Open Respiratory Archives 8 (2026) 100587

Sociedad Española de Neumología y Cirugía Torácica SEPAR

Open Respiratory Archives

www.elsevier.es/ora

Original Article

Impact-Driven Strategies for Optimizing Inhaled Therapy Adherence in COPD: The OPTIMO Delphi Consensus

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ARTICLE INFO

Article history:
Received 24 October 2025
Accepted 20 January 2026
Available online 3 February 2026

Keywords:
COPD adherence
Delphi method
Inhaled therapy optimization
Once-daily dosing
Adherence assessment tools

ABSTRACT

Introduction: Medication adherence is an important challenge in the management of COPD, with poor adherence negatively impacting symptom control, disease progression, and healthcare resource utilization.
Objetives: This study aimed to achieve multidisciplinary consensus on practical, prioritized interventions for improving adherence and clinical results in stable COPD treatment.
Material and methods: A modified Delphi study was carried out by a panel of COPD management experts to evaluate suboptimal adherence. The Delphi questionnaire, completed in two rounds, comprised 84 statements across six domains: non-adherence, its impact, contributing factors, assessment methods, improvement strategies, and prioritization. Agreement was rated using a 9-point Likert scale and consensus considered as ≥70% agreement.
Results: Seventy-three multidisciplinary experts completed the questionnaire, reaching consensus on 74 of 84 statements. The panel identified high-impact, easy-to-implement interventions, culminating in a practical decalogue for optimizing inhalation therapy. Two key strategies were emphasized: simplifying and unifying inhalation regimens, and empowering patients. While all adherence assessment tools were considered useful, only digital and automated methods were deemed feasible in routine practice. Treatment optimization was also associated with reducing inhalation frequency by using long-acting molecules, and tailoring device selection to patient capacity.
Conclusion: The resulting decalogue provides structured expert guidance for healthcare professionals, highlighting once-daily dosing, simplified devices, and patient engagement as the interventions considered most likely to improve adherence in COPD.

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https://doi.org/10.1016/j.opresp.2026.100587

Estrategias con impacto para optimizar la adherencia a la terapia inhalada en la EPOC: Consenso Delphi OPTIM

Palabras clave:
Adherencia en EPOC
Método Delphi
Optimización de la terapia inhalada
Dosificación una vez al día
Herramientas para evaluar la adherencia

RESUMEN

Introducción: La adherencia al tratamiento es un desafío importante en el manejo de la EPOC, ya que una baja adherencia afecta negativamente el control de los síntomas, la progresión de la enfermedad y el uso de recursos sanitarios.
Objetivo: Este estudio tuvo como finalidad alcanzar un consenso multidisciplinar sobre intervenciones prácticas y prioritarias para mejorar la adherencia y los resultados clínicos en el tratamiento de la EPOC estable.
Material y métodos: Se llevó a cabo un estudio Delphi modificado con un panel de expertos en el manejo de la EPOC para evaluar la adherencia subóptima. El cuestionario Delphi, completado en dos rondas, incluyó 84 afirmaciones distribuidas en seis áreas: falta de adherencia, su impacto, factores contribuyentes, métodos de evaluación, estrategias de mejora y priorización. El grado de acuerdo se valoró mediante una escala Likert de 9 puntos, y se consideró consenso cuando se alcanzaba un $\geq$70% de acuerdo.
Resultados: Setenta y tres expertos multidisciplinares completaron el cuestionario, alcanzando consenso en 74 de las 84 afirmaciones. El panel identificó intervenciones de alto impacto y fácil implementación, que culminaron en un decálogo práctico para optimizar la terapia inhalada. Se destacaron dos estrategias clave: simplificar y unificar los regímenes de inhalación, y empoderar a los pacientes. Aunque se consideraron útiles todas las herramientas de evaluación de la adherencia, solo los métodos digitales y automatizados se consideraron viables en la práctica rutinaria. La optimización del tratamiento también se relacionó con la reducción de la frecuencia de inhalación mediante el uso de moléculas de acción prolongada, y con la adaptación del dispositivo a la capacidad del paciente.
Conclusión: El decálogo resultante ofrece recomendaciones prácticas para los profesionales sanitarios, destacando la dosificación una vez al día, los dispositivos simplificados y la implicación del paciente como las intervenciones más efectivas para mejorar la adherencia en la EPOC.

Introduction

Chronic obstructive pulmonary disease (COPD) is a significant cause of healthcare use, morbidity and mortality worldwide.[1] COPD is a heterogeneous lung disease characterized by chronic respiratory symptoms (dyspnea, cough and sputum production, etc.) caused by damage or dysfunction in the respiratory tract (as bronchitis and/or bronchiolitis) and/or alveoli (as emphysema), which produce persistent and progressive airflow obstruction.[2] The prevalence of COPD varies from one country to another, and is often related to tobacco smoking and air pollution (outdoor, occupational and household).[2] The economic burden of COPD is considerable, comprising approximately 56% of the total costs of respiratory diseases in the European Union: 38.6 billion euros.[2] As one of the three most common causes of death in the world, COPD affects in low- and middle-income countries, where nearly 90% of deaths are described.[3] The projections for the future indicate that the prevalence and burden of COPD will grow over the next decades, because of continued exposure to the risk factors of COPD and the aging of the population.[2]

Ensuring adherence to treatment in COPD continues to be a significant concern, with non-adherence rates to COPD medication ranging from 22% to 93%, depending on the study (50% of the studies reported non-adherence in more than a half of patients).[2] This inadequate adherence has a direct impact on symptom control, patients' quality of life (QoL), exacerbation frequency, and overall disease progression, ultimately leading to poorer clinical outcomes and greater demand for healthcare resources and costs. Therefore, adherence to inhaled therapy is critical for controlling symptoms and preventing exacerbations in patients with stable COPD.[2,3]

As recommended by GOLD guidelines, a simplified treatment enhances adherence and provides long-term results. Inhaled therapies have evolved significantly, aiming to improve COPD management by incorporating long-acting, high-affinity molecules that reduce the frequency of inhalations and simplify posology. Despite these advances, adherence remains suboptimal, highlighting the need for further optimization in disease management.[2]

Several barriers have been identified that hinder adherence, including the complexity of inhaled treatment regimens (multiple devices, multiple daily doses and several inhalations per intake), lack of patient training and understanding about their condition and treatment, and insufficient follow-up and clinical support.[4,5] Therefore, there is an urgent need to identify and implement short-, medium- and long-term solutions that improve treatment adherence, with the goal of reducing the negative impact of non-adherence and improving long-term COPD control.[6–8] However, it is necessary to analyze more factors that influence adherence and the tools available for its evaluation.

The primary objective of the OPTIMO (Optimization of Inhaled Therapy for Improving COPD Control) study was to achieve a multidisciplinary consensus on the prioritized interventions that have the greatest impact and ease of implementation for optimizing and improving the control of stable COPD. So, in this study we evaluated the impact of non-adherence and the factors that could potentially influence it, including patient-dependent factors, healthcare professional (HCP)-dependent factors, healthcare system-related factors, and treatment-related factors (duration of action of the molecules, dosage, number of inhalers, number of inhalations per intake, etc.).

Material and methods

Study design

A modified Delphi study was conducted involving healthcare professionals on the management of COPD from various parts of Spain (hereinafter referred to as 'the Delphi expert panel'), using online questionnaires involving two structured rounds of questions.

The modified Delphi method, a widely embraced scientific approach, offers a structured and systematic means of reaching

consensus in situations with limited or conflicting evidence. An iterative methodology is used, where expert opinions are gathered anonymously using structured questionnaires across multiple rounds.[9] The study was carried out in three stages (Supplementary Fig. S1): (1) A narrative literature review followed by iterative Scientific Committee (SC) meetings to draft, refine, and consolidate the Delphi questionnaire; (2) Two successive rounds of online surveys to obtain the opinion of the Delphi expert panel about the items on the statement list; and (3) Analysis and discussion of the results with the SC to draw conclusions.

The Delphi questionnaire was divided into seven sections (Supplementary Table S1) and consisted of 84 statements on a Likert-type scale (75 items included in the 1st round, with 9 new additions introduced in the 2nd round). Data were analyzed globally. The consensus thresholds were predefined as ≥70% panelists agreement on a statement before data collection, which minimizes subjective interpretation and ensures methodological transparency.

Participants

The SC consisted of ten experts in the treatment of patients with COPD from three medical specialties: 4 pulmonologists, 4 primary care physicians and 2 internal medicine physicians. The experts conducted the scientific literature and developed a questionnaire addressing key issues about adherence to inhaled treatment in stable COPD. The SC also approved and analyzed the statistical results obtained from the two rounds.

A total of 75 experts, with clinical activity in different regions of Spain and in different types of hospitals (public and private), were requested to participate in the survey (February–July 2024) as panelists (Supplementary Fig. S2). The inclusion criteria were: (1) Active professionals with 3 or more years of experience since completing training in their specialty; (2) Ongoing professional relationship with COPD patients; and (3) Great involvement in COPD research and development: (a) authorship in scientific publications on COPD, (b) membership of scientific societies/working groups with a special focus on COPD, and/or (c) participation in some kind of training or congress with focus on COPD.

Two rounds of Delphi consensus

Following the Delphi method, an iterative approach was developed to reach consensus on the statements. The Delphi questionnaire was answered online in two rounds. In the 1st round, the Delphi expert panel rated their agreement with each statement on a Likert scale (1–3 = disagree, 4–6 = neutral, and 7–9 = agree) (Supplementary Table S2). The expert panel in an anonymous manner and individually provided feedback to each statement based on non-adherence, its impact, causes, associated factors and possible interventions.

The results of the 1st round were discussed by the SC in an online meeting (May 2024), and statements without consensus were revised by the SC. Consensus was defined as ≥70% of responses within the agreement (7–9) or disagreement (1–3) range, consistent with prior Delphi studies.[10–14] The statements that progressed to the 2nd round were those that did not achieve consensus in the 1st round (i.e., statements agreed with or disagreed with by <70% of participants in the 1st round) and new statements to further explore certain issues. Final agreement percentages for all statements are shown in the results.

New items were added in the 2nd round to explore certain statements in more detail, and a new section (Section 7: Actions that are easier to implement and have a greater impact on clinical practice) (Supplementary material – Questionnaires) was added to prioritize the actions that would be the easiest to implement and would have the greatest impact on adherence. To facilitate this process, an updated questionnaire was distributed for re-evaluation – comprising statements that lacked consensus in the 1st round, the newly added 9 statements and the new section consisting of two questions. The results were evaluated and discussed by the SC during the concluding meeting (September 2024).

Table 1
Characteristics of the expert panel.

Characteristics	*N* = 73
Sex (%)	
Man (*M*)	52.1%
Woman (*W*)	47.9%
Mean age (SD), years	43.3 (9.0)
Medical specialty (%)	
Primary care (PC); *n* = 25	40.0% (W), 60.0% (M)
Internal Medicine (IM); *n* = 23	43.5% (W), 56.5% (M)
Pulmonology (P); *n* = 25	60.0% (W), 40.0% (M)
Professional experience caring for COPD patients (%)	
3–10 years	30.2% (PC), 17.4% (IM), 72% (P)
11–15 years	24.0% (PC), 30.4% (IM), 12.0% (P)
16–20 years	12.0% (PC), 4.3% (IM), 4.0% (P)
>20 years	32.0% (PC), 47.8% (IM), 12.0% (P)
Patients with COPD visited per month	
<10	4.0% (PC), 4.3% (IM), 0% (P)
10–25	48.0% (PC), 26.1% (IM), 4.0% (P)
25–50	20.0% (PC), 43.5% (IM), 32.0% (P)
50–100	24.0% (PC), 21.7% (IM), 24.0% (P)
100–150	4.0% (PC), 0% (IM), 20.0% (P)
>150	0% (PC), 4.3% (IM), 20.0% (P)
Professional activity (%)	
Public	94.6% (PC), 87.8% (IM), 88.0% (P)
Private	5.4% (PC), 12.2% (IM), 12.0% (P)
Type of centers for Primary care	
Rural	28.0%
Semi-urban	24.0%
Urban	48.0%
Type of hospital for Internal Medicine (IM) and Pulmonology (P)	
Primary	8.7% (IM), 8.0% (P)
Secondary	21.7% (IM), 28.0% (P)
Tertiary	69.6% (IM), 64.0% (P)

Notes: Rural: <2000 inhabitants; Semi-urban: ≤10,000 inhabitants; Urban: >10,000 inhabitants; Primary: Centers where preventive activities are carried out, as well as provision of Local Health Plan activities, general medical consultations, general dentistry, clinical laboratory and low complexity imaging, hospitalization, emergency care and low complexity childbirth; Secondary: Hospitals where they provide external medical consultation, hospitalization and emergency care of basic specialties, delivery and Cesarean sections of medium complexity, general and specialized dental care, nutritional consultations, psychology, optometry and support therapies for functional rehabilitation; Tertiary: Hospitals that provide medical care in activities aimed at restoring health and rehabilitating users referred by the other levels, and who present conditions of high diagnostic and treatment complexity through one or more medical, surgical or medical–surgical specialties.
Abbreviations: COPD, chronic obstructive pulmonary disease; IM, internal medicine; PC, primary care; P, pulmonology; SD, standard deviation.

Statistical analysis

For nominal/ordinal variables, relative frequencies were employed for description. For continuous variables, measures of central tendency and dispersion were computed. IBM SPSS Statistics 27 was used to perform all statistical analyses.

Results

Profile of Delphi panelists

A total of 73 participants completed the questionnaire for the 1st and 2nd rounds. Table 1 provides details of panelists profile. The

Table 2
Results of the two rounds of the Delphi process for the statements in Section 2 – Lack of adherence and Section 3 – Impact and consequences of non-adherence.

Statements/Items	% of agreement		Consensus	*p*-Value
Lack of adherence	1st round	2nd round		
Section 2 – Lack of adherence				
Evolution of inhaled therapies has contributed to improved adherence in COPD patients[a]	–	91.8	Yes	–
Inhaled therapies available for COPD have evolved in recent years[a]	–	98.0	Yes	–
As with other chronic diseases in adults, poor adherence to inhaled therapy is one of the main challenges in the management of COPD	83.6	–	Yes	–
Despite the evolution of inhaled therapies, therapeutic adherence has not improved in recent years and remains a challenge in the treatment of COPD	46.6 (non-agreement: 26.0%)	52.1 (non-agreement: 20.5%)	No	0.744
Low adherence to inhaled therapy has negative clinical consequences for the ongoing control of COPD symptoms	92.0	–	Yes	–
Section 3 – Impact and consequences of non-adherence				
Poor adherence to inhaled therapy has negative clinical consequences on future COPD risk	92.0	–	Yes	–
Low adherence to inhaled treatment increases the risk of moderate and serious exacerbations	96.0	–	Yes	–
Low adherence to inhaled treatment increases the risk of hospitalization	96.0	–	Yes	–
Low adherence to inhaled treatment increases the risk of disease progression	92.0	–	Yes	–
Low adherence to inhaled treatment increases comorbidities worsening	92.0	–	Yes	–
Low adherence to inhaled treatment increases the risk of death	96.0	–	Yes	–
The worse control of the disease due to low adherence has socio-economic consequences (productivity reduction, work absenteeism and disability)	96.0	–	Yes	–
Low adherence to inhaled treatment has negative consequences in the healthcare system (increased use of resources and higher overall healthcare costs derived from admissions or urgent care)	96.0	–	Yes	–
Greater adherence to treatment can result in an increase in the costs of maintenance treatment dispensed in pharmacy, but that increase is smaller than the increase in general healthcare costs derived from low adherence	96.0	–	Yes	–

Abbreviations: COPD, chronic obstructive pulmonary disease.
[a] Item added in the 2nd round.

geographical distribution of participants across the autonomous community in which they carry out their medical activity was homogeneous (Supplementary Fig. S3). Most of the panelists work in an academic medical center (91.8%), 82.2% are active members of national and/or international scientific societies, 61.6% had participated in the past year in some kind of training or scientific congress with special focus on respiratory pathology or COPD, 41.1% had contributed in the past 5 years as an investigator in clinical trials or as an author in COPD-related publications, and 37% belong to a working group with a special focus on respiratory pathology or COPD.

Consensus

Initially, out of the 75 proposed items in the 1st round, consensus was achieved on 65 (86.7%) (Supplementary Figs. S4 and S5). In the 2nd round, the unresolved 10 items underwent further evaluation, and 9 new items were added to explore certain issues in more depth. Finally, consensus was achieved on 74 items (88.1%), but not on 10 other items (11.9%) (Fig. S4) (consensus or non-consensus for each item is shown in Tables 2 and 3).

Overcoming non-adherence for better outcomes

Results of the questionnaire about the lack of adherence (Section 2) and the impact and consequences of non-adherence (Section 3) showed that the panelists considered, among other aspects, that the evolution of inhaled therapies—such as improvements in inhaler devices, simplified treatment regimens with combination therapies, and enhanced medication formulations—has contributed to improving therapeutic adherence in patients with COPD (91.8% agreement) (Table 2), and that poor adherence to inhaled treatment increases the risk of moderate and severe exacerbations (96.0%) (Table 2). The panelists also agreed that poor adherence to inhaled therapy is one of the main challenges in the management of COPD (83.6%), that it has negative clinical consequences (92.0%), that it is associated with negative socio-economic consequences (96%) and with higher risk of: hospitalization (96%), disease progression (92%), comorbidities worsening (92%) and death (96%) (Table 2).

Key factors affecting treatment adherence

Results of the questionnaire about causes and factors potentially impacting on adherence (Section 4) showed that panelists considered, among other aspects (Table 3), the following:

- **Patient-related** factors – Panelists agreed that a greater proportion of patients, especially those who manifest problems with the medication or are less adherent, prefer treatments with a lower number of daily inhalations (94.5%). Greater symptomatology and severity of COPD favor adherence (agreement 82.3%), and that the following aspects hinder adherence: non-involvement of patients in decision-making (agreement 95.9%), insufficient understanding of COPD and its treatment by the patient (98.6%), low educational level/low income (78.1%), limited family support or the institutionalization of the patient (76.7%), adverse effects of previous treatments (82.2%), polypharmacy (80.8%), depression or smoking (75.3%), and patients' perception of low effectiveness of treatment (91.8%).
- **Healthcare professional-related** factors – Panelists considered that several aspects hinder adherence: insufficient patient training (critical errors) (agreement 97.3%), insufficient follow-up of adherence (98.6%), lack of clear explanation of COPD physiopathology, management and objectives (98.6%), and poor multidisciplinary communication and coordination between HCPs (90.4%).
- **Healthcare system-related** factors – Panelists considered that the availability of the same therapy at home and hospital favors adherence (agreement 91.8%), and that several aspects hinder

Table 3
Results of the two rounds of the Delphi process for the statements in Section 4 – Causes and factors potentially impacting on adherence.

Statements/Items	% of agreement		Consensus	*p*-Value
Causes and factors potentially impacting on adherence	1st round	2nd round		
Patient-related factors				
There is a relationship between older age and higher average adherence	49.3 (non-agreement: 12.3%)	50.7 (non-agreement: 11.0%)	No	0.260
Without considering polypharmacy or possible physical or sensory limitations, average adherence in elderly patients is usually higher[a]	–	56.2 (non-agreement: 9.6%)	No	–
There is a relationship between greater severity of the disease and higher average adherence	71.2	–	Yes	–
There is a relationship between greater impact of symptoms associated with the disease and greater mean adherence[a]	–	82.3	Yes	–
There is a relationship between lower lung function and higher mean adherence[a]	–	65.8 (non-agreement: 9.6%)	No	–
The presence of comorbidities such as depression or smoking is related to lower mean adherence	75.3	–	Yes	–
The presence of adverse events prior to similar treatments is related to lower mean adherence	82.2	–	Yes	–
Polypharmacy is related to lower mean adherence	80.8	–	Yes	–
Limited understanding or low level of patient comprehension about the disease and the prescribed treatment is related to lower mean adherence	98.6	–	Yes	–
Not involving the patient in therapeutic decision-making is related to lower mean adherence	95.9	–	Yes	–
A patient's low educational level and/or income are related to lower mean adherence	78.1	–	Yes	–
The patient's perception of polypharmacy is associated with a greater preference for regimens that require fewer daily inhalations	94.5	–	Yes	–
Personal and social beliefs about treatment affect adherence	86.3	–	Yes	–
Personal perception of low treatment effectiveness is related to lower mean adherence	91.8	–	Yes	–
The patient's social circumstances affect the level of adherence	87.7	–	Yes	–
Limited family support or institutionalization of the patient is related to lower mean adherence	76.7	–	Yes	–
Healthcare professional-related factors				
A lack of clear explanation, to the patient by the healthcare professional, of the pathophysiology of the disease, its management and the therapeutic objectives is related to lower mean adherence	98.6	–	Yes	–
Insufficient training of the patient in inhalation technique is related to lower mean adherence	95.9	–	Yes	–
Insufficient training of the patient in inhalation technique is related to a greater number of basic errors	98.6	–	Yes	–
Insufficient follow-up of the level of adherence by professionals in check-ups is related to lower mean adherence	98.6	–	Yes	–
Inadequate communication and multidisciplinary coordination among healthcare professionals (medicine, nursing, pharmacy) is related to a lower level of adherence	90.4	–	Yes	–
Healthcare system-related factors				
Lack of coordination in the transition from hospital care to primary care after admission is related to lower mean adherence	83.6	–	Yes	–
Frequent changes of inhalation device when the patient is seen by different professionals or in different services (primary care, outpatient clinics, emergencies, hospitalization, etc.) are related to lower average adherence	95.9	–	Yes	–
Temporary changes in inhaled therapy during hospital admission due to unavailability of medication in hospital are associated with lower mean adherence	61.6	–	Yes	–
Changes in inhaled therapy initiated by the physician during hospital admission have a negative impact on patient adherence upon discharge[a]	–	52.1 (non-agreement: 13.3%)	No	–
In an admitted patient, the possibility of having the same inhaled therapy that they use at home has a positive impact on adherence after admission[a]	–	91.8	Yes	–
Higher treatment costs and their financing (copayment for certain therapies) are related to a lower level of adherence	76.7	–	Yes	–
Treatment-related factors				
A therapeutic regimen composed of several different inhalers is related to lower mean adherence and a higher number of critical errors	94.5	–	Yes	–
A higher frequency of administration (more times per day) is related to lower mean adherence	84.9	–	Yes	–
A higher number of inhalations in each intake is related to lower mean adherence	84.9	–	Yes	–
According to my clinical experience, a higher proportion of patients, especially those who report problems with medication or are less adherent, prefer treatments with fewer daily inhalations.	89.0	–	Yes	–
The lower frequency of administration (single daily dose) provided by molecules with a longer duration of action (>24 h), is related to higher average adherence because it simplifies the treatment and improves its results	97.3	–	Yes	–
The lower frequency of administration (single daily dose) provided by molecules with a longer duration of action (>24 h) results in an uninterrupted (or plateau) therapeutic effect that reduces the window of non-protective effect between doses	89.0	–	Yes	–

Table 3 (*Continued*)

Statements/Items	% of agreement		Consensus	*p*-Value
Causes and factors potentially impacting on adherence	1st round	2nd round		
Lower frequency of administration (fewer times per day) increases the possibility of overdose and complete non-adherence	9.6 (non-agreement: 78.1%)	–	No	–
In regimens where the frequency of administration is lower (fewer times per day), the possibility of overdose (the patient taking a dose more times than indicated) increases[a]	–	8.2 (non-agreement: 78.1%)	No	–
Complex inhalation devices or those with a greater number of steps for each inhalation increase the likelihood of critical errors and reduce adherence to treatment	97.3	–	Yes	–
Devices with a high volume or those requiring a spacer chamber make portability and treatment adherence difficult	72.7	–	Yes	–
Inhalation devices that require maintenance or cleaning, including spacer chambers, add complexity and reduce treatment adherence	76.7	–	Yes	–

Abbreviations: COPD, chronic obstructive pulmonary disease.

[a] Item added in the 2nd round.

adherence: frequent changes of device (95.9%), changes of the inhaled therapy during hospital admission (72.6%), lack of coordination in the transition from hospital to primary care (83.6%), and costs and funding limitations (76.7%). There was no consensus about the influence of changes in inhaled therapy after hospital discharge (agreement 52.1%; non-agreement 13.3%).

- **Treatment-related** factors – Panelists considered that several aspects that improve adherence are: a single daily dose provided by molecules with a longer duration of action (>24 h) because it simplifies the treatment, improves its outcomes (agreement: 97.3%) and results in an uninterrupted (or plateau) therapeutic effect that reduces the non-protective effect window between doses (89.0%). Panelist also considered that some aspects that hinder adherence are: a higher frequency of administration (more times per day) or a greater number of inhalations in each intake (84.9%) and therapeutic regimens with multiple inhalers or complex inhalers (more steps, voluminous, or maintenance/cleaning required) (97.3%).

Evaluation of adherence: tools and feasibility

Results of the Delphi study section on adherence assessment (Section 5) showed consensus on the utility of all the tools and calculations presented for adherence assessment (Table 4): test of adherence to inhalers (TAI) (agreement 74.0%), Morisky-Green test (76.7%), Batalla test (78.1%), Haynes–Sackett test (75.3%), electronic records of withdrawal in pharmacies (81.7%), and Proportion of Days Covered (PDC = % doses taken vs. prescribed) (76.7%).

Nevertheless, when asked about their feasibility in real clinical practice there was only agreement on: electronic records of withdrawal in pharmacies (agreement 81.7% and 78.9%, respectively), digital tools and smart inhalers (84.9% and 72.5%, respectively), availability of an indicator in the IT system which automatically shows the PDC (% doses taken at pharmacy vs. prescribed) (76.7% and 89.4%, respectively) (Table 4).

Time for action: prioritization of interventions to improve adherence and outcomes

Results of the Delphi study about interventions to improve adherence and therapeutic management (Section 6) and its prioritization based on ease of implementation and patient impact (Section 7) showed that panelists considered, among other aspects (Table 5), the following:

- With regard to the optimization of treatment, participants responded that inhalers that allow treatment changes (escalation and de-escalation) without changing the device and without the need for actuation-inhalation coordination (agreement 100%), and simple, portable and maintenance-free devices (98.6%) would contribute to the optimization of treatment. Also, simplification of treatment (98.6%), reduction of daily inhalations as well as the number of inhalations per intake (98.6%), and innovation with long-acting molecules with less frequent administration (97.3%) would favor the optimization of treatment. Panelists also considered limiting the use of devices that require coordination between actuation and inhalation, or the use of a spacer chamber, only to patient profiles for whom such use is clinically necessary (PIFR < 30 L/min) would be beneficial to improve adherence to inhaled therapy in COPD (89.0%).
- Panelists considered that patient empowerment by therapeutic training programs (including treatment goals, inhalation technique, regimens) (agreement 97.3%), patient involvement (device preferences and frequency of administration) (98.6%), and integration into the daily routine (associating the intake of medicines with established daily activities) (97.3%) would improve adherence.
- There was a high level of consensus that integrated support and active monitoring promote adherence: digital tools (incorporation of reminders, adherence tracking apps and smart inhalers [agreement 89.0%]), treatment of comorbidities (diagnosis and treatment of depression, addictions and others [98.6%]), social and family support (patient associations/social support services [95.9%]), follow-up and monitoring (increased by HCPs, with tools to assess adherence and review inhaler technique [97.3%]), and multidisciplinary collaboration (nursing and community pharmacy [100%]).

Fig. 1a shows the 10 prioritized actions that are easier to implement and with a greater impact on adherence, resulting in a decalogue for inhalation therapy optimization useful in clinical practice (Fig. 1b). The most voted actions are based on unifying and simplifying inhaled treatment and empowering the patient.

Discussion

This study found unanimous consensus (100%) on the negative consequences of non-adherence and its impact on treatment outcomes. This aligns with real-world studies showing that non-adherence leads to poor COPD control, increased disease progression, exacerbations, hospitalizations, mortality, and socioeconomic consequences like reduced productivity, absenteeism, work incapacity, and higher healthcare costs.[15–17]

Unlike previous Spanish Delphi studies – mainly focused on device selection or technical aspects of inhalation therapy – this

Table 4
Results of the two rounds of the Delphi process for the statements in Section 5 – Adherence assessment.

Statements/Items	% of agreement		Consensus	*p*-Value
Adherence assessment	1st round	2nd round		
The information provided by the TAI is useful in real clinical practice for patient monitoring and assessing adherence to inhaled therapy	74.0	–	Yes	–
The information provided by the Morisky–Green test is useful in real clinical practice for patient monitoring and assessing adherence to inhaled therapy	76.7	–	Yes	–
The information provided by the disease knowledge test (Batalla Test) is useful in real clinical practice for patient monitoring and assessing adherence to inhaled therapy	78.1	–	Yes	–
The information provided by the self-reported adherence test (Haynes–Sackett) is useful in real clinical practice for patient monitoring and assessing adherence to inhaled therapy	75.3	–	Yes	–
The information provided by the electronic record of drug withdrawal in pharmacies is useful in real clinical practice for patient monitoring and in assessing adherence to inhaled therapy	81.7	–	Yes	–
The information provided by the calculation of Proportion of Covered Days (PDC = % doses taken vs prescribed) is useful in real clinical practice for patient monitoring and assessing adherence to treatment	76.7	–	Yes	–
The information provided by digital tools and smart inhalers is useful in real clinical practice for patient monitoring and assessing adherence to treatment	84.9	–	Yes	–
The use of TAI is feasible/realistic in my real clinical practice, taking into account the resources required to implement it (time, personnel) and the characteristics of the tool (length, simplicity)	58.9 (non-agreement: 11.0%)	52.9 (non-agreement: 14.0%	No	0.862
The use of the Morisky–Green test is feasible/realistic in my real clinical practice, taking into account the resources required to implement it (time, personnel) and the characteristics of the tool (length, simplicity)	61.6 (non-agreement: 9.6%)	51.7 (non-agreement: 23.3%)	No	0.284
The use of the disease knowledge test (Batalla Test) is feasible/realistic in my real clinical practice, taking into account the resources required to implement it (time, personnel) and the characteristics of the tool (length, simplicity)	67.1 (non-agreement: 6.8%)	52.6 (non-agreement: 24.6%)	No	0.047
The use of the self-reported adherence test (Haynes–Sackett) is feasible/realistic in my real clinical practice, taking into account the resources required to implement it (time, personnel) and the characteristics of the tool (length, simplicity)	68.5 (non-agreement: 9.6%	50.0 (non-agreement: 25.9%)	No	0.092
The use of the electronic record of drug withdrawal in pharmacies is feasible/realistic in my real clinical practice, taking into account the resources required to implement it (time, personnel) and the characteristics of the tool (length, simplicity)	78.9	–	Yes	–
The calculation of Proportion of Days Covered (PDC = % doses taken vs. prescribed) is feasible/realistic in my real clinical practice, taking into account the resources required to implement it (time, personnel) and the characteristics of the tool (length, simplicity)	67.1 (non-agreement: 15.1%)	47.5 (non-agreement: 21.3%)	No	0.166
The availability of an indicator in the computer system that automatically shows the proportion of days covered (PDC = % doses withdrawn from pharmacy vs. prescribed) would be useful to evaluate patient adherence[a]	–	89.4	Yes	–
The use of digital tools and smart inhalers is feasible/realistic in my real clinical practice, taking into account the resources required to implement it (time, personnel) and the characteristics of each tool (length, simplicity)	72.5	–	Yes	–

Abbreviations: COPD, chronic obstructive pulmonary disease; TAI, test of adherence to inhalers.
[a] Item added in the 2nd round.

study offers a multidimensional prioritization of interventions considered by experts to have the greatest potential impact on adherence. The resulting ten-point action plan consolidates these insights into a practical and context-specific framework tailored to the Spanish healthcare system.[11,18]

There was a clear consensus that adherence is influenced by multiple factors. Starting from treatment-related ones, panelists' opinions are aligned with those of previous studies,[4,19–22] demonstrating that the single-daily inhaled treatments show significantly better patient adherence and persistence, compared to multiple-daily dose treatments.[20] For instance, a recent large US cohort study found that once-daily inhalation of FF/UMEC/VI SITT vs. four daily inhalations of BUD/GLY/FOR SITT results in significantly greater adherence and persistence at 6 and 12 months.[22] Over one year, BUD/GLY/FOR users (1460 inhalations/year) received almost one month less treatment than FF/UMEC/VI patients (365 inhalations/year). These compliance differences may be linked to effectiveness, as seen in two large-cohort studies where FF/UMEC/VI showed better outcomes for exacerbations and all-cause mortality vs. BUD/GLY/FOR.[23,24] This is also shown in recent predictive modeling studies, in which once-daily is linked to a lower probability of exacerbations.[25] The availability of once-daily long-acting bronchodilators from various manufacturers is seen as a paradigm shift and has been linked to improved COPD patient outcomes, including symptom control, dyspnea, exacerbations, FEV1, hyperinflation, physical activity, and quality of life.[26] The Delphi expert panel agreed that limiting the use of devices requiring coordination between actuation and inhalation, or those with a spacer chamber, to patients who clinically need them (PIFR < 30 L/min) could simplify treatment and improve adherence in COPD. This is supported by the evidence that dry powder inhalers (DPIs) present the lowest rates of critical errors, while metered-dose inhalers (MDIs) with spacer chambers present the highest rates.[27] This recommendation seem feasible, as previous research and a recent hospitalized-patient real-world studies confirm that over 90% of COPD patients achieve peak inspiratory flow rates (PIFR) ≥ 30 L/min.[27,28] The findings of this Delphi are aligned with those of other studies and international guidelines, which reinforce the importance of combining molecules in a single inhaler for improved.[2,29–35]

Table 5
Results of the two rounds of the Delphi process for the statements in Sections 6 and 7 – Interventions to improve adherence and therapeutic management.

Statements/Items	% of agreement		Consensus	*p*-Value
Interventions to improve adherence and therapeutic management	1st round	2nd round		
Increasing patients' knowledge about their disease by means of a therapeutic training program would be useful to improve adherence to inhaled therapy in COPD	97.3	–	Yes	–
Involving the patient in the treatment strategy, and taking into account their preferences regarding devices and frequency of administration (daily doses) would be useful to improve adherence to inhaled therapy in COPD	98.6	–	Yes	–
Unifying inhaled treatment whenever clinically possible in a single device would favor adherence to inhaled therapy	100	–	Yes	–
Simplifying treatment whenever clinically possible (fewer daily doses and fewer inhalations per dose) would be useful to improve adherence to inhaled therapy in COPD	98.6	–	Yes	–
Simplifying treatment whenever clinically possible (simple devices, with the fewest possible steps, portable, without the need for maintenance or cleaning) would be useful to improve adherence to inhaled therapy in COPD	98.6	–	Yes	–
Using inhalers that allow treatment changes (escalation or de-escalation) without changing the device would promote adherence and reduce the number of critical errors	100	–	Yes	–
The widespread use of drugs with lower administration frequency (fewer doses per day) that has been applied to other chronic treatments (e.g. hypertension) would also promote adherence and treatment results in COPD	97.3	–	Yes	–
Promoting innovation in the pharmacology of inhaled treatments to develop molecules that, due to their affinity with the receptor and their duration of action, allow the time between doses to be spaced out and the frequency of administration to be reduced as much as possible, would be useful to improve adherence to inhaled therapy in COPD	97.3	–	Yes	–
Limiting the use of devices that require coordination between pressing and inhaling or a spacer chamber only to patient profiles in which such use is clinically necessary (PIFR < 30 L/min) would be useful to improve adherence to inhaled therapy in COPD	89.0	–	Yes	–
Associating the intake of treatment with an already established daily routine would be useful to improve adherence to inhaled therapy in COPD	97.3	–	Yes	–
Diagnosing and treating comorbidities that negatively affect adherence, such as depression or addictions (smoking), would be useful to minimize their impact on adherence to inhaled therapy in COPD	98.6	–	Yes	–
Promoting social/family support (e.g. by informing about patient associations, social work, etc.) would be useful to improve adherence to inhaled therapy in COPD	95.9	–	Yes	–
Improving follow-up and more frequent monitoring of efficacy, tolerability and adherence by healthcare professionals would be useful to improve adherence to inhaled therapy in COPD	97.3	–	Yes	–
Implementing the use of tools to assess adherence in clinical practice would be useful to improve adherence to inhaled therapy in COPD	86.3	–	Yes	–
Conducting behavioral interviews and periodically reviewing and retraining the patient in inhalation technique would be useful to improve adherence to inhaled therapy in COPD	95.9	–	Yes	–
Improving collaboration between healthcare professionals and involving nursing and community pharmacists in patient training and follow-up would be useful to improve adherence to inhaled therapy in COPD	100	–	Yes	–
Incorporating digital tools where possible (reminders, adherence recording applications or smart inhalers) would be useful to improve adherence to inhaled therapy in COPD	89.0	–	Yes	–

Abbreviations: COPD, chronic obstructive pulmonary disease.

Indeed, these nuances further support the need to consider patient-related factors when addressing adherence. Consensus was reached on the general association between lower dosing frequency and improved adherence. A proportion of panelists reported dissent, noting variability in clinical experience; consequently, experts emphasized the need to individualize therapy by considering patient preferences, perceived symptom control and device convenience.

Regarding patient-related factors, the expert panel in this Delphi highlights the need to increase patient understanding of COPD, improve inhaler use training, and involve the patient in decision-making, which has been mentioned before by other authors.[2,8,36–38] Experts agreed that patients with more advanced or symptomatic disease tend to adhere better to their treatments, although existing evidence is not clear on this point.[39–42] The same occurs with the fact that low educational level or low income can reduce a patient's ability to manage and adhere to treatment.[2,43]

Among the factors originating in the healthcare system or among the HCPs, inadequate monitoring of treatment adherence and technique, along with lack of structured and interdisciplinary follow-up visits were emphasized as significant contributors to non-adherence.[44,45] Another important factor identified was that temporary variations in treatment during hospitalization can confuse patients and lead to poorer adherence.[8,46–48]

To our knowledge, this is the first multidisciplinary consensus resulting in prioritized actions with the greatest impact and ease of implementation, resulting in a practical decalogue for inhalation therapy optimization in real practice. This Spanish multidisciplinary Delphi study underscores two fundamental lines of action: simplifying and unifying the inhalation treatment and empowering the patient.

In the OPTIMO study, no consensus was reached on some items. There was no consensus on whether reduced lung function leads to better adherence. Some believe advanced COPD patients might adhere more, while others think disease burden and comorbidities complicate compliance. Reduced lung function does not always correlate with increased disease burden, making this relationship complex.[39–42] The relationship between age and adherence is unclear. Younger patients might be less responsible, while older patients may struggle due to cognitive decline, polypharmacy, or physical limitations. Evidence does not show that age alone predicts lower adherence. Clinicians may find factors like disease burden, cognitive state, and overall health more significant.[39,40,49,50] A recent retrospective study including middle-aged to older COPD

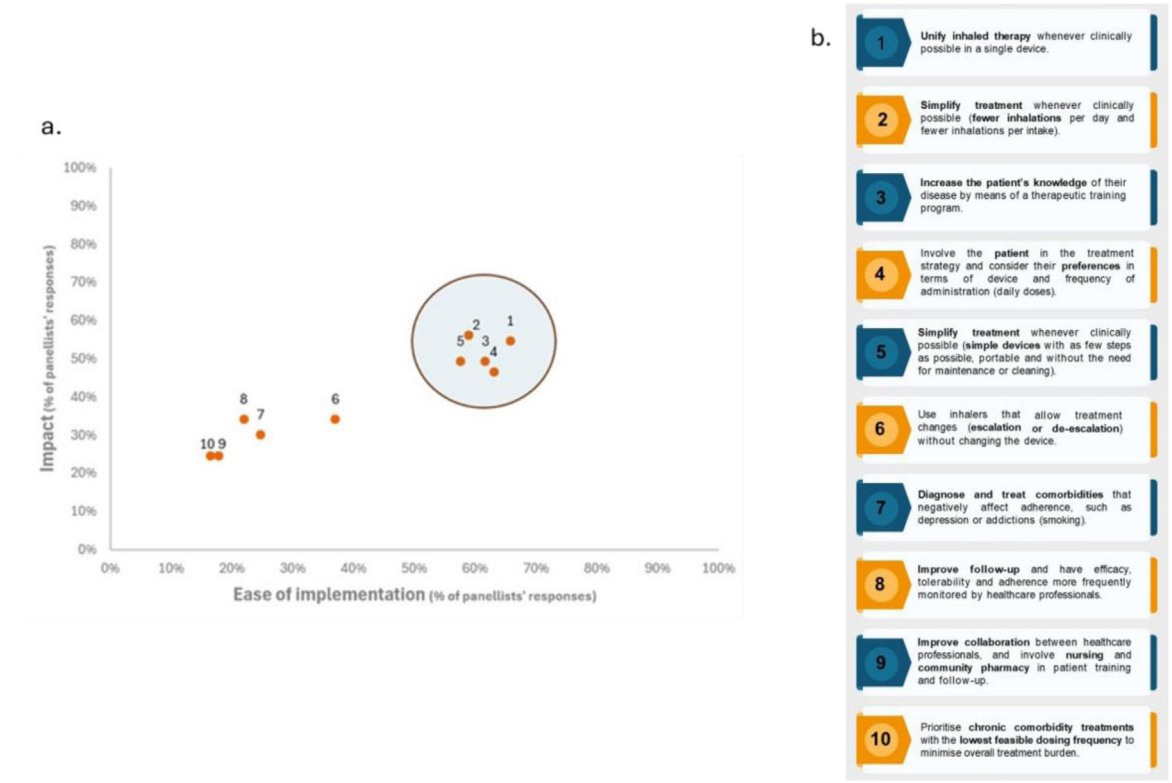

Fig. 1. Expert recommendations to improve adherence to inhalation therapy. (a) Top 10 multidisciplinary actions prioritized by the expert panel based on ease of implementation and expected impact on patient adherence and (b) Decalogue for inhalation therapy optimization, summarizing key recommendations from the expert panel, also ranked by ease of implementation and impact on adherence.

patients suggests that older patients might have been more adherent to their treatment if its regimen had been simpler.[22]

The main strengths of this study are: high consensus and a practical focus, with prioritized actionable points for improving adherence in real practice; being the first Spanish Delphi consensus on COPD management, inclusion of many expert panelists from multiple specialties, and the Delphi method ensuring honest responses and reduced bias through anonymity and iterative rounds for refined, informed answers.

The present study is subject to several limitations, some of which are inherent to the Delphi methodology. Since these findings reflect structured expert opinion and should be interpreted within the inherent subjectivity of it. The decalogue does not replace evidence-based guideline recommendations but complements them by prioritizing actions considered most feasible and impactful in real-world Spanish clinical practice. Notably, the absence of direct interaction among panelists may have constrained opportunities for in-depth discussion; however, this limitation was partially addressed through the establishment of a scientific committee tasked with interpreting the results. Additionally, potential biases related to the questionnaire and sponsorship may have influenced the responses, as the questionnaire, while grounded in compiled scientific evidence, ultimately relies on the subjective opinions of experts.

A further limitation of the study is the absence of respiratory nurses within both the scientific committee and the expert panel. Although the Delphi process included statements that explicitly addressed the role of nursing in inhaler education, technique reinforcement, and adherence support, the perspectives of nursing professionals—who are key actors in the day-to-day management of COPD—were not directly represented. Similarly, the viewpoints of patients and community pharmacists were not included. Considering the increasingly multidisciplinary nature of COPD care, and the active participation of nurses and pharmacists in clinical practice and scientific initiatives in Spain, future consensus exercises should ensure the inclusion of these stakeholders. Their contribution would likely enrich the interpretation of barriers and facilitators to adherence, strengthen the external validity of the proposed recommendations, and help refine the implementation strategies derived from this consensus.

Moreover, the exclusion of perspectives from patients represents a notable gap. Finally, given that the panel was composed of Spanish professionals only, the findings reflect national clinical practice and organizational characteristics. This enhances applicability within Spain but limits international generalizability, especially considering variability in COPD care models across countries.

Building on these findings, several future directions emerge. First, implementing the proposed decalogue may support more structured and patient-centered approaches to optimizing inhalation therapy. Second, strengthening the involvement of community pharmacists and nursing professionals in routine follow-up appears essential, given their pivotal role in patient education, inhaler technique support, and adherence monitoring. Third, future Delphi or consensus initiatives should broaden stakeholder representation to include respiratory nurses, patients, and pharmacists, whose perspectives were not captured in this study and would substantially enrich the interpretation and applicability of the recommendations. Finally, identifying real-world barriers and developing practical facilitators for the use of adherence-monitoring tools remain key goals to support sustained improvements in COPD management.

Conclusion

This multidisciplinary panel of COPD experts agreed on 17 actions to support the optimization of adherence and treatment outcomes. Through a structured consensus process, the panel identified high-priority, feasible interventions, which were consolidated into a ten-point guidance framework for inhalation therapy optimization. These expert-derived recommendations complement existing evidence-based guidelines by highlighting strategies perceived as most impactful in real-world Spanish clinical practice, including treatment simplification, the use of long-acting therapies and user-friendly devices, and the empowerment of patients through training and shared decision-making.

Use of artificial intelligence

No artificial intelligence tools were used to generate, analyze, or draft the scientific content of this manuscript.

Ethical considerations and informed consent

This study is a Delphi expert consensus survey and does not constitute a clinical trial. The participants were healthcare professionals recognized as experts in the management of Chronic Obstructive Pulmonary Disease (COPD), who were asked to provide their opinions on specific issues related to treatment adherence and disease control. No patients were involved in the study, and the experts did not undergo any interventions or biological sample collection.

In accordance with the ISPOR Good Practices for Outcomes Research (2017), specifically sections 9.2 and 9.3 from Appendix 9, and the EPHMRA Code of Conduct (2023), specifically sections 1.2 and 1.3, as well as examples from similar published studies, ethical review is not required for this type of non-interventional research.

Only experts who provided consent to participate through the online platform were included in the Delphi survey. Data were analyzed anonymously, ensuring confidentiality and privacy. Additionally, the questionnaire content does not pertain to clinical trials or scientific research involving patient data, nor does it compromise the physical or psychological integrity of any subject.

Funding

This study was sponsored by GlaxoSmithKline (GSK), which provided funding to Adelphi Targis for the design and conduct of the Delphi survey and for medical writing support. The sponsor had no role in the identification of experts, development of the questionnaire, data analysis, interpretation of results, formulation of conclusions, or decisions related to manuscript content. All scientific decisions were made independently by the scientific committee. The study was conducted in accordance with the Farmaindustria Code of Good Practices.

Authors' contributions

All authors meet the criteria established by the International Committee of Medical Journal Editors (ICMJE) for authorship: (1) substantial contributions to the conception, design, data acquisition, analysis, or interpretation; (2) drafting or critical revision for important intellectual content; (3) final approval of the version to be published; and (4) agreement to be accountable for all aspects of the work.

Conflicts of interest

MTY reports personal fees and/or non-financial support from Almirall, Astellas, Astra Zeneca, Bayer, Bial, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, Daiichi Sankyo, Esteve, Faes, Ferrer, Grunenthal Pharma, GSK, Janssen, Lilly, MSD, Novartis, Novo Nordisk, Organon, Sanofi, Servier, and Viatris outside the submitted work.

JDMV reports personal fees and/or non-financial support from AMGEN, EP Health Marketing, S.L., GSK, and Live-Med Iberia, S.L. outside the submitted work.

FNR reports personal fees and/or non-financial support from AstraZeneca, Boehringer Ingelheim, Chiesi, EP Health Marketing S.L., Esteve, Ferrer, GSK, Kern Pharma, Lundbeck, Menarini, MSD, Novartis, Novo Nordisk, Pfizer, Sanofi, and Viatris outside the submitted work.

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MBAO reports personal fees and/or non-financial support from Adventia Pharma, AstraZeneca, Boehringer Ingelheim, Chiesi, FAES, Fresenius Kabi, GSK, Neuraxpharm, Nestlé Health Science and Zambon outside the submitted work.

PGM reports personal fees and/or non-financial support from GSK outside the submitted work.

CGV reports personal fees and/or non-financial support from Bial, Chiesi, GSK and Sanofi outside the submitted work.

EDD reports personal fees and/or non-financial support from Aflofarm, Astra-Zeneca, Bial, Boheringer, Chiesi, GSK, Menarini, Novartis and Zambon outside the submitted work.

BAN reports personal fees and/or non-financial support from AstraZeneca, Boehringer Ingelheim, Chiesi, Gilead, GSK, Laboratorios BIAL, Laboratorios Menarini, MSD, Sanofi, Zambon. outside the submitted work.

JMES reports personal fees and/or non-financial support from GSK and Boehringer Ingelheim outside the submitted work.

AMF is an employee of GSK and holds stocks/shares in GSK.

Acknowledgments

This study was sponsored by GSK, which funded Adelphi Targis to design and conduct the survey following the Delphi methodology and to provide medical writing support for drafting the publication. The authors would like to thank all COPD experts who independently participated in the Delphi questionnaire, as well as Maria Ruart, PhD, Ana Fernández, MSc, Laura Barajas, and Mónica Pantín for their editorial assistance and project management support.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.opresp.2026.100587.

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