The patient's role in the spread and control of bacterial resistance to antibiotics

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As the ultimate consumers, patients play an important role in the emergence, spread and control of bacterial resistance to antibiotics. Improved knowledge of antibiotics and the problem of resistance, as well as a better understanding of beliefs, pressures/concerns, and expectations, from both the patient's and physician's perspectives, are fundamental for controlling antibiotic use. There is growing evidence to suggest that empowering patients through implementation of patient-centered health-care strategies, such as shared decision-making, in conjunction with educational initiatives help to change attitudes and behavior, and improve access to and completion of appropriate antimicrobial therapy. This, in turn, may help to control the development and spread of resistance to antibiotics.

Keywords Patient, public information, patient education, antibiotic resistance, shared decision-making

INTRODUCTION

Patients are the end consumers of all medical treatments, including antibiotics. While this fact appears obvious, its implications are not always fully appreciated by authorities responsible for the design and delivery of health-care services. Bacterial resistance to antibiotics is among the most important health-care problems of our time. This paper explores the role of the patient in the emergence, spread, and control of bacterial resistance to antibiotics from both the consumer's and physician's perspectives. It focuses on community-acquired respiratory tract infections (RTIs), as these account for the majority of antibiotic prescriptions in the community.

Overcoming Antimicrobial Resistance was the title of the World Health Organization (WHO) Report on Infectious Diseases for 2000 [1]. The report identified three key issues that have implications for the patient's role in bacterial resistance:

- Inadequate access to medical services and antimicrobial drugs. This remains a key problem in developing countries, and is also likely to be important amongst the poorer sections of society in developed countries, e.g. the 45 million people without health insurance in the USA [2];
- Unnecessary use of antimicrobial drugs for the wrong infections, or when no infection is present;
- Not taking a full course of treatment, sharing medication with other people, or keeping part of the course for another occasion. Also, where antibiotics are available without prescription, patients may elect to buy the cheapest antibiotic without regard to its effectiveness.

It is easy to present the role of patients in negative terms. For example, the WHO report includes the following paragraph:

> 'Patient demand for antimicrobials—sometimes the result of TV, Internet, magazine or newspaper advertising—also spurs the development of resistance. In a 1997 study undertaken in Europe, physicians cited patient pressure as the number one reason why they prescribed the wrong antibiotics. In the United States, 95% of physicians surveyed had seen an average of seven patients in the previous six months who had requested specific drugs as a result of advertising. Of physicians questioned, 70% admitted that patient pressure forced them to prescribe drugs they

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> might otherwise have avoided. In a 1995 study undertaken in Peru, two-thirds of those health workers surveyed claimed that their primary source of information came from medical journals. Researchers concluded otherwise, and wrote that advertising appeared to be a key information source. The authors went on to say that this factor ''tended to promote irrational drug use''.'

Although these statements were somewhat negative, the WHO report endeavored to move beyond this to explore the potential benefits of empowering patients through the implementation of patient-centered health-care strategies, arguing that greater patient involvement will improve access to and completion of appropriate antimicrobial treatment. Critical to this discussion is a clear definition of the terms 'patient' and 'need'. By patient we mean people who are accessing health care. By 'need' we mean capacity to benefit from antimicrobial treatment. Before discussing the theory and process of patient-centered care in the treatment of community-acquired RTIs this paper first outlines the knowledge, beliefs and expectations that both patients and doctors bring to consultations in this setting.

KNOWLEDGE, BELIEFS, AND EXPECTATIONS

Patients

Knowledge and beliefs

Beneficial effects of antibiotics. In 1969, the Surgeon General of the United States stated that 'We can close the book on infectious diseases caused by bacteria.' Statements like these generated the impression among the public that antibiotics are invincible cures. This type of sentiment is still evident. A survey of 5379 people from nine countries revealed that 87% thought that antibiotics speed recovery from respiratory infections and that 74% perceived them as 'strong drugs', 51% as a 'savior', 45% as 'dependable' and 16% as 'gentle' [3]. Most people perceive antibiotics as an effective treatment for acute RTIs. However, misperceptions exist regarding the difference between bacterial and viral infections and the appropriate use of antibiotics [4,5].

At the same time, the public are subjected to an intensely negative view of bacteria through the advertisement of a range of antibacterial products. The overall impression is that antibiotics are keeping an overwhelmingly hostile world of bacteria at bay. Search the Internet with the term 'antibacterial' and a bewildering number of products impregnated with antimicrobials are found, from sock, carpet and mattress 'fresheners' to high-chairs and toys. There has been some fight back against these products. For example the United States Environmental Protection Agency brought an enforcement action against Hasbro Inc. for unsubstantiated claims about the public health benefits of antibacterial toys. Nonetheless, advertising of these products and of home cleaning agents presents the public with a strong negative message about bacteria or 'germs'.

Harmful effects of antibiotics. The Internet does provide some counterbalance to the mainly negative portrayal of bacteria in the media. Information about the importance of the normal human bacterial flora is readily available on the world-wide web. Search for 'normal bacterial flora' and there are a growing number of informative websites with a more balanced view of the complex relationship between humans and bacteria (e.g. http://gsbs.utmb.edu/microbook/ch006.htm). The following extract is published at the Earthlife website (http://www.earthlife.net/prokaryotes/human.html):

> 'Many people may think of bacteria only as the causative agents of disease, however, the disease causing species only represent a very small percentage of the total number of species of bacteria. It will come as a surprise then to realize that we as human beings live in harmony with millions of bacteria all the time. Most of these bacteria live within us, harmlessly going about their short lives without causing us any problems at all. Some in fact may even be beneficial. A small percentage live on us rather than in us, these are relatively few in numbers of individuals and number of species compared with our internal flora but they and their progeny will be there all our lives.'

Even this extract provides only a single, tentative statement that the normal human flora 'may even be beneficial'. In fact the reality is that the normal flora fulfils key roles both in digestion and as a key component of our host defenses [6]. Nonetheless, the message does not seem to have got through to the public, perhaps in part due to the messages implicit in information sheets about

antibiotics. These suggest that it is only 'unnecessary' antibiotics that are harmful and tend to portray a very negative relationship between bacteria and human health. In reality, antibiotics always damage the normal human bacterial flora: the key question is when do the benefits of treatment outweigh the inevitable risks? Prescribing is more likely to be influenced when risks to individuals from antibiotics (rather than trial evidence for marginal benefit) are emphasized [7].

Antibiotic resistance. Misperceptions also exist regarding bacterial resistance to antibiotics. Patients will commonly say that taking antibiotics may cause they themselves to become resistant to antibiotics. They rarely say that antibiotics cause their bacteria to become resistant. The aforementioned multinational survey of 5379 people found that 59% believed that antibiotics could undermine their natural immunity [3]. When asked about negative features only a minority named any. None of the respondents mentioned antibiotic resistance as a negative consequence of taking antibiotics.

Expectations

Patients' expectations regarding antibiotic prescribing and consultations for acute respiratory symptoms in primary care have mainly been studied in North America and Western Europe (Table 1).

Symptoms that require antibiotic treatment. Patients present with symptoms (runny nose, tiredness, cough) rather than diagnoses (sinusitis, influenza, bronchitis). They want rapid relief from their symptoms and are less concerned with bacterial eradication. Only a minority (37%) of 5379 people believed that antibiotics should be taken for the 'common cold' whereas a majority believed they should take antibiotics for sore throat (72%), fever (67%), earache (65%), thick catarrh (64%), bad cough (65%), and flu (64%) [3]. Surveys of patients visiting their doctor with acute respiratory symptoms show that most are expecting to receive antibiotics [10,11,14,16,18,19]. Belief that their symptoms are caused by bacterial infection is a powerful stimulus to seek antibiotic treatment [3,19]. However, 40% of students with upper respiratory symptoms expected to receive antibiotics even if they believed that they had a viral infection [19]. Furthermore, there is some evidence that patients know the kinds of symptoms that are likely to induce doctors to prescribe and will report symptoms such as sinus pain or productive cough with green sputum even when they do not have them [3,15].

Previous experience of antibiotics. Previous use of antibiotics prompts patients to expect antibiotics when the same symptoms occur again [4,7,15]. Conversely, strategies that persuade patients that they do not need antibiotics for an episode also give them confidence that they do not need to consult their doctor when they have similar symptoms in the future [23,24]. Patients who have lived in countries where antibiotics are available without prescription are more likely to demand antibiotics and to obtain antibiotics without prescription, even when they have moved to countries where this is theoretically impossible. For example, 26% of subjects surveyed in the USA said that they had obtained antibiotics without prescription, either from pharmacies or from a supplier outside the USA [18]. Information from other countries where antibiotics are only available on prescription also suggests that people regularly obtain antibiotics without prescription [3].

Return to normal activity (work/school/day-care). The symptoms of 'minor' respiratory infections can seriously disrupt patients' lives. In a study of 79 patients with acute bronchitis, it took 3–4 weeks before most patients were well and able to perform all their usual daily activities again [25]. Similarly, the majority of ambulatory patients with community-acquired pneumonia were not fully recovered 30 days after the onset of symptoms [26]. Providing patients with information about the likely time course of their symptoms significantly reduces the chance of repeat consultation, regardless of whether or not they received antibiotics at the initial consultation [27].

Erosion of confidence in doctors. On both sides of the Atlantic, recent high-profile cases in which doctors were shown to be negligent or worse are bound to erode the public's trust in doctors [28,29]. A doctor's reluctance to prescribe antibiotics may be perceived by the patient as an attempt to save money from the over stretched health-care budget. Doctors are concerned that not prescribing antibiotics will disturb their future relationship with patients and families in their practice [30].

Table 1 Studies of patient expectations for antibiotic prescribing and consultations for acute respiratory symptoms in primary care

Country	Subjects	Reported influence of expectations
USA [8]	1368 children attending 44 practices in the Ambulatory Sentinel Practice Network	Parental expectation that an antibiotic would be given was associated with a twofold increase in the likelihood of a diagnosis of bronchitis and a halving in the likelihood of a diagnosis of an upper respiratory tract infection (RTI)
USA [9]	266 patients attending two outpatient clinics	Patients at the intervention clinic received a patient-based educational intervention. Antibiotics were prescribed to 64% and 85% of patients at the intervention and control clinics, respectively ($P < 0.001$). Patient satisfaction with the visit did not differ between intervention and control clinics (69% of intervention and 63% of control clinic patients reported very good or excellent satisfaction; $P > 0.2$). After adjustment for age, sex, duration of illness before the visit, reason for visit, and clinician specialty, there was no difference between intervention and control clinics in the proportion of patients reporting very good or excellent satisfaction (adjusted relative risk for high satisfaction at the intervention clinic, 1.1[95% Confidence Interval [CI], 0.81–1.3])
USA [10]	113 patients with symptoms of acute RTI	Sixty-five per cent of patients expected to receive antibiotics. Physicians had some ability to perceive this expectation and frequently prescribed antibiotics for patients who expected them. Antibiotics were prescribed to >75% of patients with sinusitis or bronchitis and to 18% of those diagnosed with viral infections. No association was found between prescription for antibiotics and patient satisfaction. However, patient satisfaction correlated with the patients' report that they understood the illness and that the physician spent enough time with them
Germany [11]	Ten general practitioners and 185 randomly identified patients	Nearly half of the patients expected a drug prescription from their doctor; 68% received one. Doctors recognized the expectation of a prescription in only 40.7% of patients; 82.6% of patients expecting a drug were issued a prescription. Nearly all patients (45/48) who expected a drug according to their doctor's judgement left the surgery with a prescription, and 58.4% of the remaining patients were prescribed a drug. There was no difference in satisfaction scores between patients whose expectations were or were not fulfilled
USA [12]	237 patients with acute respiratory symptoms attending one practice	Patients' most important goal was to obtain a diagnosis (57%). They usually got more reassurance, medication, and personal interest than they had expected ($P = 0.0001$). In a multivariate model, patients' satisfaction was related to the degree of personal interest and reassurance they had received and whether they felt they had received the right medication ($r^2 = 0.45$, $P = 0.0001$)
USA [13]	104 patients (>14 years) with upper RTI from three practices	Stress scores were calculated for each patient's family using several standard instruments. Measures of stress and support were related to the use of medical services, seeking additional medical care, extra phone calls, and longer perceived duration of illness. Physicians prescribed more medications, ordered more laboratory tests, and scheduled more return visits for patients with high stress or low support scores
USA [14]	210 patients (aged >18 years) with upper RTI symptoms attending a walk-in clinic	The 210 patients were categorized into two groups: those who believed that antibiotics were necessary (157[75%]) and those who believed antibiotics were unnecessary (53[25%]). The only statistically significant difference between the two groups was in patients with sinus pain: 109 (69%) wanted antibiotics compared with 23 (43%) who did not ($P < 0.001$). Of the 210 patients, 130 completed postvisit questionnaires, 129 (99%) of whom reported satisfaction with the clinic visit. All patients who either desired or received antibiotics indicated they would likely seek medical care for future upper RTIs

Table 1 continued

USA [15]	298 outpatient visits for acute RTIs in 18 family practices	Patients were observed to pressure physicians for medication. The types of patterns identified were direct request, candidate diagnosis (a diagnosis suggested by the patient), implied candidate diagnosis (a set of symptoms specifically indexing a particular diagnosis), portraying severity of illness, appealing to life circumstances, and previous use of antibiotics. Also, clinicians were observed to rationalize their antibiotic prescriptions by reporting medically acceptable reasons and diagnoses to patients
USA [16]	10 physicians and 295 parents from two private pediatric practices	Fifty per cent of parents expressed a previsit expectation for antibiotics. Among these parents, only 1% made a direct verbal request for them. Even when no direct requests for antibiotics were made, physicians still perceived an expectation for antibiotics 34% of the time. Among parents who did not receive expected antibiotics, those offered a contingency plan from the physician (i.e. the possibility of receiving antibiotics in the future if their child did not get better) had a significantly higher mean satisfaction score than parents not receiving a contingency plan (76 vs. 58.9; $P < 0.05$)
USA [17]	10 physicians and 306 parents of children with acute respiratory symptoms from two private pediatric practices	Based on multivariate analysis, physicians' perceptions of parental expectations for antibiotics was the only significant predictor of prescribing for conditions of presumed viral etiology. When physicians thought a parent wanted an antibiotic, they prescribed them 62% of the time vs. 7% of the time when they did not think the parent wanted them. However, physician prescribing behavior was not associated with actual parental expectations for receiving antibiotics. In addition, when physicians thought the parent wanted a drug, they were also significantly more likely to give a bacterial diagnosis (70% of the time vs. 31% of the time). Failure to meet parental expectations regarding communication events during the visit was the only significant predictor of parental satisfaction. Failure to provide expected antibiotics did not affect satisfaction
USA [18]	192 adults from an urban community	A majority of subjects reported a belief in the effectiveness of antibiotics for upper RTIs and indicated they are likely to seek care for these conditions. Many (26%) had obtained antibiotics from sources other than a physician's prescription (e.g. directly from pharmacists or a supplier outside the United States). Subjects with a cultural background from countries where antibiotics are available over the counter were more likely to use antibiotics not prescribed by a physician than those from countries with variably enforced regulations or the United States (40%, 30%, and 20%, respectively; $P = 0.049$)
USA [19]	129 students with upper RTI symptoms	Fifty-five per cent of students expected an antibiotic prescription. Antibiotic expectation was significantly more likely among students who thought they had a bacterial vs. a viral infection (90% vs. 40%; $P < 0.01$). A clear diagnosis, an explanation of the rationale for treatment, and an antibiotic prescription were significantly associated with patient satisfaction. Clinicians prescribed an antibiotic for 36% of the students; only 13% of these 46 students had requested an antibiotic during the visit
Belgium, Columbia, France, Italy Morocco, Spain, Thailand, Turkey, UK [3]	Telephone interviews of 5379 subjects randomly selected (approximately 600 per country)	The majority of those questioned believed (but did not necessarily expect) that for most RTIs, antibiotics should be prescribed: sore throat, 72%; fever, 67%; earache, 65%; thick catarrh, 64%; bad cough, 65%; and flu, 64%; but common cold, only 37%. Of those questioned 11% admitted that they had , to exaggerate symptoms to get antibiotics from their physician. Twenty-four per cent of respondents said that they routinely saved part of the course for future use, but the percentage varied widely by country (from 4% of the 600 interviewees in the UK to 41% in Italy).

Table 1 continued

UK [20]	716 patients with sore throat	Most people (69%) had their concerns very well dealt with; this was a better predictor of whether patients were very satisfied (odds ratio 88.6; CI 38.4–177.4) than whether an antibiotic was prescribed (odds ratio 2.97; CI 1.54–5.74). Satisfaction was not predicted by any other variable
UK [21]	787 patients with lower RTIs and 76 general practitioners	Eighty-four per cent of patients thought that their symptoms were caused by an infection, 83% thought that antibiotics would help and 71% expected a prescription. Doctors thought that 20% of antibiotic prescriptions were definitely indicated and 20% were definitely not indicated. Doctors considered antibiotics definitely indicated in only 1% of the group in whom patient pressure influenced the prescribing decision. Patients who did not receive an antibiotic that they wanted were much more likely to express dissatisfaction. Dissatisfied patients reconsulted for the same symptoms twice as often as satisfied patients
Canada [22]	20 family physicians seeing patients with acute infections over a 2-day period	Perceived patient demand was reported in 124 (48%) of 260 physician–patient encounters; however, in almost 80% of these encounters, physicians did not think that the demand had much influence on their decision to prescribe an antibiotic. When clinical need was uncertain, 28 (82%) of 34 patients seeking an antibiotic were prescribed one, and physicians reported that they were influenced either 'moderately' or ''quite a bit'' by perceived patient demand in over 50% of these cases
USA [4]	961 adults from the community of Kentucky and Louisiana	Seventy-two per cent of patients would seek care for a condition of 5 days' duration with cough, sore throat, and discolored nasal discharge. Sixty-one per cent believed that antibiotics are effective for a condition of 5 days' duration with cough, sore throat, and clear nasal discharge; 79% said that they believed antibiotics are effective when there is discolored nasal discharge ($P = 00001$). The strongest predictor of both likelihood of utilization and belief in effectiveness of antibiotics was usual use of antibiotics for the upper RTI symptom complexes. The authors concluded that patients lack understanding of the normal presentation of an upper RTI and the effectiveness of antibiotics as a treatment

Doctors and other health-care professionals

Knowledge and beliefs

Studies into the knowledge and beliefs held by health-care professionals regarding antibiotics are summarized in Table 2.

Beneficial effects of antibiotics. Infectious diseases still kill more people than either cardiovascular diseases or cancer, but over the past century, doctors in developed countries have seen a marked reduction in mortality from these diseases [36–38]. Most doctors probably overestimate the contribution of antibiotics to this decline [39–41]. In Sweden, linear regression analysis showed that mortality rates declined faster in septicemia, syphilis and nonmeningococcal meningitis after the introduction of antibiotics. In contrast, for the 10 other infectious diseases studied (scarlet fever, erysipelas, acute rheumatic fever, puerperal sepsis, meningococcal infection, bronchitis, pneumonia, tuberculosis, typhoid fever, and acute gastroenteritis) no such accelerated decline in mortality could be detected [39]. A similar analysis in The Netherlands focused on evidence for a longer lasting acceleration of the mortality decline after the introduction of antibiotics. Estimated differences in per cent per annum mortality change were 10% or larger for puerperal fever, scarlet fever, rheumatic fever, erysipelas, otitis

Table 2 Surveys of professionals about antibiotic prescribing for acute respiratory symptoms in primary care

Country	Subjects	Prescribed antibiotics	Factors influencing antibiotic prescription
USA [31]	265 members of the American Board of Family Practice	63% for bronchitis	Smoking (90% use antibiotics as first-choice treatment in smokers). Physicians' age, sex, years in practice, and location did not influence their decisions
USA [32]	444 members of the American College of Clinical Pharmacy		Antibiotics were recommended for upper respiratory tract infections (RTIs) or bronchitis more often if patients' symptoms included discolored nasal discharge or sputum. Board-certified pharmacists were less likely to recommend antibiotics
Canada [33]	136 primary-care family physicians and pediatricians	24% to children with cough	The proportion of doctors who would prescribe antibiotics increased to 45% when symptoms had worsened in the 24 h before the office visit
Australia [34]	20 general practitioners		Cough productive of yellow sputum; presence of sore throat; fever; and colored nasal mucus increased the probability of an antibiotic being prescribed.
USA [35]	366 pediatricians and family physicians	86% for bronchitis; 42% for the common cold	Ninety-seven per cent of physicians agreed that overuse of antibiotics is a major factor contributing to the development of antibiotic resistance, and 83% agreed that they should consider selective pressure for resistance in their decisions on providing antibiotic treatment for upper RTIs in children in their practices. However, many reported practices do not conform to the recently published principles for judicious antibiotic use

media, tuberculosis, and bacillary dysentery [40]. Both studies suggest that antibiotics made a small but important contribution to the decline in mortality from acute infections in the 20th century. Nonetheless, health-care professionals and the public need to be reminded that improvements in public health were responsible for most of this achievement.

Doctors should also be aware that antibiotics only have a modest impact on the symptoms of acute bacterial RTIs [42–52]. Any discussion about prescribing antibiotics in general practice needs to start from an honest appraisal of the modest benefits that they achieve for these infections [7]. Too much emphasis on the distinction between viral and bacterial infections can create an artificial dichotomy, where antibiotics provide no benefit against viral infections but are seen as essential to recovery from bacterial infections [7].

Harmful effects of antibiotics. As with patients, many doctors may have little appreciation of the importance of the normal bacterial flora to human health and of the damaging effect of antibiotics on this flora. The normal flora of the throat [53,54], gut [55,56], and vagina [57,58] form an important barrier to colonization by pathogenic bacteria or fungi that is disturbed by prior administration of antibiotics. This protective effect results both from the formation of a physical barrier and from metabolic effects [56]. The metabolic effects of the normal gut flora also have important implications for the risk of breast and colon cancer [59–61] and there is epidemiological evidence linking antibiotic use in women with an increased risk of breast cancer [62]. Antibiotic treatment undoubtedly increases the risk of colitis caused by *Clostridium difficile* [63,64] and of vaginal candidiasis [65].

Antibiotic resistance and antibiotic prescribing. While most doctors acknowledge that antibiotic use relates to antibiotic resistance, they are loath to admit that their own prescribing contributes to the problem. Rather, they are liable to pin the blame on

other doctors (primary-care doctors blame their hospital colleagues and vice versa). If doctors from primary and secondary care are cornered, they will probably unite temporarily in order to blame veterinary surgeons.

Twenty-five per cent of 392 family physicians surveyed in British Columbia, Canada, did not believe that prior antibiotic use increased personal risk for acquiring drug-resistant infection. Moreover, 23% did not believe that antibiotic use was an important factor in promoting resistance in their communities [66]. In reality, there is good evidence linking prior exposure to antibiotics to significantly increased risk of infection with drug-resistant bacteria, both in the community [67] and in hospital [68]. This relationship is clearly seen in studies that collect data on exposure to antibiotics and isolation of resistant bacteria from individual patients [67,68]. However, ecological studies with data from populations of patients are likely to obscure the relationship between antibiotic exposure and resistance [68].

Expectations

Howie [30] identified four nonbacteriological determinants of antibiotic prescribing for respiratory symptoms:

- The doctor's anxiety about his or her workload;
- The response of doctors to social pressures;
- Misinterpretation of underlying reasons for a consultation;
- Fear of the possible development of sequelae to streptococcal illness.

Subsequent studies of the factors that influence antibiotic prescribing support the importance of these four determinants. For example, in one study doctors explained their prescription of antibiotics to patients whom they did not think had a genuine clinical need on the basis of the pressure from patients to do so, combined with social factors and the doctor's own workload [69]. Several of the studies in Table 1 show that doctors commonly misinterpret the reasons for a patient's consultation and their expectations for antibiotic treatment.

Even when doctors acknowledge the relationship between prescribing and resistance, and the need for prudent prescribing against RTIs, their reported prescribing practices do not conform to recently published principles for prudent antibiotic use [35]. One reason for this may be that doctors find it difficult to differentiate between RTIs, in particular bronchitis and pneumonia. In a qualitative study of coughing involving 24 community physicians in the UK, clinical signs and symptoms often left the physicians with reasonable diagnostic doubt. Their prescribing behavior was also determined by both doctor- and patient-related factors (e.g. having missed pneumonia once, patient expectations). The 'chagrin factor' explains why these factors lead to a shift in the action threshold, in favor of antibiotics [70].

Increasing patient demand. It should not be assumed that doctors inevitably give way to pressure from patients to prescribe and it is important to measure doctors' perceptions about pressure separately [71]. While it may be true that doctors are more likely to feel pressurized if the patient expects a prescription, 52% (220/420) of doctors in one study did not feel under pressure when the patient hoped to receive a prescription [72].

Pressure to see more patients. Doctors in primary and secondary care are under pressure to see more patients and most believe that it takes longer to reassure a patient that they do not need an antibiotic than simply to prescribe one [7]. Interviews with 21 primary-care doctors in the UK revealed that they believed that if a prescription was issued then the consultation was short and the patient seemed satisfied. A typical doctor's opinion was, 'You can't just say, ''It's viral, you don't need antibiotics, go away,'' because they feel they're being fobbed off. They feel that their illness is not being taken seriously' [7]. Conversely, attempting to change patients' beliefs and expectations in the consultation was often perceived as time consuming and unrewarding. One practitioner said, 'You spend 15 min trying to educate them, when they will go out disillusioned, come back the next day and see someone else, making you feel 5 min would be better spent just giving them a prescription and getting rid of them' [7].

Conflicts of interest between the patient, the provider organization, and public health. Under managed care in its various forms, restrictions on clinicians have now become commonplace. Modern information systems make it possible for managers to monitor and control practitioners' behavior by such measures as utilization review, incentives and

disincentives, and pre-authorization for procedures and referrals. This is often so destructive of professional morale that it may become self-defeating. Self-imposed limits are more tolerable than those imposed from above, but if doctors stand to gain from the decisions themselves, their interests are potentially in conflict with those of their patients [73]. Managed care is a relatively recent development that focuses on the tensions between the cost and quality of care [74]. However, doctors have always had to balance their conflicting duties: 'fidelity' to the interests of an individual patient and 'stewardship' for the health-care resources that are entrusted to them by society [75].

The 'principal-agent' relationship was developed in mainstream economics to model situations in which the consumer is ill-informed, but can use an agent to make decisions on his or her behalf [76]. In applying this concept to health, most of the literature has focused on the doctor–patient relationship, in which the doctor makes decisions on behalf of the patient purely in relation to the patient's interests. However, there has been some extension of the notion of agency to the relationship between citizens and those making health-care decisions on their behalf. A form of societal agency relationship is envisaged where the principals are citizens and the aim is to maximize social welfare rather than patient utility [76]. It is debatable whether a doctor can act as a perfect agent both for an individual patient and for the citizens that he or she serves. Conflict between the (implicit) role of societal agent and the (explicit) role of patient advocate is intrinsic to the doctor's role [77–82], and can be expected to increase as the oft-quoted 'gap' between demand and supply widens. If doctors are to act as both the patient's and the citizen's agent they may be left with moral and ethical problems preventing them from making disinterested rationing decisions [76].

The problem of antibiotic resistance provides an important focus for debate on these key issues because the conflict of interests between individual patients and society is not due to constraints on health-care budgets.

Attitudes to practice guidelines. There is increasing concern about the quality, reliability and independence of practice guidelines. A review of 431 guidelines published between 1988 and 1998 found that 67% did not report any description of the type of organizations involved in the development process, 88% gave no information on searches for published studies, and 82% did not give any explicit grading of the strength of recommendations. There was improvement over time at including search details (from 2% to 18%; $P < 0.001$) and explicit grading of evidence (from 6% to 27%; $P < 0.001$). The authors concluded that, despite improvement over time, the quality of practice guidelines developed by specialty societies is unsatisfactory [83]. The AGREE (Appraisal of Guidelines for REsearch & Evaluation) project is a response to this problem. Funded by the European Union, AGREE is developing guidance on good practice for guideline developers (http://www.agreecollaboration.org).

While guideline developers may have reached a consensus about good practice, their standards do not reflect the current beliefs of practitioners. A survey of 1199 doctors in Italy revealed that practice guidelines were generally perceived to be less useful than other sources of medical information (e.g. personal experience, conferences, colleagues, articles, the Internet, and textbooks) [84]. Most physicians thought that guidelines were developed for cost-containment reasons and expressed concerns about their limited applicability to individual patients and local settings. Furthermore, most respondents did not favor the involvement of health professionals other than physicians in guideline development. Thus, having a multidisciplinary guideline group, which is regarded as a key element of good practice, may actually make a guideline less credible to practicing doctors.

Efficacy and availability of alternatives to antimicrobial treatment. Anti-inflammatory drugs are underused in acute RTIs [85]. For example, despite evidence of their effectiveness, two studies have shown that bronchodilators are only prescribed for 6–17% of patients with bronchitis [31, 86]. Patient information about the likely course of symptoms for acute RTIs, combined with advice about symptomatic relief, is a powerful alternative to antibiotic prescribing [87].

Fear of litigation for malpractice. Many doctors distrust guidelines because they do not believe that they are sufficiently sensitive to important differences between individual patients [84,88]. Doctors who are high prescribers of antibiotics show other evidence of a defensive attitude in their practice [89].

Doctors are unsure whether following a guideline will be sufficient defense against a charge of negligence if they do not prescribe antibiotics to a patient who subsequently is shown to have a serious bacterial infection [84]. Unfortunately there is some basis for this fear. A court can declare a policy or guideline as insufficient or unacceptable; the court is sovereign and can decide upon the standard according to its own legal policies, which are usually aimed at improving public health. Thus, if the court finds a certain policy—even one approved by official bodies—to be insufficient, it can declare it as nonstandard and set its own standard. The following quote is from the book *International Medical Malpractice Law*, 'A common practice (regardless if founded on guidelines) simply may not be good enough to fulfill the standard required by the law' [90]. In 1993 the Supreme Court of Canada expressed the view that 'conformity with standard practice (based on policy or guidelines) in a profession does not necessarily insulate a doctor from negligence where the standard of practice itself is negligent' [91]. In the UK, the House of Lords has stated the view that the court can, in rare cases, reach a conclusion that a professional standard is not based on a rational analysis, and that the experts express views that are not logical or responsible [92]. However, such situations are rare and the court will usually accept an antibiotic policy as a standard and act accordingly.

Influences on antibiotic prescribing

Various factors are reported to influence the prescribing of antibiotics by doctors (Tables 2 and 3). The most consistently reported influence is the nature of the patient's symptoms. Reporting of discolored secretions (nasal discharge or sputum) and sinus tenderness are strongly associated with prescribing [32,34,69,89,94,95,98,101]. There is also evidence that doctors rationalize their prescribing by reporting medically acceptable diagnoses, such as bronchitis or sinusitis [8,15,35,100]. A doctor's perception of either high stress or low social support is associated with increased antibiotic prescribing [13]. This is consistent with the results of studies that have examined the influence of non-bacteriological factors on prescribing [30,69]. If doctors perceive that patients are expecting antibiotics, they are more likely to provide diagnoses such as bronchitis [8,15] and more likely to prescribe antibiotics [11,17].

High prescribers of antibiotics tend to be high prescribers of other drugs [104,105]. There is no consistent evidence about characteristics such as age of the prescriber or time since qualification as predictors of prescribing; few of the studies that examine these variables use multivariate analysis to adjust for other associated variables. When this is done, the age of the prescriber does not appear to be an important predictor of prescribing [100,105]. In comparison with other practices, those that train junior doctors in primary care have been shown to prescribe fewer antibiotics as well as a higher proportion of formulary drugs [105]. Of course, budgetary limitations also are an increasingly important influence on antibiotic prescribing.

Patient–doctor interaction: bridging the gap

Patient–doctor communication is a dual process whereby two players with different objectives and backgrounds try to find a joint solution to a problem. Patients should play an active part in reaching this solution in order to maximize the acceptability and effectiveness of treatment. Several studies include information about the interaction between patients and doctors (Tables 1,2,3). Despite their different designs and settings, several common findings emerge:

- Satisfaction is increased by providing information (including a diagnosis), enough time and reassurance, combined with an interest in the patient's problems [10,12,16,17,19]. In one study, failure to meet parental expectations regarding communication events during the visit was the only significant predictor of parental satisfaction [17]. Failure to provide expected antimicrobials did not affect satisfaction in this study nor in two additional studies [9,10].
- Doctors are not good at recognizing patient expectations. In formal studies, they correctly identify $<50\%$ of patients who are expecting antibiotic treatment [10,11,17,20].
- Some patients seem to be all too aware of what influences doctors to prescribe antibiotics. They exert pressure on the doctor to prescribe, using tactics such as suggesting candidate diagnoses that are more likely to elicit a prescription or exaggerating the severity of their symptoms or their lack of social support [3,15].

The results of these studies are consistent with those of more general studies of patient

Table 3 Studies of influences on antibiotic prescribing for acute respiratory symptoms in primary care

Country	Subjects	Prescribed antibiotics	Factors influencing the consultation
USA [93]	1525 adult patients with acute bronchitis	85% of patients with bronchitis	Purulent nasal discharge; sinus tenderness moderately associated with antibiotic prescribing. Patient age, gender, duration of illness or days off work did not influence prescribing
USA [94]	Adult patients with upper respiratory illness	33% of all upper respiratory tract infections (RTIs)	Purulent nasal discharge, green phlegm, and tonsillar exudates were each independently associated with antibiotic prescribing
Japan [95]	302 patients with bronchitis and 1165 with upper RTIs	68% of patients with bronchitis	Purulent sputum, pharyngeal exudates, chest signs, and pyrexia were significantly associated with antibiotic prescribing
USA [96]	National Ambulatory Care Surveys 1980–94	66% of patients with bronchitis	In every year of the study, white, non-Hispanic patients aged <65-year-old were more likely to receive antibiotics than nonwhite patients or patients aged 65 or older. There was a significant increase in prescribing from 59% of patients in1980 to 70% in 1994
New Zealand [97]	Computerized records of 100 222 consultations from 17 practices	78% of all upper RTIs	There was no statistically significant difference in the likelihood of a successful outcome with or without antibiotic therapy ($\chi^2 = 0.76$; $P > 0.05$)
USA [98]	482 patients (>4 years)		In an adjusted model, the variables significantly associated with antibiotic prescribing were physical findings of sinus tenderness, rales/rhonchi, discolored nasal discharge, and postnasal drainage. The presence of clear nasal discharge on examination was negatively associated with prescribing
Canada [99]	4344 children (<16 years) attending offices or urgent care centers	76% of children with pharyngitis and 90% of children with bronchitis	Urgent care physicians were significantly more likely than pediatricians or family physicians to prescribe immediate antibiotics and to disregard guidelines
USA [35]	7531 encounters with children aged 1–6 years	43% of all encounters; 72% of upper RTI office visits; 11% of checkups; 18% of telephone calls	There was wide variability in the overall antibiotic-use rates among the 25 physicians (1–10 courses per child per year). There was an even wider variability in some diagnosis-specific rates; bronchitis and sinusitis in particular. Those with the highest antibiotic prescribing rates had up to 30% more return office visits. Physicians who prescribed antibiotics for purulent rhinitis were more likely to see parents who believed that their children should be evaluated for cold symptoms
USA [89]	722 patients with a runny nose, blocked nose, or cough		The best independent predictor of an antibiotic prescription was the individual antibiotic prescribing rate, which expresses the personal habit of the general practitioner in prescribing antibiotics (adjusted odds ratio [OR] 5.27, 95% confidence interval [CI] 3.22–8.62). Others were the diagnostic labels: 'sinusitis' (adjusted OR 2.80, 95% CI 1.2–6.49) and 'flu–like syndrome' (adjusted OR 0.08, 95% CI 0.01–0.45), and the sign 'sinus tenderness' (adjusted OR 4.37, CI 2.15–8.89). The antibiotic prescribing behavior intensified with an increased tendency to prescribe medication in general (beta = 0.46; $P < 0.001$) and with an increased defensive attitude (beta = 0.22; $P < 0.05$)

Table 3 continued

Country	Subjects	Prescribed antibiotics	Factors influencing the consultation
USA [15]	298 outpatient visits for upper RTIs in 18 practices	68% of all visits	79% of antibiotic prescriptions were determined to be unnecessary according to the Centers for Disease Control and Prevention guidelines. Patients were observed to pressure physicians for a prescription
USA [100]	Patients with acute infections attending 73 practices	Low prescribers; high prescribers	Low prescribers and high prescribers were of similar ages and saw similar numbers of patients of similar ages with very similar presenting complaints. Both groups diagnosed urinary tract and skin and soft-tissue infections at similar rates, but differed markedly in their rates of diagnoses of RTIs. High prescribers diagnosed bacterial RTIs in 65.4% (147/225) of their patients; low prescribers diagnosed bacterial RTIs in 31.0% (66/213 ($P < 0.001$)
The Netherlands [101]	Nationwide survey of 335 000 patients attending 161 family physicians	33% of first contacts for otitis media, upper RTI, sinusitis, and tonsillitis	An antibiotic was prescribed most frequently for sinusitis (72%) and acute tonsillitis (74%), but much less frequently for otitis media and acute upper RTI
UK [102]	518 patients with acute lower RTIs	76%	Thirty per cent of patients reconsulted for similar symptoms within the next 28 days (29% of those who were given antibiotics and 33% of those who were not). Forty-one per cent of patients who had seen their general practitioner 15 or more times in the previous 2 years reconsulted, compared with 13% of those who had made fewer than 5 visits
UK [69]	1089 adults with lower RTIs visiting 115 general practitioners	75%	The doctors stated that only 33% of prescriptions were definitely indicated and that 20% were definitely not needed. Logistic multivariate analysis revealed that all of the following were independent predictors of antibiotic prescribing: age of general practitioners and patients, discolored sputum, fever, signs on chest examination, and 'other factors'. These 'other factors' included patient pressure, social factors, physician work pressure, and prior experience with the patient. They were particularly likely to be associated with prescribing to patients whom the doctors thought did not need antibiotics
USA [103]	531 pediatric office visits to physicians participating in the National Ambulatory Medical Care Survey	75% of children with bronchitis	Antibiotics were prescribed to 44% of patients with common colds, 46% with upper RTIs, and 75% with bronchitis. After controlling for confounding factors, antibiotics were prescribed more often for children aged 5–11 years than for younger children (OR, 1.94; 95% CI, 1.13–3.33) and rates were lower for pediatricians than for nonpediatricians (OR, 0.57; 95% CI, 0.35–0.92)

interactions with doctors in prescribing decisions. They also reveal misunderstandings relating to patient information unknown to the doctor; doctor information unknown to the patient; conflicting information; disagreement about attribution of side-effects; failure of communication about the doctor's decisions; and relationship factors. All these misunderstandings were associated with lack of patient participation in the consultation in terms of the voicing of expectations and preferences or the voicing of responses to doctors' decisions and actions [106].

Doctors feel more confident about making prescribing decisions when they know the patient [69,107]. However, the doctor is unlikely to know patients who present with acute RTIs. Patients will either make an urgent appointment during office hours or seek help out of hours. In most health-care systems it is increasingly unlikely that they will see their regular doctor. Moreover a high proportion of patients with infections are otherwise healthy so that even their family doctor may not know them well.

PATIENT-CENTERED CARE

What is patient-centered care?

There is a great deal of confusion among health-care professionals about what exactly it means to practice patient-centered medicine. This confusion is unsurprising in view of the many terms used to describe related concepts such as patient-centered care, shared decision-making, patient empowerment, informed patient choice, and concordance. In order to develop effective patient-centered interventions for reducing unnecessary antibiotic prescribing, it is important to understand the similarities and differences between such concepts. Here we will describe the main approaches in order to identify what we believe to be the key issues.

Patient-centered care

Patient-centered care is best described as a general philosophy whereby the patient is valued as a person and is seen as a partner in the process of medical care, rather than as an inferior and passive recipient of professional expertise. It also recognizes that there is more to illness than physical symptoms and capitalizes on the therapeutic nature of the consultation itself. Patient-centered care has been defined and measured as a professional attitude (e.g. valuing the patient), as a knowledge set (e.g. about what is important to patients), and as a set of skills (e.g. sharing with the patient in decision-making and being responsive to the patient's feelings). In fact, it is a broad construct encompassing all these factors [108]. While there is a general consensus that patient-centeredness involves the doctor being open and responsive to the concerns and needs of patients (including their need for information and participation in decision-making), there is no one agreed definition. Attempts have nevertheless been made to 'operationalize' patient-centered care as a set of behaviors. For example, a six-component 'patient-centered clinical method' has been proposed [109], which comprises:

- Exploring the disease experience;
- Understanding the whole person;
- Finding common ground regarding management;
- Incorporating health promotion and disease prevention;
- Enhancing the doctor–patient relationship;
- Being realistic.

Patient participation

This is a broad and loosely defined concept encompassing shared decision-making, patient education (including initiatives to promote public understanding such as the National Patient Library [110] in the USA) and involvement of patients or consumer advocates in the process of policy and guideline development [111].

Patient empowerment

Through the emergence of the Internet, public campaigns by patient groups, and publicity surrounding medical disasters, patients have transformed from passive participants in the health-care system to active players who are aware that their personal wellbeing is at stake. Nowadays, instead of blindly following the paternalistic health-care system in which the doctor was regarded as always knowing what was best, patients expect to be well-informed and involved in decisions relating to their own health. Thus, empowerment has been broadly defined as '... a social process of recognizing, promoting and enhancing people's abilities to meet their own needs, solve their own problems and mobilize the necessary resources in order to control their lives' [112].

The process of patient empowerment entails helping the person to develop a sense of control by educating them appropriately and encouraging them to participate actively in medical encounters [113]. The concept is closely linked with consumerism: 'Consumerist behavior is only likely to occur when the patient feels empowered to question the doctor, make independent judgements, or seek out alternative sources of information' [114].

Informed choice

This approach focuses on ensuring that patients have all the facts they need to come to a decision (i.e. available treatment options and their associated risks and benefits). In other words, it emphasizes communication of information from the professional to the patient. Once this has been achieved, the patient must make the choice or decision themselves, either alone or aided by relatives or friends if desired. In the 'pure' version of the informed choice model the doctor stands back from the decision so as not to lead the patient. However, in practice the doctor may offer or be asked to offer an opinion in addition to stating the evidence [115].

Not surprisingly, much of the work on informed choice has been conducted from the point of view of avoiding future litigation when healthcare choices (e.g. about surgery) have to be made.

Enablement

The term 'enablement' has often been used interchangeably with empowerment, although in recent years it has come to describe a measurable outcome of patient-focused consultations, rather than a process *per se*, incorporating satisfaction with the consultation and improved knowledge and self-efficacy. The outcome should be that the patient feels empowered and that he or she has been helped [116].

Shared decision-making

Shared decision-making describes a process whereby the patient is actively encouraged to participate in decision-making about their health care. Reaching a shared decision involves several stages:

- *Information exchange between doctor* and *patient*. This information could include evidence or opinion about lifestyle preferences/anxieties/personal circumstances.
- *Deliberation of alternative treatment options*. The patient and doctor state their preferences. Consensus may be reached quickly or via a process of persuasion and negotiation. Doctor and patient may agree to disagree.
- *Deciding what treatment to implement*. The patient and professional work together to build consensus on the preferred treatment option. If consensus cannot be reached the deliberation phase may still be regarded as a shared event (as views were shared) but the outcome of the deliberation, i.e. the decision, is not.

Qualitative research has identified a number of additional substages or 'competencies' involved in shared decision-making (Table 4) [117].

Concordance

In 1995, a Royal Pharmaceutical Society working group was formed to explore what was known about the difficulties patients have in taking medication as prescribed. This heralded a change in

Table 4 Competencies required by professionals for informed shared decision-making [117]

1.	Develop a partnership with the patient
2.	Establish or review the patient's preferences for information (e.g. amount and format)
3.	Establish or review the patient's preferences for a role in decision-making (such as risk taking and degree of involvement of self and others) and the existence and nature of any uncertainty about the course of action to take
4.	Ascertain and respond to patient's ideas, concerns, and expectations (e.g. about disease management options)
5.	Identify choices (including ideas and information that the patient may have) and evaluate the research evidence in relation to the individual patient
6.	Present (or direct patients to) evidence, taking into account competencies 2 and 3, framing effects (i.e. how presentation of the information may influence decision-making), etc. Help patient to reflect on and assess the impact of alternative decisions with regard to his or her values and lifestyle
7.	Make or negotiate a decision in partnership with the patient and resolve conflict
8.	Agree an action plan and complete arrangements for follow up

emphasis from simple compliance to what became known as 'concordance' [118]. The philosophy underlying concordance recognizes that the reasons why patients do not comply with medication can be complex and can vary from person to person. These reasons include poor understanding of the condition or treatment; maladaptive attitudes towards the medication or illness; practical barriers to medication use; and rational choices based on personal utilities. The process of achieving concordance involves two-way communication whereby the patient and doctor share information about the illness, its treatment and the patient's barriers to compliance, to give a common understanding of the problem and its origins. Solutions should be negotiated in the light of this new understanding and the decision about how to proceed should be shared by both parties. Embedded in this approach is the idea that the patient's right to choose must be respected even if their ultimate decision is medically 'wrong', provided that their choice is appropriately informed. The concept of concordance overlaps closely with the other models of shared decision-making. The focus of concordance research has been long-term medication for chronic illnesses.

Implementing shared decision-making

Patient interventions

Patient–doctor interaction. Shared decision-making can be implemented at the individual patient–doctor level via several interventions. Firstly, it is important for the physician to ascertain the patient's reasons for and expectations from the consultation.

Secondly, there should be a negotiated treatment approach, involving careful explanation and reassurance if antibiotics are not used. This can be reinforced by giving the patient a prescription with a negotiated agreement to 'save' it for a few days to see if the symptoms resolve by themselves. The delayed prescription approach has been evaluated in three randomized trials. The majority of patients did not pick up their antibiotics (i.e. 55% of patients with cough [119], 69% with sore throat [23], and 76% with otitis media [24]). Furthermore, patients who had been persuaded not to redeem their prescription for an antibiotic were less likely to consult or expect antibiotics in the future for similar symptoms. These findings are consistent with those from an observational study of parents who did not receive expected antibiotics. In this study, parents who were offered a contingency plan from the physician (i.e. the possibility of receiving antibiotics in the future if their child did not get better) had a higher mean satisfaction score than those who did not (76 vs. 58.9; $P < 0.05$) [16]. Similarly, in another observational study 50% of patients did not redeem their 'back-up' prescriptions and 96% reported satisfaction with their care [120].

Finally, there should be provision of advice regarding the duration of symptoms and symptomatic relief. This may be in the form of a 'prescription' to give an 'outcome' to the consultation. Also, questionnaires completed in the waiting room and information sheets have been used. A randomized trial showed that provision of information leaflets significantly reduced the number of repeat consultations for patients with symptoms of lower RTI, regardless of whether or not they had received antibiotics [27].

Together, these data suggest that patient empowerment is likely to be a successful strategy for reducing antibiotic prescribing and infection control in primary care, just as it is in secondary care [121].

Having considered several of the most common approaches to patient involvement, we now turn to practical advice regarding the question of how best to modify patient demand for antibiotics. Unlike other examples of health behavior change, where the emphasis is largely on motivating people to avoid risky behaviors (e.g. smoking) or engage in healthy behaviors (e.g. taking exercise), the primary behavioral change sought in the case of antibiotic prescribing is reduced patient demand. This behavioral change requires modification of patient expectations.

As already noted, the informed choice model of patient involvement emphasizes the importance of provision of information, which is intended to enable patients to make rational choices. In the case of antibiotics for minor conditions such as sore throat, such information might commonly involve evidence about the probability of the symptoms having a viral rather than a bacterial cause, the likely time course of symptoms, and the likely ineffectiveness of antibiotics in changing that time course. In some cases it may include some discussion of population resistance. However, qualitative research indicates that patients may

not understand such information or may harbor the belief that it does not apply to them, and hence may either persist in demanding antibiotics or come away from the consultation feeling disgruntled if they are not prescribed [7]. With regard to the information itself, the concept of population resistance may be too abstract for the patient (or even the doctor) to grasp and a more effective method of persuasion may be to emphasize risks to the individual patient, such as side-effects and the possibility of 'their' bacteria becoming resistant.

It is also important to consider doctors' concerns that not meeting patients' expectations may jeopardize their future therapeutic relationship [7]. Such concerns may explain doctors' common failure to broach the subject of alternative strategies and instead simply to administer antibiotics in the belief that this will satisfy the patient. Patients, on the other hand, indicated that they would appreciate more information on these matters [7]. This finding is supported by several studies that have found that patient satisfaction is primarily influenced by information and reassurance rather than by antibiotic prescribing [7,9,10,17, 122,123]. In focus groups, parents also indicated that they would be satisfied with the consultation even if antibiotics were not prescribed, provided the physician explained the reasons for the decision [124].

In view of the importance of elucidating and tackling underlying concerns and expectations as an aid to decision-making for both the patient and professional, it is likely that the shared decision-making approach will be more useful in the case of antibiotic prescribing than the informed choice approach [125]. The shared decision-making approach involves a number of stages in which the doctor and patient exchange information pertinent to their perspectives, discuss the advantages and disadvantages of alternative treatment strategies, and come to an agreement about the way forward.

The process of shared decision-making can be illustrated by showing how it would be applied to specific cases [125]. For example: a patient presents with a sore throat and requests antibiotics. The doctor first takes a history and examines the patient and concludes that the source of infection is most likely viral. The following stages then occur:

- *Information exchange*. The doctor should communicate information about the patient's symptoms, his/her opinion about the cause, the availability of alternative treatment options, and evidence about their likely effectiveness (including areas of uncertainty). The doctor should elicit the patient's feelings about their symptoms, barriers such as past experiences of apparently successful antibiotic therapies, their level of understanding about the condition and its treatment, and their preference for an active or passive role in the decision-making process. Alternative treatment options include immediate antibiotic prescription, prescription of anti-inflammatory or pain-relieving drugs, advice to seek 'over the counter' sore throat remedies, and delayed antibiotic prescription. Delayed antibiotic prescription can be achieved by asking the patient to wait 3 days and then, if the throat is still sore, either return to the office or telephone for a prescription, or by providing a prescription at the first consultation which the patient agrees to have dispensed only if symptoms persist.
- *Deliberation of alternative treatment options*. The doctor should state his/her preferred treatment strategy, making sure the patient has understood the reasoning for this choice. The patient should state his or her preference, bearing in mind the doctor's advice, the alternatives that have been presented, and their own concerns.
- *Deciding what treatment to implement*. The doctor and patient should attempt to reach agreement on a way forward. If consensus is not possible, the patient may choose to accept the doctor's preference or insist that his or her own preference be met. In the latter case the individual clinician must decide what is acceptable, although a wholly patient-centered approach would respect the patient's right to choose.

Of course, such an approach must be tailored to the individual patient. For example, patients may vary in the extent to which they prefer to be involved in treatment decisions. Some patients indicate that they do not state their expectations regarding a consultation because they believe that it should be the doctor's responsibility to assess the situation and decide what should happen [7]. Clearly, it is important to elicit these views early on. Likewise symptom severity and relative risk averseness for different patients will influence a doctor's appraisal of alternative management options. For example, patients with severe sore throat may be less likely to accept a wait and see

approach, whilst patients who are averse to risk may prefer to receive a prescription for anti-inflammatories or painkillers as a means of obtaining rapid relief whilst avoiding the risk of side-effects from antibiotics. Although the process of achieving shared, informed decisions may require additional time in the first instance, it may be reasoned that well-informed patients will be less likely to present with inappropriate demands for antibiotics in the future, reducing long-term health-care costs. Such strategies should ideally be combined with effective mass media campaigns to promote better understanding of the issues associated with antibiotic prescribing for sore throat.

Public information campaigns. The mass media frequently cover health-related topics, are the leading source of information about important health issues, and are targeted by those who aim to influence the behavior of health professionals and patients. A *Cochrane Systematic Review* has identified 17 studies (randomized trials, controlled clinical trials, controlled before and after studies, or interrupted time-series analyses) that have evaluated the effectiveness of mass media interventions on health-service utilization. The participants were health-care professionals, patients, and the general public. Fourteen studies evaluated the impact of formal mass media campaigns, and three looked at media coverage of health-related issues. All but one of the studies concluded that mass media was effective. The authors concluded that those engaged in promoting better uptake of research information in clinical practice should consider mass media as one of the tools that may encourage the use of effective services and discourage the use of those with unproven effectiveness [126].

In Belgium, a public information campaign on antibiotic resistance was associated with an 18% reduction in antibiotic consumption the month after the campaign period. This was statistically significant after adjustment for seasonal changes in acute respiratory infection [127]. It is imperative that patient organizations are actively involved in the development of such education campaigns in order to ensure that the perspective of the patient has been taken into account.

Doctor interventions

AGREE is a project funded by the European Union that aims to standardize the development of evidence-based guidelines. Their recommendations (http://www.agreecollaboration.org) and those of other groups such as the Scottish Intercollegiate Guidelines Network (SIGN) [111] recognize the importance of including patients' views in the development of practice guidelines.

The importance of including patients' views is illustrated by a study of the implementation of a guideline that aimed to reduce hospital admission for patients with community-acquired pneumonia who were at low risk of developing complications [88]. The guideline was developed with physicians working in an accident and emergency department. After implementation of the guideline physicians were still admitting 44% of patients whom, by their own agreed criteria, had mild pneumonia that did not require hospitalization. The explanations given for nonadherence with the guidelines were largely due to patient-related factors. For example, physicians stated that the guideline did not accurately assess the risk of individual patients, patients or their carers were not happy for the patient to be discharged, or that the patient's home circumstances were not suitable for outpatient care [88].

There is now a large literature on methods for changing the behavior of doctors and other health-care professionals. The Cochrane Library includes seven systematic reviews demonstrating the effectiveness of a variety of educational methods in practice [126,128–133]. However, to summarize the current state of knowledge: there are 'no magic bullets' [134]. All of the methods have been shown to work in some circumstances but not in others. The problem is that there is still no generic method for predicting which interventions will work with specific people and settings.

The Cochrane collaboration is currently supporting two reviews of interventions to improve antibiotic prescribing, one in ambulatory care and one in hospital inpatients. The protocols for both reviews are available on the Cochrane website (http://www.update-software.com/cochrane). Two studies suggest that interventions targeted at education of both public and health-care professionals are more likely to succeed than educational interventions targeted at either group alone. In Cuba, combined intervention decreased antibiotic prescribing by 63%, compared with a 23% decrease for professional education alone, and a 2% increase for public education alone. There was a 48% increase in the control practices who

received no intervention [135]. In the USA, a practice-based educational intervention alone using patient information leaflets was ineffective: prescribing declined from 78% to 76% compared with a change from 82% to 77% in control practices. However, the addition of a household-based educational intervention resulted in a significant decline in antibiotic prescription rates (from 74% to 48%; $P = 0.003$) [136].

System interventions

Shifting the costs of prescribing from the insurer to physicians in a staff model of a health maintenance organization (HMO) did not appear to influence antibiotic prescribing in a study of patients in whom upper RTIs ($n = 334$) or acute bronchitis ($n = 218$) were diagnosed within a 12-month period. For upper RTIs, antibiotic prescribing was significantly higher in the HMO population than in the fee for service group (31% vs. 20%; $P = 0.02$). In patients with acute bronchitis, HMO patients were also more likely to have an antibiotic prescribed, but the difference was not statistically significant (82% vs. 73%; $P = 0.11$). Further analyses showed that, while HMO physicians were more likely to prescribe antibiotics, they were less likely to prescribe other medications for acute bronchitis or to use diagnostic tests for evaluation of patients with upper RTIs or bronchitis [137].

In Denmark, reductions in the reimbursement of antibiotics prescribed for certain infections was associated with a marked reduction in prescribing. In a prospective study, the prescribing behavior of 553 primary-care doctors in 1990 (after reimbursement was reduced) was compared with that in 1987 (before reimbursement was reduced). In 1987, 7607 patients were treated compared with 5765 in 1990. The relative number of patients treated for sinusitis, other upper RTIs, acute bronchitis, pneumonia, and upper gynecological infections was significantly lower in 1990 than in 1987. Other infections, particularly those that are often diagnosed by culture or microscopy by the doctors themselves, increased significantly. They included tonsillitis and urinary tract infections. The authors concluded that reimbursement can be a very powerful tool controlling the use of antibiotics by general practitioners [138].

Evaluation of interventions

The Cochrane Effective Practice and Organization of Care group (EPOC) website provides access to a series of methodology papers and a checklist for assessment of reports of interventions designed to change clinical practice (http://www.abdn.ac.uk/hsru/epoc/). In addition to controlled trials, Cochrane EPOC reviews include quasi-experimental study designs, such as controlled before and after studies and interrupted time-series analyses [139]. Uncontrolled before and after studies almost always overestimate the impact of interventions [140] and give no indication of changes that would have occurred without the intervention. Controlled before and after studies compare the impact of an intervention in, for example, a hospital or primary-care group with a comparable site. The EPOC methodology papers provide advice on ensuring comparability of intervention and control sites and on statistical methods for comparing changes in both sites. An interrupted time-series analysis uses the intervention site as its own internal control by comparing several measurements before and after the intervention. The most common errors in interrupted time series are to have too few data points before the intervention and to base statistical analysis on a comparison of average measures before and after the intervention rather than on an analysis of time trends. At least three measurements are required before and after the intervention to analyze trends. However, the larger the number of data points before the intervention, the more reliable the results.

OPPORTUNITIES FOR IMPROVEMENT AND IMMEDIATE ACTION

Strategies for involving patients in developing countries must recognize the fundamental need for improvement in access to medical services, including antibiotic treatment. In other words, in developing countries the first barrier to overcome is becoming a patient in the first place.

General health literacy is improving through the influence of new media, including the Internet. There are already some excellent websites that provide information for consumers, both about antibiotics and about the importance of the normal flora to human health. For example:

- *Alliance for the Prudent Use of Antibiotics* (*APUA*) (http://www.healthsci.tufts.edu/apua/Patients/patient.html). This association has an excellent website with a consumer page and good links to other sources of information. Health-care

consumers can learn how they can help to improve the use of antibiotics by understanding the drugs and by following their doctors' advice about taking them.

- *Do Bugs Need Drugs?* (http://www.dobugsneeddrugs.org). This is a Canadian website designed to inform consumers and the public about antibiotics and their effects. This website provides information for health-care professionals, the public, teachers, parents' and children. Guidelines for managing RTIs, including colds, flu, sore throat, cough, earaches, sinus infections, chest colds (bronchitis) and pneumonia, can be found in the Parent and the Health-care Professional Sections.
- *NIPA: Canada's National Information Program on Antibiotics* (http://www.antibiotics-info.org/anti01.html). NIPA is a group of health-care organizations dedicated to promoting the appropriate use of antibiotics. This website contains information for consumers and health-care professionals on a variety of topics surrounding the rising issue of antibiotic resistance in Canada.

A patient-centered approach to the management of RTIs, as well as other conditions, may require longer consultations between patients and doctors. This may necessitate changes in health-care systems that are beyond the scope of this paper. Increased consultation time needs to be accompanied by changes in attitudes (away from the paternalistic toward a more patient-centered approach), improved health literacy and consulting behavior among patients, and improved communication skills among physicians. However, these changes are all achievable.

Education of patients and doctors is not only concerned with providing facts; it is also concerned with changing beliefs and attitudes. In relation to antibiotics this means increasing awareness of the risks of antibiotic treatment to the individual. There is currently an excessive emphasis on a binary approach to bacterial infection: patients either have bacterial infection or they do not. Doctors are angered by advice such as 'don't prescribe antibiotics for viral sore throats'. If they knew for certain that the patient had a viral infection, they would not prescribe an antibiotic. The problem is that they are faced with patients who might have bacterial infection and their current belief is 'if in doubt, treat'. Patient leaflets carry messages such as 'unnecessary antibiotics may be harmful'. The decision to prescribe antibiotics is therefore a balance between expected risks and benefits. The distinction between necessary and unnecessary prescribing is only important for the benefit side of this equation. The reality of the risk side of the equation is that every course of antibiotics we take damages the normal flora, whether the treatment was necessary or unnecessary. Doctors need to feel confident that not prescribing antibiotics is sometimes in the best interests of the patient. For example, patients need to understand that if they have acute bronchitis they will be ill for about 2 weeks whether or not they take antibiotics and that, at best, antibiotics may shorten the illness by a day.

Patients present with symptoms, not infections, and doctors have to help them to understand the probability a of bacterial infection. They can then assess the relative beneficial vs. harmful effects of antibiotics. In this complex situation, decision-support tools can be used to help the doctor and the patient before, during, and after the consultation (Figure 1). Information provided before the consultation may be critical to change the knowledge, attitudes, and beliefs of patients or doctors to a point where they are ready to employ shared decision-making during or after the consultation. Key players include patient networks/organizations, pharmacists, employers, schools, nurseries/child carers, the pharmaceutical industry, governments, and the media. A recent Cochrane review has confirmed the effectiveness of mass media campaigns for influencing the way that the public makes decisions about their use of health care [126].

IMPORTANT AREAS OF UNCERTAINTY

Is shared decision-making feasible in routine clinical practice?

To be successful this requires significant changes in attitudes (away from paternalistic, toward a more patient-centered approach), improved communication skills among physicians, and improved health literacy and consulting behavior among patients. Changes in attitudes need to be supported by changes in health-care systems, including either increased consultation time or changes in the way that consultations occur with much more preparation of the patient and the doctor before the consultation.

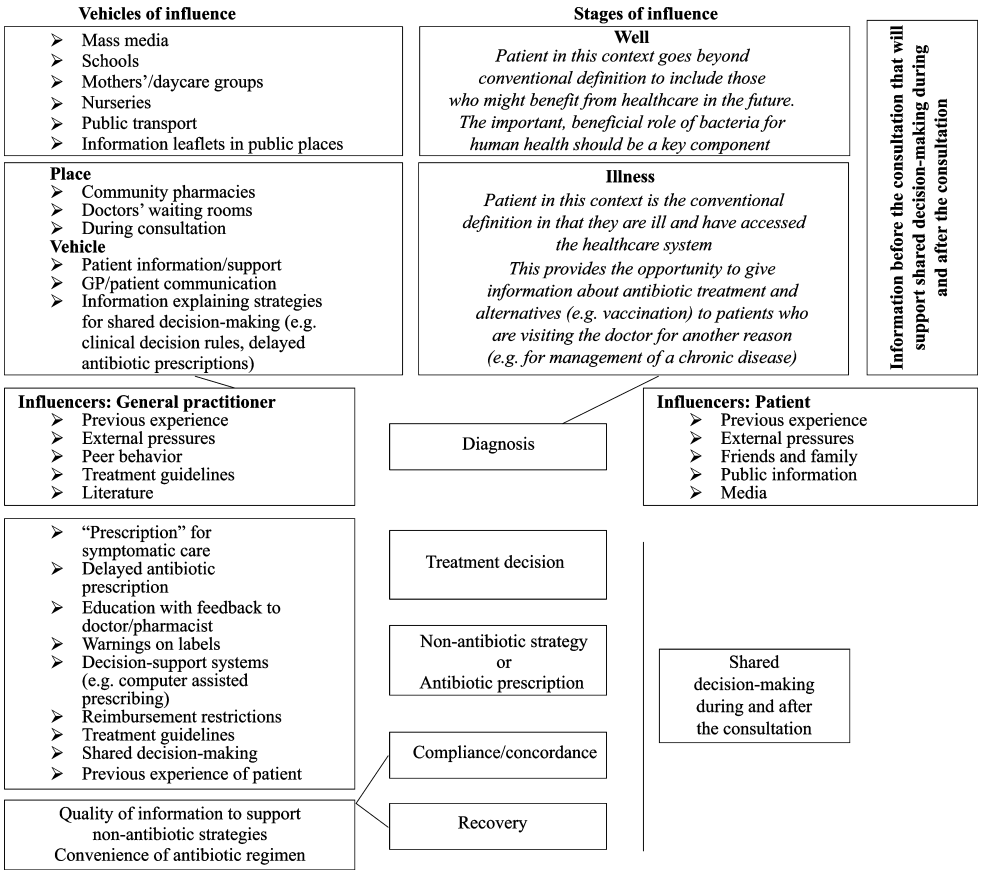

Figure 1 Intervention: when and how to communicate. We know that almost any intervention works some of the time and fails to work part of the time—but why? The above model tries to illustrate the different points of intervention, the vehicles for intervention, and the pros and cons of directing action at this stage.

Will the shared decision-making and patient-centered approaches developed in chronic illnesses work in acute infections?

The principles are the same, as far as sharing decisions is concerned, but the emphasis may be different, depending on the condition and the type of behavior you want to change. For example, in many chronic diseases the emphasis is on encouraging preventive behaviors (antismoking or safe sex) or on compliance with effective, long-term treatment. It remains to be determined whether strategies that work in these contexts will be equally effective for changing the expectations of people with sore throats.

How important are cultural differences between and within countries?

A key limitation of existing research is that it is dominated by studies from the USA or Western Europe (Tables 1,2,3). We have very limited information on the importance of cultural variation between countries/regions (and even within multicultural societies) to the appropriateness and application of patient-centered health care and shared decision-making. However, the limited available evidence suggests that cultural variations are very important. At the same time, although cultural variations clearly exist in discussing priorities for health care, there seems to be a universal agreement on the importance of certain aspects of health-care decision-making, such as the doctor–patient relationship, information and support, and availability of and access to treatment [141].

Which patients want to engage in shared decision-making?

Even within a uniform cultural group, there will be varying enthusiasm for shared decision-making.

Not all patients want to be empowered at all times; some might prefer to leave decisions about their health care to an expert whom they trust. Age, ethnicity, gender and social class may all influence habits, preferences and expectations.

CONCLUSIONS

Being the ultimate consumers of antibiotics, patients are fundamental to any efforts to control antibiotic usage and resistance. Informed public representation must be encouraged.

The debate on antibiotic prescribing and resistance needs to move beyond the traditional assumptions about patients' demand for antibiotics. Patients may lack knowledge about correct antibiotic use and may be subject to cultural bias against 'germs' combined with little knowledge of the risk that resistance may have for their health. However, the evidence suggests that there has been gross overestimation of the importance of patient demands as drivers of antibiotic prescribing and resistance. The explanation lies in physicians' misperceptions of patients' more fundamental needs and health-care expectations.

We have identified evidence that supports initiatives to encourage shared decision-making as a driver for behavioral change. However, these initiatives would need to be underpinned by educational initiatives in order to achieve broader changes in attitudes. Patient organizations offer a unique means of access to the patient's perspective. Public information campaigns do work but the effect of any individual campaign is transient so these interventions must be sustained.

Research should focus on extending the encouraging results regarding the effectiveness of shared decision-making in upper RTIs. As all of the research so far is from Western Europe and North America, we need evidence that the same success can be achieved in other cultural settings. At the same time we need evidence about the role of shared decision-making in other disease areas, especially those where problems are less easy to deal with without medical help (e.g. cystitis). Finally, we need research on methods for educating the public about antibiotic resistance and the role of bacteria in human health. At present, few patients really understand these issues and prescribers are only a little better informed.

REFERENCES

1. World Health Organization. *Report on Infectious Diseases. Overcoming antimicrobial resistance.* Geneva: World Health Organization, 2000; [http://www.who.int/infectious-disease-report/2000/index.html).
2. Sommers B. Provision of healthcare: how much, if any, are we entitled to. *Princet J Bioeth* 2000; 3: 59–69.
3. Pechere JC. Patients' interviews and misuse of antibiotics. *Clin Infect Dis* 2001; 33(Suppl. 3): S170–3.
4. Mainous AG III, Zoorob RJ, Oler MJ, Haynes DM. Patient knowledge of upper respiratory infections: implications for antibiotic expectations and unnecessary utilization. *J Fam Pract* 1997; 45: 75–83.
5. Collett CA, Pappas DE, Evans BA, Hayden GF. Parental knowledge about common respiratory infections and antibiotic therapy in children. *South Med J* 1999; 92: 971–6.
6. Isenberg HD. Pathogenicity and virulence: another view. *Clin Microbiol Rev* 1988; 1: 40–53.
7. Butler CC, Rollnick S, Pill R, Maggs-Rapport F, Scott N. Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats. *BMJ* 1998; 317: 637–42.
8. Vinson DC, Lutz LJ. The effect of parental expectations on treatment of children with a cough: a report from ASPN. *J Fam Pract* 1993; 37: 23–7.
9. Gonzales R, Steiner JF, Maselli J, Lum A, Barrett PH Jr. Impact of reducing antibiotic prescribing for acute bronchitis on patient satisfaction. *Eff Clin Pract* 2001; 4: 105–11.
10. Hamm RM, Hicks RJ, Bemben DA. Antibiotics and respiratory infections: are patients more satisfied when expectations are met? *J Fam Pract* 1996; 43: 56–62.
11. Himmel W, Lippert-Urbanke E, Kochen MM. Are patients more satisfied when they receive a prescription? The effect of patient expectations in general practice. *Scand J Prim Health Care* 1997; 15: 118–22.
12. Sanchez-Menegay C, Hudes ES, Cummings SR. Patient expectations and satisfaction with medical care for upper respiratory infections. *J Gen Intern Med* 1992; 7: 432–4.
13. Frank S, Zyzanski S, Alemagno S. Upper respiratory infection: stress, support, and the medical encounter. *Fam Med* 1992; 24: 518–23.
14. Ray DA, Rohren CH. Characteristics of patients with upper respiratory tract infection presenting to a walk-in clinic. *Mayo Clin Proc* 2001; 76: 169–73.
15. Scott JG, Cohen D, DiCicco-Bloom B, Orzano AJ, Jaen CR, Crabtree BF. Antibiotic use in acute respiratory infections and the ways patients

pressure physicians for a prescription. *J Fam Pract* 2001; 50: 853–8.
16. Mangione-Smith R, McGlynn EA, Elliott MN, McDonald L, Franz CE, Kravitz RL. Parent expectations for antibiotics, physician–parent communication, and satisfaction. *Arch Pediatr Adolesc Med* 2001; 155: 800–6.
17. Mangione-Smith R, McGlynn EA, Elliott MN, Krogstad P, Brook RH. The relationship between perceived parental expectations and pediatrician antimicrobial prescribing behavior. *Pediatrics* 1999; 103: 711–18.
18. McKee MD, Mills L, Mainous AG III Antibiotic use for the treatment of upper respiratory infections in a diverse community. *J Fam Pract* 1999; 48: 993–6.
19. Haltiwanger KA, Hayden GF, Weber T, Evans BA, Possner AB. Antibiotic-seeking behavior in college students: what do they really expect? *J Am Coll Health* 2001; 50: 9–13.
20. Little P, Gould C, Williamson I, Warner G, Gantley M, Kinmonth AL. Clinical and psychosocial predictors of illness duration from randomised controlled trial of prescribing strategies for sore throat. *BMJ* 1999; 319: 736–7.
21. Macfarlane J, Holmes W, Macfarlane R, Britten N. Influence of patients' expectations on antibiotic management of acute lower respiratory tract illness in general practice: questionnaire study. *BMJ* 1997; 315: 1211–14.
22. Miller E, MacKeigan LD, Rosser W. Effects of perceived patient demand on prescribing anti-infective drugs. *CMAJ* 1999; 161: 139–42.
23. Little P, Williamson I, Warner G, Gould C, Gantley M, Kinmonth AL. Open randomised trial of prescribing strategies in managing sore throat. *BMJ* 1997; 314: 722–7.
24. Little P, Gould C, Williamson I, Moore M, Warner G, Dunleavey J. Pragmatic randomised controlled trial of two prescribing strategies for childhood acute otitis media. *BMJ* 2001; 322: 336–42.
25. Verheij T, Hermans J, Kaptein A, Mulder J. Acute bronchitis: course of symptoms and restrictions in patients' daily activities. *Scand J Prim Health Care* 1995; 13: 8–12.
26. Marrie TJ, Peeling RW, Fine MJ, Singer DE, Coley CM, Kapoor WN. Ambulatory patients with community-acquired pneumonia: the frequency of atypical agents and clinical course. *Am J Med* 1996; 101: 508–15.
27. Macfarlane JT, Holmes WF, Macfarlane RM. Reducing reconsultations for acute lower respiratory tract illness with an information leaflet: a randomized controlled study of patients in primary care. *Br J Gen Pract* 1997; 47: 719–22.
28. Smith R. All changed, changed utterly. British medicine will be transformed by the Bristol case. *BMJ* 1998; 316: 1917–18.
29. Smith R. One Bristol, but there could have been many. Radical change is essential but hard to achieve. *BMJ* 2001; 323: 179–80.
30. Howie JG. Some non-bacteriological determinants and implications of antibiotic use in upper respiratory tract illness. *Scand J Infect Dis* 1983; 39(Suppl.): 68–72.
31. Oeffinger KC, Snell LM, Foster BM, Panico KG, Archer RK. Treatment of acute bronchitis in adults. A national survey of family physicians. *J Fam Pract* 1998; 46: 469–75.
32. Mainous AG III, MacFarlane LL, Connor MK, Green LA, Fowler K, Hueston WJ. Survey of clinical pharmacists' knowledge of appropriateness of antimicrobial therapy for upper respiratory infections and acute bronchitis. *Pharmacotherapy* 1999; 19: 388–92.
33. Davy T, Dick PT, Munk P. Self-reported prescribing of antibiotics for children with undifferentiated acute respiratory tract infections with cough. *Pediatr Infect Dis J* 1998; 17: 457–62.
34. Murray S, Del Mar C, O'Rourke P. Predictors of an antibiotic prescription by GPs for respiratory tract infections: a pilot. *Fam Pract* 2000; 17: 386–8.
35. Watson RL, Dowell SF, Jayaraman M, Keyserling H, Kolczak M, Schwartz B. Antimicrobial use for pediatric upper respiratory infections: reported practice, actual practice, and parent beliefs. *Pediatrics* 1999; 104: 1251–7.
36. Armstrong GL, Conn LA, Pinner RW. Trends in infectious disease mortality in the United States during the 20th century. *JAMA* 1999; 281: 61–6.
37. Pinner RW, Teutsch SM, Simonsen L *et al.* Trends in infectious diseases mortality in the United States. *JAMA* 1996; 275: 189–93.
38. Taylor R, Lewis M, Powles J. The Australian mortality decline: cause-specific mortality, 1907–1990. *Aust N Z J Public Health* 1998; 22: 37–44.
39. Hemminki E, Paakkulainen A. The effect of antibiotics on mortality from infectious diseases in Sweden and Finland. *Am J Public Health* 1976; 66: 1180–4.
40. Mackenbach JP, Looman CWN. Secular trends of infectious disease mortality in The Netherlands. 1911–1978: quantitative estimates of changes coinciding with the introduction of antibiotics. *Int J Epidemiol* 1988; 17: 618–24.
41. Wolleswinkel-van den Bosch JH, Looman CW, Van Poppel FW, Mackenbach JP. Cause-specific mortality trends in The Netherlands. 1875–1992: a formal analysis of the epidemiologic transition. *Int J Epidemiol* 1997; 26: 772–81.
42. Anthonisen NR, Manfreda J, Warren CPW, Hershfield ES, Harding GKM, Nelson NA. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Int Med* 1987; 106: 196–204.

43. Bent S, Saint S, Vittinghoff E, Grady D. Antibiotics in acute bronchitis: a meta-analysis. *Am J Med* 1999; 107: 62–7.
44. Del Mar CB, Glasziou PP. Antibiotics for sore throat. *Cochrane Database Syst Rev* 2000; 4: CD000023.
45. Kaiser L, Lew D, Hirschel B *et al*. Effects of antibiotic treatment in the subset of common-cold patients who have bacteria in nasopharyngeal secretions. *Lancet* 1996; 347: 1507–10.
46. Saint S, Bent S, Vittinghoff E, Grady D. Antibiotics in chronic obstructive pulmonary disease exacerbations. A meta-analysis. *JAMA* 1995; 273: 957–60.
47. Stalman W, van Essen GA, van der Graaf Y, de Melker RA. The end of antibiotic treatment in adults with acute sinusitis-like complaints in general practice? A placebo-controlled double-blind randomized doxycycline trial. *Br J Gen Pract* 1997; 47: 794–9.
48. Arroll B, Kenealy T. Antibiotics for the common cold. *Cochrane Database Syst Rev* 2000; 2: CD000247.
49. Becker L, Glazier R, McIsaac W, Smucny J. Antibiotics for acute bronchitis. *Cochrane Database Syst Rev* 2000; 2: CD000245.
50. Glasziou PP, Hayem M, Del Mar CB. Antibiotics for acute otitis media in children. *Cochrane Database Syst Rev* 2000; 2: CD000219.
51. Shann F, D'Souza RM, D'Souza R. Antibiotics for preventing pneumonia in children with measles. *Cochrane Database Syst Rev* 2000; 4: CD001477.
52. Williams JW Jr, Aguilar C, Makela M *et al*. Antimicrobial therapy for acute maxillary sinusitis. *Cochrane Database Syst Rev* 2000; 2: CD000243.
53. Sanders CC, Sanders WE, Harrowe DJ. Bacterial interference: Effects of oral antibiotics on the normal throat flora and its ability to interfere with group A streptococci. *Infect Immun* 1976; 13: 808–12.
54. Sanders CC, Nelson GE, Sanders WE. Bacterial interference IV. Epidemiological determinants of the antagonistic activity of the normal throat flora against group A streptococci. *Infect Immun* 1977; 16: 599–603.
55. Hentges DJ, Stein AJ, Casey SW, Que JU. Protective role of intestinal flora against infection with *Pseudomonas aeruginosa* in mice: influence of antibiotics on colonization resistance. *Infect Immun* 1985; 47: 118–22.
56. Que JU, Casey SW, Hentges DJ. Factors responsible for increased susceptibility of mice to intestinal colonization after treatment with streptomycin. *Infect Immun* 1986; 53: 116–23.
57. Herthelius BM, Hedstrom KG, Mollby R, Nord CE, Pettersson L, Winberg J. Pathogenesis of urinary tract infections – amoxicillin induces genital *Escherichia coli* colonization. *Infection* 1988; 16: 263–6.
58. Herthelius M, Gorbach SL, Mollby R, Nord CE, Pettersson L, Winberg J. Elimination of vaginal colonization with *Escherichia coli* by administration of indigenous flora. *Infect Immun* 1989; 57: 2447–51.
59. Gorbach SL, Goldin BR. The intestinal microflora and the colon cancer connection. *Rev Infect Dis* 1990; 12(Suppl. 2): S252–61.
60. Gorbach SL. Estrogens, breast cancer, and intestinal flora. *Rev Infect Dis* 1984; 6(Suppl. 1): S85–90.
61. Adlercreutz H, Fotsis T, Heikkinen R *et al*. Excretion of the lignans enterolactone and enterodiol and of equol in omnivorous and vegetarian postmenopausal women and in women with breast cancer. *Lancet* 1982; 2: 1295–9.
62. Knekt P, Adlercreutz H, Rissanen H, Aromaa A, Teppo L, Heliovaara M. Does antibacterial treatment for urinary tract infection contribute to the risk of breast cancer? *Br J Cancer* 2000; 82: 1107–10.
63. Fekety R. Antibiotic-associated diarrhoea and colitis. *Curr Opin Infect Dis* 1995; 8: 391–7.
64. Bartlett JG. Antibiotic-associated diarrhoea. *Clin Infect Dis* 1992; 15: 573–81.
65. MacDonald TM, Beardon PHG, McGilchrist MM, Duncan ID, Mckendrick AD, McDevitt DG. The risks of symptomatic vaginal candidiasis after oral antibiotic therapy. *Q J Med* 1993; 86: 419–24.
66. Paluck E, Katzenstein D, Frankish CJ *et al*. Prescribing practices and attitudes toward giving children antibiotics. *Can Fam Physician* 2001; 47: 521–7.
67. Steinke D, Davey PG. The association between antibiotic resistance and community prescribing. *A Critical Review of Bias and Confounding in* published studies. *Clin Infect Dis* 2001; 33: S193–205.
68. Harbarth S, Harris AD, Carmeli Y, Samore MH. Parallel analysis of individual and aggregated data on antibiotic exposure and resistance in gram-negative bacilli 13647. *Clin Infect Dis* 2001; 33: 1462–8.
69. Macfarlane J, Lewis SA, Macfarlane R, Holmes W. Contemporary use of antibiotics in 1089 adults presenting with acute lower respiratory tract illness in general practice in the UK: implications for developing management guidelines. *Respir Med* 1997; 91: 427–34.
70. Coenen S, Van Royen P, Vermeire E, Hermann I, Denekens J. Antibiotics for coughing in general practice: a qualitative decision analysis. *Fam Pract* 2000; 17: 380–5.
71. Ukoumunne OC, Britten N. Pressure on doctors to prescribe needs measuring directly. *BMJ* 1998; 317: 818.
72. Britten N, Ukoumunne O. The influence of patients' hopes of receiving a prescription on doctors' perception and the decision to prescribe: a questionnaire survey 3272. *BMJ* 1997; 315: 1506–10.

73. McWhinney IR. Primary care: core values. Core values in a changing world. *BMJ* 1998; 316: 1807–9.
74. Dixon J, Holland P, Mays N. Primary care: core values developing primary care: gatekeeping, commissioning, and managed care. *BMJ* 1998; 317: 125–8.
75. Sabin JE. Fairness as a problem of love and the heart: a clinician's perspective on priority setting. *BMJ* 1998; 317: 1002–4.
76. Coast J. Citizens, their agents and healthcare rationing: an exploratory study using qualitative methods. *Health Econ* 2001; 10: 159–74.
77. Tehan S, Whittaker J. A multi-centre double blind prospective study comparing the efficacy and tolerance of augmentin with the combination of cephradine plus metronidazole as surgical prophylaxis. *Surg Res Comm* 1989; 6: 97–105.
78. West SK, Brandon BM, Stevens AM. Drug utilization review in an HMO: I. introduction and examples of methodology. *Med Care* 1977; 15: 505–14.
79. Dormandy JA, Belcher G, Broos P *et al*. Prospective study of 713 below-knee amputations for ischaemia and the effect of a prostacyclin analogue on healing. *Br J Surg* 1994; 81: 33–7.
80. Foster JE, Harpur ES, Garland HO. An investigation of the acute effect of gentamicin on the renal handling of electrolytes in the rat. *J Pharmacol Exper Ther* 1992; 261: 38–43.
81. Smith MD, Duong NM, Hoa NT *et al*. Comparison of ofloxacin and ceftriaxone for short-course treatment of enteric fever. *Antimicrob Agents Chemother* 1994; 38: 1716–20.
82. Department of Health. *Improving prescribing*. London: Department of Health, 1993.
83. Grilli R, Magrini N, Penna A, Mura G, Liberati A. Practice guidelines developed by specialty societies: the need for a critical appraisal. *Lancet* 2000; 355: 103–6.
84. Formoso G, Liberati A, Magrini N. Practice guidelines: useful and 'participative' method? Survey of Italian physicians by professional setting. *Arch Intern Med* 2001; 161: 2037–42.
85. Butler CC, Rollnick S, Kinnersley P, Jones A, Stott N. Reducing antibiotics for respiratory tract symptoms in primary care: consolidating 'why' and considering 'how'. *Br J Gen Pract* 1998; 48: 1865–70.
86. Mainous AG III, Zoorob RJ, Hueston WJ. Current management of acute bronchitis in ambulatory care: The use of antibiotics and bronchodilators. *Arch Fam Med* 1996; 5: 79–83.
87. Cates C. An evidence based approach to reducing antibiotic use in children with acute otitis media: controlled before and after study. *BMJ* 1999; 318: 715–6.
88. Halm EA, Atlas SJ, Borowsky LH *et al*. Understanding physician adherence with a pneumonia practice guideline: effects of patient, system, and physician factors. *Arch Intern Med* 2000; 160: 98–104.
89. De Sutter AI, De Meyere MJ, De Maeseneer JM, Peersman WP. Antibiotic prescribing in acute infections of the nose or sinuses: a matter of personal habit? *Fam Pract* 2001; 18: 209–13.
90. Giesen D. *International Medical Malpractice Law*. Dordrecht, The Netherlands: Kluwer Academic Publishers, 1988.
91. Dominion Law Reports. *ter Neuzen v. Korn*. Ontario Canada: Canada Law Book, 4th Series, 2001; 103: 473–520.
92. House of Lords. *Judgements—Bolitho v. City and Hackney Health Authority*, 90–9. London: Judicial Office, House of Lords, 1997.
93. Gonzales R, Barrett PH Jr, Crane LA, Steiner JF. Factors associated with antibiotic use for acute bronchitis. *J Gen Intern Med* 1998; 13: 541–8.
94. Gonzales R, Barrett PH Jr, Steiner JF. The relation between purulent manifestations and antibiotic treatment of upper respiratory tract infections. *J Gen Intern Med* 1999; 14: 151–6.
95. Kawamoto R, Asai Y, Nago N, Okayama M, Mise J, Igarashi M. A study of clinical features and treatment of acute bronchitis by Japanese primary care physicians. *Fam Pract* 1998; 15: 244–51.
96. Metlay JP, Stafford RS, Singer DE. National trends in the use of antibiotics by primary care physicians for adult patients with cough. *Arch Intern Med* 1998; 158: 1813–18.
97. McGregor A, Dovey S, Tilyard M. Antibiotic use in upper respiratory tract infections in New Zealand. *Fam Pract* 1995; 12: 166–70.
98. Dosh SA, Hickner JM, Mainous AG III, Ebell MH. Predictors of antibiotic prescribing for nonspecific upper respiratory infections, acute bronchitis, and acute sinusitis. An UPRNet study. Upper Peninsula Research Network. *J Fam Pract* 2000; 49: 407–14.
99. Pennie RA. Prospective study of antibiotic prescribing for children. *Can Fam Physician* 1998; 44: 1850–6.
100. Hutchinson JM, Jelinski S, Hefferton D, Desaulniers G, Parfrey PS. Role of diagnostic labeling in antibiotic prescription. *Can Fam Physician* 2001; 47: 1217–24.
101. de Melker RA, Kuyvenhoven MM. Management of upper respiratory tract infections in Dutch family practice. *J Fam Pract* 1994; 38: 353–7.
102. Holmes WF, Macfarlane JT, Macfarlane RM, Lewis S. The influence of antibiotics and other factors on reconsultation for acute lower respiratory tract illness in primary care. *Br J Gen Pract* 1997; 47: 815–18.

103. Nyquist AC, Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. *JAMA* 1998; 279: 875–7.
104. Steffensen FH, Schonheyder HC, Sorensen HT. High prescribers of antibiotics among general practitioners—relation to prescribing habits of other drugs and use of microbiological diagnostics. *Scand J Infect Dis* 1998; 29: 409–13.
105. Steinke DT, Bain DJG, MacDonald TM, Davey PG. Practice factors that influence antibiotic prescribing in general practice in Tayside. *J Antimicrob Chemother* 2000; 46: 509–12.
106. Britten N, Stevenson FA, Barry CA, Barber N, Bradley CP. Misunderstandings in prescribing decisions in general practice: qualitative study. *BMJ* 2000; 320: 484–8.
107. Nazareth I, King M. Decision making by general practitioners in diagnosis and management of lower urinary tract symptoms in women. *BMJ* 1993; 306: 1103–6.
108. Mead N, Bower P. Patient-centeredness: a conceptual framework and review of the empirical literature. *Soc Sci Med* 2000; 51: 1087–110.
109. Stewart M, Belle Brown J, Weston WW *et al. Patient-centered medicine. Transforming the Clinical Method.* Thousand Oaks, CA: Sage Publications, 1995.
110. Lerner JC, The National Patient Library. Evidence-based information for consumers. *Int J Technol Assess Health Care* 1998; 14: 81–96.
111. Scottish Intercollegiate Guidelines Network SIGN. *Guidelines: an Introduction to SIGN Methodology for the Development of Evidence-based Clinical Guidelines.* Edinburgh: Royal College of Physicians of Edinburgh, 1999; 39: 1–34.
112. Gibson CH. A concept analysis of empowerment. *J Adv Nurs* 1991; 16: 354–61.
113. Ouschan R, Sweeney JC, Johnson LW. Dimensions of patient empowerment: implications for professional services marketing. *Health Mark Q* 2000; 18: 99–114.
114. Lupton D. Consumerism, reflexivity and the medical encounter. *Soc Sci Med* 1997; 45: 373–81.
115. Charles C, Gafni A, Whelan T. Decision-making in the physician–patient encounter: revisiting the shared treatment decision-making model. *Soc Sci Med* 1999; 49: 651–61.
116. Banks JC, Howie JGR. Reducing consultations for symptoms of cystitis using a health education leaflet. *Br J Gen Pract* 1998; 48: 1595–6.
117. Towle A, Godolphin W. Framework for teaching and learning informed shared decision making. *BMJ* 1999; 319: 766–71.
118. Mullen PD. Compliance becomes concordance. *BMJ* 1997; 314: 691–2.
119. Dowell J, Pitkethly M, Bain J, Martin S. A randomised controlled trial of delayed antibiotic prescribing as a strategy for managing uncomplicated respiratory tract infection in primary care. *Br J Gen Pract* 2001; 51: 200–5.
120. Couchman GR, Rascoe TG, Forjuoh SN. Back-up antibiotic prescriptions for common respiratory symptoms. Patient satisfaction and fill rates. *J Fam Pract* 2000; 49: 907–13.
121. McGuckin M, Waterman R, Storr J *et al.* Evaluation of a patient-empowering hand hygiene programme in the UK. *J Hosp Infect* 2001; 48: 222–7.
122. Trepka M, Belongia E, Chyou P, Davis J, Schwardz B. The effect of a community intervention trial on parental knowledge and awareness of antibiotic resistance and appropriate antibiotic use in children. *Pediatrics* 2001; 107: E6.
123. Butler CC, Rollnick S, Pill R, Maggs-Rapport F, Stott N. Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats. *BMJ* 1998; 317: 637–42.
124. Barden LS, Dowell SF, Schwartz B, Lackey C. Current attitudes regarding use of antimicrobial agents: results from physician's and parents' focus group discussions. *Clin Pediatr (Phila)* 1998; 37: 665–71.
125. Butler CC, Kinnersley P, Prout H, Rollnick S, Edwards A, Elwyn G. Antibiotics and shared decision-making in primary care. *J Antimicrob Chemother* 2001; 48: 435–40.
126. Grilli R, Freemantle N, Minozzi S *et al.* Mass media interventions: effects on health services utilisation. *Cochrane Database Syst Rev* 2000; 2: CD000389.
127. Bauraind I, Vanden Bremt I, Bogaert M *et al.* Evaluation of the impact of a public campaign for a more rational use of antibiotics in Belgium. In: *Program and Abstracts of the 41st Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, USA*, 2001 [abstract LB-9].
128. Freemantle N, Harvey EL, Wolf F *et al.* Printed educational materials: effects on professional practice and healthcare outcomes *Cochrane Database Syst Rev* 2000; 2: CD000172.
129. Thomson O'Brien MA, Oxman AD, Davis DA, Haynes RB, Freemantle N, Harvey EL. Audit and feedback versus alternative strategies: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2000; 2: CD000260.
130. Thomson O'Brien MA, Oxman AD, Davis DA, Haynes RB, Freemantle N, Harvey EL. Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev* 2000; 2: CD000259.
131. Thomson O'Brien MA, Oxman AD, Davis DA, Haynes RB, Freemantle N, Harvey EL. Educational outreach visits: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev* 2000; 2: CD000409.

132. Thomson O'Brien MA, Oxman AD, Haynes RB, Davis DA, Freemantle N, Harvey EL. Local opinion leaders: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev* 2000; 2: CD000125.
133. Walton RT, Harvey E, Dovey S, Freemantle N. Computerised advice on drug dosage to improve prescribing practice. *Cochrane Database Syst Rev* 2001; 1: CD002894.
134. Oxman A, Thomson M, Davis D, Haynes B. No magic bullets: a systematic review of 102 trials of interventions to improve professional practice. *CMAJ* 1995; 153: 1423–31.
135. Gonzalez OE, Armas PL, Bravo G Jr, Cabrales EJ, Rosales CR, Abreu SG. Prescription of antibiotics for mild acute respiratory infections in children. *Bull Pan Am Health Organ* 1996; 30: 106–17.
136. Gonzales R, Steiner JF, Lum A, Barrett PH Jr. Decreasing antibiotic use in ambulatory practice: impact of a multidimensional intervention on the treatment of uncomplicated acute bronchitis in adults. *JAMA* 1999; 281: 1512–19.
137. Hueston WJ, Mainous AG III, Brauer N, Mercuri J. Evaluation and treatment of respiratory infections: does managed care make a difference? *J Fam Pract* 1997; 44: 572–7.
138. Friis H, Bro F, Eriksen NR, Mabeck CE, Vejlsgaard R. The effect of reimbursement on the use of antibiotics. *Scand J Prim Health Care* 1993; 11: 247–51.
139. Cook TD, Campbell DT. *Quasi Experimentation. Design and Analysis Issues for Field Settings.* Boston: Houghton Mifflin Company, 1979.
140. Soumerai SB, McLaughlin TJ, Avorn J. Improving drug prescribing in primary care: a critical analysis of the experimental literature. *Milbank Q* 1989; 67: 268–317.
141. Grol R, Wensing M, Mainz J *et al.* Patients' priorities with respect to general practice care: an international comparison. *Fam Pract* 1999; 16: 4–11.