

# Poor adherence to antibiotic prescribing guidelines in acute otitis media—obstacles, implications, and possible solutions

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**Abstract** Many countries now have guidelines on the clinical management of acute otitis media. In almost all, the public health goal of containing acquired resistance in bacteria through reduced antibiotic prescribing is the main aim and basis for recommendations. Despite some partial short-term successes, clinical activity databases and opinion surveys suggest that such restrictive guidelines are not followed closely, so this aim is not achieved. Radical new solutions are needed to tackle irrationalities in healthcare systems which set the short-term physician–patient relationship against long-term public health. Resolving this opposition will require comprehensive policy appraisal and coordinated actions at many levels, not just dissemination of evidence and promotion of guidelines. The inappropriate clinical rationales that underpin non-compliance with guidelines can be questioned by evidence, but also need specific developments promoting alternative solutions, within a framework of whole-system thinking. Promising developments would be (a) physician training modules on age-appropriate analgesia and on detection plus referral of rare complications like mastoiditis, and (b) vaccination against the most common and serious bacterial pathogens.

**Keywords** Otitis media · Burden · Antibiotic resistance · Antibiotic prescription · Public health policy · Guidelines · Antibiotic prescribing · Acute otitis media · Policy framework · Behavior change · Vaccination

## Abbreviations

OM Otitis media  
AOM Acute otitis media  
OME Otitis media with effusions

## Introduction: the challenge of marginal efficacy

Otitis media (OM) is a very common childhood infection of the middle ear facilitated by seasonal respiratory viruses. Incidence peaks between 6 months and 2 years, by which age over 90% of children have had at least one episode of acute OM (AOM) [72]. A proportion will develop OM with effusion (OME), with consequences which reach well into mid-childhood [53]. AOM is generally self-limiting, but its recurrence and frequency entail high direct healthcare costs [50] and indirect costs for parents [42], as well as burden on family quality of life [14]. Despite a superficial familiarity, OM still poses many challenges of definition, assessment, and indications for treatment.

Even with insensitive traditional culture methods, about 70% of middle ears in AOM yield bacterial isolates [96], so most of properly diagnosed (and severe) AOM is seen as bacterial [55, 67]. Over-inclusive diagnosis by non-specialists may result in antibiotic prescribing for conditions that are not actually bacterial. Routine microbiological assessment (by paracentesis) is impractical and mostly thought unethical. Hence, antibiotics give frustratingly small benefits [39, 56, 61] compared to temporizing care with analgesics [88]. Even with appropriate diagnosis, the overall clinical effectiveness of antibiotics remains low for reasons which are now well understood, including: poor penetration into the middle ear mucosa [19]; inaccessibility of bacteria in the form of biofilm [48]; little symptomatic

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benefit in the first 24 h [39, 86]; generally favorable clinical course in most patients if untreated [84]; and poor adherence to treatment regimens [15]. The treatment dilemma is intensified by the emergence of strains resistant to antibiotics [9], which has become the main stimulus to guidelines, discussed further below.

Recent reductions in consultations for AOM [78, 102, 103] are too large and pervasive to be due to one single factor. Guidelines must have contributed, in part, to “de-medicalization” of AOM. The exact contribution of changes in clinical practice and health systems are hard to distinguish so guidelines are best seen as flags of a trend rather than the root cause. Trials suggest that the contribution of pneumococcal vaccination to all-cause reduction in OM is no more than modest [18, 28, 80] and observational studies on all-cause OM consultations post-vaccine are poorly controlled for background trends like the de-medicalization from guidelines [93]. Reduction in the more serious (and more clearly diagnosable) pneumococcal OM is not in question.

Antibiotic prescription rates *per consultation* for AOM remain high in most countries (approximately 80% of all consultations) [102], and especially in children <2 years [72]. This may be due to a fixed notion of an appropriate prescription rate. Parents’ criteria for consultation may have become both higher and narrower (family-level triage) making more consultations justify a prescription. A further possibility is time pressure as an opportunity cost: the relatively modest cost to the healthcare system of many antibiotics, against the personnel cost for assessment and explanation required in rational prescribing, create an incentive to over-prescribe. The multiple possible explanations for stable prescription rates per consultation amid reduced consultations add to the present requirement for a whole-system examination of the main policy dilemmas around antibiotics in OM, separate from mere promotion of guidelines.

### Antibiotic resistance—the driver for change

At recent rates of spread of resistance, the low rate of discovery of new antimicrobials will soon compromise mankind’s ability to fight serious infections, including prophylaxis to control infection during surgery [58, 101]. Bacteriological time series data reflect the selection pressures for the development of antibiotic resistance. The European Surveillance of Antimicrobial Consumption findings from 2001 [40], replicated in 2004 [97], established firmly the link between antibiotic consumption and resistance. Countries can be at differing phases of a cycle in consumption and bacterial response [29]: rates of resistance have been rising in Ireland and Finland, but remain low in

Germany and The Netherlands. Encouragingly, reducing prescription rates in France, Belgium, and Spain, (former) high-consumption countries, seem to be giving lower levels of resistance (Fig. 1) [29].

OM is a major public health issue because it is a prime target for rational prescribing [24]. It dominates antibiotic consumption, even in low-consumption countries with low OM concern [87]. Secondly, the high incidence and low antibiotic efficacy in OM favor mutation and survival of resistant strains. In infants <2 year, 90% of antibiotic prescriptions are for OM [72], and the number and proximity of contacts in child day care create a particularly effective “forcing ground” for the spread of resistance [43], reflected in locally differing prescription rates for OM [6]. Thus OM particularly justifies guidelines and related developments to restrict prescribing.

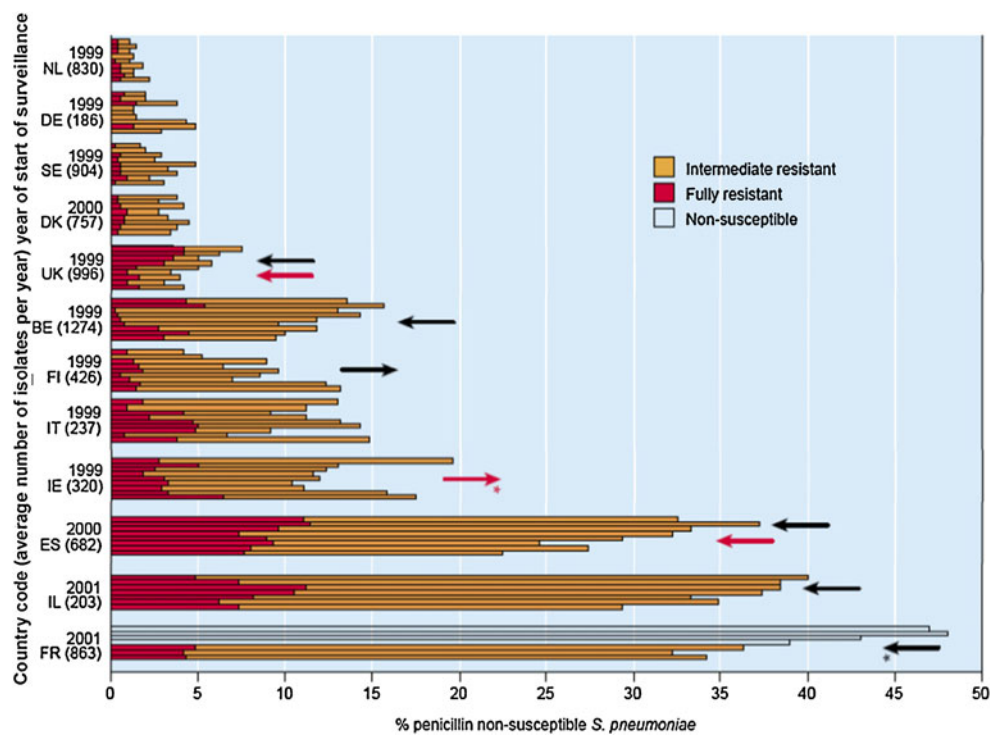
### Guidelines: formulation and presentation

Guidelines on management of AOM (and of upper respiratory tract infections more generally) draw on shared evidence and clinical insights from a coherent literature. They recommend “watchful waiting” in children >2 years with uncomplicated AOM, and limit immediate prescription to those most likely to benefit, i.e., the very young and those with a firm diagnosis (Table 1). All guidelines stratify eligible patients by age, duration, and severity, although the recommended cut-offs differ between countries. These details are probably less important than whether a guideline recommends watchful waiting as an option or as favored good practice: for example in the child over 2 years and severely ill or still symptomatic after 48 h, in North America antibiotics are “recommended” whereas in Europe antibiotics are “optional”. Feedback and/or sanctions on prescribing practice should be more influential than a recommendation versus an option. Particular clinical options tend to be exercised if the alternative is perceived as therapeutically inactive [18, 46, 62] and naming is an important part of marketing. The professional term (“watchful waiting” or equivalent) guides physician behavior, but may not reduce parental concerns: “age-appropriate analgesia with active monitoring” would more judiciously reassure parents.

### Are guidelines alone effective in changing practice?

Evidence-based recommendations are necessary, but insufficient drivers of change. Within an intervention study, short-term performance improvements (reductions in antibiotic prescribing) can be shown, without apparently compromising parental satisfaction [18, 62, 63]. However,

**Fig. 1** Trends between 1999 and 2007 in penicillin-resistant *Streptococcus pneumoniae* by country. Reproduced with permission from European Antimicrobial Resistance Surveillance System Annual report 2007 [29]. Available at: <http://www.earss.rivm.nl>. Data retrieved February 2009. Each bar represents the findings from a single year. The arrows indicate the significant trends observed for all resistant strains (black arrows) or fully penicillin-resistant strains (red arrows). The stars indicate significant trends in the overall national data that were, non-significantly, supported by data from laboratories reporting all 9 years. IE Ireland, IL Israel, IT Italy, BE Belgium, NL Netherlands, DK Denmark, FI Finland, FR France, DE Germany, ES Spain, SE Sweden, UK United Kingdom



where physicians know their performance is observed, such “Hawthorn effects” [38] are expected. This highly controlled evidence shows feasibility and non-harm of rational prescribing, but does not guarantee long-term adherence to guidelines.

There remain wide variations in antibiotic prescribing across Europe [27, 31, 97] and between Europe and the USA [40], with growing consumption and high resistance in Asia [90]. The important global question is therefore whether guidelines will make a *large enough* difference *soon enough*. This urgency requires the analysis of policy options broader than dissemination of guidelines, particularly supplementary actions that may help adherence. Guidelines are alien to much medical tradition, but other pressures for change in physician role are occurring for separate reasons, e.g., partnership with, and explanation to, patients. With a judicious lead and explanation, parents can change their expectations and behavior, assisting compliance with guidelines [32, 33]. Effective implementation of guidelines on any condition can require physicians to give advice based on the limited efficacy or unfavorable benefit-to-harm ratio of whole groups of medicines [66]. In the present phase of transition to more patient-centered practice, progressive explanation of more appropriate antibiotic use requires the complementary use of age-appropriate pain management, following a more traditional model of practice. It is surprising that explicit analgesic alternatives have been little developed, promoted, or trialed.

**Reasons for non-adherence**

Non-adherence to guidelines is based on the clinical predicament as experienced by physicians, not on reasoned counter-claims that guidelines’ aims are somehow inappropriate. The literature (e.g., Cabana [17]) identifies seven overlapping classes of reason for poor adherence, many of them cultural, physician inertia, lack of appropriate incentives, lack of detailed knowledge due to poor dissemination, conflict of interest, parental pressure, insufficient use of appropriate analgesia, uncertain diagnosis, and concerns over possible complications from not treating infection. Different types of policy response are required by reasons based on (a) practical obstacles, (b) clinical counter-arguments that may be part-justified, and (c) veiled excuses not to practice effectively or reflectively.

**Multi-dimensional cultural differences and the vicious spiral**

Major differences exist between countries in medical beliefs and practices [74] for economic and cultural reasons. Compared to Northern and Western Europe, Southern and Eastern European countries have greater use of antibiotics [41]. The very low (until recently) antibiotic prescription rate for AOM in the Netherlands for OM [34], has been offset by a high rate of early surgical intervention, often for recurrent AOM rather than OME.

**Table 1** Examples of national guidelines in AOM: scope and recommended first-line treatment

Guideline	Scope	First-line treatment
American Academy of Pediatrics and American Academy of Family Physicians (AAP/AAFP 2004) [5]	Pain management, initial observation versus antibacterial treatment, appropriate choices of antibacterials, and preventive measures	Analgesia Following certain diagnosis <2 years: antibiotics; >2 years; watchful waiting
Scottish Intercollegiate Guidelines Network (SIGN 2003) [88]	Detection, management, referral and follow-up of AOM and OM with effusion	Analgesia first-line Delayed antibiotic treatment after 72 h
National Institute of Clinical Excellence, UK (NICE 2008) [70]	Clinical effectiveness and cost effectiveness of antibiotic management strategies for respiratory tract infections	AOM—no antibiotic or delayed antibiotics And/or antibiotics for severe cases Bilateral AOM in children younger than 2 years AOM in children with otorrhoea
Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS 2005) [2]	Best use of antibiotics for respiratory tract infection	<2 years: antibiotics >2 years: watchful waiting unless symptoms are severe then use antibiotics And/or delayed treatment after re-evaluation at 48–72 h
Ontario Guidelines Advisory Committee 2002 [71]	Antibiotic treatment in OM	For purulent OM with effusion or minimally symptomatic AOM Amoxicillin prescription to be filled within a week at the parent's discretion, if symptoms are worsening Or deferred treatment following phone call to physician
Guidelines of the German society for pediatric infectious diseases [36]	Treatment of AOM	Symptomatic treatment (analgesia, nose drops) and watchful waiting for 24–72 h if second look is assured. Antibiotics first line (amoxicillin) in severe disease, age <6 months, risk factors
Nederlands Huisarts Genootschap (NHG) [69]	Treatment of AOM	Analgesia (paracetamol) In case of worsening disease or children <2 year with bilateral acute OM: amoxicillin for 1 week (recommended alternatives azithromycin for 3 days or cotrimoxazole for 5–7 days)
Spanish Pediatric Association [23]	Treatment of AOM	Symptomatic treatment (paracetamol, ibuprofen) Children >2 years without poor prognostic factors, analgesic with reassessment after 48 h Antibiotic is recommended treatment for: Mild or moderate condition: amoxicillin, then amoxicillin-clavulanate (if clinical failure at 48–72 h of treatment) Severe conditions or less than 6 months: amoxicillin-clavulanate then if clinical failure at 48–72 h of treatment, tympanocentesis and treatment according to results of Gram staining and antibiotic sensitivity Previous treatment failure (lack of clinical response): amoxicillin-clavulanate then ceftriaxone, then tympanocentesis and treatment, according to Gram stain, culture, and sensitivity

The Franco-German contrast between two generally similar countries shows how cumulative differences in health beliefs, social determinants, and regulatory practice produced in France a rate of antibiotic consumption twice that of Germany [49]. Such accumulations of several factors [85] resist change if they are mutually reinforcing, forming vicious spirals (Fig. 2). But a spiral can also permit large changes, if any of the links become greatly

weakened, e.g., the belief in high efficacy of antibiotics for AOM.

#### Parental pressure: the burden of OM on the family

Breaking the spiral requires acknowledgement of the range of impacts of OM on the family (absence from work with

possible loss of earnings, extra childcare, loss of family quality of life, and lowered resilience of the parents to cope with other problems) [14]. These have not so far been summarized in a single index, but pressures for consultation and antibiotic use do reflect these impacts, and so carry implications for the economic and other choices being modeled. When watchful waiting was incorporated by Meropol et al. [65] in a formal decision analysis, it was suggested that work days lost by parents of children older than 2 years (compared with <2), due to prolonged episodes of OM, could pose a genuinely grounded policy obstacle to rational prescribing.

**Physician inertia**

Databases on actual clinical activity [3, 81, 83] and surveys of clinician opinion or professed practice [1, 37, 57, 99] show poor adherence to guidelines in the real world [82], making it unlikely that repeating summaries of evidence can achieve desired changes. One aspect of this inertia is shift in diagnostic habit, concealing discrepancies between recommended practice and actual prescribing behavior. Some displacement of former AOM into the separate diagnosis of OME was noted in the UK [95, 102] recently illustrating the contradictions of performance management. (Antibiotics are even less effective in OME, so rarely used, and not subject to the same guideline strictures.)

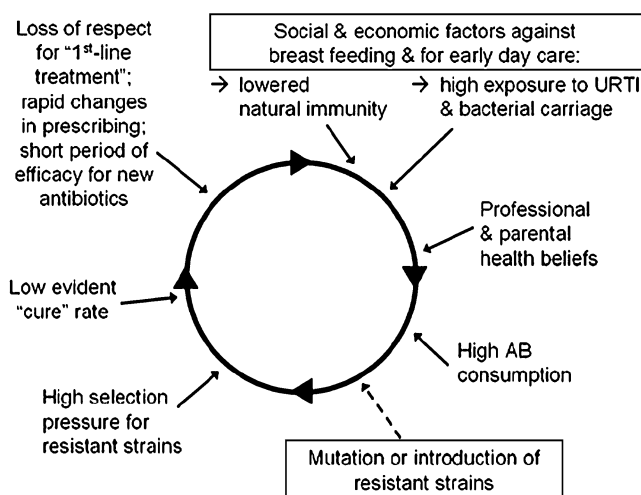
**Conflicts of interest**

In some healthcare systems, a patient/parent can easily change physician and/or consult more than one practice. In

combination with payment by item of service, these arrangements make it difficult for physicians to challenge patient health beliefs [89] and intensify the conflict of interest between present doctors or parents (to prescribe) and future patients (to withhold). The conflict becomes extreme in countries where poorly paid doctors receive a commission on drugs prescribed.

**Fears over the adverse consequences of restricted prescribing**

OM is not zero-risk: some AOM cases progress to complications such as mastoiditis and intracranial abscess. However, any recent increase in acute mastoiditis with restraints on prescription is uncertain from the low event rate and is too small to form a valid objection to guidelines [94]. The prevention of mastoiditis by routine antibiotic treatment of AOM has not been directly established [98]. Thompson and colleagues (2009) showed in a reference population of 2.6 million that, although antibiotics roughly halved the risk of mastoiditis, two-thirds of mastoiditis cases did not have a known antecedent OM [94]. Thus the estimated number-needed-to-treat to prevent one episode of mastoiditis, is unacceptably high [94] and routine antibiotic use may even mask mastoiditis. Physicians and public emphasize the avoidance of serious complications, so progress here requires not merely revisiting the wording of guidance, but support for an alternative action: training and dissemination to encourage prompt referral of suspected mastoiditis to specialists.



**Fig. 2** Vicious seven-stage spiral of antibiotic resistance in a core transmission group of preschoolers illustrated in the contrast between France and Germany. The boxes indicate forces which would exist without the spiral but which help to drive it

**Diagnosis of OM versus severity and persistence of disease**

General practitioners are broadly aware of the distinction between bacterial and viral infection [16]. In children’s ear problems, such awareness does not seem to restrain antibiotic prescription, perhaps because the known viral facilitation does not rule out bacterial origin or bacterial development (the prophylactic attitude to mastoiditis being one extreme). The uncertainties here make the etiological assumption, (hence antibiotic prescription) culturally arbitrary [25]. Until a low-cost non-invasive method to distinguish bacterial from viral etiology in OM becomes available, pragmatic guidelines cannot handle this issue satisfactorily.

Diagnosis of AOM by physicians is currently suboptimal, with both false-positive and false-negative errors [76]. But this is only the first step to treatment. Proportionate clinical response to the severity and persistence/recurrence of OM is

required. In epidemiological research this nuancing only arrived in 1997 for AOM [4] and 1993 for OME [91]. To cater simply for single-episode diagnosis and treatment, AOM guidelines have not adequately addressed the graduation issue [48] and the necessary evidence base for it has not been seriously sought. Proportionate response to severity and recurrence requires integrating information over time, hence either high linkage and accessibility of clinical data or long-term knowledge of the child and family, or both. In the present transitional era, neither can be assumed.

### Possible contributions to a solution

Given these obstacles, various policy elements must be considered for reducing resistance.

### Risk factor reduction

Guidelines from the American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP) have encouraged prevention of OM through reducing modifiable risk factors. Theoretically, there is some scope for reducing the size and influence of the core transmission group [26] via limited use of day care or small groups; breast feeding beyond 3 months protects against risk for early OM [5]. However, risk factor intervention in recurrent AOM meets limited parental willingness to change behavior [13, 65]. Given (a) the general difficulty in changing health-related behaviors by education, (b) the fact that some risk factors are already subject to public health advice, and (c) the modest relative risk values for single factors, risk modification is not generally promising.

### Training and role evolution for physicians

A large body of research on guideline implementation [8, 12, 37] identifies the most effective forms and channels of information when updating practice [12, 60]. But healthcare systems are not mechanistic sets of processes that can be enduringly optimized: over-use of particular media degrades their influence with time. For details within conventional medical paradigms (e.g., which specific antibiotics are appropriate for first- and second-line management in a particular setting), physician update education has seemed effective [77]. To support more radical change adequately, issues need to be grouped into packages important enough to command attention and a well-developed educational component then rolled out, as in France where one package improved guideline acceptance [45] and reduced antibiotic resistance.

De-medicalization (helping patients find alternative non-medical solutions) has not been a natural role for physicians. However, the era of the physician as part educator of the patient and especially as the moderator of other information sources (such as the internet) began 20 years ago in advanced countries. Evaluations are beginning to appear of ways within CME to train this educational role of physicians [54]. Major recent changes in the management of chronic conditions may offer principles and precedents for preparing of materials and procedures that “work”.

### Decision support

A new habit may be more readily adopted when supported by a facility that solves an acknowledged problem; here information technology offers possibilities. Evidence on reminders and prompts built into computerized decision support systems suggests at least short-term reductions in antimicrobial use and improved appropriateness of antimicrobial selection [60], but feedback on performance against target rates may be more important.

Incentives and related structural changes to manage care

Where healthcare is funded by co-payment systems, financial incentives to patients can be built in or removed. Despite some evidence of incentives changing clinical practice [22], revising payment structures takes resources, and creates complexities needing to be consolidated or removed later. Incentives to doctors may have unforeseen consequences (currently insufficiently researched) such as the erosion of professional motivation towards appropriate and cost-effective practice. Alternative responsibility structures such as pharmacist-led collaborative care, despite some evidence of effectiveness towards rational prescribing [60] may not be politically realistic.

### Public information campaigns

In Iceland [7] and USA [100] correlations have been shown between physicians' practices and knowledge or attitudes about OM. But what is cause and what is effect here? Various education campaigns (international, national, regional, and practice-level) including the recent “European Antibiotic Awareness Day” have improved public knowledge on antibiotic prescribing, but when used in isolation have not changed attitudes nor prescribing practice [52, 64, 73, 92]. The evidence for effectiveness of non-targeted campaigns is at best equivocal [60]. In contrast, assessment of attitudes informed directly by the physician shows improved compliance [8].

## Vaccination

Non-typeable *Haemophilus influenzae* (NTHi) and *Streptococcus pneumoniae* account for approximately 80% of OM cases worldwide [44], with NTHi becoming the new frontier as pneumococcal vaccination spreads [98]. These two pathogens are responsible for the more severe forms and sequelae of OM, so effective vaccination against them could materially reduce OM's clinical impact and wider burden [68, 75]. Where antibiotic consumption and other health costs for childhood OM are high, the cost-saving argument for vaccination explicitly against OM is already in place. Where antibiotic consumption is low, the vaccination scenario is more complex: cost-savings would need to be accumulated over several disease categories associated with the two main OM pathogens [44, 59] and the benefits, including indirect protection, may need to be measured and accumulated over the severities and prevalences of these same categories.

The conjugate heptavalent pneumococcal vaccine, PCV7 (7vCRM, *Prevnar*<sup>TM</sup>/*Prevenar*<sup>TM</sup>), was introduced primarily to prevent invasive pneumococcal disease (IPD: sepsis, meningitis, pneumonia, and bacteraemia) by universal vaccination of infants [79], and it appears in some countries to also benefit adults through herd protection. The large reduction in IPD was accompanied by a small reduction in all-cause OM, this via a moderate reduction in pneumococcal OM [10, 11, 51]. To be described as “for” OM, i.e., effective against most of the most severe OM, a vaccine would also require good coverage of pneumococcal serotypes and of NTHi. An innovative formulation (PhiD-CV, prototype of the recently licensed *Synflorix*<sup>TM</sup>) has shown significant efficacy against AOM from both NTHi and *S. pneumoniae* pathogens [21, 80]. Further trials are currently assessing its effectiveness more fully. PCV7 introduction led to a shift in the level of acceptable IPD risk in febrile children, with implications for reduced healthcare use [35]. Further such shifts in risk perception could help dismantle the vicious spiral, by giving confidence not to prescribe prophylactically against rare complications [47]. There is already preliminary evidence in OM that presence of a vaccination program confers such confidence: 3 years after introduction of PCV7 in France, antibiotic consumption, as well as carriage of both resistant and non-resistant strains were reduced in vaccinated children [20]. Prescribing is the chief selection pressure in the bacteriological changes post vaccination, so to further encourage rational prescribing at introduction of vaccines must slow the need for updating them [30]. To provide further evidence for policy decisions, opportunities should be seized for 2×2 studies, powered for a more-than-additive combination of introducing vaccination with new (or re-issued) guidelines. This could provide the desired direct evidence for the probable positive synergy

between vaccination and rational prescribing policies against antibiotic resistance.

## Conclusions

Adherence to guidelines for rational prescribing in AOM has been poor, so mere existence of guidelines has not reduced prescription rates sufficiently or enduringly. Policy initiatives have to directly attack the clinical rationales that permit continuing physician inertia. Immediately, the following three steps would help to break the vicious spiral of antibiotic resistance:

- Strengthening physician education, training, and continuing professional training towards prevention and explanation, integrated with clinical decision support and feedback; also encouraging continuity of care to manage irrational demand downwards, while providing assurance and monitoring risk
- Two specific training modules for generalist pediatricians and family practitioners promoting age-appropriate analgesia and the efficient early identification and management of symptomatic mastoiditis
- Vaccination against the most serious pathogens for OM, shifting the clinical emphasis away from prophylaxis against serious complications, and from low-effectiveness, especially in high-prescription countries of older first-line treatments. The shift in perceived risk following high-coverage vaccination against OM should help to break the vicious spiral, but opportunities should be seized to test this conjecture, and to document the *a priori* partnership whereby improved adherence to guidelines would decrease replacement pressures and so ease the vaccine development and updating cycle

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