of 89%, LR+ 4.0 (CI 95%, 1.6–9.9), and a negative likelihood ratio (LR–) of 0.8 (CI 95%, 0.7–0.9). A third trial (n=172) found that the overall clinical impression for the presence or absence of COPD was associated with an 83% sensitivity, 81% specificity, LR+ 4.26 (CI 95%, 2.9–6.3), and LR– 0.21 (CI 95%, 0.12–0.37) for the diagnosis of COPD. Two of the remaining studies only examined multivariate analysis and as a result these studies were not included. The sixth study was not included in the evidence summary due to lack of sensitivity, specificity, or LR measurement.¹

A separate cross-sectional analysis evaluated the prevalence of low lung function among 4,461 Vietnam-era army veterans with abnormal medical history and physical examination data.² The sample consisted of 2,008 current smokers, 1,292 former smokers, and 1,161 patients who had never smoked. Findings evaluated in this study included history of smoking, signs and/or symptoms of respiratory disease, and a history of respiratory disease. Signs of respiratory disease included poor lung expansion, hyperresonance, dullness on percussion, decreased breath sounds, crackles, wheezes, and/or rubs. Low lung function was defined as having an FEV1 <81% of predicted value, FVC <80%, or an FEV1/FVC ratio <0.7. Pulmonary function tests were subsequently obtained on all participants. Current signs of respiratory disease were associated with a sensitivity of 14% and a specificity of 94% for the diagnosis of COPD (LR+ 2.3; LR– 0.91).

A third cross-sectional analysis (n=161) evaluated the accuracy of several clinical elements in diagnosing COPD. Patients underwent a clinical examination and blinded spirometer testing.³ COPD was defined as having an FEV1/FVC ratio <0.7. Multivariate analysis found that 3 elements of the clinical examination were indicative of COPD: a self-reported history of COPD (LR+ 4.4; LR– 0.5), wheezing on examination (LR+ 2.9; LR– 0.8), and a forced expiratory time >9 seconds (LR+ 4.6; LR– 0.8).

### Are antibiotics effective in acute flares of chronic asthma?

#### Evidence-Based Answer

In patients with acute asthma flares, at least 3 weeks of macrolide therapy added to standard asthma care may be associated with improved symptom control (SOR: B, meta-analysis of RCTs). There does not appear to be any benefit with amoxicillin (SOR: B, meta-analysis) or macrolide therapy for 16 weeks (SOR: B, RCTs).

A 2013 meta-analysis of 12 RCTs involving 831 patients examined the effectiveness of macrolides (clarithromycin, azithromycin, and troleandomycin) for asthma management.¹ Antibiotics were prescribed during an acute episode for a minimum 3-week course.

There was no effect on forced expiratory volume in 1 second (FEV1) (8 trials, n=381; standardized mean difference [SMD] 0.05, 95% CI, –0.14 to 0.25) between the antibiotic group and control. However, significant increases were noted in peak expiratory flow (4 trials, n=419; weighted mean difference [WMD] 6.7 L/min; 95% CI, 1.4–12) and reduction in symptoms (variety of scales used, ranges not provided) (8 trials, n=478; WMD –0.46; 95% CI, –0.60 to –0.32).¹

A 2005 Cochrane review of 2 double-blind RCTs examined the effectiveness of antibiotics in 115 acute asthma exacerbations involving 93 patients. The first of the 2 trials was a 1982 double-blind RCT of 71 exacerbations in 60 adults that found improved FEV1 in the placebo group compared with amoxicillin 500 mg 3 times daily (duration not specified; no data provided). The second was a 1974 double-blind RCT of 44 exacerbations among 33 children that found hetacillin 100 mg/kg for 24 hours, followed by 225 mg 4 times daily for 6 days did not reduce length of stay in the hospital (MD –0.10 days; 95% CI, –0.53 to 0.33). Data were not pooled between the 2 studies due to heterogeneity.²

A 2012 RCT examined clarithromycin therapy for 40 acute pediatric asthma exacerbations.³ Although treatment group assignment was double-blinded, treatment itself was open. In addition to standard therapy of beta-agonist, systemic steroids, and anticholinergics, patients were given 3 weeks of clarithromycin 15 mg/kg or no additional medication.

By follow-up at 12 weeks, children treated with clarithromycin had more symptom-free days.

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(78 vs 69 days; \( P < .001 \)), fewer exacerbations (9 vs 19; \( P = .013 \)), and shorter exacerbation duration (5 vs 7.5 days; \( P < .0001 \)). Additionally, FEV1 at 6- and 12-week follow-up improved in the clarithromycin group (1.9 L at inclusion, 2.0 L at 6 weeks; \( P < .004 \); and 2.1 L at 12 weeks; \( P < .001 \)), but not in the control group (2.15 L at inclusion, 2.2 L at 6 weeks; \( P = .164 \); and 2.2 L at 12 weeks; \( P = .07 \)).

In 2010, a double-blinded, placebo-controlled RCT of 92 adult patients with mild-moderate persistent asthma examined improvement in asthma control with longer term clarithromycin.\(^4\) Patients were given 16 weeks of clarithromycin 500 mg twice daily or placebo in addition to fluticasone MDI. The Juniper Asthma Control Questionnaire was used to assess their response to treatment pre- and post-clarithromycin. No improvement in asthma control or reduction in rescue bronchodilator use was seen when compared with placebo.

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The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Medical Department of the US Army or the US Army Service at large.


**Is biofeedback an effective treatment for tension headaches in adults?**

Evidence-Based Answer
The answer is unclear (No SOR given, disputed meta-analysis and conflicting RCTs).

A 2008 meta-analysis of 45 pre-post, controlled trials and RCTs involving a total of 1,289 patients with tension-type headaches examined biofeedback for headache disorders.\(^1\) Studied populations showed marked heterogeneity in age, location, and sex (73% of patients were women). Inclusion criteria required that patients meet specified headache diagnostic criteria. Biofeedback was evaluated as treatment alone or in combination with behavior therapy. Outcomes were measured by standardized headache diaries, with follow-up at least 3 months’ duration, and at least 4 patients were included per treatment group. The primary outcome was pain relief as measured by headache diaries; secondary measures were muscle tension and various psychological and behavioral outcomes. Electromyographic biofeedback (EMG-FB) comprised 92% of all biofeedback treatments employed. The average duration of each session was 43 minutes, with a mean of 11 sessions conducted.

Compared with both placebo and waiting-list control groups, EMG-FB yielded statistically significant effect sizes (an effect size of 0.2 is considered small, 0.6 moderate, and 1.2 large) for measures of medication use, headache intensity and duration, anxiety, and self-efficacy (**TABLE**).\(^1\)

However, a Centre for Reviews and Dissemination of the National Institute for Health Research published a critique of the above meta-analysis in 2010.\(^2\) Authors noted only 28 of the 45 trials above were controlled trials. Reanalysis of these RCTs showed that biofeedback yielded a significant medium effect size (ES) on headache reduction compared with placebo controls (N=165; ES 0.50, 95% CI, 0.26–0.75). Because statistical and clinical heterogeneity were not clearly reported and conclusions were drawn from both controlled and uncontrolled studies, they recommended caution regarding any strong conclusions from the above meta-analysis. A more restrictive meta-analysis limited to pooled data from 11 RCTs examined the use of biofeedback for chronic tension headaches in

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Mean weighted effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication index(^*)</td>
<td>18</td>
<td>0.42 (0.26–0.57)</td>
</tr>
<tr>
<td>Headache index(^*)</td>
<td>30</td>
<td>0.80 (0.57–1.09)</td>
</tr>
<tr>
<td>Headache intensity</td>
<td>27</td>
<td>0.70 (0.50–0.85)</td>
</tr>
<tr>
<td>Headache duration</td>
<td>13</td>
<td>0.46 (0.26–0.64)</td>
</tr>
<tr>
<td>Headache frequency</td>
<td>28</td>
<td>0.82 (0.56–1.07)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>9</td>
<td>0.52 (0.27–0.80)</td>
</tr>
<tr>
<td>Depression</td>
<td>5</td>
<td>0.54 (0.03–1.02)</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>5</td>
<td>0.62 (0.25–0.65)</td>
</tr>
</tbody>
</table>

Total patient numbers in outcome analysis were not identified.

Effect size of 0.2 is considered small, 0.6 moderate, and 1.2 large.

\(^*\)Medication and headache indexes were not defined.