AMERICAN ACADEMY OF PEDIATRICS
AMERICAN ACADEMY OF FAMILY PHYSICIANS

Subcommittee on Management of Acute Otitis Media

CLINICAL PRACTICE GUIDELINE

Diagnosis and Management of Acute Otitis Media

ABSTRACT. This evidence-based clinical practice guideline provides recommendations to primary care clinicians for the management of children from 2 months through 12 years of age with uncomplicated acute otitis media (AOM).

The American Academy of Pediatrics and American Academy of Family Physicians convened a committee composed of primary care physicians and experts in the fields of otolaryngology, epidemiology, and infectious disease. The subcommittee partnered with the Agency for Healthcare Research and Quality and the Southern California Evidence-Based Practice Center to develop a comprehensive review of the evidence-based literature related to AOM. The resulting evidence report and other sources of data were used to formulate the practice guideline recommendations. The focus of this practice guideline is the appropriate diagnosis and initial treatment of a child presenting with AOM.

The guideline provides a specific definition of AOM. It addresses pain management, initial observation versus antibacterial treatment, appropriate choices of antibacterials, and preventive measures. Decisions were made based on a systematic grading of the quality of evidence and strength of recommendations, as well as expert consensus when definitive data were not available. The practice guideline underwent comprehensive peer review prior to formal approval by the partnering organizations.

This clinical practice guideline is not intended as a sole source of guidance in the management of children with AOM. Rather, it is intended to assist primary care clinicians by providing a framework for clinical decision making. It is not intended to replace clinical judgment or establish a protocol for all children with this condition. These recommendations may not provide the only appropriate approach to the management of this problem.

ABBREVIATIONS. AOM, acute otitis media; AAP, American Academy of Pediatrics; AAFP, American Academy of Family Physicians; AHRQ, Agency for Healthcare Research and Quality; EPC, Southern California Evidence-Based Practice Center; MEE, middle-ear effusion; OME, otitis media with effusion; CAM, complementary and alternative medicine.

INTRODUCTION

Acute otitis media (AOM) is the most common infection for which antibacterial agents are prescribed for children in the United States. As such, the diagnosis and management of AOM has a significant impact on the health of children, cost of providing care, and overall use of antibacterial agents. The illness also generates a significant social burden and indirect cost due to time lost from school and work. The estimated direct cost of AOM was $1.96 billion in 1995. In addition the indirect cost was estimated to be $1.02 billion.[1] During 1990 there were almost 25 million visits made to office-based physicians in the United States for otitis media, with 809 antibacterial prescriptions per 1000 visits, for a total of more than 20 million prescriptions for otitis media–related antibacterials. While the total number of office visits for otitis media decreased to 16 million in 2000, the rate of antibacterial prescribing was approximately the same (802 antibacterial prescriptions per 1000 visits for a total of more than 13 million prescriptions).[2–4] An individual course of antibacterial therapy can range in cost from $10 to more than $100.

There has been much discussion recently as to the necessity for the use of antibacterial agents at the time of diagnosis in children with uncomplicated AOM. Although in the United States the use of antibacterial agents in the management of AOM has been routine, in some countries in Europe it is common practice to treat the symptoms of AOM initially and only institute antibacterial therapy if clinical improvement does not occur. For the clinician, the choice of a specific antibacterial agent has become a key aspect of management. Concerns about the rising rates of antibacterial resistance and the growing costs of antibacterial prescriptions have focused the attention of the medical community and the general public on the need for judicious use of antibacterial agents. Greater resistance among many of the pathogens that cause AOM has fueled an increase in the use of broader-spectrum and generally more expensive antibacterial agents.

It is the intent of this guideline to evaluate the published evidence on the natural history and management of uncomplicated AOM and to make recommendations based on that evidence to primary care clinicians, including pediatricians, family physicians, physician assistants, nurse practitioners, and emergency department physicians, as well as otolaryngologists. The scope of the guideline is the diagnosis and management of uncomplicated AOM in children from 2 months through 12 years of age without signs or symptoms of systemic illness unrelated to the middle ear. It applies only to the otherwise healthy child without underlying conditions that may alter the natural course of AOM. These conditions include, but are not limited to, anatomic abnormalities such as cleft palate, genetic conditions such as Down syndrome, immunodeficiencies, and the presence of cochlear implants. Also excluded are

children with a clinical recurrence of AOM within 30 days or AOM with underlying chronic otitis media with effusion (OME).

METHODS

To develop the clinical practice guideline on the management of AOM, the American Academy of Pediatrics (AAP) and American Academy of Family Physicians (AAFP) convened the Subcommittee on Management of Acute Otitis Media, a working panel composed of primary care and subspecialty physicians. The subcommittee was cochaired by a primary care pediatrician and a family physician and included experts in the fields of general pediatrics, family medicine, otolaryngology, epidemiology, infectious disease, and medical informatics. All panel members reviewed the AAP policy on conflict of interest and voluntary disclosure and were given an opportunity to present any potential conflicts with the subcommittee's work.

The AAP and AAFP partnered with the Agency for Healthcare Research and Quality (AHRQ) and the Southern California Evidence-Based Practice Center (EPC) to develop the evidence report, which served as a major source of data for these practice guideline recommendations.[1] Specific clinical issues addressed in the AHRQ evidence report were the 1) definition of acute otitis media, 2) natural history of AOM without antibacterial treatment, 3) effectiveness of antibacterial agents in preventing clinical failure, and 4) relative effectiveness of specific antibacterial regimens. The AHRQ report focused on children between 4 weeks and 18 years of age with uncomplicated AOM seeking initial treatment. Outcomes included the presence or absence of signs and symptoms within 48 hours, at 3 to 7 days, 8 to 14 days, 15 days to 3 months, and more than 3 months and the presence of adverse effects from antibacterial treatment. EPC project staff searched Medline (1966 through March 1999), the Cochrane Library (through March 1999), HealthSTAR (1975 through March 1999), International Pharmaceutical Abstracts (1970 through March 1999), CINAHL (1982 through March 1999), BIOSIS (1970 through March 1999), and Embase (1980 through March 1999). Additional articles were identified by review of reference lists in proceedings, published articles, reports, and guidelines. Studies relevant to treatment questions were limited to randomized, controlled trials. For natural history, prospective and retrospective comparative cohort studies were also included. A total of 3461 titles were identified initially for additional review. Of these, 2701 were excluded and 760 required article review. Finally, 72 English language and 2 foreign-language articles were fully reviewed. Results of the literature review were presented in evidence tables and published in the final evidence report.

New literature about otitis media is constantly being published. While the systematic review done by AHRQ could not be replicated with new literature, members of the Subcommittee on Management of Acute Otitis Media reviewed additional articles published through September 2003. Articles were nonsystematically evaluated for quality of methodology and importance of results. Articles used in the AHRQ review also were reevaluated for their quality. Conclusions were based on the consensus of the subcommittee after the review of newer literature and reevaluation of the AHRQ evidence. Of significance is that the literature includes relatively few cases of uncomplicated AOM in children older than 12 years. The subcommittee therefore limited this guideline to children from 2 months through 12 years of age.

The evidence-based approach to guideline development requires that the evidence in support of a policy be identified, appraised, and summarized and that an explicit link between evidence and recommendations be defined. Evidence-based recommendations reflect the quality of evidence and the balance of benefit and harm that is anticipated when the recommendation is followed. The AAP definitions of evidence-based recommendations are shown in Table 1.

TABLE 1. Guideline Definitions for Evidence-based Statements

Statement	**Definition**	**Implication**
Strong Recommendation	A strong recommendation in favor of a particular action is made when the anticipated benefits of the recommended intervention clearly exceed the harms (as a strong recommendation against an action is made when the anticipated harms clearly exceed the benefits) and the quality of the supporting evidence is excellent. In some clearly identified circumstances, strong recommendations may be made when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	A recommendation in favor of a particular action is made when the anticipated benefits exceed the harms, but the quality of evidence is not as strong. Again, in some clearly identified circumstances, recommendations may be made when high-quality evidence is impossible to obtain but the anticipated benefits outweigh the harms.	Clinicians would be prudent to follow a recommendation, but should remain alert to new information and sensitive to patient preferences.
Option	Options define courses that may be taken when either the quality of evidence is suspect or carefully performed studies have shown little clear advantage to one approach over another.	Clinicians should consider the option in their decision making, and patient preference may have a substantial role.
No Recommendation	No recommendation indicates that there is a lack of pertinent published evidence and that the anticipated balance of benefits and harms is presently unclear.	Clinicians should be alert to new published evidence that clarifies the balance of benefit versus harm.

A draft version of this practice guideline underwent extensive peer review by committees and sections within the AAP, reviewers appointed by the AAFP, outside organizations, and other individuals identified by the subcommittee as experts in the field. Members of the subcommittee were invited to distribute the draft to other representatives and committees within their specialty organizations. The resulting comments were reviewed by the subcommittee and, when appropriate, incorporated into the guideline.

RECOMMENDATION 1: ***To diagnose acute otitis media the clinician should confirm a history of acute onset, identify signs of middle-ear effusion (MEE), and evaluate for the presence of signs and symptoms of middle-ear inflammation. (This recommendation is based on observational studies and a preponderance of benefit over risk; see Table 2.)***

TABLE 2. Definition of Acute Otitis Media

A diagnosis of acute otitis media requires 1) a history of acute onset of signs and symptoms, 2) the presence of MEE, and 3) signs and symptoms of middle-ear inflammation.

Elements of the definition of AOM are all of the following:

1. Recent, usually abrupt, onset of signs and symptoms of middle-ear inflammation and MEE.

2. The presence of MEE that is indicated by any of the following:
   a. Bulging of the tympanic membrane
   b. Limited or absent mobility of the tympanic membrane
   c. Air fluid level behind the tympanic membrane
   d. Otorrhea

3. Signs or symptoms of middle-ear inflammation as indicated by either
   a. Distinct erythema of the tympanic membrane OR
   b. Distinct otalgia (discomfort clearly referable to the ear[s] that results in interference with or precludes normal activity or sleep)

Children with AOM usually present with a history of rapid onset of signs and symptoms such as otalgia (or pulling of the ear in an infant), irritability in an infant or toddler, otorrhea, and/or fever. These findings, other than otorrhea, are nonspecific and frequently overlap those of an uncomplicated viral upper respiratory infection.[5,6] In a prospective survey among 354 children who visited a physician for acute respiratory illness, fever, earache, and excessive crying were frequently present (90%) in those with AOM. However, these symptoms were also prominent among children without AOM (72%). Other symptoms of a viral upper respiratory infection, such as cough and nasal discharge or stuffiness, often precede or accompany AOM, and are nonspecific also. Accordingly, clinical history alone is poorly predictive of the presence of AOM, especially in younger children.[5]

The presence of MEE is commonly confirmed with the use of pneumatic otoscopy[7] but can be supplemented by tympanometry[8] and/or acoustic reflectometry.[9–12] MEE also can be demonstrated directly by tympanocentesis or by the presence of fluid in the external auditory canal as a result of tympanic membrane perforation.

Visualization of the tympanic membrane with identification of an MEE and inflammatory changes is necessary to establish the diagnosis with certainty. To visualize the tympanic membrane adequately it is essential that cerumen obscuring the tympanic membrane be removed and that lighting is adequate. For pneumatic otoscopy, a speculum of proper shape and diameter must be selected to permit a seal in the external auditory canal. Appropriate restraint of the child to permit adequate examination may be necessary also.

The findings on otoscopy indicating the presence of MEE and inflammation associated with AOM have been well defined. Fullness or bulging of the tympanic membrane is often present and has the highest predictive value for the presence of MEE. When combined with color and mobility, bulging is also the best predictor of AOM.[7,13,14] Reduced or absent mobility of the tympanic membrane during performance of pneumatic otoscopy is further evidence of fluid in the middle ear. Opacification or cloudiness, other than that caused by scarring, is also a consistent finding and is caused by edema of the tympanic membrane. Redness of the tympanic membrane due to inflammation may be present and must be distinguished from the pink erythematous flush evoked by crying or high fever, which is usually less intense and remits as the child quiets down. In bullous myringitis blisters may be seen on the tympanic membrane.[15] When the presence of middle-ear fluid is difficult to determine, the use of tympanometry or acoustic reflectometry[16] can be helpful in establishing a diagnosis.

A major challenge for the practitioner is to discriminate between otitis media with effusion (OME) and AOM.[17,18] OME is more common than AOM. OME may accompany viral upper respiratory infections, be a prelude to AOM, or be a sequela of AOM.[19] When OME is mistakenly identified as AOM, antibacterial agents may be prescribed unnecessarily.[20,21] Clinicians should strive to avoid a false-positive diagnosis in children with middle-ear discomfort caused by eustachian tube dysfunction and retraction of the tympanic membrane or when acute viral respiratory infection is superimposed on chronic preexisting MEE.

The diagnosis of AOM, particularly in infants and young children, is often made with a degree of uncertainty. Common factors that may increase uncertainty include the inability to sufficiently clear the external auditory canal of cerumen, a narrow ear canal, or inability to maintain an adequate seal for successful pneumatic

otoscopy or tympanometry. An uncertain diagnosis of AOM is most often caused by inability to confirm the presence of MEE.[22] Acoustic reflectometry can be helpful, because it requires no seal of the canal and can determine the presence of middle-ear fluid through only a small opening in the cerumen.[10,11] When the presence of middle-ear fluid is questionable or uncertain, a diagnosis of AOM may be considered but cannot be confirmed. Although every effort should be made by the clinician to differentiate AOM from OME or a normal ear, it must be acknowledged that, using all available tools, uncertainty will remain in some cases. Efforts to improve clinician education must be increased to improve diagnostic skills and thereby decrease the frequency of an uncertain diagnosis. Ideally, instruction in the proper examination of the child's ear should begin with the first pediatric rotation in medical school and continue throughout postgraduate training.[18] Continuing medical education should reinforce the importance of and retrain the clinician in the use of pneumatic otoscopy. By including the degree of certainty into the formation of a management plan, the everyday challenge of pediatric examinations is incorporated into decision making.

A certain diagnosis of AOM meets all 3 of the criteria: rapid onset, presence of MEE, and signs and symptoms of middle-ear inflammation. The clinician should maximize diagnostic strategies, particularly to establish the presence of MEE, and should consider the certainty of diagnosis in determining management. Clinicians may wish to discuss the degree of diagnostic certainty with parents or caregivers at the time of initial AOM management.

RECOMMENDATION 2: ***The management of AOM should include an assessment of pain. If pain is present, the clinician should recommend treatment to reduce pain. (This is a strong recommendation based on randomized, clinical trials with limitations and a preponderance of benefit over risk.)***

Many episodes of AOM are associated with pain.[23] Although pain is an integral part of the illness, clinicians often see otalgia as a peripheral concern not requiring direct attention.[24] The AAP has published the policy statement "The Assessment and Management of Acute Pain in Infants, Children, and Adolescents"[25] to assist the clinician in addressing pain in the context of illness. The management of pain, especially during the first 24 hours of an episode of AOM, should be addressed, regardless of the use of antibacterial agents.

Various treatments of otalgia have been used, but none has been well studied. The clinician should select a treatment based on a consideration of benefits and risks and, wherever possible, incorporate parent or caregiver and patient preference (Table 3).

TABLE 3. Treatments for Otalgia in Acute Otitis Media

Modality	Comments
Acetaminophen, ibuprofen[26]	Effective analgesia for mild to moderate pain, readily available, mainstay of pain management for acute otitis media.
Home remedies (no controlled studies that directly address effectiveness) Distraction External application of heat or cold Oil	May have limited effectiveness.
Topical agents Benzocaine (Auralgan®, Americaine Otic®)[27] Naturopathic agents (Otikon Otic Solution®)[28]	Additional, but brief, benefit over acetaminophen in patients >5 y Comparable to ametocaine/phenazone drops (Anaesthetic®) in patients >6 y
Homeopathic agents[29,30]	No controlled studies that directly address pain
Narcotic analgesia with codeine or analogs	Effective for moderate or severe pain; requires prescription; risk of respiratory depression, altered mental status, gastrointestinal upset, and constipation
Tympanostomy/myringotomy[31]	Requires skill and entails potential risk

RECOMMENDATION 3A: ***Observation without use of antibacterial agents in a child with uncomplicated AOM is an option for selected children based on diagnostic certainty, age, illness severity, and assurance of follow-up. (This option is based on randomized controlled trials with limitations and a relative balance of benefit and risk.)***

The "observation option" for AOM refers to deferring antibacterial treatment of selected children for 48 to 72 hours and limiting management to symptomatic relief. The decision to observe or treat is based on the child's age, diagnostic certainty, and illness severity. To observe a child without initial antibacterial therapy, it is important that the parent or caregiver has a ready means of communicating with the clinician. There also must be a system in place that permits reevaluation of the child. If necessary the parent or caregiver also must be able to conveniently obtain medication.

This option should be limited to otherwise healthy children 6 months to 2 years of age with non-severe illness at presentation *and* an uncertain diagnosis *and* to children 2 years of age and older without severe symptoms at presentation *or* with an uncertain diagnosis. In these situations observation provides an opportunity for the patient to improve without antibacterial treatment. The association of age younger than 2 years with increased risk of failure of watchful waiting and the concern for serious infection among children younger than 6 months influence the

decision for immediate antibacterial therapy. Consequently, the panel recommends an age-stratified approach that incorporates these clinical considerations along with the certainty of diagnosis (Table 4).

TABLE 4. Criteria for Initial Antibacterial Agent Treatment or Observation in Children With Acute Otitis Media

Age	Certain Diagnosis	Uncertain Diagnosis
<6 mo	Antibacterial therapy	Antibacterial therapy
6 mo–2 y	Antibacterial therapy	Antibacterial therapy if severe illness; observation option* if non-severe illness
≥2 y	Antibacterial therapy if severe illness; observation option* if non-severe illness	Observation option*

This table was modified with permission from the New York State Department of Health and the New York Region Otitis Project Committee.[32,33]
*Observation is an appropriate option only when follow-up can be ensured and antibacterial agents started if symptoms persist or worsen. Nonsevere illness is mild otalgia and fever <39°C in the past 24 hours. Severe illness is moderate to severe otalgia or fever ≥39°C.
A certain diagnosis of acute otitis media meets all 3 criteria: 1) rapid onset, 2) signs of middle-ear effusion, and 3) signs and symptoms of middle-ear inflammation.

Placebo-controlled trials of AOM over the past 30 years have consistently shown that most children do well, without adverse sequelae, even without antibacterial therapy. Between 7 and 20 children must be treated with antibacterial agents for 1 child to derive benefit.[34–36] By 24 hours, 61% of children have decreased symptoms whether they receive placebo or antibacterial agents. By 7 days approximately 75% of children have resolution of symptoms.[37] The AHRQ evidence report meta-analysis showed a 12.3% reduction in the clinical failure rate within 2 to 7 days of diagnosis when ampicillin or amoxicillin was prescribed compared with initial use of placebo or observation (number needed to treat: 8).[1]

In 1990 the Dutch College of General Practitioners adopted a guideline for the management of AOM that recommended treating symptoms without antibacterial agents for 24 hours (for those 6 to 24 months old) or 72 hours (for those older than 24 months) and adding antibacterial agents if no improvement is evident at reassessment. A 1999 revision to this early guideline does not distinguish the younger age group for special consideration.[38] Although this guideline has been widely adopted in the Netherlands, its use in other countries requires consideration of the availability of access to care for follow-up and the presence of an adult who can adequately monitor the child's course. Although there are no controlled studies that address the question as to whether the Dutch guideline has resulted in more complications following AOM, van Buchem and colleagues[39,136] found that only 2.7% of 4860 Dutch children older than 2 years given only symptomatic treatment developed severe illness, defined by persistent fever, pain, or discharge after 3 to 4 days. Only 2 children developed mastoiditis. One case of mastoiditis was

present at initial assessment, and the other developed within the first week and resolved promptly with oral antibacterial agents.

Randomized trials of observation with symptomatic treatment have been few. A recent randomized trial in general practice in the United Kingdom compared providing immediate antibacterial therapy with delaying antibacterial agents for 72 hours in children aged 6 months to 10 years.[40] Seventy-six percent of children in the delayed treatment group never required antibacterial agents. Seventy percent of the delayed antibacterial group were symptomatically better at 3 days, whereas 86% of the immediate treatment group were better. Immediate use of antibacterial agents was associated with about 1-day-shorter illness and one-half teaspoon a day less acetaminophen consumption but no difference in school absence, pain, or distress scores. Among children with fever or vomiting on day 1, those receiving immediate antibacterial agents were 21% less likely to have distress on day 3. In children without fever or vomiting, immediate antibacterial agents decreased distress on day 3 by only 4%.[41] This study, however, was limited due to the use of imprecise criteria for the diagnosis of AOM and the use of low doses of amoxicillin (125 mg, 3 times a day, for 7 days for all patients regardless of weight) in the treatment group.

The likelihood of recovery without antibacterial therapy differs depending on severity of signs and symptoms at initial examination. Kaleida et al[42] divided patients into severe and non-severe groups based on degree of fever, a scoring system based on duration and severity of pain or apparent discomfort, and estimated parental anxiety. In the non-severe group, initial treatment failure occurred in 3.8% more children who received placebo rather than amoxicillin. In the severe group of children, the initial failure rate on placebo plus myringotomy was 23.5% versus an initial failure rate of 9.6% on amoxicillin alone (a difference of 13.9%).

Several investigators report poorer outcomes in younger children. A greater number of penicillin-resistant strains of pneumococci are isolated in those younger than 18 months, compared with older children,[43] and are associated with an increased bacteriologic failure rate in children younger than 2 years.[44–47] The study by Kaleida and colleagues also shows a greater initial clinical failure rate (9.8%) in children younger than 2 years than in those older than 2 years (5.5%) who were in the placebo group.[42]

Routine antibacterial therapy for AOM is often cited as the main reason for the decrease in the incidence of mastoiditis in the antibacterial era.[48,49] By the 1950s, mastoiditis (frequent in the pre-antibacterial agent era[48]) had decreased dramatically. Although some have expressed concern about a possible resurgence,[50,51] such concern is not supported by published data.

The AHRQ evidence report on AOM concluded that mastoiditis is not increased with initial observation, provided that children are followed closely and antibacterial therapy is initiated in those that do not improve. Pooled data from 6 randomized trials and 2 cohort studies showed comparable rates of mastoiditis in children (0.59%) who received initial antibacterial therapy and children (0.17%) who received placebo or observation ($P = 0.212$). External validity might be limited, however, because some trials excluded very young children or those with severe illness.[1]

Recently published case series of pediatric mastoiditis show that acute mastoiditis is most common in infants and young children, and can be the presenting sign of AOM in a patient with no prior middle-ear disease.[50–60] Routine antibacterial therapy of AOM is not an absolute safeguard against mastoiditis and other complications because most cases (36%–87%) have received prior antibacterial agent therapy.[50,53,57–59,61–63]

Van Zuijlen et al[64] compared national differences in acute mastoiditis rates from 1991 to 1998 for children 14 years of age or younger. Incidence rates were higher in The Netherlands, Norway, and Denmark (in which antibacterial agents are not necessarily given on initial diagnosis of AOM) than in the United Kingdom, Canada, Australia, and the United States in which antibacterial agents are prescribed in more than 96% of cases. However, despite initial use of antibacterial agents more than twice as often in Norway and Denmark than in The Netherlands, mastoiditis rates in all 3 countries were comparable.

Thus current evidence does not suggest a clinically important increased risk of mastoiditis in children when AOM is managed only with initial symptomatic treatment without antibacterial agents. Clinicians should remain aware that antibacterial agent treatment might mask mastoiditis signs and symptoms, producing a subtle presentation that can delay diagnosis.[56,59,61]

Although bacteremia may accompany AOM, particularly in children with a temperature higher than 39°C,[65] there is little evidence that routine antibacterial treatment for otitis media prevents bacterial meningitis. In a study of 4860 children with AOM who did not receive antibacterial therapy, no cases of bacterial meningitis were observed.[39] However, in a study involving 240 children between 6 and 24 months of age, 1 child in the placebo group was subsequently diagnosed as having meningitis.[66] In another report, positive blood cultures were equally common in children with bacterial meningitis regardless of whether they received preadmission treatment with antibacterials for AOM (77% and 78%).[67] Thus, as with mastoiditis, the incidence of meningitis in those with AOM is unlikely to be influenced by initial treatment of AOM with antibacterial agents.

The incidence of invasive pneumococcal disease has decreased since the introduction of the protein-polysaccharide conjugate vaccine (PPV7). There has been a 69% decline in children younger than 2 years between 1998 to 1999 and 2001. The decline in this age group for invasive disease caused by vaccine serotypes during that period was 78%.[68] How this will affect the risk of AOM-associated invasive pneumococcal disease is not yet known.

As noted by Dagan and McCracken,[69] studies comparing efficacy of different antibacterial agents or placebo compared with antibacterial therapy often have significant design flaws that may influence the outcome of the studies. Methodologic considerations include enrollment criteria, sample size, diagnostic criteria, dosing regimens, definition and timing of outcome criteria, age, severity of symptoms, race, immune system, compliance, virulence and resistance of the infecting organism, duration of antibacterial therapy, and the presence of an underlying respiratory infection. One of the most important issues among the design characteristics of the studies of otitis media is the definition of AOM used in the individual investigations. If studies that evaluate the impact of antibacterial therapy on the clinical course of children with AOM have weak definitions of AOM (that allow the inclusion of children who are more likely to have OME than AOM), recipients of placebo will not respond significantly differently from those who receive antibacterial therapy.

Given the sum of the available evidence, clinicians may consider observation with symptomatic treatment as an option for initial management of selected children with AOM. If the "observation option" is used, the clinician should share with parents or caregivers the degree of diagnostic certainty and consider their preference. The potential of antibacterial therapy at the initial visit to shorten symptoms by one day in 5% to 14% of children can be compared with the avoidance of common antibacterial side effects in 5% to 10% of children, infrequent serious side effects, and the adverse effects of antibacterial resistance. When considering this option, the clinician should verify the presence of an adult who will reliably observe the child, recognize signs of serious illness, and be able to provide prompt access to medical care if improvement does not occur. If there is worsening of illness or if there is no improvement in 48 to 72 hours while a child is under observation, institution of antibacterial therapy should be considered. Reexamination may be warranted if discussion with the parents raises concern as to the degree of illness.

Strategies for following children being managed with initial observation include a parent-initiated visit and/or phone contact for worsening condition or no improvement at 48 to 72 hours, a scheduled follow-up appointment in 48 to 72 hours, routine follow-up phone contact, or use of a safety-net antibiotic prescription to be filled if illness does not improve in 48 to 72 hours.[70,71] Clinicians should determine the most appropriate strategy for

their practice setting, taking into account the availability and reliability of the reporting parent/caregiver, available office resources, cost to the health care system and the family, and the convenience of the family. An assessment of the potential risk of inappropriate use of an antibacterial agent in a patient who may be worsening or who may have a condition other than AOM must also be made. Table 5 summarizes the data on initial observation versus initial antibacterial agent treatment of AOM.

TABLE 5. Comparative AOM Outcomes for Initial Observation Versus Antibacterial Agent*

AOM Outcome	**Initial Antibacterial Therapy**	**Initial Observation**	***P* Value**
Symptomatic relief at 24 hours[37,72]	60%	59%	NS
Symptomatic relief at 2–3 days[72]	91%	87%	NS
Symptomatic relief at 4–7 days[72]	79%	71%	NS
Clinical resolution at 7–14 days[72]	82%	72%	NS
Pain duration, mean days[73]	2.8	3.3	NS
Crying duration, mean days[73]	0.5	1.4	<.001
Analgesic use, mean doses[66]	2.3	4.1	.004
Fever duration, median days[66]	2.0	3.0	.004
Incidence of mastoiditis or suppurative complications[1]	0.59%	0.17%	NS
Persistent MEE at 4–6 weeks[72]	45%	48%	NS
Persistent MEE at 3 months[72]	21%	26%	NS
Antibacterial agent–induced diarrhea or vomiting[74]	16%	—	—
Antibacterial agent–induced skin rash[74]	2%	—	—

* NS, not significant.

RECOMMENDATION 3B: ***If a decision is made to treat with an antibacterial agent, the clinician should prescribe amoxicillin for most children. (This recommendation is based on randomized clinical trials with limitations and a preponderance of benefit over risk.)***
When amoxicillin is used, the dose should be 80 to 90 mg/kg/day. (This option is ***based on extrapolation from microbiologic studies and expert opinion, with a preponderance of benefit over risk.)***

If a decision is made to treat with antibacterial agents, there are numerous medications that are clinically effective. The choice of first-line treatment should be based on the anticipated clinical response as well as the microbiologic flora likely to be present. The justification to use amoxicillin as first-line therapy in most patients with

AOM relates to its general effectiveness when used in sufficient doses against susceptible and intermediate resistant pneumococci, as well as its safety, low cost, acceptable taste, and narrow microbiologic spectrum.[75]

In patients who have severe illness (moderate to severe otalgia or fever of 39°C or higher[42]) and in those for whom additional coverage for β-lactamase-positive *Haemophilus influenzae* and *Moraxella catarrhalis* is desired, therapy should be initiated with high-dose amoxicillin-clavulanate (90 mg/kg per day of amoxicillin component, with 6.4 mg/kg per day of clavulanate in 2 divided doses).[76] This dose has sufficient potassium clavulanate to inhibit all β-lactamase-producing *H influenzae* and *M catarrhalis.*

Many clinical studies comparing the effectiveness of various antibacterial agents in the treatment of AOM do not carefully define standard criteria for diagnosis of AOM at entry, or for improvement or cure at follow-up. Another way to measure the outcome of treatment of AOM with various antibacterial agents is to assess bacteriologic efficacy. Although this does not provide a one-to-one correlation with clinical effectiveness, there is a definite concordance between the two.[77–79] Children who experience a bacteriologic cure improve more rapidly and more often than children who experience bacteriologic failure. Carlin et al[79] showed an 86% agreement between clinical and bacteriologic response. Dagan et al[77] showed that 91% of clinical failures at or before day 10 were culture positive at days 4 to 5. If we use bacteriologic cure as a surrogate for clinical efficacy, there is strong evidence that drugs that achieve antibacterial concentrations that are able to eradicate pathogens from the middle-ear fluid are the preferred selection.[80,81]

Numerous studies have shown that the common pathogens in AOM are *Streptococcus pneumoniae*, non-typeable *H influenzae,* and *M catarrhalis*.[82,83] *S pneumoniae* has been recovered from the middle-ear fluid of approximately 25% to 50% of children with AOM, *H influenzae* from 15% to 30%, and *M catarrhalis* from about 3% to 20%.[83] There is some evidence that the microbiology of AOM may be changing as a result of routine use of the heptavalent pneumococcal vaccine. Block et al[84] showed an increase in *H Influenzae* from 39% to 52% of isolates in children 7 to 24 months of age with AOM and a decrease in *S pneumoniae* from 49% to 34% between 1992–1998 and 2000–2003. Viruses, including respiratory syncytial virus, rhinovirus, coronavirus, parainfluenza, adenovirus, and enterovirus, have been found in respiratory secretions and/or MEE in 40% to 75% of AOM cases and in MEE without bacteria in 5% to 22% of cases, and may be responsible for many cases of apparent antibacterial agent “failure.” In approximately 16% to 25% of cases of AOM, no bacterial or viral pathogen can be detected in MEE.[19,85,86]

Currently approximately 50% of isolates of *H influenzae* and 100% of *M catarrhalis* derived from the upper respiratory tract are likely to be beta-lactamase positive nationwide.[87] Between 15% and 50% (average: 30%) of upper respiratory tract isolates of *S pneumoniae* are also not susceptible to penicillin; approximately 50% of these are highly resistant to penicillin (minimum inhibitory concentration: 2.0 μg/mL or higher) and the remaining half are intermediate in resistance (minimum inhibitory concentration: between 0.1–1.0 μg/mL).[88–91] The mechanism of penicillin resistance among isolates of *S pneumoniae* is not associated with β-lactamase production but rather an alteration of penicillin-binding proteins. This phenomenon, which varies considerably according to geographic location, results in resistance to penicillins and cephalosporins.

Data from early studies of patients with AOM show that 19% of children with *S pneumoniae* and 48% with *H influenzae* cultured on initial tympanocentesis who were not treated with antibacterial agents cleared the bacteria at the time of a second tympanocentesis 2 to 7 days later.[92] Estimates are that approximately 75% of children infected with *M catarrhalis* also experience bacteriologic cure, based on resolution after treatment with an antibacterial agent to which it is not susceptible (amoxicillin).[93,94] Only *S pneumoniae* that are highly resistant to penicillin will not respond to conventional doses of amoxicillin.[95] Accordingly, approximately 80% of children with AOM will respond to treatment with high-dose amoxicillin including many caused by resistant pneumococci. The higher dose will yield middle-ear fluid levels that exceed the minimum inhibitory concentration of all *S pneumoniae* that are intermediate in resistance to penicillin and many, but not all, highly resistant *S pneumoniae*.[76] Risk factors for the presence of bacterial species likely to be resistant to amoxicillin include attendance at child care, recent receipt (less than 30 days) of antibacterial treatment, and age younger than 2 years.[96,97]

If the patient is allergic to amoxicillin and the allergic reaction was not a type I hypersensitivity reaction (urticaria or anaphylaxis), cefdinir (14 mg/kg per day in 1 or 2 doses), cefpodoxime (10 mg/kg per day, once daily), or cefuroxime (30 mg/kg per day in 2 divided doses) can be used. In cases of Type I reactions, azithromycin (10 mg/kg per day on day 1 followed by 5 mg/kg per day for 4 days as a single daily dose) or clarithromycin (15 mg/kg per day in 2 divided doses) can be used in an effort to select an antibacterial agent of an entirely different class. Other possibilities include erythromycin-sulfisoxazole (50 mg/kg per day of erythromycin) or sulfamethoxazole-trimethoprim (6–10 mg/kg per day trimethoprim). Alternative therapy in the penicillin-allergic patient who is being treated for infection that is known or presumed to be caused by penicillin-resistant *S pneumoniae* is clindamycin at 30 to 40 mg/kg per day in 3 divided doses. In the patient who is vomiting or cannot otherwise tolerate oral

medication, a single dose of parenteral ceftriaxone (50 mg/kg) has been shown to be effective for the initial treatment of AOM.[98,99]

The optimal duration of therapy for patients with AOM is uncertain. Studies comparing standard duration of treatment (10 days) to short duration treatment (1–7 days) were often characterized by limitations including inadequate sample size (therefore having low or limited statistical power), few or no children younger than 2 years, exclusion of otitis-prone children, lack of standardized or stringent criteria for the diagnosis of AOM or for improvement or cure, use of an antibacterial medication that had less than optimal efficacy against common middle-ear pathogens, use of lower than recommended dosage of a medication, and lack of analysis of outcome by age.[100] Not surprisingly, the results of these studies were variable. Several more recent studies have been reported addressing the issue of duration of therapy.[101–105] The results favoring standard 10-day therapy have been most significant in children younger than 2 years and suggestive of increased efficacy in those 2 to 5 years of age. Thus, for younger children, and for children with severe disease, a standard 10-day course is recommended.[106] For children 6 years of age and older with mild to moderate disease, a 5- to 7-day course is appropriate.

RECOMMENDATION 4: ***If the patient fails to respond to the initial management option within 48 to 72 hours, the clinician must reassess the patient to confirm AOM and exclude other causes of illness. If AOM is confirmed in the patient initially managed with observation, the clinician should begin antibacterial therapy. If the patient was initially managed with an antibacterial agent(s), the clinician should change the antibacterial agent(s). (This recommendation is based on observational studies and a preponderance of benefit over risk.)***

When antibacterial agents are prescribed for AOM, the time course of clinical response should be 48 to 72 hours. With few exceptions, the first 24 hours of therapy are characterized by a stabilization of the clinical condition. Early during this period the patient may actually worsen slightly. In the second 24 hours, the patient should begin to improve. If initially febrile, the patient is expected to defervesce within 48 to 72 hours. Irritability should improve and sleeping and eating patterns should begin to normalize.[37] If the patient is not improved by 48 to 72 hours, either another disease is present or the therapy that has been chosen was not adequate. When observation has been the chosen management and spontaneous improvement has not been noted by 48 to 72 hours, antibacterial therapy is indicated to limit the duration of further illness.

The patient should be given clear instructions at the initial visit as to when and how to communicate continuation or worsening of signs and symptoms to the clinician to expedite a change in treatment.

Antibacterial agent choice after initial failure of observation or first-line antibacterial therapy should be based on the likely pathogen(s) present and on clinical experience. If the patient was treated with initial observation, amoxicillin should be started at a dose of 80 to 90 mg/kg/day. For patients who have severe illness (moderate to severe otalgia or temperature 39°C or higher[42]), in those for whom additional coverage for β-lactamase positive *H influenzae* and *M catarrhalis* is desired, and for those who had been treated initially with amoxicillin and did not improve, high-dose amoxicillin-clavulanate (90 mg/kg per day of amoxicillin component, with 6.4 mg/kg per day of clavulanate in 2 divided doses)[76] should be used. Alternatives in patients with a history of a non-type I allergic reaction to penicillins are cefdinir, cefpodoxime, or cefuroxime.[88] In cases of type I reactions, alternatives are azithromycin, clarithromycin, erythromycin-sulfisoxazole, or sulfamethoxazole-trimethoprim. Ceftriaxone (50 mg/kg per day), given for 3 consecutive days, either intravenously or intramuscularly, can be used in children with vomiting, or in other situations that preclude administration of oral antibacterial agents. In the treatment of AOM unresponsive to initial antibacterial therapy, a 3-day course of ceftriaxone has been shown to be better than a 1-day regimen.[99] Although trimethoprim-sulfamethoxazole and erythromycin-sulfisoxazole have traditionally been useful as first- and second-line therapy for patients with AOM, recent pneumococcal surveillance studies indicate that resistance to these 2 combination agents is substantial.[90,95] Therefore, when patients fail to improve while receiving amoxicillin, neither trimethoprim-sulfamethoxazole[107] nor erythromycin-sulfisoxazole are optimal for antibacterial therapy.

A patient who fails amoxicillin-potassium clavulanate should be treated with a 3-day course of parenteral ceftriaxone due to its superior efficacy against *S pneumoniae* compared with alternative oral antibacterials.[91] If AOM persists, tympanocentesis should be recommended to make a bacteriologic diagnosis. If tympanocentesis is not available, a course of clindamycin may be considered for the rare case of penicillin-resistant pneumococcal infection not responding to the previous regimens. If the patient still does not improve, tympanocentesis with Gram stain, culture, and antibacterial agent sensitivity studies of the fluid is essential to guide further therapy. Table 6 summarizes antibacterial options.

TABLE 6. Recommended Antibacterial Agents for Patients Who Are Being Treated Initially With Antibacterial Agents or Who Have Failed 48 to 72 Hours of Observation or Have Failed Initial Management With Antibacterial Agents

Temperature ≥39°C and/or Severe Otalgia	**At Diagnosis for Patients Being Treated Initially With Antibacterial Agents**		**Clinically Defined Treatment Failure at 48–72 Hours After Initial Management With Observation Option**		**Clinically Defined Treatment Failure at 48–72 Hours After Initial Management With Antibacterial Agents**	
	Recommended	**Alternative for Penicillin Allergy**	**Recommended**	**Alternative for Penicillin Allergy**	**Recommended**	**Alternative for Penicillin Allergy**
No	Amoxicillin 80–90 mg/kg per day	Non-type I: cefdinir, cefuroxime, cefpodoxime; type I: azithromycin, clarithromycin	Amoxicillin 80–90 mg/kg per day	Non-type I: cefdinir, cefuroxime, cefpodoxime; type I: azithromycin, clarithromycin	Amoxicillin-clavulanate (90 mg/kg per day of amoxicillin component, with 6.4 mg/kg per day of clavulanate)	Non-type I: ceftriaxone, 3 days; type I: clindamycin
Yes	Amoxicillin-clavulanate (90 mg/kg per day of amoxicillin with 6.4 mg/kg per day of clavulanate	Ceftriaxone, 1 or 3 days	Amoxicillin-clavulanate (90 mg/kg per day of amoxicillin with 6.4 mg/kg per day of clavulanate)	Ceftriaxone, 1 or 3 days	Ceftriaxone, 3 days	Tympanocentesis, clindamycin

Once the patient has shown clinical improvement, follow-up is based on the usual clinical course of AOM. Persistent MEE after resolution of acute symptoms is common and should not be viewed as a need for active therapy. Two weeks after an episode of AOM, 60% to 70% of children have MEE, decreasing to 40% at 1 month and 10% to 25% after 3 months.[37(161–162)] OME must be differentiated clinically from AOM and requires additional monitoring, but not antibacterial therapy. Assurance that OME resolves is particularly important for children with cognitive or developmental delays that may be impacted adversely by transient hearing loss associated with MEE.

RECOMMENDATION 5: ***Clinicians should encourage the prevention of AOM through reduction of risk factors. (This recommendation is based on strong observational studies and a preponderance of benefits over risks.)***

A number of factors associated with early or recurrent AOM are not amenable to change, for example, genetic predisposition, premature birth, male gender, Native American/Inuit ethnicity, family history of recurrent otitis media, presence of siblings in the household, and low socioeconomic status.[108–113]

During infancy and early childhood, reducing the incidence of respiratory tract infections by altering child care center attendance patterns can significantly reduce the incidence of recurrent AOM.[108,114] The implementation of breastfeeding for at least the first 6 months also seems to be helpful against the development of early episodes of AOM.[108,109] Avoiding supine bottle-feeding ("bottle propping"),[115] reducing or eliminating pacifier use in the second 6 months of life,[116] and eliminating exposure to passive tobacco smoke[117,118] have been postulated to reduce the incidence of AOM in infancy; however, the utility of these interventions is unclear.[108,109,114,119,120]

Immunoprophylaxis with killed[121] and live-attenuated intranasal[122] influenza vaccines has demonstrated more than 30% efficacy in prevention of AOM during the respiratory illness season. Most of the children in these studies were older than 2 years. A controlled study among infants and toddlers 6 to 23 months of age failed to demonstrate any efficacy of killed vaccine in preventing AOM.[123] Pneumococcal conjugate vaccines have proven effective in preventing vaccine-serotype pneumococcal otitis media, but their overall benefit is small, with only a 6% reduction in the incidence of AOM.[124–126] Medical office visits for otitis were reduced by 7.8% and antibiotic prescriptions by 5.7% in a large clinical practice after introduction of the pneumococcal conjugate vaccine.[127] Respiratory syncytial virus, parainfluenza virus, and adenovirus vaccines currently under development hold additional promise for prevention of ear infections.

RECOMMENDATION 6: ***Complementary and alternative medicine (CAM) for treatment of AOM. (No recommendations are made based on limited and controversial data.)***

Increasing numbers of parents and caregivers are using various forms of nonconventional treatment for their children.[128,129] The types of treatments used can differ depending on the ethnic background and belief system of the family and the availability of alternative medicine in a particular community. Treatments that have been used for AOM include homeopathy, acupuncture, herbal remedies, chiropractic treatments, and nutritional supplements.[130] Many physicians ask parents, caregivers, or older children if they are using medicines, supplements, or other means to maintain health or treat specific conditions[131]; however, parents or caregivers are often reluctant to tell their physicians that they are using complementary or alternative treatments.[132] Although most treatments are harmless, some are not. Some can have a direct and dangerous effect, whereas others may interfere with the effects of conventional treatments.[30] Clinicians should become more informed about complementary and alternative therapies, ask if they are being used, and be ready to discuss potential benefits or risks.[133]

To date there are no studies that conclusively show a beneficial effect of alternative therapies used for AOM. Recent interest in the use of CAM has led to research efforts to investigate its efficacy.[134] It is difficult to

design and conduct studies on certain forms of CAM because of the unique nature of the treatment.[135] Any study conducted will need to show proof of effectiveness of a specific therapy when compared with the natural history of AOM. Conclusions regarding CAM cannot be made until research evidence is available.

FUTURE RESEARCH

Despite the voluminous literature about AOM there are still many opportunities for future research to continue to clarify the accurate diagnosis and most effective management of this common condition. Most important is that future studies address concerns regarding the quality and applicability of many studies in AOM.[21,69,78,100] Future studies should use standardized criteria for diagnosis, outcome, and severity of illness; increase sample size, which in general has been too limited to identify small but significant differences in clinical outcome; include children younger than 2 years and older than 12 years; use doses of medication shown to achieve adequate levels in the middle ear to successfully treat the target organisms; and stratify outcomes by age and severity of illness. In addition studies done in limited geographic areas must be replicated in other areas to ensure generalizability. Some of the studies that should be considered include:

- Additional validation of standard definitions of AOM
- New or improved technologies for objective diagnosis of MEE
- Efficacy of education programs to improve clinician diagnostic skills
- Additional studies on pain management including topical, CAM, and role of tympanocentesis/myringotomy in pain management
- Large population-based studies on the benefits and risks of the "observation option" looking at antibacterial use; bacterial resistance; incidence of adverse events; long-term effects on hearing; persistence of MEE; and parent, patient, and clinician satisfaction
- Continued development of new antibacterial agents to address potential changes in resistance patterns of organisms responsible for AOM (studies on new agents must be appropriately designed and have adequate sample size to show clinical efficacy equal to or better than current agents.)
- Randomized, controlled trials on duration of treatment in all age groups
- Vaccine research directed at more of the causative organisms of AOM
- Additional studies on potential measures to prevent AOM

SUMMARY

This clinical practice guideline provides evidence-based recommendations for the definition and management of AOM in children from 2 months through 12 years of age without signs or symptoms of systemic illness unrelated to the middle ear. It emphasizes accurate diagnosis and adherence to a consistent definition of AOM. Management of the pain associated with AOM is identified as an essential aspect of care. An option to observe a select group of children with AOM with symptomatic therapy for 48 to 72 hours is supported by evidence and may potentially lead to decreased use of antibacterial agents. If a decision is made to treat with an antibacterial agent, amoxicillin at a dose of 80 to 90 mg/kg per day is recommended as the initial antibacterial agent of choice for most children. Additional guidance is given for choosing an antibacterial agent when an alternative to amoxicillin is indicated. Also addressed is evidence related to the prevention of AOM and the role of CAM in the treatment of AOM. The recommendations are summarized in Fig 1.

Fig 1. Management of AOM

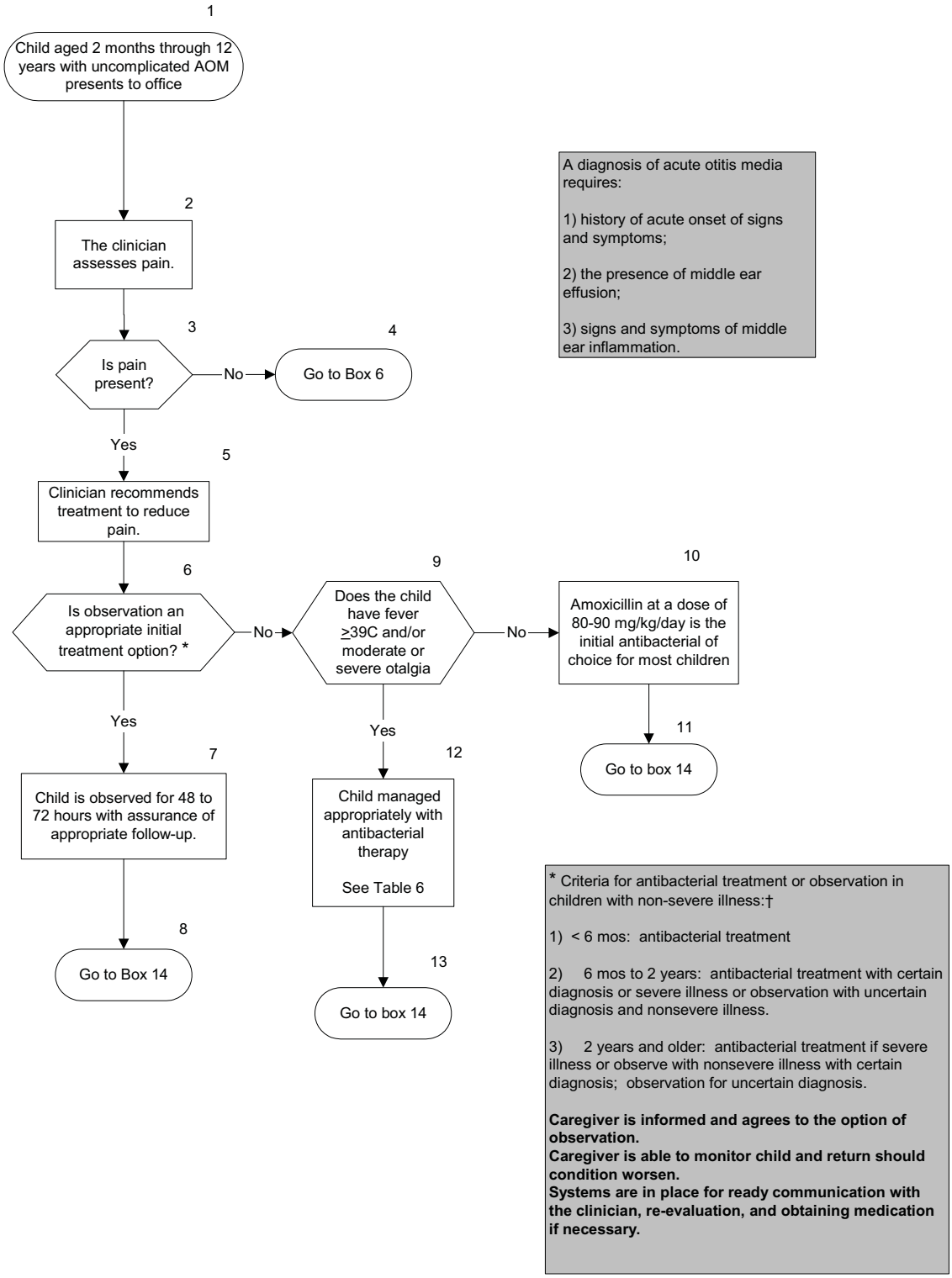
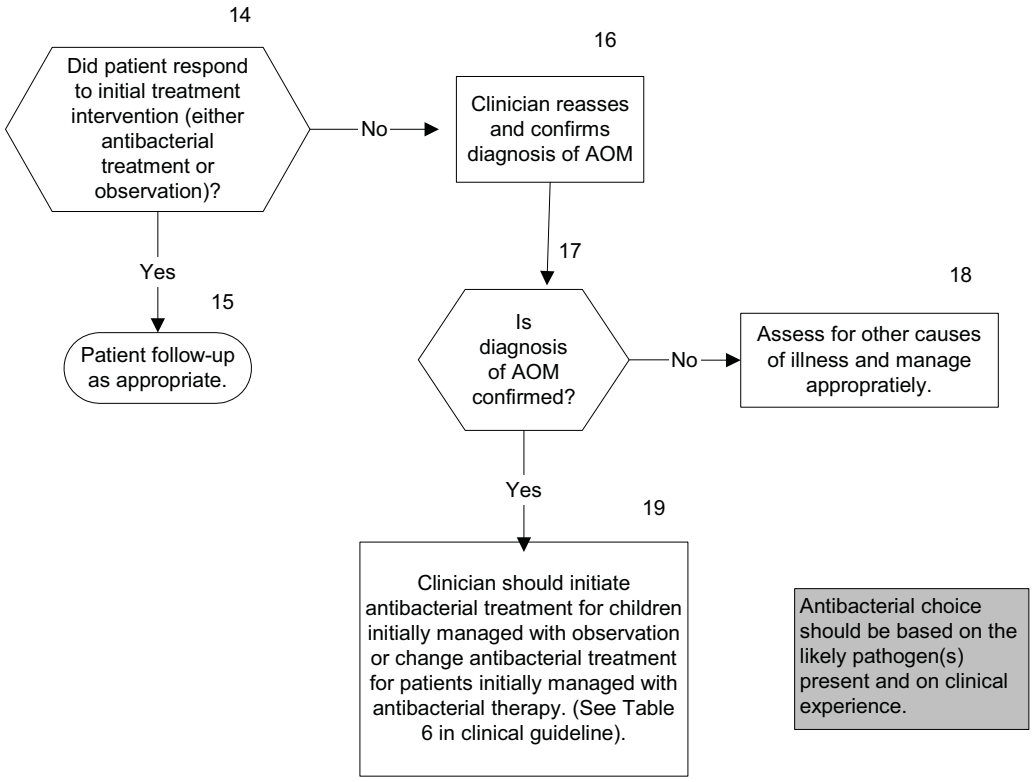


Fig 1. Management of AOM, continued



CONCLUSIONS

1. Recommendation: To diagnose acute otitis media the clinician should confirm a history of acute onset, identify signs of middle-ear effusion, and evaluate for the presence of signs and symptoms of middle-ear inflammation.
2. Strong recommendation: The management of AOM should include an assessment of pain. If pain is present, the clinician should recommend treatment to reduce pain.

3A. Option: Observation without use of antibacterial agents in a child with uncomplicated AOM is an option for selected children based on diagnostic certainty, age, illness severity, and assurance of follow-up.

3B. Recommendation: If a decision is made to treat with an antibacterial agent, the clinician should prescribe amoxicillin for most children.

Option: When amoxicillin is used, the dose should be 80–90 mg/kg/day.

4. Recommendation: If the patient fails to respond to the initial management option within 48 to 72 hours, the clinician must reassess the patient to confirm AOM and exclude other causes of illness. If AOM is confirmed in the patient initially managed with observation, the clinician should begin antibacterial therapy. If the patient was initially managed with an antibacterial agent, the clinician should change the antibacterial agent.
5. Recommendation: Clinicians should encourage the prevention of AOM through reduction of risk factors.
6. No recommendation: There is insufficient evidence to make a recommendation regarding the use of CAM for AOM.

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The recommendations in this guideline do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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