Cancer and men who have sex with men: a systematic review

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Disparities in cancer burden between specific populations are widely acknowledged, including differences associated with sexual orientation. We searched PubMed for articles about cancer in men who have sex with men. Of the 410 publications that we identified, 47 reports were eligible for inclusion and review. Most addressed issues of cancer prevention, followed by diagnosis, survivorship, detection, and cancer treatment. Disparities exist mainly in the prevalence of viruses linked to cancers. Knowledge about sexual orientation and cancer is skewed towards infection-related cancers, so information about the association between sexual orientation and other cancers, and social and cultural causes for disparities in cancer, is less available. Men who have sex with men are still a largely overlooked minority group in this respect. Future research should examine the effects of sexual orientation on cancer, from prevention to survivorship.

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Introduction

In the USA, men have a 44% probability of being diagnosed with an invasive cancer over their lifetime, and cancer is the leading cause of death in men.[1] US estimates suggested that 822 300 men would be diagnosed with new invasive cancer and 300 400 would die from cancer in 2011.[1] Because of improvements in detection and treatment of many cancers, survival has improved, and the number of US men living with cancer in 2007 had increased to 5·4 million.[2] US federal and non-federal agencies spend billions of dollars on surveillance, cancer prevention efforts, and cancer research. These agencies acknowledge the existence of cancer disparities related to gender, age, race and ethnic origin, income, social class, disability, geographical location, and sexual orientation, and have tried to eliminate these health disparities.

Analysis of existing US cancer surveillance data has inferred that 36 720 cancer deaths (43% of all cancer deaths) in men aged 25–64 years in 2007 could have been avoided if educational and racial disparities were eliminated.[1] Because of the absence of sexual orientation data in cancer registries, estimates that link cancer deaths to men's sexual orientation are not available, which hinders the elimination of cancer disparities associated with sexual orientation substantially.

We review published work that focuses on cancer and sexual orientation in men by focusing on the cancer control continuum—a framework that defines the cancer trajectory (prevention, detection, diagnosis, treatment, survivorship, and end of life).[3] Each point on this continuum should be examined for differences between sexual orientations to discover which aspects need to be researched further to eliminate disparities associated with sexual orientation. Because men and women differ with respect to cancer, we selected to focus on men. To include all components of sexual orientation—behaviour, identity, and attraction—we have included data on men with a gay or bisexual identity as well as other men who have sex with men (MSM). For the purposes of this Review, we use the term MSM to encompass gay and bisexual men and all other men who engage in sexual activity with other men.

Methods

Search strategy and selection criteria

On Feb 20, 2012, one author (UB) searched PubMed with the keywords "cancer" and ("homosexuality" or "bisexuality" or "gay" or "bisexual" or "not exclusively heterosexual" or "sexual minority" or "men who have sex with men"), restricting the search to studies in men, published from Jan 1, 2001, to Dec 31, 2011. We then applied the following selection criteria: availability of an abstract; a minimum sample size of ten individuals; use of primary data, which excluded case studies and review articles; assessment of a point on the cancer control continuum; and inclusion of heterosexual men or an appropriate comparison group that included heterosexual men. We excluded articles that did not meet all these criteria and then reviewed the full text of the remaining studies. We applied the same eligibility criteria to the full text of these articles, again excluding those that did not comply with our criteria and that did not have a full text available in English.

Data synthesis

For each eligible study we noted the geographical location where the data were obtained when possible, and other characteristics of the study sample and the group with which MSM were compared. We report on how MSM were defined by the investigators of each study, and have retained each study's terminology when discussing the results—ie, we refer to homosexual, gay, or MSM depending on the term chosen by each study's investigators. We classified studies according to the point along the cancer control continuum that was assessed. Of the studies that covered several aspects along the continuum, we used the main aspect of each study for classification.

Results

Study selection and characteristics

The initial search strategy resulted in 410 reports, of which we eliminated 339 that did not comply with our inclusion criteria. After application of the same criteria to the full text of the remaining 71, the most frequent reason for exclusion was that the study did not compare MSM with an appropriate comparison group (figure).

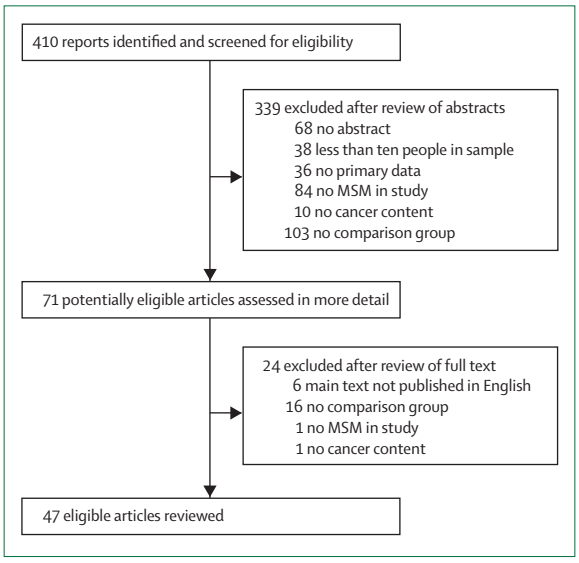

Figure: **Summary of application of eligibility criteria for inclusion into the review**
MSM=men who have sex with men.

Six articles were excluded because the full text was not in English, which prevented us from extracting sufficient detail. Another two studies were excluded because, after reading the full text, we discovered that neither MSM nor cancer content had been considered.

47 articles qualified for inclusion in this systematic review (table). Publications were unequally distributed along the cancer control continuum, with 30 studies addressing issues of cancer prevention,[4–33] nine diagnosis,[36–44] five survivorship,[46–50] two detection,[34,35] and one treatment.[45]

Prevention

Most articles that assessed cancer prevention, with few exceptions, focused on viruses linked to cancers.

Human papillomavirus (HPV) as a risk factor for head and neck cancers

Only one study focused on oral HPV as a cause of oropharyngeal cancer and head and neck squamous cell carcinoma.[4] The study sample consisted of outpatients without cancer and a sample of male college students aged 18–23 years, who provided detailed behavioural information, self-reported either as heterosexual or as homosexual or bisexual, and provided oral samples for HPV testing. The findings showed that the risk of oral HPV infection did not differ by sexual orientation.

HPV and other risk factors for anal cancer

12 studies focused on risk factors for anal cancer, including HPV infection in the anal canal.[5–16] One aetiological study of HPV and anal cancer compared a representative sample of patients with anal cancer with a control group without cancer from the general population, distinguishing between not exclusively heterosexual and heterosexual individuals.[5] In the patients with cancer, more tumours of men who were not exclusively heterosexual contained HPV DNA than did tumours of heterosexual men (98% *vs* 78%; p=0·004), and not being exclusively heterosexual significantly increased the risk of anal cancer (odds ratio [OR] 17·3, 95% CI 8·2–36·1).[5]

Nyitray and colleagues did two studies[6,7] of the same convenience samples of MSM and men who have sex with women (MSW), both without HIV, from Brazil, Mexico, and Florida. In the first study,[6] anal HPV prevalence differed according to sexual orientation. 4–10 times more MSM had HPV infection than did MSW (any one type of HPV, 47·2% [95% CI 39·6–54·8] of MSM *vs* 12·2% [10·5–14·1] of MSW; oncogenic HPV, 27·3% [20·7–33·9] *vs* 6·8% [5·5–8·3]; and several types of HPV, 33·0% [26·1–40·4] *vs* 3·2% [2.3–4.3]).[6] The second study[7] reported results after following up both groups for a median of 6·7 months. The findings showed that anal HPV was transient in MSW but persistent in MSM—eg, 16·0% of MSM versus 1·6% of MSW had persistent oncogenic infection, and 5·1% of MSM had HPV-16 compared with none of the MSW.[7] Another study assessed adolescents aged 13–18 years with and without HIV who displayed high-risk homosexual, bisexual, or heterosexual behaviour.[8] The prevalence of anal HPV infection did not differ with HIV status, but anal HPV infection and abnormal anal cytology were highest in boys with a homosexual or bisexual orientation.[8]

A study of 445 men with HIV attending an AIDS clinic in Brazil compared anal HPV infection in MSM with men who have sex with men and women (MSWM) and MSW.[9] MSWM were more likely to have non-oncogenic HPV (OR 4·22, 95% CI 1·77–10·11) or oncogenic HPV (OR 7·33, 3·43–15·70) than were MSW. MSM were also more likely to have non-oncogenic HPV (OR 4·76, 1·38–16·40) or oncogenic HPV (OR 7·92, 2·69–23·35) than were MSW. Similarly, a French study of HIV-clinic outpatients assessed HPV infection and anal squamous intraepithelial lesions in heterosexual men with HIV who injected drugs but had no history of anal intercourse and MSM with HIV.[10] MSM had a greater prevalence of HPV infection than did heterosexual men who injected drugs (85% *vs* 46%; p<0·001). Of the men with HPV, more MSM were infected with several types of HPV than were heterosexual men who injected drugs (61% *vs* 26%; p=0·006), and more MSM had cytologic abnormalities than did men who injected drugs (72% *vs* 36%; p<0·001). In men with anal squamous intraepithelial lesions, distribution of grade did not significantly differ by sexual orientation.[10] Conversely, a study with a small sample of 74 men recruited from a Spanish HIV clinic and consisting of 52 MSM (12 bisexual) and 22 heterosexual men, concluded that the prevalence of HPV infection in the anus, penis, and mouth did not differ by sexual orientation.[11]

Focus of study	
Prevention	
D'Souza et al, 2009[4]	HPV as a risk factor for head and neck cancers
Daling et al, 2004[5]	HPV and other risk factors for anal cancer
Nyitray et al, 2011[6]	HPV and other risk factors for anal cancer
Nyitray et al, 2011[7]	HPV and other risk factors for anal cancer
Moscicki et al, 2003[8]	HPV and other risk factors for anal cancer
Guimaraes et al, 2011[9]	HPV and other risk factors for anal cancer
Piketty et al, 2003[10]	HPV and other risk factors for anal cancer
Sirera et al, 2006[11]	HPV and other risk factors for anal cancer
Abramowitz et al, 2007[12]	HPV and other risk factors for anal cancer
Wilkin et al, 2004[13]	HPV and other risk factors for anal cancer
Weis et al, 2011[14]	HPV and other risk factors for anal cancer
Silva et al, 2011[15]	HPV and other risk factors for anal cancer
Piketty et al, 2008[16]	HPV and other risk factors for anal cancer
Brewer et al, 2010[17]	Understanding of HPV and vaccination
Hernandez et al, 2010[18]	Understanding of HPV and vaccination
McRee et al, 2010[19]	Understanding of HPV and vaccination
Atkinson et al, 2003[20]	HHV-8 as a risk factor for Kaposi's sarcoma
Engels et al, 2007[21]	HHV-8 as a risk factor for Kaposi's sarcoma
Mbulaiteye et al, 2006[22]	HHV-8 as a risk factor for Kaposi's sarcoma
Nascimento et al, 2005[23]	HHV-8 as a risk factor for Kaposi's sarcoma
Renwick et al, 2002[24]	HHV-8 as a risk factor for Kaposi's sarcoma
Souza et al, 2004[25]	HHV-8 as a risk factor for Kaposi's sarcoma
Szalai et al, 2005[26]	HHV-8 as a risk factor for Kaposi's sarcoma
Widmer et al, 2006[27]	HHV-8 as a risk factor for Kaposi's sarcoma
Kouri et al, 2004[28]	HHV-8 as a risk factor for Kaposi's sarcoma
Crum et al, 2003[29]	HHV-8 as a risk factor for Kaposi's sarcoma
Centers for Disease Control and Prevention, 2004[30]	HBV and HCV as risk factors for non-Hodgkin lymphoma and hepatocellular carcinoma
Franceschi et al, 2006[31]	HBV and HCV as risk factors for non-Hodgkin lymphoma and hepatocellular carcinoma
Wieland et al, 2011[32]	Merkel cell polyomavirus
Blosnich et al, 2010[33]	Risk factors for lung cancer
(Continues in next column)	

Focus of study	
(Continued from previous column)	
Detection	
Rosa-Cunha et al, 2010[34]	Anal cancer
Heslin et al, 2008[35]	Prostate and colorectal cancer
Diagnosis	
Allardice et al, 2003[36]	Cancers in HIV/AIDS cohorts
Ebrahim et al, 2004[37]	Cancers in HIV/AIDS cohorts
Atkinson et al, 2004[38]	Cancers in HIV/AIDS cohorts
Engels et al, 2002[39]	Cancers in HIV/AIDS cohorts
Galceran et al, 2007[40]	Cancers in HIV/AIDS cohorts
Lanoy et al, 2009[41]	Cancers in HIV/AIDS cohorts
Mayor et al, 2003[42]	Cancers in HIV/AIDS cohorts
Frisch et al, 2003[43]	Cancer in the general population
Cress and Holly, 2003[44]	Cancer in the general population
Treatment	
Motofei et al, 2011[45]	Prostate cancer
Survivorship	
Monforte et al, 2008[46]	Survival and mortality
Sackoff et al, 2006[47]	Survival and mortality
Holly et al, 2002[48]	Survival and mortality
Boehmer et al, 2011[49]	Survival and mortality
Boehmer et al, 2011[50]	Self-reported health

HPV=human papillomavirus. HHV-8=human herpesvirus 8. HBV=hepatitis B virus. HCV=hepatitis C virus.

Table: **Studies defined according to the cancer control continuum**

Three studies assessed both sexual orientation and receptive anal intercourse as risk factors for anal cancer.[12–14] Each study recruited a sample of people with HIV from an HIV clinic, with all three assessing the prevalence of and factors associated with squamous intraepithelial lesions and condyloma, and two[13,14] comparing abnormal cytological results and anal intraepithelial neoplasia. Results showed that sexual orientation and receptive anal intercourse are independent correlates of condyloma, abnormal cytological results, histological dysplasia, and anal intraepithelial neoplasia.[12–14] However, findings from each study showed that the absence of receptive anal intercourse does not rule out anal intraepithelial neoplasia or abnormal cytological results, and therefore encourage screening of all populations with HIV. A Brazilian study recruited consecutive individuals with and without HIV from an outpatient clinic who presented with colorectal complaints and had differing risk factors for anal squamous intraepithelial lesions.[15] MSM with HIV were significantly more likely to have anal squamous intraepithelial lesions than were women with HIV, men and women without any anal cancer risk factors, heterosexual men with HIV, men and women without HIV who did not have receptive anal intercourse, and women without HIV who did have receptive anal intercourse. The results suggest that both HIV infection and receptive anal intercourse are significant correlates of anal squamous intraepithelial lesions.[15]

Piketty and colleagues[16] assessed the prevalence of anal cancer over time in the context of the introduction of combination antiretroviral therapy (cART) in France by analysing data from the French Hospital Database on HIV. The prevalence of anal cancer was higher in MSM with HIV than in women and heterosexual men, and increased over time (eg, 18·2 per 100 000 MSM with HIV had anal cancer in the pre-cART period compared with 45·1 per 100 000 in the early cART period and 75·1 per 100 000 during the cART period).[16]

HPV knowledge and vaccination

A population-based survey of US men aged 18–59 years assessed men's HPV-related knowledge and understanding of risk factors related to genital warts, oral cancer, and anal cancer.[17] When the investigators compared gay or bisexual men with heterosexual men,

they noted that significantly more gay or bisexual men knew that HPV can cause genital warts and anal cancer and that HIV increases the risk of genital warts, oral, and anal cancer, and more believed they knew a lot about genital warts, oral, and anal cancer, than did heterosexual men. Beliefs about risk factors for HPV-related disease differed according to sexual orientation.[17]

Two survey studies focused on the acceptability of HPV vaccination.[18,19] Hernandez and colleagues[18] studied a convenience sample of MSM and heterosexual men and concluded that significantly less heterosexual men (68%) than MSM (75%) intended to be vaccinated (adjusted OR 0·54, 95% CI 0·30–0·97).[18] Results of a nationally representative study of US gay or bisexual and heterosexual men showed that gay or bisexual men had a greater interest in HPV vaccination than did heterosexual men (73% *vs* 37%).[19] However, when HPV vaccination was framed as a cancer prevention activity, the intent to undergo vaccination did not significantly differ by sexual orientation.

Human herpesvirus type 8 (HHV-8) as a risk factor for Kaposi's sarcoma

HHV-8 has been shown to predispose people to Kaposi's sarcoma. Ten studies assessed the prevalence and correlates of HHV-8, with most concluding that MSM have disproportionally higher HHV-8 infection rates than do comparison groups.[20–27] One exception to this finding was reported by Kouri and colleagues[28] who studied various populations in Cuba. The investigators concluded that homosexuality or bisexuality was not significantly associated with HHV-8 infection in patients with AIDS with or without Kaposi's sarcoma after they compared these patients with a simulated general low-risk population comparison sample consisting of blood donors and kidney transplant recipients without HIV.[28]

Evidence of sexual transmission of HHV-8 in MSM was derived from several studies that used different comparison groups. A study in Brazil compared individuals from the general population without risk for HHV-8 with individuals at risk for sexually transmitted diseases, including MSM without HIV.[25] The prevalence of HHV-8 in MSM was 32·6% compared with 1·0–4·1% in the general population, depending on age group. A study in San Francisco compared MSM who used injection drugs with heterosexual men and women who used injection drugs.[20] HHV-8 seroprevalence was significantly greater in MSM than in heterosexual men and women, suggesting that MSM who inject drugs have a greater risk of HHV-8 infection through both sexual and bloodborne transmission. Findings from a cohort study that took place in Amsterdam showed that a greater proportion of MSM had HHV-8 infection than did other men, and that HHV-8 seropositivity was not associated with injection drug use.[24] Engels and colleagues[21] studied participants in the US National Health and Nutrition Examination Survey and concluded that the prevalence of HHV-8 in MSM was substantially higher than in heterosexual men (8·2% *vs* 1·3%).

Similarly, results of studies of patients with HIV have showed that HHV-8 is more prevalent in MSM than in other men. A Swiss HIV cohort study[27] reported that the prevalence of HHV-8 and prevalence over time of Kaposi's sarcoma lesions were significantly higher in MSM than in heterosexual men, but that oral HHV-8 DNA detection did not differ with sexual orientation. Results of a Hungarian sample of patients with HIV with and without Kaposi's sarcoma showed that of the patients without Kaposi's sarcoma, more homosexual men had HHV-8 infection than did bisexual or heterosexual patients.[26] An analysis of data from US military men with HIV identified correlates of HHV-8 seropositivity and compared MSM with heterosexual men.[29] Although HHV-8 was more prevalent in MSM than in heterosexual men, this difference was not statistically significant. However, correlates of HHV-8 significantly differed with sexual orientation. MSM infected with hepatitis B virus (HBV) or herpes simplex virus type 2 (HSV-2) were significantly more likely to have HHV-8 infection than were MSM without HBV or HSV-2 (with HBV, OR 2·17; with HSV-2, OR 2·60). These infections did not significantly affect the prevalence of HHV-8 infection in heterosexual men. Rather, in heterosexual men, marital status and race were associated with HHV-8 infection. Studies of patients with AIDS identified further differences. The National Cancer Institute's AIDS cohort study[22] reported a significantly greater prevalence of HHV-8 infection in MSM than in women and heterosexual men, and identified correlates of HHV-8 that differed according to sexual behaviour. In MSM, HHV-8 was significantly associated with hepatitis, gonorrhoea, genital warts, and nitrate inhalant use.[22] Finally, a study of patients with AIDS and Kaposi's sarcoma in Brazil that characterised the strains of Kaposi's sarcoma-associated herpes virus reported significant associations of specific strains with sexual orientation.[23] Homosexual and bisexual men clustered in subtype A, whereas heterosexual men and women clustered in subtype C, which led the investigators to conclude that different networks of sexual transmission exist.

Hepatitis (B or C) as risk factor for non-Hodgkin lymphoma and hepatocellular carcinoma

US national disease surveillance data of acute HBV infection, which can result in liver cancer, suggested that HBV declined by 67% overall between 1990 and 2002.[30] However, the proportion of MSM with HBV increased from 7% to 18% in the same period. Using data and blood samples from a Swiss HIV cohort study, Franceschi and colleagues[31] examined the link between non-Hodgkin lymphoma and seropositivity for antibodies of HBV and hepatitis C virus (HCV) in patients with HIV and

non-Hodgkin lymphoma who were matched to controls without non-Hodgkin lymphoma.[31] They identified that neither HBV nor HCV infection was associated with non-Hodgkin lymphoma. MSM had a higher HBV-to-HCV infection ratio than did heterosexuals and people who used intravenous drugs, suggesting that the efficiency of sexual transmission is greater for HBV than for HCV.

Merkel cell polyomavirus as a risk factor for Merkel cell carcinoma

A German case-control study assessed MSM with HIV and a control group of presumably heterosexual (sexual orientation was not assessed) men without HIV for the presence of Merkel cell polyomavirus, which has been linked to Merkel cell carcinoma.[32] Although Merkel cell polyomavirus DNA loads were high (53·9%) in both groups, prevalence of Merkel cell polyomavirus did not differ significantly between patients and controls.

Risk factors for lung cancer

Blosnich and colleagues[33] focused on smoking and acute respiratory illnesses as risk factors for lung cancer in sexual minorities because evidence suggests that a history of chronic bronchitis and impaired lung function are risk factors for lung cancer. This study analysed a national, but not representative, sample of 75 164 college students aged 18–24 years who reported having a heterosexual, gay or lesbian, bisexual, or unsure sexual orientation.[33] It compared each sexual orientation group's likelihood of acute respiratory illness, which was defined as streptococcal pharyngitis, bronchitis, sinus infection, or asthma. The study's models adjusted for age, sex, race, HIV status, and binge drinking and smoking. The likelihood of gay or lesbian college students having had streptococcal pharyngitis was significantly greater than for heterosexual college students (OR 1·38), and bisexuals were more likely to have had the following respiratory illnesses than were heterosexuals: sinus infection (OR 1·15); asthma (OR 1·37); and bronchitis (OR 1·19). These analyses were not stratified by sex.

Detection

Patient–provider communication about anal health has been identified as key for identification of symptoms that might be associated with anal cancer.[34] Using survey data of patient self-reports from an existing HIV cohort, Rosa-Cunha and colleagues[34] assessed whether patients had discussed anal health with an HIV primary care provider.[34] In this sample of patients with HIV, MSM were 5·56 times more likely to have discussed anal health than were women, compared with heterosexual men who were 2·31 times more likely then were women to have discussed anal health.[34]

Using representative population-based data from California, Heslin and colleagues[35] compared gay or bisexual men's reports of screening for prostate and colorectal cancer with heterosexual men's screening rates. Compared with heterosexual men, gay or bisexual men were almost twice as likely to have undergone screening for colorectal cancer (OR 1·67, 95% CI 1·06–2·65), but had significantly lower odds of having had an up-to-date prostate-specific antigen test (0·61, 0·42–0·89).

Diagnosis

In the diagnosis category, most studies focused on cancers in cohorts with HIV or AIDS.[36–42] Studies reporting ORs or standardised incidence ratios (SIR) compared risk with that of the general population and between various HIV risk categories. The SIR of a sample of Scottish patients with HIV for AIDS-related and non-AIDS-related cancers was 11 times that of the general population, with homosexual and bisexual men having an SIR of 21·4—higher than for heterosexuals (5·9) and patients in other HIV risk groups.[36] Engels and colleagues[39] used the AIDS–Cancer Match Registry, a linkage of AIDS and cancer registry data from 11 US states, to calculate SIRs for non-Hodgkin lymphoma and liver cancer relative to the general population. Homosexual men who did and did not inject drugs had lower risks of liver cancer than people with haemophilia and people who injected drugs, but still substantially higher risks than the general population (homosexual men, SIR 5·5; homosexual men who injected drugs, SIR 8·9). The SIR for non-Hodgkin lymphoma was calculated for all non-Hodgkin lymphoma subtypes of low, intermediate, high, and unspecified grade. For low, intermediate, and high grades, homosexual men had higher SIRs than did people with haemophilia, people who injected drugs, and heterosexuals. Depending on the grade, SIRs ranged from 4·6 to 155. A Spanish study that linked AIDS and cancer registry data calculated SIRs for Kaposi's sarcoma, non-Hodgkin lymphoma, and any invasive cancer.[40] Of all HIV risk categories, men with homosexual or bisexual contact had the highest SIR for Kaposi's sarcoma (3003·23) and any invasive cancers (SIR 53·94), whereas heterosexual women had the highest SIR for non-Hodgkin lymphoma (272·34), closely followed by men with homosexual or bisexual contact (SIR 240·66). A study that matched AIDS and cancer registry data from nine US states assessed incidence of various skin cancers.[41] In patients with AIDS, incidences of Merkel cell carcinoma (SIR 11) and sebaceous carcinoma (SIR 8·1) were higher than in the general population, but did not significantly differ between HIV risk categories. MSM had the highest incidence of melanoma (SIR 1·6) of all the HIV risk categories and were the only HIV risk group that exceeded melanoma risks of the general population. The risk of appendageal carcinomas was significantly greater in both MSM (SIR 6·8) and MSM who inject drugs (SIR 11) than in the general population.

In an AIDS surveillance dataset that included data from 17 western European countries, Ebrahim and

colleagues[37] assessed how often cancer (eg, Kaposi's sarcoma, lymphoma) was the initial AIDS-defining illness for several HIV risk categories. From 1994 to 2001, homosexual and bisexual men had the highest decline in Kaposi's sarcoma as the initial AIDS-defining cancer of all HIV risk categories. Kaposi's sarcoma in people who used intravenous drugs also significantly declined, but at a lower rate, whereas those whose sexual orientation was undetermined had a significant increase over the same period. Lymphoma as the AIDS-defining illness did not differ by risk group over this period.[37] A study of HIV/AIDS patients in Puerto Rico assessed differences in prevalence of non-Hodgkin lymphoma between HIV risk groups, distinguishing between AIDS-defining and non-AIDS-defining non-Hodgkin lymphoma.[42] Injection drug use was more prevalent in patients with AIDS-defining non-Hodgkin lymphoma, whereas homosexual or bisexual contact was more prevalent in patients with non-AIDS-defining non-Hodgkin lymphoma. By linking US state and metropolitan area AIDS and cancer registry data, Atkinson and colleagues[38] estimated incidence of Kaposi's sarcoma in patients with AIDS, concluding that MSM had the highest incidence of Kaposi's sarcoma (5·7 per 100 person-years) compared with heterosexual men (0·7 per 100 person-years) and women (0·4 per 100 person years).[38] Furthermore, when each sex and sexual orientation group was differentiated by injection drug use, results between the groups did not differ, with the exception of MSM—ie, MSM who injected drugs had a significantly lower incidence of Kaposi's sarcoma than did MSM who did not inject drugs (4·7 per 100 person-years *vs* 5·8 per 100 person-years).

Two studies assessed cancer in populations not characterised by HIV/AIDS.[43,44] A Danish study focused on cancer prevalence, using data from Denmark's Civil Registration System to identify men in homosexual partnerships.[43] Although men in homosexual partnerships were significantly more likely to have cancer (OR 2·1) than the general population, these high rates were a result of AIDS-related cancers, such as Kaposi's sarcoma (OR 136·0), non-Hodgkin lymphoma (OR 15·1), and anal squamous carcinoma (OR 31·2). After exclusion of AIDS-related cancers, the rate of cancers for men in homosexual partnerships was not significantly different from the general population.[43] To compensate for an absence of information about the sexual orientation of patients with cancer in US cancer registries, Cress and Holly[44] used California Cancer registry data on anal cancer to compare patients by demographics and county of residence. Men who resided in San Francisco county had a significantly raised rate of anal cancer compared with other counties and with the state of California overall. The investigators concluded that the greater incidence of anal cancer in San Francisco was associated with the greater proportion of MSM living in San Francisco than in other counties.[44]

Treatment

We identified only one study that assessed treatment of cancer for MSM.[45] The study examined sexual function in Romanian heterosexual and homosexual men with prostate cancer who were given a non-steroidal antiandrogen.[45] Homosexuals had worse erectile function that decreased at a faster rate during treatment than did heterosexual men's erectile function. Homosexual men showed lower sexual functioning on most subscales related to antiandrogen treatment than did heterosexual men.

Survivorship

Of studies in the survivorship category, most addressed overall survival or mortality. Two studies focused on mortality in people with AIDS, discerning between AIDS-related and non-AIDS-related mortality.[46,47] In a study of patients with AIDS in New York City, Sackoff and colleagues[47] noted that non-AIDS-related deaths increased between 1999 and 2004, with 21% of all deaths caused by cancer, making cancer the third most common non-AIDS-related cause of death in these patients.[47] Of the non-AIDS-defining deaths, 9·4 deaths per 10 000 were linked to lung cancer in all people with AIDS, with 5·2 deaths per 10 000 in MSM, and 2·5 deaths per 10 000 were linked to liver cancer in all people with AIDS, with 1·7 per 10 000 in MSM. Finally, the prevalence of rectal and anal cancer was 1·6 per 10 000 in all people with AIDS and in the subset of MSM. In a study of 11 combined HIV cohorts from the USA, Europe, and Australia, Monforte and colleagues[46] assessed cancer mortality as a result of AIDS-related deaths (Kaposi's sarcoma; non-Hodgkin lymphoma, either systemic or of the brain; or cervical cancer) and non-AIDS-related deaths (cancer of the lung, anal canal, gastrointestinal tract, liver, urogenital tract, oral cavity, nasopharynx, or larynx, or haematological cancer excluding non-Hodgkin lymphoma, or cancer of other sites).[46] Adjusted models of AIDS-related mortality showed significant differences in mortality between risk categories, and the odds of mortality were significantly higher for homosexual men than for heterosexual men, heterosexual women, or men who injected drugs. Risk category was not significantly associated with non-AIDS-defining mortality.

In a large epidemiological study of risk estimates for non-Hodgkin lymphoma in the San Francisco Bay area, non-Hodgkin lymphoma subtype significantly differed by sex and sexual orientation.[48] Homosexual men were more likely to have high-grade non-Hodgkin lymphoma then were heterosexual men or heterosexual women. Homosexual men had the shortest survival and heterosexual men had the longest survival. After considering individuals who were not interviewed (either because they died or because the investigators received their information after the study had ended), the revised estimated OR for non-Hodgkin lymphoma in homosexual men with HIV was 50, more than double

the original estimate of 20. Using Surveillance, Epidemiology and End Results data, Boehmer and colleagues[49] examined the relation between colorectal cancer incidence, mortality, and density of MSM within US counties (derived from census data for same-sex partner households). After controlling for other demographics, they identified a significant positive association between density of MSM and colorectal cancer incidence and mortality.[49]

The same group then used data that were representative of the adult population of California to assess the prevalence of any cancer diagnosis and cancer survivors' self-reported health according to sexual orientation, distinguishing between gay, bisexual, and heterosexual individuals.[50] They noted that gay men were more likely to report a diagnosis of cancer than were heterosexual men (OR 1·9). Furthermore, gay men were diagnosed at a significantly younger age (42 years) than were heterosexual men (52 years). Cancer survivors' self-reports of being in fair or poor health did not significantly differ by sexual orientation.

Discussion

The goal of our review was to synthesise known disparities in cancer statistics and to identify gaps in knowledge about MSM (ie, gay, bisexual, and other MSM) and cancer. We noted that existing research focused most heavily on risk factors for cancer, providing evidence of disparities in the prevalence of viruses linked to cancers. The most evidence available was about HPV, showing that MSM have a higher prevalence of anal HPV infection than do comparison groups—a finding that applied to people with and without HIV. However, MSM were also more aware and knowledgeable about HPV and had a greater willingness to be vaccinated than did comparison groups. We noted a similar pattern in the second most well studied virus, HHV-8 (associated with Kaposi's sarcoma)—most studies documented that, of people with and without HIV, MSM had a higher prevalence of HHV-8 than did comparison groups. Moreover, HBV infection has increased over time in MSM, whereas it has decreased in the general population. Finally, only one study[33] focused on non-viral risk factors for cancers—acute respiratory disease and smoking—concluding that MSM had consistently greater odds of acute respiratory illnesses, with and without controls for smoking.

Results of the two studies[34,35] that focused on detection showed some advantages for MSM—providers were more likely to discuss anal health with MSM with HIV than with heterosexual men and women with HIV, and MSM had more colorectal cancer screening. However, substantial evidence from epidemiological studies shows disparities in cancer incidence or prevalence, although most evidence was derived from HIV/AIDS cohorts. MSM with HIV had more AIDS-related and non-AIDS-related cancers than did others with HIV. Alternatively, studies that focused on populations other than those with HIV had contradictory findings. Investigators of one study[43] concluded that cancer disparities exist only with respect to AIDS-related cancers. Others documented a higher prevalence in MSM of anal cancer,[44] colorectal cancer,[49] or any cancer type[50] than in the general population. The only cancer treatment study, which focused on prostate cancer, concluded that MSM's sexual function was worse after treatment than was heterosexual men's.[45] Finally, cancer survivorship studies suggested that cancer survivors' self-reported health did not differ significantly according to sexual orientation,[50] but MSM do not survive for as long after being diagnosed with non-Hodgkin lymphoma[48] as do heterosexual men or women, and have higher colorectal cancer mortality.[49] In populations with AIDS, MSM had more AIDS-related cancer deaths than did other individuals with HIV/AIDS, and non-AIDS-related mortality was prevalent, but evidence of disparities between sexual orientations was inconclusive.

With few exceptions,[43,44,48–50] information on sexual orientation disparities in cancer incidence and mortality is not available for the general population, and is mostly inferred from populations with HIV/AIDS. One main reason for this bias could be the absence of sexual orientation data in cancer registries. In populations with HIV/AIDS, much of the evidence documenting cancer burden disparities is derived from studies that linked cancer registries to AIDS registries, which store data on sexual risk behaviour.[39–41] If sexual orientation data continues to be omitted from medical records of the general population, data for people with HIV/AIDS will continue to be more readily available than for the general population.

We also suggest that evidence of cancer disparities between sexual orientations is skewed towards information related to immunosuppression and infectious causes. Thus, information is available on AIDS-related cancers, such as Kaposi's sarcoma and lymphoma, and cancers with infectious causes (eg, HPV), which are prevalent in populations infected with HIV, but is lacking for other cancer types. Most non-infectious cancers have yet to be studied in the context of sexual orientation. Almost 50% of cancers are linked to environmental and lifestyle factors, such as smoking, diet, and alcohol, but despite being at the centre of public awareness and a mainstay of media attention,[51] studies of how they differ according to sexual orientation were mostly absent from this review. By contrast, only about 18% of cancers are caused by infection,[52] but studies of this cancer type dominated this review. Eligibility criteria for this review were such that all articles addressed cancer explicitly, which resulted in identification of articles that dealt mostly with infectious causes, even though studies documenting differences in lifestyle behaviours by sexual orientation are well established.[53]

Two more reasons might contribute heavily towards explaining the restricted scope of the available knowledge

on MSM and cancer. First, cancer initially emerged as a concern for MSM in the context of HIV/AIDS. Thus, rightfully, cancer researchers became involved in the discovery and treatment of HIV/AIDS-related malignancies and the virology of cancer. Second, the narrow understanding of sexual orientation might be a contributing factor. In studies of this type, sexual orientation is often defined only by sexual behaviour or sexual acts that can transmit infections. However, a broader understanding of sexual orientation that not only embraces sexual behaviour, but also defines sexual minorities as socially and culturally distinct groups, is needed. This approach calls for a comprehensive cancer research agenda to identify the determinants of cancer disparities caused by sexual orientation, in line with the work that has examined racial, ethnic, or economic disparities in cancer.[54] When this broader framework of sexual orientation is used, gaps in the knowledge about MSM and cancer can be seen—eg, an absence of research on MSM's interactions with the health-care system, including with oncologists and other providers; treatment decision-making; participation in clinical cancer trials; and information about support available to MSM living with cancer, their partners or spouses, and their families.

In conclusion, our review of the evidence suggests that sexual orientation is still largely overlooked in the context of cancer. Significant research efforts should be devoted to examination of the effects of sexual orientation along the cancer control continuum. To bring knowledge about cancer in MSM on a par with other minority groups, a framework of social justice that incorporates social and behavioural research and that systematically documents the nature and cause of inequities associated with MSM and cancer should be put in place to inform future efforts.

Contributors

UB searched the scientific literature and led the writing, TPC provided clinical knowledge, and MAC provided conceptual input. All authors interpreted the findings and contributed in significant ways to the final article by reviewing and discussing earlier drafts.

Conflicts of interest

We declare that we have no conflicts of interest.

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