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Acute otitis media guidelines in selected developed and developing countries: uniformity and diversity

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ABSTRACT

Background Acute otitis media (AOM) is a common childhood disease, with an enormous economic and healthcare-related burden. Guidelines and consensus papers for AOM diagnosis and management were published in many countries. Our objective was to study the differences and similarities between these protocols in developing and developed countries.

Methods The keywords: 'acute otitis media' AND 'children' AND ['treatment' or 'management'] AND ['guideline' or 'consensus'] were used in various electronic databases between 1 January 1989 through 31 December 2015. Overall, 99 sources from 62 countries were retrieved: 53 from 22 developed countries, and 46 from 40 developing countries. Representative guidelines from America (the USA, Argentina), Europe (Italy, Moldova), Africa (South Africa, Tanzania, Ethiopia), Asia (Japan, Afghanistan, Sri Lanka),and Oceania (South Australia, Fiji) were compared.

Results Paediatric societies publish guidelines in most developed countries; in developing countries, the Ministry of Health usually initiates guideline formulation. Most guidelines use the same diagnostic criteria and offer watchful waiting in mild–moderate scenarios. Amoxicillin is the suggested first-line antibiotic, whereas options for second-line and third-line therapies vary. Duration of therapy varies and is usually age dependent: 5–7 days for children <2 years and 10 days for children >2 years in developed countries, while duration and age groups vary greatly in developing countries. Reduction of AOM risk factors is encouraged in developed countries, but rarely in developing countries.

Conclusions Guidelines for AOM from developing and developed countries are similar in many aspects, with variation in specific recommendations, due to local epidemiology and healthcare accessibility. Formulation of regional guidelines may help reduce AOM burden.

What is already known on this topic?

- Acute otitis media (AOM) is a common childhood disease, which creates a major healthcare and economic burden.
- In developed and developing countries, national guidelines and consensus papers address AOM diagnostic and therapeutic issues in order to reduce overdiagnosis and overtreatment.
- There is a huge diversity of AOM diagnosis and management guidelines.

What this study adds?

AOM guidelines from developed and developing countries have more similarities than differences.

INTRODUCTION

Acute otitis media (AOM) is one of the most common childhood diseases, representing the most common indication for antibiotic prescription and outpatient visits in children in the USA and other countries.[1–5] AOM is a substantial cause of health services use (office visits, antibiotic costs), potential complications (ie, acute mastoiditis, meningitis) and indirect costs (ie, absence from school or work). Reduced susceptibility to antibiotics among bacteria commonly causing AOM is also a major concern.[6 7] In order to reduce the burden of AOM and limit antibiotic prescriptions, various professional guidelines and consensus statements have been published. These position papers were created in order to assist physicians to accurately diagnose AOM and offer treatment options, reduce risk factors and encourage vaccination.

The first AOM management guidelines were published in the Netherlands in 1989.[8] The guidelines were drafted following the studies of van Buchem *et al*,[9 10] who opposed the traditional approach of antibiotic therapy administration to *all* children presenting with AOM, and offered a 'watchful waiting' approach in selected scenarios. The Dutch guidelines were aimed at general practitioners, who treat the majority of children with AOM.

Many countries followed the innovative Dutch practice and published their own guidelines based on local epidemiology data and accessibility to healthcare facilities. A few guidelines were revised, following changes in the epidemiology, antibiotic susceptibility of pathogens and implementation of preventive interventions, such as vaccines. These guidelines and consensus statements differ in various aspects, such as the methodology of AOM diagnosis, age range included; times when antibiotic therapy can be withheld; the types of antibiotic therapy, dosage and duration; and the option for additional therapy (table 1). When comparing the content of some guidelines with others, there are even some conflicting statements. To date, there are no papers that reviewed this topic.

Due to the increasing number of AOM guidelines in different countries, we studied the unifying and diverging points of guidelines from selected developing and developed countries in order to detect common elements, as well as differences.

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MATERIALS AND METHODS

We searched for the following keywords: 'acute otitis media' AND 'children' AND ['treatment' or 'management'] AND ['guideline' or 'consensus'] in various electronic databases: MEDLINE (via PubMed), Ovid Medline, Google Scholar and Clinical Evidence (BMJ Publishing). These databases were searched from 1 January 1989 through 31 December 2015 (see online supplementary table S1). Publications that described the diagnosis/treatment of other forms of otitis media (ie, otitis media with effusion), AOM in adults and papers focusing on AOM-related complications (ie, acute mastoiditis) were excluded.

The initial search yielded 99 national guidelines, consensus papers and position documents from 62 countries, in addition to 3 official position papers published by the WHO,[2] the Agency for Healthcare Research and Quality, from the US Department of Health and Human Services (Rockville, Maryland, USA)[1] (figure 1 and online supplementary table S2). We categorised countries as either 'developed' or 'developing' according to the definitions of the 2014 United Nations Statistical Annex (accessed 30 June 2016: http://www.un.org/en/development/desa/policy/wesp/wesp_current/2014wesp_country_classification.pdf). According to this classification, 53 guidelines were from 22 developed countries, and 46 from 40 developing countries. Some AOM guidelines were incorporated within upper respiratory tract infections guidelines.

Table 1 Differences in acute otitis media (AOM) guidelines worldwide

Variable	Options
Methodology of AOM diagnosis	Wide or limited description
Age of patients	Infants and young children, or also including teenagers
'Watchful waiting' option	Restricted for various clinical scenarios in different ages, not always clear
Antibiotic treatment	Different antibiotic families, doses and duration of therapy
Myringotomy	Early in the disease course or not all
Complementary and alternative medicine	Optional in some, discouraged or ignored by others

Since it was impossible to compare all the retrieved guidelines, we initially sought to compare guidelines from one developed country and one developing country from each continent. However, due to the large variability between guidelines in developing countries we decided to include more guidelines from developing countries. Ultimately, 12 representative guidelines from 7 developing and 5 developed countries were compared. Our eligibility criteria for guideline selection were if guidelines (1) were published or revised within the last 5 years; in order to assess the impact of the introduction of different vaccines; (2) were in English or could be found on the web and easily translated; (3) were issued by a local expert society(ies) or association(s) or by the local Ministry of Health; (4) had a title, abstract and content that were detailed and consistent with similar clinical guidelines; and (5) if we had full access to the text and references.

Developed countries

Two reviewers independently chose to compare AOM guidelines from Italy (*Europe*),[11] the USA (*Americas*),[12] Japan (*Asia*),[13 14] South Australia (*Oceania*),[15] and South Africa (*Africa*).[16] We were forced to make these exceptions: (1) for *Oceania*, guidelines from the state of South Australia were chosen, which were the most appropriate detailed publication from this region, but cannot be considered as a national guideline; (2) for *Europe*, several countries met the inclusion criteria, such as Italy, the UK, Spain and the Netherlands. We decided to analyse the Italian guidelines, which were the most comprehensive; and (3) for *Africa*, South Africa was selected as a developed country, although categorised as being only partly developed due to the lack of other developed countries in this continent.

Developing countries

The same reviewers chose Tanzania (Africa),[17] Ethiopia (Africa),[18] Moldova (Europe),[19] Argentina (America),[20] Fiji (Oceania),[21] Afghanistan (Asia)[22] and Sri Lanka (Asia).[23]

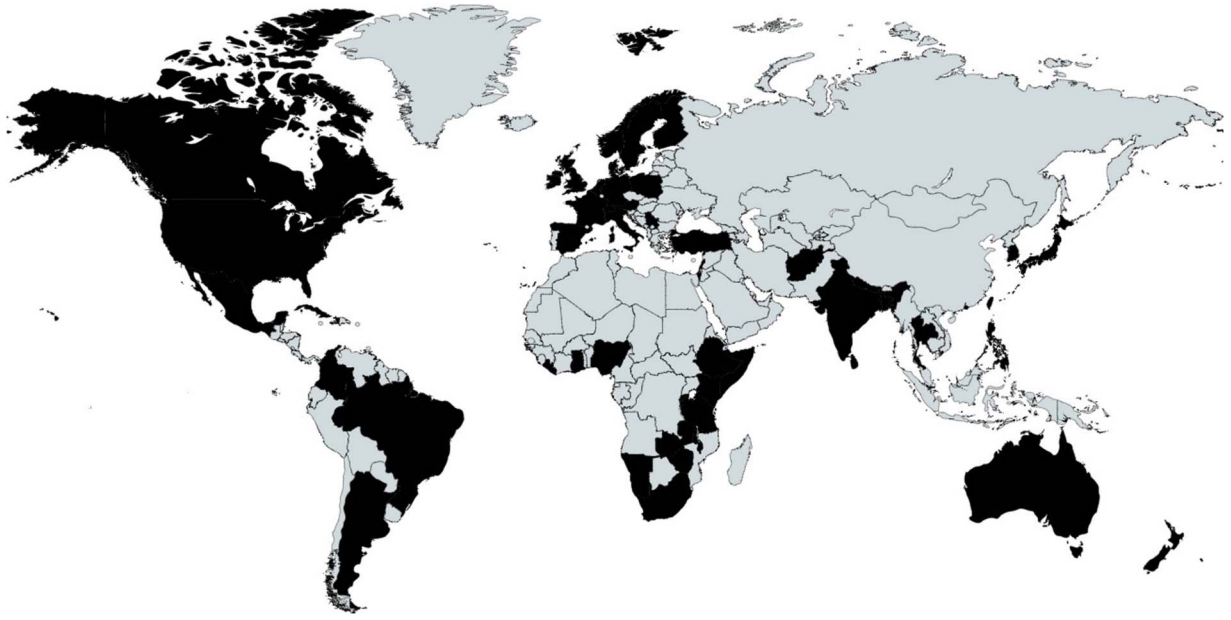

Figure 1 Countries with consensus papers and/or national guidelines for acute otitis media diagnosis and treatment (blackened).

We were forced to make these exceptions: (1) for *Oceania*, Fiji was chosen because its guidelines were the most recent and comprehensive ones from that region; (2) for *Europe*, Moldova (written in the local native language) was chosen as a representative since there are almost no developing countries in Europe; and (3) For *America*, Argentina was chosen as a representative developing country, although published in Spanish.

For selected guidelines, we compared their characteristics, criteria for AOM diagnosis, treatment options and recommended preventive measures, if there were any. We believe that selected guidelines represent not only the geographical region in terms of the local demographics and access to healthcare facilities but also regarding AOM epidemiology and disease burden.

RESULTS

Founders of guidelines

Bibliographic details of the selected AOM guidelines are presented in tables 2 and 3. Most guidelines were drafted by professional paediatric societies since paediatricians are the primary healthcare providers for children with AOM. For developed countries, Japan is an exception: since otolaryngologists are the primary healthcare providers for children with AOM, they drafted the local guidelines. In contrast, the Ministry of Health was usually the author of guidelines in developing countries, except in Argentina, where the professional Paediatric Society and the Society of Infectious Diseases issued the local guidelines.

Table 2 Guidelines for acute otitis media (AOM) management from five developed countries

Country	USA	ITA	JPN*	ZAF	AUS†
Author	American Academy of Pediatrics, American Academy of Family Physicians	Italian AOM Guideline Multidisciplinary Working Group: Italian Society of Pediatrics, Italian Society of Pediatric Otolaryngology, Italian Preventative Pediatrics Society	Subcommittee of Clinical Practice Guideline for Diagnosis and Management of AOM in Children: Japan Otological Society, Japan, Society for Pediatric Otorhinolaryngology, Japan Society for Infectious Diseases in Otolaryngology	Infectious Diseases Society of Southern Africa, Southern African Society for Pediatric Infectious Diseases, Federation of Infectious Diseases Societies of Southern Africa, National Institute of Communicable Diseases and Medical Research Council, Ampath National Laboratory Services	South Australia Child Health Clinical Network, South Australian Paediatric Clinical Guidelines Reference Committee
Target audience	Primary care clinicians (paediatricians, family physicians), emergency department physicians, otolaryngologists, physician assistants, nurse practitioners	Paediatricians, otolaryngologists	Otolaryngologists	Health providers across South Africa	All clinical, medical, nursing, allied health, emergency, dental, mental health, pathology in the public health sector
Year	2013	2010	2012 (update, 2013)	2015	2014
Age range population	6 months to 12 years	2 months to 12 years	<15 years	Birth–adolescence	Birth–adolescence
Age subgroups	6–23 months; >24 months	<6 months; 6–24 months; >24 months	None	<2 years; ≥2 years	<6 months; 6–24 months; >24 months

*Guidelines were published in 2012; updated in 2013.
†The treatment of AOM in Aboriginal and Torres Strait Islander Populations is addressed elsewhere.
AUS, Australia; ITA, Italy; JPN, Japan; ZAF, South Africa.

Table 3 Guidelines for acute otitis media management from seven developing countries

Country	AFG	LKA	TZA	ETH	FJI	ARG	MDA
Author	Ministry of Public Health*	Ministry of Health*	Ministry of Health and Social Welfare*	Food, Medicine and Healthcare Administration and Control Authority of Ethiopia*	National Drugs and Therapeutics Subcommittee*	Argentinian Societies of Infectious Diseases, Pediatrics, Medicine, Bacteriology, Mycology and Clinical Parasitology	Ministry of Health
Target audience	All primary-level health workers	All primary-level health workers	All primary-level health workers	Primary healthcare workers	Primary healthcare workers	–	Family doctors, nurses, paediatricians, otolaryngologists
Year	2013	2014	2013	2014	2011	2012	2011†
Age range population	All age groups	All age groups	All age groups	All age groups	All age groups	All age groups	All age groups
Age subgroups	<5 years; >5 years	<6 months; 6–24 months; >24 months	<5 years; >5 years	–	<2 months; 2–12 months; 1–5 years	<2 years; >2 years	<3 years; >3 years

*Supported/aided by an external health agency, such as the WHO.
†Guidelines were published in 2011; updated in 2013.
AFG, Afghanistan; ARG, Argentina; ETH, Ethiopia; FJI, Fiji; LKA, Sri Lanka; MDA, Moldova; TZA, Tanzania.

Age

Not all age groups are covered, even in detailed guidelines (eg, the USA). Very young infants are excluded in 2/5 of the selected guidelines from developed countries (<2 months, Italy; <6 months, the USA). These exclusions do not exist in guidelines from developing countries. In developed countries, the upper age limit was either early adolescence (12 years for the USA and Italy, 15 years in Japan) or undefined in 2/5, while in developing countries the upper age limit was not mentioned. In 4/5 selected developed countries guidelines, there were age subgroups: younger children (<2 years) and older children (>2 years), which emphasises the higher incidence of AOM in younger children. Age categorisation was more detailed in 2/5 guidelines from developing countries (<2 or <6 months, 2–12 months or 6–24 months and >1 or >2 years). Other guidelines from developing countries used other age limits (<5 years or older (Afghanistan, Tanzania), <3 years or older (Moldova), <2 years or older (Argentina)).

Diagnosis

All guidelines from developed countries highlighted the need for accurate AOM diagnosis and encouraged the removal of blocking cerumen (tables 4 and 5). However, removing earwax is not discussed in guidelines from developing countries. In previous guidelines, indirect means for AOM diagnosis were accepted (ie, tympanometry). Current guidelines from developed countries recommend that diagnosis should be based on three major criteria: (1) constitutional signs and symptoms (fever, ear tugging, otalgia), (2) tympanic membrane (TM) bulging and (3) presence of middle ear effusion. The Japanese guidelines broadly detailed the TM examination, preferably by using oto-microscopy or oto-endoscopy, and allow the diminished light reflex and/or TM bullar formation to serve as supplemental criteria for diagnosis. In developing countries, these criteria are listed in most guidelines. The use of pneumatic otoscopy is discussed and allowed in 3/7 guidelines (Sri Lanka, Argentina and Moldova).

Table 4 Diagnostic criteria in guidelines for acute otitis media (AOM) management from five developed countries

Country	USA*	ITA	JPN†	ZAF	AUS
TM characteristics (contour, colour, translucency)	+	+	+	+	+
Otorrhoea	+	+	+	–	–
Fever	+	+	+	+	+
Otalgia	+	+	+	+	+
Use of pneumatic otoscopy (mobility)‡§	+	+	+	+	–
Use of tympanometry	–	+¶	+	+	–
Hearing loss, dizziness	–	–	–	+	–

*Distinction between severe and non-severe AOM.
†AOM severity is classified as mild/moderate/severe, according to age, fever, crying, TM hyperaemia or protrusion and otorrhoea.
‡Mobility: normal/increased/decreased/absent.
§After removal of cerumen, if present.
¶Limited to uncertain cases.
AUS, Australia; ITA, Italy; JPN, Japan; TM, tympanic membrane; ZAF, South Africa.

Table 5 Diagnostic criteria in guidelines for acute otitis media management from seven developing countries

Country	AFG	LKA	TZA	ETH	FJI	ARG	MDA
Tympanic membrane characteristics (contour, colour, translucency)	+	+	+	+	+	+	+
Otorrhoea	+/–	+	+/–	+/–	+	+/–	+
Fever	+	+	+	+	–	+	+
Otalgia	+	+	+	+	–	+	+
Use of pneumatic otoscopy (mobility)	–	+	–	–	–	+	+*
Use of tympanometry	–	–	–	–	–	–	+*
Hearing loss, dizziness	–	–	+	–	–	–	+*

*Use of pneumatic otoscopy/tympanometry and concern for hearing loss in the 2011 guidelines only.
AFG, Afghanistan; ARG, Argentina; ETH, Ethiopia; FJI, Fiji; LKA, Sri Lanka; MDA, Moldova; TZA, Tanzania.

Treatment

Watchful waiting in mild–moderate AOM scenarios is now the standard of care in all guidelines from developed countries (tables 6 and 7), where follow-up is possible. In comparison, watchful waiting is an option in 3/7 guidelines from developing countries (Sri Lanka, Argentina and Moldova). Amoxicillin is universally accepted as the first-line antibiotic therapy, both in developing and developed countries, but in different doses (30–100 mg/kg/day), usually given three times a day. There is a wide variety of suggested second-line and third-line antibiotic therapies, as well as for the recommended duration and dosage. Unlike earlier guidelines, newer guidelines encourage the use of systemic (but not topical) analgesia. Myringotomy is reserved for more advanced, complicated cases, which are unresponsive to antibiotic therapies (the USA, Japan, South Africa). Other treatments, such as steroids, antihistamines, nasal steroid sprays or local/systemic decongestants, are either discouraged or ignored in all guidelines from developed countries, but are mentioned in guidelines from two developing countries (Moldova and Sri Lanka). Of note, the Japanese guidelines are the only ones that mention the use of local/systemic decongestants in children with AOM, and complementary and alternative medicine in the form of probiotic products containing *Lactobacillus bifidus* or *Clostridium butyricum* is recommended as a concomitant treatment. Ventilation tube insertion is discussed in 4/5 guidelines from developed countries and is proposed for children with recurrent AOM.

Prevention

Some, but not all, guidelines from developed countries mention important means for prevention by reduction of AOM risk factors (ie, limiting exposure to cigarette smoke or encouraging breast feeding), and call for childhood immunisation with pneumococcal conjugate vaccines (PCVs) and yearly influenza vaccinations (tables 8 and 9). Of note, prevention methods for AOM are mentioned only in one guideline from developing countries (Afghanistan; reducing exposure to cigarette smoke).

DISCUSSION

Our study of selected guidelines revealed that AOM diagnosis and management guidelines from industrialised, developed countries and developing countries share many common principles. Minor differences exist due to differences in local epidemiology, healthcare policy, accessibility to health facilities and health expenditure. The use of antibiotics in the treatment of AOM remains controversial. The 'watchful waiting' option is popular in developed countries, but less in developing countries, where follow-up is sometimes not possible. The major differences

Table 6 Treatment options in guidelines for acute otitis media management from five developed countries

Country	USA	ITA	JPN	ZAF	AUS
Watchful waiting*	+	+	+	+	+
ABx therapy—first-line	AMOX (80–90 mg/kg, twice a day); AMOX-CLAV (90 mg/kg, twice a day)	*Mild*: AMOX (50 mg/kg twice a day /three times a day) *Severe*: AMOX-CLAV (80–90 mg/kg/day, twice a day, three times a day	*Mild*: AMOX *Moderate*: AMOX *Severe*: AMOX (maximal dose of 1500 mg)	AMOX (80–90 mg/kg, twice a day); AMOX-CLAV (90 mg/kg twice a day)	AMOX (15 mg/kg three times a day) or 30 mg/kg twice a day)
ABx therapy—second-line		*Mild*: Cefaclor (40–50 mg/kg twice a day) *Severe*: Cefpodoxime (8 mg/kg twice a day); CEFR (30 mg/kg twice a day)	*Moderate*: high-dose AMOX, AMOX-CLAV, cefditoren pivoxil *Severe*: myringotomy+ AMOX-CLAV/cefditoren pivoxil (maximal dose of 600 mg)	AMOX-CLAV (90 mg/kg twice a day); CEFT (50 mg/kg/day), CEFR (30 mg/kg twice a day), cepodoxime (16 mg/kg twice a day)	AMOX-CLAV (25 mg/kg three times a day), CEFR (10–15 mg/kg/dose, depending on age)
ABx therapy—third-line	Cefdinir (14 mg/kg/day, 1–2 doses); CEFR (30 mg/kg twice a day) Cefpodoxime (10 mg/kg twice a day) OR CEFT (50 mg/kg)	N/A	*Moderate*: high-dose cefditoren pivoxil, tebipenem pivoxil (maximal dose of 600 mg/day), tosfloxacin (maximal dose 360 mg/d) *Severe*: myringotomy+ tebipenem pivoxil/tosfloxacin, intravenous ampicillin or CEFT	CEFT (50 mg/kg/day); clindamycin (90–150 mg/kg three times a day), with or without a second- or third-generation cephalosporin	Admit to paediatric service for intravenous treatment (eg, CEFT)
Duration (days)	10 in children <2 years; 7 in children 2–5 years; 5 in children >6 years; intramuscular/intravenous once daily CEFT, 3	10; in children >2 years, 5 are sufficient	*Mild* :5 *Moderate* and *severe*: reassess after 3, when needed, complete 7	<2 years, 7; >2 years, 5; intramuscular/intravenous once daily CEFT, 3; clindamycin, 5–7	5
Myringotomy	+†	–	+	+	–
Systemic analgesics	+	+ (Paracetamol, ibuprofen)	+ (Acetaminophen 10 mg/kg)	+ (Paracetamol 10–15 mg/kg, 4–6-hourly, or ibuprofen 5–10 mg/kg 8-hourly)	+ (Paracetamol 15 mg/kg/dose or ibuprofen 10 mg/kg/dose)
Local analgesics	+	+ (>3 years)	–	–	+ (in cases where systemic analgesia is unsuccessful)
Local/systemic decongestants	–	–	+	–	–
Steroids	–	–	–	–	–
Antihistamines	–	–		–	–
CAM	–	–	+ (Consider use of *Lactobacillus bifidus* or Miyarisan when administering antibiotics)	–	–

*Watchful waiting is usually optional for 2–3 days.
†Myringotomy is considered in children who failed initial antibiotic therapy (48–72 hours).
ABx, antibiotic therapy; AMOX, amoxicillin; AMOX-CLAV, amoxicillin-clavulanate; AUS, Australia; CAM, complementary and alternative medicine; CEFR, cefuroxime axetil; CEFT, ceftriaxone; ITA, Italy; JPN, Japan; ZAF, South Africa.

between developing and developed countries are the suggestions for prevention, mostly in guidelines from developed countries.

Recommending amoxicillin as the first-line therapy has been found to positively affect the resistance patterns of *Streptococcus pneumoniae* isolated from middle ear fluid or AOM-associated otorrhoea in French and Israeli PCV immunised children.[24 25] Disagreement on the dosage and duration of antibiotic therapy were noted in the studied guidelines. In addition, there is disagreement concerning the second-line and third-line antibiotic treatments. This could be because local epidemiology and healthcare costs largely contribute to these decisions. In addition, local data on antibiotic resistance patterns among causative bacteria of AOM may mean national guidelines to suggest certain antibiotic therapies over others. One common antibiotic found in second-line and third-line treatments is ceftriaxone (in 5/12 guidelines). This third-generation cephalosporin has an excellent activity against Gram-positive bacteria, the major causative agents of AOM.

In our opinion, healthcare authorities in developing countries could also focus on AOM prevention in their guidelines. The relative high costs of PCVs and influenza vaccinations may make these preventive measures unaffordable in some developing countries.

In most guidelines from developing countries, there is a statement about when to transfer a child to hospital. This indicates that many physicians work in remote areas, where access to advanced healthcare facilities is limited. Guidelines from developing countries do not address the option of surgical therapy

Table 7 Treatment options in guidelines for acute otitis media (AOM) management from seven developing countries

Country	AFG*	LKA†	TZA	ETH	FJI	ARG	MDA
Watchful waiting	–	+	–	–	–	+‡	+§
ABx therapy—first-line	TMP/SMX or AMOX	AMOX, 30 mg/kg, three times a day	Penicillin V or AMOX, 40 mg/kg, three times a day	AMOX: >6 years—250 mg three times a day; <6 years—125 mg three times a day, ampicillin, 50–100 mg/kg twice a day or 100–200 mg/kg twice a day	AMOX or TMP/SMX, twice a day	AMOX, 80–100 mg/kg, twice a day	AMOX 80–100 mg/kg three times a day, or ampicillin, 80–100 mg/kg, four times a day, or AMOX-CLAV, 50–100 mg/kg, twice a day /three times a day, or CEPH, 25–50 mg/kg, three times a day /four times a day, or CEFT, 70–100 mg mg/kg, twice a day
ABx therapy—second-line	–	CLOX, or CEPH	–	AMOX-CLAV	–	AMOX-CLAV, CEFT	–
ABx therapy—third-line	–	AMOX-CLAV, CEFR, CEFT	–	–	–	–	–
Duration (days)	5–7	5–7	7	10	5	5–10	7–10
Myringotomy	–	–	+/–	+/–	–	+/–	–
Systemic analgesics	+	+	+	+	–	+	+
Local analgesics	–	–	–	–	–	–	+
Local/systemic decongestants	–	–	+	–	–	–	+
Steroids	–	–	–	–	–	–	–
Antihistamines	–	–	–	–	–	–	+
CAM	–		–	–	–	–	–
Other	Ear cleaning if otorrhoea present	–	–	–	–	–	–

*Guideline distinguishes between children <5 or >5 years for length of treatment: 5 and 7 days, respectively.
†Treatment is correlated to patient's age (<6 or >6 years) and severity of disease.
‡Watchful waiting for 72 hours is possible in a child >2 years, with mild unilateral AOM and without comorbidities.
§Watchful waiting for 72–96 hours is possible; however, antibiotic treatment is indicated when there is no effect anti-inflammatory for 3 days, AOM during the last month or antibiotic therapy during the last month, child age >1 year or recurrent AOM episodes.
ABx, antibiotic; AFG, Afghanistan; AMOX-CLAV, amoxicillin-clavulanate; ARG, Argentina; CAM, complementary and alternative medicine; CEFR, cefuroxime axetil; CEFT, ceftriaxone; CEPH, cephalexin; CLOX, cloxaciliin; ETH, Ethiopia; FJI, Fiji; LKA, Sri Lanka; MDA, Moldova;TMP/SMX, trimethoprim/sulfamethoxazole; TZA, Tanzania.

Table 8 Preventive strategies in guidelines for acute otitis media (AOM) management from five developed countries

Country	USA	ITA	JPN	ZAF	AUS
Pneumococcal conjugate vaccine immunisation	+	+	+	+	–
Influenza immunisation	+	+	–	–	–
Handwashing	–	+	–	–	–
Reduction in exposure to smoking	+	+		–	–
Day care attendance	+	–	+	–	–
Pacifier usage limit*	+	+	+	–	–
Breast feeding	+ (6 months)	–	+	–	–
Ventilating tube insertion	+†	–	+	+	+
Chemoprophylaxis‡	–	–	–	–	–
Adenoidectomy	–	–	–	–	–

*Its elimination in the second 6 months of life may reduce AOM burden.
†Offered for recurrent AOM (≥3 episodes/6 months or ≥4 episodes/1 year).
‡Long-term, low-dose antibiotics to prevent recurrent episodes.
AUS, Australia; ITA, Italy; JPN, Japan; ZAF, South Africa.

for recurrent AOM cases, which require specialised facilities and trained physicians, of which some or all may not be found in developing countries.

To our knowledge, there are no AOM guidelines in large developing countries like China or Russia, and even the Indian guidelines are not accepted nationwide. Studies from developing countries provide some disturbing data on extensive unjustified use of antibiotics for AOM, high antibiotic resistance of *S pneumoniae* isolated from AOM cases, including multidrug resistance phenotypes, and high complication rate.[26–29] In Russian children with pneumococcal AOM, 45% of the pneumococci were penicillin-non-susceptible and 30% had multidrug resistance phenotype.[26] Another Russian study found that the rate of unjustified outpatient antibiotic prescriptions in children with respiratory infections was estimated at 40%.[27] In PCV-unimmunised Chinese children with pneumococcal AOM, a significant proportion of clones were also resistant to antibiotics.[28] In India, otolaryngologists reported that they treated 98% of AOM episodes with antibiotics, and amoxicillin/clavulanic acid was the first-line therapy.[29] We acknowledge limitations in our study: (1) we focused on only 12 guidelines. However, our main findings are similar to guidelines we did not review in detail (data not shown); and (2) there are known differences in the paediatric outpatient antibiotic prescribing rate internationally. For example, in European countries, Holstiege *et al*[30] looked at the prescription rates between 2005 and 2008, and found significant differences, with Italy (chosen in this study to represent Europe) having the highest rate, while the Netherlands (which pioneered the guidelines) having the lowest.

Due to the global nature of AOM, if developing countries with large populations do not implement strategies to reduce AOM and limit antibiotic uses, we expect to see an increase in bacterial resistance, which may spread worldwide. In contrast, countries that implemented AOM guidelines have already

Table 9 Preventive strategies in guidelines for acute otitis media management from seven developing countries

Country	AFG	LKA	TZA	ETH	FJI	ARG	MDA
Pneumococcal conjugate vaccine	–	–	–	–	–	–	–
Influenza immunisation	–	–	–	–	–	–	–
Handwashing	–	–	–	–	–	–	–
Reduction in exposure to smoking	+	–	–	–	–	–	+
Day care attendance	–	–	–	–	–	–	–
Pacifier usage limit	–	–	–	–	–	–	–
Breast feeding	–	–	–	–	–	–	–
Ventilating tube insertion	–	–	–	–	–	–	
Chemoprophylaxis	–	–	–	–	–	–	–
Adenoidectomy	–	–	–	–	–	–	–
Others	Proper treatment of pharyngitis or upper respiratory tract infection, minimise risk factors, keep ear dry	–	–	–	–	–	Alcohol avoidance of the parents, limit consumption of allergic product, adequate treatment of nasopharyngeal pathology

AFG, Afghanistan; ARG, Argentina; ETH, Ethiopia; FJI, Fiji; LKA, Sri Lanka; MDA, Moldova TZA, Tanzania.

reported reduced rates of appropriate antibiotic prescription for AOM and low resistance rates in isolated pathogens.[24 25 31]

CONCLUSIONS

The analysed AOM guidelines from developing and developed countries revealed many unifying notions but some diversity. Ideally, it could be suggested that the similar parts of the guidelines could serve as the basis for future international cooperation in the formulation of 'global' guidelines, which need to be in line with the local epidemiology. The use of stringent criteria in AOM diagnosis, restraint in antibiotic use, adoption of the 'watchful waiting' approach as the primary option for most uncomplicated cases and the integration of preventative methods (including environmental changes and childhood vaccination) is recommended in these future guidelines.

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REFERENCES

1 Zhou F, Shefer A, Kong Y, *et al*. Trends in acute otitis media-related health care utilization by privately insured young children in the United States, 1997–2004. *Pediatrics* 2008;121:253–60.
2 Marom T, Tan A, Wilkinson GS, *et al*. Trends in otitis media-related health care use in the United States, 2001–2011. *JAMA Pediatr* 2014;168:68–75.
3 Grossman Z, Silverman BG, Porter B, *et al*. Implementing the delayed antibiotic therapy approach significantly reduced antibiotics consumption in Israeli children with first documented Acute otitis media. *Pediatr Infect Dis J* 2010;29:595–9.
4 Marchisio P, Cantarutti L, Sturkenboom M, *et al*. Burden of acute otitis media in primary care pediatrics in Italy: a secondary data analysis from the Pedianet database. *BMC Pediatr* 2012;12:185.
5 Monasta L, Ronfani L, Marchetti F, *et al*. Burden of disease caused by otitis media: systematic review and global estimates. *PLoS ONE* 2012;7:e36226.
6 Angoulvant F, Cohen R, Doit C, *et al*. Trends in antibiotic resistance of *Streptococcus pneumoniae* and *Haemophilus influenzae* isolated from nasopharyngeal flora in children with acute otitis media in France before and after 13 valent pneumococcal conjugate vaccine introduction. *BMC Infect Dis* 2015;15:236.
7 Pumarola F, Marès J, Losada I, *et al*. Microbiology of bacteria causing recurrent acute otitis media (AOM) and AOM treatment failure in young children in Spain: shifting pathogens in the post-pneumococcal conjugate vaccination era. *Int J Pediatr Otorhinolaryngol* 2013;77:1231–6.
8 van Buchem FL. [The treatment of acute otitis media]. *Ned Tijdschr Geneeskd* 1989;133:290–2.
9 van Buchem FL, Dunk JH, van't Hof MA. Therapy of acute otitis media: myringotomy, antibiotics, or neither? A double-blind study in children. *Lancet* 1981;2:883–7.
10 van Buchem FL, Peeters MF, van 't Hof MA. Acute otitis media: a new treatment strategy. *Br Med J (Clin Res Ed)* 1985;290:1033–7.
11 Marchisio P, Bellussi L, Di Mauro G, *et al*. Acute otitis media: From diagnosis to prevention. Summary of the Italian guideline. *Int J Pediatr Otorhinolaryngol* 2010;74:1209–16.
12 Lieberthal AS, Carroll AE, Chonmaitree T, *et al*. The diagnosis and management of acute otitis media. *Pediatrics* 2013;131:e964–99.
13 Subcommittee of Clinical Practice Guideline for Diagnosis and Management of Acute Otitis Media in Children (Japan Otological Society, Japan Society for Pediatric Otorhinolaryngology, Japan Society for Infectious Diseases in Otolaryngology). Clinical practice guidelines for the diagnosis and management of acute otitis media (AOM) in children in Japan. *Auris Nasus Larynx* 2012;39:1–8.
14 Kitamura K, Iino Y, Kamide Y, *et al*. Clinical practice guidelines for the diagnosis and management of acute otitis media (AOM) in children in Japan—2013 update. *Auris Nasus Larynx* 2015;42:99–106.
15 Network SCHC. *South Australian Paediatric Practice Guidelines—Acute Otitis Media in Children*. SA Child Health Clinical Network, 2014.
16 Brink AJ, Cotton M, Feldman C, *et al*. Updated recommendations for the management of upper respiratory tract infections in South Africa. *S Afr Med J* 2015;105:344–52.
17 Ministry of Health and Social Welfare. *Standard treatment guidelines and essential medicines list*. 4th edn. The United Republic of Tanzania, 2013. http://www.who.int/selection_medicines/country_lists/Tanzania_STG_052013.pdf
18 Food, Medicine and Healthcare Administration and Control Authority of Ethiopia. *Standard treatment guidelines for primary hospital*. 3rd edn. Ethiopia, 2014:466–8. http://apps.who.int/medicinedocs/documents/s21693en/s21693en.pdf
19 Health Ministry. *Otita Medie Acută La Copii. Protocol Clinic National*. Moldova, 2011. http://old.ms.gov.md/_files/10999-Protocol%2520clinic%2520na%25C5%25A3ional%2520%25E2%2580%259EOtita%2520medie%2520acut%25C4%2583%2520la%2520copil%25E2%2580%259D%252C%2520actualizat%25202011.pdf21
20 Lopardo G, Calmaggi A, Clara L, *et al*. [Consensus guidelines for the management of upper respiratory tract infections]. *Medicina (B Aires)* 2012;72:484–94.
21 Ministry of Health, Government of Fiji. National Drugs and Therapeutics Subcommittee. *Antibiotic Guidelines*. editor, 3rd edn, Fiji, 2011:18, 61. http://www.health.gov.fj/wp-content/uploads/2015/04/Antibiotic-Guidelines-3rd-edition-2011.pdf
22 Ministry of Public Health. *National Standard Treatment Guidelines for the Primary Level*. Afghanistan, 2013:87–90. http://apps.who.int/medicinedocs/documents/s21744en/s21744en.pdf
23 Ministry of Health. *Management of Respiratory Tract Infections in Children*. Sri Lanka, 2014:90–4. http://www.gampcs.org/wp-content/uploads/2014/10/Management-of-respiratory-tract-infections-in-children.pdf

24 Kempf M, Varon E, Lepoutre A, *et al*. Decline in antibiotic resistance and changes in the serotype distribution of *Streptococcus pneumoniae* isolates from children with acute otitis media; a 2001–2011 survey by the French Pneumococcal Network. *Clin Microbiol Infect* 2015;21:35–42.

25 Marom T, Avraham E, Cinamon U, *et al*. The effect of immunization with pneumococcal conjugated vaccines on *Streptococcus pneumoniae* resistance patterns in acute otitis media. *J Microbiol Immunol Infect* 2015.

26 Mayanskiy N, Alyabieva N, Ponomarenko O, *et al*. Bacterial etiology of acute otitis media and characterization of pneumococcal serotypes and genotypes among children in Moscow, Russia. *Pediatr Infect Dis J* 2015;34:255–60.

27 Rachina S, Kozlov R, Jarkova L, *et al*. PATRIOT Study Group. Prescribing of systemic antimicrobials for respiratory infections in children in primary care in Russia [Abstract P0370]. In: 24th ECCMID, Barcelona, Spain, 2014.

28 Ding Y, Geng Q, Tao Y, *et al*. Etiology and epidemiology of children with acute otitis media and spontaneous otorrhea in Suzhou, China. *Pediatr Infect Dis J* 2015;34:e102–6.

29 D'silva L, Parikh R, Nanivadekar A, *et al*. A Questionnaire-Based Survey of Indian ENT Surgeons to Estimate Clinic Prevalence of Acute Otitis Media, Diagnostic Practices, and Management Strategies. *Indian J Otolaryngol Head Neck Surg* 2013;65(Suppl 3):575–81.

30 Holstiege J, Schink T, Molokhia M, *et al*. Systemic antibiotic prescribing to paediatric outpatients in 5 European countries: a population-based cohort study. *BMC Pediatr* 2014;14:174.

31 Palma S, Rosafio C, Del Giovane C, *et al*. The impact of the Italian guidelines on antibiotic prescription practices for acute otitis media in a paediatric emergency setting. *Ital J Pediatr* 2015;41:37.

Acute otitis media guidelines in selected developed and developing countries: uniformity and diversity

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