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ORIGINAL PAPER

HIV Prevalence Among Tuberculosis Patients in Sub-Saharan Africa: A Systematic Review and Meta-analysis

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Abstract

HIV associated tuberculosis (TB) morbidity and mortality is a major concern in sub-Saharan Africa. Understanding the level of HIV infection among TB patients is vital for adequate response. We conducted a systematic review and meta-analysis to estimate the prevalence of HIV in TB patients in sub-Saharan Africa. We searched PubMed, EMBASE, Web of Science and CINAHL databases. A meta-analysis with a random-effects model was performed. Potential sources of heterogeneity in the prevalence estimates were explored using meta-regression analysis. We identified 68 studies that collectively included 62,969 TB patients between 1990 and 2017. The overall estimate of HIV prevalence in TB patients was 31.8% (95% CI 27.8–36.1). There was substantial heterogeneity in the prevalence estimates in Southern, Central, Eastern, and Western sub-Saharan Africa regions (43.7, 41.3, 31.1 and 25.5%, respectively). We noted an apparent reduction in the estimate from 33.7% (95% CI 27.6–40.4) in the period before 2000 to 25.7% (95% CI 17.6–336.6) in the period after 2010. The Eastern and Southern sub-Saharan Africa region had higher prevalence [34.4% (95% CI 29.3–34.4)] than the Western and Central region [27.3% (95% CI 21.6–33.8)]. The prevalence of HIV in TB patients has declined over time in sub-Saharan Africa. We argue that this is due to strengthened HIV prevention and control response and enhanced TB/HIV collaborative activities. Countries and regions with high burdens of HIV and TB should strengthen and sustain efforts in order to achieve the goal of ending both HIV and TB epidemics in line with the Sustainable Development Goals.

Keywords HIV · TB · Prevalence · Sub-Saharan Africa · Meta-analysis

Introduction

Globally, it is estimated that around 10.4 million tuberculosis (TB) cases occurred in 2016; out of which 1.3 million people died among HIV-negative people with an additional 374,000 deaths among HIV-positive people [1]. Overall, it is also estimated that 1.7 billion people are infected with M. tuberculosis. However, only 5–15% will develop TB disease during their lifetime. The risk of developing active TB differs markedly according to the presence of HIV infection and other risk factors. People living with HIV are 26–31 times more likely to develop active TB than people without HIV [1]. The burden of TB is greater in areas with higher HIV prevalence [2, 3]. The HIV epidemic poses a paramount challenge to TB prevention and control in sub-Saharan Africa. According to the World Health Organization (WHO), there were an estimated 1.2 million new cases of TB amongst people living with HIV in 2016, 71% of whom were living in Africa [1]. The WHO has recommended a package of collaborative TB/HIV activities that will reduce

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the burden of HIV infection in presumptive and diagnosed TB patients by providing: HIV testing and counselling, cotrimoxazole preventive therapy, antiretroviral therapy for HIV-positive TB patients, and other HIV prevention interventions, treatment and care [4].

In many high HIV prevalence settings, concerted measures have been taken to prevent and control HIV/AIDS since 2000. These have reduced the burden of HIV-associated TB morbidity and mortality [5]. In 2016, TB incidence and mortality rates have decreased by an average of 2% and 3% per year, respectively, since 2000. The pace of decline has varied among different WHO regions. In sub-Saharan Africa countries including Ethiopia, Kenya, Lesotho, Namibia, the United Republic of Tanzania, Zambia and Zimbabwe, there has been a decline in TB incidence, TB mortality rate and HIV-associated TB between 1990 and 2017 [6, 7]. Nevertheless, HIV is still challenging TB control efforts and an accelerated response is needed to produce a 4–5% annual decline in order to achieve the "End TB" milestone for the region in 2020 [1].

The accelerated response towards "End TB" targets require consolidated evidence on the burden of HIV in TB patients. Two systematic reviews [8, 9] and one narrative review [10] have been published on the burden of HIV in TB and/or TB in HIV coinfection. However, they do not include all studies done in sub-Saharan African and do not attempt to show HIV prevalence in TB patients distinctly. According to a systematic review and meta-analysis of the global prevalence of HIV/TB and/or TB/HIV co-infection in countries (excluding China) in 2013, the prevalence of co-infection [31.2% (95% CI 19.3–43.2)] in African countries was higher than for the rest of the world [8]. Therefore, it is important to exclusively report HIV prevalence and its trend over time in TB patients in the sub-Saharan Africa where about half of the high TB burden countries are located.

In this study we aimed to systematically review the existing literature and quantify the prevalence of HIV in TB patients over three different distinct time periods across regions in sub-Saharan Africa.

Methods

Search Methods for Identifying Studies

We searched PubMed, EMBASE, Web of Science and CINAHL electronic databases using a predefined search strategy (Supplementary material I). Studies reporting HIV infection in TB patients which were published up to September 14, 2017 were included. In addition to the articles we retrieved from our literature search, we hand-searched the references of all the relevant articles to ensure that we did not exclude eligible studies. Searches were limited to human studies (all age groups) conducted in sub-Saharan Africa countries and published in English language.

Eligibility Criteria

Studies were eligible for inclusion if the prevalence of HIV in TB patients was presented or could be calculated from available data. All study designs including prevalence surveys, and published reports of programmatic activities were included.

Studies were excluded if the language of publication was not English, if they only reported the prevalence (not reported people screened for HIV test and HIV tested positive TB patients), were reviews were conducted in a special population (e.g. miners), or if they only reported prevalence of TB or HIV.

Data Extraction

All searched studies were imported into EndNote X8 database and duplicate records were removed. YG examined studies using the title and abstract to remove irrelevant studies. The full-text of eligible articles was independently retrieved by two authors (YG and YA) for final inclusion using inclusion/exclusion criteria with a predesigned assessment form.

YG and YA extracted information from selected studies using a data extraction form and inconsistencies were resolved by discussion. For each study, information on geographical location, year of publication, study periods, sample size and sampling strategies, study type, clinical form of TB, age group of the study population, and the diagnostic algorithms of TB and HIV were extracted.

Definitions

For the purpose of this analysis, we categorised HIV prevalence by three research periods and two WHO sub-Saharan Africa regions. We further divided the two regions into four. The research period was defined by the duration of the study: before 2000, 2000 to 2010 and after 2010. These periods were set based on key milestones in the HIV/AIDS and TB/HIV control programs. In the early 2000s, ART scale-up commenced in some health facilities in sub-Saharan Africa countries [11]; between 2000 and 2010, TB/HIV collaborative activities were launched, and HIV/AIDS care and treatment services strengthened in sub-Saharan Africa countries [12]. Since 2010 WHO has been updating its HIV/AIDS treatment guidelines to initiate ART with 350 or less than 350 cell counts. Currently people living with HIV have treatment initiated irrespective of CD4-cells count [13].

Geographic location of studies was categorised as Eastern, Southern, Western and Central regions. These regions

were further classified into Central, Eastern, Southern and Western sub-Saharan Africa regions.

Quality Assessment

We used the Newcastle–Ottawa Scale adapted for cross-sectional studies and used by Modesti et al. [14] and Nliwasa et al. [15] to assess the methodological quality of each study. In the scale score of exposure (tuberculosis) and outcome (HIV prevalence in TB patients) measurement of each study was assessed based on the national standard tuberculosis and HIV diagnosis and test procedures of the included countries. Self-reported exposure and outcomes were excluded because TB and HIV disease results are not reported unless confirmed by a health professional. Two stars are given to the studies that assess the outcome (HIV prevalence in active TB patients) with the antibody test and one star is given for medical records linkage to HIV testing (Supplementary Table I).

For each study, the maximum overall score was seven. The overall quality of the studies was categorised into two based on the total scores given using the domain; high quality (studies with an average score or above) and low quality (studies with a score of below average) (Supplementary Table II).

Statistical Analyses

Meta-analysis was undertaken to calculate the pooled HIV prevalence and its 95% CI using a random-effects model (to account for heterogeneity of HIV-prevalence) using the *metafor* package which carries out meta-analysis for proportions in R (version 3.3.3, the R foundation for Statistical Computing, Vienna, Australia).

A meta-analysis for a proportion includes studies that do not use control groups unlike other types of meta-analysis. We also need to transform data to improve the statistical properties [16]. The logit transformation method was used and back-transformed to calculate the final pooled estimate and 95% CI. The Shapiro–Wilk normality test ($W = 0.9811$, p value $= 0.3905$) showed that the transformed data had a normal distribution. Restricted maximum-likelihood estimation (REML) is used to estimate model parameters.

Between-study heterogeneity was assessed with the I^2 statistic, which describes the percentage of variation between studies, compared to the overall variation [17]. An influential study diagnostic test, i.e., Cook's distance (the *influence* function and *baujat plot* in R) was used to identify studies which introduced additional residual heterogeneity [18]. Sensitivity analysis was assessed by removing outliers (higher and lower prevalence) and low quality studies. We checked this using the 'leave one out' approach (*leaveout* function of R) [19].

Subgroup analysis was conducted by assuming a common between-study variance component across sub-groups and meta-regression were used to explore heterogeneity further [20, 21]. Subgroup analysis compared Central (reference category) with Eastern, Western, and Southern sub-Saharan African and research periods (before 2000 compared with between 2000 and 2010 inclusive and after 2010) and type of TB (all forms of TB versus Pulmonary TB).

Potential publication bias was investigated using funnel plots. This was further examined using Begg's test which examines the rank correlation between the log odds ratio and the meta-analysis weight [22]. Trim and fill plot analysis was also used for assessing publication bias.

Data on TB and HIV infections per 100,000 population for each country were obtained from UNAIDS and UN Millennium Development Goals databases [23, 24] and used to extract national estimates for the year of completion of the study period. We included significant variables ($p < 0.05$) into a meta-regression model using the *metareg* function of R [25].

Results

Characteristics of Included Studies

A total of 1, 490 articles were initially identified in our search. After the exclusion of duplicate references (143) and non-relevant studies (1157), a full text review was conducted for 190 articles. Finally, 68 articles were included in the meta-analysis (Fig. 1).

Among the 68 eligible studies published from 1990 to 2017, 26 were conducted before 2000 [26–51] were from 2000 to 2010 [52–81], and 12 were after 2010 [82–93]. With respect to age group, 36 studies included adults, eight studies included children and 24 studies were unclassified. One-third (22 studies) were conducted on pulmonary tuberculosis (PTB) and 46 studies were not classified by type of TB. Two studies estimated prevalence in special populations: pregnant women [63] and prisoners [88]. The sample size of the studies ranged from 74 to 10, 612, with a combined total of 62,969 TB patients included to estimate HIV prevalence in TB patients. HIV prevalence was 32.5% (95% CI 24.8–41.2) among PTB patients and 31.5% (95% CI 27–34.4%) among uncategorised TB patients.

More than half of included studies were from the Eastern region; eighteen were in Ethiopia [26, 44, 48, 51, 53, 59, 63, 67, 72, 75, 77, 78, 80, 81, 83, 84, 88, 90], seven in Tanzania [32, 37, 38, 47, 60, 71, 79], five in Kenya [31, 62, 65, 73, 74], one in Eretria [61] and one in Uganda [28]. Twelve articles were included from the Southern region; four in South Africa, four in Zambia [30, 34, 64, 91], two in Zimbabwe [29, 33], one in Angola [76] and one in Malawi [46].

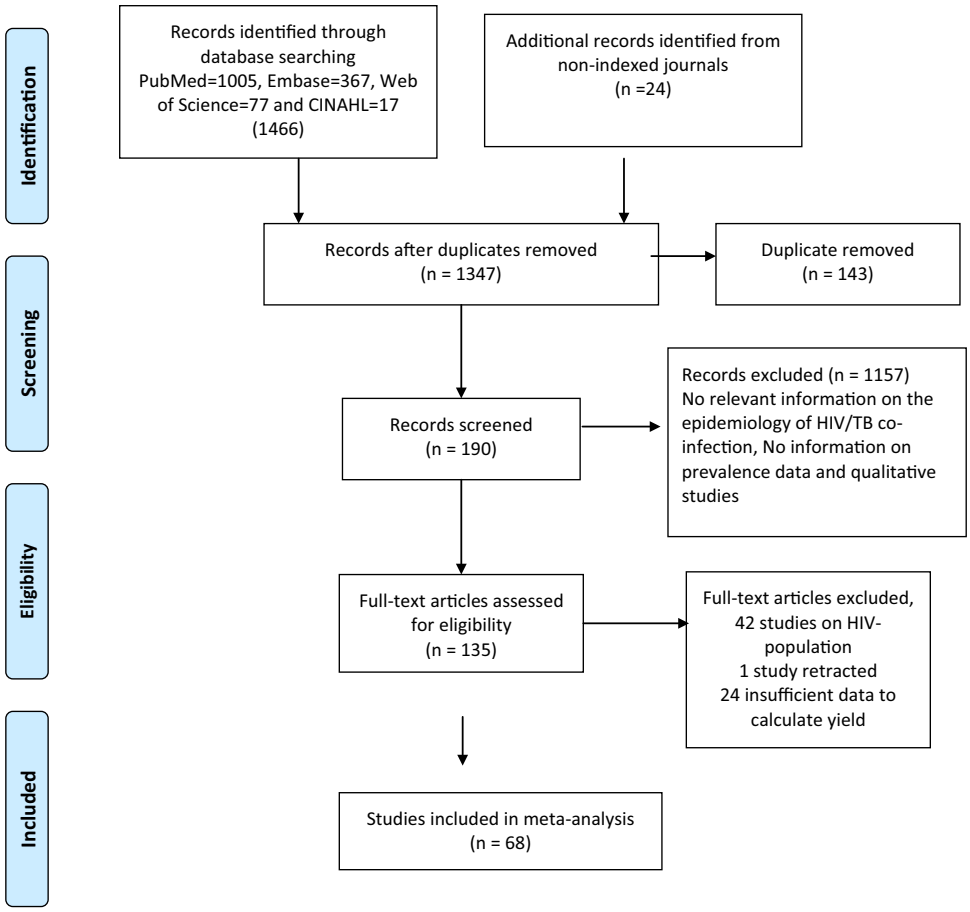

Fig. 1 Flow chart of selection of eligible studies for inclusion in systematic review and meta-analysis of prevalence of HIV in TB patients in sub-Saharan Africa, 2017

Nearly one-third of included studies were from the Western Sub-Saharan Africa region; fourteen in Nigeria [43, 49, 50, 52, 54, 55, 57, 58, 68, 69, 86, 87, 89, 92], three in Cote d'Ivoire [27, 35, 36], two in Ghana [56, 93], one in Burkina Faso [39] and one in Togo [70]. Only three studies were included in the Central sub-Saharan Africa regions; two in Cameroon [66, 82] and one in Republic of Congo [85] (Table 1).

Prevalence of HIV in Tuberculosis Patients

The overall estimates of HIV prevalence ranged from 6% in Ethiopia [88] to 72% in Zambia [64] study. Most estimates were between 20 and 30% of the population. Low estimates (less than 20%) occurred in 16 studies [26, 28, 35, 43, 49, 50, 52–54, 58, 61, 63, 75, 87, 88, 93]. Forty-four studies presented age-specific HIV prevalence. The prevalence among children and adults were 31.4% (95% CI 17.1–50.2) and 31.1% (95% CI 26.5–36.0), respectively.

The overall estimates of HIV prevalence in TB patients was 31.8% (95% CI 27.8–36.1) using a random-effects model. The I^2 statistic (98%, $P < 0.01$) indicated substantial heterogeneity among the studies.

The highest HIV prevalence in TB patients was estimated to be in the Southern region, 43.7% (95% CI 35.05–52.70; $I^2 = 99\%$) with a range of 23% [91] to 72% [64] in the Zambia followed by the Central region (41.3%, 95% CI 30.4–51.2; $I^2 = 98\%$) ranging from 31% in Republic of Congo [85] to 51% in Cameroon [66]; Eastern region 31.1% (95% CI 25.4–37.5; $I^2 = 98\%$) ranging from 6% in Ethiopia to 60% [88] in Kenya [65] and Western region 25.5% (95% CI 19.7–32.3; $I^2 = 98\%$) ranging from 12% [43] to 72% in the Nigeria [86] (Fig. 2).

There were an apparent reduction in prevalence of HIV in TB from before 2000, [33.7% (95% CI 27.6–40.4); $I^2 = 98\%$, $p < 0.01$) to after 2010, 25.7% (95% CI 17.6–36.0); $I^2 = 98\%$, $p < 0.01$)] (Fig. 3).

HIV prevalence in TB patients was 34.41% (95% CI 29.27–39.94%) in Eastern and Southern regions and 27.30% (95% CI 21.63–33.82%) in Western and Central regions of sub-Saharan Africa. A significant decline was observed in Southern and Eastern Africa region, where HIV prevalence is highest, from before 2000, 38.15% (95% CI 31.25–45.55, $I^2 = 97\%$), to after 2010, 18.87%, 95% CI 11.01–30.42, $I^2 = 95\%$) (Fig. 4).

In the Western and Central region, where HIV prevalence is relatively low, an increase was observed from before 2000,

Table 1 Characteristics of included studies in systematic review and meta-analysis of prevalence of HIV in TB patients in sub-Saharan Africa, 1990–2017

Study	Location	Research period	Age group	Study design	Types of TB	Presumptive and diagnosis TB (n)	HIV positive TB patient, n (%)
Eastern, sub-Saharan Africa							
Hailu et al. [26]	Ethiopia	1988–1989	Adult	Retrospective	PTB	106	7
Migliori et al. [28]	Uganda	1987–1989	All age	Case–control	All forms	323	59
Nunn et al. [31]	Kenya	1985–1990	Adult	Retrospective	All forms	161	37
Van den Broek et al. [32]	Tanzania	1991	Adult	Case–control	All forms	441	132
van Cleeff et al. [37]	Tanzania	1990	Adult	Case–control	All forms	128	66
Chum et al. [38]	Tanzania	1991–1993	Adult	Prevalence survey	All forms	6715	2139
Demissie et al. [44]	Ethiopia	1998–1998	Adult	Cross-sectional	PTB	236	107
Range et al. [47]	Tanzania	1994–1998	Adult	Prevalence survey	All forms	10,612	4653
Bruchfeld et al. [48]	Ethiopia	1996	Adult	Case–control	PTB	168	96
Yassin et al. [53]	Ethiopia	2002	All age	Prospective study	All forms	500	97
Van der Werf et al. [61]	Eritrea	2004–2005	Adult	Cross-sectional	All forms	220	26
Kassu et al. [59]	Ethiopia	2003	Adult	Cross-sectional	All forms	257	134
Range et al. [60]	Tanzania	2001–2002	Adult	Cross-sectional	PTB	532	232
Datiko et al. [63]	Ethiopia	2004–2005	Adult	cross-sectional	All forms	1308	226
Odhiambo et al. [65]	Kenya	2003–2005	All age	Cross-sectional	All forms	2193	1327
Chakaya et al. [62]	Kenya	2002–2006	All age	Cross-sectional	PTB	732	372
Ayenew et al. [67]	Ethiopia	2009	Adult	Case–control	All forms	235	85
Ligidi et al. [72]	Ethiopia	2007	Adult	Cross-sectional	All forms	258	68
van't Hoog et al. [73]	Kenya	2006–2007	Adult	Prevalence survey	PTB	101	52
Kamenju et al. [71]	Tanzania	2008–2009	All age	Retrospective	PTB	205	103
Nyamogoba et al. [74]	Kenya	2007–2009	All age	Cross-sectional	All forms	274	117
Teklu et al. [75]	Ethiopia	2004 to 2008	All age	Retrospective	All forms	459	36
Yadeta et al. [83]	Ethiopia	2009–2011	Adult	Cross-sectional	All forms	668	215
Kebede et al. [77]	Ethiopia	2009–2010	Adult	Cross-sectional	All forms	353	137
Keflie et al. [78]	Ethiopia	2007	All age	Cross-sectional	PTB	335	96
Mihret et al. [80]	Ethiopia	2007–2010	Adult	Cross-sectional	PTB	418	97
Denegetu et al. [84]	Ethiopia	2011	Adult	Cross-sectional	All forms	579	117
Kishimba et al. [79]	Tanzania	2006–2010	Children	Retrospective	All forms	2284	905
Belay et al. [81]	Ethiopia	2009–2010	Adult	Cross-sectional	PTB	99	40
Gebrecherkos et al. [88]	Ethiopia	2015	Adult	Cross-sectional	PTB	282	17
Tarekegne et al. [90]	Ethiopia	2009–2012	All age	Retrospective	All forms	2005	404
Gellete et al. [51]	Ethiopia	1993–1994	Adult	Cross-sectional	All forms	450	199
Southern, sub-Saharan Africa							
Pozniak et al. [29]	Zimbabwe	1988–1989	Adult	Retrospective	All forms	906	363
Chintu et al. [30]	Zambia	1990–1991	Children	Case–control	All forms	237	88
Luo et al. [34]	Zambia	1991–1992	Children	Cross-sectional	All forms	120	67
Houston et al. [33]	Zimbabwe	1988–1999	Adult	Case–control	All forms	1434	610
Colvin et al. [40]	South Africa	1998	All age	Cross-sectional	PTB	182	56
Karstaedt et al. [41]	South Africa	1995–1996	Adult	Retrospective	All forms	412	185
Churchyard et al. [42]	South Africa	1988–1990	Adult	Cross-sectional	All forms	3465	1040
Madhi et al. [45]	South Africa	1996–1997	Children	Prospective study	PTB	161	68
Kiwanuka et al. [46]	Malawi	1998	Children	Cross-sectional	PTB	102	72
Mwinga et al. [64]	Zambia	2004–2006	All age	Cross-sectional	All forms	2072	1497
Valadas et al. [76]	Angola	2007	All age	Retrospective	All forms	1906	712
Chanda-Kapata et al. [91]	Zambia	2013–2014	Adult	Prevalence survey	All forms	151	36

Table 1 (continued)

Study	Location	Research period	Age group	Study design	Types of TB	Presumptive and diagnosis TB (n)	HIV positive TB patient, n (%)
Western, sub-Saharan Africa							
De Cock et al. [27]	Cote d' Ivore	1989–1990	Adult	Cross-sectional	All forms	2043	821
Sassan-Morokro et al. [35]	Cote d' Ivore	1989–1990	Children	Retrospective	All forms	289	34
Richards et al. [36]	Cote d' Ivore	1981–1991	All age	Retrospective	All forms	3271	1426
Malkin et al. [39]	Burkina Faso	1988–1990	Adult	Prospective study	PTB	422	97
Onipede et al. [43]	Nigeria	1995–1996	Adult	Case–control	All forms	79	10
Moses et al. [49]	Nigeria	1997–1998	Adult	Retrospective	PTB	58	11
Daniel et al. [54]	Nigeria	2001–2002	All age	Cross-sectional	PTB	269	40
Ige et al. [55]	Nigeria	1998–2002	All age	Retrospective	All forms	640	180
Daniel et al. [54]	Nigeria	2000–2004	Children	Retrospective	All forms	78	8
Adjei et al. [56]	Ghana	2001	All age	Cross-sectional	PTB	108	51
Odaibo et al. [50]	Nigeria	2000	All age	Cross-sectional	PTB	2752	527
Salami et al. [57]	Nigeria	2000–2004	Adult	Retrospective	All forms	744	297
Daniel et al. [58]	Nigeria	1999–2003	Children	Cross-sectional	All forms	76	8
Dagnra et al. [70]	Togo	2007	Adult	Cross-sectional	All forms	569	135
Erhabor et al. [68]	Nigeria	2006	Adult	Cross-sectional	All forms	120	30
Pennap et al. [69]	Nigeria	2007–2008	All age	Retrospective	All forms	257	106
Gomerep et al. [86]	Nigeria	2009–2011	All age	Retrospective	All forms	305	220
Ojiezeh et al. [87]	Nigeria	2008–2012	All age	Retrospective	PTB	342	58
Ranti et al. [89]	Nigeria	2008–2011	All age	Retrospective	All forms	386	113
Osei et al. [93]	Ghana	2012–2015	All age	Retrospective	All forms	1633	297
Chinedu et al. [92]	Nigeria	2013–2016	All age	Retrospective	All forms	1704	372
Central, sub-Saharan Africa							
Sume et al. [66]	Cameron	2003–2006	All age	Retrospective	PTB	865	446
Namme et al. [82]	Cameron	2007–2011	Adult	Cross-sectional	All forms	749	311
Linguissi et al. [85]	Congo	2011	Adult	Cross-sectional	PTB	425	133

23.00% (95% CI 15.07–33.43; $I^2 = 99\%$) to after 2010, 31.5% (95% CI 19.41–46.76; $I^2 = 99\%$) (Fig. 5).

Sub-group Analysis and Meta-regression

Sub-group analysis showed that research period ($p = 0.34$), population category ($p = 0.89$), type of TB ($p = 0.81$), sample size ($p = 0.28$) and study type ($p = 0.76$) were not significantly associated with HIV prevalence. Regions within sub-Saharan Africa ($p = 0.02$, $R^2 = 9.05\%$) and study quality ($p = 0.042$, $R^2 = 5.01\%$) were significantly associated with HIV prevalence; together, they explained 12.04% of heterogeneity.

In univariate meta-regression analyses, type of TB (PTB or uncategorised TB), population category (adults compared with children and all age groups), sample size (≤ 500 or > 500) and TB prevalence per 100,000 population were not significantly associated with HIV prevalence in TB (Table 2). However, significant variation was found for geographical region (Central or other regions) and HIV prevalence per 100,000 population. These variables accounted for variation, measured by R^2 as follows: $R^2_{\text{region}} = 9.05\%$, $P_{\text{region}} = 0.021$; $R^2_{\text{HIV}} = 7.87\%$, $P_{\text{HIV}} = 0.011$. A multivariate mixed-effects meta-regression model was fitted using geographical region and HIV prevalence per 100,000 population as covariates. These two variables accounted for 13.3% of the heterogeneity in the HIV prevalence in TB patients estimates ($R^2_{\text{region+HIV}} = 13.3\%$, $P_{\text{region + HIV}} = 0.0070$).

Influence of Study Quality on HIV Prevalence in TB Patients

Sensitivity analysis was assessed by systematically removing outliers (high and lower prevalence) and low-quality studies. There was no material difference in the estimate of HIV prevalence [31.9% (95% CI 28.6–35.4)

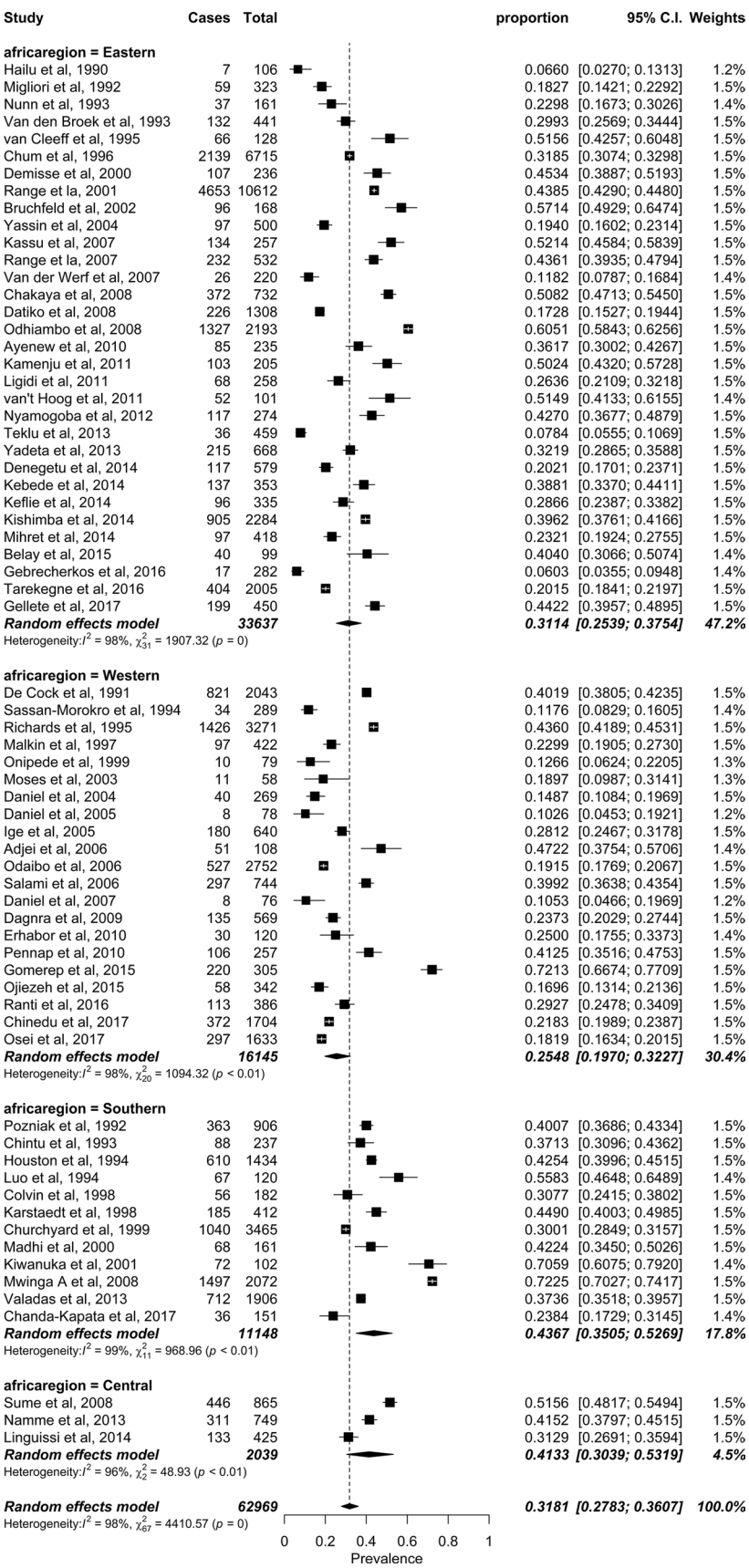

Fig. 2 Forest plots for prevalence of HIV in TB patients from studies by regions in sub-Saharan Africa region

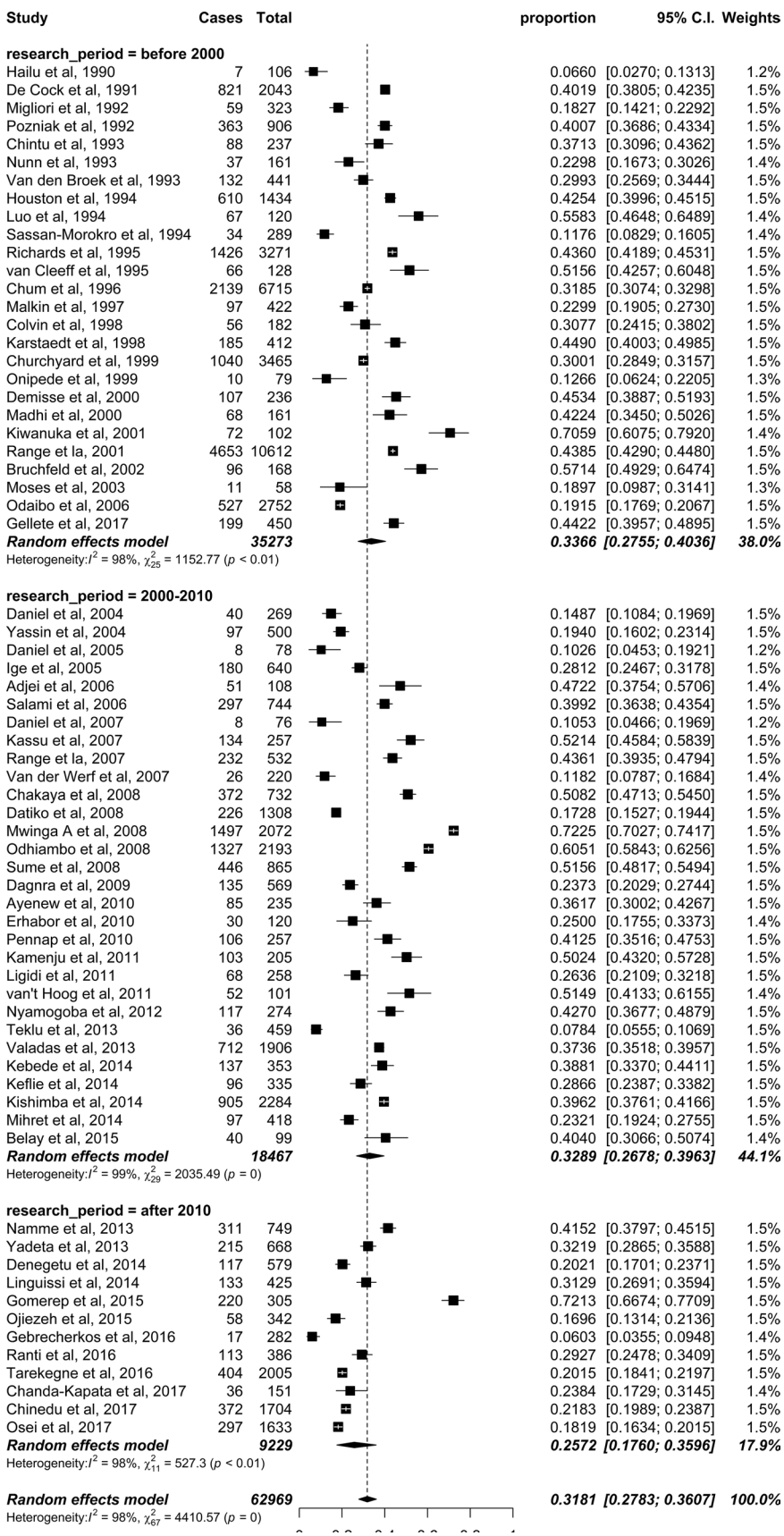

Fig. 3 Forest plots for prevalence of HIV in TB patients from studies by study periods in sub-Saharan Africa region

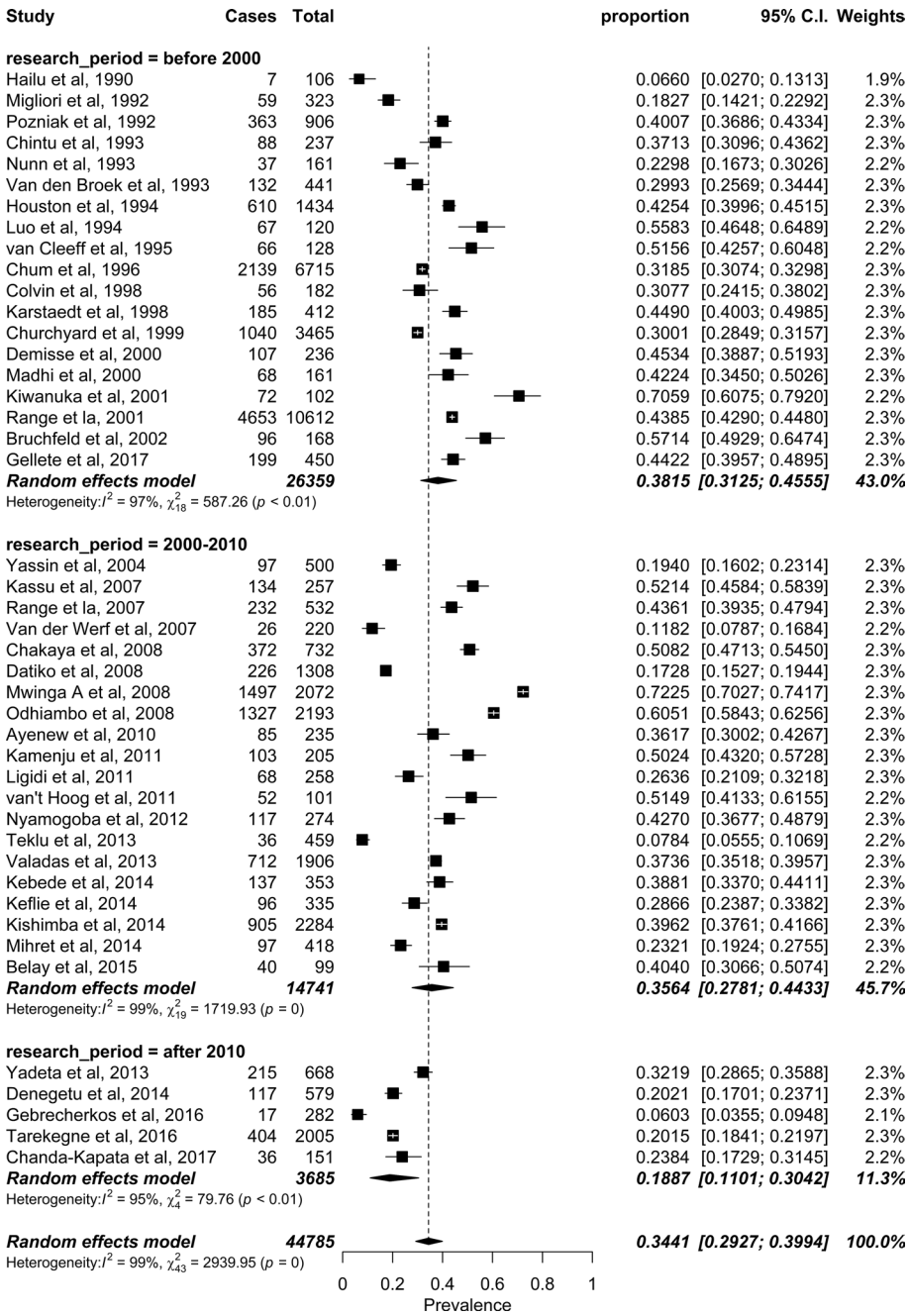

Fig. 4 Forest plots for prevalence of HIV in TB patients from studies Eastern and southern regions in sub-Saharan Africa

and 33.63% (95% CI 29.3–38.2)] when removing outliers and low-quality studies, respectively (Supplementary Table III).

Publication bias was assessed using a funnel plot (Fig. 6). Each point represents an individual study. The points are distributed asymmetrically, indicating the existence of publication bias. However, Begg's test demonstrated non-significant publication bias (p = 0.2518).

Discussion

The overall pooled prevalence of HIV infection in TB patients in sub-Saharan Africa was 31.8% (95% CI 27.8–36.1) with an apparent reduction from 33.7% (95% CI 27.5–40.4) before 2000 to 25.7% (95% CI 17.6–36.0) after 2010. The Eastern and Southern sub-Saharan Africa

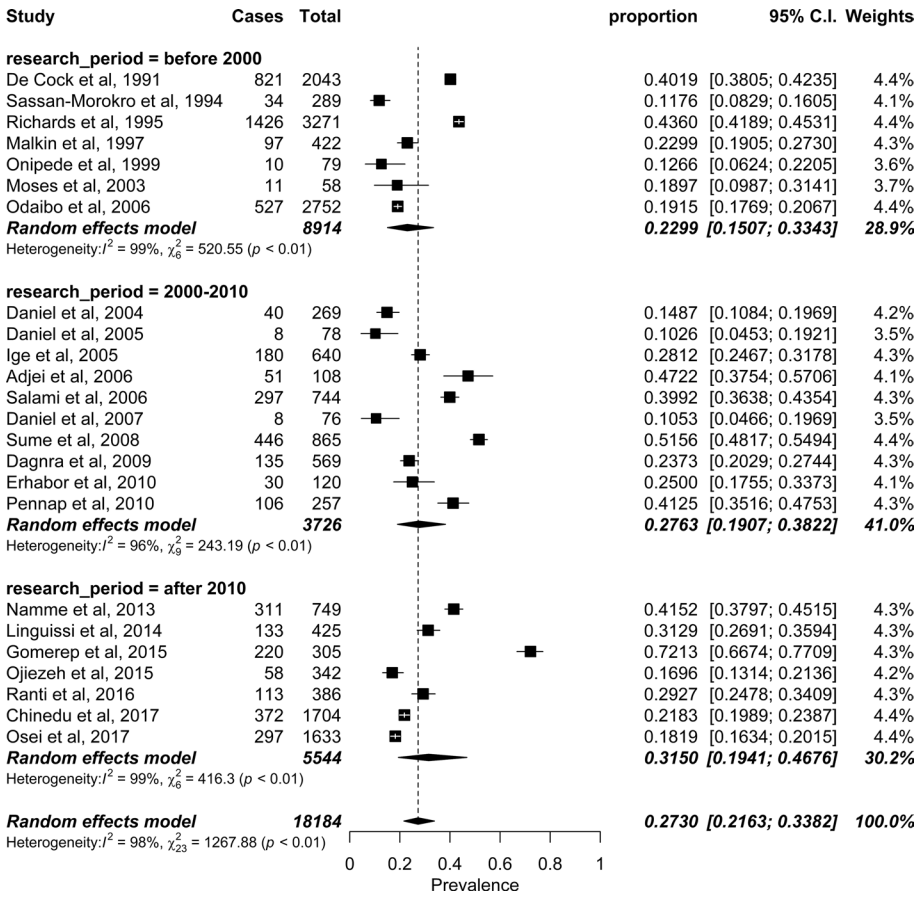

Fig. 5 Forest plots for prevalence of HIV in TB patients from studies Western and central regions in sub-Saharan Africa

region had a higher HIV prevalence [34.4% (95% CI 29.3–34.4)] than the Western and Central sub-Saharan Africa region [27.3% (95% CI 21.6–33.8)]. The prevalence of HIV dropped significantly in the Eastern and Southern sub-Saharan African region, from 38.15% (95% CI 31.25–45.55) before 2000 to 18.87% (95% CI 11.01–30.42) after 2010, while it increased in Western and Central sub-Saharan African region over time, from 23.00% (95% CI 15.07–33.43) before 2000 to 31.5% (95% CI 19.41–46.76) after 2010.

A previous meta-analysis of HIV/TB co-infection prevalence in countries excluding China [9] reported a lower prevalence (25%) than the present review. This is because our analysis included only studies conducted in the sub-Saharan region where HIV prevalence is higher compared with regions included in the previous studies. However, the WHO series of global TB reports showed that the incidence of HIV infection in Africa region has gradually decreased from 130 in 2000 to 75 per 100,000 population in 2016 [1].

Globally, HIV/AIDS and TB/HIV control measures have been strengthened and services scaled up since 2000 [94]. The prevalence of HIV in TB declined progressively in South-East regions, while it remains high in West-Central region from before 2000 to the after 2010 [6]. We argue that the discrepancy in the implementation of these activities explains our findings that the trend of HIV prevalence among TB patients varies across regions in sub-Saharan Africa.

The 2018 UNAIDS report indicated that in Eastern and Southern sub-Saharan Africa regions antiretroviral therapy (ART) coverage has increased from about 26% in 2010 to about 66% in 2017 [6], whereas in Western and Central region ART coverage has increased from about 14% in 2010 to 40% in 2017, which is lagging behind the rest of sub-Saharan Africa [23]. Moreover, the high number of people who do not know their HIV status is a key barrier [95]. Despite these gaps, huge decisive steps have been made towards meeting the 90–90–90 targets. In 2016, in the Eastern and Southern sub-Saharan Africa, almost all people living with HIV in the region, who were aware of their status were on treatment [95]. Therefore, the substantial reduction in HIV prevalence among TB patients in the Eastern and Southern region is likely to be due to effective scaling up of HIV prevention and ART programmes among the general population in addition to other similar activities, including TB/HIV collaborative activities.

Our meta-regression analysis showed that geographical region and population prevalence of HIV are sources of

Table 2 Univariate and multivariate meta-regression for prevalence of HIV infection among TB patients

	Meta-regression coefficient (%)	95% CI	P
Univariate meta-regression			
Types of TB (all forms compared with PTB)	0.0512	− 0.3603 to 0.4627	0.8072
Population by age category			
Adult (15-year and above)	Ref		
All age	0.1013	− 0.3167 to 0.5194	0.4751
Children (< 15-years)	0.0415	− 0.5922 to 0.6753	0.1285
Population TB prevalence per 100,000 population	0.0003	− 0.0012 to 0.0019	0.6935
Research period (before 2000 compared with after 2000)	0.1311	− 0.2630 to 0.5252	0.5144
Sample size (> 500 compared with ≤ 500)	− 0.2103	− 0.5961 to 0.1755	0.2853
Geographical region			0.0215*
Central	Ref		
Eastern	− 0.4375	− 1.3318 to 0.4568	0.3377
Southern	0.1003	− 0.8565 to 1.0570	0.8372
Western	− 0.7191	− 1.6350 to 0.1967	0.1238
Population prevalence of HIV/AIDS per 100,000 population	0.0001	0.0000 to 0.0002	0.0107**
Multivariate meta-regression			
Geographical region			
Central	Ref		
Eastern	− 0.3976	− 1.2717 to 0.4765	0.3726
Southern	− 0.0890	− 1.0416 to 0.8635	0.8547
Western	− 0.7506	− 1.6456 to 0.1443	0.1002
Population prevalence of HIV/AIDS per 100,000 population	0.0001	0.0010 to 0.0002	0.0460*

**p-value = 0.01, *p-value < 0.05

heterogeneity. Western sub-Saharan Africa region had a significantly lower prevalence of HIV in TB patients than Central, Eastern or Southern regions. Prevalence of HIV among TB patients is positively associated with HIV prevalence in the general population in countries of origin of the studies, which is consistent with a previous systematic review and successive WHO reports [1, 8, 96]. However, these two variables explained only 13.3% of the heterogeneity. Other characteristics that were not reported in the original articles such as types of diagnostic tools for TB and HIV, types of HIV, types of TB, data collection methods, or by study methods could cause this heterogeneity.

The findings of this study have important practical relevance and implications toward achieving the goal of ending TB in line with the WHO's ''End TB'' Strategy [97]. This is especially so for countries with high TB and HIV burden. The evidence that HIV prevalence among TB patients has fallen from the level before 2000 to that after 2010 in regions with high HIV prevalence and better HIV and TB/HIV response implies that the response has been effective. Countries and regions with high burdens of TB and HIV, which are lagging in response, need to strengthen their HIV and TB/HIV response packages. This is important to reduce the burden of HIV among TB patients, and vice versa [4].

The fast-tracking of the HIV response has been a focus of HIV high-burden countries mainly in South and East sub-Saharan Africa, while most countries in the Western and Central Africa region have neglected to provide adequate response [98, 99]. We argue, based on the results of this review, that fast-tracking the HIV response including TB/HIV collaborative activities in these sub-Saharan Africa regions would reduce the overwhelming double burden of these infections on the health care system [1]. This review calls for strengthened HIV prevention, routine HIV testing, treatment, and care for TB patients in Western and Central regions in sub-Saharan Africa [4, 97, 100].

This review has acknowledged the following potential limitations: (1) all published reports and articles might not have been included in our database search, particularly those in country-specific journals; (2) the pooled prevalence of HIV is estimated among TB patients who have access to HIV testing in TB diagnostic and treatment health facilities and likely overestimate the real prevalence; (3) types of TB, types of HIV, mean age and age group were not reported in most articles; (4) TB diagnostic methods and HIV testing methods also varied between studies and over time and by country. Thus, the findings from this review may not be generalizable to countries not included in this review.

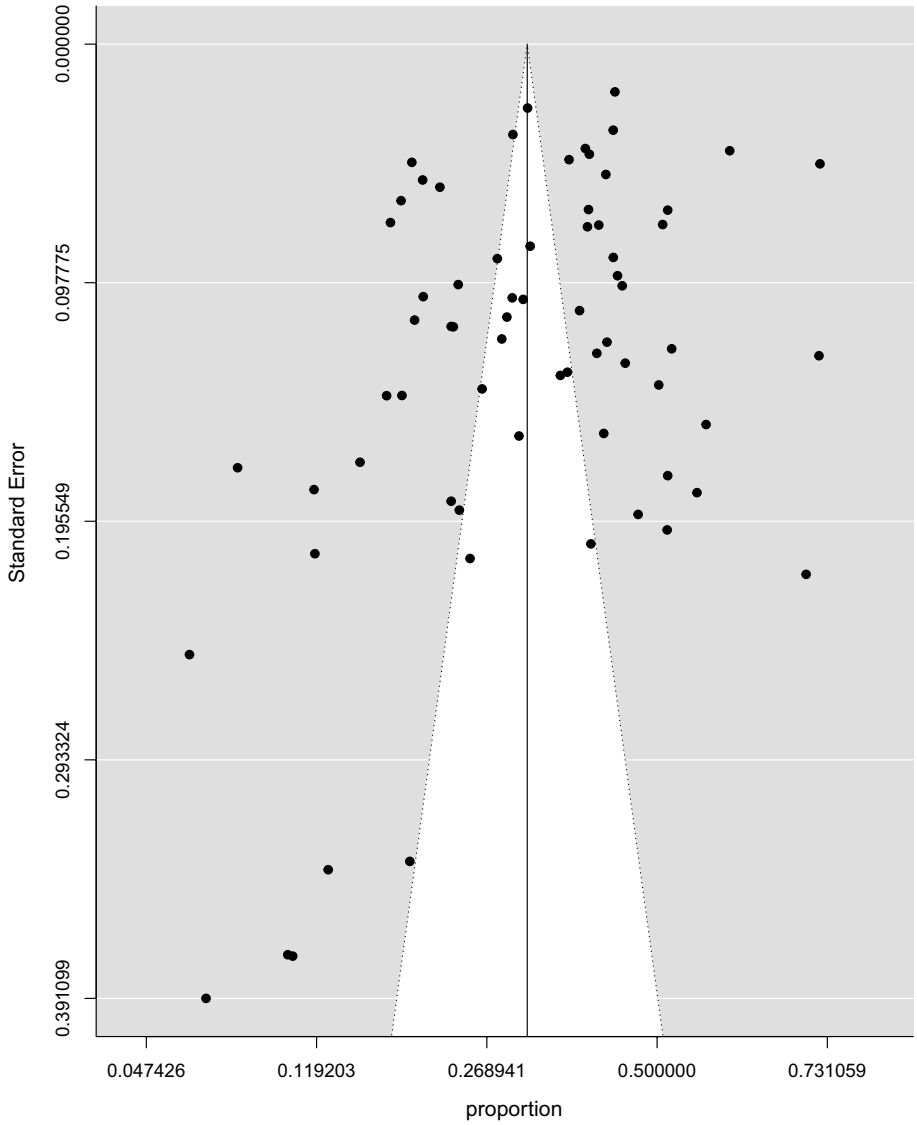

Fig. 6 Funnel plots for prevalence of HIV in TB patients in sub-Saharan Africa

Nevertheless, the review has strengths: it identified 68 studies published from 1990 to 2017, which allowed us to pool results from 62,969 TB patients tested for HIV. The review provides evidence to enable countries in the sub-Saharan Africa region to evaluate their TB/HIV collaborative activities, particularly routine HIV testing, prevention, treatment, care and support, and to strengthen their efforts to achieve the goal of ending TB by 2035 and HIV by 2030.

Conclusion

Overall, the prevalence of HIV infection among TB patients has steadily declined in sub-Saharan Africa from 1990 to 2017. This reduction is most pronounced in Eastern and Southern sub-Saharan Africa regions, showing the effectiveness of the HIV response and extended TB/HIV collaborative activities in these regions. On the contrary, there was an increase in HIV prevalence in TB patients in Western and Central regions of sub-Saharan Africa, where the response to HIV and TB/HIV has been relatively inadequate. Our systematic review and meta-analysis sheds light on the significance of the HIV and TB/HIV response toward the goal of ending TB and HIV in sub-Saharan Africa and beyond.

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Author Contribution YAG, YA, GW and RSM conceived the research question and study design. YAG performed the electronic database search, data abstraction, analysis and wrote the first draft of the article. YAG supervised and reviewed the database search, data analysis and interpretation. GW, CG, RSM and HG supervised the research process

and provided comments. All authors reviewed subsequent versions and approved the final version of the manuscript.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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