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A Cost-Utility Analysis of 5 Strategies for the Management of Acute Otitis Media in Children

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Objective To assess whether antimicrobial therapy in young children with acute otitis media reduces time to resolution of symptoms, overall symptom burden, and persistence of otoscopic evidence of infection. We used a cost-utility model to evaluate whether immediate antimicrobial treatment seems to be worthwhile, and if so, which antimicrobial agent is most cost effective.

Study design We compared the cost per quality-adjusted life-day of 5 treatment regimens in children younger than 2 years of age with acute otitis media: immediate amoxicillin/clavulanate, immediate amoxicillin, immediate cefdinir, watchful waiting, and delayed prescription (DP) for antibiotic.

Results The 5 treatment regimens, listed in order from least effective to most effective were DP, watchful waiting, immediate cefdinir, immediate amoxicillin, and immediate amoxicillin/clavulanate. Listed in order from least costly to most costly, the regimens were DP, immediate amoxicillin, watchful waiting, immediate amoxicillin/clavulanate, and immediate cefdinir. The incremental cost-utility ratio of immediate amoxicillin compared with DP was $101.07 per quality-adjusted life-day gained. The incremental cost-utility ratio of immediate amoxicillin/clavulanate compared with amoxicillin was $2331.28 per quality-adjusted life-day gained.

Conclusions In children younger than 2 years of age with acute otitis media and no recent antibiotic exposure, immediate amoxicillin seems to be the most cost-effective initial treatment. *(J Pediatr 2017;189:54-60).*

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Acute otitis media (AOM) is the most frequent reason that children in the United States receive antimicrobial therapy. Evidence from 2 recent randomized, placebo-controlled clinical trials in young children diagnosed with AOM using stringent criteria indicates that antimicrobial therapy compared with watchful waiting (WW) results in faster symptomatic relief, lower rates of treatment failure, and lesser persistence of otoscopic evidence of infection.[1,2] Nonetheless, the question remains whether risks and costs of antimicrobial therapy, particularly in children younger than 2 years of age, outweigh its benefits. The lack of clarity results in part from difficulties in integrating respective benefits and harms of the various available therapies. For example, 1 study compared children 6 months to 10 years of age receiving a delayed prescription (DP) for antibiotic, mainly amoxicillin, which parents could fill after 72 hours if children failed to improve, with children receiving immediate antimicrobials, albeit at lower dose than currently recommended in the United States. The latter group had, on average, 1.1 fewer days of illness and 0.72 fewer nights with disturbed sleep, but twice as much diarrhea.[3]

Accordingly, it seemed worthwhile to analyze available data systematically in an effort to determine whether immediate antimicrobial treatment seems justified and, if so, which antimicrobial agent is most cost effective. A cost-utility analysis is particularly well-suited for this task because all outcomes, whether positive, such as reduction of symptoms, or negative, such as diarrhea, can be combined into a single metric, namely, quality-adjusted life-days (QALDs) accrued, which can be compared across treatment options.

Accordingly, we constructed a decision-analytic model to compare the cost effectiveness of 5 frequently used options for managing children with AOM. We also explored the impact of inaccurate diagnosis on the relative cost effectiveness of these treatment options.

AOM	Acute otitis media
AOM-SOS scale	Acute Otitis Media Severity of Symptom Scale
DP	Delayed prescription
ICER	Incremental cost-effectiveness ratio
QALD	Quality-adjusted life-day
WW	Watchful waiting

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Methods

We compared the clinical and economic outcomes of 5 treatment strategies in a hypothetical cohort of symptomatic children younger than 2 years of age who were diagnosed with AOM, based on symptoms and otoscopic findings. As recommended by the Panel on Cost-Effectiveness in Health and Medicine,[4] we adopted a societal perspective and included both direct and indirect medical costs in our model. We do, however, also report results from the payer's perspective (ie, including only direct medical costs).[5] We constructed and analyzed our decision tree using TreeAge Pro software (TreeAge, Williamstown, Massachusetts).

We set a time horizon of 30 days because most of the benefits and harms attributable to an episode of AOM occur within this period, and because previous studies have failed to find an association between treatment modality and incidence of late (beyond 30 days) recurrences of AOM.[6-8]

We compared 5 treatment strategies: immediate amoxicillin/clavulanate (90/6.4 mg/kg/day for 10 days), immediate amoxicillin (90 mg/kg/day for 10 days), immediate cefdinir (14 mg/kg/day for 10 days), WW, and DP. Parents of children in the DP group would be given a prescription for amoxicillin as rescue treatment that could be filled if their children's symptoms did not improve as quickly as the parents had expected. Parents of children in all other groups would be asked to return for an office visit if their children were not improving.

The **Figure** (available at www.jpeds.com) shows the structure of the decision tree. For each of the other 4 treatment strategies, we considered 3 possible outcomes within the first 7 days: improved symptoms, persistent symptoms, or mastoiditis. Children in whom symptoms had improved satisfactorily would continue on the initially prescribed treatment regimen, and would be reevaluated only if symptoms recurred within 30 days. Children would be categorized as having persistent symptoms if they experienced any of the following during the initial 7 days of therapy: worsening or lack of improvement in scores on the Acute Otitis Media Severity of Symptom Scale (AOM-SOS),[7-9] otorrhea associated with perforation of the tympanic membrane, or hospitalization for an otitis-related reason other than mastoiditis. In all branches except for the DP branch, such children would be reevaluated; those with evidence of continuing infection on examination would be categorized as having early clinical failure and would be prescribed rescue antimicrobial therapy, consisting of amoxicillin, or in children for whom amoxicillin or amoxicillin/clavulanate had been initially prescribed, amoxicillin/clavulanate. Children with persistent symptoms but without evidence of continuing infection would be categorized as having early clinical success and would continue to be managed according to the original treatment strategy. In the DP branch, children whose symptoms failed to improve within 48 hours of diagnosis were assumed to have been started on antimicrobial therapy without the need for a consultation; those whose symptoms continued to persist would be reevaluated by a clinician. Children with acute mastoiditis would be evaluated initially in the office, then hospitalized and receive intravenous antimicrobial therapy for an average of 3.2 days.[9] After discharge, they would receive antimicrobial therapy orally for 30 days.[10]

Children experiencing a second episode of AOM during the 30-day analytic period would be treated with amoxicillin/clavulanate if the children had received antimicrobial therapy initially, and with amoxicillin if they had not, for 10 days. Because few children would be expected to experience more than 3 episodes of AOM within a 30-day period, we modeled a maximum of 3 episodes. We did not consider complications of AOM other than acute mastoiditis because such complications are rare. In **Table I**, the probabilities of outcomes in relation to the various treatment strategies considered in the decision-analytic model are summarized.

Table I. Conditional probabilities of outcomes in relation to treatment strategies used in the cost-utility model

	Designated initial treatment strategy				
	DP	Immediate amoxicillin	WW	Immediate amoxicillin/clavulanate	Immediate cefdinir
Treatment outcomes*	Probability (%) of outcome occurrence (range used in the model)				
Persistent symptoms days 1-7	45 (37-53)	32 (24-40)†	45 (37-53)	29 (21-37)	34 (26-42)†
Early clinical failure days 1-7	100	16 (5-27)†	37 (25-49)	11 (1-21)	20 (8-32)†
AOM recurrence days 8-30	27 (16-38)	26 (0-59)†	27 (9-45)	25 (0-66)	26 (0-54)†
Early clinical success days 1-7	0	84 (73-95)†	63 (51-75)	89 (79-99)	80 (68-92)†
AOM recurrence days 8-30	0	16 (4-28)†	21 (8-34)	15 (3-27)	17 (5-29)†
Improved symptoms days 1-7	55 (47-63)	68 (60-76)†	55 (47-63)	71 (63-79)	66 (58-74)†
AOM recurrence days 8-30	12 (5-19)	5 (1-9)†	12 (5-19)	4 (0-8)	6 (1-11)†
Mastoiditis§	0.038 (0.032-0.044)	0.018 (0.015-0.021)	0.038 (0.032-0.044)	.018 (.015-.021)	.018 (.015-.021)
Diarrhea	12 (7-15)‡	18 (12-24)¶	5 (2-8)	24 (17-31)	11 (9-13)¶
Diaper rash¶	4 (0-10)‡	6 (1-15)**	2 (0-6)	11 (6-17)	5 (2-8)
Body rash¶	3 (1-4)‡	3 (2-4)**	3 (1-4)	5 (3-6)	1 (0-2)

*All data based on Hoberman et al 2011[2] unless otherwise indicated.
†Calculated using bacteriologic efficacy (see **Appendix**; available at www.jpeds.com).
‡Calculated from WW branch considering the proportion of children who would have received antimicrobials.
§From Thompson et al.[11]
¶We systematically reviewed available studies and, if multiple studies were available, used meta-analysis to arrive at these pooled estimates.
**Because of the paucity of data, we used data from studies of both low and high-dose amoxicillin.