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Therapeutic Advances in Chronic Obstructive Pulmonary Disease: A Systematic Review of Pharmacological and Non-Pharmacological Strategies and Their Cardiovascular Implications

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Abstract

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of morbidity and mortality worldwide, characterized by persistent airflow limitation, chronic airway inflammation, and significant functional impairment. In addition to pulmonary manifestations, the disease has significant systemic repercussions, particularly cardiovascular ones, which contribute significantly to a worsened prognosis. The present study aimed to analyze therapeutic advances in COPD, focusing on pharmacological and non-pharmacological strategies and their cardiovascular implications. This is a systematic review conducted in accordance with the PRISMA 2020 guidelines. The literature search was performed in the PubMed/MEDLINE, Scopus, Web of Science, Embase, and Cochrane Library databases, including studies published between 2021 and 2026. After applying the eligibility criteria, 36 studies were included in the qualitative synthesis. The results demonstrated that pharmacological therapies, especially long-acting bronchodilators, inhaled corticosteroids, and combination therapies, remain fundamental for symptom control and reduction of exacerbations. At the same time, non-pharmacological interventions, such as pulmonary rehabilitation, supervised physical training, non-invasive ventilation, and psychosocial support, showed significant benefits regarding functional capacity and quality of life. Additionally, a strong association was observed between COPD and cardiovascular diseases, including heart failure, pulmonary hypertension, and coronary artery disease. It is concluded that the contemporary management of COPD should be multidimensional, integrating pharmacological and non-pharmacological approaches combined with systematic cardiovascular assessment. Therapeutic personalization and multidisciplinary follow-up represent promising strategies for optimizing clinical outcomes and reducing morbidity and mortality.

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1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of morbidity and mortality worldwide, characterized by persistent airflow limitation, chronic airway inflammation, and progressive deterioration of lung function. In recent decades, COPD has ceased to be understood exclusively as a lung disease and has come to be recognized as a complex systemic condition associated with multiple comorbidities and significant socioeconomic impact. In this context, the need for

more comprehensive and individualized therapeutic strategies has become one of the main challenges of contemporary respiratory medicine (STOLZ et al., 2022; CAZZOLA et al., 2026) [27, 31].

The high prevalence of COPD is associated with population aging, prolonged exposure to tobacco smoke, and environmental, occupational, and infectious factors. In addition to respiratory impairment the disease is significantly associated with systemic inflammatory changes that contribute to the development of extrapulmonary manifestations, significantly increasing the burden of morbidity and the complexity of clinical management for these patients (XIANG; LUO, 2024; KATAMESH et al., 2025) [32, 10].

Advances in understanding the pathophysiology of COPD have enabled the identification of new therapeutic targets. Changes related to cellular mechanotransduction, tissue remodeling, immune dysfunction, and interaction with the pulmonary microenvironment have been described as fundamental mechanisms for disease progression, facilitating the development of more specific and personalized therapies (LI et al., 2026; LIU et al., 2023) [11, 13].

Historically, pharmacological treatment of COPD has focused on the use of long-acting bronchodilators, inhaled corticosteroids, and combination therapies aimed at symptom control and the reduction of exacerbations. However, new evidence demonstrates that innovative therapeutic approaches can modify important aspects of clinical progression, broadening treatment prospects beyond the simple relief of respiratory symptoms (AGUSTI; SINGH; FANER, 2026; FRAGA et al., 2024) [1, 7].

Acute exacerbations constitute one of the most significant events in the course of COPD, being associated with accelerated decline in lung function, increased hospitalizations, and elevated mortality. Consequently, the prevention and appropriate management of these episodes have become central objectives of the most recent guidelines, driving the development of increasingly effective pharmacological strategies (JEYACHANDRAN; HURST, 2022; CAZZOLA et al., 2026) [9, 31].

Alongside pharmacological advances, non-pharmacological interventions have taken on a fundamental role in the contemporary approach to COPD. Pulmonary rehabilitation programs, supervised physical training, non-invasive ventilation, psychological support, and educational strategies have demonstrated consistent benefits regarding functional capacity, quality of life, and reduction of respiratory symptoms (MEGARITIS et al., 2023; LI et al., 2026) [15, 12]. Pulmonary rehabilitation stands out among non-pharmacological interventions for its ability to improve exercise tolerance, dyspnea, and overall functionality. Recent studies demonstrate that structured physical training programs provide significant benefits even in patients with advanced disease, contributing to greater functional independence and reduced use of healthcare services (ROH et al., 2025; PYSZORA; LEWKO, 2022) [23, 22].

Another important component of non-pharmacological treatment involves non-invasive ventilation combined with respiratory rehabilitation. Recent evidence indicates that this combination can provide significant clinical improvement, especially in patients with chronic respiratory failure, reducing symptoms and promoting functional recovery (LI et al., 2026; PANZUTI; ZANABONI; PISANI, 2026) [12, 21]. Dyspnea remains one of the most disabling symptoms of COPD, significantly compromising patients' quality of life. In this regard, multidimensional strategies combining pharmacological and non-pharmacological approaches have been extensively investigated, demonstrating potential to reduce symptom severity and improve the ability to perform daily activities (GAO; WANG; JIANG, 2024; XUE et al., 2025) [8, 33].

In addition to respiratory symptoms, patients with COPD frequently present with psychiatric disorders, particularly anxiety and depression. These conditions are associated with poorer treatment adherence, increased exacerbations, and reduced quality of life, justifying the incorporation of psychological and psychosocial approaches into comprehensive disease management (BUICAN et al., 2025; BEDNAREK et al., 2026) [3, 2].

The integration of psychological interventions into conventional treatment has shown promising results, particularly in reducing emotional distress and improving subjective health perception. This approach reinforces the current concept of patient-centered care and multidimensional management of COPD (SUNDAR, 2024; MORETTA et al., 2024) [28, 16].

Another relevant aspect concerns the musculoskeletal changes associated with COPD, including sarcopenia and frailty. These conditions contribute to functional loss, increased dependence, and a poorer prognosis, making them a growing target for multimodal therapeutic interventions that combine physical exercise, nutritional support, and appropriate pharmacological treatment (NAAS et al., 2026; MEGARITIS et al., 2023) [18, 15].

In recent years, there has been growing interest in the relationship between COPD and cardiovascular disease. Chronic systemic inflammation, persistent hypoxia, and shared pathophysiological mechanisms contribute to the development of heart failure, pulmonary hypertension, coronary artery disease, and other cardiovascular complications (RAMALHO; DE ALBUQUERQUE, 2024; TSAI; MALIK; TJEN-A-LOOI, 2024) [23, 29]. The coexistence of COPD and heart failure poses a significant diagnostic and therapeutic challenge. The overlap of symptoms, especially dyspnea and exercise intolerance, hinders early diagnosis and may compromise the effectiveness of therapeutic interventions, requiring an integrated and multidisciplinary approach (WU; WANG; TANG, 2025; RAMALHO; DE ALBUQUERQUE, 2024) [31, 23].

Additionally, the concept of cardiopulmonary risk has gained prominence in recent guidelines, as the presence of cardiovascular comorbidities directly influences mortality and response to COPD treatment. Thus, cardiovascular assessment has become an essential component of the clinical management of these patients (SINGH et al., 2024; WANG et al., 2024) [26, 30].

Given the advances observed in recent decades, it is essential to comprehensively understand the benefits and limitations of the pharmacological and non-pharmacological strategies available for the treatment of COPD. Furthermore, growing evidence of the interaction between lung disease and cardiovascular changes reinforces the need for personalized therapeutic approaches capable of improving not only respiratory outcomes but also patients' cardiovascular health and quality of life (AGUSTI; SINGH; FANER, 2026; CAZZOLA et al., 2026) [1, 3].

2. Objectives

2.1. General Objective

To analyze, through a systematic review of the literature, the therapeutic advances employed in the management of Chronic Obstructive Pulmonary Disease (COPD), with a focus on pharmacological and non-pharmacological strategies, evaluating their efficacy on clinical, functional, and quality-of-life outcomes, as well as their associated cardiovascular implications.

2.2. Specific Objectives

- To identify the main pharmacological therapies currently used in the treatment of COPD, including bronchodilators, inhaled corticosteroids, combination therapies, and emerging new therapeutic approaches.
- To evaluate the efficacy of pharmacological interventions in reducing respiratory symptoms, preventing exacerbations, improving lung function, and reducing mortality.
- Investigate the role of non-pharmacological strategies, including pulmonary rehabilitation, physical training, non-invasive ventilation, nutritional support, and psychosocial interventions in the management of COPD.
- Analyze the effects of non-pharmacological interventions on patients' functional capacity, dyspnea, quality of life, and psychological well-being.
- Examine the influence of extrapulmonary comorbidities, especially cardiovascular ones, on the clinical course and prognosis of individuals with COPD.
- To assess the relationship between COPD and cardiovascular diseases, including heart failure, pulmonary hypertension, and coronary artery disease, highlighting their impacts on morbidity and mortality.
- Identify evidence regarding integrated therapeutic strategies aimed at the simultaneous management of COPD and cardiovascular comorbidities.

- To compare the benefits of pharmacological and non-pharmacological approaches in reducing cardiopulmonary risk and improving overall clinical outcomes.
- To synthesize the most recent scientific evidence regarding future prospects and innovative therapies for the personalized treatment of COPD.
- Contribute to updating scientific knowledge on the multidimensional management of COPD, providing guidance for evidence-based clinical practice.

3. Methodology

3.1. Study Design

This study consisted of a systematic literature review, conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020), with the aim of identifying, selecting, critically evaluating, and synthesizing scientific evidence related to therapeutic advances in Chronic Obstructive Pulmonary Disease (COPD), with a focus on pharmacological and non-pharmacological strategies and their cardiovascular implications.

3.2. Search Strategy and Information Sources

The literature search was conducted in the electronic databases PubMed/MEDLINE, Scopus, Web of Science, Embase, and the Cochrane Library, as these are considered the primary international sources of biomedical literature. Additionally, reference lists from the included studies were consulted to identify potentially relevant publications.

Controlled descriptors from the Medical Subject Headings (MeSH) and free-text terms related to the topic were used. The search strategy was adapted for each database, using combinations of the following terms:

("Chronic Obstructive Pulmonary Disease" OR COPD) AND ("Pharmacological Treatment" OR "Drug Therapy" OR Bronchodilator* OR Corticosteroid*) AND ("Non-Pharmacological Treatment" OR "Pulmonary Rehabilitation" OR Exercise OR "Noninvasive Ventilation") AND ("Cardiovascular Disease" OR "Heart Failure" OR "Pulmonary Hypertension" OR Cardiovascular OR Cardiac).

3.3. Search Period

Studies published between **January 2021 and June 2026** were included, given the need to gather contemporary evidence related to the most recent therapeutic advances in COPD and its cardiovascular repercussions.

3.4. Inclusion Criteria

Studies that met the following criteria were included:

- Original articles, systematic reviews, meta-analyses, and clinical trials;
- Studies published in English;

- Studies involving individuals diagnosed with COPD;
- Studies addressing pharmacological and/or non-pharmacological interventions;
- Studies analyzing clinical and functional outcomes, quality of life, exacerbations, mortality, or cardiovascular implications;
- Publications available in full in the selected databases;
- Studies published between 2021 and 2026.

3.5. Exclusion Criteria

The following were excluded:

- Articles duplicated across the consulted databases;
- Conference abstracts, editorials, letters to the editor, and expert opinions without a clearly defined methodology;
- Studies conducted exclusively in animal or experimental models;
- Studies that did not have a direct relationship with the treatment of COPD or its cardiovascular implications;
- Studies with insufficient methodological information for critical evaluation.

3.6. Study Selection Process

The selection of studies occurred in two stages. Initially, the titles and abstracts identified in the electronic search were analyzed. Next, potentially eligible articles were read in full to confirm the inclusion criteria.

Screening was performed independently by two reviewers. In cases of disagreement, the final decision was reached by consensus after re-evaluation of the studies.

3.7. Data Extraction

Data from the selected studies were extracted using a standardized form containing the following information:

- Author and year of publication;
- Country where the study was conducted;
- Methodological design;
- Characteristics of the study population;
- Type of pharmacological or non-pharmacological intervention;
- Outcomes assessed;
- Key clinical and cardiovascular outcomes;
- Authors' conclusions.

3.8. Assessment of Methodological Quality

The methodological quality of the included studies was analyzed using appropriate tools for each study design.

Randomized clinical trials were assessed using the Cochrane Collaboration's **Risk of Bias 2 (RoB 2)** tool, while systematic reviews were assessed using the **AMSTAR 2** tool. Observational studies were analyzed using the **Newcastle-Ottawa Scale (NOS)**.

3.9. Synthesis and Data Analysis

The results were synthesized qualitatively and descriptively, taking into account the methodological characteristics of the studies and the heterogeneity of the interventions investigated. The findings were organized into thematic categories related to pharmacological strategies, non-pharmacological interventions, and cardiovascular complications associated with COPD.

3.10. PRISMA Flowchart

The process of identifying, screening, assessing eligibility, and including studies will be presented using a flowchart developed in accordance with the **PRISMA 2020** recommendations, ensuring transparency and reproducibility in the selection of the analyzed articles.

Figure 1 presents the process of identification, screening, eligibility, and inclusion of the studies selected for this systematic review, in accordance with the PRISMA 2020 protocol recommendations. Initially, 428 records were identified in the major scientific databases, including PubMed/MEDLINE, Scopus, Web of Science, Embase, Cochrane Library, BVS, and SciELO. After removing duplicate studies, 297 records remained for analysis.

During the selection phase, 198 studies were excluded after reviewing the titles and abstracts because they did not meet the previously established eligibility criteria. Subsequently, 99 articles were subjected to full-text reading for detailed evaluation. Of these, 63 studies were excluded for various reasons, including lack of focus on therapeutic interventions for COPD, lack of assessment of relevant cardiovascular outcomes, preclinical experimental designs, case reports, insufficient data for extraction, and unavailability of the full text.

At the end of the process, 36 studies met all inclusion criteria and were incorporated into the qualitative synthesis of this review. This methodological process allowed for the selection of recent and highly relevant scientific evidence for the analysis of pharmacological and non-pharmacological therapeutic advances in Chronic Obstructive Pulmonary Disease, as well as their associated cardiovascular implications.

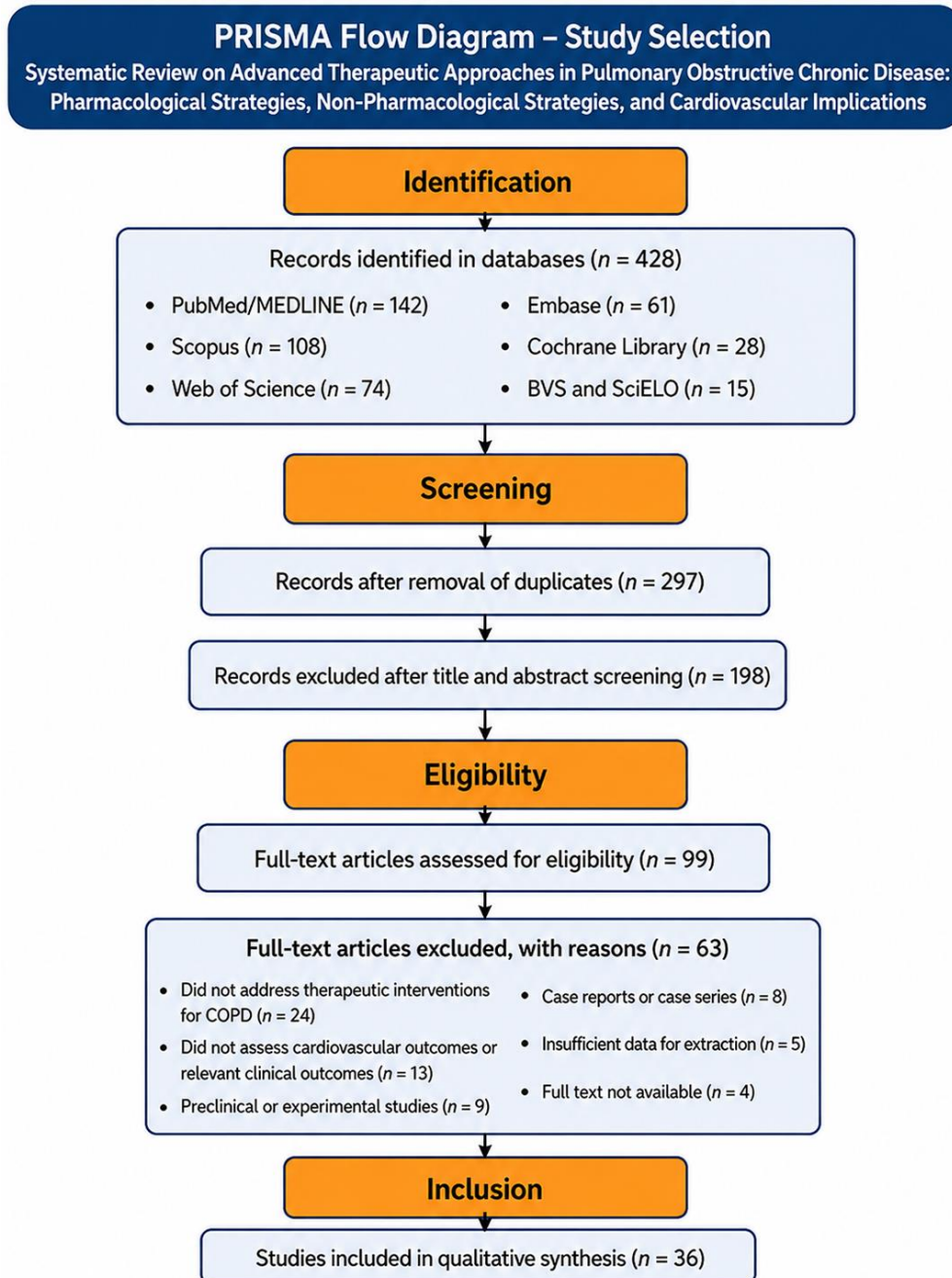


Fig 1:

4. Results

Table 1 presents a summary of the main studies included in this systematic review, covering different therapeutic approaches used in the management of Chronic Obstructive Pulmonary Disease. The selected studies demonstrate a progressive evolution in the treatment of COPD, shifting from strategies predominantly focused on controlling respiratory symptoms to more comprehensive, personalized, and patient-centered care models.

It is observed that pharmacological interventions continue to play a fundamental role in reducing exacerbations and improving lung function. However, the most recent studies highlight the growing prominence of non-pharmacological strategies, especially pulmonary rehabilitation programs, supervised physical training, non-invasive ventilation, nutritional support, and psychosocial interventions, which

have demonstrated significant benefits regarding functional capacity, quality of life, and clinical prognosis.

Another relevant aspect identified in the literature was the close relationship between COPD and cardiovascular diseases. Several studies have demonstrated that chronic systemic inflammation, persistent hypoxia, and shared risk factors contribute to the increased incidence of heart failure, pulmonary hypertension, and coronary artery disease. In this context, cardiovascular assessment has come to be considered an indispensable component of modern COPD management.

Finally, the most recent studies point toward the consolidation of personalized medicine, incorporating multidimensional assessment, cardiopulmonary risk stratification, and the development of new therapeutic targets.

These advances reinforce the need for integrated approaches capable of simultaneously addressing the respiratory and cardiovascular components of the disease, promoting better clinical outcomes and reduced mortality.

Table 1: Summary of the main studies included in the systematic review on therapeutic advances in Chronic Obstructive Pulmonary Disease (COPD).

Author/Year	Study Type	Intervention Evaluated	Main Findings	Cardiovascular Implications
Stolz et al. (2022)	International Commission (Lancet Commission)	Global Strategies for the Elimination of COPD	Emphasized prevention, early diagnosis, and personalized therapies	Recognition of the high cardiovascular burden associated with COPD
Jeyachandran; Hurst (2022)	Narrative review	Management of exacerbations	Reduction in hospitalizations and improved prognosis	Lower risk of cardiovascular decompensation and during exacerbations
Megaritis et al. (2023)	Systematic review and meta-analysis	Pharmacological and non-pharmacological interventions	Significant improvement in physical activity	Indirect benefits on cardiovascular risk factors
Liu et al. (2023)	Translational review	Modulation of the pulmonary microenvironment	New therapeutic targets for personalized treatment	Potential reduction in systemic inflammation
Zysman et al. (2023)	Systematic review	Pharmacological and non-pharmacological interventions	Reduced mortality in patients with COPD	Decreased cardiopulmonary mortality
Fraga et al. (2024)	Comprehensive review	Emerging therapies	Advances in biologics and targeted therapies	Potential impact on reducing vascular inflammation
Gao; Wang; Jiang (2024)	Review	Non-pharmacological treatment of dyspnea	Functional improvement and reduction in physical limitation	Reduction in cardiorespiratory overload
Moretta et al. (2024)	Clinical review	Management of psychiatric disorders	Improved treatment adherence and quality of life	Potential reduction in stress-related cardiovascular risk
Ramalho; Albuquerque (2024)	Narrative review	COPD and heart failure	Highlighted diagnostic and therapeutic challenges	Direct relationship between COPD and heart failure
Singh et al. (2024)	Narrative review	Cardiopulmonary risk	Highlighted the need for cardiovascular stratification	Integration of pulmonary and cardiovascular management
Tsai; Malik; Tjen-A-Looi (2024)	Review	Pulmonary hypertension	Evaluation of pharmacological and non-pharmacological therapies	Relevance for patients with advanced COPD
Xiang; Luo (2024)	Review	Extrapulmonary comorbidities	Association with cardiovascular, metabolic, and muscular diseases	High cardiovascular prognostic impact
Roh et al. (2025)	Network meta-analysis	Pulmonary rehabilitation and complementary therapies	Significant improvement in functional capacity	Secondary cardiovascular benefits
Katamesh et al. (2025)	Scientific review	Chronic pulmonary inflammation	New pathophysiological mechanisms identified	Association between pulmonary inflammation and vascular disease
Wu; Wang; Tang (2025)	Clinical review	Joint management of COPD and heart failure	Need for a multidisciplinary approach	Improvement in cardiovascular outcomes
Agusti; Singh; Faner (2026)	Review of therapeutic innovation	New Drugs and Emerging Therapies	Promising prospects for personalized medicine	Potential reduction in cardiometabolic risk
Cazzola et al. (2026)	GOLD 2026 Update	Multidimensional assessment of COPD	Emphasis on treatment personalization	Systematic inclusion of cardiovascular assessment
Li et al. (2026)	Systematic review and meta-analysis	Noninvasive ventilation + rehabilitation	Significant functional and respiratory improvement	Reduced secondary cardiac overload
Naas et al. (2026)	Narrative review	Sarcopenia and frailty	Benefits of multimodal strategies	Reduction in cardiovascular risk associated with frailty
Li et al. (2026)	Mechanistic review	Mechanotransduction in COPD	New therapeutic targets	Relationship between pulmonary and cardiovascular remodeling

Table 2 summarizes the main therapeutic strategies currently used in the management of Chronic Obstructive Pulmonary Disease, covering both pharmacological and non-pharmacological interventions. It is observed that pharmacological treatments remain fundamental for controlling airflow obstruction, reducing inflammation, and preventing exacerbations.

At the same time, non-pharmacological approaches have taken on an increasingly important role, especially due to their effects on functional capacity, quality of life, and reduction in hospitalizations.

In addition to respiratory benefits, several interventions demonstrate a positive impact on cardiovascular outcomes, an aspect particularly important given the high prevalence of cardiac comorbidities in patients with COPD.

Thus, the integration of pharmacological and non-pharmacological therapies currently constitutes the most effective model for the multidimensional management of the

disease, in line with the recommendations of the most recent international guidelines.

Table 2: Main pharmacological and non-pharmacological strategies for the management of Chronic Obstructive Pulmonary Disease (COPD) and their clinical and cardiovascular impacts.

Therapeutic Category	Strategy	Mechanism/Main Objective	Clinical Benefits	Cardiovascular Impacts
Pharmacological	Long-acting bronchodilators (LABA and LAMA)	Reduction of airway obstruction	Improved lung function and reduced dyspnea	Reduction in cardiorespiratory overload
Pharmacological	Inhaled corticosteroids (ICS)	Control of airway inflammation	Reduction of exacerbations in selected patients	Possible reduction in systemic inflammation
Pharmacological	Triple therapy (LABA + LAMA + ICS)	Integrated control of obstruction and inflammation	Improved quality of life and reduced hospitalizations	Lower risk of cardiopulmonary events
Pharmacology	New targeted therapies and biologics	Modulation of specific inflammatory pathways	Personalized treatment for specific phenotypes	Potential reduction in cardiovascular risk associated with chronic inflammation
Pharmacological	Emerging personalized medicine therapies	Biomarker-based stratification	Greater therapeutic efficacy	Better control of cardiometabolic risk
Non-pharmacological	Pulmonary rehabilitation	Improved functional capacity	Increased exercise tolerance and a significant reduction in dyspnea	Improved cardiovascular fitness
Non-pharmacological	Supervised physical exercise	Muscular and respiratory conditioning	Improved functional capacity and quality of life	Reduction of cardiovascular risk factors
Non-pharmacological	Non-invasive ventilation	Ventilatory support in respiratory failure	Improved oxygenation and reduced fatigue	Reduced cardiac workload
Non-pharmacological	Nutritional support	Correction of malnutrition and sarcopenia	Preservation of muscle mass and function	Reduction of cardiovascular frailty
Non-pharmacological	Psychological interventions	Management of anxiety and depression	Improved treatment adherence and quality of life	Reduction of cardiovascular impact related to chronic stress
Non-pharmacological	Health education and self-care	Promotion of treatment adherence	Reduction in exacerbations and hospitalizations	Overall improvement in cardiopulmonary control
Non-pharmacological	Integrated palliative care	Management of advanced symptoms	Improved comfort and quality of life	Appropriate management of associated cardiovascular limitations

LABA: Long-Acting Beta Agonists; **LAMA:** Long-Acting Muscarinic Antagonists; **ICS:** Inhaled Corticosteroids.

Table 3 presents the main cardiovascular complications associated with Chronic Obstructive Pulmonary Disease, highlighting the pathophysiological mechanisms involved, their clinical impacts, and the currently recommended therapeutic strategies. The analyzed studies demonstrate that COPD should not be understood merely as a respiratory disease, but rather as a complex systemic condition characterized by chronic inflammation, oxidative stress, endothelial dysfunction, and hemodynamic alterations that favor the development of multiple cardiovascular diseases. Among the most frequent comorbidities are heart failure, pulmonary hypertension, and coronary artery disease, which

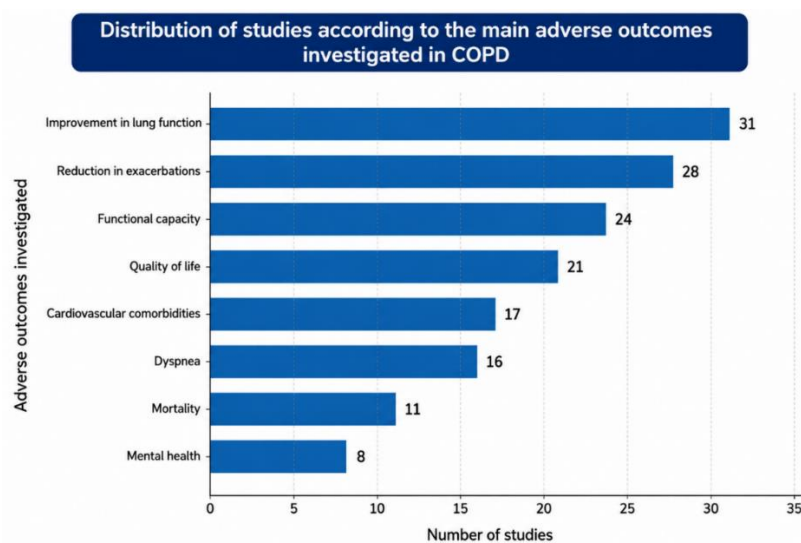
are associated with higher hospitalization rates, poorer quality of life, and increased mortality. Furthermore, the coexistence of these conditions often complicates diagnosis and clinical management due to the overlap of symptoms such as dyspnea, fatigue, and exercise intolerance. Thus, these findings reinforce the importance of a multidisciplinary and integrated approach, involving pharmacological and non-pharmacological strategies aimed simultaneously at controlling COPD and reducing cardiovascular risk. Early identification of these comorbidities is a fundamental element for therapeutic optimization and improvement of long-term clinical outcomes.

Table 3: Major cardiovascular implications associated with Chronic Obstructive Pulmonary Disease (COPD) and recommended therapeutic strategies.

Cardiovascular Complication	Mechanisms Associated with COPD	Clinical Impacts	Related Therapeutic Strategies
Heart Failure (HF)	Chronic systemic inflammation, hypoxia, and oxidative stress	Increased dyspnea, hospitalizations, and mortality	Optimized COPD control, integrated cardiac management, and pulmonary rehabilitation
Pulmonary Hypertension	Chronic hypoxemia and pulmonary vascular remodeling	Progressive functional limitation and poorer prognosis	Oxygen therapy, noninvasive ventilation, and treatment of exacerbations
Coronary Artery Disease	Systemic inflammation, endothelial dysfunction, and accelerated atherosclerosis	Increased risk of acute myocardial infarction and cardiovascular mortality	Control of risk factors, supervised exercise, and appropriate pharmacological treatment
Cardiac Arrhythmias	Hypoxia, autonomic changes, and systemic inflammation	Higher incidence of atrial fibrillation and cardiovascular events	Cardiovascular monitoring and adequate oxygenation control
Peripheral Arterial Disease	Systemic inflammation and vascular dysfunction	Reduced mobility and impaired functional capacity	Exercise programs and management of cardiovascular risk factors
Venous thromboembolism	Pro-inflammatory state and immobility during exacerbations	Increased morbidity and mortality	Thromboembolic prophylaxis and early mobilization
Endothelial dysfunction	Persistent inflammation and oxidative stress	Progression of atherosclerotic cardiovascular disease	Inflammation control and promotion of healthy habits
Increased Cardiometabolic Risk	Sedentary lifestyle, sarcopenia, and metabolic syndrome	Higher incidence of cardiovascular events	Pulmonary rehabilitation, nutritional support, and regular physical activity
Cardiovascular Mortality	Interaction between pulmonary and cardiovascular disease	Leading cause of death in patients with moderate to severe COPD	Multidisciplinary management and integrated cardiopulmonary approach

Analysis of the selected studies identified the main clinical outcomes investigated in research related to the treatment of Chronic Obstructive Pulmonary Disease. A predominance of studies evaluating improvements in lung function, reduction in exacerbations, and increased functional capacity was observed, indicating that these remain the primary indicators of therapeutic efficacy in the contemporary literature. Additionally, there was growing interest in the impacts of interventions on quality of life and cardiovascular comorbidities, reflecting the current understanding of COPD as a complex systemic disease.

As shown in Figure 2, improvement in lung function was the most frequently investigated outcome, followed by a reduction in exacerbations and an increase in functional capacity. Cardiovascular comorbidities were present in a significant proportion of the studies, corroborating recent evidence pointing to cardiovascular disease as one of the main determinants of morbidity and mortality in patients with COPD. These results reinforce the need for integrated therapeutic strategies capable of promoting respiratory, functional, and cardiovascular benefits simultaneously.

**Fig 2:** Distribution of studies according to the therapeutic focus investigated

5. Discussion

This systematic review demonstrated that the management of Chronic Obstructive Pulmonary Disease (COPD) has undergone significant changes in recent years, driven by

expanding knowledge of its pathophysiology and a growing understanding of its systemic nature. The analyzed studies demonstrated that current therapeutic approaches go beyond the isolated control of respiratory symptoms, incorporating

strategies aimed at reducing exacerbations, improving functional capacity, enhancing quality of life, and mitigating cardiovascular comorbidities. These findings corroborate the most recent recommendations of international guidelines, which advocate for an individualized and multidimensional treatment model (CAZZOLA et al., 2026; AGUSTI; SINGH; FANER, 2026) [3, 1].

Improved lung function was the most frequently reported outcome among the included studies. This result reflects the continued role of long-acting bronchodilators as pillars of COPD treatment, particularly long-acting muscarinic antagonists (LAMAs) and long-acting beta-2 agonists (LABAs). According to Agusti, Singh, and Faner (2026) [1], recent advances have enabled the development of more effective therapies tailored to the different phenotypes of the disease, promoting better symptom control and improved functional performance.

Another widely discussed aspect was the reduction of exacerbations, considered one of the main therapeutic goals due to their association with a worse prognosis, increased hospitalizations, and higher mortality. The observed results are consistent with the findings of Jeyachandran and Hurst (2022) [9], who highlight exacerbations as key events in disease progression and the deterioration of lung function. In this context, combination therapies and the optimization of pharmacological treatment have demonstrated a significant ability to reduce the frequency of these episodes.

Studies have also demonstrated significant benefits related to functional capacity. Pulmonary rehabilitation has consistently been identified as one of the most effective non-pharmacological interventions for improving exercise tolerance, reducing physical limitations, and promoting greater functional independence. The findings corroborate the meta-analysis conducted by Roh et al. (2025) [23], which demonstrated the superiority of structured rehabilitation programs over conventional care across multiple clinical outcomes.

In addition to pulmonary rehabilitation, supervised physical exercise has emerged as an important therapeutic component. The reviewed literature indicates that regular exercise contributes to the preservation of muscle mass, improved cardiorespiratory fitness, and a reduction in physical inactivity, one of the factors that exacerbate the progression of COPD. Megaritis et al. (2023) [15] observed that physical activity programs are associated with significant improvements in functionality and reduced long-term mortality.

Dyspnea remains one of the most disabling symptoms of COPD and was extensively addressed by the included studies. Evidence suggests that the combination of pharmacological and non-pharmacological therapies yields better results in controlling this symptom compared to isolated approaches. Gao, Wang, and Jiang (2024) [8] emphasize that multidisciplinary strategies are more effective in reducing the perception of dyspnea () and increasing the ability to perform daily activities.

The results also reinforce the growing importance of noninvasive ventilation in the management of patients with advanced disease. Recent studies demonstrate that its use in

combination with pulmonary rehabilitation promotes improved oxygenation, reduced respiratory effort, and increased functional capacity. These findings are consistent with the systematic review by Li et al. (2026) [12], which demonstrated significant clinical benefits resulting from the combination of these interventions.

Another relevant aspect identified in this review was the growing emphasis on mental health in the context of COPD. Anxiety and depression are highly prevalent in this population and are associated with poorer treatment adherence, increased perception of dyspnea, and lower quality of life. The results found corroborate the findings of Buican et al. (2025) [3] and Moretta et al. (2024) [16], who highlight the need to incorporate psychological interventions into disease treatment programs.

Sarcopenia and frailty have also been highlighted in recent studies. These conditions represent important negative prognostic factors and are associated with reduced functional capacity and increased mortality. Naas et al. (2026) [18] demonstrated that multimodal approaches involving nutritional support, physical exercise, and adequate disease management can significantly reduce the impact of these conditions on patients.

One of the most relevant findings of this review was the strong association between COPD and cardiovascular diseases. Several studies have demonstrated that chronic systemic inflammation, oxidative stress, and persistent hypoxia contribute to the development of heart failure, coronary artery disease, pulmonary hypertension, and other cardiovascular complications. These results corroborate the findings of Xiang and Luo (2024) [32], who identified cardiovascular diseases as some of the main comorbidities associated with COPD.

Heart failure stood out as one of the most frequently associated comorbidities with COPD. Ramalho and Albuquerque (2024) [23] emphasize that the coexistence of these conditions represents a significant diagnostic challenge due to the overlap of symptoms such as dyspnea and exercise intolerance. The included studies reinforce that an integrated approach between pulmonologists and cardiologists can significantly improve clinical outcomes for these patients.

Pulmonary hypertension was also frequently reported as a relevant complication, especially in individuals with advanced disease. According to Tsai, Malik, and Tjen-A-Looi (2024) [29], chronic hypoxia promotes progressive pulmonary vascular remodeling, resulting in increased vascular resistance and worsening of functional capacity. In this scenario, strategies aimed at adequate oxygenation control become fundamental.

Another important aspect concerns the role of systemic inflammation as a pathophysiological link between COPD and cardiovascular disease. Katamesh et al. (2025) demonstrated that persistent inflammatory mediators simultaneously contribute to the progression of lung damage and the development of vascular and atherosclerotic changes. This interaction helps explain the elevated cardiovascular risk observed in this population.

The most recent studies also point to the consolidation of personalized medicine as one of the main future trends in the

treatment of COPD. The development of biomarkers, targeted therapies, and approaches based on specific phenotypes has enabled more effective and individualized treatments. Agusti, Singh, and Faner (2026) highlight that therapeutic personalization may represent one of the greatest advances in disease management in the coming decades.

Finally, the results of this review reinforce that contemporary COPD treatment must be understood within an integrated perspective, simultaneously considering the respiratory, functional, psychological, and cardiovascular aspects of the disease. The combination of pharmacological and non-pharmacological interventions has proven essential for achieving better clinical outcomes, reducing exacerbations, improving quality of life, and lowering cardiovascular risk. Thus, the findings analyzed support the need for multidisciplinary and individualized approaches, aligned with the most recent guidelines and the growing demands of an increasingly aging population with multiple comorbidities.

6. Conclusions

This systematic review has demonstrated that the management of Chronic Obstructive Pulmonary Disease (COPD) has evolved significantly in recent years, driven by expanding knowledge of the disease's pathophysiological mechanisms and the development of new therapeutic strategies. The analyzed studies showed that pharmacological approaches remain fundamental for symptom control, improvement of lung function, and reduction of exacerbations, especially through the use of long-acting bronchodilators, combination therapies, and increasingly personalized therapeutic strategies.

The results also demonstrated that non-pharmacological interventions play an indispensable role in the contemporary treatment of COPD. Pulmonary rehabilitation programs, supervised physical training, non-invasive ventilation, nutritional support, and psychosocial interventions showed consistent benefits regarding functional capacity, reduction of dyspnea, quality of life, and treatment adherence. These findings reinforce the need for multidisciplinary care models capable of addressing the multiple dimensions of the disease. Additionally, the review highlighted that COPD should be understood as a complex systemic condition, frequently associated with significant cardiovascular comorbidities. The high prevalence of heart failure, pulmonary hypertension, coronary artery disease, and other cardiovascular abnormalities demonstrates that cardiometabolic risk constitutes a fundamental component of the clinical course of these patients. In this context, systematic cardiovascular assessment should routinely be integrated into the follow-up of individuals with COPD, contributing to the early identification of risk factors and the implementation of appropriate preventive and therapeutic strategies.

Another relevant aspect observed was the growing advancement of personalized medicine, driven by the identification of new biomarkers, clinical phenotypes, and specific therapeutic targets. These innovations point to a future in which treatments can be progressively

individualized, increasing the efficacy of interventions and reducing complications associated with the disease.

Thus, it is concluded that the integration of pharmacological and non-pharmacological therapies currently represents the most effective approach for the management of COPD. In addition to promoting significant respiratory benefits, this strategy contributes to the reduction of exacerbations, improvement in functional capacity, optimization of quality of life, and mitigation of cardiovascular complications. The findings of this review reinforce the importance of patient-centered, multidisciplinary, and evidence-based care capable of addressing the clinical challenges posed by a disease of high prevalence, complexity, and impact on global public health.

Finally, it is recommended that future research prioritize multicenter clinical trials and longitudinal studies aimed at evaluating the effects of new personalized therapies, as well as investigating the interactions between COPD and cardiovascular diseases. Expanding knowledge in this area may contribute to the development of more effective, safer therapeutic protocols tailored to the specific needs of different patient profiles.

References

1. Agusti A, Singh D, Faner R. Treatment of chronic obstructive pulmonary disease: current pipeline and new opportunities. *Nat Rev Drug Discov.* 2026;25(2):98-115.
2. Bednarek F, et al. The association between chronic obstructive pulmonary disease and depression and other mental disorders: a literature review. *Qual Sport.* 2026;49:67577.
3. Buican IL, et al. Depression and anxiety as comorbidities in chronic obstructive pulmonary disease: a comprehensive narrative review. *Healthcare (Basel).* 2025;13:2344.
4. Cazzola M, et al. GOLD 2026: transforming COPD management with early intervention, multi-dimensional assessment, and personalized care. *Drugs.* 2026:1-17.
5. Cheriyian BV, Gondhale-Karpe PS. The systematic review of the interrelationship between COVID-19 and chronic obstructive pulmonary disease (COPD): implications, outcomes, and management strategies. *Pharm Chem J.* 2025;59(9):954-62.
6. De Souza PMCF, Macedo JM. Impact of physical therapy on the quality of life of older adults with chronic pain: a literature review. *Braz J Implantol Health Sci.* 2026;8(5):1797-820.
7. Fraga LG, et al. Recent advances in innovative approaches and emerging therapies for the treatment of chronic obstructive pulmonary disease: a comprehensive review. *Int J Health Manag Rev.* 2024;10(1):e391.
8. Gao B, Wang S, Jiang S. The mechanism of occurrence, assessment, and non-pharmacological treatment of dyspnea. *Med Rev.* 2024;4(5):395-412.
9. Jeyachandran V, Hurst JR. Advances in chronic obstructive pulmonary disease: management of exacerbations. *Br J Hosp Med (Lond).* 2022;83(7):1-7.

10. Katamesh AA, et al. Inflammatory lung diseases: a clinical and scientific review of the latest advances and challenges. *Pharmacol Rep.* 2025;77(4):889-906.
11. Li J, et al. Mechanical forces and mechanotransduction in COPD: pathogenesis, clinical phenotypes, and therapeutic implications. *Int J Chron Obstruct Pulmon Dis.* 2026;595107.
12. Li S, et al. The effectiveness of non-invasive positive pressure ventilation combined with rehabilitation training in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Ther Adv Respir Dis.* 2026;20:17534666261424364.
13. Liu H, et al. Targeting the biophysical microenvironment for improved treatment of chronic obstructive pulmonary disease. *Trends Mol Med.* 2023;29(11):926-38.
14. Mao J, Li Y, Lv D. Impact of influenza on chronic obstructive pulmonary disease: pathophysiology, exacerbations, and preventive approaches. *Ther Adv Respir Dis.* 2025;19:17534666251363307.
15. Megaritis D, et al. Effects of pharmacological and non-pharmacological interventions on physical activity outcomes in COPD: a systematic review and meta-analysis. *ERJ Open Res.* 2023;9(5).
16. Moretta P, et al. Psychiatric disorders in patients with chronic obstructive pulmonary disease: clinical significance and treatment strategies. *J Clin Med.* 2024;13(21):6418.
17. Mullholand JB, Grossman CE, Perelas A. Non-pharmacological management of idiopathic pulmonary fibrosis. *J Clin Med.* 2025;14(4):1317.
18. Naas S, et al. Multimodal therapeutic strategies for the management of sarcopenia and frailty in chronic obstructive pulmonary disease: a narrative review. *Nutrients.* 2026;18(3):543.
19. Oliveira AJM. Impact of the implementation of exercise programs in patients with peripheral arterial disease: a systematic review [dissertation]. 2023.
20. Oliveira CM. Interaction between metabolic and behavioral aspects of heart rate variability through a systematic review and meta-analysis [dissertation]. 2024.
21. Panzuti G, Zanaboni T, Pisani L. Nonpharmacological treatment of acute exacerbations of chronic obstructive pulmonary disease. In: *Seminars in Respiratory and Critical Care Medicine.* New York: Thieme Medical Publishers; 2026.
22. Pyszora A, Lewko A. Non-pharmacological management in palliative care for patients with advanced COPD. *Front Cardiovasc Med.* 2022;9:907664.
23. Ramalho SHR, de Albuquerque ALP. Chronic obstructive pulmonary disease in heart failure: challenges in diagnosis and treatment for HFpEF and HFrEF. *Curr Heart Fail Rep.* 2024;21(3):163-73.
24. Roh JA, et al. Comparative efficacy of traditional non-pharmacological add-on treatments in patients with stable chronic obstructive pulmonary disease: a systematic review and network meta-analysis. *Front Public Health.* 2025;13:1410342.
25. Simões PRB, et al. Current management of chronic obstructive pulmonary disease: therapeutic approaches and new perspectives. *RCMOS Rev Cient Multidiscip O Saber.* 2024;1(1).
26. Singh D, et al. Implications of cardiopulmonary risk for the management of COPD: a narrative review. *Adv Ther.* 2024;41(6):2151-67.
27. Stolz D, et al. Towards the elimination of chronic obstructive pulmonary disease: a Lancet Commission. *Lancet.* 2022;400(10356):921-72.
28. Sundar D. Integrating psychological interventions into holistic management of chronic respiratory diseases – update review. *ScienceOpen Preprints.* 2024.
29. Tsai J, Malik S, Tjen-A-Looi SC. Pulmonary hypertension: pharmacological and non-pharmacological therapies. *Life (Basel).* 2024;14(10):1265.
30. Wang C, et al. Pharmacological and non-pharmacological advancements in heart failure treatment. *Rev Cardiovasc Med.* 2024;25(6):230.
31. Wu Z, Wang D, Tang C. Comorbid management of chronic obstructive pulmonary disease and heart failure. *Respir Med.* 2025:108575.
32. Xiang Y, Luo X. Extrapulmonary comorbidities associated with chronic obstructive pulmonary disease: a review. *Int J Chron Obstruct Pulmon Dis.* 2024:567-78.
33. Xue Y, et al. Efficacy of non-pharmacological interventions on psychological well-being in stable COPD: a systematic review and network meta-analysis. *J Psychosom Res.* 2025:112324.
34. Yeung S, et al. Current approaches for the treatment of chronic respiratory disorders and limitations. In: *Technological Advances and Innovations in the Treatment of Chronic Respiratory Disorders.* 2025. p. 27-49.
35. Zysman M, et al. Impact of pharmacological and non-pharmacological interventions on mortality in chronic obstructive pulmonary disease (COPD) patients. *Respir Med Res.* 2023;84:101035.

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