Acute otitis media (AOM) is the most common condition for which antibiotics are prescribed for US children; however, wide variation exists in diagnosis and treatment.

**Objectives** To perform a systematic review on AOM diagnosis, treatment, and the association of heptavalent pneumococcal conjugate vaccine (PCV7) use with AOM microbiology.

**Data Sources** PubMed, Cochrane Databases, and Web of Science, searched to identify articles published from January 1999 through July 2010.

**Study Selection** Diagnostic studies with a criterion standard, observational studies and randomized controlled trials comparing AOM microbiology with and without PCV7, and randomized controlled trials assessing antibiotic treatment.

**Data Extraction** Independent article review and study quality assessment by 2 investigators with consensus resolution of discrepancies.

**Results** Of 8945 citations screened, 135 were included. Meta-analysis was performed for comparisons with 3 or more trials. Few studies examined diagnosis; otoscopic findings of tympanic membrane bulging (positive likelihood ratio, 51 [95% confidence interval (CI), 36-73]) and redness (positive likelihood ratio, 8.4 [95% CI, 7-11]) were associated with accurate diagnosis. In the few available studies, prevalence of *Streptococcus pneumoniae* decreased (eg, 33%-48% vs 23%-31% of AOM isolates), while that of *Haemophilus influenzae* increased (41%-43% vs 56%-57%) pre- vs post-PCV7. Short-term clinical success was higher for immediate use of ampicillin or amoxicillin vs placebo (73% vs 60%; pooled rate difference, 12% [95% CI, 5%-18%]; number needed to treat, 9 [95% CI, 6-20]), while increasing the rate of rash or diarrhea by 3% to 5%. Two of 4 studies showed greater clinical success for immediate vs delayed antibiotics (95% vs 80%; rate difference, 15% [95% CI, 6%-24%] and 86% vs 70%; rate difference, 16% [95% CI, 6%-26%]). Data are absent on long-term effects on antimicrobial resistance. Meta-analyses in general showed no significant differences in antibiotic comparative effectiveness.

**Conclusions** Otoscopic findings are critical to accurate AOM diagnosis. AOM microbiology has changed with use of PCV7. Antibiotics are modestly more effective than no treatment but cause adverse effects in 4% to 10% of children. Most antibiotics have comparable clinical success.

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www.jama.com

See also Patient Page.

CME available online at www.jamaarchivescme.com and questions on p 2186.
In light of these additional studies and practice changes, we conducted a systematic review to support the new AOM practice guidelines (currently in preparation) from the American Academy of Pediatrics. We report on the evidence for (1) the precision and accuracy of AOM diagnosis, (2) the association of PCV7 use with changes in AOM microbial epidemiology, (3) the decision about whether to treat with antibiotics, and (4) the comparative effectiveness of different antibiotics for uncomplicated AOM in average-risk children and associated antibiotic-related adverse events.

METHODS

Literature Search and Study Selection

We searched PubMed, the Cochrane Controlled Clinical Trials Register Database, the Cochrane Database of Reviews of Effectiveness, and the Web of Science for articles published January 1999 through July 2010 on AOM diagnosis, treatment outcomes, and association of PCV7 use with changes in AOM microbiology using Medical Subject Headings terms (eg, *otitis media*, *vaccines*), key words (eg, *diagnostic microbiology*, *therapy*), and individual antibiotic terms. This search supplemented a previous January 1966 through March 1999 search with additional key words for PCV7 and newer antibiotics.11 We performed reference mining of relevant systematic reviews.

We included articles in any language that studied children aged 4 weeks to 18 years. We excluded studies on children with immunodeficiencies and craniofacial anomalies. Systematic reviews, randomized controlled trials (RCTs), controlled clinical trials, and observational studies were included in the initial search; case reports, clinical overviews, editorials, and practice guidelines were excluded.

Observational studies were considered for the PCV7 and diagnostic questions but excluded for the treatment question. For the PCV7 question, only articles that assessed AOM microbiology (using middle ear fluid) both before and after PCV7 implementation were included. For the diagnostic question, we considered studies of children that performed independent comparisons of signs or symptoms with a clear criterion standard; studies using clinicians in training were excluded. For the antibiotic comparative effectiveness question, only studies that examined clinical improvement as an outcome (not just microbiologic findings) were included. The search strategy and inclusion/exclusion criteria are detailed elsewhere.19

Data Abstraction

Two investigators (T.R.C., M.A.L.) independently reviewed titles and abstracts for potentially relevant articles. They then independently abstracted data from the full-text articles using structured review forms that included inclusion/exclusion criteria, outcome measures, and study quality. Disagreements were resolved by consensus; the principal investigators (P.G.S., G.S.T.) resolved remaining disagreements. The study biostatistician abstracted data (verified by a clinician investigator) for pooled analyses. One investigator independently abstracted treatment-related adverse event data.

Quality Assessment

We used the Jadad criteria to assess RCT quality,15 AMSTAR16 to assess systematic review quality, and QUADAS17 to assess diagnostic study quality.

Data Synthesis

For diagnostic studies, we report summary data, including sensitivities and specificities, when available. The number of studies was insufficient to allow pooling of data across studies. Furthermore, the criterion standards for the diagnostic studies varied widely.

For studies examining the association between PCV7 use and changes in AOM microbial epidemiology, we report summary data; the studies were too few in number and lacked enough consistency across study design and population for pooled analysis.

For treatment studies, an adequate number of articles was identified for pooled analyses of some comparisons. Comparisons were grouped by individual antibiotics rather than by antibiotic class to maximize the clinical relevance of our findings. The only a priori exception was to group ampicillin with amoxicillin because of similarity. When 3 or more articles examined the same comparison, we used the DerSimonian and Laird random-effects model to pool rate differences across studies.18 Sensitivity analysis was performed for pooled significant findings. For pooled estimates, we report the I² statistic and P value for the χ² test of heterogeneity, which tests the null hypothesis that individual study results are homogeneous.19,20 I² values near 100% represent high degrees of heterogeneity. For assessment of publication bias in our pooled analyses, we report the Egger asymmetry test.

We used Stata version 10.0 to perform the meta-analyses.21 The study received a waiver of institutional review board review from the RAND Human Subjects Protection Committee.

RESULTS

The literature searches and reference mining yielded 8945 titles. After removal of duplicates and clearly irrelevant titles, 738 went for further review. After 2 rounds of screening, 55 articles were accepted and combined with 80 articles identified from the 2001 systematic review.11 These included 4 articles (3 research articles plus 1 systematic review) on diagnosis, 6 on PCV7-microbiology, and 125 on antibiotic treatment (FIGURE 1).

AOM Diagnosis

In clinical practice, 3 criteria are used to diagnose AOM: (1) acute symptoms of infection, (2) evidence of middle ear inflammation, and (3) presence of middle ear effusion (MEE).12 Published research focuses on what constitutes acute symptoms of infection and what physical findings are associated with middle ear inflammation or effusion. A challenge with
interpreting this research is the lack of a consistent gold standard, which varied from otolaryngologist-made diagnosis to tympanocentesis.

We identified 1 systematic review and 3 additional studies that addressed the question of diagnostic accuracy and precision in identifying any or all of the 3 criteria. Detailed data on these studies are available in our evidence report; findings suggest that certain otoscopic signs are strongly associated with AOM, while data on the importance of symptoms as a predictor of AOM are less convincing.

Symptoms. A 2003 review by Rothman et al found that ear pain (sensitivities: 54%, 60%, 100%; specificities: 82% and 92%; positive likelihood ratio [LR], 3.0 [95% confidence interval (CI), 2.1 to 4.3]; positive LR, 7.3 [95% CI, 4.4 to 12.1]) and ear rubbing (sensitivity: 42%; specificity: 87%; positive LR, 3.3 [95% CI, 2.1 to 5.1]) were modestly associated with AOM diagnosis. The review by Rothman et al included 4 studies examining specific symptoms among 965 total participants. In 2 of the studies, participants were recruited from otolaryngology practices and may not be representative of the general population of children with AOM. A more recent single study found that among 469 children aged 6 to 36 months presenting to primary care offices with parent-suspected AOM, AOM diagnosis was not associated with occurrence, duration, or severity of parent-reported symptoms (eg, ear rubbing, ear pain, fever). In another study subsequent to the review by Rothman et al, 22% of AOM cases diagnosed by a general practitioner were concurrently diagnosed by an otolaryngologist as otitis media with effusion, viral otitis, or a normal tympanic membrane.

PCV7 and AOM Microbial Epidemiology

Six studies examined the association between PCV7 use and changes in AOM microbial epidemiology (Table). These studies fit into 2 categories: observational studies of AOM isolates both before and after the 2000 licensure of PCV7 and PCV7 efficacy

**Table.** Studies Examining Association Between PCV7 Use and Changes in AOM Microbial Epidemiology

<table>
<thead>
<tr>
<th>Study</th>
<th>Reference</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takata et al.</td>
<td>11</td>
<td>Increased PCV7 coverage and decreased PCV7 serotype isolation.</td>
</tr>
<tr>
<td>Rothman et al.</td>
<td>5</td>
<td>Decreased serotype 1 serotype isolation.</td>
</tr>
</tbody>
</table>

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**Acute Otitis Media in Children**

RCTs examining AOM-related organisms.

Most studies found that *Haemophilus influenzae* became more prevalent as an AOM isolate and that *Streptococcus pneumoniae* became less prevalent although it remained important.\(^{30,31,33}\) In an observational study of children with persistent AOM or AOM with treatment failure, the proportion of *S pneumoniae* MEE isolates decreased (from 44% in 1998-2000 to 31% in 2001-2003, \(P = .02\)), while the proportion of *H influenzae* isolates increased (from 43% in 1998-2000 to 57% in 2001-2003, \(P = .01\)).

### Table. Studies of the Effects of Heptavalent Pneumococcal Conjugate Vaccine on Microbial Epidemiology of Acute Otitis Media

<table>
<thead>
<tr>
<th>Source</th>
<th>Age</th>
<th>Setting and Inclusive Years</th>
<th>Participants</th>
<th>Streptococcus pneumoniae</th>
<th>Haemophilus influenzae</th>
<th>All Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort studies</td>
<td></td>
<td></td>
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<tr>
<td>Block et al</td>
<td>7-24 mo</td>
<td>Pediatric practice, United States, 1992-1998 and 2000-2003</td>
<td>379 patients with severe or refractory AOM 1992-1996: n = 336 isolates 2000-2003: n = 83 isolates For serotype analysis: 1992-1996: n = 132 <em>S pneumoniae</em> isolates 2000-2003: n = 22 <em>S pneumoniae</em> isolates</td>
<td>31% vs 48% ((P = .007)) PCV7 serotypes: 36% vs 70% ((P = .005)) Non-PCV7 serotypes: 22% vs 23% PCV7-related serotypes: 32% vs 8% ((P = .005))</td>
<td>56% vs 41% ((P = .01)) PCV7 serotypes: 52% vs 76% ((P &lt; .01)) Non-PCV7 serotypes: 32% vs 12% ((P &lt; .01)) PCV-related serotypes: 13% vs 10% P values are trend over time, 1999-2002 Only <em>S pneumoniae</em> examined Only <em>S pneumoniae</em> examined</td>
<td></td>
</tr>
<tr>
<td>McEllistrem et al</td>
<td>Not reported</td>
<td>S hospitals in the United States, 1999-2002</td>
<td>505 isolates (No. of children not specified) 1999: n = 162 isolates 2000: n = 126 isolates 2001: n = 115 isolates 2002: n = 82 isolates</td>
<td>2002 vs 1999: PCV7 serotypes: 52% vs 76% ((P &lt; .01)) Non-PCV7 serotypes: 32% vs 12% ((P &lt; .01)) PCV-related serotypes: 13% vs 10% P values are trend over time, 1999-2002 Only <em>S pneumoniae</em> examined Only <em>S pneumoniae</em> examined</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brook and Gober</td>
<td>5 mo-12 y</td>
<td>Outpatient practice, United States, 1993-1998 and 2001-2006</td>
<td>100 patients with AOM with new spontaneous perforation 1992-1998: n = 61 isolates 2001-2006: n = 63 isolates</td>
<td>44% vs 54% Serotypes not reported</td>
<td>24% vs 18% MSSA: 8% vs 8% MRSA: 10% vs 0% ((P &lt; .05))</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Randomized controlled trials</th>
<th>Age</th>
<th>Setting and Inclusive Years</th>
<th>Participants</th>
<th>Streptococcus pneumoniae</th>
<th>Haemophilus influenzae</th>
<th>All Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eskola et al</td>
<td>Infants &lt; 2 mo</td>
<td>8 clinics in Finland, 1995-1999</td>
<td>1662 (with 2596 episodes of AOM) Vaccine group: n = 1177 AOM episodes with confirmed MEF Control group: n = 1267 AOM episodes with confirmed MEF For serotype analysis: Vaccine group: n = 271 <em>S pneumoniae</em> isolates Control group: n = 414 <em>S pneumoniae</em> isolates</td>
<td>23% vs 33% ((P &lt; .001)) PCV7 serotype: 40% vs 60% ((P &lt; .001)) Non-PCV7 serotype: 46% vs 23% ((P &lt; .001)) PCV-related serotype: 15% vs 20%</td>
<td>27% vs 23% ((P = .02)) PCV7 serotype: 40% vs 60% ((P &lt; .001)) Non-PCV7 serotype: 46% vs 23% ((P &lt; .001)) PCV-related serotype: 15% vs 20% M catarrhalis: 32% vs 30%</td>
<td></td>
</tr>
<tr>
<td>Veenhoven et al</td>
<td>12-84 mo</td>
<td>2 hospitals in the Netherlands, 1998-2002</td>
<td>383 patients with recurrent AOM; 181 with MEF samples Vaccine group: n = 60 AOM episodes with culture-positive MEF Control group: n = 54 AOM episodes with culture-positive MEF For serotype analysis: Vaccine group: n = 13 <em>S pneumoniae</em> isolates Control group: n = 19 <em>S pneumoniae</em> isolates</td>
<td>22% vs 35% Serotype analysis: PCV7 serotype: 31% vs 42% Non-PCV7 serotype: 70% vs 58% PCV-related serotype: not reported</td>
<td>35% vs 43% Staphylococcus aureus: 34% vs 17% ((P = .004)) Group A S aureus: 10% vs 7%</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: MEF, middle ear fluid; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; PCV7, heptavalent pneumococcal conjugate vaccine.

\(^a\)P values are provided for comparisons with \(P < .05\).
2001-2003, \( P = .01 \). Another study found an increase (as a proportion of all \( S \) \( pneumoniae \) isolates) in nonvaccine serotype \( S \) \( pneumoniae \) and a decrease in vaccine serotype \( S \) \( pneumoniae \) (non-PCV7 \( S \) \( pneumoniae \) from 12% in 1999 to 32% in 2002, \( P < .01 \)). In a vaccine-efficacy RCT, investigators found a greater proportion of \( S \) \( pneumoniae \) isolates in the control group (33%) than in the PCV7 group (23%) \( (P < .001) \). It is important to note that study findings did not always reach statistical significance, and most studies focused on patients with severe or persistent AOM.

**Antibiotics for Uncomplicated AOM**

One hundred twenty-five articles compared the effectiveness of antibiotic treatment options in uncomplicated AOM. Older articles that examined antibiotics no longer typically used for AOM are not discussed here but are included in the evidence reports.14,36

**Benefits of Antibiotic Treatment**

Evidence about the benefits of treating with antibiotics comes from 2 types of studies: placebo-controlled studies of immediate use of antibiotics and studies comparing immediate use of antibiotics with a strategy of observation with possible delayed treatment (“wait-and-see” or “prescription-to-hold”).

**Ampicillin or Amoxicillin vs Placebo**

We identified 8 studies that compared ampicillin or amoxicillin with placebo. One did not report clinical success (only pain resolution) and was not included in the pooled analysis.37

In pooled analysis of the remaining 7 RCTs, the random-effects pooled rate difference for success by day 14 was estimated at 12% (95% CI, 5% to 18%), with a 73% success rate for ampicillin/amoxicillin and a 60% success rate for placebo. The number needed to treat \((NNT)\) for clinical success was 9 (95% CI, 0 to 9) \( (P < .001) \). It is important to note that study findings did not always reach statistical significance, and most studies focused on patients with severe or persistent AOM.

**Other Antibiotics vs Placebo**

We identified 5 studies that compared other antibiotics with placebo \( (eTable 1) \), but they are not included in pooled analysis because we examined the overall benefit of antibiotics more commonly prescribed for AOM \( (ie, \ amoxicillin) \) over placebo.

**Immediate vs Delayed Antibiotics**

We identified 4 studies of delayed treatment approaches; 2 reported higher rates of clinical success with immediate compared with delayed use of antibiotics.45,46 and 2 found no difference.47,48 One article reported rates of 95% vs 80% \( (rate\ difference, 15% [95\% CI, 6% to 24%]; \ NNT, 7 [95\% CI, 4 to 17]) favoring amoxicillin over the wait-and-see approach for parent-perceived success at day 12,49 whereas the other reported rates of 86% vs 70% \( (rate\ difference, 16% [95\% CI, 6% to 26%]; \ NNT, 6 [95\% CI, 4 to 17]) \), also favoring amoxicillin over the prescription-to-hold approach for parent-perceived clinical success at day 3.45 Thirty-four percent46 and 24%48 of participants in the delayed antibiotic groups in these studies received delayed antibiotics, respectively.

**Short-term Harms of Antibiotic Treatment**

The risk of harms from antibiotic treatment for AOM has been less well studi-
ied than the benefits. Four of the 7 placebo-controlled studies reported on harms. One reported the counterintuitive, although not statistically significant, result of more cases of rash and diarrhea in placebo-treated patients than in amoxicillin-treated patients.44 Pooled analysis of the other 3 trials yielded rates of 13% vs 8% for diarrhea (pooled rate difference, 5% [95% CI, 0% to 10%]; I² = 23%; P = .30), while 2 individual studies had a rate difference of 4% (4% vs 0%) and 3% (8% vs 5%) for rash; these differences did not reach statistical significance. These point estimates are compatible with published estimates of the rate of rash (3%-10%) and diarrhea (5%-10%).50-53 In the studies by Little et al45 and Spiro et al., the rate of diarrhea was higher for the antibiotic group than for the prescription-to-hold group (19% vs 9%; rate difference, 10% [95% CI, 2% to 18%]) and 23% vs 8%; rate difference, 14% [95% CI, 6% to 22%] for the 2 studies, respectively), with a number needed to harm (NNH) of 10 (95% CI, 6 to 50) and 7 (95% CI, 5 to 17), respectively.54McCormick et al64 reported no difference in the rate of antibiotic-related adverse events, and Neumark et al65 did not examine adverse events. In RCTs comparing amoxicillin with other antibiotics, the proportion of amoxicillin-treated children reporting rash ranged from 2% to 11% and the proportion reporting diarrhea ranged from 3% to 16%.54-60

Long-term Harms of Antibiotic Treatment

None of the studies evaluated the rates of longer-term adverse effects of immediate antibiotic treatment, including antibiotic resistance.

Antibiotic Comparative Effectiveness
eTable 2 describes selected antibiotic comparative effectiveness studies and pooled analyses for comparisons examining 3 or more studies. The Egger test was not suggestive of publication bias for any of the pooled analyses.

The success rate differences were statistically nonsignificant in the pooled analyses comparing ampicillin/amoxicillin vs ceftriaxone (4 trials, F = 50.7%), ampicillin/amoxicillin vs cefixime (4 trials, F = 22.9%), ampicillin/amoxicillin vs cefaclor (4 trials, F = 13.0%), amoxicillin-clavulanate vs ceftriaxone (5 trials, F = 22.9%), cefaclor vs azithromycin (3 trials, F = 0%), and amoxicillin-clavulanate vs 5 days of azithromycin (5 trials, F = 62.2%) and vs 3 or fewer days of azithromycin (7 trials, F = 84.1%).

Statistically significant differences between treatment regimens were found in a few individual studies. Amoxicillin-clavulanate was superior to cefaclor (97% vs 84%; rate difference, 13% [95% CI, 5% to 21%]);10; 10 days of amoxicillin-clavulanate was superior to 5 days of azithromycin (86% vs 70%; rate difference, 16% [95% CI, 2% to 30%])62; 5 days of amoxicillin-clavulanate was not as effective as 7 to 10 days (77% vs 88%; rate difference, −11% [95% CI, −20% to −3%] in the study by Cohen et al63 and 71% vs 87%; rate difference, −16% [95% CI, −24% to −8%] in the study by Hoberman et al64); and 5 days of cefitubut was not as effective as 10 days of cefitubutin (78% vs 98%; rate difference, −20% [95% CI, −28% to −12%]).55

Antibiotic-Related Adverse Events

In the pooled comparisons, use of ampicillin/amoxicillin resulted in a lower rate of diarrhea than cefixime (14% vs 21%; rate difference, −8% [95% CI, −13% to −4%]; NNH, 12 [95% CI, 8 to 25]; I² = 0%), and use of amoxicillin-clavulanate resulted in a higher rate of diarrhea than 1 dose of ceftriaxone (20% vs 9%; rate difference, 11% [95% CI, 7% to 16%]; NNH, 9 [95% CI, 6 to 15]; I² = 10.8%) and higher rates of any adverse event compared with 5 days of azithromycin (26% vs 9%; rate difference, 16% [95% CI, 7% to 25%]; NNH, 6 [95% CI, 4 to 14]; I² = 81.9%).

COMMENT

We identified several important findings for AOM diagnosis, microbiology, and antibiotic management.
superiority of any other antibiotic over amoxicillin.

In most cases of uncomplicated AOM when amoxicillin is appropriate (eg, excluding children with penicillin allergy and those who previously did not improve after a course of amoxicillin), there is no evidence for first-line use of higher-cost antibiotics (eg, cefdinir, cefixime). For a 20-kg child with AOM, a 7-day course of cefdinir costs approximately $96, compared with $34 for an equivalent course of amoxicillin (pricing information available at http://www.drugstore.com). In an analysis of data from the National Ambulatory Medical Care Survey, among visits for AOM (visits for a new problem without additional diagnoses requiring antibiotic therapy), amoxicillin was prescribed in 49%, amoxicillin-clavulanate in 16%, cefdinir in 14%, and other cephalosporins in 6%.13 If just half of the 14% of the estimated 8 million children who visit a physician for AOM annually were to receive amoxicillin instead of cefdinir (assuming the other half were appropriately prescribed cefdinir because of a non–type-1 penicillin allergy), the estimated annual savings would exceed $34 million. This estimate does not account for potential additional savings from adopting a less aggressive approach to antibiotic prescribing that might avoid a certain number of prescriptions altogether.

This review has several limitations that must be considered. First, article screening and data abstraction were not blinded, which may potentially introduce bias. However, there is evidence that blinding does not alter the results of meta-analyses.68 Second, we may not have identified some relevant evidence. For example, we did not search EMBASE or seek unpublished data. We used statistical tools to detect publication bias but found no evidence of it in our pooled analyses. Additionally, our findings on diagnosis and microbiology are greatly limited by the small number of studies; thus, caution should be used in interpreting our findings for these topics. To account for variation in study quality, we performed sensitivity analyses that pooled only high-quality studies. Third, the studies varied widely in their definitions of clinical success and in AOM diagnostic criteria. Some studies that did not use all 3 AOM diagnostic criteria may have included participants without AOM but with otitis media with effusion or no middle-ear abnormality at all.99,70 Lastly, our pooled analyses included studies completed before and after the licensing of PCV7. It is not clear how the changing microbiology of AOM may have influenced study findings; the heterogeneity of AOM over the past 20 years might favor an analysis that does not include pooling data from studies before and after 2000.90

One remaining question is what new evidence about antibiotic comparative effectiveness is needed. It is not enough to show statistical significance or lack thereof; the clinical importance of any difference must also be considered. This requires knowing the minimal clinically important difference (MCID) for treatment of AOM. Although there currently is no agreed-on value for the MCID, assuming an MCID of 5% (representing a “small” effect size, according to Cohen’s classification71) means that when existing evidence falls entirely within or outside of this MCID, equivalence or significance can be concluded; when it does not, it can be concluded that more information is needed. Using this definition, we can conclude equivalence for 2 of the 8 pooled analyses in eTable 2 and that effects are inconclusive for the remaining 6. The MCID has important implications for our conclusions; for example, in contrast to a previous systematic review,7 we are unable to make definitive conclusions regarding the equivalency of short- vs long-term regimens analyzed by antibiotic when considering an MCID of 5%, except for 7 to 10 days of cefaclor vs 3 days of azithromycin.

To account for both statistical and clinical significance, sample sizes for AOM comparative effectiveness studies need to be large. Because approximately 80% of AOM cases resolve spontaneously,67 most RCTs will be able to test superiority of different antibiotics with only the remaining 20%. If the success rate is 88% for the treatment group and 80% for the control group, a sample size of 1150 per group would provide a 95% CI of the difference of 5% to 11%, which is outside the ±5% MCID; this sample size is much larger than that of any published AOM comparative effectiveness study.

CONCLUSIONS

We found evidence to guide the diagnosis and management of AOM in children; however, further research is needed that (1) examines clinicians’ diagnostic accuracy and precision using the 3 AOM diagnostic criteria; (2) continues surveillance of AOM microbiology, especially in view of the newly approved PCV13; and (3) produces more high-quality studies on AOM management that include clear diagnostic criteria, a better-defined menu of clinical success measures that are universally applied, and more investigation into the comparative antibiotic-related adverse event rates that assesses whether any antibiotic regimen is superior to amoxicillin.

Author Contributions: Dr Shekelle had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Coker, Chan, Shekelle, Takata.

Acquisition of data: Coker, Chan, Newberry, Limbos, Takata.

Analysis and interpretation of data: Coker, Chan, Newberry, Limbos, Suttorp, Shekelle, Takata.

Drafting of the manuscript: Coker, Chan, Shekelle, Takata.

Critical revision of the manuscript for important intellectual content: Coker, Chan, Newberry, Limbos, Suttorp, Shekelle, Takata.

Statistical analysis: Chan, Suttorp.

 Obtained funding: Shekelle.

Administrative, technical, or material support: Newberry.

Study supervision: Shekelle, Takata.

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the collection, management, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

Disclaimer: The authors of this article are responsible for its contents. No statement in this article should be construed as an official position of the AHRQ or the US Department of Health and Human Services.


Additional Contributors: Roberta Shanman, MLS (RAND Library), conducted the literature searches.

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AneesA Motala, BA, and Breanne Johnsen, BS (EPC, RAND Health), conducted the literature searches.

AHRQ. Aneesa Motala, BA, and Breanne Johnsen, BS (EPC, RAND Health), conducted the literature searches.

JAMA. Aneesa Motala, BA, and Breanne Johnsen, BS (EPC, RAND Health), conducted the literature searches.


22. Stata. Measuring inconsistency in meta-analyses.


The educator is like a good gardener, whose function is to make available healthy, fertile soil in which a young plant can grow strong roots; through these it will extract the nutrients it requires. The young plant will develop in accordance with its own laws of being, which are far more subtle than any human can fathom, and will develop best when it has the greatest possible freedom to choose exactly the nutrients it needs.

—E. F. Schumacher (1911-1977)