



Family determinants as a risk factor for chronic obstructive pulmonary disease: a systematic review

Ana Martins,¹ Susana Vasques,² Paulo Santos³⁻⁴

ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a preventable respiratory disease, with repercussions in quality of life. Worldwide COPD is a leading cause of mortality. Cigarette smoking is the most debated risk factor, but it's important to identify other determinants at stake. Family context and behaviors have an impact on the individual's health.

Objective: This systematic review aims to characterize family determinants as possible risk factors for the development of COPD.

Methods: A systematic search was conducted in PubMed, followed by a three-step selection process. Data were processed by two independent reviewers and studies were gathered based on pre-defined variables. English written, articles about risk factors for COPD related to the familiar context, meta-analysis, case-control, cohort, and cross-sectional studies were included. The family determinants considered were childhood maltreatment, education level of the patient, socioeconomic status and family history of tobacco.

Results: From 196 references retrieved, inclusion and exclusion criteria were applied, and eight studies were included. This review found six articles about education, one about socioeconomic status, one about family history of tobacco and one about childhood maltreatment as possible risk factors. One of the studies was a meta-analysis that did not contain any of the other studies included.

Conclusions: Little evidence is available on the effect of family determinants in the development of COPD. The studies reported an association between COPD and low socioeconomic status and low education and interaction with childhood maltreatment.

Keywords: Chronic obstructive pulmonary disease; Family; Risk factors.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined by airflow obstruction that is not fully reversible. It is a preventable and treatable common respiratory disease.¹ Spirometry is used as a diagnostic tool and the presence of a post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of COPD.¹

Worldwide COPD is a leading cause of morbidity and mortality.²⁻³ In 2010, the number of cases of COPD was estimated to be 384 million, with a global prevalence of 11.70% (CI95%, 8.40-15.00%).⁴ According to the World Health Organization (WHO), COPD is the fourth cause of death in the world.⁵ About 3 million people die every year with COPD and it is expected that, by 2030, it will be the third leading cause of death worldwide.⁶⁻⁷

Cigarette smoking is the most debated known risk factor for COPD. However, COPD also develops in non-smokers.⁸ Besides, the burden of COPD is still increasing even though the smoking rate has recently decreased.⁹

Besides the genetic factors, there are many environ-

1. Faculdade de Medicina, Universidade do Porto.

2. Médica Interna de Medicina Geral e Familiar. USF Ermesinde, ACeS Grande Porto III – Maia/Valongo.

3. Departamento de Medicina da Comunidade, Informação e Decisão em Saúde (MEDCIDS). Faculdade de Medicina, Universidade do Porto.

4. Centro de Investigação em Tecnologias e Serviços de Saúde (CINTESIS). Universidade do Porto.

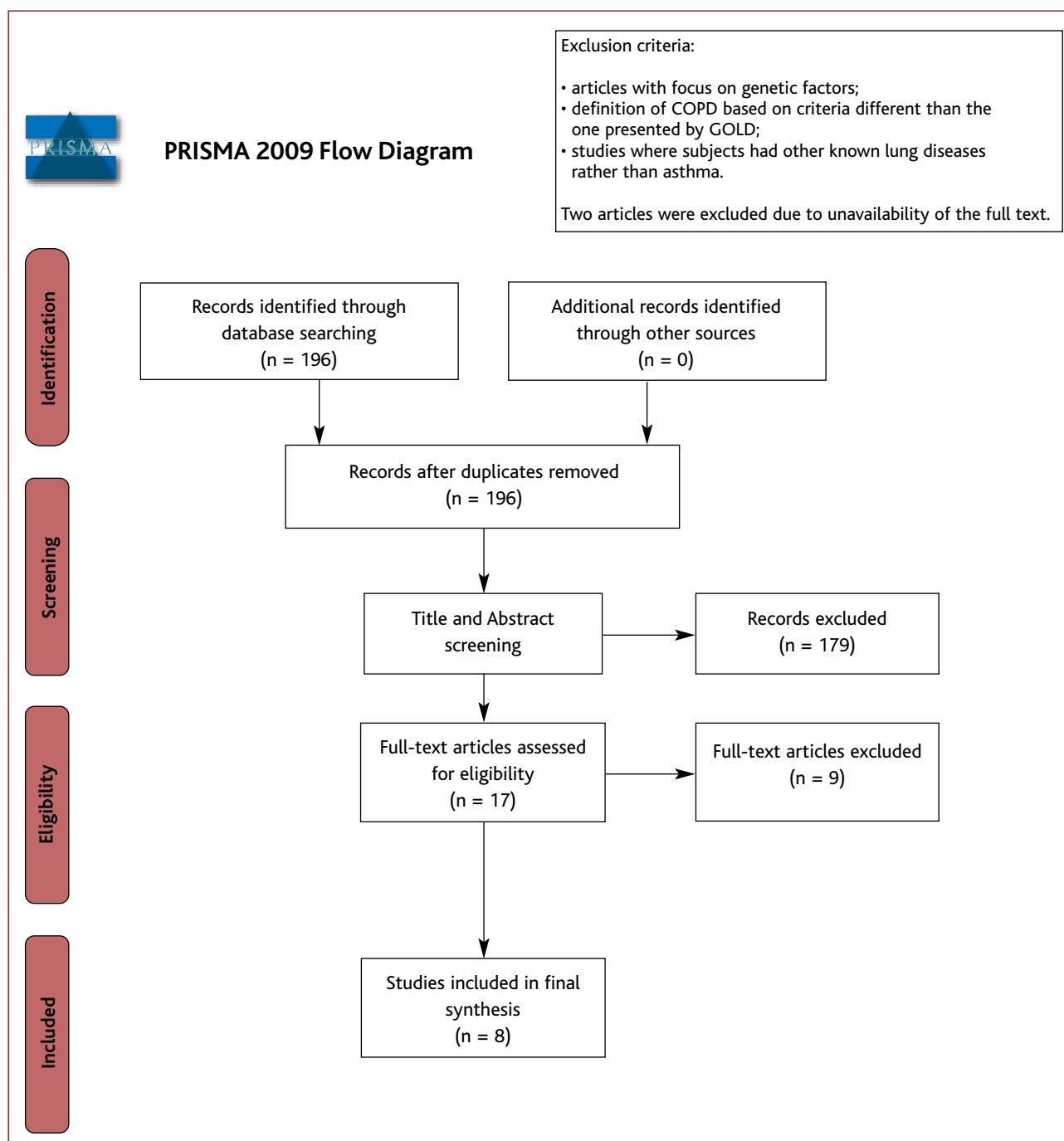


Figure 1. PRISMA flow diagram of article selection.

mental factors associated with the incidence of COPD. Factors that influence disease development include age and sex, exposure to particles, infections, lung growth and development. The role of childhood maltreatment,

education, socioeconomic status and family history of tobacco is still open to debate.¹

Social determinants of health represent conditions in which individuals are born and live that play an

TABLE I. Data from individual studies

Author Date	Type of article	Description of the article	Nr. of studies	Total cases	Total controls
Yang <i>et al.</i> (2017)	Systematic review and meta-analysis	Identify risk factors for COPD among adults in Chinese mainland Case control or cohort design studies	9	3,861	4,319
Ding <i>et al.</i> (2015)	Case control study	Study the risk factors for COPD in Li population in Hainan Province > 40 years by random sampling between 2012 and 2014	1	277	307
Zhou <i>et al.</i> (2009)	Cross-sectional study	COPD in Chinese nonsmokers \geq 40 years Data of 12,471 nonsmokers and 1,024 smoking COPD patients were analyzed	1		
Hooper <i>et al.</i> (2012)	Cross-sectional study	BOLD study 14 countries			
Hersh (2011)	Case control study	Non-Hispanic white and non-Hispanic black Age 45-50 years	1	821	776
Johannessen (2012)	Case control study	Age: 40-79 years Cases – post-bronchodilator FEV1/FVC < 0.7 – and controls – normal spirometry. Patients performed extensive questionnaires regarding some risk factors for COPD, which included level of education	1	433	325
Grisbgy (2015)	Cohort study	Age: 35-95 years Spirometry was performed in all participants 11,042 participants			
Shields (2016)	Cohort study	15,902 respondents to the 2012 Canadian Community Health Survey 3 types of CM: CPA, CSA and CEIPV Checklist of conditions: chronic bronchitis, emphysema or COPD			

Notes: CEIPV = childhood exposure to intimate partner violence; CI = confidence interval; CM = childhood maltreatment; CPA = childhood physical abuse; CSA = childhood sexual abuse; OR = odds ratio; SES = socio economic status.

* After adjustment for the effect of smoking. Effect per group, assuming a linear effect over the four groups of highest level of education: none, primary (primary or middle school); secondary (secondary school); tertiary (technical/vocational college or university).

**Adjusted for age.

‡ - Adjusted for age, other sociodemographic factors, smoking status, and mental and substance use disorders.



Studied Variable and Results

Low Education level (≤ 9 years)

OR=1.609 (CI95%, 1.206-2.147; $p=0.001$)

Education level

OR=0.50 (CI95%, 0.31-0.82; $p=0.000$)

Control: \leq elementary school

Group: \geq middle school

Education level

0 year: OR=1.44 (CI95%, 0.95-2.17; $p=0.001$)

1-9 years: OR=1.97 (CI95%, 1.28-3.02; $p=0.001$)

≥ 10 years: OR=1

Education level*

OR=0.81 (CI95%, 0.74-0.89; $p<0.001$)

Education level

Attended-college or technical school: 488 (59.4%) cases subjects. 557 (71.8%) control subjects

Attended-college or technical school: OR=0.48 (0.37-0.61); $p<0.001$

Family History of Smoking

Parental history of smoking: 693 (85.5%) case subjects, 636 (82.9%) control subjects

Parental history of smoking: OR=1.22 (0.82-1.83); $p=0.32$

Education level

Higher, n (%) 41 (10) case. 75 (25) control

Intermediate, n (%) 263 (65) case. 185 (62) control

Lower, n (%) 102 (25) case. 39 (13) control

After adjusted analysis:

♀ Intermediate: OR=1.39 (0.57-3.37)

Lower: OR=1.86 (1.01-3.42); $p<0.05$

♂ Intermediate: OR=2.68 (1.10-6.53); $p<0.05$

Lower: OR=1.03 (0.51-2.07)

Socioeconomic status

Monthly household income: OR=0.96 (0.93, 0.99); $p=0.01$

Median household size: OR=1.08 (0.90, 1.30); $p=0.42$

Secondary school or higher: OR=0.73 (0.55, 0.98); $p=0.04$

Composite SES index: OR=1.23 (1.05, 1.43); $p=0.01$

Childhood maltreatment

♀ CPA: OR=1.78 (CI95%, 1.27-2.5; $p<0.01$) **

CSA: OR=1.45 (CI95%, 1.04-2.01; $p<0.05$) ||

CSA severe and frequent (≥ 3 times) 1.73 (CI95%, 1.05-2.84; $p<0.05$) ||

CEIPV: OR=1.70 (CI95%, 1.07-2.70; $p<0.05$) ||

♂ CEIPV: OR=2.08 (CI95%, 1.32-3.25; $p<0.01$) **

Severe and frequent CPA: OR=2.64 (CI95%, 1.32-3.25; $p<0.05$) **

active role in their health. These include situations like early childhood experiences and development, social support and educational opportunities. Therefore, family context and behaviors have an impact in the individual's health.¹⁰

Primary care plays a crucial role in the continuity of care, since the early onset of risk factors to the development and progression of COPD, putting it in the best position to act preventively, especially in high-risk individuals and their respective families. Tobacco smoking and environmental exposure to pollutants are quite known factors. It is important to identify other determinants at stake. The aim of this review is to characterize family determinants as possible risk factors for the development of COPD in order to early detect high-risk individuals.

METHODS

A systematic search was conducted in PubMed between November 10 and January 22, 2019, using as a query a combination of 'family', 'risk factors' and 'Pulmonary Disease, Chronic Obstructive'. English written articles and articles performed in humans were included. No time limits were applied. Subsequently, a selection process was carried out in three stages. The data was processed by two independent reviewers and the information was collected based on pre-defined variables. In the first step, titles and abstracts were selected, and articles proceeded to the second stage after the inclusion by at least one reviewer. Within the second stage, full-text was evaluated and the disagreements were discussed and solved by consensus.

Inclusion criteria were: articles about risk factors for COPD related to the familiar context, case-control studies, cohort studies, meta-analysis, and cross-sectional studies. Exclusion criteria were: articles with a focus on genetic factors; those in whom COPD defined by spirometry was explicitly based on spirometric criteria different than the one presented by GOLD; studies where subjects had other known lung diseases except asthma.

Data on the significance of each study were pooled, with a statistically significant value defined as $p<0.05$. This review was performed based on Items Preferred Reports for Systematic Reviews and Guidance Indicators for Meta-Analyses (PRISMA).¹¹ PRISMA checklist is available on supplementary file.



RESULTS

From 196 references retrieved, inclusion and exclusion criteria were applied, and eight studies were included in the final revision. The flow diagram summarizing the study identification and selection is shown in Figure 1. This review found six articles about education, one about socioeconomic status, one about family history of tobacco and one about childhood maltreatment as possible risk factors for COPD (Table I). One of the studies was a meta-analysis that did not contain any of the other studies included. In seven studies, COPD was defined by post-bronchodilator spirometry criteria ($FEV_1/FVC < 0.7$). In another study, the presence of COPD was only based on questionnaire answers.

Education level

All six studies showed an association between low educational level and COPD.

One of the studies showed that lower educational achievement was associated with COPD in women (OR=1.86; CI95%, 1.01-3.42; $p < 0.05$). In men, the level of education was also a risk factor for COPD (OR=2.68; CI95%, 1.10-6.53; $p < 0.05$).¹² However, the categorization of education level is not explicit enough.

Education level equal or inferior to ninth grade was a risk factor for COPD.¹³

Low educational level was associated with stages I-IV COPD in non-smokers. Stage 0 was not found to be associated with education to the same degree as stages II or higher and stage I. Lower educational level was a risk factor for non-smoking COPD patients (0 years: OR=1.44; CI95%, 0.95-2.17, and 1-9 years: OR=1.97; CI95%, 1.28-3.02).¹⁴ It should be noted that stage 0 (chronic obstruction with preserved lung function) is no longer part of the GOLD criteria for COPD. A higher level of education was strongly and significantly associated with less disease (OR=0.81; CI95%, 0.74-0.89; $p < 0.001$).¹⁵

In other study, high educational level (defined as middle school or higher) seemed to be protective for COPD (OR=0.50; CI95%, 0.31-0.82; $p < 0.001$), but it didn't confirm after the adjustment in a multivariate model including exposure to pollutants.¹⁶

Socioeconomic status

One study evaluated the relation between socioeco-

nomical status and COPD. Lower composite socioeconomic status index was associated with higher odds of having COPD (OR=1.23; CI95%, 1.05-1.43; $p = 0.01$), and higher household income showed to be protective (OR=0.96; CI95%, 0.93-0.99; $p = 0.01$). However, the authors were not able to adjust for occupation, which could influence the association between socioeconomic status and COPD.¹⁷

Family history of smoking

The relationship between parental history of smoking and childhood environmental tobacco smoke exposure was studied. Although the history of smoking in the relatives is very common (more than 80%), it didn't seem to be a significant predictor of COPD (OR=1.22; CI95%, 0.82-1.83; $p = 0.32$).¹⁸

Childhood maltreatment

COPD was related to childhood maltreatment in children according to sex. Among women, the binary childhood physical abuse was significantly associated with COPD after controlling for age (OR=1.78; CI95%, 1.27-2.5; $p < 0.01$). A dose-response relationship was found between childhood physical abuse and COPD when severity and frequency were considered (OR=3.51; CI95%, 1.82-6.77, for severe and frequent childhood physical abuse and OR=2.44; CI95%, 1.50-3.98, for severe childhood physical abuse, ≤ 10 times). After fully adjustment controlling for smoking status and other covariates, the association persisted both with childhood sexual abuse (OR=1.45; CI95%, 1.04-2.84; $p < 0.05$) and childhood exposure to intimate partner violence (OR=1.70; CI95%, 1.07-2.7; $p < 0.05$), but not with childhood physical abuse. The authors also noticed that, among females that never smoked, childhood physical abuse and childhood exposure to intimate partner violence were associated with COPD, but not childhood sexual abuse (childhood physical abuse, OR=2.29; CI95%, 1.17-4.47; $p < 0.05$; childhood exposure to intimate partner violence, OR=3.15; CI95%, 1.26-7.91; $p < 0.05$).

Among males, COPD was associated with childhood exposure to intimate partner violence (OR=2.08; CI95%, 1.32-3.25; $p < 0.01$) and severe and frequent childhood physical abuse (OR=2.64; CI95%, 1.32-3.25; $p < 0.05$) but this association did not persist after the fully adjusted model. The authors found that smoking and mental



and substance use disorders were important mediators in associations between childhood maltreatment and COPD. The associations that persisted after the full adjustment suggest that other pathways may be involved in the associations between childhood maltreatment and COPD.¹⁹

This systematic review assessed family determinants as a risk factor for the development of COPD. We considered family determinants such as childhood maltreatment, education level, socioeconomic status and family history of tobacco. According to the data available, low socioeconomic status is associated with the development of COPD.²⁰⁻²¹

All six articles about education level showed an association between a lower level of education and the development of COPD. One showed no significant correlation with education, suggesting it isn't a high-risk factor for COPD.¹⁶ The association between family history of smoking and COPD was not significant.¹⁸ One article found that smoking and mental and substance use disorders were important mediators in the associations between childhood maltreatment and COPD.¹⁹

Therefore, education level and socioeconomic status are important family determinants that play a role in the development of COPD.

Nevertheless, only eight articles were included in the final synthesis and some limitations can be pointed out. The definition of the level of education was not equal between the studies analyzed and in one of the studies, it was not defined. Education is also closely related to socioeconomic status. In one of the studies, socioeconomic status was defined by educational achievement, but it can also be measured by other individual factors. The article about childhood maltreatment refers not only to violence in the family but also in school and neighborhood, so we cannot attribute the entire effects to the role of the family. Also, it is prone to recall bias, which could have interfered with the associations between childhood maltreatment, smoking, and COPD.

This systematic review has a few limitations. Due to the heterogeneity of the data collected, we could not perform a quantitative meta-analysis. Also, neither a publication bias nor quality assessments were performed. Nevertheless, our conclusions are an appropriate summary of the current evidence available on this topic.

CONCLUSION

Little evidence is available on the effect of family behaviors or environment conditionings in the development of Chronic Obstructive Pulmonary Disease, a preventable cause of chronic morbidity and mortality.¹ The studies gathered reported an association between COPD and low socioeconomic status and with low education and interaction with childhood maltreatment. Although tobacco and environment exposure to pollutants are the main factors to pay attention in the risk estimation for COPD, it is important to identify other potential conditioners, especially in primary prevention, selecting those patients to stress the tobacco eviction and cessation and to protect from hostile environments, such as low socioeconomic status and low education.

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CONFLICT OF INTERESTS

The authors declare they do not have any conflict of interests.

CORRESPONDING AUTHOR

Ana Martins

E-mail: anainesvm@gmail.com

<https://orcid.org/0000-0003-1799-3048>

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Supplementary file PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	NA
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., web address), and, if available, provide registration information including registration number.	4



Supplementary file (continuation)
PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
METHODS			
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	NA
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	NA
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.	NA
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5; Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12;13; Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	NA
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	5;6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA



Supplementary file (*continuation*)
PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
RESULTS			
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	6;7
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	6:7
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	8
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	NA

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. *PLoS Med.* 2009;6(7): e1000097

RESUMO

DETERMINANTES FAMILIARES COMO FATOR DE RISCO PARA DOENÇA PULMONAR OBSTRUTIVA CRÓNICA: UMA REVISÃO SISTEMÁTICA

Introdução: A doença pulmonar obstrutiva crónica (DPOC) é uma doença respiratória evitável, com uma repercussão na qualidade de vida. A DPOC é uma das principais causas de morte. O tabaco é o fator de risco mais debatido, mas é importante identificar outros determinantes. O contexto e comportamentos familiares apresentam um impacto na saúde individual.

Objetivo: Esta revisão sistemática pretende caracterizar determinantes familiares como possíveis fatores de risco para o desenvolvimento de DPOC.

Métodos: Uma pesquisa sistemática foi conduzida na PubMed, seguida por um processo de seleção com três fases. A informação foi processada por dois revisores independentes e os estudos foram escolhidos com base em variáveis pré-definidas. Estudos em inglês, artigos sobre fatores de risco para DPOC relacionados com o contexto familiar, estudos de meta-análise, casos-controlo, coorte e transversais foram incluídos. Os determinantes familiares considerados foram maus tratos na infância, nível socioeconómico, educação e história familiar de tabaco.

Resultados: Após a aplicação de critérios de inclusão e exclusão foram incluídos oito artigos de 196 encontrados. Esta revisão encontrou seis artigos sobre educação, um sobre o nível socioeconómico, um sobre história familiar de tabaco e um sobre maus tratos na infância como possíveis fatores de risco. Um dos estudos consiste numa meta-análise, a qual não inclui os outros estudos.

Conclusões: Existe pouca evidência disponível sobre o efeito de determinantes familiares no desenvolvimento da DPOC. Os estudos incluídos mostraram uma associação entre DPOC e um baixo nível educacional e baixo nível socioeconómico e uma interação com abusos na infância.

Palavras-chave: Doença pulmonar obstrutiva crónica; Família; Fatores de risco.