Thesis for doctoral degree (Ph.D.) 2016

HIV Preventive Interventions, Sampling Methods and Sexual Risk Behaviour among Men who have Sex with Men

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Stockholm 2016





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Public Defense Friday February 26, 2016 at 9.00am Inghe Lecture Hall, Widerströmska Huset, Tomtebodavägen 18a

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ABSTRACT

Background: Gay, bisexual and other men who have sex with men (MSM) are at high risk of HIV globally. HIV rates among MSM in Europe show increasing trends, in contrast to declining trends in the general population. During the last five years, an increase in reported HIV cases among foreign-born MSM have been observed in Sweden. Representative data about the MSM population is difficult to collect due to lack of a sampling frame. Respondent driven sampling has been developed to access hidden groups and achieve high response rates. Online sampling methods such as Web-based Respondent driven sampling and stratified sampling in a Web community are new and innovative ways of reaching MSM.

Aims: To systematically gather and review evidence for HIV prevention interventions among men who have sex with men in the European Union/European Economic Area and to test and evaluate different sampling methods to study sexual risk behaviour among Men who have sex with Men.

Methods: A systematic review of HIV preventive interventions among MSM applying the Highest Available Standard of Evidence grading framework was performed to inform European guidelines. Web-based respondent driven sampling was implemented to study sexual risk behaviour and Internet use among MSM. Stratified sampling in a Web community was performed to study HIV testing and prevention uptake among foreign-born MSM living in Sweden. Finally, the samples of MSM in Sweden achieved through Web-based respondent driven sampling, stratified sampling in a Web community, time location sampling and online banner survey sampling, were compared regarding sociodemographics and sexual risk behaviour for HIV.

Results: In total, twenty-four interventions were reviewed and fifteen interventions were graded to be strongly, probably or possibly recommended. Condom use, peer outreach, peerled groups, and universal coverage of antiretroviral treatment were found to be strongly recommended. Web-based respondent driven sampling generated a sample of MSM whom all reported unprotected anal intercourse with at least one casual and one regular sex partner in the past twelve months. Stratified sampling in a Web community produced a sub-sample of foreign-born MSM of which 45% had tested for HIV during the past twelve months. A fifth of participants had never tested. Having talked with a prevention worker in the last year was associated with having tested for HIV in the same time frame. The four different sampling strategies used to study sexual risk behaviour among MSM in Sweden captured participant samples that differed regarding sociodemographic characteristic and reported sexual behaviour.

Conclusions: Condom use, peer outreach, peer-led groups, and universal coverage of antiretroviral treatment are evidence-based corner stones of HIV preventive interventions for MSM. Web-based respondent driven sampling reached MSM engaging in sexual risk behaviour and holds promise for online interventions and referrals to prevention programmes. To achieve higher uptake of HIV testing among foreign-born MSM in Sweden outreach programmes could be scaled up and evaluated. Future studies could benefit from using different sampling methods to achieve comprehensive data and validate findings across samples of MSM.

Key words: HIV prevention, Men who have Sex with Men, Sampling Methods, Non probability sampling, Respondent Driven Sampling, Sexual risk behaviour, Epidemiology, Public Health

LIST OF SCIENTIFIC PAPERS

- I. **Strömdahl S**, Hickson F, Pharris A, Sabido M, Baral S, Thorson A. A systematic revie of evidence to inform HIV prevention interventions among men who have sex with men in Europe. *Eurosurveillance 2015 Apr* 16;20(15). pii: 21096.
- II. Strömdahl S, Lu X, Bengtsson L, Liljeros F, Thorson A. Implementation of Web-Based Respondent Driven Sampling among Men Who Have Sex with Men in Sweden. *PLoS One. 2015 Oct* 1;10(10):e0138599.
- III. Strömdahl S, Liljeros F, Ekéus Thorson A, Ingemarsdotter Persson K, Forsberg B.HIV Testing and Prevention among Foreign-born Men Who Have Sex with Men: An Online Survey from Sweden. *Manuscript*.
- IV. Strömdahl S, Ingemarsdotter Persson K, Forsberg B, Berglund T, Kühlmann-Berenzon S, Tikkanen R, Velicko I, Bergström J, Lu X, Bengtsson L, Ekéus Thorson A. Sampling strategies used in Sweden to study sexual risk behaviour for HIV/STI among men who have sex with men: Online banner survey, time location sampling, Web respondent driven sampling and stratified sampling in a Web community. *Manuscript*.

These articles will be referred to by their Roman numerals (I-IV).

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LIST OF ABBREVIATIONS

MSM Men who have Sex with Men

HIV Human Immunodeficiency Virus

AIDS Aguired Immunodeficiency Syndrome

STI Sexually Transmitted Infections

ART Antiretroviral Treatment

ECDC European Centre for Disease Prevention and Control

EU The European Union

EEA European Economic Area

UAI Unprotected Anal Intercourse

RDS Respondent Driven Sampling

WebRDS Web-based Respondent Driven Sampling

TLS Time Location Sampling

HASTE Highest Attainable Standard of Evidence

GRADE Grading of Recommendations, Assessment, Development

and Evaluation

PICO Population, Intervention, Comparison, Outcome model

MeSH Medical Subject Headings

LGBTI Lesbian, Gay, Bisexual, Trans and Intergender

RFSL The Swedish Foundation of LGBTI Rights / Riksförbundet

för homosexuellas, bisexuellas, transpersoners och queeras

rättigheter

SSWC Stratified Sampling in a Web Community

EMIS European MSM Internet Survey

PEP Post-Exposure Prophylaxis

PrEP Pre-Exposure Prophylaxis

1 INTRODUCTION

My interest for this thesis topic was sparked by a few different events. During the first years in medical school I volunteered in a programme providing peer education to Swedish youth on sexual health including sexual health around same sex practices. This work provided an introduction to the topic.

Later in 2005, during a course at a rural dispensary in the Northern part of Tanzania, I witnessed the mass death due to AIDS. The roll out of the first treatment programme in the area had just started and the life saving treatment also had a large societal impact, saving children from becoming orphans. This experience motivated me to contribute in the fight against the HIV pandemic.

A few months later I was introduced to the Division of International Health at the Karolinska Institutet where colleagues guided me into the field of epidemiology and global health. I was hooked. Around the same point in time I was introduced to the HIV situation among men who have sex with men (MSM) living in Sweden through clinical work at a MSM clinic. This work provided insights into the disproportionate burden of HIV in this group. I have continued to work with MSM patients in periods, in parallel to my thesis research.

This path eventually took me to a Master in Public Health, research among key populations for HIV in low income settings and work at the World Bank to scale up HIV services in Sub Saharan Africa. Finally, I had the opportunity to further my knowledge through the research work presented in this thesis. The research presented here is inspired by patients' stories, which provided insights to the thesis topics.

Hereby follows a short introduction to the thesis work, which in most parts follows the chronological order of when the studies were performed. The thesis aims to contribute with improved knowledge regarding evidence based HIV prevention and sampling methods to reach gay men and other men who have sex with men for study purposes and HIV preventive interventions.

A systematic review was performed to inform a European guidance for HIV prevention among men who have sex with men issued by the European Centre for Disease Prevention and Control in 2015. The guidance work and dissemination thereof by the ECDC contributed with knowledge sharing between different diverse European setting and most importantly provide leadership for the scale up of HIV preventive interventions for MSM in the European Union and European Economic Area (EU/EEA) (1).

Studies among MSM often lead to questions around the representativeness of findings to the larger MSM population in a country or geographical area. As MSM represents a population without a known sampling frame there is a need for additional strategies to probability sampling to recruit MSM to studies. For example there is no national register of MSM living in Sweden as this is prohibited to protect the group, but there are meeting venues both in real life and online where researchers may access MSM. Online strategies are interesting to explore as people globally spend increasing amounts of time on the Internet. Therefore, two different Web-based studies were implemented as part of this thesis. Web-based respondent driven sampling applied peer recruitment within the online social network of MSM. In addition, Sweden's largest Web community for Lesbian, Gay, Bisexual, Transgender and Intergender member registry was used for stratified sampling.

To further our understanding of differences and similarities in samples of MSM participants recruited through different sampling methods, four studies performed between 2010 and 2013 were compared. The included sampling methods 2010 and 2013 in Sweden to study sexual risk behaviour among MSM include an online banner survey, time location sampling, Webbased respondent driven sampling and stratified sampling in a Web community.

2 BACKGROUND

2.1 THE GLOBAL HIV EPIDEMIC

In 2014 the global burden of human immunodeficiency virus (HIV) (2) was estimated to include 36.9 million people living with HIV (3). Among adults between the ages of 15 and 49 years HIV prevalence was estimated at 0.8% (4). Encouragingly, we are now seeing a globally declining trend in new HIV infections and decreasing morbidity and mortality due to HIV and AIDS. Access to antiretroviral treatment (ART) and improved treatment regimens are important factors behind these trends (5).

The HIV Epidemic among Men who have Sex with Men

Gay, bisexual and other men who have sex with men (MSM) are disproportionally affected by HIV compared to other adult males in every setting where data are available (6). HIV rates reported among MSM show an increasing trend, in contrast to the declining trends reported in the general population (7). In high-income countries data reveal male-predominant HIV epidemics, with a male: female median case ratio of 2.5: 1 (8).

The European HIV Epidemic among Men who have Sex with Men

About 30 000 persons were newly diagnosed with HIV in 2014 in the European Union/European Economic Area (EU/EEA). This translates to a rate of 5.9 diagnoses per 100 000 people. Sex between men was estimated to account for 42% of these cases (9). Since 2005, MSM represents the only key population for HIV where an increase in HIV diagnoses has been observed in EU/EEA (10). Between 2004 and 2013, the increase of HIV diagnoses among MSM was estimated to be 33% (11). In some European settings steep increases of more than 100% of newly diagnosed HIV cases among MSM are observed during this time period, including Bulgaria, Cyprus, Czech Republic, Hungary, Romania, and Slovakia. HIV prevalence among MSM was estimated to be at or above 5% in 14 of the 26 EU/EEA countries reporting national data in 2013 (12).

The Swedish HIV Epidemic among Men who have Sex with Men

Since the beginning of surveillance of the HIV epidemic in Sweden 1983 until December 2014, totally 11247 people have been diagnosed and reported to be living with HIV in Sweden. An estimated 6800 people were living with HIV in Sweden in April 2015, of which a third were MSM, which translates to 69 out of 100 000 persons in the Swedish population (13).

The latest national surveillance data available in Sweden are from 2014. During this year, 473 new cases of HIV were reported of which 272 were male and 199 female. Of these newly reported cases, 83% reported transmission abroad either while travelling or before migrating to Sweden, 14% reported transmission in Sweden and in 3% the country of transmission is unknown (13). The key populations MSM and people who inject drugs are both represented in the HIV epidemic in Sweden. Figure 1 shows the trends in newly reported cases due to domestic transmission, where MSM represents the group with the most cases of HIV transmission that takes place in Sweden.

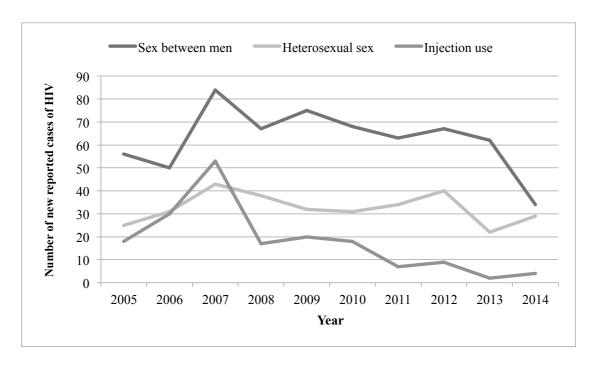


Figure 1. Number of reported new cases of HIV per transmission route where transmission is reported to have occurred in Sweden during 2005 to 2014. Monitoring data from the Public Health Agency of Sweden (13)

HIV prevalence among MSM in Sweden was estimated in 2012 to be between 2-6%, compared to an estimated HIV prevalence of 0.06% in the general population of Sweden (14). During 2010-2014, an average of 130 new HIV cases per year were reported due to sexual transmission between men. Half of these cases were reported among foreign-born MSM, which is an increase compared to 40% during the previous five year period (2005-2009) (15). The proportion of newly reported HIV cases among foreign-born MSM resulting from sex between men while in Sweden is increasing as well, from 26 percent between 2005 to 2009 to 36 percent between 2010 to 2014 (13). Indicating that foreign-born MSM are at risk of HIV while in Sweden.

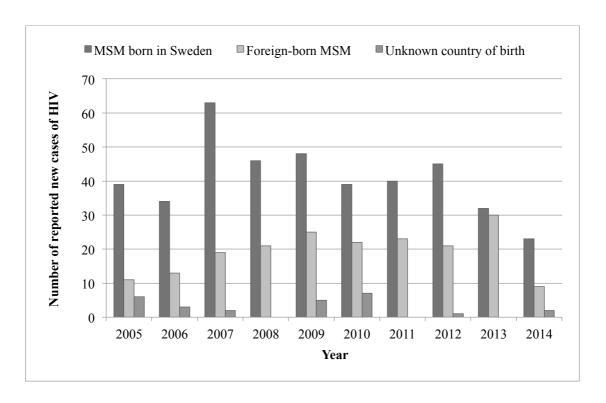


Figure 2. Number of reported new cases of HIV resulting from sex between men while in Sweden. Monitoring data from the Public Health Agency of Sweden (13)

2.2 MEN WHO HAVE SEX WITH MEN

The term 'men who have sex with men' refers to the population of men engaged in same-sex sexual behaviour irrespective of sexual orientation (homosexual, bisexual, heterosexual, or gay) and gender identity (male, female, transgender, queer). The term was introduced in research on HIV to capture the larger group of men engaging in sex with men and not only those identifying as homosexual (16-19). This is beneficial for including all at risk of HIV due to male same sex practices and MSM have become the standard term within HIV prevention work and research (20). It is important to note that individual men belonging to this population may not refer to themselves as MSM, rather gay, bisexual, straight or experimenting. It can be beneficial to gather sexual identity data in studies of MSM in order to take differences between sub groups of MSM into account.

Biological males with female identities are generally referred to as transgender women. Transgender women might share some heightened HIV risks with MSM, such as unprotected receptive anal intercourse and local sexual networks. However, their female gender identity may place them in a different population and they are not included as MSM in this thesis work. In addition, data shows a higher HIV burden among transgender women indicating a different epidemic scenario (21). I use the term 'men who have sex with men' recognizing the diversity of this population and the limitations of this term.

2.3 SEXUAL TRANSMISSION OF HIV

HIV-1 is the predominant existing HIV type worldwide and the focus in this thesis and here referred to as HIV (3). HIV-1 is further divided into four groups (M, N, O, P), where M stands for the majority of the global HIV epidemic (22). The contagiousness of HIV during sex is an important determinant of the HIV epidemic among MSM. We have limited knowledge of biological determinants of HIV transmission due to that randomized trials cannot be performed with regards to ethical considerations. However, data reveals several factors that impact the HIV transmission probability, including factors relating to the person living with HIV, the person exposed to HIV and the virus itself (23-25).

The risk of HIV-1 transmission during penile-vaginal intercourse between a seropositive and seronegative partner has been estimated across studies to be 0.04% per act in female to male transmission risk and 0.08% per act in male to female transmission risk (23). For receptive anal intercourse the per act risk is estimated to be 1.4% (24). The risk of HIV transmission at insertive anal intercourse is lower than at receptive anal intercourse (24, 26, 27). These estimates are uncertain and the HIV transmission risk varies both in between different individuals and over time for the same individual (24).

The extent of infectiousness in the person living with HIV is determined by the amount of HIV there is in the blood and body fluids (28). An estimate of this amount can be measured through determining the HIV viral load in a blood specimen (29). During the acute HIV infection stage, a period of weeks to months after the HIV infection has occurred, there are high amounts of virus in body fluids (30). During this period the immune system has not yet fully started to defend the body against the virus. The virus replicates quickly and can achieve a high viral load. Later the immune system keeps the viral load at lower levels during the asymptomatic phase of the HIV infection. If the HIV infection is not treated, high viral load are present at the late stage of infection when the body's immune system is weakened by the virus (31).

The per act risk of HIV transmission at penile-vaginal intercourse during the acute phase is estimated to be about nine times higher than during the asymptomatic stage, and about seven times higher during the late phase (23). Estimations for the per act risk of HIV transmission at receptive anal intercourse during the acute and late phase has been estimated to 18%, however with a very wide 95% confidence interval of 2.08-24.6, reflecting diversity in the pooled data used for this estimate (24). Successful antiretroviral treatment can decrease the viral load to undetectable levels thereby the risk of HIV transmission becomes close to 0 (32).

The versatility of the insertive/receptive sexual role among MSM enables quicker onwards transmission in comparison to male-female vaginal sex where the insertive and receptive roles are biologically determined (7, 33).

Other sexually transmitted infections (STI) affect the risk of HIV transmission. Genital ulcer disease increases the risk of HIV transmission at penile-vaginal intercourse about five times (23). Gonorrhoea has been estimated to increase HIV transmission at UAI about seven times and anal warts has been estimated to increase the risk of HIV transmission at UAI four times (26).

2.4 RISK FOR HIV AMONG MSM

In the studies presented here sexual risk behaviour for HIV among MSM at the individual level is defined as unprotected anal intercourse (UAI) with male sex partners of positive or unknown HIV status. To facilitate understanding of HIV risk among MSM, the individual risk level may be placed in a larger perspective (34).

At the individual level, risk involves frequency of unprotected anal intercourse, number of male sex partners, concurrent sex partners and number of lifetime sex partners (35-40). Sexual transmitted infections such as genital ulcer disease, gonorrhoea and anal warts adds to the risk of transmission at UAI (26). Other additional risk behaviours for HIV such injecting drug use and male sex work also contributes to HIV risk among MSM (41-44). Non-injecting drug use such as use of party drugs (Cocaine, Crack, Amfetamin, Ecstacy, LSD, GHB, Heroin) as well as binge drinking of alcohol can cause an increase in sexual risk taking by disinhibition (45). High usage of poppers, nitrite inhalants, among MSM have been reported across Europe (46-49). Nitrite inhalants cause peripheral vasodilatation and may decrease anal sphincter muscle tone, potentially leading to more traumatic sexual intercourse or more direct exposure to HIV target cells. However, this has not been established (50).

The local sexual network represent another level of risk. Sexual networks among MSM holds an important role for HIV transmission, the prevalence of HIV and STI in the local sexual network affects individual HIV risk. Clusters of HIV transmission have been reported indicating outbreaks within certain sexual networks of MSM (51-53). In addition, normative behaviour in the sexual network around condom and lubricant use may lead to an increased or decreased risk of HIV.

At the MSM community level access to HIV prevention services including MSM competent voluntary HIV testing and counselling, STI testing and treatment, information and behavioural HIV prevention holds an important role to modify HIV risk among MSM.

The societal level affects risk by either promoting or hindering a MSM friendly societal climate. Ensuring LGBTI rights through legislation and implementation thereof enables access to and uptake of prevention and care. Stigma around same sex practices similarly affects HIV risk through hindering access and uptake.

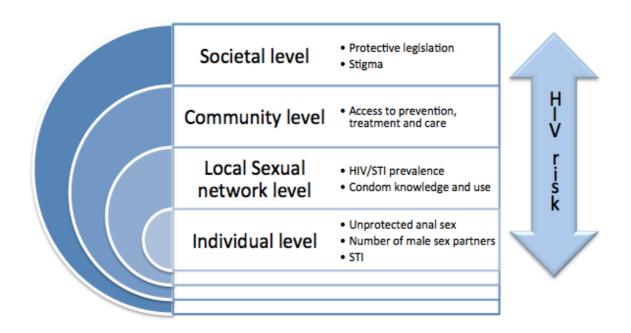


Figure 3. Factors at the societal level, community level, local sexual network level and individual level affect HIV risk for the individual

Health impact of stigma around same sex practices between men

MSM are persecuted for their sexual behaviour in large parts of the world, thereby many MSM to not disclose as MSM (54). Stigma can be divided into enacted stigma such as hate crimes against, and discrimination of MSM, and perceived stigma. Perceived stigma includes perceiving being unequally treated due to sexual orientation. Within the health care system perceived stigma can for example lead to not disclosing as MSM to health care workers, thereby not being offered MSM specific services. Stigma has also been found to contribute to late HIV testing, leading to late diagnosis of HIV (55). Internalized stigma or homonegativity

refers to a process where lesbian, gay and bisexual persons internalize society stigma as part of their self-image. Internalized homonegativity has been found to be associated with sexual risk behaviour and not testing for HIV among MSM in Europe (56-58). All these levels of stigma contribute to MSM being considered a population that is hard to reach for study purposes and intervention programmes and referred to as a hidden population (59-61).

2.5 CHALLENGES WHEN STUDYING MSM

MSM populations are of unknown size and parts of the population may be 'hidden' and therefore 'hard to reach' due to stigma around same sex practices (62). A registry of sexual preference in a population is rare. In many settings such as Sweden law prohibits such registry to ensure protection of minority groups (63). Therefore, it is not possible to define a sampling frame for MSM in most countries (64). Studies on sexual behaviour in the general population could include sub-samples of MSM. Such studies would require very large number of participants in order to capture a sufficient sub-sample of a minority group such as MSM. This is an uncommon approach due to economical constraints and feasibility.

Further, there is a reported trend of low response rates in national public health surveys in several European countries. Low response rates may introduce significant bias. In addition, a low response rate makes it more difficult to reach a sufficient number of MSM (65-67).

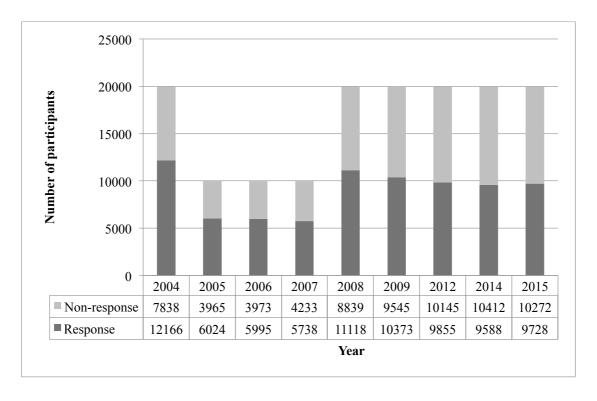


Figure 4. Response rates in the Swedish national public health survey 2004-2015 (66)

To address these challenges non-probability sampling methods have been used to a large extent in national surveillance studies evaluating HIV/STI prevalence and sexual risk behaviour among MSM (62). To improve national surveillance of HIV and sexual risk behaviour for HIV in order to inform prevention programming we need a better understanding of how these sampling methods work in real life.

The fundamental challenge for research among MSM is the absence of proper sampling frames, which is a challenge that most likely will remain. Therefore the key lies in furthering our understanding of other ways of reaching MSM for study purposes and producing population estimates.

2.6 OVERVIEW OF SAMPLING METHODS

To gain knowledge about a population of interest you can gather information about all individuals in that population by complete enumeration, which can also be called a census. Pending on the population size, this can be both time consuming and expensive. Another strategy is to sample some individuals out of the population of interest i.e. to study the whole by the part. When the sample is representative of the population of interest you can estimate population characteristics. This means that the characteristics of the sample approximate the characteristics in the whole population of interest. Thereby the results from the sample population can be inferred to the whole population.

2.6.1 Probability sampling

A sampling frame of the population under study must be established in probability sampling. In order to create a representative sample, each person in the sampling frame is assigned the same probability of being sampled. This can be achieved by simple random sampling. For example a random sample can be selected by assigning every individual in the population with a number and then letting a random numbers table or computerized version of this generate a sample (68).

Another way of sampling is a systematic sampling approach. In systematic sampling you select every Xth individual in the sampling frame from a randomly selected starting point, for example every third individual. In systematic sampling it's important that the ordering of the population does not correlate with the characteristics of interest. This approach is useful for on-site studies where the sampling frame is not available at the beginning of the study. For example every third patient visiting a clinic can be selected for the study in this manner (69).

Probability sampling can be achieved when the selection probability/inclusion probability of each person in the population of interest can be established. The selection probability/inclusion probability can be used to assign weights to individuals according to their selection probability, thereby generating estimates approximating the characteristics of the population of interest (68).

When there is a particular interest in certain subgroups within the population stratified sampling can be applied. The population is then divided into strata by characteristics such as female and male. Each stratum is then sampled using the simple random sampling approach, which then requires a smaller sample (68). This approach allows researchers to estimate properties of the strata subgroups. Another advantage is that sampling is performed in more homogenous groups when first divided into strata.

Another approach is to define clusters or groups of the population of interest (68). For example defining clusters by geographical location. The clusters constitute the sampling frame, from which a random sample of is drawn. Secondly, sampling of individuals is performed within each selected cluster. The defined clusters may be different from the general population if interest. In addition individuals within a cluster often share characteristics, which are different between clusters. Thereby, the variability of estimates becomes larger than in simple random sampling and a larger sample size is needed.

2.6.2 Non-probability sampling

For some populations it is not possible to define a sampling frame. Then samples are selected in other ways, usually referred to as non-probability sampling.

Convenience sampling

In convenience sampling researchers recruit individuals who are accessible for example due to location and time. For example, facility-based sampling in a clinic catering to MSM or a gay club. The online version of convenience sampling is banner survey adds on websites recruiting study participants (70, 71).

Convenience sampling is an easy and economical way of gathering data. This method can quickly provide useful information about the target group. However participants are selected due to accessibility, which may correlate to study outcomes (72). For example a study that aims to assess sexual risk behaviour for HIV among MSM using convenience sampling at an STI/HIV-testing clinic for MSM will probably get an overrepresentation of persons engaging

in sexual risk behaviour in the study sample due to that those MSM visiting such a clinic may be there due to STI symptoms or sexual health issues. Thereby the assessment of sexual risk behaviour cannot be generalized to the larger population of MSM, including those not visiting a HIV clinic for MSM.

Snowball sampling

Snowball sampling is a form of chain referral sampling (73). Initially, several persons who fit the study criteria and that are accessible to the researchers are identified and invited to participate in the study. After participation, participants are asked to invite persons they know who also fulfil the study population criteria. The sample then increases quickly in size like 'a rolling snowball', thereof the name (74).

A few different aspects need to be considered in snowball sampling. Respondents who volunteer to participate and refer friends/peers to the study are probably more accessible, cooperative and interested/invested in the aim of the study. This introduces volunteerism and salience bias (75). When referring friends or peers to the study this will most probably not be done by random selection of all friends/peers. For example, a participant may choose to invite close friends rather than acquaintances. Another example from MSM studies may be that participants will not invite MSM friends who they know are not comfortable disclosing as MSM. Persons with large social networks may be overrepresented as they are more likely to be invited by friends (76). If they are over sampled and if their characteristics differ to those with small social networks regarding the studied outcomes, bias may be introduced. For example MSM with large social networks could in addition to having many MSM friends (being popular), possibly also have a higher frequency of male sex partners. In a study of sexual risk behaviour for HIV, this may lead to overestimating the number of male sex partner.

Time Location Sampling

Targeted sampling combines different aspects of venue sampling and stratified sampling, by performing an assessment and ethnographic mapping to identify places where the study population meet, such as a gay bar or a street corner for male sex work (77). For each location identified, enrolment plans are developed, so called quotas. Sampling is then performed in the identified places according to the quotas. Estimating the density of study population members in the defined places can be used to assign proportional sampling quotas (78). A further development of targeted sampling is time location sampling (TLS) (also referred to as time-space sampling) (79). In addition, TLS gathers information regarding

when the venues are visited by the target population and divide the venues in venue-day-time units. The list of venue-day-time units constitutes a sampling frame from which a random set of venue-day-time units are drawn. The selected venues are then visited at the selected time to recruit study participants. Recruitment can be performed by either asking everyone there to participate or by systematic sampling (79, 80).

Weighting in TLS usually takes into account the probability of being sampled in the following way: i) the probability that the person attends the venue in the sampling frame on the sampling time, ii) the probability that the person attends the sampling venue given attendance at some other venue included in the sampling frame during the same day iii) the proportion of potential venue sampling time on the day sampling occurred iv) the sampling fraction at this particular sampling event (79, 81). Based on these data, the probability of inclusion can be estimated. Thereby TLS approximates probability sampling. Limitations of TLS includes that it may be difficult and time consuming to list and include all the venues that MSM visit. Those not attending the venues included in the sampling frame are excluded (59).

Respondent driven sampling

Respondent driven sampling (RDS) is an extended form of chain referral sampling within a social network of the population of interest (61). The method was developed with the target to increase response rates by using peer recruitment and giving incentives (61, 82). RDS starts by selecting a few persons (usually five to fifteen) who fit the study population criteria and invite them to participate, these persons are called 'seeds'. Efforts are usually made to have a diverse set of seeds regarding characteristics that are important in the study population. For example, in MSM studies it can be of value to have seeds of different sexual orientation (gay, straight, bisexual) (83, 84).

After having participated in the study, the seeds are given a certain amount (usually three) invitations coupons to the study to give to friends who fit the study inclusion criteria. To let participants invite peers themselves removes some privacy concern when studying a partly stigmatized population such as MSM (61). The restricted number of invitation coupons enables the recruitment process chain to reach far into the social network, finally reaching individuals with few social contacts (76).

Participants are reimbursed for time spent or given a small economical incentive to participate in the study themselves. In addition, they are given the same economical incentive for each friend they successfully recruit who participates in the study (76). This process has

been shown to create a long recruitment chains and a high response rate. The invitation coupons contain a serial code, which makes it possible to follow the recruitment chain i.e. who recruits whom in the sample.

Every participant is asked for their number of contacts or size of her/his personal network, which is also called 'degree' (85). The personal network size is used to establish a participants probability of being included i.e. it reflects upon the number of people within the study population that could invite the participant to the study. Participants with large social networks are oversampled and participants with small social networks are under sampled in RDS. To establish the social networks size or degree for each study participant allows adjusting for this differential in sampling probability. Common questions asked to measure participants network size are:

'How many persons do you know who fulfil the study population criteria of ...?' or

'How many friends who also fulfil the study population criteria would you invite to participate in this study if there was no limitation?'

Proportion estimates can be calculated using the RDS estimator called RDSII according to the formula below (85).

$$\hat{P}_{A} = \left(\frac{n_{A}}{n}\right) \left(\frac{\hat{\delta}_{U}}{\hat{\delta}_{A}}\right)$$

Where n_A is the number of individuals with characteristic A, n is the total sample size, $\hat{\delta}_U$ is the mean degree of all individuals in the sample and $\hat{\delta}_A$ is the mean degree of individuals with characteristic A in the sample.

Recently a new RDS estimator has been suggested, RDSI^{ego} (86). To increase the accuracy of the degree, respondents are also asked regarding the composition of their personal network. For example, *'What proportion of your friends live in the same city as you?'* Such questions can only be applied to information participants know about their friends, thereby hidden behaviours may be difficult to include. Simulations of networks and empirical data among female sex workers in China show that this estimator is robust to variations in the network and preference in peer recruitment, leading to less bias in estimates (87).

It has statistically been shown that the RDS proportion estimates are unbiased when certain assumptions, called the RDS criteria are fulfilled:

- (i) Relationships are reciprocal, i.e. there is the same chance of A recruiting B as of B recruiting A.
- (ii) The network forms a single component i.e. each individual in the study population has a chance of being invited.
- (iii) Respondents can accurately report the size of their social network, degree.
- (iv) Sampling of peer recruitment is done with replacement i.e. a study participant can participate more than once.
- (v) Each participant recruits one peer from his/her friends i.e. only one invitation coupon is distributed to each study participant.
- (vi) The peer recruitment is a random selection among all the participant's friends.

If these assumptions are fulfilled the sample composition will converge to a stable level, usually referred to as equilibrium, of proportions of key characteristics of study participants that is independent from the characteristics of the seeds (85). Distribution of key variables such as sociodemographic variables will remain stable when recruiting additional participants after equilibrium has been reached. Thereby sample calculations in RDS studies are usually not performed, rather recruitment continues until additional recruitment waves do not change the composition of the sample (85, 88). Variance in RDS estimates can depend on the structures of the social network the RDS process samples within. If there is a high degree of homophiliy, i.e. participants are connected with participants who are similar to themselves, variance will increase (89). Weak connections between different parts of the social network can also produce a high variance in estimates (90).

In real life implementation of RDS the RDS criteria may not always be met (90-94). Reciprocal relationships are usually not established or measured (i). Accurately reporting network size may be difficult for participants (iii) (95). Sampling is usually conducted without replacement thereby each respondent is only allowed to participate once (iv). It's common to use more than one invitation coupon, usually three (v). Study participants who receive an invitation coupon may be more likely to recruit a close friend rather than choosing randomly among all friends within the social network, particularly if the study touches upon a sensitive topic such as sexual behaviour (vi) (86, 91, 96, 97). Due to these differences, it has been recommended to report data regarding the six RDS criteria in RDS studies (98).

Violations of the RDS criteria have been reported to affect the population estimates in different ways (89, 99). Bias can be expected to be large if the network is directed or if participants invites friends / peers based on characteristics that are related to the study outcome (100). RDS in a dense network reduces variance, while variance increases if participants choose to invite close rather than distant friends. However, RDS simulations on social networks report that sampling without replacement, low response rates and some error in the reported network size, degree, does not affect the population estimates to a large extent (87, 94, 100).

RDS has been shown to be successful in recruiting so called 'hard to reach populations' due to stigma, such as part of the MSM population, and additionally creating high response rates (61, 76, 83). These factors are both very valuable features of a sampling method particularly developed to study hidden groups.

RDS has been implemented online as web-based respondent driven sampling (WebRDS). Online sampling can cover large geographical areas. In addition, costs are decreased in online compared to real life implementation. The online forum also provides privacy and convenience for the participant who can participate at their own chosen time and place. WebRDS has been implemented among students at Cornell University in the US, Facebook users in the US, and the general population in Thailand and the Netherlands, for different study purposes (92, 101-104). In addition, WebRDS has been implemented among MSM in Vietnam to study sexual risk behaviour for HIV and recruitment worked well among Internetusing MSM (105). WebRDS is a promising way to reach MSM for studies on sexual risk behaviour. However, like all online methods it is limited in the sense that you cannot easily collect biological samples to estimate HIV or STI prevalence..

3 AIM AND OBJECTIVES

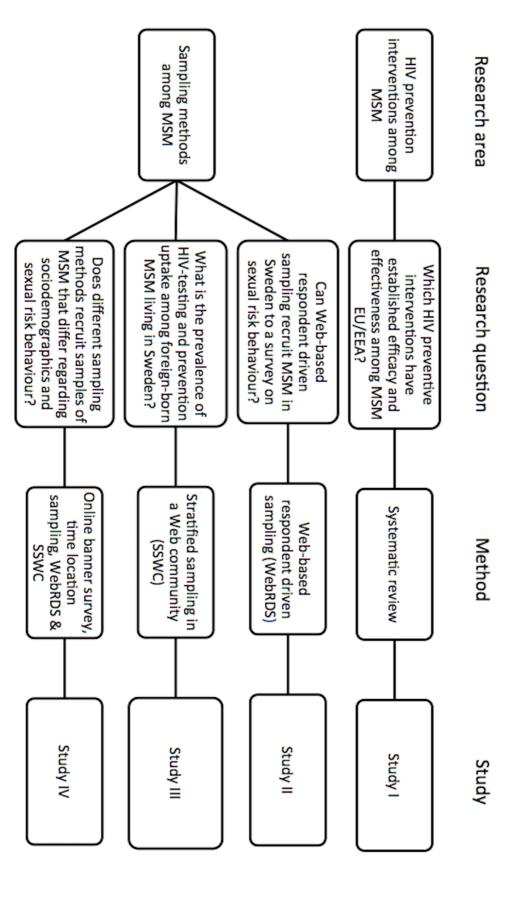
Overall Aim of the PhD thesis

To systematically gather and review evidence for HIV preventive interventions among men who have sex with men in the European Union and European Economic Area, and to test and evaluate different sampling methods to study sexual risk behaviour among Men who have Sex with Men (MSM).

Specific Objectives

- 1) To gather and review systematically studies on HIV prevention interventions among MSM in relation to implementation data from the European Union and European Economic Area (Study I)
- 2) To implement Web-based Respondent Driven Sampling among MSM in Sweden to analyse sexual risk behaviour (Study II)
- 3) To examine HIV testing and prevention uptake among foreign-born MSM living in Sweden (Study III)
- 4) To compare and analyse similarities and differences in sociodemographics and sexual risk behaviour among samples of MSM participants recruited by four different sampling methods used in Sweden (Study IV)

STUDY MATRIX



4 METHODS

OVERVIEW OF STUDY DESIGN

The studies presented here first evaluate the evidence for HIV prevention interventions for MSM and implementation data thereof from the European Union and European Economic Area by performing a systematic review and applying the Highest Attainable Standard of Evidence framework. Different sampling strategies were used to examine sexual risk behaviour among MSM living in Sweden. The focus is on implementation and evaluation of the web-based sampling methods WebRDS and stratified sampling in a Web-community, both new and innovative strategies. Finally, four samples of MSM recruited through WebRDS, stratified sampling in a Web community, time location sampling and online banner survey sampling, are analysed regarding similarities and differences.

4.1 SYSTEMATIC REVIEW METHODOLOGY (STUDY I)

The objectives of this review was to identify and describe studies evaluating the efficacy and effectiveness of HIV prevention interventions among MSM in relation to implementation data from the European Union and European Economic Area. The gathered evidence was graded according to the Highest Attainable Standard of Evidence (HASTE) framework as described in table 1 (106). The review was performed to inform the development of a guidance on this topic by the European Centre for Disease Prevention and Control (ECDC) (1).

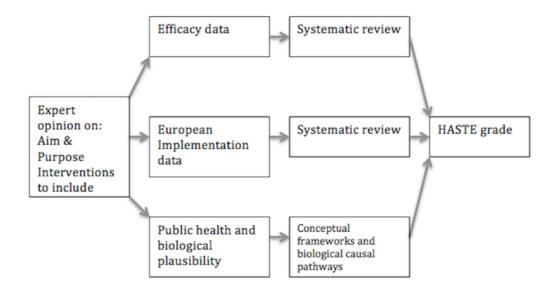


Figure 5. Work process for the systematic review of HIV preventive interventions among MSM

Table 1. Highest Attainable Standard of Evidence System for HIV Interventions (HASTE). Modified from Baral et al (48)

HASTE grading level		Strength of Recommendation	Explanation
Grade 1		Strong	 High plausibility Efficacy is consistent Large body of consistent implementation data
Grade 2	Grade 2a	Conditional - Probable	 Plausibility Limited efficacy data Consistently effective from implementation data
	Grade 2b	Conditional - Possible	 Plausibility Limited or inconsistent efficacy data Limited or paucity of implementation data*
	Grade 2c	Conditional - Pending	PlausibilityOn-going efficacy trials
Grade 3		Insufficient	 Undefined plausibility Inconsistent data Inconsistent or paucity of implementation data
Grade 4		Inappropriate	 Consistent data demonstrating lack of efficacy Consensus from implementation data of inappropriate intervention

Systematic review process

We started out by making a comprehensive list of known interventions which address primary HIV transmission among MSM (Appendix I). We aimed to capture biomedical, psychosocial, and programmatic interventions for the umbrella review. This process included consulting an expert review group gathered by ECDC, which included medical, social science

and policy experts, programme implementers from non-governmental organizations and government representatives.

A systematic review was then performed for each intervention included. The Population, Intervention, Comparison, Outcome (PICO) model was used to develop inclusion criteria and search terms per intervention (107). The population for the intervention was MSM as defined earlier in this thesis. All types of comparison and studies without a comparison were included. Outcomes included were biological such as prevalence and incidence of HIV, self-reported diagnoses of HIV infection and self-reported behavioural outcomes on condom use or UAI. Previous systematic reviews performed on these topics were included. Implementation studies were only included if performed in European setting. Non-peer reviewed literature was not included, however guided further searches for literature.

Electronic searches were performed in PubMed, Embase, Medline, Cinahl, Psycinfo, the Cochrane library and the World Health Organization publication database. The search included medical subject headings (MeSH) terms for HIV or AIDS, and terms associated with MSM and the specific interventions reviewed. Searches were performed between 10 December 2012 and 8 February 2013 (Appendix II).

Titles of articles located through the search process were screened independently by myself and another researcher to exclude those who did not fit the inclusion criteria. For titles deemed relevant, the articles abstract was reviewed and included if the study met the inclusion criteria. When it was unclear from the abstract whether or not the inclusion criteria was met, the full article was reviewed.

A pre-designed form that included details on individual study design, methods of recruitment, sampling frame, sample size, location, response rate, analysis performed, results, confounders, and reported outcomes was used for data extraction from the included studies. Then a critical appraisal using a checklist approach to assess the quality and methodology of each individual study was performed (108). The appraisal was performed independently and in parallel by myself and another researcher to ensure consistency and that nothing was missed. The data was compiled per intervention and then reviewed by myself, another researcher and a senior researcher.

Implementation studies were, when data was available, appraised for availability, acceptability, uptake, feasibility of implementation, implementation costs, and effectiveness of the intervention among MSM in the European setting.

We reviewed the gathered evidence per intervention according to the HASTE grading framework. First I and another researcher independently graded the interventions. Then a senior researcher reviewed the grading. Discrepancies were discussed within the team of coauthors. Biological and public health plausibility was determined through a process of discussions within the team of co-authors.

4.2 WEB-BASED RESPONDENT DRIVEN SAMPLING (STUDY II)

WebRDS had prior to this study been implemented among MSM in Vietnam and worked well to recruit a sample of MSM online (105). The method holds promise to overcome some challenges when aiming to study a 'hidden' population such as providing a high sense of confidentiality and convenience for study participants. Based on this, we sat out to implement the WebRDS sampling method for the first time among MSM living in Sweden to study Internet use and sexual risk behaviour for HIV.

Formative studies

I started out by interviewing key persons within the MSM community regarding the social network structure and Internet behaviour within the MSM group. Key informants were accessed through a collaboration with the Swedish Foundation of LGBTI Rights in Stockholm (RFSL Stockholm). In addition, I spent time observing activities on Sweden's' and Scandinavia's' largest LGBTI Web community that is called Qruiser and is owned by the QX publishing house (109), from hereon referred to as the Web community. This enabled me to understand the context, social networks, dating, finding new sex partners and how quick hook-ups for sex took place on the Web community. From this formative research we concluded that there seemed to be a well-connected social network of MSM online. Thereby, WebRDS may have potential to work as a sampling method within this population.

Study design and population

The study population of MSM was defined as reporting being a man, 15 years old or older (as this is the legal age for when consenting individuals may engage in sexual acts in Sweden), having had any type of sex including oral sex or fondling with another man (110). In addition, participants were required to have an email address to be able to recruit peers in the WebRDS software.

The study is of cross-sectional design and the survey was implemented online from July 11, 2012 to January 21, 2013.

Web survey

The survey consisted of a questionnaire developed taking into account previous Swedish and international studies on this topics among MSM (111-113). We applied the experiences from the WebRDS team's work in Vietnam when designing the survey and aimed to develop an easy to answer survey that would take about fifteen minutes to complete (105). The final survey was available in Swedish and included modules on sociodemographic information, number of sex partners and sex partners for UAI, and Internet use (Appendix III).

The personal network size of individuals was estimated by asking the question:

"How many MSM who are 15 years or older, would you like to invite to this study by the described online recruitment process, if possible to invite more than four?"

In addition, participants were asked how many persons who fit the study criteria they had been in contact with online during the last seven days. The online survey and WebRDS recruitment webpage was piloted with ten key informants. These key informants were of different age (15-25, 25-35, 35-55, >55 years old) and represented a diversity of sexual orientations. The key informants evaluated the web survey and the time it took to participate to ensure user-friendliness and appropriate questions. Some improvements were implemented to ensure that it was user-friendly.

WebRDS recruitment

The same WebRDS software that was used in the Vietnamese study among MSM was used both to implement the web survey and WebRDS recruitment process (105). All communication between the survey webpage and the data server was encrypted.

The recruitment started with thirteen seeds that were identified through the collaboration with the Swedish Federation for LGBTI Rights (four seeds) and through online recruitment of MSM members on the Web community (nine seeds). Two different strategies of recruitment of seeds were used to try to capture diverse seeds (84). To reflect the diversity within the MSM population the seeds were selected from different age groups (15-25, 25-35, 35-55, >55 years old), sexual orientation (homo-, bi- sexual, transgender) and place of residence (urban or rural county). On the Web community seeds were recruited by sending an invitation message to the most recent member who logged in on July 11, 2012 per county of residence, registered as being male and looking for men. Nine Web community members responded positively and were selected as seeds. These seeds represented different age group and reported living in different counties. The seeds were informed regarding the study and the

function of them as seed participants. Invitations to participate were sent via email or message in their Web community inbox including a unique link. The link took them to a web page where the study information was repeated and they could give their consent to participate by an active click that took them to the web survey.

After having answered the web survey, participants were invited to recruit friends / peers via email messages. Each participant could recruit a maximum of four peers. At the last page of the web survey participants were asked to enter their email address. Four recruitment emails with four unique links to the web survey were sent to this email address. Seeds could either forward these invitation emails to friends / peers, or copy the link and send through the online media of their preference (Web community, chat, Facebook, smart phone).

An unexpected server failure took place on August 23 which interrupted the WebRDS and web survey until September 20, 2012. Participants were informed about the server failure when they tried to reach the web survey. In addition, the most recent participant in each recruitment chain was sent an information email. When the server was functioning again, one month later, new invitation emails were sent to inform the last person that participated in the recruitment chain that it was possible to recruit and participate An additional sixteen seeds were invited on September 20, 2012 and another eight seeds on November 2, 2012. These seeds were invited via the Web community, using the same procedure as described previously, and represented a diversity of age groups and counties of residence in Sweden.

Incentive for participation

Participants were offered an incentive to participate and to recruit friends to participate. Participants were given a gift certificate for one month of the highest standard of membership at the Web community (monetary value of approximately 4 USD in 2012). This may be a rather low economical value for an incentive in a high-income setting such as Sweden (88). However, key informants evaluated the incentive to be attractive and suitable for diverse subgroups of MSM.

Data cleaning

In total, 148 participants answered the survey through the WebRDS software program. Double participation was identified through duplication of email addresses and eighteen participants were removed. Participants were further excluded due to not fulfilling the inclusion criteria, four reported being a woman and two reported never having had sex with a man. Respondent who answered the web survey very quickly, in less than three minutes,

were excluded due to that it was deemed infeasible to read and answer the questionnaire in such short time frame. One participant was removed for this reason. Seeds were included in the sample. A total sample of 123 participants remained. Seeds were included in the sample.

Analysis

RDS estimates were calculated using the RDSII estimator and a design effect of 2 (85). Both the data and RDS estimates are reported in study II (98). We evaluated the sampling process regarding if the sample composition stabilized with increasing number of participants. We aimed to analyse equilibrium by the criteria in the RDS literature, however our recruitment process did not fulfil these (85). Therefore, we compared the achieved sample with and without the last 40 respondents to see if the sample composition was still changing.

In order to strengthen our decision to include seeds in the final sample for analysis we have performed the analysis with (n=123) and without (n=90) the eligible seeds included. As shown in the table below this did not contribute with any major difference in results

Table 2. The Web RDS participant sample with and without the seeds included

Variable	Covariate	Mean /proportion	Mean /proportion
Age		32.06	30.31
Nationality	Swedish	0.86	0.90
County of residence	Stockholm county	0.25	0.26
Education	Tertiary	0.29	0.24
	Secondary	0.51	0.58
	Vocational training	0.12	0.11
	Primary (grade 1-9)	0.08	0.07
Occupation	Unemployed	0.21	0.24
Sexual orientation	Homosexual	0.75	0.76
	Bisexual	0.23	0.22
	Heterosexual	0.03	0.03
	Asexual	0.02	0
	Don't know	0.03	0.03
Network size	Reported number of MSM possible to invite	31.03	31.59

4.3 EXAMINATION OF HIV TESTING AND PREVENTION UPTAKE AMONG FOREIGN-BORN MSM (STUDY III)

According to Swedish national surveillance data foreign-born MSM living in Sweden are a part of the MSM population that have a higher risk of HIV, therefore this group is of particular interest to study (114). To understand HIV-testing and prevention uptake is of interest to improve these services for foreign-born MSM.

The Public Health Agency of Sweden in collaboration with the Karolinska Institutet performed this study of sexual risk behaviour among MSM as part of national HIV surveillance in Sweden in 2013. Stratified sampling in a Web community was used to invite participants.(115). The Web community for LGBTI previously mentioned has a member registry that served as the sampling frame (109). Thereby this sampling procedure can only capture those MSM and those foreign-born MSM who are members of the Web community.

This study analyses the sub-sample of foreign-born MSM within this larger study. The sampling method was not designed to capture foreign-born MSM specifically, rather MSM in general. The stratified sampling approach is not taken into account in the analysis, rather the raw data is presented. The motivation for this choice is that we do not know to what extent foreign-born MSM are represented in the chosen sampling strata of age and county of residence on the Web community. In addition, we cannot account for systematic non-response of foreign-born MSM.

Study design options when aiming to study foreign-born MSM

Foreign-born MSM living in Sweden represents a heterogeneous group and are not likely to be interconnected in one social network, rather they are part of a larger network of MSM and form diverse sub-groups within this network. Therefore RDS could probably capture sub-groups of foreign-born MSM or could be performed to capture a specific sub-group such as for example Latino MSM if a well connected social network exists. A RDS study among Central and East European foreign-born MSM in London report difficulties in RDS recruitment that that might be due to that this group was not be well-connected in the study setting, which indicates that RDS may not be suitable for some groups of foreign-born MSM (116).

Study design and population

This study is of cross-sectional design and took place online between October 1 and 30, 2013. The Web community member registry was used as sampling frame (109). Being registered as

living in Sweden, 15 years or older and not being registered as a woman defined Web community members' eligibility for the study. Thereby a sampling frame of 52 979 Web community members was established.

Stratified sampling was performed by the age strata of 15-25, 26-35, 36-46, 47 and above years old. In addition, the 21 Swedish counties were used as strata. The stratified random sampling procedure then selected 14 514 Web community membership registered that met the eligibility criteria. Invitations were sent via a message to their inbox at the Web community site with an active link to the web survey. Out of those invited, 2751 participated in the web survey. Thereby producing a response rate of 19%. Out of the participants, 289 reported being born abroad. Forty-five of these were adopted and were excluded as they were not expected to share the experiences of foreign-born migrants. Thereby this sampling strategy provided a sample of 244 MSM participants born abroad and living in Sweden. This sample of participants was included in the data analysis.

Web survey

The web survey was developed by a multi-disciplinary team including researchers, representatives of the Swedish Public Health Agency and different NGO's representing the MSM community. Previous Swedish study questionnaires were taken into account (111-113). In addition, efforts were made to include the same sociodemographic variables as in study II to ease a comparison. The web survey included modules on sociodemographics, condom use, sexual risk behaviour, HIV/STI-testing and experience of HIV/STI prevention interventions and programmes. The final web survey was piloted with eleven MSM informants to ensure appropriateness, simple language and user-friendliness.

Analysis

The achieved sample of 244 foreign-born MSM is treated as a convenience sample in the data analysis. Descriptive data analysis was performed. The chi-square and t-test was used regarding socio-demographic, sexual identity and practice variables, HIV/STI-testing and experience of HIV/STI preventive interventions. The main outcome variable was defined as having tested for HIV within the past 12 months. Eighteen variables were analysed with univariate logistic regression and t-test to identify factors associated with the outcome. Collinearity test led to that one variable, living with HIV, showing a variance inflation factor of >10 was excluded. No significant interaction was found between the included variables. The variables with a p-value under 0.05 were included in the final model for multivariate logistic regression analysis.

4.4 EVALUATION OF SAMPLING METHODS USED TO STUDY SEXUAL RISK BEHAVIOUR AMONG MSM (STUDY IV)

Between 2010-2013, four different sampling strategies were used in Sweden to study sexual risk behaviour among MSM; online banner survey sampling, TLS, WebRDS, and stratified sampling in a Web community (SSWC). This study aims to analyse the samples of MSM achieved by the four different sampling strategies regarding similarities and differences regarding sociodemographics and sexual risk behaviour.

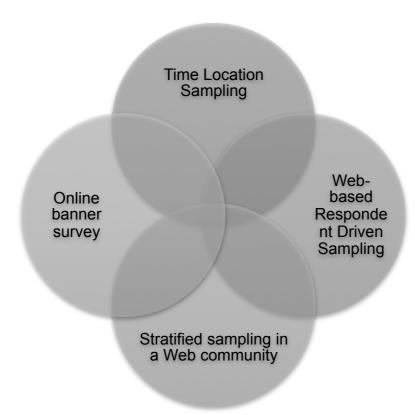


Figure 6. The different sampling methods used to study sexual risk behaviour among MSM may recruit samples of participants that have similarities and differences. In addition, there may be some overlap between samples.

Data collection methods and analysis

The European MSM Internet Survey (EMIS) web survey was implemented using online banner survey sampling from the 4th of June to the 31st of August 2010 (117). A convenience sample of over 180 000 men answered the EMIS questionnaire online, of which 3089 resided in Sweden and were included in this analysis. The European study Sialon II was implemented using TLS in identified MSM venues in Stockholm between May 11 to August 16, 2013. The WebRDS study is described previously in this thesis,

under study II. The MSM survey in Sweden that used SSWC is described previously in this thesis under study III.

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Analysis

Analysis was described and performed for socio-demographic variables, sexual orientation, and sexual risk behaviour for HIV/STI variables. TLS estimates were analysed as a two-stage sampling procedure using a weighting procedure based on the inverse of the probability that a person was sampled. RDS estimates were calculated using the RDSII estimator and a design effect of 2. The survey using stratified sampling in a web-community applied stratified sampling with unequal probability of inclusion by age and county of residence, which was adjusted for in the analysis. In addition, estimates were adjusted for non–response with inverse probability of weighting for each age and county of residence strata when analysing data.

4.5 ETHICAL CONSIDERATIONS

The utmost measures were taken to protect the individuals in the studies II, III and IV from identification so as to keep their anonymity. Participants were given clear information on all aspects of the study before deciding on whether they should participate in the study or not. All participants gave their consent to participate in the study. In the web surveys applying webRDS, stratified sampling in a Web community and banner survey consent was given online by an active click, saying yes to participate. Participants could skip any part of the study or question at any time. Participants had the possibility to end the study at any time point and thereby opt out of the study altogether. Data was then deleted and not included in the studies.

The WebRDS survey included a log out button to provide a quick exit. This button removed the survey from the computer. The WebRDS study web page provided detailed information on how to delete browser history. The unique links to the web survey in the invitation messages to the study could only be used from one computer at the time. If inactive, the web survey logged out after ten minutes. Data traffic and storage was encrypted to ensure data safety. In Study II and III, the study information web page was designed to give detailed study information in a positive and informative manner. In Study II, III and IV no personal identifiable data such as personal identification number or full name was collected. In study II, the WebRDS participants were given the option to give their email address. An email address could represent a type of personal identifiable data, but participants could also choose to keep their anonymity by using a temporary email address created only for this study purpose.

No person was coerced or put under pressure at any time of the data collection. All interactions with participants were designed and performed with utmost respect given to the individual. Collected data were kept on one pass word protected computer in a pass word protected file. In addition a backup was kept on a hard drive in locked facilities at the Karolinska Institutet.

5 RESULTS

5.1 SYSTEMATIC REVIEW FINDINGS

Main finding

The HIV prevention interventions condom use, peer outreach, peer-led groups, and using universal coverage of antiretroviral treatment and treatment as prevention were found to be strongly recommended as HIV prevention interventions for MSM. In total, 24 interventions were reviewed and 15 interventions were graded to be strongly, probably or possibly recommended according to the HASTE grading framework. A paucity of implementation data from the European Union and European Economic Area was found for most interventions.

Interventions assigned a strong recommendation, HASTE grade 1

For four interventions quality data was available to support a strong recommendation. Condom use, peer outreach, peer-led groups, and using universal coverage of antiretroviral treatment and treatment as prevention all held high plausibility, consistent efficacy data and implementation data.

Interventions assigned a probable recommendation, HASTE grade 2a

Four interventions were assigned a probable recommendation, fulfilling the criteria of plausibility, limited efficacy data and consistently effective implementation data. Voluntary counselling and testing for HIV, using condom-compatible lubricant, using post-exposure prophylaxis (PEP), and individual counselling for MSM living with HIV were assigned a probable recommendation.

Interventions assigned a possible recommendation, HASTE grade 2b

For the seven interventions; individual counselling for MSM, peer-led group interventions targeting MSM living with HIV, Internet-based HIV prevention messages, interventions in sex-on-premises venues, social marketing interventions, pre-exposure prophylaxis (PrEP) and voluntary medical male circumcision, a level of possible recommendation was found. All these interventions demonstrated plausibility, however limited or inconsistent efficacy data and limited or paucity of implementation data.

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Interventions assigned a pending recommendation, HASTE grade 2c

A pending recommendation was assigned to five interventions, including training for health care providers to offer comprehensive care for MSM, MSM-competent health clinics, voluntary anonymous partner notification, campaigns for Lesbian, Gay, Bisexual and Trans equality; and female condom use for anal intercourse. For these interventions plausibility was established and there were on-going efficacy trials.

Interventions assigned an insufficient recommendation, HASTE grade 3

An insufficient level of evidence was found for the four interventions; sero-sorting, to avoid taking semen in the mouth/unprotected oral sex, to avoid use of poppers at UAI and to avoid alcohol binge-drinking. These interventions were assigned an undefined plausibility, inconsistent efficacy data and inconsistent or paucity of implementation data.

5.2 EXPERIENCES FROM IMPLEMENTATION OF WEBRDS AMONG MSM

Main finding

The WebRDS produced a sample of 123 eligible participants, who all reported sexual risk behaviour for HIV during the last 12 months. Recruitment was initially rapid, however after a server failure it was slow. Future studies need to further improve and evaluate the WebRDS method.

WebRDS recruitment process

The recruitment chains varied in length between one to nine waves. The sample of eligible participants is composed of seventeen recruitment chains with at least two connected respondents. In addition, 41 isolated respondents due to exclusion of their links according to the exclusion criteria or being a seed and not recruiting additional participants. Three recruitment chains reached more than three waves. Two seeds and five participants were successful at recruiting the maximum of four friends / peers. Out of the 123 eligible participants 33 were seeds.

Initially the recruitment process was active, recruiting two thirds of the final sample during the first 47 days of recruitment. However, after the server failure recruitment was slow. Ten out of the thirteen recruitment chains that were interrupted by the server failure did not start again after being re-invited. The three recruitment chains that did start recruiting after the server breakdown, recruited in total six more respondents.

To analyse to what extent the sample composition was still changing at the end of the recruitment process, we compared the WebRDS sample with and without the last 40 respondents. A change in proportion between the sample with and without the last 40 respondents showed a change of 0.02 of MSM living in Stockholm, 0.03 having a university education, 0.025 being unemployed, and 0.002 in having a Web community gold membership was found. Numeric change between the sample with and without the last 40 respondents for age was 2.5 and for average personal network size 0.23.

Characteristics of study participants

The mean age among participants was 32 years, with a range from 19 to 73 years old. About half of the respondents (51%) had finalized secondary school and 28% had university-level education. Participants reported residence in the 18 of Sweden's 21 counties, reaching MSM in rural areas with low population density. The majority (75%) reported being homosexual and about a fifth reported being bisexual. The majority (60%) of participants checked their email once or more per day. Web community membership was common and 79% reported having at least one member profile registered.

Sexual risk behaviour for HIV among participants

All respondents reported having had UAI with at least one regular and one casual sex partner during the last 12 months. On average participants reported having had UAI with three casual sexual partners during the past year. The average of male casual sex partners was seven during the past year.

5.3 HIV TESTING AND PREVENTION UPTAKE AMONG FOREIGN-BORN MSM

Main finding

About half (45%) of participants in this study had tested for HIV during the last twelve months. 20% of participants had never tested for HIV. Participants who had lived in Sweden less than or equal to five years were more likely to have tested for HIV during the last 12 months. Having talked about HIV/STI with a prevention worker in the last year was associated with having tested for HIV. In addition, having had a STI-test during the last 12 months was associated with having had a HIV-test in the same time frame.

Sociodemographics of participants

The median age among participants was 36 years, with the youngest being sixteen years and oldest participant being 73 years old. Over half (57%) had tertiary education and three participants had not completed lower secondary school. The majority (67%) held an employment and 16% were students.

Median time spent living in Sweden was 15 years, ranging from less than one year to 58 years. Over half (57%) held Swedish citizenship and 25% held a permanent residency permit. One participant was in the process of seeking asylum at the time they answered the survey. The majority of participants (68%) were born in Europe, a fifth were born in Asia (20%), about a tenth in South America (11%) and North America (9%) respectively, and around 1% in Africa.

Sexual identity and behaviour among participants

The majority (64%) identified as homosexual and about a fourth (23%) as bisexual. Half (50%) reported being single, 35% were in a relationship with a man and 10% with a woman. The median number of sexual partners during the last twelve months was four. About a fourth (26%) reported having had sex with both men and women during the last twelve months. Frequency of male partners for UAI was on average 2, and the median was 0.

HIV/STI testing and prevention service experience among participants

Close to half (45%) had tested for HIV during the last twelve months. A fifth reported never having tested for HIV. Self-reported HIV prevalence among participants was 4%. The majority (88%) felt certain regarding their HIV serostatus, while 11% reported being uncertain. Almost a fifth (17%) reported not knowing where to access HIV testing. Among those who had never tested for HIV, the most common reason given was that 'I've never thought of it' or due to perceiving that 'I don't take risks'. A fifth of those never tested reported that they don't know where to access HIV-testing. 2% reported having been denied a HIV-test by health personnel. Having tested for STIs during the last twelve months was reported by 37% of participants. A third reported never having tested for STIs. During the past twelve months most participants reported having read online (66%) and / or printed information (54%) on HIV/STI. Half of participants had received free condoms and about a third had talked about HIV/STI with a prevention worker in the same time period. The majority (76%) of participants requested rapid test for HIV. In addition, the majority wanted easily accessible condoms and lubricants in places where MSM meet (76%). Other requested services included; anonymous HIV-testing, MSM-friendly clinics, HIV/STI testing outside of the health care setting, vaccination for hepatitis A, B and HPV and the possibility to have condoms and lubricants sent via mail. Over half requested (58%) web-based HIV/STI information.

Associations with having tested for HIV during the past twelve months

In univariate logistic regression analysis the following variables were found to be significantly associated with having tested for HIV during the last 12 months: having lived in Sweden less than or equal to 5 years (OR 1.87, 95%CI 1.04-3.36), knowledge of where to test for HIV (OR 2.21, 95%CI 1.03-4.74), having had other STI-tests than HIV in the last 12 months (OR 18.94, 95%CI 9.31-38.54), talked about HIV/STI with a prevention worker in the last 12 months (OR5.33 95%CI 2.94-9.65), received free condoms in the last 12 months (OR 2.23, 95%CI 1.30-3.82), read online about STI/HIV in the last 12 months (OR2.56, 95%CI 1.42-4.60), read printed information about HIV/STI in the last 12 months (OR1.86 95%CI 1.09-3.19). After multivariate adjustment three variables remained significantly associated with the outcome; having lived in Sweden less than 5 years (aOR 3.39 95%CI 1.49-7.73), having tested for other STIs than HIV in the last 12 months (aOR 26.54 95%CI 10.49-67.19) and talked to a HIV/STI prevention worker in the last 12 months (aOR 4.10 95%CI 1.68-9.97).

5.4 DIFFERENCES IN SAMPLES OF MSM PARTICIPANTS

Main finding

The four different sampling strategies used to study sexual risk behaviour for HIV among MSM in Sweden captured samples of MSM that differed regarding socio-demographic characteristic and sexual behaviour. Particularly, large discrepancies on reported sexual risk behaviour were found in the different samples of MSM.

Sociodemographics of respondents

TLS and WebRDS achieved sample populations with a mean age of 33 and 32 years old respectively. The banner survey and stratified sampling in a web-community both reached an on average older sample population of MSM with the mean age of 37. The majority of the samples had a secondary or tertiary education. Tertiary education differed to some extent between the samples. More than half of the banner survey sample was comprised of men with a tertiary education, as compared to slightly more than a quarter (27%) in the WebRDS sample. Unemployment varied from 6% in the banner survey to 15% in the WebRDS sample. TLS reached a sample of MSM with a large proportion of foreign-born MSM (28%). While WebRDS and the banner-survey both reached populations with about a fifth born abroad. SSWC reached 15% born abroad. Regarding residence in non-urban counties, 42% of the WebRDS sample, 35% of the SSWC sample and 27% of the banner survey sample reported living in counties other than the three large urban areas in Sweden.

Sexual identity, behaviour and HIV/STI-testing among respondents

In the banner survey, TLS and WebRDS participant samples some 76-79% of participants identified as homosexuals, while in SSWC less than two thirds identified as homosexuals.

All respondents in the WebRDS reported more than one sexual partner during the last 12 months. This differed from the other studies, where 12% of the TLS sample, 9% of the online banner survey sample and 4% of the stratified sampling in a Web community reported not having had any sexual partner during the last 12 months. Further all WebRDS participants reported UAI with a casual male sex partner during the last year, while the majority of the other samples had not engaged in UAI with a casual male sex partner. The proportion of sample participants reporting having had UAI with 2-5 casual male sex partners during the

last 12 months differed somewhat, between 13-18% in the three web survey participant samples. The TLS study measured the number of casual male sex partners for UAI during the last 6 months, and a fifth of participants reported UAI with one partner and about a sixth reported UAI with 2-5 casual male sex partners during this time period.

A slight difference in the percentage of participants reporting living with HIV were found, reaching from 2% in TLS to 5% in the banner survey sample. HIV testing frequency differed as well, with 61% of the TLS sample, 43% of SSWC sample and 30% of the banner survey sample reporting having been tested for HIV during the last 12 months.

STI testing during the last 12 months was somewhat lower in the online banner survey and SSWC participant samples compared to the TLS participants, among whom the same proportion (61%) had tested both for HIV and STIs. Lower STI testing rates were reported in the SSWC sample (37%) and online banner survey sample (38%). The highest proportion (19%) reporting having been diagnosed with an STI during the last 12 months was found among TLS participants. While a tenth of the SSWC sample and a twentieth of the banner survey sample reported having had an STI during the last 12 months

6 DISCUSSION

Future directions of evidence-based HIV prevention among MSM

The systematic review findings are consistent with the 2010 World Health Organization systematic review that used the GRADE framework (120). There are synergies and dependency between the recommended interventions, therefore combining interventions into programmes is desirable for HIV prevention among MSM (121). For example, an HIV-testing service may achieve high uptake when implemented in combination with peer outreach and social marketing. The delivery modes that were evaluated to be recommended include peer-led interventions, outreach activities and group intervention programmes, supporting findings from a previous World Bank literature review of HIV prevention services for MSM in low and middle income countries (6).

Antiretroviral treatment prevention strategies rely on HIV-testing

Scaling up ART is a most important target both for HIV prevention and for health among MSM living with HIV as according to the World Health Organization guidelines (122). In order to do so, HIV-testing is a key intervention. Thereby antiretroviral treatment prevention strategies rely on behavioural prevention strategies to increase HIV-testing (121). Between 38-61% of MSM participants in study IV had tested for HIV within the last year, indicating a need for increased access to and uptake of regular HIV-testing linked to ART and care among MSM living in Sweden. A scale-up of the preferred services among foreign-born MSM in study III, rapid test, testing outside of the health care setting, anonymous testing and MSM clinics could facilitate higher uptake of HIV-testing. Social marketing has been shown to increase uptake of testing among MSM in the United States and these strategies could be beneficial to apply to increase uptake of testing in Sweden as well (123).

Sweden is, in most parts, a sparsely populated country relying on primary health care facilities to serve the population as the first point of contact with the health care system. The primary health care system covers all areas of Sweden and could be helpful in scaling up testing for MSM and other risk groups to increase coverage of HIV testing. Rapid HIV test services could be offered by trained staff at the primary health care level with quick referrals of those testing positive to HIV clinics. In addition, geographically strategically located primary health care units could be trained to offer comprehensive care and HIV/STI testing

for MSM. A promising approach has been evaluated in Australia where a study introducing comprehensive HIV/STI testing for MSM by a trained nurse at the primary health care level have shown significant increase in testing rates (124). These add on services at already existing primary health care units would increase access to comprehensive HIV/STI testing for MSM living all over Sweden including rural areas. Implementation of such programmes would need to be evaluated both regarding quality assurance and uptake of services in the target populations.

Since the systematic review presented here was performed confirmatory studies have been reported supporting Pre Exposure Prophylaxis (PrEP) as HIV prevention for MSM in the European setting. Therefore there is a need to update the assigned grading for this intervention, which today would have been assigned a grade 2a for probable recommendation as efficacy data is available, limited implementation data is available and biological plausibility is established (125-129). However, drug approval by the European Medicines Agency for emtricibine and tenofovir disoproxil fumarate (TDF/FTC), brand-named Truvada, to be used as PrEP is still pending thereby limiting the possibility of usage in Europe.

Making PrEP accessible for MSM in Sweden and Europe may contribute to decrease transmission (33, 125, 128, 129). Some MSM participants in all four studies reported a high number of casual sex partner for UAI. If these sex partners are of positive HIV serostatus this would indicate a risk of HIV and a potential benefit of PrEP. MSM living in Sweden that while travelling to other cities or countries, where HIV prevalence is higher, and engage in condomless sex increase their HIV risk at the local sexual network level. This group may also benefit for on demand PrEP use (125).

Post Exposure Prophylaxis (PEP) is available as a part of standard care in Sweden. There may be potential for an increase in uptake by making these services more easily available for MSM (130). In addition information about when to use and where to access PEP can be included in behavioural interventions such as peer education. Studies from Amsterdam and Denmark report low uptake of PEP among MSM and strategies to increase uptake may be relevant for several European settings where PEP is part of standard of care (131-133). As PEP should be initiated as soon as possible after a risk of transmission has occurred, initial treatment could be given at all emergency room units (as already implemented in Sweden) and at primary health care units to enable quick initiation of treatment. The initial treatment may be followed up with referrals to specialised clinics for decision regarding continued PEP and follow-up. Increased correct usage of PEP may also contribute to diminish HIV incidence among MSM.

Online strategies to increase uptake of HIV-testing

The web-based sampling strategies presented here may also be applied for recruiting MSM into online interventions providing information and counselling with referral to the nearest testing site and prevention programme. As the majority of participants in both study II and III reported having used or preferred online information regarding HIV, further development of online prevention seems promising. The next step could include interactive features where the visitor enters information regarding sexual behaviour to enable tailored information on HIV and STI. A pilot study among MSM in Sweden of an Internet-based intervention based on the information-motivation-behavioural skills model report a decrease in number of casual sex partners among participants (134). Smartphone applications also holds promise (135, 136). These applications could provide information regarding the closest facility where you can test for HIV/STI and opening hours based on the person's geographical location. Voluntary anonymous partner notification smartphone applications may also be useful. In addition, information regarding safe sex and where to test could be incorporated in existing dating smartphone applications for MSM.

Peer education and outreach work

Peer outreach work to promote testing, distribute condoms and lubricants, and provide information and counselling may be of advantage particularly to groups of MSM such as foreign-born MSM and MSM visiting sex venues (137). Peer outreach acts as a first point of contact that can offer information and refer to other services, thereby increasing uptake of these services as seen in study III where having talked to a prevention worker was associated with recent HIV-testing among foreign-born MSM.

Implementing and evaluating structural interventions

Structural barriers also limit the effect of HIV prevention programmes by reducing service uptake and compromising the quality of offered services. 38% of European MSM respondents in the European Survey of Lesbian, Gay, Bisexual and Transgender persons conducted in 2012 reported that they have not disclosed their sexual orientation to a health care provider (54). The lack of this information in the counselling process limits the opportunity for MSM-competent health services. Structural interventions aiming to decrease stigma, homophobia and discrimination against MSM may achieve an open climate where

MSM feel safe to disclose and enrol in prevention and treatment programmes more frequently. As these structural changes take place there is a need to evaluate in order to guide future improvements in design and implementation. For example, LGBTI rights will hopefully be improved through structural and policy changes in diverse European settings over the next decade. The opportunity to evaluate the health impact regarding HIV, mental health, and life quality, of these structural changes should not be missed.

Scale-up of prevention among foreign-born MSM

Foreign-born MSM who have recently arrived to Sweden represents a sub-population of people migrating/fleeing to Sweden. As registers of those migrating to Sweden are available this provides opportunities for probability sampling. These registers may also be used to offer this group comprehensive health information and services, which is provided today in parts of Sweden (138, 139). Scale-up of these services are needed and could include sexual health promotion through counselling, information about where to seek HIV/STI testing, treatment and care, being offered HIV/STI-testing and information regarding LGBTI rights and services such as MSM clinics.

Prevention among foreign-born MSM that have lived in Sweden for various amounts of time will benefit from inclusion in HIV prevention programming for all MSM. These programmes may benefit from including culturally sensitive strategies and several different languages used by foreign-born MSM. For example peer outreach in Spanish at venues Latino MSM visit may be beneficial. An evaluation of foreign-born MSM's experience of sexual health clinics in Britain suggests that services needs to be culturally sensitive and also address possible confidentiality concerns (140).

Limitations, challenges and advantages with the HASTE grading framework (Study I)

In this study, a lack of European effectiveness studies was found both regarding new interventions such as implementation of Pre Exposure Prophylaxis (PrEP) programmes and regarding existing interventions such as Post Exposure Prophylaxis (PEP) and voluntary partner notification. The lack of implementation data is a limitation to the systematic review process and also to our understanding on how the reviewed interventions perform in the real life setting. Future evaluations of these interventions would aid in further establishing the evidence base and guide future program implementation.

When designing the systematic review we looked at different ways of evaluating data. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) has been widely endorsed as the most effective methods to grade the current state of evidence of clinical interventions and has informed the development of clinical practice guidelines by the World Health Organization. The GRADE system is built on the traditional hierarchy of evidence (141). The highest quality of evidence is derived from randomized double-blinded controlled trials, followed by unblinded randomized controlled trials, prospective cohort studies, case-control studies, clinical case series and lastly consensus among experts. The GRADE system was developed to evaluate individual level efficacy of clinical interventions by applying the hierarchy of evidence studies and can serve as the basis to evaluate public health interventions as well (141). Public health interventions tend to be context-specific and multifaceted. The existing evidence from randomized controlled trials evaluating public health interventions with biological endpoints for MSM populations are limited (120). Therefore, the GRADE system needs to be complemented when reviewing evidence on HIV preventive interventions among MSM. The HASTE system builds on the GRADE system and was developed specifically to evaluate evidence regarding HIV/STI interventions among most at-risk populations, in particular MSM (106).

The HASTE framework allowed for an inclusive approach to available data and was particularly helpful for highlighting implementation data. In the grading process we spent considerable time on thoroughly discussing the differences between HASTE grade 2a probable, 2b possible and 2c pending- for recommendation. These grades are somewhat overlapping, which requires careful consideration when assigning them. For example, PEP and PrEP holds the same evidence for plausibility. PrEP had at the time limited efficacy data and no implementation data (127). While, for PEP limited efficacy data was found and implementation data reported that PEP was available in most European settings (131-133). The difference in available implementation data led to assigning these interventions different grades, grade 2a for PEP and 2b for PrEP.

Some interventions that have been implemented for long time periods based on plausibility have a sufficient amount of implementation experience but lack efficacy data. These interventions are difficult to place within the HASTE framework. For example voluntary anonymous partner notification have established plausibility, but no efficacy data or on-going trial was found. Implementation data from the European setting was sufficient and reported willingness among MSM index partner to notify their sex partners (142, 143). For grade 2c, the original HASTE framework states that plausibility should be established and that there are

on-going efficacy trials. This intervention was assigned grade 2c even though not fulfilling the criteria of on-going efficacy trials. We thereby made an adjustment to the original HASTE grading framework. The adjustment was helpful for this review and we propose that it will be evaluated in future reviews using HASTE.

Behavioural and biological outcomes were assigned the same value according to the inclusion criteria for this review. As HIV incidence studies are rare we included all available and relevant efficacy data. This leads to that universal antiretroviral treatment which is shown to lead to decrease in HIV transmission and peer outreach that is shown to reduce UAI were both assigned a strong recommendation. However we expect different size of intervention effectiveness regarding decreasing HIV incidence in the MSM population for these two interventions. This review's grading process does not take the expected decrease in HIV incidence into account.

Future development and use of Web-based sampling strategies

The online banner survey, WebRDS and stratified sampling in a Web community discussed in study IV all used Sweden's largest Web community for LGBTI for recruitment in different ways. The Web community is an active social forum, however usage has decreased during the last five years (109). New online social forums have become available including other Web communities, chats and smartphone applications. Future web-based studies may need to consider a variety of online forums. In particular smartphone applications used for dating among MSM may be a potential opportunity for web-based sampling, surveys and interventions (136, 144). WebRDS recruitment could also benefit from applying several online options to recruit peers including smartphone applications such as Grindr, chats, FaceBook and other online social forums. Random probability sampling, such as stratified sampling in a Web community, may also be performed among other online social forums member registers. It could be helpful to sample from several member registers in order to capture a wider population of MSM.

To validate findings between different samples of MSM, such as in study IV, may provide a more comprehensive understanding of the samples of MSM captured and help in interpreting the results. The WebRDS and TLS sample included younger participants in comparison to the banner survey and stratified sampling in a Web community. All sample were on average younger than the male population of Sweden (145, 146). The opposite have been reported from two recent studies among MSM in China that found that TLS participants were on

average older than online banner survey participants and RDS participants (147, 148). These data highlights the diversity between settings and implementation of the sampling methods. The age difference between samples is relevant for understanding the differences in participants' employment status, education level, HIV serostatus and HIV/STI testing experience in the different samples. These outcomes may be related to age as well. WebRDS captured MSM with lower education levels. This finding is consistent with previous RDS among MSM in Brazil and China (148-150).

All participants in the WebRDS reported having had one or more casual male sex partners for UAI in the last 12 months, while more than half of the participants in the other samples reported no casual sex partners for UAI during the same time period. Thereby three sampling methods validate each other, except the WebRDS. This discrepancy can possibly be explained by that the WebRDS recruitment chains were short and early in RDS recruitment hence MSM with large social networks may be oversampled. Having a large social network may imply having more opportunity for sex and thereby sexual risk behaviour (151). Similar proportions of participants in the four samples reported six or more casual male sex partners for UAI in the past 12 months, indicating that the sampling methods can be used to indicate the validity of the data across the samples for some variables.

Web-based or venue based sampling through meeting places and online forums that are also used for finding new sex partners may have implications for measuring sexual risk behaviour for HIV/STI (152). A comparison of an online banner survey and a sub sample of MSM from a national probability sample in the United Kingdom report higher sexual risk behaviour among the online banner survey participants (71). Similar findings are reported in a comparison of studies among the general population in Sweden (153).

Non-probability samples or probability samples with low response rates estimates should be interpreted with caution regarding generalizing results to the larger population of MSM. In most cases inference is not possible.

Monitoring the HIV epidemic among MSM

Different high income countries use different sampling strategies and methods to gather HIV monitoring data of MSM. There are particularly discrepancies regarding collecting only behavioural or in addition also biological data when surveys are perfomed. Most countries within the European Union / European Economic Area including Sweden report on newly diagnosed cases of HIV and transmission route (12). In addition the Public Health Agency of Sweden have gathered behavioural data among MSM in two online banner surveys (2004, 2006) and the stratified sampling in a Web community study described previously (111, 112). Two large European studies have also been implemented in Sweden as described earlier, EMIS and Sialon II (113, 154). Thereby behavioural data have been collected on repeated occasions applying different sampling methods, while biological data i.e. HIV-testing to estimate HIV prevalence in a sample of MSM have been collected once, in 2013.

Monitoring data studies for HIV among MSM in low and middle income countries have to a large extent used RDS sampling for recruitment to HIV Integrated Biological and Behavioural Surveillance Surveys (155). On the contrary biological and behavioural monitoring data among MSM in the United States are gathered by applying TLS in metropolitan areas (80). RDS are being used in the United States for gathering monitoring data on two other key populations for HIV, people who inject drugs and heterosexual adults at increased risk of HIV (156). In Canada, another high income setting, RDS has been used to study several key populations for HIV such a MSM, street youth and people who inject drugs (157). When comparing RDS among these three populations, the recruitment process among MSM was less successful. Aglipay et al. reports that this may be due to the study design and problems with informing MSM regarding the peer recruitment process, however MSM may also have smaller social networks in this setting (157). The different sampling methods used in different settings points towards that RDS and TLS both works well to sample MSM and the methods have different advantages and disadvantages.

Measuring HIV prevalence in a sample of MSM provides insights to the risk of HIV at the local sexual network level. While, behavioural data on UAI provides insights to the risk of HIV at the individual level. UAI only poses a considerable risk of HIV when performed with a sex partner living with HIV and manifest HIV viral blood count. Thereby behavioural and biological data complements each other to provide insights into the HIV epidemic and HIV risk among MSM. Another benefit from gathering biological data as part of monitoring data is to contribute towards increased uptake of testing.

Future efforts of monitoring HIV risk among MSM living in Sweden could benefit from gathering biological and behavioural data. A real life RDS among MSM living in Sweden could employ both real life and web-based peer recruitment with referrals to a study site. A multi-site study may be beneficial in order to reach MSM living in different parts of the country, as Sweden covers a vast geographical area. All of the previously used web-based sampling methods could also be explored to recruit participant to a web survey with an add on referral for anonymous HIV-testing at the nearest clinic. In order to motivate participants to part take in testing incentives could be explored. For example, iTunes song gifting was recently found to be a low-cost efficient methods for recruitment of MSM in the United States (158).

Future monitoring of the HIV epidemic among MSM will most probably continue to involve web-based strategies as Internet use increase globally. Further development of these strategies including the latest online technology such as smartphone and tablet applications holds promise for both research and interventions among MSM.

Limitations of used sampling strategies (Study II-IV)

When studying sexual behaviour there is a risk of bias due to self-reporting. Thereby reporting bias, recall bias and social desirability bias may be introduced (159-161). Social desirability bias may have been reduced by the privacy of the online setting and by not collecting personal identifier data. To diminish recall bias we asked about sexual risk behaviour within a specific time frame to enable participants to focus and recall only for this period (161, 162). However, recall bias may still exist in the data. The same kind of bias may exist in the individual studies examining behavioural outcomes included in the systematic review (study I). In addition, salience bias may have been introduced meaning that some individuals who are interested in the study topic may be more inclined to respond to the study (75).

The different web-based sampling methods presented in study II-IV all have limitations. The online banner survey recruited the largest sample of MSM, but represents a convenience sample. Thereby generalizability of findings to the Internet active MSM population is limited. This sampling method may however be useful when data is needed quickly and at low cost, as it has proven ability to recruit MSM across diverse settings (70, 163, 164).

The time location sampling study provide estimates that are generalizable to the established sampling frame of MSM visiting selected venues in Stockholm and provides a good option when aiming to target MSM in urban areas. In addition TLS offers the opportunity for biological samples in addition to gathering behavioural data. However additional strategies are needed in order to capture MSM not residing in urban areas.

The WebRDS recruitment produced short recruitment chains, similarly to WebRDS studies among the general population in the Netherlands and Thailand (101, 102, 165). Therefore the study may have captured MSM with large social networks, which has implication for the study outcome of sexual risk behaviour. Another limitation is that the web survey format was not adjusted for smart phone and tablets, which should be explored in future studies to ease participation. For example a person may receive the invitation while checking their email inbox on the buss but cannot answer the survey immediately on their smart phone. The invitation email may have been forgotten by the next time the person checks their email on a computer leading to non response. Since the analysis of study II was performed a new RDS estimator has been suggested and evaluated to perform better in comparison to the RDSII estimator used (86, 87). Future RDS analysis may benefit from using the new recommended estimator

The stratified sampling among the member registry of a Web community achieved a crude overall response rate of 19%. Data was not available in order to know to what extent foreignborn differed from other participants regarding response rate. The findings achieved may be generalizable to the member register of the Qruiser Web community if systematic drop out did not occur, but systematic drop out has been reported from two previous online banner surveys among men and women in Sweden and MSM in the United States (166, 167). In addition, the MSM population living in Sweden may differ in many aspects from the Web community registry. The formative interview studies performed indicated that some MSM have multiple memberships and profiles on the Web community. Thereby one person can have been invited twice through two different Web community profiles.

Foreign-born MSM having recently arrived in Sweden may not be inclined to answer a web survey due to language barrier, being in an asylum process or a hidden refugee, and not wanting to answer questions regarding a stigmatized topic such as same sex practices. In addition, newly arrived MSM may not know of or be members of the Web community where sampling took place. Further strategies are needed to reach this group of foreign-born MSM. One optin could be probability sampling among newly arrived migrants/refugees that may capture sufficient sub-samples of MSM.

In study IV, the four studies presented are diverse using different sampling methods of which there is no 'golden standard', thereby only allowing for a descriptive comparison. Inference of the study participant populations to the general population of MSM living in Sweden can only be done with great caution.

6.1 CONCLUSIONS

- Condom use, peer outreach, peer-led group interventions and universal coverage of
 antireotrviral treatment were strongly recommended as HIV prevention among MSM
 according to the HASTE grading framework. In addition, HIV-testing was deemed
 essential to achieve coverage of antiretrovial treatment.
- A lack of implementation studies of HIV prevention among MSM from the European Union / European Economic Area was identified.
- Web-based Respondent Driven Sampling among MSM recruited participants that all reported having had unprotected anal intercourse with at least one regular and one casual sex partner during the past year.
- Having lived in Sweden less than or equal to five years, having talked with a
 prevention worker and having had a STI test during the last 12 months was associated
 with having tested for HIV during the same time period among foreign-born MSM.
- Preferred testing services among foreign-born MSM participants were rapid HIV test, anonymous testing, testing outside of the health care system and testing at MSM clinics.
- Online banner survey sampling, time location sampling, Web-based Respondent
 Driven Sampling and stratified sampling in a Web community to study sexual risk
 behaviour among MSM in Sweden captured samples of MSM that differed regarding
 sociodemographic characteristics and sexual behaviour.

6.2 RECOMMENDATIONS

- Scale-up of HIV-testing, coverage of antiretroviral treatment, peer outreach, peer-led group interventions, and condom promotion and distribution are recommended as HIV prevention among MSM within the European Union and European Economic Area.
- Future studies to evaluate implementation and effectiveness of interventions would be benefical to guide scale-up of these interventions within the European Union and European Economic Area.
- To further improve the Web-based Respondent Driven Sampling method, the software could be adapted to smart phones and tablets, and aply recruitment strategies on different online social platforms.
- Web-based Respondent Driven Sampling may hold promise for recruiting MSM engaging in sexual risk behaviour to web-based HIV prevention interventions including referrals to testing for HIV and sexually transmitted infections.
- Prevention outreach activities, individual- and group- counselling to promote uptake
 of HIV testing should be applied and evaluated among foreign-born MSM as well as
 other MSM living in Sweden.
- By applying different sampling strategies among MSM comprehensive data can be achieved and findings can be validated across the samples.

7 SUMMARY IN SWEDISH / SVENSK SAMMANFATTNING

Hiv-prevention, urvalsmetoder och sexuellt riskbeteende bland män som har sex med män

Homosexuella, bisexuella och andra män som har sex med män, benämns inom hälso- och sexualitetsrelaterad forskning för "män som har sex med män" och förkortas MSM. MSM har en förhöjd risk för humant immunbristvirus, hiv, och är en viktig grupp för riktade preventionsinsatser. Antalet nydiagnostiserade fall av hiv bland MSM i Europa ökar i kontrast till att antalet minskar bland den generella populationen. I Sverige är sex mellan män den vanligaste överföringsvägen av hiv vid inhemsk smitta. Under de senaste åren har en ökning av hiv fall bland utlandsfödda MSM rapporterats. Ytterligare preventionsinsatser behövs bland MSM i Sverige, i Europa och globalt.

Representativitet i data för MSM populationen är svår att uppnå. Stigma kring MSM försvårar även rekrytering till forskningsstudier och gruppen kallas ofta för en dold grupp. För att lösa problemet har andra rekryteringsstrategier för forskningsstudier av dolda grupper utvecklats. "Respondent driven sampling" är en metod som använder sig av studiedeltagarnas sociala kontakter vilket har visat ge en hög svarsfrekvens. Internetbaserad rekrytering till studier har visats nå MSM. En fördel med Internet-baserade studier är att de ger en hög grad av upplevd anonymitet bland studiedeltagare och kan besvaras vid den tidpunkt och på den plats som passar den enskilde.

Studierna som presenteras här har som syfte att bidra till ökad kunskap kring effektiv hivprevention och urvalsmetoder för nå MSM. För att nå MSM och studera sexuellt
riskbeteende så använde vi oss av web-baserad "respondent driven sampling" samt ett
stratifierat urval av MSM medlemmar på ett internetforum. Båda urvalsmetoderna användes
för första gången i Sverige.

Studie I granskade och utvärderade systematiskt hiv-preventiva interventioner bland MSM i Europa (Europeiska Unionen och det Europeiska ekonomiska samarbetsområdet). Tjugofyra olika hiv-preventiva interventioner för MSM inkluderades varav femton interventioner uppfyllde kraven för att räknas som evidensbaserad hiv-prevention för MSM. Studien visar att de fyra interventionerna: kondomanvändning, uppsökande

preventionsverksamhet av och för MSM, MSM-ledda gruppaktiviteter med preventionsbudskap och antiretroviral behandling för personer som lever med hiv uppfyller evidens för en stark rekommendation. Hiv-testning bland MSM är grundläggande för att möjliggöra antiretroviral behandling för de personer som lever med hiv. Studieresultaten användes sedan som evidensgrund för att utveckla europeiska riktlinjer kring prevention bland MSM av European Centre for Disease Prevention and Control.

Studie II implementerade och utvärderade web-baserad "respondent driven sampling" som metod för att studera sexuellt riskbeteende bland MSM i Sverige. Alla studiedeltagarna rapporterade att de haft haft analsex utan kondom med en eller flera tillfälliga manliga sexpartner, och en eller flera regelbundna sexpartner under det senaste året. Studien visade därmed att deltagarna är en grupp av MSM som kan ha nytta av preventionsinsatser. Web-baserad "respondent driven sampling" kan i framtiden användas för att implementera web-baserade interventioner bland MSM som tar sexuella risker.

Studie III undersökte hiv-testning och prevention bland utlandsfödda MSM i Sverige genom ett stratifierat urval av MSM som är medlemmar på ett Internetforum. Ungefär hälften (45 %) av deltagarna hade testat sig för hiv senaste året medan en femtedel aldrig hade testat sig. Att ha talat med en person som arbetar med hiv-prevention under senaste året var signifikant associerat med att ha testat sig inom samma tidsperiod. Resultaten stärker att uppsökande preventionsverksamhet kan främja testning bland utlandsfödda MSM.

Studie IV analyserade likheter och skillnader med avseende på sociodemografiska faktorer och sexuellt riskbeteende i fyra olika urval av MSM som insamlats mellan 2010 och 2013 i Sverige. Utöver urvalen av MSM från studie II och III så studerades två ytterligare urval. Dels deltagarna i en webbenkät som annonserades via länkar på websidor för MSM ("online banner survey"), och dels data som samlats in på fysiska mötesplatser för MSM så kallad "time location sampling". De fyra urvalen av MSM studiedeltagare skiljde sig avseende sociodemografiska variabler och sexuellt riskbeteende. Sammantaget gav data från flera urvalsmetoder en ökad förståelse för sexuellt riskbeteende bland MSM. Framtida studier kan dra nytta av att kombinera urvalsmetoder för att validera insamlad data mellan flera urval av MSM.

För att vända hiv-situationen bland MSM i Europa rekommenderas en ökad satsning på implementering av evidensbaserad hiv-prevention. Web-baserade urvalsmetoder visade på möjlighet att rekrytera en bred representation av MSM och bör vidareutvecklas både för forskningsstudier och för implementering av preventiva interventioner. Utvärdering av data från olika urvalsmetoder bidrar med att ge en större förståelse för sexuellt riskbeteende bland MSM.

8 ACKNOWLEDGEMENTS

First and most importantly, I would like to thank all study participants for sharing their experiences and contributing to this research.

Thank you to the Division of Global Health (IHCAR), currently included in the Department of Public Health Sciences at the Karolinska Institutet for letting me embark on this journey. It has been most inspiring to be part of our fantastic research community.

I'm most grateful to my supervisor team Anna Ekéus Thorson, Fredrik Liljeros and Birger Forsberg. Thank you for support, guidance, inspiration and laughter throughout this journey.

Anna, first thank you for giving me the opportunity to perform this thesis work with you. Your guidance, inspiring talks and reminders to always look for the bigger picture have been most valuable. You have provided support and freedom for me to develop and pursue my own research ideas, which I really appreciate. You're a remarkable researcher and role model, thanks for all your generous advice.

Fredrik, thank you for your enthusiasm, encouragement and all the study design and statistic sessions where you've generously welcomed my questions. And for introducing me to the world of sociology and social networks. You're a truly pedagogic teacher who brings out the best in your students. It's been great fun to discuss, thank you for sharing brilliant ideas and lending me a seat on your green 'professor' couch during these years.

Birger, thank you for providing mentorship, encouragement and strategic advise throughout this work. Receiving supporting emails from you are always encouraging and bring a smile to my face. You're also living proof that there is time to do everything, quite inspiring.

Helena Hervius-Askling, my PhD mentor and all time supporter. Thank you for all the lunches filled with encouragement, support and advise. For pushing me to develop, being a role model and sharing life lessons.

Thank you to my co-author team, Linus Bengtsson, Xin Lu and Kristina Ingemarsdotter Persson. Thank you for fun times, great discussions, support and friendship!

Hans Rosling, thank you for the inspiration, encouragement, constructive criticism and all the doors you have opened for me. Most importantly for encouraging me to be data focused, data critical and only rely on a fact-based view of the world.

Thank you to all colleagues in the research group on Global health, HIV/AIDS and Sexual and Reproductive Health and Rights. Especially to Anna Mia Ekström for giving me the opportunity to work and develop within your team. You're a great source of inspiration.

Thank you to the leaders of IHCAR and PHS during my time here, Vinod Diwan, Cecilia Stålsby Lundborg and Lucie LaFlamme, for creating this space of high impact research

across diverse global settings. And special thanks to Marie Hasselberg for help and support with all the formal parts of doctoral education.

Thank you to all colleagues and friends at IHCAR over the years for corridor talks, fikas and laughters: Abela Agnarsson, Anastasia Pharris, Anna Bergström, Anders Klingberg, Anneli Eriksson, Asli Kulane, Ashish Pathak, Andreas Mårtensson, Ayesha De Costa, Anders Ragnarsson, Birgitta Rubensson, Cecilia Lindsjö, Charlotta Zacharias, Christian Unge, Claudia Hanson, Dell Saulnier, Dorcus Kiwanuka Henriksson, Elin Larsson, Elisabeth Faxelid, Erika Saliba, Gaetano Marrone, Galit Zeluf, Hana Taha, Hanani Tabana, Helena Nordenström, Helga Naburi, Helle Mölsted Alvesson, Ingvild Odsbu, Jessica Pååfs, Joel Monárrez-Espino, Johan Von Schreeb, Karin Källander, Karin Båge, Keshab Deuba, Ketsekone Phrasisombath, Kim Brolin, Klara Johansson, Kristi Sydney, Linda Sanneving, Lisa Blom, Mariano Salazar, Martin Camitz, Martin Gerdin, Martina Vallin, Mattias Larsson, Meena Daivadanam, Niklas Karlsson, Oliver Dyar, Patricia Awitii, Pham Nguyen Ha, Rachel Irwin, Ritva Rissanen, Sandeep Nerkar, Sara Thomsen, Senia Rosales, Sigridur Baldursdottir, Simon Walusimbi, Tobias Alfén, Theodora Mbunda, Tim Baker, Ulrika Baker, Yanga Zembe and Ziad El-Khatib.

My warmest thank you also goes to the administration at PHS for all timely help over the years: Gun-Britt Eriksson, Kersti Rådmark, Bo Planstedt, Andreas Sandin, Elisabeth Kaven, Pia Olsson, Marie Dokken, Marita Larsson and Anita Thyni.

Thank you to my PhD colleagues Veronika Fridlund, Hernan Mondani, and Amir Rostami at the Sociology Department at Stockholm University for interesting discussions and making me feel at home at SU.

Thank you to my pre-defense reviewers, Luis Correa Da Rocha, Jaran Eriksen and John Dusabe, for valuable input.

Thank you to the Swedish Research School of Global Health for providing peer support, fun discussions and great workshops.

Thank you to the Swedish network of PhD students studying sexual health for inspirational meetings. A special thank you to Ronny Tiikkanen for advise and sharing insights.

Stefan Baral, thank you for inspiration, support and giving me the opportunity to learn from your expertise.

I would like to thank the Public Health Agency of Sweden for providing support for this research and for good collaborations. Thank you Torsten Berglund, Louise Mannheimer, Staffan Hallin, Charlotte Deogan, Inga Velicko, Jakob Bergström and Sharon Kühlmann-Berenzon.

Thank you to the European Centre for Disease Prevention and Control for good collaborations. Special thanks to Anastasia Pharris, Teymur Noori and Otilia Sfetcu. In addition thank you to Ford Hickson for critical research advice. And thank you to Meritxell Sabidó for good team work.

Thank you to all colleagues at the MSM clinic Venhälsan at Södersjukhuset. It's been a pleasure to work with and learn from all of you. Special thanks to Göran Bratt, Bo Hejdeman, Lena Lindborg, Anders Blaxhult, Katarina Gyllensten, Erik Sandström, Lars Moberg, Sven Grützmeier, Lena Sandreiser, Lena Björklund, Kajsa Flisager, Ulla-Karin Hallgren, Magnus Göransson, Tilde Gray och Ronnie Ask.

Thank you to the Swedish national Federation of LGBTI Rights/RFSL for good collaborations and inspiring meetings, your work matters! Special thanks to Nicklas Dennermalm, Olov Lindblad, Carolina Orre and Filip Garcia.

Thank you Ingrid Lundberg for support to doctoral studies in the first place.

Thanks to all fantastic friends for sharing both the fun and tricky parts of life, and who have helped me to think of other things than this thesis, a most important part!

Last but not least, thanks to my family Inger, Carl and Lars, who have supported me through all my aspirations in life of which this PhD work is just one leg of the journey. You are my foundation that makes it all possible, you mean the world to me.

Johan, your ever-lasting support and enthusiasm throughout this process have been invaluable. Life is so much more fun with you in it. Thank you for being there and being you.

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10 APPENDICES

Appendix I: Number of articles found through search strategies, screened and included according to inclusion criteria

Interventions	Articles identified through searches	Nr. of articles included addressing efficacy	Nr. of articles included addressing implementation
Condom use	130	1	3
HIV Treatment as Prevention (TaSP)	9	2	4
Peer-led group interventions	326	2	0
Peer outreach	326	2	0
Voluntary HIV counselling and testing (VCT)	717	2	8
Condom-compatible lubricant use (when using condoms)	130	5	2
Post-exposure prophylaxis (PEP)	28	3	2
Individual counselling for MSM living with HIV	327	4	2
Peer-led group interventions targeting MSM living with HIV	326	1	2
Sex venue-based interventions	25	1	8
Social marketing interventions	476	3	7
Individual counselling for MSM	327	2	1
Internet-based HIV prevention messages	40	6	4
Training for health care providers to provide comprehensive care for MSM	225	0	1
MSM friendly clinics	234	0	1
Voluntary anonymous partner notification	126	0	7
Voluntary Medical male circumcision	49	3	2
Pre-exposure prophylaxis (PrEP)	4	1	0
Campaigns for Lesbian, Gay, Bisexual and Trans equality	3	0	1
Female condom use	4	3	1
Sero-sorting	9	3	4
Avoid ejaculation of semen orally	226	3	0
Avoiding poppers during anal intercourse	5	0	0
Reducing alcohol binge drinking among MSM	119	1	0
Summary	3865	48	60

Appendix II: Search Strategies and MeSH terms per intervention

Condom use and Condom-compatible lubricant use

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(Homosexuality or homosexual OR bisexuality or bisexual OR gay OR "men who have sex with men" OR MSM) AND (condom or condoms or lubricant) AND (cohort)

(Homosexuality or homosexual OR bisexuality or bisexual OR gay OR transgender OR transsexual OR bisexual OR "men who have sex with men" OR MSM) AND (condom or condoms or lubricant) AND (Europe) AND (implementation)

HIV Treatment as Prevention (TaSP)

(Homosexuality or homosexual OR bisexuality or bisexual OR gay OR "men who have sex with men" OR MSM) AND (antiretroviral treatment as prevention) AND (chemoprophylaxis) AND (HIV) AND (test and treat)

Peer-led group interventions for MSM and targeting MSM living with HIV

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(Homosexuality OR homosexual OR bisexuality OR gay OR transgender OR transsexual OR bisexual OR "men who have sex with men" OR MSM) AND (HIV OR AIDS OR STI IR STD OR sexually transmitted diseases OR sexually transmitted infections) AND (random allocation OR intervention studies OR program evaluation OR random OR randomize OR randomized OR randomly) AND ("2010/01/01"[Date - Publication] : "3000"[Date - Publication])

Peer outreach

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(Homosexuality OR homosexual OR bisexuality OR gay OR transgender OR transsexual OR bisexual OR "men who have sex with men" OR MSM) AND (HIV OR AIDS OR STI IR STD OR sexually transmitted diseases OR sexually transmitted infections) AND (random allocation OR intervention studies OR program evaluation OR random OR randomize OR randomized OR randomly) AND ("2010/01/01"[Date - Publication] : "3000"[Date - Publication])

Voluntary testing and counselling for HIV (VCT)

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(Homosexuality OR homosexual OR bisexuality OR bisexual OR gay OR transgender OR transsexual OR "men who have sex with men" OR MSM) AND (HIV OR AIDS) AND (testing OR counselling OR "testing and counselling") AND ("2010/01/01"[Date - Publication]: "3000"[Date - Publication])

Post-exposure prophylaxis (PEP)

(HIV) AND Post-exposure prophylaxis AND Men who have sex with men) AND homosexual

Individual counselling for MSM and MSM living with HIV

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(Homosexuality OR homosexual OR bisexuality OR gay OR transgender OR transsexual OR bisexual OR "men who have sex with men" OR MSM) AND (HIV OR AIDS OR STI OR STD OR sexually transmitted diseases OR sexually transmitted infections) AND (random allocation OR intervention studies OR program evaluation OR random OR randomize OR randomized OR randomly) AND ("2010/01/01"[Date - Publication] : "3000"[Date - Publication])

Internet-based interventions

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw]) OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR (placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR control* [tw] OR prospectiv* [tw] OR volunteer* [tw]) OR non-randomi*[tw] OR before after study[tw] OR time series[tw] OR case control[tw] OR prospective cohort[tw] OR retrospective cohort[tw] OR cross- section*[tw] OR prospective[tw] OR retrospective[tw] OR research design [mh:noexp] OR comparative study[mh] OR evaluation studies[mh] OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw] OR longitud*[tw] OR descripti*[title/abstract] OR study[title/abstract] OR evaluat*[title/abstract] OR pre-post[tw] OR (pre-test[tw] AND post-test[tw]) NOT (animals [mh] NOT human [mh])) AND (HIV Infections[MeSH] OR HIV[MeSH] OR hiv[title/abstract] OR hiv-1*[title/abstract] OR hiv- 2*[title/abstract] OR hiv1[title/abstract] OR hiv2[title/abstract] OR hiv infect*[title/abstract] OR human immunodeficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR human immuno-deficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR ((human immun*) AND (deficiency virus[title/abstract])) OR acquired immunodeficiency syndrome[title/abstract] OR acquired immunedeficiency syndrome[title/abstract] OR acquired immuno-deficiency syndrome[title/abstract] OR acquired immune-deficiency syndrome[title/abstract] OR ((acquired immun*) AND (deficiency syndrome[title/abstract])) HIV Infections[MeSH] OR HIV[MeSH] OR hiv[title/abstract] OR hiv-1*[title/abstract] OR hiv-2*[title/abstract] OR hiv1[title/abstract] OR hiv2[title/abstract] OR hiv infect*[title/abstract] OR human immunodeficiency virus[title/abstract] OR human immunedeficiency virus[title/abstract] OR human immuno-deficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR ((human immun*) AND (deficiency virus[title/abstract])) OR acquired immunodeficiency syndrome[title/abstract] OR acquired immunedeficiency syndrome[title/abstract] OR acquired immuno-deficiency syndrome[title/abstract] OR acquired immune-deficiency syndrome[title/abstract] OR ((acquired immun*) AND (deficiency syndrome[title/abstract])) OR Sexually Transmitted Diseases[Mesh] OR sexually transmitted[title/abstract] OR Syphilis[Mesh] OR syphilis[title/abstract]) OR hepatitis[Mesh] OR hepatitis[title/abstract]) AND 20 (Homosexuality, Male[Mesh] OR Bisexuality[Mesh] OR Transsexualism[Mesh] OR homosexual*[title/abstract] OR gay[title/abstract] OR homosexual*[title/abstract] OR MSM[tw] OR "men who have sex with men"[title/abstract] OR "same-sex"[title/abstract] OR queer[title/abstract] OR bisexual[title/abstract]) AND ((tailor*[title/abstract] OR targeted[title/abstract] OR targetted[title/abstract] individualised[title/abstract] OR individualized[title/abstract] OR interactive*[title/abstract] OR interactive*[title/abstract]) (hyperlink*[title/abstract] **AND** OR hypermedia[title/abstract] OR Internet[title/abstract] OR on-line[title/abstract] OR online[title/abstract] OR web[title/abstract] OR web-based[title/abstract] OR website[title/abstract] OR WWW[title/abstract] OR WWW-

based[title/abstract] OR net-based[title/abstract] OR Internet[Mesh])) AND ("2010/01/01"[Date - Publication]) = "3000"[Date - Publication])

Interventions in sex-on-premises venues

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw]) OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR (placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR control* [tw] OR prospectiv* [tw] OR volunteer* [tw]) OR non-randomi*[tw] OR before after study[tw] OR time-series[tw] OR case control[tw] OR prospective cohort[tw] OR retrospective cohort[tw] OR cross-section*[tw] OR prospective[tw] OR retrospective[tw] OR research design [mh:noexp] OR comparative study[mh] OR evaluation studies[mh] OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw] OR longitud*[tw] OR descripti*[title/abstract] OR study[title/abstract] OR evaluat*[title/abstract] OR pre-post[tw] OR (pre-test[tw] AND post-test[tw]) NOT (animals [mh] NOT human [mh])) AND (HIV Infections[MeSH] OR HIV[MeSH] OR hiv[title/abstract] OR hiv-1*[title/abstract] OR hiv-2*[title/abstract] OR hiv1[title/abstract] OR hiv2[title/abstract] OR hiv infect*[title/abstract] OR human immunodeficiency virus[title/abstract] OR human immunedeficiency virus[title/abstract] OR human immuno-deficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR ((human immun*) AND (deficiency virus[title/abstract])) OR acquired immunodeficiency syndrome[title/abstract] OR acquired immunedeficiency syndrome[title/abstract] OR acquired immuno-deficiency syndrome[title/abstract] OR acquired immune-deficiency syndrome[title/abstract] OR ((acquired immun*) AND (deficiency syndrome[title/abstract])) HIV Infections[MeSH] OR HIV[MeSH] OR hiv[title/abstract] OR hiv-1*[title/abstract] OR hiv-2*[title/abstract] OR hiv1[title/abstract] OR hiv2[title/abstract] OR hiv infect*[title/abstract] OR human immunodeficiency virus[title/abstract] OR human immunedeficiency virus[title/abstract] OR human immuno-deficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR ((human immun*) AND (deficiency virus[title/abstract])) OR acquired immunodeficiency syndrome[title/abstract] OR acquired immunedeficiency syndrome[title/abstract] OR acquired immuno-deficiency syndrome[title/abstract] OR acquired immune-deficiency syndrome[title/abstract] OR ((acquired immun*) AND (deficiency syndrome[title/abstract])) OR Sexually Transmitted Diseases[Mesh] OR sexually transmitted[title/abstract] OR Syphilis[Mesh] OR syphilis[title/abstract]) (Homosexuality, Male[Mesh] OR Bisexuality[Mesh] AND OR gay[title/abstract] Transsexualism[Mesh] homosexual*[title/abstract] OR OR OR homosexual*[title/abstract] OR MSM[tw] OR "men who have sex with men"[title/abstract] OR OR OR "same-sex"[title/abstract] queer[title/abstract] bisexual[title/abstract] OR transgender[title/abstract] OR transsexual[title/abstract] OR transexual[title/abstract] (Bathhouse*[title/abstract] OR bath house*[title/abstract] OR bathouse*[title/abstract] OR sex club*[title/abstract] OR sauna*[title/abstract] OR public sex environment*[title/abstract] OR PSE[title/abstract] OR PSEs[title/abstract] OR commercial sex environment*[title/abstract] OR CSE[title/abstract] OR CSEs[title/abstract] OR sex facilitating business*[title/abstract] OR SFB[title/abstract] OR SFBs[title/abstract] OR sex venue*[title/abstract] OR sex premises[title/abstract]) AND ("2010/01/01"[Date - Publication]: "3000"[Date - Publication])

Social marketing interventions

(Homosexuality[title/abstract] OR homosexual[title/abstract] OR bisexuality[title/abstract] OR bisexual[title/abstract] OR gay[title/abstract] OR transgender[title/abstract] OR transsexual[title/abstract] OR "men who have sex with men"[title/abstract] OR MSM[title/abstract] OR MD (media[title/abstract] OR Social Marketing[Mesh] OR mass media[title/abstract] OR campaign[title/abstract] OR mass communication[title/abstract] OR multi media[title/abstract] OR

multimedia*[title/abstract] OR audivisual OR equipment[title/abstract] patient OR visual information[title/abstract] OR radio[title/abstract] information[title/abstract] OR leaflet[title/abstract] OR posters* OR pamphlet* OR print television[title/abstract] media[title/abstract] OR printed media[title/abstract] OR skit* OR talk media[title/abstract] OR broadcast* OR film* OR telecommunication* OR (multimedia[title/abstract] marketing[title/abstract]) OR promotional[title/abstract]) AND ("1990/01/01"[Date - Publication] : "3000"[Date - Publication])

Pre-exposure prophylaxis (PrEP)

(Homosexuality or homosexual OR bisexuality or bisexual OR gay OR "men who have sex with men" OR MSM) AND (Antiretroviral chemoprophylaxis) AND (PrEP) AND (Pre-exposure prophylaxis) AND (HIV)

Voluntary medical male circumcision

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(homosexuality, male OR bisexual OR gay OR transgender OR MSM OR homosexual* OR male homosexual OR transsexualism) AND (male circumcision OR male circumcisions OR circumcis* OR uncircumcis*) AND (HIV Infections[MeSH] OR HIV[MeSH] OR hiv[tw] OR hiv-1*[tw] OR hiv-2*[tw] OR hiv1[tw] OR hiv2[tw] OR hiv infect*[tw] OR human immunodeficiency virus[tw] OR human immunodeficiency virus[tw] OR human immunodeficiency virus[tw] OR human immunodeficiency virus[tw] OR acquired immunodeficiency syndrome[tw] OR acquired immunodeficiency syndrome[tw] OR acquired immunodeficiency syndrome[tw] OR acquired immunodeficiency syndrome[tw] OR ((acquired immun*) AND (deficiency syndrome[tw]) OR "sexually transmitted diseases, viral"[MESH:NoExp]) AND ("2010/01/01"[Date - Publication] : "3000"[Date - Publication])

Training for health care providers to offer comprehensive care for MSM

(HIV Infections[MeSH] OR HIV[MeSH] OR hiv[title/abstract] OR hiv-1*[title/abstract] OR hiv-2*[title/abstract] OR hiv1[title/abstract] OR hiv2[title/abstract] OR hiv infect*[title/abstract] OR human immunodeficiency virus[title/abstract] OR human immunedeficiency virus[title/abstract] OR human immuno-deficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR ((human immun*) AND (deficiency virus[title/abstract])) OR acquired immunodeficiency syndrome[title/abstract] OR acquired immunedeficiency syndrome[title/abstract] OR acquired immuno-deficiency syndrome[title/abstract] OR acquired immune-deficiency syndrome[title/abstract] OR ((acquired immun*) AND (deficiency syndrome[title/abstract])) HIV Infections[MeSH] OR HIV[MeSH] OR hiv[title/abstract] OR hiv- 1*[title/abstract] OR hiv-2*[title/abstract] OR hiv1[title/abstract] OR hiv2[title/abstract] OR hiv infect*[title/abstract] OR human immunodeficiency virus[title/abstract] OR human immunedeficiency virus[title/abstract] OR human immuno-deficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR ((human immun*) AND (deficiency virus[title/abstract])) OR acquired immunodeficiency syndrome[title/abstract] OR immunedeficiency syndrome[title/abstract] OR acquired immuno-deficiency acquired syndrome[title/abstract] OR acquired immune-deficiency syndrome[title/abstract] OR ((acquired immun*) AND (deficiency syndrome[title/abstract])) OR Sexually Transmitted Diseases[Mesh] OR sexually transmitted[title/abstract] OR Syphilis[Mesh] OR syphilis[title/abstract]) OR hepatitis[Mesh] OR hepatitis[title/abstract] OR anorectal care[title/abstract] OR anorectal health[title/abstract] OR comprehensive OR comprehensive care[title/abstract] health care[title/abstract]) **AND** (Homosexuality[title/abstract] OR homosexual[title/abstract] OR bisexuality[title/abstract] OR bisexual[title/abstract] OR gay[title/abstract] OR transgender[title/abstract] transsexual[title/abstract] OR "men who have sex with men"[title/abstract] OR MSM[title/abstract])

AND ((((patients care[title/abstract] OR clinical skill[title/abstract] OR "health services needs and demand" OR "professional practice" OR "clinical practice" OR "doctor patient relation") OR ((provider[title/abstract] OR professional[title/abstract] OR physician[title/abstract] OR nurse[title/abstract] OR clinician[title/abstract] OR practitioner[title/abstract]) AND (experience OR skill OR train OR competence OR training)))) AND ("1990/01/01"[Date - Publication]: "3000"[Date - Publication])

MSM competent clinics

(Homosexuality OR homosexual OR bisexuality OR bisexual OR gay OR transgender OR transsexual OR "men who have sex with men" OR MSM) AND (HIV OR AIDS) AND ("MSM clinics" OR "STI clinics" OR "sexual health clinics" OR "primary health care" OR "comprehensive care") AND ("1990/01/01"[Date - Publication] : "3000"[Date - Publication])

Voluntary anonymous partner notification

(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw]) OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR (placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR control* [tw] OR prospectiv* [tw] OR volunteer* [tw]) OR non-randomi*[tw] OR before after study[tw] OR time-series[tw] OR case control[tw] OR prospective cohort[tw] OR retrospective cohort[tw] OR cross-section*[tw] OR prospective[tw] OR retrospective[tw] OR research design [mh:noexp] OR comparative study[mh] OR evaluation studies[mh] OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw] OR longitud*[tw] OR descripti*[title/abstract] OR study[title/abstract] OR evaluat*[title/abstract] OR pre-post[tw] OR (pre-test[tw] AND post-test[tw]) NOT (animals [mh] NOT human [mh])) AND (HIV Infections[MeSH] OR HIV[MeSH] OR hiv[title/abstract] OR hiv-1*[title/abstract] OR hiv-2*[title/abstract] OR hiv1[title/abstract] OR hiv2[title/abstract] OR hiv infect*[title/abstract] OR human immunodeficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR human immuno-deficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR ((human immun*) AND (deficiency virus[title/abstract])) OR acquired immunodeficiency syndrome[title/abstract] OR acquired immunedeficiency syndrome[title/abstract] OR acquired immuno-deficiency syndrome[title/abstract] OR acquired immune-deficiency syndrome[title/abstract] OR ((acquired immun*) AND (deficiency syndrome[title/abstract])) HIV Infections[MeSH] OR HIV[MeSH] OR hiv[title/abstract] OR hiv-1*[title/abstract] OR hiv-2*[title/abstract] OR hiv1[title/abstract] OR hiv2[title/abstract] OR hiv infect*[title/abstract] OR human immunodeficiency virus[title/abstract] OR human immunedeficiency virus[title/abstract] OR human immuno-deficiency virus[title/abstract] OR human immune-deficiency virus[title/abstract] OR ((human immun*) AND (deficiency virus[title/abstract])) OR acquired immunodeficiency syndrome[title/abstract] OR acquired immunedeficiency syndrome[title/abstract] OR acquired immuno-deficiency syndrome[title/abstract] OR acquired immune-deficiency syndrome[title/abstract] OR ((acquired immun*) AND (deficiency syndrome[title/abstract])) OR Sexually Transmitted Diseases[Mesh] OR sexually transmitted[title/abstract] OR Syphilis[Mesh] OR syphilis[title/abstract]) (Homosexuality, Male[Mesh] OR Bisexuality[Mesh] AND Transsexualism[Mesh] OR homosexual*[title/abstract] OR gay[title/abstract] OR homosexual*[title/abstract] OR MSM[tw] OR "men who have sex with men"[title/abstract] OR "same-sex"[title/abstract] OR queer[title/abstract] OR bisexual[title/abstract] OR transgender[title/abstract] OR transsexual[title/abstract] OR transexual[title/abstract] AND (contact tracing[title/abstract] OR contact-tracing[title/abstract] OR partner notification[title/abstract] partner referral[title/abstract] OR expedited-partner treatment[title/abstract] OR expedited-partner therapy[title/abstract]) AND ("1990/01/01"[Date - Publication] : "3000"[Date - Publication])

Campaigns for Lesbian, Gay, Bisexual and Trans equality

(Homosexuality or homosexual OR bisexuality or bisexual OR gay OR "men who have sex with men" OR MSM) AND (structural interventions) AND (legalization) AND (advocacy) AND (same sex practices)

Female Condom Use for Anal Sex among MSM

(Homosexuality or homosexual OR bisexuality or bisexual OR gay OR "men who have sex with men" OR MSM) AND (female condom) AND (Femidom)

Sero-sortiong

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(Homosexuality OR homosexual OR bisexuality OR gay OR transgender OR transsexual OR bisexual OR "men who have sex with men" OR MSM) AND ((serosorting OR Serosort* OR Seroposition* OR Seroadapt* OR Sero-sort* OR Sero-position* OR Sero-adapt* OR (HIV and "partner selection") OR AIDS and "partner selection" OR HIV and "partner choice" OR aIDS and "partner choice" OR "strategic positioning" OR "sexual harm reduction" OR Seroguessing)) AND ("2010/01/01"[Date - Publication])

To avoid semen in the mouth/unprotected oral sex

(Homosexuality or homosexual OR bisexuality or bisexual OR gay OR "men who have sex with men" OR MSM) AND ((oral sex) AND (oral hiv transmission))

Avoiding nitrate inhalants/poppers at UAI

(Homosexuality or homosexual OR bisexuality or bisexual OR gay OR "men who have sex with men" OR MSM) AND ((poppers) AND (amyl-nitrate))

Interventions to reduce alcohol binge-drinking

A systematic review performed in 2010 was included. In addition, the search strategy of this systematic review was updated from up until 8 February 2013.

(Homosexuality OR homosexual OR bisexuality OR gay OR transgender OR transsexual OR bisexual OR "men who have sex with men" OR MSM) AND (HIV OR AIDS OR STI OR STD OR sexually transmitted diseases OR sexually transmitted infections OR hepatitis) AND (alcohol OR alcoholbinge OR "alcohol-binge drinking" OR substance use) AND (random allocation OR intervention studies OR program evaluation OR random OR randomize OR randomized OR randomly) AND ("1990/01/01" [Date - Publication] : "3000" [Date - Publication])

Appendix III: Questionnaire Study II

Studie för män som har sex med män

Karolinska Institutet genomför den här studien för att utvärdera hur man bäst når män som har sex med män med enkätundersökningar för att studera risk för sexuellt överförbara sjukdomar. Studien vill nå män med olika ålder och bakgrund. Delta om du är en man, känner dig som en man eller var född som man och är 15 år eller äldre. Mer information om studien (*Läs mer*)

Här frågar vi angående sociodemografisk information för att förstå vilken del av gruppen, män som har sex med män, som studien når. (Läs mer)

1. Vilko	et år är du född?
2. Född	les du i Sverige
	Ja Nej
2b. Vill	ket land föddes du i?
3. Vilko	et län bor du i?
4. Vilko	en är din högst avslutade utbildning?
	Grundskola, årskurs 1–6 Grundskola, årskurs 7–9 Gymnasieskola, folkhögskola Eftergymnasial utbildning, KY-utbildning Högskole-/universitets-utbildning/kurs Forskarutbildning
5. Vilko alternat	et av följande beskriver bäst din nuvarande sysselsättning? Du kan svara med ett eller två iv.
	Anställd Student Arbetslös Egenföretagare Pensionerad
6. Iden	tifierar du dig som man?
	Ja Nej Annat:
7. Född	les du med biologiskt manligt kön?
	Ja Nej Annat:

□ Ja □ Nej
9. Hur definierar du din sexuella läggning? Du kan svara med ett eller flera alternativ. Homosexuell Bisexuell Heterosexuell Sexuell Asexuell Annat:
Här frågar vi angående sexuellt beteende, för att bättre förstå risk för sexuellt överförbara sjukdomar bland män som har sex med män. (Läs mer)
10. Hur många män har du regelbundet haft sex med senaste 12 månaderna? Med regelbundet sex menar vi att ni har träffats vid flera tillfällen och haft sex, såsom en pojkvän, make, knullkompis eller andra regelbundna partners.
11. Hur många män har du regelbundet haft anala samlag utan kondom med under de senaste 12 månaderna?
12. Hur många tillfälliga manliga partners har du haft sex med senaste 12 månaderna? Med tillfällig partner så menar vi att ni har träffats vid ett tillfälle och haft sex, såsom 'one night stands'.
13. Hur många tillfälliga manliga partners har du haft analt samlag utan kondom med under de senaste 12 månaderna?
Här frågar vi angående hur du använder Internet och om ditt sociala nätverk för att kunna utvärdera om den här sortens studier på internet är ett bra sätt att nå alla inom gruppen män som har sex med män. (Läs mer)
14. Hur ofta har du kollat något av dina epostkonton de senaste 7 dagarna? Räkna både privat
mail och jobbmail.
mail och jobbmail. □ Inte alls □ 1-3 gånger totalt □ 4-6 gånger totalt □ 1-5 gånger per dag □ Mer än 5 gånger per dag □ Jag är inloggad på min mail större delen av tiden
☐ Inte alls ☐ 1-3 gånger totalt ☐ 4-6 gånger totalt ☐ 1-5 gånger per dag ☐ Mer än 5 gånger per dag

Här frågar vi angående hur du använder QX Qruiser, ett web-Community för homosexuella, bisexuella, transgender och queer samt deras vänner. QX Qruiser har tidigare använts för att hitta deltagare till studier, därför vill vi förstå QX Qruisers roll bättre. Det hjälper oss att förstå vilka vi når med den här studien och hur vi kan förbättra studien för att alla män som har sex med män ska ha samma chans att delta. (Läs mer) 21. Är du medlem på Qruiser? □ Ja □ Nei 22. Har du guldmedlemskap på Qruiser? □ Ja □ Nei 23. Av de X män som har sex med män som du har haft kontakt med via Internet under de senaste 7 dagarna, hur många är medlemmar på Qruiser? Det är viktigt för studien att du försöker uppskatta även om det inte blir exakt. ☐ Alla, eller nästan alla (80-100%) ☐ Mer än hälften (60-80%) ☐ Hälften (40-60%) ☐ Mindre än hälften (20-40%) ☐ Ett fåtal (0-20%) □ Inga (0%) □ Vet ei 24. Hur många av din/dina Qruiserprofiler har du varit inloggad på under de senaste två månaderna? \Box 0 \Box 1 \square 2 □ 3 eller fler Här frågar vi angående den Qruiserprofil som du använder mest, studien använder den här informationen för att utvärdera om studien når alla delar av gruppen män som har sex med män. (Läs mer) 25a. Hur många gånger har du varit inloggad på den Qruiserprofil som du använder mest de senaste 7 dagarna? ☐ Inte alls

25b. Vilken ålder har du registrerat på den Qruiserprofil som du använder mest / på din Qruiserprofil?

□ 1-3 gånger totalt
□ 4-6 gånger totalt
□ 1-5 gånger per dag

Mer än 5 gånger per dag

Jag är inloggad större delen av tiden

25c. Vilket län har du registrerat på den Qruiserprofil som du använder mest / på din Qruiserprofil?
25d. Vad har du registrerat för sexuell läggning på den Qruiserprofil du använder mest / på din Qruiserprofil?
 ☐ Homosexuell ☐ Bisexuell ☐ Experimentell ☐ Queer ☐ Heterosexuell ☐ Asexuell ☐ Vet ej / Annat 25e. Vilken sorts kontakt har du registrerat att du söker efter på den Qruiserprofil du
använder mest / på din Qruiser profil? Du kan svara med ett eller flera alternativ.
☐ Chat ☐ Vänskap ☐ Sex ☐ Relation ☐ Har ej registrerat
25f. Vad har du registrerat för civil status på den Qruiserprofil du använder mest / på din Qruiser profil?
☐ Singel ☐ Har en partner ☐ Har flera partners ☐ Har en partner som jag bor med ☐ Förlovad ☐ Gift ☐ Har ej registrerat
25g. Hur många favoriter har du på den Qruiserprofil du använder mest / på din Qruiser profil? Dubbelkolla gärna på din Qruiserprofil om du inte kommer ihåg.
25h. Vad har du registrerat för sysselsättning på den Qruiserprofil du använder mest / på din Qruiser profil?
 □ Anställd □ Student □ Arbetslös □ Egenföretagare □ Pensionerad □ Har ej registrerat

Här frågar vi angående den Qruiserprofil som du använder näst mest, studien använder den här informationen för att utvärdera om studien når alla delar av gruppen män som har sex med män. (Läs mer)

26a. Hur många gånger har du varit inloggad på den Qruiserprofil som du använder näst mest

de senaste	e 7 dagarna?
□ 1 □ 4 □ 1 □ N	te alls -3 gånger totalt -6 gånger totalt -5 gånger per dag Mer än 5 gånger per dag ag är inloggad större delen av tiden
26b. Vilke	en ålder har du registrerat på den Qruiserprofil som du använder näst mest?
26c. Vilke	t län har du registrerat på den Qruiserprofil som du använder näst mest?
26d. Vad l	har du registrerat för sexuell läggning på den Qruiserprofil du använder näst mest?
	omosexuell Bisexuell Experimentell Queer Heterosexuell Asexuell et ej / Annat
	n sorts kontakt har du registrerat att du söker efter på den Qruiserprofil du använde Du kan svara med ett eller flera alternativ.
	nat Zänskap Sex Relation Har ej registrerat
26f. Vad h	nar du registrerat för civil status på den Qruiserprofil du använder näst mest?
□ H □ H □ F □ C	ingel Har en partner Har flera partners Har en partner som jag bor med Förlovad Gift Har ej registrerat
_	många favoriter har du på den Qruiserprofil du använder näst mest? Dubbelkolla din qruiserprofil om du inte kommer ihåg.
26h. Vad 1	har du registrerat för sysselsättning på den Qruiserprofil du använder näst mest?
□ S □ A □ F	nställd Student Arbetslös Egenföretagare Pensionerad Har ej registrerat

Här frågar vi angående din tredje Qruiserprofil, studien använder den här informationen för att utvärdera om studien når alla delar av gruppen män som har sex med män. (Läs mer)

27a. Hur många gånger har du varit inloggad på din <i>tredje</i> Qruiserprofil de senaste 7 dagarna?
☐ Inte alls ☐ 1-3 gånger totalt ☐ 4-6 gånger totalt ☐ 1-5 gånger per dag ☐ Mer än 5 gånger per dag ☐ Jag är inloggad större delen av tiden
27b. Vilken ålder har du registrerat på din <i>tredje</i> Qruiserprofil?
27c. Vilket län har du registrerat på din <i>tredje</i> Qruiserprofil?
27d. Vad har du registrerat för sexuell läggning på din tredje Qruiserprofil?
 ☐ Homosexuell ☐ Bisexuell ☐ Experimentell ☐ Queer ☐ Heterosexuell ☐ Asexuell ☐ Vet ej / Annat
27e. Vilken sorts kontakt har du registrerat att du söker efter på din <i>tredje</i> Qruiserprofil? Du kan svara med ett eller flera alternativ.
☐ Chat ☐ Vänskap ☐ Sex ☐ Relation ☐ Har ej registrerat
27f. Vad har du registrerat för civil status på din tredje Qruiserprofil?
☐ Singel ☐ Har en partner ☐ Har flera partners ☐ Har en partner som jag bor med ☐ Förlovad ☐ Gift ☐ Har ej registrerat
27g. Hur många favoriter har du på din <i>tredje</i> Qruiserprofil? Dubbelkolla gärna med din qruiserprofil om du inte kommer ihåg.
☐ (Box to add number 0-) ☐ Vet ei

27h. Vad har du registrerat för sysselsättning på din tredje Qruiserprofil?		
	Anställd Student Arbetslös Egenföretagare Pensionerad Har ej registrerat	
28. Om	du vill ha information om säkrare sex, vart vänder du dig då? Du kan svara med ett eller	
	ternativ.	
	Vänner Familj Partner Skola/universitet Sjukvårdspersonal Mottagningar för sexuellt överförbara sjukdomar Mottagningar riktade till män som har sex med män, såsom Venhälsan & Gayhälsan	
	Ungdomsmottagning	
	RFSL:s sexperter	
	Noaks Ark RFSU	
	Hjälplinje (telefon)	
	www.sentry.nu	
	Söker på internet	
	Tidning/tidskrift	
	Bok/böcker	
	Annat:	
	Inte aktuellt	
ш	Vet ej	