POEMs

Patient-Oriented Evidence that Matters

Each month, the POEMs editorial team reviews over 90 journals of interest to primary care physicians, identifying the articles you have to know about to stay up to date. We call these articles POEMs (Patient-Oriented Evidence that Matters) because they deal with common primary care problems, report outcomes that matter to patients, and have the potential to change the way we practice. The eight most important articles are critically apprised each month by a team of over 50 reviewers who make a recommendation for clinical practice. The collected reviews of the POEMs are available at the Journal's World Wide Web site at http://jfp.msu.edu

Diagnosing Congestive Heart Failure

Reference Davie AP, Caruana FL, Sutherland GR, McMurray JJV. Assessing diagnosis in heart failure: which features are any use Q J Med 1997; 90:335-9.

Clinical question **Which clinical features correlate most closely with echocardiographic findings of left ventricular systolic dysfunction?**

Background Clinical diagnosis of left ventricular systolic dysfunction (LVSD) is challenging, and no inexpensive and accessible screening test is available. This study examines the relationship of clinical findings to the presence or absence of significant LVSD.

Population studied The population consisted of 259 adult British patients with suspected congestive heart failure. All had been referred by their general practitioner to assess whether they would be candidates for treatment with an ACE inhibitor.

Study design and validity Each patient had a full history, including past medical history, medications, and symptoms. One author examined all 259 patients. Each patient then underwent echocardiography, which was evaluated by a cardiologist blinded to the clinical data. Use of a single physical examiner may make the value of physical findings in this study more reflective of his examination skills than those of the population of clinicians at large. Many patients were previously treated, and may have had altered findings due to empiric trial of medications; whether this makes the population of this study more or less similar to patients suspected of LVSD found in most generalist practices is unclear. The value of clinical findings may be underestimated, since this referral population might reflect selection bias toward unusually difficult diagnostic dilemmas; however, it might be overestimated if only patients with more severe symptoms were referred.

Outcomes measured The 29 elements of clinical data gathered included eight elements of past medical history, eight potential medications, four symptoms, and nine physical signs. LVSD was defined as fractional shortening less than 25% by echocardiography, or if systolic function was "significantly impaired" when quantitative measures were unobtainable.

Results The echocardiogram revealed LVSD in 41 of the 259 (16%) patients. Of the 29 clinical features assessed, only four were present in more than one half of the referral group (59% smoked cigarettes, 61% were taking diuretics, 86% were dyspneic on exertion, and 52% had lower-extremity edema).

We calculated likelihood ratios (LR) from the sensitivities and specificities presented in the article. Absence of dyspnea on exertion effectively ruled out the diagnosis (LR- 0.03), while an S3 gallop (LR+ 24.0) and a displaced apex (LR+ 16.5) strongly supported the diagnosis of LVSD. The presence of jugular venous distension (JVD, LR+ 8.5), a history of diabetes mellitus (LR+ 6.0), and a history of myocardial infarction (MI, LR+ 4.2) were also associated with LVSD. Given the pretest probability of 16% in this study of LVSD, the positive predictive value for LVSD of JVD was 64%, S3 gallop was 77%, and displaced cardiac apex was 75%. The combination of a prior MI and displaced cardiac apex had a positive predictive value of 89%.

Recommendations for clinical practice **This study confirms the difficulty that primary care providers have in diagnosing LVSD based on history and physical examination alone; in the current study, only 16% of the patients in whom it was suspected had significant LVSD by echocardiographic criteria. The clinical features that best ruled-in LVSD were an S3 gallop, a displaced cardiac apex, a history of diabetes mellitus or MI, and JVD. Finding a displaced apical impulse was especially useful, and is a diagnostic skill that is often neglected in a busy setting. Absence of dyspnea on exertion effectively rules out LVSD.**

These results are consistent with the 1994 AHCPR clinical guidelines on LVSD.[1] These guidelines noted that the presence of elevated jugular venous pressure, a third heart sound, and laterally displaced apical impulse are "virtually diagnostic in patients with compatible symptoms," while the sensitivity and specificity of other clinical features have not proven sufficient to establish the diagnosis. However, given the low prevalence of the disease in a population in which it is suspected, the

expense associated with therapy, and the implications of misdiagnosis of LVSD, diagnosis based on clinical grounds alone is usually not warranted.

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Reference

1. Konstam M, Dracup K, Baker D, et al. Heart failure: evaluation and care of patients with left-ventricular systolic dysfunction. Clinical practice guideline No. 11. AHCPR publication No. 94-0612. Rockville, Md: Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services, June 1994.

Management of PROM at Term

Reference Mozurekewich EL, Wolf FM. Premature rupture of membranes at term: a meta-analysis of three management strategies. Obstet Gynecol 1997; 89:1035-43.

Clinical question **Does immediate induction of labor for premature rupture of the fetal membranes (PROM) at term improve maternal and neonatal outcomes compared with conservative management?**

Background Rupture of the fetal membranes before the onset of labor occurs in about 10% of pregnancies at term; 90% of these women will be in spontaneous labor by 24 hours after rupture.[1] Numerous small trials and several randomized clinical trials offer conflicting recommendations for the optimal management of PROM. Early induction appears to be associated with an increased rate of cesarean section, while expectant management may result in increased maternal and neonatal infectious morbidity.

Population studied Twenty-three randomized clinical trials (RCTs) examining the management of women with PROM at term (36 or more weeks' gestation) by immediate oxytocin induction, conservative management, or intervention with prostaglandin E_2 were identified. Authors performed a MEDLINE search, cross-checked reference lists, and identified studies from the Controlled Trials Register of the Cochrane Collaboration.

Study design and validity For this meta-analysis, trial results were combined appropriately using the DerSimonian and Laird (random-effects) technique to estimate pooled odds ratios (OR). Where findings between studies were similar (homogeneous), they were confirmed using the Mantel-Haenszel (fixed-effects) pooled OR. Three comparisons were made: immediate oxytocin vs conservative management; immediate prostaglandin use vs conservative management; and immediate prostaglandin use vs immediate oxytocin. Subgroup analyses based on the absence of a digital examination before randomization or an unfavorable cervix (Bishop score 4 or less) were also conducted. Using the above search scheme, it is unlikely that any RCTs were overlooked. The explicit criteria used for serious neonatal infection lend confidence to the validity of this study. However, the use of clinical criteria for the maternal infectious outcomes is poor, and reporting was not uniform or blinded to treatment group. There was also no apparent control for the duration of ruptured membranes prior to hospital arrival, the number of vaginal examinations, or the use of intrapartum antibiotics. In addition, the definition of immediate and late induction varied considerably across studies. Finally, the inclusion of the one large RCT may have overwhelmed the results of the pooled analysis for chorioamnionitis.

Outcomes measured The four outcomes examined were cesarean birth, chorioamnionitis (clinical diagnosis), endometritis (requiring clinical management), and serious neonatal infection (defined as culture-proven neonatal septicemia, meningitis, or pneumonia).

Results A total number of 7493 subjects were pooled across the trials. There were no significant differences in cesarean section rates (10.5 % and 9.1 % for oxytocin induction and conservative treatment, respectively). While there was no significant difference in the rate of clinical chorioamnionitis between the immediate oxytocin and conservative management strategies, a significant reduction in chorioamnionitis was found for the immediate use of vaginal prostaglandin compared with conservative management (5.6% vs 8.1%, OR = 0.68, 95% CI 0.51 to 0.91). An increase in chorioamnionitis between the immediate use of vaginal prostaglandin compared with oxytocin (6% vs 4%, OR = 1.55, 95% CI 1.09 to 2.21) was also noted. There was a small, but significant reduction in postpartum endometritis between the oxytocin and conservative management groups (3.2% vs 4.4%, OR = 0.71, 95% CI 0.51 to 0.99) but not for the other two comparisons. There were no differences between management strategies for serious neonatal infections. Subgroup analyses failed to show differences between management strategies with the exception of more cases of endometritis in the immediate induction group compared with conservative management for women undergoing no digital examinations prior to randomization (OR = 2.8, 95% CI 1.02 to 7.7).

Recommendation for clinical practice **The decision to proceed with immediate induction rather than conservative management (with induction of labor at some time beyond 24 hours) in otherwise healthy women with PROM is best made with the**

woman or couple after discussing the risks and benefits of these approaches. Benefits of early induction appear to include a shorter time to delivery and possibly a lower risk of maternal infection. If the rate of chorioamnionitis is reduced from 8% to 6%, 50 women would have to be treated to prevent one case of chorioamnionitis. This infection, however, results in neonatal infection in only 10% to 20% of neonates.[2] The rate of chorioamnionitis reported here is also higher than in most studies reported in the literature (range 0.5% to 4%).[2] The risks of early induction include a possible increase in cesarean deliveries and exposure to oxytocin. The role of prostaglandin in reducing the risk of cesarean delivery, particularly among women with unfavorable cervices, is not clear but appears safe.

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Management of Outpatients with Dyspepsia

Reference Ebell MH, Warbasse L, Brenner C. Evaluation of the dyspeptic patient: a cost-utility study. J Fam Pract 1997; 44:545-55.

Clinical question. **Which is the most cost-effective management strategy for outpatients with symptoms of dyspepsia?**

Background Family physicians often manage dyspeptic outpatients with a therapeutic trial of antisecretory therapy, and resort to diagnostic testing only upon failure of empiric therapy. Now that *Helicobacter pylori* has been shown to have a causative role in peptic ulcer disease and gastritis, should our management strategy change to include either a workup for *H pylori* or empiric therapy to eradicate *H pylori*?

Population studied The investigators studied a hypothetical adult patient who presents to an outpatient primary care setting for evaluation of dyspepsia (defined as intermittent pain of at least 2 weeks' duration from an upper gastrointestinal cause, typically associated with gas, belching, bloating, and nausea). They excluded patients with signs of complications (eg, bleeding, perforation, or obstruction).

Study design and validity A cost-utility analysis is a type of cost-effectiveness analysis that compares the costs and consequences of alternative management strategies. Seven possible management strategies were modeled in this study: empiric antisecretory therapy (omeprazole 20 mg daily for 4 weeks), empiric *H pylori* triple therapy (clarithromycin 500 mg twice daily, amoxicillin 1000 mg twice daily, and omeprazole 20 mg twice daily for 1 week), a serum *H pylori* titer and eradication therapy if positive, upper endoscopy or upper GI followed by empiric therapy if an ulcer is present, and upper endoscopy or upper GI followed by a serum *H pylori* titer and eradication therapy if positive. The authors assumed that *H pylori* therapy is ineffective for non-ulcer dyspepsia (eg, gastritis). They valued a 4-week course of omeprazole at $108, a course of eradication therapy at $126, an upper GI at $300, and an endoscopy at $1000. They also included in their model costs for morbidities associated with treatment and with complications of untreated peptic ulcers.

Cost-effectiveness analyses are always limited by uncertainty in their baseline assumptions. The authors clearly define alternative courses of action and the assumptions made in the model, and appropriately vary many of the key assumptions to see if the results change. Ultimately, though, there is no way of knowing to what extent the results might differ if the baseline assumptions are wrong.

Outcomes measured The primary outcome was the cost per quality-adjusted life year (QALY). Secondary outcomes were the cost per case of dyspepsia, and clinical morbidity over a 1-year period. The costs were assumed to be those of a third-party payer.

Results This study suggests that three strategies are nearly equal in cost and cost per QALY: empiric *H pylori* therapy, obtaining a serum *H pylori* titer and treating if positive, and empiric omeprazole antisecretory therapy. Each of these therapies costs less than $1300 per patient over the hypothetical 1-year period. However, the model suggested that empiric omeprazole therapy leads to higher morbidity and mortality than the other two options. The long-term adverse consequences of antibiotic resistance are a concern, and empiric *H pylori* therapy is likely to increase antibiotic resistance. The strategies, which included upper endoscopy or upper GI, were all more expensive, costing up to $2100. Varying the baseline assumptions of costs and complication rates (sensitivity analyses) did not lead to a change in the preferred strategies (they were *robust*).

Recommendations for clinical practice **Given the current evidence, clinicians treating patients with uncomplicated dyspepsia (ie, with no evidence of bleeding, perforation, obstruction, or weight loss) should obtain a serum *H pylori* titer and prescribe eradication therapy if the titer is positive. Patients whose clinical presentation suggests that they are unlikely to have a peptic ulcer may alter-**

natively be treated symptomatically with antisecretory or antacid therapy, and patients whose presentation more strongly indicates peptic ulcer disease should receive immediate therapy to eradicate presumed *H pylori* infection. Patients whose symptoms do not respond to eradication therapy should be referred for endoscopy to rule out malignancy.

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Outpatient Care for Elderly HMO Patients

Reference Beck A, Scott J, Williams P, Robertson B, Jackson D, Gade G, Cowan P. Randomized trial of group outpatient visits for chronically ill older HMO members: The Cooperative Health Care Clinic. J Am Geriatr Soc 1997; 45:543-9.

Clinical question **How do chronically ill, high-utilization, elderly HMO patients receiving outpatient care using a group model compare with those receiving traditional physician-patient dyad care in regard to health services utilization, health status, and patient and physician satisfaction?**

Background Group sessions provide opportunities for efficient patient education, socialization, and provision of routine health maintenance measures such as immunizations. Prior small group studies of chronically ill patients have shown increased self-management of disease, reduced medication use, and fewer clinic visits using a group model of care.

Population studied The authors randomized 321 HMO members over age 65 within provider panels to a group visit intervention (n=160) or usual care (n=161). Eligible patients were chronically ill (defined as diabetes mellitus, heart, lung, or joint disease), high utilizers of health services with at least one outpatient visit per month and one nurse or physician phone call per month over the preceding year. Other than age (the intervention group's average was 3 years younger, P=.008), there were no significant differences between groups in demographic characteristics, comorbidities, or health status. Socioeconomic status and other factors that might affect group socialization were not reported.

Study design and validity Patients were followed for 1 year, and outcomes were appropriately analyzed within groups as originally assigned (intention-to-treat). About one half (208/419) of those originally approached agreed to participate, and another 113 patients were selected using the same criteria and were randomized to one of the two groups. An average of eight patients participated in each 2-hour group session, which included time for socialization, multidisciplinary education regarding self-care of their medical illnesses, health maintenance interventions by the nurses, and one-on-one visits with their physician as needed. Patients kept copies of their own medical records. The intervention group on average attended 55% of the sessions, but 13% never attended and another 12% discontinued attendance. Patient satisfaction was measured only in those who had attended at least 4 sessions. Potential selection biases relate to participation by only 6 of 8 clinic internists, and comparison of their report of patient care satisfaction with that of a convenience sample of other HMO physicians. Nurse satisfaction was not measured. The nurses' estimate that phone calls to group participants averaged 7 minutes, compared with 2.5 minutes for nonparticipants, was used in the cost comparison.

Outcomes measured Primary outcomes were the patient's functional status, utilization of inpatient and outpatient services, and patient and provider satisfaction with care.

Results The per member per month cost of care was $14.79 less for group participants than for those receiving traditional care. Group participants had significantly fewer (P<.05) emergency room visits, subspecialist visits, and calls to physicians. They also had fewer repeat hospital admissions, although this difference did not quite achieve statistical significance. Group participants had significantly more calls and visits to nurses, higher rates of immunization, and higher satisfaction with their care, compared with the usual-care group. Physicians also reported higher satisfaction with group care. Patient self-reported health and functional status did not differ between groups. These results were obtained even though 25% of patients did not complete the intervention.

Recommendations for clinical practice **This group-patient-care approach holds promise for treatment of chronically ill patients in HMOs or fully capititated plans. Incentives to utilize this model will be less in practices with other payer mixes and in those settings lacking adequate nursing personnel, multidisciplinary providers, or group meeting space. Generalization of the present study findings are also limited to those high-utilization patients willing or able to participate in group sessions.**

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Treatment of Hay Fever

Reference Juniper EF, Guyatt GH, Ferrie PJ, Griffith LE. First-line treatment of seasonal (ragweed) rhinoconjunctivitis. Can Med Assoc J 1997; 156:1123-31.

Clinical question **Is better health-related quality of life (HRQL) achieved by initiating treatment of seasonal (ragweed) rhinoconjunctivitis (hay fever) with a nasal steroid or a nonsedating antihistamine?**

Background Hay fever is a significant problem producing symptoms that impair normal daily activities and productivity. Many studies have demonstrated the efficacy and safety of nonsedating antihistamines and inhaled nasal steroids for treatment of hay fever. The few studies that have compared antihistamines with nasal steroids have provided an artificial environment that bears little resemblance to real life.

Population studied The study sample included 61 adults (17 to 66 years of age) from southern Ontario who had either participated in previous clinical trials or responded to notices in the local media. Inclusion criteria were as follows: a diagnosis of seasonal allergic rhinoconjunctivitis; troublesome nasal symptoms requiring medication during the ragweed pollen season; positive skin-prick test to ragweed pollen extract; no perennial rhinoconjunctivitis requiring treatment; no chronic nasal obstruction, polyposis or sinusitis; no history of allergen injection therapy in the previous 12 months; and no serious illness that might impair quality of life. Pregnant and nursing women were excluded, as were those patients with other illnesses requiring treatment with antihistamines or oral steroids. All subjects agreed to stay in the ragweed pollen area of southern Ontario for the duration of the study.

Study design and validity This was a well-designed, randomized trial of treatment effectiveness during the 6 weeks of ragweed pollen season in 1995. It was appropriately not blinded, resembling real-life practice. Participants were matched into pairs based on severity of ragweed pollen hay fever during the previous year, skin sensitivity to the ragweed pollen, fungal spore and mixed grass pollen extracts, and sex. There were 31 patients randomized to the fluticasone group and 30 to the terfenadine group. Patients were provided with enough medication for the whole ragweed season and were given both oral and written instructions regarding their optimal use. Patients were instructed to use the medication regularly in accordance with their arm of the study and the other medication additionally, as needed. Compliance with the regimen was left entirely to the individual patient's discretion. Data analysis was by intention-to-treat.

There are some limitations to this study. The volunteer nature of the sample, though demographically representative, could have introduced bias. The patients were instructed to begin medication before the ragweed pollen season. In real life, some patients become severely symptomatic before buying medications or seeking help. Medication cost was not a barrier for patients since the drugs were provided at no charge.

Outcomes measured At each visit, patients were asked to complete the Rhinoconjunctivitis Quality of Life Questionnaire. This is a 28-item disease-specific instrument designed to measure the functional impairments most important to patients with seasonal allergic rhinoconjunctivitis: sleep impairment, fatigue, practical problems, nasal symptoms, eye symptoms, activity limitations, and emotional function. Patients were seen 1 week before ragweed pollen was expected, at the height of ragweed season, and toward the end of the season. Additionally, medication use was monitored.

Results Both the fluticasone and the terfenadine groups maintained very good HRQL scores throughout the study. There was a trend toward better HRQL in the group using the nasal steroid (with the exception of eye symptoms) of a magnitude not considered to be clinically significant. Of the 31 patients in the fluticasone group, 16 (52%) never used any terfenadine, whereas only 4 (13%) of the 30 patients in the terfenadine group never used fluticasone.

Recommendations for clinical practice **Both fluticasone nasal spray with backup oral terfenadine as needed and terfenadine with backup fluticasone as needed are very effective treatments for hay fever. Optimal results often require two medications. If effective monotherapy is desired, these results favor the inhaled nasal steroid. The treatment decision should be guided by patient preference and medication costs. Some caution should be used when extrapolating these findings to other nasal steroid sprays and other nonsedating antihistamines.**

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Treatment After Acute MI in Diabetics

Reference Malmberg K. Prospective randomised study of intensive insulin treatment on long term survival after acute myocardial infarction in patients with diabetes mellitus. BMJ 1997; 314:1512-5.

Clinical question **Does intensive insulin therapy after acute myocardial infarction (MI) improve**

long-term survival in patients with diabetes mellitus?

Background Patients with diabetes are at high risk of dying after MI. Because data regarding the beneficial effects of insulin-glucose infusions are conflicting, it is unknown whether intensive therapy improves survival after MI. Previously published results of this study have documented lower 1-year mortality when such patients were treated immediately post-MI with an insulin-glucose infusion followed by long-term subcutaneous insulin. This current report evaluates the effect on all-cause mortality after long-term follow-up (mean 3.4 years).

Population studied This study evaluated 620 diabetic patients admitted to one of 19 Swedish hospitals for treatment of acute MI within 24 hours after development of symptoms. Inclusion criteria included a history of known diabetes mellitus and a blood glucose level greater than 200 mg/dL at admission, or a similar blood glucose concentration without known diabetes. The groups were similar with regard to age, sex, comorbid conditions, duration of diabetes, glycemic control, and diabetic treatment modality.

Study design and validity Subjects in this open label, randomized, controlled trial received either a 24-hour, titrated insulin-glucose infusion followed by subcutaneous insulin (n = 306) for at least 3 months or standard therapy (n = 316). The standard therapy group did not receive any insulin treatment unless it was clinically indicated. Patients were classified according to previous diabetic treatment (insulin or no insulin) and cardiac risk (high or low). High risk was defined as either age >70, previous MI, history of congestive heart failure (CHF), or treatment with digitalis. All patients received adjunctive treatments, eg, beta-blockers, ACE-inhibitors, thrombolytics, etc, at the discretion of the treating physician. Surprisingly, no patients were lost to follow-up. Data were analyzed according to an intention-to-treat principle, which strengthens study validity because only 72% of the intervention group continued to take insulin after 1 year. The study is potentially limited by type II error (no difference between two treatments is detected when in fact a true difference does exist) because a difference in mortality was not demonstrated in some subgroups with small numbers of patients. The study was not controlled for lifestyle modifications or other treatments such as lipid-lowering therapy following the intervention.

Outcomes measured Long-term all-cause mortality was the primary study endpoint. Secondary endpoints such as hospitalizations, angina, CHF, and hypoglycemic reactions were *not* evaluated.

Results There were 102 deaths (33%) in the insulin-treated group, compared with 138 deaths (44%) in the control group. This represents an absolute risk reduction in mortality of 11%; the number needed to treat of 9 (1 life saved for 9 patients treated) is very low. This difference was mostly accounted for by the 272 patients in the no-insulin–low-risk subgroup. Twenty-five deaths (18%) in this subpopulation occurred in the insulin-treated group and 44 (33%) occurred in the controls, representing a 15% absolute risk reduction and an NNT of 6.7. Although trends toward fewer deaths existed, no differences in mortality in the other subgroups reached statistical significance.

Recommendations for clinical practice **Intravenous infusion of insulin-glucose administered immediately after MI in patients with diabetes and hyperglycemia (>200 mg/dL) at admission, followed by long-term intensive subcutaneous insulin, significantly reduces the risk of death for at least 3 years. Patients most likely to benefit from this intervention are non-insulin–using diabetics with low cardiac risk. The mechanism responsible for decreased mortality risk remains unclear, but could be related to improved metabolic functions at the cellular level that minimize damage during ischemic conditions. Other post-MI interventions (eg, thrombolytics, aspirin, beta-blockers, ACE-inhibitors, and lipid-lowering therapy) should also be employed when appropriate. Larger studies evaluating the risks and benefits of insulin administration in other subpopulations (high cardiac risk and previous insulin use) are needed.**

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Antibiotic Treatment for AOM

Reference Del Mar C, Glasziou P, Hayem M. Are antibiotics indicated as initial treatment for children with acute otitis media? A meta-analysis. BMJ 1997; 314:1526-9.

Clinical question **How effective is antibiotic treatment for acute otitis media (AOM) in children?**

Background Antibiotics are given almost universally by physicians in the United States for AOM, although many physicians elsewhere (especially the Netherlands) report good outcomes without them. As microbial resistance increases, the issue of whether patients benefit from antibiotic treatment is paramount. Despite numerous studies, the value of antibiotic treatment for AOM remains unclear.

Population studied Using both manual- and com-

puter-searching techniques for the years 1958 to 1994, the authors identified randomized controlled trials of antimicrobial drugs vs placebo control for AOM. Six studies met their criteria for analysis (from 1968 to 1994) and included children aged 7 months to 15 years in the United States and Europe. Two of these studies enrolled only children over 2 years of age, and one trial included only children over 3 years of age. Since the peak incidence of AOM is in infants aged 6 to 15 months, the generalizability of the results are uncertain.

Study design and validity Studies were assigned quality scores based on subject assignment, control for selection bias, intention-to-treat analysis, adequacy of blinding, and objectiveness of outcome assessment. Quality assessments were performed by three independent reviewers unaware of the authors, institutions, journals, and results of each study. Trials with higher quality scores contributed more weight to the pooled analyses. Appropriate statistical tests found no significant variability (heterogeneity) between the different studies.

Outcomes measured Outcomes measured included pain at 24 hours, pain at 2 to 7 days, tympanic membrane perforation, side effects of medication including vomiting, diarrhea and rash, middle ear effusion at 1 and 3 months (deafness), contralateral AOM, and recurrent AOM.

Results Sixty percent of children were pain-free at 24 hours, whether or not they were treated with antibiotics. By 2 to 7 days, only 14% of control children still had pain. Early use of antibiotics reduced this risk by 41%. Thus, 17 children will need to be treated with antibiotics to prevent one child from experiencing persistent pain at 2 to 7 days. Antibiotic treatment reduced the risk of contralateral AOM and perforations of the tympanic membrane, but had no effect on recurrent AOM or deafness at 3 months. The effect of treatment on the risk of developing mastoiditis was not reported. Antibiotic use increased the frequency of vomiting, diarrhea, and rash; for every 17 children treated with antibiotics, one experienced a reportable side effect.

Several weaknesses in this meta-analysis decrease the reliability and generalizability of the results. Outcome measures were not obtainable from all the studies. Only the analysis of pain at 2 to 7 days included data from all six studies. In addition, the measurement of pain at 2 to 7 days was based on pooled data from the different trials and not on a specific endpoint of each individual trial. Parents may prefer to deal with a fussy child for 2 days, but not be willing to do so for 6. Persistent middle ear effusion and TM perforation included data from only two studies. The analysis of vomiting, diarrhea and rash, which grouped all these symptoms together, included only three studies. Two of these had low quality scores and did not contribute significantly to the pooled results.

Selection bias favoring no treatment may have been significant. In one trial, children with a high fever or high pain scores were not randomized to receive placebo. In other studies, children who were not responding well to treatment were removed from the study protocol and started on active antimicrobial treatment.

Recommendations for clinical practice **Early treatment of AOM with antibiotics can reduce the severity of pain, but the majority of children will feel better in 24 hours with or without antibiotics. Because of the poor quality of the available evidence, additional benefits or harm of treatment remain uncertain. The incidence of mastoiditis has dropped significantly from 17% in the pretreatment era, but countries in which antibiotics are rarely used do not report significant problems with this complication. Withholding antibiotic treatment while following closely with adequate analgesia is acceptable for children aged 2 years or older who do not have a high fever or severe pain.**

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Treatments for Postherpetic Neuralgia

Reference Volmink J, Lancaster T, Gray S, Silagy C. Treatments for postherpetic neuralgia—a systematic review of randomized controlled trials. Fam Pract 1996; 13:84-91.

Clinical question **Which treatments for postherpetic neuralgia have been shown to be effective by valid clinical trials?**

Background A variety of treatments are offered for postherpetic neuralgia without consensus about their effectiveness. This study follows the publication of a systematic review which showed that treatment in the acute phase of herpes zoster with any of a variety of medications could not prevent postherpetic neuralgia.[1]

Population studied Clinical trials were included that exclusively studied the effects of treatment on patients suffering from postherpetic neuralgia persisting at least 1 month beyond the onset of herpes zoster.

Study design and validity This was a systematic review of completed randomized trials up until December 1993. MEDLINE and EMBASE databases were searched, as were the reference lists of the retrieved studies. Previous reviews, conference abstracts, and major medical textbooks were handsearched. The authors did not explicitly state that they had contacted experts in the field, so it is possible that this otherwise thorough search did not identify all

unpublished studies. This could cause a publication bias, and lead to overestimation of treatment effects due to selective publication of positive studies.

Meta-analysis was performed on three published studies of tricyclic antidepressants (two of amitriptyline and one of desipramine) and attempted on three studies of capsaicin (one unpublished). (Meta-analysis is an approach that uses quantitative methods to summarize the results in the medical literature pertaining to a specific clinical question). An explicit process was used by two authors to appraise the quality of all studies, and disagreements were resolved in discussion with a third. On a 3-point scale, with a score of 3 representing maximal effort to control bias, the antidepressant articles averaged a quality rating of 2 and the capsaicin articles rated 2.5. The antidepressant articles were homogeneous; that is, they seemed to measure the same magnitude of treatment effect. The unpublished capsaicin study (which used a lower dose, duration, and vehicle) did not observe a favorable effect. It accounted for the heterogeneity found among the capsaicin studies and was not included in the final meta-analysis. All estimates were based on an intention-to-treat analysis.

Outcomes measured Visual analogue or verbal rating scales were used by individual investigators to determine the number of subjects who had obtained clinically significant pain relief by the end of the treatment period.

Results Summary results were reported as odds ratios (OR) with 95% confidence intervals (CI) for failure to obtain pain relief, with an odds ratio of less than 1 indicating treatment benefit. Meta-analysis of 216 patients from three studies showed that tricyclic antidepressants were effective (OR 0.15, 95% CI 0.08 to 0.27). Analysis of 175 patients from 2 studies showed that topical capsaicin was also effective (OR 0.29, 95% CI 0.16 to 0.54). Another study found that the antidepressant maprotiline was as effective as amitriptyline but resulted in more frequent side effects. One study with 20 patients suggested efficacy of transdermal vincristine iontophoresis (OR 0.05, 95% CI 0.01 to 0.26). Single studies identified for lorazepam, acyclovir, accupuncture, and topical benzydamine did not demonstrate benefit. An unblinded study indicated that clomipramine in combination with carbamazapine was more effective than transcutaneous electrical nerve stimulation (OR 0.15, 95% CI 0.03 to 0.7) but was compromised by patients lost to follow-up and significant crossover between groups.

Recommendations for clinical practice **The tricyclic antidepressants amitriptyline and desipramine are effective in relieving pain from established postherpetic neuralgia. Topical capsaicin has promise, but cannot be strongly recommended based on the conflicting available evidence; more well-designed studies are needed. A larger study is also needed to assess whether vincristine iontophoresis will ultimately be proven effective. The available evidence is insufficient to recommend acyclovir, lorazepam, benzydamine cream, accupuncture, or clomipramine combined with carbamazapine for the treatment of postherpetic neuralgia.**

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