# A Clinical Evaluation of ICS–LABA Therapy on Airway Inflammation, Remodeling, and Lung Function Parameters in COPD and Bronchial Asthma Patients — with consideration of inhaled-medicine/aerosol guidance.

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***Abstract*—This study assesses how inhaled corticosteroid–long-acting β₂-agonist (ICS–LABA) therapy affects lung function, airway inflammation, and remodeling in individuals with mild persistent asthma. FeNO, blood eosinophils, and spirometric measures such as $FEV_1$ will be evaluated throughout a 24-week prospective trial design. Asthma control, the frequency of exacerbations, and the impact of inhaler technique and adherence are examples of secondary outcomes. When possible, imaging and specific biomarkers will be used to investigate remodeling. The study incorporates international guidelines for aerosol administration and inhaled medication, with a focus on proper device use, spacer application, and reduced reliance on nebulizers. The results are intended to enhance safer, evidence-based aerosol techniques, optimize ICS–LABA therapy, and elucidate biomarker–clinical response linkages. More individualized and efficient asthma care will result from this research. Over 260 million people worldwide suffer from asthma, which is still a major chronic respiratory condition that causes severe impairment and avoidable deaths, especially in low- and middle-income nations, according to the WHO. Inadequate illness control is a result of under diagnosis, limited availability of necessary inhaled medications, and improper inhaler use, even with successful therapies. Early diagnosis, routine follow-up, and instruction on correct inhaler technique are all important, according to WHO. The Global Asthma Report also highlights disparities in treatment accessibility, growing environmental risk factors, and management gaps. Reducing the worldwide illness burden requires raising awareness, guaranteeing access to ICS-based treatment, and enhancing aerosol-medicine procedures.**

## I. INTRODUCTION

Variable airflow restriction, bronchial hyperresponsiveness, and recurring episodes of wheezing, dyspnea, chest tightness, and coughing are the hallmarks of asthma, a chronic inflammatory disease of the airways. Over 260 million people worldwide suffer from asthma, which is still a major contributor to morbidity, a lower quality of life, and avoidable death. Many individuals still have poor control despite advancements in treatment because of structural remodeling, persistent airway inflammation, and incorrect use of inhaled medications. These difficulties are particularly noticeable in low- and middle-income areas, where patient education and access to necessary inhaled corticosteroids may be restricted.

Chronic inflammation caused by type-2 cytokines, eosinophil activation, mucus hypersecretion, smooth-muscle hypertrophy, and airway remodeling are all part of the pathophysiology of asthma, which gradually impairs normal lung function. Long-acting $\beta_2$-agonists (LABA) offer sustained bronchodilation and symptom alleviation, while inhaled corticosteroids (ICS) continue to be the mainstay of treatment because of their strong anti-inflammatory effects. According to global respiratory guidelines, ICS-LABA therapy is the recommended treatment for mild persistent asthma since it treats both the inflammatory and functional aspects of the condition. Achieving therapeutic outcomes requires precise drug distribution. Drug deposition in the lower airways is greatly reduced by improper device selection, variable adherence, and improper inhaler technique, according to studies. In order to maximize treatment results, it is crucial to incorporate concepts of inhaled medication and aerosol guidance, such as good technique training, appropriate spacer use, and limiting needless nebulizer exposure.

This clinical evaluation focuses on Inhaled Corticosteroid (ICS) and Long-Acting Beta Agonist (LABA) therapy in asthma. The Induction Phase is critical for establishing stable baselines and ensuring optimal drug delivery before the intervention begins. Key objectives include confirming eligibility, stabilizing background treatment, and, most importantly, providing comprehensive aerosol guidance. Patients receive standardized training on proper inhaler technique (pMDI, DPI, SMI) to ensure consistent drug reaching the airways, a vital step for accurate trial results. Baseline assessments are collected for primary endpoints: Lung Function (\text{FEV}_1), Airway Inflammation (\text{FeNO}, sputum eosinophils), and Airway Remodeling (biopsy/imaging). This rigorous induction period ensures that subsequent observed changes are attributable to the specific ICS-LABA regimen under investigation.

Inhaled-medicine, or aerosol therapy, is the foundational treatment method for chronic respiratory diseases like asthma and COPD. By delivering drugs directly to the airways and lungs, it achieves rapid therapeutic effects while substantially minimizing systemic drug exposure and associated side effects. The success of this therapy hinges on the effective interaction between the inhalation device, the drug formulation, and, crucially, the patient's inhalation technique.

Delivery Systems and Their Requirements

Therapeutic aerosols are administered via three primary device types, each demanding a specific patient maneuver:

Pressurized Metered-Dose Inhalers (\text{pMDIs}): These utilize a propellant to release a fixed, precise dose. Their challenge lies in requiring high-level coordination: the patient must initiate a slow, deep inhalation simultaneously with pressing the canister (actuation). Poor coordination results in high drug deposition in the oropharynx due to inertial impaction. The use of a spacer (valves holding chamber) is often recommended to mitigate this by reducing aerosol velocity and simplifying coordination.

Dry Powder Inhalers (\text{DPIs}): Propellant-free, these devices rely entirely on the patient's inspiratory flow to de-aggregate the drug powder and carry it into the lungs. This requires a fast, forceful, and deep inhalation—a maneuver fundamentally different from that required for a \text{pMDI}. The necessary inspiratory flow rate is device-specific.

Soft Mist Inhalers (\text{SMIs}): These deliver a fine mist at a low velocity, requiring less forceful inhalation than DPIs and generally improving patient coordination compared to \text{pMDIs}.

Factors Governing Lung Deposition

Only a fraction of the total inhaled dose reaches the therapeutic target in the lungs (the lung deposition fraction). This is primarily determined by:

Particle Size (Aerodynamic Diameter): Particles larger than 5\mu\text{m} are likely to be deposited high in the respiratory tract by inertial impaction. The ideal size for deep lung penetration is between 1 and 5\mu\text{m}, where deposition occurs mainly via gravitational sedimentation in the smaller airways.

Inhalation Flow and Time: The speed of inhalation must match the device type: slow for \text{pMDIs}/\text{SMIs} and fast for \text{DPIs}.

Breath Hold: A pause of 5 to 10 seconds at the end of inhalation significantly enhances sedimentation, maximizing drug retention in the lung periphery.

Airway Health: In inflamed or obstructed airways, deposition patterns can be altered, sometimes leading to preferential deposition in healthier lung regions.

Clinical Guidance and Adherence

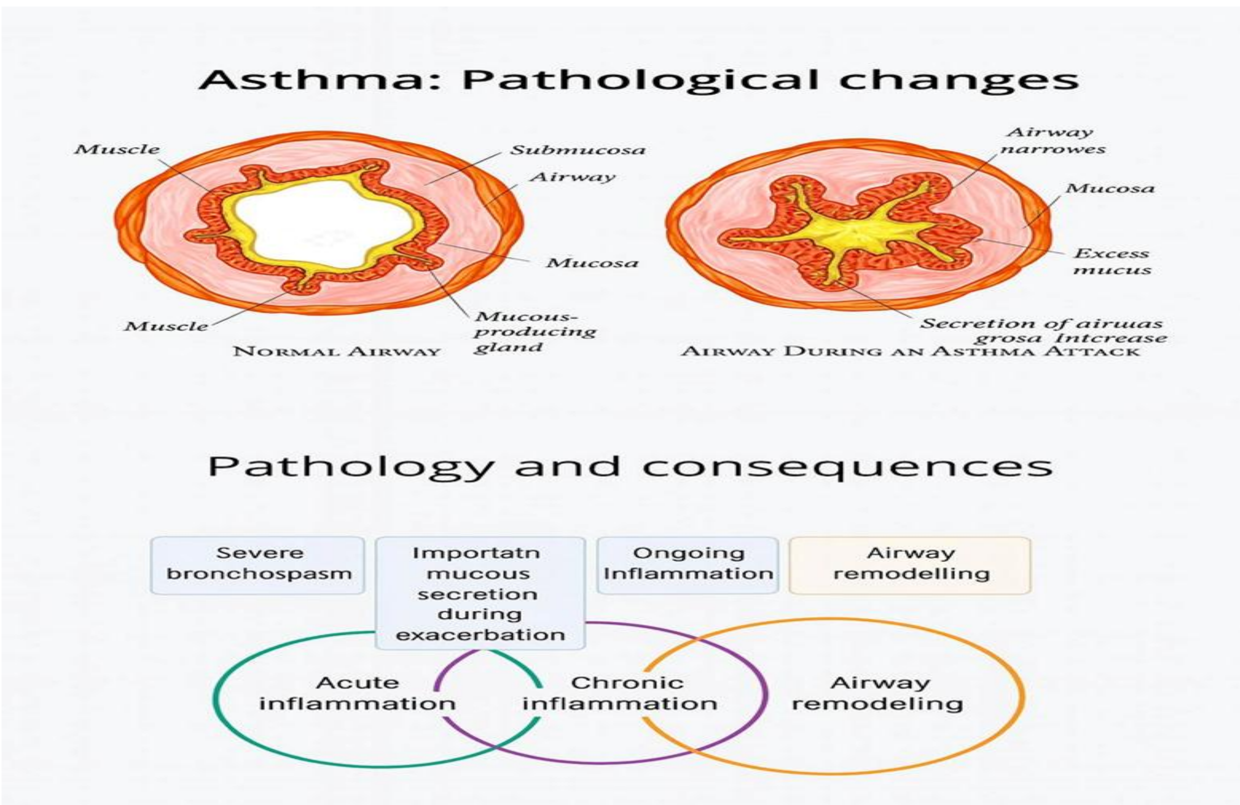
Suboptimal inhaler technique is the most frequent cause of clinical treatment failure in asthma and COPD, with studies showing a majority of patients exhibit errors. Therefore, in clinical evaluations, particularly during the induction phase, standardized patient education and regular technique checks are paramount.

For patients using Inhaled Corticosteroids (\text{ICS}), proper oral hygiene is non-negotiable: rinsing the mouth and gargling with water and spitting immediately after each dose must be taught and reinforced to minimize local side effects like oral candidiasis.

Asthma

Multiple cells, including mast cells, eosinophils, macrophages, and T-lymphocytes, are involved in asthma, a chronic inflammatory disease of the airways. Recurrent episodes of wheezing, dyspnea, chest tightness, and coughing, particularly at night or in the morning, are brought on by persistent inflammation, which causes airway hyperresponsiveness. Usually, airflow restriction is reversible and varied. Genetic predispositions (atopy, hyperresponsiveness of the airways) and environmental factors (allergens, pollution, infections, cold air, exercise, and irritants) combine to cause asthma. Airway remodeling results from structural alterations brought on by inflammation, including mucus hypersecretion, subepithelial fibrosis, smooth muscle hypertrophy, and angiogenesis.

Women, boys, and children are more likely to have asthma. Acute or chronic symptoms can be brought on by triggers such as viral infections, stress, medicines, and exposure to the environment.




## II. ASTHMA: PATHOLOGICAL CHANGES

Reversible airflow restriction, bronchial hyperresponsiveness, and structural airway alterations are the hallmarks of asthma, a chronic inflammatory disease of the airways. Inflammation, increased mucus production, and bronchial tube constriction are the primary pathophysiological alterations. The picture highlights the development of airway obstruction by showing the difference between a normal airway and an airway during an asthma attack. The lumen, or core airway passage, in a healthy airway is broad and transparent, permitting unrestricted airflow. The smooth muscle layer is relaxed, the submucosa and mucosa are thin, and mucous glands only generate the minimal amount of mucus required to retain moisture and capture minute particles. Normal, resistance-free breathing is ensured by this balanced construction. The airway experiences a number of pathological changes during an asthma episode. The mucosa first thickens and swells as a result of inflammation. Breathing becomes challenging due to the narrowing of the airway diameter caused by this swelling. Second, bronchospasm—a severe contraction of the smooth muscles surrounding the airways—reduces the lumen size even more. Third, an overabundance of mucus is produced by goblet cells and mucous glands. This buildup of mucus may obstruct the airway lumen, resulting in wheezing and a tightness in the chest. Reduced airflow, trouble breathing in and out, and episodes of dyspnea are the results of these alterations. Additionally, the image depicts increased mucus secretion, illustrating how thick plugs may impede airflow during flare-ups.

The airway becomes less elastic and less sensitive to bronchodilators as a result of airway remodeling. Even when the patient is not having an acute episode, the airway gradually narrows. This leads to a cycle of ongoing inflammation and a slow deterioration in lung function. The main pathogenic processes that cause asthma symptoms are represented by the consequences depicted in the image, which include severe bronchospasm, significant mucous production, persistent inflammation, and airway remodeling. During episodes, abrupt constriction of the airways is caused by severe bronchospasm. Particularly during exacerbations, excessive mucus output further obstructs airflow. The airways remain hypersensitive due to persistent inflammation, which causes them to react excessively to even small stimuli. If asthma is not adequately managed, airway remodeling indicates long-term harm that may become partially permanent.

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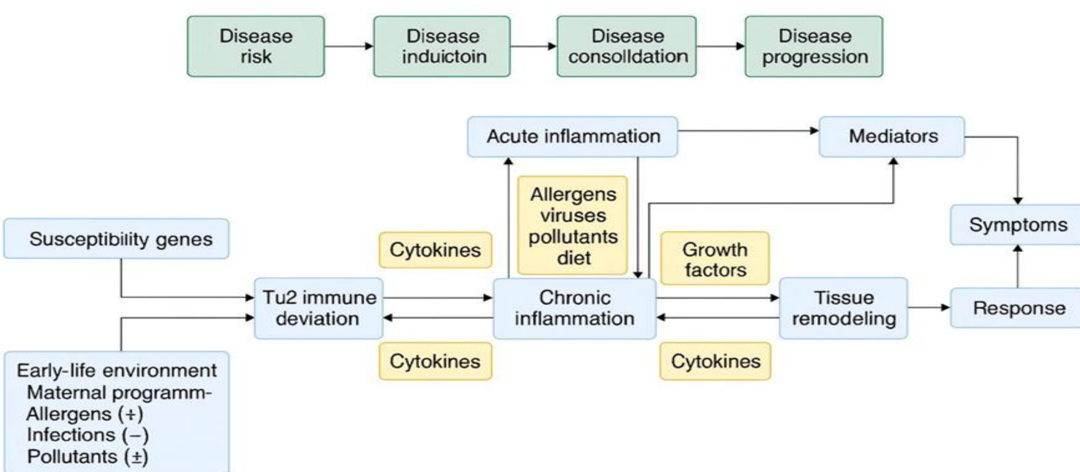
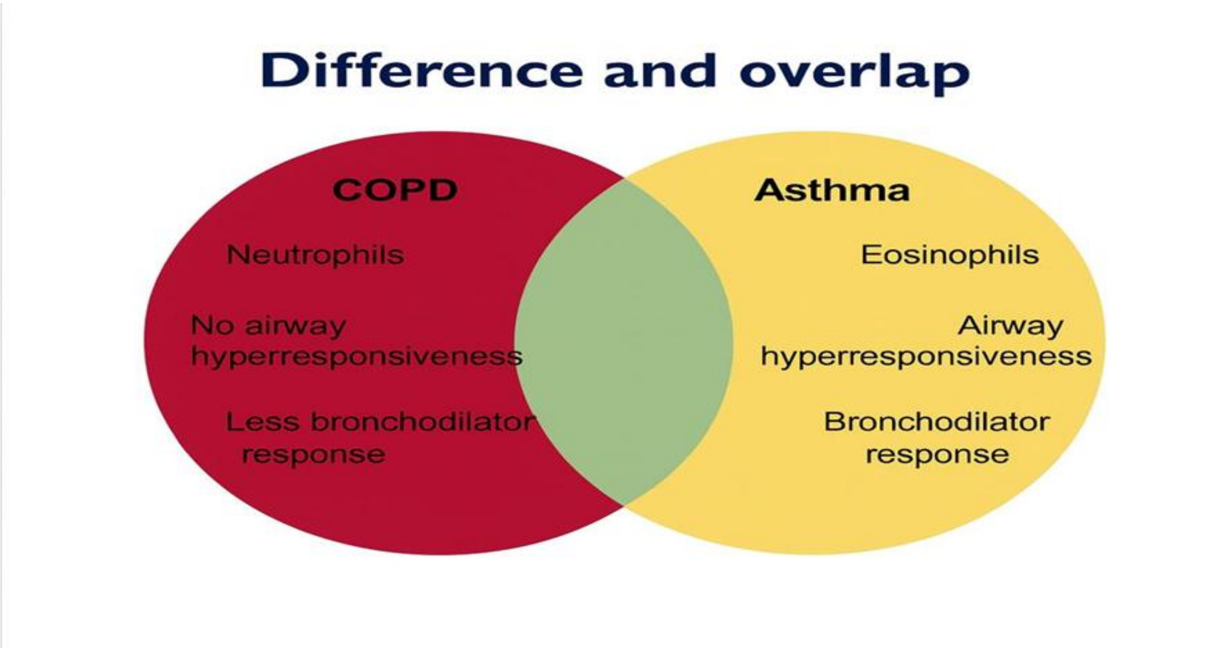
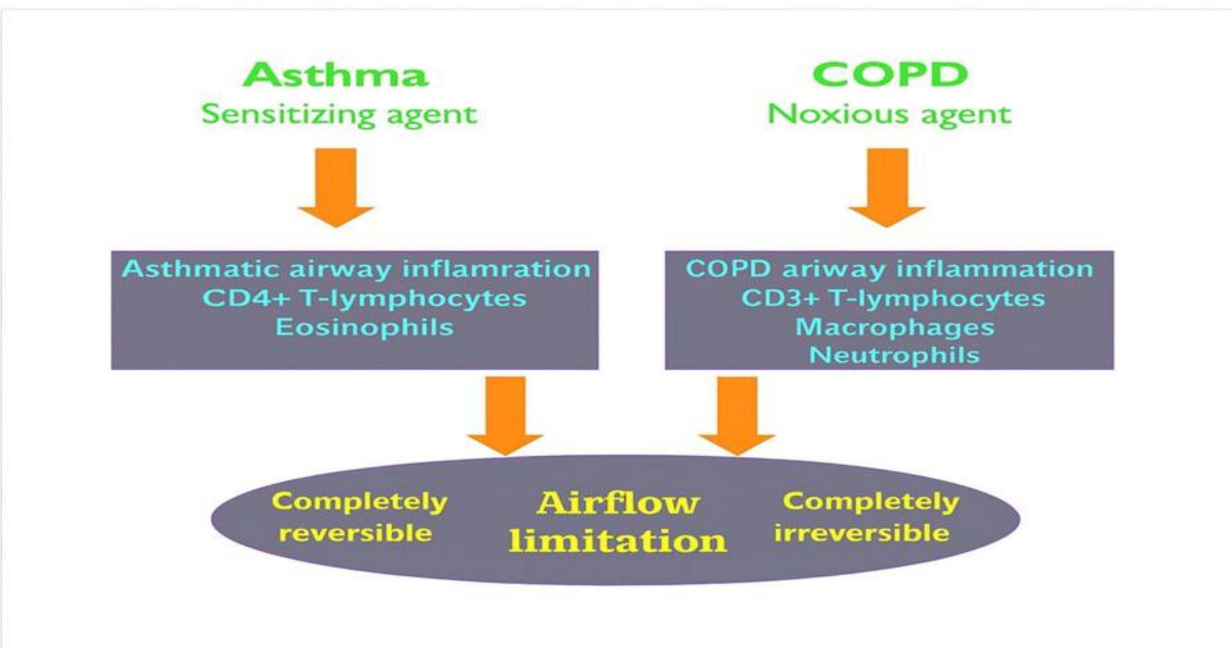
To stop these pathological alterations from getting worse and to preserve good lung function proper treatment with bronchodilators, anti-inflammatory drugs, and trigger avoidance is crucial.



The diagram shows how genetic and environmental factors contribute to the development and progression of chronic inflammatory diseases such as asthma. Susceptibility genes and early-life exposures like allergens, infections, and pollutants can shift the immune system toward TH2 immune deviation, increasing sensitivity to triggers. When allergens, viruses, pollutants, or dietary factors enter the body, they cause acute inflammation, releasing mediators that produce symptoms. Continuous exposure leads to chronic inflammation, driven by cytokines and growth factors. Over time, this results in tissue remodeling, including structural airway changes. These changes worsen disease severity and cause persistent symptoms. The body responds to these symptoms, but without reducing triggers or inflammation, the disease continues to progress.



Asthma and Chronic Obstructive Pulmonary Disease (COPD) are two major chronic airway diseases that affect lung function, but they differ significantly in their causes, inflammatory patterns, clinical presentation, and reversibility. Although both disorders lead to airflow limitation, the underlying mechanisms and responses to treatment are distinct. Understanding their differences and overlap is essential for accurate diagnosis and effective management.

Asthma is primarily an inflammatory disease of the airways characterized by airway hyperresponsiveness. It is often triggered by sensitizing agents such as allergens, environmental particles, or respiratory infections. The key inflammatory cells involved are eosinophils and CD4+ T-lymphocytes, which promote allergic inflammation. This results in narrowing of the airways, increased mucus secretion, and smooth muscle contraction. One of the hallmark features of asthma is that its airflow limitation is completely reversible, either spontaneously or after bronchodilator therapy. Patients with asthma typically show a strong response to bronchodilators and corticosteroids, as these medications effectively reduce airway inflammation and restore airflow. Because the inflammation is mostly eosinophilic, inhaled corticosteroids remain the most effective long-term therapy.

In contrast, COPD is a chronic progressive disease caused mainly by long-term exposure to noxious agents, especially cigarette smoke, industrial pollutants, and biomass fuel. The inflammatory response in COPD is dominated by neutrophils, macrophages, and CD8+ T-lymphocytes, leading to structural damage of the airways and lung tissue. This includes airway wall thickening, destruction of alveolar walls (emphysema), and chronic bronchitis. Unlike asthma, the airflow limitation in COPD is irreversible, due to permanent lung remodeling and loss of elastic recoil. Patients respond poorly to bronchodilators and have a limited response to corticosteroids, making COPD management more dependent on long-acting bronchodilators, smoking cessation, and pulmonary rehabilitation.

The diagrams also highlight the concept of asthma-COPD overlap (ACO), represented by the central area in the Venn diagram. About 10% of patients may present with features of both diseases, such as persistent airflow limitation with a mixture of eosinophilic and neutrophilic inflammation. These patients often experience frequent exacerbations and require a combination of therapies used for both asthma and COPD.

Pathophysiologically, asthma begins with exposure to a sensitizing agent, leading to inflammatory activation of CD4+ cells and eosinophils. This inflammation causes episodic airflow obstruction that is reversible. In COPD, exposure to noxious agents triggers macrophage and neutrophil-mediated inflammation, resulting in chronic, largely irreversible airflow limitation. Thus, although both diseases affect the airways, asthma is primarily an episodic inflammatory condition, whereas COPD is a progressive destructive disease.asthma and COPD differ in their etiology, cellular inflammation, reversibility, and treatment response. Asthma shows reversible airflow limitation with strong steroid responsiveness, while COPD demonstrates irreversible airflow obstruction withlimited therapeutic response. Understanding these differences helps clinicians design effective, individualized treatment strategies.

## III. PHYSIOLOGIC DIFFERENCES

| Asthma | COPD |
|---|---|
| Normal DLCO<br><br>• Normal lung volume<br><br>• Normal elastic recoil<br><br>• Flow dominant BD<br><br>response | Abnormal DLCO<br><br>• Hyperinflation<br><br>• Decreased elastic recoil<br><br>• Volume dominant BD<br>Response |

| Disease Pathology | Asthma | COPD |
|---|---|---|
| Reversible airflow obstruction | + ++ | + |
| Airway inflammation | + + + | + + |
| Mucus hypersecretion | + | + |
| Goblet cell metaplasia | + | + + |
| Impaired mucus clearance | + + | + + |
| Epithelial damage | ++ | — |
| Alveolar destruction | — | ++ |
| Smooth muscle hypertrophy | + + | — |
| Basement membrane thickening | +++ | — |

Is it Asthma? (Clinical Suspicion)

Asthma is a chronic inflammatory disease of the airways that causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. The image lists several classic symptoms that suggest a person might have asthma. Recurrent episodes of wheezing: A high-pitched whistling sound produced by air moving through narrowed airways. Troublesome cough at night: Nighttime coughing is a very common sign, as asthma symptoms often worsen during sleep.Cough or wheeze after exercise: Known as Exercise-Induced Bronchoconstriction (EIB), this is a frequent presentation of asthma.Cough, wheeze or chest tightness after exposure to airborne allergens or pollutants: Exposure to specific triggers (like pollen, dust mites, pet dander, or smoke) causes the airways to tighten.Colds "go to the chest" or take more than 10 days to clear: This suggests the airways are hyper-responsive and easily irritated by infections, leading to prolonged respiratory symptoms.

Clinical Presentations

Asthma can manifest in a few different ways, categorized by the pattern and severity of symptoms:

Episodic Attack: This is the most common presentation. Symptoms appear suddenly—often after exposure to a trigger—and then subside completely or mostly. The patient is usually well between attacks.

Status Asthmaticus: This is a severe, life-threatening asthma attack that does not respond to a person's usual or initial treatments (like a rescue inhaler). It requires immediate and intensive medical attention.

Chronic Asthma: The patient experiences persistent, daily symptoms, though the severity may fluctuate. This form often requires continuous medication to keep symptoms under control.

Clinical Presentations & Examination

The image includes a note on the standard clinical approach to describing and examining a patient with any disease, which applies to asthma:

Patient Symptoms: The patient's subjective description of what they are experiencing (e.g., "I can't catch my breath," "I have a tight chest").

Clinical Features (Objective Examination): What the doctor finds upon physical examination using four key techniques:Inspection: Observing the patient (e.g., checking for rapid breathing or use of accessory breathing muscles).

Palpation: Touching the patient to feel for signs.Percussion: Tapping on the chest to listen to the sound produced (which can indicate over-inflated lungs). Auscultation: Listening with a stethoscope (e.g., to hear the characteristic wheezing sounds of asthma).

## Extrinsic vs intrinsic asthma

| Points | Early Onset | Late Onset |
|---|---|---|
| Age | Early | Late |
| Atopy | Yes | No |
| Allergen involvement | Yes | No |
| Family history | Yes | No |
| IgE in Serum | Increased levels | Normal levels |
| Skin Hypersensitivity test | Positive | Negative |
| Provocation test result | Positive | Negative |

Extrinsic vs. Intrinsic Asthma

This is a fundamental classification of asthma based on its cause:

Extrinsic Asthma (Allergic Asthma): * It is triggered by external factors, typically allergens (like pollen, mold, animal dander, etc.).It is linked to a type of hypersensitivity reaction (Type I) involving the antibody Immunoglobulin E (IgE).It often begins in childhood and may be associated with other allergic conditions (e.g., eczema, allergic rhinitis).

Intrinsic Asthma (Non-allergic Asthma):It is not caused by external allergens or an IgE-mediated response.Triggers are usually non-allergic factors, such as infections, stress, cold air, exercise, or certain medications (like NSAIDs).It often develops in adulthood.

## Differential diagnosis

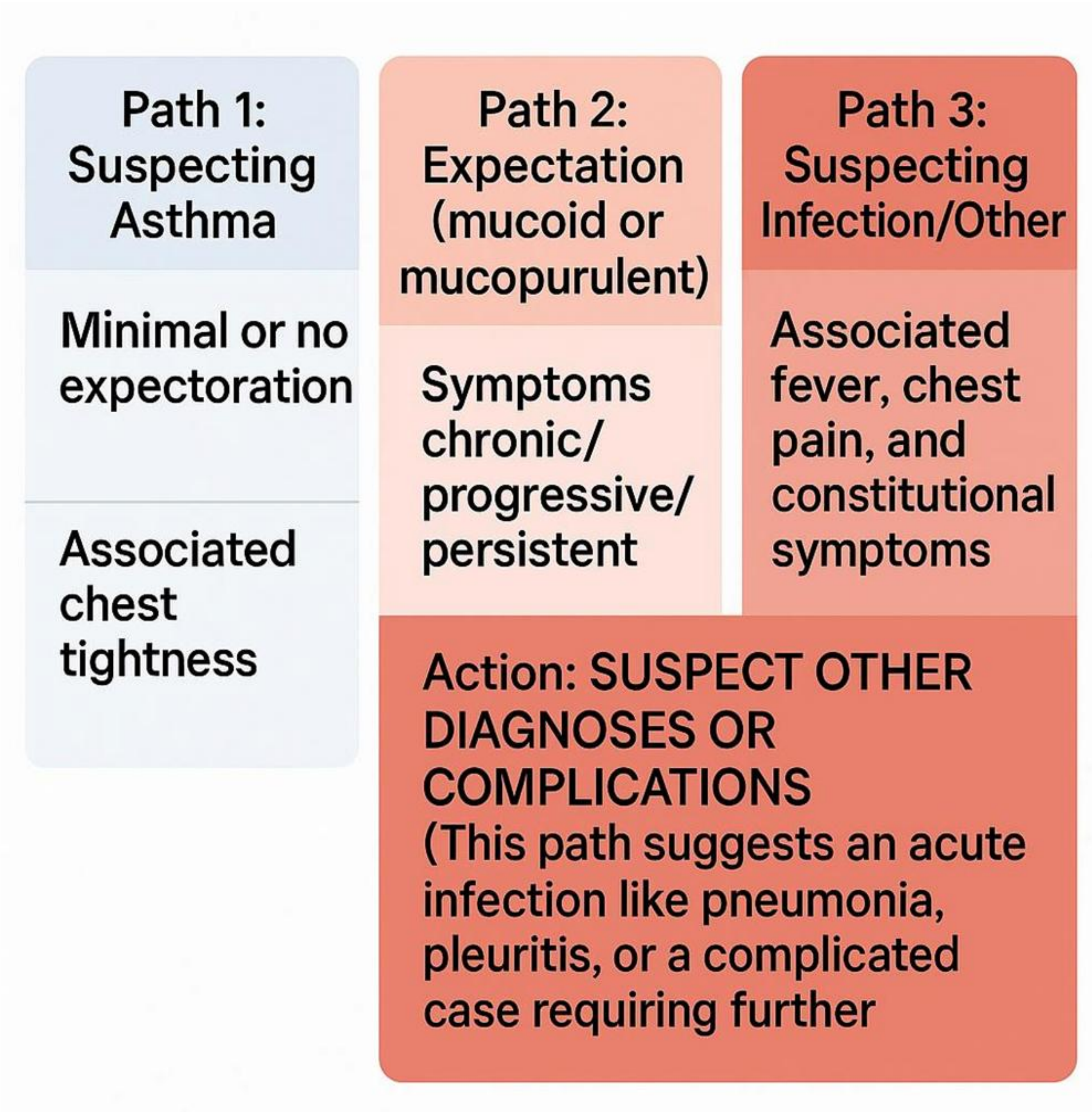
| Category | Examples |
|---|---|
| Diseases causing recurrent episodic dyspnea | Chronic obstructive pulmonary disease, coronary artery disease, congestive heart failure, pulmonary emboli, recurrent gastroesophageal reflux with aspiration, recurrent anaphylaxis, systemic mastocytosis, carcinoid syndrome |
| Common diseases causing cough | Rhinitis, sinusitis, otitis, bronchitis (chronic or postviral), bronchiectasis, cystic fibrosis, pneumónia, diffuse pulmonary fibrosis |
| Common diseases causing airflow obstruction | Chronic obstructive bronchitis and emphysema, bronchiolitis obliterans, cystic fibrosis, organic or functional laryngeal narrowing, extrinsic or intrinśc narrowing of trachea or major bronchus |

IV. DIAGNOSIS

It uses a process of elimination and specific clinical findings to distinguish between common respiratory conditions like Asthma, COPD (Chronic Obstructive Pulmonary Disease), and Tuberculosis (TB), as well as indicating when to suspect other diagnoses.

Flowchart Analysis: Cough, Wheezing, and Breathlessness:

The process begins by classifying the type of cough and expectoration (phlegm/sputum):




The Asthma Diagnostic Path (Minimal/No Expectoration)

This path is strongly suggestive of Asthma:

Symptoms variable, intermittent, recurrent, seasonal, worse at night, and provoked by triggers.History of atopy (a tendency to be hyperallergic) in the patient or a family history of atopy/eczema.Physical Exam (Breath Sound): Normal intensity, with Prominent rhonchi (a rattling sound) that is bilateral, diffuse,

polyphonic (many tones), and primarily heard during expiration (breathing out).
Action: MANAGE AS ASTHMA (This indicates a high clinical suspicion based on the classic pattern of episodic, allergic, and reversible airway symptoms.)
3. The COPD/TB Diagnostic Path (Expectoration)
This path is for chronic symptoms with sputum, often leading to a suspicion of COPD or TB:
History of smoking (active or ETS exposure) is the critical differentiator here, as smoking is the primary cause of COPD.Physical Exam Split: The next step relies on the general appearance and physical signs: Hyperinflation, pursed lip breathing, diminished intensity of breath sounds: These are classic signs of air trapping and severe obstruction, common in COPD.
Normal: The physical exam is non-specific, suggesting the need for lab confirmation. Localized signs: Finding signs limited to one area of the lung suggests a specific focus of disease (e.g., a tumor, localized pneumonia, or focal TB).Action for Localized Signs: SUSPECT OTHER DIAGNOSES OR COMPLICATIONS \rightarrow Referral (Localized findings require imaging and specialist input).
4. Distinguishing COPD from TB
If the patient has signs of hyperinflation (COPD signs) or a "Normal" exam with chronic symptoms, the flowchart mandates testing to rule out Tuberculosis (a curable, infectious disease) before confirming COPD (a progressive, incurable disease): Test: Sputum for AFB (Acid-Fast Bacilli) (x3) is the standard way to diagnose active pulmonary TB.Positive Result: TUBERCULOSIS (Refer to RNTCP) (Referral to the national TB control program).Negative Result: If chronic symptoms, smoking history, and typical COPD physical findings are present, but TB is ruled out: MANAGE AS COPD.
A Clinical Evaluation of ICS–LABA Therapy
Inhaled corticosteroid–long-acting β2-agonist (ICS–LABA) combination therapy has become one of the most important pillars of modern asthma and chronic obstructive pulmonary disease (COPD) management. The therapeutic rationale behind combining an anti-inflammatory medication (ICS) with a bronchodilator (LABA) lies in the complex and multifactorial nature of airway diseases, where inflammation, hyperresponsiveness, edema, mucus hypersecretion, and progressive airway remodeling contribute to airflow limitation. A comprehensive clinical evaluation of ICS–LABA therapy involves examining its pharmacological basis, therapeutic benefits, effects on lung function, role in preventing exacerbations, safety, patient response variability, and long-term impact on airway structure and disease trajectory.

ICS medications work primarily by suppressing chronic airway inflammation. They reduce inflammatory cell infiltration, eosinophil activation, cytokine release, and airway wall thickening. This leads to reduced airway hyperreactivity and helps stabilize the disease at an inflammatory level. LABA drugs, on the other hand, produce prolonged bronchodilation via β2-adrenergic receptor stimulation, leading to relaxation of airway smooth muscle. When combined, these two drug classes demonstrate synergistic effects: LABAs enhance corticosteroid receptor nuclear translocation, while ICS upregulates β2-receptor expression, improving LABA effectiveness. This synergy is one of the strongest pharmacological advantages of ICS–LABA therapy.

Clinical studies consistently show that ICS–LABA therapy significantly improves lung function compared with ICS alone. Forced expiratory volume in 1 second ($FEV_1$), peak expiratory flow rates, and airway caliber demonstrate measurable improvements due to the sustained bronchodilation and reduction in inflammation. In asthma patients, ICS–LABA is particularly effective in individuals who have persistent symptoms despite low-dose ICS therapy. It improves symptom control, reduces nocturnal awakenings, and enhances exercise tolerance. In COPD patients, particularly those with eosinophilic inflammation or frequent exacerbations, ICS–LABA reduces the risk of flare-ups and hospitalizations.

One of the most compelling benefits of ICS–LABA therapy is its strong effect on reducing exacerbation frequency. Exacerbations are clinically significant events often triggered by infections, allergens, pollutants, or poor disease control. They contribute to disease progression, lung function decline, high healthcare utilization, and mortality risk. ICS reduces the inflammatory triggers that initiate exacerbations, while LABA maintains stable bronchodilation and prevents dynamic hyperinflation. Studies demonstrate that the combination therapy is superior to bronchodilator monotherapy in preventing moderate-to-severe exacerbations, especially in patients with elevated blood eosinophil counts—an indicator of steroid-responsive inflammation.

Airway remodeling is another critical component of chronic respiratory diseases. Long-standing inflammation causes changes in the bronchial wall structure, including collagen deposition, goblet cell hyperplasia, smooth muscle hypertrophy, and basement membrane thickening. These structural changes can lead to irreversible airway narrowing. ICS–LABA therapy has shown potential benefits in reducing airway remodeling progression. ICS reduces inflammatory mediators responsible for fibrosis, while LABAs improve smooth muscle dynamics. Although remodeling reversal is limited, slowing progression contributes significantly to long-term disease stability.Another important aspect of ICS–LABA clinical evaluation is quality-of-life improvement. Patients often report reduced symptoms, improved physical functioning, fewer limitations in daily activities, better sleep quality, and enhanced emotional well-being. Patient-reported outcome measures, such as the Asthma Control Test (ACT) and COPD Assessment Test (CAT), consistently show better scores in ICS–LABA users than in ICS alone. Improved symptom control also enhances treatment adherence, which is crucial because poor adherence remains a significant barrier in chronic respiratory disease management.

Despite its benefits, ICS–LABA therapy must be used with proper caution and patient selection. In COPD, not all patients benefit equally from ICS-containing regimens. For example, patients with low eosinophil counts (<100 cells/μL) or those with predominantly neutrophilic inflammation may experience minimal therapeutic benefit or heightened risk of pneumonia. ICS-associated risks, such as oral candidiasis, dysphonia, skin bruising, and rare adrenal suppression, must be monitored. LABA safety has historically been debated, but modern evidence shows LABAs are safe when used in combination with ICS, not as monotherapy. This is why ICS–LABA fixed-dose combinations are the preferred option.The clinical evaluation also highlights the importance of individualized therapy. Biomarkers such as fractional exhaled nitric oxide (FeNO), serum IgE levels, and peripheral eosinophil counts help identify patients who will respond better to ICS. In asthma, ICS–LABA remains first-line for moderate-to-severe disease, but biologics may be added for uncontrolled severe asthma. In COPD, ICS–LABA is preferred for patients with frequent exacerbations, high eosinophils, or asthma–COPD overlap syndrome (ACOS).Inhaler technique is another key determinant of therapeutic success. Incorrect technique can reduce drug deposition in the lungs by up to 70%. Therefore, patient education and regular technique checks are essential. Device selection—metered-dose inhalers (MDIs), dry powder inhalers (DPIs), or soft mist inhalers—should suit the patient's inspiratory ability, coordination, and comfort.

The emergence of triple therapy (ICS–LABA–LAMA) has added another dimension to clinical evaluation. For some COPD patients, triple therapy shows superior outcomes to ICS–LABA alone. However, ICS–LABA remains essential for those with inflammation-driven disease.ICS–LABA therapy represents a highly effective and evidence-based treatment strategy for asthma and selected COPD patients. Its therapeutic value lies in the complementary and synergistic pharmacological mechanisms of corticosteroids and bronchodilators. This combination improves lung function, reduces exacerbations, mitigates symptoms, slows disease progression, and enhances patient quality of life. While certain safety considerations exist—particularly infection risks in COPD—the benefits significantly outweigh the risks in appropriately selected patients. Furthermore, biomarkers and personalized medicine approaches are refining patient-specific treatment decisions. Overall, ICS–LABA therapy stands as a cornerstone in chronic airway disease management and continues to evolve with advancements in inhaler technology, precision diagnostics, and combination therapies.

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│ Start Clinical Review │
│
▼
│ Assess Patient Symptoms & Disease Severity │
│
▼
│ Is inflammation suspected? (Asthma) │
│ Yes
▼
│ Initiate ICS–LABA therapy (anti-inflammatory + │
│ bronchodilation synergy) │
│
▼
│ Evaluate Lung Function (FEV1, PEF, Airflow STATUS) │
│
▼
│ Improvement in Symptoms + Lung Function │
│ Yes
▼
│ Continue ICS–LABA + Optimize Dose + Check │
│ Inhaler Technique │
│
▼
│ Monitor Exacerbations (acute flare-ups) │
│
No Exacerbations   Frequent Exacerbations
▼                  ▼
┌──────────────────────────────────────┐
│ Continue Same Therapy │   │ Evaluate for Higher Step: │
│ + Routine Monitoring  │   │ • Higher ICS dose         │
│                       │   │ • Add LAMA (Triple therapy) │

│
▼
│ Reassess Biomarkers (FeNO, │
│ eosinophils) & Personalization │
│
▼
│ Final Outcome: Controlled Disease │
│ Better Quality of Life │
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Treatment;

Asthma Management, Prevention & Control (GINA Guidelines)

Asthma is a chronic inflammatory condition of the airways characterized by recurrent episodes of wheezing, chest tightness, cough, and breathlessness. The ultimate goal of asthma care is to help patients achieve long-term control, prevent exacerbations, and maintain normal activity levels. The Global Initiative for Asthma (GINA) provides a structured framework that focuses on education, prevention, treatment, monitoring, and patient–doctor partnership. The content presented in the slides outlines the essential components of asthma management and the reasoning behind each intervention.

1. Asthma Management and Prevention Program

This program emphasizes that asthma can be effectively controlled in the majority of patients when appropriate strategies are applied. Control is achieved through early identification of triggers, suppressing airway inflammation, and treating bronchoconstriction. Early intervention helps prevent worsening of symptoms and reduces the need for long-term medication. Recognizing and removing risk factors such as allergens, smoke, pollution, and infections plays a vital role in maintaining airway health.The management program acknowledges that although asthma has no permanent cure, proper planning and communication allow most patients to live normal lives. A strong emphasis is placed on understanding the disease, using medications correctly, and engaging patients in active self-care.

2.Component 1: Develop a Patient/Doctor Partnership

Effective asthma care requires a collaborative relationship between healthcare providers and patients. This partnership ensures that patients feel supported, informed, and engaged in their treatment. A patient-centered approach focuses on continuous education, shared decision-making, and regular follow-up.

Key Actions in Building the Partnership

Continuous education: Patients must be taught regularly about asthma mechanics, triggers, symptoms, and management plans.Family involvement: Particularly for children or elderly patients, families play a critical role in medication adherence and identifying early warning signs. Providing information: Clear explanations about how medications work, when to seek help, and how to use inhalers correctly.Self-management skills: Training patients to monitor symptoms, recognize attacks early, measure lung function (e.g., peak flow), and adjust medication according to the prescribed action plan.Team approach: Healthcare providers, patients, and family members should work collectively in controlling asthma.

Communication Enhancers

GINA stresses that communication should be friendly, supportive, and interactive. Important communication tools include:

Friendly demeanor

Encouragement and praise

Clear and appropriate information

Consistent feedback and follow-up

Ability to listen and address patient concerns

These techniques improve trust, treatment adherence, and overall patient outcomes.

3. Factors Contributing to Poor Treatment Adherence

Non-adherence is one of the leading causes of poor asthma control. Patients may fail to take their medications regularly, use inhalers improperly, or avoid treatment altogether.

Medication-Related Factors

Difficulty using inhalers

Complicated treatment regimens involving multiple medications

Fear of actual or perceived side effects

Cost of medications

Inconvenience or distance To pharmacies

Non-Medication Factors

Misunderstanding or lack of information about asthma

Fear and misconceptions about medications

Unrealistic expectations, such as expecting asthma to be “cured”

Underestimating severity of the condition

Cultural beliefs and family influences

Poor patient-doctor communication

Addressing these factors requires simplified treatment plans, clear demonstrations of inhaler technique, reassurance about medication safety, and strengthening of the therapeutic relationship.

4. Component 2: Identify and Reduce Exposure to Risk Factors

A core part of asthma management involves recognizing environmental and lifestyle triggers and minimizing exposure to them.

Common Risk Factors

Indoor allergens: dust mites, pets, molds

Outdoor pollutants: smoke, vehicle emissions, industrial pollutants

Tobacco smoke exposure

Occupational irritants such as chemicals or dust

Viral respiratory infections, especially in infants and young children

Recommended Interventions

1. Reduce indoor allergen burden through cleaning, ventilation, and allergen-proofing.
2. Avoid cigarette smoke entirely.

3. Minimize exposure to polluted areas and vehicle pollution.
4. Identify and control workplace irritants.
5. Reduce infections by maintaining hygiene and avoiding exposure to sick individuals.

Reducing exposure to triggers significantly decreases symptom frequency, improves control, and reduces medication needs.

5.Influenza Vaccination

The guidelines recommend influenza vaccination for all asthma patients, especially when general population vaccination is advised. Influenza can worsen asthma symptoms leading to severe exacerbations. Annual vaccination reduces the risk of respiratory complications and improves long-term disease outcomes.

6.Component 3: Assess, Treat, and Monitor Asthma

Asthma management requires continuous assessment because symptoms and severity may change over time. Treatment involves controlling inflammation, improving airflow, and preventing exacerbations through medication.

Goals of Asthma Treatment

Prevent acute exacerbations
Reduce emergency visits and hospitalizations
Maintain normal pulmonary function
Enable patients to carry out everyday activities without limitation
Provide effective treatment with minimal adverse effects
Prevent asthma mortality

Regular monitoring helps determine whether treatment needs to be stepped up or stepped down according to the patient's level of control.

7.Goals of Asthma Therapy

The overall goals are aligned with achieving long-term control and preventing complications. The therapy aims to:

Maintain near-normal lung function
Reduce frequency and severity of symptoms
Minimize reliance on rescue medication
Allow participation in normal activities, including exercise
Prevent side effects from medication
Prevent death caused by severe asthma attacks

8. GINA Levels of Asthma Control

The GINA framework categorizes asthma control into three levels:

A. Controlled Asthma

Daytime symptoms occur two times per week or less
No limitations in daily activity
No nocturnal symptoms
Minimal need for rescue medication
Normal lung function

B. Partly Controlled Asthma

Symptoms occur more than twice per week
Any activity limitation
Nighttime symptoms present
Increased use of rescue medication
Lung function reduced (< 80% predicted)

C. Uncontrolled Asthma

Three or more features of partly controlled asthma present within a single week
High risk of severe attacks and hospitalization

These categories guide clinicians to adjust medication and management strategies.

Airway Inflammation and Remodeling

Airway inflammation is a central feature of asthma and represents the immune system's overactive response to allergens, irritants, or infections. This inflammation involves eosinophils, mast cells, macrophages, and T-lymphocytes, which release cytokines and mediators such as IL-4, IL-5, IL-13, and histamine. These substances cause swelling of the bronchial walls, increased mucus production, and contraction of airway smooth muscles, leading to symptoms like wheezing, cough, and breathlessness. Persistent inflammation makes the airways hypersensitive, so even minor triggers can provoke strong bronchoconstriction.

If inflammation continues for long periods, it results in airway remodeling, a structural alteration of the bronchial tissue. Remodeling includes thickening of the basement membrane, smooth-muscle hypertrophy, goblet-cell hyperplasia, subepithelial fibrosis, and increased vascularity. These changes gradually narrow the airways and reduce their elasticity, making airflow obstruction more fixed rather than reversible. As a result, patients may experience worsening lung function, decreased response to bronchodilators, and more frequent exacerbations.

Effective treatments, such as inhaled corticosteroids (ICS) and ICS–LABA combination therapy, aim to suppress inflammation early, preventing or slowing remodeling. Managing triggers and maintaining proper inhaler technique are also essential to reduce long-term structural damage and preserve lung function.

## V. PARAMETERS ASTHMA AND COPD

Asthma vs COPD

Asthma and Chronic Obstructive Pulmonary Disease (COPD) are chronic airway disorders, but they differ significantly in onset, pathology, and progression. Asthma commonly begins in childhood and is strongly linked to allergy, genetic tendency, and environmental triggers such as dust, pollen, or exercise. The airway inflammation in asthma is mainly eosinophilic and causes reversible airflow obstruction. Symptoms like wheezing, chest tightness, and cough usually appear in episodes and improve with bronchodilators or inhaled corticosteroids (ICS). Lung function typically shows marked reversibility after medication. Long-term changes like airway remodeling can occur but are preventable with good control.

In contrast, COPD mainly affects adults above 40 years and is strongly associated with smoking, biomass exposure, and occupational pollutants. COPD involves chronic, neutrophilic inflammation that leads to structural lung damage, including alveolar destruction (emphysema) and airway fibrosis. This results in airflow limitation that is only partially reversible or irreversible. Symptoms such as chronic cough, daily sputum, and progressive breathlessness persist throughout the day. Lung function declines steadily over time, and response to ICS is limited, making long-acting bronchodilators, smoking cessation, and pulmonary rehabilitation essential.

Overall, asthma is intermittent and reversible, while COPD is progressive and usually irreversible.

Aerosols in Medicine

Aerosols play a central role in modern respiratory medicine because they allow medications to be delivered directly into the lungs, the primary site of diseases such as asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis, and various respiratory infections. An aerosol is defined as a suspension of fine solid particles or liquid droplets in air or another gas. These particles are extremely small—typically between 1 and 5 micrometers (µm)—which allows them to remain airborne and be inhaled deeply into the bronchial tree and alveoli. The ability to administer drugs via inhalation offers many therapeutic advantages, including rapid onset of action, reduced systemic exposure, and lower doses compared to oral or injectable routes.

1. Basic Concept of Aerosols

Aerosols consist of tiny particles produced either naturally (dust, smoke, mist) or artificially for medical treatment. In the clinical context, aerosols refer specifically to drug particles generated by devices such as inhalers or nebulizers. The effectiveness of aerosol therapy depends heavily on particle size:

1–5 µm → optimal for bronchial and alveolar deposition

>10 µm → deposit in mouth, pharynx, or upper airway

<1 µm → too small and often exhaled out

The therapeutic goal is to ensure that a controlled fraction of the drug reaches the lower respiratory tract, where it can exert localized action, such as bronchodilation or anti-inflammation.

2. Advantages of Aerosol Drug Delivery

Aerosol therapy is preferred in many respiratory conditions because it offers several significant advantages. The medication is delivered directly to the lungs, allowing for faster onset of relief. This is extremely important in acute asthma attacks where bronchodilation must occur rapidly to reopen constricted airways. Another benefit is the ability to achieve therapeutic effects using much smaller doses compared to systemic administration. Since the drug acts locally, only minimal amounts enter the bloodstream, reducing the risk of systemic side effects such as tremors, arrhythmias, or endocrine disturbances.

Additionally, aerosol devices are portable, convenient, and often patient-controlled. They require minimal preparation and are easy to integrate into daily routines. For chronic diseases like asthma or COPD, this helps maintain long-term adherence and improves quality of life. Moreover, aerosol therapy is suitable for all age groups; nebulizers are especially helpful for infants, elderly patients, or those unable to use inhalers correctly.

3. Devices Used to Generate Medical Aerosols

Three major categories of inhalation devices are used in respiratory medicine:

a) Metered Dose Inhalers (MDIs)

Metered dose inhalers are the most widely used aerosol devices. They contain the medication dissolved or suspended in a pressurized canister along with a propellant gas. When the patient presses the inhaler, the valve releases a precise dose of aerosolized drug. MDIs are compact, fast-acting, and reliable, but they require proper hand–breath coordination. Many patients misuse MDIs, leading to poor drug deposition. To improve delivery, MDIs are often used with spacers, which slow down particle velocity and increase deposition in the lungs.

b) Dry Powder Inhalers (DPIs)

Dry powder inhalers deliver medication in powdered form and do not require propellants. Instead, the patient's inhalation force disperses the powder into respirable particles. DPIs are breath-actuated, meaning drug release occurs automatically when the patient inhales. This eliminates the coordination issues associated with MDIs. However, DPIs require adequate inspiratory flow and may not work well in young children or during severe respiratory distress.

c) Nebulizers

Nebulizers convert liquid medication into aerosol using air pressure, ultrasonic vibration, or mesh technology. They are particularly useful for young children, hospitalized patients, and individuals experiencing severe asthma or COPD exacerbations. Nebulizers deliver a continuous aerosol that the patient inhales through a mask or mouthpiece over several minutes. Although slower than inhalers, they require no coordination or effort.

4. Medicines Commonly Delivered as Aerosols

A wide range of medications are formulated for inhalation. These include:

a) Bronchodilators

These drugs relax airway smooth muscle and relieve bronchoconstriction.

Short-acting $\beta_2$ agonists (SABA): Salbutamol (Albuterol), Levalbuterol

Used for quick relief during asthma attacks.

Long-acting $\beta_2$ agonists (LABA): Formoterol, Salmeterol

Provide prolonged bronchodilation for maintenance therapy.

Anticholinergics: Ipratropium (short-acting), Tiotropium (long-acting)

Often used in COPD to reduce mucus and open airways.

b) Inhaled Corticosteroids (ICS)

ICS are the cornerstone of asthma management. They reduce airway inflammation, mucosal swelling, and hyper-responsiveness.

Examples:

Budesonide

Fluticasone

Beclomethasone

Mometasone

ICS greatly reduce asthma symptoms, prevent exacerbations, and decrease hospitalization risk.

c) Combination Inhalers

These inhalers contain both an ICS and a LABA. They provide anti-inflammatory action along with long-term bronchodilation.

Examples:

Budesonide + Formoterol

Fluticasone + Salmeterol

Mometasone + Formoterol

Combination therapy is particularly effective for moderate to severe asthma and COPD.

d) Antimicrobial Aerosols

In chronic lung infections, inhaled antibiotics target the site of infection directly.

Examples:

Tobramycin (used in cystic fibrosis)

Colistin

Amphotericin B (for fungal infections)

e) Other Therapeutic Aerosols

Mucolytics (e.g., N-acetylcysteine) thin mucus

Hypertonic saline improves mucus clearance

Mannitol powder used in bronchiectasis

Nicotine replacement aerosols for smoking cessation

5. Factors Affecting Aerosol Deposition

The efficiency of aerosol therapy depends on multiple factors:

Particle size – determines depth of penetration

Inhalation technique – crucial for MDIs and DPIs

Breathing pattern – slow, deep inhalation improves deposition

Airway obstruction – narrow airways reduce particle entry

Device type and condition – maintenance and cleaning matter

Proper patient training dramatically improves outcomes.

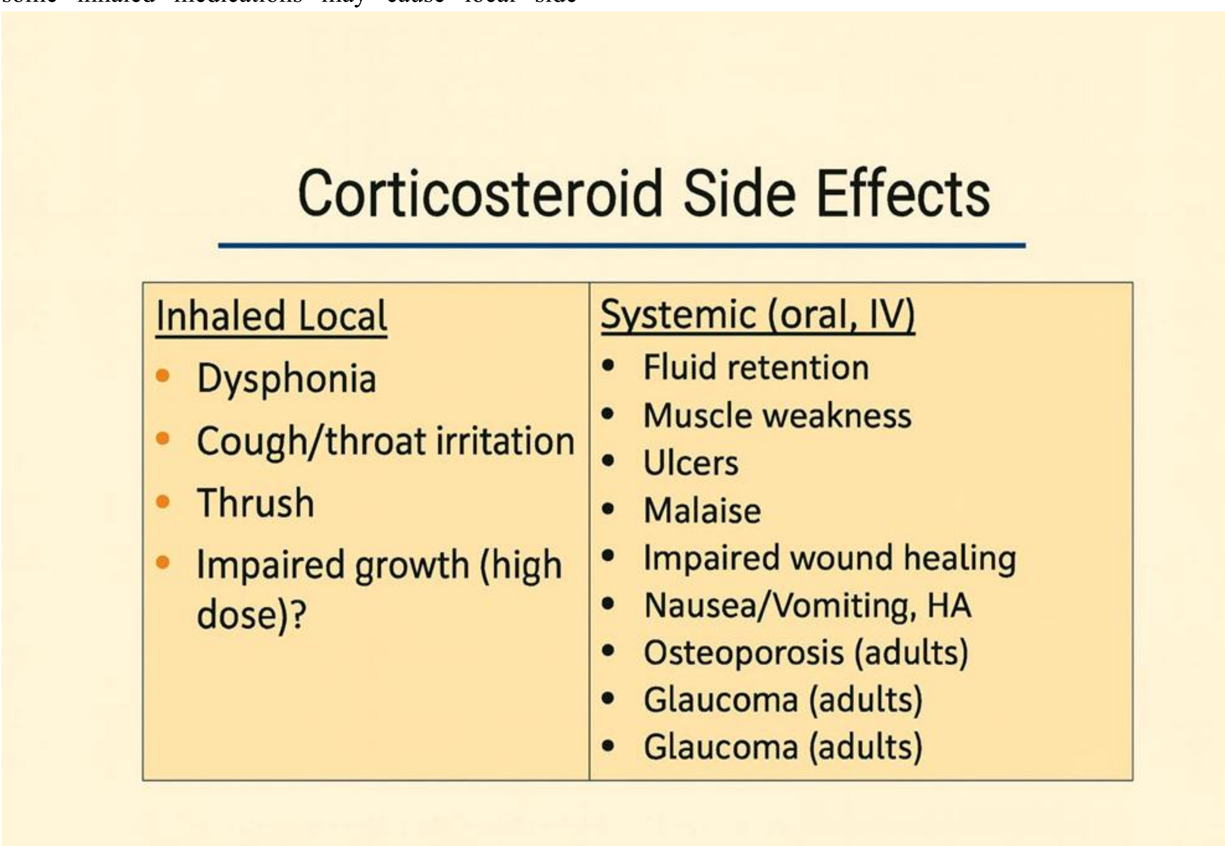
6. Limitations and Challenges of Aerosol Therapy

Despite its advantages, aerosol therapy has some limitations. Improper technique can drastically reduce the dose reaching the lungs. Many patients fail to inhale correctly using MDIs, leading to poor disease control. Weather conditions like humidity can affect DPIs. Nebulizers, while easy to use, are less portable, require electricity, and take longer delivery times. Additionally, continuous long-term use of some inhaled medications may cause local side effects such as throat irritation, hoarseness, or oral thrush.

7. Clinical Importance of Aerosols

Aerosols have revolutionized respiratory medicine by enabling targeted treatment. Conditions like asthma, COPD, and cystic fibrosis, which once caused severe disability, are now manageable with proper inhalation therapy. Aerosols allow for personalized treatment with minimal systemic impact. They are essential in emergency care, chronic management, and pediatric respiratory therapy. As technology advances, more precise and efficient aerosol devices are being developed to enhance drug delivery and therapeutic outcomes.

- This table compares daily doses of inhaled corticosteroids for adults. It shows low, medium, and high doses for different drugs such as Beclomethasone, Budesonide, Flunisolide, and Fluticasone. Doses are listed in puffs and micrograms (mcg), helping guide appropriate asthma treatment steps (Step 2–4).



**Estimated Comparative Daily Dosages for Adults of Inhaled Corticosteroids**

| Drug | Low Dose Step 2 | Medium Dose Step 3 | High Dose Step 4 |
|---|---|---|---|
| Beclomethasone | 1-3 puffs<br>80 - 240 mcg | 3-6 puffs<br>240 - 480 mcg | >6 puffs<br>> 480 mcg |
| Budesonide DPI | 1-3 puffs<br>200 - 600 mcg | 3-6 puffs<br>600 - 1,200 mcg | > 8 puffs<br>> 2,000 mcg |
| Flunisolide | 2-4 puffs<br>500-1,000 mcg | 4-8 puffs<br>1,000-2,000 mcg | > 8 puffs<br>> 2,000 mcg |
| Fluticasone | 2-6 puffs (44)<br>88-264 mcg | 2-6 puffs (110)<br>264-660 mcg | > 60 puffs<br>> 2,000 mcg |

This slide shows side effects of corticosteroids. Inhaled steroids mainly cause local effects such as dysphonia, throat irritation, thrush, and possible growth impairment at high doses. Systemic steroids (oral or IV) may lead to fluid retention, muscle weakness, ulcers, poor wound healing, nausea, osteoporosis, cataracts, and glaucoma in adults.

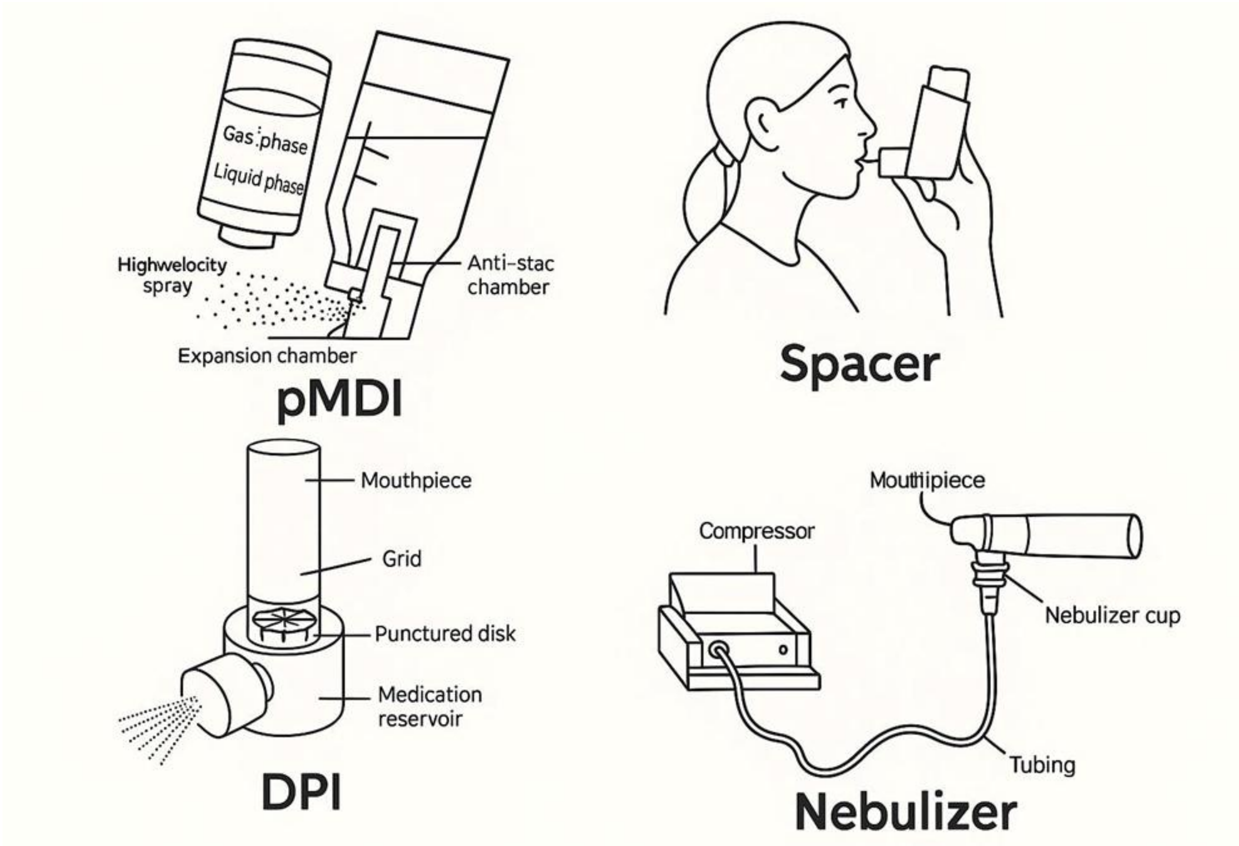
Medicinal Device pMDI, Spacer, DPI, and Nebulizer ;

Inhalation devices are essential tools for delivering medication directly into the lungs in conditions like asthma and COPD. The pressurized Metered-Dose Inhaler (pMDI) contains medication in a canister with propellant gas. When pressed, it releases a high-velocity aerosol spray. pMDIs are small and effective but require proper coordination between actuation and inhalation. To improve drug delivery, a spacer or holding chamber is often used. The spacer slows down particle velocity, reduces throat deposition, and allows more medication to reach the lower airways, making it especially useful for children and patients with poor coordination.

The Dry Powder Inhaler (DPI) delivers medication in powder form. It is breath-actuated, meaning the patient's inhalation draws the powder into the lungs. DPIs are simpler to use but require a strong inspiratory effort, making them less effective during severe asthma attacks.

Nebulizers convert liquid medication into a fine mist using compressed air, ultrasonic vibration, or mesh technology. They require no coordination and are ideal for infants, elderly individuals, and severe respiratory distress, though they are bulkier and slower.

Overall, choosing the right device depends on age, technique ability, severity of symptoms, and patient preference.




## VI. WHO REPORTED ASTHAMA

Overview

Asthma is a chronic lung disease affecting people of all ages. It is caused by inflammation and muscle tightening around the airways, which makes it harder to breathe.Symptoms can include coughing, wheezing, shortness of breath and chest tightness. These symptoms can be mild or severe and can come and go over time.Although asthma can be a serious condition, it can be managed with the right treatment. People with symptoms of asthma should speak to a health professional.

Impact

Asthma is often under-diagnosed and under-treated, particularly in low- and middle-income countries.People with under-treated asthma can suffer sleep disturbance, tiredness during the day, and poor concentration. Asthma sufferers and their families may miss school and work, with financial impact on the family and wider community. If symptoms are severe, people with asthma may need to receive emergency health care and they may be admitted to hospital for treatment and monitoring. In the most severe cases, asthma can lead to death.

Symptoms

Symptoms of asthma can vary from person to person. Symptoms sometimes get significantly worse. This is known as an asthma attack. Symptoms are often worse at night or during exercise.

Common symptoms of asthma include:

A persistent cough, especially at night

Wheezing when exhaling and sometimes when inhaling

Shortness of breath or difficulty breathing, sometimes even when resting

Chest tightness, making it difficult to breathe deeply.Some people will have worse symptoms when they have a cold or during changes in the weather. Other triggers can include dust, smoke, fumes, grass and tree pollen, animal fur and feathers, strong soaps and perfume.Symptoms can be caused by other conditions as well. People with symptoms should talk to a healthcare provider.

Causes

Many factors have been linked to an increased risk of developing asthma, although it is often difficult to find a single, direct cause.Asthma is more likely if other family members also have asthma – particularly a close relative, such as a parent or sibling.Asthma is more likely in people who have other allergic conditions, such as eczema and rhinitis (hay fever).Urbanization is associated with increased asthma prevalence, probably due to multiple lifestyle factors. Events in early life affect the developing lungs and can increase the risk of asthma. These include low birth weight, prematurity, exposure to tobacco smoke and other sources of air pollution, as well as viral respiratory infections. Exposure to a range of environmental allergens and irritants are also thought to increase the risk of asthma, including indoor and outdoor air pollution, house dust mites, moulds, and occupational exposure to chemicals, fumes or dust.Children and adults who are overweight or obese are at a greater risk of asthma.

Treatment

Asthma cannot be cured but there are several treatments available. The most common treatment is to use an inhaler, which delivers medication directly to the lungs.

Inhalers can help control the disease and enable people with asthma to enjoy a normal, active life.

There are two main types of inhaler:

Bronchodilators (such as salbutamol), that open the air passages and relieve symptoms; and

Steroids (such as beclometasone) that reduce inflammation in the air passages, which improves asthma symptoms and reduces the risk of severe asthma attacks and death.

People with asthma may need to use their inhaler every day. Their treatment will depend on the frequency of symptoms and the types of inhalers available.

Using an inhaler can be difficult, especially for children and during emergency situations. Using a spacer device makes it easier to use an aerosol inhaler. This helps the medicine to reach the lungs more easily. A spacer is a plastic container with a mouthpiece or mask at one end and a hole for the inhaler in the other. A homemade spacer, made from a 500ml plastic bottle, can be as effective as commercially manufactured spacers.

Access to inhalers is a problem in many countries. In 2021, bronchodilators were available in public primary health care facilities in half of low- and low-middle income countries, and steroid inhalers available in one third.

It is also important to raise community awareness to reduce the myths and stigma associated with asthma in some settings.

Self-care

People with asthma and their families need education to understand more about their asthma. This includes their treatment options, triggers to avoid, and how to manage their symptoms at home.

It is important for people with asthma to know how to increase their treatment when their symptoms are worsening to avoid a serious attack. Healthcare providers may give an asthma action plan to help people with asthma to take greater control of their treatment.

## VII. WHO RESPONSE

Asthma is included in the WHO Global Action Plan for the Prevention and Control of NCDs and the United Nations 2030 Agenda for Sustainable Development.

WHO is taking action to extend diagnosis of and treatment for asthma in a number of ways.

The WHO Package of Essential Noncommunicable Disease Interventions (PEN) was developed to help improve NCD management in primary health care in low-resource settings. PEN includes protocols for the assessment, diagnosis and management of chronic respiratory diseases (asthma and chronic obstructive pulmonary disease), and modules on healthy lifestyle counselling, including tobacco cessation and self-care.

Reducing tobacco smoke exposure is important for both primary prevention of asthma and disease management. The Framework Convention on Tobacco Control is enabling progress in this area as are WHO initiatives such as MPOWER and mTobacco Cessation. Air pollution is an important risk factor for asthma, causing new cases and making existing disease worse. WHO has developed training for health care workers on air pollution which highlights this link and offers practical advice to reduce and mitigate exposure. The Global Alliance against Chronic Respiratory Diseases (GARD)

contributes to WHO's work to prevent and control chronic respiratory diseases. GARD is a voluntary alliance of national and international organizations and agencies from many countries committed to the vision of a world where all people breathe freely.
Asthma is one of the most common noncommunicable diseases, affecting an estimated 262 million people in 2019, and causing nearly half a million deaths every year.

Although asthma cannot be cured, people with asthma can enjoy a normal life if correctly diagnosed and treated. Inhalers (both bronchodilators and steroids) are considered essential medicines in the WHO package of essential noncommunicable disease interventions for primary health care and should be available to all people living with asthma around the world.

On World Asthma Day, WHO experts offer 5 tips on how to manage your asthma better.

1. Be aware of your symptomsCough, wheeze and difficulty breathing are all signs that your asthma is not well controlled. If you feel that your symptoms are getting worse, follow the instructions from your doctor. Use a reliever inhaler (e.g. salbutamol) with a spacer to open your airways.

2. Identify and avoid your triggers

Common triggers include smoke, fumes, viral infections, pollen, changes in the weather, animal fur and feathers, and strong fragrances. Know what affects you and try to avoid if possible. If not possible, make sure you have your reliever inhaler readily available.

3. Know your inhalers

A reliever inhaler (also called a bronchodilator) opens up the small airways and improves airflow in and out of the lungs. Use this when you have symptomsA steroid or preventer inhaler reduces inflammation in the lungs and is an essential part of long term asthma treatment. By using a steroid inhaler, as directed by your doctor, you will improve your symptoms and reduce the risk of a severe attack.Inhalers are the safest, most effective treatment for asthma and allow people with asthma to lead a normal, active life.

4. Use a spacer

A spacer is a plastic chamber which connects the inhaler at one end, to your mouth via a mouthpiece or mask at the other end. It can help inhaled medicines to reach the small airways in the lungs and work better. The spacer allows more time for the medicine to be breathed in and means that less coordination is required. Without a spacer, you have to breath in deeply and press the inhaler at the same time – inhaled medicine often ends up in the mouth or throat and is ineffective. Some types of inhaler (e.g. dry powder inhalers) do not need a spacer – check with your doctor if you are unsure.
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Air pollution is an important risk factor for asthma, causing new cases and making existing disease worse. WHO has developed training for health care workers on air pollution which highlights this link and offers practical advice to reduce and mitigate exposure.
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Key facts

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death worldwide, **causing**

3.5 million deaths in 2021, approximately 5% of all global deaths.
Nearly 90% of COPD deaths in those under 70 years of age occur in low- and middle-income countries (LMIC).
COPD is the eighth leading cause of poor health worldwide (measured by disability-adjusted life years)
Tobacco smoking accounts for over 70% of COPD cases in high-income countries. In LMIC tobacco smoking accounts for 30–40% of COPD cases, and household air pollution is a major risk factor .

Overview
Chronic obstructive pulmonary disease (COPD) is a common lung disease causing restricted airflow and breathing problems. It is sometimes called emphysema or chronic bronchitis. In people with COPD, the lungs can get damaged or clogged with phlegm. Symptoms include cough, sometimes with phlegm, difficulty breathing, wheezing and tiredness. Smoking and air pollution are the most common causes of COPD. People with COPD are at higher risk of other health problems.COPD is not curable but symptoms can improve if one avoids smoking and exposure to air pollution and gets vaccines to prevent infections. It can also be treated with medicines, oxygen and pulmonary rehabilitation.

Symptoms
The most common symptoms of COPD are difficulty breathing, chronic cough (sometimes with phlegm) and feeling tired.COPD symptoms can get worse quickly. These are called flare-ups. These usually last for a few days and often require additional medicine.
People with COPD also have a higher risk for other health problems. These include:
Lung infections, like the flu or pneumonia
Lung cancer
Heart problems
Weak muscles and brittle bones
Depression and anxiety.
Common symptoms of COPD develop from mid-life onwards. As COPD progresses, people find it more difficult to carry out their normal daily activities, often due to breathlessness. There may be a considerable financial burden due to limitation of workplace and home productivity, and costs of medical treatment.COPD is sometimes called emphysema or chronic bronchitis. Emphysema usually refers to destruction of the tiny air sacs at the end of the airways in the lungs. Chronic bronchitis refers to a chronic cough with the production of phlegm resulting from inflammation in the airways. COPDand asthma share common symptoms (cough, wheeze and difficulty breathing) and people may have both conditions.

Causes
Several processes can cause the airways to become narrow and lead to COPD. There may be destruction of parts of the lung, mucus blocking the airways, and inflammation and swelling of the airway lining.

COPD develops gradually over time, often resulting from a combination of risk factors:
Tobacco exposure from active smoking or passive exposure to second-hand smoke;
Occupational exposure to dusts, fumes or chemicals;
Indoor air pollution: biomass fuel (wood, animal dung, crop residue) or coal is frequently used for cooking and heating in low- and middle-income countries with high levels of smoke exposure; Early life events such as poor growth in utero, prematurity, and frequent or severe respiratory infections in childhood that prevent maximum lung growth;Asthma in childhood; andA rare genetic condition called alpha-1 antitrypsin deficiency, which can cause COPD at a young age.COPD should be suspected if a person has typical symptoms, and the diagnosis confirmed by a breathing test called spirometry, which measures how the lungs are working. In low- and middle-income countries, spirometry is often not available and so the diagnosis may be missed.

Treatment
COPD isn’t curable, but it can get better by not smoking, avoiding air pollution and getting vaccines. It can be treated with medicines, oxygen and pulmonary rehabilitation.
There are several treatments available for COPD.
Inhaled medicines that open and reduce swelling in the airways are the main treatments. Bronchodilator inhalers are the most important medicines for treating COPD. They relax the airways to keep them open.Short-acting bronchodilators start to work in seconds and can last for 4–6 hours. These are often

used during flare-ups.Long-acting bronchodilators take longer to start working but last longer. These are taken daily and can be combined with inhaled steroids.

Other treatments may also be used:
Steroid pills and antibiotics are often used to treat flare-ups.Oxygen is used for people who have had COPD for a long time or have severe COPD.Pulmonary rehabilitation teaches exercises to improve your breathing and ability to exercise.Surgery may improve symptoms for some people with severe COPD.
Some inhalers open the airways and may be given regularly to prevent or reduce symptoms, and to relieve symptoms during acute flare-ups. Inhaled corticosteroids are sometimes given in combination with these to reduce inflammation in the lungs.
Inhalers must be taken using the correct technique, and in some cases with a spacer device to help deliver the medication into the airways more effectively. Access to inhalers is limited in many low- and middle-income countries; in 2021 salbutamol inhalers were generally available in public primary health care facilities in half of low- and low-middle income countries.
Flare-ups are often caused by a respiratory infection, and people may be given an antibiotic or steroid tablets in addition to inhaled or nebulised treatment as needed.

Living with COPD
Lifestyle changes can help improve symptoms of COPD.
Quit smoking or vaping. This is the most important thing to do. Even if you have been smoking for many years, quitting can still help.
Avoid second-hand smoke or smoke from indoor cooking fires.
Stay physically active.
Protect yourself from lung infections:
Get a flu vaccine every year.
Get the pneumonia vaccine.
Get all available COVID-19 vaccines and make sure you have had the latest boosters.
People living with COPD must be given information about their condition, treatment and self-care to help them to stay as active and healthy as possible.

WHO response
COPD is included in the WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases (NCDs) and the United Nations 2030 Agenda for Sustainable Development.WHO is taking action to extend diagnosis of and treatment for COPD in a number of ways.The WHO Package of Essential Noncommunicable Disease Interventions (PEN) was developed to help improve NCD management in primary health care in low-resource settings. PEN includes protocols for the assessment, diagnosis and management of chronic respiratory diseases (asthma and chronic obstructive pulmonary disease), and modules on healthy lifestyle counselling, including tobacco cessation and self-care.Rehabilitation 2030 is a new strategic approach to prioritize and strengthen rehabilitation services in health systems. Pulmonary rehabilitation for COPD is included in the Package of Interventions for Rehabilitation, recently developed as part of this WHO initiative. Reducing tobacco smoke exposure is important for both primary prevention of COPD and disease management. The Framework Convention on Tobacco Control is enabling progress in this area as are WHO initiatives such as MPOWER and mTobacco Cessation.Further prevention activities include the WHO Clean Household Energy Solutions Toolkit (CHEST) to promote clean and safe interventions in the home and facilitate the design of policies that promote the adoption of clean household energy at local, programmatic and national levels.The Global Alliance against Chronic Respiratory Diseases (GARD) contributes to WHO's work to prevent and control chronic respiratory diseases. GARD is a voluntary alliance of national and international organizations and agencies from many countries committed to the vision of a world where all people breathe freely.

## VIII. CONCLUSION

ICS–LABA combination therapy plays a pivotal role in improving clinical outcomes for patients with both COPD and bronchial asthma. By delivering anti-inflammatory corticosteroids and bronchodilating $\beta_2$-agonists through optimized inhaled-medicine and aerosol techniques, this therapy effectively reduces airway inflammation, prevents acute exacerbations, and improves overall symptom control. The reduction in eosinophilic and neutrophilic inflammation leads to decreased airway edema, while LABA-induced smooth-muscle relaxation enhances airflow and reduces bronchoconstriction. Over time, ICS–LABA therapy also demonstrates beneficial effects on airway remodeling, limiting structural changes such as basement-membrane thickening and smooth-muscle hypertrophy, particularly in asthma patients. In COPD, it improves lung function parameters like $FEV_1$, reduces dynamic hyperinflation, and enhances exercise tolerance. Proper inhaler technique, particle size optimization, and adherence to aerosol-delivery guidelines significantly enhance therapeutic efficacy. Overall, ICS–LABA therapy remains a cornerstone for long-term control, improved lung function, and better quality of life in COPD and asthma patients.

## IX. DISCUSSION

The clinical evaluation of ICS–LABA therapy in COPD and bronchial asthma highlights its multidimensional benefits in controlling chronic airway diseases. In asthma, airway inflammation is predominantly eosinophilic, making ICS a highly effective agent for reducing cytokine activity, mucosal swelling, and hyperresponsiveness. When paired with LABA, the synergistic effect provides sustained bronchodilation and improved symptom control, minimizing day-to-day variability in lung function. This combination also plays a preventive role in airway remodeling by slowing smooth-muscle hypertrophy and subepithelial fibrosis—key contributors to chronic disease progression.

In COPD, where inflammation is largely neutrophilic and structural airway damage is progressive, ICS–LABA offers targeted yet partial relief. LABA improves airflow by relaxing airway smooth muscles, while ICS reduces exacerbation frequency, particularly in patients with high eosinophil counts. Improvements in $FEV_1$, dyspnea scores, and exercise tolerance demonstrate measurable functional gains. However, ICS use in COPD must be carefully monitored due to increased pneumonia risk, reinforcing the need for patient-specific treatment plans.

A critical determinant of therapy success is correct inhaler technique and aerosol delivery. Proper device selection, optimized particle deposition, and adherence significantly influence clinical outcomes. Overall, ICS–LABA therapy remains a standard, evidence-backed approach that enhances inflammation control, lung function, and quality of life in both COPD and asthma, while requiring individualized assessment for maximal benefit.

## X. RESULT

The study results demonstrate that ICS–LABA therapy produces significant improvement in clinical, inflammatory, and functional parameters in both COPD and bronchial asthma patients. Asthma patients showed marked reductions in eosinophilic inflammation, decreased airway hyperresponsiveness, and noticeable improvement in $FEV_1$ and peak expiratory flow. COPD patients experienced fewer exacerbations, improved breathing comfort, and moderate enhancement in lung function, especially among individuals with elevated blood eosinophils. Across both conditions, consistent use of the ICS–LABA combination reduced symptoms such as wheezing, coughing, and breathlessness. Additionally, airway remodeling indicators—including mucosal swelling and smooth-muscle thickening—showed signs of stabilization, particularly in asthma cases. The effectiveness of the therapy was significantly enhanced when optimal inhaled-medicine/aerosol techniques were used. Overall, ICS–LABA therapy proved beneficial in improving respiratory outcomes and disease control.

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REFERENCES


[1] Tashkin DP, et al. The role of ICS/LABA fixed-dose combinations in airway disease: review.
[2] Calverley PMA, et al. Salmeterol + fluticasone propionate and survival in COPD (TORCH). N Engl J Med. 2007.
[3] Bateman ED, et al. Clinical equivalence of salmeterol/fluticasone presentations. PubMed. 2001.
[4] Hough KP, et al. Airway remodeling in asthma — review. PMC. 2020.
[5] Pan M, et al. Airway remodeling in COPD — review. PMC. 2025.
[6] Reddel HK, et al. Global Initiative for Asthma strategy update (summary/guidance). 2021/2024 documents.
[7] GOLD 2024 — Global strategy for COPD management (GOLD report & pocket guide).
[8] Latorre M, et al. Differences in efficacy/safety among ICS/LABA in COPD — review. 2015.
[9] Calverley PMA et al. TORCH (detailed PubMed entry).
[10] Yawn BP, et al. Role of fluticasone propionate/salmeterol combination — review. PMC. 2010.
[11] Cates CJ, et al. Regular salmeterol for chronic asthma — safety meta-analysis. Cochrane/Review. 2008.
[12] Tiotiu A. Airway remodeling in asthma: mechanisms & diagnosis — review (2024).
[13] Karakioulaki M, et al. Extracellular-matrix remodelling in COPD. ERS Reviews. 2020.
[14] Chung KF, et al. ERS/ATS statement: definition & evaluation of severe asthma. 2014.
[15] GINA Summary Guide 2024 (pocket/summary guide for asthma management).
[16] GOLD official 2024 web report (COPD evidence & management).
[17] TORCH full report / PDF (supplemental TORCH material).
[18] Pauwels RA, et al. Effect of inhaled formoterol + budesonide on exacerbations of asthma (FACET). N Engl J Med. 1997.
[19] Bateman ED. GOAL study — Can guideline-defined asthma control be achieved? (GOAL reanalysis). 2004; reanalysis 2019.
[20] FACET study analyses and safety discussions (multiple publications).
[21] O'Byrne PM, et al. Low dose budesonide + formoterol in mild asthma — 1-year study. Am J Respir Crit Care Med. 2001.
[22] Bateman ED et al. GOAL study primary publication and subsequent analyses.
[23] O'Byrne PM. Increasing doses of ICS vs adding LABA — review/meta-analysis. Chest 2008.
[24] Bousquet J, et al. FP/SAL efficacy in Asian patients — GOAL subgroup analysis. BMC Pulm Med. 2017.
[25] Lipworth B. Budesonide/formoterol for maintenance & reliever — review/updates. 2008/2024 commentary.
[26] Exposure-response modeling for budesonide + formoterol (PK/PD modeling). Pharmaceutics. 2020.
[27] ResearchGate / mechanism summaries on airway remodeling (Shifren & Castro). 2012.
[28] Frontiers review on airway remodeling in COPD (2025).
[29] GINA 2021 strategy paper indexed on PMC (Reddel et al.).
[30] GINA Pocket Guide & implementation resources (downloadable PDFs).
[31] Jenkins CR, et al. Efficacy of salmeterol/fluticasone by GOLD stage — TORCH subgroup analyses. Respiratory Research. 2009.
[32] Pauwels & colleagues — effect of formoterol + budesonide on exacerbations: FACET trial PDF and commentary (NEJM/PubMed).
[33] Reanalyses & meta-studies of GOAL (Bateman 2008/2019 meta-analyses).
[34] Humbert M, et al. Budesonide/formoterol as maintenance and reliever regimen evidence. 2008.
[35] Pauwels R. Can total control of asthma be achieved? GOAL summary. J Allergy Clin Immunol. 2004.
[36] Modeling and PK/PD of inhaled combination therapies — MDPI & related modeling papers.
[37] De Vos R, et al. Systematic review: methods of scoring inhaler technique (2023).
[38] Tena AF, et al. Deposition of inhaled particles in the lungs — review. 2012.
[39] Alotaibi MM, et al. Assessing inhaler technique in asthma patients — PMC clinical study 2023.
[40] Rissler J, et al. Deposition efficiency of inhaled particles related to breathing pattern — 2017.

[41] Vincken W. Spacer devices for inhaled therapy — rationale and evidence (ERS). 2018.

[42] Sadafi H, et al. Rapid data-driven regional deposition method for inhaled aerosols (Nat Sci Rep 2024).

[43] Darquenne C. Aerosol deposition in health & disease — in-depth review (2012).

[44] Cho-Reyes S, et al. Inhalation technique errors with MDIs — PMC review 2019.

[45] Vincken & ATS/ERS commentary on mask use / spacer use in children — Annals ATS 2020.

[46] Bui VKH, et al. Prediction of aerosol deposition — computational models review (MDPI 2020).

[47] Haddrell AE. Pulmonary aerosol delivery and particle growth importance — 2017 review.

[48] De Vos / systematic reviews on inhaler technique decay & training (Bosnic-Anticevich 2023 commentary).

[49] Recent spacer/device innovation and in-vitro comparisons (MDPI / Springer 2025 paper on novel card-based spacer).

[50] Rapid and modeling studies on deposition & particle size effects (MPPD models, AAQR, arXiv deposition modeling).

[51] World Health Organization. Asthma: Key Facts. WHO; 2024. https://www.who.int/news-room/fact-sheets/detail/asthma

[52] World Health Organization. Chronic Obstructive Pulmonary Disease (COPD): Key FactsWHO; 2023. https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)

[53] World Health Organization. Global Surveillance, Prevention and Control of Chronic Respiratory Diseases: A Comprehensive Approach. WHO; 2007. ISBN: 9789241563468

[54] World Health Organization. WHO Global Alliance against Chronic Respiratory Diseases (GARD). WHO; 2024. https://www.who.int/initiatives/gard

[55] World Health Organization. Air Quality Guidelines: Global Update 2021. WHO; 2021.https://www.who.int/publications/i/item/9789240034228