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HIV infection in Men who have Sex with Men (MSM):
Risk-Taking Behaviours and Drivers of Increased Infection

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**DISSERTAÇÃO PARA A OBTENÇÃO DO GRAU DE DOUTOR EM SAÚDE INTERNACIONAL
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HIV infection in Men who have Sex with Men (MSM): Risk-Taking Behaviours and Drivers of Increased Infection

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II. Dias S, Gama A, Fuertes R, Mendão L, Barros H. Risk-taking behaviours and HIV infection among sex workers in Portugal: results from a cross-sectional survey. *Sex Transm Infect.* 2015; 91(5):346-52. doi: 10.1136/sextrans-2014-051697.

III. Gama A, Martins MRO, Mendão L, Barros H, Dias S. HIV Infection, Risk Factors and Health Services Use among Male-to-Female Transgender Sex Workers: A Cross-sectional Study in Portugal. *AIDS Care.* 2017 May 25:1-8. doi: 10.1080/09540121.2017.1332736. [Epub ahead of print].

IV. Gama A, Martins MO, Dias S. HIV research with Men who have Sex with Men (MSM): Advantages and challenges of different methods for most appropriately targeting a key population. *AIMS Public Health.* 2017; 4(3):221-39. doi: 10.3934/publichealth.2017.3.221.

V. Dias S, Gama A. [Community-based participatory research in public health: potentials and challenges]. *Rev Panam Salud Publica.* 2014; 35(2):150-4. PMID: 24781097.

LIST OF COMMUNICATIONS

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Dias S, Gama A, Pingarilho M, Simões D, Mendão L, Martins, MO. Utilização de serviços de saúde e prevalência do VIH em trabalhadoras do sexo migrantes e nacionais em Portugal: estamos a providenciar os serviços necessários? Apresentação oral. 4º Congresso Nacional de Medicina Tropical. Lisboa, Portugal, 19-21 de abril de 2017.

Gama, A. HIV among Men who have Sex with Men: The Influence of Cruising Venues in Risk Behaviors. Oral presentation. National Meeting of Public Health PhD Students. Porto, Portugal, 13th July 2016.

Gama, A. Comportamentos de risco e infecção pelo VIH em trabalhadores do sexo homens, transgénero e mulheres em Portugal. Poster. 6[as]Jornadas Científicas do IHMT. Lisboa, Portugal. 11 de dezembro de 2015.

Dias, S., Gama, A., Fuertes, R., & Mendão, L. The promising of participatory approach in HIV health promotion research. Oral presentation. 21st IUHPE World Conference on Health Promotion. Pattaya, Thailand. 25th-29th August 2013.

Dias, S., Gama, A., Simões, D., Rego, I., & Mendão, L. Male-to-female transgender sex workers in Portugal: Sexual health behaviours. Oral presentation. 1st International Conference on LGBT Psychology and related fields. Lisbon, Portugal. 20th-22nd June 2013.

Dias, S., Gama, A., Fuertes, R., Simões, D., Fernandes, R., & Mendão, L. Transgender sex workers use of health services for HIV information, prevention and testing. Oral presentation. 1st International Conference on LGBT Psychology and related fields. Lisbon, Portugal. 20th-22nd June 2013.

their love and support. To my brother for his contagious good spirit and companionship. To the kids, my nephews, for the laughs.

To all my friends, who near or far were always present despite my absence.

"So the problem is not so much to see what nobody has yet seen, as to think what nobody has yet thought concerning that which everybody sees."

— Arthur Schopenhauer (1851)

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ABSTRACT

HIV incidence among men who have sex with men (MSM) has risen in most Western countries. This has been largely attributed to increased high-risk sexual behaviours that occur from combinations of drivers operating in specific social, economic, cultural, and political contexts. MSM constitute a key population at increased risk for HIV, but not all MSM are at equivalent risk. Male and transgender sex workers (SW) are MSM subgroups considered most vulnerable to HIV infection. So far, knowledge on drivers of increased HIV among MSM is limited. Difficulties in reaching hard-to-reach groups have challenged research with key populations. Several methods for recruiting difficult-to-access populations have emerged.

This thesis intends to contribute to improve knowledge on prevalence of HIV, high risk behaviours and its determinants among MSM in Portugal. The specific objectives are to: 1)Estimate the prevalence of HIV and assess high-risk behaviours among a population of MSM in Portugal; 2)Explore and understand the complex links of HIV risk-taking practices and the adoption of protective measures among MSM most vulnerable groups; and 3)Critically analyse different methods for most effectively targeting MSM in HIV research and reach those most-at-risk. This thesis is expected to contribute to improve knowledge on HIV burden and risk factors among MSM in Portugal, and identify prevention needs to inform actions for reducing the spread of infection in MSM. This thesis is also expected to contribute to conducting future research with this hard-to-reach population. This work was based on the literature review on HIV and MSM developed throughout the thesis, the results obtained in the cross-sectional studies conducted about the prevalence of HIV, high-risk behaviours and drivers of infection among MSM, and the critical review of the methods for most appropriately targeting MSM in HIV research.

Our findings show a high prevalence of HIV among the MSM studied – 8.8% (95%CI: 7-11%). More than a third of respondents reported visiting venues where MSM frequently seek sexual partners and have sex (cruising venues). A significantly higher proportion of cruising venues' visitors reported to be HIV-positive (14.6% [95%CI: 11-18%] vs. 5.5% [95%CI: 4-7%] among non-visitors). Cruising venues' visitors also engage more frequently in high-risk sexual behaviours as multiple sexual partners, group sex, and unprotected anal sex. Our findings show that different subgroups of MSM present disparate levels of HIV risk. Male SW presented high levels of HIV infection (5.0% [95%CI: 1-10%] self-reported; 10.7% [95%CI: 0-23%] reactive to rapid test), and reported frequently high-risk sexual behaviours as multiplicity of sexual partners, inconsistent condom use and drugs use. Among transgender SW (TSW), the proportion of HIV infection was 14.9% [95%CI: 8-21%]; findings show an overlap of sexual risk behaviours and an association of poor socioeconomic context with increased HIV risk and underuse of health services. Emerging methods for most effectively targeting MSM in HIV research - chain-referral, venue-based, respondent-driven, time-location, internet sampling methods, and community-based participatory approach - face common challenges but present several advantages on recruitment efficiency, especially of most-vulnerable subgroups, and evidence obtained on MSM's needs.

There are diverse risk profiles of MSM population. Tailored interventions should integrate strategies to reduce risk behaviours, intensify harm reduction, improve uptake of HIV testing and promote access to HIV health services, while tackling socioeconomic, partnering, and structural contexts conducive to increased risk. Further research

producing relevant knowledge more 'translatable' into effective actions that address MSM's health needs and improve health gain is needed.

RESUMO

A incidência da infecção pelo VIH em homens que praticam sexo com homens (HSH) tem aumentado na maioria dos países ocidentais. Tal tem sido atribuído ao aumento de comportamentos de risco resultantes de combinações de factores que operam em contextos sociais, económicos, culturais e políticos específicos. Os HSH constituem uma população-chave em maior risco para o VIH, mas nem todos os HSH se encontram em igual nível de risco. Homens e pessoas transgénero trabalhadores do sexo (TS) são subgrupos de HSH considerados particularmente vulneráveis à infecção pelo VIH. O conhecimento actual sobre os factores do aumento da infecção pelo VIH em HSH é limitado. As dificuldades em alcançar grupos de difícil acesso têm desafiado a investigação com populações-chave. Neste contexto têm emergido vários métodos para recrutar estas populações.

Esta tese pretende contribuir para aumentar o conhecimento sobre a prevalência do VIH, comportamentos de risco e seus determinantes em HSH em Portugal. Os objectivos desta tese são: 1)Estimar a prevalência do VIH e examinar os comportamentos de risco numa população de HSH em Portugal: 2)Explorar e compreende as complexas ligações de práticas de risco para o VIH e a adopção de medidas protectoras em grupos mais vulneráveis de HSH; e 3)Analisar criticamente diferentes métodos para alcançar mais adequadamente HSH na investigação em VIH e alcançar os grupos em maior risco. Com esta tese espera-se contribuir para um melhor conhecimento sobre a prevalência de VIH e factores de risco em HSH em Portugal, e identificar necessidades de prevenção para informar acções com vista à redução da transmissão do VIH nos HSH. Com esta tese espera-se também contribuir para o desenvolvimento de investigação futura com esta população de difícil acesso. O presente trabalho baseia-se na revisão de literatura sobre VIH e HSH desenvolvida ao longo do período da tese, nos resultados obtidos nos estudos transversais realizados sobre a prevalência de VIH, comportamentos de risco e factores da infecção em HSH, bem como na análise crítica dos métodos para alcançar mais adequadamente HSH na investigação em VIH.

Os nossos resultados mostram uma elevada prevalência de VIH nos HSH estudados - 8.8% (IC95%: 7-11%). Mais de um terço dos inquiridos reportou frequentar locais onde HSH procuram parceiros sexuais e têm relações sexuais (locais de encontro sexual). Uma proporção significativamente mais elevada de frequentadores de locais de encontro sexual reportou ser VIH-positivo (14.6% [IC95%: 11-18%] vs. 5.5% [IC95%: 4-7%] nos não-frequentadores). Os frequentadores de locais de encontro sexual também reportam mais frequentemente comportamentos sexuais de risco como múltiplos parceiros sexuais, sexo em grupo e sexo anal desprotegido. Os nossos resultados indicam que diferentes subgrupos de HSH apresentam diferentes níveis de risco para o VIH. Homens TS apresentam elevados níveis de infecção pelo VIH (5.0% [IC95%: 1-10%] auto-reportado; 10.7% [IC95%: 0-23%] resultado reactivo ao teste rápido), e reportam frequentemente comportamentos sexuais de risco como a multiplicidade de parceiros sexuais, o uso inconsistente do preservativo e o uso de drogas. Nos indivíduos transgénero TS, a proporção de infecção pelo VIH foi de 14.9% [IC95%: 8-21%]; os resultados mostram uma intersecção de comportamentos sexuais de risco e uma associação de contextos socioeconómicos desfavoráveis com um aumento do risco para o VIH e reduzida utilização dos serviços de saúde. Métodos emergentes para alcançar mais adequadamente HSH na investigação em VIH – de referência em cadeia, baseados em locais, orientados

pelos respondentes, de tempo-local, por internet, e abordagem de investigação baseada na comunidade – enfrentam desafios comuns, mas apresentam várias vantagens ao nível da eficiência do recrutamento, especialmente de subgrupos mais vulneráveis, e da evidência obtida sobre as necessidades dos HSH.

Existem diferentes perfis de risco na população de HSH. Intervenções adequadas devem integrar estratégias para reduzir comportamentos de risco, intensificar a redução de danos, aumentar a realização do teste para o VIH e promover o acesso aos serviços de saúde e VIH, abordando os contextos socioeconómicos, relacionais e estruturais que conduzem a um maior risco. É necessária investigação que produza conhecimento relevante e mais "traduzível" em acções efectivas, que respondam às necessidades em saúde dos HSH e contribuam para ganhos de saúde.

Palavras-chave: VIH; Comportamentos de risco; HSH; Homens trabalhadores do sexo; Indivíduos transgénero trabalhadores do sexo; Métodos.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AIDS - Acquired Immunodeficiency Syndrome

ART - Antiretroviral Therapy

CDC - US Centers for Disease Control and Prevention

ECDC - European Centre for Disease Prevention and Control

EU/EEA - European Union/European Economic Area

GSE - Group sexual encounters

HIV - Human Immunodeficiency Virus

HSH - Homens que particam sexo com homens

INSA - Instituto Nacional de Saúde Doutor Ricardo Jorge

LGBT - Lesbian, gay, bisexual and transgender

MSM - Men who have sex with men

PLWHA - People living with HIV/AIDS

PrEP - Pre-exposure prophylaxis

RDS - Respondent-driven sampling

SES – Socioeconomic status

STIs - Sexually transmitted infections

SW - Sex worker

TLS - Time-location sampling

TSW - Transgender sex worker

UAI - Unprotected anal intercourse

UNAIDS - Joint United Nations Programme on HIV/AIDS

USA - United States of America

WHO - World Health Organization

1. GENERAL INTRODUCTION

1. GENERAL INTRODUCTION

1.1. HIV among Men who have Sex with Men (MSM)

1.1.1. Current HIV epidemic trends

In the last decades, Human Immunodeficiency Virus (HIV) infection has evolved into a chronic disease with effective combination of antiretroviral therapy (Chu & Selwyn 2011; Deeks et al. 2013; Fee & Krieger 1993). However, HIV infection continues to be a concern in global public health. The latest estimates from Joint United Nations Programme on HIV/AIDS (UNAIDS) covering 160 countries indicate that in 2015 there were 2.1 million [1.8 million–2.4 million] new HIV infections worldwide, adding up to a total of 36.7 million [34.0 million–39.8 million] people living with HIV (UNAIDS 2016). Surveillance data published by the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) Regional Office for Europe indicate that, in 50 of 53 countries in the WHO European Region, 153 407 new HIV diagnoses were reported in 2015, corresponding to a rate of 17.6 per 100 000 population in this region (ECDC/WHO Regional Office for Europe 2016).

Portugal is one of the western European countries with the highest burden of HIV infection (ECDC/WHO Regional Office for Europe 2016). The most recent available estimates indicate that, in the European Region, Portugal had one of the highest incidence rates in 2015 (9.5 new HIV diagnoses per 100 000 population) (ECDC/WHO Regional Office for Europe 2016) and had the second highest HIV prevalence in 2011 - 0.7% [0.6-1.0%] (among adults aged 15-49 years old) (UNAIDS 2012a).

The emergence of Acquired Immunodeficiency Syndrome (AIDS) as a global threat has served to highlight the diversity of lifestyles and complexity of sociocultural subgroups which need to be considered in health action and policy (Faugier & Sargeant 1997). Key populations suddenly assumed a new importance due to the challenge they now pose to public health (Faugier & Sargeant 1997). In line with current consensus definitions used by UNAIDS and WHO, "key populations" are groups who, due to specific higher-risk behaviours in combination with interpersonal, socio-political, and cultural contexts, are at increased risk of HIV (UNAIDS 2015; WHO 2014). In low-level and concentrated epidemics, key populations include men who have sex with men, injecting drug users, sex workers and transgender people (UNAIDS 2015; WHO 2014). In Portugal, a country with concentrated HIV epidemic, prevention within key

populations is considered a priority for the National Program for HIV/AIDS Infection 2012-2016 (DGS/Programa Nacional de Prevenção e Controlo da Infeção VIH/SIDA 2013).

1.1.2. The burden of HIV among MSM

Men who have sex with men (MSM) refer to men who irrespective of their sexual identities and orientations (homosexual, bisexual, heterosexual, others) have sexual relations with men (Young & Meyer 2005). For the sake of clarity, the abbreviation "MSM" is used throughout this thesis.

Against the background of low or declining HIV prevalence in the general population in most Western countries, MSM continue to be disproportionately affected by HIV infection, with continuous rise of incidence rates (Baral et al. 2007; ECDC 2013a; UNAIDS 2014).

Back in the early 1980s, the initial spread of the HIV/AIDS epidemic was followed by an expansion of prevention efforts and a decline in sexual risk activities at the population level (Blower & van Griensven 1993; Boily et al. 2004; Boily et al. 2005). But with the introduction of antiretroviral therapy (ART) in the mid-1990s, HIV infection evolved into a chronic disease changing the dynamics of the HIV/AIDS epidemic (Boily et al. 2004; Boily et al. 2005; Chu & Selwyn 2011; Deeks et al. 2013). More thoroughly, according to the literature, in the early years of the epidemic AIDS-related mortality/morbidity disproportionately depleted the population of individuals engaging in high-risk behaviours, which decreased the availability of men willing to engage in risk-taking practices (Blower & van Griensven 1993; Boily et al. 2004; Boily et al. 2005). As Boily and colleagues (2005) refer, in such a context those MSM who intended to engage in high-risk sexual practices might be left with no option than having less sexual partners or less risky sex (Boily et al. 2005). This along with prevention resulted in a decrease in risky sexual behaviours observed among MSM (Boily et al. 2005; Carne et al. 1987; Lau et al. 1992). Later on, the introduction of ART available at population level allowed to restore the quality of life of treated AIDS patients, who then could return to be sexually active (Boily et al. 2005; Dukers et al. 2001). By reducing HIV-related effects, favouring return to a more active sexual life and potentially slowing transmission due to reduced infectivity of HIV-positive individuals, ART also enabled the replenishment of the pool

of individuals willing to engage in high-risk taking behaviours (Boily et al. 2004; Boily et al. 2005; Porco et al. 2004). This along with other factors pointed out in the literature including prevention and safer-sex fatigue, low perception of HIV as a threat and optimism towards the risk of developing AIDS among HIV-positive individuals due to the availability of ART, contributed to increased high-risk taking behaviours among this population (Boily et al. 2005; Crepaz et al. 2004; Ostrow et al. 2002).

In the most recent decades, the rise of HIV among MSM has been of great concern (Beyrer et al. 2012; Likatavicius et al. 2008; WHO 2011). New emergence and resurgence of HIV infection among MSM were observed in many parts of the world. There has been increased newly identified HIV epidemics among MSM in Asia, Africa, and Latin America (Cáceres et al. 2008; de Lind van Wijngaarden et al. 2009; van Griensven 2007) and it has been observed a resurgence of HIV infection among MSM in the Western world (ECDC/WHO 2011; Jaffe et al. 2007; Likatavicius et al. 2008). Recent data estimate that 42.2% of the new HIV diagnoses reported in the European Union/European Economic Area (EU/EEA) in 2015 were attributed to sex between men (ECDC/WHO Regional Office for Europe 2016). The number of HIV diagnoses reported among MSM increased from 7 796 cases in 2006 to 9 858 cases in 2014, and the proportion of all HIV diagnoses attributed to sex between men increased from 33% of cases in 2005 to 42% of cases in 2015 (ECDC/WHO Regional Office for Europe 2016). On the other hand, the number of HIV diagnoses due to all other modes of transmission decreased (ECDC/WHO Regional Office for Europe 2016).

In Portugal, the HIV incidence in MSM has markedly arisen, being one of the European countries with the highest number of newly diagnosed cases attributed to homosexual transmission (ECDC 2013b; INSA 2016). National official data from Instituto Nacional de Saúde Dr. Ricardo Jorge (INSA) indicate a trend of increasing number of HIV diagnosed cases attributed to sex between men in the last decade, in contrast with a reduction of the number of cases attributed to injecting drug use and heterosexual transmission (INSA 2016). According to recent data, 24.1% of the 776 newly notified cases in 2012 were attributed to sex between men (INSA 2016) and that proportion reached 40.5% in 2015 (INSA 2016).

1.2. Factors associated with increased HIV risk among MSM

The rise of HIV infection in MSM has been largely attributed to a steady increase in high risk sexual behaviours (Chen et al. 2002; Koblin et al. 2006). Particularly, it has long been demonstrated that unprotected anal intercourse (UAI) with an HIV-positive man is the major behavioural risk factor for HIV transmission among MSM (Darrow et al. 1983; Jin et al. 2009; McDaid & Hart 2010). Evidence also supports that receptive UAI is substantially more infectious than insertive UAI (Baggaley et al. 2010; Koblin et al. 2006).

In biological terms, rectal mucosa lacks the protective humoral immune barrier present in cervicovaginal secretions (Bélec et al. 1995) and is more susceptible to traumatic abrasions which may facilitate transmission (Levy 1993). In contrast to heterosexual transmission, in which men always take the insertive role and women the receptive role in penetrative sex, in sex between men, men can take either the insertive or receptive role (Baggaley et al. 2010; Jin et al. 2009). Therefore, anal intercourse, especially receptive, has a crucial role driving HIV epidemics among MSM (Baggaley et al. 2010).

Some evidence has suggested that a reduction in anal intercourse infectiousness due to ART occurs (Bezemer et al. 2008; Cooper et al. 2002; Quinn et al. 2000). However, despite the scarcity of data on HIV transmission risk in the era of ART among MSM with high treatment rates and at low viral loads (Attia et al. 2009; Jin et al. 2009; Wilson et al. 2008), the residual infectiousness could still present a high risk to partners, as reviewed elsewhere (Baggaley et al. 2010; Bezemer et al. 2008).

Within a biomedical perspective, the behaviours that directly cause the acquisition or onward transmission of HIV, such as UAI with a HIV-positive partner, are positioned and understood as 'biological' routes of HIV transmission (Kippax 2008). The biomedical model is premised on the ideology of individualism, considering individuals "free" to "choose" health behaviours (Fee & Krieger 1993). But some of the critiques of the biomedical model reside in its exclusive focus on biological and individual-level factors, leaving little place for understanding how behaviours are related to social conditions and constraints or how communities shape individuals' lives (Fee & Krieger 1993).

Patterns of behaviour arise from combinations of drivers operating in specific social, economic, cultural, and political contexts (Auerbach et al. 2011). As proposed by researchers, rather than the "individual" behaviour, a focus on the sexual behaviour as a

social practice, formed in the relations between people with reference to the interpersonal contexts and networks in which they are enacted, produced within prevailing socio-cultural, economic and political structures and regulated by social norms is essential (Kippax 2008). Deeper understanding of the socio-cultural, economic and political forces by which risk behaviours are organized and in which they are produced and patterned is needed in order to better comprehend risk for HIV infection and identify particular patterns of risk in particular settings (Auerbach et al. 2011; Baral et al. 2013a; Kippax 2008; Poundstone et al. 2004).

Therefore, there is an increasing recognition of the importance of identifying the drivers of HIV acquisition and transmission, i.e. the factors that increase the likelihood of HIV infection (Auerbach et al. 2011; Baral et al. 2013a; Kippax 2008; Poundstone et al. 2004). Several models have been used to visually represent theoretical explanations of biological, social and structural influences on disease processes, and can serve as useful guides for research to characterize drivers of HIV risk at each of those levels (Auerbach et al. 2011; Baral et al. 2013a; Parker & Aggleton 2003; Poundstone et al. 2004).

In particular, social ecological models are based on the premise that while individual level risks are necessary for the spread of disease, they are insufficient to explain population level epidemic dynamics - they are only one component affecting the transmission of HIV among populations (Baral et al. 2013a; Poundstone et al. 2004). In this sense, the social ecological models underlaid by the ecosocial theory seek to integrate social and biological reasoning and a dynamic and ecological perspective to develop new insights into determinants of population distributions of disease and social inequalities in health (Krieger 2001a; Krieger 2001b; Krieger 2001c). Therefore, the social ecological models have been used to explain the complex associations between social and structural factors, individual practices, the physical environment and health (Baral et al. 2013a; Krieger 2001b; Poundstone et al. 2004). These models contextualize individuals' behaviours using dimensions that include intrapersonal/individual (e.g. knowledge, attitudes, behaviour), interpersonal/network (social networks, social support), community (e.g. relationships among organizations/institutions), and public policy (e.g. local, state, national laws) to provide a framework for describing the interactions between these levels (Baral et al. 2013a; McLeroy et al. 1988).

Few models have been developed to guide the measurement of individual level risks, both biologic and behavioural, as well as higher order levels of risk in the context of HIV infection, in order to help visualize multi-level domains of HIV infection risks (Baral et al. 2013a). Auerbach and colleagues (Auerbach et al. 2011) developed a model to assess social and structural drivers of HIV to inform intervention development. Poundstone and colleagues presented a heuristic framework of the social epidemiology of HIV that highlights the social and structural determinants of the epidemic (Poundstone et al. 2004). Other models have examined ecological-level risk factors for HIV such as structural violence and social factors such as stigma and discrimination (Lane et al. 2004; Parker & Aggleton 2003). Most recently, built on past frameworks, Baral and colleagues developed the modified social ecological model that encapsulates individual HIV transmission risks in the context of social and structural drivers of the epidemic, besides adding the stage or level of the HIV epidemic to the social ecological model (Baral et al. 2013a).

The following subheadings focus on some of the main individual-, social- and structural-level factors that have driven HIV infection among MSM according to the literature.

1.2.1. Individual-level factors

Individual factors include biologic, sociodemographic, psychological and behavioural characteristics that may influence the risk of HIV acquisition or transmission (Baral et al. 2013a; McLeroy et al. 1988; Poundstone et al. 2004). While biological factors directly affect the likelihood of HIV infection, other factors have an indirect effect on HIV infection, placing one at risk or reducing that risk by influencing the ability of individuals to protect themselves and others from acquiring or transmitting HIV infection (Auerbach et al. 2011; Baral et al. 2013a; Kippax 2008).

Biologic factors

As regards biologic factors, the literature has documented the interdependence of HIV infection and other sexually transmitted infections (STIs) (Wasserheit 1992). In fact, similar sexual behaviours place people at high risk of both infections and there is clear evidence that STIs increase the likelihood of HIV transmission (Wasserheit 1992).

Studies have found that, besides HIV infection, MSM are also at greater risk for STIs compared to heterosexual populations, including Gonorrhoea, Chlamydia and Genital herpes (Chow et al. 2011; Pathela et al. 2011; Remis et al. 2016; Wolitski & Fenton 2011). Moreover, research has shown that HIV-infected MSM have a higher prevalence of co-infection with other STIs than HIV-negative MSM (Chin-Hong et al. 2009; Remis et al. 2016). These STIs may cause anogenital ulcers or mucosal inflammation, facilitating the transmission of HIV (Butler et al. 2008; Hunt 2012; Rebbapragada & Kaul 2007; Remis et al. 2016).

Besides STIs, circumcision status is also a biological factor associated with HIV infection. In the last decades, evidence has demonstrated that male circumcision performed by well-trained medical professionals reduces the risk of female-to-male HIV transmission by half (Auvert et al. 2005; Gray et al. 2007; WHO 2011). A systematic review of most recent research has documented the efficacy of male circumcision in preventing HIV acquisition among MSM, yet with differences based on predominant sexual roles in anal sex. While among males who practised primarily receptive anal sex there was no relation between circumcision and HIV infection, among those who engaged mostly in insertive anal sex circumcision was associated with a protective effect for HIV infection (WHO 2011; Wiysonge et al. 2011).

Sociodemographic factors

Additionally, sociodemographic factors are associated with HIV infection. Sociodemographic characteristics predispose vulnerabilities linked to social and structural inequities. These vulnerabilities in turn may heighten unprotected sexual behaviour and increase the likelihood of HIV acquisition (Halkitis & Figueroa 2013). A sociodemographic factor associated with HIV infection is age. Estimates indicate that young people (aged 15–24 years) accounted for 35% of all new HIV infections worldwide in people over 15 years of age in 2013 (WHO 2015). Data on the levels of HIV risk and protective behaviours among young MSM in particular has been limited (WHO 2015). Nevertheless, the available evidence has shown that young MSM are often at greater risk of engagement in behaviours that put them at risk of HIV, such as frequent unprotected sex and greater use of drugs or alcohol (Mustanski et al. 2011; WHO 2015). Young MSM are often more vulnerable than older MSM to the effects of homophobia, manifested in

discrimination, bullying, harassment, family disapproval, social isolation and violence, as well as self-stigmatization (WHO 2015). These can have serious repercussions for their physical and mental health, their emotional and social development, as well as their ability to access sexual health services, HIV testing, counselling and treatment (Santos et al. 2013; UNAIDS 2014; WHO 2015).

On the other hand, most recently older people have been considered one of the populations that have been left behind by the AIDS response (UNAIDS 2014). Current epidemiologic data show changes in the demographics of the HIV-positive population, with this population aging and the rate of newly detected infections in the elderly rising (CDC 2014; ECDC 2013b). Data from Western countries, and as reported by UNAIDS, primarily reflects the HIV epidemic up to the age of 49 years. However, some data in the elderly have been reported (Nguyen & Holodniy 2008). In high-income countries, the sub-population of people aged ≥50 years old has represented approximately 30% of the adult population living with HIV, and this proportion has rising (CDC 2014; UNAIDS 2013; UNAIDS 2014). Some factors have contributing to the positive association between increasing age and increasing rates of HIV/AIDS. First, ART currently available to treat HIV infection has been successful in effectively prolonging the lives of people living with HIV in high-income countries (UNAIDS 2014). The high life expectancy of a person living with HIV who achieves and maintains viral suppression on ART is now similar to that of a person who has not acquired HIV (Nakagawa et al. 2013; UNAIDS 2014). With the introduction of ART, survival following HIV diagnosis risen considerably and, as a result, treated HIV-infected patients live longer, being able to continue being sexually active (Nguyen & Holodniy 2008). Finally, older populations tend to present late for HIV testing (Hall et al. 2013). Factors associated with late diagnosis of HIV infection in older people include routine HIV screening being uncommon in this age group, poor awareness of HIV risk factors and failure of health care providers to consider HIV infection in this patient population (Grabar et al. 2006; Mack & Ory 2003; Nguyen & Holodniy 2008).

Social vulnerability, often manifested by lower socio-economic status, also contributes to MSM increased vulnerability to HIV infection. Several research has linked poverty with sexual risk taking in MSM (Frye et al. 2006; Halkitis & Figueroa 2013). A study of young MSM in New York City found that those of lower socioeconomic status (SES) were more likely to engage in unprotected receptive anal intercourse than those of

higher SES (Rosario et al. 2006). As documented elsewhere, poverty, socioeconomic deprivation and marginalization of gay men leads many to engage in high risk transactional sex in order to secure essential material resources (Figueroa et al. 2015; Halkitis & Figueroa 2013; Zhang et al. 2012). Moreover, men who are economically disadvantaged may have less access to gay health-related resources (Frye et al. 2006; Halkitis & Figueroa 2013).

Sexual orientation

Recently, several researchers have examined sexual orientation as a potential individual-level factor associated with risk for HIV infection (Everett 2013; Malebranche 2008; Young & Meyer 2005). The term sexual orientation refers to each person's capacity for profound emotional, affectional and sexual attraction to (and intimate and sexual relations with) individuals of any sex (UNAIDS 2015). The term 'sexual minority' has been employed with greater frequency to capture a diverse population of individuals whose sexual identity, behaviour, and attraction do not reflect a completely heterosexual orientation (Everett 2013). Nevertheless, merging sexual identity with behaviour may be problematic as much research has established that identity and behaviour often do not perfectly align (Everett 2013; Reback & Larkins 2010; Wells et al. 2011). For instance, in a study with MSM identified through a national population-based survey in the United States of America (USA), 5% of males reported a same-sex relationship, of which only 38% identified as gay, while 40% identified as heterosexual and 22% identified as bisexual (Xu et al. 2010).

The fact is that sexual behaviours occur between individuals who have self-determined sexual orientation identities that may be differentially related to HIV risk factors (Everett 2013). Some studies have suggested that gay-MSM report more sexual partners and a higher prevalence of HIV than heterosexual-MSM (Everett 2013; Wolitski et al. 2006; Xu et al. 2010). Other studies have shown that gay, lesbian, and bisexual individuals experience higher rates of physical and sexual victimization in both adolescence and in adulthood which, in turn, are associated with increased HIV risk in adulthood (Everett 2013; Haydon et al. 2011; Roberts et al. 2010). Moreover, in a study analysing the content of adds/profiles posted on one of the most popular MSM websites that specifically fosters unprotected sex showed that gay and bisexual men who preferred

to have sex under the influence of drugs were more likely to prefer to engage in receptive anal sex (Klein 2009). On the other hand, men who considered themselves to be heterosexual were the most likely to prefer to engage in insertive anal sex (Klein 2009).

Psychological factors

The literature has documented a number of psychological characteristics that correlate with high-risk sex behaviour among MSM (Kelly & Kalichman 1998; Kooyman 2008; Parsons et al. 2003). These psychosocial characteristics include perceptions, beliefs and attitudes toward HIV/AIDS, risk and sexual orientation. Particularly, research identified as positively associated with increased risk behaviours among MSM factors like lower sense of AIDS-related fatalism, the perception that AIDS antiretroviral drugs have made HIV/AIDS less of a health concern now than in prior years and consequent low perceived risk (Gold 2000; Halkitis et al. 2003; Kooyman 2008), as well as AIDS fatigue and feeling "burned out" by worrying about becoming HIV-infected (Halkitis et al. 2003; Kooyman 2008; Parsons et al. 2003). Other factors associated with HIV risk behaviours relate to perceptions toward condom use, especially the reinforcement of unsafe sex value and the belief that sex is more pleasurable when condoms are not used (Carballo-Diéguez et al. 2004; Kelly & Kalichman 1998; Mansergh et al. 2002), the belief that engaging in unprotected sex is an expression of masculinity and individual choice (Adam 2005; Carballo-Diéguez & Bauermeister 2004; Halkitis et al. 2003; Ridge 2004), a fear of being rejected sexually by partners who dislike condoms (Sheon & Crosby 2004), and a feeling of greater sense of emotional connectedness to sexual partners with whom one had unprotected rather than protected sex (Theodore et al. 2004; Mansergh et al. 2002).

Another important aspect in the psychological processes of MSM is the perception of their sexuality. Indeed, self-stigma toward homo/bisexuality and homophobia may increase HIV risk. In recent studies, MSM having negative attitudes toward their sexual orientation were more likely to engage in risk sexual behaviours (Folch et al. 2009; Saavedra et al. 2008). A cross-sectional study conducted with 850 MSM in Catalonia, Spain, found that of those who characterised themselves as homosexual or bisexual (97.7% of the total sample), 7.5% had a high degree of internalised homophobia (Folch et al. 2009). Furthermore, men who found it difficult to live with their homo/bisexuality

and had a high level of internalised homophobia were also more likely to have unprotected sex with casual partners (Folch et al. 2009). Other studies have shown an association between internalised homophobia and sexual risk behaviours (Huebner et al. 2002; Ross et al. 2013; Williamson 2000). While on one hand internalised homophobia has been reported to be an obstacle to prevention campaigns (Huebner et al. 2002), it has also been associated with low self-esteem and greater consumption of alcohol and drugs, which hamper the practice of safe sex (Williamson 2000).

Behavioural factors

At the behavioural level, acquisition risks among MSM have focused on the highest probability exposure, i.e. UAI, and specifically on receptive anal intercourse, as previously described in this Introduction section (Baral et al. 2013a; Koblin et al. 2006). But in addition to UAI, studies examining risk factors for HIV incidence have found independent associations with increased number and concurrency of sexual partners, and drug use (ECDC 2013b; Koblin et al. 2006).

Multiple sex partners is a recognized risk for HIV infection, especially among MSM (Kalichman & Grebler 2010; Kelly et al. 2010; Klein 2013; Koblin et al. 2006). Behavioural surveillance data from MSM indicate an increase in the frequency of UAI with casual partners (ECDC 2013b; Elam et al. 2008). A survey with MSM using London gyms conducted as part of a behavioural surveillance programme found that the proportion of men reporting high sexual risk with a casual partner increased between 1998 and 2003, as did the percentage of HIV positive men reporting UAI (Elford 2004).

Particularly concurrent partnerships, i.e. overlapping sexual partnerships where intercourse with one partner occurs between two intercourse acts with another partner within six months (UNAIDS 2015), lie at the root of generalised HIV epidemic and have been of public health concern among MSM (UNAIDS 2009a; Tieu et al. 2014). Multiple and concurrent partnerships have been associated with unprotected sex and the spread of HIV at the network level (Amirkhanian 2014; Bohl et al. 2009; Rosenberg et al. 2012; Tieu et al. 2014).

Concurrent partnerships potentiate the epidemic spread of HIV by influencing not only the rapidity of spread of HIV in the initial epidemic phase but also the total number of individuals who become infected (Gorbach & Holmes 2003). Concurrency reduces the

time between acquisition and subsequent exposure, which decreases the time to onward transmission and increases the likelihood of exposing one's partners to each other and the likelihood that a newly infected individual transmits HIV to an uninfected partner during the highly infectious acute period of HIV infection (period of high viremia) (Rosenberg et al. 2012; UNAIDS 2009a; Wohlfeiler & Potterat 2005). Concurrency can accelerate HIV spread by expanding sexual network size, enhancing network connectivity, and increasing rate and efficiency of infectious disease transmission within and across networks before individuals have knowledge of or treatment for an infection (Aral 2010; Gorbach & Holmes 2003; Morris & Kretzschmar 1995; Rosenberg et al. 2013). In a prospective online study of MSM in the USA, prevalence of concurrency was high (45%) (Rosenberg et al. 2012), compared to that reported among heterosexual counterparts in a nationally representative survey (11%) (Adimora et al. 2007), but consistent with the sparse evidence on MSM (Cassels et al. 2010; Choi et al. 2008). In a multi-site cross-sectional survey of gay, lesbian, bisexual, and transgender persons from seven metropolitan areas in the USA, prevalence of concurrency in MSM population was high (55%) and, of those who reported concurrency, 76% reported unprotected sex with more than one of their partners. Also, more than 75% of MSM believed that at least one of their sexual partners also had concurrent partners (Cassels et al. 2010).

Drug use is another behavioural-level factor associated with higher vulnerability to HIV (ECDC 2013b; WHO 2011). Alcohol and drug use/dependence among many MSM is considered a concern, and is linked to significant morbidity and mortality (Stall et al. 2001; WHO 2011). Research suggests that MSM populations are more likely to report higher use of alcohol and drugs than the general population (Li & McDaid 2014; Ruf et al. 2006; Vosburgh et al. 2012). While the role of injecting drug use in increasing the risk for HIV infection through sharing contaminated injection equipment is well documented (Metzger et al. 1993), harmful use and dependence on alcohol and other substances is also associated with compromised judgement and decreased ability to adopt preventive practices leading to risky sexual behaviour (ECDC 2013b; George & Stoner 2000; WHO 2011). A study on alcohol and drug use during UAI among a community-based sample of gay and bisexual men in Scotland revealed that more than three-quarters of men always/sometimes used alcohol during UAI and one-fifth used a stimulant or other recreational/illicit drugs (Li & McDaid 2014). Authors found associations of alcohol and

drug use to UAI with more than one partner and with casual partners (Li & McDaid 2014). Another study conducted with gay and bisexual men in New York City found a strong and statistically significant correlation between stimulants use and history of recent repeated UAI (Klitzman et al. 2000).

The literature has documented some motivations for drug use among MSM. Some research suggests that most MSM who report drug use are not drug dependent but instead use drugs for specific purposes (such as when partying, socialising or seeking or having sex, or in specific periods of stress such as an HIV diagnosis, struggles in the process of 'coming out', experience of depression or anxiety) (Bourne 2012; Santos et al. 2011). Drugs often serve a very deliberate purpose in helping individuals to relax, to socialise, to mitigate social unease and to gain confidence in seeking sexual partners (Bourne 2012; Fazio et al. 2011). Further to this, a significant body of research indicates that some drugs are often used by MSM to psychologically enhance sexual experience, to maintain sexual activity over long periods of time and to facilitate sexual desires by dissipating sexual inhibitions (Bourne 2012; Halkitis et al. 2005; Kurtz 2005; Semple et al. 2009). Recently, it has been documented the emergent phenomenon of 'chemsex' (intentional sex under the influence of psychoactive drugs, mostly among MSM) with little evidence indicating a link with transmission risk behaviours such as injecting drug use and UAI (Bourne et al. 2015; McCall et al. 2015). Drugs may also help individuals with diagnosed HIV, in particular, to 'cognitively escape' from fear of rejection and negative self-perception and to cope with broader emotional and physical demands of living with HIV on a daily basis (Bourne 2012; Semple et al. 2002).

1.2.2. Social-level factors
Preventative and epidemiological research on HIV risk has advanced by going beyond egocentric data on sexual behaviour and individual correlates to include data from social-level factors of importance to HIV/AIDS epidemiology. These factors refer to the socio-cultural environment and include partnerships' characteristics, social and sexual networks, and sex environments.

Partnerships

It has been documented that many MSM have short-term casual partnerships, while others have long-term steady partnerships (Gorbach & Holmes 2003). Individual sexual encounters may be totally anonymous or they may involve awareness of each other's identity (Prestage et al. 2001). Men may have sex just once or several times or they may have had ongoing sexual contact over many years (Prestage et al. 2001). Partnership type may be identified by serostatus of the partner, that is, positive serostatus, negative serostatus, or unknown serostatus and the partnerships may be sero-concordant or sero-discordant (Gorbach & Holmes 2003; Prestage et al. 2001). In this context, it has been increasingly acknowledged the need for a better understanding of the variation of dynamics across partnerships, as well as the roles of certain types of sexual partnerships in creating or reducing risk for HIV (Gorbach & Holmes 2003).

Partnerships may be characterized in terms of partner' characteristics, type and frequency. As the population ages and the size of the population living with HIV increases, partnerships between youth and elders have become more frequent among MSM (Hurt et al. 2010). In a qualitative study of MSM' preferences for selection of sex partners, about a half of participants indicated age of a potential partner as a specific draw, alongside other physical features (Adam 2000). Among many younger MSM, relationships with older men connote stability, emotional maturity, and mentorship (Adam 2000; Hurt et al. 2010). For older men, having a younger partner may provide a sense of power or virility and frame aging in a positive light (Adam 2000; Hurt et al. 2010). MSM seeking long-term partnerships seem to narrow their desired age range, whereas those looking for a partner for casual sex generally have less stringent requirements for partner age (Gobrogge et al. 2007; Hurt et al. 2010). The age-mixing with older sex partners among young adults has been associated with risk of HIV infection (Hurt et al. 2010). A case-control study conducted with a sample of young MSM in North Carolina, USA, demonstrated that young MSM who select older sex partners have significantly greater odds of acquiring HIV infection (Hurt et al. 2010).

A common categorization of partnerships focuses on the type of partner: "main/stable/steady/regular partner" versus "casual/occasional partner" (Gorbach & Holmes 2003). Previous research has suggested an association between partner type and sexual risk behaviour in MSM (Cambou et al. 2014; Knox et al. 2010; Macaluso et al.

2000). In general, ''stable'' or primary partnerships are associated with a greater perception of commitment between partners, while ''non-stable'' partnerships including casual, anonymous or transactional sexual relations, typically do not involve emotional intimacy (Cambou et al. 2014; Gorbach & Holmes 2003; Knox et al. 2010). Accordingly, UAI has been more commonly reported in primary partnerships when compared to casual partnerships among both HIV-infected and HIV-uninfected MSM (Cambou et al. 2014; Moreau-Gruet et al. 2001; Rocha et al. 2013). The greater intimacy presumed in ''stable'' partnerships can be seen as both protective (supporting open communication about HIV and encouraging mutually protective behaviour within the partnership), and potentially harmful (inhibiting condom use within a partnership which is incorrectly believed to be monogamous and free of infection) (Cambou et al. 2014; Gorbach & Holmes 2003; Knox et al. 2010). Other epidemiologic studies confirm a higher overall prevalence of UAI with stable compared with casual partners among MSM suggesting that the greater sense of familiarity, commitment, and/or intimacy common in these relationships may lead to a minimization of the importance of condom use during anal intercourse (Brian S Mustanski et al. 2011; Sanchez et al. 2007; WHO 2015).

In terms of sexual partners' frequency, group sex is one such practice that may contribute to the high prevalence of HIV among MSM (Rice et al. 2016). This broad term describes sexual acts involving more than one person at a time, and may include threesomes, spontaneous group sex or organized sex parties (Grov et al. 2013a; Rice et al. 2016). In an online study of MSM in the USA it was found that 88% of men had taken part in some type of group sexual encounters (GSE) at one point in their lives (Grov et al. 2013a). The authors also found that those men who had engaged in a GSE might be at greater risk for transmitting HIV than those who had never taken part in a GSE (Grov et al. 2013a). Indeed, GSE may increase HIV transmission for several reasons (Friedman et al. 2008; Mimiaga et al. 2011; Rice et al. 2016). On one hand, research has found that men who participate in GSE are more likely to endorse other high-risk behaviours outside of GSE (Grov et al. 2013a; Mimiaga et al. 2011; Rice et al. 2016; Solomon et al. 2011). MSM who participate in GSE are more likely to be HIV-positive, report drug use and report UAI in the past 3 months, compared to MSM who do not participate in GSE (Grov et al. 2013a). In another study of 540 MSM aged 18–29 years old, 8.7% had attended a sex party in the past 3 months. These men reported significantly higher numbers of

lifetime and recent male sexual partners and were more likely to report drug use in their lifetime than men who had not attended sex parties (Solomon et al. 2011).

On the other hand, high-risk behaviours often occur alongside GSE (Mimiaga et al. 2010; Phillips et al. 2014; Pollock & Halkitis 2009; Rice et al. 2016). In a study of 311 gym-attending MSM it was found that 23% reported having been to a sex party in the previous 6 months (Pollock & Halkitis 2009). Other study of 40 MSM who either attended or hosted sex parties in Massachusetts revealed that more than a half had used alcohol or drugs, and 25% had UAI during their most recent sex party attended (Mimiaga et al. 2010).

The described studies and others published worldwide illustrate the great amount of research indicating that MSM who attend organized sex parties engage in higher rates of UAI. However, less is known about prevalence of UAI among MSM who engage in spontaneous group sex or threesomes (Grov et al. 2013a). The online study of MSM in the USA previously mentioned aimed to compare behavioural and social characteristics of groups of men who engaged in threesomes, spontaneous group sex and organized sex parties (Grov et al. 2013a). The authors found that rates of receptive UAI were significantly higher for men who had engaged in spontaneous group sex (43.3%) than for the other two groups. Men who engaged in spontaneous group sex as their last GSE were also more likely than others to engage in hazardous alcohol use and stimulant drug use during that encounter. As noted by the authors, the wider range of sexual behaviours experienced during spontaneous group sex may be characteristic of the innate spontaneity of the event, or may be related to greater substance use during events, as drugs and alcohol reduce inhibitions (Grov et al. 2013a; Mansergh et al. 2008; Ostrow et al. 2009).

Social and sexual networks

Over the recent years there has been considerable research interest in studying HIV risk among MSM from network perspectives, through analysis and mapping of social and sexual networks involved in disease transmission (Amirkhanian 2014; Delva et al. 2016; Hurt et al. 2015; Leung et al. 2015; Verre et al. 2014). Indeed, while high-risk taking behaviour and long lived asymptomatic infections play a role in maintaining the prevalence of HIV infection, they fail to explain persistence of infection in local areas,

suggesting that sexual network approaches may be needed to account for persistence of HIV in local populations (Aral 2002).

The concept of networking underlies the nature of sexual HIV transmission in that, rather than isolated from social context, sexual interactions between individuals are embedded in concrete, ongoing systems of social relations and may be described using network theoretical constructs (Amirkhanian 2014; Kelly et al. 2012). The social connections that exist between individuals constitute 'social networks' and the sexual encounters constitute components of 'sexual networks' (Amirkhanian 2014). While overlap between social and sexual networks of MSM is often high, each type of network plays a unique role important for understanding and preventing HIV transmission (Amirkhanian 2014; Liu et al. 2009; Morris & Kretzschmar 1995). Social networks play a key role in shaping the sexual networks within which sexual mixing occurs (Ruan et al. 2011). While MSM sex partners are often selected from within their social network, on the other hand social networks exert strong social influence on the individual sexual behaviour of network members (Amirkhanian 2014; Choi et al. 2007; Smith et al. 2004). Social networks constitute micro-environments in which individuals interact, provide and receive information and social support, and share peer norms, attitudes, linkages with sexual partners and similar risk circumstances (Amirkhanian 2014; Choi et al. 2007).

In the HIV/AIDS field, members of the same network often have in common not only similar views and attitudes about risk but also shared levels of risky sexual practices (Amirkhanian 2014; Kelly et al. 2010). Some studies in which data were collected from network members found that individuals with elevated risk levels tend to belong to the same networks (Amirkhanian et al. 2006; Kelly et al. 2010). Low normative support for safer sex and lack of disapproval of risky sex within networks were found to be associated with high-risk behaviours (Amirkhanian et al. 2006; Kelly et al. 2010; Peterson et al. 2009; Schneider et al. 2013).

The perspective that sexual risk behaviours are situated within the context of network socialisation has forced the need to empirically examine characteristics of individuals' networks (Kelly et al. 2012). Various network characteristics have been associated with being HIV-positive and engaging in HIV risk behaviour (Amirkhanian 2014; Hao et al. 2014; Schneider et al. 2012). Recent research suggests that network attributes such as structure, size, density, homophily, sexual mixing and bridging are

important risk factors of greater HIV incidence in MSM populations, beside frequent risky practices (Amirkhanian 2014; Smith et al. 2004).

The social networks relevant for HIV transmission have complex and dynamic structures (Amirkhanian 2014; Delva et al. 2016). Importantly, social networks evolve over time as individuals end current relationships and form new ones. Through this dynamic process, new potential HIV transmission pathways emerge, whereas others are interrupted (Kelly et al. 2012; Leung et al. 2015; Smith et al. 2004; Verre et al. 2014).

In terms of the network size (the total number of individuals in a sexual network), research has found that MSM with larger sexual network size were more likely to have UAI with sexual network partners (Choi et al. 2007; Scott et al. 2015). On the other hand, network density refers to the overall network connectedness and is defined as the proportion of actual ties among people, from all possible links (dyads, triads or components of four or more elements) (Doherty et al. 2005). In denser sexual networks there are potentially higher contact rates among people, which create more opportunities for transmission and, thus, are considered riskier (Doherty et al. 2005).

Other network characteristic associated with HIV risk is homophily, i.e. the propensity to engage in partnerships with others who share similar characteristics (Delva et al. 2016; Kelly et al. 2012). Networks may consist of similarly high- or low-risk members (i.e. many or few members with HIV infection) or disproportions of high- and low-risk members that may differentially lead to risk for HIV (Bingham et al. 2003).

A network-related aspect considered particularly pertinent to the spread of HIV is sexual mixing (Doherty et al. 2005). Sexual mixing refers to the types of contact patterns within and across risk groups (Doherty et al. 2005; Laumann & Youm 1999). Assortative mixing occurs when individuals with same level of risk typically have sex with each other more often than with others outside their risk-level group. Conversely, dissortative mixing occurs when people with differential risk form partnerships and this has been shown to increase the odds of infection (Bingham et al. 2003; Doherty et al. 2005).

Finally, bridging of sexual network groups has been identified as a predictor of the emergence and maintenance of HIV transmission within a population (Doherty et al. 2006; Spicknall et al. 2009). Bridging generally refers to the formation of sexual partnerships between people of high HIV risk with lower-risk individuals, leading to

linkage of networks and greater risk of HIV acquisition and transmission across networks (Doherty et al. 2006; Tieu et al. 2015).

Sex venues

In addition, a focus on social and spatial contexts may help understanding HIV transmission patterns in MSM (Amirkhanian 2014; Duncan et al. 2014; Oster et al. 2013). Indeed, assessing the venues where people report meeting sexual partners has been described as a way to capture indirect, yet valuable, information on social and sexual networks (Doherty et al. 2005; Latkin et al. 2012; Verre et al. 2014). Affiliation with certain venues where MSM socialize and engage in sexual activity have been found to substantially elevate the risk of HIV infection (Amirkhanian 2014; Duncan et al. 2014).

Lately, considerable attention has been given to the contexts that increase MSM exposure to HIV risk, such as venues where MSM frequently seek sexual partners and have sex (Melendez-Torres et al. 2016; Reisen et al. 2010; Vanden Berghe et al. 2011). These are so called cruising venues and include commercial venues (gay bathhouses, sex clubs, adult bookstore, adult movie houses) and free public spaces (beaches, parks and toilets) (Lee et al. 2012; Leung et al. 2015; Reisen et al. 2010; WHO 2011). Several studies show that MSM who visit sex venues are more likely to engage in high-risk sexual behaviours, suggesting that some venue-specific characteristics can significantly influence MSM sexual behaviours (Aynalem et al. 2006; Binson et al. 2001; Reisen et al. 2010; Reisner et al. 2009). These characteristics include physical space, sexual norms, and risk-behaviour patterns at the venue (Grov et al. 2010; Grov et al. 2013b; Zhao et al. 2013).

In recent years, more MSM in many countries have started using internet and mobile applications as a convenient method for sex partner seeking and selection (Bolding et al. 2007; Kelly et al. 2012; Ko et al. 2012; Leung et al. 2015). The use of the internet for sex has been a concern as it facilitates access to a greater number of partners as well as access to risk subcultures (Doherty et al. 2005; Kelly et al. 2012). Some research has found that MSM who meet sexual partners online have a higher number of sex partners, are more likely to engage in UAI and to be at increased risk for HIV (Berry et al. 2008; Kelly et al. 2012; Ostergren et al. 2011).

Overall, in sex settings MSM frequently meet other men for casual, usually anonymous, sexual encounters (Aynalem et al. 2006; Klein 2012; Reisen et al. 2010; Reisner et al. 2009). Research has shown that sex with partners who are barely known to the individual is quite common among MSM and appears to be rising (Bolding et al. 2007; Klein 2012; Tewksbury 2008). Other research has shown that frequenting public sex venues, where anonymous sex is often the norm, is commonplace among MSM, with large proportions of MSM acknowledging that they had recently gone to such venues and a sizable proportion frequenting different types of public sex venue overtime (Binson et al. 2001; Klein 2012; Parsons et al. 2003). Relatively recent evidence suggests that during the last decades there has been a re-emergence of sex in public places, implying a simultaneous increase in MSM's opportunities for and interest in engaging in anonymous sex (Klein 2012; Reece & Dodge 2003).

In some research, MSM expressed that when they have anonymous sex they are not concerned about contracting sexually transmitted infections and engage in a variety of risky sexual practices with their anonymous sex partners, such as condomless sex (Klein 2012; Reece & Dodge 2003). In a study HIV-positive gay and bisexual men, authors found that more than a half had anal sex with anonymous partners and two thirds had unprotected sex (Semple et al. 2004). Also, the great majority of the participants did not disclose their HIV-positive serostatus to their anonymous sex partners. This is in great part because there is a strong set of social norms that establish the importance of silent interactions whenever anonymous sex is involved (Klein 2012; Semple et al. 2004). In such encounters, verbal communication is unexpected, inappropriate, almost always inhibited and considered a violation of the norms of the sexual space, principally because silence contributes to the anonymity that draws many men to such sex environments to have anonymous sex in the first place (Klein 2012; Reece & Dodge 2003; Richters 2007). As a result, there is a low likelihood that disclosures about HIV or discussions about the use of condoms or other safer sex methods occur (Klein 2012; Reece & Dodge 2003). Other authors have concluded that risky behaviour may occur in situations in which the sexual activity is disconnected from interpersonal relations and interaction/negotiation (Diaz et al. 1999). In a study with an ethnically diverse sample of HIV-positive MSM from the New York City and San Francisco metropolitan areas, men who had sex in commercial sex environments perceived themselves to have less responsibility towards

protecting their sex partners from HIV infection, compared with men who did not have sex in those environments (Parsons et al. 2003). In addition, sex in public cruising settings often occurs as hidden, illicit encounters with minimal influence of prevention messages or normative influences regarding expectations for safer sex (Diaz et al. 1999; Klein 2012; Somlai et al. 2001).

1.2.3. Structural-level factors

There is no singular definition of structural drivers but they can be conceptualized as those social, economic, organizational, and political factors which contribute to social inequities (Baral et al. 2013a). One of those factors refer to stigma.

Stigma and discrimination

Stigmatization related to HIV can be an additional burden and increase risk of transmission (Mahajan et al. 2008; Mayer et al. 2008; Valdiserri 2002; WHO 2015). A study of young MSM living with HIV found that those who experienced high levels of HIV stigma were significantly more likely to engage in unprotected sex while under the influence of substances (Radcliffe et al. 2010). Among people living with HIV/AIDS (PLWHA) in Cape Town, South Africa, those who experienced stigma or discrimination were less likely to disclose their HIV status to their sexual partner, and non-disclosure was associated with transmission-risk behaviour such as multiple sexual partners and unprotected intercourse with non-concordant sexual partners (Simbayi et al. 2007).

In addition, stigmatizing attitudes towards homosexuality, and discriminatory behaviour towards people with a homosexual orientation, are major obstacles affecting the lives and health of MSM (Mahajan et al. 2008; Peretti-Watel et al. 2007; WHO 2015). In a social psychology perspective, sexual orientation-based discrimination manifests the heteronormativity and homophobia that characterize the values and attitudes inherent in a sex-gender-sexuality system (Frye et al. 2015; Westbrook & Schilt 2014). This system depends upon the cultural stigma associated with homosexuality and gender identity deviance to legitimize its oppressive function (Frye et al. 2015). In this perspective, men who identify as gay or bisexual and who engage in same-sex sexual behaviour are socially considered as transgressing the prescribed heterosexual and masculine norms, and thus they are often targets for acts of discrimination (Frye et al. 2015).

Social discrimination experience often translates into adverse health behaviours and ultimately poor health outcomes (Frye et al. 2015). Sexual minority stress theory advances that certain environments increase the likelihood of experiencing personal stress events (Frye et al. 2015; Meyer 1995). Extended social stress theory posits that sexual minorities experience chronic stress in their daily interactions due to being members of stigmatized groups, including social discrimination based on perceived sexual orientation (Frye et al. 2015; Meyer 1995). Increased stress due to experience of sexual orientation-based discrimination may contribute to depression, drug and alcohol use and/or sexual compulsivity as a coping mechanism (Frye et al. 2015). Empirical evidence has documented that the negative health effects of sexual orientation-based discrimination include psychological distress, substance use and risky sexual behaviour (Frye et al. 2015; Jeffries et al. 2013; Wolitski & Fenton 2011).

In addition, self-stigmatization is also linked to HIV risk behaviour (WHO 2015). It has been found that, particularly among young MSM, anxiety, loneliness, and fear of rejection affect the self-perception and sense of worth and can lead to self-stigmatization, i.e. feelings of depression, low self-esteem and anger, or self-harming acts (WHO 2015). In recent studies, MSM having negative attitudes toward their sexual orientation were more likely to engage in risk sexual behaviours (Folch et al. 2009; Saavedra et al. 2008). Conversely, men who accept their sexual orientation are more psychologically healthy, have higher self-esteem, are more likely to disclose their HIV status with casual sex partners and are less likely to engage in sexual risk-taking (WHO 2015).

The effects of sexual orientation-based stigma and discrimination on MSM health may be reinforced by violence (Folch et al. 2009). In a prospective study of 521 young MSM in a Canadian city, 16% reported having experienced physical assault related to actual or perceived sexual orientation (Lampinen et al. 2008). Compared with men who did not report such an assault, men who experienced sexual orientation–related assault were more likely to report forced or coerced sexual relations and to be HIV positive (Lampinen et al. 2008).

Access and utilization of HIV health services

At last, the increased vulnerability of MSM to HIV is strongly related to lack of access to and reduced utilization of health services and HIV interventions (UNAIDS

2009b; WHO 2011). According to reports from 20 countries, the percentage of MSM reached by HIV prevention programmes fell from 59% to 40% between 2009 and 2013 (UNAIDS 2014). It has been put forward that, due to stigma, discrimination and fear of public exposure, MSM are less likely to access appropriate HIV treatment, care and support than other groups and often experience barriers to quality health care (ECDC 2013b; Institute of Medicine 2011; UNAIDS 2009b; WHO 2011).

From a socio-ecological perspective, barriers to accessing health care can be categorized into personal and structural (Andersen 1995; Dutton 1986; Institute of Medicine 2011; Sheeran & Abraham 1996; Travassos & Martins 2004).

At personal level, MSM may delay or avoid seeking HIV-related information, care and services as they may be less inclined to disclose their sexual orientation and other health-related behaviours in health care settings (WHO 2011). By fearing stigma and discrimination from health-care providers and being aware of incomprehension around issues of same-sex behaviour, many MSM often choose to keep their sexual behaviour or orientation hidden, which reduces their access to appropriate guidance and information about HIV and the risks of unprotected sex (CDC 2003; WHO 2015). Other reasons for MSM opting not to disclose their sexual orientation or behaviours to healthcare providers include concern with confidentiality and previous negative experiences with provider-patient encounters (Mayer et al. 2008). A cross-sectional study with 506 MSM in El Salvador revealed that only 30.2% of participants had used health services in the previous year (Andrinopoulos & Hembling 2013). Almost two thirds reported that they had experienced discrimination from a healthcare provider because they were MSM, and more than a half considered that they had received poorer quality services because they were MSM and reported being refused services because they were MSM (Andrinopoulos & Hembling 2013). Also, 39.2% of the participants had not tested for HIV in the previous year, with the most common reasons for not testing being the concern about confidentiality, the long wait time to receive the results, the belief that the provider would judge them, not wanting others to find out their sexual orientation and fear of receiving the test result (Andrinopoulos & Hembling 2013). In this context, effective healthcare may be compromised as MSM fears and concerns with revealing their sexual orientation and behaviours may lead them to seek healthcare at an early stage, resulting in missed opportunities for timely diagnosis and treatment (Clark et al. 2001).

In addition, perceived low risk for infection has been described as one of the reasons that MSM delay testing (WHO 2015). In a survey of young MSM in seven metropolitan areas of the USA, almost 6 out of 10 respondents thought they were at low risk of being infected (MacKellar et al. 2005). However, low uptake of HIV testing can also be because those who perceive themselves at high risk of HIV fear learning that they are HIV positive (Moyer et al. 2007). Although these psychosocial barriers can be traced to HIV and sexual stigma, many MSM may also experience barriers to care related to their membership in other marginalized groups in society (e.g., racial/ethnic minorities, low-income groups, and those from certain geographic locations) (Institute of Medicine 2011).

On the other hand, structural barriers limit access to health care and often relate to the health care system (Institute of Medicine 2011). Manifestations of structural stigma at institutional level have effect on access to health services and individual decision-making to seek health care, as described above. Discrimination or insensitivity on the part of healthcare providers in particular have been shown to deter some MSM from seeking HIV testing, counselling and treatment, especially if they feel they will need to disclose their same-sex behaviour to service-providers (WHO 2015; Wilson et al. 2011). Such reluctance may be especially strong for MSM who do not identify as gay (Bernstein et al. 2008).

Discrimination from healthcare providers may be exacerbated by lack of training and awareness (WHO 2015). In fact, MSM populations have a variety of health needs that should be addressed, including concerns regarding sexual health and emotional wellbeing (WHO 2011). But it has been advanced that sexual health counselling provided by clinicians frequently addresses only heterosexual behaviour in part because training curricula do not include issues around same-sex behaviours and homosexuality (WHO 2015). A survey of paediatricians in the USA found that while most discussed sexual activity with their adolescent patients during preventive care visits, 82% rarely or never discussed homosexuality (Henry-Reid et al. 2010). In the aforementioned study conducted with MSM in El Salvador, participants were asked to provide the most important characteristics they considered a healthcare provider supportive of MSM should have (Andrinopoulos & Hembling 2013). Most common features included: being a healthcare provider with whom the participant feels comfortable asking questions about

sexual behaviour and HIV/STIs, who maintains patient confidentiality, who has sufficient knowledge about the health needs of MSM, who does not judge the participant negatively, and who treats the patient with dignity and respect (Andrinopoulos & Hembling 2013).

1.3. Most vulnerable MSM subgroups: Male sex workers and male-to-female transgender persons who do sex work

As described in the previous sections, MSM constitute a population at increased risk for HIV, however not all MSM are at equivalent risk (Reisner et al. 2009). One of the subgroups of the MSM population most vulnerable to HIV infection is that of males who do sex work (Geibel et al. 2010).

The term sex worker (SW) refers to female, male and transgender adults and young people who receive money or goods in exchange for sexual services, either regularly or occasionally (Harcourt & Donovan 2005; UNAIDS 2009c; UNAIDS 2015). Sex work is viewed as extremely widespread, yet the actual number of people involved is difficult to determine (Vandepitte 2006). Sex work varies in terms of the level of formality or organisation and the settings in which it occurs, which range from dedicated establishments and private homes to hotels, bars and streets or parks. Individuals may sell sex as a full-time occupation, part-time, or occasionally to meet specific economic needs (TAMPEP 2009; UNAIDS 2009c). Although lesser than women, men also engage in sex work in diverse social and cultural settings. Male SW frequently report sexual contacts both with male and female partners, representing a potential for heterosexual and homosexual transmission (UNAIDS 2002).

Evidence from different parts of the globe have shown a very high prevalence of HIV among male SW (Baral et al. 2015). A review of HIV prevalence reports from 81 sites across 19 countries between 2000 and 2012, appeared in peer-reviewed journals or non-peer reviewed sources, revealed a median HIV prevalence of 7.8% among male SW from 8 European countries, a median HIV prevalence of 12.5% among male SW from five African countries and estimates of HIV burden ranging from 5% to 31% among male SW in North America (Baral et al. 2015). Authors also found that male SW present either higher or equivalent burdens of HIV compared to other populations (female SW, MSM not engaged in sex work, men in general) in several settings (Baral et al. 2015).

Owing to the increased vulnerability to HIV compared to other MSM who never exchanged sex for money or goods, male SW have been considered to be a key population for HIV prevention (Estcourt et al. 2000; Tang et al. 2015).

The heightened risk for HIV acquisition and transmission among male SW operates through a variety of behavioural and biological risks at the individual level. SW in general may experience high-risk sexual exposures through high numbers of sexual partners, high concurrency of these partners and inconsistent condom use (Baral et al. 2012). Among male SW in particular high risk behaviours include multiple sexual partners and frequent unprotected anal intercourse (Tang et al. 2015). HIV transmission among SW may also be exacerbated by the intersection of injection drug use and sex work through parenteral exposures from shared injection equipment (Baral et al. 2012; Strathdee et al. 2008). In addition, the history and current levels of other STIs compounds SW risks to HIV infection (Yi et al. 2010).

Although the main risk practices identified among SW are unprotected sex and injection drug use (Baral et al. 2012), the degree of exposure to HIV risk and the adoption of risk behaviours among SW may vary across work environments, economic situation and sociocultural context. In this sense, risk for HIV may differ among different strata of SW (Harcourt & Donovan 2005; Rekart 2005). The environmental conditions in which sex work occurs have a profound impact on HIV risk (UNAIDS 2009c). Outdoor SW, who are isolated from labour and social protection systems, report high vulnerability to HIV risk behaviours and violence (Church et al. 2001; El-Bassel et al. 2001; Yi et al. 2010). Frequently, the health and safety of these SW are compromised by the inability to assert control over their working environments and negotiate safer sex (Ferguson & Morris 2007; Li et al. 2012; Morisky et al. 2006; Shannon et al. 2010). Also, SW frequently have insufficient access to adequate health services, HIV preventive materials, diagnosis and management of sexually transmitted infections, drug treatment, social and legal support (Rosenheck et al. 2010; UNAIDS 2009c). In particular, some SW are migrants who often are in irregular situation and experience difficulties in accessing to health care (ECDC 2013c). SW, especially those male, may also be victimized by discriminatory attitudes, violence, and sexual exploitation, and by association with other populations that are highly vulnerable to HIV exposure, as MSM and injecting drug users (UNAIDS 2005). In addition, men involved in sex-work subculture do not easily identify

themselves as sex workers nor as homosexual, and are therefore missed by regular health care (Verhaegh-Haasnoot et al. 2015).

Another subgroup of MSM particularly vulnerable to HIV include male-to-female transgender persons (De Santis 2009). Male-to-female transgender persons (hereafter designated 'transgender') are individuals who were assigned male sex at birth but who identify themselves as women, irrespective of anatomy or medical interventions (Institute of Medicine 2011). The transgender population is diverse in gender identity, expression, and sexual orientation. Some transgender individuals have undergone medical interventions to alter their sexual anatomy and physiology, others wish to have such procedures in the future, and others do not (Institute of Medicine 2011). Transgender people can be heterosexual, homosexual, or bisexual in their sexual orientation (Institute of Medicine 2011). Expectedly, there are health differences between transgender and non-transgender people (Institute of Medicine 2011).

Although lesbian, gay, bisexual and transgender (LGBT) groups are separate populations, they frequently are considered as a group. The primary driving force behind combining these populations is that they are non-heterosexual or gender nonconforming (Institute of Medicine 2011). Also, these populations are often combined in some way for research purposes. In some HIV research, study participants are frequently combined in a single category that may include gay men, bisexual men, transgender women, and men who do not identify as any of the above but still have sex with other men. However, combining these populations in this way obscures differences among them (Institute of Medicine 2011). Most of the research on LGBT populations has focused on lesbians and gay men. Much less research has been conducted on bisexual and transgender people (Institute of Medicine 2011).

Transgender people born male may share some behavioural risks with MSM, most importantly receptive anal intercourse, but their female gender identity places them in quite different risk levels, with higher vulnerability and specific health needs (Beyrer et al. 2012; WHO 2011).

Emerging data from international epidemiologic studies show a disproportionate burden of HIV in transgender people compared with other populations (Baral et al. 2013b; De Santis 2009; Mayer et al. 2013; Operario et al. 2008; Poteat et al. 2015). In a systematic review, pooled HIV prevalence in transgender population worldwide was

19.1% (95% CI: 17.4-20.7) (Baral et al. 2013b). Transgender persons experience a variety of psychosocial challenges including discrimination, stigmatization, and marginalization from society, which affect the employment, education, and housing opportunities for transgender persons (Clements-Nolle et al. 2008), impact on mental health (Clements-Nolle et al. 2001; Morgan & Stevens 2008), and render this population at greater risk for HIV infection (De Santis 2009; Herbst et al. 2008). Sex work might further contribute to HIV risk in transgender women (De Santis 2009; Operario et al. 2008; Poteat et al. 2015).

The proportion of sex work in transgender population is uncertain, although studies have estimated to be as high as 44% (Schulden et al. 2008) and to vary between 24% and 75% (Herbst et al. 2008). Research have found that transgender individuals who engage in sex work have a greater HIV prevalence than other transgender groups (Baral et al. 2013b; Operario et al. 2008; Reback et al. 2005) and other sex workers (male or female) (Baral et al. 2013b). A systematic review and meta-analysis of 25 studies with data from 6405 participants recruited mostly in large metropolitan cities from 14 countries in 5 continents found a higher overall crude non-weighted HIV prevalence in transgender people engaged in sex work (27.3%), compared to that found in transgender people not engaged in sex work (14.7%), in male sex workers (15.1%) and in biologically female sex workers (4.5%) (Operario et al. 2008). In this sense, transgender sex workers (TSW) have been identified by UNAIDS and WHO as a key population at risk for HIV within the worldwide epidemic response (UNAIDS 2012b; WHO 2011).

HIV vulnerability of TSW reflects a complex interaction of multilevel risks (Baral et al. 2013b; Beyrer et al. 2015; De Santis 2009; Poteat et al. 2015). High-risk behavioural factors include condomless anal sex, particularly condomless receptive anal sex, with male partners including clients, stable and casual partners (Baral et al. 2013b; De Santis 2009; Nemoto et al. 2014; Operario et al. 2011; Poteat et al. 2015). When engaging in sex work, transgender individuals are often the receptive partners during unprotected anal intercourse (De Santis 2009; Edwards et al. 2007). The context of sex work is also characterized by multiple sexual partners, which increase HIV exposure risk (De Santis 2009; Schulden et al. 2008). Also, substance misuse has been linked to increased sexual risk-taking in transgender populations (Clements-Nolle et al. 2008; De Santis 2009; Hotton et al. 2013; Nuttbrock et al. 2013; Poteat et al. 2015). High levels of drug use and needle sharing have been reported in transgender women, and drugs are often used in the

context of sex with partners and clients (Clements-Nolle et al. 2001; Edwards et al. 2007; Poteat et al. 2015).

At structural level, many forms of stigma related to gender identity, gender expression, perceived sexual orientation, and involvement in sex work can create intensely hostile environments for TSW (Beyrer et al. 2015). Because transgender individuals challenge gender norms, they are often socially, economically, politically, and legally marginalized (Bockting et al. 2013; Boyce et al. 2012; Poteat et al. 2015). This context along with fear of rejection may reduce TSW's access to health services (Beyrer et al. 2015; Poteat et al. 2015). Also, marginalization reduces access of transgender people who live with HIV to prevention, treatment, care and support (Poteat et al. 2015). In addition, TSW often report that sexual health services ignore their needs, focusing instead on other at-risk populations such as natal female sex workers or men who have sex with men (Boyce et al. 2012; Poteat et al. 2015). Furthermore, TSW are at greater risk for sexual violence from both clients and intimate partners (De Santis 2009; Decker et al. 2015; Poteat et al. 2015).

Although MSM subgroups such as male SW and TSW are generally considered to be at increased risk for HIV infection, there is few data available on HIV burden and vulnerability among these populations that could inform adequate prevention strategies and interventions.

1.4. Challenges in research on HIV among MSM

Lately, bio-behavioural surveillance surveys measuring HIV prevalence and associated risk behaviours among MSM have widely expanded. However, a critical issue in HIV research with MSM is gathering information from non-representative samples. Given the recent trends of HIV in MSM, and considering the multiplicity of socio-behavioural profiles and levels of HIV risk, relevant methodological questions arise: are the subgroups that have been studied so far the most imperative ones? Are there subgroups with higher risk behaviours being understudied? Are we reaching those who matter the most?

The main function of HIV/AIDS surveillance is to provide an understanding of local epidemics, including the source of new infections over time and the behavioural and biological factors driving HIV transmission in order to provide a basis for designing and

evaluating appropriate interventions (Brown 2003; Magnani et al. 2005). In order to be effective, it is crucial that surveillance efforts focus on the segments of national populations that play an important role in HIV transmission (Magnani et al. 2005).

An essential attribute of public health surveillance is that data should be representative (and thus generalizable) of the population under surveillance (CDC 2001). In contexts where a disease is highly prevalent in the general population and a large proportion of the population comes into contact with health services, routine reporting by healthcare-providing institutions serves as a surveillance mechanism (Brookmeyer 2010; Magnani et al. 2005). In most developing countries, the main sources of routinely available HIV surveillance data have been pregnant women seeking antenatal care and sexually transmitted disease patients (Brookmeyer 2010; Magnani et al. 2005). When there is a lack of facility-based data, general population surveys can provide adequate HIV surveillance data, although at a higher cost. Survey-based public health surveillance of health status and related behaviours in general population has been common practice (Magnani et al. 2005). With regard to HIV/AIDS, population-based surveys have provided much of the general population behavioural surveillance data available in developing countries (Brookmeyer 2010; Magnani et al. 2005).

In scientifically rigorous endeavours the preferred approach for surveillance has been probability sampling, in which sample elements are chosen randomly from a known sample frame (Lohr 2010; Magnani et al. 2005). Such conventional approach traditionally targets the general and most easily accessible populations, but often it only captures a small fraction of the total population of some subgroups (Lohr 2010; Magnani et al. 2005). Given the trends of HIV in MSM, and considering the multiplicity of socio-behavioural profiles and levels of HIV risk, relevant methodological questions arise: are the subgroups that have been studied so far the most imperative ones? Are there subgroups with higher risk behaviours being understudied? Are we reaching those who matter the most? In order to be effective, it is crucial that surveillance efforts focus on the segments of populations which play an important role in HIV transmission (Magnani et al. 2005). The behaviours and HIV status of those covered and missed by conventional surveillance efforts can differ quite substantially. Hence, there is a great hazard of surveillance data failing to 'capture' significant pockets of infection that can lead to a more generalized spread of HIV if not contained (Magnani et al. 2005). The omission of

key populations as MSM from surveillance systems leaves significant gaps in our knowledge and understanding of the HIV/AIDS epidemics (Magnani et al. 2005).

There are major challenges in researching key populations as MSM. In addition to the inexistence of a sampling frame for this subgroup, creating a useful sampling frame generally is either unfeasible or excessively expensive making it impossible to use traditional probability-based sampling methods for MSM and obtaining 'representative' samples (Faugier & Sargeant 1997; Magnani et al. 2005; Mills et al. 1998). Also, key populations as MSM often represent a small proportion of the general population, and therefore obtaining statistically reliable data for such subpopulations through household surveys would require prohibitively large sample sizes (Lohr 2010; Magnani et al. 2005; Sadler et al. 2010). Lastly, when the risk-taking behaviours which justify the inclusion of most-at-risk subgroups in HIV surveillance are considered deviant or illegal within society and are stigmatized (e.g. sex between men, sex work), conventional household surveys are unlikely to produce accurate surveillance data (Magnani et al. 2005). In such cases, individuals are generally reluctant to participate in research efforts to measure their infection status and risk behaviours, and subsequently jeopardize revealing personal and sensitive information to others (Gorbach et al. 2009; Johnston et al. 2010; Magnani et al. 2005; Sadler et al. 2010).

Accurately measuring the prevalence of HIV and behaviours over time in key populations, such as MSM, is essential to planning and implementing cost effective, targeted prevention programs (Johnston et al. 2010; Mills et al. 2004; Pisani et al. 2003; WHO/UNAIDS 2002; Zaba et al. 2005). Over the past decades, several methods for recruiting difficult-to-access populations for surveillance and research purposes have emerged (Heckathorn 1997; MacKellar et al. 1996; Platt et al. 2006; Semaan et al. 2002; Thompson & Collins 2002; Yeka et al. 2006). Some of the most innovative methods for collecting data on trends of HIV prevalence and behavioural risk factors of key populations include snowball, venue-based, respondent-driven, time-location and internet sampling methods (Abramovitz et al. 2009; Atkinson & Flint 2001; Bowen 2005; Malekinejad et al. 2008; Muhib et al. 2001; Pachankis et al. 2015; Stueve et al. 2001).

In recent years, the important role of community-based participatory approach in undertaking research with hard-to-reach populations has been increasingly recognized (DiStefano et al. 2013; Minkler 2000; Olshansky 2008; Parrado et al. 2005; Wallerstein

& Duran 2006). Participatory research integrates a collaborative approach with involvement of communities, professionals, political decision-makers, and academics to produce knowledge, incorporating the different perspectives and experiences of these stakeholders (Israel et al. 1998). Community-based participatory approach may particularly help researchers choose the methods that most appropriately target MSM, relying on community partners and 'insiders' knowledge on the best strategies to locate and approach these groups.

1.5. Relevance of the theme

So far, the knowledge on drivers of increased HIV among MSM is limited. This thesis intends to contribute to improve knowledge on prevalence of HIV, high risk behaviours and its determinants among MSM in Portugal, a population that has been relatively understudied and is considered most at risk to HIV infection. This thesis is also expected to contribute to conducting future research with this hard-to-reach population. Finally, this thesis is expected to contribute to improving evidence base and identify HIV prevention needs to inform national HIV programs aimed at reducing the spread of infection in MSM. This will be based on the literature review on HIV and MSM developed throughout the thesis, the results obtained in the studies conducted on the prevalence of HIV, high risk behaviours and associated factors among MSM, and the critical review of the methods to most appropriately target MSM in HIV research.

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2. OBJECTIVES

2. OBJECTIVES

The overall aim of this thesis is to improve knowledge on prevalence of HIV infection, high risk behaviours and its determinants among MSM in Portugal.

The specific objectives are:

1) To estimate the prevalence of HIV and assess high risk behaviours among a population of MSM in Portugal.

> *Study I: Cruising Venues as a Context for HIV Risky Behaviour among Men who have Sex with Men*

2) To explore and understand the complex links of HIV risk-taking practices and the adoption of protective measures among MSM most vulnerable groups.

> *Study II: Risk-taking Behaviours and HIV Infection among Sex Workers in Portugal: Results from a Cross-sectional Survey*

> *Study III: HIV Infection, Risk Factors and Health Services Use among Male-to-Female Transgender Sex Workers: A Cross-sectional Study in Portugal*

3) To critically analyse different methods to most effectively target MSM in HIV research and reach those most-at-risk.

> *Study IV: HIV Research with Men who have Sex with Men (MSM): Advantages and Challenges of Different Methods for Most Appropriately Targeting a Key Population*

> *Study V: [Community-based Participatory Research in Public Health: Potentials and Challenges]*

This thesis is therefore based on five papers, each with their background, methods, results and discussion sections.

3. RESULTS

Study I – Cruising venues as a context for HIV risky behavior among men who have sex with men

Ana Gama, Ana Abecasis, Marta Pingarilho, Luís Mendão, Maria O. Martins, Henrique Barros, Sónia Dias

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ORIGINAL PAPER

Cruising Venues as a Context for HIV Risky Behavior Among Men Who Have Sex With Men

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Henrique Barros[3] · Sónia Dias[1]

Abstract We examined differences in sexual risk behaviors, HIV prevalence, and demographic characteristics between men who have sex with men (MSM) who visit different types of venues to meet sexual partners, and identified correlates of high-risk behaviors. A cross-sectional behavioral survey was conducted with a venue-based sample of 1011 MSM in Portugal. Overall, 36.3 % of MSM usually visit cruising venues to meet sexual partners (63.7 % only visit social gay venues). Cruising venues' visitors reported higher HIV prevalence (14.6 % [95 % CI 11–18 %] vs. 5.5 % [95 % CI 4–7 %]). Visiting cruising venues was more likely among those older, reporting high number of male sexual partners, group sex, and unprotected anal sex with a partner whose HIV status was unknown. Cruising venues play an important role in increasing risk of HIV transmission among MSM who frequent them. Venue-focused behavioral interventions that promote healthy sexual behaviors are needed.

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Introduction

In most industrialized countries, the incidence rates of HIV infection have declined in the overall population; however, among men who have sex with men (MSM), the incidence of HIV continues to rise (Alkaiyat, Schaetti, Liswi, & Weiss, 2014; Beyrer et al., 2012; UNAIDS, 2012). This trend has been associated with increased laxity in safe sexual practices and adoption of high-risk sexual behaviors due to the perception that HIV/AIDS is less serious in the era of highly active antiretroviral therapy (Aynalem et al., 2006; Beyrer et al., 2012; Le Vu et al., 2012; Vanden Berghe et al., 2011). Therefore, MSM are considered a key population at increased risk of HIV transmission, though different subgroups present disparate levels of HIV/STI risk (Reisner et al., 2009; WHO, 2014).

Lately, considerable attention has been given to the environmental contexts that increase MSM exposure to HIV risk, such as cruising venues where MSM frequently seek sexual partners (Binson et al., 2001; Melendez-Torres, Nye, & Bonell, 2015; Vanden Berghe et al., 2011). These venues include commercial venues (gay bathhouses and sex clubs) and free public spaces (beaches, parks, and toilets) (Binson et al., 2001; Reisen, Iracheta, Zea, Bianchi, & Poppen, 2010). In these settings, MSM frequently seek sex with anonymous or casual partners (Aynalem et al., 2006; Binson et al., 2001; Reisen et al., 2010). Previous studies showed that MSM who visit sex venues are more likely to engage in high-risk sexual behaviors, suggesting that some venue-specific characteristics can significantly influence MSM sexual behaviors (Aynalem et al., 2006; Binson et al., 2001; Reisen et al., 2010; Reisner et al., 2009). These characteristics include physical space, sexual norms, and risk-behavior patterns at the venue (Grov, Golub, & Parsons, 2010; Grov, Hirshfield, Remien, Humberstone, & Chiasson, 2013; Zhao et al., 2013).

Given the association between sex venues and sexual risk found in the literature, a comparison of the characteristics of

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MSM subgroups that attend different venues and a deeper understanding of the role of cruising venues in the spread of HIV is extremely important. Such knowledge would help conceive effective tailored and venue-specific prevention strategies.

Our aim was to examine differences in sexual risk behaviors, HIV prevalence, and demographic characteristics between MSM who visit different types of venues to meet sexual partners, and identify correlates of high-risk behaviors.

Method

Participants

A cross-sectional behavioral survey was conducted with MSM in Portugal. A community-based participatory research approach was used (Dias & Gama, 2014; Wallerstein & Duran, 2006), in which a Community Advisory Board (CAB) including representatives of non-governmental and governmental organizations, academics, and MSM was formed and actively participated in all phases of the project, as the study design, elaboration of the questionnaire, results interpretation, and discussion. Community partners were also involved in the data collection process.

There is no adequate sampling frame for this population enabling to draw a probability sample of MSM in Portugal. Therefore, this study used a venue-based sampling method to recruit participants (Muhib et al., 2001). In order to estimate a sample that would be large enough for detailed analyses, the sample size was calculated assuming a hypothetical worst-case prevalence of HIV infection of 50 %, at 95 % confidence level with precision of 3.5 %, which resulted in a sample size estimate of 784 MSM. Initially, a geographic and network mapping was conducted based on a formative research developed by the CAB. The mapping allowed us to list venues where MSM gather and to systematically identify data collection sites. Recruitment teams of outreach workers from local non-governmental organizations working on HIV prevention, including for LGBT, and MSM peers from community-based organizations (CBOs) were sent to those venues and systematically approached potential participants inviting them to participate in the study. The inclusion criteria were being ≥18 years old and having had sex (anal or oral) with a man in the last 12 months. Participants were recruited from gay bars/clubs, cafes, local CBOs, and community events. Additionally, the recruited respondents were asked to advertise the study among their social networks and peers. Overall, 1046 MSM were enrolled (665 MSM, 63.6 %, recruited in CBOs and 381 MSM, 36.4 %, recruited in other venues), between January and September of 2011.

Measures

Data were collected in the recruitment sites (in private spaces) through a paper-and-pencil structured questionnaire administered by peers trained for data collection. The questionnaire included closed-ended questions on socio-demographics (age, educational level, occupational status, and income), sexual behaviors (group sex was defined as sex with at least 2 partners simultaneously; unprotected anal sex was defined as having had anal sex without condom in the last 12 months; substance consumption before/during the last sexual intercourse included alcohol and illicit substances), coverage in HIV prevention campaigns (including having been reached with HIV prevention programs in the last 12 months and having received free condoms in the last 12 months), HIV testing, and reported HIV infection. Participants were also asked about venues they usually visit to meet sexual partners. Similar to prior studies, for the purpose of this analysis, "cruising venues" comprised venues where sexual contact on site is possible (gay saunas, beaches and parks); "social gay venues" comprised gay clubs, bars, discos where it is not possible to have sexual contact on site, and internet chats (Binson et al., 2001; Reisen et al., 2010). Although internet chats are technically not venues (i.e., physical spaces), for ease in discussing findings, we use the term "social gay venue" to describe this setting.

The refusal rate was 23.2 %. No significant differences were found between refusals and participants regarding age and education. No information was collected about reasons for refusal.

Anonymity of participants was ensured (no personal identifying information was collected), and confidentiality was guaranteed; informed consent was obtained from all participants. The study was approved by the Ethics Committee for Health of the North Regional Health Administration.

Statistical Analysis

Visitors of cruising venues and of social gay venues were compared across HIV prevalence, sexual risk behaviors, demographic characteristics, and coverage in HIV prevention campaigns. Differences were tested for significance using Pearson's χ^2 and Fisher's exact tests for categorical variables, and ANOVA tests for continuous variables.

We performed bivariate and multivariate logistic regression analyses to measure the association of visiting cruising venues with HIV infection, sexual risk behaviors, and demographic characteristics. We also conducted bivariate and multivariate logistic regression analyses in order to explore the association of high-risk sexual behavior (unprotected anal sex with a partner whose HIV serostatus was unknown) with type of venues visited, self-reported HIV status, and coverage in prevention campaigns. All the variables that remained significantly associated with the variables "visiting cruising venues" and "unpro-

tected anal sex with a partner whose HIV serostatus was unknown" at a significance level of $p < 0.05$ were included in the final multivariate models. Associations were measured calculating the odds ratio (OR) and its 95 % confidence interval (CI). Finally, the Hosmer–Lemeshow goodness-of-fit test was used to assess both models fit. Statistical analyses were conducted using IBM SPSS Statistics 22.0 software.

Results

Overall, 1046 MSM were enrolled in the study. Of these, 1011 responded to the question about the venues that were usually visited to meet sexual partners. The remaining 35 subjects were excluded from analysis. Overall, 644 (63.7 %) MSM reported to visit social gay venues and 367 (36.3 %) to visit cruising venues to meet sexual partners (of the latter, 89.4 % reported to visit both cruising venues and social gay venues).

Demographic and behavioral characteristics are shown in Table 1. In total, 43.2 % of participants were 25–34 years old,

and about one third was older; 39.6 % had higher education, 39.4 % secondary, and 21.0 % elementary; 71.5 % were employed, 16.4 % were student, and 10.3 % were unemployed; 58.0 % reported income >1000 euro. MSM who visit cruising venues were significantly older, had lower education, were more frequently unemployed, and reported lower income than MSM who visit social gay venues.

Overall, nearly 25 % of participants had their first anal intercourse at age 15 or younger. The mean number of male sexual partners in the previous year reported by participants was 15.1 ± 36.6. A higher proportion of cruising venues' visitors had their first anal intercourse at age 15 or younger. Also, cruising venues' visitors reported higher mean number of male sexual partners in the previous year. Approximately 70 % of the total participants reported having had sex with occasional partners in the last 12 months, 61.4 % had with regular partners, 26.0 % reported group sex, and 5.4 % had sex with client partners. A greater proportion of cruising venues' visitors reported sex with occasional partners, with client partners and group sex in the past year, while a lower proportion had sex with regular partners. A lower proportion of

Table 1 Type of venues used to meet sexual partners according to participants' demographic characteristics, risk behaviors, and reported HIV infection

	Total	Venues usually visited to meet sexual partners		*p* value
		Cruising venues	Social gay venues	
	n (%)	*n* (%)	*n* (%)	
Total	1011 (100)	367 (36.3)	644 (63.7)	
Sociodemographics				
Age (in years)				
18–24	247 (24.5)	62 (16.9)	185 (28.7)	<0.001
25–34	437 (43.2)	151 (41.3)	286 (44.4)	
35–44	206 (20.4)	94 (25.7)	112 (17.4)	
≥45	120 (11.9)	59 (16.1)	61 (9.5)	
Educational level				
Elementary	210 (21.0)	99 (27.5)	111 (17.3)	0.001
Secondary	394 (39.4)	136 (37.8)	258 (40.3)	
Higher	396 (39.6)	125 (34.7)	271 (42.3)	
Occupational status				
Employed	707 (71.5)	271 (75.3)	436 (69.3)	<0.001
Unemployed	102 (10.3)	51 (14.2)	51 (8.1)	
Retired	18 (1.8)	12 (3.3)	6 (1.0)	
Student	162 (16.4)	26 (7.2)	136 (21.6)	
Income				
≤1000 euro	416 (42.0)	172 (48.5)	244 (38.4)	0.002
>1000 euro	575 (58.0)	183 (51.5)	392 (61.6)	
Sexual risk exposures				
Age at first anal intercourse				
≤15	243 (24.8)	108 (30.8)	135 (21.5)	0.001
16–17	249 (25.4)	82 (23.4)	167 (26.5)	
18–20	273 (27.9)	102 (29.0)	171 (27.2)	
≥21	215 (21.9)	59 (16.8)	156 (24.8)	

Table 1 continued

	M (SD)	M (SD)	M (SD)	*p* value
In the last 12M				
Number of male sexual partners	15.1 (36.6)	28.4 (54.8)	7.5 (15.0)	<0.001
	n (%)	*n* (%)	*n* (%)	*p* value
In the last 12M				
Sex with regular partners	608 (61.4)	165 (46.2)	443 (70.0)	<0.001
Sex with occasional partners	690 (70.1)	312 (87.6)	378 (60.1)	<0.001
Sex with client partners	52 (5.4)	30 (8.7)	22 (3.5)	0.001
Sex with sex workers	48 (5.0)	22 (6.4)	26 (4.2)	0.135
Group sex	253 (26.0)	146 (41.2)	107 (17.3)	<0.001
Condom use with regular partners				
Consistent (always)	314 (52.5)	101 (62.3)	213 (48.9)	0.003
Inconsistent (sometimes/rarely/never)	284 (47.5)	61 (37.7)	223 (51.1)	
Condom use with occasional partners				
Consistent (always)	545 (81.5)	238 (79.1)	307 (83.4)	0.149
Inconsistent (sometimes/rarely/never)	124 (18.5)	63 (20.9)	61 (16.6)	
Condom use in group sex				
Consistent (always)	205 (83.7)	115 (79.9)	90 (89.1)	0.054
Inconsistent (sometimes/rarely/never)	40 (16.3)	29 (20.1)	11 (10.9)	
Unprotected anal sex with a partner whose HIV serostatus was unknown	170 (23.7)	89 (33.5)	81 (18.0)	<0.001
Unprotected anal sex with a partner whose HIV serostatus was different from his own	41 (7.0)	18 (9.0)	23 (5.9)	0.168
Substance consumption before/during the last sexual intercourse	356 (35.2)	153 (41.7)	203 (31.5)	0.001
HIV prevention campaigns				
Reached by HIV prevention programs in the last 12M	385 (38.8)	138 (38.0)	247 (39.3)	0.697
Received free condoms in the last 12M	835 (82.7)	324 (88.3)	511 (79.5)	<0.001
HIV testing and reported infection				
Having ever been tested for HIV	889 (88.4)	341 (93.7)	548 (85.4)	<0.001
Reported HIV status				
HIV negative	731 (72.8)	258 (71.1)	473 (73.8)	<0.001
HIV positive	88 (8.8)	53 (14.6)	35 (5.5)	
Don't know	185 (18.4)	52 (14.3)	133 (20.7)	

SD standard deviation, *12M* 12 months

cruising venues' visitors reported inconsistent condom use with regular partners, while a higher proportion reported inconsistent condom use in group sex, unprotected anal sex in the last year with a partner whose HIV serostatus was unknown, and substance consumption before/during the last sexual intercourse.

MSM who visit cruising venues reported more frequently having received free condoms in the previous year and having ever been tested for HIV than other venues' visitors. MSM who visit cruising venues reported less frequently not knowing their serostatus for HIV compared to social gay venues' visitors.

Overall, 14.6 % (95 % CI 11–18 %) of cruising venues' visitors reported to be HIV positive, while a significantly lower proportion of visitors of other venues reported seropositivity [5.5 % (95 % CI 4–7 %)].

The logistic regression analysis (Table 2) showed that MSM who usually visit cruising venues to meet sexual partners were significantly more likely to be older ($\geq$45 years old) (OR 3.01, 95 % CI 1.56–5.84), to have increasing number of sexual partners (OR 1.02, 95 % CI 1.01–1.04), to engage in group sex (OR 2.22, 95 % CI 1.47–3.34) and in unprotected sex with a partner whose HIV serostatus was unknown (OR 1.67, 95 % CI 1.09–2.55), and to be HIV positive (OR 2.31, 95 % CI 1.07–4.98). Cruising venues' visitors were also less likely to have higher education (OR 0.37, 95 % CI 0.23–0.59).

Results of the association of unprotected anal sex with type of venues visited, behavioral factors, HIV infection, and coverage in HIV prevention campaigns are shown in Table 3. The multivariate analysis showed that engagement in unprotected anal sex in

Table 2 Factors associated with visiting cruising venues to meet sexual partners

	n (%)	p value	Crude OR (95 % CI)	Adjusted OR (95 % CI)[a]
Age				
18–24	62 (25.1)	<0.001	1	1
25–34	151 (34.6)		1.57 (1.11–2.23)*	1.40 (0.88–2.23)
35–44	94 (45.6)		2.50 (1.68–3.73)***	1.79 (1.02–3.15)*
≥45	59 (49.2)		2.89 (1.82–4.57)***	3.01 (1.56–5.84)**
Educational level				
Elementary	99 (47.1)	0.001	1	1
Secondary	136 (34.5)		0.59 (0.42–0.83)**	0.64 (0.40–1.02)[†]
Higher	125 (31.6)		0.52 (0.37–0.73)***	0.37 (0.23–0.59)***
	M (SD)	p value	Crude OR (95 % CI)	Adjusted OR (95 % CI)[a]
Number of male sexual partners in the last 12M	28.4 (54.8)	<0.001	1.04 (1.03–1.05)***	1.02 (1.01–1.04)***
	n (%)	p value	Crude OR (95 % CI)	Adjusted OR (95 % CI)[a]
Group sex in the last 12M				
No	208 (28.9)	<0.001	1	1
Yes	146 (57.7)		3.36 (2.50–4.52)***	2.22 (1.47–3.34)***
Unprotected anal sex in the last 12 M with a partner whose HIV serostatus was unknown				
No	177 (32.4)	<0.001	1	1
Yes	89 (52.4)		2.30 (1.62–3.26)***	1.67 (1.09–2.55)*
Reported HIV status				
HIV negative	258 (35.3)	<0.001	1	1
HIV positive	53 (60.2)		2.78 (1.77–4.37)***	2.31 (1.07–4.98)*
Don't know	52 (28.1)		0.72 (0.50–1.02)	0.67 (0.41–1.10)
Hosmer–Lemeshow goodness-of-fit, χ^2 (df), p value				5.2 (8), 0.732

OR odds ratio, *CI* confidence interval, *SD* standard deviation, *12M* 12 months

[†]　$p < 0.10$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

[a]　Adjusted for age, educational level, number of male sexual partners in the last 12 months, group sex in the last 12 months, unprotected anal sex in the last 12 months with a partner whose HIV serostatus was unknown, and reported HIV status

Table 3 Type of venues visited, behavioral factors, HIV infection, and coverage in HIV prevention campaigns associated with unprotected anal sex in the last 12M with a partner whose HIV serostatus was unknown

	n (%)	p value	Crude OR (CI 95 %)	Adjusted OR (CI 95 %)[a]
Venues usually visited to meet sexual partners				
Social gay venues	81 (18.0)	<0.001	1	1
Cruising venues	89 (33.5)		2.30 (1.62–3.26)***	1.76 (1.17–2.66)**
	M (SD)	p value	Crude OR (CI 95 %)	Adjusted OR (CI 95 %)[a]
Number of male sexual partners in the last 12M	25.4 (44.9)	<0.001	1.01 (1.01–1.02)***	1.01 (1.00–1.01)*
	n (%)	p value	Crude OR (CI 95 %)	Adjusted OR (CI 95 %)[a]
Group sex in the last 12M				
No	98 (19.5)	<0.001	1	1
Yes	65 (34.4)		2.17 (1.49–3.14)***	1.60 (1.03–2.47)*
Substance consumption before/during the last sexual intercourse				
No	98 (21.1)	0.009	1	1
Yes	72 (30.0)		1.54 (1.08–2.19)*	1.64 (1.11–2.43)*
Reported HIV status				
HIV negative	105 (20.3)	0.001	1	1
HIV positive	22 (39.3)		2.54 (1.43–4.52)**	1.88 (0.96–3.70)[†]
Don't know	42 (30.7)		1.73 (1.14–2.65)*	2.14 (1.32–3.45)**
Reached by HIV prevention programs in the last 12M				
Yes	53 (17.5)	0.001	1	1
No	114 (28.5)		1.88 (1.30–2.71)**	1.69 (1.14–2.52)**
Hosmer–Lemeshow goodness-of-fit, χ^2 (df), p value				8.6 (8), 0.380

OR odds ratio, *CI* confidence interval, *SD* standard deviation, *12M* 12 months

[†] $p < 0.10$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

[a] Adjusted for venues usually visited to meet sexual partners, number of male sexual partners in the last 12 months, group sex in the last 12 months, substance consumption before/during the last sexual intercourse, reported HIV status and reached by HIV prevention programs in the last 12 months

the last 12 months with a partner whose HIV serostatus was unknown was more likely among cruising venues' visitors (OR 1.76, 95 % CI 1.17–2.66), MSM who reported higher number of male sexual partners (OR 1.01, 95 % CI 1.00–1.01), those who engaged in group sex (OR 1.60, 95 % CI 1.03–2.47), those who consumed substances before/during the last sexual intercourse (OR 1.64, 95 % CI 1.11–2.43), those reporting not knowing their HIV serostatus compared to those HIV negative (OR 2.14, 95 % CI 1.32–3.45), and those not reached with HIV prevention campaigns in the last 12 months (OR 1.69, 95 % CI 1.14–2.52).

Discussion

This study provided insight into characteristics of MSM who visit different types of venues to meet sexual partners and examined differences in HIV prevalence and risk behaviors, being one of the few studies in Europe.

More than a third of respondents reported frequently visiting cruising venues to meet sexual partners. A significantly higher proportion of cruising venues' visitors (14.6 %) reported to be HIV positive, when compared to those who visit social gay venues (5.5 %). Our reported prevalence data are in line with other European studies with MSM where similar range of prevalence estimates were found (1.3–19.7 % in EMIS survey, 2.6–17.0 % in SIALON I project) (Marcus, Hickson, Weatherburn, & Schmidt, 2012; Mirandola et al., 2009), despite data being collected in different contexts and with different methodologies. In our study, as in others, older MSM tend to seek sexual contact at cruising venues, while younger MSM more frequently use the internet and gay bars (Vanden Berghe et al., 2011). As HIV infection is more prevalent in older age groups, it was expected to find higher HIV infection within those settings. Other potential explanation for a higher proportion of HIV-positive MSM visiting cruising venues relates

to the possibility of non-disclosure to partners in such places, where there is a decreased expectation for verbal or direct communication because of the casual or anonymous nature of the sexual encounters (Bird & Voisin, 2011; Wei, Lim, Guadamuz, & Koe, 2012). In more anonymous settings, disclosure may be also mitigated by perceived serostatus based on circumstantial evidence and normative assumptions based on the setting of the encounter (Parsons et al., 2006; Rönn, White, Hughes, & Ward, 2014).

Our findings indicate that MSM who frequently visit cruising venues to meet sexual partners also engage more frequently in high-risk sexual behaviors as having higher number of male sexual partners, engaging in group sex, and having unprotected sex with a partner whose HIV serostatus was unknown, similarly to other studies (Aynalem et al., 2006; Binson et al., 2001; Parsons & Halkitis, 2002). Also, factors as higher number of male sexual partners, engagement in group sex, and substances consumption before/during the last sexual intercourse were associated with unprotected anal intercourse, consistently with other research (Mimiaga et al., 2011; Reidy et al., 2009; Tang et al., 2013). It has been put forward that the environment of cruising venues potentially fosters the engagement in sex acts with multiple anonymous partners (Aynalem et al., 2006). Indeed, some authors suggest that in these venues, men tend to engage in unprotected sex while detached from any sense of connection to their sexual partners, as a means for coping with needs for sexual sensation seeking or sexual adventurism (Aynalem et al., 2006; Parsons & Halkitis, 2002). This potentially reduces the feeling of responsibility of protecting himself and casual sexual partners from HIV transmission (Aynalem et al., 2006; O'Leary, Horvath, & Rosser, 2013; Parsons & Halkitis, 2002). In line with this, other research has underscored the role of risk seeking as a predictor of HIV acquirement/transmission (Conner, Stein, & Longshore, 2005; Parsons & Halkitis, 2002). High-risk seekers are likely to be more impulsive, disinhibited, and to engage more frequently in high-risk sexual behaviors, leading them to be at increased risk for HIV infection (Conner et al., 2005).

An important finding is that a considerable proportion of MSM reported not knowing their HIV serostatus and these MSM were more likely to engage in unprotected anal intercourse with a partner whose HIV serostatus was unknown. These findings are particularly striking, given that a substantial number of MSM in our study reported having never been tested for HIV. Moreover, MSM not reached with HIV prevention were more likely to engage in unprotected anal intercourse. Our results highlight that these particular subgroups of high-risk-taking MSM who are unaware of their HIV serostatus and who remain out of scope of current prevention actions are in great need of HIV prevention efforts. These findings are also of particular interest as they reinforce that sexual health education and HIV prevention initiatives within venues may be effective and should be supported (Binson et al., 2001).

The limitations of this study must be acknowledged. As the study sample was not randomly recruited, the results may not reflect the situation of MSM in general. As a matter of fact, the lack of research with key populations so far has been due greatly to difficulties in reaching these groups for population-based health research (Magnani, Sabin, Saidel, & Heckathorn, 2005). Secondly, as data are self-reported, response bias and social stigma may have inhibited some participants to disclose their HIV serostatus and risk behaviors. Nevertheless, the high response rate and the obtained data on reported HIV prevalence make us confident of the responses' validity. In a worst-case scenario, our data underestimate the HIV prevalence and risks for infection among MSM. But we have no reasons to believe that such underestimation should be uneven in different groups of venues' visitors. Finally, although the demographic profile of individuals who refused to participate in the study was similar to those who participated, we did not collect information about reasons for refusal nor about reported HIV infection, so it is not possible to determine to what extent HIV prevalence and related risk behaviors might have differed between participants and refusals.

Our results provide evidence of the relationship between environments where MSM meet other MSM for sex and risk behavior. The findings show that cruising venues are a context that fosters engagement in unprotected sex, playing an important role in increasing risk of HIV transmission among MSM. Venue-focused behavioral interventions as promotion of condom use and HIV testing are needed. This may contribute to enhance safer sex practices, to decrease unawareness of HIV infection, and consequently to reduce transmission. Strategies focused on people living with HIV should also be supported. Cruising venues should be considered as an optimal setting to reach high-risk MSM for HIV research and targeted prevention interventions.

Compliance with Ethical Standards

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional

and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in this study.

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Study II – Risk-taking behaviors and HIV infection among sex workers in Portugal: Results from a cross-sectional survey
Sónia Dias, Ana Gama, Ricardo Fuertes, Luís Mendão, Henrique Barros

Epidemiology

Risk-taking behaviours and HIV infection among sex workers in Portugal: results from a cross-sectional survey

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ABSTRACT

Objectives Sex workers (SW) are key populations at an increased risk of HIV infection. This study aimed to characterise risk-taking behaviours and assess HIV prevalence among SW in Portugal.

Methods A cross-sectional survey was conducted with 1040 SW using a participatory research approach. SW were recruited in sex-work locations and community-based organisation offices. Data were collected through a questionnaire with trained interviewers. An HIV rapid test was performed in 213 respondents.

Results Reported HIV prevalence was 8%: 17.6% of man-to-woman transgenders, 7.4% of women and 5% of men. Of SW reportedly living with HIV, 52.2% reported ever injecting drug use. Inconsistent condom use with clients in the last month was higher among male SW (26.5%) and with non-paying partners in the last year was higher among women (71.3%). Among reported HIV-positive SW, the proportions of inconsistent condom use were high. In multivariate regression analysis, reported HIV infection remained significantly higher among transgenders (OR 6.4; 95% CI 1.7 to 24.3), those older (OR 5.1; 95% CI 1.3 to 21.1), working outdoors (OR 5.4; 95% CI 1.9 to 15.6), having ever used psychoactive substances (OR 4.1; 95% CI 2.2 to 7.7) and earning ≤€1000 per month (OR 2.6; 95% CI 1.2 to 5.9). Of those who had an HIV rapid test, 8.9% were reactive; 73.7% were unaware of their seropositivity.

Conclusions The HIV infection burden in SW is high. Efforts to promote HIV testing must be sustained in order to reduce undiagnosed infection. The diverse risk profiles of SW must be addressed in targeted HIV interventions. Prevention interventions should be systematically implemented within most-at-risk subgroups of SW.

INTRODUCTION

HIV continues to be a major concern in public health.[1] Sex workers (SW) have been considered to be at an increased risk of HIV infection. Limited data about HIV prevalence among SW in Europe show wide variation between countries,[2,3] being estimated to be >1% in 22 countries and >5% in six of these countries (6.1%–22.2%).[2]

Sex work is viewed as extremely widespread; yet, the actual number of people involved is difficult to determine.[4] Sex work varies in terms of formality or organisation and settings in which it occurs, ranging from dedicated establishments and private homes to hotels, bars and streets or parks.[5,6]

Little scientific attention has been given to the heightened behavioural, social and structural vulnerabilities of SW to HIV. Increased risk of HIV infection can result from multiple exposures: large number and concurrency of sexual partners, inconsistent condom use,[7,8] intersection with injecting drug use[9,10] and presence of other sexually transmitted infections (STIs).[7,11] In addition, among SW, infection risk and the adoption of unsafe behaviours vary across economic strata, sociocultural context and work environments.[12] Outdoor sex work is associated with higher vulnerability to HIV and violence.[13] The health and safety of these SW are frequently compromised by the inability to assert control over their working environments and negotiate safer sex.[7] Access to health services is often hindered by discriminatory attitudes and social exclusion, particularly among men and transgenders.[6,14] Additionally, criminalisation and enforcement-based policies can impact directly and indirectly on HIV vulnerability.[3,15]

Despite the widely recognised importance of characterising the burden of HIV among SW, epidemiological and socio-behavioural data remain scarce in Europe. In particular, there is no information on HIV prevalence among SW in Portugal, one of the countries presenting the largest burden of infection in Europe.[16] It probably reflects the difficulty of addressing hidden populations, which are stigmatised and not represented in traditional national HIV surveillance systems.[4] Injecting drug users have driven the Portuguese HIV epidemic, but sexually transmitted cases are arising. Routine surveillance data showed that in 2011 about 62% of the newly diagnosed infections were related to heterosexual and 26.2% to homosexual/bisexual transmission and 9.6% to injecting drug use.[17] The contribution of sex work to transmission of HIV in the country remains unknown. Thus, we aimed to characterise risk-taking behaviours and assess HIV prevalence among SW in Portugal.

METHODS

Behavioural study

A cross-sectional survey of SW was conducted using a participatory research approach. A Community Advisory Board (comprising SW, representatives of non-governmental and governmental organisations, and academics) actively participated in the study design, implementation and interpretation of results. SW were defined as 'female, male and transgender adults and young people who received
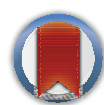
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money or goods in exchange for sexual services, either regularly or occasionally' whatever the settings.[6] The study inclusion criteria were being ≥18 years old and reporting sex work in the last 12 months. To estimate the sample size that would be large enough for detailed analyses, we assumed a hypothetical worst case prevalence of 50%, at 95% confidence level with precision of 3.5%; it was estimated that 784 SW would be required. Given that there is no adequate sampling frame of this population enabling to draw a probability sample of SW in Portugal, this study used a convenience sampling approach to generate a sufficiently robust sample that could capture different elements of the population. In a first stage, a geographic and network mapping was conducted based on a formative research with community partners in which the locations and networks where SW congregate were systematically listed to identify data collection sites. We sampled SW from the three large urban centres in Portugal: Great Lisbon (n=470), Great Porto (n=424) and Coimbra (n=146). Data were collected in venues frequented by large and diverse numbers of SW, including sex-work locations (streets, bars, private residences) and community-based organisations targeted at SW. Interviewers approached eligible respondents inviting them to participate. After data collection, respondents were asked to advertise the study among persons involved in sex work from their social networks. In total, 1040 SW were enrolled in the study.

Data were collected between January and September 2011 using a questionnaire administered by trained interviewers recruited from community organisation partners. Interviewer training included a presentation of study's purpose, ethical considerations, instrument, data collection procedures and practice of interviewing techniques through role plays. The questionnaire comprised information on socio-demographic characteristics, sex-work setting, sexual behaviour, drug use, HIV testing, prevention initiatives, HIV infection and other STIs.

The study was approved by the Ethics Committee for Health of North Regional Health Administration (No.18.09CES). Before responding to the questionnaire, participants were informed of the purpose and procedures of the study; confidentiality was guaranteed and informed consent was obtained. All participants were given information leaflets on HIV prevention and the testing services available.

HIV prevalence study (rapid test)

Throughout 1 month, we offered an HIV rapid test to every respondent in sex-work venues in the centre of Lisbon using a mobile unit that provided adequate conditions of privacy and room for pretest/post-test counselling. Logistic constraints limited the provision of HIV rapid tests in other areas of the country and for the whole study period. Of the 272 eligible participants who were approached, 213 accepted to be tested onsite using a finger-stick whole-blood rapid test (see online supplementary figure 1). Those with a reactive HIV test were referred to HIV care services for confirmatory testing and linkage to care. All the participants referred had their positive result confirmed. A numerical code was used to link behavioural and biological information, maintaining participant anonymity.

Statistical analysis

χ^2 Or exact Fisher test was used for comparisons. The magnitude of univariate and multivariate associations among reported HIV infection and socio-demographic, behavioural and environmental factors was estimated by means of OR and 95% CIs calculated using logistic regression. A $p<0.05$ was set to retain variables in the model. For statistical analysis, SPSS V.19.0 was used.

RESULTS

Characteristics of participants

Overall, the refusal rate was 35%; no significant differences were found between refusals and respondents on gender, age and education. As shown in table 1, 853 participants (82%) were women, 106 (10.2%) men and 81 (7.8%) transgenders (man-to-woman). Men were significantly younger and more frequently non-nationals than transgenders and women. Transgenders had a higher level of education. More female SW reported lower incomes and worked outdoor (in streets/cars). Most outdoor SW were Portuguese (71.7% vs 34.9% indoor, p<0.001; among non-nationals, Africans: 53.5% outdoor vs 4.1% indoor, Europeans: 19.4% vs 3.3%, Latin Americans: 27.1% vs 92.6%, p<0.001) (data not shown in table). Also, the majority of outdoor SW had a monthly income ≤€1000 (75.1% vs 40.0% indoor, p<0.001) and had ≤9 schooling years (84.5% vs 52.5% indoor, p<0.001).

Of those who had an HIV rapid test (n=213), 176 were women (82.6%), 28 men (13.2%) and nine transgenders (4.2%) (data not shown). No significant gender differences were found regarding age (overall, 59.6% were ≤35 years old) and nationality (50.2% were Portuguese). More women reported low income (≤€1000: 73.5% vs 50.0% of transgenders and 42.9% of men, p=0.009) and worked outdoors (85.8% vs 55.6% of transgenders and 47.6% of men, p<0.001).

HIV risk behaviour

A higher number of clients was more frequently reported by transgenders than men and women. Men declared a higher number of non-paying partners. Inconsistent condom use with clients was higher among men (26.5%) and with non-paying partners was higher among women (71.3%). Condom failure and forced sexual relations were reported, with no significant gender differences (table 1). Forced sexual relations were more likely among outdoor SW (14.3% vs 5.3% indoor, p<0.001) (data not shown in table). Those who had forced sexual relations reported more frequently inconsistent condom use with clients (19.8% vs 10.1%, p=0.003).

Ever use of psychoactive substances was reported by 68.9% of men, 46.9% of transgenders and 31.1% of women. Ever injecting drug use was more prevalent among women (18.1%) than men (13.7%) or transgenders (7.9%) (table 1). Injecting drug use was also higher among Portuguese SW (22.4% vs 3.3% non-nationals, p<0.001) and outdoor SW (25.4% vs 1.7% indoor, p<0.001). Those who ever injected drugs also reported more frequently having had forced sexual relations (23.3% vs 14.4%, p=0.085) (data not shown).

HIV testing and prevention

Most participants reported having been tested for HIV (table 2). Further analysis showed a higher proportion of those never tested among non-nationals (24.1% vs 18.9% of nationals; p=0.05), but no significant differences were found across education, sex-work setting, number of partners and drug use. Those SW who ever tested compared with those never tested reported more frequently consistent condom use with clients and non-paying partners (90.2% vs 81.6%, p=0.001; 36.5% vs 25.9%, p=0.010) and having been reached by HIV prevention programmes (44.2% vs 24.4%, p<0.001).

HIV prevalence

Self-reported HIV infection

Of those ever tested for HIV, 66 (8%, 95% CI 6.0 to 10.0) reported living with HIV: 17.6% of transgenders (95% CI 8.0 to 27.0),

Epidemiology

Table 1 Characteristics and risk behaviours of the participants by gender

	Female		Male		Transgender		
	n	%	n	%	n	%	p Value
Total (N=1040)	853	82.0	106	10.2	81	7.8	
Characteristics							
Age (years) (n=1040)							
18–25	152	17.8	36	34.0	17	21.0	<0.001*
26–35	315	36.9	54	50.9	36	44.4	
36–45	204	23.9	12	11.3	16	19.8	
≥46	182	21.4	4	3.8	12	14.8	
Nationality (n=1038)							
Portuguese	479	56.3	53	50.0	55	67.9	0.047*
Non-national	372	43.7	53	50.0	26	32.1	
Region of origin (n=440)							
Africa	94	26.0	3	5.8	1	3.8	<0.001†
Latin America	227	62.7	48	92.3	25	96.2	
Europe	41	11.3	1	1.9	0	0.0	
Schooling (years) (n=1027)							
≤9	520	61.8	58	54.7	38	47.5	0.022*
≥10	321	38.2	48	45.3	42	52.5	
Household monthly income (n=995)							
≤€1000	512	62.6	55	55.6	38	48.7	0.030*
>€1000	306	37.4	44	44.4	40	51.3	
Sex-work setting (n=968)							
Outdoor	460	57.4	31	36.1	30	37.5	<0.001*
Indoor	301	37.5	48	55.8	38	47.5	
Both	41	5.1	7	8.1	12	15.0	
Risk behaviours							
Number of clients in the last working day (n=989)							
None	26	3.2	1	1.0	0	0.0	0.013*
1–3	447	55.0	73	73.0	39	51.3	
4–6	220	27.1	16	16.0	23	30.3	
≥7	120	14.8	10	10.0	14	18.4	
Number of non-paying partners in the last 12 months (n=959)							
None	155	19.6	7	7.4	15	20.3	<0.001*
1	480	60.7	30	31.9	32	43.2	
2	84	10.6	6	6.4	11	14.9	
≥3	72	9.1	51	54.3	16	21.6	
Condom use with clients in the last month (n=1016)							
Consistent	758	91.0	75	73.5	66	81.5	<0.001*
Non-consistent (sometimes/never)	75	9.0	27	26.5	15	18.5	
Condom use with non-paying partners in the last 12 months (n=755)							
Consistent	176	28.7	32	39.0	34	57.6	<0.001*
Non-consistent (sometimes/never)	438	71.3	50	61.0	25	42.4	
Condom failure in the last 6 months (n=939)‡							
Never	437	55.7	40	50.0	34	45.9	0.195*
At least once	348	44.3	40	50.0	40	54.1	
Forced sexual relations in the last 12 months (n=1000)§							
Yes	80	9.7	12	12.2	9	11.4	0.680*
No	743	90.3	86	87.8	70	88.6	
Ever use of psychoactive substances (n=1040)							
Yes	265	31.1	73	68.9	38	46.9	<0.001*
No	588	68.9	33	31.1	43	53.1	
Ever injected drugs (n=376)¶							
Yes	48	18.1	10	13.7	3	7.9	0.226*
No	217	81.9	63	86.3	35	92.1	

The significance level for the p-values presented in italics is <0.05.
*χ^2 test.
†Exact Fisher test.
‡Condom failure includes slippage and breakage.
§Forced sexual relations by any type of partner in any setting.
¶Of those who ever used psychoactive substances.

Table 2 HIV prevention initiatives, HIV testing, self-reported HIV infection and STI by gender

	Female		Male		Transgender		
	n	%	n	%	n	%	p Value
HIV prevention initiatives and HIV testing							
Reached by HIV prevention programmes in the last 12 months (n=1003)							
Yes	344	41.6	40	41.2	40	50.0	*0.344**
No	482	58.4	57	58.8	40	50.0	
Received free condoms in the last 12 months (n=1022)							
Yes	770	91.4	86	86.9	75	92.6	*0.282**
No	72	8.6	13	13.1	6	7.4	
Ever tested for HIV (n=974)							
Yes	628	78.2	79	77.5	59	85.5	*0.348**
No	175	21.8	23	22.5	10	14.5	
Tested for HIV in the last 12 months (n=762)†							
Yes	483	76.7	57	75.0	44	78.6	*0.891**
No	147	23.3	19	25.0	12	21.4	
Self-reported HIV infection and STI							
HIV-positive	50	7.4	4	5.0	12	17.6	*0.007**
For how long HIV-positive status was known (years) (n=62)							
<1	6	12.8	1	25.0	0	0.0	*0.383‡*
1–5	16	34.0	2	50.0	6	54.5	
>5	25	53.2	1	25.0	5	45.5	
STI-positive in the last 12 months	58	9.9	6	7.4	4	6.9	*0.620‡*

The significance level for the p-values presented in italics is <0.05.
*χ^2 test.
†Of those who had ever been tested for HIV.
‡Exact Fisher test.
STI, sexually transmitted infection.

7.4% of women (95% CI 5.0 to 9.0) and 5% of men (95% CI 1.0 to 10.0) (table 2). In additional analysis, approximately 10% of participants admitted not knowing their current serostatus. Recalling at least one STI episode in the last 12 months was more frequent among HIV-positive than HIV-negative participants (24.4%, 10/41 vs 6.8%, 39/577, p=0.001).

Among SW reportedly living with HIV, transgenders more often reported inconsistent condom use with clients (33.3%, 4/12), than men (25.0%, 1/4) and women (8.9%, 4/45), (p=0.034). The opposite was observed with non-paying partners: 43.6% (17/39) of women, 33.3% (1/3) of men and 18.2% (2/11) of transgenders (p=0.086). Condom failure was referred by 54.4% and forced sexual relations by 15.4% of reported HIV-positive SW (no significant differences across gender). Ever injecting drug use was reported by 52.2% of HIV positives (vs 10.6% among HIV negatives): 66.7% (2/3) of men, 57.1% (20/35) of women and 25.0% (2/8) of transgenders (p=0.099). Among these injecting drug users, 55.0% referred that the probable mode of HIV transmission was sharing injection material.

HIV infection (rapid test)
Of the 213 SW who accepted to be tested, 8.9% (n=19) were reactive: 22.2% (n=2; 95% CI 0.0 to 56.0) of transgenders, 10.7% (n=3; 95% CI 0.0 to 23.0) of men and 8% (n=14; 95% CI 4.0 to 12.0) of women. Of the 19 who tested HIV positive, 14 (73.7%, 95% CI 52.0 to 95.0) had reported being HIV negative or not knowing their serostatus: two transgender cases, three men and nine (64.3%) of positive women. Around 64% (9/14) of unknown HIV-positives were non-nationals: 55.6% (five) women, 22.2% (two) men and 22.2% (two) transgenders.

Of the 14 HIV-positive participants unaware of their status, 42.9% inconsistently used condoms with clients: 50% (1/2) of transgenders, 44.4% (4/9) of women and 33.3% (1/3) of men.

About 75.0% (6/8) inconsistently used condoms with non-paying partners: all women (3/3), 66.7% (2/3) of men and 50.0% (1/2) of transgenders. Condom failure occurred in 33.3%. Forced sexual relations were reported by 33.3%. Around 43% reported ever consuming psychoactive substances: all men (3/3), 50% (1/2) of transgenders and 22.2% (2/9) of women. No unknown HIV-positive participant reported ever injecting drug use.

Factors associated with self-reported HIV infection
In the multivariate model, reported HIV infection remained significantly higher among transgenders (OR 6.4; 95% CI 1.7 to 24.3), those older (OR 5.1; 95% CI 1.3 to 21.1), earning ≤€1000 per month (OR 2.6; 95% CI 1.2 to 5.9), having used psychoactive substances (OR 4.1; 95% CI 2.2 to 7.7) and doing outdoor sex work (OR 5.4; 95% CI 1.9 to 15.6) compared with indoor. HIV infection was lower among non-nationals (OR 0.4; 95% CI 0.1 to 0.9) compared with Portuguese (table 3).

DISCUSSION
This is the first Portuguese survey conducted in a large sample of SW to characterise risk behaviours and assess HIV prevalence. The frequency of high-risk sexual behaviours remains concerning. Even with gender differences, SW reported high client frequency, multiple partners and engagement in unprotected sex with clients and non-paying partners. A high reported prevalence of HIV was found, particularly among transgenders. Other European studies show highly disparate levels of infection in different SW populations.[8] [18–20] It is worth noting that in general risk behaviours were frequent among reported HIV-positive SW but also among those screened who tested positive and did not know their seropositivity. The risk of sexual behaviours undertaken combined with HIV prevalence

Table 3 Factors associated with self-reported HIV infection*

	N	HIV prevalence n (%)	Crude OR (CI 95%)	Adjusted OR (CI 95%)†
Age (years)				
18–25	152	3 (2.0)	1	1
26–35	326	28 (8.6)	4.67 (1.40 to 15.60)	5.64 (1.52 to 20.93)
36–45	204	19 (9.3)	5.10 (1.48 to 17.57)	5.65 (1.47 to 21.79)
≥46	146	16 (11.0)	6.11 (1.74 to 21.45)	5.14 (1.25 to 21.11)
Gender				
Male	80	4 (5.0)	1	1
Female	680	50 (7.4)	1.51 (0.53 to 4.29)	1.00 (0.31 to 3.21)
Transgender	68	12 (17.6)	4.07 (1.25 to 13.29)	6.35 (1.66 to 24.26)
Nationality (missing=1)				
Portuguese	480	59 (12.3)	1	1
Non-national	347	7 (2.0)	0.15 (0.07 to 0.33)	0.35 (0.14 to 0.90)
Household monthly income (missing=29)				
>€1000	298	9 (3.0)	1	1
≤€1000	501	53 (10.6)	3.80 (1.85 to 7.82)	2.62 (1.16 to 5.91)
Ever use of psychoactive substances				
No	527	20 (3.8)	1	1
Yes	301	46 (15.3)	4.57 (2.65 to 7.90)	4.06 (2.16 to 7.67)
Sex-work setting (missing=55)				
Indoor	308	5 (1.6)	1	1
Outdoor	418	52 (12.4)	8.61 (3.40 to 21.83)	5.43 (1.90 to 15.56)
Both	47	5 (10.6)	7.21 (2.00 to 25.97)	2.61 (0.63 to 10.79)

*Excluding those participants who reported having never been tested.
†Adjusted for age, gender, nationality, household monthly income, ever use of psychoactive substances and sex-work setting.

increases the likelihood of spreading of HIV to general population. This indicates that both SW and their clients/non-paying partners are key populations to be targeted as they may act as bridging populations.

Self-reported HIV prevalence was significantly higher among drug users compared with non-drug users (15.3% vs 3.8%). Among HIV-positive SW, 52.2% ever injected drugs. This is consistent with research demonstrating that HIV infection is driven largely by the overlap of injecting drug use and sex work.[10] [11] [21] Our study also found a higher proportion of injecting drug users working outdoors which heightens vulnerability to HIV infection. As in earlier surveys, SW working in streets presented higher levels of infection than those working in brothels, clubs and apartments.[3] [22] Outdoor SW had lower income and educational levels. In a context of socioeconomic disadvantage, these SW are more likely to engage in higher risk behaviours.[7] [13] We observed that among outdoor SW, a higher proportion engaged in inconsistent condom use with clients (12.9% vs 8.1% of indoor SW, p=0.063). Additionally, an important proportion of SW experienced forced sexual relations (14.3% vs 5.3% of indoor, p<0.001), which increases vulnerability to HIV. As noted in the literature, policies supporting safer environments and integrated interventions including harm-reduction programmes should be promoted.[23] [24]

The results from the rapid tests show that 74% of the SW who tested HIV positive (reactive test) were unaware of their serostatus. Among these, 64.3% were migrants from highly endemic areas. Although the sample screened was small and CIs were wide, this can be an important finding. Those unaware of their HIV status are at risk of transmitting HIV to others through high-risk behaviours. Early diagnosis is crucial to limit further transmission of HIV.[25] This finding may partly explain the higher self-reported HIV prevalence among Portuguese SW

compared with non-nationals. Other possible explanations for this disparity are that a larger proportion of Portuguese SW worked outdoor, reported lower income and higher injecting drug use than non-nationals.

Our findings indicate a considerable HIV testing rate and proportion of participants tested during the previous year. In Europe, data on HIV testing among SW are scarce and the reported rates vary considerably between countries, ranging from 33% in Czech Republic and 35% in France to 93.8% in Belgium and 100% in Greece.[26] The rate of HIV testing found in our study may be a positive outcome of prevention programmes among SW implemented in the last few years as community-based HIV testing initiatives. Nevertheless, the proportion of SW who never tested for HIV is worth highlighting. Indeed, these reported more frequently inconsistent condom use with both clients and non-paying partners. In Portugal, HIV testing is non-mandatory and can be done anonymously, confidentially and for free. Potential reasons for not getting tested are mistrust of health services, confidentiality, fear of discrimination or exclusion, lack of awareness of services available and low self-perception of HIV risk.[27] Unfortunately, we did not collect data on duration of sex work and so we cannot determine its effect on HIV-testing behaviour. There remains a need to understand factors that may underlie unwillingness to be tested. Yet, our findings reinforce that efforts should be made to increase HIV testing, particularly among individuals who do not perceive themselves to be at risk or who do not contact healthcare services.[28] Particular emphasis should be given to increase health service use by migrant SW.[6] [13] Furthermore, as supported by other studies,[29] [30] integrating outreach strategies for HIV prevention is valuable: having been reached by HIV prevention programmes in the previous year appeared positively associated with having been tested for HIV.

Almost a fourth of reported HIV-positive SW reported an STI. STIs increase the risk of HIV infection by increasing HIV infectiousness and susceptibility.[25] In a context of frequent high-risk sexual exposure, STIs may have a stronger role on HIV infection and transmission. Preventing and controlling STIs are key strategies in controlling the spread of HIV/AIDS, and HIV/STI programmes and services should be integrated for SW.

Limitations of this study must be acknowledged. First, due to sampling procedure, results may not reflect the situation of the SW population in general. Nevertheless, interviewing SW at different times and working places allowed reaching a heterogeneous sample of 1040 SW comprised of outdoor and indoor, nationals and non-nationals, with reported HIV and other STIs. The socioeconomic characteristics of our sample are in line with recent data on sex work in Europe showing high rates of low education and low income among SW.[5] Also, the socio-demographic profile of individuals who refused to participate in the study was similar to those who participated. However, as we did not collect information about reasons for refusal to behavioural study or to rapid test, it is not possible to determine to what extent HIV prevalence and related risk behaviours might have differed between participants and refusals. Second, given the relatively low numbers of HIV positives, the wide CIs of the OR in the multivariate analysis and the missing data in some variables, results must be treated with caution. Finally, to include those of low-level literacy and migrants, we opted for an interview-administered questionnaire. Interviewers might have interpreted the responses in a biased way, although they were trained thoroughly prior to fieldwork. Social desirability and recall bias also potentially led to under-reported risk behaviours and HIV infection from respondents. Nevertheless, the high response rate and the obtained data on reported HIV prevalence make us confident of the validity of the responses. Overall, the HIV burden in SW population could be under-represented.

Research among SW remains relatively scarce, which reflects the ongoing challenge in studying this population. Further research is required for an indepth understanding of the effect of sex work-related variables and factors that increase vulnerability.

In conclusion, to prevent further transmission of HIV it is essential to acknowledge the diverse risk profiles of SW and address the links between these key features and HIV/STIs. The findings of this study suggest most-at-risk subgroups that need to be additionally focused for future prevention interventions and research such as transgenders, drug users and those who are unaware of HIV status. Safe sex promotion should also pay attention to HIV-positive SW. Overall, targeted interventions aimed at improving uptake of testing and reducing risky behaviours in this population should be sustained.

Key messages

- ▶ The HIV burden in sex workers (SW) is high and the overlap between drug use and sex work is a major driver of HIV infection.
- ▶ The prevalence of risky sexual behaviour among SW, such as high numbers of partners and inconsistent condom use with clients and non-paying partners, is concerning.
- ▶ The findings suggest a potential high level of undiagnosed infection among SW.
- ▶ Prevention interventions should be systematically implemented particularly within most-at-risk subgroups of SW including transgenders, drug users and those not tested for HIV.

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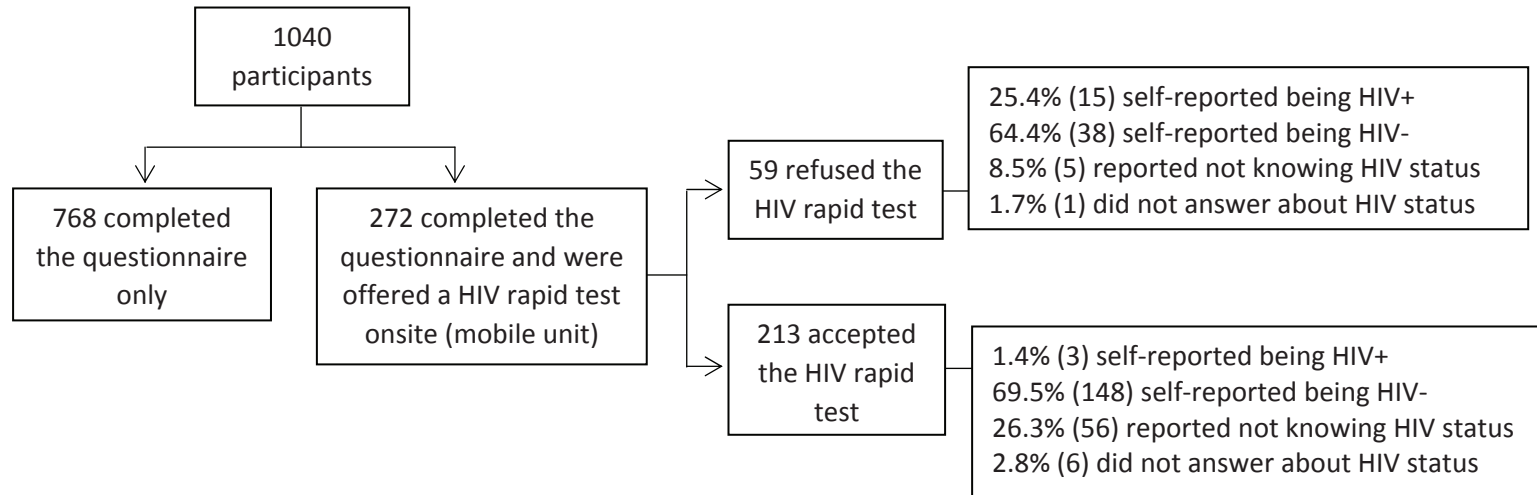
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Figure 1. Study flowchart with a focus on offer and uptake of HIV rapid test.

```
                        ┌─────────────────┐
                        │      1040       │
                        │   participants  │
                        └─────────────────┘
                 ┌───────────────┴───────────────┐
                 ▼                               ▼
    ┌─────────────────────┐      ┌─────────────────────────┐
    │  768 completed      │      │  272 completed the      │
    │  the questionnaire  │      │  questionnaire and were │
    │  only               │      │  offered a HIV rapid test│
    │                     │      │  onsite (mobile unit)   │
    └─────────────────────┘      └─────────────────────────┘
```

59 refused the HIV rapid test

25.4% (15) self-reported being HIV+
64.4% (38) self-reported being HIV-
8.5% (5) reported not knowing HIV status
1.7% (1) did not answer about HIV status

213 accepted the HIV rapid test

1.4% (3) self-reported being HIV+
69.5% (148) self-reported being HIV-
26.3% (56) reported not knowing HIV status
2.8% (6) did not answer about HIV status

Study III – HIV infection, risk factors and health services use among male-to-female transgender sex workers: A cross-sectional study in Portugal
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HIV Infection, risk factors and health services use among male-to-female transgender sex workers: a cross-sectional study in Portugal

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ABSTRACT

Male-to-female transgender sex workers (TSW) have been identified as a key population at risk for HIV. This study examined risk behaviors and HIV prevalence among TSW, and described health services use. A participatory cross-sectional survey was conducted with 125 TSW recruited in locations and networks where sex workers congregate. HIV-risk behaviors were common among participants. Inconsistent condom use with clients in the previous month was reported by 12.0% of participants and was associated with Portuguese nationality, inconsistent condom use with non-paying partners and not been reached by HIV prevention programs in the previous year. Ever use of psychoactive substances was reported by 61.6% of participants and was associated with being non-employed, doing full-time sex work, having higher number of non-paying partners and having never used health services. Also, ever use of psychoactive substances was negatively associated with older age and Portuguese nationality. About 34% of the participants reported having not been tested in the previous 12 months; 20.2% never used the health services. Overall, 14.9% (95%CI: 8.0–21.0%) reported being HIV-positive. Of those, 22.2% (95%CI: 1.0–43.5%) had unprotected sex with clients in the previous month, 26.7% (95%CI: 1.3–52.0%) had unprotected sex with non-paying partners in the previous year, 13.3% (95%CI: 0.0–33.0%) had ever injected drugs, 60.0% (95%CI: 23.0–97.0%) reported a past STI and 33.3% (95%CI: 2.0–64.6%) had currently HIV/STI co-infection. The socioeconomic, relational or partnering, and structural contexts conducive to increased risk are warranting further investigation. This knowledge would be valuable to inform prevention programs. HIV interventions, including secondary prevention, should address specific needs of TSW. Outreach initiatives aimed to reach TSW who are difficult to access can play a role in promoting access to health services and reducing HIV infection and transmission.

Introduction

Emerging research show a disproportionate burden of HIV in male-to-female transgender people (Baral et al., 2013; De Santis, 2009). Male-to-female transgender persons (hereafter designated "transgender") are assigned male sex at birth but identify themselves as women, irrespective of anatomy or medical interventions (Institute of Medicine, 2011). Worldwide, pooled HIV prevalence in transgender population is 19.1% (Baral et al., 2013).

The proportion of sex work in transgender population is uncertain, although studies have estimated to be 24%–75% (Herbst et al., 2008; Schulden et al., 2008). A systematic review of 25 studies found a crude non-weighted HIV prevalence of 27.3% in transgender individuals engaged in sex work (Operario, Soma, & Underhill, 2008), higher than in other transgender populations or other sex workers (SW) (Operario et al., 2008; Reback, Lombardi, Simon, & Frye, 2005).

HIV vulnerability of transgender SW (TSW) reflects a complex interaction of multilevel risks (Beyrer et al., 2015; De Santis, 2009). High-risk behavioral factors include condomless anal sex, multiple sexual partners and substance misuse (Nemoto, Bödeker, Iwamoto, & Sakata, 2014; Reback et al., 2005). At structural level, socioeconomic disadvantage as well as stigma and marginalization related to gender identity and involvement in sex work can create hostile environments for TSW. This context along with fear of rejection may reduce TSW's access to health services (Beyrer et al., 2015; Poteat et al., 2015).

Information on HIV burden and vulnerability among TSW is scarce. This study aims to examine risk behaviors

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and HIV prevalence among TSW, and describe health services use.

Methods

A cross-sectional study was conducted with SW in Portugal using a participatory approach (Dias & Gama, 2014). Detailed methods are described elsewhere (Dias, Gama, Fuertes, Mendão, & Barros, 2015). Briefly, based on a formative research with community partners, a geographic and network mapping was conducted to systematically list locations and networks where SW congregate and subsequently identify data collection sites. Data were collected in sex-work locations (streets, bars, private residences) and community-based organizations targeted at SW. Respondents were asked to advertise the study among peers from their social networks. A total of 125 TSW were enrolled in the study (refusal rate = 28.3%; no significant differences found between refusals and respondents on age and education). Participants were sampled from the two largest urban centers in Portugal. Data were collected using a pen-and-paper questionnaire administered face-to-face by trained interviewers recruited from community partners. The study was approved by the Ethics Committee for Health of North Regional Health Administration (No.18.09CES).

Measures

Sociodemographic characteristics included age, nationality, living with a partner, educational level, professional situation (employed – having a job excluding sex work) and household monthly income. Characteristics of sex-work activity comprised frequency (full-time; occasionally) and setting (outdoor – in streets or cars; indoor – in private apartments or nightclubs/bars). Sexual behaviors included number of clients in the last working day and number of non-paying partners in the last 12 months, condom use with clients in the last month and with non-paying partners in the last 12 months, experience of forced sexual relations in the last 12 months and condom failure in the last 6 months. Drug use information included ever use of psychoactive substances (only illicit drugs included) and ever injection of drugs. Participants were asked about HIV testing ever/ last 12 months, being reached by HIV prevention programs and having received free condoms in the previous 12 months, ever use of health services (general services from the National Health Service), and ever use of services to obtain HIV information. Participants self-reported their current serostatus for HIV and STI, and STI in the past.

Statistical analysis

Descriptive statistics and Chi-square tests were conducted to summarize characteristics of the participants. Bivariate logistic regression analysis was conducted to examine the correlates of high-risk behaviors. Ninety-five percent confidence intervals (CI) were calculated for characteristics of HIV-positive respondents. Statistical analyses were conducted using IBM-SPSS Statistics 22.0. (See Supplementary Text 1 for statistical details).

Results

Sociodemographic and sex-work characteristics

Table 1 shows the participants' sociodemographic and sex-work characteristics.

HIV-risk behaviors

HIV-risk behaviors were common among participants, including inconsistent condom use with clients (12.0%) and with non-paying partners (47.6%), and ever consumption of psychoactive substances (61.6%) (Table 1). (See Supplementary Table 1 for reasons for condomless sex).

Factors associated with HIV-risk behaviors

Inconsistent condom use with clients in the last month was significantly associated with Portuguese nationality, inconsistent condom use with non-paying partners and not been reached by HIV prevention programs (Table 1). Ever use of psychoactive substances was significantly associated with non-employed situation, full-time sex work, higher number of non-paying partners, and never use of health services. Also, ever use of psychoactive substances was negatively associated with older age and Portuguese nationality (Table 1).

HIV testing and utilization of health services

In total, 34.4% of the participants had not been tested for HIV in the previous 12 months (Table 1). About 20.0% reported having never used the health services. Sociodemographic and sex work-related factors associated with ever utilization of health services are presented in Table 2.

HIV infection

Overall, 14.9% (95%CI: 8.0–21.0%) reported being HIV-positive. Characteristics of HIV-positive participants are shown in Table 3.

Table 1. Sociodemographics, sex-work characteristics, partnerships, risk behaviours, utilization of health services, HIV testing and prevention initiatives, and factors associated with HIV risk behaviours.

	Total		Non-consistent condom use with clients in the last month		Crude OR (95% CI)	p	Ever use of psychoactive substances		Crude OR (95% CI)	p
	n	%	n	%			n	%		
Total	125	100	15	12.0			77	61.6		
Sociodemographics										
	mean	s.d.	mean	s.d.			mean	s.d.		
Age (years) (n = 125)	32.0	8.9	33.6	10.3	1.02 (0.97–1.08)	0.453	30.2	7.3	0.94 (0.90–0.98)	0.005
	n	%	n	%			n	%		
Nationality (n = 125)										
Non-national	67	53.6	3	4.4	1		52	76.5	1	
Portuguese	58	46.4	12	21.1	5.57 (1.49–20.85)	0.011	25	43.9	0.25 (0.12–0.55)	<0.001
Living with a partner (n = 122)										
Yes	34	27.9	4	11.8	1		21	61.8	1	
No	88	72.1	10	11.4	0.96 (0.28–3.30)	0.950	55	62.5	1.03 (0.46–2.33)	0.940
Educational level (n = 125)										
Elementary	64	51.2	8	12.5	1		36	56.3	1	
Secondary (high-school)	58	46.4	6	10.3	0.81 (0.26–2.49)	0.710	39	67.2	1.60 (0.76–3.34)	0.214
Higher	3	2.4	1	33.3	3.50 (0.28–43.16)	0.328	2	66.7	1.56 (0.13–18.04)	0.724
Professional situation (n = 119)										
Employed	27	22.7	4	14.8	1		10	37.0	1	
Non-employed	92	77.3	10	10.9	0.70 (0.20–2.44)	0.577	66	71.7	4.31 (1.75–10.65)	0.002
Household monthly income (n = 120)										
>1000€	40	33.3	7	17.5	1		21	52.5	1	
≤1000€	80	66.7	7	8.8	0.45 (0.15–1.39)	0.167	54	67.5	1.88 (0.86–4.09)	0.112
Sex work characteristics										
Frequency (n = 110)										
Occasionally	26	23.6	4	15.4	1		7	26.9	1	
Full-time	84	76.4	6	7.1	0.42 (0.11–1.63)	0.212	61	72.6	7.20 (2.67–19.38)	<0.001
Setting (n = 124)										
Indoor	75	60.5	9	12.0	1		49	65.3	1	
Outdoor/Both	49	39.5	6	12.2	1.02 (0.34–3.08)	0.967	27	55.1	0.65 (0.31–1.36)	0.254
Partnerships										
	median		median				median			
Number of clients in the last working day (n = 119)	3		3		0.99 (0.78–1.26)	0.945	4		1.04 (0.89–1.21)	0.634
Number of non-paying partners in the last 12 months (n = 118)	1		2		1.01 (0.95–1.06)	0.962	2		1.09 (1.01–1.18)	0.025
Risk behaviours										
	n	%	n	%			n	%		
Non-consistent (sometimes/never) condom use with clients in the last month (n = 125)	15	12.0	–	–	–	–	11	73.3	1.83 (0.55–6.13)	0.325
Non-consistent (sometimes/never) condom use with non-paying partners in the last 12 months (n = 103)	49	47.6	11	22.4	4.92 (1.28–18.87)	0.020	34	69.4	1.95 (0.87–4.39)	0.105
Forced sexual relations in the last 12 months (n = 122)[a]	9	7.4	1	11.1	0.96 (0.11–8.32)	0.962	4	44.4	0.46 (0.12–1.79)	0.261
Condom failure in the last 6 months (n = 117)	55	47.0	9	16.4	3.85 (0.99–15.03)	0.053	31	56.4	0.71 (0.34–1.50)	0.368
Ever use of psychoactive substances (except alcohol and medication) (n = 125)	77	61.6	11	14.3	1.83 (0.55–6.13)	0.325	–	–	–	–

(Continued)

Table 1. Continued.

	Total		Non-consistent condom use with clients in the last month		Crude OR (95% CI)	p	Ever use of psychoactive substances		Crude OR (95% CI)	p
	n	%	n	%			n	%		
Ever injected drugs (n = 104)	3	2.9	1	33.3	0.21 (0.02–2.53)	0.220	3	100	–	–
Health services utilization										
Ever used the health services (n = 124)										
Yes	99	79.8	11	11.1	1		55	55.6	1	
No	25	20.2	3	12.0	1.09 (0.28–4.25)	0.900	22	88.0	5.87 (1.65–20.89)	0.006
Ever used services to obtain HIV information (n = 125)										
Yes	81	64.8	13	16.0	1		45	55.6	1	0.059
No	44	35.2	2	4.5	0.25 (0.05–1.16)	0.076	32	72.7	2.13 (0.96–4.73)	0.062
HIV testing and prevention initiatives										
Ever tested for HIV (n = 125)										
Yes	122	97.6	14	11.5	1		74	60.7	–	
No	3	2.4	1	33.3	3.86 (0.33–45.34)	0.283	3	100	–	–
Tested for HIV in the last 12 months (n = 125)										
Yes	82	65.6	9	11.0	1		47	57.3	1	
No	43	34.4	5	12.5	1.16 (0.36–3.71)	0.804	27	67.5	1.55 (0.70–3.42)	0.281
Reached by HIV prevention programs in the last 12 months (n = 124)										
Yes	71	57.3	4	5.6	1		46	64.8	1	
No	53	42.7	10	18.9	3.89 (1.15–13.21)	0.029	31	58.5	0.77 (0.37–1.59)	0.475
Received free condoms in the last 12 months (n = 125)										
Yes	111	88.8	12	10.8	1		68	61.3	1	
No	14	11.2	3	21.4	2.25 (0.55–9.22)	0.260	9	64.3	1.14 (0.36–3.62)	0.827

[a]Forced sexual relations by any type of partner in any setting.

Table 2. Sociodemographic and sex work-related factors associated with ever utilization of health services.

| | Ever utilization of health services | | | | |
| | Yes | | No | | |
	n	%	n	%	Test statistic, p
Total	99	79.8	25	20.2	
Sociodemographics					
Nationality (n = 124)					
Non-national	45	67.2	22	32.8	χ2 (1) = 14.55, p < 0.001
Portuguese	54	94.7	3	5.3	
Educational level (n = 124)					
Elementary	54	85.7	9	14.3	χ2 (2) = 2.85, p = 0.235
Secondary (high-school)	43	74.1	15	25.9	
Higher	2	66.7	1	33.3	
Professional situation (n = 118)					
Employed	26	100	0	0.0	χ2 (1) = 8.07, p = 0.004
Non-employed	69	75.0	23	25.0	
Household monthly income (n = 120)					
≤1000€	63	78.7	17	21.3	χ2 (1) = 0.23, p = 0.628
>1000€	33	82.5	7	17.5	
Sex work characteristics					
Frequency (n = 109)					
Occasionally	24	96.0	1	4.0	χ2 (1) = 5.70, p = 0.017
Full-time	62	73.8	22	26.2	
Setting (n = 123)					
Indoor	56	75.7	18	24.3	χ2 (1) = 1.83, p = 0.176
Outdoor/Both	42	85.7	7	14.3	

Discussion

This study found a high level of HIV infection among TSW, as in other research (Operario et al., 2008). High-risk behaviors such as unprotected sex were reported by TSW, namely among those HIV-positive. Unprotected sex with clients was more likely among TSW at low socioeconomic level, reinforcing that contexts of social disadvantage increase exposure to HIV risk. Many TSW are compelled to engage in unprotected sex especially with clients that pay extra money for condomless sex (Poteat et al., 2015; Reback et al., 2005).

Participants who had unprotected sex with clients were also more likely to have unprotected sex with non-paying partners. Additionally, other behavioral risks like multiple partners, forced sexual relations and condom failure were found. This overlap of sexual risk behaviors suggests that complex multi-related factors are linked to increased risk for HIV infection and transmission. Nevertheless, the higher inconsistent condom use with non-paying partners than with clients indicates that psychosocial aspects, like low risk perception and relationship intimacy, can act as barriers to condom use (Nemoto, Operario, Keatley, & Villegas, 2004; Operario, Nemoto, Iwamoto, & Moore, 2011). Future research especially focusing on qualitative approaches to explore characteristics of non-paying and client partners, experiences of violence and condom failure, contexts of social vulnerability of TSW and its impact on HIV risk would be valuable.

Drug use was observed among TSW, and in an important proportion of those HIV-positive. This is consistent with research showing that HIV infection is driven largely by the intersection of drug use and sex work (Stockman & Strathdee, 2010; Strathdee et al., 2011). In our study, psychoactive substances use was significantly more likely among non-employed, full-time and non-national TSW. As documented elsewhere, migrant SW often live in poorer socioeconomic conditions and face additional vulnerabilities, such as substance use and marginalization related to gender identity and ethnicity (Decker et al., 2015). In a context of socioeconomic disadvantage, sex work is a common mean to finance drugs use (Nemoto et al., 2004; Reback et al., 2005). It has been reported that drugs are often used in the context of sex with partners and clients, and in addition needles are sometimes shared with clients who pay for their services with drugs (Clements-Nolle, Marx, Guzman, & Katz, 2001; Strathdee et al., 2011). Further studies are needed to understand the influence of patterns of drug use in HIV risk-taking behaviors, in order to inform integrated interventions that include harm reduction strategies (Rekart, 2005).

Furthermore, a significant group of TSW underuse health services, especially those more socially vulnerable. Social exclusion impairs this group's ability to access health services and HIV prevention programs (Dos Ramos Farías et al., 2011). This is a relevant finding because not been reached with HIV prevention

Table 3. Sociodemographics, sex-work characteristics, partnerships, risk behaviours, prevention initiatives and other reported infections of self-reported HIV-positive participants.

	HIV+ (self-reported)		
	n	%	95% CI
Total (*n* = 121)	18	14.9	8.0–21.0
Sociodemographics			
	mean	s.d.	
Age (years) (*n* = 121)	34.4	8.8	30.1–38.8
	n	%	
Nationality (n = 121)			
Non-national	8	44.4	19.0–70.0
Portuguese	10	55.6	30.1–81.0
Educational level (n = 121)			
Elementary	10	55.6	30.1–81.0
Secondary (high-school)	8	44.4	19.0–70.0
Higher	0	0.0	0.0–0.0
Professional situation (n = 115)			
Employed	1	6.3	0.0–19.6
Non-employed	15	93.7	80.4–100
Household monthly income (n = 116)			
≤1000€	15	83.3	64.3–100
>1000€	3	16.7	0.0–35.7
Sex work characteristics			
Frequency (*n* = 107)			
Occasionally	0	0.0	0.0–0.0
Full-time	13	100	100–100
Setting (n = 120)			
Indoor	9	50.0	24.4–75.6
Outdoor/Both	9	50.0	24.4--75.6
Partnerships			
	median		
Number of clients in the last working day (*n* = 116)	3		3.0–4.0
Number of non-paying partners in the last 12 months (*n* = 116)	2		1.0–8.0
Risk behaviours			
	n	%	
Non-consistent (sometimes/never) condom use with clients in the last month (*n* = 121)	4	22.2	1.0–43.5
Non-consistent (sometimes/never) condom use with non-paying partners in the last 12 months (*n* = 99)	4	26.7	1.3–52.0
Forced sexual relations in the last 12 months (*n* = 118)[a]	3	16.7	0.0–36.0
Condom failure in the last 6 months (*n* = 113)	9	56.2	28.9–83.5
Ever use of psychoactive substances (except alcohol and medication) (*n* = 121)	13	72.2	49.0–95.0
Ever injected drugs (*n* = 104)	2	13.3	0.0–33.0
HIV prevention initiatives			
Not reached by HIV prevention programs in the last 12 months (*n* = 120)	8	44.4	19.0–69.9
Not received free condoms in the last 12 months (*n* = 121)	2	11.1	0.0–27.2
Other reported infections			
Past STI (*n* = 99)	6	60.0	23.0–97.0
Current HIV/STI co-infection (*n* = 107)	4	33.3	2.0–64.6

[a]Forced sexual relations by any type of partner in any setting.

programs appeared positively associated with inconsistent condom use with clients.

This study had limitations. The use of a convenience sample means that findings may not be generalized to TSW in general. Data may be biased towards individuals who frequently attend venues or have larger social networks. Nevertheless, recruiting TSW at different times and working places allowed reaching a relatively large and heterogeneous sample. Data were self-reported potentially inhibiting disclosure of HIV serostatus and risk behaviors. In a worst-case scenario the HIV burden

and risk in TSW population could be underestimated. Given the low numbers of HIV-positive participants and the missing data in some variables, results must be treated with caution. Nevertheless, findings shed light on HIV among TSW, a group understudied and under-addressed.

Conclusions

Our findings show a high HIV burden and risk among TSW. The socioeconomic, relational or partnering, and

structural contexts conducive to increased risk are warranting further investigation in order to inform prevention programs. Culturally tailored HIV interventions, including secondary prevention, are needed to address specific needs of TSW. Outreach initiatives aimed to reach TSW who are difficult to access and are most at risk can play a role in promoting access to health services and reducing HIV infection and transmission.

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Supplementary Table 1 – Reasons for condomless sex

Table 1. Reasons for condomless sex with clients and with non-paying partners.

	n	%
Reasons for condomless sex with clients		
Client refused to use condom (n=15)	7	46.7
Client paid higher price for unprotected sex (n=15)	6	40.0
Dislike using condom (n=15)	3	20.0
Condoms are expensive (n=15)	1	6.7
Didn't have any condom at the moment (n=15)	1	6.7
Condom reduces pleasure (n=15)	1	6.7
Reasons for condomless sex with non-paying partners		
Didn't think it was necessary (n=48)	9	18.8
Condoms are expensive (n=48)	8	16.7
Condom reduces pleasure (n=48)	6	12.5
Dislike using condom (n=48)	4	8.3
Didn't think about it (n=48)	2	4.2
Partner refused to use condom (n=48)	1	2.1
Didn't have any condom at the moment (n=48)	1	2.1

Supplementary Text 1 – Additional statistical details

Statistical analysis

Descriptive statistics (means, medians and proportions) were used to describe sociodemographic and behavioural characteristics of the participants, as well as utilization of health services, HIV testing, prevention initiatives, reported HIV infection and other STI. Chi-square tests were performed to compare the proportion of utilization of health services across sociodemographic and sex-work characteristics. Bivariate logistic regression analysis was conducted to examine the factors (related to sociodemographics, sex-work activity, partnerships, risk behaviours, health services utilization and HIV prevention initiatives) correlating with high-risk behaviours ('Non-consistent condom use with clients in the last month' and 'Ever use of psychoactive substances'). Ninety-five percent confidence intervals (CI) were calculated around proportions, mean and medians for characteristics of HIV-positive respondents. Statistical analyses were conducted using IBM SPSS Statistics 22.0.

Study IV – HIV research with Men who have Sex with Men (MSM): Advantages and challenges of different methods for most appropriately targeting a key population
Ana Gama, Maria O. Martins, Sónia Dias

100

Review

HIV Research with Men who Have Sex with Men (MSM): Advantages and Challenges of Different Methods for Most Appropriately Targeting a Key Population

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Abstract: The difficulty in accessing hard-to-reach populations as men who have sex with men presents a dilemma for HIV surveillance as their omission from surveillance systems leaves significant gaps in our understanding of HIV/AIDS epidemics. Several methods for recruiting difficult-to-access populations and collecting data on trends of HIV prevalence and behavioural factors for surveillance and research purposes have emerged. This paper aims to critically review different sampling approaches, from chain-referral and venue-based to respondent-driven, time-location and internet sampling methods, focusing on its main advantages and challenges for conducting HIV research among key populations, such as men who have sex with men. The benefits of using these approaches to recruit participants must be weighed against privacy concerns inherent in any social situation or health condition. Nevertheless, the methods discussed in this paper represent some of the best efforts to effectively reach most-at-risk subgroups of men who have sex with men, contributing to obtain unbiased trends of HIV prevalence and HIV-related risk behaviours among this population group.

Keywords: HIV; Men who have sex with men; surveillance; research; sampling methods

1. Introduction

1.1. HIV Epidemic Trends and Burden among Men who Have Sex with Men (MSM)

The Human Immunodeficiency Virus (HIV) infection continues to be a concern in global public health. Surveillance data published by the European Centre for Disease Prevention and Control and the World Health Organization (WHO) Regional Office for Europe indicate that, in 50 of 53 countries in the WHO European Region, 153,407 new HIV diagnoses were reported in 2015, corresponding to a rate of 17.6 per 100,000 populations in this region [1].

The emergence of Acquired Immunodeficiency Syndrome (AIDS) as a global threat has served to highlight the diversity of lifestyles and complexity of socio-cultural subgroups which need to be considered in health policy [2]. In low-level and concentrated epidemics, key populations (which are at increased risk for acquiring and transmitting HIV and other infections due to specific higher-risk behaviours, in combination with interpersonal, socio-political, and cultural contexts) include injecting drug users, female sex workers, and men who have sex with men (MSM) [3,4].

Against the background of low or declining HIV prevalence in the general population, MSM continue to be disproportionately affected by HIV infection [5,6]. In recent years, there has been increased concern about newly identified epidemics of HIV infection among MSM in Asia, Africa, and Latin America [7,8] and the resurgence in HIV infection among MSM in the Western world [9–11]. Recent data estimates that 25.6% of new HIV diagnoses reported in the WHO European Region in 2015 were attributed to sex between men [1]. The number of HIV cases among MSM in Europe increased 27% between 2004 and 2009, more than the HIV cases acquired through heterosexual contact or among injecting drug users [12].

Besides biological vulnerability of MSM to HIV infection (unprotected anal sex represents high risk of transmission) [13], the escalation of HIV/sexually transmitted infections (STI) in MSM has been largely attributed to a steady increase in high risk sexual behaviours, such as unprotected sex, and multiple and concurrent sexual partners [14,15].

1.2. HIV Surveillance in MSM: a Crucial yet Challenging Endeavour

The main function of HIV/AIDS surveillance is to provide an understanding of local epidemics, including the source of new infections over time and the behavioural and biological factors driving HIV transmission in order to provide a basis for designing and evaluating appropriate interventions [16].

An essential attribute of public health surveillance is data should be representative (and thus generalizable) of the population under surveillance [17]. In contexts where a disease is highly

prevalent in the general population and a large proportion of the population comes into contact with health services, routine reporting by healthcare-providing institutions serves as a surveillance mechanism [16,18]. In most developing countries, the main sources of routinely available HIV surveillance data have been pregnant women seeking antenatal care and sexually transmitted disease patients [18]. When there is a lack of facility-based data, general population surveys can provide adequate HIV surveillance data, although at a higher cost. Survey-based public health surveillance of health status and related behaviours in general population has been common practice [16]. With regard to HIV/AIDS, population-based surveys have provided much of the general population behavioural surveillance data available in developing countries [16,18].

In scientifically rigorous endeavours, the preferred approach for surveillance is probability sampling in which sample elements are chosen randomly from a known sample frame [16,19]. Such conventional surveillance approach traditionally targets the general and most easily accessible populations, but often it only captures a small fraction of the population of some subgroups [16,19]. In order to be effective, it is crucial that surveillance efforts focus on the segments of populations which play an important role in HIV transmission [16]. The behaviours and HIV status of those covered and missed by conventional surveillance efforts can differ quite substantially. Hence, there is great hazard of surveillance data failing to capture significant pockets of infection that can lead to a more generalized spread of HIV if not contained [16]. Accurately measuring the prevalence of HIV and behaviours over time in key populations, as MSM, is essential to planning and implementing cost-effective, targeted prevention programs [20–24].

1.3. Sampling of Key and Difficult-to-Access Populations as MSM

A primary challenge for surveillance of key populations is obtaining "representative" samples [16,25]. In fact, there is no list or sampling frame for these subgroups, which makes it unfeasible to create a useful sampling frame and use traditional probability-based sampling methods [2,16]. Also, key populations as MSM often represent a small proportion of the general population, therefore obtaining statistically reliable data for such subpopulations through household surveys would require prohibitively large sample sizes [16,19,26]. Lastly, when the risk-taking behaviours which justify the inclusion of most-at-risk subgroups in HIV surveillance are considered deviant or illegal within society and are stigmatized, conventional household surveys are unlikely to produce accurate surveillance data [16]. This is the case for MSM. Since the behaviours in which these subpopulations engage are frequently stigmatized, they are generally reluctant to participate in research efforts to measure their infection status and risk behaviours, and subsequently jeopardize revealing personal and sensitive information to others [16,20,26,27].

Therefore, the difficulty in accessing such hard-to-reach populations presents a dilemma for HIV surveillance, as their omission from surveillance systems leaves important gaps in our knowledge and understanding of the HIV/AIDS epidemics [16]. The importance of including these

populations has highlighted the need for alternative sampling strategies which are both feasible and capable of producing realistic estimates, with minimal levels of bias for population subgroups which are not efficiently "captured" using conventional surveillance data collection strategies [16,19]. Special attention has been drawn to the development of sampling methods which provide valid estimates of infection rates, behaviours, and contextual factors among their members for meaningful surveillance. In particular, the use of non-random sampling techniques has been increasingly recognized [2].

Over the past decades, several methods for recruiting difficult-to-access populations for surveillance and research purposes have emerged [28–32]. This paper aims to critically review different sampling approaches with a focus on its main advantages and challenges for conducting HIV research among key populations as MSM.

2. Sampling Approaches for Conducting HIV Research among Key Populations as MSM

As broadly acknowledged, implementing a simple random sampling approach, though valuable from a statistical perspective, in the context of most vulnerable populations can be extremely expensive, inconvenient or impossible [33]. Alternatively, non-probabilistic methods have been frequently used to reach most-at-risk populations [33].

2.1. Chain-referral and Venue-based Sampling Methods

Many HIV surveillance studies conducted in the last decades have relied on non-probability sampling methods, such as chain-referral sampling to recruit members of the target group. These methods work on the assumption that peers are better able to recruit members of a hidden population than researchers [16,30].

2.1.1. Snowball Sampling

One of the most commonly used methods is Snowball sampling, which has been considered particularly effective in locating members of special populations when the focus of the study is on a sensitive issue [2,16,31]. Snowball sampling entails identifying an initial number of subgroup members from whom the desired data are gathered, and who then serve as "seeds" to help identify other subgroup members to be included in the sample, according to the inclusion criteria defined by the researchers. These individuals, in turn, are asked to provide information on other subgroup members, and the process continues until either a target sample size is reached or the sample becomes "saturated" (i.e. new sample subgroup members fail to provide information that differs from that obtained from members interviewed previously) [16]. The snowball sampling can be placed within a set of link-tracing or chain referral methodologies, the basic assumption being the

existence of some kind of "linkage" with other people in the sample population [2,34]. Such sampling methodologies are portrayed as being created by a series of referrals that are made within a circle of people who know one another. This cyclical nature permits loops, in which a person named in a later wave in turn names someone from an earlier wave, and so on [2,34].

Snowball sampling was conceptually designed as a sample recruitment method that offered a way to overcome many of the recruitment challenges associated with inviting difficult-to-reach communities to join health-care research studies. The experience that was gained over many years of use generated a body of knowledge about both the benefits and limitations of this approach [26].

One of the benefits of snowball sampling is its potential to shorten the time and diminish the cost required to assemble a participant group of sufficient size and diversity from the specific target group [26,34,35]. Another benefit of snowball sampling is when the study's participants who are sought, they are so well integrated with the mainstream community that it is difficult to identify individual group members, as is often the case of MSM. Community informants can help to identify which individuals with potentially eligible criteria are actually from the community of focus [26]. This is even more pertinent when the study's eligibility criteria involve characteristics that some people consider to be very private (e.g. men's engagement in sex with other men). In this sense, a main benefit of snowball sampling is the possibility to reach particular most-vulnerable subgroups through community key-informants, who otherwise could not be identified by the researchers and included in the research. Additionally, a particular advantage of snowball sampling is the inherent trust it encourages among potential participants, which can help to increase the likelihood that the identified person will agree to talk with the researcher [26,34].

Nonetheless, probability sampling methods are considered to be the gold standard for recruiting participants who are most likely to be representative of the larger population from which they are drawn. Thus, the downside to snowball sampling is that it is a non-probability method [26,34]. Snowball sampling lacks validity in representation because the composition of the sample is dependent upon the choice of seeds (initial recruits) and the size of recruitment chains (the number of recruits per participant) [35]. Although initial seeds in snowball sampling may be in theory randomly chosen, in practice this is difficult, if not impossible, to carry out. As a practical matter, initial seeds in snowball sampling tend to be chosen via convenience sampling [16]. Also, the sample composition is heavily influenced by the choice of initial seeds, and in practice, the method also tends to be biased towards favouring more cooperative individuals, as opposed to randomly chosen subjects and those that are part of larger personal networks [16,26,35]. So, in a study that uses a snowball recruitment strategy, any conclusion reached may be particularly biased; for example, the sample may include an over-representation of individuals with numerous social connections who share similar characteristics [16,19,26]. In a study conducted in Fortaleza, Brazil in 2002–2005, community-based behavioural surveys of MSM were conducted as part of a comprehensive Second Generation HIV Surveillance system [35]. In that period, MSM were sampled through different sampling strategies, including the snowball method as well as intercepting and interviewing

members of the MSM population in venues where MSM met, which was previously mapped through formative research. Interviewing MSM and asking them to identify others to be recruited to the survey made this method the least costly survey method in the study. However, the snowball sample comprised significantly more MSM in the higher social classes than other methods samples, and consequently data collected through snowball sampling over-represented men with financial resources [35].

Additionally, chain referral methods like snowball sampling do carry the inherent risk of disclosure of personal information to others. The participants may be reluctant to contact other individuals whom they believe to have a certain characteristic, as that may represent a disclosure of information about themselves or information that has been obtained in a personal and private context., When contacted by the source, the named individuals are faced with the challenge of deciding whether to disclose information about their personal status to the outsider, in order to claim their eligibility for participation in the research study [26,34].

In face of the drawbacks of chain-referral methods, mostly related to its dependence on the characteristics and dynamics of the network of participants, alternative methods have been put forward, as venue-based methods.

2.1.2. Venue-based Sampling

Venue-based techniques seek to recruit respondents in places and at times where they would reasonably be expected to gather, and to collect data from them within that place [36,37]. In this sense, the initial phase of identification of venues relies on the specific characteristic(s) being sought (e.g. venues where MSM gather), and, for a comprehensive sampling, researchers need to collect information on the target population's attendance habits, such as frequency of attendance at the venue, frequency of attendance at other venues, and time spent in the venue [37]. Overall, the venue-based method allows convenient access to the target population without having to rely on participants and network connections, therefore circumventing some of the biases associated with chain-referral methods.

Nevertheless, some sampling biases may also be introduced in using venue-based method. A significant limitation is the assumption that all members of the target population attend venues that researchers can access [36,37]. Actually, some members of the population may not attend the venues or may do so very rarely, having a near zero probability of being recruited compared with population members who attend often. For example, in a research project aimed to evaluate the effects of multicomponent, community level intervention for promoting safer sex behaviour among young 15–25 year old MSM in United States of America, the venue-based method was used to recruit participants for the surveys, and some limitations were described [37]. Young MSM have characteristics which make them a hard-to-reach population, even with a venue-based approach [37]. Due to age restrictions for entering many establishments where MSM socialize, young men are less

likely to be found at venues such as bars. In addition, young MSM from ethnic minority populations may identify more with their ethnic groups than with the gay community, and may not frequent well-known gay-identified establishments [37]. Also, the venues which researchers are able to visit and where they collect data may themselves introduce a bias. This is particularly pertinent in research aimed to provide estimates of HIV prevalence and risk behaviours, as different venues where MSM socialize present disparate levels of prevalence of HIV infection and high-risk sexual behaviours, as shown in the literature [38–40]. Another limitation is that individuals attending highly-frequented venues may have a lower probability of being enrolled than those attending low-density venues [37]. The information on the target population's frequency of attendance at the venue is sometimes difficult to assess and mainly depends on the accuracy of attendees' recall. Moreover, having a complete or representative list of venues and attendance times is a key step to ensure that the method is efficiently carried out; however, reliance on the identified universe of venues and times may lead to a bias of over- or under-representation of venues attended by some social networks [37].

2.1.3. Combination of Methods

Given the limitations in reaching and collecting relevant data from particularly difficult-to-access subgroups of most-at-risk populations as MSM, several recent studies have been using combinations of snowball/chain referral sampling methods and venue-based recruitment strategies [36,40–42]. As a non-probability sampling approach, the combination with venue-based sampling extends the ideas of snowball sampling to include a formative research consisting in an initial ethnographic assessment aimed at identifying the various networks or subgroups that might exist in a targeted setting [16,43]. In such formative research, the adoption of community-based participatory research approach has been valued [44,45]. This approach promotes community partners' involvement in the research process, and enables to integrate their expertise and knowledge on the study population' characteristics and contexts, allowing for a more accurate formative research [46]. The use of these two different approaches has contributed to obtaining broad samples of most vulnerable populations. In a participatory HIV behavioural survey conducted with MSM in Portugal, combining venue-based and chain referral sampling methods allowed investigators to reach a sample of 1,046 MSM comprised of diverse subgroups potentially difficult-to-access, as those unemployed and with lower incomes, reporting high-risk taking behaviours, HIV-positive and those never tested for HIV [38]. The study had a high acceptance from MSM, which translated into high recruitment and retention rates—overall, 76.8% of MSM accepted to participate in the survey [38]. This was possible due to the recruitment strategy adopted. Recruitment teams of outreach workers from local non-governmental organizations working on HIV prevention, and MSM peers from community-based organizations were sent to different venues where MSM gathered to recruit participants, previously mapped through a formative research developed by the Community

Advisory Board of the project. Simultaneously, respondents were asked to advertise the study among their social networks, in an attempt to reach potential eligible peers [38]. Nevertheless, a main limitation of the study, that has also been reported in several other research using similar sampling methods, is the impossibility to infer the results from the study sample to the MSM in general due to the fact that the study sample was not randomly recruited [2,16,38].

As a major concern of non-probabilistic sampling methods being the fact that the selection bias limits the validity of the sample and potentially the quality of data, attempts have been made to improve the statistical accuracy of samples obtained by these techniques [34].

2.2. Respondent-driven Sampling

A sampling method specifically designed to overcome some of the biases associated with traditional chain-referral sampling methods is Respondent-driven sampling (RDS) [47]. RDS has rapidly become popular and widely used, being applied in more than 120 studies in over 20 countries involving more than 30,000 participants [48,49]. RDS has being used for surveillance of populations most-at-risk for HIV/AIDS as MSM, injecting drug users and sex workers in many countries worldwide [35,49,50]. A systematic literature review found that MSM were more frequently recruited by semi-probabilistic methods as RDS, in line with the WHO recommendations on methods for conducting HIV surveillance among populations most at risk for HIV [33,51]. Particularly, RDS has been currently used by the U.S. Centers for Disease Control and Prevention to help track the HIV epidemic and provide data for public-health decision-making [48,52,53].

RDS presents two key innovations for sampling difficult-to-reach populations as MSM: a design for sampling from the target population that relies on a structured system of recruitment procedures, involving recruitment of peers by their peers, a dual system of incentives and a coupon system; and a corresponding strategy for estimating properties of the target population based on the resulting sample, employing post-stratification weighting procedures [16,43,47,48,53,54].

The recruitment starts with an initial set of seed respondents, usually selected by convenience sampling or other methods, who are given coupons to recruit others from the target population [16,47,52]. The recruitment process continues in waves, with seeds recruiting first-wave respondents, first-wave respondents recruiting the second-wave respondents, and so on until a pre-determined sample size is achieved or an equilibrium is reached – the point at which sample characteristics cease to fluctuate and theoretically approximate the characteristics of participants' networks [16,47,52,54]. The coupon system is used to monitor the number of peers one can recruit into the study, and recruitment information is used to link recruiters to recruits [43,47]. Respondents are typically given an incentive (often money) for interview completion, and then for each peer successfully recruited [16,43,47,52,54].

Afterwards, estimation methods are applied to account for the non-random sample selection in an attempt to generate unbiased estimates for the target population [43,52]. Individuals with more

contacts in the target population are more likely to be recruited [55]. Therefore, to adjust for this selection bias, respondents are asked to estimate how many people they know in the hidden population, and the inverse of each person's estimate is then used as a weight to discount the respondents most likely to be sampled [48,53].

The RDS method is similar to snowball sampling in that it involves chain-referral sampling, but the implementation of the recruitment process allows for the calculation of selection probabilities [16]. In addition, the method has greater external validity because it is not limited to subgroup members who are accessible at sites, but rather extends the sample to all potential members of a subgroup selected for surveillance by accessing respondents through their social networks [16]. Several studies conclude that RDS is an appropriate, efficient and fast way to recruit large samples of hard-to-reach populations as MSM, highlighting that the demographics of samples recruited through RDS reflect the general demographics of the population in similar study locations [16,47,50,52,54,56]. RDS lends statistical rigor to conventional snowball sampling through longer recruitment chains, recruitment limits, and the collection of data used to statistically adjust the biases inherent in how persons of similar characteristics are networked and likely to recruit each other [28,35,56,57]. A main advantage of RDS over other non-probability methods for sampling hidden populations is that the long sampling chains reduce, or ideally eliminate, the biases induced by the convenience sampling of seeds [43].

However, as with all population-based studies, RDS is not immune from sampling bias as shown in several studies [47,48,52,54]. Some of those biases include differential recruitment effectiveness (when some groups are better at recruiting than others), differential recruitment patterns (also known as homophily, the individuals' tendency to associate with other individuals with similar socio-demographic and behavioural characteristics), and heterogeneity in degree (differences between groups in terms of network size, with subjects in larger network being over-sampled because more recruitment paths lead to them) [47,52]. Other studies have shown that recruitment efficiency of RDS may vary by population density and by the ability to recruit productive seeds [54]. Post-stratification weighting is proposed as a way to correct sampling bias in RDS samples, but it cannot fully account for bias introduced by non-random selection from personal networks [54]. Indeed, such weighting is a mathematically appropriate technique for characterizing recruitment probabilities in a sample from a network if RDS assumptions are met and respondents are able to estimate their popularity with reasonable accuracy, which is not always the case [53,54].

These biases may increase the design effect of respondent-driven sampling, which measures the increased variation of the estimates [52,58]. While RDS is an efficient means of recruiting samples of hidden populations, inaccuracies in estimates of network sizes may lead to biases [54]. Recent research indicates that the accuracy of the RDS approach is sensitive to the assumptions it makes about the social network of the underlying population [43,48,53]. Indeed, the accuracy of RDS estimates is affected by the structure of the underlying social network, the distribution of traits within the network, and the recruitment dynamics [48,53]. Consequently, according to some studies

assessing RDS efficiency, RDS estimates are much less precise and its variability is significantly larger than generally believed [48,52]. Overall, RDS statistical-inference methods can fail and the confidence intervals may be too narrow [52]. A study investigating the performance of RDS by simulating sampling from 85 known network populations of sex workers and drug users found that variance of RDS is typically 5–10 times greater than that of simple random sampling and, moreover, standard RDS confidence intervals are misleadingly narrow [48]. In this sense, the authors put forward that some RDS studies may lack sufficient power to identify changes in behaviour and disease prevalence with statistical confidence [48]. This implies collecting larger sample sizes than would be needed from random sampling to maintain the same level of statistical power [53].

2.3.   Time-location Sampling

Another approach that has seen increasing use in recent years is Time-location sampling (TLS). This is a venue-based method that came into use to sample hard-to-reach populations, primarily MSM, in the late 1980s to early 1990s [20,59], and takes advantage of the fact that some hidden populations tend to gather or congregate at certain types of locations [16,29,37]. MSM often congregate in commercial and non-commercial venues, as gay bars and "cruising areas", known to attract MSM [16,38]. In TLS, such venues are enumerated in a preliminary ethnographic mapping or formative research exercise. The method entails identifying days and times when the target population congregates at the specific locations, constructing a sampling frame from which to choose a probability sample of time and location units [16,20,35,37,60]. Data are gathered from either all or a sample of subgroup members found at the site during the pre-defined time interval. The number of group members at each location provides a sampling weight that can be a priori used to draw a self-weighting sample, or post priori in analysis [16]. Because probabilities of selection can be calculated, TLS qualifies as a probability sampling method [16,20,29,31,37].

The major contribution of TLS over other cluster sampling methods is the ability to account for the fact that populations of interest are not statically associated with a particular location, and often move between multiple locations during the course of a single day. As such, TLS allows researchers to construct a sample with known properties, make statistical inference to the larger population of location visitors, and theorize about the introduction of biases that may limit generalization of results to the target population [20,31]. TLS has been used widely for routine biological and behavioural surveillance surveys among most-at-risk populations that are concentrated in specific geographical areas that may "float" among locations [20,61–63].

In an HIV bio-behavioural survey implemented in nine European cities and countries, a total sample of 3,661 MSM was reached, recruited through TLS in a diverse set of physical public or private locations, including commercial venues such as cafes, discos/clubs, bars, sex shop, sex cinema, saunas, spas, etc. as well as non-commercial venues, such as cruising settings and special events [64]. Excluded were venues that specifically serve HIV positive members of the priority

population. Indeed, including these types of venues would introduce sampling biases by artificially increasing representation of HIV-positive individuals in the final sample [64]. The construction of sampling frames is allowed to generate a statistically representative sample from "hidden" and most-at-risk populations among MSM. Once the initial list of venues was elaborated based on the findings of the formative research, MSM venues and venue-day-time (VDT) units were identified and two sampling frames constructed. The first sampling frame (or venues sampling frame) comprised a list of venues that met the attendance requirements and were also willing to participate (eligible venues). The second sampling frame (VDT sampling frame) comprised a list of venue-specific sampling periods of four hours each. Following completion of the final sampling frame, a three-stage sampling plan to select venues, VDTs, and participants was used [64]. This semi-probabilistic method enabled to obtain relevant evidence for MSM prevention campaigns and for effective epidemiological surveillance, based on the estimation of HIV/STI prevalence and of the undiagnosed infections in the MSM population, the identification of sexual risk behaviour patterns, and a detailed knowledge of the heterogeneity of prevention needs in different contexts [65].

However, TLS method has several limitations. Some locations may be missed, particularly sites that are exceptionally discrete, while others may not have sufficient numbers of eligible group members [16,20]. A significant proportion of subgroup members may tend not to frequent the selected sites, which is relevant given that the behaviours and HIV status of subgroup members who do not visit gathering venues differ from those who do [16,20,37]. Logistically, identification of all gathering venues can in theory be achieved given sufficient time and resources for sampling frame development, but there are practical limits to the resources that can be committed to such activities on a regular basis [16]. Also, the venues where members of MSM subgroups congregate frequently change over time resulting from economical or law enforcement actions, which implies updating the sampling frame before each round of data collection, and this has high costs associated with it [16,20]. The nature of the recruitment sites is itself a limitation. MSM attending bars and dance clubs may not want to participate in biobehavioural surveys in which they might learn their HIV status [16]. Some recruitment venues may also be unsafe, with the potential to jeopardize community researchers' security [20]. Finally, accounting for non-participation may be challenging when owners forbid recruitment on their property, or in public locations where it is impractical or illegal to recruit participants [20]. A major question is whether non-response is differential in diverse settings when subgroup members are approached to participate in a surveillance survey [20]. All these limitations of TLS method are potentially important sources of sampling bias.

2.4. *Internet Sampling*

With increasing access to the Internet and growing popularity among MSM in seeking sex partners online, the Internet has also been increasingly used to recruit MSM in HIV research [66,67]. The advantages of using this method are faster recruitment, lower operational costs and a greater

level of anonymity provided to participants, which allows potentially capture more MSM without self-disclosure of their sexual orientation, compared with those recruited in person and from venues [36,68–70]. Also, Internet sampling is the method that reaches a higher number of respondents. A systematic literature review showed that Internet sampling reached a total of 225,320 participants in 33 selected studies, compared to 82,004 participants reached by RDS in 77 studies, and 55,193 participants reached by TLS in 42 studies [51]. One of the strengths of the European MSM Internet Survey (EMIS), administered across 38 European countries, was that it reached the largest and most geographically diverse dataset to examine country-level stigma and the pathways through which it operates to suppress both HIV-risks and HIV-precautions among MSM [67].

Nevertheless, Internet sampling is subject to selection biases, as it can only sample those MSM who have access to the Internet, and may sample particular subgroups who engage in certain risk behaviours associated to Internet use. For instance, in EMIS the participants who were reached differed from the broader population of MSM, over-representing younger men and men with diagnosed HIV. Additionally, the degree and direction in which this selection bias may under- or overestimate the relationship between sample characteristics and HIV outcomes is difficult to predict and control [67,69].

The advantages and limitations of each sampling strategy are summarized in Table 1.

Table 1. Advantages and limitations of each sampling strategy.

Sampling strategy	Advantages	Limitations
Snowball sampling	• Short time and reduced cost to assemble a large and diverse participant group. • Trust of potential participants and increased likelihood that they will agree to talk with the researcher. • Collaboration of community informants to identify and reach most-vulnerable subgroups from the community under study.	• Non-probability method lacks validity in representation. • Sample composition heavily influenced by the choice of initial seeds. • Potential bias towards favouring more cooperative, as opposed to randomly chosen subjects, and those that are part of larger personal networks. • Inherent risk of disclosure of personal information to others, participants may be reluctant to disclose information about themselves or information about their peers that has been obtained in a personal and private context.
Venue-based sampling	• Convenient access to the target population without having to rely on participants and network connections, while also avoiding some biases associated with chain-referral methods.	• Lack of access to some venues attended by the target population. • Potential to not reach some members of the population as they may not attend the identified venues. • Difficulty to access accurate information about the target population's frequency of attendance at the venue.

		• Potential bias of over/under-representation of venues attended by some social networks due to reliance on the identified universe of venues and times.
Respondent-driven sampling	• Estimation methods applied in an attempt to generate unbiased estimates for the target population. • Greater external validity. • Lends statistical rigor to snowball sampling through: - longer recruitment chains - recruitment limits -collection of data used to statistically adjust for the recruitment biases.	• Differential recruitment effectiveness (when some groups are better at recruiting than others) • Differential recruitment patterns (homophily: individuals' tendency to associate with other individuals with similar characteristics; heterogeneity in degree: differences between groups in terms of network size, with subjects with larger network sizes being over-sampled). • Implies collecting large sample sizes to ensure statistical power.
Time-location sampling	• Construct a sample with known properties, allows theorize about the introduction of biases that may limit generalization of results to the target population. • Possibility to make statistical inference to the larger population of location visitors.	• Some locations may be missed, particularly sites that are exceptionally discrete, while others may not have sufficient numbers of eligible group members. • The venues where members of MSM subgroups congregate frequently change over time. • The nature of the recruitment sites itself may reduce the acceptability of potential participants to enrol in the study and/or can affect the disclosure of information by participants.
Internet sampling	• Faster recruitment. • Lower operational cost. • Greater level of anonymity provided to participants. • Reaches higher number of respondents.	• Selection bias, it can only sample those who have access to the Internet. • Potential over-sampling of subjects with higher levels of internet use and/or users of higher number of online networks.

3. Conclusions

Given the critical importance of understanding HIV epidemics, high quality surveillance systems are necessary. The need to find more effective and efficient recruitment strategies is paramount. Appropriate sampling approaches are at the core of any high quality surveillance system, especially when attempting to track transmission dynamics among populations that play a critical role in the transmission of HIV, and that are "hidden" or hard-to-reach [16,26]. The varying approaches face common challenges. The definition of the study population continues to be

challenging as there is no consensus on who the MSM group includes (consider men who had only anal sex or also oral sex? Men had sex with men in their lifetime or in the last year?). According to UNAIDS Terminology Guidelines, the term men who have sex with men "describes males who have sex with males, regardless of whether or not they also have sex with women or have a personal or social gay or bisexual identity" [71]. This is a useful concept because it also includes men who self-identify as heterosexual but who occasionally have sex with other men. Indeed, an additional global challenge has been to identify this especially hard-to-reach MSM subgroup. Nevertheless, the methods discussed in this paper represent some of the best efforts thus far to find feasible sampling approaches and recruitment strategies that effectively reach most-at-risk and hard-to-reach subgroups of MSM, contributing to obtain unbiased trends of HIV prevalence and HIV-related risk behaviours among these populations.

The benefits and limitations of the described strategies should be carefully evaluated against its benefits and limitations in each specific context, in order to select the optimal strategy. Also, the benefits of using these approaches to recruit participants for HIV research must be weighed against the privacy concerns that are inherent in any individual social situation or health condition [26].

In recent years, the important role of community-based participatory approach in undertaking research with hard-to-reach populations has increasingly been recognized [38,44,45]. Participatory research integrates a collaborative approach with involvement of communities, professionals, political decision-makers, and academics to produce knowledge, incorporating the different perspectives and experiences of these stakeholders [46]. Community-based participatory approach may particularly help researchers choose the methods that most appropriately target MSM, relying on community partners and "insiders" knowledge on the best strategies to locate and approach these groups.

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Conflict of Interest

All authors declare no conflicts of interest in this paper.

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Study V - [Community-based participatory research in public health: potentials and challenges].
Sónia Dias, Ana Gama

Investigação participativa baseada na comunidade em saúde pública: potencialidades e desafios

Sónia Dias[1] *e Ana Gama*[1]

SINOPSE

No campo da saúde pública, advoga-se uma mudança de paradigma de investigação que possibilite maior tradução do conhecimento científico em ações e políticas de saúde mais adaptadas às comunidades. Especial atenção tem sido dada à investigação participativa baseada na comunidade, pelo seu potencial em possibilitar um maior conhecimento sobre as questões complexas de saúde. Neste ensaio, refletiu-se sobre a contribuição da investigação participativa em saúde, analisando as suas perspectivas teóricas, princípios e potencialidades. Também se examinarom alguns aspectos críticos na sua implementação, realçando-se possíveis estratégias para superar esses desafios. A investigação participativa integra uma abordagem colaborativa de envolvimento das comunidades, profissionais, decisores políticos e acadêmicos na produção de conhecimento, incorporando as suas diferentes perspectivas e experiências. Essa abordagem favorece a aceitação do projeto, a adesão das comunidades ao estudo e, consequentemente, a qualidade dos dados coletados. A investigação participativa pode ser, em si só, uma intervenção: o envolvimento das comunidades pode aumentar a sua tomada de consciência sobre a importância das temáticas abordadas e capacitá-las para definir e responder às problemáticas de saúde, promovendo o seu empoderamento. Contudo, os investigadores encontram desafios na utilização dessa abordagem, relacionados com o estabelecimento e manutenção das parcerias de investigação, a partilha de controle da tomada de decisão e a conciliação das motivações e interesses dos parceiros. Mais evidência sobre o processo de implementação da investigação participativa reforçará o

seu quadro teórico, a compreensão das suas potencialidades e limitações no estudo de diferentes problemáticas, contextos e populações, e o seu papel benéfico para as comunidades.

Palavras-chave: saúde pública; pesquisa participativa baseada na comunidade.

Historicamente, a investigação em saúde pública, com uma abordagem essencialmente quantitativa e fortemente influenciada pela perspectiva biomédica, tem-se focado na produção de conhecimento sobre os fatores de risco e seus determinantes individuais em prol dos socioambientais (1). Contudo, atualmente se reconhece que, para a compreensão mais abrangente das complexas questões em saúde, a investigação tem de ser multidimensional, integrando a influência inter-relacionada de fatores ambientais, estruturais, socio-culturais e individuais (1). Nesse sentido, tem-se assistido à emergência de um corpo de investigação que transpõe as descrições quantitativas das problemáticas em saúde e incorpora os determinantes contextuais subjacentes a uma maior vulnerabilidade (2). Adicionalmente, advoga-se uma mudança de paradigma na investigação, que possibilite uma maior tradução do conhecimento científico em ações de saúde mais adaptadas às comunidades (3).

Assim, especial atenção tem sido dada à investigação participativa baseada na comunidade, pelo seu potencial em possibilitar um maior conhecimento sobre as questões complexas de saúde (4). No presente ensaio, pretende-se refletir sobre a contribuição da investigação participativa em saúde, analisando as suas perspectivas teóricas, princípios e potencialidades. Também serão examinados alguns aspectos críticos na implementação desse tipo de investigação, realçando-se possíveis estratégias para superá-los.

INVESTIGAÇÃO PARTICIPATIVA EM SAÚDE

A investigação participativa é definida por Israel et al. (1) como uma abordagem colaborativa que envolve de forma equitativa membros da comunidade, representantes de organizações ou instituições governamentais e nãogovernamentais e investigadores no processo de produção de conhecimento. Cada parceiro contribui com recursos únicos e responsabilidades partilhadas para a compreensão do fenômeno em estudo e da sua dinâmica sociocultural (1). Essa abordagem combina investigação com estratégias de capacitação comunitária para reduzir a lacuna entre o conhecimento produzido através da investigação e a tradução desse conhecimento em intervenções e políticas que melhorem a saúde das comunidades (5).

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Distingue-se de outras abordagens ao reconhecer que a comunidade não é meramente local ou cenário de investigação, mas também entidade sociocultural, valorizando o envolvimento e a influência ativa dos membros da comunidade em todo o processo de investigação (6).

O paradigma de investigação participativa surgiu nos anos 1960, quando movimentos sociopolíticos e acadêmicos desafiavam as relações entre as universidades e a sociedade e suscitavam a procura de novas teorias e práticas de investigação, com o desafio de usar o conhecimento para promover uma sociedade mais equitativa (4, 6). A abordagem participativa em investigação derivou de duas principais tradições: a investigação-ação de Kurt Lewin (anos 1940-1950), que enfatizava o envolvimento das pessoas afetadas pela problemática na resolução prática do problema através de um processo cíclico de procura de fatos, ação e avaliação; e a investigação-ação participativa baseada nos trabalhos de Paulo Freire nos anos 1970 sobre educação popular com populações vulneráveis, em que, numa perspectiva emancipatória, se desafiava o domínio político do conhecimento pelas elites, o papel das comunidades enquanto mero objeto de pesquisa, os papéis dos investigadores na academia e a sua responsabilidade na mudança sociopolítica na sociedade (4-6).

No decorrer da evolução dessa abordagem, vários autores têm-se dedicado a desenvolver uma base conceitual para a investigação participativa. Nesse contexto, Israel et al. (7) têm tido um papel importante, propondo uma sistematização dos princípios que caracterizam a investigação participativa, nomeadamente: reconhecer a comunidade como uma unidade de identidade; basear-se nas forças e recursos da comunidade; facilitar uma parceria colaborativa e equitativa em todas as fases da investigação; promover a aprendizagem conjunta e a capacitação dos parceiros; alcançar um equilíbrio entre investigação e intervenção para benefício de todos; focar-se nos problemas de saúde pública localmente relevantes e numa perspectiva ecológica; implicar a reorganização de sistemas; divulgar os resultados aos parceiros e envolvê-los na sua ampla disseminação; desenvolver um compromisso para a sustentabilidade. Outros autores têm contribuído para o desenvolvimento do campo da investigação participativa, trabalhando na construção de um modelo para a sua prática, como Cargo e Mercer (3), ou debruçando-se sobre as potencialidades dessa abordagem na investigação em saúde, como Wallerstein e Duran ou Blumenthal (4, 8).

O interesse na investigação participativa cresceu na última década, abrangendo várias organizações, universidades e centros de investigação na América Latina, América do Norte e Europa (4, 8). Alguns exemplos são as iniciativas de investigação e formação desenvolvidas pela Aliança Internacional de Pesquisa Universidades-Comunidades sobre Saúde Mental e Cidadania (parceria entre Brasil e Canadá), o *National Institute on Minority Health and Health Disparities* e *Prevention Research Centers*, nos Estados Unidos,

ou os projetos desenvolvidos pela *WHO European Healthy Cities Network* na Europa e pela Organização Pan-Americana de Saúde (PAHO) sobre avaliação de programas comunitários. A investigação participativa tem uma grande diversidade de aplicações, realizando-se através de diferentes desenhos de estudo e métodos, dependendo da questão e objetivos de investigação e da viabilidade da sua aplicação nos contextos específicos (7).

Potencialidades

A literatura mais recente tem apontado várias potencialidades na utilização da investigação participativa em saúde (6, 8). Uma das principais é a integração do conhecimento teórico-metodológico dos investigadores com o conhecimento e experiências do contexto dos parceiros. Isso contribui para uma maior compreensão dos múltiplos determinantes que produzem iniquidades em saúde e para a adoção de boas práticas que respondam às necessidades das populações (4, 5).

Os princípios da investigação participativa emergem de uma preocupação ética face a um histórico de "utilização" das comunidades (especialmente minoritárias e em maior desvantagem socioeconômica) em prol da investigação sem garantir que as comunidades se beneficiassem, bem como da influência do conceito de empoderamento comunitário, muito inspirado no trabalho de Paulo Freire. Freire defendia que o desenvolvimento da "consciência crítica" tornaria indivíduos e comunidades mais empoderados para quebrar o ciclo de vulnerabilidade. Sustentava que criar conhecimento científico com aqueles mais afetados pela questão em estudo poderia fazer a diferença na prática da saúde pública (3).

A colaboração com pessoas da comunidade permite estabelecer uma relação de confiança que facilita a aceitação do projeto e credibiliza os investigadores, possibilitando a obtenção de um elevado nível de participação e qualidade dos dados recolhidos (9). Esses aspectos assumiram particular relevância num estudo sobre saúde sexual e reprodutiva com populações imigrantes, permitindo ultrapassar dificuldades linguísticas e culturais, obter o consentimento de um elevado número de participantes e ter acesso às suas reais perspectivas e a informações de foro pessoal e sensível (10). Ainda no contexto das populações de "difícil acesso", os parceiros podem auxiliar os investigadores na identificação dos locais e redes sociais nos quais se poderá recrutar participantes e recolher dados. Esse foi o caso de um estudo de conhecimentos, atitudes e práticas sobre a infecção por HIV em trabalhadores sexuais em Portugal, em que os entrevistadores puderam abordar diversos subgrupos, como homens, transgêneros, imigrantes (nomeadamente em situação irregular) e usuários de drogas (11).

A colaboração entre acadêmicos, profissionais e comunidades no delineamento do desenho do estudo, métodos e instrumentos de coleta de dados é uma vantagem, pois contribui para tornar esses dados

mais adequados, acessíveis e relevantes para os participantes e a investigação. Como exemplo, refere-se o envolvimento dos parceiros no treinamento para atuar como entrevistadores e na construção e validação dos instrumentos para assegurar procedimentos de coleta de dados (quantitativos/qualitativos) de qualidade. Essa abordagem permite ainda incorporar questões de saúde que são percebidas pelas comunidades como prioritárias e que frequentemente não são equacionadas pelos investigadores (12). Simultaneamente, essa estratégia favorece o desenvolvimento de competências e aumenta o sentimento de responsabilidade pelo projeto (9, 13). Assim, a investigação pode ser em si só uma intervenção, devendo os investigadores reforçar essa potencialidade (14).

Em vários estudos, a inclusão dos parceiros comunitários no processo de análise e disseminação dos resultados tem possibilitado aumentar a tomada de consciência sobre a importância das temáticas abordadas (15). Por outro lado, os parceiros podem identificar outros resultados da investigação que sejam benéficos para a comunidade, isto é, que possam dar resposta às próprias necessidades em saúde (16). Esses processos participativos contribuem também para tornar as comunidades mais abertas às iniciativas políticas formuladas com base nas recomendações resultantes dessas investigações. Num estudo desenvolvido em Portugal sobre a utilização dos serviços pelos imigrantes, o envolvimento de todos os atores implicados (decisores políticos, profissionais de saúde e imigrantes) favoreceu o enriquecimento e a validação dos dados, bem como a conscientização sobre a pertinência da temática. Contribuiu também para fortalecer a capacidade dos serviços para desenvolver programas mais adequados às necessidades específicas dessas populações e dos profissionais para lidar com a diversidade (17).

Alguns aspectos críticos na utilização da investigação participativa

Embora seja cada vez mais reconhecido o valor da investigação participativa e incentivada a sua aplicação em saúde, os investigadores encontram alguns desafios na utilização dessa abordagem (7, 8). Um primeiro desafio refere-se à definição de comunidade adotada em cada projeto (15). Embora a "comunidade" seja tipicamente entendida como uma entidade local geopolítica, vários autores sugerem uma definição de comunidade mais ampla, que inclui todos os implicados na questão em estudo, que partilham características ou interesses comuns (15). Assim, para além dos seus residentes, a comunidade pode constituir-se por profissionais de saúde, organizações, decisores políticos, entre outros. Adicionalmente, uma vez que as comunidades são entidades heterogêneas, é pertinente identificar os membros que verdadeiramente a representam e que estão qualificados para consentir a investigação em nome da mesma (9). Não existindo uma única solução para todas as situações, o grupo inicial envolvido no estabelecimento da

parceira deve decidir sobre: quem é a comunidade? Quem pode representá-la? Quem a influencia? Como podem ser envolvidos? A resposta a essas questões tem impacto em todas as fases posteriores e, em última instância, nos resultados do projeto (8).

Ao longo da investigação colocam-se várias dificuldades quando se procura assegurar o envolvimento equitativo dos diversos parceiros e a partilha do controle da tomada de decisão (14). Apesar da morosidade do processo e da dificuldade em garantir a total concordância entre os diferentes parceiros, esses processos de tomada de decisão constituem uma importante oportunidade de diálogo, partilha de perspectivas e construção de relações de confiança, aspectos que potencialmente favorecem o projeto (4). Outro desafio é escolher e aplicar adequadamente diferentes metodologias, o que influencia os resultados da investigação. Assim, vários autores têm enfatizado que os padrões de rigor e qualidade científicos devem ser assegurados (8). Efetivamente, os diferentes parceiros nem sempre estão capacitados para realizar algumas atividades inerentes à investigação, como a análise de dados quantitativos/qualitativos, o que pode produzir vieses com consequências para a interpretação dos resultados. Na prática, reconhecendo que os parceiros têm diversos níveis de competências e experiências, o mais apropriado será encontrar diferentes graus de envolvimento dos parceiros nas várias atividades.

A investigação participativa varia conforme os seus objetivos e o contexto em que se desenvolve a parceria. Um desafio coloca-se assim em assegurar que, independentemente da diversidade na implementação dessa abordagem, a investigação se mantenha coerente com os princípios que orientam os processos e resultados de uma investigação participativa, contribuindo para um aumento do conhecimento e beneficiando as comunidades (4, 7).

A atual ênfase na tradução do conhecimento em práticas mais adequadas às necessidades reais torna relevante a questão da aplicabilidade dos resultados obtidos nas investigações. Nesse âmbito surge frequentemente um paradoxo: o aumento da relevância e da especificidade da investigação nas comunidades em estudo pode dificultar a generalização dos resultados; por outro lado, as recomendações de boas práticas resultantes da investigação mais tradicional são muitas vezes desajustadas às comunidades mais vulneráveis, frequentemente sub-representadas nesses estudos. De fato, cada vez mais, decisores políticos, profissionais de saúde e comunidades questionam a validade social e cultural dos estudos conduzidos por equipes que pouco conhecem as comunidades, a cultura e o contexto em que conduzem a investigação (3). Nesse debate, embora os resultados obtidos com a investigação participativa sejam considerados relevantes e de elevada aplicabilidade nos contextos em que ocorre, também se reconhece a necessidade de mais evidências que maximizem as potencialidades dessa abordagem (3, 8).

Outro desafio na investigação participativa é o fato de frequentemente os parceiros terem diferentes

motivações e interesses subjacentes. Por exemplo, o financiamento para investigar uma questão específica em saúde pode não coincidir com o que os outros parceiros consideram como questão prioritária – nesses casos, os parceiros podem querer abordar outras preocupações da comunidade, ou mostrar-se resistentes a investigações que desafiem os valores, atitudes e práticas adotadas (18). A negociação é uma estratégia que permite ultrapassar essas tensões, podendo-se, inicialmente, centrar o trabalho na resposta a prioridades específicas da comunidade e, ao longo do processo de investigação, incorporar o diálogo para uma maior compreensão dos determinantes de vulnerabilidade e das estratégias que minimizam o seu impacto (7, 18). Também frequentemente os parceiros comunitários não estão sensibilizados para os procedimentos metodológicos necessários para assegurar o rigor científico da investigação, estando mais empenhados em dar resposta a questões tangíveis da sua realidade (16).

Adicionalmente, os investigadores podem sentir pressão quando pretendem estabelecer relações recíprocas e compromissos duradouros com as comunidades, dado que o meio acadêmico prioriza a produção rápida de publicações científicas (8). No entanto, assiste-se a uma valorização dos projetos de investigação participativa por parte das entidades financiadoras, com incentivo para publicar não só os resultados, mas também os processos envolvidos nesse tipo de investigação (3).

CONSIDERAÇÕES FINAIS

A investigação participativa tem contribuído para um conhecimento mais aprofundado, possibilitando o acesso às perspectivas e experiências das comunidades e compreender a influência dos aspectos socioculturais e contextuais na saúde das populações (4). A participação das comunidades no processo de investigação tem sido essencial para dar acesso a grupos mais vulneráveis e que tendem a estar sub-representados nos estudos que utilizam métodos de investigação mais tradicionais (4).

Simultaneamente, a investigação participativa pode constituir em si uma intervenção, ao permitir capacitar as comunidades para definir e responder às problemáticas de saúde e promover o seu papel enquanto agentes de mudança na prevenção e redução da doença (13, 16). Vários autores têm realçado o potencial desse tipo de investigação para traduzir o conhecimento em práticas e estratégias de ação mais adequadas e eficazes (8, 14). Essa abordagem tem sido utilizada com populações culturalmente diversas, de diferentes contextos sociais e de difícil acesso, demonstrando a sua utilidade e versatilidade no estudo de várias questões de saúde.

Progressivamente, tem-se assistido ao crescimento do interesse nessa abordagem, sendo consensual a necessidade de mais evidências sobre o seu processo de implementação - como é conduzida, que condições favorecem a participação e a colaboração entre os diversos parceiros, qual o papel dos serviços de saúde no suporte dessa abordagem e como as variações na sua implementação influenciam os resultados obtidos (3, 7). Tal conhecimento permitirá reforçar o quadro teórico e a compreensão da utilidade, potencialidades e limitações da investigação participativa em diferentes problemáticas de saúde, contextos e populações (8). É ainda importante um maior conhecimento do impacto da investigação participativa no empoderamento das comunidades e nos resultados em saúde, compreendendo de forma mais global o seu papel benéfico para as comunidades (14).

Apesar de ainda em desenvolvimento, o potencial da investigação participativa tem sido valorizado, assistindo-se a um gradual investimento em formação nessa área e na implementação de projetos com essa abordagem (19). Tal realidade reflete-se no fato de as entidades financiadoras cada vez mais incentivarem a realização de investigações que promovam a participação das comunidades na produção de conhecimento, bem como na consequente implementação de iniciativas para melhorar a sua saúde (6, 20).

Em suma, tem sido reconhecida a contribuição da investigação participativa para obter um maior conhecimento sobre a saúde das populações, que se traduza em efetivos ganhos em saúde. Contudo, um dos principais desafios desta abordagem é garantir que, na multiplicidade de contextos em que a investigação participativa pode ser implementada, sejam assegurados os princípios que a caracterizam, como o envolvimento equitativo dos parceiros e o equilíbrio entre investigação e intervenção para benefício de todos os atores.

Conflitos de interesse. Nada declarado pelos autores.

SYNOPSIS

Community-based participatory research in public health: potentials and challenges

A change in the research paradigm towards a method that more readily allows the translation of scientific knowledge into more community-oriented health actions and policies has been advocated in the field of public health. Special attention has been paid to community-based participatory research, which has the potential to allow the production of deeper knowledge of complex health issues. The present essay reflects on the contributions of participatory research in health, analyzing its theoretical perspectives, principles, and strengths. Some key aspects relating to the implementation of participatory research are also examined, underscoring possible strategies to face this challenge. Participatory research integrates a collaborative approach with involvement of communities, professionals, political decision-makers, and academics to produce knowledge, incorporating the different perspectives and experiences of these stakeholders. This approach facilitates acceptance of the project and engagement of communities, and consequently enhances the quality of the data collected. Participatory research may

work in and of itself as an intervention: the involvement of communities may increase their awareness about the importance of the research themes and serve as training to define and address health issues, promoting empowerment. Nevertheless, researchers face challenges in applying this approach. Such challenges are related to the establishment and maintenance of research partnerships, the sharing of decision-making control, and the reconciliation of the motivations and interests of partners. More evidence regarding

the process of implementation of participatory research will strengthen the method's theoretical framework and provide further understanding regarding its potential and limitations to address various problems, contexts, and populations, and clarify its beneficial role for communities.

Key Words: public health; community-based participatory research.

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4. GENERAL DISCUSSION AND CONCLUSIONS

4. GENERAL DISCUSSION AND CONCLUSIONS

The rise of HIV infection among MSM has been a concern in global public heath, demanding a strong response from researchers, professionals and policy-makers to address the problem and seek solutions. Yet, research among MSM has been relatively scarce, which reflects the ongoing challenge in studying this population.

This thesis intends to contribute to improve knowledge on prevalence of HIV infection, high risk behaviours and its determinants among MSM in Portugal, a population that has been understudied despite being considered most-at-risk to HIV infection. This work is also expected to contribute in conducting future research with this difficult-to-access population.

In this section we summarize and discuss the main findings and describe the limitations of the work conducted. Moreover, we also analyse the implications of our findings for future research, intervention and policy, and present final conclusions.

4.1. Main findings

This thesis shows a high prevalence of HIV among the MSM studied – 8.8% (95%CI: 7-11%). Our reported prevalence data are in line with other European studies with MSM where similarly high prevalence estimates were found (1.3–19.7% in EMIS survey, 2.4–18.0% in SIALON II project) (Mirandola et al. 2016; Marcus et al. 2012), despite data being collected in different contexts and with different methodologies.

The rate of high-risk sexual behaviours such as unprotected anal intercourse (UAI) is concerning. In our study, inconsistent condom use with occasional partners in the previous year was reported by 18.5% of participants, with regular partners by 47.5% and in group sex by 16.3% (Study I). Although these findings may not be representative of the general MSM population due to the sampling method and potential selection biases, the high rates of UAI are in line with those investigated in other research, showing also a heterogeneity in risk-taking behaviours (Cambou et al. 2014; Knox et al. 2010; Macaluso et al. 2000; Moreau-Gruet et al. 2001; Rocha et al. 2013).

In our work we explored the contexts that increase MSM exposure to HIV risk, more specifically different locations where MSM frequently seek sexual partners. In our study we found that more than a third of respondents reported frequently visiting venues where MSM frequently seek sexual partners and have sex – generally named "cruising

venues". A significantly higher proportion of cruising venues' visitors (14.6% [95%CI: 11-18%]) reported to be HIV positive, when compared to those who visit social gay venues (5.5% [95%CI: 4-7%]). In our study, as in others, older MSM tend to seek sexual contact at cruising venues, while younger MSM more frequently use the internet and gay bars (Vanden Berghe et al. 2011). Several data indicate that HIV infection is more prevalent in older age groups (Nguyen & Holodniy 2008; UNAIDS 2013; UNAIDS 2014), and therefore it was expected to find higher HIV infection within those settings. Other potential explanation for a higher proportion of HIV-positive MSM visiting cruising venues relates to the possibility of non-disclosure to partners in such places, where there is a decreased expectation for verbal or direct communication because of the casual or anonymous nature of the sexual encounters (Bird & Voisin 2011; Wei et al. 2012). In more anonymous settings, disclosure may be also mitigated by perceived serostatus based on circumstantial evidence and normative assumptions based on the setting of the encounter (Parsons et al. 2006; Rönn et al. 2014). Our findings indicate that MSM who frequently visit cruising venues to meet sexual partners also engage more frequently in high-risk sexual behaviours as having higher number of male sexual partners, engaging in group sex, and having unprotected sex with a partner whose HIV serostatus was unknown, similarly to other studies (Aynalem et al. 2006; Binson et al. 2001; Parsons & Halkitis 2002). Also, factors as higher number of male sexual partners, engagement in group sex, and substances consumption before/during the last sexual intercourse were associated with unprotected anal intercourse, consistently with other research (Mimiaga et al. 2011; Reidy et al. 2009; Tang et al. 2013). It has been put forward that the context of cruising venues potentially fosters the engagement in sex acts with multiple anonymous partners (Aynalem et al. 2006). Indeed, some authors suggest that in these venues, men tend to engage in unprotected sex while detached from any sense of connection to their sexual partners, as a means for coping with needs for sexual sensation seeking or sexual adventurism (Aynalem et al. 2006; Parsons & Halkitis 2002). This potentially reduces the feeling of responsibility of protecting himself and casual sexual partners from HIV transmission (Aynalem et al. 2006; O'Leary et al. 2013; Parsons & Halkitis 2002). In line with this, other research has underscored the role of risk seeking as a predictor of HIV acquirement/transmission (Conner et al. 2005; Parsons & Halkitis 2002). High-risk seekers are likely to be more impulsive, disinhibited, and to engage more

frequently in high-risk sexual behaviours, leading them to be at increased risk for HIV infection (Conner et al. 2005).

An important finding is that a considerable proportion of MSM reported not knowing their HIV serostatus and these MSM were more likely to engage in unprotected anal intercourse with a partner whose HIV serostatus was unknown. These findings are particularly striking, given that a substantial number of MSM in our study reported having never been tested for HIV. Moreover, MSM not reached with HIV prevention were more likely to engage in unprotected anal intercourse. Our results highlight that these particular subgroups of high-risk-taking MSM who are unaware of their HIV serostatus and who remain out of scope of current prevention actions are in great need of HIV prevention efforts. These findings are also of particular interest as they reinforce that sexual health education and HIV prevention initiatives within venues may be effective and should be supported (Binson et al. 2001).

Though MSM are considered a key population at increased risk of HIV transmission, different subgroups present disparate levels of HIV risk. In our work we studied subgroups of the MSM population most vulnerable to HIV infection as male sex workers (SW) (Study II). The findings show that the frequency of high-risk sexual behaviours is concerning: around one fourth of male SW reported having had ≥4 client partners in the previous working day and more than a half reported ≥3 non-paying partners in the previous year; over a quarter reported inconsistent condom use with clients and almost two thirds with non-paying partners; about 70% had ever used psychoactive substances and a proportion of 13.7% had ever used injecting drugs.

The prevalence of HIV infection found was high: 5.0% (95%CI: 1-10%) of male SW self-reported being HIV positive and 10.7% (95%CI: 0-23%) of those who had a HIV rapid test had a reactive result. Other European studies show high levels of infection in male SW populations (Belza 2005; Mc Grath-Lone et al. 2014; Van Veen et al. 2010; Verster et al. 2001). It is worth noting that risk behaviours were frequent among reported HIV-positive SW but also among those screened who tested positive and did not know their seropositivity. The risk of sexual behaviours undertaken combined with HIV prevalence increases the likelihood of spreading of HIV to general population. This indicates that both SW and their clients/non-paying partners are key populations to be targeted as they may act as bridging populations.

A high proportion of HIV-positive male SW had ever injected drugs. This is consistent with research demonstrating that HIV infection is driven largely by the overlap of injecting drug use and sex work (El-Bassel et al. 2010; Stockman & Strathdee 2010; Strathdee et al. 2011). Additionally, an important proportion of male SW (12.2%) experienced forced sexual relations, which increases vulnerability to HIV.

Our findings indicate a considerable HIV testing rate and proportion of participants tested during the previous year (Study II). In Europe, data on HIV testing among SW in general are scarce and the reported rates vary considerably between countries, ranging from 33% in Czech Republic and 35% in France to 93.8% in Belgium and 100% in Greece (ECDC 2010). The rate of HIV testing found in our study may be a positive outcome of prevention programmes among SW implemented in recent years as community-based HIV testing initiatives. Nevertheless, the proportion of male SW who never tested for HIV (22.5%) is worth highlighting. Indeed, SW who never tested for HIV reported more frequently inconsistent condom use with both clients and non-paying partners. In Portugal, HIV testing is non-mandatory and can be done anonymously, confidentially and for free. Potential reasons for not getting tested are mistrust of health services, confidentiality, fear of discrimination or exclusion, lack of awareness of services available and low self-perception of HIV risk (Deblonde et al. 2010). Unfortunately, we did not collect data on duration of sex work and so we cannot determine its effect on HIV-testing behaviour. There remains a need to understand factors that may underlie unwillingness to be tested, especially among male SW.

The results from the rapid tests show that all the male SW who tested HIV positive (had a reactive test) (n=3) were unaware of their serostatus (Study II). Although the sample screened was small, this can be an important finding. Those unaware of their HIV status are at risk of transmitting HIV to others through high-risk behaviours. Early diagnosis is crucial to limit further transmission of HIV (Del Romero et al. 2010). Our findings reinforce that efforts should be made to increase HIV testing, particularly among individuals who do not perceive themselves to be at risk or who do not contact healthcare services (Dias et al. 2011). Furthermore, as supported by other studies (Platt et al. 2011; Shahmanesh et al. 2008), integrating outreach strategies for HIV prevention is valuable: having been reached by HIV prevention programmes in the previous year appeared positively associated with having been tested for HIV.

In our work we studied another subgroup of MSM considered most vulnerable to HIV infection: male-to-female transgender persons who do sex work. We examined risk behaviours and HIV prevalence among transgender sex workers (TSW), and described health services use (Study III). TSW in this study reported a high level of HIV infection (14.9% [95%CI: 8-21%]), similarly to findings reported in other research that used both self-reported data and serological HIV testing (Dos Ramos Farías et al. 2011; Nemoto et al. 2004a; Operario et al. 2008). As expected, our estimate of HIV prevalence among male-to-female TSW is higher than estimates from studies with female SW and men who have sex with men (Dos Ramos Farías et al. 2011; Operario et al. 2008).

Another relevant result was the high levels of HIV risk behaviours such as unprotected sex found among TSW, and in particular among those HIV-positive, consistent with other research (De Santis 2009). Unprotected sex with clients was more likely among TSW at low socioeconomic level, reinforcing that contexts of social disadvantage increase exposure to HIV risk (Nemoto et al. 2004b; Poteat et al. 2015; Reback et al. 2005). Earlier qualitative findings suggest that many TSW are compelled to engage in unprotected sex with clients that pay extra money for condomless sex (Nemoto et al. 2004b; Nemoto et al. 2006).

Participants who had unprotected sex with clients were also more likely to have unprotected sex with non-paying partners. Additionally, other behavioural risks like multiple partners, forced sexual relations and condom failure were found. This overlap of sexual risk behaviours suggests that complex multi-related factors are linked to increased risk for HIV infection and transmission. Nevertheless, the higher inconsistent condom use with non-paying partners than with clients indicates that psychosocial aspects, like low risk perception and relationship intimacy, can act as barriers to condom use (Nemoto et al. 2004b; Operario et al. 2011). Although we did not explore social and psychological factors associated with sexual risk behaviours, in previous focus group studies on the context of sex with main partners, transgender participants described need for affection and personal connection, and stated that condoms undermined feelings of intimacy and threatened their connection with those partners (Nemoto et al. 2004b; Nemoto et al. 2006). On the other side, in the context of sex with casual partners, participants described feelings of gender validation and attractiveness associated with receiving sexual attention from men (Nemoto et al. 2004b; Nemoto et al. 2006).

Drug use was observed among TSW, and in an important proportion of those HIV-positive. This is consistent with research showing that HIV infection is driven largely by the intersection of drug use and sex work, as also found in male SW (as previously referred) (Stockman & Strathdee 2010; Strathdee et al. 2011). In our study, psychoactive substances use was significantly more likely among non-employed, full-time and non-national TSW. As documented elsewhere, migrant SW often live in poorer socioeconomic conditions and face additional vulnerabilities, such as substance use and marginalization related to gender identity and ethnicity (Decker et al. 2015). In a context of socioeconomic disadvantage, sex work is a common mean to finance drugs use (Nemoto et al. 2004b; Reback et al. 2005; Latkin et al. 2003; Zohrabyan et al. 2013). It has been reported that drugs are often used in the context of sex with partners and clients, and sex work conducted under the influence of drugs has been associated with lower rates of condom use (Strathdee et al. 2011). In addition, needles are sometimes shared with clients who pay for their services with drugs (Clements-Nolle et al. 2001; Nemoto et al. 2004b; Poteat et al. 2015; Reisner, M. Mimiaga, et al. 2009; Strathdee et al. 2011).

Furthermore, our study shows that a significant group of TSW underuse health services, especially those more socially vulnerable. Although we did not assess reasons for underuse of health services, other research have shown that TSW tend to experience extreme social marginalization related to stigma and discrimination based on sex work and gender identity (De Santis 2009; Divan et al. 2016). This social exclusion and isolation impairs this group's ability to access health services and HIV prevention programs (Dos Ramos Farías et al. 2011). This is a relevant finding because not been reached with HIV prevention programs appeared positively associated with inconsistent condom use with client partners. In this sense, developing outreach health structures and initiatives for HIV prevention may be valuable in contributing to risk reduction and health gain. Specially outreach teams, which are frequently able to reach TSW who are difficult to access, who underuse health services and who are most at risk, can play a role in promoting access to health services and reducing HIV infection and transmission, and should be supported.

The limitations of these studies must be acknowledged. The cross-sectional design of the Studies I, II and III limits causal interpretations of the findings. Another limitation relates to the sampling procedures. Although the Studies I, II and III achieved diverse and

large samples, we did not use a random sampling method to select the study participants. The available information in Portugal does not allow constructing sampling frames for the target population. Consequently, it is difficult to ensure representativeness of MSM, SW and transgender people (hard-to-reach populations). As the study samples were not selected randomly from the target population, results obtained in the Studies I, II and III may be biased and no inferences can be made for the whole (unknown) population.

As a matter of fact, the lack of research in general with key populations so far has been due greatly to difficulties in reaching these groups for population-based health research (Magnani et al. 2005). Indeed, the difficulty in accessing hard-to-reach populations such as MSM has presenting a dilemma for HIV surveillance. Given the critical importance of understanding HIV epidemics, high quality surveillance systems are necessary. The need to find more effective and efficient recruitment strategies is paramount. Appropriate sampling approaches are at the core of any high quality surveillance system, especially when attempting to track transmission dynamics among populations that play a critical role in the transmission of HIV, and that are 'hidden' or hard-to-reach (Magnani et al. 2005; Sadler et al. 2010). The importance of including these populations has highlighted the need for alternative sampling strategies which are both feasible and capable of producing realistic estimates, with minimal levels of bias for population subgroups which are not efficiently 'captured' using conventional surveillance data collection strategies (Lohr 2010; Magnani et al. 2005). Special attention has been drawn to the development of sampling methods which provide valid estimates of infection rates, behaviours, and contextual factors among their members for meaningful surveillance. In particular, the use of non-random sampling techniques has been increasingly recognized (Faugier & Sargeant 1997).

In our critical analysis of different methods for most effectively targeting MSM in HIV research and reach those most-at-risk, we focused on some of the most common sampling approaches (Study IV). One of them is non-probability sampling methods such as chain-referral sampling. These methods work on the assumption that peers are better able to recruit members of a hidden population than researchers (Magnani et al. 2005; Platt et al. 2006). In addition, venue-based methods have been put forward, seeking to recruit respondents in places and at times where they would reasonably be expected to gather and to collect data from them within that place (Guo et al. 2011; Muhib et al. 2001).

As a major concern in non-probabilistic sampling methods being the fact that the selection bias limits the validity of the sample and potentially the quality of data, attempts have been made to improve the statistical accuracy of samples obtained by these techniques (Atkinson & Flint 2001). In this sense, two approaches that have seen increasing use in recent years is Respondent-driven sampling (RDS) and Time-location sampling (TLS). With increasing access to the Internet and growing popularity among MSM in seeking sex partners online, the Internet has also been increasingly used to recruit MSM in HIV research (Bowen 2005; Pachankis et al. 2015).

The varying methods face common challenges. The definition of the study population continues to be challenging as there is no consensus on who the MSM group includes (consider men who had only anal sex or also oral sex? Men who had sex with men in their lifetime or in the last year?). According to UNAIDS Terminology Guidelines, the term men who have sex with men "describes males who have sex with males, regardless of whether or not they also have sex with women or have a personal or social gay or bisexual identity" (UNAIDS 2015b). This is a useful concept because it also includes men who self-identify as heterosexual but who occasionally have sex with other men. Indeed, an additional global challenge has been to identify this especially hard-to-reach MSM subgroup. Nevertheless, the discussed methods present several advantages in terms of recruitment efficiency (particularly of most-vulnerable subgroups), and evidence obtained on MSM's needs and relevant HIV interventions priorities. Overall, those methods represent some of the best efforts thus far to find feasible sampling approaches and recruitment strategies that effectively reach most-at-risk and hard-to-reach subgroups of MSM, contributing to obtain unbiased trends of HIV prevalence and HIV-related risk behaviours among these populations.

The benefits and limitations of the described strategies must be carefully evaluated against its benefits and limitations in each specific context, in order to select the optimal strategy. Also, the benefits of using these approaches to recruit participants for HIV research must be weighed against the privacy concerns that are inherent in any individual social situation or health condition (Sadler et al. 2010).

Another relevant issue is the adhesion to research initiatives of communities, particularly most vulnerable groups who tend to be understudied in studies that use more traditional research methods (Wallerstein & Duran 2006). In this sense, an approach

increasingly recognized as valuable in undertaking research with hard-to-reach populations has been the community-based participatory (DiStefano et al. 2013; Minkler 2000; Olshansky 2008; Parrado et al. 2005; Wallerstein & Duran 2006). In our work we reflected on the contributions of participatory approach in health research, analysing its theoretical perspectives, principles, strengths and challenges (Study V).

Participatory research has contributing to the production of deeper knowledge of complex health issues in the sense that it potentially facilitates access to the communities' perspectives and experiences and helps to understand the influence of sociocultural and contextual aspects in populations' health (Wallerstein & Duran 2006). Alongside, participatory research may constitute itself an intervention by its potential in capacitating communities to define and respond to their health concerns and promoting their role as actors of change in disease prevention and reduction (Deren et al. 2005; Parrado et al. 2005). Several authors have highlighted this approach's potential to help translation of scientific knowledge into more community-oriented health actions and policies in the field of public health (Blumenthal 2011; Ramsden et al. 2010). This research approach has been used with culturally diverse populations, from different social contexts and difficult to access, demonstrating its utility and versatility in the investigation of health issues.

Progressively there has been an increasing interest in participatory research approach, and it is consensual the need of further evidence on its implementation process – how it is conducted, which conditions favour the participation and collaboration of the partners and how the variations on the implementation of this approach influence the results obtained (Cargo & Mercer 2008; Israel et al. 2008). Such knowledge will strengthen the theoretical background of the participatory research approach and provide further understanding of its utility, potentialities and limitations regarding different health problems, contexts and populations (Blumenthal 2011). More evidence on this approach will also be relevant to comprehend its impact in communities' empowerment and health outcomes, providing a more global perspective of its beneficial role for communities (Ramsden et al. 2010).

The recognition of the participatory research approach has been reflected in the gradual investment in training in this area and in the increasing implementation of projects using this approach (Green & Mercer 2001; Minkler 2000; Minkler & Wallerstein 2008).

Nevertheless, a main challenge is to ensure that, within the multiple contexts in which participatory research can be implemented, the principles that characterize it (equitable involvement of the partners and balance between research and intervention for the benefit of all actors) are respected.

In general, our work intended to contribute in conducting future research with MSM. The high HIV infection rates and the disparate risk levels among MSM found in this thesis and in international research support the need to further investigate and capture the changes in the trends of the HIV/AIDS epidemic, its determinants and socio-behavioural risk profiles in MSM, in order to make recommendations about interventions that have a meaningful impact on HIV epidemics (Auerbach et al. 2011). There are multiple and complex drivers of increased HIV infection among MSM beyond those explored in this study. More research is needed to complement the current national and international evidence.

More specifically, several areas of potential interest for research emerged in this work. Particularly, further research would be valuable on seroadaptation practices, that have been reported among MSM as forms of "negotiated safety" (Cassels & Katz 2013; Guzman et al. 2005; Lattimore et al. 2011; Siegler et al. 2013; Truong et al. 2006). Seroadaptation is a potential harm reduction strategy that includes a diverse set of behaviours that use HIV status to inform sexual decision-making (Cassels & Katz 2013). Some of these behaviours include serosorting (a person chooses a sexual partner known to be of the same HIV serostatus, often to engage in unprotected sex, in order to reduce the risk of acquiring or transmitting HIV), and seropositioning (also known as strategic positioning, it is the act of choosing a different sexual position or practice depending on the serostatus of one's partner) (Cassels & Katz 2013). Although seroadaptive behaviours may be a potential harm reduction strategy for individuals who choose not to use condoms, they are not necessarily effective risk reduction strategies as they do not protect against other STIs and potential risks such as HIV superinfection and drug resistance (ECDC 2013; WHO 2011). Considering that recent research shows that many different populations of MSM are engaging in seroadaptive behaviours, and many are doing so intentionally (Cassels & Katz 2013), more studies should be conducted to examine the dimension of this phenomenon among this population and identify the demographic, socioeconomic, psychosocial and behavioural associated factors.

Future studies should also further investigate contexts of potential increased HIV risk: bisexual relationships (men who have sex with both men and women) and its potential for bridging high-low risk sexual networks; effect of sex-work characteristics on HIV risk; influence of patterns of drug use in risky sexual behaviour; engagement in sex parties; specific risky sexual practices as barebacking and fisting; prevalence of other sexually transmitted infections.

Additional research of interest is to examine the role of psychosocial aspects (such as HIV risk perception, internalized homophobia, socio-emotional systems underlying risk seeking and risk taking, relational or partnering context) in the increasing risk of HIV acquisition and transmission among MSM, and its correlates (Folch et al. 2009; Saavedra et al. 2008). Research is also needed on structural factors that contribute for great vulnerability to HIV among these populations, including patterns of healthcare seeking for HIV prevention, testing, treatment and care (utilization of services and barriers to access), broader effects of social stigma towards HIV/AIDS and homosexual behaviour, and effects of migration and mobility in sexual behaviours and dynamics of infection.

Finally, further research using qualitative and mixed methods may be extremely valuable to explore the behavioural, sociocultural, contextual and structural determinants of increased HIV vulnerability among MSM population and most-at-risk subgroups, as well as their prevention needs.

4.2. Implications of the study for public health intervention

This work does suggest a number of implications for HIV public health intervention and policy. Given the high levels of HIV infection and risky sexual behaviours, targeted efforts are needed to focus on HIV prevention interventions with MSM.

While effective antiretroviral therapies are available, the implementation of a "test-and-treat" strategy faces challenges related to drug and program implementation costs associated with widespread testing and treatment, treatment retention and healthcare workforce capacity (Farmer et al. 2001; Harries et al. 2001; Kulkarni et al. 2013; Poundstone et al. 2004). In this strategy, individuals would be routinely tested for HIV, and those who are identified as being HIV infected would be started on ART immediately, irrespective of their stage of disease, to thereby reduce their likelihood of transmitting the

infection (Kulkarni et al. 2013). Also, the development of an effective HIV vaccine may take more years (Cohen & Dolin 2013; Ensoli et al. 2014; Verma et al. 2016). These constraints accentuate the urgent need to tackle the multiple determinants of HIV/AIDS through sound policies and programs (Poundstone et al. 2004).

There is emerging consensus among researchers, programmers and policy-makers that, after three decades of AIDS, it is time to shift from an 'emergency' framework to a long-term response (Auerbach et al. 2011). A key component of this shift is a change in focus from individualistic, urgency-based biomedical and behavioural interventions to new approaches that also address underlying social-structural drivers of patterns of practices that influence vulnerability and facilitate the spread of HIV (Auerbach et al. 2011; Coates et al. 2008; Kurth & Wasserheit 2011). Stating that particular social-structural factors 'do' or 'do not' lead to HIV transmission may be too simplistic. In alternative, focus should be on discussing how, in what circumstances, and among whom particular combinations of factors contribute to HIV vulnerability (Auerbach et al. 2011). For example, despite the evidence of effective behavioural interventions, behaviour change alone is unlikely to result in sustained reduction in HIV transmission (Coates et al. 2008; McDaid & Hart 2010). Programmes and interventions aimed at reducing the sexual risk need to address sexual practices as they are enacted and within its multiple cultural forms (concurrency of partners, anonymous sex, sex work). HIV health promotion efforts that simply address the 'behaviour' (condom use) may miss the point as it fails to consider the several sociocultural meanings and circumstances of the practices within which condoms might be used (Kippax 2008).

In alternative, combination HIV prevention strategies have been considered to be the way forward, given the growing recognition that it might optimize HIV prevention impact (Coates et al. 2008; Kurth & Wasserheit 2011; McDaid & Hart 2010; Piot et al. 2008). As defined by UNAIDS, combination HIV prevention 'seeks to achieve maximum impact on HIV prevention by combining human rights-based and evidence-informed behavioural, biomedical and structural strategies in the context of a well-researched and understood local epidemic' (UNAIDS 2015b). Combination HIV prevention interventions aim to modify social conditions and address the key drivers of HIV vulnerability that affect the ability of individuals to protect themselves and others from acquiring or transmitting HIV infection (Auerbach et al. 2011; Baral et al. 2013).

Combination prevention may have synergistic effects and may help to achieve the highest levels of effectiveness in reducing HIV transmission by offering multicomponent packages of evidence-based biomedical, behavioural, and structural interventions that address risk factors at the individual, dyadic, sexual network, and community levels (ECDC 2015; Kurth & Wasserheit 2011; UNAIDS 2015a).

Within a biomedical approach, pre-exposure prophylaxis (PrEP) is a method to reduce the risk of HIV infection in HIV-negative adults who are at high risk of HIV exposure through a treatment that includes the use of oral antiretrovirals in order to prevent the virus from establishing a permanent infection (ECDC 2015; Grant et al. 2010). PrEP is the first biomedical intervention with proven efficacy to reduce HIV acquisition in MSM and transgender people (Cohen et al. 2015). Recent findings from several clinical trials have demonstrated a substantial reduction in the rate of HIV acquisition for men who have sex with men (MSM), men and women in heterosexual HIV-discordant couples, and injecting drug users who were prescribed daily oral antiretroviral PrEP (Baeten et al. 2012; CDC 2014; Choopanya et al. 2013; Grant et al. 2010). The demonstrated efficacy of PrEP was in addition to the effects of repeated condom provision, sexual risk-reduction counselling, and the diagnosis and treatment of STIs (CDC 2014). In the extension of a large clinical trial (iPrEx OLE) conducted among MSM and transgender women, the results showed that good adherence to PrEP was associated with a risk reduction of 84% for HIV infection (ECDC 2015; Grant et al. 2014). Also, modelling studies suggest that PrEP could substantially reduce HIV incidence among MSM and may be cost effective if targeted to the highest risk populations (Cohen et al. 2015; Desai et al. 2008; Juusola et al. 2012; Paltiel et al. 2009). These studies provide strong evidence on the efficacy of PrEP and indicate that serious consideration should be given to its inclusion in HIV prevention programs, especially for those MSM most at risk of acquiring infection (ECDC 2015). Indeed, the use of PrEP has been recommended by international institutions (WHO, US Centers for Disease Control and Prevention - CDC) as an additional prevention option within a comprehensive HIV prevention package for sexually-active MSM at considerable risk of HIV acquisition (CDC 2014; WHO 2014).

As PrEP becomes more available in Europe, MSM who are HIV-negative and at high risk of HIV exposure can be provided information and counselling about PrEP for HIV, and about the importance of regular HIV testing. But providing isolated counselling

interventions may be insufficient for sustained behaviour change (ECDC 2015). It is suggested that counselling interventions, which usually address HIV/STIs information, behaviour, sexuality and risk reduction issues, can benefit from being combined with other services when appropriate, including prevention, testing and treatment (ECDC 2015). However, further research on PrEP is needed, especially to assess its cost-effectiveness, the potential associated risk of developing drug-resistance, and the potential associated impact on condom use and STIs acquisition (ECDC 2015).

At a behavioural intervention level, HIV-positive people, including MSM, have been often left behind those at risk of HIV infection in HIV prevention efforts (van Kesteren et al. 2007). Yet, to have an impact on the sexual transmission of HIV, prevention interventions also need to reach those most at risk for transmitting HIV (King-Spooner 1999; van Kesteren et al. 2007). In our studies, HIV-positive participants reported several risk behaviours. In this sense, strategies focused on MSM living with HIV should be supported. Secondary prevention programs focusing on risk reduction strategies, as minimizing condomless sex, may be relevant to assist HIV-positive MSM in adopting and maintaining safer sexual behaviours for reducing the transmission of HIV and other STIs (ECDC 2015; van Kesteren et al. 2007). Also, secondary prevention interventions may help to reduce stigma and empower HIV-positive male SW and transgender SW to negotiate safer sex with their clients and non-paying sexual partners.

Among the MSM subgroups of male SW and transgender SW relevant proportions of reported HIV-positive reported a STI. STIs increase the risk of HIV infection by increasing HIV infectiousness and susceptibility (Del Romero et al. 2010). In a context of frequent high-risk sexual exposure, STIs may have a stronger role on HIV infection and transmission. Preventing and controlling STIs are key strategies in controlling the spread of HIV/AIDS, and HIV/STIs programmes and services should be integrated for SW.

Prevention interventions should target those most at risk of HIV transmission considering the settings and the circumstances in which risk behaviour occurs (McDaid & Hart 2010). Our results provide evidence of the relationship between contexts where MSM meet other men for risky sexual behaviour, showing that cruising venues are a context that fosters engagement in unprotected sex and therefore play an important role in increasing risk of HIV transmission among MSM. In this sense, cruising venues should

be considered as an optimal setting to reach high-risk MSM and provide targeted HIV prevention strategies (Grov et al. 2013; Ostergren et al. 2011; Reisner, M. J. Mimiaga, et al. 2009; Vanden Berghe et al. 2011; Zhao et al. 2013). Venue-focused behavioural interventions as promotion of condom use and HIV testing may contribute to enhance safer sex practices, to decrease unawareness of HIV infection, and consequently to reduce infection. Moreover, social networks and the places where they form can successfully serve as facilitators for efficiently delivering HIV prevention interventions to MSM community members, such as the distribution of condoms and the dissemination of public health messages (Amirkhanian 2014; Doherty et al. 2005).

Our work also provides evidence of the association of HIV infection and risk with high vulnerability contexts, as those related to sex work, injecting drug use and socioeconomic disadvantage. These findings reinforce that, as noted in the literature, policies supporting safer environments and integrated interventions including harm reduction programs should be supported (Deering et al. 2014; Shannon & Csete 2010).

In a structural intervention perspective, combination prevention interventions should comprise provision of MSM-competent health care. Local points of care offering comprehensive sexual health care, including health promotion, counselling, peer support, prevention, HIV testing, STIs screening, adequate diagnostics and treatment, should be developed (ECDC 2015).

HIV testing specifically is recommended to be easily accessible and offered in an inclusive and non-discriminatory manner in order to be acceptable and accessible for MSM (ECDC 2015). Several international guidelines as those from ECDC and CDC recommend at least annual testing for sexually active MSM (Branson et al. 2006; ECDC 2015). In this sense, voluntary and confidential HIV counselling and testing should be provided in a variety of ways, including routine offering of tests in clinics and community-based settings and outreach initiatives, in order to easy access of, and cover the, target groups (ECDC 2015).

Recently published guidelines from WHO and the Joint United Nations Programme on HIV and AIDS (UNAIDS) recommend provider-initiated opt-out screening in concentrated and low level epidemics at STIs services and other health services for most at-risk populations (ECDC 2015; WHO 2007). In the opt-out testing approach, an HIV test is offered as part of routine STIs screening, and all clients are

informed about HIV testing and are tested for HIV unless they decline (ECDC 2015). Currently opting out is not a standard HIV testing strategy in Europe because routine comprehensive STIs screening is not implemented in all European settings (ECDC 2015). Nevertheless, there is a general trend towards recommending more routine HIV testing (ECDC 2015; Mounier-Jack et al. 2008). Potential benefits of opt-out are expansion of HIV testing, early diagnosis resulting in clinical benefit to the HIV-positive individual, and the reduction of HIV transmission (Bartlett et al. 2008; ECDC 2015). But testing for HIV should not be limited to health facilities. It should be promoted and offered in community-based settings (ECDC 2015). Research indicate that rapid HIV testing and counselling in community settings delivered by trained staff or peers can increase the uptake of HIV testing among MSM and can reach populations of men that have previously not accessed HIV testing (Lorenc et al. 2011; Parisi et al. 2013). MSM have also expressed preference for rapid testing over conventional testing in some European settings (Chen et al. 2010; Meulbroek et al. 2013). Testing in community settings, such as testing centres located in easily accessible areas and schedules, or through outreach/mobile services can allow easier access to and uptake of HIV testing services. Community-based settings provide an environment for testing that may be comfortable for difficult-to-reach groups. Also, community-based testing services can be delivered by trained peers, which can improve the uptake and acceptability of services for some MSM (ECDC 2015).

It is important to consider that interventions found to be successful in one setting may not readily transfer, requiring cultural adaptation (Kurth & Wasserheit 2011). In fact, prevention needs and preferences of MSM may vary by individual and over time (ECDC 2015). Therefore, offering and implementing prevention packages in collaboration with, or by, the target group may have a great influence in the success of prevention programmes (Chang et al. 2013; ECDC 2015). Peer outreach activities have been shown to be effective across several countries and income levels (ECDC 2015), and in one systematic review were associated with a 30% reduction in UAI compared with minimal or no HIV prevention (Lorimer et al. 2013). Peers are other MSM who are able to positively influence group norms and support members of the same group to maintain healthy sexual behaviours since they are seen as credible and non-judgmental role models. Peer characteristics such as age, sexual identity or HIV status may help them

more effectively reach certain groups of MSM. Community-based peer interventions can take place online, off-line and via mobile phone apps and have the capacity to reach individuals who would not normally participate in facility-based interventions (ECDC 2015).

4.3. Limitations

In Studies I, II and III, the fact that recruitment of participants took place at socialization venues may potentially lead to a sample bias by preferentially reaching individuals with common demographic and behavioural characteristics, who attend venues more frequently and/or who have larger social networks. Nevertheless, interviewing participants at different times and places allowed reaching heterogeneous samples of MSM, male SW and transgender SW with reported HIV infection and diverse high risk behaviours. Data were self-reported which may have potentially inhibited some participants to disclose their HIV serostatus and risk behaviours due to the sensitivity of many of the questions and social stigma. Social desirability and recall bias may have also potentially led to under-reported HIV infection and risk behaviours from respondents. However, the high response rates and the obtained data on reported HIV prevalence make us confident of the validity of the responses. In a worst-case scenario, our data underestimate the HIV prevalence and risks for infection among the studied populations. Although the sociodemographic profiles of individuals who refused to participate in the studies were similar to those who participated, we did not collect information about reasons for refusal nor about reported HIV infection, so it is not possible to determine to what extent HIV prevalence and related risk behaviours might have differed between participants and refusals. Given the relatively low numbers of HIV-positive participants enrolled in the studies, the wide CIs of the OR in the multivariate analyses and the missing data in some variables, results must be treated with caution. In order to include those of low-level literacy, we opted for an interview-administered questionnaire instead of a self-administered instrument. Interviewers might have interpreted the responses in a biased way, however they were trained thoroughly prior to fieldwork. Interviewers received training on ethical considerations, data collection procedures, instrument and interviewing techniques.

Finally, the critical analyses of the methods to most effectively target MSM in HIV research and reach those most-at-risk (Studies IV and V) could have been further developed by using specific indicators to evaluate and compare the different methods in terms of utility, costs and efficacy.

Despite these limitations, our work has strengths. The cross-sectional studies were conducted using methodologies commonly used in HIV research with most vulnerable populations and followed research ethical principles, having obtained approval from qualified Ethic Committees. The obtained data on HIV prevalence, risk behaviours and its correlates among MSM and most-at-risk subgroups shed light on the HIV burden and risks, research opportunities and prevention needs of a population about which little is known.

4.4. Conclusions

Our work provides a useful insight of HIV burden, behavioural-contextual risks and associated factors among an MSM population in Portugal, including most-at-risk subgroups (male sex workers and transgender sex workers) that have been particularly understudied and under-addressed. Overall, this thesis provides information that contributes to the existing evidence base and with potential implications for public health intervention aimed to reduce HIV infection among MSM.

A main conclusion of this thesis is that there are diverse risk profiles of MSM and to prevent further transmission of HIV it is essential to address the links between these key features and HIV. Tailored HIV prevention programs and interventions should comprise strategies to reduce risk behaviours, intensify harm reduction, improve uptake of testing and promote access to HIV health services, especially targeting those who underuse the services and who are most at risk. Venue-based interventions that address context- and partner-related motivations for engaging in unprotected sex could improve general approaches to promoting condom use by acknowledging specific contextual and interpersonal dynamics that contribute to increased risk for HIV.

Globally, HIV among MSM has been under-addressed. It is warranted further research that produces meaningful and relevant knowledge, more 'translatable' into effective actions that address MSM population's health needs and that are likely to have positive impacts in health gain. Recruiting members of this difficult-to-reach population

is a challenge. In this work, our ability to recruit difficult-to-reach populations was likely the result of using participatory approach. Similar peer-based approaches could be used to provide culturally appropriate HIV prevention services for MSM, including male and transgender SW. Finally, settings of research initiatives, particularly with most vulnerable and hard-to-reach populations, can simultaneously be valuable contexts for conducting HIV prevention initiatives, including providing information on HIV preventive measures, HIV testing and treatment.

4.5. References

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