

Implementing AHRQ Effective Health Care Reviews

Helping Clinicians Make Better Treatment Choices

Therapies for COPD Exacerbations in Adults

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Key Clinical Issue

What are the benefits and harms of pharmacologic and nonpharmacologic treatments for exacerbations of chronic obstructive pulmonary disease (COPD) in adults?

Evidence-Based Answer

In adults with exacerbations of COPD, antibiotic therapy increases the clinical cure rate and decreases the clinical failure rate. (Strength of Recommendation [SOR]: A, based on consistent, good-quality patient-oriented evidence.) Systemic corticosteroid therapy improves dyspnea and reduces the clinical failure rate. (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.) Titrated oxygen reduces mortality when compared with high flow oxygen. (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.) Resistance training improves dyspnea and quality of life. (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.) Early pulmonary rehabilitation initiated during hospitalization improves dyspnea.¹ (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

COPD affects 10% of the global population. In the United States, it affects 15 million people, is the fourth leading cause of death, and costs the health care system \$32 billion each year.¹ COPD is a chronic disease marked by exacerbations that impact quality of life and are potentially fatal. This Agency for Healthcare Research and Quality (AHRQ)

review was conducted to evaluate the effectiveness and harms of pharmacologic and nonpharmacologic treatments for COPD exacerbations in adults.¹

The review included 98 randomized controlled trials (RCTs) encompassing 13,401 patients. When compared with placebo, antibiotic therapy improved the clinical cure rate (three RCTs with 683 patients; odds ratio [OR] = 2.03; 95% CI, 1.47 to 2.80) and decreased the clinical failure rate by the end of the intervention (two RCTs with 405 patients; OR = 0.54; 95% CI, 0.34 to 0.86). Clinical cure was defined as improvement in signs and symptoms; clinical failure was defined as a lack of improvement in signs and symptoms or the need for additional treatment. There were no differences in clinical failure rates at the longest follow-up, hospital readmissions at 30 days, repeat exacerbations at 30 days, or adverse events. Multiple comparisons among antibiotics, doses, and durations were mostly insufficient for showing an improvement in clinical cure and failure rates, repeat exacerbations, and mortality.

In general, systemic corticosteroids were more effective than placebo in improving dyspnea on a numeric scale (two RCTs with 154 patients; standardized mean difference = 0.40; 95% CI, 0.07 to 0.70) and reducing clinical failure rate at the end of the intervention (two RCTs with 217 patients; OR = 0.01; 95% CI, 0.00 to 0.13). Some evidence indicated that total adverse events were higher with systemic corticosteroids compared with placebo (rate ratio = 1.55; 95% CI, 1.14 to 2.10), but there was no difference in serious adverse events such as gastrointestinal

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to produce evidence to improve health care and to make sure the evidence is understood and used. A key clinical question based on the AHRQ Effective Health Care Program systematic review of the literature is presented, followed by an evidence-based answer based upon the review. AHRQ's summary is accompanied by an interpretation by an *AFP* author that will help guide clinicians in making treatment decisions. For the full review go to <https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-221-copd-final-report.pdf>.

This series is coordinated by Kenny Lin, MD, MPH, deputy editor.

A collection of Implementing AHRQ Effective Health Care Reviews published in *AFP* is available at <https://www.aafp.org/afp/ahrq>.

CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 519.

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Comparison of Treatments for COPD Exacerbation: Critical Outcomes

Comparator	Outcome	Number of trials and participants	Findings	Strength of evidence
Antibiotic therapy				
Placebo	Clinical cure rate at end of intervention	3 RCTs with 683 patients	OR = 2.03; 95% CI, 1.47 to 2.80 Improvement	●●○
Placebo	Clinical failure rate at end of intervention	2 RCTs with 405 patients	OR = 0.54; 95% CI, 0.34 to 0.86 Improvement	●●○
Placebo	Clinical failure rate at longest follow-up	2 RCTs with 570 patients	OR = 0.82; 95% CI, 0.58 to 1.14 No change	●○○
No antibiotics	30-day hospital readmission	1 RCT with 194 patients	OR = 1.72; 95% CI, 0.68 to 4.36 No change	●○○
Placebo or no antibiotics	Repeat exacerbation at 30 days	2 RCTs with 229 patients	OR = 1.69; 95% CI, 0.78 to 3.68 No change	●○○
Placebo or no antibiotics	Adverse events	Multiple studies	No change	●○○
Systemic corticosteroids				
Placebo	Dyspnea	2 RCTs with 154 patients	SMD = 0.40; 95% CI, 0.07 to 0.70 Improvement	●○○
Placebo	Clinical failure rate at end of intervention	2 RCTs with 217 patients	OR = 0.01; 95% CI, 0.00 to 0.13 Improvement	●○○
Placebo	Serious adverse events	2 RCTs	Rate ratio = 0.73; 95% CI, 0.27 to 1.97 No change	●○○
Placebo	Total adverse events	4 RCTs	Rate ratio = 1.55; 95% CI, 1.14 to 2.10 More adverse events	●●○

continues

COPD = chronic obstructive pulmonary disease; OR = odds ratio; RCT = randomized controlled trial; SMD = standardized mean difference; WMD = weighted mean difference.

bleeding, hypertension, or psychiatric disorders. The evidence was insufficient to compare different corticosteroids with respect to dyspnea, clinical failure, and death. Evidence was insufficient to compare different routes of administration and duration of corticosteroid use. The evidence was insufficient to determine the effects of other pharmacologic agents, including inhaled antibiotics, inhaled corticosteroids, magnesium, and mucolytics.

Resistance training involving the upper and lower body with progressively increased elastic band tension and number of exercise repetitions for nine days was helpful in relieving dyspnea (one RCT with 60 patients; weighted mean difference [WMD] = -2.11 on the 10-point Modified Borg scale, small effect; 95% CI, -3.50 to -0.72) and improving quality of life (one RCT with 60 patients; WMD = 18.70 on the 100-point EQ-5D visual analog scale, small effect; 95% CI, 5.06 to 32.34) when compared with no resistance training. Evidence was insufficient to demonstrate a benefit of resistance training with respect to hospital readmissions and mortality.

Whole-body vibration improved quality of life (one RCT with 49 patients; WMD = -12.02 on the 100-point St. George's Respiratory Questionnaire, small effect; 95% CI, -21.41 to -2.63) when compared with no vibration. Titrated oxygen (to keep oxygen saturation between 88% and 92%) improved prehospital and in-hospital mortality at the longest follow-up (one RCT with 214 patients; OR = 0.36; 95% CI, 0.14 to 0.88) when compared with high flow oxygen. There was no evidence of benefit associated with chest physiotherapy. Early pulmonary rehabilitation initiated during hospitalization for exacerbation was found to improve six-minute walking difference (three RCTs with 253 patients; WMD = 20.02; 95% CI, 12.06 to 28.67), but there was not enough evidence to show a readmission or mortality benefit. There was no significant difference in adverse events between those who received nonpharmacologic therapies and those who did not.

This AHRQ review emphasizes many therapies that family physicians are already using for their patients experiencing COPD exacerbations, such as antibiotics and corticosteroid

Comparison of Treatments for COPD Exacerbation: Critical Outcomes

Comparator	Outcome	Number of trials and participants	Findings	Strength of evidence
Resistance training				
No resistance training	Dyspnea	1 RCT with 60 patients	WMD = -2.11; 95% CI, -3.50 to -0.72 Improvement	●○○
No resistance training	Quality of life at end of intervention	1 RCT with 60 patients	WMD = 18.70; 95% CI, 5.06 to 32.34 Improvement	●○○
Whole-body vibration				
No whole-body vibration	Quality of life	1 RCT with 49 patients	WMD = -12.02; 95% CI, -21.41 to -2.63 Improvement	●○○
Titration oxygen				
High flow oxygen	Mortality at longest follow-up	1 RCT with 214 patients	OR = 0.36; 95% CI, 0.14 to 0.88 Improvement	●○○
Vitamin D supplementation				
Placebo	Quality of life at longest follow-up	1 RCT with 70 patients	WMD = -4.67; 95% CI, -6.00 to -3.35 Improvement	●○○

Strength of evidence scale

- **High:** High confidence that the evidence reflects the true effect. Further research is very unlikely to change the confidence in the estimate of effect.
- **Moderate:** Moderate confidence that the evidence reflects the true effect. Further research may change the confidence in the estimate of effect and may change the estimate.
- **Low:** Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
- **Insufficient:** Evidence either is unavailable or does not permit a conclusion

COPD = chronic obstructive pulmonary disease; OR = odds ratio; RCT = randomized controlled trial; SMD = standardized mean difference; WMD = weighted mean difference.

Adapted from Dobler CC, Morrow AS, Farah MH, et al. Pharmacologic and nonpharmacologic therapies in adult patients with exacerbation of COPD: a systematic review. Comparative Effectiveness Review No. 221. (Prepared by the Mayo Clinic Evidence-Based Practice Center under contract no. 290-2015-00013-1.) AHRQ publication no. 19(20)-EHC024-EF. Rockville, Md.: Agency for Healthcare Research and Quality; October 2019. Accessed January 24, 2020. <https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-221-copd-final-report.pdf>

therapy, while also suggesting that magnesium and mucolytics may not be helpful. Nonpharmacologic therapies such as resistance training and whole-body vibration may be beneficial. The American Academy of Family Physicians is developing a clinical practice guideline based on the AHRQ review. Current guidelines from the U.S. Department of Veterans Affairs/U.S. Department of Defense and the Global Initiative for Chronic Obstructive Lung Disease recommend a five- to seven-day course of antibiotics and systemic corticosteroids with titrating oxygen therapy to maintain a saturation of 88% to 92% for adults with COPD exacerbations.^{2,3}

Editor's Note: AFP SOR ratings are different from the AHRQ Strength of Evidence ratings. Dr. Saguil is a contributing editor for AFP.

The views expressed in this article are the author's and do not reflect the official policy or position of the Uniformed Services

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