Prevalence of chronic obstructive pulmonary disease in the global population with HIV: a systematic review and meta-analysis

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Summary

Background In recent years, the concept has been raised that people with HIV are at risk of developing chronic obstructive pulmonary disease (COPD) because of HIV infection. However, much remains to be understood about the relationship between COPD and HIV infection. We aimed to investigate this association by assessing studies that reported the prevalence of COPD in the global population with HIV.

Methods In this systematic review and meta-analysis, we assessed observational studies of COPD in people with HIV. We searched PubMed, Embase, Web of Science, and Global Index Medicus, with no language restriction, to identify articles published until June 21, 2017, and we searched the reference lists of the retrieved articles. Eligible studies reported the prevalence of COPD or had enough data to compute these estimates. We excluded studies in subgroups of participants selected on the basis of the presence of COPD; studies that were limited to other specific groups or populations, such as people with other chronic respiratory diseases; and case series, letters, reviews, commentaries, editorials, and studies without primary data or an explicit description of methods. The main outcome assessed was prevalence of COPD. Each study was independently reviewed for methodological quality. We used a random-effects model to pool individual studies and assessed heterogeneity (I^2) using the χ^2 test on Cochrane's Q statistic. This study is registered with PROSPERO, number CRD42016052639.

Findings Of 4036 studies identified, we included 30 studies (151 686 participants) from all WHO regions in the meta-analysis of COPD prevalence. 23 studies (77%) had low risk of bias, six (20%) had moderate risk of bias, and one (3%) had high risk of bias in their methodological quality. The overall prevalence of COPD was 10·5% (95% CI 6·2–15·7; I^2=97·2%; six studies) according to the lower limit of normal definition of COPD, and 10·6% (6·9–15·0; 94·7%; 16 studies) according to the fixed-ratio definition. COPD prevalence was higher in Europe and among current and ever smokers, and increased with level of income and proportion of participants with detectable HIV viral load. Prevalence of COPD was significantly higher in patients with HIV than in HIV-negative controls (pooled odds ratio 1·14, 95% CI 1·05–1·25, I^2=63·5%; 11 studies), even after adjustment for tobacco consumption (2·58, 1·05–6·35, 74·9%; four studies).

Interpretation Our findings suggest a high prevalence of COPD in the global population with HIV, and an association with HIV. As such, COPD deserves more attention from HIV health-care providers, researchers, policy makers, and stakeholders for improved detection, overall proper management, and efficient control of COPD in people with HIV. Efforts to address this burden should focus on promoting the decrease of tobacco consumption and adherence to highly active antiretroviral therapy to reduce viral load.

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See Comment page e126

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable, non-curable, and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation due to airway or alveolar abnormalities, which are usually caused by substantial exposure to noxious particles or gases.[1] The chronic airflow limitation that characterises COPD is caused by a mixture of diseases of the small airways (eg, obstructive bronchiolitis) and parenchymal destruction (eg, emphysema).[1] COPD is one of the major contributors to global years of life lost, with attributable death rates ranked third worldwide in 2010; it is projected to be the fifth largest in terms of disease burden, and the fourth largest cause of death by 2030.[2–4] The total number of estimated COPD-related deaths was about 3 million in 2015 (5% of total deaths globally). The major risk factor for COPD is tobacco consumption.[5]

In recent years, the risk of people with HIV developing COPD due to having HIV has increased.[6–8] The widespread use of combined antiretroviral therapy has improved the survival of people with HIV, leading to the emergence of COPD as a noteworthy concern in this population.[8–10] After recent WHO recommendations

Research in context

Evidence before this study

Results from several original observational studies and narrative reviews have suggested that the prevalence of chronic obstructive pulmonary disease (COPD) would be increased in people with HIV and even higher than in the general population. Findings from studies with similar designs also suggested an association between HIV infection and COPD. We could identify no systematic review including a meta-analysis reporting the prevalence of COPD in the global population with HIV, or reporting the association between HIV and COPD, before this study.

Added value of this study

To the best of our knowledge, this study is among the first to assess the prevalence of COPD in the global population with HIV, and the association between HIV infection and COPD in a systematic review, including meta-analyses. By doing so, we can provide an accurate estimate of the prevalence of COPD in people with HIV. Using strong and robust statistical methods, we found an association between HIV and COPD, even after adjustment for tobacco consumption, the leading risk factor for COPD. We have also shown a high prevalence of COPD in HIV-positive individuals. We identified three factors favouring an increase in the prevalence of COPD among HIV-positive people: tobacco consumption (a common factor between people with HIV and the general population), the presence of a detectable HIV viral load (in HIV-positive people only), and country level of income. We found that the prevalence of COPD in HIV-positive people increased with the level of income of the country. This finding should be further investigated in future studies.

Implications of all the available evidence

We expect that findings from this research will prompt implementation of appropriate policy towards improving awareness, regular diagnosis, and proper management of COPD in HIV-positive people worldwide. We advocate actions leading to a reduction in tobacco consumption. In the absence of sufficient evidence on the role of antiretroviral therapy in the prevention of COPD and in the light of our findings, we also advocate for targeted actions that favour the occurrence of undetectable viral load, including expanding the use of and adherence to antiretroviral therapy.

promoting the initiation of antiretroviral therapy, regardless of age and CD4 cell count, the burden of COPD might be increased in people with HIV because of an increase in life expectancy.[11] HIV infection is a leading cause of morbidity and mortality, with an increasing economic burden,[9] and at the end of 2015, there were 37 million people living with HIV worldwide.[12] Although the high burden of COPD and HIV is clearly known, the relationship between COPD and HIV infection is still not well understood.

To the best of our knowledge, there are no systematic reviews and meta-analyses investigating COPD in HIV-positive populations and addressing the prevalence and association between these diseases. In this study, we aimed to synthesise data on the prevalence of COPD in the global population with HIV and data on the association between exposure to HIV infection and COPD.

Methods

Search strategy and selection criteria

In this systematic review and meta-analysis, we searched PubMed, EMBASE, Web of Science, and Global Index Medicus to identify all relevant cohort, cross-sectional, and case-control studies published on COPD in the global population with HIV, published up to June 21, 2017, without language restrictions. The main search strategy for PubMed is presented in the protocol.[13] This search strategy was adapted to fit with other databases. To supplement these database searches, references of all relevant studies were also screened to identify additional potential data sources.

To be included in this review, primary studies had to be observational studies of people with HIV and report the prevalence of COPD, or have enough data (eg, number of COPD cases and sample size) to compute these estimates. We excluded studies in subgroups of participants selected on the basis of the presence of COPD; studies that were limited to other specific groups or populations, such as people with other chronic respiratory diseases; and case series, letters, reviews, commentaries, editorials, and studies without primary data or explicit description of methods. For studies published in more than one report (duplicates), we considered the most comprehensive study that reported the largest sample size.

Two authors (JJB and AMK) independently screened the titles and abstracts of articles retrieved from the literature search, and the full texts of potentially eligible articles were obtained and further assessed for final inclusion. Disagreements were resolved through discussions between JJB and AMK until a consensus was reached.

Data analysis

Two authors (JJB and AMK) independently extracted relevant information, including first author, publication year and period of participants' recruitment, country of recruitment, site, study design, sampling method, sample size, mean or median age, age range, HIV-related data (eg, time since diagnosis, proportion on antiretroviral treatment, CD4 cell count, proportion with undetectable viral load), proportion of male participants, profile of tobacco smoking, ascertainment of COPD and diagnostic criteria, and the number of participants with COPD. A WHO region and level of income was assigned to each

study according to the country of recruitment. Disagreements were reconciled through discussion and consensus between JJB and AMK. When relevant data were not available, we directly contacted the corresponding author of the study to request the information.

We assessed the methodological quality of included studies for measuring association between exposure to HIV infection and COPD using the Newcastle–Ottawa Scale for non-randomised comparative studies[14] and an adapted version of the risk of bias tool for prevalence studies, which was developed by Hoy and colleagues[15] for prevalence estimates. Two authors (JJB and AMK) independently assessed study quality, with disagreements resolved by consensus or arbitration of a third author (SLA).

We did data analyses using the meta packages of R (version 3.2.2). We calculated unadjusted prevalence of COPD on the basis of crude numerators and denominators provided by individual studies. Only studies with the same diagnostic criteria for COPD were pooled. We used four COPD diagnostic criteria: post-bronchodilator forced expiratory volume in 1s (FEV_1)/forced vital capacity (FVC) ratio (ie, fixed ratio) of less than 0·70; FEV_1/FVC less than 5% of the age-dependent lower limit of normal (LLN); the International Classification of Diseases definition (ICD); and patient-reported COPD.[16,17] The LLN method is recognised as a much more accurate method than the others.[16] To keep the effect of studies with extremely small or extremely large prevalence estimates on the overall estimate to a minimum, we stabilised the variance of the study-specific prevalence using the Freeman–Tukey double arc-sine transformation before pooling the data with the random-effects meta-analysis model.[18] When substantial heterogeneity was detected ($p<0·05$), we did subgroup and meta-regression analyses to investigate the possible sources of heterogeneity. We planned to do a multivariable meta-regression analysis by including study-level factors that were significant (at $p<0·2$) in the model, and in the presence of at least ten (both dependent and independent) variables. For each of the study-level characteristics, we compared different proportions of potential subgroups across the studies. We used the symmetry of funnel plots and did the Egger test to assess the presence of publication and selective reporting bias.[19]

To measure the association between HIV and COPD, we did a meta-analysis using the random-effects method of DerSimonian and Laird[20] to pool weighted odds ratios (OR) of COPD risk estimates. We excluded studies with COPD diagnosed on the basis of patient reporting and included those presenting COPD prevalence data both in HIV-positive and HIV-negative individuals. We did a sensitivity analysis including only studies in which the tobacco consumption was comparable between people with HIV and their control (HIV-negative people). The symmetry of contour-enhanced funnel plots was used to explore publication bias and Harbord test was done to assess the presence of publication bias.[21] Additionally, we did meta-regression to assess the influence of different study factors on the pooled effect estimates. A p value of less than 0·10 was considered indicative of statistically significant publication bias. Heterogeneity across included studies was assessed using the χ^2 test for heterogeneity with a 5% level of statistical significance,[22] and by using the I^2 statistic, for which a value of 50% was considered to imply moderate heterogeneity.[23] Inter-rater agreements between investigators for study inclusion and methodological quality assessment were assessed using Cohen's κ.[24]

This systematic review is registered in the PROSPERO International Prospective Register of systematic reviews, registration number CRD42016052639, and the protocol has been published elsewhere.[13]

Role of the funding source

There was no funding source for this study. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

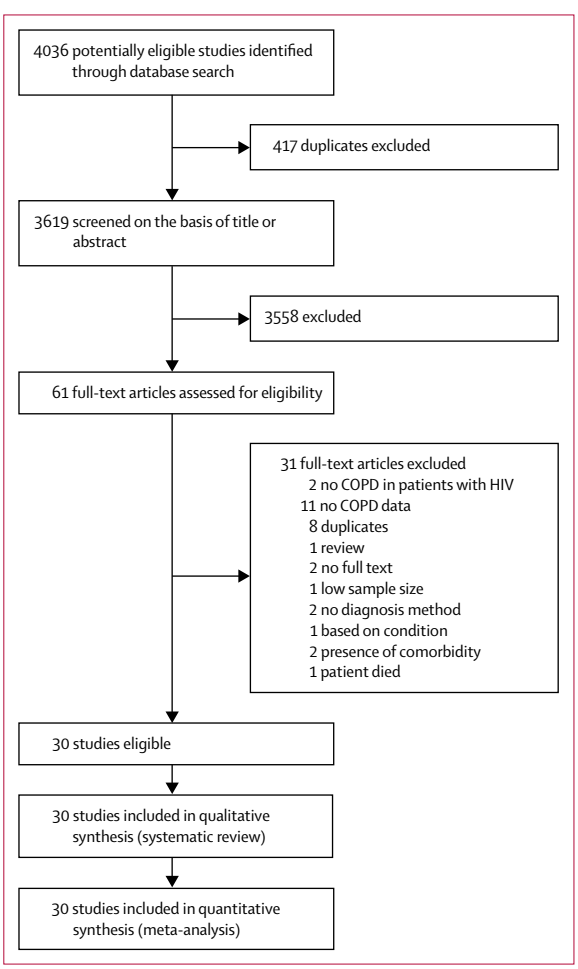

Figure 1: **Study selection**

Results

We initially identified 4036 records. After elimination of duplicates, 3619 records remained. We screened the titles and abstracts and excluded 3558 irrelevant records. Agreement between investigators on abstract selection was κ=0·78. We scrutinised full texts of the remaining 61 papers for eligibility, of which 31 were excluded (figure 1).[25–55] Finally, 30 full texts were included in the meta-analysis (figure 1).[56–85] The inter-rater agreement between investigators was κ=0·93 for study inclusion and κ=0·92 for data extraction.

Table 1 summarises the characteristics of included studies. 18 studies were from the Americas (Canada, Colombia, and the USA),[57–69,71,74,76,81,82] six were from Europe (Denmark, France, Italy, Spain, and UK),[70,72,75,76,79,80] four were from Africa (Cameroon, Nigeria, South Africa, and Uganda),[47,56,77,83] and one was from Japan.[77] One multi-regional study included all WHO regions.[38] The fixed-ratio definition was used in 16 studies,[47,56,61,62,64,66,70,72–73,75,78–81,83] LLN was used in six,[38,47,56,66,75,83] ICD was used in five,[38,47,56,58,66,75,83] and patient-reported criteria were used in nine studies.[59,65,67–69,74,76,77,82] One study was in Spanish.[76]

	Number of studies	Description
Publication year	NA	2006–2017
Period of inclusion of participants	NA	1984–2014
Income of country		
Low income	1	..
Lower-middle income	2	..
Upper-middle income	2	..
High income	24	..
Design		
Cross sectional	28	..
Cross-sectional analysis of cohort study	2	..
Timing of data collection		
Prospective	27	..
Retrospective	3	..
Site		
Hospital-based	24	..
Population-based	6	..
Sampling method		
Random	3	..
Consecutive	23	..
Not described	4	..

Table 1: **Characteristics of included studies**

Mean or median age of participants varied from 33 to 57 years (range 18–101). The proportion of male participants varied from 0 to 100% in all included studies. The proportion of participants who were tobacco smokers at the time of the study varied from 5% to 100%, with 8–29% being former smokers, and 0–87% being never smokers. The proportion of participants with a history of tuberculosis ranged from 1% to 42% (10 studies); history of bacterial bronchopneumonia ranged from 8% to 28% (six studies), and pneumocystis pneumonia varied from 4% to 16% (8 studies). The proportion of injectable-drug users varied from 12% to 44% (14 studies). Median or mean CD4 cell count varied from 139 to 648 cells per mm³ (19 studies). The mean or median time since diagnosis of HIV infection varied from 8 to 17 years (7 studies). Use of antiretroviral therapy varied from 25% to 98% (20 studies). The proportion of regular alcohol use or alcohol use disorder varied from 3% to 60% (11 studies). The proportion of hepatitis C virus infection varied from 12% to 74% (7 studies). The proportion of undetectable viral load varied from 10% to 92% (17 studies).

All 30 studies (n=151 686 participants) were included in the meta-analysis for COPD prevalence (table 2). Regarding methodological quality, 23 (77%) had low risk of bias, six (20%) had moderate risk of bias, and one (3%) had high risk of bias. In all WHO regions, there was an overall prevalence of 10·5% (95% CI 6·2–15·7) according to the LLN definition and 10·6% (95% CI 6·9–15·0) according to the fixed-ratio definition (figure 2). There was symmetry for funnel plots investigating publication bias (appendix, pp 9–12), corroborated by the Egger test (table 2).

In subgroup analyses for regions (appendix, pp 5–6), the prevalence of spirometry-defined COPD was higher in Europe than in other regions (appendix, pp 13–16). Prevalence significantly increased with level of income (appendix, pp 17–20). The prevalence did not differ by sex, regardless of diagnostic criteria used (appendix, pp 21–23). When using fixed-ratio criteria, prevalence increased from never smokers to former smokers to

See Online for appendix

	Studies (n)	Participants (n)	Prevalence (95% CI)	I^2 (95% CI)	p value		
					Heterogeneity	Egger test	Difference criteria
LLN	6	2462	10·5% (6·2–15·7)	92·7% (86·7–95·9)	p<0·0001	p=0·385	p=0·007
Fixed ratio	16	4717	10·6% (6·9–15·0)	94·7% (92·8–96·1)	p<0·0001	p=0·295	..
ICD	6	137 528	5·6% (4·6–6·7)	98·4% (97·7–98·9)	p<0·0001	p=0·248	..
Patient-reported	9	10 455	8·7% (3·3–16·1)	99·1% (98·9–99·3)	p<0·0001	p=0·106	..

Studies are categorised by definition of chronic obstructive pulmonary disease. LLN=post-bronchodilator FEV_1/FVC less than 5% age-dependent lower limit of normal. FEV_1=post-bronchodilator forced expiratory volume in 1 s. FVC=forced vital capacity. Fixed ratio=post-bronchodilator FEV_1/FVC less than 0·70. ICD=International Classification of Diseases.

Table 2: **Summary statistics of chronic obstructive pulmonary disease prevalence in people with HIV**

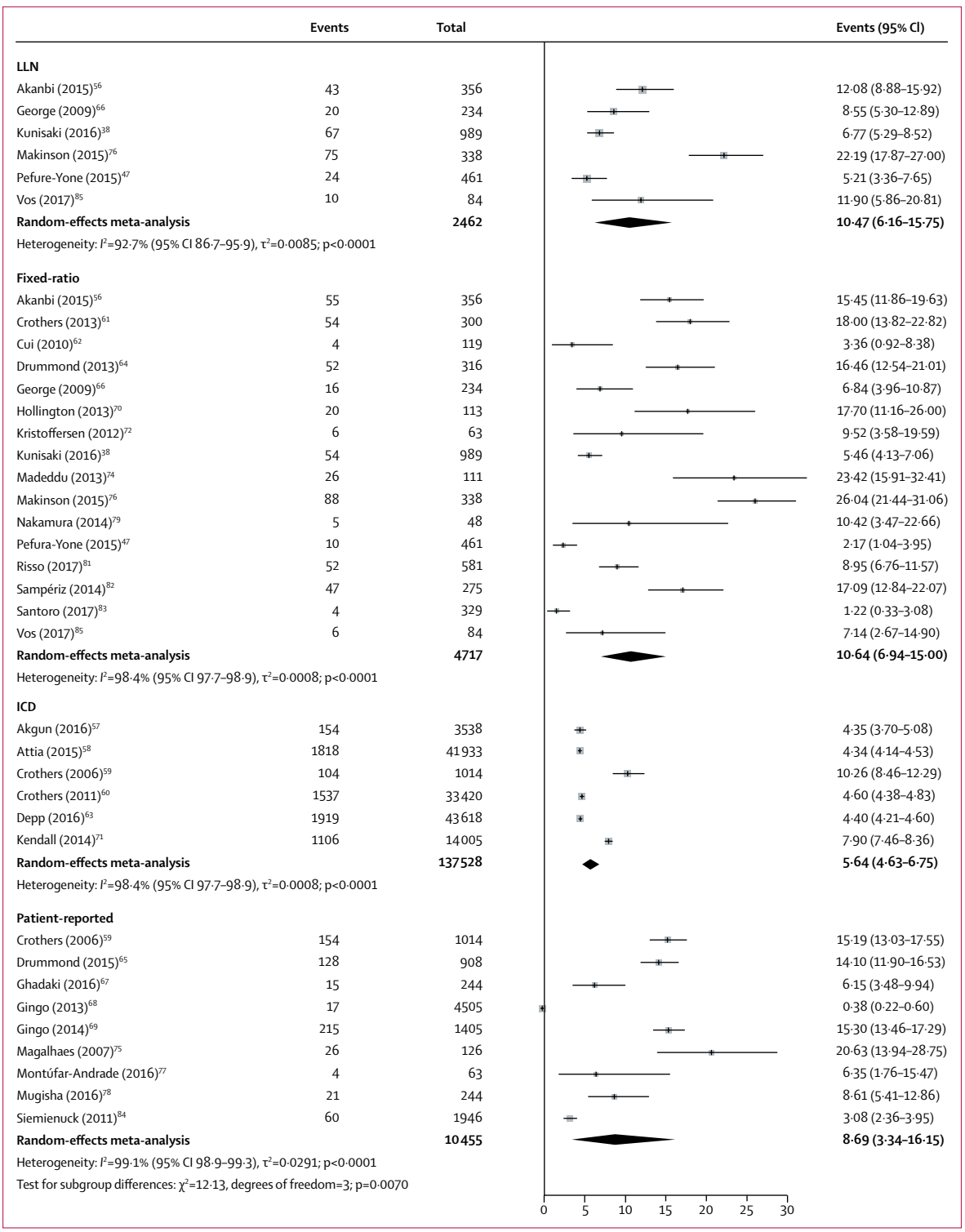

Figure 2: **Random-effects meta-analysis results for prevalence of COPD in the global population with HIV, by diagnostic criteria**
LLN=post-bronchodilator FEV_1/FVC less than 5% age-dependent lower limit of normal. FEV_1=post-bronchodilator forced expiratory volume in 1 s. FVC=forced vital capacity. Fixed-ratio=post-bronchodilator FEV_1/FVC less than 0·70. ICD=International Classification of Diseases.

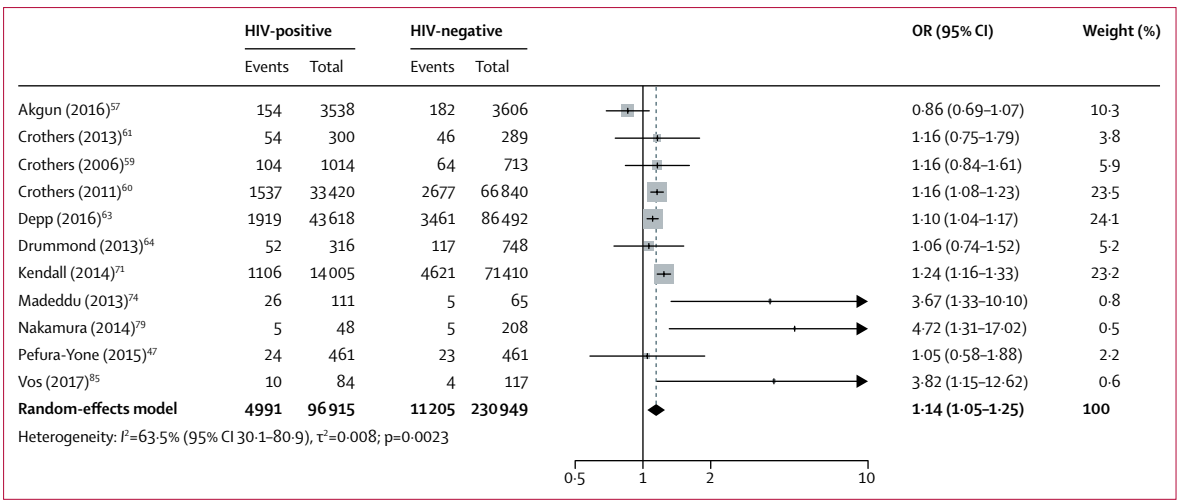

Figure 3: **Forest plot of the association between exposure to HIV infection and COPD**

current smokers (appendix, p 24). Meta-regression was only possible for fixed-ratio criteria. The prevalence of COPD increased with the proportion of current smokers, ever smokers, and detectable viral load (appendix, p 7).

We included 11 studies in the meta-analysis for the measurement of the association between HIV infection exposure and COPD. Prevalence of COPD was significantly higher among patients with HIV than in their HIV-negative counterparts (pooled OR 1·14, 95% CI 1·05–1·25; figure 3). Nine (82%) studies had low risk of bias and two (18%) had moderate risk of bias in their methodological quality. None had high risk of bias. There was most probably missing data on the top left-hand-side of the counter-enhanced plot for publication bias, as confirmed by the Harbord test (p=0·066). This finding increased the plausibility that publication bias is the underlying cause of this funnel asymmetry (appendix, p 26). The sensitivity analysis including only studies with no significant difference in tobacco consumption between HIV-positive and HIV-negative participants (n=4), showed an association between COPD and HIV (pooled OR 2·58, 95% CI 1·05–6·35; I^2=74·9%; appendix, p 25). In the univariable meta-regression analysis, neither study characteristics nor participant characteristics were associated with the OR (appendix, p 8).

Discussion

This systematic review and meta-analysis summarises available evidence on the global prevalence of COPD in people with HIV and the association between HIV infection and COPD. There were several key findings: global prevalence of COPD varies from 5·6% to 10·6% depending on diagnostic criteria used; prevalence of COPD in HIV-positive people was higher in Europe and among current smokers, and increased with detectable HIV viral load and level of income; and there was an association between exposure to HIV infection and COPD even after adjusting for tobacco consumption status.

COPD prevalence differed with respect to diagnostic criteria used. Prevalence was lower when using ICD and patient-reported criteria rather than spirometry-based criteria. This finding can be explained by the fact that COPD can be underreported by patients themselves. In our study, the prevalence of COPD in people with HIV is in the range of that reported in the general population (4–20%).[84] Only direct comparison, as we have done in this study, can allow conclusions to be drawn about a potential difference between COPD prevalence in the general population and in people with HIV. In fact, the use of indirect comparison has many drawbacks. First, the calculation methods can differ. Also, as in the general population, great variability in prevalence can occur between HIV-positive individuals from various study sites, and could explain the high between-study heterogeneity noted, no matter which diagnostic criteria are. The highest prevalence of COPD in Europe could be explained by the fact that, according to WHO 2015 data, the age-standardised prevalence of tobacco smoking was the highest in Europe (27%).[85]

We found that prevalence significantly increased with level of income. This finding should be investigated in future studies. We found a higher prevalence of COPD in HIV-positive current smokers than in former smokers and in those who had never smoked. It is well documented that tobacco is a major cause of COPD both in the general population and in people with HIV.[84,86] Prevalence did not increase with age when fixed-ratio criteria were used. This finding is inconsistent with other studies reporting the association of increasing age and the occurrence of COPD.[5,87] This difference might be explained by the fact that we used fixed-ratio criteria in meta-regression instead of LLN criteria, which consider age. Similar to the general population, we did not find a difference when comparing sex, probably because of

high levels of tobacco smoking among women in high-income countries, and the higher risk of exposure to indoor air pollution (such as solid fuel used for cooking and heating) for women in low-income and middle-income countries.[5] This result counterbalances the high consumption of tobacco in men compared with women, regardless of geographical location.

We also found that the prevalence of fixed-ratio-diagnosed COPD increased with the proportion of participants with detectable viral load and not with CD4 cell count. The presence of viral proteins at the pulmonary level might stimulate the recruitment of leucocytes into the respiratory tract. This stimulation could lead to the production of inflammatory cytokines and chemokines, as well as proteases that cause tissue destruction, airway thickening, and clinical expression of COPD.[9] The absence of an association between CD4 cell count and COPD can be explained by the fact that tissue inflammation in COPD is characterised by the predominance of neutrophils, CD8 cells, and macrophage infiltration, rather than by CD4 cell count.[6,9]

As suggested in narrative reviews,[6,7,9,86,87] exposure to HIV infection is a predisposing factor in COPD. In our study, the association persisted after adjustment for the main cause of COPD, tobacco consumption. Results from studies[6,7,9,86,88] suggest complex interplay mechanisms, including increased consumption of tobacco in patients with HIV, increased susceptibility to lung infections and colonisation, inadequate inflammatory response, increased apoptosis in lung tissue, increased oxidative stress, accumulation of cytotoxic lymphocytes in the lung tissue, recurrent pulmonary infections (especially tuberculosis), low socioeconomic status, and the direct effect of HIV antiretroviral medicines. Unfortunately, because of insufficient data to compare HIV-positive people who are naive to antiretroviral therapy with those who have experience of therapy, it was not possible to investigate the association between COPD and antiretroviral therapy. The unexplained heterogeneity in the pooled estimates could be attributed to study-level factors not considered in our analysis, but mainly because these factors were not assessed in the included studies.

Our findings have important policy implications for the management of HIV because, among the 37 million people living with HIV worldwide,[12] close to 4 million might have COPD. Policy makers should be aware of this to better prepare and strengthen health systems for proper management of this condition in this population, the people of which could have pharmacological interactions of drugs for COPD and antiretroviral therapy. It is well known that antiretroviral therapy can reduce viral load. So, with the introduction of the test and treat WHO policy for HIV care, it is expected that the burden of COPD will be reduced in people with HIV, since our findings show an association between high COPD prevalence and increase in proportion of people with detectable HIV viral load. Furthermore, concrete measures should be taken to act on the risk factors identified by this study, including tobacco smoking. When implementing public health strategies to curb the burden of tobacco smoking, people with HIV might need more attention because of the double burden from HIV infection and consequences of tobacco smoking. Data from Burden of Obstructive Lung Disease Initiative, especially the one including HIV-positive individuals from Malawi, can help to build strategies to curb the COPD burden.[89] Several other reasons could explain the heterogeneity found in our study, including CD8 cell count, use of highly active antiretroviral therapy, history of tuberculosis and pneumocystis pneumonia, second-hand smoking, genetic factors (like α1 antitrypsin deficiency), air pollution, wood smoke and other biomass exposure, and occupational dusts and chemicals. Unfortunately, we were unable to investigate these conditions as a source of heterogeneity because of insufficient data or low number of studies reporting these variables. They might deserve more attention in future studies.

There was no publication bias for prevalence, suggesting that we were unlikely to have missed studies that could alter the findings. There was publication bias for studies reporting data measuring the association between HIV and COPD, suggesting the publication or non-publication of research findings depending on the nature and direction of the results; however, there was no small-study effect on the findings. Included studies that measured the association between HIV infection and COPD were assessed as having low and moderate risk of bias in their methodological quality. Most of the included studies for prevalence estimates of COPD in people with HIV people were assessed as having low risk of bias in their methodological quality. As determined by the meta-regression analyses, methodological quality of studies had no effect on both of the overall estimates.

To the best of our knowledge, this paper is among the first systematic reviews that uses meta-analysis to summarise data about prevalence of COPD in people with HIV. It is also the first to investigate the association between exposure to HIV infection and COPD in a meta-analysis. Strengths of this study include the use of a predefined and published protocol, a comprehensive search strategy, and involvement of two independent investigators in all stages of the review process. Results suggest that we were unlikely to have missed studies that could have altered the meta-analysis results. We used strong and robust statistical methods.

Nevertheless, the findings of this study should be interpreted with caution. Firstly, the meta-regression analysis was based on univariate analyses. Since a small number of studies were included, it was not possible to control for potential confounders simultaneously using multivariable meta-regression analysis. Secondly, all included studies were observational, which could lead to bias because of unmeasured confounders, including

second-hand smoking, genetic factors, and environmental conditions. Third, none of the studies included in this study assessed the relationship between the condition and antiretroviral therapy (difference between patients on antiretroviral therapy and those not on therapy and the specific regimens increasing the risk of COPD). Finally, there were not enough studies for subgroup comparison and most of studies were from settings with low HIV burden. Therefore, the findings in subgroup analyses should be interpreted with caution.

The results of this study suggest a high prevalence of COPD in the global population with HIV, and its association with HIV. As such, COPD should also be prioritised among HIV health-care providers, policy makers and stakeholders from the health sector for improved detection, overall proper management, and efficient control of COPD in people with HIV. This study supports the need for specific strategies to reduce the risk of COPD among HIV-positive people worldwide. Strategies to address this burden should focus on promoting the decrease of tobacco consumption and initiation of highly active antiretroviral therapy to reduce viral load. More studies are needed to identify plausible causal pathways for a better description of the association between HIV infection and COPD, particularly the involvement of antiretroviral therapy, since the future face of HIV epidemiology will change as a result of WHO recommendations to initiate antiretroviral therapy in the test and treat era.

Contributors

JJB, AMK, and SLA conceived the study and designed the protocol. JJB conceived the literature search. JJB and AMK selected the studies. JJB, AMK, and SLA extracted the relevant information. JJB and ATS synthesised and interpreted the data. JJB and AMK wrote the first draft of the paper. JJB, AMK, SLA, and ATS critically revised successive drafts of the paper and approved its final version.

Declaration of interests

We declare no competing interests.

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