

## Special Article

## The 7 Cardinal Sins of COPD in Spain

 José Luis Izquierdo<sup>a,\*</sup>, Ciro Casanova<sup>b</sup>, Bartolomé Celli<sup>c</sup>, Salud Santos<sup>d</sup>, Oriol Sibila<sup>e</sup>,  
 Patricia Sobradillo<sup>f</sup>, Alvar Agusti<sup>e,g</sup>

<sup>a</sup> Department of Medicine and Medical Specialties, Universidad de Alcalá, Alcalá de Henares, Madrid, Respiratory Medicine, Hospital Universitario de Guadalajara, Guadalajara, Spain

<sup>b</sup> Department of Respiratory Medicine-Research Unit, Hospital Universitario Nuestra Señora de la Candelaria, Universidad de la Laguna, Santa Cruz de Tenerife, Spain

<sup>c</sup> Brigham and Women's Hospital, Boston, MA, USA

<sup>d</sup> Department of Respiratory Medicine, Hospital Universitario de Bellvitge, IDIBELL, L'Hospitalet de Llobregat, Barcelona, Universitat Barcelona, CIBERES, Spain

<sup>e</sup> Department of Respiratory Medicine, Institut Clínic Respiratori, Universitat Barcelona, IDIBAPS, CIBERES, Spain

<sup>f</sup> Department of Respiratory Medicine, Hospital Universitario de Cruces, Barakaldo, Biscay, Spain

<sup>g</sup> Department of Respiratory Medicine, Institut Clínic Respiratori, Universitat Barcelona, IDIBAPS, CIBERES, Spain

## ARTICLE INFO

## Article history:

Received 23 November 2021

Accepted 17 December 2021

Available online 7 January 2022

## Keywords:

 Chronic obstructive pulmonary disease  
 bronchitis  
 emphysema  
 exacerbations  
 prevention  
 healthcare system  
 smoking  
 diagnosis

## ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a public health problem due to its high prevalence (11% in the adult population in Spain), increasing incidence, and great social and economic impact. Despite this, it is underdiagnosed (and, therefore, undertreated) at a rate of around 80%. In this paper, a group of respiratory physicians specializing in COPD discuss 7 fundamental problems (“cardinal sins”) that contribute to this situation, with the explicit aim of proposing specific solutions that may help to improve this unfavorable state of affairs.

© 2022 SEPAR. Published by Elsevier España, S.L.U. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

## Introduction

Chronic obstructive pulmonary disease (COPD) is a major public health problem due to its high prevalence (11% in the adult population in Spain), increasing incidence associated with population aging, and great social and economic impact.<sup>1–3</sup> Despite this, around 80% of patients with COPD remain undiagnosed (and, therefore, untreated) and, in patients who have been diagnosed, the disease is often not confirmed by an appropriate diagnostic test (spirometry). As a result, treatment may not conform to national and international scientific recommendations.

Five years ago, Marin et al. published an excellent editorial in which they proposed 10 patient-focused “commandments” aimed at simplifying the treatment of COPD patients.<sup>4</sup> In this document, a group of respiratory medicine specialists with experience in the diagnosis and treatment of COPD patients in Spain take a contrasting approach and identify and discuss the “7 cardinal sins” of *disease management* in Spain (not of treatment of the individual patient

with COPD). The strategic objective of this discussion is to propose solutions that can be implemented to benefit COPD patients and improve the rational use of healthcare resources.

### The 7 cardinal sins of COPD in Spain

Table 1 lists the 7 cardinal sins discussed below and the actions proposed for correction. This “list” is the result of a discussion among the authors. Some readers may feel that other “sins” have been omitted from the list and/or others may disagree with those included. In any case, the authors hope to generate a discussion that will interest patients, healthcare professionals and administrators.

#### Ephemeral public health plans

The Spanish National Health System (NHS) COPD Strategy, approved by the Interterritorial Council in 2009, cited various shortcomings in the organization of care, and established objectives and recommendations for improving the entire NHS.<sup>5</sup> In its 2014 update, it became apparent that the degree of implementation of these proposals was “moderate”, and that while some activities had been started, their achievement was “limited and variable”.<sup>6</sup>

\* Corresponding author.  
 E-mail address: [jose-luis.izquierdo@uah.es](mailto:jose-luis.izquierdo@uah.es) (J. Luis Izquierdo).

**Table 1**  
The 7 cardinal sins of COPD in Spain in 2021 and proposed solutions.

Cardinal sin	Proposed solution
1. Ephemeral public health plans	<ul style="list-style-type: none"> <li>• Close monitoring of approved actions with public accountability</li> <li>• Alliance with media on the importance of the disease and lack of implementation of approved programs</li> </ul>
2. Lack of coordination in care	<ul style="list-style-type: none"> <li>• Multidisciplinary units, led by Respiratory Medicine</li> <li>• Integrated care programs</li> </ul>
3. Diagnostic issues	<ul style="list-style-type: none"> <li>• Advanced practice nursing in the COPD process</li> <li>• Day hospital for the management of severe patients</li> <li>• Expand the use of spirometry in Primary Care</li> <li>• Train Primary Care staff in the correct use of spirometry</li> <li>• Improve knowledge of the disease in Primary Care and other medical specialties</li> <li>• Improve knowledge of the disease in nursing staff</li> </ul>
4. Stigmatizing and stigmatized disease	<ul style="list-style-type: none"> <li>• Improve knowledge of the disease and its symptoms in the general population</li> <li>• COPD is not just a disease caused by cigarette smoking</li> <li>• It can begin in infancy and worsen through adolescence and early adulthood</li> <li>• It does respond to prevention and treatment</li> <li>• Early diagnosis and treatment should prevent disability in the elderly</li> </ul>
5. Need for early action	<ul style="list-style-type: none"> <li>• Perform spirometry studies in young people (&lt;30 years)</li> <li>• Identify respiratory health risk factors.</li> </ul>
6. Clinical practice guideline adherence	<ul style="list-style-type: none"> <li>• Reduce variability between CPGs. Simple messages avoiding discrepancies and proposals that generate confusion.</li> <li>• Update guidelines regularly.</li> <li>• Disseminate guidelines appropriately.</li> <li>• Audit their impact on clinical practice.</li> </ul>
7. Education of the population and patients	<ul style="list-style-type: none"> <li>• Improve awareness in the general population:</li> <li>• Informative campaigns in health media, social media and the general media</li> <li>• Identify a public figure who puts a face to COPD</li> <li>• Improve the education of COPD patients and their families/caregivers:</li> <li>• Simple and homogeneous educational material between the different care levels</li> <li>• Support for patient associations</li> </ul>

Furthermore, several autonomous regions in Spain have been generating their own documents, plans and care processes, but few end up being implemented. An expert report published in 2020 stated that<sup>3</sup>:

“... so far, this [creating a structure for the management of COPD in Spain] has not been possible due to a lack of commitment and strategic initiatives coordinated and shared by political bodies and health authorities, managers, scientific societies, health professionals, associations and patient federations, media and related sectors”.

A real commitment is required to strengthen the National COPD Strategy and Regional Plans that includes the periodic evaluation of quantitative and qualitative indicators of their implementation and effectiveness. We also propose the creation of a *Respiratory Health Plan*<sup>3</sup> that goes beyond COPD and addresses the importance of respiratory health in general, as the example of the COVID-19 pandemic has recently shown<sup>7</sup>; this would include funding for respiratory health prevention and promotion programs, early diagnosis and treatment of the most common respiratory diseases (including COPD), the understanding that forced spirometry is a non-invasive, inexpensive, reproducible test that provides information on respiratory health (with an impact on population aging),<sup>8</sup> and a firm commitment to training, innovation and research in this area.

#### *Lack of coordination in care*

Several healthcare areas and medical specialties are involved in the diagnosis and treatment of COPD, but there is no document defining their specific roles, how they should be coordinated and who is responsible for patient follow-up at each stage in the process.<sup>3</sup> This results in undesirable variability in care, as shown by the COACH audit carried out in 63 randomly selected primary care centers in Spain<sup>9</sup>. This variability is also observed in the management of exacerbations. The AUDIPOC audit investigated the health outcomes of 5178 patients discharged following COPD exacerbation in 129 hospitals throughout Spain, and revealed huge

differences between autonomous regions, hospitals and professionals in variables as important as mortality (ranging from 0% to 35%) and early hospital readmission (0%–62%).<sup>10</sup>

COPD is a complex and heterogeneous disease that requires a personalized diagnostic and therapeutic approach, based on the “treatable traits” of each individual patient<sup>11</sup>; “standard” treatment for all patients is of no use.<sup>12</sup> However, not all COPD patients are evaluated by specialists, so decisions affecting the most severe patients are not always made by the most experienced professionals. A recent study showed that, in primary care (PC), only 10% of patients diagnosed with COPD had been seen by a respiratory medicine specialist, while 24% of patients with a cardiac condition had been seen by a cardiologist.<sup>13</sup>

Improving care coordination is feasible. The creation of multidisciplinary functional units, led by respiratory medicine, facilitates the approach and organization of the entire COPD care process, from its prevention and early diagnosis, through complications and intercurrent exacerbations, to the final phase of life. Integrated COPD care programs are associated with lower costs and fewer readmissions.<sup>14</sup> Day hospitals for the management and monitoring of severe patients play a key role in the care coordination process, by improving access to alternative emergency services, while avoiding contact with patients who attend the general emergency department and facilitating continuity of care.<sup>15</sup> Finally, the role of advanced practice nursing is also fundamental in improving the continuity and quality of care provided to patients with COPD.<sup>16–18</sup>

#### *Diagnostic issues*

The diagnosis of this disease is well described in clinical practice guidelines (CPG).<sup>1,19</sup> Diagnosis is based on an assessment of respiratory symptoms, patient exposure to risk factors such as tobacco smoke and other harmful gases, and airflow limitation determined by post-bronchodilator spirometry. In principle, these patients should not be difficult to identify, but the evidence on the diagnosis of the disease in Spain suggests just the opposite. COPD is a disease with a high rate of diagnostic error, and this includes both underdiagnosis (almost 80% of COPD patients are undiag-

nosed) and, therefore, untreated<sup>20</sup> and overdiagnosis (attribution of a COPD diagnosis to certain clinical presentations that are not actually COPD).

The impact of underdiagnosis is very serious, since failing to correctly diagnose patients with COPD in the early stages of their disease or detect it in advanced stages significantly reduces the possibility of mitigating disease progression and preventing exacerbations,<sup>21</sup> thereby increasing the use of healthcare resources and healthcare costs associated with patient management.<sup>22</sup> In Spain, more than 1.5 million people are currently unaware that they have COPD and are therefore not receiving the treatment and care they require.

Overdiagnosis is also a major public health problem. Studies, both national and international, carried out mainly in the PC setting, have shown that 30%–60% of patients classified as COPD or who have received treatment for COPD do not meet the diagnostic criteria established in clinical guidelines.<sup>23,24</sup> A prospective study in Spain calculated the prevalence of COPD overdiagnosis in PC at 42.7%.<sup>25</sup> This has substantial adverse consequences, in terms of both health (erroneous prescriptions of treatments and follow-ups) and costs (high use of resources by these patients).

Several factors help to explain these diagnostic problems. The most important include the misuse of spirometry in PC, either due to lack of access to spirometers in the centers (a situation that is increasingly rare), or due to underuse of the devices (lack of time and appropriately trained staff). Other problems include the non-specificity of symptoms or the belief that smoking is the only causative factor. For example, we now know that various situations during pregnancy, childhood and adolescence influence the development of COPD (not necessarily in relation to smoking) in adulthood.<sup>26</sup> Finally, an additional factor that contributes to diagnostic errors is the lack of knowledge of this disease and its symptoms among the general population.<sup>3</sup>

### *Stigmatizing and stigmatized disease*

Traditionally, COPD has been understood (and explained, both professionally and socially) as a disease that is self-inflicted by smoking, appears in old age (in people in their sixties or seventies), and is progressive and irreversible.<sup>27–29</sup> For this reason, it has historically been thought that smokers are to blame for their own condition, stigmatizing further both smokers and the disease and transferring responsibility to the patient.<sup>30,31</sup> We are inclined to forget that smoking is more than a simple habit, or an activity associated with a lifestyle that is harmful to health, but reflects in most cases an addiction to nicotine, making it yet another item on the list of chronic addictive diseases that also includes drug addiction or alcoholism.<sup>32,33</sup>

This stigmatization of the smoker and the disease has several practical consequences. First, some smokers who experience coughing and dyspnea (possible COPD symptoms) interpret these symptoms (correctly) as the result of their smoking.<sup>34</sup> However, because they do not want to feel ill due to their addiction, they tend to withdraw and cut down their daily and social activity in order to reduce exercise-associated respiratory distress, and delay seeking professional help until their symptoms already require urgent attention.<sup>34,35</sup> Moreover, disease stigmatization affects not only the patient but also some healthcare professionals, who may adopt attitudes and practices that could contribute in part to late diagnosis, underdiagnosis or misdiagnosis, or to the idea that “little can be done”.<sup>36</sup>

This stigmatized view of COPD must change radically in the light of recent research showing that this perspective is clearly biased and incomplete. While smoking is a key (preventable) risk factor for COPD, it is not the only one. Today we know that other types

of exposures (for example, to biomass smoke) and other events in the early stages of life (prematurity, low birth weight, repeat infections, poor nutrition) alter lung development and can facilitate the development of COPD in adulthood (even in young adults).<sup>37</sup> Therefore, COPD is not related exclusively to smoking, nor does it appear exclusively in the later stages of life.<sup>26,38</sup>

To combat this stigmatization and its nihilistic consequences on therapy, COPD must be presented to the population and health professionals as a preventable and treatable disease that must be diagnosed at an early stage in order to improve patient outcomes.

### *Need for early action*

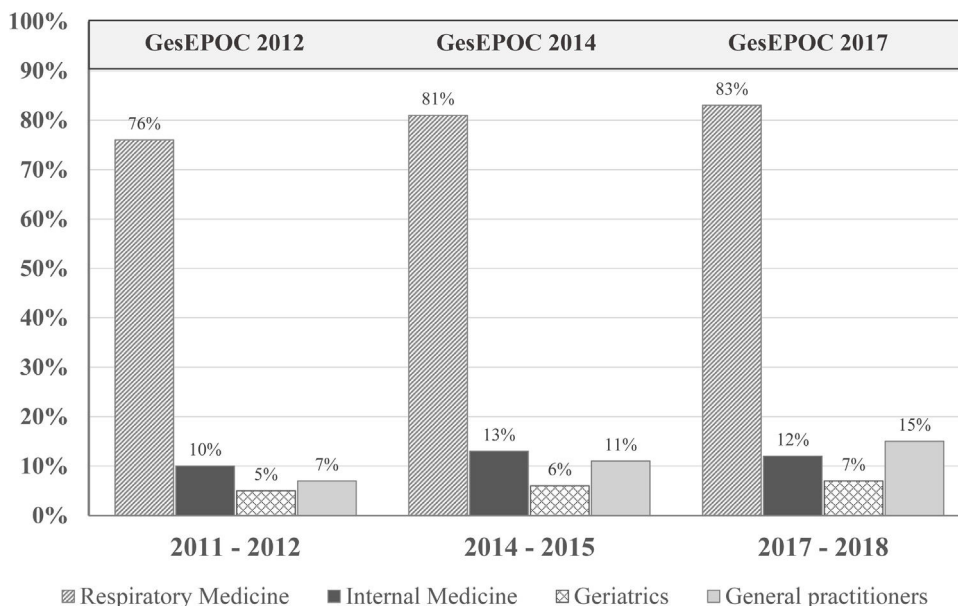
An early COPD diagnosis can impact positively on disease progression.<sup>39</sup> This should prompt us to review our performance in this regard. The results of an audit carried out between 2014 and 2015 in 59 Spanish hospitals in patients diagnosed with COPD followed up in outpatient clinics, showed that the mean age of the patients was 70 years and that, in the case of patients under 55 years, medical professionals tended to adhere less to treatment guidelines.<sup>27</sup> We must break away from the classic concept of COPD as a self-inflicted disease caused by smoking<sup>27</sup> that affects older men and whose progression is prevented only by smoking cessation.<sup>28,29</sup>

The current definition of COPD based on forced expiratory volume in 1 s (FEV<sub>1</sub>)/forced vital capacity (FVC) ratio is very specific,<sup>1,19</sup> but today we know that this parameter is not very sensitive for detecting clinical (cough and chronic expectoration), physiological (decreased diffusing capacity for carbon monoxide [DLCO] or excessive drop in FEV<sub>1</sub>) and structural (areas of emphysema on computed tomography) lung changes which may precede spirometric obstruction.<sup>19</sup> These changes have also been shown to adversely affect patient quality of life and, in some cases, to alter the course of the disease. This “spirometric-silent” period is currently a hotly debated scientific topic. Along these lines, the concept of “pre-COPD” has been recently proposed, in keeping with other medical specialties that have adopted the notion of a “pre-disease” state (e.g. pre-diabetes or pre-hypertension).<sup>41,42</sup> In these therapeutic areas, the “pre-disease” stage does not mean that all patients will develop the pathology, but it identifies a certain at-risk population for closer and more individualized follow-up.

This new scenario for diagnosing and managing COPD at an earlier stage has been reinforced by observational studies in large patient cohorts. These have shown that at least 50% of patients diagnosed with COPD at 65 years of age already had lung function changes at 25 years of age.<sup>43</sup> The natural history of the disease in this group of patients is different and closely related to lung development in the early years of life. However, this heterogeneity has not been taken into account in drug trials, and the possible differential effect of COPD treatment in this group of patients is unknown.

### *Clinical practice guideline adherence*

The main objective of CPGs is to reduce variability in clinical practice and improve effectiveness in disease management (in this case, COPD) through recommendations based on the best available scientific evidence (generally randomized clinical trials [RCTs] in large populations of carefully selected patients).<sup>44</sup> A 2018 multicenter cross-sectional study in Spain found frequent deviations from the GOLD and Spanish COPD (GesEPOC) guidelines in clinical practice.<sup>45</sup> In fact, several studies question their real usefulness.<sup>23,40,44</sup> for several reasons. First, RCTs are necessary for assessing the efficacy and safety of any drug and are essential in the regulatory procedure, but their external validity is limited by the strict inclusion and exclusion criteria that determine the specific



**Fig. 1.** Patients who have undergone spirometry to confirm the diagnosis of COPD in the last decade. The publication of the Spanish COPD guidelines (GesEPOC) and its updates has had little impact in improving the quality of the diagnosis in real life. Adapted from Izquierdo et al. (2021).<sup>23</sup>

characteristics of the study population.<sup>46</sup> Moreover, the applicability of the recommendations is not always taken into account when drawing up the CPG, although methods are now available to evaluate their implementation in the population, almost in real time.<sup>23</sup> If a CPG fails to improve COPD management, its format and objectives should be reconsidered. Finally, the abundance of CPGs does not imply higher quality or practical utility. Variability between CPGs must be reduced, some confusing discrepancies must be eliminated, they must be continuously updated and appropriately disseminated, and their real clinical impact must be audited (Fig. 1).

#### Education of the population and patients

Several studies in our setting show that the general public has a very poor understanding of COPD, including those at high risk of developing the disease.<sup>47,48</sup> This lack of knowledge has also been found among their caregivers.<sup>49</sup> Finally, we should mention that educational programs for patients and their family circle are implemented heterogeneously in different health areas.

This poor knowledge of the disease makes early diagnosis and treatment difficult,<sup>50</sup> and hampers the implementation of self-care interventions in patients with COPD that may encourage smoking cessation, improve the inhalation technique, reduce anxiety and depression levels, and improve quality of life and use of health resources (unscheduled visits to emergency services, number of hospitalizations and length of hospital stays).<sup>51</sup> The World Health Organization (WHO) global action plan for the prevention and control of non-communicable diseases (NCDs) 2013–2020 recommends empowering people with NCDs to better manage their own disease, and that education, incentives and tools for care and self-management are provided, including through the use of new information and communication technologies (ICT) such as eHealth or mHealth.<sup>52</sup>

Last but not least, a disease such as COPD, due to its prevalence, burden and social impact, should be well known to the general public, so that they can participate accordingly in its prevention, early detection and patient support.

#### Conclusions

The 7 sins discussed here emerged from a debate among 7 respiratory medicine specialists with experience in COPD diagnosis, treatment and research. Our view, however, represents only part of the complex network of professionals, patients, caregivers, and administrators involved in the disease. Here, we discuss 7 elements we believe to be important, and propose specific initiatives to improve the current situation and, thereby, help to prevent and treat COPD earlier and better. In fact, a *Lancet Commission* of international experts is currently discussing whether such initiatives could eventually result in the “eradication” of COPD.<sup>53</sup> The initiatives discussed here may help to achieve this goal at some point in the future.

#### Conflict of interests

Dr JL Izquierdo reports having received compensation for Advisory Boards and consultation fees from: Astra Zeneca, Bayer, Boehringer Ingelheim, Chiesi, GSK, Grifols, Menarini, Novartis, Orion, Pfizer, Sandoz Teva.

Dr C. Casanova reports having received fees and/or financial support for research projects of AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Menarini y Novartis.

Dr. Bartolome R Celli reports having received compensation for Advisory Boards and consultation fees from: Glaxo Smith Kline, Boehringer-Ingelheim, Astra Zeneca, Novartis, Pulmonx, CHIESI, Menarini and Bayer. He does not have shares or interest in any company, neither does any member of my family. He has not received or had any relationship with tobacco money.

Dra S. Santos, does not present any conflict of interest with the present study.

Dr O. Sibila, does not present any conflict of interest with the present study.

Dra P. Sobradillo, does not present any conflict of interest with the present study.

Dr A. Agusti, reports having received fees and/or financial support for research projects of AZ, Chiesi, GSK, Menarini.



## Acknowledgments and funding

The authors would like to thank Dr. Susana Cañón and Dr. Blanca Piedrafita (Medical Statistics Consulting, S.L., Valencia, Spain) for their help in preparing and editing this article, in accordance with Good Publication Practice (GPP3) guidelines and thanks to the funding provided by AstraZeneca.

## References

- Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD. 2021 Report; 2021. Available from: <https://goldcopd.org/2021-gold-reports/>.
- García A, Hidalgo A, Rivera B, López E, Espín J, Oliva J, et al. Libro Blanco sobre la Carga Socio-Económica de la EPOC. Madrid: Instituto Max Weber; 2015. Available from: <https://weber.org.es/publicacion/libro-blanco-sobre-la-carga-socio-economica-de-la-epoc/>
- Ancochea J, Aguilar J, de Lucas P, Fernández A, García Río F, Gracia D, et al. La epoc en España: reflexión sobre la situación actual y propuesta de soluciones 2021. EIDON. 2020;54:151–87, <http://dx.doi.org/10.13184/eidon.54.2020.151-187>.
- Marin JM, Cote C, Casanova C, Pinto-Plata V, Montes de Oca M, Divo MJ, et al. Simplificando las guías: los 10 mandamientos de la EPOC. Arch Bronconeumol. 2016;52:179–80, <http://dx.doi.org/10.1016/j.arbres.2016.01.012>.
- Ministerio de Sanidad y Política Social. Estrategia en EPOC del Sistema Nacional de Salud. Aprobada por el Consejo Interterritorial del Sistema Nacional de Salud el 3 de junio de 2009; 2009. Available from: <https://www.msbs.gob.es/organizacion/sns/planCalidadSNS/docs/EstrategiaEPOCSNS.pdf>.
- Ministerio de Sanidad SSEL. Actualización de la Estrategia en EPOC del Sistema Nacional de Salud. Informe de enero; 2014. Available from: [https://www.msbs.gob.es/organizacion/sns/planCalidadSNS/pdf/EPOC\\_version\\_junio\\_2014.pdf](https://www.msbs.gob.es/organizacion/sns/planCalidadSNS/pdf/EPOC_version_junio_2014.pdf).
- Crispi F, Crovetto F, Larroya M, Camacho M, Tortajada M, Sibila O, et al. Low birth weight as a potential risk factor for severe COVID-19 in adults. Sci Rep. 2021;11:2909, <http://dx.doi.org/10.1038/s41598-021-82389-9>.
- Agusti A, Fabbri LM, Baraldi E, Celli B, Corradi M, Faner R, et al. Spirometry: a practical lifespan predictor of global health and chronic respiratory and non-respiratory diseases. Eur J Intern Med. 2021;89:3–9, <http://dx.doi.org/10.1016/j.ejim.2021.04.027>.
- Abad-Arriaz M, Moran-Rodríguez A, Mascarós E, Quintana C, Abad L, Núñez Palomo S, et al. Community Assessment of COPD Health Care (COACH) study: a clinical audit on primary care performance variability in COPD care. BMC Med Res Methodol. 2018;18:68, <http://dx.doi.org/10.1186/s12874-018-0528-4>.
- Pozo-Rodríguez F, López-Campos JL, Álvarez-Martínez CJ, Castro-Acosta A, Agüero R, Hueto J, et al. Clinical audit of COPD patients requiring hospital admissions in Spain: AUDIPOP study. PLoS ONE. 2012;7:e42156, <http://dx.doi.org/10.1371/journal.pone.0042156>.
- Agusti A, Bel E, Thomas M, Vogelmeier C, Brusselle G, Holgate S, et al. Treatable traits: toward precision medicine of chronic airway diseases. Eur Respir J. 2016;47:410–9, <http://dx.doi.org/10.1183/13993003.01359-2015>.
- Agusti A. The path to personalised medicine in COPD. Thorax. 2014;69:857–64, <http://dx.doi.org/10.1136/thoraxjnl-2014-205507>.
- Cho EE, McCreedy GC, Wong HH, Stanbrook MB, Gershon AS. Which physicians are taking care of people with COPD? Chest. 2019;155:771–7, <http://dx.doi.org/10.1016/j.chest.2018.12.018>.
- Trout D, Bhansali AH, Riley DD, Peyler FW, Lee-Chiong TL. A quality improvement initiative for COPD patients: a cost analysis. PLoS ONE. 2020;15:e0235040, <http://dx.doi.org/10.1371/journal.pone.0235040>.
- Huertas D, Montón C, Marín A, Solanes I, López-Sánchez M, Pomares X, et al. Effectiveness of a respiratory day hospital program to reduce admissions for exacerbation in patients with severe COPD: a prospective, multicenter study. COPD. 2017;14:304–10, <http://dx.doi.org/10.1080/15412555.2017.1279598>.
- Ferrone M, Masciantonio MG, Malus N, Stitt L, O'Callahan T, Roberts Z, et al. The impact of integrated disease management in high-risk COPD patients in primary care. npj: Primary Care Respir Med. 2019;29, <http://dx.doi.org/10.1038/s41533-019-0119-9>.
- Helvacı A, Gok Metin Z. The effects of nurse-driven self-management programs on chronic obstructive pulmonary disease: a systematic review and meta-analysis. J Adv Nurs. 2020;76:2849–71, <http://dx.doi.org/10.1111/jan.14505>.
- Arriero-Marín JM, Orozco-Beltrán D, Carratalá-Munuera C, López-Pineda A, Gil-Guillen VF, Soler-Cataluña JJ, et al. A modified Delphi consensus study to identify improvement proposals for COPD management amongst clinicians and administrators in Spain. Int J Clin Pract. 2021;75, <http://dx.doi.org/10.1111/ijcp.13934>.
- Miravittles M, Calle M, Molina J, Almagro P, Gómez J-T, Trigueros JA, et al. Spanish COPD guidelines (GesEPOC) 2021. Updated pharmacological treatment of stable COPD. Arch Bronconeumol. 2021, <http://dx.doi.org/10.1016/j.arbr.2021.03.014>.
- Soriano JB, Alfageme I, Miravittles M, de Lucas P, Soler-Cataluña JJ, García-Río F, et al. Prevalence and determinants of COPD in Spain: EPISCAN II. Arch Bronconeumol. 2021;57:61–9, <http://dx.doi.org/10.1016/j.arbr.2020.07.017>.
- Welte T, Vogelmeier C, Papi A. COPD: early diagnosis and treatment to slow disease progression. Int J Clin Pract. 2015;69:336–49, <http://dx.doi.org/10.1111/ijcp.12522>.
- Larsson K, Janson C, Ställberg B, Lisspers K, Olsson P, Kostikas K, et al. Impact of COPD diagnosis timing on clinical and economic outcomes: the ARCTIC observational cohort study. Int J Chronic Obstruct Pulmon Dis. 2019;14:995–1008, <http://dx.doi.org/10.2147/COPD.S195382>.
- Izquierdo JL, Morena D, González Y, Paredero JM, Pérez B, Graziani D, et al. Clinical management of COPD in a real-world setting. A big data analysis. Arch Bronconeumol (Engl Ed). 2021;57:94–100, <http://dx.doi.org/10.1016/j.arbres.2019.12.025>.
- Diab N, Gershon AS, Sin DD, Tan WC, Bourbeau J, Boulet LP, et al. Underdiagnosis and overdiagnosis of chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2018;198:1130–9, <http://dx.doi.org/10.1164/rccm.201804-0621CI>.
- Golpe R, Díaz-Fernández M, Mengual-Macén N, Sanjuán-López P, Martín-Robles I, Cano-Jiménez E. Sobrediagnóstico de enfermedad pulmonar obstructiva crónica en atención primaria. Prevalencia y condicionantes. SEMERGEN. 2017;43:557–64, <http://dx.doi.org/10.1016/j.semerg.2016.11.006>.
- Agustí A, Hogg JC. Update on the pathogenesis of chronic obstructive pulmonary disease. N Engl J Med. 2019;381:1248–56, <http://dx.doi.org/10.1056/nejma1900475>.
- Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J. 1977;1:1645–8, <http://dx.doi.org/10.1136/bmj.1.6077.1645>.
- Anthonisen NR, Connett JE, Murray RP. Smoking and lung function of lung health study participants after 11 years. Am J Respir Crit Care Med. 2002;166:675–9, <http://dx.doi.org/10.1164/rccm.2112096>.
- Anthonisen NR, Skeans MA, Wise RA, Manfreda J, Kanner RE, Connett JE. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. Ann Intern Med. 2005;142:233–9, <http://dx.doi.org/10.7326/0003-4819-142-4-200502150-00005>.
- Mooren K, van der Linden G, Pool K, Engels Y. The attitudes of pulmonologists regarding smoking behavior of their patients with advanced COPD: a qualitative research. Int J Chron Obstruct Pulmon Dis. 2019;14:2673–9, <http://dx.doi.org/10.2147/copd.s216274>.
- Breathe. The Lung Association. Lung disease stigma report 2018; 2018. Available from: <https://www.lung.ca/sites/default/files/StigmaReportSeptemberFINAL.pdf>.
- Compton WM, Thomas YF, Stinson FS, Grant BF. Prevalence, correlates disability, and comorbidity of DSM-IV drug abuse and dependence in the United States. Arch Gen Psychiatr. 2007;64:566, <http://dx.doi.org/10.1001/archpsyc.64.5.566>.
- Klinke ME, Jónsdóttir H. Smoking addiction in chronic obstructive pulmonary disease: Integrating neurobiology and phenomenology through a review of the literature. Chron Respir Dis. 2014;11:229–36, <http://dx.doi.org/10.1177/1479972314546764>.
- Lewthwaite H, Jensen D, Ekstrom M. How to assess breathlessness in chronic obstructive pulmonary disease. Int J Chronic Obstruct Pulmon Dis. 2021;16:1581–98, <http://dx.doi.org/10.2147/copd.s277523>.
- Halding AG, Heggdal K, Wahl A. Experiences of self-blame and stigmatisation for self-infliction among individuals living with COPD. Scand J Caring Sci. 2011;25:100–7, <http://dx.doi.org/10.1111/j.1471-6712.2010.00796.x>.
- Tálaro C, de Oca MM, Halbert R, Perez-Padilla R, Jardim JRB, Muñoz A, et al. Diagnostic labeling of COPD in five Latin American cities. Chest. 2007;131:60–7, <http://dx.doi.org/10.1378/chest.06-1149>.
- Sanchez-Salcedo P, Divo M, Casanova C, Pinto-Plata V, de-Torres JP, Cote C, et al. Disease progression in young patients with COPD: rethinking the Fletcher and Peto model. Eur Respir J. 2014;44:324–31, <http://dx.doi.org/10.1183/09031936.00208613>.
- Agusti A, Faner R. Chronic obstructive pulmonary disease pathogenesis. Clin Chest Med. 2020;41:307–14, <http://dx.doi.org/10.1016/j.ccm.2020.05.001>.
- Price D, Freeman D, Cleland J, Kaplan A, Cerasoli F. Earlier diagnosis and earlier treatment of COPD in primary care. Prim Care Respir J. 2011;20:15–22, <http://dx.doi.org/10.4104/pcrj.2010.00060>.
- Calle Rubio M, López-Campos JL, Soler-Cataluña JJ, Alcázar Navarrete B, Soriano JB, Rodríguez González-Moro JM, et al. Variability in adherence to clinical practice guidelines and recommendations in COPD outpatients: a multi-level, cross-sectional analysis of the EPOCONSUL study. Respir Res. 2017;18, <http://dx.doi.org/10.1186/s12931-017-0685-8>.
- Celli BR, Agustí A. COPD: time to improve its taxonomy? ERJ Open Res. 2018;4:00132–2017, <http://dx.doi.org/10.1183/23120541.00132-2017>.
- Han MK, Agustí A, Celli BR, Criner G, Halpin DMG, Roche N, et al. From GOLD 0 to Pre-COPD. Am J Respir Crit Care Med. 2021;203:414–23, <http://dx.doi.org/10.1164/rccm.202008-3328pp>.
- Lange P, Celli B, Agustí A, Boje Jensen G, Divo M, Faner R, et al. Lung-function trajectories leading to chronic obstructive pulmonary disease. N Engl J Med. 2015;373:111–22, <http://dx.doi.org/10.1056/nejmoa1411532>.
- Gisbert JP, Alonso-Coello P, Piqué JM. ¿Cómo localizar, elaborar, evaluar y utilizar guías de práctica clínica? Gastroenterol Hepatol. 2008;31:239–57, <http://dx.doi.org/10.1157/13117903>.
- Izquierdo JL, Miravittles M, Esquinas C, Pérez M, Calle M, López Campos JL, et al. Characteristics of COPD patients managed in Respiratory Medicine Departments in Spain, according to GOLD groups and GesEPOC clinical phenotypes. Arch Bronconeumol (Engl Ed). 2018;54:559–67, <http://dx.doi.org/10.1016/j.arbr.2018.09.006>.

46. Miravittles M, Vogelmeier C, Roche N, Halpin D, Cardoso J, Chuchalin AG, et al. A review of national guidelines for management of COPD in Europe. *Eur Respir J*. 2016;47:625–37, <http://dx.doi.org/10.1183/13993003.01170-2015>.
47. Miravittles M, Calle M, Molina J, Almagro P, Gómez J-T, Trigueros JA, et al. Actualización 2021 de la Guía Española de la EPOC (GesEPOC) Tratamiento farmacológico de la EPOC estable. *Arch Bronconeumol*. 2012;48, <http://dx.doi.org/10.1016/j.arbres.2021.03.005>.
48. de Queiroz MC, Moreira MA, Jardim JR, Barbosa MA, Minamisava R, Gondim Hdel C, et al. Knowledge about COPD among users of primary health care services. *Int J Chron Obstruct Pulmon Dis*. 2015;10:1–6, <http://dx.doi.org/10.2147/copd.s71152>.
49. Nakken N, Janssen DJA, van den Bogaart EHA, Muris JWM, Vercoulen JH, Custers FL, et al. Knowledge gaps in patients with COPD and their proxies. *BMC Pulmon Med*. 2017;17, <http://dx.doi.org/10.1186/s12890-017-0481-8>.
50. Calle Rubio M, Rodríguez Hermosa JL, Miravittles M, López-Campos JL. Conocimiento de la enfermedad pulmonar obstructiva crónica, presencia de síntomas respiratorios crónicos y uso de la espirometría en la población española: estudio CONOCEPOC 2019. *Arch Bronconeumol*. 2020, <http://dx.doi.org/10.1016/j.arbres.2020.07.036>.
51. Folch A, Orts-Cortés MI, Hernández-Carcereny C, Seijas-Babot N, Macia-Soler L. Programas educativos en pacientes con Enfermedad Pulmonar Obstructiva Crónica. Revisión integradora. *Enferm Glob*. 2017;16:537–55, <http://dx.doi.org/10.6018/eglobal.16.1.249621>.
52. Regional Office for E, Slama-Chaudhry A, Golay A, World Health Organization. Patient education and self-management support for chronic disease: methodology for implementing patient-tailored therapeutic programmes. *Public Health Panorama*. 2019;5:357–61.
53. Dransfield M, Stolz D, Kleinert S. Towards eradication of chronic obstructive pulmonary disease: a Lancet Commission. *Lancet*. 2019;393:1786–8, [http://dx.doi.org/10.1016/s0140-6736\(19\)30950-x](http://dx.doi.org/10.1016/s0140-6736(19)30950-x).