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# Respiratory problems in diabetes mellitus a preventive approach from primary care

**Diabetes mellitus (DM) is a systemic disease characterized by chronic hyperglycemia, low-grade inflammation, and increased oxidative stress. Traditionally, the main target organs have been associated with microvascular involvement—retina, kidney, and peripheral nervous system—responsible for high cumulative morbidity, while macrovascular complications account for most of the mortality associated with the disease.**

However, in recent decades, it has been recognized that other organs with an extensive capillary bed, such as the lung, may be progressively and subclinically affected by the same pathophysiological mechanisms. This growing evidence has driven interest in diabetes-associated lung diseases, a field still underexplored but of increasing clinical relevance, especially in the context of population aging and multimorbidity.

Although the association between diabetes and deterioration of lung function is supported by observational studies and meta-analyses, the translation of these findings into a distinct clinical entity remains incomplete.

## LUNG AS A TARGET ORGAN OF DIABETES: PULMONARY FIBROSIS AND RESTRICTIVE PATTERN

Diabetic lung disease shares pathophysiological mechanisms similar to those involved in microvascular or small vessel damage in other organs, progressively and structurally affecting the lung and producing redistribution of pulmonary perfusion with the appearance of areas with altered ventilation/perfusion ratio.

On the other hand, the thoracic cage and lung parenchyma are structures rich in collagen and elastin, proteins particularly susceptible to non-enzymatic glycosylation induced by chronic hyperglycemia. This process promotes the binding of sugar to proteins and tissues, altering their structure and function. It may increase tissue stiffness and reduce lung compliance, favoring the development of a restrictive pattern in pulmonary function tests. In some patients, this functional deterioration could progress toward structural changes compatible with pulmonary fibrosis; although the term "diabetes-associated **pulmonary fibrosis**" has been used, this entity is not currently defined as a distinct disease.

An impaired lung function in people with diabetes is usually insidious and subclinical, making early detection difficult. In this context, spirometry can provide relevant information for the evaluation of diabetic patients with respiratory symptoms, allowing better functional characterization and appropriate stratification of cardiovascular and respiratory risk. However, in the absence of symptoms, systematic screening with pulmonary function tests is not recommended, and the most effective preventive measure remains **adequate glycemic control**.

**Spirometry** should be considered as the initial study in patients with diabetes who present respiratory symptoms, as well as in those with a history of smoking, concomitant lung diseases, or other respiratory risk factors.

## RESPIRATORY INFECTIONS AND PNEUMONIA

DM-related chronic hyperglycemia and immune dysfunction contribute to both increased susceptibility to respiratory infections and a more unfavorable clinical course compared with the general population. Alterations in innate and adaptive immunity, together with low-grade inflammation and oxidative stress, favor greater severity and prolongation of infectious episodes.

Bacterial pneumonia is more frequent and more severe in people with diabetes. Among the most implicated microorganisms are *Streptococcus pneumoniae*, with a significantly increased risk of invasive pneumococcal disease, *Staphylococcus aureus*, and gram-negative bacteria belonging to the Enterobacteriaceae family, such as *Klebsiella pneumoniae and Escherichia coli*. DM has also been associated with an increased risk of tuberculosis, especially in patients with poor glycemic control; however, systematic screening for Mycobacterium tuberculosis is not recommended unless epidemiological or clinical risk factors justify high clinical suspicion.

Similarly, viral respiratory infections, particularly those caused by influenza viruses and rhinoviruses, are associated with increased risk of hospitalization, complications, and adverse outcomes in patients with diabetes. This increased vulnerability justifies the implementation of reinforced preventive strategies in this high-risk group.

**Primary prevention** is a key tool to reduce morbidity and mortality associated with respiratory infections in people with diabetes. Among the most effective measures are adequate glycemic control, health education aimed at early detection of respiratory »

SPIROMETRY CAN PROVIDE RELEVANT INFORMATION FOR THE EVALUATION OF DIABETIC PATIENTS WITH RESPIRATORY SYMPTOMS, ALLOWING BETTER FUNCTIONAL CHARACTERIZATION AND ADEQUATE STRATIFICATION OF CARDIOVASCULAR AND RESPIRATORY RISK

| VACCINE | RECOMMENDATIONS IN SPAIN | ADA 2026 (BASED ON CDC) |
|---|---|---|
| **Influenza (flu)** | Annual vaccination in individuals ≥60 years and in people with chronic diseases, including diabetes | Annual vaccination in all people with diabetes |
| **Pneumococcus** | Vaccination at ≥65 years and in risk groups. In many AC, PCV13/PCV15 ± PPSV23 schedule | Preference for PCV20 or PCV21 as a single dose, or PCV15 followed by PPSV23 |
| **COVID-19** | Seasonal vaccination targeted to older adults and risk groups, including diabetes | Updated vaccination recommendation according to campaigns in people with comorbidities |
| **RSV (respiratory syncytial virus)** | Recently introduced in older adults or at-risk groups depending on regional programs; not yet systematic | Vaccination at ≥75 years or 60–74 years with high risk |

**TABLE 1.** General vaccination recommendations in adults with DM.
AC: Autonomous Communities; American Diabetes Association; Centers for Disease Control and Prevention (CDC); high-valency conjugate vaccines (PCV).

» symptoms, and systematic vaccination against the main respiratory pathogens, especially pneumococcus and influenza virus, from the time of diabetes diagnosis and with longitudinal follow-up in health care settings.

## VACCINATION IN PEOPLE WITH DM

People with DM have a higher risk of infections and associated complications due to immunological alterations related to chronic hyperglycemia and the frequent presence of other comorbidities. For this reason, major clinical guidelines recommend systematically reviewing vaccination status and ensuring administration of indicated vaccines according to age and risk factors. As a separate topic, prevention of pneumococcal disease in adults is fundamental. In recent years, the availability of high-valency conjugate pneumococcal vaccines has modified the preventive approach in at-risk populations, including people with diabetes.

Recent evidence indicates that high-valency conjugate vaccines (PCV20 and PCV21) generate a more potent and durable immune response against serotypes responsible for pneumococcal disease in adults than the polysaccharide vaccine PPSV23. Although PPSV23 covers more serotypes, it induces less robust and shorter-lasting immunity, especially in people with comorbidities such as diabetes, and does not significantly reduce nasopharyngeal colonization.

Clinical and observational studies show that conjugate vaccines are associated with a greater reduction in pneumonia and invasive pneumococcal disease, in addition to contributing to decreased transmission. In the Spanish context, cost-effectiveness analyses indicate that a strategy based on a single dose of PCV20 is more efficient than sequential regimens with PCV15 followed by PPSV23 in older adults and risk groups, including patients with diabetes.

Current recommendations from the ***American Diabetes Association*** (ADA 2026) follow adult vaccination schedules established by health authorities, with special emphasis on vaccines against influenza, **pneumococcus, hepatitis B, herpes zoster, COVID-19, and other vaccines indicated according to age or clinical situation**.

***Table 1*** summarizes the main vaccines that prevent respiratory tract infections in people with diabetes mellitus.

## ANTIDIABETIC TREATMENT AND PULMONARY EFFECT

In recent years, several observational studies and cohort analyses have suggested that some groups of antidiabetic drugs may be associated with a more favorable respiratory profile in patients with diabetes mellitus and pulmonary comorbidity. Among them, sodium-glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1 RA) have shown the most consistent results.

In population-based studies, treatment with SGLT2i or GLP-1 RA has been associated with a significant reduction in the risk of moderate and severe exacerbations of chronic obstructive pulmonary disease (COPD), as well as lower rates of hospitalizations for respiratory causes, compared with other antidiabetic drugs such as dipeptidyl peptidase-4 (DPP-4) inhibitors or sulfonylureas. The magnitude of benefit observed is similar between both pharmacological groups and greater than that described with DPP-4 inhibitors in relation to respiratory outcomes.

Of note, regardless of the agent used, improved glycemic control is associated »

» with improvement in spirometric parameters and reduction of central airway obstruction, highlighting the fundamental role of metabolic control in preventing deterioration of lung function.

From a mechanistic perspective, SGLT2i have demonstrated anti-inflammatory and antioxidant effects, partly mediated by inhibition of the NOD-like receptor family, pyrin domain containing 3 (NLRP3) inflammasome, which may contribute to reducing pulmonary inflammation and tissue damage. Furthermore, decreased glucose in airway secretions may limit bacterial proliferation and reduce the risk of respiratory infections. Other proposed effects include reduced endogenous $CO_2$ production, potentially relevant in patients with ventilatory limitation or a tendency toward hypercapnia.

GLP-1 receptor agonists, in turn, appear to modulate airway inflammation by reducing proinflammatory cytokines such as IL-13 and IL-33 and decreasing bronchial hyperresponsiveness. In various studies, improvements have been observed in spirometric parameters such as forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC), as well as lower incidence of respiratory exacerbations, hospitalizations, and, more preliminarily, pulmonary fibrosis.

In comparative analyses, both pharmacological groups show similar respiratory benefits, with no clinically relevant differences between them. These effects are maintained across subgroups defined by spirometric pattern—obstructive or restrictive—and degree of frailty, although reduction in hospitalizations due to COPD appears more pronounced in less frail patients, while protection against pneumonia is consistently observed across all levels. D

## CONCLUSIONS

- Diabetes-related lung diseases often evolve subclinically, but their recognition is important due to their impact on quality of life, risk of respiratory infections, and overall morbidity and mortality.
- Adequate glycemic control, optimization of antidiabetic treatment (prioritizing, when clinically indicated, the use of SGLT2i and GLP-1 RA), systematic vaccination, and health education constitute fundamental pillars in the prevention and management of these complications.
- Further research into diabetes-associated lung diseases will contribute to improving preventive and therapeutic strategies in a context of high prevalence and increasing healthcare burden.

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