

resulting in the need for additional treatment. Acute exacerbations of COPD are generally characterized by increased dyspnea, increased frequency and severity of cough, and potentially increased sputum.⁵ Patients experiencing acute exacerbations of COPD are at increased risk of mortality and morbidity, lower quality of life, increased hospital admissions, and a progressive decline in lung function.⁶⁻¹³

The goals for management of acute exacerbations of COPD include symptom resolution and recovery from the exacerbation episode via improving airflow and gas exchange in addition to reducing lung inflammation. Prevention or reduction of severity of subsequent exacerbation episodes is also a goal for many management and prevention strategies. Typical interventions used for the management of COPD exacerbations include corticosteroids, systemic antibiotics, inhaled bronchodilators, and supplemental oxygen. Surprisingly, there is limited evidence for many of these treatments in this population.¹⁴ Recently, the role of mucolytics and aminophyllines has been studied based on their mechanism of action to aid in thinning and clearing of mucus and improving dyspnea, respectively.^{15,16}

Several nonpharmacologic treatments have also been assessed for management and/or prevention of COPD exacerbations, including pulmonary rehabilitation programs, chest physiotherapy, and nutritional supplements. Chest physiotherapy includes the use of breathing techniques, vibration/percussion of the chest, and autogenic drainage (using breathing to loosen mucus). Vitamin D and omega-3 fatty acid supplements have also been highlighted as potential therapies for the prevention and management of acute exacerbations of COPD.¹⁴

Although much of the literature centers on inpatient treatment of patients with acute exacerbations of COPD, most U.S. patients with COPD are managed by primary care physicians.¹⁷ Appropriate coordination of care between subspecialists and primary care physicians is important for prevention and management of acute exacerbations of COPD.

Methods
SYSTEMATIC REVIEW

In 2019, the Agency for Healthcare Research and Quality (AHRQ) published comparative effectiveness review no. 221, Pharmacologic and Nonpharmacologic Therapies in Adult Patients With Exacerbation of COPD: A Systematic Review.¹⁸ The systematic review was conducted by the Mayo Clinic Evidence-Based Practice Center. The report was published on the AHRQ website, as well as in two additional systematic review articles.^{14,19}

The report included studies evaluating the effectiveness of systemic antibiotics, systemic corticosteroids, and other pharmacologic and nonpharmacologic therapies. The authors also searched for studies of the effectiveness of combinations of treatments and compared different regimens of

antibiotics and corticosteroids. Effectiveness of treatments was stratified by severity of disease where appropriate. The target population was defined as adults who experienced exacerbation events related to COPD. The Mayo Clinic Evidence-Based Practice Center worked with key informants and a technical expert panel consisting of stakeholders, including physician and patient representatives. Family physicians served in both groups. The report included the following key questions represented by the analytic framework in *Figure 1*.¹⁸

Key Question 1. In adult patients with exacerbations of COPD, what are the benefits and harms of systemic corticosteroids and antibiotics compared with placebo or standard care?

Key Question 2. In adult patients with exacerbations of COPD, what are the benefits and harms of emerging and other pharmacologic and nonpharmacologic therapies compared with placebo or standard care?

Key Question 3. In adult patients with exacerbations of COPD, what are the benefits and harms of combinations of treatments that are individually effective (based on empirical evidence in stable COPD)?

Key Question 4. In adult patients with exacerbations of COPD, what is the comparative effectiveness of different regimens of antibiotics and systemic corticosteroids based on type of agents (e.g., broad-spectrum vs. narrow-spectrum antibiotics), delivery modes (e.g., intravenous, oral), and durations of treatment?

Constructing the Guideline

The AAFP’s Commission on Health of the Public and Science appointed a group to develop the guideline. Members of the guideline development group included physicians with expertise in guideline development, family medicine, internal medicine, and pulmonary medicine, in addition to a consumer representative. This group followed the guideline development process that can be found in the AAFP *Clinical Practice Guideline Manual*.²⁰ The group reviewed the evidence from the AHRQ evidence report and used a modified version²⁰ of the GRADE²¹ system to rate the quality of the evidence for each outcome and the overall strength of each recommendation. The strength of recommendation reflects the extent to which one can be confident that the desirable effects of an intervention outweigh the undesirable effects and reflects the degree to which there is evidence of improved patient-oriented health outcomes (*Table 1*).

The quality of evidence is based on the certainty of the evidence. High-quality evidence means the authors have high certainty in the estimate of effect, and additional studies most likely will not change the outcome.^{22,23} Low-quality evidence means that the authors have lower certainty in the estimate of effect, and additional studies will likely change the result.

The AAFP also issues guideline recommendations without a rating when appropriate (e.g., those that will be helpful to a clinician but for which there is no direct evidence to support the recommendation). The AAFP labels these as “good practice points.”^{21,24}

The guideline development group prioritized patient-oriented clinical outcomes, which included mortality, quality of life, clinical cure, and treatment failure. Interventions, such as lung function tests, that improved intermediate outcomes but did not improve the identified patient-oriented outcomes, were not included in the recommendations. The wording of the recommendations reflects the strength and direction of the recommendation, and the quality of the evidence was listed parenthetically. Guideline recommendations were finalized based on consensus of the guideline development group after completion of GRADE evidence-to-decision frameworks, which enabled consideration of the strength of the evidence in addition to issues of feasibility, acceptability, equity, and patient preferences and values (*Table 2*).¹⁸

Patient/Consumer Perspective

Patient preferences and perspective were sought during all stages of guideline development. AHRQ routinely includes patients in the development of evidence reviews to provide input on the scope and key questions. Additionally, all AHRQ evidence reviews are available for public review and comment before being finalized. As part of the guideline development process, the AAFP included a consumer representative in the guideline development group. This member participated throughout the guideline process and was a voting member of the panel. In addition to providing insight into patient preferences during development of the recommendations, the patient representative assisted in developing the supporting text for the guideline. Patient representatives were also included in the peer-review process.

Peer Review

The guideline was peer-reviewed by relevant internal and external stakeholders, including patients and representatives from family medicine, pulmonology, and internal medicine.

All comments and any modifications based on those comments were documented. The AAFP Commission on Health of the Public and Science and AAFP board of directors reviewed and approved the final version of the guideline.

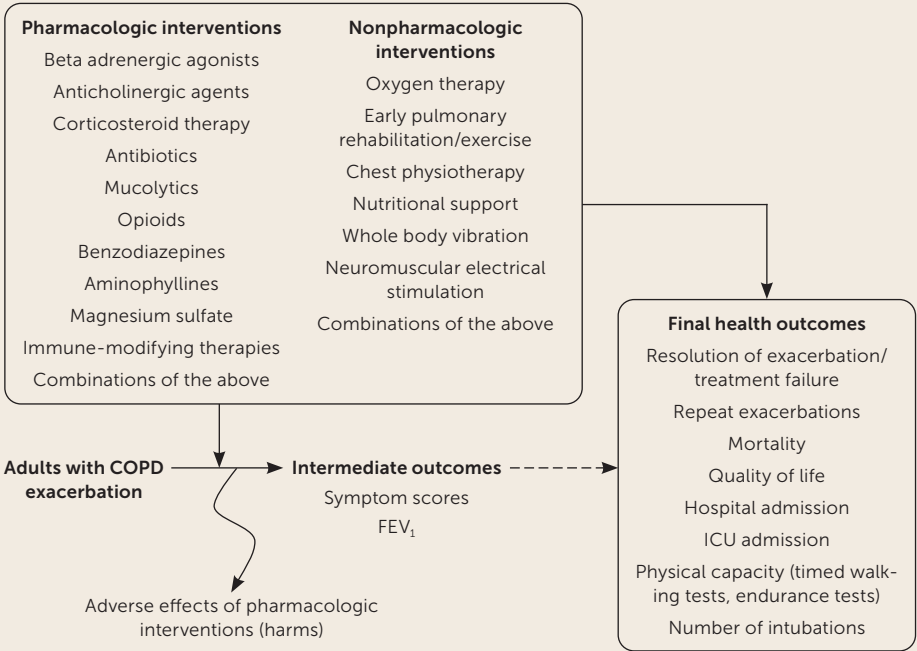
Conflict of Interest

The AAFP considers both financial and intellectual conflicts of interest (COI), which were solicited in writing at the beginning of the guideline process and updated verbally at each subsequent call. No panel member disclosed any COI. Policies for disclosures and management of COI are outlined in the AAFP *Clinical Practice Guideline Manual*.²⁰

Guideline Updating

All AAFP guidelines are scheduled for review five years after completion. Guidelines are reviewed at a shorter interval if new evidence becomes available.

FIGURE 1



AHRQ = Agency for Healthcare Research and Quality; COPD = chronic obstructive pulmonary disease; FEV₁ = forced expiratory volume in one second; ICU = intensive care unit.

Analytic framework for key questions in the AHRQ evidence review.

Adapted from Dobler CC, Morrow AS, Farah MH, et al. AHRQ comparative effectiveness review number 221. Pharmacologic and nonpharmacologic therapies in adult patients with exacerbation of COPD: a systematic review. Agency for Healthcare Research and Quality. October 2019. Accessed February 1, 2021. <https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-221-copd-final-report.pdf>