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REVIEW ARTICLE

Risk of prostate cancer in men with HIV/AIDS: a systematic review and meta-analysis

Dianqin Sun[1] · Maomao Cao[1] · He Li[1] · Jiansong Ren[1] · Jufang Shi[1] · Ni Li[1] · Wanqing Chen[1]

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Abstract

Background Although previous studies have shown a decreased incidence of prostate cancer in men with HIV/AIDS, the consensus has not been reached. Our aim is to conduct a systematic review and meta-analysis to assess the risk of prostate cancer among people with HIV/AIDS.

Methods We systematically searched PubMed, Web of Science, Embase, and Cochrane Library until March 2020. Cohort studies were included if they compared the prostate cancer risk between people with HIV/AIDS and uninfected controls or the general population. The summary standardized incidence ratio (SIR) and 95% confidence interval (CI) were calculated using a random-effects model.

Results A total of 27 studies were included for analysis, with more than 2780 males with HIV/AIDS developing prostate cancer. The results showed that HIV infection was associated with a decreased risk of prostate cancer incidence (SIR, 0.76; 95% CI, 0.64–0.91; $P = 0.003$), with significant heterogeneity ($P < 0.001$; $I^2 = 91.6\%$). A range of sensitivity analyzes did not significantly change the results.

Conclusions Our study shows that people with HIV/AIDS have a lower incidence of prostate cancer compared with the general population. However, significant heterogeneity exists among the included studies. Further prospective studies with better designs are needed to elucidate the association between HIV infection and prostate cancer.

Introduction

Human immunodeficiency virus (HIV) continues to be a major threat to human health globally. Approximately 37.9 million people were estimated to be living with HIV in 2018 [1]. The advent of highly active antiretroviral treatment (HAART) in 1996 marks a milestone. With the spread of HAART, people with HIV or acquired immune deficiency syndrome (AIDS) have achieved a longer life expectancy. The profound change of survival rates and consequent aging of HIV patients has led to a shift in cancer spectrum from AIDS-defining cancers (non-Hodgkin lymphoma, cervical cancer, and Kaposi sarcoma) to non-AIDS-defining cancers [2–4]. The association between HIV and non-AIDS-defining cancers has also received more attention.

Higher standardized incidence rates were observed in people with HIV compared with the general population for many specific types of non-AIDS-defining cancers including cancers of the liver, stomach, anus [5, 6]. However, prostate cancer is an intriguing exception. Previous studies [7–10] have shown a decreased risk of prostate cancer in men living with HIV/AIDS. Altering hormone levels seem to be an explanation for this phenomenon, given the higher frequency of hypogonadism in men with HIV [11, 12]. In addition, some preclinical studies [13, 14] suggested that HIV protease inhibitors (PIs) had an antineoplastic effect against prostate cancer. But several epidemiological studies [15–18] did not support the association between HIV infection and prostate cancer or even concluded the opposite. The census has not been reached.

Two meta-analyzes [5, 6] published more than 10 years ago found a decreased risk of prostate cancer in men with HIV/AIDS. Rather than focusing on prostate cancer, these

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✉ Wanqing Chen
chenwq@cicams.ac.cn

[1] National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, 100021 Beijing, China

analyzes explored the incidence of different cancer types. Besides, several new studies [4, 15, 16, 19–31] and opposite findings have been reported in the last decade. There is a need for a quantitative analysis with a focus on prostate cancer using the latest evidence. Thus, we conducted this systematic review and meta-analysis to further characterize the risk of prostate cancer in men with HIV/AIDS.

Material and methods

The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42020173680) and was reported following the PRISMA (preferred reporting items for systematic reviews and meta-analyses) statement [32].

Literature search

We systematically searched PubMed, Web of Science, Embase, and Cochrane Library until March 2020. No restrictions or filters were applied. The detailed search strategy was listed in the Supplementary Table S1. We also manually reviewed reference lists of original and review articles to ensure that all relevant studies were included.

Selection criteria

Studies were included if they met the following criteria: (1) comparing the prostate cancer risk between people with HIV/AIDS and uninfected controls or the general population, (2) reporting the quantitative effect estimates (odds ratio, relative risk [RR], hazard ratio [HR], standardized incidence ratio [SIR], or others), at least adjusted for age, (3) designed as cohort studies (prospective or retrospective), (4) published as original articles in English. Studies were excluded if they reported mortality data only. We treated the data from each region and period as a separate study for the meta-analysis. When there were two or more publications with overlapping data (by region and study period), we selected only the study with the largest sample size or more comprehensive information, and if these were also similar, we included the most recent study.

Two investigators (DS and MC) independently screened the identified records for eligibility. Any disagreement in the process of the literature search and selection was resolved by a third investigator (WC).

Data extraction

Several variables from primary studies were extracted, including the name of the first author, publication year, country, study period, the number of cases of prostate cancer in people with HIV/AIDS, the number of males with HIV/AIDS, cohort entry, reference population, outcome assessment method, average age, effect size, and its corresponding 95% confidence interval (CI), covariates adjusted in the multivariate analysis. When more than one multivariate model was conducted, we extracted the effect estimate from the model adjusted for the largest number of covariates. We also extracted results of subgroup analyzes in the original articles and gave a summary in this systematic review.

Quality assessment

The study quality was assessed using the Newcastle–Ottawa Quality Assessment Scale (NOS), which consists of eight items about participants' selection, study group comparability, and assessment of the outcome. The NOS scale ranges from 1 (the lowest quality) to 9 (the highest quality) points.

Statistical analysis

The SIRs and their corresponding 95% CIs were considered as the measure of the association between HIV infection and the risk of prostate cancer. Following previous meta-analysis [33], when studies did not report SIR, either RR, HR, or IRR was extracted and considered as equal to SIR. When studies [34] reported 0 observed cases, 0.1 was used to calculate the SIR with its exact CIs [35]. For studies [4, 7, 9, 29, 36] that reported separate estimates by cancer diagnosis period, we combined them into one estimate and calculated its 95% CI with the method described in Supplementary Table S2. In the case of studies [25] that reported several estimates for multiple regions, we included all estimates in the analysis because the estimates were derived from nonoverlapping populations.

The pooled SIR and its corresponding 95% CI were calculated by the inverse variance method of DerSimonian and Laird [37]. Standard error estimates of the natural logarithm of the SIR in each study were calculated as $\sigma = (\ln\alpha - \ln\mathrm{SIR})/1.96$, where α is the upper 95% confidence limit. We used a random-effects model to account between-study heterogeneity. Statistical heterogeneity within individual studies was quantified using I^2 statistic, where 51–75% indicates moderate heterogeneity, and above 75% indicates high heterogeneity [38]. To explore sources of heterogeneity, we conducted subgroup analyzes by study characteristics variables, including country income category, comparison population, outcome measurement method, level of standardization. For the country income category, following the previous article [39], studies were divided into "High-income country" and "Low- and middle-income country" according to the World Bank standard

classifications for gross national income per capita of the study sites at the mid-year of the study period. We also performed the meta-regression by the following continuous study-level variables: publication year, the number of people with HIV/AIDS, the number of cases in men with HIV/AIDS, NOS score. We used a sequential approach proposed by Patsopoulos et al. [40] to evaluate the consistency of effect estimates when heterogeneity was reduced. Briefly, studies contributing the largest part to heterogeneity were excluded sequentially and cumulatively until I^2 was <50%.

To evaluate the robustness of the results, we re-estimated the overall effect after omitting one study at a time. Some studies [8, 15, 17, 18, 20, 24, 25, 27, 41, 42] reported estimates and 95% CIs to only one decimal place, which introduced the rounding error and perhaps constrained our ability to exactly represent the existing evidence. We did an additional analysis removing two studies [15, 18], of which extracted CIs were nonsymmetrical and results significantly changed after transformation. The potential small-study effects and publication bias were graphically evaluated by the funnel plot. We also conducted Egger's test for asymmetry, where P value < 0.1 was considered significant. Statistical analyzes were performed with the Stata software (Version 14.0; StataCorp). $P < 0.05$ (two-sided) were considered as significance level.

Results

Literature search results

Figure 1 shows the study selection process. After initial database searching and removing duplicate records, 3028 records were identified. For the 145 records qualifying for the full-text review, 26 records were removed for the article type, 54 studies were excluded for the absence of prostate cancer incidence, 4 studies without reference population were also excluded. We further excluded four studies [43–46], of which effect estimates were not adjusted or standardized by age, four [47–50] that were not designed as cohort studies, four [51–54] that were not published in English. Finally, 49 articles were included in the review. For the meta-analysis, another 22 studies were removed due to overlapping participants (Supplementary Table S3). Overall, 28 estimates from 27 studies were included in our meta-analysis, since one study [25] included data from two different cohorts.

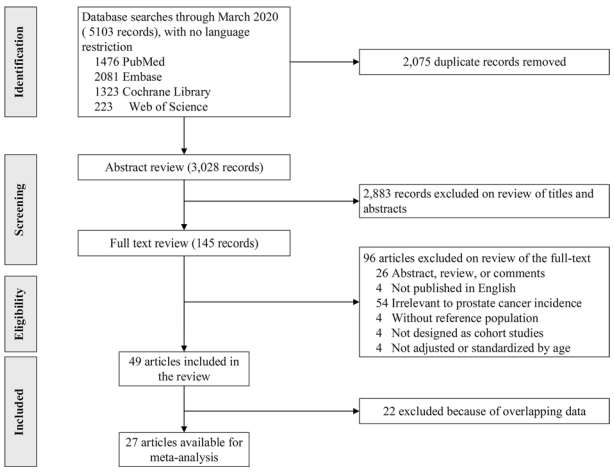

Fig. 1 Flow-chart of study selection. The diagram was made according to the preferred reporting items for systematic reviews and meta-analyses statement.

Study characteristics and quality assessment

Table 1 gives an overview of the characteristics of the included cohorts. There were more than 0.6 million men with HIV/AIDS from 11 countries included in the studies. Over 2780 cases of prostate cancer were observed. The number of men with HIV/AIDS included in each cohort varied from 1734 to 57,428, and the number of prostate cancer cases ranged from zero to more than 1000. Most studies were published after 2000, but study periods ranged from 1981 to 2013. Most included studies could ensure that the exposure precedes the outcome. But six studies [7, 10, 16, 19, 20, 36] calculated the person years at risk from the 5 years before AIDS diagnosis to the date of cancer diagnosis, which made it possible that cases before HIV infection were included in the analysis. The rationale behind the six studies was that the median duration of HIV infection is at least 5 years before AIDS [55]. It seems appropriate when the six studies aimed at investigating the impact of HIV infection. The majority of studies relied on registries or administrative data to confirm a cancer diagnosis. Overall, the qualities of the included studies varied, with NOS values between 4 and 8 (Supplementary Table S4). More than half of them got 7 or above points.

Risk of prostate cancer in men with HIV/AIDS

The random-effects meta-analysis demonstrated that people living with HIV/AIDS had a lower risk of prostate cancer than the general population. The pooled SIR was 0.76 (95% CI, 0.64–0.91; $P = 0.003$), with significant heterogeneity ($P < 0.001$; $I^2 = 91.6\%$) (Fig. 2). The results of sensitivity analysis by omitting each study one time were relatively consistent, with the SIR varying between 0.71 and 0.79 (all $P < 0.05$) (Fig. S1 in the Supplementary). After removing two studies [15, 18] that contained non-symmetrical CIs, the pooled SIR was 0.71 (95% CI, 0.60–0.85; $P < 0.001$).

Table 1 Characteristics of included studies.

Study	Country	Period	Outcome measurement method	Comparison group	Number of males with HIV/AIDS	Number of observed cases	Effect size (95% CI)	Level of adjustment or standardization
Serraino et al. [18]	France Italy	1982–1997 1988–1998	Combination[a]	General population	5281	1	SIR: 20.6 (0, 117.8)	Age
Gallagher et al. [10]	USA	1981–1994	Registry linkage	General population	10,083	37	SIR: 0.70 (0.48, 0.95)	Age, region, race
Herida et al. [9]	France	1992–1999	Medical record	General population	57,428	9	SIR: 0.45 (0.23, 0.86)	Age
Newnham et al. [41]	UK	1985–2001	Registry linkage	General population	26,080	5	SIR: 0.9 (0.3, 2.0)	Age, period
Mbulaiteye et al. [17]	Uganda	1988–2002	Registry linkage	General population	4184	2	SIR: 2.9 (0.3, 11.0)	Age, period
Long et al. [42]	USA	1996–2005	Combination	General population	1734	5	SIR: 0.6 (0.2, 1.5)	Age, race, calendar year
Patel et al. [8]	USA	1992–2003	Medical record	General population	41,632	39	SIR: 0.6 (0.4, 0.8)	Age, race
Maso et al. [7]	Italy	1986–2004	Registry linkage	General population	17,122	2	SIR: 0.29 (0.07, 1.18)	Age, period, registry
Leeuwen et al. [36]	Australia	1982–2004	Registry linkage	General population	18,794	24	SIR: 0.5 (0.34, 0.75)	Age, state/territory, calendar year
Powles et al. [61]	UK	1983–2007	Medical record	General population	9948	4	SIR: 0.57 (0.15, 1.45)	Age, period
Shiels et al. [31]	USA	1992–1995	Registry linkage	General population	NA[b]	34	SIR: 0.42 (0.29, 0.59)	Age, race, calendar year, registry
Franceschi et al. [29]	Switzerland	1985–2006	Registry linkage	General population	NA[b]	10	SIR: 1.3 (0.7, 2.41)	Age, period, registry
Albini et al. [28]	Italy	1999–2009	Combination	General population	3660	7	SIR: 1.1 (0.53, 2.32)	Age
Franzetti et al. [34]	Italy	1985–2011	Medical record	General population	4382	0	SIR: 0.016 (0.004, 0.586)[c]	Age
Marcus et al. [26]	USA	1996–2007	Registry linkage	HIV-uninfected population	17,424	74	RR: 0.73 (0.57, 0.92)	Age, race, smoking, alcohol/drug abuse, obesity, diabetes, region[d]
Chen et al. [16]	Taiwan, China	1998–2009	Registry linkage	General population	13,778	17	SIR: 3.48 (2.03, 5.57)	Age, period
Akarolo-Anthony et al. [27]	Nigeria	2005–2012	Registry linkage	General population	7246	1	SIR: 0.4 (0, 16.9)	Age, period
Raffetti et al. [24]	Italy	1986–2009	Combination	General population	12,116	8	SIR: 0.5 (0.3, 1.0)	Age

Table 1 (continued)

Study	Country	Period	Outcome measurement method	Comparison group	Number of males with HIV/AIDS	Number of observed cases	Effect size (95% CI)	Level of adjustment or standardization
Castilho et al. [25]	Brazil	1998–2010	Medical record	General population	1956	1	SIR: 0.3 (0, 1.6)	Age
Castilho et al. [25]	USA	1998–2010	Medical record	General population	2970	4	SIR: 0.4 (0.1, 1.0)	Age, race, calendar year
Yanik et al. [22]	USA	2004–2011	Registry linkage	HIV-uninfected population	NA[b]	NA[b]	HR: 0.78 (0.63, 0.98)	Age, race, calendar year
Lee et al. [23]	USA	2006–2012	Medical record	General population	50,960	119	SIR: 0.54 (0.45, 0.58)	Age
Park et al. [4]	USA	1997–2012	Registry linkage	HIV-uninfected population	43,668	664	IRR: 0.99 (0.91, 1.08)	Age, race
Godbole et al. [15]	India	1996–2008	Registry linkage	General population	20,865	3	SIR: 4.4 (0.9, 12.8)	Age, period
Dutta et al. [21]	USA	1996–2010	Combination	HIV-uninfected population	2800	19	IRR: 1 (0.55, 1.82)	Age, race, period
Tanaka et al. [19]	Brazil	1997–2012	Registry linkage	General population	NA[b]	49	SIR: 1 (0.76, 1.33)	Age
Coghill et al. [30]	USA	1996–2012	Registry linkage	General population	NA[b]	1522	SIR: 0.48 (0.46, 0.51)	Age, race, calendar year, registry
Hessol et al. [20]	USA	1985–2013	Registry linkage	General population	3656	129	SIR: 0.6 (0.5, 0.7)	Age, race, calendar year

CI confidence interval, *SIR* standardized incidence ratio, *RR* relative risk, *IRR* incidence rate ratio, *HR* hazard ratio, *NA* not available.

[a]Combination indicates that both medical record and registry database were used.

[b]No exact figures were reported in the original studies.

[c]The original study reported 0 observed cases, 0.1 was used to calculate the SIR with its 95% CI.

[d]For Kaiser Permanente of Northern California subset, model restricting to participants with a previous PSA test further included testosterone deficiency, with an adjusted RR of 0.55 (95% CI: 0.39–0.80).

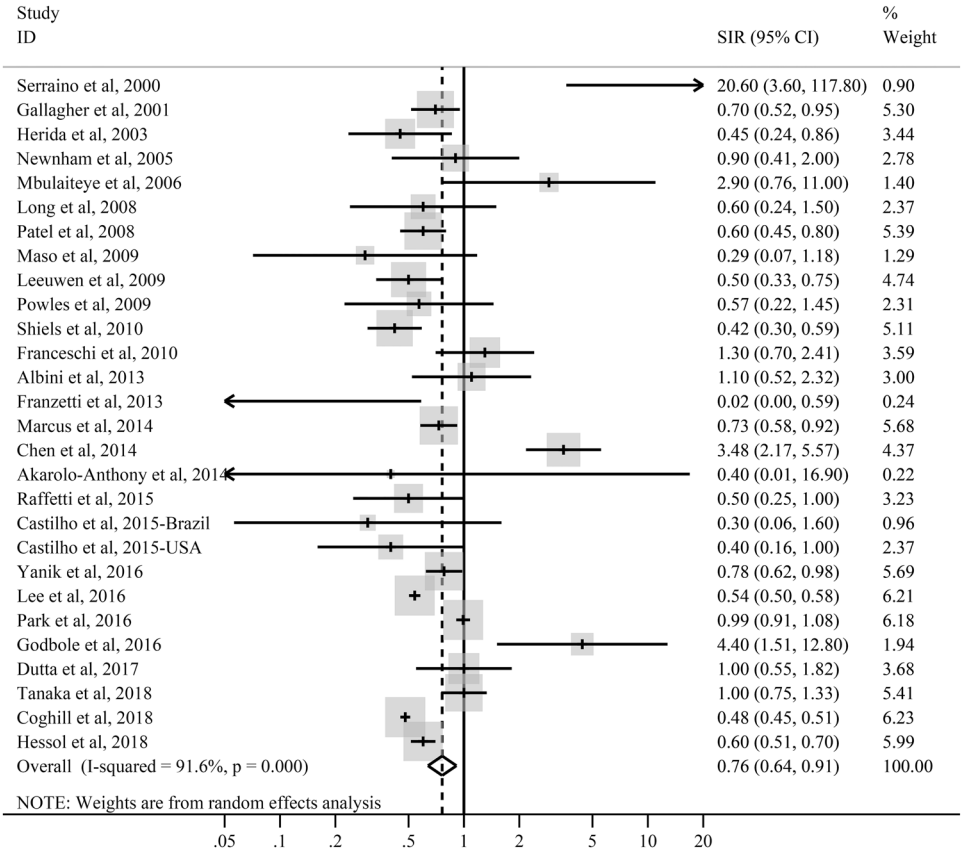

Fig. 2 Incidence of prostate cancer in men with HIV/AIDS. Horizontal lines with arrows reflect that the range of 95% confidence intervals exceeds the axis *X*'s limits. The gray boxes represent the statistical weight of the study, and the dashed vertical line indicates the line of no effect. SIR indicates standardized incidence ratio.

Table 2 Standardized incidence ratios for subgroup analyzes.

Subgroup	Number	SIR (95% CI)	I^2, %	P^b	P^c
Comparison group					0.755
General population	24	0.72 (0.61, 0.86)	85.3	<0.001	
HIV-uninfected population	4	0.86 (0.71, 1.04)	64.8	0.036	
Outcome measurement method					0.838
Registry linkage	16	0.85 (0.66, 1.10)	94.6	<0.001	
Medical record	7	0.76 (0.64, 0.91)	0	0.495	
Combination[a]	5	1.11 (0.52, 2.35)	75.5	0.003	
Country/area					0.149
High-income country	23	0.71 (0.59, 0.86)	92.4	<0.001	
Low- and middle-income country	5	1.39 (0.57, 3.41)	65.3	0.021	
Level of adjustment or standardization					0.803
Only age	8	0.73 (0.46, 1.15)	83.0	<0.001	
More than age	20	0.79 (0.62, 0.99)	93.0	<0.001	

CI confidence interval, *SIR* standardized incidence ratio.

[a]Combination indicates that both medical record and registry database were used.

[b]*P* values were for heterogeneity within a subgroup.

[c]*P* values were for heterogeneity between subgroups based on the meta-regression.

Heterogeneity, subgroup analyzes, and meta-regression

Pooled SIRs did not significantly change across all subgroup analyzes, with 95% CIs overlapping between pooled effect estimates (Table 2). For the meta-regression, no association between SIR and publication year, NOS score, the number of males with HIV/AIDS, or the number of prostate cancer cases was observed (Fig. S2). When we sequentially removed studies [4, 15, 16, 18, 19, 23, 30]

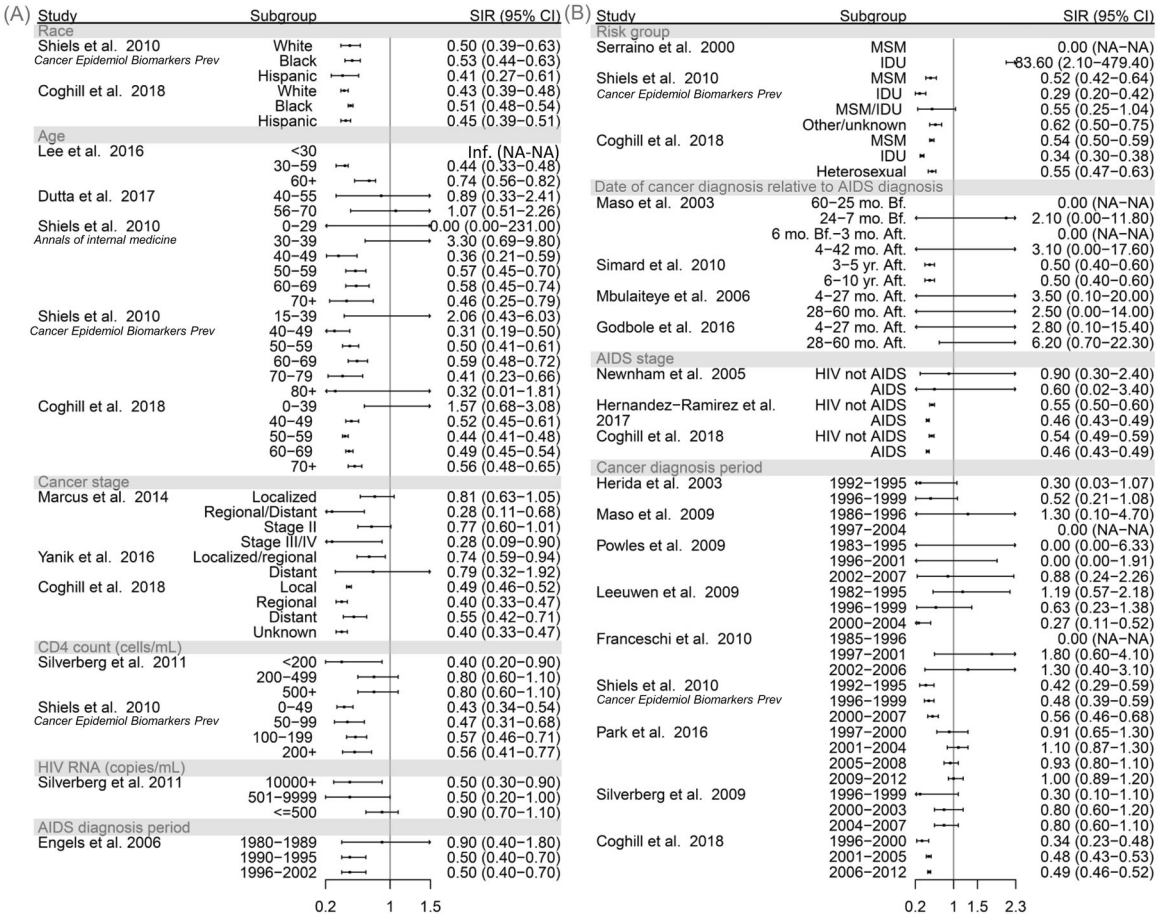

Fig. 3 Summary of subgroup analyzes in the original articles. **a** subgroup analyzes by race, age, cancer stage, CD4 count, HIV RNA copies, AIDS diagnosis period; **b** subgroup analyzes by risk group, period relative to AIDS diagnosis or registration, AIDS stage, cancer diagnosis period. SIR standardized incidence ratio; MSM men who have sex with men; IDU injection drug user; mo. month; yr. year; Bf. before; Aft. after.

accounting for the largest share of heterogeneity until I^2 was <50% ($I^2 = 44.9\%$), pooled SIR was 0.65 (95% CI, 0.56–0.75), which was similar to the original estimate.

Small-study effects and publication bias

Visual inspection of the funnel plot did not provide evidence for asymmetry (Fig. S3 in the Supplementary). The Egger regression test also did not detect a potential publication bias ($P = 0.13$).

Summary of subgroup analyzes in the original articles

Among studies included in the review, there were subgroup analyzes conducted based on demographic characteristics (race [30, 31], age [21, 23, 30, 31, 56], HIV risk group [18, 30, 31]), HIV disease progression (CD4 count [31, 57], HIV RNA copies/mL [57], AIDS stage [30, 41, 58], period relative to AIDS diagnosis [15, 17, 59, 60]), cancer diagnosis period [4, 7, 9, 29–31, 36, 61, 62], and cancer stage [22, 26, 30] (Fig. 3).

Discussion

This systematic review and meta-analysis found significantly decreased prostate cancer incidence in people living with HIV/AIDS compared with the general population. Overall, the pooled SIR was 0.76 and remained steady in a range of sensitivity analyzes, indicating an approximately a quarter lower prostate cancer incidence in men with HIV/AIDS compared with the general population. However, there was substantial heterogeneity, and thus our findings should be interpreted with caution.

Previous two meta-analyzes reported that the pooled SIRs of prostate cancer in men with HIV/AIDS were 0.70 (95% CI, 0.55–0.89) with evidence until 2007 [6] and 0.69 (95% CI, 0.55–0.86) with evidence until 2009 [5], separately. These two analyzes explored incidence ratios of

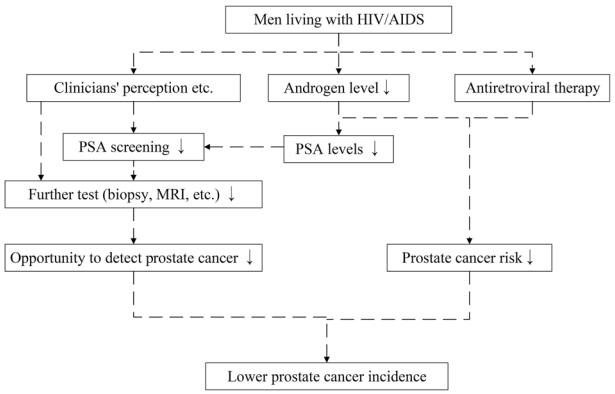

Fig. 4 Potential explanations for lower prostate cancer incidence in men living with HIV/ADS. Please read the graph from top to bottom. PSA prostate-specific antigen; MRI Magnetic resonance imaging.

different types of cancers and gave a full picture of the association between HIV and cancer. For prostate cancer, 9 and 6 studies were included in the two studies, respectively. Our study included substantially more and latest studies, with a focus on prostate cancer, and gave a relatively comprehensive review on the risk of prostate cancer in people with HIV/AIDS. We also conducted a range of analyzes to test the robustness of the results. Furthermore, we summarized the results of subgroup analyzes in the original studies to show whether the association was consistent among different categories of people with HIV (Fig. 3).

To a certain extent, subgroup analyzes in the original studies could indicate the potential interaction or even suggest the mechanism underlying the association. However, subgroup analyses were subject to limitations, of which results should be explained with caution. Two studies [30, 31] conducted subgroup analyses by race and found a significant deficit in prostate cancer risk for people with HIV across racial groups. When considered by age, the decline of prostate cancer risk was limited to the old but not in younger men [23, 30, 31, 56], which could be due to the heterogeneity of early-onset prostate cancer or limited case size. Furthermore, two studies [31, 57] showed that HIV-infected men with the lowest CD4 count had the lowest risk of prostate cancer. It could suggest that the severity of immunodeficiency may impact the association between HIV infection and prostate cancer risk while taking into account the lower incidence of prostate cancer in immunosuppressed transplant recipients compared with the general population [63]. In addition, following the guidelines [64], clinicians are less likely to recommend PSA tests to men with very low CD4 counts, since this population is expected to have much lower life expectancy [65].

Although yet there has been no clear evidence of why men infected with HIV have lower prostate cancer incidence, some possible epidemiological or biological explanations have been proposed (Fig. 4). First, previous studies [26, 66] have suggested that lower incidence in HIV-infected men might be the consequence of decreased prostate-specific antigen (PSA) screenings. Shiels et al. [31] found that only 18.7% of males with AIDS from low-income families in Baltimore had received PSA screenings, compared with 57% of the general men in America. But limitations of this study are obvious, of which the sample was not representative. In contrast with the study by Shiels et al. [31], the study by Marcus et al. [26] found that compared with HIV-uninfected men, men with HIV were more likely to receive a PSA test by age 55. This comparison may be more reliable since HIV-positive and HIV-negative men in the study by Marcus et al. [26] were from the same health care delivery system and had equal opportunities to access health care. Furthermore, Marcus et al. [26] made an additional analysis by restricting participants to those with previous PSA tests and still found a decreased prostate cancer risk among men with HIV (RR: 0.55 (95% CI: 0.39–0.80)). It may suggest that the lower prostate cancer incidence in men with HIV was not attributable to differential PSA tests. However, PSA testing is only part of the whole screening procedure. In addition to PSA screenings, HIV status may directly alter rates of further tests as well, such as magnetic resonance imaging and biopsy, considering less access to health care in this population [67]. Biopsies could be performed less frequently in men with HIV when it is difficult to weigh the risk and benefit. Since bleeding is one of the most frequent complications of prostate biopsy [68], clinicians have reasons to consider the risk of HIV transmission, though the rate for HIV seroconversion following a needlestick exposure is relatively low (0.23%) [69]. Besides, the safety of prostate biopsies for people with HIV must be considered, given that thrombocytopenia sometimes occurs in this patient population [70]. When stratified by cancer stage, consistent risk declines were observed in HIV-infected men [26, 30]. This provides further evidence that the lower prostate cancer incidence was not attributable to the lack of screenings in this population since distant-stage tumors are not generally screen-detected [30].

Another possible explanation is the altering testosterone levels in men with HIV/AIDS. Androgens are necessary for prostate cancers to grow [71], while hypogonadism is more common among men infected with HIV [12, 72]. However, the study by Marcus et al. [26] found that the association between prostate cancer and HIV persisted after further adjustment for testosterone deficiency. But this evidence could not reject the hypothesis that the decreased androgen level is only a part of reasons. Finally, antiretroviral therapy (ART) may be another potential link between HIV infection and decreased prostate cancer incidence. Preclinical

evidence [13, 14, 73, 74] has shown that HIV PIs have antiproliferative activity in prostate cancer cell lines. Chao et al. [75] found an inverse relationship between prostate cancer risk and ART use, specifically PI use in HIV-infected men. In addition, a clinical trial [76] suggested that increased dosages of efavirenz, a nonnucleoside reverse transcriptase inhibitor, might benefit the treatment of metastatic castration-resistant prostate cancer, though 600 mg of the drug did not statistically improve the PSA nonprogression rate.

Data on prostate cancer mortality among men with HIV and the general population could help us further understand the association between HIV infection and prostate cancer. The study by Hessol et al. [77] found no statistically significant difference in prostate cancer mortality between people with AIDS and the general population, with a standardized mortality rate of 1.14 (95% CI: 0.52–1.75). Two studies by Coghill et al. [78, 79] reporting association of HIV infection with cancer-specific mortality among prostate cancer patients. The study [78] published in 2015 showed that HIV-infected patients had higher cancer-specific mortality compared with HIV-uninfected patients (HR: 1.57; 95% CI: 1.02, 2.41). The more recent study [79] further adjusted the treatment effect and found that the elevation in cancer-specific mortality changed to be not statistically significant (HR: 1.65; 95% CI: 0.98, 2.79). Given that HIV-infected people with cancer tend to have lower treatment rates [67, 80], the more recent study could be more reliable. Actually, it is difficult to get the true cancer-specific mortality in HIV-infected patients, since this patient population tends to have multiple serious diseases and the cause of death is hard to determine. Current evidence is limited and rare. The role of HIV/AIDS in the progression of prostate cancer warrants further research.

Our study has some limitations that should be considered. First of all, significant heterogeneity was also observed in our meta-analysis. This was anticipated given the variation in case ascertainment methods, study quality, and the distribution of risk factors in different populations. Secondly, the small number of prostate cancer cases in most cohorts and rounding errors brought by some studies could lead to imprecise effect estimates, which may also result in the heterogeneity between studies. Another potential limitation was that residual and unmeasured confounding existed in included studies. Further better-designed studies are still needed.

In conclusion, our meta-analysis shows that men with HIV/AIDS have a lower prostate cancer incidence compared with the general population. Our findings support the need for further studies to address the epidemiological or biological pathways that affect the incidence of prostate cancer in men with HIV/AIDS.

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Compliance with ethical standards

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

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