Original research

Physicians' knowledge, perceptions, and behaviour towards antibiotic prescribing: A systematic review of the literature

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Abstract

Background: Knowledge, perceptions and prescribing behaviour are key to antibiotic prescribing. The aim of this paper is to systematically review this. **Method**: An extensive literature search from 1990–2014. **Results**: 19 articles were included; 8 in ambulatory care, 7 in hospital settings, and 4 in both, across all countries. Physicians still have inadequate knowledge and misconceptions about antibiotic prescribing. Moreover, some physicians although aware that antibiotics are of limited benefit in some conditions still prescribed them. Several factors influenced prescribing including patients' expectations, severity and duration of infections, uncertainty over diagnosis, potentially losing patients, and influence of pharmaceutical companies. Pocket-sized guidelines seen as an important source of information for physicians. **Conclusion**: Inadequate knowledge of prescribing is prevalent among physicians. However, many physicians were interested in improving their antibiotic prescribing. Multifaceted interventions targeting all key stakeholders including patients are needed to improve future antibiotic prescribing.

Key words: antibiotics, irrational use of medicines, patients, prescribing behaviour, physicians, systematic reviews, resistance

Introduction

Infectious diseases were the leading cause of morbidity and mortality before the discovery of antibiotics. This changed with their advent through researchers including Paul Ehrlich and Alexander Fleming, turning once fatal diseases into more manageable health problems (1-4). Advances in scientific and medical technology has resulted in the development of new antibiotics as well as generic antibiotics, with the latter in particular providing easy accessibility at affordable costs (5). Antibiotics are now commonly prescribed to patients in ambulatory care (6-9). However, greater accessibility has resulted in irrational and excessive use, leading to increasing antibiotic resistance (5, 10-14). Increasing antimicrobial resistance is seen as one of the most critical problems facing healthcare systems (15), with estimates that antimicrobial resistance (AMR) infections currently cause approximately 50,000 deaths a year in Europe and the US alone (1). This increases to several hundred thousand deaths each year when other countries are included (1). The continual rise in AMR is envisaged to result in 10 million deaths annually by 2050 unless checked. As a consequence, AMR infections could be a leading cause of death by 2050. This death rate will reduce GDP by 2% to 3.5% by 2050 and costing the world up to US$100trillion (1). Some common infections, especially those

caused by antibiotic resistant bacteria, are becoming more difficult to treat, causing life-threatening illnesses and potentially death (16). The combination of overuse of antibiotics for minor infections, misuse and under use due to lack of access and financial support in certain settings, has been a key driver of resistance. This phenomenon has been termed selective pressure (15).

Increasing antibiotic resistance poses a threat to health and healthcare systems in both developed and developing countries (17). In high-income countries, continuing high rates of antibiotic use in hospitals, the community, and agriculture have contributed to selection pressure that has sustained resistant strains (18), forcing a shift to more expensive and more broad spectrum antibiotics. In low-income and middle-income countries (LMICs), the high burden of infectious diseases and the unregulated access to antimicrobials has resulted in the emergence of antibiotic resistance (17). This is not helped by the increasing use of antibiotics to treat viral upper respiratory tract infections (URTIs), inappropriate prescribing of antibiotics for infections such as pneumonia, purchasing of antibiotics without a prescription as well as the challenges involved with determining current antimicrobial usage and AMR rates in LMIC countries to provide a baseline for future interventions and policies (19-25). Inappropriate use of antibiotics is also not helped by currently limited adherence to guidelines among physicians in LMIC countries; greater though among physicians in public (40%) than private-for-profit sector facilities at <30% (26).

It is now acknowledged that the rational use of antibiotics is one of the most important steps to slow down the development and spread of resistant bacteria (27). The inappropriate use of antibiotics has been attributed to a number of factors. These include physicians' non-adherence to treatment guidelines, lack of knowledge and training regarding antibiotics, lack of diagnostic facilities, uncertainty over the diagnosis, pressure from pharmaceutical industry, fear of clinical failure, financial benefits for physicians, pressure from patients to prescribe antibiotics regardless of the indication coupled with lack of time of physicians to educate patients. In LMIC countries, there are also concerns with the extent and implementation of regulations surrounding the dispensing of antibiotics including self purchasing (19, 21, 24, 25, 28-34). Moreover, antibiotic misuse or overuse has promoted the perception among the public that these medicines are the preferred treatment for instance for URTIs. This in turn induces patients to demand antibiotics, hastening the growth of resistant bacteria (25, 30, 35). To help combat the irrational use of antibiotics, stringent diagnostic criteria for URTIs have been recommended by the Centers for Disease Control and Prevention (CDC) in collaboration with the American academy of Paediatrics (AAP) and the American Academy of Family Physicians. In United Kingdom, the National Institute for Health and Clinical Excellence (NICE) introduced in 2008 a guideline for antibiotic prescribing in respiratory tract infections. Despite these efforts and guidelines, physicians still manage URTIs with considerable variation (19, 20, 30, 36-38).

Consequently, a better understanding of the determinants of antibiotic prescribing among physicians is essential for introducing and implementing targeted interventions to reduce future antibiotic prescribing and potential resistance (17, 20, 21, 26), with physician prescribing behaviour playing a key role in the utilisation of antibiotics (39). Hence, adequate knowledge and appropriate education are essential. Physicians' understanding of when antibiotics are needed, and more importantly when they are not, should subsequently reduce their prescribing (40, 41). However, there will be challenges especially in LMIC countries (19, 21, 33, 34, 42).

Since changes in prescribers' knowledge and behavior are prerequisite for changes in antibiotic prescribing pattern, it is important to understand what physicians know about antibiotics, how they acquire and maintain their knowledge, and what factors influence their prescribing practice. Understanding prescribers' perspectives could lead to the development of more effective interventions and strategies to promote the rational use of antibiotics. Consequently, the aim of this paper is to systematically review the knowledge, perceptions, and behavior of physicians regarding antibiotic prescribing to guide future strategies.

Methodology

An extensive literature search was performed to identify published studies related to medical practitioners' perceptions, knowledge, attitude, practice, belief, and behaviour regarding antibiotic prescribing and antibiotic use. The search strategy was to identify cross-sectional observational studies and experimental studies; applied either qualitative or quantitative methods or both. PRISMA

(Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement and guidelines were followed when performing the search and the identification of possible studies (43).

Relevant studies were identified by a comprehensive search of several electronic databases. These included Scopus, PubMed, ISI Web of Knowledge, Proquest, Science Direct online library and Google Scholar. The bibliography of the retrieved studies was also checked for potential studies. The search strategy involved using Boolean operators for combinations of several keywords to identify the relevant articles. The key words used in the search included (antibiotic(s) OR antimicrobials) AND (prescribing OR resistance) AND (knowledge OR practice) AND (attitude OR perception). For prescribers, the following keywords were used: prescriber(s), general practitioner(s), doctor(s) and physician(s). Articles related to antibiotic use in dental practices were excluded from the systematic review. We acknowledge that particularly in LMIC countries the prescribing and dispensing may be undertaken by non-physicians, e.g. pharmacists, even when this is not permitted (21, 44). However, these papers have been excluded from the review as our focus was on physicians.

To make the review relevant to current practice, the search was restricted to the studies published between 1990 and 2014. Only articles published in the English language were included. All results were listed and evaluated by reading the abstracts. To determine whether the studies met the required criteria, the lists of titles and abstracts from the searches were examined by two researchers independently. Where doubt remained, the full article was examined by two of the researchers to determine whether it is relevant, with the final inclusion of the article undertaken in a consensus meeting involving the authors.

The methodology, including summarizing the quality and limitations of studies, follows previously published studies (45-47).

Results

The search process resulted in 1633 titles and abstracts. After removing duplicates, 1052 studies were screened, of which 764 were excluded on the basis of title. Further assessment of title and abstracts led to the identification of 145 studies not meeting eligibility criteria, as they were not related to the topic and did not investigate perceptions, attitude or knowledge of the prescribers towards antibiotics. The remaining (n= 143) were full-text assessed for eligibility for inclusion in the study. Seventy eight studies were then excluded as their main findings did not discuss issues related to our review objectives. A further 46 studies were excluded as they did not assess physicians' perceptions and knowledge, but rather looking at the prescribing patterns and variability in antibiotic usage. This left 19 articles for inclusion in the review (Table 1).

Insert Table 1.

The PRISMA diagram for this review is shown in Figure 1.

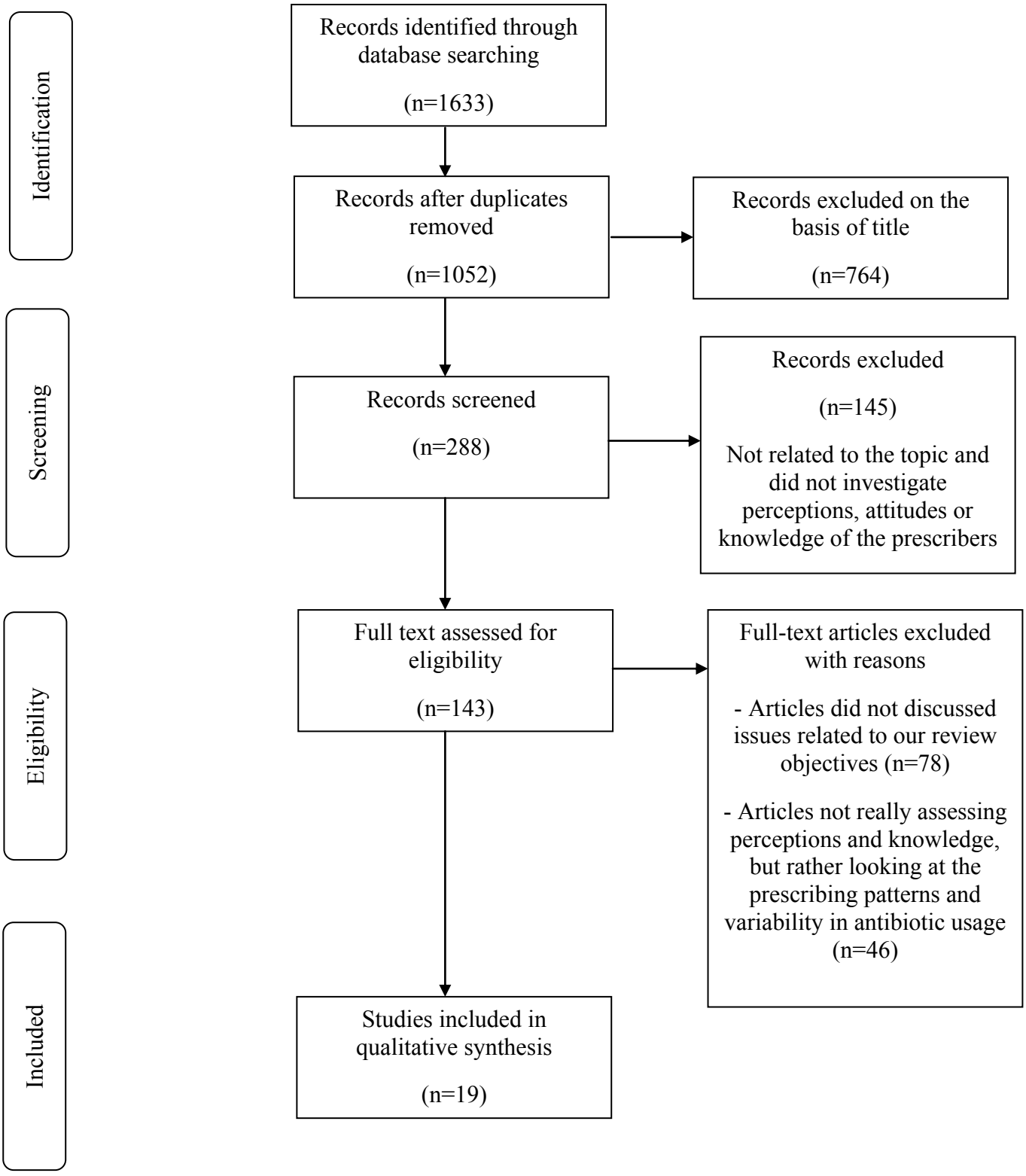

Figure 1: The PRISMA Diagram (The template is adapted with modification from Moher et al. 2009 (43)).

Methodological quality

Each study was reviewed and a consensus meeting was convened to ensure quality assurance. The most prominent pitfall identified was a lack of generalizability of the study results to whole populations, as most studies were restricted to certain geographical areas, countries, or provinces/ regions. There were two studies in which limitations were not mentioned by the authors (48, 49). In addition, three of the studies had a response rate less than 50% (29, 50, 51), which can be a limitation to the generalization of the results of these studies. In some of the studies, participants were from different specialties and treating different infectious diseases (51-54), while other studies were specific and a certain disease condition such as paediatric common colds (49), URTIs (29, 35, 50, 55, 56), and surgical site infections (57). In some of the studies, the authors stated that the respondents may be triggered to the topic and gave socially desirable answers [23]. Four of the included studies (56, 58-60) incorporated qualitative methodology and although they addressed the topic with an in-depth exploration, their findings are not possible to be generalized.

- *Characteristics of selected studies*

The study setting was ambulatory care in eight studies (29, 35, 48, 49, 56, 60-62), hospital setting in seven studies (51, 52, 54, 57, 63, 64) and both primary and hospital care in four studies (39, 50, 55, 58). Sixteen studies focused solely on physicians, while three studies included pharmacists, patients or the general public. However, for the studies that also reported results related to other groups, e.g. pharmacists and/or patients, only their results related to physicians are reported in this review.

In these studies, the response rates varied widely from 33% to 87% (Table 1). The lowest response rate (33%) was reported in a Spanish study. By using telephone call reminder and follow up, Wester *et al* and Mohan *et al* achieved higher response rates, 87% and 84.4% respectively (35, 53).

With respect to the disease/clinical condition, ambulatory care infections including URTIs, diarrhoea, the common cold and sore throats were the subject of 11 studies (29, 35, 39, 48-50, 55, 56, 58, 60, 61, 64). Other studies targeted infections in various specialties in hospital settings. As shown in Table 1, it is important to note that the study variables and objectives varied between the different studies. Some of them focused on knowledge and other studies focused on attitudes or beliefs or prescribing practices.

Main findings

The findings will be divided into five sections starting with the knowledge of physicians regarding the prescribing of antibiotics

- *Knowledge of physicians regarding the prescribing of antibiotics*

Six studies evaluated the knowledge of physicians towards antibiotic use and resistance (39, 51, 53, 54, 64, 65).

Three studies, from the United States (US), UK and Peru, assessed doctor's knowledge regarding antibiotic use in upper respiratory tract infections (URTIs) (29, 61, 64). In the US study, 99.5% of the surveyed residents thought they had at least average knowledge about the treatment of URTIs (29). Most participants agreed that there was no need to start antibiotics in mild cases of URTIs in the US (81%) and Peru (76%), but a considerable percentage thought that more symptomatic events, such as patients with purulent nasal discharge, would need an antibiotic (29, 64). Physicians in UK acknowledged that antibiotics were prescribed too often for URTIs in primary care settings, although they were aware of the evidence for the limited effect of antibiotic treatment in this situation (61). Moreover in these studies, physicians commented on reducing antibiotic usage in URTIs and the relationship with the treatment outcome (49, 61, 64).

Cho *et al* in Korea conducted a study on the prescribing of antibiotics in children with a common cold. The study showed that physicians in this study agreed that they could reduce by more than a quarter their antibiotic use without jeopardizing their patients' treatment outcome. Nevertheless, 72.8% of physicians believed antibiotics could reduce the occurrence of complications. In other studies,

physicians in United Kingdom (61) and Peru (64) thought that prescribing narrow spectrum antibiotics, and prescribing them occasionally, could do little or no harm in terms of the development of antibiotic resistance. Chamany *et al* (50) in the US found that majority of the physicians (92%) agreed that fewer antibiotics will reduce the risk of antibiotic resistance. However they were concerned about patients' dissatisfaction if antibiotics were not prescribed. Consequently, 64% of them thought it was necessary, and would eventually prescribe antibiotics to their patients with upper respiratory tract infections. Similar results were reported by physicians in Europe where they felt that antibiotic prescribing should be minimized to prevent escalating of antibiotic resistance (56).

- *Attitudes and confidence level in making antibiotic decisions*

Five studies assessed confidence levels among the physicians in their prescribing of antibiotics. There was a strong consistency among physicians with respect to their confidence level in making decisions on antibiotic prescribing. Some doctors especially junior doctors or those in their internship always discussed URTI care with senior physicians (59%-98%), yet only 2.8% to 5.4% of them did not feel confident making decisions regarding treatment (29, 39, 65). Some of the physicians in Peru and DR Congo (31% and 54.5% respectively) agreed it is difficult to select the correct antibiotics for their patients (39, 64). However in one study by Srinivasan *et al*, those who reported they were very confident in their antimicrobial use did not appear to have a better knowledge regarding antibiotics than those who were not confident (54). Despite their confidence, physicians find it difficult to select correct antibiotics for their patients. As a result, physicians do consult a colleague when prescribing antibiotics (39). However, this is less likely in the private sector where physicians prescribe in isolation

82% of respondents in a US study opted to use a diagnostic test (rapid antigen detection test or culture) to help decision making in the management of URTIs (29). However in two studies conducted in LMICs (35, 52), doctors did not favour using laboratory services due to a lack of, or limited, diagnostic facilities coupled with a delay in receiving the test results; alternatively, the belief that it is not necessary. In addition, in countries where payments for healthcare services are by the patient, i.e. out-of-pocket payments, physicians did not want to burden their patients with laboratory fees where they could not afford these (60).

- *Awareness towards antibiotic resistance*

Most of the studies reported that physicians had a general idea about the problem of resistance and its consequences. However, the majority of the studies reported that physicians had a low level of knowledge regarding the prevalence of antibiotic resistance rates in their local settings (39, 51, 53, 64, 65). For example, Pulcini et al. showed that only 16% of young doctors in a French hospital knew the actual proportion of community acquired-*Escherichia coli* resistant to fluoroquinolones (65). Similarly, only 10% respondents in DR Congo knew about *Klebsiella* spp. resistant to ceftriaxone (39). However, physicians who specialized in infectious disease (ID) estimated antibiotic resistance rate more accurately compared to physicians in general medicine and other non-ID subspecialists (53). In two of the studies, senior residents in Spain and junior doctors in United Kingdom knew more about the prevalence of MRSA compared to other physicians in their practicing centres (51, 65). In these studies, years of practice and past training experience did not influence physicians' knowledge level.

Physicians from three studies (48, 49, 61) agreed that antibiotic overuse in outpatients contributed to the emergence of resistance. Contrary to this, participants from three studies considered antibiotic use in secondary healthcare or hospital setting as the main contributor to the existence of resistance (56, 58, 59). Encouragingly, over 90% of physicians in two studies in the US agreed that there would be a reduced risk of antibiotic resistance infections if fewer and better use of antibiotics were practiced (50, 54).

- *Source of information and familiarity with guidelines*

Several studies evaluated the main sources of information used by physicians regarding antibiotics. The majority of the physicians in the studies were familiar with guidelines related to antibiotics, but still some were not using them. For example in Sudan, only 32.6% of physicians referred to Sudan National Formulary (SNF)or the British National Formulary (BNF), while the remainder did not use any reference source for their decision making (57). Physicians in Peru referred to the Sanford Guide on

Antimicrobial Therapy for information regarding antibiotics, and considered it as a very useful source (64). Similarly, 66.3% of physicians in DR Congo referred to guidelines when making treatment choices. However, the WHO Guidelines appeared to be the least popular as an information source as only 26.6% of them stated they used them as a reference (39). Physicians in Spain appreciated the recommendations contained in clinical guidelines; however, preferred these to be adapted to the local situation (59).

Pocket-based antibiotic guidelines were rated as the most useful source of information. For example, the majority (98%) of the respondents in a US study and 50% in two public hospitals in Peru used 'The Sanford Guide', a pocket-sized guideline (39, 54). Physicians in India wanted antibiotic guidelines to be provided in all community hospitals to assist them in their appropriate use (60). However, 36% of respondents in Peruvian hospitals said the national guideline was not useful, while 25% said they were not familiar with it (64).

In several studies, pharmaceutical companies were regarded as one of the major influences of antibiotic prescribing. For example, 20% of the physicians in US reported that their interaction with pharmaceutical representatives influenced their own antimicrobial selections (54). Similar result were found in a Spanish study by Vazque-Lago *et a*l where physicians attributed a very clear influence from pharmaceutical promotion and advertising when it came to choosing antibiotics (59). However in Trinidad, general practitioners did not feel pressured by pharmaceutical companies promotional efforts to prescribe antibiotics to their patients (35). Other than clinical guidelines and information provided by the pharmaceutical companies, physicians also believed in educational courses and internet-based information to assist with future prescribing of antibiotics (39, 64).

- *Practice and factors influencing prescribing behaviour*

Several factors were reported in the literature that could influence prescribing behaviour. 73% of physicians in Korea reported that parents expected an antibiotic prescription during the consultation. Consequently, 40% of them prescribed antibiotics even if they felt these were unnecessary (49). Similar results have been found in DR Congo where 62% of physicians perceived patients pressure being a contributing factor to the overuse of antibiotics in the community (39). However in South Africa, the prescribers reported that they were least influenced by patients' request or expectations (52).

Among other reported reasons for prescribing antibiotics were the severity of illness and duration of infections (35), to avoid secondary bacterial infections (35, 55), or because of uncertainty between bacterial or viral infections (55), following patients' request or perceived request (49, 50, 60, 61, 66), and afraid of losing patients (49, 60). More than half of European primary care paediatricians (65.1%) reported of using delayed antibiotic prescribing in management of URTIs, a method which is recommended by the National Institute for Health and Clinical Excellence (NICE) (55).

Other factors influencing the prescribing of antibiotics, including economic factors as well as the availability and supply of antibiotics, were not typically mentioned in the papers incorporated into this review. However, it is acknowledged they do influence prescribing (19, 21, 25).

Discussion

The same sections will be discussed to provide future guidance

- *Knowledge among physicians regarding antibiotics and antibiotic resistance*

This systematic review showed that physicians had a general idea about antibiotic resistance as a clinical problem, but they were underestimating its prevalence. Knowledge of antibiotic resistance rates was not related to the level of experience among the practitioners. In this aspect, physicians have an overview of resistance as a problem, showing a high level of awareness that this may jeopardize future patient care. However, few perceived that antibiotic resistance was an important problem in their own clinical practice, suggesting that many physicians see the risk of antibiotic resistance as more theoretical than actual, possibly weakening the motivation for behaviour change (53). Although many doctors agreed that reducing antibiotics will reduce the risk of antibiotic resistance, there is still there a high proportion reporting they would prescribe antibiotics for conditions

for which antibiotics are not usually indicated. This indicates that several external factors may also influence their prescribing. Identified factors included avoiding patients' dissatisfaction, and sometimes their own belief that the antibiotic would be necessary (50). Also, they may believe that they are more effective as physicians when they prescribe medications to treat their patients, even though this may be unnecessary. However, this is speculation at this stage and needs further research. In any event, this underscores the importance of educational sessions including active drugs and therapeutic committees (DTCs) and dissemination of guidelines as well as the availability of local resistance data to improve future antibiotic prescribing (20, 24, 25, 51, 67).

Regarding their practice, physicians believed that wide and easy access to up-to-date information would allow them to make more informed decisions about antibiotic prescribing, including selecting narrow-spectrum antibiotics that are most likely to be effective (56). However, the low average score of knowledge regarding antibiotic use and resistance suggests that antimicrobial education has been suboptimal (54). Reduced knowledge has made physicians, as well as the patients, believe that antibiotics are standard treatment for a number of conditions even if this may not be the case. It is also believed that physician personal experience with antibiotic resistance will increase their awareness about the importance of harmful effects caused by antibiotic resistance (53). Knowledge and appropriate antibiotic use may also improve as physicians advance through education, training and clinical practice. Consequently, improving antibiotic prescribing through training physicians in continuing medical education programmes, and issuing clinical guidelines for their appropriate use based on local microbiological data, are important strategies(60).

The review by *Huttner et al* showed that a number of interventions can be used to educate physicians regarding the prescribing of antibiotics. These include academic detailing, audit and feedback of prescribing behaviour as well as the distribution of guidelines (68, 69). Other authors have shown that the implementation of guidelines and subsequent improvement in prescribing is enhanced by keeping them up-to-date, involving all key stakeholders in their compilation, as well as incorporating multiple components in their implementation (26, 70). This includes active dissemination strategies coupled with monitoring and feedback of prescribing patterns as well as keeping guidelines simple and limited in number (69-77). Trust in those developing the guidance is also important given the appreciable potential for bias (72, 73, 78). Multiple interventions can be divided into managerial approaches alongside educational interventions (20). Managerial interventions include computerized decision support systems, prescribing indicators, community case management programmes, formulary restrictions and prior authorisations (19, 20, 25, 79). The added influence of multiple interventions alongside educational activities to favourably influence physician prescribing has also been shown in other disease areas with interventions including indicators, financial incentives to all key stakeholder groups and prescribing restrictions (80-83). Barriers to change not only relate to physicians but other parties including patients, health care systems, available resources, leadership and the current political environment. Consequently, strategies need to be tailored and targeted at different levels to improve the future use of medicines including antibiotics (70).

- *Attitudes and confidence level in making antibiotic decisions*

Many studies in the literature reported that junior physicians or physicians in training were less confident about antibiotic prescribing compared to attending physicians with more years of clinical experience. Low knowledge of antibiotics may account for less confidence among the physicians in their ability to use antibiotics optimally (54). Physicians without a recent formal teaching or training on antimicrobials were less knowledgeable compared to those with exposure to formal teaching, suggesting that when education does occur it is effective (54).

Furthermore, physicians in the first year of practice chose antibiotics more frequently for viral URTIs than did those in longer period of practice (29). This suggests it is important that the rational use of antibiotics and antibiotic resistance are adequately covered and emphasized during medical education. Junior doctors should also be a target group for future interventions to improve antibiotic prescribing.

- *Practice and factors influencing prescribing behaviour*

Patient demand and perceived need for a quick relief of their symptoms does appear to promote inappropriate antibiotic use. Attempting though to change patient's beliefs and expectations during the

consultation is often perceived as time-consuming and unrewarding (61). Physicians, especially those at outpatient settings, do respond to the demands of patients by prescribing antibiotics rather than providing explanations why antibiotics are not needed. This though can raise concerns that some physicians practice 'throwing antibiotics at everything', taking the easy way out rather than spending some time discussing potential treatments including why not prescribing antibiotics with their patients (50). However, in today's healthcare system where physicians in many countries have only a few minutes to fully evaluate the patient, make a diagnosis and prescribe a treatment, and given the increasingly litigious nature of society, they frequently find themselves under tremendous pressure to prescribe an antibiotic even when this may not be appropriate (4).

These findings highlight the need for training for physicians to educate patients in the rational use of antibiotics, especially in outpatient settings, in order to improve their practice. Educational interventions and campaigns to improve antibiotic prescribing must also target patients as they do influence prescribing decision. Patient campaigns could include education by healthcare professionals, distribution of leaflets and posters in public places, e.g. shopping malls, bus stations, and clinics as well as mass media including newspaper advertisements and possibly the TV, building on examples in the literature that have resulted in a more judicial use of antibiotics (68).

A number of campaigns have been successfully undertaken across countries to improve antibiotic use. This includes Australia, Chile, Europe and Korea. A summary of the programmes and their impact are contained in Table 2.

Table 2 – Summary details of programmes to influence the subsequent use of antibiotics and their impact

Country	Summary details and impact
Australia (20)	• The National Prescribing Service (NPS) conducted an antibiotic promotion programme to promote the quality use of antibiotics • The programme targeted general practitioners (GPs), pharmacists and consumers, with activities including academic retailing or clinical audits, prescribing feedback (for GPs), newsletters and promotional materials to consumers via radio, TV, and local newsletters. In addition, books and resources were distributed to GPs and community pharmacies • The programme has resulted in a major reduction in antibiotic use, e.g. reducing the number of antibiotic prescriptions for URTIs from 80 per 1000 consultations in 1996 to 50 per 1000 consultations in 2007
Chile (20)	• A new regulation in 2000 prohibiting the dispensing of antibiotics without prescription was associated with a reduction in overall sales of antibiotics in the private sector • Utilisation declined from 0.34 DDD/1000 inhabitant-days (UD$37,603,688) in 1996 to 0.25 DDD/1000 inhabitant-days (UD$32,141,856) in 2000
Europe – France (42)	• Launching of the multifaceted national programme 'Keep Antibiotics Working' targeting all key stakeholders in 2001 • This programme was coupled with the public service campaign 'Antibiotics are not automatic' every winter since 2002 • Compared to the pre-intervention period (2000–2002), the total number of antibiotic prescriptions per 100 inhabitants, adjusted for the frequency of flu-like symptoms during the winter season, decreased by 26.5% in the 2003-2007 period. The greatest reduction in antibiotic use (-36%) was seen among children
Europe – Italy (84)	• A community-based educational intervention was instigated to improve antibiotic prescribing in the outpatient setting • This included posters, brochures, and advertisements in the local media targeting the community coupled with a newsletter on antibiotic resistance targeting pharmacists and physicians • The multifaceted programme subsequently significantly improved antibiotic prescribing
Europe –	• Multifaceted interventions were conducted from 1999/ 2000 onwards in

Slovenia (85)	Slovenia • This involved all key stakeholder groups including the Ministry of Health, Health Insurance, physician groups and patients • The multifaceted programmes reversed a 24% increase in antibiotic consumption during the 1990s to a 31% reduction by 2012 compared with the late 1990s. Expenditure on antibiotics was decreased by 53%
Europe – Sweden (86, 87)	• The multifaceted Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance (STRAMA) — had a major contribution to reducing antibiotic use in Sweden • Over ten years (1995-2004), antibiotic use for outpatients decreased from 15.7 to 12.6 DDDs per 1000 inhabitants per day, and from 536 to 410 prescriptions per 1000 inhabitants per year
Korea (20, 34)	• A national policy was introduced in 2000 prohibiting the dispensing by general practitioners of medicines including antibiotics • This was associated with a reduction in antibiotic use from 80.3 to 72.8% for viral illness episodes and from 91.6 to 89.7% for bacterial illness episodes

In 2008, the Centre for Clinical Practice at National Institute for Health and Clinical Excellence (NICE) developed a guideline for antibiotic prescribing in upper respiratory tract infections for adults and children in ambulatory care. They emphasized delayed antibiotic prescribing as a safe method of implementing alternatives to immediate antibiotic prescribing for acute uncomplicated URTIs to promote their rational use (88). In the US, pharmacists are being encouraged to become a part of antimicrobial stewardships in hospitals to improve subsequent antibiotic use with future implications for the community (89).

In line with implementing suggested prescribing approaches, communication skills and certainty of the diagnosis ranked among the highest indirect factors influencing antibiotic prescription (90). Physicians may feel that using prescriptions to bring a difficult consultation to a conclusion was the only way to get through a busy clinical schedule (91). This factor is also related to patients' expectations, where some studies showed that improvement in communication between physician and patients can reduce patients' expectation to antibiotic treatment (92-94).

In Malaysia, activities were undertaken by the Ministry of Health (MOH) to improve patients' knowledge of their medicines as well as improve antibiotic prescribing. General initiatives included 'Know Your Medicine' campaign initiated in 2010, based on the 5Rs, i.e. **R**ight patient, **R**ight medicine, **R**ight dose, **R**ight route and **R**ight time. This involved communication campaigns in hospitals, media, and the community including supermarkets, religious places, schools and community halls. Initiatives to improve the prescribing of antibiotics included the establishment of the Infection Control and National Antibiotic Committee in Malaysia in 2000, with monitoring of antibiotic utilization patterns ongoing since 2005 (95). This has been conducted under the annual National Medicines Use Survey. Future activities include ascertaining point prevalence data where patient level data will be collected and fed back to physicians to improve future antibiotic prescribing as well as campaigns with patients.

- *Source of information and familiarity with guidelines*

In the various studies, there were several information sources available to physicians. These include colleagues, pharmaceutical company representatives, guidelines, electronic data sources, and medical journals. Pharmaceutical companies appear to exert appreciable influence on antibiotic usage. This was demonstrated by Sondergaard *et al*, who showed that visits from pharmaceutical representatives had a significant impact of physicians' subsequent prescribing (96). Similar result has been reported in by McGettigan *et al*, who found that information on new medicines prescribed had come from pharmaceutical representatives in 42% of cases (97). This is not surprising, as pharmaceutical companies engage in an appreciable number of activities to enhance the funding and utilisation of their medicines (98-101). However, some physicians reported that they prescribed promoted medicines within a certain time period and when the promotion from pharmaceutical companies stopped, physicians claimed they would also stop prescribing the medicines (59).

Typically, information provided by pharmaceutical companies ranked among highest choice of references among physicians. This highlights the prominent role of pharmaceutical industry as a key

source of information about medicines, especially in low and middle income countries (17, 102, 103). This is of concern as drug promotion, especially in developing countries, may not always be evidence-based adversely impacting on future care (17, 104, 105). Undue pressure on healthcare providers by pharmaceutical companies may also increase inappropriate use (43,76). Consequently, it is important to counteract this influence if this adversely affects the rational use of medicines. Several countries have taken steps in this regard (83, 106-108). In Croatia, pharmaceutical companies are required to report all their promotional expenses as well as financial remuneration to physicians for prescribing. Contact between pharmaceutical company representatives and physicians is also limited, enforced through financial penalties (83). In South Korea, by law pharmaceutical companies must not pay for physicians to participate in conferences, leading to fines for abuse (106). In the US, pharmaceutical companies are now required to report their gifts and payments to physicians (108). These countries provide examples on how relationships between pharmaceutical companies and healthcare professionals can be addressed to reduce their influence on future prescribing, reducing potential concerns (109).

Pocket-sized treatment guidelines seem to be most popular as an information source, suggesting that small and handy types of references are more preferred and more accessible. This is important as poor adherence to guidelines increases medication risks and decreases antibiotic benefit through wrong choices and dosing by physicians (58).

We are aware that eleven of the included studies were conducted in developed countries (29, 49-51, 53-56, 59, 63, 110), while eight studies were conducted in developing countries including Bangladesh, DR Congo, India, Lesotho, Peru, Sudan and Trinidad and Tobago (35, 39, 48, 52, 57, 58, 60, 64). There are appreciable differences in healthcare delivery between developed and LMICs, with limited information and lack of resources creating barriers to accessing and providing adequate healthcare in developing countries. This does create differences. Having said this, physician knowledge of resistance appeared adequate across studied countries with most studies reporting that physicians had a general idea about the problem of resistance and its consequences. However, this did not always translate into appropriate prescribing of antibiotics. This may be due to patient pressure to prescribe antibiotics among both developed and developing (LMIC) countries. Differences between countries included the fact that in developed countries, internet based information served as a common resource of information. This is in contrast with the developing (LMIC) countries where internet resources are used by only some physicians. Limited access to internet connection and other electronic facilities has made information from the internet more difficult to access compared to other available resources (39). This though is likely to change in the future. Knowledge and perceptions among physicians in LMICs may also be different. They agree that antibiotic prescriptions can be reduced; however, they believed that prescribing narrow spectrum of antibiotics occasionally are safe(64). Choosing correct antibiotics are often difficult in LMICs due to a lack of local guidelines and limited access to up-to-date international guidelines; therefore the majority of physicians will consult a colleague when doing so (39, 64). Physicians in LMIC also believe laboratory tests may not always be necessary, due in part to limited of diagnostic facilities, delay in receiving the test results, and many patients unable to afford laboratory fees (60). Physicians in LMIC countries may also feel pressured by pharmaceutical company promotions; however, this is not universal (21, 35, 98). Other factors influencing antibiotic utilization in LMIC countries relate to the health system, i.e. unavailability of the recommended antibiotic (24), oversupply of antibiotics and near-expiry antibiotics in some primary healthcare centers (21), as well as economic benefits from prescribing certain antibiotics over others(21, 24, 33) .

We are also aware that we included different physician specialties. This is because of the very limited number of studies that only concentrate on one physician group. For example, *Fakih et al* included residents from different specialties, i.e. internal medicine, family medicine, emergency medicine and paediatrics (29), *Grossman et al* and *Cho et al* included primary care/ family physicians and paediatricians (49, 55), *Pulcini et a*l included physicians from different medical and surgical specialties (63), and *Srinisavan et al* studied physicians from different medical specialties including general medicine, emergency medicine, Obstetrics/ gynaecology, surgery and neurology (54).

Other limitations include the fact that the literature search was carried out based on electronic databases to which the authors' university library subscribed. As a result, it is possible that some studies might not have been retrieved. In addition, papers that were published in languages other than English were excluded from the review. Moreover, the review focused on the recent literature,

i.e., from 1990 and onwards. However, we believe this is justified because older studies might not be relevant to current practices. Nevertheless, overall we believe the findings of this systematic review are robust and can provide excellent guidance for the future to promote the rational use of antibiotics.

Conclusion

It is evident from the various studies that inappropriate prescribing and knowledge of antibiotics is a concern among physicians in general and young physicians in particular, with physicians willing to prescribe antibiotics even for viral illnesses. Several factors appear to influence prescribing behavior. These include demands from patients, pharmaceutical company marketing activities, limited up-to-date information sources and physicians afraid of losing their patients. Inappropriate prescribing of antibiotics when it occurs also appears to be related to inadequate knowledge or training on the appropriate prescribing of antibiotics. It was encouraging to see that physicians were interested in learning more and improving their prescribing practice to address this. The majority of the physicians in the studies also wanted more feedback on their antibiotic prescribing decisions. Issues of supply, healthcare infrastructure as well as financial incentives can also affect subsequent antibiotic prescribing and utilization especially in LMIC countries.

This provides guidance for the future given the projected mortality and financial implications if the increase in inappropriate antibiotic prescribing and AMR is unchecked. Typically, multifaceted and multilevel interventions strategies that target all key stakeholders, including physicians and patients, are needed to improve the rational use of antibiotics thereby helping reduce resistance development.

Conflicts of interest
Dr Faridah Aryani Md Yusof is employed by the Ministry of Health in Malaysia. Otherwise the authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those already mentioned

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Key points

- Understanding physicians' knowledge regarding antibiotics, how this knowledge is acquired and maintained, as well as factors influencing the prescribing of antibiotics is key to introducing future strategies to enhance the rational use of antibiotics. As a result, help reduce future resistance development
- A systematic review was undertaken to assess current knowledge to provide future direction. This eventually involved 19 papers from 1633 titles and abstracts once only pertinent papers were included. The studies were across healthcare sectors and involved both developed and developing countries
- The main findings showed that some physicians still have inadequate knowledge and misconceptions about antibiotic prescribing. In addition, whilst aware that antibiotics are of limited benefit or unnecessary for some conditions they were still prescribed
- Influencers of physician prescribing included patients' requests and expectations, severity and duration of infections, belief that antibiotics can prevent secondary bacterial infections, uncertainty between bacterial or viral infections, potential losing of patients if antibiotics are not prescribed, influence of pharmaceutical companies and limited access to information sources on antibiotic prescribing
- Pocket-size guidelines were seen as the most important source of information on antibiotic prescribing. This along with future training and feedback will help improve future antibiotic prescribing
- Educating patients is also important to improve the future rational use of antibiotics

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Table 1 Description of studies reporting on knowledge, attitude, beliefs and practices among physicians regarding antibiotic prescribing

Author(s) and year	Country of study	Study design	Survey characteristics	Response rate/sample size	Study population
Grossman et al (2012)	A multi-country study involving 21 countries from Europe	Cross-sectional web-based questionnaire	- 69 Questionnaire was pretested with national coordinators of EAPRASnet (European Academy of Pediatrics Research in Ambulatory Setting Network), and changes made following their comments. - Data collection was carried out using a Web-based survey posted on European Academy of paediatrics homepage. Respondents were invited to participate via email using a mailing list in EAPRASnet. Paediatricians not belonging to the network were prompted by the Coordinators to visit the hompage and fill in the survey. Three reminders were sent out via email	- 695 respondents answered the questionnaire; 685 were valid responses. - 397 were EAPRASnet members and 288 were paediatricians visiting the web page through the embedded link.	- Primary Care setting - Paediatricians and Physicians - Mean age 50.9 (±7.5 years) - 47.6% female; 52.4% male - Respondents from 21 countries, predominantly from Germany, Spain and Italy (27.3%, 24.7%, 19.4%, respectively) - 86.9% were primary care paediatricians and 13.1%physicians.
Fakih et al. (2003)	Michigan, USA	Cross-sectional Self-completed questionnaire	- Institutional board reviews and program directors' approval were obtained from graduate medical education programs involved in internal medicine and family practice in southeastern Michigan. Then, the survey was mailed to every program director to distribute it to their resident physicians. - Survey included 22 Likert scale-based questions and 9 multiple-choice answers.	- 48% (n=182) from 11 primary care programs responded. - They were from Internal medicine (IM) 61.6% (n=112), family practice (FP) 25.8% (n=47), emergency medicine (EM) 10.8% (n=19), and medicine-paediatrics (MP) 2.2% (n=4)	- Primary care setting - 52.5% male; 47.5% female - Participating resident physicians were in postgraduate years; Year 1 (63 residents [34.6%]) Year 2 (45 [24.7%]) Year 3 (57 [31.3%]) Year (8 [4.4%])

Cho et al. (2004)	Korea	Cross-sectional Self-completed questionnaire	- Using simple random sampling, 600 physicians from two specialties—family practice and paediatrics (300 from each specialty). - Questionnaire was pre-tested with 15 family physicians and 20 paediatricians. - Questionnaires were mailed three times with a pre-paid return envelope. Follow-up telephone calls were made to non-responders.	75% (n=409) (74.2% for family physicians and 75.4% for paediatricians)	- Primary care setting - 75.1% male; 24.9% female - > 90% were solo practitioners in urban areas. - They see approximately 80 patients in a usual day
Pulcini et al. (2010)	France and United Kingdom	Cross-sectional Self-completed questionnaire	- Survey involved junior doctors in two public teaching hospitals; Dundee, Scotland, UK and Nice, France. - Participants were identified using data provided by Human Resource Department. - The questionnaire was developed in consultation with a group of experts, and was piloted with 10 junior doctors. - In Dundee, the questionnaires were distributed at the beginning of a compulsory training session. - In Nice, questionnaires were sent by email and could be returned by fax, E-mail or mail. Reminders emails were sent after 3 weeks for non-responders, and a telephone call reminders after 6 weeks.	73% (n=139)	- Hospital setting - 82 participants were from medical specialties, and 39 from surgical specialties.

Thriemer et al. (2013)	DR Congo	Cross-sectional Self-completed questionnaire	- A Purposive sample of last year medical students (who are prescribing as part of their practice) and prescribing medical doctors - Questionnaire was distributed and collected by trained collaborators - Medical students were recruited at the University Hospital of Kisangani. - Medical doctors were visited on site after making an appointment - The respondents filled in the questionnaire forms, with collaborators available for explanation.	94.4% (n=184)	- Hospital and health centers (outpatient) setting. - Medical doctors and medical students accounted for 78 (42.3%) and 106 (57.6%) of respondents respectively. - Among medical doctors, 11.5% (n=11) has less than 1 year work experience; 38.5% 1-3 years; 23.1% 4-6 years; 26.9% more than 10 years. - 54.4% prescribed antibiotics more than once a day; 15.2% 1-2 times; 17.4% 3-5 times per week. -
Butler et al. (1998)	South Wales, UK	Qualitative study with semi-structured interviews	- A sampling frame was constructed to identify the general practitioners (GPs) according to their size of practices. - Interviews were conducted with GPs and lasted 10-35 minutes. - The semi-structured interviews were piloted with four GPs. - All questions were open. New questions were added as the interviews progressed. When no new themes emerged, the interviews were ended.	21 GPs recruited	- Primary care setting - 17 of the GPs had qualified in Britain, 13 held MRCGP, working experience between one and 28 years.
Sutradhar et al. (2014)	Bangladesh	Cross-sectional Self-completed questionnaire	- The survey was done in 24 Upazila Health Complexes and 112 Union Health Centers of Dhaka and Rajashi divisions. - Questionnaires were pilot-tested prior to the main survey. - The survey was done by inteviewers, following a face-to-face interview protocol. - Questionnaires were given only to the spontaneously interested candidates during the survey.	580 physicians	- Outpatient setting (health centers) - Registered physicians practicing in the Upazila Health Complexes and Union Health Centers

Srinisavan et al. (2004)	Baltimore, USA	Cross-sectional Self-completed questionnaire	- A 75-item survey was developed, including 10-item antimicrobial quiz. - The survey was administered to the house staff physicians at John Hopkin Hospital. - Surveys were distributed on campus and by electronic mail to the participants. - Surveys were re-sent every 2 and 4 week for those who had not returned them.	- 67% (n=179) responded as follows: - General medicine 86 (83%), -Emergency medicine 23(64%) - Obe/Gyn 15 (50%) - Surgery 40 (48%) - Neurology 5 (33%)	- Hospital setting - 32% was in the first year of residency; 23% second year; 31% third year; 13% beyond that. - Emergency house staff prescribed antibiotics the most (78% prescribing more than once a day;33% Ob/Gyn; 25% surgery; 20% medicine)
Mohan et al. (2004)	Trinidad and Tobago	Cross-sectional Self-completed questionnaire	- Questionnaires were distributed among GPs from central and east Trinidad, from the respective branches of the Trinidad and Tobago Medical Association. - Letters were mailed to the doctors followed by telephone calls inviting them to participate.	84.4% (n=92)	- Primary care setting - Doctors working in primary healthcare in the public sector were excluded. - 88% male (81); 12% (11) female. - - Mean age: 52.55 years - 26.1% had >30 years of practice; 41.3% less than 20 years
Garcia et al. (2011)	Peru	Cross-sectional Self-completed questionnaire	- The Survey was done with residents (physicians in training) and attending physicians (staff physicians) from two public hospitals, Cayetano Heredia (CHH) and Arzobispo Loayza (ALH), both are tertiary, teaching hospital located in urban areas. - Questionnaire content was based on a previous survey in US, adapted into Peruvian system. Prior to administration, it was reviewed by a team of 6 infectious disease physicians.	82% (n=260)	- Hospital setting - 53% (135) residents (physicians in training) and 47% (121) attending physicians (staff physicians after completing training and specialization) - 55% of respondents has less than 5 years working experience

Chandy et al. (2013)	South India, India	Qualitative study using focus group discussion (FGD)	- Recruitment was done through purposive sampling. Open invitations were given through respective associations, selection based on their willingness and ability to commit time for the FGD. - Discussion was guided by a moderator, who communicated the objective of the discussion, and used a semi-structured discussion guide with predefined themes.	Two groups of 6 doctors each, from urban and rural area.	- Doctors were mainly in private practice and hospital, from urban and rural areas. - Age range for urban doctors: 33-63 years, while 29-54 for rural doctors.
Woods et al. (2013)	A multi-country study from Europe	Qualitative study, using a semi-structured interview and a fixed category survey	- Primary care clinicians were selected randomly from Genomics to combat Resistance against communiti-acquired LRTI in Europe (GRACE). - Interviews were conducted by a trained interviewer. A pre-piloted interview topic guide was used to facilitate the interviews.	80 interviews were conducted.	- 41% were female participant. - Mean age 43 years. - Mean years in practice; 16 years
Zaki et al. (2012)	Sudan	Cross-sectional hospital based interview study	- Participants were selected randomly from private and governmental hospitals. - The survey used a 16-item antimicrobial quiz questionnaire.	72.4% (n=181)	- 86.7% practitioners were from governmental hospital while 13.3% practitioners were from private hospitals.
Chamani et al. (2005)	USA	Cross-sectional self-completed questionnaire	- Questionnaires were distributed among American College of Obtetricians and Gynecologists (ACOG) Fellows. - Questionnaires were sent by mail. Non-responders received second mailing after 6 weeks of first mailing.	48% (n=428)	Obstetricians and Gynecologists in ambulatory settings within USA who manage upper respiratory tract infections (URIs) in non-pregnant patients.
Navarro-San Francisco et al. (2013)	Spain	Cross-sectional self-completed questionnaire	- The survey was conducted with all resident doctors in 5 teaching hospitals in 4 different cities (Madrid, Sevile, Murcia and Barakaldo) - This is an online survey. A link to the questionnaire was emailed to all	33.05% (n=279)	844 residents in various specialties

			participants. - Residents received 3 reminders during the 8 weeks of survey		
Vazquez Lago et al. (2011)	Spain	Qualitative study using focus group discussion (FGD)	- The study used a theoretical model based on previous systematic review. - Participants were recruited with the support of Galician Association of Family and Community Medicine. Potential participants were contacted by telephone or email. - Each FG was made of 4-10 GPs, sessions were held in the meeting room at the respective health centers at the time reserved for teaching activities.	44% (n=33)	- GPs in the Spanish NHS in Galicia actively engaged in healthcare. - 14 female (42.4%) and 19 male (57.6%)
Kotwani et al. (2010)	India	Qualitative study using focus group discussion (FGD)	- Three FGD conducted; 1 group composed exclusively doctors from private sectors, one group for public sector doctors and the third group contained doctors from both sectors. - The FGDs was conducted with the help of a topic guide. - Results from a completed antibiotic use and resistance study were given to participants at the beginning of FGDs.	36 doctors participated in 3 FGDs	Primary care doctors practicing in both private and public sectors
Adorka et al. (2013)	Lesotho	Cross-sectional self-completed questionnaire	- The survey was conducted in 5 Health Service Areas in Lesotho. - Questionnaires were distributed and collected by the principal researcher.	76% (n=51)	All doctors and nurses who prescribed antibiotics.
Wester et al. (2002)	Chicago, USA	Cross-sectional self -completed questionnaire	- The survey was conducted in 4 Chicago hospitals. - A 94-item self-administered questionnaire was used to collect information.Questionnaires were distributed among prescribers. After 2 weeks, phone calls were made to remind non-respondents.	87% (n=424)	Physicians included: All internal medicine residents and attending physicians, who cared for a minimum of 60 inpatients in that year. (excluding cardiologist and neurologist)