control group (OR=0.33, CI: 0.12 to 0.90) (41).

### **2.3) Interactive online educational program (one study)**

There was just one study in this group. Little et al. 2016 provided the participants (a random selection of adults in the computerised practice registers from 35 practices) with an access to an interactive website for 20 weeks. The website delivered tailored advice on visiting/not visiting a physician and methods of self-management for URTIs. The results of the study showed that antibiotic prescription did not differ significantly between the intervention and control groups in the first six months after the intervention (RR=1.02, CI: 0.82 to 1.43) or after longer follow-ups (12 months) (RR=1.00, CI: 0.74 to 1.33) (42).

### **2.4) Mass media (one study)**

Only one study examined the effect of mass media as intervention and compared it to the control group by reporting 36 data points. Two sequential mass media campaigns were used in the Lambert et al. study. The campaigns consisted of a short cartoon strip about the effects of antibiotics and self-care for managing self-limited health problems. This was accompanied by leaflets, posters, as well as TV (was added in the second intervention), radio and local newspaper coverage. Given the limited conclusions which could be drawn from the original analysis in the manuscript, we re-analyzed the data using an ITS approach. Our analysis did not incorporate the control population

but allowed the effect of the intervention to be assessed in the intervention population, while controlling for the pre-intervention level and secular trend. The results were adjusted for autocorrelation. Regarding prescription rate, after the first intervention, the change in slope was 0.39 (CI: -1.87 to 2.65) and the change in level was -8.94 (CI: -23.31 to 5.42). After the second intervention, the change in slope was calculated as -2.11 (CI: -5.75 to 1.54) and the change in level as -1.40 (CI: -17.40 to 14.60) (29).

### **Secondary outcomes**

Secondary outcome measures of our interest that were reported by included studies composed of: patients' satisfaction with the treatment or consultation, patients' beliefs on the effectiveness of antibiotics for URTIs and re-consultation. A summary of these results are provided in table 2.

**Table 2) The effect of interventions on patients’ satisfaction, beliefs and re-consultation.**

		<b>Patients’ satisfaction<sup>1</sup></b>	<b>Beliefs<sup>2</sup></b>	<b>Re-consultation<sup>3</sup></b>
<b>Delayed prescription</b>	<b>Arroll 2002</b> (delayed vs. immediate )	Intervention: 96% Control: 94% OR=1.47 (CI: 0.32 to 6.85)	Intervention: 76% Control: 76% OR=1.02 (CI: 0.45 to 2.28)	Intervention: 73% Control: 65% OR=1.50 (CI: 0.71 to 3.17)
	<b>Little 1997</b> (delayed vs. immediate)	Intervention: 93% Control: 96% OR=0.61 (CI: 0.25 to 1.49)	Intervention: 60% Control: 87% OR=0.22 (CI: 0.13 to 0.36)	Intervention: 57% Control: 79% OR=0.35 (CI: 0.22 to 0.55)
	<b>Little 2001</b> (delayed vs. immediate)	Intervention: 77% Control: 91% OR=0.32 (CI: 0.16 to 0.65)	Intervention: 46% Control: 76% OR=0.24 (CI: 0.14 to 0.40)	Intervention: 63% Control: 83% OR=0.35 (CI: 0.20 to 0.62)
	<b>Little 2014<sup>4</sup></b> (different variants of delayed prescriptions vs. no antibiotic)	Delayed re-contact: 74% Post-dated: 80% Delayed collection: 88% Delayed patient-led: 89% Likelihood ratio test X <sup>2</sup> =2.38 (P-value=0.67)	Delayed re-contact: 74% Post-dated: 73% Delayed collection: 72% Delayed patient-led: 66% Likelihood ratio test X <sup>2</sup> =1.62 (P-value=0.80)	Delayed re-contact: 18% Post-dated: 10% Delayed collection: 14% Delayed patient-led: 14% Likelihood ratio test X <sup>2</sup> =2.97 (P-value=0.56)
	<b>Poza Abad<sup>5</sup> 2016</b> (delayed collection vs. immediate and delayed patient-led vs. immediate)	P-value <sup>6</sup> = 0.14	Delayed collection: 84.4% Immediate: 91.8% OR=0.37 (CI: 0.14 to 0.99)  Delayed patient-led: 81% Immediate: 91.8% OR=0.37 (CI: 0.14 to 0.98)	Delayed collection: 69.1% Immediate: 85.7% OR=0.62 (CI: 0.19 to 2.06)  Delayed patient-led: 69.0% Immediate: 85.7% OR=0.35(CI: 0.1 to 1.30)
<b>Patient/public information</b>	<b>Francis 2009</b> (interactive booklet vs. control)	Intervention: 90.2% Control: 93.5% OR= 0.64 (CI: 0.33 to 1.22)		Intervention: 55.3% Control: 76.4% OR=0.34 (CI: 0.20 to 0.57)
	<b>Little 2016</b> (online educational program vs. control)			Intervention: 19.3% Control: 19.3% OR=0.93 (CI: 0.73 to 1.16)

1) The outcome was reported as “satisfaction with the consultation” in all studies except for Little 2001 study, in which it was reported as “satisfaction with the treatment approach”. OR>1 means more satisfaction in the intervention group compared to the control group. OR<1 means less satisfaction in the intervention group compared to the control group.

2) The belief outcome was “Antibiotics are effective” for all studies. OR<1 means more disbelief in the effectiveness of antibiotics in the intervention group compared to the control group. OR>1 means less disbelief in the effectiveness of antibiotics in the intervention group compared to the control group.

3) Re-consultation was reported only in Little 2014 (within one month after the consultation) and Little 2016 (within one year after enrolment) studies, all other studies reported the intention to re-consult in future. OR<1 means less re-consultation in the intervention group compared to the control group. OR>1 means more re-consult in the intervention group compared to the control group.

4) All intervention groups (different variants of delayed prescriptions) were compared to “no antibiotic”.

5) The P-values are reported to compare the difference between delayed collection, delayed patient-led, immediate prescription and no prescription.

6) No more data were available.

### **Patients' satisfaction with the treatment or consultation**

Five studies reported patients' satisfaction with the consultation and one study reported the patients' satisfaction with the treatment. Some of these studies reported the number of participants who were "very satisfied", some combined the "very satisfied" and "moderately satisfied" groups together and some studies did not mention any further details.

In delayed prescription group, two studies from UK reported less satisfaction in the intervention group compared to the control group, while the results were significant in only one of them (33, 36). One study from New Zealand reported higher satisfaction (though this was not statistically significant) in the intervention group (30). In Little et al. 2014 study there was no significant difference in satisfaction between different variants of delayed prescription (35). Poza Abad et al. reported no significant difference between delayed collection, delayed patient-led and immediate prescription groups regarding patients' satisfaction (34).

In the patient/public information and education group, only one study which used booklets as intervention measured satisfaction which showed less satisfaction in the intervention group, however it was not statistically significant (40).

### **Patients' beliefs on the effectiveness of antibiotics for URTIs**

Four studies compared participants' beliefs on the effectiveness of antibiotics between the patients in the delayed prescription group and immediate prescription group. Two studies from UK and one study from Spain showed significant better results in the intervention groups (33, 34, 36). One study from New Zealand reported no difference between control and intervention groups (30). In Little et al. 2014 study there was no significant difference between different variants of delayed

prescription regarding patients' beliefs (35). No studies in the information and education group measured this outcome.

### **Re-consultation**

Five studies in delayed prescription group evaluated patients' willingness to re-consult for similar illnesses in near future or re-consultation rate. Two studies from UK and one study from Spain reported less intention to re-consult in the intervention groups; however, the results were significant only in two studies (33, 34, 36). One study from New Zealand reported greater intention to re-consult in the intervention group though this was not statistically significant (30). In Little et al. 2014 study there was no significant difference between different variants of delayed prescription regarding re-consultation (35).

Two studies in the patient/public information and education group (from UK) (one applied booklets, the other applied online educational program) reported less re-consultation in the intervention group, while the results were statistically significant in only one study (40, 42).

## **Discussion**

### **Summary of main results**

This systematic review synthesised evaluations of patient-oriented interventions to reduce unnecessary use of antibiotics for URTIs. The 14 studies that were included in our review focused on either delayed prescription of antibiotics or information and education materials as their interventions. Our meta-analysis revealed that almost all studies with delayed prescription significantly reduced use of antibiotics for URTIs. Our subgroup analysis showed that the

prescriptions that were given at a later time and the prescriptions that were given at the index consultation had similar effects in reducing antibiotic use in patients.

The effect of interventions in the information and education group varied highly among different types of educational materials. The results suggested that providing information/education via online educational program or mass media (each evaluated in one study) might not have a significant effect on antibiotic prescription; however one study that used educational sessions plus booklets disclosed promising effects on reducing antibiotic use. Furthermore, applying booklets, pamphlets or videotapes demonstrated inconsistent results on antibiotic prescription; it seems that when these interventions were provided by a physician rather than a researcher and were discussed verbally in a face-to-face visit they led to better results.

Changes in patients' satisfaction, beliefs on the effectiveness of antibiotics and re-consultation were only reported in a few studies. In the delayed prescription group, only four studies compared patients' satisfaction between delayed prescription and immediate prescription groups, of which one study from New Zealand reported higher satisfaction in the intervention group (non-significant) and two studies from a single group in UK reported less satisfaction in the intervention group (only one was significant). One study from Spain only mentioned that the difference between delayed collection, delayed patient-led and immediate prescription groups was not significant. In the patient/public information and education group, patients' satisfaction was only reported in one study (interactive booklets) from UK which showed less satisfaction in the intervention group. Re-consultation was reported in four studies in the delayed prescription group; three of them (one from Spain and two from the UK) showed less re-consultation in the intervention groups, while the study from New Zealand showed the opposite results. Two UK studies in the patient/public information and education group (interactive booklets and online

educational program) reported fewer re-consultations in the intervention group. Patients' beliefs on the effectiveness of antibiotics were only studied in delayed prescription group and showed a significant change in favour of the intervention in three studies (one from Spain and two from the UK) and no change in the study from New Zealand. The difference between the results of the study from New Zealand and other studies (Europe) might be explained in part by the location of studies. Differences in cultural or socioeconomic backgrounds of participants in different settings could have affected the results.

## **Strengths and limitations of the study**

We believe that one of the major strengths of this review is the comprehensive literature search in various databases; however our study has a number of limitations:

We limited our search to English language studies which may have caused missing some studies in this field. We identified some studies where the educational interventions were directed at both patients and healthcare providers. We excluded these studies as we were interested in the effects of just targeting patients. We also excluded the studies that promoted shared decision making or communication between the patients and healthcare providers. However, we included the studies with delayed prescription, because we believe it is the patient who decides to collect or fill the prescription. A few studies in our review included LRTIs in addition to URTIs (34, 35, 37); since the major focus of these studies was URTIs, we did not exclude them.

Our systematic review was dependent on the results provided in the included studies and therefore, was influenced by the ways they reported their outcomes:

Some studies lacked clear data on the effect size and only provided P-values. Secondary outcomes were measured and reported in multiple ways. Patients' satisfaction and beliefs on the effectiveness of antibiotics for URTIs were examined using diverse questionnaires and scales. Re-consultation was defined with various times to follow-up in different studies and some studies had evaluated patients' intentions to re-consult in the future and not the actual re-consultation rate. All these differences in measuring and reporting the outcomes in different studies or lack of enough data made pooling the data inappropriate.

There were also two issues regarding the use of antibiotics. First, antibiotic use was measured by relying on patients' reports in most of the studies. This may have introduced social desirability bias which could have distorted the estimates of antibiotic use. Second, some studies reported antibiotic prescription instead of antibiotic use. It is not clear how many of these prescriptions resulted in actual use of antibiotics.

Finally, there were some concerns on interpreting the results of the Mainous et al. study (37). First of all, it was a cluster RCT, but the authors did not mention any adjustments for the clustering effect. Second, they reported "mean percentage of episodes receiving antibiotics" in the control and intervention groups as their outcome; as mentioned by the authors in the manuscript, individuals could have more than one episode of care and it made it difficult to judge if the post intervention difference between control and intervention groups was merely due to difference in antibiotic prescription or was a result of difference both in antibiotic prescription and number of episodes.

## **Agreements and disagreements with other studies**

Other systematic reviews have evaluated the effect of different patient-oriented interventions on antibiotic use. However, most of them have not evaluated the quality of included studies or have focused on only specific kind of interventions (e.g. delayed prescriptions). Some reviews only focused on patient-oriented interventions (43, 44, 45, 46) while others also included interventions that targeted healthcare providers (47, 48, 49). Andrews et al. and Vodicka et al. reported the effect of interventions on antibiotic use specifically in children (44, 48).

In general, most reviews shared similar results. Consistent with our results, Thoolen et al., Spurling et al., Andrews et al., Arnold et al. and McDonagh et al. concluded that delayed prescriptions resulted in a significant decrease in antibiotic use. It was also noticed that this decrease did not affect patients' satisfaction (44, 45, 46, 47, 49).

Similar to our results, there was not a consensus among reviews on the effectiveness of educational methods on reducing antibiotic use. One review reported no or small benefit from printed educational materials (48). O'Sullivan et al. examined the effect of written information for patients and concluded that providing written information to parents of children can lead to a decrease in antibiotic use with no negative effect on patients' satisfaction. However they included only two studies in their review and it is difficult to make firm conclusions about the effectiveness of all written information for patients based on these sparse data (43). McDonagh et al. concluded that clinic-based educational materials for parents (e.g. posters, pamphlets, interactive videos) reduce overall prescription of antibiotics. Some of the differences between the results of this study and other studies could be explained by differences in their inclusion criteria. A broader range of designs including observational studies were included in this study. Consistent with our results,

McDonagh et al. agreed that public educational campaigns are not effective in reducing antibiotic use (49).

We only included studies that had been conducted in primary care settings; however some of the studies in emergency department share the same results as our study (50, 51).

## **Implications for practice**

Some patient-oriented interventions are effective in reducing antibiotic use for URTIs in patients. This is of great importance in terms of the ultimate goal, which is dealing with the problem of antibiotic resistance.

The results of this study are consistent with other studies that delayed prescription of antibiotics reduces the antibiotic use for URTIs. This strategy can be adopted by healthcare providers and policy makers. To implement this strategy, we may need to train doctors to explain to the patients when and how the prescriptions can be accessed.

The effect of interventions that only focused on patients' or public education varied according to the type of materials used and the way they were applied. We found the interventions that were delivered face to face or through a session and were discussed verbally by the doctors showed promising effects on decreasing antibiotic use or prescription. This highlights the role of active education versus passive methods and the importance of physicians' role to explain the contents of educational materials to patients.

## **Implications for research**

The effectiveness of different patient-oriented interventions on reducing antibiotic use is discussed in multiple studies. Conducting more studies of this kind (especially about the delayed prescriptions) in similar settings is unlikely to provide any new insights in understanding their effectiveness. However, we lack enough data on patients' satisfaction with these interventions. In our review, the studies from UK and New Zealand showed different direction of effect for satisfaction, suggesting that there may be cultural or contextual factors that modify the intervention acceptability. Research is needed to investigate the factors that affect intervention acceptability and therefore patients' satisfaction among different settings.

There may also be some opportunities in combining different components of effective interventions to design new multifaceted interventions (e.g. mixing delayed prescriptions with pamphlets/booklets). Further research is needed to identify and evaluate the most effective combinations.

Our results show the effectiveness of delayed prescriptions on reducing antibiotic use. However, when implementing these strategies, we should also consider the associated costs. Although delayed prescriptions do not impose further cost by themselves, additional funds may be required to train the doctors and staff to adopt this strategy. Regarding educational methods, we should consider the direct costs of the educational materials in addition to the training. Other than cost, there may be some practical challenges in implementation of these interventions. Further research is required to focus on the feasibility and costs of implementing these interventions.

Better reporting of interventions' details (who delivered the interventions, the settings in which they were delivered, how often they were delivered) would make it easier to compare the

interventions or to adopt them. Most studies in our review also lacked the description of co-interventions or assessment of fidelity.

Some studies in our review reported antibiotic prescription as their outcome. However, not all patients actually use their prescriptions. On the other hand, the studies that reported antibiotic use instead of antibiotic prescription relied on patients' self reports which may introduce desirability bias. It is important to choose a common outcome to allow us to measure the real antibiotic use by patients.

Finally, qualitative research can help to realize why some interventions are more effective in some settings and less effective in others. These methods can also be beneficiary in understanding patients' concerns with the treatments or consultations in order to achieve a higher satisfaction.

## **Conclusion**

Our study focused on addressing patients to decrease the unnecessary use of antibiotics for URTIs. Patient-oriented interventions have been studied in two major categories: delayed antibiotic prescription and patient/public information and education materials. There is evidence that delayed prescription of antibiotics reduces antibiotic use by patients. The effects of educational intervention varied among different educational methods and materials, but were smaller than the effect of delayed prescriptions. However, it seems that providing education through sessions or pamphlets/booklets (especially if delivered by a healthcare provider and discussed verbally) may decrease antibiotic use or prescription.

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# Appendix 1

## Criteria for considering studies for the review

Study characteristics	Include	Exclude
Participants	<ul style="list-style-type: none"> <li>Public, healthy individuals or patients of all age groups with upper respiratory tract infections (such as sinusitis, pharyngitis, sore throat, otitis media, common cold and acute cough) who seek treatment in any general practice setting.</li> </ul>	<ul style="list-style-type: none"> <li>Patients with lower respiratory tract infections (LRTIs) and those with chronic lung conditions (such as chronic obstructive pulmonary disease (COPD)) will be excluded.</li> </ul>
Interventions	<ul style="list-style-type: none"> <li>Any intervention that is directed to patients, parents of patients (when the patients are children), public or healthy individuals) to reduce unnecessary use of antibiotics for URTIs in primary care setting.</li> </ul>	<ul style="list-style-type: none"> <li>Interventions that are directed to healthcare providers or clinical staff will be excluded.</li> <li>The interventions that target patients indirectly (the primary and main effect of the intervention are directed to healthcare providers and patients benefit secondarily from that effect) will be excluded.</li> <li>Patient decision aids</li> </ul>
Comparisons (19)	<ul style="list-style-type: none"> <li>These comparisons will be included:               <ul style="list-style-type: none"> <li>Interventions directed at patients/public versus no intervention.</li> <li>Interventions directed at patients/public versus standard or usual care.</li> <li>One form of intervention directed at patients/public versus another.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Other comparisons will be excluded.</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>Primary outcomes:               <ul style="list-style-type: none"> <li>Prescription or use of antibiotics for URTIs in primary care setting.</li> </ul> </li> <li>Secondary outcomes:               <ul style="list-style-type: none"> <li>Public/patients' satisfaction with the treatment/consultation.</li> <li>Public/patients' beliefs that antibiotics are effective for URTIs.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Studies that do not report the primary outcome will be excluded.</li> </ul>

	<ul style="list-style-type: none"> <li>○ Re-consultation for the same illness in the next two weeks.</li> </ul>	
Study designs (19)	<ul style="list-style-type: none"> <li>• Randomized controlled trials (RCTs)</li> <li>• Quasi-RCTs (a trial in which randomization is attempted but subject to potential manipulation, such as allocating participants by day of the week, date or birth, or sequence of entry into trial).</li> <li>• CBA (Controlled Before and After) studies are included if: <ul style="list-style-type: none"> <li>○ There are at least two intervention sites and two control sites;</li> <li>○ The timing of the periods for study for the control and intervention groups is comparable (that is, the pre- and post- intervention periods of measurement for the control and intervention groups should be the same);</li> <li>○ The intervention and control groups are comparable on key characteristics.</li> </ul> </li> <li>• ITS (Interrupted Time Series) studies will be included if: <ul style="list-style-type: none"> <li>○ The intervention occurred at a clearly defined point in time, and this was specified by the researchers;</li> <li>○ There were at least three data points before and three data points after the intervention was introduced.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• CBA and ITS will not be included if they do not meet the mentioned criteria.</li> <li>• Other kinds of studies (e.g. observational, reviews) will be excluded.</li> </ul>
Language	English studies will be included.	Studies of other languages will be excluded.

## Appendix 2

### Search strategy

1. exp Patient Education as Topic/
2. exp Consumer Health Information/
3. exp Pamphlets/
4. exp Decision Support Techniques/
5. exp Health Promotion/
6. exp Computer-Assisted Instruction/
7. motivational interviewing/ or distance counselling/
8. counselling/ or directive counselling/
9. exp Information Services/
10. exp Mass Media/
11. exp Social Media/
12. self care/ or exp self administration/ or exp self medication/
13. health education/ or exp consumer health information/ or exp health fairs/ or exp teach-back communication/
14. exp Teaching Materials/
15. exp Patient Participation/
16. exp Decision Making/
17. exp social support/
18. exp Consumer Participation/
19. exp Cooperative Behaviour/
20. exp Behaviour Therapy/
21. exp Problem Solving/
22. exp Postal Service/
23. exp "Delivery of Health Care"/
24. exp "Cost Sharing"/
25. exp Insurance, Health, Reimbursement/ or exp Reimbursement, Incentive/
26. exp Motivation/
27. (Delay* adj2 prescrip*).ti,ab.
28. (Health adj2 Promot*).ti,ab.
29. (Computer* adj2 assist* adj2 education?).ti,ab.
30. (Motivat* adj2 Interview*).ti,ab.
31. Counsel*.ti,ab.
32. (Inform* adj2 Service*).ti,ab.
33. mass media.ti,ab.
34. social media.ti,ab.
35. self care.ti,ab.
36. (health adj2 educat*).ti,ab.
37. (teaching adj2 material?).ti,ab.
38. (decision? adj2 mak*).ti,ab.
39. decision support techniques/
40. decision aid*.ti,ab.
41. (patient? adj2 participat*).ti,ab.
42. (patient? adj2 involv*).ti,ab.
43. (patient? adj2 support?).ti,ab.
44. (social adj2 support?).ti,ab.
45. (patient? adj2 educat*).ti,ab.
46. (facilitat* adj2 communicat*).ti,ab.
47. (health adj2 inform*).ti,ab.
48. pamphlet?.ti,ab.
49. booklet?.ti,ab.
50. (educat* adj3 video?).ti,ab.

51. (educat* adj3 book?).ti,ab.
52. brochure?.ti,ab.
53. (Computer* adj2 interact*).ti,ab.
54. (health* adj2 behavior?).ti,ab.
55. (health* adj2 behaviour?).ti,ab.
56. (consumer? adj2 particip*).ti,ab.
57. (support* adj2 behavior?).ti,ab.
58. (support* adj2 behaviour?).ti,ab.
59. (cooperat* adj2 behavior?).ti,ab.
60. (cooperat* adj2 behaviour?).ti,ab.
61. (inform* adj2 material?).ti,ab.
62. (educat* adj3 video?).ti,ab.
63. (behavior adj2 therapy).ti,ab.
64. (behaviour adj2 therapy).ti,ab.
65. (problem adj2 solving).ti,ab.
66. Group programme?.ti,ab.
67. action plan?.ti,ab.
68. post* service?.ti,ab.
69. Mass mailing?.ti,ab.
70. (mail* adj2 distribut*).ti,ab.
71. (mail? adj2 order*).ti,ab.
72. (Financial adj2 intervention?).ti,ab.
73. (Financial adj2 incentive?).ti,ab.
74. Harm reduc*.ti,ab.
75. (cost? adj2 shar*).ti,ab.
76. co-payment?.ti,ab.
77. copayment?.ti,ab.
78. reimburs*.ti,ab.
79. (health adj2 campaign?).ti,ab.
80. (wellness adj2 campaign?).ti,ab.
81. (consumer? adj2 involv*).ti,ab.
82. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81
83. exp Respiratory Tract Infections/
84. exp Sinusitis/
85. sinusitis.ti,ab.
86. respiratory tract infection?.ti,ab.
87. (respiratory adj2 infection?).ti,ab.
88. exp Pharyngitis/
89. pharyngitis.ti,ab.
90. sore throat?.ti,ab.
91. exp Laryngitis/
92. laryngitis.ti,ab.
93. exp Tonsillitis/
94. Tonsil?itis.ti,ab.
95. exp Otitis Media/
96. otitis media.ti,ab.
97. (inflammation? adj2 middle ear).ti,ab.
98. exp Common Cold/
99. common cold?.ti,ab.
100. chest cold?.ti,ab.
101. coryza?.ti,ab.
102. catarrh?.ti,ab.
103. exp Rhinitis/
104. Rhinitis.ti,ab.
105. rhinosinusitis.ti,ab.
106. exp Epiglottitis/

107. epiglottitis.ti,ab.
108. Epiglottitis.ti,ab.
109. exp Tracheitis/
110. Tracheitis.ti,ab.
111. exp Influenza, Human/
112. influenza?.ti,ab.
113. flu?.ti,ab.
114. flue?.ti,ab.
115. grippe?.ti,ab.
116. pharyngalgia?.ti,ab.
117. pharyngeal pain?.ti,ab.
118. (pharyn* adj2 infection?).ti,ab.
119. (pharyn* adj2 inflammation?).ti,ab.
120. throat infection?.ti,ab.
121. strep* throat.ti,ab.
122. throat pain?.ti,ab.
123. throat ache?.ti,ab.
124. 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123
125. 82 and 124
126. exp Anti-Bacterial Agents/
127. antibiotic?.ti,ab.
128. antibacterial?.ti,ab.
129. anti?bacterial?.ti,ab.
130. antibiotic?.ti,ab.
131. antimycobacterial?.ti,ab.
132. anti?mycobacterial?.ti,ab.
133. bacteriocid*.ti,ab.
134. antibacter*.ti,ab.
135. exp Penicillins/
136. penicillin?.ti,ab.
137. exp Amoxicillin-Potassium Clavulanate Combination/ or exp Amoxicillin/
138. amoxicillin.ti,ab.
139. coamoxiclav*.ti,ab.
140. amoxi-Clavulanate.ti,ab.
141. amoxiClavulanate.ti,ab.
142. Co-Amoxiclav*.ti,ab.
143. exp Cephalosporins/
144. Cephalosporin*.ti,ab.
145. exp Ceftriaxone/
146. ceftriaxone.ti,ab.
147. exp Cefixime/
148. cefixime.ti,ab.
149. Azithromycin/
150. azitrocin.ti,ab.
151. Azit?romycin.ti,ab.
152. Cefotaxime/
153. cefotaxime.ti,ab.
154. exp Ampicillin/
155. ampicillin?.ti,ab.
156. Doxycycline/
157. doxycycline.ti,ab.
158. Cephalexin/
159. cephalixin.ti,ab.
160. Erythromycin/
161. erythromycin.ti,ab.
162. betalactam?.ti,ab.
163. beta?lactam?.ti,ab.

164. anti?biotic?.ti,ab.
165. 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133 or 134 or 135 or 136 or 137 or 138 or 139 or 140 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156 or 157 or 158 or 159 or 160 or 161 or 162 or 163 or 164
166. 125 and 165
167. exp Primary Health Care/
168. primary care.ti,ab.
169. primary health care.ti,ab.
170. physicians/ or general practitioners/ or physicians, family/ or physicians, primary care/
171. family physician?.ti,ab.
172. family doctor?.ti,ab.
173. general doctor?.ti,ab.
174. general physician?.ti,ab.
175. general practitioner?.ti,ab.
176. family practitioner?.ti,ab.
177. exp Family Practice/
178. family practice.ti,ab.
179. general practice.ti,ab.
180. General Practice/
181. first-line care?.ti,ab.
182. first line care?.ti,ab.
183. general medical practice.ti,ab.
184. GP?.ti,ab.
185. 167 or 168 or 169 or 170 or 171 or 172 or 173 or 174 or 175 or 176 or 177 or 178 or 179 or 180 or 181 or 182 or 183 or 184
186. 166 and 185

## Appendix 3

### Data extraction form

Reviewing details	Reviewer	
	Date of data extraction	
	Study Number	
	Study ID (First Author family name followed by publication year)	
Methods	Design (RCT, cluster RCT, quasi-experimental, CBA, ITS)	
	Country where the research took place	
	Unit of randomization (if applicable)	
	Number of sites, if applicable	
	Number of arms or groups (including control groups); briefly describe each	
	Inclusion criteria for participation in the study	
	Exclusion criteria for participation in study	
	Methods used to analysis data? Has any adjustment been used?	
Participants	Description (e.g. Patients/consumers; carers; parents of patients/consumers; health professionals; well people in the community)	
	Setting (e.g. Community, home, primary health centre, acute care hospital, extended care facility)	
	Age (Provide total, and group specific information)	
	Gender (% male/ %female)	
	Number of persons allocated to each arm?	
	Number of missing persons in each arm? Reasons?	
	Number of participants in each arm?	
Interventions	Intervention(s) name (Include a brief name or phrase that describes the intervention)	
	Intervention target (The intervention was delivered at patients, parents, community, public?)	
	How was the intervention(s) delivered? (face-to-face, by phone, mail, poster, leaflet, decision aid, in a consultation/educational session)	
	The content of intervention(s)	
	Co-interventions: Describe the delivery of any co-interventions	
	Who delivered the intervention?	
	Where was the intervention provided? (Describe the features of the setting (location) that might be relevant to intervention delivery)	
	How often intervention was provided?	
	Was the intervention modified or adapted during the study? (If such modifications happen, why, what, how and when the intervention was changed should be described.)	
	Assessment of fidelity (if intervention fidelity was assessed, describe the extent to which the intervention was delivered as intended.)	
	Description of control/usual care	
Outcomes	Primary outcome(s)	

	Method of assessing primary outcome measures e.g., phone survey, questionnaire	
	Primary outcome measurement time points	
	Secondary outcome(s)	
	Method of assessing secondary outcome measures e.g., phone survey, questionnaire	
	Secondary outcome measurement time points	
Results	The outcome for which the result is reported. (For each outcome, add another complete row for entering the results.)	
	Type of outcome (continuous or dichotomous)	
	Number of participants in control group	
	Baseline data in Control group	
	Post intervention data in control group	
	Change in control group (provide p-value or CI if available)	
	Number of participants in intervention group	
	Baseline data in intervention(s) group	
	Post intervention data in intervention(s) group	
	Change in intervention(s) group (provide p-value or CI if available)	
	Post-intervention comparison between intervention and control groups (Risk Difference, Odds Ratio, Risk ratio) (provide p-value or CI if available)	
	SMD (if available) (provide p-value or CI if available)	
	Notes	
	Risk of bias	Appendix 4

## Appendix 4

### Risk of bias assessment in RCT studies

Was the allocation sequence adequately generated?	
Was the allocation adequately concealed?	
Were baseline outcome measurements similar?	
Were baseline characteristics similar?	
Were incomplete outcome data adequately addressed?	
Was knowledge of the allocated interventions adequately prevented during the study?	
Was the study adequately protected against contamination?	
Was the study free from selective outcome reporting?	
Was the study free from other risks of bias?	

### Risk of bias assessment in ITS studies

Was the intervention independent of other changes?	
Was the shape of the intervention effect pre-specified?	
Was the intervention unlikely to affect data collection?	
Was knowledge of the allocated interventions adequately prevented during the study?	
Were incomplete outcome data adequately addressed?	
Was the study free from selective outcome reporting?	
Was the study free from other risks of bias?	

## Appendix 5

### Characteristics of included studies

<b>Alexandrino 2016</b>	
<b>Methods</b>	RCT, 2 arms <b>Study setting:</b> Portugal, 10 private daycare centers.
<b>Participants</b>	Caregivers (parents or legal tutors) of children aged up to 3 years old. <b>Number of participants:</b> 177
<b>Interventions</b>	Health Education Session (HES) about respiratory infections on the indicators of individual health and health care utilization of daycare children. The HES had a mean duration of 1 hour and 30 minutes. It covered the following five domains: prevention of ARI, first signs and symptoms of ARI, worsening signs of ARI, medication and nasal clearance techniques. The HES was conducted by a respiratory physiotherapist among small groups of 10–15 caregivers at the daycare centre. At the end of the HES, the participants received a small booklet with a summary of the information.
<b>Outcomes</b>	<b>Primary:</b> Impact of HES on the indicators of individual health and health care utilization (signs of respiratory infections, respiratory infections diagnosed by the child’s doctor, health care utilization of medical consultations, emergency services and/or antibiotics, absenteeism, nasal clearance techniques). <b>Secondary:</b> Association between the caregivers’ use of nasal clearance techniques and respiratory infections. • Antibiotic use was measured by filling a diary of records by participants.
<b>Notes</b>	<b>Funding:</b> none

<b>Arroll 2002</b>	
<b>Methods</b>	RCT, 2 arms <b>Study setting:</b> New Zealand, one family practice (15 physicians)
<b>Participants</b>	Patients presenting with the common cold who requested antibiotics or whose physicians thought they wanted them. For young children, the parents indicated whether or not they wanted antibiotics. <b>Number of participants:</b> 129
<b>Interventions</b>	Delayed antibiotic prescription: the Intervention group was given a prescription for antibiotics with instructions to fill it after 3 days if symptoms failed to improve.

<b>Outcomes</b>	<p><b>Primary:</b> Antibiotic use (taking at least one dose of antibiotic)</p> <p><b>Secondary:</b> Symptom score, satisfaction, patient's intention to visit a physician for the next cold, patients' beliefs on the effectiveness of antibiotics.</p> <ul style="list-style-type: none"> <li>• No details on measurement of antibiotic use.</li> </ul>
<b>Notes</b>	<b>Funding:</b> Health Research Council

<b>Francis 2009</b>	
<b>Methods</b>	Cluster RCT, 61 clusters, 2 arms <b>Study setting:</b> UK, general practices.
<b>Participants</b>	Children (6 months to 14 years) consulting with a respiratory tract infection (cough, cold, sore throat, earache for seven days or less) and their parents. <b>Number of participants:</b> 558
<b>Interventions</b>	Interactive booklet on respiratory tract infections. It consisted of eight pages on respiratory tract infections in children, designed to be used within the consultation and then provided to parents as a take home resource, to facilitate the use of certain communication skills, mainly exploring the parent's main concerns, asking about their expectations, and discussing prognosis, treatment options, and any reasons that should prompt re-consultation.
<b>Outcomes</b>	<p><b>Primary:</b> The proportion of children who attended a face-to-face consultation about the same illness during the two week follow-up period.</p> <p><b>Secondary:</b> Antibiotic prescribing, antibiotic consumption, future consulting intentions, and parental satisfaction, reassurance, and enablement.</p> <ul style="list-style-type: none"> <li>• Antibiotic use was measured by a telephone administered questionnaire with the child's parent or guardian.</li> </ul>
<b>Notes</b>	<b>Funding:</b> Medical Research Council and the Welsh Assembly Government in the form of a joint Health Services Fellowship for NF. Funding for the development of the training website was from an educational grant from Pfizer UK. The South-East Wales Trials Unit was funded by the Welsh Office for Research and Development. This study was sponsored by Cardiff University.

<b>Lambert 2007</b>	
<b>Methods</b>	ITS <b>Study setting:</b> UK, a single geographical population in the North East of England.
<b>Participants</b>	People of the community
<b>Interventions</b>	Mass media education. A regional mass media campaign used in two consecutive years. It was led by a cartoon character called 'Moxy Malone'

	<p>who was developed specifically for this regional campaign. The character was given dialogue that included simple messages ‘facts’ and ‘fictions’ about the effects of antimicrobials, and about the availability of community pharmacists to support self-care for the management of usually self limiting health problems. These messages were drawn together under the title of ‘Antibiotics- tracking down the truth’, which appeared as a short cartoon strip, with supporting leaflets and posters. In addition, the campaign received editorial coverage from local newspapers, TV and radio. In both years, advertisements were run on local radio with posters on buses and local Metro system. Printed materials (leaflets and posters) were made available to GP surgeries throughout the target area. In the second phase, regional television advertising was added, with the same artwork and character.</p> <ul style="list-style-type: none"> <li>• The timing of the campaigns was chosen to coincide with the annual peak in consultations for respiratory infections.</li> </ul>
<b>Outcomes</b>	<p><b>Primary:</b> Prescribing rates prescribing rates (items) for all microbial agents.</p> <p><b>Secondary:</b> Analysing factors that had a possible effect on the prescribing of antibacterial drugs.</p> <ul style="list-style-type: none"> <li>• The volumes prescribed were derived from the Prescription Pricing Authority database.</li> </ul>
<b>Notes</b>	<ul style="list-style-type: none"> <li>• The Moxy Malone campaign was not the only intervention being used to tackle inappropriate antimicrobial prescribing at this time. The undocumented co-interventions may have affected the results.</li> </ul> <p><b>Funding:</b> None.</p>

<b>Lee 2017</b>	
<b>Methods</b>	<p>RCT, 2 arms</p> <p><b>Study setting:</b> Singapore, primary care setting.</p>
<b>Participants</b>	<p>Patients aged 21 years and above, presenting with at least one of four URTI symptoms (runny nose, blocked nose, cough or sore throat) for seven days or less.</p> <p><b>Number of participants:</b> 914</p>
<b>Interventions</b>	<p>Patients in the intervention arm were educated verbally and by using pamphlets on causes of URTIs and when antibiotics are appropriate to treat URTIs. The intervention pamphlets and counselling scripts specifically addressed key misconceptions identified in the previous study of URTI patients at local primary care clinics.</p>
<b>Outcomes</b>	<p><b>Primary:</b> The proportion of patients in each arm prescribed antibiotics.</p> <p><b>Secondary:</b> Patients’ agreement on a 4-point scale to the following three statements: that the education had improved their understanding about causes of</p>

	<p>URTI, that they were worried about the side effects of antibiotics, and that antibiotics are not needed most of the time for URTI.</p> <ul style="list-style-type: none"> <li>• Antibiotic prescription was measured by an interviewer-assisted post-consultation questionnaire.</li> </ul>
<b>Notes</b>	<b>Funding:</b> Saw Swee Hock School of Public Health.

<b>Little 1997</b>	
<b>Methods</b>	<p>RCT, 3 arms.</p> <p><b>Study setting:</b> UK, general practices.</p>
<b>Participants</b>	<p>Patients aged 4 years and over with sore throat and an abnormal physical sign in the throat;</p> <p><b>Number of participants:</b> 716</p>
<b>Interventions</b>	<p>Intervention group 1: no antibiotics.</p> <p>Intervention group 2: patients were offered antibiotics, but the patient could collect the prescription from the surgery if symptoms were not starting to settle within three days.</p>
<b>Outcomes</b>	<p><b>Primary:</b> Antibiotic use.</p> <p><b>Secondary:</b> Duration of antibiotic use, resolution of symptoms, believe that antibiotics were effective, intention to consult in future episodes, satisfaction, time off school or work.</p> <ul style="list-style-type: none"> <li>• Antibiotic use was measured by filling a daily diary by participants and a doctors' documentation sheet.</li> </ul>
<b>Notes</b>	<b>Funding:</b> This work was supported by Wessex NHS regional research and development funds. One of the authors was supported by the Wellcome Trust.

<b>Little 2001</b>	
<b>Methods</b>	<p>RCT, 2 arms.</p> <p><b>Study setting:</b> UK, general practices.</p>
<b>Participants</b>	<p>Children aged 6 months to 10 years, who attended their doctor with acute otalgia and otoscopic evidence of acute inflammation of the ear drum (dullness or cloudiness with erythema, bulging, or perforation).</p> <p><b>Number of participants:</b> 315</p>
<b>Interventions</b>	<p>Delayed treatment with antibiotics. Parents were asked to wait for 72 hours after seeing the doctor before considering using the prescription.</p> <p>Parents were instructed that if their child still had substantial otalgia or fever after the 72 hours or was not starting to get better then they should come and collect the prescription for antibiotics, which was left at the practice's reception.</p>
<b>Outcomes</b>	<p><b>Primary:</b> Use and collection of antibiotic prescriptions.</p> <p><b>Secondary:</b></p>

	<p>Symptoms resolution and analgesia use, absence from school or nursery, satisfaction, belief that antibiotics are very effective, intention to consult doctor in future, side effects.</p> <ul style="list-style-type: none"> <li>Antibiotic use was measured by filling a daily diary by participants and a doctors' documentation sheet.</li> </ul>
<b>Notes</b>	<b>Funding:</b> NHS Research and Development (South West and South East Regions). One of the authors was supported by the Medical Research Council.

<b>Little 2014</b>	
<b>Methods</b>	RCT, 5 arms. <b>Study setting:</b> UK, primary care setting.
<b>Participants</b>	Patients aged 3 years and over with a respiratory tract infection diagnosed by the health professional. <b>Number of participants:</b> 556
<b>Interventions</b>	Intervention groups: 1) Patient led: the patient was given antibiotics and asked to wait to use them. 2) Post-dating: the patient was given antibiotics, but post dated. 3) Collection: patients were given instructions to wait but could request antibiotics from front desk. 4) Re-contact/phone: patients were asked to contact/phone the surgery to leave message for doctor/nurse to request antibiotics and they were able to come to reception. 5) No offer of prescription but a clinical review for worsening symptoms.
<b>Outcomes</b>	<b>Primary:</b> Symptom severity. <b>Secondary:</b> Any antibiotic use in the 14 days after recruitment, side effects, mean temperature, duration of symptoms, return with new or worsening symptoms or complications of intervention, belief in the effectiveness of antibiotics and satisfaction. <ul style="list-style-type: none"> <li>Antibiotic use was measured by filling a diary by participants.</li> </ul>
<b>Notes</b>	<ul style="list-style-type: none"> <li>A non-randomised group was added later in the study that received immediate prescription of antibiotics.</li> </ul> <b>Funding:</b> It was funded by the National Institute for Health Research under its Programme Grants for Applied Research programme.

<b>Little 2016</b>	
<b>Methods</b>	RCT, 2 arms. <b>Study setting:</b> UK, primary care setting.
<b>Participants</b>	Adult patients (aged 18+ years). <b>Number of participants:</b> 2923
<b>Interventions</b>	Interactive website providing tailored advice. It was reinforced by email prompts and reminders to use the website; patients were given information

	<p>about the natural history, self-care advice and advice about the use of over-the-counter medication.</p> <p>Participants had access to the website for 20 weeks. On logging onto the website, users could select tailored advice on (1) whether and why they need/do not need to consult the GP and (2) how to self-care for RTIs. Patients selecting consultation advice completed questions about their symptoms and medical history, and were then presented with tailored advice recommending either self-management (for mild symptoms), for more severe symptoms phoning the ‘NHS Direct’ helpline, which provided nurse-led advice about the need to seek further medical help, or alternatively, seeking medical attention. Patients were given the opportunity to challenge this advice by selecting further in-depth information.</p>
<b>Outcomes</b>	<p><b>Primary:</b> General practitioner consultation.</p> <p><b>Secondary:</b> The use of antibiotics, contacting NHS Direct for phone-based advice, the duration of symptoms, the number of days where work/normal activities were impaired, re-consultation, hospitalization.</p> <ul style="list-style-type: none"> <li>• The use of antibiotics was documented as prescription of antibiotics, from patient records.</li> </ul>
<b>Notes</b>	<p><b>Funding:</b> This study was funded by the National Institute for Health Research Programme Grants for Applied Research programme.</p>

<b>Mainous 2000</b>	
<b>Methods</b>	<p>Cluster RCT, 4 clusters, 4 arms.</p> <p><b>Study setting:</b> USA, primary care setting.</p>
<b>Participants</b>	<p>Primary care physicians managing paediatric respiratory infections. Patients aged less than 18 years old who were diagnosed with respiratory tract infections.</p> <p><b>Number of participants:</b> 269 physicians (115 in patient education group and control groups)</p>
<b>Interventions</b>	<p>There were three intervention groups: 1) Performance feedback about antibiotic prescribing, 2) patient education materials about antibiotic use, and 3) both feedback and education materials.</p> <p>The patient education intervention consisted of a letter without information on costs and profiling and patient education pamphlets, “Your Child and Antibiotics.” The pamphlets were produced in 1997 by the American Academy of Paediatrics with co-sponsorship by the Centers for Disease Control and Prevention (CDC) and the American Society for Microbiology.</p>
<b>Outcomes</b>	<p><b>Primary:</b> Change in antibiotic prescribing.</p>

	<p><b>Secondary:</b> Comparison of diagnosis before and after the intervention.</p> <ul style="list-style-type: none"> <li>• Antibiotic prescribing was measured by using Medicaid drug claims.</li> </ul>
<b>Notes</b>	<ul style="list-style-type: none"> <li>• The outcome (antibiotic prescription) was reported for episodes of care, defined as one patient-physician consultation. A patient could have more than one consultation per disease. So, counting on episodes of care instead of patients or episodes of disease, may have introduced some issues on unit of analysis.</li> <li>• There was no information on cluster size or adjustments for the effect of clustering in the study.</li> </ul> <p><b>Funding:</b> Department of Public Health, Commonwealth of Kentucky.</p>

<b>Pshetizky 2003</b>	
<b>Methods</b>	<p>RCT, 2 arms. <b>Study setting:</b> Israel, primary care setting.</p>
<b>Participants</b>	<p>Parents of children aged 3 months to 4 years diagnosed with acute otitis media (AOM). <b>Number of participants:</b> 81</p>
<b>Interventions</b>	<p>The intervention group received a structured explanation and a prescription for antibiotics to be used if symptoms did not improve within 48 h.</p> <p>The explanation was short and included the following points: AOM is part of an upper respiratory tract infection, it has been well established that in most cases children will recover regardless of antibiotic prescription, dangerous late complications from AOM unfortunately may occur regardless of whether antibiotics were or were not delivered in the course of the acute illness, and parents were recommended in cases of high fever or severe pain to administer Paracetamol prescribed according to the child's weight.</p>
<b>Outcomes</b>	<p><b>Primary:</b> Antibiotic use</p> <p><b>Secondary:</b> Taking antibiotic on first day, association between administration of antibiotics and other variables.</p> <ul style="list-style-type: none"> <li>• Antibiotic use was measured by interviewing the parents by phone using a structured questionnaire by a blinded interviewer.</li> </ul>
<b>Notes</b>	<ul style="list-style-type: none"> <li>• The numbers of events reported were different from the reported percentages.</li> </ul> <p><b>Funding:</b> Not reported.</p>

<b>Poza Abad 2016</b>	
<b>Methods</b>	<p>RCT, 4 arms. <b>Study setting:</b> Spain, primary care setting.</p>

<b>Participants</b>	<p>Patients were older than 18 years and had 1 of the following acute, uncomplicated respiratory infections: acute pharyngitis, rhinosinusitis, acute bronchitis, or exacerbation of mild-to-moderate chronic obstructive pulmonary disease (COPD). In all cases, the physician had reasonable doubt as to whether to treat with an antibiotic.</p> <p><b>Number of participants:</b> 398</p>
<b>Interventions</b>	<p>There were three intervention groups:</p> <p>1) Delayed patient-led prescription strategy (given an antibiotic at first consultation), 2) delayed prescription collection strategy requiring patients to collect their prescription from the primary care reception desk 3 days after the first consultation, and 3) no antibiotic strategy.</p> <p>Delayed prescription strategies consisted of prescribing an antibiotic to take only if the symptoms worsened or if there was no improvement several days after the medical visit (If they noted no improvement after 5 days (in cases of pharyngitis) or after 10 days (in cases of other infections).</p>
<b>Outcomes</b>	<p><b>Primary:</b> Duration and severity of symptoms.</p> <p><b>Secondary:</b> Antibiotic use, satisfaction with health care, belief in the effectiveness of antibiotics, absenteeism, risk of complications, risk of need for unscheduled health care.</p> <ul style="list-style-type: none"> <li>• Antibiotic use was measured by asking patients by phone or in the follow up visit.</li> </ul>
<b>Notes</b>	<p><b>Funding:</b> The study was sponsored through a governmental grant of the Instituto de Salud Carlos III, Spanish Ministry of Health. One of the authors reported a grant from the Jordi Gol i Gurina Foundation for a research stage at the University of Cardiff in 2013, as well as research grants from the European Commission, Catalan Society of Family Medicine, and Instituto de Salud Carlos III. One of the authors was funded by a Miguel Servet research contract from the Instituto de Salud Carlos.</p>

<b>Taylor 2005</b>	
<b>Methods</b>	<p>RCT, 2 arms.</p> <p><b>Study setting:</b> USA, primary care setting.</p>
<b>Participants</b>	<p>Healthy children younger than 24 months old, seen in the offices of primary care paediatricians. Children and their parents were recruited for the study.</p> <p><b>Number of participants:</b> 499</p>
<b>Interventions</b>	<p>Parental education promoting the judicious use of antibiotics. Parents assigned to the intervention group received a copy of the educational pamphlet, "Your Child and Antibiotics," developed by the American Academy of Paediatrics, Centers for Disease Control and Prevention and the American Society of Microbiology, and a video in which the main points discussed in the pamphlet were reinforced. The video, which was</p>

	professionally produced and ran for 5 minutes, featured one of the physicians from the study child's paediatric practice. Additional copies of "Your Child and Antibiotics," were mailed to parents of study children at 6 weeks and 6 months after enrolment.
<b>Outcomes</b>	<p><b>Primary:</b> Number of diagnoses of otitis media and sinusitis per study child, number of visits per child for which antibiotics (oral or intramuscular) were prescribed for a diagnosis of otitis media, number of visits per child for which antibiotics were prescribed for a diagnosis of otitis media and/or sinusitis and total number of antibiotics prescribed per child.</p> <p><b>Secondary:</b> Total number of visits per study patient and number of visits for URI symptoms per child.</p> <ul style="list-style-type: none"> <li>• Antibiotic prescription was measured by checking patients' medical records.</li> </ul>
<b>Notes</b>	<b>Funding:</b> The study was supported by GlaxoSmithKline in conjunction with the Aetna Foundation's Quality Care Research Fund.

<b>Worrall 2010</b>	
<b>Methods</b>	RCT, 2 arms. <b>Study setting:</b> Canada, primary care setting.
<b>Participants</b>	Adult patients (aged 18 years or older) with acute upper respiratory tract infections for whom the clinicians thought antibiotic treatment might not be necessary. <b>Number of participants:</b> 149.
<b>Interventions</b>	Post-dated delayed antibiotic prescription. A delayed prescription dated for 2 days later. The patient was asked to use the prescription only if symptoms had not improved or had worsened after 2 days.
<b>Outcomes</b>	<p><b>Primary:</b> Filling the prescription by the patients.</p> <p><b>Secondary:</b> The time it took for the patients to fill the prescriptions, the number of early filling (within 2 days), and the reasons given to the pharmacist by patients who filled their delayed prescriptions early. Filling the prescription was measured by contacting the pharmacies.</p>
<b>Notes</b>	<b>Funding:</b> Not reported.

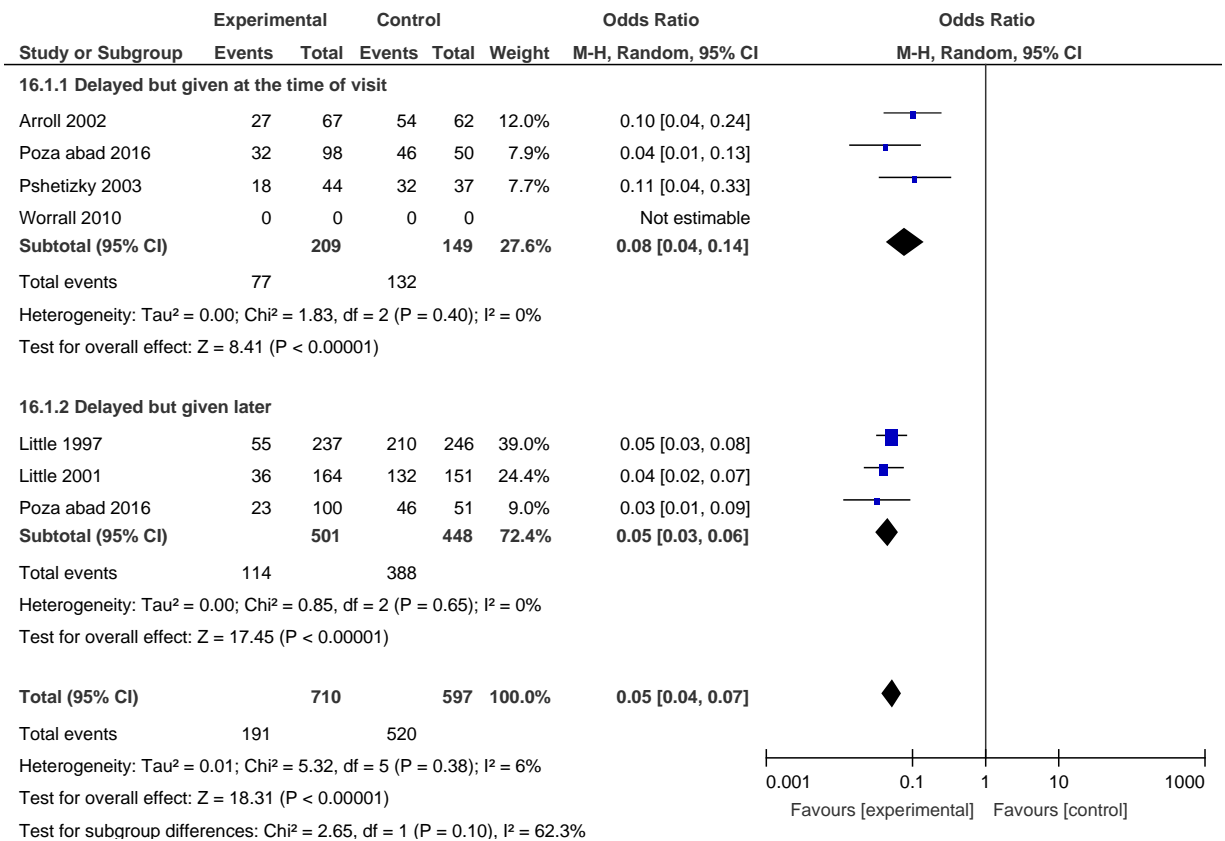
## Appendix 6

### Excluded studies and reasons for exclusion

<b>Study</b>	<b>Year</b>	<b>Reason for exclusion</b>
Belongia et al.(52)	2005	ITS: insufficient number of observations.
Cebotarenco et al. (53)	2008	CBA: Only one site.
Dowel et al.(54)	2001	The primary outcome was reported only in the intervention group.
Flottorp et al.(55)	2002	Multifaceted intervention: not possible to disentangle the effects of patient-oriented interventions.
Grover et al.(16)	2013	Before after study without a control group.
LeBlanc et al.(56)	2011	Multifaceted intervention: not possible to disentangle the effects of patient-oriented interventions.
Llor et al.(57)	2014	Multifaceted intervention: not possible to disentangle the effects of patient-oriented interventions.
Malmvall et al.(58)	2007	Multifaceted intervention: not possible to disentangle the effects of patient-oriented interventions.
McNulty et al.(59)	2010	CBA: Only one site.
Meeker et al.(60)	2014	Multifaceted intervention: not possible to disentangle the effects of patient-oriented interventions.
Plachouras et al. (61)	2014	Multifaceted intervention: not possible to disentangle the effects of patient-oriented interventions.
Rubin et al.(62)	2005	CBA: Only one site.
Sabuncu et al.(63)	2009	ITS: insufficient number of observations.
Welschen et al.(64)	2004	Multifaceted intervention: not possible to disentangle the effects of patient-oriented interventions.

## Appendix 7

### Forest plot of comparing antibiotic use between intervention and control groups after deleting the Worrall et al. Study (sensitivity analysis)



## Chapter 3

# Understanding determinants of patients' decisions to attend their family physician and to take antibiotics for upper respiratory tract infections-a qualitative descriptive study

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## **Authors' contribution**

**Sameh Mortazhejri (SM)**, developed the research protocol, completed the research ethics board applications, developed the interview guide, recruited participants, provided information to the participants and got their consent for participation, conducted all the interviews, coded the interviews, analysed the data and prepared the manuscript.

**Andrea Patey (AP)**, provided guidance and revisions on all parts of the project, helped in developing the interview guide, coded the interviews, supervised the analysis of the data and reviewed drafts of the manuscript.

**Dawn Stacey**, helped with the development of the proposal, provided comments and guidance on conducting the project and data analysis and reviewed drafts of the manuscript.

**Sacha Bhatia**, helped with the development of the proposal, provided comments and guidance on conducting the project and data analysis and reviewed drafts of the manuscript.

**Alykhan Abdulla (AA)**, helped in recruiting the participants, provided comments and guidance on conducting the project and reviewed drafts of the manuscript.

**Jeremy M. Grimshaw**, provided guidance on planning the research, supervised all parts of the project and reviewed drafts of the manuscript.

All the authors approved the final version.

## **Abstract**

**Background:** Although antibiotics have little or no benefit for most upper respiratory tract infections (URTIs), they continue to be prescribed frequently. Physicians perceive that patients' expectations influence their antibiotic prescribing practice; however, not all patients seek treatment despite similar symptoms. In this study, we aimed to explore patients' views about URTIs and identify ways they manage them (including attendance in primary care and taking antibiotics). We used the Common Sense-Self-Regulation Model (CS-SRM) of illness to explore how patients' cognitive factors affect their illness management.

**Methods:** Using a qualitative descriptive study design, adult English-speaking individuals at a Canadian health center were recruited and interviewed using semi-structured interviews based on CS-SRM. Sampling continued until saturation was achieved. The interviews were transcribed verbatim and coded by two coders according to CS-SRM dimensions (cognitive and emotional illness representations, coping strategies).

**Results:** In total 15 individuals (six females, nine males) between the ages of 18 and 69 years old were interviewed. Regarding cognitive illness representations, participants had a good knowledge about the symptoms of URTIs, prevention and controlling the symptoms. However, participants revealed some misconceptions about the causes of URTIs and expected timelines for cough to resolve. With respect to emotional illness representations, parents felt more concerned when their children showed the symptoms, especially if they could not control the fever. As regards to coping strategies, almost all participants mentioned that they only visited their doctor if their symptoms got progressively worse and they could no longer self-manage URTI symptoms. When

visiting a doctor, most participants reported that they expected to receive an examination and an explanation for their symptoms. Generally, participants believed that there was no need for antibiotics for URTIs.

**Discussion:** Our participants reported good knowledge regarding the likely lack of benefit from antibiotics for URTIs. The results suggest a discrepancy between our participants' reported reasons for visiting doctors and doctors' perceptions about patients' reason for their visit identified in previous studies. Focusing on interventions that facilitate the communication between patients and doctors, instead of providing more education to public may help in reducing the use of unnecessary antibiotics.

## Background

Upper respiratory tract symptoms are one of the commonest reasons to visit a doctor, but not all patients with similar symptoms attend their doctor. Variation in illness behaviour (i.e. the way people perceive their symptoms and evaluate and act on them) of different individuals may account for some of this diversity (1, 2).

Many primary care visits by patients with upper respiratory tract infections (URTIs) result in antibiotic prescription (3, 4). Patients' expectations or doctors' perceptions of those expectations may affect doctors' behaviours. Physicians are more likely to prescribe antibiotics if they believe that their patients expect them (5, 6). There is some evidence that some patients put pressure on their doctors to prescribe antibiotics directly by asking them or indirectly by the way they present their chief complaints (7, 8). Furthermore, studies report that physicians assume that prescribing antibiotics will lead to more satisfaction in patients (7, 9, 10). However, physicians' perceptions about their patients' wishes do not always reflect the reality (5, 10, 11, 12).

With easy access to the internet and mass media, patients are taking a more active role and are making decisions for their own healthcare (9). However, some studies report that there are still some misconceptions about the effectiveness of antibiotics for URTIs among patients (13, 14). For example, a cross sectional study on 50 years or older adults presenting to primary care clinics in Ontario reported that only 44% of participants were aware that antibiotics are not necessary to treat sinus infections (15). It should be noted that the patient sample was biased towards highly educated individuals. Therefore the results may not be generalizable to the broader population (15) and hence may have overestimated the proportion of the general population that are aware that antibiotics may not be helpful in sinusitis (and other URTIs).

To investigate individuals' expectations and beliefs in a theory based and systematic manner, we chose the Common Sense-Self-Regulation Model of illness (CS-SRM) (16) to help us understand patients' perceptions toward managing URTIs.

## **Self-Regulation Model**

Social cognitive models can help us understand factors that may influence patients' health-related behaviors (17). The CS-SRM is a model which attempts to explain patients' illness-related behaviors and provides a framework to address how individuals' perceptions and beliefs about an illness influence their behaviors toward that illness. This model can help us understand why some patients with URTIs go to doctors and ask for antibiotics, while the others prefer to manage it themselves (16).

According to CS-SRM, people develop beliefs and emotions about their illnesses (illness representations) relating to two major categories: 1) *cognitive illness representations*, and 2) *emotional illness representations*. Cognitive illness representations can be further categorized into the following dimensions (16, 18, 19):

- 1) **Identity:** represents the beliefs about a label for the disease and knowledge of the symptoms associated with it.
- 2) **Cause:** represents the beliefs regarding the factor(s) that lead to disease.
- 3) **Timeline:** represents the beliefs about the duration of the illness.
- 4) **Consequences:** represents the beliefs regarding the short-term and long-term effects of the disease on the quality of life or physical function of the person.

5) **Curability/controllability**: represents the beliefs regarding the factors that help the person to recover from or get over the illness.

Some studies have also added a sixth dimension: **prevention**, which represents the beliefs regarding the factors that help a person to prevent an illness attack (20).

These illness representations (cognitive and emotional representations) influence individuals' health behaviors toward an illness (18). Individuals develop a strategy or set of strategies to cope with those illness representations. These strategies are called action plans or coping strategies (16, 20). Coping strategies are often appraised and updated repeatedly by the individuals. People evaluate their coping strategies based on success or failure in dealing with previous episodes of an illness. Each new experience is accompanied by new information from other sources such as cultural knowledge of an illness (e.g. from media) or significant authorities like parents or doctors, resulting in the development of new illness representations. These new representations will consequently lead to new sets of coping strategies. The model is dynamic and is based on continuous feedback between different elements (16, 20). Lau et al. showed that patients with the same illness can have different illness cognitions (based on illness representations) and that these may lead to different reasons for doctor visits. This means that two different patients with the same disease can experience the disease and act differently according to their perceived illness representations (2).

The CS-SRM has mainly been applied to understand patients' illness perceptions and self-management of chronic diseases such as diabetes, Alzheimer's Disease, epilepsy, asthma (21, 22, 23, 24). While URTIs have an acute course and are typically resolved within a few days, people can experience URTIs many times during their lifetime. Therefore, using CS-SRM to understand

patients' perceptions about URTIs and their coping strategies to future URTIs may prove insightful.

In this study, we aimed to understand how individuals perceived URTIs and how their perceptions influenced their management of these URTIs. The specific objectives were:

- 1) To explore individuals' views about URTIs (including causes, treatments, prevention)
- 2) To identify the ways in which individuals manage their URTIs (including the role of self-management, primary care consultation and antibiotic use).

## **Methods**

A qualitative descriptive study using semi-structured interviews based on CS-SRM was conducted.

### **Identification of participants**

Adult English-speaking individuals with or without symptoms of URTIs presenting to a mixed urban/rural family practice in the Champlain LHIN, Ontario, Canada were eligible to participate in this study. Individuals who could not speak English, or had severe pain or illness were excluded. Individuals younger than 18 years old were also excluded.

AA identified eligible individuals and gave them a postcard with study information and the contact information (email and phone number) of the researcher (SM). Individuals willing to be interviewed were asked to meet with the researcher who was available in the clinic. The researcher provided further information about the aims and procedures of the study and sought contact from interested individuals. If individuals indicated interest, the researcher provided them with an information sheet (Appendix 1) and a consent form (Appendix 2). The information sheet stressed

that participation was voluntary and would not affect the care they would receive during their current or future visits. Participants were also informed that they could withdraw from the study at any time. Once written consent was received, a telephone interview was scheduled for a time convenient for participants.

### **Interview schedule**

The interview guide was designed in collaboration with a health psychologist with expertise in behavioural theories (AP). It included demographic questions about gender, age and level of education, as well as open-ended questions related to individuals' experiences with URTIs which were based on CS-SRM dimensions (Appendix 3). Prior to the main study, the interview guide was piloted with three individuals to ensure all dimensions of the CS-SRM were adequately covered and questions were clear for participants.

### **Interview procedure**

All interviews were conducted by one researcher (SM) and lasted for a maximum duration of 30 minutes. At the start of the interview, confirmatory verbal consent was sought for participation and recording of the interview. Participants were informed that they could skip a question if they felt uncomfortable answering it and that they could stop the interview anytime if they were no longer willing to participate in the study. Participants were reminded that there is no right or wrong answer to the questions, so they feel comfortable to share their beliefs or experiences. SM also explained the definition of URTIs to the participants. Recruitment of interview participants continued until saturation was achieved (i.e. until three consecutive interviews did not add additional concepts/ideas) (25).

## Data analysis

Interviews were transcribed verbatim and anonymised. Two coders (SM, AP) independently reviewed the interview transcripts and coded them using NVivo 10 software. The CS-SRM dimensions provided an initial coding scheme to identify the key concepts. Illness representations were coded in two major categories: *cognitive* and *emotional*. The cognitive illness representations were subcategorized into **identity, timeline, cause, consequences, curability/controllability and prevention**. Since coping strategies are not specified in the CS-SRM, the coders developed different subcategories of these strategies by reviewing all the transcripts. This resulted in identifying four major subcategories: 1) visiting doctor, 2) using antibiotics, 3) problem-focused coping and 4) self-treatment. Sources of information was added as a sub-theme to all groups if applicable, to understand what sources of information were used to help the individual to develop that specific perception or behaviour. The coders met after coding the first transcript to compare their results and develop a uniform scheme for coding the quotes. Any disagreements were discussed and resolved through consensus.

## Ethics

The study was approved by the Ottawa Health Science Network Research Ethics (OHSN-REB# 20170829-01H).

## Results

Fifteen individuals (six females, nine males) were interviewed by phone, of whom four were parents of dependent children. The interviews took between six and 36 minutes. The participants

were between 18 and 69 years old. The highest level of education was high school in five individuals, community college in four individuals and university education in six individuals.

The reliability between the two coders was assessed by an inter-rater reliability coefficient (kappa score). The kappa score ranged between 0.23 (for prevention) and 1.00. However, in 85% of the coding, the Kappa score was higher or equal to 0.8. Discrepancies between coders' initial coding were discussed and consensus was reached for all interviews.

## **Cognitive illness representations**

**Identity** When asked about their symptoms of URTIs, participants often described cough, runny or stuffed nose, post-nasal drip, sore throat, headaches and body aches. Many participants also noted that symptoms tended to be mild, although occasionally more severe symptoms (e.g. prolonged cough) could occur. One individual believed that the URTI symptoms were changing over time and that URTIs now lasted longer than before.

**Timeline** Most participants noted that they usually experienced URTIs at least once a year. There were a few participants that reported having URTIs more (two to three times a year) or less (every three to four years) often. Participants reported that the symptoms would typically last between three to 14 days; however, one individual stated that the cough often lasted for a couple of months.

**Cause** A variety of causes were mentioned by participants; close contacts with sick people at public places or kids at school, low immune system or being more susceptible, not washing the hands (especially after touching door knobs or flushing the toilet), not eating healthy or drinking enough water, season changing, cold weather and stress.

P7: *“So it was end of the year, a very stressful time period for me, so everything went up in the air and so just my body said OK enough, I can’t deal with this, you’re going down now.”*

Viruses and bacteria were stated as cause only by three people. Three participants declared that they really did not know what causes these kinds of infections.

P6: *“Maybe your immune system’s low or, bad bacteria in your system or ... it’s just I don’t know anything causes it.”*

**Consequences** The major concerns voiced by many of the participants were not being able to sleep or work. Other consequences mentioned included cough, body aches, being tired and low energy and difficulty in breathing. Another negative consequence of URTIs was not being able to see friends or enjoy trips when travelling. One participant who had a history of bronchitis was afraid that the URTI would turn into pneumonia or bronchitis.

P1: *“The most area it affects you is the mobility to go under full speed and, you know, to work.”*

**Curability/controllability** Most of the participants believed that URTIs would last for a period of time (i.e. a few days), eventually go away on their own and that there was no need for antibiotics or serious medications. Some individuals used over the counter (OTC) medications or home remedies to control the symptoms.

P11: *“You just have to put up with it because you know it’s gonna take its time and then it’s gonna get better.”*

P7: *“A cold cannot be treated by any modern medicine. All you can do is control the symptoms so that you don’t feel like you’re dying.”*

One of the participants described their cough as uncontrollable. Another participant rationalised the use of antibiotics to manage URTIs:

P1: *“I don’t really know, because bacteria needs to be treated by the antibiotics so, you know, probably there is no other way except for antibiotics.”*

**Prevention** Washing hands and staying away from sick people were primarily reported as ways of avoiding URTIs. In addition, eating healthy food and drinking lots of fluid, taking vitamins, proper sleep and being active were considered major preventative measures for URTIs by most participants. Taking flu shots, staying warm, taking raw garlic, and wiping things with alcohol were also mentioned by a few numbers of participants.

However, one participant was strongly insistent on the importance of knowledge.

P7: *“Knowledge, knowledge is the big one. Knowing what can and cannot cause it. Knowing what can prevent it. Knowing what you shouldn’t be doing; i.e. going to work and spreading it around things like that. Having that knowledge and following through with the knowledge is, I think at this point in time the best prevention.”*

### **Participants’ sources of information regarding cognitive illness representations**

Sources of information on the **Cause** of URTIs were discussed in six interviews; life experience of having previous episodes of the disease, television, internet and family members who worked as doctors or nurses were the main identified sources.

P11: *“I’m 72 years old. I have a lot of experience in life. I have all kinds of other situations I’ve been dealing with. It started when I was a kid. My mum, you know, used to tell me about how to take care of things.”*

P7: *“I’m familiar enough with my body. I’m comfortable enough knowing what I can and cannot fight off on my own.”*

Sources of information on **Curability/controllability** of URTIs were mentioned in two interviews; one individual said she used the methods that her mother used to apply to deal with URTIs for herself and her kids and preferred not look things up online. Another participant found booklets in doctors’ offices helpful for this matter.

### **Emotional illness representations**

The majority of the emotional illness representations centered around fear of the URTIs becoming something more severe. Parents felt more concerned when their children showed the symptoms. One of them found the infections very terrifying, especially if the symptoms were not manageable.

P1: *“If the fever is not manageable, if I can’t manage with Tylenol or Ibuprofen, I am afraid. You know, I don’t want to wait. I don’t want to be at night, no, no, no.”*

One of the participants called these infections irritating and noted changes in their management as they age.

P5: *“I guess as I get older, things get tougher to fight off.”*

### **Coping strategies**

Participants reported a number of coping strategies that they used to manage URTIs (See Table 1). These included self-treatment, problem-focused coping, visiting the doctor and using antibiotics.

**Self-treatment**: The majority of participants stated that they try to manage the symptoms by themselves, especially for the first few days of the disease or when the disease is not very severe.

OTC medications such as Acetaminophen, Ibuprofen, cough drops or tablets, cough syrups, Echinacea and nasal drops were widely used. The medications were applied as soon as the participants felt the symptoms.

**Visiting doctor** Almost all participants (14 individuals) mentioned that they did not routinely visit a doctor because of an URTI or at least not for the mild ones. They tried to manage it themselves. But they would consider going to doctor if the symptoms got worse, lasted longer than a few days (three to seven days, depending on the individual), if they had a high fever or problems breathing or swallowing. A few participants considered green secretions from nose or throat as a sign of getting worse.

P11: *“But if it goes into the chest, you know, like that was long, long time ago. You feel it starts to go to the chest, you start to cough or maybe green stuff is coming out of your nose then, then that’s when I go and see a doctor and ask for antibiotic.”*

P14: *“If it’s green and it’s hung on for a couple of days then I’ll take my kids to see the doctor.”*

A few participants insisted that they usually did not go to the doctor, unless they suspected a more serious illness.

P7: *“If I’m going to the doctor there is something there definitely.”*

Only one of the participants stated that she preferred to go to doctor sooner than later, especially if she felt that it was not an ordinary infection. Participants were more concerned when it came to their children; they would take them to the doctor soon after the symptoms appeared or would wait for a maximum of two days before taking them to doctor. One individual mentioned that if she could not manage her children’s fever with OTC medications, she would take them to the doctor.

The participants who did not consider going to doctor, identified different reasons for not going. Some believed it is a waste of time or money. One individual mentioned not having access to her doctor as the main reason for not going to the doctor.

P6: *“You don’t need a doctor to tell you if you have a sore throat or go get throat lozenges.”*

When visiting a doctor because of URTI, participants’ expectations varied from receiving a physical examination (including listening to their lungs), to seeking a prescription for an inhaler or puffer for their cough (Table 1). Most participants stated that they trusted their doctors and accepted their opinions; only one individual mentioned that he would seek a second opinion if his symptoms were unbearable.

**Problem-focused coping** There were a number of specific problems that would take the participants with URTIs to the doctors. These included: getting a refill for an inhaler/puffer for the cough, asking if antibiotics were needed in case of green secretions from nose or throat, having difficulty managing the fever with Acetaminophen/Ibuprofen and a long-lasting cough. All these participants mentioned that otherwise they would manage URTIs themselves without going to a doctor.

**Using antibiotics** Most participants stated that they did not use antibiotics for URTIs and they believed that antibiotics were not needed for URTIs. Some individuals mentioned that they would ask for antibiotics if the infection got into their chest or if their symptoms were unbearable, especially for their children. However, they stated that at the end they would accept the doctors’ opinions even if the doctors did not prescribe antibiotics. Only one individual revealed that he used leftover antibiotics from previous episodes.

Reasons for not using antibiotics for URTIs included concerns around bacterial resistance (mentioned by five individuals) and the fact that the antibiotics kill the good stuff in the gut (four individuals).

P4: *“Not everything requires an antibiotic. Too many being prescribed, too many antibiotics on several occasions each year, you’re growing a resistance to them.”*

P15: *“The more that people use them (antibiotics), the more the bugs are gonna get resistant which is probably a huge issue in the broad spectrum the next 20 years. It’s gonna be an enormous problem.”*

P13: *“If you take too many (antibiotics), it’s not good. Because it strips your good bacteria from your stomach and can I guess it makes you sicker.”*

A noticeable number of participants (six individuals) did not know the side effects of using antibiotics and a few of them mentioned that their doctors did not talk to them about the side effects when prescribing an antibiotic. The doctors mostly would be described as emphasizing the need to take the antibiotics with food and completing the course of treatment.

### **Participants’ sources of information regarding coping strategies**

Participants got the information from Internet (e.g. WebMD), TV, Telehealth and pharmacists. Regarding antibiotics and their side effects, most participants relied on pharmacists, medications package inserts or Internet; only one individual mentioned that she would ask her questions from the doctor.

P4: *“The expert on any form of medication is always a pharmacist.”*

Some individuals put emphasis on their lifelong experiences or common-sense, as well as the things they learnt from their mothers.

P6: *“Because you’ve done it before, gone through the process before with doctors you just might as well just do it yourself.”*

**Table 1-Participants’ coping strategies toward URTIs**

	<b>Themes (number of individuals)</b>	<b>Quotes</b>
<b>Self-treatment</b>	<ul style="list-style-type: none"> <li>• Used OTC medications (13)</li> <li>• Took a lot of water (4)</li> <li>• Took warm liquids such as tea with honey or lemon and soup (6)</li> <li>• Took multivitamins or Vitamin C (2)</li> <li>• Took more rest or sleep (5)</li> <li>• Gargled water with salt (1)</li> <li>• Took fresh air(1)</li> </ul>	<p>P2: “I just drink a lot of water and try to get a lot of rest and not do too much and they usually go away; it’s pretty quick.”</p> <p>P3: “I just go home, crawl in bed and wait ‘til it’s over.”</p> <p>P4: “I drink an awful lot of water; an awful lot of liquids like especially warm liquids that make you feel better.”</p>
<b>Visiting doctor</b>	<ul style="list-style-type: none"> <li>• Expected to receive a physical examination (4)</li> <li>• Seek a prescription for inhaler (3)</li> <li>• Seek an explanation for getting worse (3)</li> <li>• Asked if antibiotics are needed (2)</li> <li>• Interested to know doctor’s opinion (1)</li> </ul>	<p>P15: “I’m going to have his assessment as to whether it’s an infection or just an ordinary cold.”</p> <p>P2: “Well honestly I’m hoping that there’s nothing wrong with me, but sort of an explanation of why the symptoms are getting worse; if my doctor can figure that out or give me like a reason why they were getting worse.”</p> <p>P4: “I kind of wait a couple of days like 4-5 days. If I’m not feeling better then I go to a doctor and have them listen to my lungs.”</p> <p>P1: “Doctor at least can look at me and listen to my lungs and can tell me if it’s viral or if it’s bacterial.”</p>
<b>Problem-focused coping</b>	<ul style="list-style-type: none"> <li>• Getting a refill for an inhaler (2)</li> <li>• Asking if antibiotics are needed in case of green secretions from nose or throat (2)</li> <li>• Having difficulty managing the fever with Acetaminophen/Ibuprofen (2)</li> <li>• Long-lasting cough (4)</li> </ul>	<p>P15: “He can’t do anything for a general cold but, but if you get an infection in your chest they give antibiotics for that. So I’m going to have his assessment.”</p> <p>P4: “I have a puffer at home, if I need a refill, I ask the doctor for a new prescription and it usually helps with the coughing”</p> <p>P8: “I take the cough syrup and do my best and if it continues and I can’t manage it then I go to the doctors”</p>
<b>Using antibiotics</b>	<ul style="list-style-type: none"> <li>• Believed antibiotics are not needed for URTIs(9)</li> <li>• Would ask for antibiotics if the symptoms get severe (4)</li> <li>• Used left over antibiotics (1)</li> </ul>	<p>P1: “I always ask if it’s necessary to get antibiotics. If I don’t need, that’s right I, I’m happy and I will take care of myself.”</p> <p>P15: “In my case because it gets into my chest, if I have any prophylactic, if I have any Amoxicillin</p>

		<p><i>or something left over from the last course which I know I'm not supposed to do I'll take that. That doesn't treat it, doesn't make it go away faster but it makes it feel better. It's not a good thing to do for 2 reasons: 1) it's probably not helping my cold, 2) I should have taken the full course of medication he gave me the last time."</i></p>
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# Discussion

## Summary of main results

This study investigated the individuals' knowledge and beliefs about URTIs and the way they manage them using CS-SRM. Although the participants had different beliefs about the causes of these infections, they had good knowledge regarding self-management of their symptoms and preventing the infections from happening. Almost all participants mentioned that they would not go to the doctor because of these infections, unless there was a serious problem (e.g. breathing or swallowing difficulties, high fever, long-lasting cough). When visiting a doctor, participants mostly wished to be examined and to gain better understanding about what was going on in their bodies. Parents described being more cautious about their children with URTIs and would take them to doctors in earlier stages of the disease. Generally, participants trusted their doctors and accepted their opinions, even if no antibiotic was prescribed. Most participants believed that there was no need for serious medication or antibiotics and the symptoms would go away by themselves after a few days. Home remedies and OTC medications were used widely by participants to control the symptoms. We know from previous studies (7, 8) that some doctors perceive that patients expect antibiotics; however, our results suggest that doctors may overestimate patients' expectations for antibiotics. It is also important for doctors to realize that patients' satisfaction can be achieved by other actions such as thorough examinations or explanations about symptoms rather than prescribing antibiotics.

Participants' strategies for managing URTIs were described as being based on their previous experiences of these infections, common sense and things that they had learnt from their parents in childhood. They mostly relied on family members, Internet and pharmacists as sources of

information. The findings of our study suggest that there are opportunities for doctors to engage in more conversations about URTI management with patients and provide them with evidence-based information as required.

## **Strengths and limitations of the study**

To our knowledge, this is the first qualitative descriptive study in Canada to apply CS-SRM with individuals about URTIs. The semi-structured nature of the interview guide, allowed us to have a better understanding of individuals' reasons for particular behaviours. There is only one study from UK which has used CS-SRM to study expectations of patients with URTIs for consultation and antibiotics (27). Except for a few studies that have used grounded theory model (28), Theory of Planned Behaviour (29) and Andersen's behavioural model (30), most studies in this field have not used any theoretical models in their investigations (e.g. 27, 31, 32, 33, 34, 35).

Our participant sample had male and female representation and a diverse age range as well as a variety of education levels. However, by limiting our sample to English speaking individuals, we may have missed varying perceptions from other patients at the primary care practice. In addition, most individuals who were approached at the primary care practice agreed to participate in the study. We do not know if those who did not participate were different from our sample regarding their beliefs and behaviours about URTIs. Despite these limitations, our findings were supported by other studies that investigated patient perceptions about managing URTIs and provided valuable insight into improving patient-physician communication to improve self-management of URTI symptoms and reduce antibiotic prescribing.

## **Agreements and disagreements with other studies**

Our results showed that participants interviewed did not usually visit the doctor to ask for antibiotics for URTIs, which is consistent with other studies (36). Specifically, a study investigating patients in six European countries with respiratory tract infections revealed that only 2% of these patients explicitly requested antibiotics (36). Similar findings were reported from other parts of the world (UK, South Korea, Australia, China, Qatar, Denmark, Germany, USA) (27, 30, 31, 32, 33, 34, 37, 38, 39). A study from USA reported that patients put a lot of pressure on doctors for the prescription of antibiotics for URTIs by the way they presented their symptoms. However, they observed that only 6% of cases made direct requests for antibiotics (7). Another study from USA argued that doctors felt a pressure to prescribe antibiotics from the patients who suggested a candidate diagnosis, but the authors noted that an overt demand for antibiotics was unusual (40). Conversely Dosh et al. from USA reported that 60% of patients expected antibiotics (6), but included respiratory infections for which the antibiotics were sometimes necessary. In addition, these three studies are older compared to other studies and this may in part explain the difference in results. Public knowledge and beliefs may have changed in recent years because of people's easy access to different sources of information through internet or media.

When visiting a doctor, most participants in our study expected an examination or an explanation for their symptoms. Consistent with our results, a study from Netherland revealed that 90% of patients with URTIs presenting to general practices, expected information or reassurance from their doctors. Meeting this expectation by doctors provided more satisfaction to patients than prescription of antibiotics (10). According to many studies, thorough examination, explanation and reassurance were expected by patients with the symptoms of URTIs in USA, UK, South Korea, Germany, Qatar, Denmark and Netherlands (27, 28, 33, 37, 38, 41). According to our results, individuals with URTIs who visited the doctor usually reported serious problems such as trouble

breathing or fever. This is consistent with Duijn et al in Netherlands who also reported that the small number of patients, who decided to visit doctors, often had good reasons (e.g. serious symptoms, suffering for more than two weeks, respiratory comorbidity) (41).

Based on our results, these 15 participants did not primarily go to doctors because of URTIs; instead, they tried to manage the symptoms by themselves. Roberts et al. from USA and Hawking et al. from UK reported similar results (28, 29). However, visiting the doctor was often reported as the first choice for many patients with URTIs in studies from South Korea, Malaysia and Qatar (30, 33, 35). This may be in part due to lack of public knowledge about self-management of URTIs (30). Also, cultural beliefs in some parts of the world, such as believe in the effectiveness of treatments that are received from doctors, could explain these results (35).

Recently, Silverstein et al. conducted a cross sectional study on 50 years adults or older presenting to primary care clinics in Ontario and demonstrated that only 44% of participants were aware that antibiotics are not necessary to treat sinus infections, a type of URTI (15). However, most participants in our study believed that antibiotics are not needed for URTIs. The discrepancies in results may in part be due to differences in the sample characteristics. The fact that in Silverstein et al. study, sinus infections were the only URTI that have been investigated may also contribute to this discrepancy.

## **Implications for research and policy**

Our results showed that individuals with URTIs did not necessary ask for antibiotics, instead they expected a thorough examination and an explanation for their symptoms. This is contrasted by some other studies (6, 7, 8, 40) that report doctors perceive pressure from patients to prescribe antibiotics. It suggests that maybe better communication with patients could help doctors to elicit

patients' expectations and potentially reduce unnecessary prescriptions while increasing patients' satisfaction with being heard by their healthcare provider.

Individuals in our study had different perceptions about the causes of URTIs. Providing information about viruses as the main cause of most URTIs by healthcare providers or mass media may help patients feel more comfortable about not visiting doctors or taking antibiotics for these infections. Furthermore, there were misconceptions among some patients that changes in symptoms might require antibiotics (e.g. if the color of sputum changes to green, antibiotic is needed). However, there is evidence that some of these changes do not imply the need for antibiotics (42, 43). Doctors could take opportunities during patient visits to clarify the reasons for patients' concerns, as well as addressing those concerns with evidence-based information.

Our results were based on English speaking individuals' beliefs and perceptions in a single practice. However, Canada consists of individuals from different ethnicities and cultural backgrounds. Studying individuals from different locations or ethnicities may identify new concepts that are specific to those groups.

## **Conclusion**

In this study we explored 15 individuals' views about URTIs and the ways in which they managed their symptoms (including self-management, primary care consultation and antibiotic use). Participants had a good knowledge about the use of antibiotics for URTIs. They did not usually go to doctors because of URTIs, and if they went, most of the times they did not seek antibiotics, but instead they wanted to be examined and receive an explanation for their symptoms. Instead of concentrating on providing more education to public, we may benefit from interventions that

promote the communication between doctors and patients. Further work is needed to identify these interventions and implement the most effective and feasible ones in Canada.

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# Appendix 1

## Participants' information sheet

**Title of study:** Understanding determinants of patients' decisions to attend their family physician and to take antibiotics for upper respiratory tract infection

**Principal Investigator:** Dr. Jeremy Grimshaw

Telephone:

**Research coordinator:** Sameh Mortazhejri,  
The Ottawa Hospital-General Campus  
Ottawa Hospital Research Institute  
Centre for Practice Changing Research  
Telephone:  
Email:

**Funding source:** CIHR Foundation grant

Participation in this study is voluntary. Please read this Participant Informed Consent Form carefully before you decide if you would like to participate. Ask the study team as many questions as you like.

### **Why am I being given this form?**

You are being asked to participate in this research study because of your willingness to be contacted by the research team. We would like to know your knowledge and beliefs about upper respiratory tract infections (URTIs) (e.g. common cold, sore throat, sinusitis...) and the way you manage them (including attendance in primary care and taking antibiotics).

### **Why is this study being done?**

This study aims to explore the patients' current knowledge and attitude about URTIs and the way they manage them. The findings of this study could inform future studies of patient oriented interventions to improve appropriate antibiotic use for URTIs. This study will recruit patients attending the Kingsway Health Center (Family Practice), who are willing to be contacted by the research team. We estimate that a total of 15 participants will be enrolled in the study.

### **How is the study designed?**

This study is looking at participant's beliefs and experiences of URTIs. Participants will be interviewed by phone to understand their perspectives.

### **What is expected of me?**

You will be asked to participate in a single interview. The interview will be conducted by telephone at a time that is convenient to you. The interview will last about 30 minutes and will be recorded and transcribed to help the researchers record your thoughts correctly. In the interview, you will be asked about your knowledge and beliefs about URTIs and the way you manage them. You may skip any questions that make you uncomfortable or that you do not wish to answer.

**How long will I be involved in the study?**

The entire study will last approximately 4 months. Your participation in the study will consist of one single interview which takes about 30 minutes.

**What are the potential risks I may experience?**

There are no known risks to you as a participant.

You might find the interview tiring if it is lengthy. You might not like all of the questions that you are asked. You do not have to answer any questions that make you uncomfortable and you can decide to take a break or end the interview at anytime.

**Can I expect to benefit from participating in this research study?**

You may not receive any direct benefit from taking part in this study. Your participation in this research will help us reach a better understanding of people's knowledge and beliefs about URTIs and the way they manage them. This will help us formulate a plan to decide on the best strategies to reduce inappropriate antibiotic use for URTIs.

**Do I have to participate? What alternatives do I have? If I agree now, can I change my mind and withdraw later?**

Your participation in this study is voluntary. The alternative to this study is not to participate.

You may decide not to be in this study, or to be in the study now, and then change your mind later without affecting the medical care or other services to which you are entitled or are presently receiving at this institution.

If you withdraw your consent, the study team will no longer collect your personal information for research purposes. Information given before you withdraw this consent may still be used.

**Will I be paid for my participation or will there be any additional costs to me?**

You will be paid \$25 Tim Horton's or Amazon gift voucher for time taken to participate in the study.

**How is my personal information being protected?**

- All information collected during your participation in this study will be identified with a unique study number, and will not contain information that identifies you, such as your name, address, etc.
- The link between your unique study number and your name and contact information will be stored securely and separate from your study records, and will not leave this site.
- Any documents leaving The Ottawa Hospital will contain only your unique study number. This includes publications or presentations resulting from this study.

- Information that identifies you will be released only if it is required by law.
- For audit purposes only, your original records and relevant study files may be reviewed under the supervision of Dr Jeremy Grimshaw's staff by representatives from:
  - The Ottawa Health Science Network Research Ethics Board (OHSN-REB), and
  - The Ottawa Hospital Research Institute.
- Research records will be kept for 10 years, after this time they will be destroyed.

### **Questions about the Study**

If you have any questions about this study please contact Sameh Mortazhejri (research coordinator) at ... or Dr. Jeremy Grimshaw (Principal Investigator) at ....

The Ottawa Health Science Network Research Ethics Board (OHSN-REB) has reviewed the plans for this research study. The Board considers the ethical aspects of all research studies involving human participants at the Ottawa Hospital. If you have any questions about your rights as a study participant, you may contact the Chairperson at ...

## Appendix 2

### Participants' consent form

**Title of study:** Understanding determinants of patients' decisions to attend their family physician and to take antibiotics for upper respiratory tract infection

#### **Consent to Participate in Research**

- I understand that I am being asked to participate in a research study to share my knowledge and beliefs about upper respiratory tract infections (URTIs) and the way I manage them (including attendance in primary care and taking antibiotics) with the research team.
- I have read, or someone has read to me, each page of this Participant Informed Consent Form.
- All of my questions have been answered to my satisfaction.
- If I decide later that I would like to withdraw my participation and/or consent from the study, I can do so at any time.
- I voluntarily agree to participate in this study.
- I will be given a copy of this signed Participant Informed Consent Form.

Participant's Name

Participant's Signature

Date

#### **Investigator or Delegate Statement**

I have carefully explained the study to the study participant. To the best of my knowledge, the participant understands the nature, demands, risks and benefits involved in taking part in this study.

Name of Investigator/Delegate

Signature of Investigator/Delegate

Date

## Appendix 3

### Interview guide

Thank you for participating in this interview. Information you provide in this interview will be identified by a study ID code and will not be associated with your name or other personal identifying information. The purpose of the interview is to understand your point of view regarding how you manage upper respiratory infections (URTIs) (e.g. common cold, sore throat, sinusitis...). The information you provide here, including your thoughts and comments will not be shared with your family doctor, or other healthcare providers. There's no right/wrong way to answer the questions; however we are looking for honest answers. It helps us to understand the current concerns of patients.

I would like to start with some general questions:

1. Gender
2. Your age?
3. Your highest level of education?

Now, I would like to talk to you about your experience with having an upper respiratory infection and how you manage that. When I say URTI, I'm talking about respiratory infections that affect the chest, throat, nose, sinuses and ears. Chronic conditions such as asthma, chronic obstructive pulmonary disease (COPD) or the infections of lower respiratory tract (e.g. bronchitis) are not the scope of this interview.

1. How often do you usually get URTIs?
  - a. Do you remember what your last respiratory infection was like?
2. When was it? What were your symptoms like? The duration of your symptoms? The severity of your symptoms? How did it make you feel?
3. What do you think causes URTIs? (Prompts biological causes, emotional causes, environmental causes)
4. What are the consequences of URTI for you? (Prompts it may make you less effective at work? You might get complications from the URTI (e.g. chest infection)? What is the worst thing that can happen to you when you suffer from a cold?

5. What is your usual approach to looking after yourself when you have an URTI? Does it work?
6. Do you ever look up information about URTIs and how to treat them? If so, where? Under what circumstances (i.e. any particular symptoms would trigger a search?) Where do you look for information? (E.g. internet, family, friends, doctor)
7. Do you usually visit a doctor for an URTI?
  - a) If yes,
    - I. When do you go? (Prompts As soon as the symptoms appear (any particular symptoms?)? Or it takes you a few days before going to doctor?)
    - II. What are you aiming for when you see a doctor? (Prompts For a prescription? For reassurance? For a referral to a specialist?)
    - III. What factors would make you go see a doctor? (Prompts For example, the severity of the symptoms? The duration of the disease? The friends/colleagues' advices? The fear of disease complications?)
    - IV. In your experience, did visiting the doctor have any effect on your disease?
  - b) If no,
    - I. Why? (Prompts because of factors related to your time, your doctor, your disease, the medication)
    - II. In your experience, has your disease (the duration, the severity) been affected by not seeking a doctor?
8. Are you aware of the pros and cons of taking antibiotics? What sources have helped you to building this knowledge?
  - a. Does the doctor usually talk to you about the pros and cons of taking antibiotics?
  - b. Do you share your concerns with your doctor? (That you think if you don't get AB, you won't get better) or (you don't want AB, because of its side effects...)
  - c. If you took AB for your last URTI, did it shorten the duration of the disease? Relieved the symptoms?
9. How do you think URTIs can be cured?
10. Do you think that URTIs can be prevented? If yes, how?

Thank you. Is there anything else about your management of URTIs you would like to talk to me about that I haven't covered in this interview?

## **Chapter 4**

### **Discussion**

## Summary of main result

This thesis aimed to explore the potential of targeting interventions to patients to reduce unnecessary antibiotic use for upper respiratory tract infections (URTIs). I conducted two studies to explore this.

My first study was a systematic review to identify the most effective patient-oriented interventions to reduce unnecessary use of antibiotics for URTIs. We found two major categories of interventions: 1) delayed prescription, and 2) patient/public information and education. In the delayed prescription group, seven RCT studies (from UK (three studies from the same research group), Spain, New Zealand, Canada, Israel) compared delayed prescriptions with immediate prescriptions of antibiotics. The result of our meta-analysis showed that overall, the participants in the delayed prescription group were less likely than participants in the immediate prescription group to use antibiotics (OR=0.09, CI: 0.03 to 0.23). Our subgroup analysis revealed that delayed prescriptions which were given at a later time and delayed prescriptions that were given at the index consultation were similar regarding their effect in reducing antibiotic use for URTIs. Seven studies (six RCTs and one ITS) from USA, UK, Portugal and Singapore were included in the patient/public information and education group. The effect of educational interventions differed according to the education method; and since only one or two studies represented each method, it was not possible to draw conclusions on the effectiveness of each method. However, overall their effect was much smaller compared to the effect of delayed prescriptions. In general, providing information via online educational program or mass media (each was applied in only one study) did not have a significant effect on antibiotic prescription. Furthermore, applying booklets, pamphlets, letters or videotapes demonstrated inconsistent results on antibiotic prescription. Our

results suggest that providing these interventions by a doctor rather than a researcher and discussing them verbally in a face-to-face visit can be more effective in reducing inappropriate antibiotic use.

The secondary outcomes which were studied in our systematic review consisted of patients' satisfaction, patients' beliefs on the effectiveness of antibiotics and re-consultation. These outcomes were reported only in a few studies. In the delayed prescription group, patients' satisfaction was reported in only three studies; one study from New Zealand reported higher satisfaction in the intervention group (non-significant) and two studies from a single group in UK reported less satisfaction in the intervention group (only one was significant). Re-consultation was reported in four studies; three of them (one from Spain and two from the UK) showed less re-consultation in the intervention groups, while the study from New Zealand showed the opposite results. One possible explanation for the difference results between the study from New Zealand and the other studies (from Europe), is that the effect of delayed prescription on patients' satisfaction or re-consultation may vary depending on healthcare context and culture. Patients' beliefs on the effectiveness of antibiotics were investigated in four studies and three of them (one from Spain and two from the UK) showed a significant change in favour of the intervention, while the study from New Zealand showed no difference between the intervention and control groups. In the patient/public information and education group, patients' satisfaction was only reported in one study from UK which showed less satisfaction in the intervention group. Two UK studies in the patient/public information and education group both reported fewer re-consultations in the intervention group. No study in this group investigated patients' beliefs.

Building on the results of our systematic review, my second study was a qualitative descriptive study to explore individuals' knowledge and beliefs about URTIs and the way they manage their

symptoms (including attendance in primary care and taking antibiotics). We performed semi-structured interviews based on Common Sense-Self-regulation Model (CS-SRM) with English-speaking individuals presenting to a mixed urban/rural family practice. CS-SRM attempts to explain patients' perceptions and behaviours related to an illness and suggests that differences in patients' perceptions about the symptoms, cause, time-line, consequences, curability/controllability and prevention of an illness may result in variations in the way they manage that illness. In total, we interviewed 15 individuals (six females, nine males) by phone. The participants were between 18 and 69 years old. The highest level of education was high school in five individuals, community college in four individuals and university education in six individuals. The participants in our study were quite familiar with prevention and management of URTIs. Most participants believed that URTI symptoms usually went away after a few days and did not need antibiotics. They relied mostly on over the counter (OTC) medications and home remedies to control their symptoms. They were also more concerned when their children showed the symptoms and preferred to take them to doctors earlier. During doctors' visits, patients mostly expected an examination and an explanation for their symptoms. They trusted their doctors and accepted their clinical judgment even if no antibiotics were prescribed. Participants' experience of previous episodes of disease played an important role in their approach to dealing with new episodes. This experience accompanied by the guidance they obtained from Internet or pharmacists were the major sources of information for participants. Despite the participants generally being knowledgeable about managing URTIs, there were some misconceptions about some symptoms. They believed a prolonged cough or a change in the color of sputum might mean that they needed antibiotics for their URTIs. Participants also showed lack of knowledge regarding the causes of URTIs and side effects of antibiotics.

## **Agreements and disagreements with other studies**

Delayed prescription of antibiotics for URTIs is investigated in multiple reviews; however, they have rarely discussed the quality of included studies. In general, the results of these reviews are mostly consistent with our results that delayed prescriptions are effective in reducing antibiotic use (1, 2, 3, 4, 5). Similar to our results, the effect of patient/public information and education interventions varies highly among other studies according to education methods and materials being used (5, 6, 7).

Our second study revealed that patients did not usually ask for antibiotics. Different studies reported different results; while some studies stated that patients did not expect antibiotics for URTIs (8, 9, 10, 11, 12, 13, 14), a number of other studies noted the opposite results (15, 16, 17, 18). These discrepancies were observed in studies from different countries and studies within a single country. This suggests that in addition to nation-wide factors, some local factors (e.g. cultural, ethnical, socioeconomic) also affect patients' beliefs. Furthermore, the studies that reported high expectation for antibiotics only included parents/caregivers, while other studies had a mixture of parents and non-parents participants.

The results of Silverman et al. and O'Connor et al. studies suggests that doctors who see more patients are likely to prescribe more antibiotics, mostly because the high patient volumes lead to shorter consultations which consequently limits the time to discuss the lack of benefits from antibiotics or alternative ways of managing URTIs (19, 20). Consistent with these studies, our results signify the importance of a proper conversation between patients and doctors as well.

## **Discussion**

Antibiotic resistance is a major health problem and is due to inappropriate use of antibiotics in humans, as well as its extensive use in agriculture (21). To fully address the problem of antibiotic resistance, it will be important to reduce inappropriate antibiotic use in all sectors. However, for this thesis we only focused on a small part of the whole problem, specifically inappropriate antibiotic prescriptions for URTIs in primary care settings. Furthermore, we confined our study to patients as the end users of antibiotics. Antibiotic resistant bacteria cause infections that are difficult to deal with, resulting in increased mortality and morbidity. Furthermore, they impose huge costs to the healthcare system (22, 23, 24). In 2016, 65% of all prescriptions dispensed by community pharmacists in Canada were prescribed by general practitioners (GPs) which were mostly for respiratory tract infections. In 2016, 68% of diagnosed sinusitis, 58% of diagnosed otitis media and 22% of diagnosed URTIs received an antibiotic recommendation in Canada (24). However, the evidence from several systematic reviews suggest that there are no or small benefit from prescribing antibiotics for most of URTIs (25, 26, 27). According to some studies, some doctors perceive patients' expectations as a major reason for prescribing antibiotics (28, 29). We tried to investigate the potential of addressing patients to reduce unnecessary use of antibiotics from two perspectives.

As the first step, we conducted a systematic review of patient-oriented interventions. Our findings suggest that delayed prescription of antibiotics effectively reduces the use of antibiotics. This strategy can be applied in Canada; however since only one study among the included studies were conducted in Canada, it is essential to examine the requirements of implementing this strategy. For example, according to our results, patients' satisfaction with delayed prescription was different in different settings (different results in UK and New Zealand). Local healthcare system or cultural beliefs in Canada may affect the acceptability of the interventions to patients which might modify

the effect of delayed prescriptions. This highlights the importance of checking the acceptability of this strategy in Canada to ensure a long-standing and effective change within the healthcare system.

As the second step, in order to understand what aspects of these interventions may be more applicable to our settings, we studied a group of individuals to understand how they perceived and managed URTIs. Our results revealed that despite some knowledge misconceptions about causes of URTIs and side effects of antibiotics, participants generally had a good understanding about lack of benefits from antibiotics for URTIs. They mostly mentioned that they would not go to doctors because of these infections and preferred to manage it themselves. It suggests that little additional benefit would be gained from focusing only on general educational interventions on decreasing antibiotic overuse. This is consistent with the result of our systematic review that showed overall small effect for patient/public information and education interventions in reducing antibiotic use. Furthermore, our participants did not routinely ask for antibiotics. This is contrasted by some other studies, mentioning that doctors feel a pressure from patients to prescribe antibiotics (30, 31). So a better communication between doctors and patients may better elicit patients' expectations and prevents unnecessary prescriptions. Choosing Wisely Canada (CWC) in recent years has tried to promote the conversations between doctors and patients about treatment expectations. As part of their framework, they have encouraged patients to be more engaged in clinical encounters and ask questions about the necessity of treatments or procedures. CWC has also persuaded doctors to change their practice styles and to be more explicit about their clinical decisions with patients (32).

## **Implications for practice**

Although, most participants in our study did not expect antibiotics for URTIs, some of them considered asking for antibiotics when they had severe or prolonged symptoms, especially for their children. Delayed prescription of antibiotics can provide doctors with a tool to deal with patients who insist on receiving antibiotics or patients who have more severe symptoms. In addition, this method may be helpful in reassuring doctors that they have done something for the patients.

Regarding participants' misconceptions about some symptoms or side effects of antibiotics, there may be some opportunities for doctors to discuss these issues with patients during the visits. Since our participants indicated that they mostly relied on their previous experiences of disease episodes as a source of knowledge, we may benefit from providing tailored information to patients. However, we still need to determine what features of information and education interventions (booklets, pamphlets, letters or videotapes) or a combination of them works best in our settings. In addition, it is important to assess the cost-effectiveness of delivering individualized and practical information to patients.

## **Implications for research**

Research regarding unnecessary use of antibiotics for URTIs has mostly focused on healthcare providers. Except for a few studies (12, 30, 33, 34, 35, 36, 37), most studies that direct their research toward patients have mainly used quantitative methods. Addressing this topic using qualitative methods can provide a better and more detailed understanding of the reasons behind individuals' behaviours, as well as the factors that promote or discourage specific behaviours. There may also be some benefits in conducting observational studies by field researchers to inspect the patient-doctor interactions during consultations. This could reveal some real-time behavioural patterns of doctors and patients which may be difficult to identify by using other methods such as

surveys or interviews. Subsequently, the results of these studies (qualitative studies) can be applied to design a nationwide survey. The survey would allow us to estimate the overall doctors' visits because of URTIs, antibiotic use and the reasons behind these actions.

Data from other studies suggest that doctors are more likely to prescribe antibiotics if they perceive that their patients expect it (13, 38, 39, 40, 41). The participants in our study mostly did not ask for antibiotics for URTIs, rather they expected an examination and explanation for their symptoms. This suggests that there may be some misalignments between patients' expectations and doctors' perceptions of those expectations. Further research is needed to explore the barriers to proper conversations between patients and doctors. It should be investigated if it is due to high volume of patients and time constraints or due to some cultural reluctance on patients' sides to talk openly to their doctors. Once the reasons are identified, we should try to facilitate conversations between patients and doctors which could increase patients' satisfaction, as well as decreasing antibiotic use by revealing patients' expectations.

## **Conclusion**

Patient-oriented interventions to decrease the unnecessary use of antibiotics for URTIs were studied in two major categories: delayed antibiotic prescription and patient/public information and educational materials. There is evidence that delayed prescription of antibiotic can reduce the unnecessary use of antibiotics for URTIs. Although it seems that providing education through sessions or pamphlets/booklets (especially if delivered by a healthcare provider and discussed verbally) can decrease antibiotic use, the small number of included studies did not allow us to make a definite conclusion on their effectiveness.

Our results suggest that patients have a good understanding about the ineffectiveness of antibiotics for most URTIs and they prefer to manage these infections by using home remedies or OTC medications. Furthermore, patients' main reasons for visiting a doctor are to be examined and reassured. This highlights the importance of facilitating a conversation between patients and doctors to elicit patients' expectations.

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