

Clinical questionnaires for chronic obstructive pulmonary disease diagnosis: A systematic review and meta-analysis

Cuestionarios clínicos para el diagnóstico de la enfermedad pulmonar obstructiva crónica. Revisión sistemática y metaanálisis

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Abstract

Introduction: The use of early screening questionnaires for chronic obstructive pulmonary disease (COPD) in primary health care could improve underdiagnosis. Several instruments are currently available, but there is scant information on their diagnostic performance.

Objective: To determine the validity of different questionnaires for COPD diagnosis.

Materials and methods: A systematic review and a meta-analysis of diagnostic test accuracy were carried out. A search of the literature published between July 1, 1997, and June 30, 2019 was performed in PubMed, EMBASE, and LILACS databases using MeSH and DeCS terms and the PICO strategy. Based on the inclusion and exclusion criteria, two reviewers selected the articles for complete analysis. Article quality was assessed using the QUADAS instrument.

Results: 19 articles were included for analysis. Overall results were: sensitivity: 68.1% (95%CI: 66.7%-69.4%); specificity: 64.9% (95%CI: 64.3-65.5); positive likelihood ratio: 2.024 (95%CI: 1.715-2.388); negative likelihood ratio: 0.407 (95%CI: 0.289-0.573); and receiver operating characteristic area under the curve (ROC AUC): 0.75. The COPD-PS questionnaire reported the highest performance with sensitivity of 0.673 (95%CI: 0.653-0.692), specificity of 0.663 (95%CI: 0.655-0.651), and ROC AUC of 0.750. It was followed by LFQ with sensitivity of 0.840 (95%CI: 0.806-0.871), specificity of 0.312 (95%CI: 0.289-0.336), and ROC AUC of 0.730. Finally, CDQ had sensitivity of 0.798 (95%CI: 0.764-0.829), specificity of 0.517 (95%CI: 0.495-0.538), and ROC AUC of 0.727.

Conclusion: Clinical prediction instruments for COPD diagnosis have an acceptable performance. The COPD-PS, LFQ and CDQ questionnaires show a similar performance.

Keywords: Chronic Obstructive Pulmonary Disease; Surveys and Questionnaires; Reproducibility of Results (MeSH).

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Resumen

Introducción. El uso de cuestionarios de predicción clínica para el diagnóstico de la enfermedad pulmonar obstructiva crónica (EPOC) en atención primaria en salud podría mejorar el subdiagnóstico de esta enfermedad. Hoy en día existen varios instrumentos de este tipo; sin embargo, hay poca información sobre su rendimiento diagnóstico.

Objetivo. Determinar la validez del uso de los diferentes cuestionarios de predicción clínica para el diagnóstico de la EPOC.

Materiales y métodos. Se realizó una revisión sistemática con metaanálisis de prueba diagnóstica en las bases de datos PubMed, EMBASE y LILACS a partir de la estrategia PICO y utilizando términos MeSH y DeCS. Se incluyeron los estudios publicados entre julio 1 de 1997 y junio 30 de 2019. Dos revisores seleccionaron los artículos para análisis completo con base en los criterios de inclusión y exclusión. La calidad de los artículos se evaluó con el instrumento QUADAS.

Resultados. Se incluyeron 19 artículos para el análisis. En cuanto a la evaluación global de los cuestionarios se obtuvieron los siguientes datos: sensibilidad: 68.1% (IC95%: 66.7-69.4); especificidad: 64.9% (IC95%: 64.3-65.5); razón de verosimilitud positiva: 2.024 (IC95%: 1.715-2.388); razón de verosimilitud negativa: 0.407 (IC95%: 0.289-0.573) y el área bajo la curva de características del receptor (ACOR): 0.75. El cuestionario COPD-PS reportó el mayor rendimiento —sensibilidad: 0.673 (IC95%: 0.653-0.692), especificidad: 0.663 (IC95%: 0.655-0.671) y ACOR: 0.750—; seguido de LFQ —sensibilidad: 0.840 (IC95%: 0.806-0.871), especificidad: 0.312 (IC95%: 0.289-0.336) y ACOR: 0,730—, y CDQ —sensibilidad: 0.798 (IC95%: 0.764-0.829), especificidad: 0.517 (IC95%: 0.495-0.538) y ACOR: 0.727—.

Conclusión. Los instrumentos de predicción clínica para el diagnóstico de EPOC tienen un rendimiento aceptable, pues los valores de sensibilidad obtenidos a través de estos son superiores a los de la evaluación individual de la sintomatología respiratoria que se puede hacer a través de la historia clínica habitual.

Palabras clave: Enfermedad pulmonar obstructiva crónica; Encuestas y cuestionarios; Reproducibilidad de los resultados (DeCS).

Bastidas-Goyes AR, Cardozo-Niño AO, Quintero-Muñoz E, López-Gómez KA, Suárez-Escobar LP, Hernández-Santos LE. [Cuestionarios clínicos para el diagnóstico de la enfermedad pulmonar obstructiva crónica. Revisión sistemática y metaanálisis]. Rev. Fac. Med. 2021;69(1):e88706. English. doi: <https://dx.doi.org/10.15446/revfacmed.v69n1.88706>.

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most common chronic noncommunicable diseases of the lower airway,^{1,2} with an estimated prevalence of 15.7% in men and 9.93% in women worldwide. The Americas is the region with the highest reported figures, as 14.53% of the general population suffer from this disease,³ and they are associated mainly with exposure to risk factors particularly found in developing countries.⁴ Moreover, COPD is the third leading cause of early death at the global level, making it an important cause of morbidity and mortality.^{3,5}

Over the years, it has become evident that there are many limitations to diagnose COPD, with an underdiagnosis rate of up to 70% in the Americas.⁶⁻⁸ This situation considerably increases the burden of the disease for health systems and generates a higher average annual cost per patient, mainly due to complications⁹⁻¹¹ that bring along events such as decreased pulmonary function, deterioration of the health condition, increased number of hospitalizations,^{12,13} and a significant increase in mortality.¹⁴

Considering the possible underdiagnosis rates of COPD, multiple questionnaires have been used to screen or detect it in primary care services to improve diagnosis.^{15,16} Currently, the most commonly used questionnaires are COPD-PS (COPD Population Screener),^{12,17} CDQ (COPD Diagnostic Questionnaire),^{18,19} LFQ (Lung Function Questionnaire),²⁰⁻²² EGARPOC (COPD screening questionnaire from Terrassa),²³ IPAG (International Primary Care Airways Guidelines questionnaire),²⁴⁻²⁶ CAPTURE (COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk),^{6,27,28} and CAT (COPD Assessment Test).²⁹

These instruments' validity is variable because there is no uniformity in the questions or the target population, although most of them explore risk factors and clinical symptoms.^{30,31} Therefore, there is no consensus on which questionnaire is more suitable to diagnose this disease.²⁵

Haroon *et al.*³² performed a systematic review in which the CDQ questionnaire was evaluated and five studies were included for the final meta-analysis. Sensitivity of 64.5% (95%CI: 59.9-68.8) and specificity of 65.2% (95%CI: 52.9-75.8), with a cut-off point of 19.5, were observed, as well as a change in sensitivity of 87.5% (95%CI: 83.1-90.9) and specificity of 38.8% (95%CI: 27.7-51.3), with a cut-off point of 16.5. These results showed that this instrument could be useful as a screening test and, eventually, optimize the use of spirometry by improving the diagnosis of COPD.

The present research work summarizes the available data on the use of questionnaires for the diagnosis and screening of COPD. To this end, instruments were analyzed globally and individually, always taking into account the variability of the parameters evaluated by each one of them. Thus, the objective of the review was to determine the validity of the use of different questionnaires for COPD diagnosis.

Materials and methods

Protocol and record keeping

The protocol followed the PRISMA-DTA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Protocols extension for Diagnostic Test Accuracy) guideline, which establishes screening and data extraction and analysis strategies. In addition, the study protocol was submitted to the Research Committee of the Universidad de la Sabana, in Colombia, which authorized it through institutional registration number MED-263-2019.

PROSPERO Registration

https://www.crd.york.ac.uk/PROSPEROFILES/138410_STRATEGY_20190609.pdf

Eligibility criteria

The included studies were conducted in subjects who met the following criteria: being older than 30 years and being exposed to biomass and/or cigarettes, regardless of the number of packages per year; respondents in person to a survey/interview indicating the probability of having COPD, who were inpatients or outpatients regardless of the level of care provided; and patients with a confirmed diagnosis of COPD based on spirometric parameters such as FEV₁ (forced expiratory volume in the first second) / FVC (forced vital capacity) <0.7 after using beta-2 receptor agonists (B₂), FEV₁/FVC₆ (forced expiratory volume in 6 seconds) <0.7 after using B₂, or FEV₁/FVC <0.7 below the normal lower limit.

On the other hand, studies conducted in patients previously diagnosed with COPD who had exacerbations, that evaluated quality of life, and that included the diagnosis of other conditions such as lung cancer, or interstitial lung diseases such as sarcoidosis, were excluded. Likewise, studies in which spirometry was not performed after administering the questionnaires or that did not allow obtaining data directly or indirectly for the construction of 2x2 tables with their corresponding positive and negative test results frequencies were excluded.

Sources of information and search methodology

An exhaustive literature search was performed in PubMed, EMBASE and LILACS using the PICO (Patient, Intervention, Control, Outcomes) strategy and MeSH and DeCS terms. Studies published between July 1, 1997, and April 30, 2020, were included. The search strategy is described in Annex 1.

To select the studies, a group of researchers, composed of a team of experts in pulmonology and internal medicine, was created to review the titles and abstracts of the publications identified in the search. In addition, articles recommended by experts and others identified in the references of the selected articles were included.

Selection of studies

Based on the titles and abstracts identified, two reviewers independently screened potential eligible articles. In case of disagreements between the two reviewers regarding the decision to include or not an article, a third senior researcher made the decision.

Data collection

Two researchers independently extracted the relevant data from the studies and consolidated them into a

single digital database. When necessary, the authors of the articles were contacted to clarify information. Data were recorded in contingency tables to establish the variables required to analyze the validity properties of the scales.

Definitions for data extraction

The following information was extracted from the selected studies: principal author, year of publication, number of participants, methods employed, diagnostic tests used, and variables analyzed (exposure to tobacco or biomass, COPD diagnosis, questionnaire administration).

Furthermore, the following information was obtained for the COPD screening scales included in the studies: method of administration, language, cut-off point, sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratio, and receiver operating characteristic and area under the curve (ROC AUC).

Risk of bias and applicability

The methodological quality and risk of bias of the selected studies were assessed using the QUADAS (Quality Assessment of Diagnostic Accuracy Studies) instrument, where each of the items was classified as *yes*, *no*, or *x* when the response was unclear. Risk of bias was judged as *low*, *high*, or *uncertain*. If the answers to the guiding questions were *yes*, the probability of bias was *low*. In turn, if any of the answers to the guiding questions were *no*, the probability was *high*. Finally, if data were insufficient to make a judgment, the probability was *uncertain*.

Summary of results

To analyze the results, 2x2 tables were created including the corresponding true positives, true negatives, false positives, and false negatives. Likewise, for the meta-analysis, an analysis plan was designed using a hierarchical model with the representation of the summarized ROC curve. Thus, consolidated estimates of sensitivity, specificity, and diagnostic odds ratios (DOR) with 95% confidence intervals (95%CI) were presented.

Meta-analysis

For the meta-analysis of the data, forest plots of sensitivity and specificity were constructed using the statistical software Meta-DiSc version 1.4. These plots were generated to determine the between-study variance and the diagnostic accuracy of each test.

Results

Study selection

The initial search of the databases yielded 7 193 potentially relevant articles, of which 1 323 were eliminated because they were duplicates, 5 775 because they did not meet the study objective, and 80 because they did not meet the inclusion criteria, for a total sample of 15 articles selected for full-text review. Another 7 articles, which were not considered in the initial search, were included following the recommendations of experts. Of the 22 articles selected for a comprehensive review, 3 were excluded since no spirometry had been performed after administering the questionnaires. Consequently, 19 studies were finally included in the review (Figure 1).

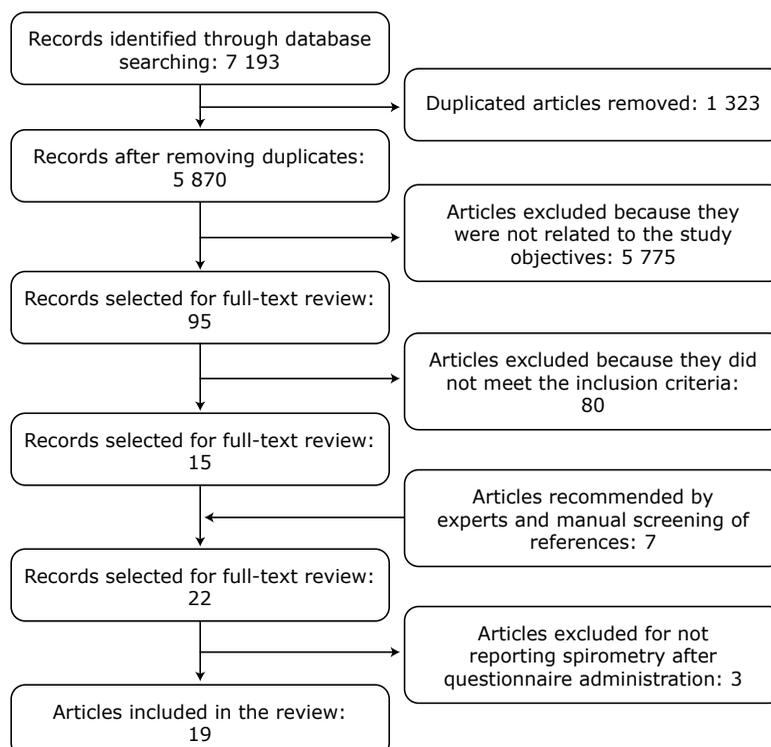


Figure 1. Flow chart for the selection of studies. Source: Own elaboration.

Study characteristics

Table 1 shows the general characteristics of the selected articles.

Table 1. General characteristics of the articles.

Characteristics	Description	Rank or number of studies
Study design	Cross-sectional	19
Participants		105-7 701
Average age (years)		55-68
Percentage of males		74%
Smoking status assessment		17
Respiratory symptom assessment		14
Number of centers	Multicenter	12
Questionnaires	COPD diagnosis	16
	Diagnostic Use and Quality of Life Questionnaire	4
Reference test	Spirometry	17
	No exact description of diagnostic values	2
Sensitivity		14%-95%
Specificity		25%-87.6%
Area under the curve		0.65-0.7

Source: Own elaboration.

Risk of bias

The results of the risk of bias assessment are presented below. As shown in Figures 2 and 3, and in Table 2, the

domains where the highest risk of bias was found were reference standard and patient selection.

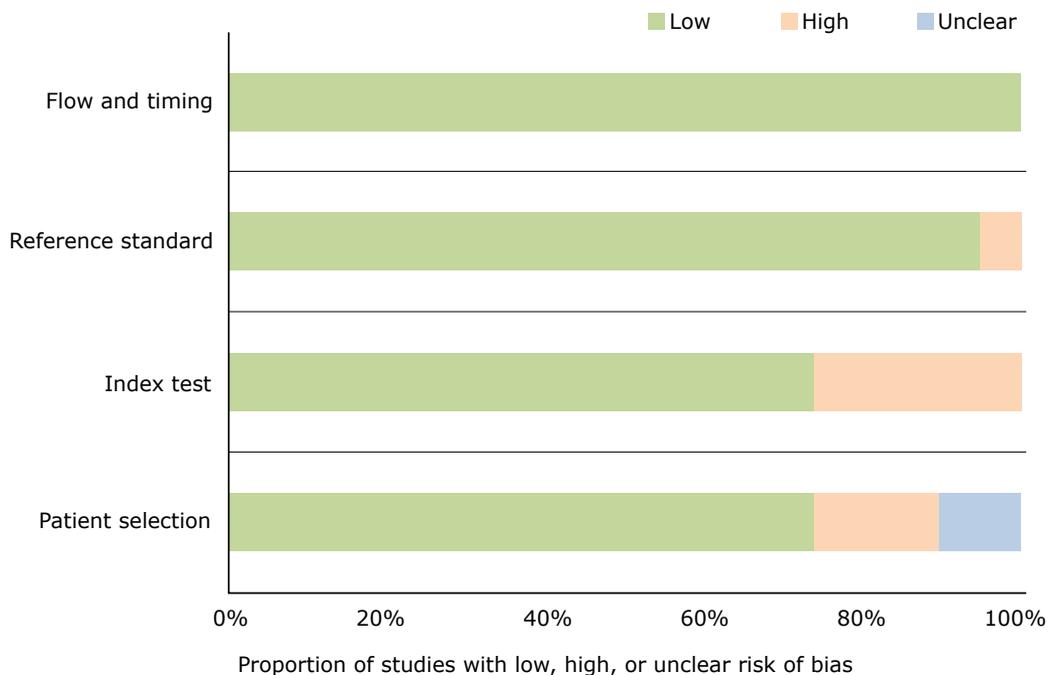


Figure 2. Risk of bias assessment.

Source: Own elaboration.

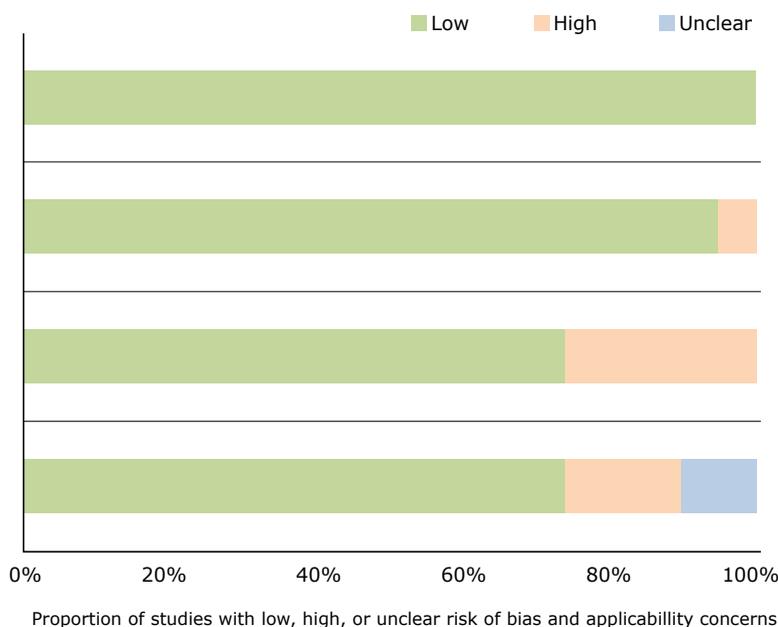


Figure 3. Risk of bias and applicability concerns. Source: Own elaboration.

Table 2. Summary of methodological quality in the studies according to the QUADAS instrument.

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Tsukuya et al. ¹⁷	Low	High	Low	Low	High	Low	Low
Stanley et al. ¹⁸	Low	Low	Low	Low	Low	Low	Low
Yawn et al. ²⁰	High	Low	Low	Low	Unclear	Low	Low
Hanania et al. ²²	High	Low	Low	Low	High	Low	Low
Llordés et al. ²³	Low	Low	Low	Low	Low	Low	Low
Martinez et al. ²⁷	Low	Low	Low	Low	Low	Low	Low
López-Varela et al. ³³	Low	High	Low	Unclear	Low	Low	Low
Mahesh et al. ³⁴	Unclear	High	Low	Low	High	Low	Low
Murgia et al. ³⁵	Low	Low	Low	Low	Low	Low	Low
Calverley et al. ³⁶	Unclear	Low	Low	Low	Low	Low	Low
Kotz et al. ³⁷	Low	Low	Low	Low	Low	Low	Low
Mintz et al. ³⁸	Low	Low	Low	Low	Low	Low	Low
Kim et al. ³⁹	Low	High	High	Low	Unclear	Low	Unclear
Price et al. ⁴⁰	Low	Low	Low	Low	Low	Low	Low
Frith et al. ⁴¹	Low	Low	Low	Low	Low	Low	Low
Yoshimoto et al. ⁴²	High	Low	Low	Low	High	Low	Low
Sichletidis et al. ⁴³	Low	Low	Low	Low	Low	Low	Low
Freeman et al. ⁴⁴	Low	High	Low	Low	Low	Low	Low
Buffels et al. ⁴⁵	Low	Low	Low	Low	Low	Low	Low

■ : Low; ■ : High; ■ : Unclear. Source: Own elaboration.

Results per study

Sensitivity and specificity

The overall sensitivity was 68.1% (95%CI: 66.7-69.4), with a heterogeneity statistic (I²) of 98.8%; the stud-

ies by Martínez et al.²⁷ and Mintz et al.³⁸ reported the highest sensitivity in the questionnaires (97.3% and 97.1% respectively), while Murgia et al.³⁵ reported the lowest sensitivity with 5.7%. On the other hand, the overall specificity was 64.9% (95%CI: 64.3-65.5), with I² of 99.7%; the highest specificity was reported by

Murgia *et al.*³⁵ with 99.7%, and the lowest by Mintz *et al.*³⁸ with 6.5%.

Tables 3, 4, 5 and 6 summarize the sensitivity, specificity and likelihood ratios analyses, and Figures 4, 5, 6, 7 and 8 present the forest plots for those variables.

Table 3. Sensitivity analysis of the questionnaires used to diagnose chronic obstructive pulmonary disease.

Study	Sen	95% Confidence interval	TP/ (TP+FN)	TN/ (TN+FP)
Tsukuya <i>et al.</i> ¹⁷	0.673	0.577-0.759	74/110	1526/2094
Stanley <i>et al.</i> ¹⁸	0.797	0.720-0.861	110/138	30/916
Yawn <i>et al.</i> ²⁰	0.730	0.661-0.792	138/189	115/198
Hanania <i>et al.</i> ²²	0.827	0.758-0.883	129/156	326/681
Llordes <i>et al.</i> ²³	0.729	0.634-0.810	78/107	175/300
Martinez <i>et al.</i> ²⁷	0.973	0.938-0.991	181/186	71/160
Lopez-Valera <i>et al.</i> ³³	0.650	0.594-0.704	201/309	774/1434
Mahesh <i>et al.</i> ³⁴	0.620	0.504-0.727	49/79	719/821
Murgia <i>et al.</i> ³⁵	0.057	0.036-0.086	21/366	3515/3526
Calverley <i>et al.</i> ³⁶	0.849	0.830-0.868	1190/1401	2835/6300
Kotz <i>et al.</i> ³⁷	0.892	0.850-0.926	248/278	92/378
Mintz <i>et al.</i> ³⁸	0.971	0.935-0.991	170/175	44/674
Kim <i>et al.</i> ³⁹	0.500	0.374-0.626	33/66	112/124
Price <i>et al.</i> ⁴⁰	0.587	0.505-0.665	91/155	511/663
Frith <i>et al.</i> ⁴¹	0.912	0.807-0.971	52/57	54/147
Yoshimoto <i>et al.</i> ⁴²	0.372	0.335-0.410	249/669	1893/2393
Sichletidis <i>et al.</i> ⁴³	0.933	0.861-0.975	84/90	208/534
Freeman <i>et al.</i> ⁴⁴	0.871	0.761-0.943	54/62	219/307
Buffels <i>et al.</i> ⁴⁵	0.568	0.501-0.633	130/229	2331/2929
Pooled Sen	0.681	0.667-0.694		

Heterogeneity chi-squared: 1514.97 (d.f.: 18) p=0.000
 Inconsistency (I-square): 98.8%
 No. of studies: 19
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

Sen: sensitivity; TP: true positive; FN: false negative; TN: true negative; FP: false positive.
 Source: Own elaboration.

Table 4. Specificity analysis of the questionnaires used to diagnose chronic obstructive pulmonary disease.

Study	Spe	95% Confidence interval	TP/ (TP+FN)	TN/ (TN+FP)
Tsukuya <i>et al.</i> ¹⁷	0.729	0.709-0.748	74/110	1526/2094
Stanley <i>et al.</i> ¹⁸	0.469	0.437-0.502	110/138	430/916
Yawn <i>et al.</i> ²⁰	0.581	0.509-0.650	138/189	115/198
Hanania <i>et al.</i> ²²	0.479	0.441-0.517	29/156	326/681
Llordes <i>et al.</i> ²³	0.583	0.525-0.640	78/107	175/300
Martinez <i>et al.</i> ²⁷	0.444	0.365-0.524	181/186	71/160
Lopez <i>et al.</i> ³³	0.540	0.514-0.566	201/309	774/1434
Manesh <i>et al.</i> ³⁴	0.876	0.851-0.898	49/79	719/821
Murgia <i>et al.</i> ³⁵	0.997	0.994-0.998	21/366	3515/3526
Calverley <i>et al.</i> ³⁶	0.450	0.438-0.462	1190/1401	2835/6300
Kotz <i>et al.</i> ³⁷	0.243	0.201-0.290	248/278	92/378
Mintz <i>et al.</i> ³⁸	0.065	0.048-0.087	170/175	44/674
Kim <i>et al.</i> ³⁹	0.903	0.837-0.949	33/66	112/124
Price <i>et al.</i> ⁴⁰	0.771	0.737-0.802	91/155	511/663
Frith <i>et al.</i> ⁴¹	0.367	0.289-0.451	52/57	54/147
Yoshimoto <i>et al.</i> ⁴²	0.791	0.774-0.807	249/669	893/2393
Sichletidis <i>et al.</i> ⁴³	0.390	0.348-0.432	84/90	208/534
Freeman <i>et al.</i> ⁴⁴	0.713	0.659-0.763	54/62	219/307
Buffels <i>et al.</i> ⁴⁵	0.796	0.781-0.810	130/229	2331/2929
Pooled Spe	0.649	0.643-0.655		

Heterogeneity chi-squared: 6660.80 (d.f.: 18) p=0.000
 Inconsistency (I-square); 99.7%
 No. of studies: 19
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

Spe: Specificity; TP: true positive; FN: false negative; TN: true negative; FP: false positive.
 Source: Own elaboration.

Table 5. Positive likelihood ratio analysis of questionnaires used to diagnose chronic obstructive pulmonary disease.

Study	LR+	95% Confidence interval	% Weight
Tsukuya <i>et al.</i> ¹⁷	2.480	2.139-2.876	5.50
Stanley <i>et al.</i> ¹⁸	1.502	1.354-1.667	5.63
Yawn <i>et al.</i> ²⁰	1.742	1.447-2.097	5.37
Hanania <i>et al.</i> ²²	1.586	1.433-1.756	5.63
Llordes <i>et al.</i> ²³	1.750	1.466-2.088	5.40
Martinez <i>et al.</i> ²⁷	1.749	1.520-2.013	5.53
Lopez <i>et al.</i> ³³	1.413	1.280-1.561	5.64
Manesh <i>et al.</i> ³⁴	4.992	3.886-6.414	5.09
Murgia <i>et al.</i> ³⁵	18.392	8.939-37.842	2.75
Calverley <i>et al.</i> ³⁶	1.544	1.497-1.594	5.74
Kotz <i>et al.</i> ³⁷	1.179	1.099-1.265	5.70
Mintz <i>et al.</i> ³⁸	1.039	1.006-1.073	5.74
Kim <i>et al.</i> ³⁹	5.167	2.866-9.315	3.33
Price <i>et al.</i> ⁴⁰	2.561	2.113-3.10	5.34
Frith <i>et al.</i> ⁴¹	1.442	1.245-1.671	5.51
Yoshimoto <i>et al.</i> ⁴²	1.781	1.571-2.020	5.57
Sichletidis <i>et al.</i> ⁴³	1.529	1.401-1.668	5.67
Freeman <i>et al.</i> ⁴⁴	3.038	2.486-3.714	5.31
Buffels <i>et al.</i> ⁴⁵	2.781	2.432-3.178	5.55
(REM) pooled LR+	2.024	1.715-2.388	

Heterogeneity chi-squared: 1119.15 (d.f.: 18) p=0.000
 Inconsistency (I-square): 98.4%
 Estimate of between-study variance (Tau-squared): 0.1242
 No. of studies: 19
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

LR+: positive likelihood ratio; REM: random effects model. Source: Own elaboration.

Table 6. Negative likelihood ratio analysis of questionnaires used to diagnose chronic obstructive pulmonary disease.

Study	LR-	95% Confidence interval	% Weight
Tsukuya <i>et al.</i> ¹⁷	0.449	0.343-0.588	5.57
Stanley <i>et al.</i> ¹⁸	0.432	0.308-0.606	5.46
Yawn <i>et al.</i> ²⁰	0.465	0.357-0.604	5.58
Hanania <i>et al.</i> ²²	0.362	0.254-0.514	5.43
Llordes <i>et al.</i> ²³	0.465	0.336-0.643	5.48
Martinez <i>et al.</i> ²⁷	0.061	0.025-0.146	4.17
Lopez-Valera <i>et al.</i> ³³	0.648	0.552-0.759	5.69
Manesh <i>et al.</i> ³⁴	0.434	0.327-0.575	5.55
Murgia <i>et al.</i> ³⁵	0.946	0.922-0.970	5.76
Calverley <i>et al.</i> ³⁶	0.335	0.295-0.380	5.72
Kotz <i>et al.</i> ³⁷	0.443	0.303-0.650	5.38
Mintz <i>et al.</i> ³⁸	0.438	0.176-1.087	4.09
Kim <i>et al.</i> ³⁹	0.554	0.432-0.709	5.59
Price <i>et al.</i> ⁴⁰	0.536	0.442-0.649	5.66
Frith <i>et al.</i> ⁴¹	0.239	0.101-0.566	4.21
Yoshimoto <i>et al.</i> ⁴²	0.794	0.746-0.844	5.75
Sichletidis <i>et al.</i> ⁴³	0.171	0.078-0.373	4.43
Freeman <i>et al.</i> ⁴⁴	0.181	0.094-0.347	4.77
Buffels <i>et al.</i> ⁴⁵	0.543	0.468-0.631	5.70
(REM) pooled LR-	0.407	0.289-0.573	

Heterogeneity chi-squared: 1826.01 (d.f.: 18) p=0.000
 Inconsistency (I-square): 99.0%
 Estimate of between-study variance (Tau-squared): 0.5279
 No. of studies: 19
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

LR-: negative likelihood ratio; REM: random effects model. Source: Own elaboration.

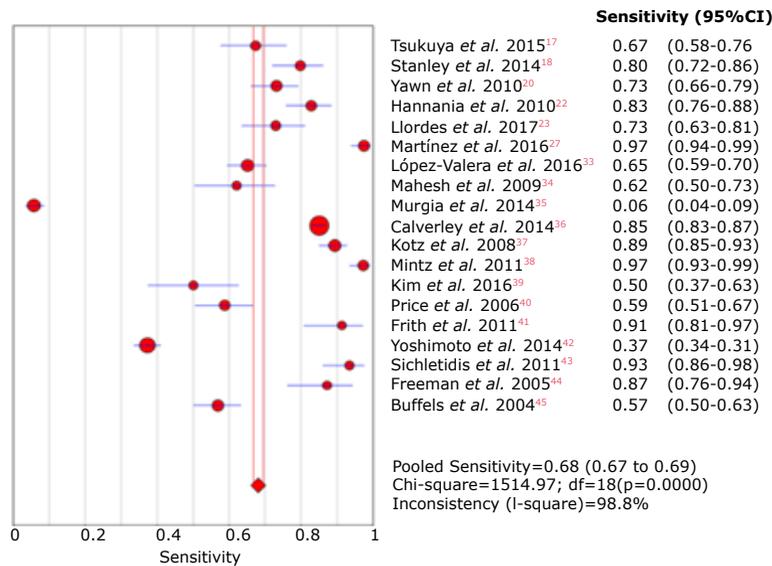


Figure 4. Forest plot for sensitivity of questionnaires used to diagnose chronic obstructive pulmonary disease. Source: Own elaboration.

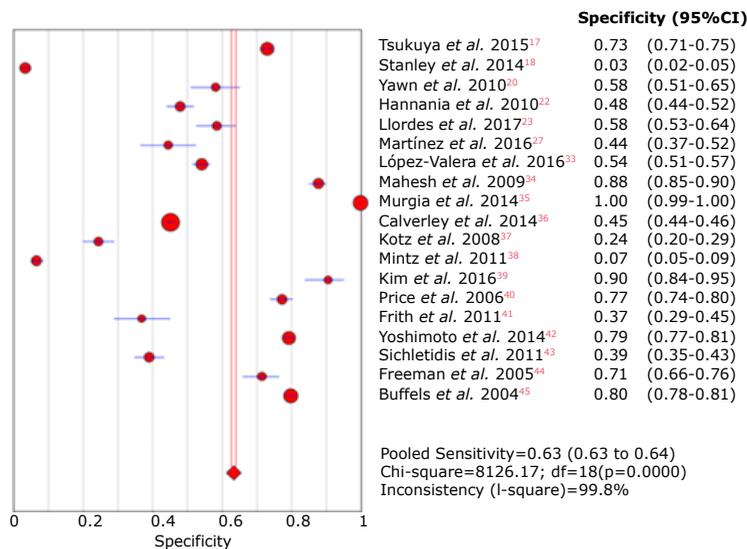


Figure 5. Forest plot for specificity of questionnaires used to diagnose chronic obstructive pulmonary disease. Source: Own elaboration.

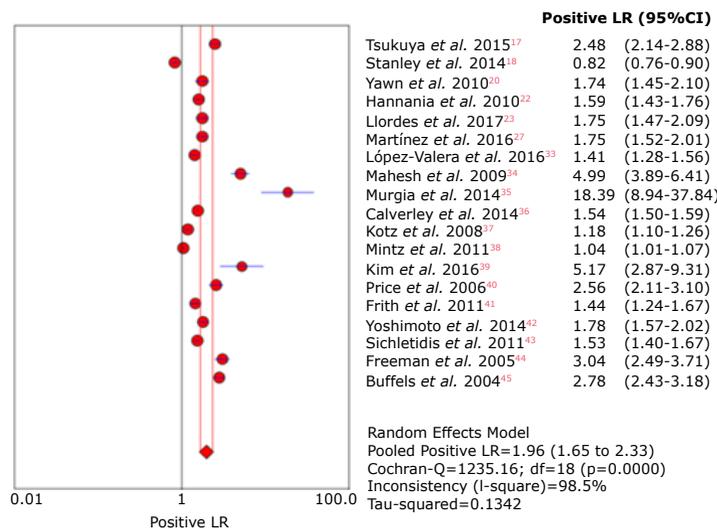


Figure 6. Forest plot for positive likelihood ratio of questionnaires used to diagnose chronic obstructive pulmonary disease. Source: Own elaboration.

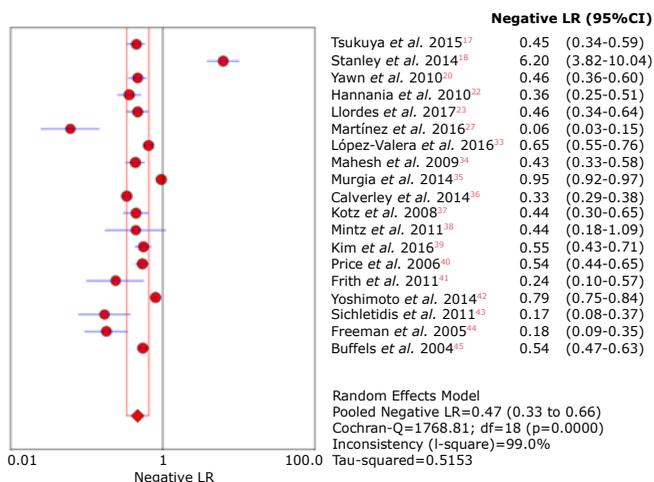


Figure 7. Forest plot for negative likelihood ratio of questionnaires used to diagnose chronic obstructive pulmonary disease.
 Source: Own elaboration.

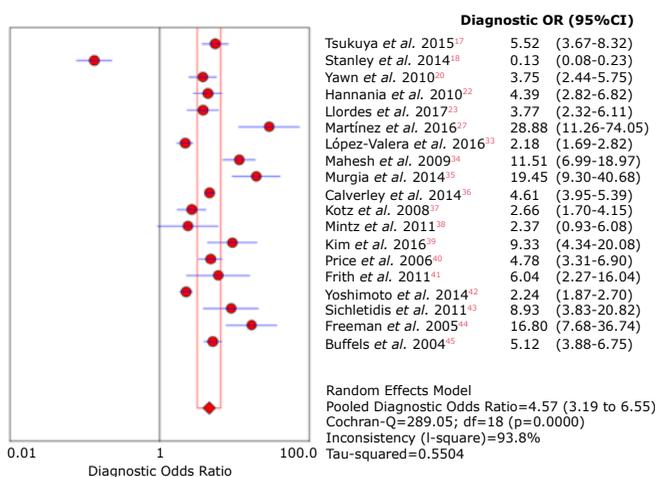


Figure 8. Forest plot for diagnostic likelihood ratio of questionnaires used to diagnose chronic obstructive pulmonary disease.
 Source: Own elaboration.

Figure 9 presents the graphic summary of the operating characteristics of the questionnaires used to diagnose COPD, while Figure 10 summarizes the analysis

of the receiver operating characteristic curves for the aggregate of the studies; the discriminative ability of the questionnaires was 0.75.

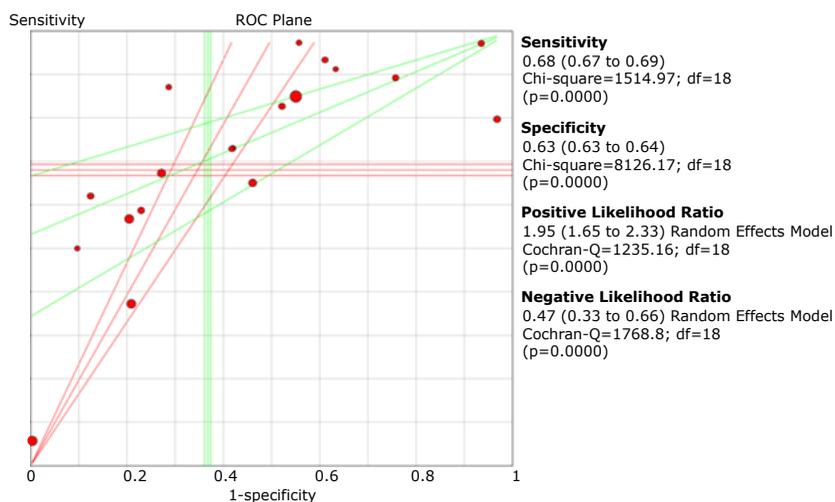


Figure 9. Summary of sensitivity, specificity and positive and negative likelihood ratios of the questionnaires assessed.
 Source: Own elaboration.

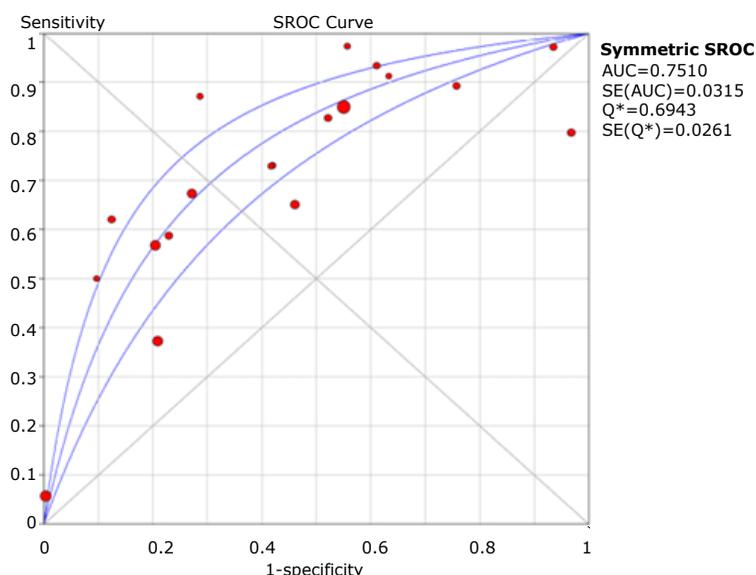


Figure 10. Summary of receiver operating characteristic and area under the curve of the questionnaires used to diagnose chronic obstructive pulmonary disease. Source: Own elaboration.

Summary of results

COPD-PS questionnaire

For a total population of 16 630 subjects, 6 studies assessed the COPD-PS questionnaire. Kim *et al.*³⁹ assessed the FEV₁/FEV₆ ratio as a diagnostic criterion, and Varela *et al.*³³ and Murgia, *et al.*³⁵ analyzed outpatients.

Sensitivity, specificity, positive and negative likelihood ratio, DOR and ROC AUC results for the COPD-PS questionnaire are shown in Tables 7, 8, 9, 10 and 11, and in Figures 11, 12, 13, 14, 15, 16 and 17.

Table 7. Sensitivity analysis of the COPD-PS questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	Sen	95% Confidence interval	TP/ (TP+FN)	TN/ (TN+FP)
Tsukuya <i>et al.</i> ¹⁷	0.673	0.577-0.759	74/110	1526/2094
Lopez-Valera <i>et al.</i> ³³	0.650	0.594-0.704	201/309	774/1434
Manesh <i>et al.</i> ³⁴	0.620	0.504-0.727	49/79	719/821
Murgia <i>et al.</i> ³⁵	0.057	0.036-0.086	21/366	3515/3526
Calverley <i>et al.</i> ³⁶	0.849	0.830-0.868	1190/1401	2835/6300
Kim <i>et al.</i> ³⁹	0.500	0.374-0.626	33/66	112/124
Pooled Sen	0.673	0.653-0.692		
Heterogeneity chi-squared: 864.03 (d.f.: 5) p=0.000 Inconsistency (I-square): 99.4% No. of studies: 6 Filter: OFF Adding 1/2 to all cells of the studies with zero events				

Sen: sensitivity; TP: true positive; FN: false negative; TN: true negative; FP: false positive. Source: Own elaboration.

Table 8. Specificity analysis of the COPD-PS questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	Spe	95% Confidence interval	TP/ (TP+FN)	TN/ (TN+FP)
Tsukuya <i>et al.</i> ¹⁷	0.729	0.709-0.748	74/110	1526/2094
Lopez-Valera <i>et al.</i> ³³	0.540	0.514-0.566	201/309	774/1434
Manesh <i>et al.</i> ³⁴	0.876	0.851-0.898	49/79	719/821
Murgia <i>et al.</i> ³⁵	0.997	0.994-0.998	21/366	3515/3526
Calverley <i>et al.</i> ³⁶	0.450	0.438-0.462	1190/1401	2835/6300
Kim <i>et al.</i> ³⁹	0.903	0.837-0.949	33/66	112/124
Pooled Spe	0.663	0.655-0.671		
Heterogeneity chi-squared: 4332.54 (d.f.: 5) p=0.000 Inconsistency (I-square): 99.9% No. of studies: 6 Filter: OFF Adding 1/2 to all cells of the studies with zero events				

Spe: Specificity; TP: true positive; FN: false negative; TN: true negative; FP: false positive. Source: Own elaboration.

Table 9. Positive likelihood ratio analysis of the COPD-SP questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	LR+	95% Confidence interval	% Weight
Tsukuya <i>et al.</i> ¹⁷	2.480	2.139-2.876	19.21
Lopez-Valera <i>et al.</i> ³³	1.413	1.280-1.561	19.59
Manesh <i>et al.</i> ³⁴	4.992	3.886-6.414	18.03
Murgia <i>et al.</i> ³⁵	18.392	8.939-37.842	10.67
Calverley <i>et al.</i> ³⁶	1.544	1.497-1.594	19.88
Kim <i>et al.</i> ³⁹	5.167	2.866-9.315	12.61
(REM) pooled LR+	3.115	2.205-4.402	

Heterogeneity chi-squared: 186.09 (d.f.: 5) p=0.000
 Inconsistency (I-square): 97.3%
 Estimate of between-study variance (Tau-squared): 0.1562
 No. of studies: 6
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

LR+: positive likelihood ratio; REM: random effects model. Source: Own elaboration.

Table 10. Negative likelihood ratio analysis of the COPD-SP questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	LR-	95% Confidence interval	% Weight
Tsukuya <i>et al.</i> ¹⁷	0.449	0.343-0.588	16.59
Lopez-Valera <i>et al.</i> ³³	0.648	0.552-0.759	16.71
Manesh <i>et al.</i> ³⁴	0.434	0.327-0.575	16.57
Murgia <i>et al.</i> ³⁵	0.946	0.922-0.970	16.78
Calverley <i>et al.</i> ³⁶	0.335	0.295-0.380	16.74
Kim <i>et al.</i> ³⁹	0.554	0.432-0.709	16.62
(REM) pooled LR-	0.530	0.193-1.455	

Heterogeneity chi-squared: 1653.13 (d.f.: 5) p=0.000
 Inconsistency (I-square): 99.7%
 Estimate of between-study variance (Tau-squared): 1.5802
 No. of studies: 6
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

LR-: negative likelihood ratio; REM: random effects model. Source: Own elaboration.

Table 11. Diagnostic odds ratio analysis of the COPD-SP questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	DOR	95% Confidence interval	% Weight
Tsukuya <i>et al.</i> ¹⁷	5.522	3.666-8.319	17.49
Lopez-Valera <i>et al.</i> ³³	2.183	1.690-2.819	18.70
Manesh <i>et al.</i> ³⁴	11.513	6.987-18.972	16.63
Murgia <i>et al.</i> ³⁵	19.451	9.300-40.678	14.13
Calverley <i>et al.</i> ³⁶	4.614	3.953-5.386	19.23
Kim <i>et al.</i> ³⁹	9.333	4.337-20.084	13.83
(REM) pooled DOR	6.510	3.846-11.019	

Heterogeneity chi-squared: 64.06 (d.f.: 5) p: 0.000
 Inconsistency (I-square): 92.2%
 Estimate of between-study variance (Tau-squared): 0.3686
 No. Studies: 6.
 Filter OFF
 Adding 1/2 to all cells of the studies with zero events

DOR: diagnostic odds ratio; REM: random effects model. Source: Own elaboration.

Table 12. Sensitivity analysis of the LFQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.

Study	Sen	95% Confidence interval	TP/ (TP+FN)	TN/ (TN+FP)
Yawn <i>et al.</i> ²⁰	0.730	0.661-0.792	138/189	115/198
Hanania <i>et al.</i> ²²	0.827	0.758-0.883	129/156	326/681
Mintz <i>et al.</i> ³⁸	0.971	0.935-0.991	170/175	44/674
Pooled Sen	0.840	0.806-0.871		

Heterogeneity chi-squared: 47.02 (d.f.: 2) p=0.000
 Inconsistency (I-square): 95.7%
 No. of studies: 3
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

Sen: sensitivity; TP: true positive; FN: false negative; TN: true negative; FP: false positive. Source: Own elaboration.

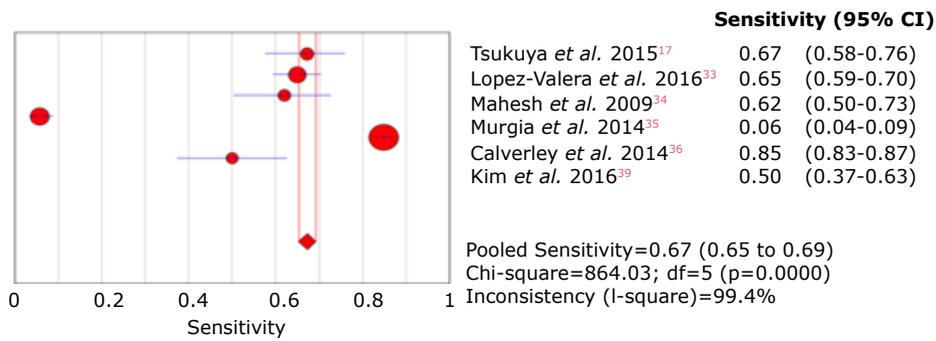


Figure 11. Forest plot for sensitivity of the COPD-SP questionnaire used to diagnose chronic obstructive pulmonary disease.
Source: Own elaboration.

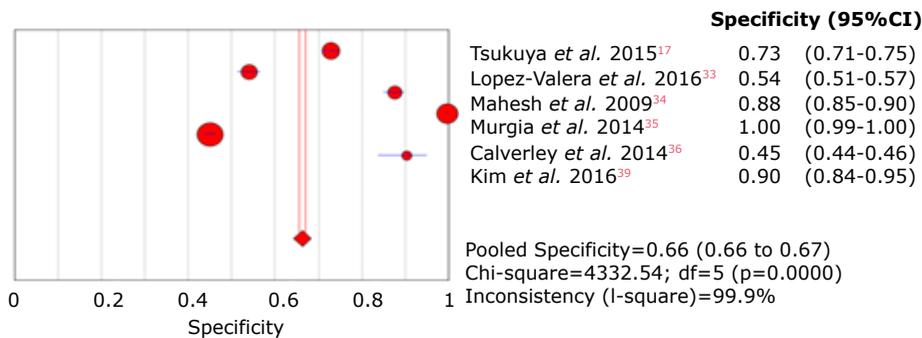


Figure 12. Forest plot for specificity of the COPD-SP questionnaire used to diagnose chronic obstructive pulmonary disease.
Source: Own elaboration.

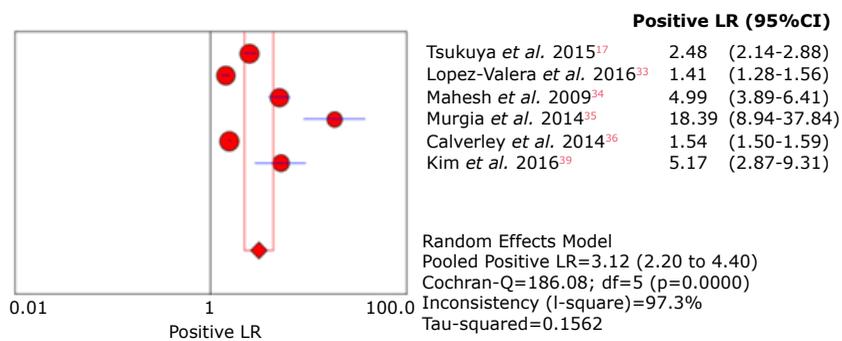


Figure 13. Forest plot for positive likelihood ratio of the COPD-SP questionnaire used to diagnose chronic obstructive pulmonary disease.
Source: Own elaboration.

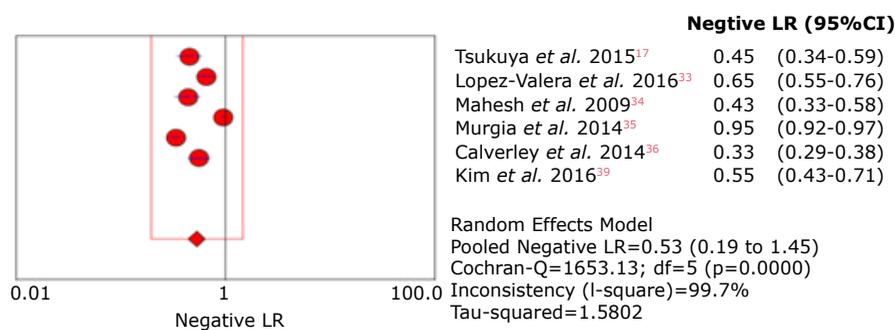


Figure 14. Forest plot for negative likelihood ratio of the COPD-SP questionnaire used to diagnose chronic obstructive pulmonary disease.
Source: Own elaboration.

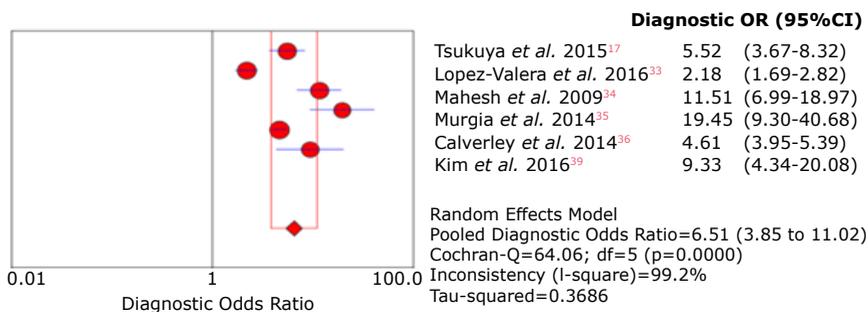


Figure 15. Forest plot for diagnostic odds ratio of the COPD-SP questionnaire used to diagnose chronic obstructive pulmonary disease. Source: Own elaboration.

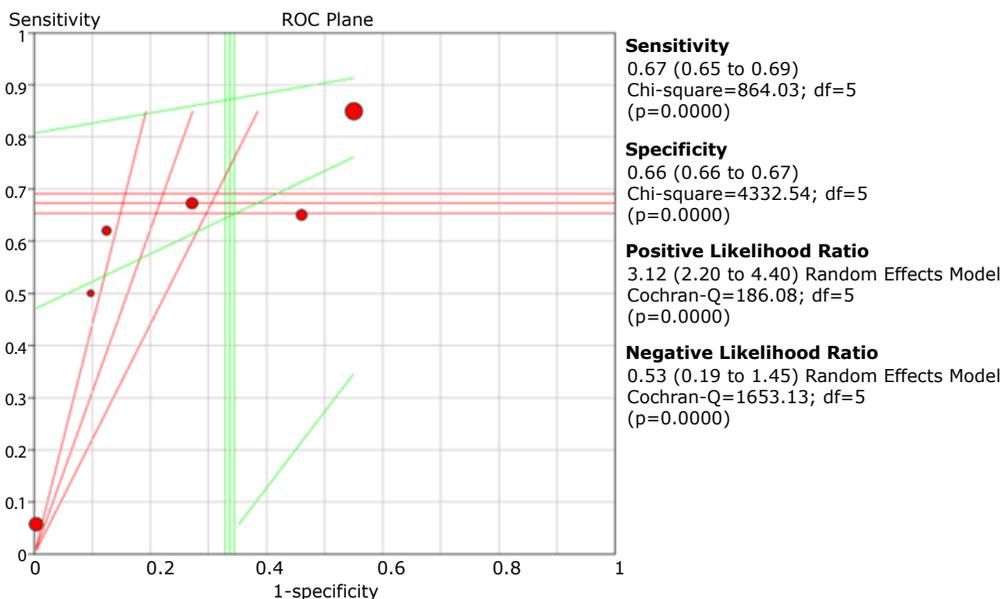


Figure 16. Summary of sensitivity, specificity, and positive and negative likelihood ratios of the COPD-SP questionnaire. Source: Own elaboration.

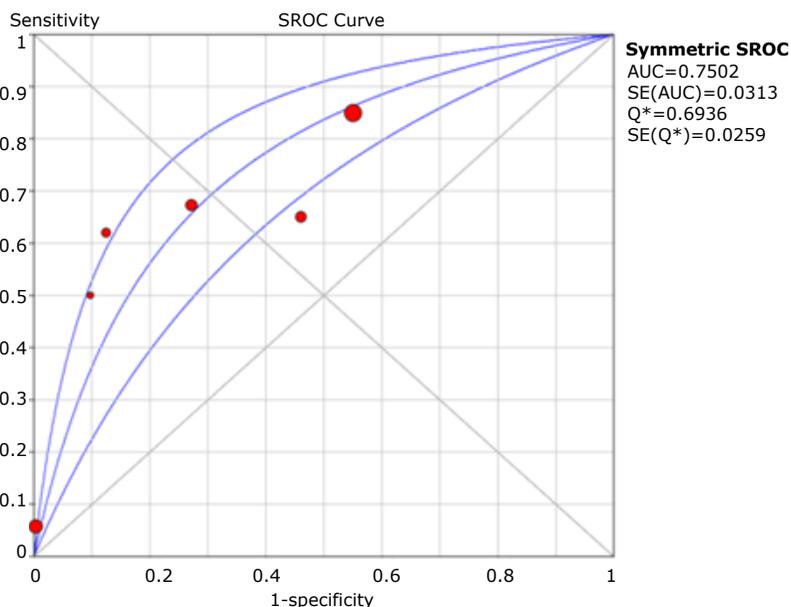


Figure 17. Summary of receiver operating characteristic and area under the curve for the COPD-PS questionnaire used to diagnose chronic obstructive pulmonary disease. Source: Own elaboration.

LFQ questionnaire

Three studies evaluated the LFQ questionnaire in a study population of 2 073 subjects. All studies assessed the FEV₁/FVC ratio as a diagnostic criterion, Mintz *et al.*³⁸ and Hanania, *et al.*²² in outpatients and Yawn *et al.*²⁰ in people from the community and outpatients.

Sensitivity, specificity, positive and negative likelihood ratio, DOR and ROC AUC results for the LFQ questionnaire are shown in Tables 12, 13, 14, 15 and 16, and Figures 18, 19, 20, 21, 22, 23 and 24.

Table 13. Specificity analysis of the LFQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.

Study	Spe	95% Confidence interval	TP/ (TP+FN)	TN/ (TN+FP)
Yawn <i>et al.</i> ²⁰	0.581	0.509-0.650	138/189	115/198
Hanania <i>et al.</i> ²²	0.479	0.441-0.517	129/156	326/681
Mintz <i>et al.</i> ³⁸	0.065	0.048-0.087	170/175	44/674
Pooled Spe	0.312	0.289-0.336		
Heterogeneity chi-squared: 391.26 (d.f.: 2) p=0.000 Inconsistency (I-square): 99.5% No. of studies: 3 Filter: OFF Adding 1/2 to all cells of the studies with zero events				

Spe: Specificity; TP: true positive; FN: false negative; TN: true negative; FP: false positive.
 Source: Own elaboration.

Table 14. Positive likelihood ratio analysis of the LFQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.

Study	LR+	95% Confidence interval	% Weight
Yawn <i>et al.</i> ²⁰	1.742	1.447-2.097	32.69
Hanania <i>et al.</i> ²²	1.586	1.433-1.756	33.49
Mintz <i>et al.</i> ³⁸	1.039	1.006-1.073	33.81
(REM) pooled LR+	1.418	0.799-2.515	
Heterogeneity chi-squared: 223.00 (d.f.: 2) p=0.000 Inconsistency (I-square): 99.1% Estimate of between-study variance (Tau-squared): 0.2527 No. of studies: 3 Filter: OFF Adding 1/2 to all cells of the studies with zero events			

LR+: positive likelihood ratio; REM: random effects model.
 Source: Own elaboration.

Table 15. Negative likelihood ratio analysis of the LFQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.

Study	LR-	95% Confidence interval	% Weight
Yawn <i>et al.</i> ²⁰	0.465	0.357-0.604	60.95
Hanania <i>et al.</i> ²²	0.362	0.254-0.514	33.97
Mintz <i>et al.</i> ³⁸	0.438	0.176-1.087	5.08
(REM) pooled LR-	0.425	0.346-0.522	
Heterogeneity chi-squared: 1.34 (d.f.: 2) p=0.512 Inconsistency (I-square): 0.0 % Estimate of between-study variance (Tau-squared): 0.0000 No. of studies: 3 Filter: OFF Adding 1/2 to all cells of the studies with zero events			

LR-: negative likelihood ratio; REM: random effects model.
 Source: Own elaboration.

Table 16. Diagnostic likelihood ratio analysis of the LFQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.

Study	DOR	95% Confidence Interval	% Weight
Yawn <i>et al.</i> ²⁰	3.749	2.445-5.750	46.60
Hanania <i>et al.</i> ²²	4.387	2.822-6.821	43.77
Mintz <i>et al.</i> ³⁸	2.375	0.927-6.081	9.63
(REM) pooled DOR	3.843	2.870-5.146	
Heterogeneity chi-squared: 1.37 (d.f.: 2) p=0.505 Inconsistency (I-square): 0.0% Estimate of between-study variance (Tau-squared): 0.0000 No. of studies: 3 Filter: OFF Adding 1/2 to all cells of the studies with zero events			

DOR: diagnostic odds ratio; REM: random effects model.
 Source: Own elaboration.

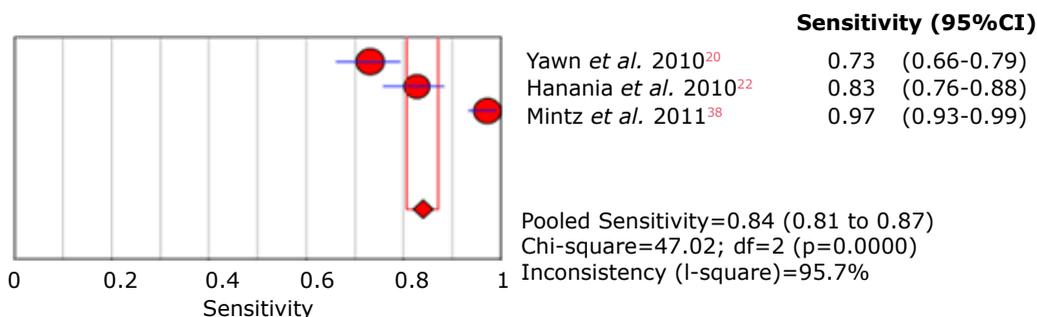


Figure 18. Forest plot of sensitivity of the LFQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.
Source: Own elaboration.

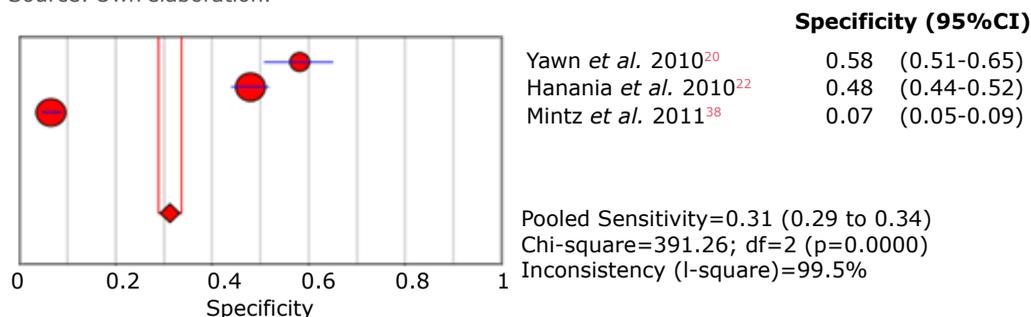


Figure 19. Forest plot of specificity of the LFQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.
Source: Own elaboration.

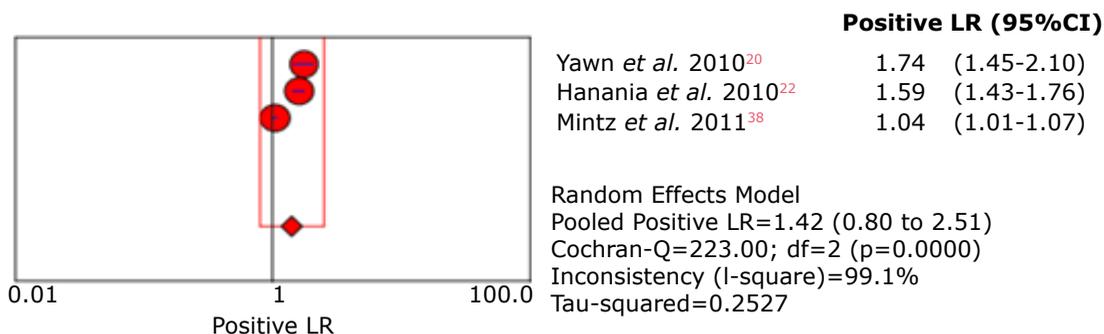


Figure 20. Forest plot of positive likelihood ratio of the LFQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.
Source: Own elaboration.

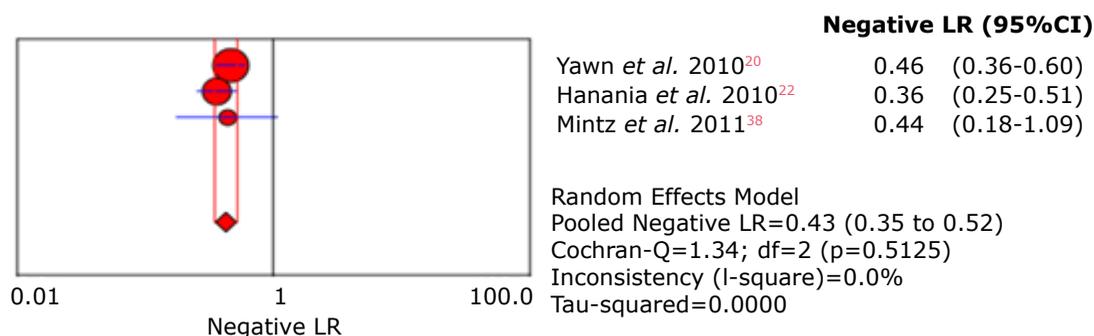


Figure 21. Forest plot of negative likelihood ratio of the LFQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.
Source: Own elaboration.

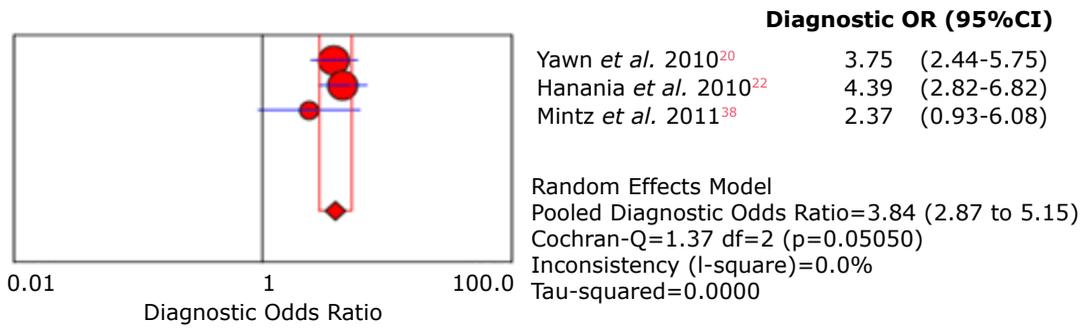


Figure 22. Forest plot of diagnostic likelihood ratio of the LFAQ questionnaire for the diagnosis of chronic obstructive pulmonary disease.
 Source: Own elaboration.

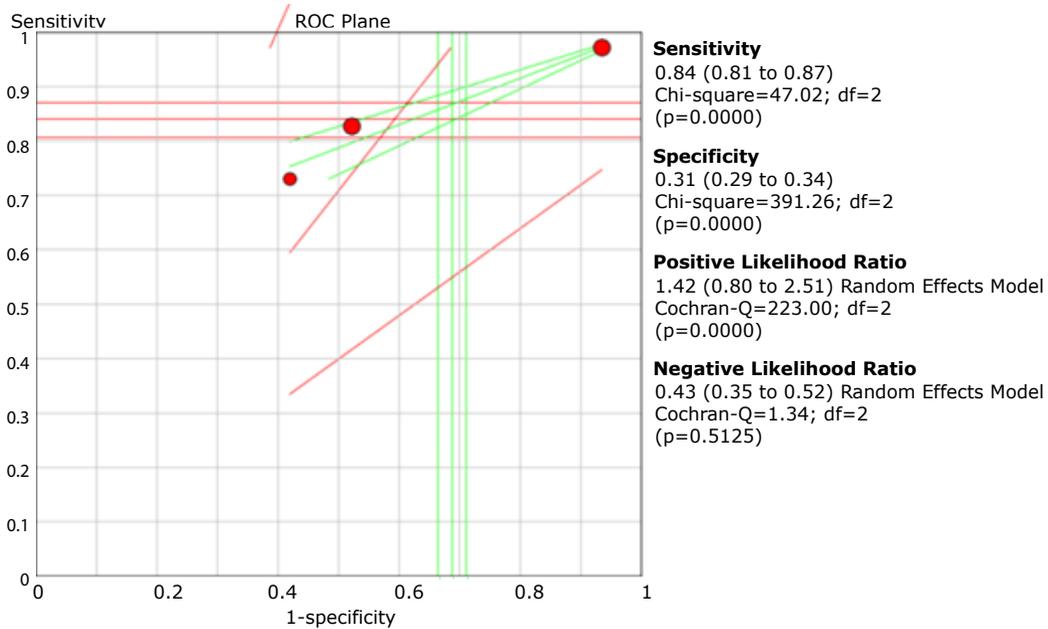


Figure 23. Summary of LFAQ questionnaire sensitivity, specificity, and positive and negative likelihood ratios.
 Source: Own elaboration.

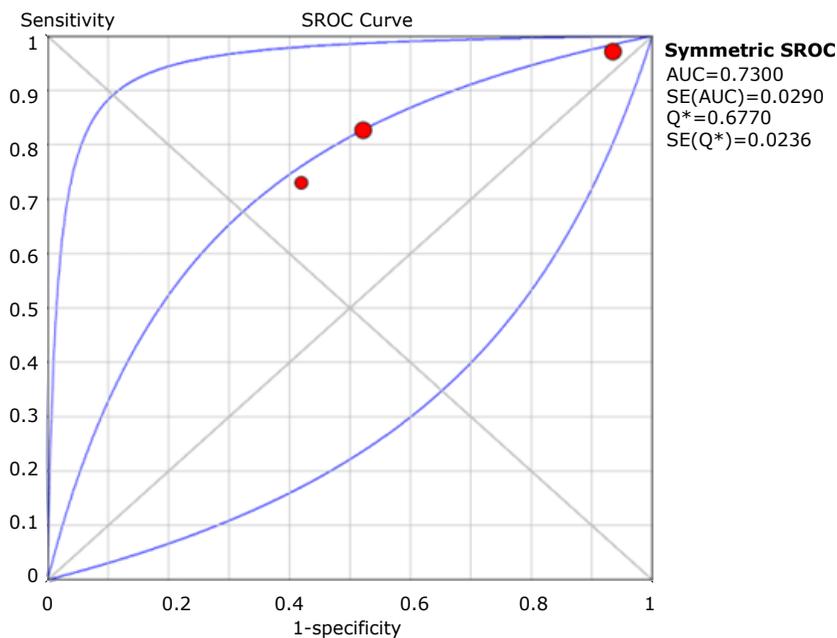


Figure 24. Summary of LFAQ questionnaire receiver operating characteristic and area under the curve for the diagnosis of chronic obstructive pulmonary disease.
 Source: Own elaboration.

CDQ questionnaire

Four studies evaluated the CDQ-38 questionnaire in a total population of 2 732 subjects. Only Frith *et al.*⁴¹ evaluated the FEV1/ FEV6 ratio as a diagnostic criterion; Stanley *et al.*¹⁸ and Frith *et al.*⁴¹ did the evaluation in outpatients, Kotz *et al.*³⁷ evaluated people from the community, and Price *et al.*⁴⁰ people from the community and outpatients.

Sensitivity, specificity, positive and negative likelihood ratio, DOR and ROC AUC results for the CDQ questionnaire are shown in Tables 17, 18, 19, 20 and 21, and in Figures 25, 26, 27, 28, 29, 30 and 31.

Table 17. Sensitivity analysis of the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	Sen	95% Confidence interval	TP/ (TP+FN)	TN/ (TN+FP)
Stanley <i>et al.</i> ¹⁸	0.797	0.720-0.861	110/138	430/916
Kotz <i>et al.</i> ³⁷	0.892	0.850-0.926	248/278	92/378
Price <i>et al.</i> ⁴⁰	0.587	0.505-0.665	91/155	511/663
Frith <i>et al.</i> ⁴¹	0.912	0.807-0.971	52/57	54/147
Pooled Sen	0.798	0.764-0.829		

Heterogeneity chi-squared: 58.90 (d.f.: 3) p=0.000
 Inconsistency (I-square): 94.9 %
 No. of Studies: 4.
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

Sen: sensitivity; TP: true positive; FN: false negative; TN: true negative; FP: false positive.
 Source: Own elaboration.

Table 18. Specificity analysis of the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	Spe	95% Confidence interval	TP/ (TP+FN)	TN/ (TN+FP)
Stanley <i>et al.</i> ¹⁸	0.469	0.437-0.502	110/138	430/916
Kotz <i>et al.</i> ³⁷	0.243	0.201-0.290	248/278	92/378
Price <i>et al.</i> ⁴⁰	0.771	0.737-0.802	91/155	511/663
Frith <i>et al.</i> ⁴¹	0.367	0.289-0.451	52/57	54/147
Pooled Spe	0.517	0.495-0.538		

Heterogeneity chi-squared: 321.26 (d.f.: 3) p=0.000
 Inconsistency (I-square): 99.1%
 No. of studies: 4
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

Spe: Specificity; TP: true positive; FN: false negative; TN: true negative; FP: false positive.
 Source: Own elaboration.

Table 19. Positive likelihood ratio analysis of the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	LR+	95% Confidence Interval	% Weight
Stanley <i>et al.</i> ¹⁸	1.502	1.354-1.667	25.61
Kotz <i>et al.</i> ³⁷	1.179	1.099-1.265	26.11
Price <i>et al.</i> ⁴⁰	2.561	2.113-3.103	23.56
Frith <i>et al.</i> ⁴¹	1.442	1.245-1.671	24.72
(REM) pooled LR+	1.583	1.199-2.090	

Heterogeneity chi-squared: 68.63 (d.f.: 3) p=0.000
 Inconsistency (I-square): 95.6%
 Estimate of between-study variance (Tau-squared): 0.0756
 No. of studies: 4
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

LR+: positive likelihood ratio; REM: random effects model.
 Source: Own elaboration.

Table 20. Negative likelihood ratio analysis of the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	LR-	95% Confidence Interval	% Weight
Stanley <i>et al.</i> ¹⁸	0.432	0.308-0.606	25.98
Kotz <i>et al.</i> ³⁷	0.443	0.303-0.650	22.00
Price <i>et al.</i> ⁴⁰	0.536	0.442-0.649	46.38
Frith <i>et al.</i> ⁴¹	0.239	0.101-0.566	5.64
(REM) pooled LR-	0.464	0.375-0.575	

Heterogeneity chi-squared: 4.50 (d.f.: 3) p=0.212
 Inconsistency (I-square): 33.4%
 Estimate of between-study variance (Tau-squared): 0.0160
 No. of studies: 4
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

LR-: negative likelihood ratio; REM: random effects model.
 Source: Own elaboration.

Table 21. Diagnostic odds ratio analysis of the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.

Study	DOR	95% Confidence Interval	% Weight
Stanley <i>et al.</i> ¹⁸	3.476	2.251-5.368	28.83
Kotz <i>et al.</i> ³⁷	2.659	1.703-4.153	28.03
Price <i>et al.</i> ⁴⁰	4.780	3.310-6.903	34.22
Frith <i>et al.</i> ⁴¹	6.039	2.273-16.042	8.92
(REM) pooled DOR	3.777	2.758-5.173	

Heterogeneity chi-squared: 4.99 (d.f.: 3) p=0.172
 Inconsistency (I-square): 39.9 %
 Estimate of between-study variance (Tau-squared): 0.0400
 No. of studies: 4
 Filter: OFF
 Adding 1/2 to all cells of the studies with zero events

DOR: diagnostic odds ratio; REM: random effects model.
 Source: Own elaboration.

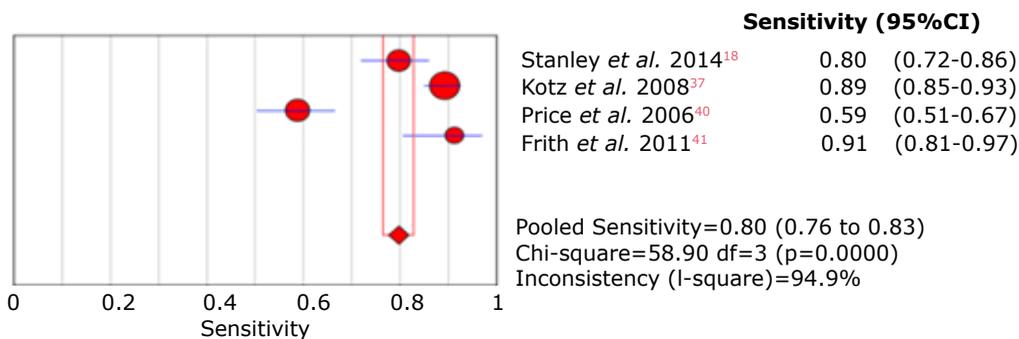


Figure 25. Forest plot for sensitivity of the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.
Source: Own elaboration.

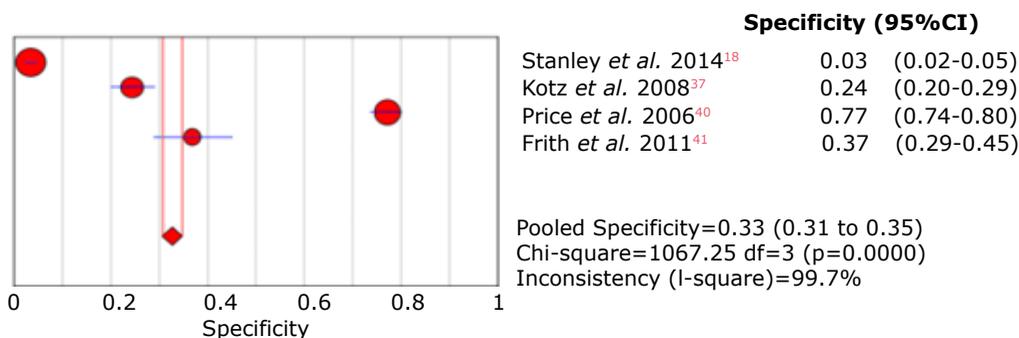


Figure 26. Forest plot for CDQ questionnaire specificity for the diagnosis of chronic obstructive pulmonary disease.
Source: Own elaboration.

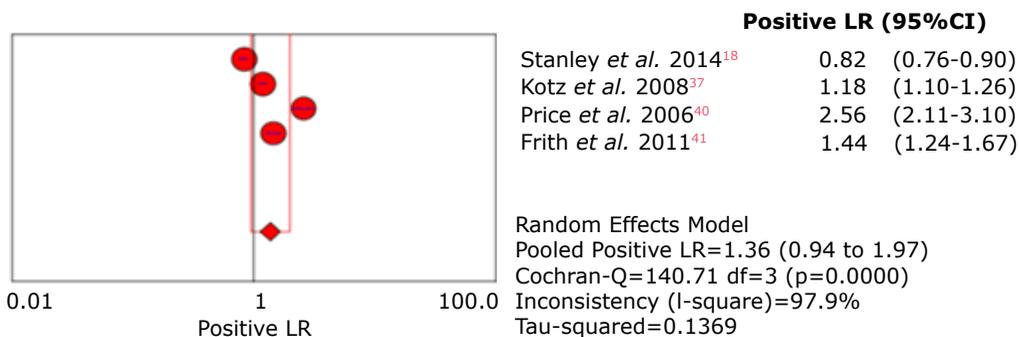


Figure 27. Forest plot for positive likelihood ratio of the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.
Source: Own elaboration.

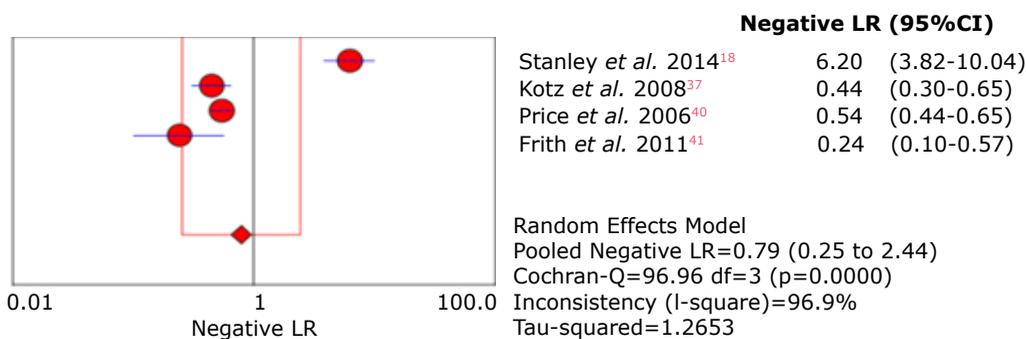


Figure 28. Forest plot for negative likelihood ratio of the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.
Source: Own elaboration.

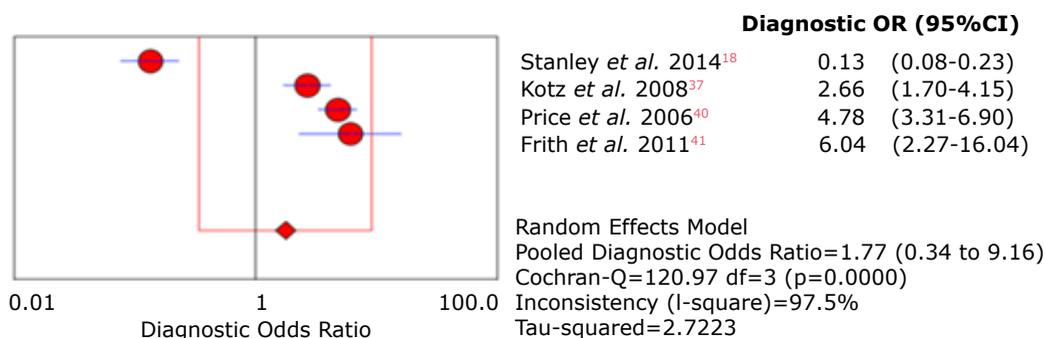


Figure 29. Forest plot for diagnostic odds ratio of the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.
Source: Own elaboration.

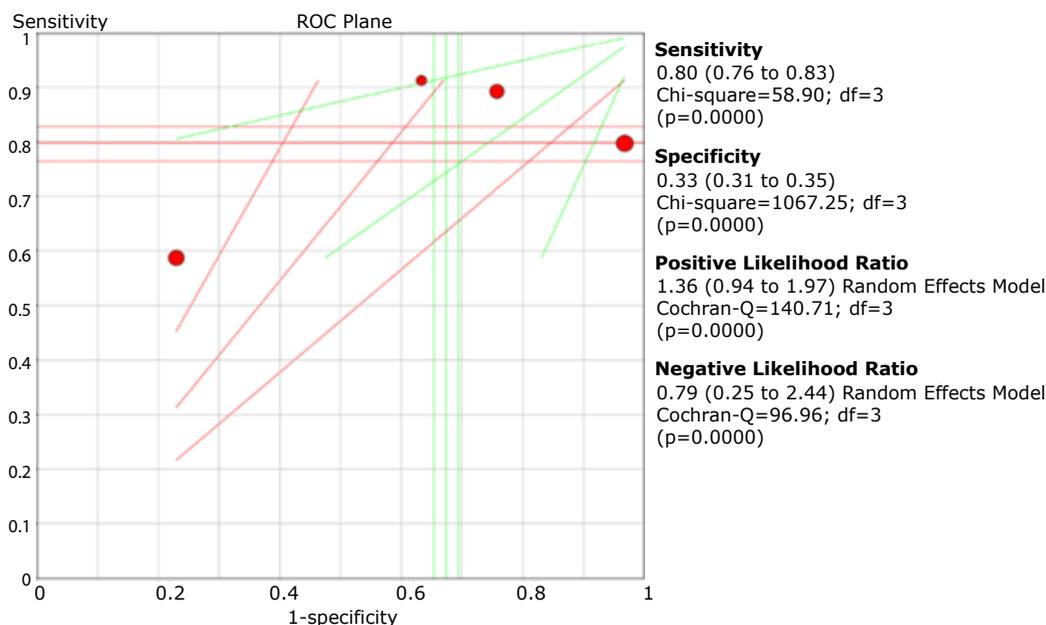


Figure 30. Summary of sensitivity, specificity, and positive and negative likelihood ratios of the CDQ questionnaire.
Source: Own elaboration.

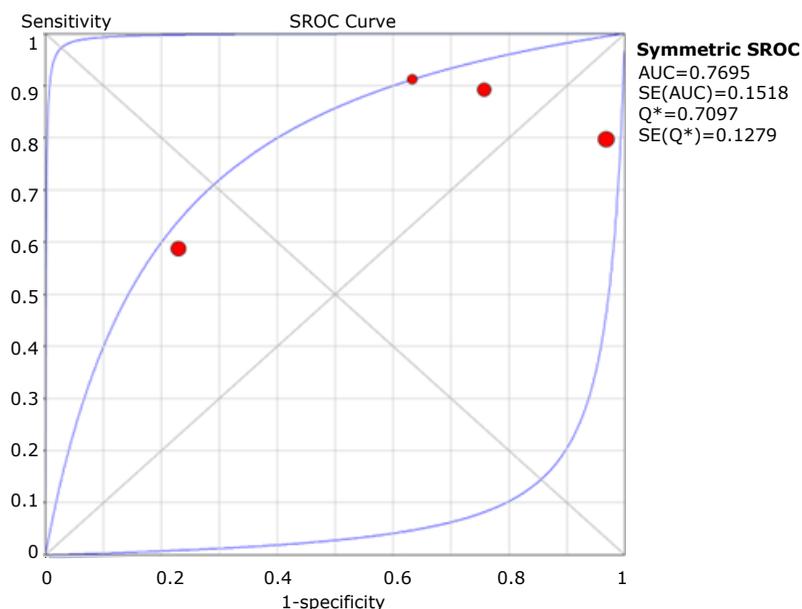


Figure 31. Summary of receiver operating characteristic and area under the curve for the CDQ questionnaire used to diagnose chronic obstructive pulmonary disease.
Source: Own elaboration.

Other questionnaires

The search did not yield any result of studies that evaluated the CAPTURE, CAT, EGARPOC, OTHER, SRHS or IPAG questionnaires, which is why summary statistics were not obtained.

Discussion

The present article is the literature review with the largest number of publications on clinical questionnaires for the diagnosis of COPD to date. The latest systematic review on this topic was conducted by Haroon *et al.*³² in 2015 and included five studies, finding that the most relevant questionnaire was CDQ. In that study, the researchers reported no additional evaluations of other currently available instruments such as COPD-PS and LFQ, which show different diagnostic yields.²⁵

In total, 19 publications that evaluated the validity of different questionnaires available for the diagnosis of COPD confirmed through spirometric values were included in the present study. The evaluated articles were conducted in different populations around the world and included subjects treated in outpatient and inpatient settings.^{24,34-36}

The overall analysis showed that the epidemiological design used in the studies was cross-sectional and that the minimum number of study subjects was 707 patients, which coincided with the reports by Haroon *et al.*³² Moreover, although only 40% of the studies reported overall statistical power or sample size, all reported information that allowed determining an overall statistical power of 80% to evaluate the scales' operational characteristics. Most studies were multicenter, and smoking status and respiratory symptoms were explicitly reported; the evaluation process was not specified only in a small number of studies.

Overall sensitivity of the questionnaires was 68.1% (95%CI: 66.7-69.4), while overall specificity was 64.9% (95%CI: 64.3-65.5), which agreed with the study by Haroon *et al.*³² where sensitivity and specificity were 64.5% (95%CI: 59.9-68.8) and 65.2% (95%CI: 52.9-75.8), respectively. Also, these results were similar to those reported by Spyrtatos *et al.*,²⁵ who evaluated the diagnostic performance of the IPAG (≥ 17), COPD-PS (≥ 5) and LFQ (≤ 18) questionnaires in a population of 3 234 individuals, finding sensitivity between 55% and 79%, and specificity between 68% and 90%. Such values decreased when their use was analyzed in the group of patients with under- or over-diagnosis of COPD, where sensitivity was between 50% and 74% and specificity between 69% and 91%; however, the sensitivity and specificity values of the three questionnaires grouped together were not presented in this article.

The study with the most weight for sensitivity and specificity was the one conducted by Calverley *et al.*³⁶ in which 7 701 subjects were evaluated, finding sensitivity of 85%; however, the highest sensitivity was described by Martínez *et al.*²⁷ and Mintz *et al.*,³⁸ both with a value of 97% and a population that together totaled 1 195 subjects. It should be noted that the GOLD, ATS and ERS criteria were used in these 3 studies to diagnose COPD, but the differences found were associated with the type of questionnaire used, namely, COPD-PS, CAPTURE, or LFQ. On the other hand, Murgia *et*

*al.*³⁵ reported the lowest sensitivity in an urban population of 3 892 subjects when evaluating the COPD-PS questionnaire; it should be noted that the studies by Calverley *et al.*³⁶ and Murgia *et al.*³⁵ were conducted in people from the community, while Martínez *et al.*²⁷ and Mintz *et al.*³⁸ assessed outpatients, which could affect to some extent the results obtained, even though the prevalence of the disease especially affects the positive predictive results.

The highest specificity was reported by Kim *et al.*³⁹ and Murgia *et al.*,³⁵ 90% and 100%, respectively; both studies evaluated the COPD-PS questionnaire in people from the community and outpatients, where the prevalence of the disease may be lower, as well as the respiratory symptomatology reported by patients. In turn, Mintz *et al.*³⁸ reported the lowest specificity with the LFQ questionnaire in outpatient subjects, which may eventually be explained by the nature of the questions and the differences in the scores.^{20,38}

The highest positive likelihood ratio was reported by Murgia *et al.*³⁵ with 18.4, while the lowest was reported by Mintz *et al.*³⁸ with 1.03. The highest negative likelihood ratio was described in the study by Martínez *et al.*²⁷ with 0.06, and the lowest in the study by Murgia *et al.*³⁵ with 0.94, thus showing great variability of results that can be explained mainly by the different types of questionnaires analyzed and the population evaluated.

The overall ROC AUC was 0.759, which was sufficient to discriminate between subjects with and without the disease; however, questionnaires with various cut-off points could also affect the validity results previously discussed, even being necessary, eventually, to consider different cut-off points according to the specific population characteristics.^{17,18} Nevertheless, the ROC AUC obtained suggests that the approach to COPD diagnosis is quite acceptable with all the questionnaires included in the study.

Sensitivity values obtained through the questionnaires evaluated are higher than those of the individual evaluation of respiratory symptoms that can be made based on the clinical history since the isolated sensitivity of history of smoking is 30-40%; expectoration, 20%; wheezing, 51%; dyspnea, 27%; and cough, 51%. This suggests that joint assessment of respiratory symptoms with targeted COPD questionnaires is superior,⁴⁶⁻⁵⁰ but specificity is similar and sometimes lower; for example, absence of dyspnea has a specificity of 88% for absence of disease.

The combined use of questionnaires and portable pulmonary function test equipment is another option for diagnosing COPD,⁵¹ and their combination can increase diagnostic performance by increasing sensitivity and specificity.⁵² In this regard, Sichletidis *et al.*⁴³ evaluated the use of the PiKo-6 portable device in combination with the IPAG questionnaire and found a sensitivity of 72% and a specificity of 97%; likewise, Kim *et al.*,³⁹ in a population of 179 subjects, found that the ROC AUC was 0.759 with the use of a portable spirometer, being superior to the value of the respiratory symptom evaluation and the use of the questionnaire alone. Nevertheless, the use of this type of device is more expensive and may require trained personnel, generating higher costs for COPD screening.^{53,54}

The large heterogeneity of the final analysis may be associated with several conditions such as the use of

different types of questionnaires, which have different questions and scores. Another cause could be related to the characteristics of the populations evaluated, with differences between people from the community, outpatients, and patients with specific risk factors. Also, some studies used the FEV₁/FEV₆ spirometric parameter, while others utilized the FEV₁/CVF ratio after using B2 <0.7. All these situations, added to the large number of studies included in the analysis, affect the heterogeneity of the results;^{55,56} however, in general terms, the risk of bias was low, and the applicability of the questionnaires was satisfactory.

Regarding the evaluation of the questionnaires separately, COPD-PS reported the highest performance with a cut-off point of 4, sensitivity of 0.673 (95%CI: 0.653-0.692), specificity of 0.663 (95%CI: 0.655-0.651), and ROC AUC of 0.750; followed by LFQ with a cut-off point of 18, sensitivity of 0.840 (95% CI: 0.806-0.871), specificity of 0.312 (95% CI: 0.289-0.336), and ROC AUC of 0.730; and CDQ with a cut-off point of 16.5, sensitivity of 0.798 (95% CI: 0.764-0.829), specificity of 0.517 (95% CI: 0.495-0.538), and ROC AUC of 0.727. It should be noted that, with regard to the other questionnaires described in the introduction, only one study was found for each instrument, which prevented the synthesis of the results.

Despite the validity results, data on the reproducibility of the questionnaires are scarce. Martínez *et al.*²⁷ report an intraclass correlation coefficient between 0.86 and 0.91 when performing the before-and-after test with the COPD-PS questionnaire, thus leaving the possibility of delving into the reliability data of the questionnaires and the cost-effectiveness and cost-utility analysis.

Conclusions

In general, clinical prediction instruments for diagnosing COPD have an acceptable performance since the sensitivity values obtained are superior to those obtained with the individual assessment of respiratory symptoms based on the clinical history. The COPD-PS, LFQ and CDQ questionnaires have a similar performance for the diagnosis of this disease since they present large heterogeneity in the results of the studies evaluated.

Conflicts of interest

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References

- Singh D, Agusti A, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, *et al.* Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease: the GOLD science committee report 2019. *European Resp J.* 2019;53(5):1099164. <https://doi.org/gf39d4>.
- Barrecheuren M, Pinto L, Mostafavi-Pour-Manshadi SMY, Tan WC, Li PZ, Aaron SD, *et al.* Identification and definition of asthma-COPD overlap: The CanCOLD study. *Respirology.* 2020;25(8):836-49. <https://doi.org/fpnj>.
- Varmaghani M, Dehghani M, Heidari E, Sharifi F, Moghaddam SS, Farzadfar F. Global prevalence of chronic obstructive pulmonary disease: Systematic review and meta-analysis. *East Mediterr Heal J.* 2019;25(1):47-57. <https://doi.org/fpnk>.
- Halbert RJ, Isonaka S, George D, Iqbal A. Interpreting COPD prevalence estimates: What is the true burden of disease?, *Chest.* 2003;123(5):1684-92. <https://doi.org/fb9t7v>.
- World Health Organization (WHO). The top 10 causes of death. Geneva: WHO; 2018 [cited 2020 Aug 9]. Available from: <https://bit.ly/3o0TPeL>.
- Labonte LE, Tan WC, Li PZ, Mancino P, Aaron SD, Benedetti A, *et al.* Undiagnosed chronic obstructive pulmonary disease contributes to the burden of health care use data from the CanCOLD study. *Am J Respir Crit Care Med.* 2016;194(3):285-98. <https://doi.org/f8xk7t>.
- Bednarek M, Maciejewski J, Wozniak M, Kuca P, Zielinski J. Prevalence, severity and underdiagnosis of COPD in the primary care setting. *Thorax.* 2008;63(5):402-7. <https://doi.org/dvbj62>.
- Quach A, Giovannelli J, Chérot-Kornobis N, Ciuchete A, Clément G, Matran R, *et al.* Prevalence and underdiagnosis of airway obstruction among middle-aged adults in northern France: The ELISABET study 2011-2013. *Respir Med.* 2015;109(12):1553-61. <https://doi.org/f729t2>.
- Martínez-Briseño D, Fernández-Plata MR, García-Sancho Figueroa MC, Pérez-Padilla R. La carga económica de la EPOC. Análisis de los costos a nivel internacional. *Neumol Cir Tórax.* 2011;70(2):118-26.
- Pérez M, Puig-Peiró R, Aceituno S, Lizán L. Impacto económico de las exacerbaciones agudas en EPOC desde la perspectiva del SNS español. *Rev Patol Respir.* 2016;19(3):88-95.
- Masa JF, Sobradillo V, Villasante C, Jiménez-Ruiz CA, Fernández-Fau L, Viejo JL, *et al.* Costes de la EPOC en España. Estimación a partir de un estudio epidemiológico poblacional. *Arch Bronconeumol.* 2004;40(2):72-9. <https://doi.org/dtnqht>.
- Martínez FJ, Raczek AE, Seifer FD, Conoscenti CS, Curtice TG, D'Eletto T, *et al.* Development and Initial Validation of a Self-Scored COPD Population Screener Questionnaire (COPD-PS). *COPD.* 2008;5(2):85-95. <https://doi.org/d6hww4>.
- Smith MC, Wrobel JP. Epidemiology and clinical impact of major comorbidities in patients with COPD. *Int J Chron Obstruct Pulmon Dis.* 2014;9:871-88. <https://doi.org/f6zxdq>.
- Soler-Cataluña JJ, Martínez-García MÁ, Román-Sánchez P, Salcedo E, Navarro M, Ochando R. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax.* 2005;60(11):925-31. <https://doi.org/fnstqc>.
- Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2020 report). GOLD; 2020.
- Colombia. Ministerio de Salud y Protección Social (MinSalud). Guía de práctica clínica basada en la evidencia para la prevención, diagnóstico, tratamiento y seguimiento de la Enfermedad Pulmonar Obstructiva Crónica (EPOC) en población adulta. Guía No. 28. Bogotá D.C.: MinSalud; 2014.
- Tsukuya G, Matsumoto K, Fukuyama S, Crawford B, Nakanishi Y, Ichinose M, *et al.* Validation of a COPD screening questionnaire and establishment of diagnostic cut-points in a Japanese general population: The Hisayama study. *Allergol Int.* 2015;64(1):49-53. <https://doi.org/f62wg9>.
- Stanley AJ, Hasan I, Crockett AJ, van Schayck OCP, Zwar NA. Validation of the COPD diagnostic questionnaire in an Australian general practice cohort: A cross-sectional study. *Prim Care Respir J.* 2014;23(1):92-7. <https://doi.org/f5wf52>.

19. Guirguis-Blake JM, Senger CA, Webber EM, Mularski RA, Whitlock EP. Screening for chronic obstructive pulmonary disease evidence report and systematic review for the US preventive services task force. *JAMA*. 2016;315(13):1378-93. <https://doi.org/cj48>.
20. Yawn BP, Mapel DW, Mannino DM, Martinez FJ, Donohue JF, Hanania NA, *et al*. Development of the lung function questionnaire (LFQ) to identify airflow obstruction. *Int J Chron Obstruct Pulmon Dis*. 2010;5(1):1-10. <https://doi.org/cfr859>.
21. Dalal AA, Demuro-Mercon C, Lewis S, Nelson L, Gilligan T, McLeod L. Validation of alternate modes of administration of the lung function questionnaire (LFQ) in subjects with smoking history. *Int J Chron Obstruct Pulmon Dis*. 2010;5:425-34. <https://doi.org/djrthk>.
22. Hanania NA, Mannino DM, Yawn BP, Mapel DW, Martinez FJ, Donohue JF, *et al*. Predicting risk of airflow obstruction in primary care: Validation of the lung function questionnaire (LFQ). *Respir Med*. 2010;104(8):1160-70. <https://doi.org/b7q7pr>.
23. Llordés M, Zurdo E, Jaén Á, Vázquez I, Pastrana L, Miravittles M. Which is the Best Screening Strategy for COPD among Smokers in Primary Care? *COPD*. 2017;14(1):43-51. <https://doi.org/fpk8>.
24. Arimura Y, Yamazaki S, Shirahama T, Matsukura S, Chiyotanda S, Nakazato M, *et al*. [Accuracy of COPD questionnaires in the general health check-up setting]. *Nihon Kokyuki Gakkai Zasshi*. 2008;46(9):693-9.
25. Spyrtatos D, Haidich AB, Chloros D, Michalopoulou D, Sichelidis L. Comparison of Three Screening Questionnaires for Chronic Obstructive Pulmonary Disease in the Primary Care. *Respiration*. 2017;93(2):83-9. <https://doi.org/fpn3>.
26. Bardapurkar S, Bardapurkar S, Gadge G. Can we diagnose COPD by just asking 8 questions? *Eur Respir J*. 2013;42(Suppl 57):1874.
27. Martinez FJ, Mannino D, Leidy NK, Malley KG, Bacci ED, Barr RG, *et al*. A new approach for identifying patients with undiagnosed chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2017;195(6):748-56. <https://doi.org/f9tp66>.
28. Londhe J, Apte K, Barne M, Salvi S. CAPTURE: A screening tool for chronic obstructive pulmonary disease or obstructive airway disease? *Am J Respir Crit Care Med*. 2018;197(2):272. <https://doi.org/fpn4>.
29. Miravittles M, Koblizek V, Esquinas C, Milenkovic B, Barczyk A, Tkacova R, *et al*. Determinants of CAT (COPD Assessment Test) scores in a population of patients with COPD in central and Eastern Europe: The POPE study. *Respir Med*. 2019;150:141-8. <https://doi.org/fpn5>.
30. Gabler NB, Duan N, Liao D, Elmore JG, Ganiats TG, Kravitz RL. Dealing with heterogeneity of treatment effects: Is the literature up to the challenge? *Trials*. 2009 ;10(1):43. <https://doi.org/btz79d>.
31. Fernandez y Garcia E, Nguyen H, Duan N, Gabler NB, Kravitz RL. Assessing Heterogeneity of Treatment Effects: Are Authors Misinterpreting Their Results? *Health Serv Res*. 2010;45(1):283-301. <https://doi.org/bmfch8>.
32. Haroon S, Jordan R, Takwoingi Y, Adab P. Diagnostic accuracy of screening tests for COPD: A systematic review and meta-analysis. *BMJ Open*. 2015;5(10):e008133. <https://doi.org/f88ndf>.
33. López-Varela MV, Montes-de Oca M, Rey A, Casas A, Stirbulov R, Di Boscio V. Development of a simple screening tool for opportunistic COPD case finding in primary care in Latin America: The PUMA study. *Respirology*. 2016;21(7):1227-34. <https://doi.org/f85fnw>.
34. Mahesh PA, Jayaraj BS, Prahlad ST, Chaya SK, Prabhakar AK, Agarwal AN, *et al*. Validation of a structured questionnaire for COPD and prevalence of COPD in rural area of Mysore: A pilot study. *Lung India*. 2009;26(3):63-9. <https://doi.org/ftv2dd>.
35. Murgia N, Brisman J, Claesson A, Muzi G, Olin AC, Torén K. Validity of a questionnaire-based diagnosis of chronic obstructive pulmonary disease in a general population-based study. *BMC Pulm Med*. 2014;14(1):49. <https://doi.org/gb3k6w>.
36. Calverley PMA, Nordyke RJ, Halbert RJ, Isonaka S, Nonikov D. Development of a population-based screening questionnaire for COPD. *COPD*. 2005;2(2):225-32.
37. Kotz D, Nelemans P, Van Schayck CP, Wesseling GJ. External validation of a COPD diagnostic questionnaire. *Eur Respir J*. 2008;31(2):298-303. <https://doi.org/dktw68>.
38. Mintz ML, Yawn BP, Mannino DM, Donohue JF, Hanania NA, Grellet CA, *et al*. Prevalence of airway obstruction assessed by lung function questionnaire. *Mayo Clin Proc*. 2011;86(5):375-81. <https://doi.org/d8ftb9>.
39. Kim JK, Lee CM, Park JY, Kim JH, Park S-H, Jang SH, *et al*. Active case finding strategy for chronic obstructive pulmonary disease with handheld spirometry. *Medicine (Baltimore)*. 2016;95(50):e5683. <https://doi.org/fpmc>.
40. Price DB, Tinkelman DG, Nordyke RJ, Isonaka S, Halbert RJ. Scoring system and clinical application of COPD diagnostic questionnaires. *Chest*. 2006;129(6):1531-9. <https://doi.org/bstdzb>.
41. Frith P, Crockett A, Beilby J, Marshall D, Attewell R, Ratnanesan A, *et al*. Simplified COPD screening: Validation of the PiKo-6® in primary care. *Prim Care Respir J*. 2011;20(2):190-8. <https://doi.org/cpd3z8>.
42. Yoshimoto D, Nakano Y, Onishi K, Hagan G, Jones P. The relationship between the COPD assessment test score and airflow limitation in Japan in patients aged over 40 years with a smoking history. *Int J Chron Obstruct Pulmon Dis*. 2014;9:1357-63. <https://doi.org/fpmg>.
43. Sichelidis L, Spyrtatos D, Papaioannou M, Chloros D, Tsiotsios A, Tsagaraki V, *et al*. A combination of the IPAG questionnaire and PiKo-6® flow meter is a valuable screening tool for COPD in the primary care setting. *Prim Care Respir J*. 2011;20(2):184-9. <https://doi.org/fprt3n>.
44. Freeman D, Nordyke RJ, Isonaka S, Nonikov DV, Maroni JM, Price D, *et al*. Questions for COPD diagnostic screening in a primary care setting. *Respir Med*. 2005;99(10):1311-8. <https://doi.org/d6vd5v>.
45. Buffels J, Degryse J, Heyrman J, Decramer M. Office spirometry significantly improves early detection of COPD in general practice: The DIDASCO Study. *Chest*. 2004;125(4):1394-9. <https://doi.org/fpv558>.
46. Schapira RM, Schapira MM, Funahashi A, McAuliffe TL, Varkey B. The Value of the Forced Expiratory Time in the Physical Diagnosis of Obstructive Airways Disease. *JAMA*. 1993;270(6):731-6.
47. Straus SE, McAlister FA, Sackett DL, Deeks JJ. Accuracy of history, wheezing, and forced expiratory time in the diagnosis of chronic obstructive pulmonary disease. *J Gen Intern Med*. 2002;17(9):684-8. <https://doi.org/dzdmv6>.
48. Straus SE, McAlister FA, Sackett DL, Deeks JJ. The accuracy of patient history, wheezing, and laryngeal measurements in diagnosing obstructive airway disease. CARE-COAD1 Group. Clinical Assessment of the Reliability of the Examination-Chronic Obstructive Airways Disease. *JAMA*. 2000;283(14):1853-7. <https://doi.org/fvc8x8>.
49. King DK, Thompson BT, Johnson DC. Wheezing on maximal forced exhalation in the diagnosis of atypical asthma. Lack of sensitivity and specificity. *Ann Intern Med*. 1989;110(6):451-5. <https://doi.org/fpn6>.

50. Holleman DR, Simel DL, Goldberg JS. Diagnosis of obstructive airways disease from the clinical examination. *J Gen Intern Med.* 1993;8(2):63-8. <https://doi.org/br72pr>.
51. Nelson SB, LaVange LM, Nie Y, Walsh JW, Enright PL, Martinez FJ, *et al.* Questionnaires and pocket spirometers provide an alternative approach for COPD screening in the general population. *Chest.* 2012;142(2):358-66. <https://doi.org/fxqp6q>.
52. Represas-Represas C, Botana-Rial M, Leiro-Fernández V, González-Silva AI, del Campo-Pérez V, Fernández-Villar A. Validación del dispositivo portátil COPD-6 para la detección de patologías obstructivas de la vía aérea. *Arch Bronconeumol.* 2010;46(8):426-32. <https://doi.org/fmwrxr>.
53. Pierce R. Spirometry: an essential clinical measurement. *Aust Fam Physician.* 2005;34(7):535-9.
54. Qaseem A, Wilt TJ, Weinberger SE, Hanania NA, Criner G, van der Molen T, *et al.* Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann Intern Med.* 2011;155(3):179-91. <https://doi.org/9mc>.
55. Malone DC, Hines LE, Graff JS. The good, the bad, and the different: A primer on aspects of heterogeneity of treatment effects. *J Manag Care Pharm.* 2014;20(6):555-63. <https://doi.org/f6f9h4>.
56. Kent DM, Rothwell PM, Ioannidis JPA, Altman DG, Hayward RA. Assessing and reporting heterogeneity in treatment effects in clinical trials: A proposal. *Trials.* 2010;11(1):85. <https://doi.org/cmpxkf>.

Annex 1. Search protocol.**PubMed**

P: population	((("Middle Aged"[Mesh]) OR ("Aged, 80 and over"[Mesh])) OR "Tobacco Smoke Pollution"[Mesh]) OR "Biomass"[Mesh] OR "Tobacco Use Disorder"[Mesh])
I: intervention	Surveys and Questionnaires, Health Surveys, Spirometry, Respiratory Function Tests ("Health Surveys"[Mesh]) OR ("Surveys and Questionnaires"[Mesh])
C: comparison	("Spirometry"[Mesh]) OR "Respiratory Function Tests"[Mesh])
O: outcome	((("Reproducibility of Results"[Mesh]) OR "Pulmonary Disease, Chronic Obstructive"[Mesh]) OR "Diagnosis"[Mesh]) OR "Early Diagnosis"[Mesh])

Filters in PubMed

Systematic reviews	((systematic review [Title/Abstract]) OR meta analysis [Title/Abstract]) OR "Meta-Analysis" [Publication Type]) OR "Review" [Publication Type]
Randomized clinical trials	((((Groups [tiab]) OR trial [tiab]) OR randomly [tiab]) OR randomized [tiab]) OR controlled clinical trial [pt]) OR randomized controlled trial [pt]
Observational studies	((("Cohort Studies"[Mesh]) OR "Longitudinal Studies"[Mesh]) OR "Prospective Studies"[Mesh]) OR "Incidence"[Mesh])

((((((((((("Middle Aged"[Mesh]) OR ("Aged, 80 and over"[Mesh])) OR "Tobacco Smoke Pollution"[Mesh]) OR "Biomass"[Mesh]) OR "Tobacco Use Disorder"[Mesh])) AND (("Health Surveys"[Mesh]) OR ("Surveys and Questionnaires"[Mesh])) AND ("Spirometry"[Mesh]) OR "Respiratory Function Tests"[Mesh])) AND ("Reproducibility of Results"[Mesh]) OR "Pulmonary Disease, Chronic Obstructive"[Mesh]) OR "Diagnosis"[Mesh]) OR "Early Diagnosis"[Mesh])) AND (((("Cohort Studies"[Mesh]) OR "Longitudinal Studies"[Mesh]) OR "Prospective Studies"[Mesh]) OR "Incidence"[Mesh])) Filters: Publication date from 1997/07/01 to 2017/07/15
Total PubMed: 3 020.

RS:

((((((((((("Middle Aged"[Mesh]) OR ("Aged, 80 and over"[Mesh])) OR "Tobacco Smoke Pollution"[Mesh]) OR "Biomass"[Mesh]) OR "Tobacco Use Disorder"[Mesh])) AND (("Health Surveys"[Mesh]) OR ("Surveys and Questionnaires"[Mesh])) AND ("Spirometry"[Mesh]) OR "Respiratory Function Tests"[Mesh])) AND ("Reproducibility of Results"[Mesh]) OR "Pulmonary Disease, Chronic Obstructive"[Mesh]) OR "Diagnosis"[Mesh]) OR "Early Diagnosis"[Mesh])) AND (((systematic review [Title/Abstract]) OR meta analysis [Title/Abstract]) OR "Meta-Analysis" [Publication Type]) OR "Review" [Publication Type]) AND ("1997/07/01"[PDate] : "2017/07/15"[PDate]))
Total: 149.

EC:

Search (((((((((((("Middle Aged"[Mesh]) OR ("Aged, 80 and over"[Mesh])) OR "Tobacco Smoke Pollution"[Mesh]) OR "Biomass"[Mesh]) OR "Tobacco Use Disorder"[Mesh])) AND (("Health Surveys"[Mesh]) OR ("Surveys and Questionnaires"[Mesh])) AND ("Spirometry"[Mesh]) OR "Respiratory Function Tests"[Mesh])) AND ("Reproducibility of Results"[Mesh]) OR "Pulmonary Disease, Chronic Obstructive"[Mesh]) OR "Diagnosis"[Mesh]) OR "Early Diagnosis"[Mesh])) AND (((((Groups [tiab]) OR trial [tiab]) OR randomly [tiab]) OR randomized [tiab]) OR controlled clinical trial [pt]) OR randomized controlled trial [pt]) AND ("1997/07/01"[PDate] : "2017/07/15"[PDate])) Filters: Publication date from 1997/07/01 to 2017/07/15
Total: 2 479

EMBASE:

'middle aged'/exp OR 'middle age' OR 'middle aged' OR 'very elderly'/exp OR 'aged, 80 and over' OR 'centenarian' OR 'centenarians' OR 'nonagenarian' OR 'nonagenarians' OR 'octogenarian' OR 'octogenarians' OR 'very elderly' OR 'very old' OR 'tobacco smoke pollution' OR 'biomass'/exp OR 'biomass' OR 'tobacco dependence'/exp OR 'dependence, tobacco' OR 'nicotine abuse' OR 'nicotine addiction' OR 'nicotine dependence' OR 'nicotine dependency' OR 'nicotism' OR 'tobacco abuse' OR 'tobacco addiction' OR 'tobacco dependence' OR 'tobacco dependency' OR 'tobacco use disorder' OR 'tobaccoism' AND ('health survey'/exp OR 'health care surveillance, registration and quality control' OR 'health survey' OR 'health surveys' OR 'population surveillance' OR 'public health surveillance' OR 'survey, health' OR 'questionnaire'/exp OR 'questionnaire' OR 'questionnaires' OR 'surveys and questionnaires' OR 'technique, delphi') AND ('spirometry'/exp OR 'breath measurement' OR 'spirometry' OR 'lung function test'/exp OR 'function test, lung' OR 'function test, pulmonary' OR 'lung function test' OR 'pulmonary function test' OR 'respiratory function test' OR 'respiratory function tests' OR 'respiratory test' OR 'ventilation test') AND ('reproducibility'/exp OR 'measurement reproducibility' OR 'reproducibility' OR 'reproducibility of results' OR 'reproductivity' OR 'chronic obstructive lung disease'/exp OR 'chronic airflow obstruction' OR 'chronic airway obstruction' OR 'chronic obstructive bronchitis' OR 'chronic obstructive bronchopulmonary disease' OR 'chronic obstructive lung disease' OR 'chronic obstructive lung disorder' OR 'chronic obstructive pulmonary disease' OR 'chronic obstructive pulmonary disorder' OR 'chronic obstructive respiratory disease' OR 'copd' OR 'lung chronic obstructive disease' OR 'lung disease, chronic obstructive' OR 'lung diseases, obstructive' OR 'obstructive lung disease' OR 'obstructive lung disease, chronic' OR 'obstructive pulmonary disease' OR 'obstructive respiratory disease' OR 'obstructive respiratory tract disease' OR 'pulmonary disease, chronic obstructive' OR 'pulmonary disorder, chronic obstructive' OR 'diagnosis'/exp OR 'bacteriologic diagnosis' OR 'diagnosis' OR 'diagnosis delay' OR 'diagnostic screening' OR 'diagnostic sign' OR 'diagnostic tool' OR 'diagnostics' OR 'disease diagnosis' OR 'medical diagnosis' OR 'physical diagnosis' OR 'early diagnosis'/exp OR 'diagnosis, early' OR 'early diagnosis') AND [1-7-1997]/sd NOT [15-7-2017]/sd
Total: 1 460.

LILACS

P	middle-aged, elderly, smoking, smoking habit, biomass	(tw:(Mediana Edad)) OR (tw:(Anciano)) OR (tw:(Tabaquismo)) OR (tw:(Hábito de fumar)) OR (tw:(Biomasa))
I	Interview, survey, and questionnaires	(tw:(Entrevista)) OR (tw:(Encuesta y cuestionarios))
C	Spirometry, pulmonary function tests	(tw:(Espirometría)) OR (tw:(Pruebas de Función Respiratoria))
O	Reliability and validity, test validity Chronic obstructive pulmonary disease Diagnosis, early diagnosis	(tw:(Confiabilidad y Validez)) OR (tw:(Validez del test)) OR (tw:(Enfermedad Pulmonar Obstructiva Crónica)) OR (tw:(Diagnóstico)) OR (tw:(Diagnóstico Precoz))

(tw:((tw:(Mediana Edad)) OR (tw:(Anciano)) OR (tw:(Tabaquismo)) OR (tw:(Hábito de fumar)) OR (tw:(Biomasa)))) AND (tw:((tw:(Entrevista)) OR (tw:(Encuesta y cuestionarios)))) AND (tw:((tw:(Espirometría)) OR (tw:(Pruebas de Función Respiratoria)))) AND (tw:((tw:(-Confiabilidad y Validez)) OR (tw:(Validez del test)) OR (tw:(Enfermedad Pulmonar Obstructiva Crónica)) OR (tw:(Diagnóstico)) OR (tw:(Diagnóstico Precoz))))

Total: 85

Total literature search: 7 193.

Filters used to search for evidence

Filters for identifying systematic reviews in PubMed and EMBASE

	PubMed	EMBASE
#1	"Review" [Publication Type]	'systematic review'/exp AND [embase]/lim
#2	"Meta-Analysis" [Publication Type]	'systematic review (topic)'/exp AND [embase]/lim
#3	Meta-analysis [Title/Abstract]	#1 OR #2
#4	Systematic review [Title/Abstract]	

((systematic review [Title/Abstract]) OR meta analysis [Title/Abstract]) OR "Meta-Analysis" [Publication Type]) OR "Review" [Publication Type]

Filters for identifying randomized clinical trials in PubMed and EMBASE

Steps	PubMed	EMBASE
#1	randomized controlled trial [pt]	randomized:ab AND [embase]/lim
#2	controlled clinical trial [pt]	'randomized controlled trial'/de AND [embase]/lim
#3	randomized [tiab]	'controlled clinical trial'/de AND [embase]/lim
#4	placebo [tiab]	placebo:ab AND [embase]/lim
#5	drug therapy [sh]	'drug therapy'/syn AND [embase]/lim
#6	randomly [tiab]	randomly:ab AND [embase]/lim

(((((Groups [tiab]) OR trial [tiab]) OR randomly [tiab]) OR randomized [tiab]) OR controlled clinical trial [pt]) OR randomized controlled trial [pt]

Filters to identify observational studies in PubMed and EMBASE.

Pasos	PubMed	EMBASE
#1	"Cohort Studies"[Mesh]	'cohort analysis'/exp AND [embase]/lim
#2	"Longitudinal Studies"[Mesh]	'longitudinal study'/exp AND [embase]/lim
#3	"Prospective Studies"[Mesh]	'prospective study'/exp AND [embase]/lim
#4	"Incidence"[Mesh]	'incidence'/exp AND [embase]/lim
#5	#1 OR #2 OR #3 OR #4	#1 OR #2 OR #3 OR #4

((("Cohort Studies"[Mesh]) OR "Longitudinal Studies"[Mesh]) OR "Prospective Studies"[Mesh]) OR "Incidence"[Mesh]