What you love might kill you. Epidemiology, time trends and risk factors for sexually transmitted infections among men who have sex with men in Norway, 1992-2013

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TABLE OF CONTENTS

SUMMARY

Sexually transmitted infections (STI) are among the infections which could potentially be permanently eradicated. Unfortunately, they remain one of most common global health problems and represent a high burden in both mortality and morbidity, causing detrimental health effects. While some of the global efforts have recently led to important decreases in new STI, many countries observed simultaneous increases of high risk behaviour and STI among men, who have sex with men (MSM), in spite of scaled-up preventative messages.

In Norway, a great bulk of research on behaviour of MSM has been conducted before the advent of effective therapy against HIV, when HIV infection was a fatal diagnosis. This study aimed to provide current behavioural overview of MSM in Norway, describe recent STI trends and analyse risk factors for a STI in this population.

We conducted a large cross-sectional study on an Internet dating website aimed at MSM. In addition, we obtained and analysed data on gonorrhoea, syphilis and HIV from The Norwegian Surveillance System for Communicable Diseases (MSIS).

Our findings corroborated that STI constitute an important and increasing public health problem among Norwegian MSM, who are disproportionally affected by STI. Similar to experiences in other affluent countries, we observed worrisome increases in incidence of gonorrhoea, syphilis and HIV among MSM. Of particular concern is observed increase in concurrent infections of either syphilis or gonorrhoea and HIV, as STIs can facilitate the transmission of HIV. The STI epidemic among MSM is concentrated to Oslo municipality, where majority of MSM in Norway have been infected.

We provided further insights into demographics, sexual practices, STI prevalence, risk factors for STI and STI transmission knowledge in a large online sample of MSM. Certain demographic factors were associated with higher risk for an STI (two income categories and unknown/non-western ethnic background). Among behavioural risk factors, associated with an STI, were a high number of sexual partners and having unsafe sex under the influence of alcohol or selected drugs.

We identified a high sexual partners' turnover and frequent concurrent sexual relationships with women among study participants. Important proportion of MSM (23.7%) in the study reported unprotected anal intercourse (UAI) with a casual or anonymous partner in the last 6 months. Many study participants admitted not revealing their sexual practices to their dedicated physician. While they were aware of the risk of HIV transmission with UAI, awareness of current increasing STI trends in Norway was poor.

We identified some limitations of our methods. The increasing trends in number of reported cases are difficult to interpret without estimates of testing activity. There is some circumstantial evidence that the testing activity did not change for syphilis and HIV in the study time. The same cannot be said for gonorrhoea, where novel methods of testing have been introduced, affecting the positive predictive value of the test outcome and adding further uncertainty with probable changes in testing scope to include different anatomical locations.

Many challenges remain ahead in fighting the STI among MSM in Norway. In this study, important gaps in STI surveillance and knowledge of STI transmission among MSM in Norway, as well as a need for

modernisation of the surveillance system (MSIS), have been identified. Conduction of regular behavioural studies, which could be supplemented by prevalence studies among MSM, would improve our current knowledge on the topic. Effective interventions to prevent further STI spread in population of MSM are recommended, as well as efforts for early detection and effective treatment of these infections. Strengthening the general knowledge among MSM on increasing STI problem in Norway, as well as education on sexual risks associated with substance use are necessary.

ABBREVIATIONS

AIDS	acquired immunodeficiency syndrome
cART	combined antiretroviral therapy for HIV treatment, this term is an attempt of some scholars to replace previous less specific and clinically less correct term (and abbreviation for) "highly active antiretroviral therapy," HAART, which is still more predominant in the literature
CI	confidence interval
CSW	commercial sex worker
ED	erectile dysfunction
HIV	human immunodeficiency virus
MSM	men who have sex with men
MSMW	men, who have sex with men and women
NGU	nongonococcal urethritis
MSIS	The Norwegian Surveillance System for Communicable Diseases
NIPH	Norwegian Institute of Public Health
PEP	post-exposure prophylaxis; short-term antiretroviral treatment to reduce the likelihood of HIV infection after potential exposure, either occupationally or through sexual intercourse
PR	prevalence ratio
PrEP	pre-exposure prophylaxis; a new HIV prevention method in which people who do not have HIV take a daily pill to reduce their risk of becoming infected
STD	sexually transmitted diseases
STI	sexually transmitted infections
UAI	unprotected anal intercourse
UAT	unlinked anonymous testing
XTC	MDMA or Ecstasy

TABLES AND FIGURES

Tables

Figures

LIST OF PAPERS

The thesis is based on the following published papers. They will be cited by their respective Roman numeral.

I. **Jakopanec I**, Schimmer B, Grjibovski AM, Klouman E, Aavitsland P. Self-reported sexually transmitted infections and their correlates among men who have sex with men in Norway: an Internet-based cross-sectional survey. BMC Infect Dis 2010;10:261.

II. **Jakopanec I**, Borgen K, Aavitsland P. The epidemiology of gonorrhoea in Norway, 1993-2007: past victories, future challenges. BMC Infect Dis 2009;9:33.

III. **Jakopanec I**, Grjibovski AM, Nilsen O, Aavitsland P. Syphilis epidemiology in Norway, 1992-2008: resurgence among men who have sex with men. BMC Infect Dis 2010;10:105.

IV. **Jakopanec I**, Grjibovski AM, Nilsen O, Blystad H, Aavitsland P. Trends in HIV infection surveillance data among men who have sex with men in Norway, 1995-2011. BMC Public Health 2013;13:144.

THESIS OUTLINE

Chapter 1	presents a brief overview over the study population, some challenges regarding availability of information on STI among MSM and some general details about STI transmission, transmission dynamics and risk factors, found to be associated with STI acquisition
Chapter 2	presents the general objectives of the study, focusing on Norwegian MSM
Chapter 3	explains the methods used to collect and analyse the study data
Chapter 4	presents the main results of the study related to specific objectives
Chapter 5	by discussion of the findings, limitations and new knowledge added
Chapter 6	summarizes the main conclusions and recommendations for policy, practice and future research in the field

Following chapter six is a list of references. The published papers that this thesis is based upon can be found in the Appendices together with surveillance reporting forms for a reportable STI in Norway.

1   INTRODUCTION

1.1   Men who have sex with men as population

"A certain tiny percentage of everyone is gay."
Dan Savage

An epidemiologist, focusing on studying patterns of disease, is in need of three categories, in order to conduct her work: person, time and place. While time and place are usually straightforward and objective terms, person or rather study population is at times more challenging to define.

In this work, I will focus on a population that has been recognised as especially vulnerable to sexually transmitted infections. This population is behaviour-defined, which by itself comes with many methodological challenges. We would perhaps be able to find a population of opera singers, smokers, bicycle riders or bird watchers; though I assume no official population registers of these persons exist to include all of them. However, if one would ask a randomly sampled population, an honest answer on these activities is probably more likely than on sexual behaviour. When it comes to sexual behaviour, we touch upon most intimate and personal information, which may unfortunately still be a source of prejudices or social and legal constraints.

1.1.1   Overview of terms

To begin any study with "men who have sex with men" (MSM) as a study population is to begin with making an error. Treating an elusive term MSM as a population is an epidemiologist's shortcut and rough generalization rather than tangible definition, as it depicts someone whose behaviour may last for a very brief period of time and is sometimes never repeated. It is thus relatively uncertain who should this term represent, especially, if we try to apply it globally.

Apart from men, who would describe their own sexual identity as "gay" or homosexual, there is a variety of men, who have sex with men, but do not necessarily share the same sexual orientation, sexual or gender identity, but would belong to a risk group for sexually transmitted infections (STI) due to their behaviour. Mayer and Carballo-Diéguez point out no consensus on specific definitions exist (1), but it is perhaps useful at this point to provide a brief overview of the terms with their (unless indicated otherwise) proposed definitions:

Gender identity: an (individual) social construct of which of the gender groups a person belongs to (transgender – perception of being "trapped in a wrong body")

Sexual orientation: erotic or affectional disposition to the same or opposite sex

Sexual identity: the way people describe themselves in terms of their sexual orientation

Sexual minority: people whose sexual orientation or practices differ from the dominant heterosexual paradigm. This term encompasses sexual orientation and gender identity, including those who identify as being lesbian, gay, bisexual, transgender or intersex, or are MSM or women who have sex with women (2).

MSM: males who have sex with males, regardless of whether or not they have sex with women or have a personal or social gay or bisexual identity (3). This concept includes men who self-identify as heterosexual but have sex with other men.

Some of the above terms may be influenced by social norms and depend on time in history and culture. Human sexual behaviour is diverse (4) and, as pointed above, any individual choices in sexuality may be intermittent, transient or once in a life time only.

1.1.2   Prevalence of same sex sexual behaviour

Among 6300 males, whose life histories were examined by Kinsey in 1948, homoerotic play has been described to be quite prevalent among preadolescent males (66%), but much less (15%) reported oral or anal-genital contact and only 4% rated themselves as exclusively homosexual for all of their lives (1). In industrialized societies the prevalence of homosexual behaviour is estimated to range between 1-10%, depending on the sampling - lifetime vs. recent contact. If the latter is limited to last year, 3-7% of men engaged in homosexual activity and behaviours that are included (1).

Social expression of homosexuality might be restrained in many cultures with legally criminalised same-sex behaviour, persistent homophobia, discrimination and human rights violation, making the estimates more difficult in such settings and data scarce or unavailable. Review of studies on lifetime prevalence male sex with men yielded figures 3-5% for East Asia, 6-12% for South and South East Asia, 6-15% for Eastern Europe and 6-20% for Latin America, while if same activity was restrained on last year only, estimates were approximately half of lifetime figures (5).

In Norway, research of sexual practices using mailed anonymous questionnaire was conducted by Norwegian Institute of Public Health on a representative population sample of 10000 persons (18-60 and later 18-49 old) in 1987 and repeated in 1992, 1997 and 2002. When asked if they ever had any form of sexual interaction with a person of the same gender, 3.6% men in 1987, 4.8% in 1992, 5.1% in 1997 and 10.7% men in 2002 confirmed. The proportions were observed to be higher among 18-24 year old men: 5.8% in 1987 and 14.1% in 2002, but naturally lower if the question was limited to a sexual interaction with a man that happened in the last year: from 1.5 % in 1987 to 3.8 % in 2002 (6, 7)}.

In the representative national sample of 19 to 26 years old Norwegian adolescents from 1994 ("Young in Norway" study), with follow-ups in 1996 and 1999/2000, same-sex sexual experience at any time in their lives was reported among 6.3% of men and 1.5% had this experience in the past 12 months. Only 1.0% reported being exclusively attracted to the same sex (4). Among those males who had same-sex sexual experience at some point, 45.3% reported they currently felt no sexual attraction to people of same sex (4).

The estimates of the prevalence of same sex intimate behaviours among men remain controversial and are fraught with methodological problems (convenience sampling, appropriateness of inclusion of diverse individuals, cultural contexts, diverse terminology) (1, 8). Thus, no single study will give an exact estimate of a specific sexual behaviour. Also, research of sexual practices in general population is time consuming, costly and largely dependent on sufficient response rate which is notoriously difficult to achieve in this topic.

1.1.3   Historical overview of MSM as at risk population for STI

Now that we addressed the diversity and temporality of same-sex sexual experiences, we briefly describe the origins of the term MSM. The term "homosexual" originated in a sexological discourse of mid-19th-century Europe, while "gay" and "lesbian" originated in subcultural contexts about 50 years later (9).

The era of sexual revolution in the West in the late 1960s and 1970s has led to forming a homosexual subculture, in which intimacy with multiple partners became a norm (1). Together with other epidemiological risk factors, this lifestyle has likely paved the way for high transmission of sexually transmitted infections, including HIV, so that homosexual men in the USA and Western Europe were the first described cases with AIDS, which seemed to disproportionally affect them in the early years of epidemic (10, 11). The term MSM originated in scientific environments for analytical purposes of HIV and AIDS surveillance in the United States and was likely used for the first time in 1988 by Mantell and Petzke (1, 9) with its original meaning "men who have sex with men but do not identify as gay" with the purpose to distinguish this group from "gay" men.

MSM depicted an epidemiological definition of at risk (for HIV transmission) group, which included straight or bisexual identified men who had anal sex with other men; it was thus a category distinctive of sexual, race or social class identity. The rapid global spread of the term, first through English-dominant countries, coincided with the rise of the Internet and accelerating scientific knowledge exchange in the STI field and was probably aided by the fact that "gay " was seen as inaccurate in many non-Western contexts (9). By the early 2000s, the term has been transformed from excluding gay men into including them, thus shortened into "men who have sex with men". It remains debatable (but of less epidemiological significance) whether and how this term should also include transgender persons (9, 12), whether it includes adults only, what sexual practices are implicit under "sex" and how often (once in a lifetime?) should they be practiced to fulfil the criteria for inclusion of MSM (12).

1.1.4   Current debate on MSM term

Having apparent limitations, the term MSM has been recognised as problematic since its early uses, when "there has been a sense that we already know MSM will not work" (9) and has, not surprisingly, been widely criticized since, but it also seems that it opened for "new possibilities for subjectivity" (i.e. identification) (9).

"…the term anticipates its own failure, yet consensus and even unexpected confirmation emerge."
Boellstorff

While the term might seem to be here to stay and is being widely used in the scientific literature, this does not imply its overall acceptance. Claims have been made recently that "MSM" may represent "a source of discomfort and offence because it reduces gay men to just their social behaviour" and that the term has been used politically as a tool to "effectively deemphasize gay communities' early role in response to HIV" (12). While I remain sceptical that any other term would be completely neutral and acceptable to all, I am in a humble agreement with Prestage, who declares MSM term as epidemiologically simplistic, socially misleading and sexologically just silly (12). This is unfortunate because we currently lack any better substitutes that can be applied globally.

To work with MSM as a study population is to introduce a constantly changing or missing denominator, a great limitation in epidemiological studies. Furthermore, same-sex sexual experiences are not widely socially accepted. This is often a stigmatized population with legal and social sanctions and restrictions still persisting in many parts of the world. Though some may occasionally declare different findings (13), MSM are in general not "an easy to reach" population and are frequently referred to as "hidden population".

Though MSM represent "at risk" population with a certain "behavioural denominator", this is a largely heterogeneous group. This research work will, however, aim to address risk (and hence behavioural and demographic) differences among MSM at risk for STI in Norway.

1.2   Ethical and legal aspects of sexually transmitted infections research

"Everyone detected with AIDS should be tattooed in the upper forearm, to protect common needle users, and on the buttock, to prevent the victimization of other homosexuals."
William F. Buckley

The proposals for, attempts and acts of social isolation and rejection due to specific sexual behaviour or STI are far from being anything novel in human history. Unacceptable abuses of STI patients have happened in the past and many of them have paid these with permanently crippling conditions (transmitted in some instances also to their children), social exclusion, shame or their own lives. Even today, a great diversity in how human rights of patients with an STI are treated in the terms of law exists among countries.

I believe I should briefly touch upon history and the development of modern human rights when it comes to STI, privacy and sexual choices to provide an insight into challenges that Norwegian society has already been facing prior to its modern legislation.

1.2.1   From forced hospitalization to modern Communicable Diseases Control Act in Norway

Similar to the US prior to 1900 (14), "venereal diseases" were considered more of a moral problem in Norway. Modernisation of the society in the early 19th century in Norway has led to increases in the population and urbanization. Poor living conditions, poverty and crowding have contributed to rapid spread of epidemics such as cholera and leprosy. It was mainly the threat of these diseases and an example of the English Public Health Act that lead to an establishment of a "Sunnhetsloven" (*The Public Health Law*) in 1860 in Norway (15) . While this law did not specifically mention any STIs, the article §21 was generally used for hospitalizing (with use of police and against their will, if necessary) of individuals, who were considered a potential source of infection or/and could not afford sufficient care (judged by a doctor) at home. These persons were identified by different authorities, including medical personnel.

An English venereologist Jonathan Hutchinson, visiting Norway in 1869, expressed his criticism towards forced hospitalization of the patients, who might have been taken from their homes by police (16).

In the first half of 19th century efforts for eliminating STI focused on screening of the female sexual workers (assumed to be a core group of STI transmission at the time), who were obliged to get regular

checks with a physician, working at police station, in order to be permitted to work (17). This practice was stopped in 1887 with prohibition of prostitution (16).

A stronger emphasis on voluntary patient cooperation in STI diagnosis and treatment came only in 1923 with a new law proposal, which was initiated by the Swedish law on venereal diseases Lex Veneris in 1918 (18).

In 1947, the STI specific law "Lov om åtgjerder mot kjønnssykdommer" (*The Law on Measures against Venereal Diseases*) addressed the necessity of a responsible physician to conduct contact tracing in the case of an STI (17). This law made it a responsibility of presumably contagious person to accept diagnostic procedures and treatment. In spite of the aforementioned changes, forced treatment was possible for patients, who refused to cooperate fully on specific measures and fully complete their treatment. It was still possible for local boards of health to use police for hospitalizing presumably infectious persons until 1995, when this option was finally removed by the new Communicable Diseases Control Act (17, 19). The purpose of the modern Norwegian Communicable Diseases Control Act is to protect the society against communicable diseases by preventing their spread, introduction to Norway and potential export to other countries. The law protects the rights of all persons in Norway, regardless of citizenship, which have the right to healthcare services, care, prevention services and treatment for those communicable diseases, which are defined as hazardous to public health. The law is regulating the activities of the health authorities, which should initiate and conduct necessary actions against the communicable diseases, hazardous to public health, as well as inform the public.

It took decades before international human rights movements formed after Second World War lead to initiatives for protection of LGBT individuals or same-sex couples (20).

In 1951, the Norwegian ministry of justice white paper recommended de-criminalization of consensual homosexual acts of adult persons originating from the Norwegian General Civil Penal Code §213 (1903), but the Justice Department and Norwegian Parliament rejected this proposal. Homosexual partnership was thus banned in Norway from 1687 until 1972, when the article §213 was removed (21). Nonetheless, the Norwegian Psychiatric Association considered same sex orientation to be a mental disorder until 1977. LGBT individuals and same sex couples rights became a focus of litigation before the European Court of Human Rights (ECtHR) in the 1980s and 1990s (20).

Due to the above history, the acting of MSM was neither public, neither organised (until 1950-ies). It is thus very difficult to present the stigma related specifically to STI and MSM in the past. We can, nonetheless, briefly touch upon some of the most interesting ethical issues in the history, at times actions committed in the name of research, as well as sexual health.

1.2.2 A bitter path to modern ethics: syphilis research in 19th and early 20th century

"One night with Venus, a lifetime with Mercury."

The current ethical framework for STI research is built on bitter lessons and many lives destroyed in the past. In the early 19th century, wet nurses were being used to breastfeed infants of wealthy families in France (and elsewhere). The information on syphilis disease in the baby was frequently being withheld from wet nurses due to fear of them rejecting the job. In different experiments, involving doctors, the

bodies of these wet nurses were both exposed to the infection (which some eventually contracted) and used as vehicles for administration of mercury through breast milk in treatment experiments, which many times included highly toxic doses and were performed without consent (22). In addition, Jenner's success with vaccination against smallpox gave rise to the idea of "syphilisation", proposed by French doctor Joseph-Alexandre Auzias-Turenne. It meant the use of pus material from hard chancres on different other body parts of patients in a hope of inducing immunity, a practice also conducted on wet nurses (22, 23).

In Norway, professor Carl Wilhelm Boeck, chief of Dermatology department at Rikshospitalet, Oslo, conducted "syphilisation" on 1075 patients in the period 1852-1870 (16). He also forbade mercury use in treatment of syphilis at his department. Safe administration of potentially efficient mercury, a toxin at any dose, was likely impossible to achieve. Carl Wilhelm's nephew Caesar Boeck succeeded him as a department chief in 1875 and conducted one of the longest studies of syphilis in the world (1891-1910), including about 2000 patients in Oslo. He continued with mercury prohibition, but discontinued syphilisation. According to aforementioned Health Law from 1860, Boeck was in power to determine the length of patients' stay in the hospital. At the time, the poor were regarded as immoral and were in more danger to be forcedly hospitalized (24). Boeck's study results suggests that average time of hospitalization was about 100 days, 1.2 months longer for women (25). The doors to the department were locked and the department was surrounded by board fences and barbed wire until 1930s (16).

Finally, the ground breaking drug arsphenamine (Salvarsan) was made available to Oslo syphilis patients in 1910 (25). Boecks' findings and those of his successors, Bruusgaard and Gjestland echoed internationally (26). In 1932, when this was highly unnecessary, unethical and openly malicious, the idea of studying a «natural course of syphilis» gave rise to the notorious Tuskegee study in Alabama, USA, in which 600 impoverished and predominantly illiterate rural African American men were lured into collaboration under promise of free meals, health services and burial insurance. At the time of enrolment in the study, 399 men were infected with syphilis and 201 were considered not infected (27). Regardless of the outcome during the study, all 600 men were left untreated for decades. While the researchers passively permitted the infection to spread to the family members of men in Tuskegee study, over one thousand individuals enrolled in Guatemala experiment were intentionally exposed to, or inoculated with, *T. pallidum*, *N. gonorrhoeae*, or *Hemophilus ducreyi* between 1946 and 1948 (27).

The above history is described here to stress the importance of doctor-patient confidentiality, right to proper information, patient consent in all procedures, right to move freely, right to accessible diagnostics and treatment (in some countries, price of healthcare services or treatment are prohibitive for poor patients to afford one) and the patients' right to have a sexual life with consenting adults without any associated stigma. These goals are not yet globally achieved.

1.2.3 Modern prosecution and stigma related to sexual practices and STI infected

Results of surveys using the People Living with HIV Stigma Index from 2008-2011 suggested that more than half HIV positive participants reported verbal insults in Kenya, Rwanda and Zambia and more than 20% were physically assaulted in Estonia, Kenya, Nigeria, Rwanda and Zambia (28).

There is a decline in number of countries with HIV-related travel restrictions. Armenia, China, Fiji, Namibia, the Republic of Korea, the Republic of Moldova, Ukraine and the United States of America have only recently lifted their bans, while other countries continue to have them (28).

Norway was the first country in the world that introduced regulations (1981), under which homosexuals as individuals and as a group became entitled to a special criminal protection against derogatory references and discrimination. The law on partnership was put to practice in 1993 and Norway was the second country in the world to have accepted such regulation of homosexual partnership. This law was replaced by a new gender-neutral law on marriage on 1st January 2009 (29).

According to the United Nations General Assembly report from 2011, there remain about 85 countries in the world in which consensual adult homosexual conduct is punishable, in at least five of them with death penalty (30).

HIV transmission is specifically criminalized in about 60 countries (as of 2012) (28). Under Section 155 of the Norwegian General Civil Penal Code (31), it is a criminal offence for a person who knows that he or she is infected with a "communicable disease, hazardous to public health" (the full list of these specified infections is regularly revised), to expose another person to the risk of becoming infected. The punishment is up to six years imprisonment if found guilty - the same for taking part in or assisting in such act. In practice and resulting in conviction, this law has been used mainly for instances of HIV exposure. It is exposure itself that is punishable, even though the actual transmission might not have taken place.

Buying sexual services is a crime in Norway under article §202Aa in Norwegian General Civil Penal Code, effective on 1 January 2009 (31). Similar initiative was evaluated by Justice Department and Parliament already in 1997, two years before Sweden banned the purchase of sex, but the proposal was dismissed. By law, it is also prohibited to further or force to prostitution. Critics of the recent legislative changes, which were supposed to prevent human trafficking, point out that sex workers in Norway cannot have work contracts, sick leave and form unions. As renting out property to prostitutes could be regarded as pimping, selling sexual services in Norway is now becoming an underground activity (32). The knowledge on sex trade among MSM in Norway is scarce.

It is clear that in many countries around the world, legal challenges remain when it comes to full respect of human rights, already supported by international human rights documents. In order to address this inconsistency and patterns of abuse, related to gender identity or sexual orientation (and other status), international human rights experts met in Yogyakarta, Indonesia, in 2006. The resulting document, "Yogyakarta principles" is a set of 29 binding legal standards with recommendations to governments, regional intergovernmental institutions, civil society and the UN (33).

1.3   Sexually transmitted infections of public health importance in MSM

"Morality is a venereal disease. Its primary stage is called virtue; its secondary stage, boredom; its tertiary stage, syphilis."
Kraus, Karl

The historical term *venereal disease* referred to a rather short list of diseases. Some propose that the expression reproductive tract infections (RTI) de-stigmatizes such conditions and is more appropriate for infections, for which sexual transmission is still debated (34). To avoid unnecessary confusion with respiratory tract infections, currently, the terms sexually transmitted disease (STD) and sexually transmitted infection (STI) are used interchangeably in the literature, though "infection" is preferred over "disease", as infections may remain without apparent symptoms – permanently or at least for long periods of time. HIV is frequently named separately to STD and STI, but in this work I will use a term sexually transmitted infection, which includes all possible pathogens, including HIV.

The total number of distinct sexually transmitted or transmissible pathogens now exceeds 35 (34) and includes some of the pathogens that occur only very rarely in Norway, for example parasites (*Phthirus pubis* and *Sarcoptes scabiei*) or shigellosis. The epidemiologic and clinical evidence is suggesting some newly identified pathogens might be sexually transmissible (transmitted by contact of mucous membranes (35)), though in some, nonsexual routes of transmission predominate (34). The list will perhaps never be exhaustive, as we have learned that new pathogens – take HIV as an example, can and do emerge. It would be beyond the scope of this work to focus on all of them, but I believe it is necessary to provide brief descriptions of STI of public health importance and their epidemiological and clinical characteristics in men. It may be of interest to first take a look at the global burden of STI.

1.3.1   Global burden of STI

STD are among the world's most common diseases, with an annual incidence exceeded only by diarrheal diseases, malaria, and lower respiratory infections (36). Worldwide, the eight most prevalent STI are infections with: *Treponema pallidum*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, genital herpes simplex virus, HIV, hepatitis B virus (HBV), and human papillomavirus (HPV); all of which cause, even without HIV, most common conditions leading to health care consultations (36).

The total number of new cases of the four STIs among adults, aged 15 - 49 years, was estimated to be 498.9 million globally in 2008. Of these, 105.7 million were cases of *C. trachomatis*, 106.1 million of *N. gonorrhoeae*, 10.6 million of syphilis and 276.4 million of *T. vaginalis*. Males accounted for 266.1 million or 53% of the new cases. Compared to 2005, this was an 11% increase in number of cases. In addition, at any point in 2008 it was estimated that 100.4 million adults were infected with *C. trachomatis*, 36.4 million with *N. gonorrhoeae*, 36.4 million with syphilis and 187.0 million with *T. vaginalis (37)*.

These numbers reveal a great public health problem and stand for potential serious health consequences for the infected globally, if the infections are not treated on time. While it may be challenging to get morbidity estimates for all STI, sexually transmitted chlamydial diseases and trichomoniasis are reported

to be among 50 most common sequelae of all disability causing diseases and injuries, with global prevalence of 2.5% for chlamydia in men and 1.4% for trichomoniasis (38).

Until 2009, more than 60 million people have been infected with HIV and nearly 30 million people have died of HIV-related causes. At the end of 2011, an estimated 34 million people were living with HIV, which also represented 0.8% of adults aged 15-49. In the same year, 1.7 million people died from AIDS (a 24% decline compared with 2.3 million in 2005)(39). While the global number of newly infected was 20% lower in 2011 (2.5 million) than in 2001, the burden of epidemic varies considerably between countries, regions and populations affected (28).

Important steps have been made to prevent mortality from STIs in the past decade, resulting in decrease of mortality due to an STI excluding HIV by 43.5% between 1990 and 2010. Unfortunately, deaths due to HIV/AIDS were still among leading causes of death and years of life lost due to premature mortality in 2010 (40). While death rates fell for most of the diseases in the past decade, age standardised death rates from HIV/AIDS increased. In 1990, HIV/AIDS was ranked 35th most common cause of death globally, but it moved to be the 6th in 2010 (40). In addition, syphilis is number 36th as a leading cause of premature mortality globally in 2010 (40).
Globally, HIV/AIDS is the 36th leading cause for years lived with disability in 2010, ranging from 1st in Southern sub-Saharan Africa to 131st in Western Europe (38).

Though a great regional variability exists in mortality and morbidity due to STI, a large proportion of them is treatable and all are preventable infections - often with simple, inexpensive interventions (36).

While there is an overall decline in HIV rates in many high-income settings (Australia, France, the UK and USA), increases among MSM are observed in the era of cART – "re-emergent epidemics" (41). Similar to HIV, other STIs are disproportionally affecting MSM in many countries, including European Union and the European Economic Area (EU/EEA) (42). STI of relevance for MSM may be identified as: HIV, gonorrhoea, syphilis, hepatitis B, hepatitis A, intestinal parasites (amoebae and *Giardia lamblia*), intestinal bacteria (especially *Shigella*) and lymphogranuloma venereum (LGV) (29). As a lot of them occur only sporadically in Norway, the detailed description of all of them would be beyond the scope of this work.

1.3.2   Bacterial infections in men

"Even diseases have lost their prestige, there aren't so many of them left. Think it over... no more syphilis, no more clap, no more typhoid... antibiotics have taken half the tragedy out of medicine. "
Louis Ferdinand Celine (1894-1961)

Louis Ferdinand Celine did not live long enough to observe the great come-back of bacterial infectious diseases, and their impressive capability to develop antibiotic resistance faster than we humans develop new antimicrobial drugs. Unfortunately, we now face problems such as multiple drug resistant gonorrhoea evolving into an untreatable disease.

In the following descriptions of selected sexually transmitted bacterial infections, I will briefly describe their relevant pathogenesis and most prevalent symptoms of infection in men.

1.3.2.1 Chlamydia and lymphogranuloma venereum (LGV)

Chlamydia trachomatis bacteria is an obligate intracellular parasite and responsible for the largest number of nongonococcal urethritis (NGU) cases, which can also be caused by *Trichomonas vaginalis, Ureaplasma urealyticum and Mycoplasma genitalium.*

Different clinical diseases, caused by *Chlamydia trachomatis*, are usually, but not exclusively, associated with different serovars. Most common genital tracts infections in men, leading to urethritis, proctitis, epididymitis and trachoma, are caused by trachoma biovar. The lymphogranuloma venereum (LGV) biovar of chlamydia causes a systemic disease. LGV proctitis may develop to ulcerative proctitis with serious sequelae, while the LGV infection of the genitourinary tract presents with inguinal adenopathy with draining buboes (1). In men, non-LGV *C. trachomatis* strain leads to urethritis in 1-3 weeks. There is a possibility of eye infection (inclusion conjunctivitis) through contact with infective genital discharges (43).

Chlamydiae do not always produce clinically apparent infections. Chlamydial infections follow a self-limited acute course and resolve into a low-grade persistent infection, which may last for years, during which exacerbations may occur (43, 44). Alternatively, the bacteria are cleared by the immune system. Azithromycin as a single-dose treatment of choice makes the therapy of genital tract infection relatively simple (43).

1.3.2.2 Gonorrhoea

Neisseria gonorrhoeae (gonococci) is a diploccocus, related to *Neisseria meningitidis* (meningococci), the etiological agent of bacterial meningitis (45).

In men, most common infection with gonococcus is acute anterior urethritis, evident after an incubation period of usually 2-5 days. The symptoms include dysuria, accompanied by a mucoid or mucopurulent discharge, which in most patients becomes purulent within a day. Without treatmet, spontaneous resolution usually follows in a few months. Complications include epididymitis, acute or chronic prostatitis, posterior urethritis, which may lead to stranguria and urinary urgency, seminal vasculitis and infections of Cowper's and Tyson's glands (46).

Rectal infections are frequent among MSM and many are asymptomatic, however symptoms (in fewer than 10% of infected) may range from anal pruritus, discharge, rectal bleeding, to overt proctitis with severe pain, tenesmus and constipation. Similarly, over 90% of pharyngeal infections are asymptomatic, though pharyngitis or tonsillitis has been anecdotally reported. Spontaneous resolution of pharyngeal gonorrhoea in a few weeks has been described (47).

While urethral infections are rarely asymptomatic in men (1-3%), asymptomatic pharyngeal and rectal infections are likely important in gonorrhoea transmission, as these men rarely seek medical attention and treatment (46). Untreated infection may persist for considerable periods and increase the risk of disseminated infection, including dermatitis-arthritis syndrome, endocarditis and meningitis.

In the past decades, a gradual selection of antibiotic resistant gonococci through chromosomal mutations (low-lever resistance to penicillins and tetracyclines) and plasmids that mediate high resistance led to ineffectiveness of penicillin and tetracycline in most areas. More expensive antibiotics

such as spectinomycin, ciprofloxacin and ceftriaxone are effective, though ciprofloxacin resistance is effectively emerging (45).

1.3.2.3   Syphilis

"It is unthinkable for a Frenchman to arrive at middle age without having syphilis and the Cross of the Legion of Honor."
Andre Gide

Similar to other members of the family *Spirochaetaceae*, treponemes, too, have a spiral shape, corkscrew motility and periplasmic flagella (endoflagella). Different human treponemal diseases (syphilis, yaws and bejel) are caused by three uncultivable subspecies of *Treponema pallidum* and transmitted by direct contact. Due to their long and thin dimensions, darkfield or phase contrast microscopy is best to visualize them. Binding of antibody to the *T. pallidum* surface is very limited and requires long incubation periods (48).

Syphilis infection may last decades and active clinical phases (primary, secondary and tertiary stage) with varying symptoms alternate with asymptomatic (latent) period. Most typically, primary painless syphilis lesion, a chancre, appears at the site of infection in one third of patients, accompanied by regional lymphadenopathy. Spontaneous chancre resolution is usually followed by secondary stage maculopapular rash of the skin, mucous membrane lesions and hypertrophic lesions in moist body cervices (condylomata lata) in a few weeks or months, accompanied by systemic lymphadenopathy (48).

Patients in the latent stage are seemingly unaffected, but the Oslo study of untreated syphilis at the turn of the twentieth century suggested that about 25% may experience relapses to secondary syphilis during the early latent stage (i.e. less than a year since infection). Untreated, about one third of infected persons developed seriously disabling or fatal late active disease with gummatous tissue destruction, cardiovascular involvement or neurosyphilis (49).

Serological tests for syphilis lack sensitivity and though some may be helpful in assessing the stage of infection, they are unreliable (50). In determining the stage, particularly in asymptomatic patients, clinicians thus rely on previously documented syphilis tests, anamnesis (i.e. most likely time of exposure, data from contact tracing, known previous treatment) and clinical evaluation. Uncertain stage in asymptomatic patients with unknown duration of infection is an important limitation of early syphilis (i.e. primary, secondary and early latent syphilis) surveillance.

While syphilis treatment remains relatively simple and inexpensive with benzathine penicillin, macrolides (a drug of choice for some patients, allergic to penicillin) resistance has been reported and is supposed to be prevalent in several countries (51).

1.3.3   Viral infections in men

1.3.3.1   Human papillomavirus

Human papillomavirus (HPV) is spread between male sexual partners through insertive or receptive anal intercourse, oral sex, digital-rectal contact and scrotal contact (1). It causes a largely transient infection which usually results in spontaneous clearance, however persistent infection with low risk oncogenic and

high risk oncogenic HPV genotypes, prevalent among MSM, can lead to extragential warts, precancerous anogenital conditions (anal dysplasia, usually slow-growing), as well as cancers of anus, penis and oropharynx (52, 53). Concurrent infections with multiple types of HPV are common and MSM are especially at risk for anal cancer, as they have higher HPV prevalence, higher incidence rate and lower clearance rate in this anatomical site than heterosexual men, while prevalence, clearance and incidence seems similar for penile and oral HPV infection (53).

HPV vaccines effectively prevent warts, penile and anal cancers and reduce high grade anal lesion among men. CDC and European Medicines Agency currently recommends the vaccine for MSM up to 26 years of age (54). Current research suggests that anal Papanicolaou (Pap) screening may be a cost effective screening method for anal cancer prevention among MSM (55).

1.3.3.2   Herpes virus

Herpes simplex virus (HSV) is one of most common sexually transmitted infections. While HSV 2 type occurs predominantly as a genital disease, HSV 1 is associated with both oropharyngeal and genital disease (56). Over the past two decades, a rising proportion of genital herpes is caused by HSV 1, particularly among college students, young heterosexual women and MSM (57). After a first local infection of epithelial cells, HSV is transported via sensory neuronal axons to the neuronal cell bodies of dorsal root ganglia, establishing a latent infection with potential subsequent brief and frequent reactivations. Severe disease is more likely among those with immunodeficient or immunosuppressed conditions (56). Most reactivations happen in a form of brief asymptomatic shedding episodes, which contribute to high HSV transmission rates (57).

1.3.3.3   Human immunodeficiency virus (HIV)

HIV is the cause of one of the most successful, lethal and widespread pandemics. The evolutionary origins of the virus and its relation to primate lentiviruses have been well established. HIV-1 and HIV-2 belong to lentivirus genus of retroviruses (RNA viruses), which do not, similar to other retroviruses, cause cancer, but establish a chronic infection that results in a long incubation period, followed by a chronic symptomatic disease ("lenti" – lat. slow)(58). HIV-2 has lower pathogenicity and slower disease progression (59).

In 1981, the infection with HIV was first recognised as an acquired immunodeficiency syndrome (AIDS), comprised by opportunistic infections and lymphadenopathy among otherwise healthy sexually active gay men in the United States (58, 60). Contrary to early beliefs that HIV emerged out of nowhere, there is now good evidence that the virus has likely been present in human population for around a century (58).

CD4^{+} T lymphocytes are a primary target of the virus and its complex direct and indirect effects ultimately lead to their depletion. The virus replicates itself in lymphoid tissues throughout the body (lymph nodes, spleen and gut-associated lymphoid tissue) and , in addition to CD4^{+} cells, also affects other cells of immune system (B cells, NK cells and CD8^{+} cells), causing aberrant immune activation (60).

The acute phase of HIV infection, lasting several weeks, is marked by HIV viremia, followed by a reduction in viral burden. This phase may include flu-like clinical symptoms such as fever, swollen lymph

nodes, throat and muscle pain, rash and malaise etc., denoting acute retroviral syndrome. The stage of clinical latency (asymptomatic or chronic HIV infection) follows, which can vary from a few weeks to twenty years or more usually with no or few symptoms and during which the virus is able to efficiently spread among the population, is still a major public health challenge (58).

While some individuals (i.e. "long-term nonprogressors") remain healthy for many years without having received any treatment, in the vast majority (over 90%) of HIV-infected patients progression to AIDS – see definition further below - is inevitable, Figure 1 (60, 61). Any particular individual's disease course may, however, vary considerably. Those with highest viral burdens (acute HIV, AIDS and rapid progressors) are most contagious (62).
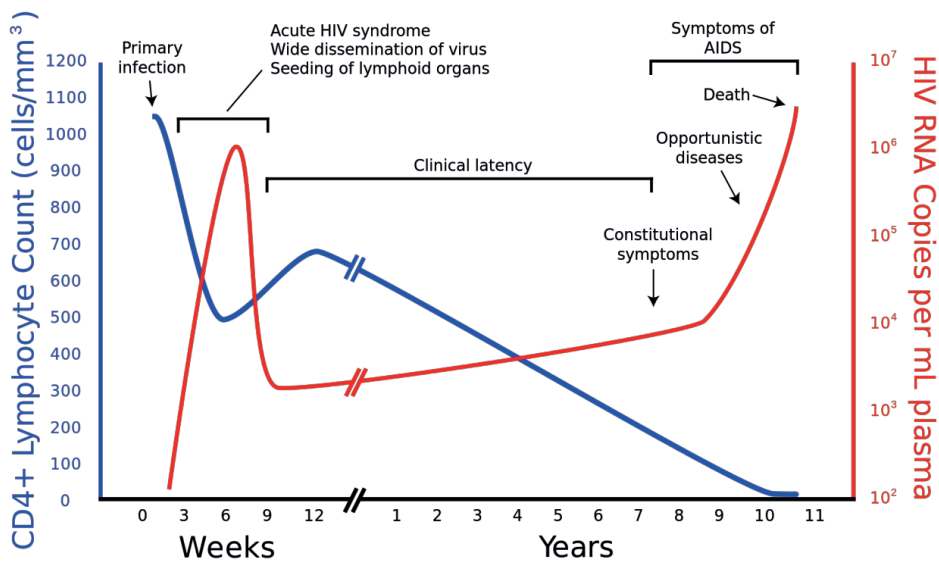
Figure 1. A generalized graph of the relationship between HIV copies (viral load) and CD4 counts over the average clinical course of untreated HIV infection. Blue line: CD4+ T cell count (cells per µL), red line HIV RNA copies per mL of plasma, secondary axis. Version published on 20:30, 13 December 2012. No copyright. With permission under the Creative Commons CC0 1.0 Universal Public Domain Dedication (61).

AIDS has a high fatality rate and survival of patients in affluent countries without treatment used to be 3-5 years after the diagnosis (59). The life expectancy is significantly prolonged if combined antiretroviral therapy (cART) is initiated early; offering near normal quality of life, provided long term good adherence is maintained (63). Since the virus invariably reappears after the cessation of suppressive treatment, presumably from cell viral reservoirs, the infection remains incurable (58).

The initial surveillance definition of an AIDS case included more than a dozen opportunistic infections and several cancers, provided other immunodeficiency causes were ruled out. The definition was later

broadened to include laboratory confirmation of HIV and additional indicator diseases. The Centers' for Disease Control (CDC) definition from 1993 included a CD4$^+$ cell count under 200/mm^3 or a CD4$^+$ T lymphocyte percentage of total lymphocytes is less than 14%, regardless of clinical status, to be indicative of AIDS. These biological criteria were not included in the European case definition (64).

Disagreement remains on when to start the treatment in diagnosed patients. While there is a global consensus that any HIV+ person with CD4 counts less than 350 cells/μl should be treated, it remains controversial whether cART is indicated in asymptomatic HIV-infected persons with CD4 counts above 350 cells/μl, or whether it is more advisable to defer treatment and monitor CD4 count (65).

In Norway, a positive HIV antibody test currently needs to be confirmed with two independent tests in the reference laboratory. Different tests (HIV antibody, HIV antibody and HIV antigen, nucleic acid amplification tests (NAAT) etc.) differ according to sensitivity, specificity and ability to detect an early infection. Fourth generation HIV combined test (antibody and p24 antigen) can be positive as early as 1-2 weeks after the exposure, greatly shortening the "window period", when the antibodies might not yet be detectable (62). Pooling sera for NAAT can be a cost-effective method of increasing the sensitivity of the testing (62).

Same technique is also used in unlinked anonymous testing (UAT) seroprevalence surveys in which residual blood samples taken for any diagnostic purposes are tested after they have been irreversibly unlinked and anonymised from their source. In this instance, explicit consent is not obtained in the UK (66), while it is necessary in the Netherlands (67). Different population groups may be targeted with UAT (new-borns, STI clinics users, intravenous drug users, MSM attending a venue etc.). In Norway, UAT has not been deemed epidemiologically necessary and has never been undertaken (67).

In July 2012, the US Food and Drugs Administration approved a rapid HIV home test, which allows users to test themselves for HIV infection at home. Home HIV tests remain a controversial public health topic.

Post-exposure prophylaxis (PEP) has proven to be highly effective in reducing the risk of acquiring HIV infection, if initiated soon after exposure and continued for 28 days (68). In July 2012, the US Food and Drugs Administration approved of daily oral tenofovir and emtricitabine for pre-exposure prophylaxis (PrEP) to prevent HIV infection in high-risk individuals in the USA, but such therapy remains highly controversial for healthy individuals (69).

1.3.4 Epidemiology of STI among MSM and STI co-infections

"To have a curable illness and to leave it untreated except for prayer is like sticking your hand in a fire and asking God to remove the flame."
Sandra L. Douglas

The initial decline of STDs among MSM due to safer sex practices in the advent of the AIDS epidemic (as well as shorter survival of those with HIV) was followed by an observed increase since the late 1990s in industrialized nations (1). Variety of causes for this unexpected increase have been suggested (70) and we shall explore some which may be applicable to MSM in Norway.

Currently, outbreaks of syphilis, lymphogranuloma venereum (LGV), hepatitis C virus infection (HCV) and other STI in many European cities suggest high-risk sexual behaviour and extensive sexual networking (42).

It should be noted that in convenience samples, the STI prevalence figures are often estimated among MSM at highest risk (8), thus a likely overestimation. Due to inevitable difficulties in reaching and screening entire population of MSM, described previously, the prevalence estimates given below might be biased. The prevalence of HIV infection among men who have sex with men in surveys in capital cities is on average 13 times higher than that in the country's general population (28). In sampling, which is many times not nationally representative, as it is more likely conducted in the capitals, European countries where HIV prevalence is ≤1% in general population, reported the following prevalence among MSM in recent years: Hungary 4%, Czech Republic 5%, Sweden 6%, Latvia 7%, Slovenia 7%, Ireland 9%, Portugal 10%, Switzerland 11%, Germany 12%, Greece 13%, Spain 13%, Netherlands 14%, France 17% (28). Between 2004 and 2009, HIV reporting rates in MSM increased in the EU/EEA from 3.5 to 4.1 per 100 000 males (42). In many countries, including Norway, data on HIV prevalence among MSM are not available or monitored regularly. Compared to heterosexual people in the same populations, MSM have higher rates of dual- and multiple-variant HIV infections (41).

Human papillomavirus (HPV) is thought to be the most common STI in developed countries (1) and the prevalence of high-risk oncogenic infection is highest in MSM (52). In HIV negative MSM, the prevalence of HPV is estimated to be 50% in HIV positive, 85% (1, 52). Among the latter, the incidence of anal cancer is twice as high as compared to HIV negative MSM (53).

The risk of acquiring HIV infection seems to be higher in those 22-34% of MSM, who carry HPV strains of high risk oncogenic potential (52). Reciprocally, existing HIV infection is a risk factor for HPV infection (epidemiological synergy). MSM with high risk HPV genotypes are more likely to be infected with other STIs, such as rectal infection with *Chlamydia trachomatis, N. gonorrhoeae* and HSV-2 (52). NGU (causing bacteria) may enhance HIV transmission and acquisition among MSM (1). The HSV infection increases the risk of HIV acquisition by two to three fold as well as HIV transmission in dually infected individuals (57).

In the European Union and the European Economic Area (EU/EEA), the proportion of HIV co-infections is highest among MSM with HCV (95–100%) and LGV (35–100%) and is lower for syphilis (20–60%) and gonorrhoea (20–35%) (42).

1.3.5   Transmission of STI associated with different sexual practices

"I never miss a chance to have sex or appear on television."
Gore Vidal

Ethical and logistical issues prevent direct estimates of efficiency of STI transmission per sexual act. The estimates thus come from longitudinal cohort studies, documenting these behaviours (1), though it should be stressed that such studies face several methodological problems (the source of infection is difficult to identify retrospectively and relationships might not be monogamous). I will address factors that play a role in infection establishing itself in a susceptible population in the next chapter and will

here discuss transmissibility – a probability for a susceptible individual to get infected during a single sexual contact with an infected individual (35).

Compared to heterosexual people, the estimation of per act risk in MSM is more complex not only because regular relationships are frequently nonmonogamous with partners of unknown STI status, but also because MSM can take either insertive or receptive role (71).

By (unspecified) sexual contact, syphilis is transferred to 30% of uninfected partners (49).

In a systematic review, the efficiency of HIV transmission for receptive unprotected anal intercourse (UAI) was estimated to be 1.4% [CI: 0.2-2.5] per act and 40.4% [CI:6.0-74.9] per partner (i.e., irrespective of duration and frequency of sex acts) with no risk difference observed between heterosexuals and MSM (72). In a study on 1427 MSM in Australia, the per-act probability for receptive UAI was 1.43% [95% CI: 0.48–2.85] if ejaculation occurred inside the rectum, and 0.65% [95% CI 0.15–1.53] with penis withdrawal prior to ejaculation.

The estimated transmission rate in the same study for insertive UAI in participants who were circumcised was 0.11% (95% CI 0.02–0.24), and it was 0.62% (95% CI 0.07–1.68) in uncircumcised men (0.16% regardless of circumcision status) (71). In the review, no transmission estimates per act were possible and transmission estimate for insertive UAI per partnership was 21.7% [95% CI: 0.2-43.3] and combined insertive and receptive UAI per partnership 39.9% [95% CI: 22.5-57.4](72).

Gonorrhoea is likely quite efficiently transmitted by insertive or receptive anal intercourse (46), considering the risk of infection for men in in a single heterosexual intercourse has been estimated to be 19.0-25.0% (73). Other STI, efficiently transmitted by anal intercourse, include: syphilis, chlamydia (including LGV), herpes simplex virus and hepatitis B (74). These infections may result in either asymptomatic or symptomatic proctitis, including itching, pain, cramps and discharge in and around the anal canal (74).

Oral HIV transmission has been estimated to be 0.4/1000 fellatio acts (1), but this is an unreliable estimate, as not many records of such transmission exist and it is thought that many factors, affecting oral health, are involved.

Pharyngeal bacterial infections are of special interest, as they are frequently asymptomatic and may, in the absence of regular testing and treatment, persist for longer periods (44). Receptive oral sex without a condom and use of anal sex toys were identified as a major risk factors of syphilis infection in a matched case-control study in France (75). Pharyngeal chlamydia, detected in 1% of Australian MSM, was not associated with pharyngeal symptoms and pharynx was the only location of the infection in 70% (44). Similar results were reported among 2197 MSM in Germany (2009-2010) with pharyngeal chlamydia detected in 1.5% (rectal in 8.0%) and pharyngeal gonorrhoea detected in 5.5% (rectal in 4.6%). As much as 38% of gonorrhoea infections were exclusively pharyngeal (76). Furthermore, only 5.1% of MSM with a pharyngeal infection reported any local symptoms (76).

Similar to oro-genital sex, which is a route of transmission for *Chlamydia trachomatis, Neisseria gonorrhoeae*, syphilis, chancroid, *Neisseria meningitidis* and respiratory organisms, oro-anal sex (rimming) is implicated in the transmission of various enteric infections (77), for example *Shigella, Giardia lamblia, Salmonella, E. hystolitica, Campylobacter, Cryptosporidium* and hepatitis A, which may

occur commonly among sexually active MSM (78). While it is unclear how readily these STI are transmitted in the acts of penile-oral and oro-anal sex, it is plausible that pharyngeal infections may have a role in anogenital infections (44), especially considering using a condom in oral sex might be practiced rarely among MSM. In one study, oro-genital transmission accounted for 26% of urethral gonorrhoea in MSM (79). Syphilis was also associated with rimming (80).

Transmission of enteric infections, causing proctocolitis or enteritis is also possible by digital-anal contact (fisting). Practices that lead to mucosal trauma (multiple sexual partners, fisting, and use of sex toys) have been explored in relation to HCV transmission. The association with HCV is less clear for HIV uninfected MSM, partially because these practices are not very prevalent, few studies followed MSM for long enough period and due to concurrent injecting of drugs. For HIV infected MSM, however, the association between these high risk practices and HCV transmission has been well established, especially in the presence of genital ulcerative disease (81). Fisting (with gloves) was also associated with syphilis transmission (80).

Nonetheless, condom use in penetrative anal sex does not guarantee protection for bacterial and protozoan STIs, which are often spread without penile penetration (74). The use of saliva as a lubricant in insertive or receptive penile-anal intercourse or fingering/fisting is a widespread practice among MSM, which might explain why MSM are at greater risk for cytomegalovirus, HBV and more recently discovered Kaposi sarcoma-associated herpes virus infections (82).

Sharing semen ("cum play") can include ejaculation over the anus, rubbing semen over the anus or using semen as lubricant during masturbation or for digital and penile penetration with potential risk for STI transmission (83). A form of semen exchange called "felching'' involves oral ingestion of semen from a partner's anus following UAI (83).

Gonococci survive only a short time outside the human body and transmission is, although unlikely, possible also directly through a shared object, such as a bath towel (45) or an inflatable doll (84). Hence, shared sexual toys may also be a means of STI transmission.

Urophilia ("watersports" or "golden showers") practices may transmit hepatitis, cytomegalovirus, genital herpes, chlamydia and gonorrhoea.

It should be pointed out that other sexual practices, not necessarily involving an anal intercourse, do come with a risk of STI transmission, which is difficult to ascertain. Examples have been given in a study of sexual practices of MSM: "nudging" (touching or rubbing of another man's anus with the penis without a condom); "dipping" (partly inserting or briefly inserting the penis into the anus without a condom, followed by immediate withdrawal); and "docking" (pulling one's foreskin over another man's penis)(85). As the authors point out, some of these practices may explain anal infections in the absence of reported anal sex.

1.4 Transmission dynamics and sexual networks

"Let me be, was all I wanted. Be what I am, no matter how I am."
Henry Miller

Members of the "core group", who have multiple sex partners and change them frequently, are more likely than members of the general population to become infected with an STI. Because the "core group" is defined primarily on behavioural grounds, members are not permanent (46). This is relevant for potential eradication of STI. Clearly, an infection cannot persist unless an infectious person transmits the disease to a susceptible person. As opposed to other infectious diseases, dependent on daily social contacts for their transmission, STI contacts might be fewer and happen intermittently. Mathematical models suggest that gonorrhoea prevalence could decline to zero, had it not been for core group members transmission, as the transmission is not 100% efficient and spontaneous cures do occur (46).

At the population level, the spread of an STI depends upon the average number of new cases of infection generated by an infected person. This can be described in terms of reproductive rate (R) which, for an STI, depends upon the efficiency of transmission – the probability of transmission in a contact between an infected individual and a susceptible one – an "attack rate" (b), the mean rate of sexual partners change (c) and the average duration of infectiousness (D) and the proportion of the population that is susceptible (e) as expressed in the form:

$$R = b * c * D * e$$

The higher the value of R, the greater the potential for the spread of the infection (35). Since sexual contacts are only intermittent, it is not surprising to learn that most of STI induce poor immunity if any at all and vaccines currently exist for only a few. In order for a STI pathogen to withstand eradication, a long period of infectivity, often months or years is necessary. Antimicrobial and antiretroviral resistance are also among important factors that may potentiate STI transmission as they typically prolong the period of infectivity (70).

Additionally, re-activation in case of herpes viruses means repeated infectivity (often preceding clinical symptoms) in some individuals and hence more successful transmission (86), resulting in a very high serological prevalence (59). By using condoms (affecting b), lowering number of sexual partners (c) and developing vaccines (e), the eradication of STI is hypothetically possible.

As we have seen in the previous chapter, different sexual practices (related to route of exposure and intensity of exposure) might be associated with different attack rates. Whether or not the exposed individual will become ill will also depend on characteristics of the pathogen (e.g. virulence of strain) (87). It should also be stressed that the above formula is too simplistic to include contact patterns in society, which are, especially in the case of STI, not random or homogenous (86). In practice, the mean rate of sexual partners change is also difficult to evaluate, as the behaviour may greatly vary by time and include concurrent sexual relationships with different people. Sexual networks, partner concurrency and patterns of partners mixing, such as random, assortative (like with like) or disassortative have been used to mathematically model the HIV epidemic (88). STI spread from core groups with high number of sexual connections (i.e. "high density networks"), in which STI are maintained endemic, to lower risk individuals

through concurrent partnerships of "bridge persons", often involving clients of sex workers or mobile men, for example migrant workers, truckers etc. (36, 88).

While hypotheses that non-gay homosexually active men might represent a group, "substantially less at risk than gay men" do exist (12), a review of studies on male same-sex behaviour in low- and middle-income countries indicates that an unexpectedly large proportion of MSM involves in heterosexual sex and many of them may lack knowledge about risks of unprotected anal intercourse and wrongfully assume it to be lower than a risk of unprotected vaginal intercourse (8). Due to bridging, the STI burden of MSM is not an unimportant and isolated public health problem. In order to interrupt the STI transmission, core and bridging groups should be targeted with prevention programs (36).

1.5   Monitoring of sexually transmitted infections transmission

"Perfect numbers like perfect men are very rare."
Rene Descartes

Effective actions in preventing the transmission of STI among in any population are: vaccination, where available, monogamous relationships, testing, thorough contact tracing, effective treatment, lowering infectivity, decreasing risk of exposure (condoms and other barriers), and vaccination.

The aims of the ongoing modern STI surveillance systems are to further our understanding of STI distribution in the community in order to inform prevention efforts or to evaluate the effectiveness of prevention interventions (14).
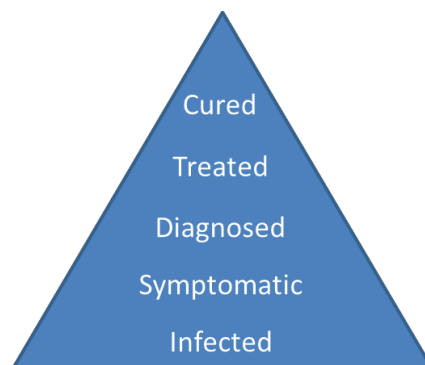
Figure 2. From infection to cure: system challenges to efficiently detect and treat all infected. Some spontaneous cures may however occur for certain STI.

Modern laboratory techniques provide affordable detection and confirmation of STIs and are important part of surveillance systems. In general, the accuracy of surveillance will depend heavily on the amount of laboratory tests performed. Changes in testing activity are likely to affect surveillance results. This is particularly problematic with asymptomatic STI, in which patient is less likely to seek medical assistance (Figure 2). Among the diagnosed cases of STI, only a certain proportion is often reported. Thus, in spite of spontaneous cure of some STI, the numbers in the surveillance system represent only the "tip of the

iceberg", as more than half of the STI will remain undiagnosed (some of those because they are predominantly asymptomatic) (36). The main types of STI surveillance activities are: case reporting, prevalence monitoring, sentinel surveillance, behavioural surveillance, population based surveys and health services and administrative data surveillance (14).

Relatively few countries have all of these activities in place and perform them regularly. Such systems tend to be complex and costly. More frequently, surveillance activities vary from country to country, from laboratory data only to clinician-reported data (with behavioural data), from database with overall national coverage to the one limited to selected sentinel sites. This is also the reason why it is difficult to compare STI data among different countries and true incidence estimates are difficult to obtain, as they might be influenced by incubation period, prevalence of asymptomatic cases, availability and cost of healthcare services and other.

Anonymous unlinked prevalence studies are an efficient way of monitoring HIV prevalence among designated population groups. In this approach, anonymous residual sera of a population group, tested for other purposes (army recruits, pregnant women, STI clinic patients etc.) are tested for a public health purpose of HIV burden estimate the population. As informed consent is not necessary, a potentially representative sample of the target population is thus obtained. By implementing pooled HIV testing of residual sera, the costs of this method decreases even further. Under The Ethical Guidelines for Epidemiological Investigations by The Council for International Organizations of Medical Sciences (CIOMS) unlinked anonymous screening should be paralleled with provision of linked confidential or anonymous voluntary HIV testing.

Surveillance data are likely to underestimate the frequency of transmission among MSM, as they rely on patient informing a healthcare worker on their often stigmatised sexual behaviour (89). While this problem is generally perceived to be of minor importance in Norway, detailed data on this issue are scarce. We can assume disclosure of sexual behaviour may be particularly difficult for MSM who originate in cultures that stigmatise behaviour of MSM, but uncertainty remains to what extent are Norwegian MSM open about their sexual practices with healthcare personnel.

1.5.1 Contact tracing

The Norwegian Communicable Diseases Control Act (17, 19) describes the responsibilities of treating physician, municipal medical officer, index patient and contacts in contact tracing (sometimes also referred to as "partner notification"). It is a responsibility of a patient to take part in and responsibility of a physician to conduct the contact tracing. Contact tracing should be only done for those STD, which are by the law defined as " the communicable diseases, hazardous to public health": HIV, gonorrhoea, syphilis, genital chlamydia (including LGV), hepatitis A, B and C. Other STD are not considered hazardous to public health under Norwegian legislation and there is no obligation to conduct contact tracing for them.

According to the Communicable Diseases Control Act (19), the following conditions must be fulfilled for the contact tracing to be required: 1. the disease should be currently recognized as hazardous to public health, 2. conducting contact tracing is feasible, 3. principles of infection control require that the contact tracing is performed (17, 19).

In Norway, all contacts have the right to free testing, doctor check-up and treatment if there is a suspicion they might be infected with infection, recognized as hazardous to public health.

1.6 The role of risk behaviour and risk factors in transmission of sexually transmitted infections

"I can resist everything except temptation."
Oscar Wilde

If durable decreases of STIs are to achieved in the population of MSM, a wide spectrum of factors that potentiate transmission needs to be addressed at the personal, interpersonal, community and structural level (1). Already in 2005, Fenton and Imrie grouped risk factors to account for increases in STI rates among MSM in Western Europe and US into individual level factors, infectious agents, sociocultural environment and biomedical environment (capability of effective interventions by health services) (70).

I have addressed factors related to infectious agents previously. I will now briefly touch on some other factors, particularly those, that might seem irrational in the light of available knowledge of safe sex practices in the affluent countries.

1.6.1 Individual level factors

Several risk factors, associated with increased risk taking for STI transmission, have been identified among MSM: lack of willingness to change one's sexual behaviours, emotional distress, ongoing substance use, past sexual abuse, (unprotected) sex with familiar partners, a diminished sense of sexual control and sexual compulsivity (1). Combined with sexual risk behaviours (unsafe sex, high number of sex partners, sexual concurrency, serosorting and payment for sex), demographic changes (increased survival of HIV positive due to cART, higher prevalence of HIV and increased prevalence of same-sex experiences) are also thought to contribute to the increases of STI among MSM(70).

Intentional UAI, in which STI transmission is a possibility, has been referred to as "barebacking" and carries connotations of something risky and exhilarating (90). While the possibility of a controversial subculture with "bug chasing" (intentional UAI with a HIV serodiscorcondant partner) and corresponding "gift giving" has been explored by some researchers (91). Such practices, however remain marginal and the epidemiological data suggest that the majority of MSM do not intentionally seek UAI (90).

Further non-condom based strategies to lower the risk of infection might sometimes be employed at the act of UAI, such as strategic sexual positioning (in which HIV-negative barebackers are more likely to be insertive - "top" - rather than receptive - "bottom" - in UAI with anonymous or casual partner), "coitus interruptus" (lowering exposure to semen) and serosorting (searching for partners of same HIV serostatus) (71, 91). These practices may be negotiated online before the intercourse on specialized websites, some of which cater exclusively to barebackers.

Reported condom use with UAI does not always equal safe sex, as many MSM may choose to engage in risky "cum play" with their partner on the same occasion, due to semen potentially having great symbolic and personal importance for gay men, while others, however, might see semen exchange as "toxic and a source of danger" (83).

While erection enhancing drugs may be taken for valid reasons, many seem to take them unsupervised by healthcare personnel (92). A study 18–25 year old college males showed that 12.7% had a lifetime history of erectile dysfunction (ED) and 24.8% reported ED related to condom usage; only one participant experiencing ED discussed his condition with a doctor (93). While majority (57%) has taken erection enhancing drugs to treat ED, 29% took them to enhance sexual performance (93). A study among those who take these drugs recreationally suggested they are more likely MSM and engage in higher risk sexual behaviours (92).

While some of the sexual risk taking might be intentional, other behaviour creates an environment where the choice of safe practices is less likely to occur: for example, psychoactive substances were proposed to be used as a disinhibitor for risky sexual practices, leading to traumatic sex and mucosal damage (81). Methamphetamine ("meth") and sildenafil citrate (Viagra) have been shown to be associated with high risk behaviour (unprotected sex acts) and STI (HBV, syphilis and HIV) incidence, however it is the combination of meth, Viagra and nitrite inhalants (poppers), frequently taken to enhance sexual performance in sexual marathons, that has been associated with the highest risk for HIV seroconversion (94). Poppers is a peripheral vasodilator, used to facilitate anal penetration and more likely to be used during ''rougher'' sex (95). Also other drugs like Ecstasy (XTC), cocaine, and Viagra may lead to an increase in risky sexual behaviour (91). Party-n-play (PnP) preference, i.e., mixing legal/illegal drugs and sex, or being "a party boy" may be disclosed on the Internet profile of sex-seeking MSM (91).

Studies suggested that those, who consume any alcohol, drink before/during sex and binge drink may be at a higher risk for HIV infection (96). Associations found between alcohol use and increased sexual risk behaviour, while demonstrated by some studies, are more inconsistent compared to aforementioned psychoactive substances, and assumed to be a result of more complex behavioural patterns (97). The hypothetic explanations for higher risk of sexual behaviour with alcohol consumption ("unrestrained sexual behaviour") include:

1. psychoactive properties of alcohol (alcohol myopia theory – alcohol intoxication causes more extreme behaviour by impairment of cognitive capacity to systematically process risk-relevant information),

2. psychological expectancy properties (alcohol expectancy theory or "reverse causation" – those wanting to pursue risky sex use alcohol as a disinhibiting substance or as a cultural signal of their sexual availability in public settings),

3. personality traits such as sexual sensation seeking: risk prone individuals with sensation seeking personality type are more likely to drink alcohol and engage in sexual risk behaviour (98).

Individual patterns of alcohol consumption are influenced by diverse social contexts, thus, alcohol use in association with risky sexual behaviour is more challenging to study. While a clear (behavioural) causal inference has not been established (97) and does not seem dose-dependent (96), there is a biological plausible causal role of alcohol in the acquisition of HIV and other infections, as alcohol exposure induces immune deficiencies resulting in increased susceptibility to bacterial and viral pathogens (96). Many studies confirm, however, MSM being particularly at risk for alcohol and drug abuse compared to other subpopulations (99, 100) or being less likely to abstain from drinking or accept abstinence as a treatment goal (101).

1.6.2   Socio-cultural environment factors

The distinction between individual and socio-cultural environment factors is somewhat arbitrary. Many factors mentioned in the previous section might be influenced by social and cultural environment. For example, in the first decades of HIV epidemic, the UAI was assumed to occur due to poor planning, unintentional incidents, relapses, and mutual consent between partners, but since, social scientists proposed more complex macro-, meso-, interpersonal-, and intrapersonal level factors like homonegativity, community norms, partner intimacy, and drug use, which all converge to influence the likelihood that an individual will bareback (90).

Increased international mobility has led to an increasing risk for STI among MSM. Research of sexual encounters per week suggests travelling as an independent predictor of increased sexual activity and an opportunity for sexual mixing (102). The risks for STI are increased on holiday due to exposure to new sexual networks and the prevalence of STIs in the foreign community, the partner exchange rate, high-risk sexual practices, lack of condom use (including UAI) and substance abuse (102, 103). The risks taken while travelling, however, differ greatly on the purpose of travel and its associated destination (destinations with "party atmosphere" like gay resort, hot spot vs. other, availability of a large number of male commercial sex workers) (103)."Circuit parties", scheduled weekend-long dance parties in different cities globally, are frequently attended by MSM, exhibiting high levels of risk behaviour, such as recreational drug use and high risk sexual behaviour (70).

Some bigger cities in Europe (Barcelona, Berlin, Paris etc.) have invested in LGBT tourism and attract MSM for their cultural and festive experiences (104) and as they became a popular destination in the community of MSM, many of them also reported outbreaks or increases in STI.

Prior to their travel, some MSM explore online to find potential sex partners and risk behaviours in this group has been suggested to be the highest (103). Overall, the Internet is gaining popularity as a social networking tool and is now a widespread and acceptable way to meet partners for dates and relationships. The popularity of online dating is driven by convenience of access, larger user base, greater anonymity and flexible self-presentation options (105). Some of these properties are particularly utilised by non-gay identified and bisexual men. While some studies suggested that the use of Internet to find sexual partners might be an independent risk factor for STIs (as in the outbreak of syphilis in San Francisco, linked to a chat room), others could not establish such association and proposed that online sex seeking may be a marker, rather than the cause of risky behaviour (106). Undoubtedly, the Internet enables rapid worldwide dissemination of ideas and new behavioural norms and ultimately links sexual networks that may traverse vast physical distances (70). This interesting topic has been explored further in our study.

The hypothesis that the emerging use of geosocial networking smartphone applications (GSN apps) targeting MSM may influence the STI transmission is plausible, due to their seemingly narrow purpose of "cruising" or "hooking up". These apps typically include geolocating feature, which enables consensual identification of members in the geographical proximity and disclosure of one's own location details (107). While some pioneer research among GSN apps users (young MSM) suggested high rates of sexual partnering and UAI(108), the assumption that GSN apps are only used to facilitate sexual encounters is an oversimplification (107).

1.7   Epidemiological study designs used in investigating sexually transmitted infections

"What is not in the open street is false, derived, that is to say, literature."
Henry Miller

Means of getting a fully representative population sample of MSM might be impossible to achieve and the question of an objective denominator is doomed to stay unanswered. Studies, done on non-representative, self-selected (convenient) samples of men recruited through gay magazines, organisations, bars, clubs or personal networks are more likely to recruit those with self-identification as gay or bisexual and active participants of such networks (4), potentially excluding other MSM. As more inventive patterns of recruitment of MSM are emerging, Prestage's criticism that MSM are largely (in excess of 90%) represented by gay men in samples of "virtually every study" in Australia (12), is no longer justified.

While large cohort studies are pricy and may be inconvenient for behavioural monitoring among high risk MSM, they are more frequently applied among HIV positive patients to study their health outcomes, immunological processes of HIV infection, drug efficiency and phylogenetic changes of the virus (for example, The Swiss HIV Cohort Study). By numbers of selected patients (N=297), a smaller cohort study was also done on HIV positive in Oslo 1988-1993 to study the onset of AIDS (109). Birth cohort longitudinal studies, inclusive of entire population, may answer questions on STI prevalence in the population and risk factors for STI incidence, such as, for example HSV-2 incidence rates study and associated risk factors (number of partners, age period and gender susceptibility) in New Zealand (110). Large repeated cross-sectional cohort studies (i.e., pseudolongitudinal studies) may answer detailed questions on sexual behaviour and attitudes and the trends in those, for example Natsal surveys (111) in Britain.

In the recent years, Internet recruitment has been shown to be an efficient and cheap way to recruit MSM (112), however recruiting through social networks or specialised gay websites increases the likelihood of assortativity and sampling bias. Nonetheless, such recruitment offers possibility to approach MSM, not identified as gay. A study of an online Nordic community has, for example, recruited male website members with either preference for male contacts or preference for both men and women, resulting in a relatively low proportion of MSM, who identify as "homosexual" (39.7%) and a higher proportion of those, who identify themselves as "bisexual" (36.8 %) or "experimental" (18.0%) (105). In an attempt to lower assortativity, snow-ball techniques (respondent driven sampling) are frequently applied (113).

Compared to cohort studies, case-control studies are usually considerably less costly and time consuming as there is no need to obtain information on everyone in the source population (114). Case-control studies may be, for example, conducted among MSM visiting STI clinics. A multicentre case-control study conducted at 72 sites in different regions in Germany from 2008-2010 studied risk factors for recent HIV seroconversion among MSM (115), while another case-control study conducted in Lille, a large urban area of northern France, studied risk factors for primary, secondary or early latent syphilis (75).

Randomised controlled trials are often used to assess novel treatment or prophylaxis approaches, for example association of PrEP with changes in sexual behaviour among MSM (116) or behavioural interventions using online digital media (117).

2   SETTING AND AIMS OF THE THESIS

"I don't know the question, but sex is definitely the answer."
Woody Allen

2.1   Setting

The population of Norway, a sparsely populated Scandinavian country with physical borders to Sweden, Finland and Russia, increased, predominantly due to intense immigration, from 4.3 million in 1995 to 5.0 in 2012 (118). The number of men increased from 2.1 million in 1995 to 2.5 in 2012. The expected life span for men born in 2011 was 79 years and is expected to increase up to 90 years in 2100 (118).

Similar to many industrialized countries, the Norwegian population is aging and the number of persons, aged 67 years and older will double from 610 000 in 2002 to 1.1-1.4 million in 2050, with a predicted proportional increase from 13% to 18% of total population in 2050 (118).

Proportion of immigrants and persons with at least one of the parents being an immigrant (second generation immigrants) increased from 4.3% in 1992 to 11.4% in 2010. In January 2013, first generation immigrants represented 12% and second generation immigrants represented 2% of Norwegian population. Most immigrants settle in the capital Oslo, where first and second generation immigrants represented 30% in January 2013 (118).

Norway is one of the most affluent countries in the world with a prosperous economy and a low unemployment rate (3.1% est. 2012). In 2012, reported 55300 USD GDP per capita ranked Norway among first 10 countries globally. Out of 185 United Nations member states, Norway is ranked first on Human Development Index (2011 and 2012), a measure, based on life expectancy, literacy, education, standards of living and quality of life scores (119).

Healthcare services, primarily funded through taxes, are provided on the principle of equal access to all inhabitants. The coverage for welfare services and expenses is universal through the National Insurance Scheme, assuring everybody a minimum of social security, regardless of income, and is administered by National Insurance Administration (*Ny arbeids og velferdsvorvaltning* - NAV). Healthcare has a three level structure: national/state level (responsible for national health policies), four regional health authorities responsible for specialist healthcare services and subsequent municipalities responsible for primary healthcare services (120). According to WHO estimates, the total health expenditure as percentage of gross domestic product (GDP) was 9% in 2009.

Adult prevalence rate of HIV/AIDS in Norway was 0.1% (2009 estimate). Though 1064 cases of AIDS were reported from 1983-2013 in Norway (121), past data from the Oslo HIV-cohort study (1988-1993) have suggested Norwegian MSM being at higher risk of developing AIDS than injecting drug users or heterosexual persons (adjusted for CD4+ level at the beginning of the study)(109).

Data for this study was collected during 1992-2012. This research was started during my training in European Programme for Intervention Epidemiology Training programme (EPIET) in 2007 at the Norwegian Institute of Public Health (NIPH), organized by European Centre for Disease Prevention and Control (ECDC) in Stockholm, Sweden, during which guidance and feedback were provided both by

mentors/facilitators and peer trainees. The researchers, who contributed to this study, were predominantly based at the NIPH, a governmental national competence institution responsible for health issues related to forensic medicine, physical and mental health, epidemiology, surveillance and prevention of communicable diseases and prevention of harmful environmental influences.

2.2   Aims of the study

The main aim of the study was to present the burden of selected STIs among MSM in Norway, their trends and some of the most common risk factors associated with high risk of STI acquisition, including sexual behavioural data. As the data on MSM in Norway are scarce, the secondary aim of the study was to acquire some sociodemographic data on this population.

The specific objectives of this study were to:

- Provide a demographic and behavioural overview of men who have sex with men in Norway (paper I and supplementary unpublished data)
- Describe the distribution and secular trends of sexually transmitted infections among men who have sex with men in Norway (paper I, II, III, IV)
- Analyse risk factors for STI among men who have sex with men in Norway (paper I and supplementary unpublished data)

3   MATERIAL AND METHODS

3.1   Data sources

Paper II, III and IV are based on the Norwegian Surveillance System for Communicable Diseases database, (*Meldingssystem for smittsomme sykdommer - MSIS)* managed at NIPH. STI reporting has a long tradition in Norway. From 1876, VD cases were reported in Oslo and from 1882 in other cities; and a national system of reporting was introduced in 1922 (16). The modern MSIS was implemented nationwide in 1975 (122) with named AIDS reporting introduced in 1983 and anonymous HIV reporting in 1986 (67).

STI testing is available at various settings including general practitioners, hospitals, youth clinics and STI clinics in Norway. All reference laboratories are obliged to report any gonorrhoea, syphilis or HIV positive results anonymously to the Norwegian Institute of Public Health (NIPH) using a unique reference number. The laboratory sends one part of the form with the reference number to NIPH and the other part, carrying the same reference number, to the referring clinician, who provides more detailed data, including epidemiological data of the patient to the NIPH. Ensuring high coverage of reporting, the NIPH may contact the clinician who failed to submit their part of the form or has sent an incomplete report.

At NIPH, only newly recognised cases with early syphilis, defined as laboratory confirmed, primary, secondary or early latent syphilis (less than a year since infection) are entered into the MSIS database (paper III). In the case of HIV, CD4+ level at diagnosis is not reported. In addition to the main diagnosis (reportable STI), currently, only one concurrent STI can be recorded in MSIS, so this is usually done with a prioritisation of syphilis as a reported concurrent STI, followed by gonorrhoea (paper IV). In the surveillance data, we defined MSM as cases who told their physician prior to reporting that they most likely got infected by another man (homosexual transmission).

The data were updated with most recent years, including 2013 data, collected from MSIS database on the 9th January 2014. On this date, the collection of case reports for 2013 was not yet officially closed.

Paper I is based on data from an Internet cross-sectional survey on members of the Norwegian MSM-oriented website. The survey was initiated by the NIPH in cooperation with "Gay and Lesbian Health Norway" and conducted from 1 to 19th October 2007. Only men, who lived in Norway and reported having sex with a man at least once in their life, were included in the analysis.

3.2   Ethical and legal aspects

This research did not include any interventions.

Participants in the Internet cross-sectional survey (paper I) were presented online with the aims of the study, eligibility information and were offered informed consent before entering the study. Only consenting participants were directed to the web-based survey instrument. The survey was of no direct benefit to the respondents. No personal identifiers were collected.

The study was approved by the Regional Committee for Medical and Health Research Ethics, Southern Norway, and by the Norwegian Data Inspectorate.

In papers II-IV, we used anonymous or de-identified data from MSIS. The data was used according to directives of the Communicable Diseases Control Act (19), the MSIS and Tuberculosis Register Regulations (123) and the Health Register Act (124). The MSIS is administered by the NIPH and the data is used for the public health function of surveillance. As the use of data for our study was aligned with legislation directives and associated public health function, approval from the Regional Committee for Medical and Health Research Ethics was not considered necessary.

3.3   Cross-sectional study design (prevalence survey)

In paper I, we used the cross-sectional study design, in which associations between the outcome and explanatory (independent) variables are studied at a single point of time (a "snapshot"). The advantages of cross-sectional studies are that they are relatively inexpensive, take up little time to conduct, can estimate prevalence of outcome of within a sampling population, enable studying associations of many outcomes and risk factors, and are useful for public health planning. While loss to follow up is not possible, the response rates might affect the representativeness of the sample (125).

Since the dependent and independent variables are measured at the same time, it is difficult to make causal inference (low evidence grade). In addition, this design might lack power for statistical significance, especially when the outcome studied is a rare disease (126). Particularly in the case with longer-lasting infections, there is a prevalence-incidence bias, as any risk factor resulting in death will be under-represented among those with the disease (125).

3.4   Statistical methods

Descriptive statistics with frequency distribution were used for presentation of the characteristics of MSM, diagnosed with gonorrhoea, syphilis or HIV (and reported to MSIS) or sampled in an Internet-based cross-sectional survey. Bivariate comparisons were performed using Pearson's chi squared test (paper III) or Poisson regression with robust variance estimates (paper I and IV). In the latter case, the strength of association was given by crude prevalence ratios (PR) with 95% confidence intervals (CI). The level of statistical significance was set at 0.05.

Chi-squared test of independence can be used to analyse the association of two categorical variables with two or more possible values. The test compares the observed frequency distribution of mutually exclusive outcomes in a categorical variable to the expected (hypothesized) values (127), if the variables were independent. The chi-squared numeric result relates to the probability of observed data given the null hypothesis (i.e., no association between the variables) is true.

Chi-square = Σ $(O-E)^2/E$

The chi square value is the sum of the squared difference between observed (O) and expected number (E), that is, deviation, divided by the expected number (128) - for all possible categories or table cells (127). This final result is then assessed against a standard reference table according to degrees of freedom (Df, C – number of table columns, R – number of rows) in the contingency table (127).

Df = (C-1) x(R-1)

Underlying assumptions of the chi-squared test of independence are that observations are independent and that the sample size is sufficiently large (128).

Associations between the outcome and categorical independent variables with and without adjustment for potential confounders were studied by Poisson regression with robust variance estimates. Poisson regression models the natural log of the outcome as a linear function of the independent variables (log-linear model) and permits direct estimation of prevalence ratios (129). The model assumes that the probability of occurrence is constant over time and that occurrences of an outcome are independent of one another (130) - an unlikely situation when occurrence of an STI is the outcome of primary interest. As prevalence data in a cross–sectional study follow a binomial distribution, the variance of the coefficients results in wider confidence intervals compared to those based on the binomial distribution. This is explained by comparing the binomial variance, p(1-p) with a maximum of 0.25 when p=0.5 with Poisson variance, λ, that grows steadily with the intensity of the process. That is, the variance estimated by the Poisson model will be very close to the binomial variance when the outcome is rare, but will be increasingly greater as the outcome becomes more frequent (underdispersion). Using robust variance estimates seems to improve this issue and Poisson regression with robust variance may be a better alternative for the analysis of cross-sectional studies with binary outcomes than logistic regression (129).

The strength of association in multivariable model using Poisson regression with robust variance estimates was estimated (in multivariable model) with adjusted prevalence ratios with 95% confidence intervals (CI) (papers I and IV).

Linear regression analysis was used to estimate trends over time. Taking into account possible autocorrelation and different variability of the data between the years (heteroskedasticity), the regression coefficients for linear trends were evaluated using Prais-Winsten autoregression for gonorrhoea (paper II) and linear regression with Newey-West procedure (paper III) for syphilis and HIV (paper IV).

Prais-Winsten procedure models a first order autoregressive linear model, but does not adjust for heteroskedasticity (131). We used this model in cases where we identified autocorrelations by the Durbin Watson test and did not observe any heteroskedasticity. If the latter was found, then we used the Newey-West procedure.

The Newey – West variance estimator is an extension of the commonly used sandwich robust variance estimator, which produces consistent estimates when there is possible heteroskedasticity in addition to autocorrelation in the data (132, 133). The number of cases of the studied infections in the Norwegian population in the current year correlates with the number of infection in the previous year(s). Moreover, the variance is not constant over time, indicating heteroskedasticity in our data. Thus, the use of the Newey-West procedure provides more appropriate estimates of standard errors than the standard ordinary least-squares regression. In most cases our data had only the first order autocorrelation.

Multivariable analysis studies associations of risk factors and their relative contribution to outcome, but it is worth emphasizing that the statistical methods (or significant associations) cannot prove causality (130). Multivariable models in our papers included variables, associated with the outcome at p<0.15 in crude analysis as well as potential confounders and risk factors, previously shown as predictors of STI.

Using empiric criteria for choosing variables is not ideal, as variables, not significantly related to the outcome in bivariate analysis, could potentially be associated with the outcome in multivariable analysis, for example if suppresser effect exists (134).

If two or more variables are closely related to one another, the model may not be able to reliably assess the independent contribution of each of them – a case of multicollinearity (130). Hence, the procedure of running a correlation coefficient matrix was done before entering the variables into the models to detect potential problems.

Where the categories unknown or missing were statistically different in the crude analysis from the rest of the categories within a variable, they were entered in multivariable analysis as a separate category, otherwise they were excluded. If there was zero variance in a category, we excluded this category from the analysis.

Missing data is a problem with multivariable analysis, as those subjects will be tossed out of the analysis, even if the subject has valid values on the other variables. While deleting cases with missing values remains the most common method of dealing with missing data in clinical research, this decreases the power of the analysis and may bias the study (134). With some exceptions, in which new categories were introduced to represent missing data, our data had a high proportion of completeness, thus making the bias due to exclusion of missing data unlikely. As described in section 3.1, efforts were routinely made to obtain missing data in MSIS.

3.5   Extended results

The internet study contained 119 questions. By the time of writing this summary, only one peer-reviewed article has been published (paper I) based on the study. Since no report was ever published, I added some selected results of interest from the 2007 study into the Results section. I am humbly aware that doing so might seem confusing and unnecessary for the sole purpose of this thesis; however my intention was to use the Results section as a communication channel for those interested in the field. Likewise, I have decided to update the surveillance data with the data up to and including 2013, to comment on latest developments in the trends and STI transmission among MSM in Norway.

I am aware that the extended results section might be a general disadvantage and make the thesis summary less concise, but I find it of value to present these data. In order not to further expand the topics beyond my published work, not all presented results are discussed in detail in the Discussion.

4   MAIN RESULTS

In this chapter, I will present the main findings from each paper. I will also supplement them with additional previously unpublished data to shed further light on the findings. This mainly relates to updates of the time series presented in papers II-IV (more recent years added) and to further details from the survey presented in paper I.

4.1   Demographic and behavioural overview of men who have sex with men in Norway (paper I)

First, I present a closer look of some sociodemographic data from the large survey sample of MSM in 2007 including 16-74 years old male members (N=2430) of a MSM-oriented Norwegian website, who lived in Norway and reported having sex with a man at least once in their life is of interest. This is more detailed than presented in paper I, where aggregated cultural background was used.

Table 1. Self-reported cultural background by place of residence of MSM responding to the Internet-based cross-sectional study, 2007, unpublished data, and Statistics Norway data

Municipality	Cultural background, study participants				Proportion of men with immigrant background by county in 2007)*
	Unknown N= 34 (%)	Norwegian N=2265 (%)	Immigrant background, N=131 (%)	Total number of participants N=2430, %	
Akershus	1 (2.)	149 (6.6)	12 (9.2)	161 (6.6)	10.1
Aust-Agder	0	24 (1.1)	3 (2.3)	27 (1.1)	6.0
Buskerud	1 (2.9)	83 (3.7)	3 (2.3)	87 (3.6)	9.8
Finmark	0	13 (0.6)	0	13 (0.5)	4.5
Hedmark	1 (2.9)	62 (2.7)	2 (1.5)	65 (2.7)	4.6
Hordaland	7 (20.6)	187 (8.3)	3 (2.3)	197 (8.1)	6.5
Møre og Romsdal	2 (5.6)	45 (2.0)	1 (0.8)	48 (2.0)	4.0
Nord-Trøndelag	0	21 (0.9)	1 (0.8)	22 (0.9)	3.1
Nordland	0	68 (3.0)	1 (0.8)	70 (2.9)	3.6
Oppland	0	57 (2.5)	1 (0.8)	58 (2.4)	4.6
Oslo	14 (41.2)	976 (43.1)	74 (56.5)	1064 (43.8)	24.8
Rogaland	4 (11.7)	139 (6.1)	10 (7.6)	153 (6.3)	8.5
Sogn og	0	18 (0.8)	1 (0.8)	19 (0.8)	4.2

Fjordane					
Sør-Trondelag	3 (8.8)	160 (7.1)	3 (2.3)	166 (6.8)	5.9
Telemark	0	37 (1.6)	1 (0.8)	38 (1.6)	6.7
Troms	0	62 (2.7)	6 (4.6)	68 (2.8)	4.5
Vest-Agder	0	31 (1.4)	1 (0.8)	32 (1.3)	8.3
Vestfold	0	64 (2.8)	6 (4.6)	70 (2.9)	7.2
Østfold	1 (2.9)	64 (2.8)	2 (1.5)	67 (2.8)	9.1
Not applicable**	0	5	0	5 (0.2)	0

*includes immigrants and those born in Norway with immigrant parents, data from Statistics Norway

** declared they currently live in Norway

The median age for Internet survey respondents was 31 years. In comparison, the median age for MSM, diagnosed with gonorrhoea was 31 years (paper II), 36 years for MSM diagnosed with HIV (paper IV) and 37 years for MSM diagnosed with syphilis (paper III).

The majority of the Internet cross-sectional survey participants were highly educated (57.6 %) and earned a taxable income in 2005. Majority (71.8%) had a job, while students were a second biggest group in employment category (18.3%, unpublished data). A small proportion (3.8%) was retired or received social support, a proportion, similar to those without current employment (3.2%, unpublished data).

4.1.1 Sexual and social behaviour

The majority of the Internet cross-sectional survey participants reported to be living alone (50.8%), 15.9% lived together with their male partner, 11.6% lived with other tenants, 9% lived with their parents, 6.3% were in a partnership (only one of these also declared to be living with a female partner), 3.3% reported they live with their spouse, 2.0% lived with the female partner, 1.7% lived with their own biological children and 0.4% lived with a partner and their children (unpublished data).

4.1.1.1 Sexual debut (unpublished data)

"It's better to break ones heart than to do nothing with it."
Isaac Asimov

Among the MSM participating in the Internet survey in 2007, 1 148 (47.2%) responded they never had sex with a woman. The age of MSM at first sexual intercourse with a woman (N=1299) varied from 10 to "more than 50 years" (median 17 years). Only 4% were older than 25 years when they had their first intercourse with a woman and 187 (14.4%) reported having the intercourse before the legal age of consent (15 years) in Norway.

Similarly, age of first sexual intercourse with a man varied from 10 to "more than 50 years" with 17 years as a median (N=2428), however as much as 581 (23.9%) were younger than 15 years.

4.1.1.2   Sexual identity, social relations and sexual practices

As mentioned in the introduction, sexual orientation might differ from sexual practices. I compared the answers from our 2007 survey (paper I, merged categories, herby detailed) with the results of the European MSM Internet Survey (EMIS) among MSM in 2010(135), Table 2:

Table 2. Sexual identity in two different surveys in the population of MSM in Norway, (2007, 2010).

Internet study on MSM (2007)					the European MSM Internet Survey (EMIS (2010), Norwegian answers	
Declared sexual orientation	N (%)	Sex with a woman (anytime in life), N (%)	Current steady relationship with a woman, N (%)	Current steady relationship with a man, N (%)	Declared sexual orientation	N (%)
Homosexual	1805 (74.3)	764 (59.6)	56 (23.7)	792 (84.6)	Gay or homosexual	1717 (82.0)
Homosexual with some heterosexual inclination	283 (11.6)	217 (16.9)	36 (15.2)	100 (10.7)		
Bisexual	225 (9.3)	205 (16.0)	93 (39.4)	33 (3.5)	Bisexual	232 (11.1)
Heterosexual	7 (0.3)	6 (0.5)	4 (1.7)	2 (0.2)	Straight or heterosexual	9 (0.4)
Heterosexual with some homosexual inclination	70 (2.9)	66 (5.1)	40 (16.9)	1 (0.1)	Don't usually use a term	118 (5.6)
I am uncertain of my sexual orientation	40 (1.6)	24 (1.9)	7 (2.9)	8 (0.8)	Any other term	19 (0.9)
Total	2430 (100)	1282	236	936		2096 (100)

A majority of MSM (1492, 61.4%) in the 2007 survey revealed they are currently not in a steady relationship with a man. On the other hand, 9.7% had a steady relationship with a woman and 33.7%

(819) with a man. Of the latter, 81 had a steady relationship with both a woman and a man. Interestingly, 19 (17-56 years old) had a current steady relationship with a woman, even though they never had sex with one.

Ten percent of the study sample (N=242) reported more than ten sexual partners in the previous six months. While majority of those without a steady partner reported having more than three male sex partners in the last six months , those reporting a current steady relationship with a man were not necessarily sexually monogamous, Table 3. Increasing length of a steady relationship was not reflected on a higher proportion of monogamy.

Table 3. Number of male sexual partners in the last 6 months by the reported length of a steady relationship with a man, N=2430, Internet survey of MSM, 2007 (unpublished data).

N of male sex partners in the last 6 months	In a steady relationship with a man (N=819), for:			Currently without a steady partner (N=1492)	Unknown partner status (N=119)	Total N (%)
	0-6 months (N = 201)	7 months - 5 years (N=325)	More than 5 years (N=293)			
None	2	4	4	162	3	175 (7.2)
1-2	74	216	134	486	68	978 (40.2)
>3	125	105	155	842	47	1274 (52.4)
Unknown number of sex partners	0	0	0	2	1	3 (0.1)

MSM engaged in the 2007 survey rarely used a condom during oral sex (Table 4). While some high risk sexual practices were rare, inconsistent use of a condom with insertive or receptive UAI was prevalent.

Table 4. Frequency of sexual practices among 2252 men, who reported having a male sexual partner in the last 6 months, unpublished data from Internet survey of MSM in 2007 (unpublished data).

Sexual practice	Reported frequency (%)					
	Always	**Frequently**	**Sometimes**	**Rarely**	**Never**	**Unknown**
Mutual masturbation	633 (28.1)	729 (32.4)	455 (20.2)	260 (11.5)	125 (5.5)	50 (2.2)
Giving oral sex (fellatio) without a condom	753 (33.4)	894 (39.7)	367 (16.3)	141 (6.3)	70 (3.1)	27 (1.2)
Giving oral sex with a condom	32 (1.4)	43 (1.9)	117 (5.2)	352 (15.6)	1578 (70.1)	130 (5.6)
Receiving oral sex without a condom	728 (32.3)	852 (37.8)	340 (15.1)	152 (6.7)	138 (6.1)	42 (1.9)
Receiving oral sex with a condom	32 (1.4)	49 (2.2)	105 (4.7)	331 (14.7)	1577 (70.0)	158 (7.0)
Insertive anal intercourse without a condom	111 (4.9)	212 (9.4)	309 (13.7)	483 (21.4)	1054 (46.8)	83 (3.7)
Insertive anal intercourse with a condom	246 (10.9)	416 (18.5)	514 (22.8)	425 (18.9)	577 (25.6)	74 (3.3)
Receptive anal intercourse without a condom	107 (4.7)	208 (9.2)	282 (12.5)	421 (18.7)	1156 (51.3)	78 (3.5)
Receptive anal intercourse with a condom	235 (10.4)	363 (16.1)	475 (21.1)	431 (19.1)	664 (29.5)	84 (3.7)
Licking of anus (rimming)	66 (2.9)	296 (13.1)	530 (23.5)	557 (24.7)	740 (32.9)	63 (2.8)
Insertive fisting	10 (0.4)	47 (2.1)	115 (5.1)	222 (10.0)	1756 (78.0)	102 (4.5)
Receptive fisting	10 (0.4)	41 (1.8)	97 (4.3)	172 (7.6)	1834 (81.4)	98 (4.3)
Sexual play with urine ("watersports")	13 (0.6)	33 (1.5)	105 (4.7)	207 (9.2)	1808 (80.3)	86 (3.8)

Sharing of sexual toys	11 (0.5)	29 (1.3)	138 (6.1)	260 (11.5)	1721 (76.4)	93 (4.1)
Threesome or group sex	5 (0.2)	84 (3.7)	321 (14.2)	610 (27.1)	1152 (51.1)	80 (3.5)

4.1.2 Contact with healthcare services and HIV testing

It is generally assumed that MSM in Norway are open about having sex with men, at least with their family physician, however the results from 2007 study suggest that almost a half (46.4%) of MSM from the study sample may not be open about their sex with men with their physician, Table 5.

Table 5. Revealing sex with men to a dedicated primary care physician by sexual orientation, N=2430, unpublished data from Internet survey of MSM in 2007.

	When you are in contact with your primary care physician, do you tell him/her you have sex with men?			
Declared sexual orientation	**Yes**	**No**	**Missing answer**	**Total**
Homosexual , N (%)	1088 (60.3)	693 (38.4)	24 (1.3)	1805 (100)
Homosexual with some heterosexual inclination, N (%)	107 (37.8)	171 (60.4)	5 (1.8)	283 (100)
Bisexual, N (%)	53 (23.6)	170 (75.6)	2 (0.9)	255 (100)
Heterosexual , N (%)	1 (14.3)	6 (85.7)	0	7 (100)
Heterosexual with some homosexual inclination, N (%)	3 (4.3)	64 (91.4)	3 (4.3)	70 (100)
I am uncertain of my sexual orientation, N (%)	16 (40.0)	23 (57.5)	1 (2.5)	40 (100)
Total	1268	1127	35	2430

It may be that it is difficult for a patient to initiate a conversation about their sexual habits, so this information is often not shared with a physician. Furthermore, a lot of study participants (39.3%) felt that their sexual health is not taken into consideration at primary care physician and that physicians do not initiate a conversation about this topic, (unpublished data). Still, a large majority (49.0%) of participants indicated that they would choose their primary care physician to be checked for STI. A specialized STI clinic in Oslo was a second choice (21.4%, unpublished data).

When asked if they have ever been tested for HIV, 10 participants did not respond, while 679 (27.9) responded they have never been tested. Of the latter, 51% (349) had more than two sexual partners in the previous six months. Of those 1741 (71.7%) of survey participants, who confirmed they ever took HIV test, 744 (42.7%) were tested 2-4 times and additional 388 (22.3%) 5-9 times. More than a half (963, 55.3%) were tested within the last year (unpublished data).

Those 679, who were never tested for HIV, were asked for the reasons of why they have not yet done so (several answers possible). Majority (489, 72%) thought they were not at risk and 304 (44.8%) responded they felt healthy. Some (178, 26.2%) claimed they always choose safe partners and 149 (21.9%) responded they did not choose to be tested due to being in a steady relationship. About 20% (135, 19.9%) admitted to postponing the HIV test and a similar proportion (136, 20.0%) was afraid of the consequences of a positive result. Interestingly, 98 (14.4%) did not know where they could be tested. A small proportion (57, 8.4%) have been avoiding the test because they were afraid of blood, needles or doctors, did not expect support and understanding from their friends if tested positive (42. 6.2%) or did not want counselling before or after the test (25, 3.7%, unpublished data).

Among those MSM, diagnosed with HIV in Norway in the years 2002-2011, more than a third (33.9%), had not been tested prior to their positive HIV test (paper IV).

4.1.3 Assumptions, opinions and knowledge about STI

The participants of the 2007 survey were also asked certain questions about their assumptions, opinions and knowledge of trends and transmission of STI (Tables 6 and 7, unpublished data).

Those who responded that they ever had a date in reality with a partner they met online (with or without sex, N=2209) were also asked if the Internet has changed their sexual practices and habits. To this, majority (63.0%) responded it they experienced a change and 46.5% (1027) said they now have more partners. These 2209 MSM were also asked if the last partner they met online revealed their HIV status before the meeting and 49.3% (1090) answered they did not do so, while 31.5% reported their partner revealed being HIV positive or negative. Similarly, 50.9% (1124) also said they did not reveal their own HIV status to the man they were meeting with, but 32.6% did so. Among those, who reported partial or no use of a condom during anal sex with their last online partner, 46.8% (245/523) reported communicating about their partner's HIV status in advance.

Among all sampled MSM (N=2430), 30.8% never asks their sexual partners of their HIV status and further 20.8% do so only rarely. However, majority (1852, 76.2%) expressed disagreement with the statement that is easy to find out the HIV status of their sexual partners, though finding a sexual partner with a similar HIV status to theirs is preferable (Table 7, unpublished data).

Table 6. Assumptions and knowledge about STI, N=2430, unpublished data from Internet survey of MSM in 2007.

Questions on assumptions and knowledge	Evaluation of risk of HIV transmission with UAI :		What are the trends of gonorrhoea among MSM in Norway today?		I think that HIV positive, who take medicines, are less infectious	
Evaluated risk level	a. with ejaculation inside partner N=2430 (%)	b. without ejaculation N=2430 (%)	Trend assumption	N=2430 (%)	Level of agreement	N=2430 (%)
No risk	19 (0.8)	35 (1.4)	Falling trend	76 (3.1)	Disagree completely	1826 (75.1)
Little risk	62 (2.5)	241 (9.9)	Unchanged trend	284 (11.7)	Disagree a bit	155 (6.4)
Some risk	291 (12.0)	697 (28.7)	Increasing trend	1049 (43.2)	Indifferent	200 (8.2)
Big risk	591 (24.3)	876 (36.0)	I do not know	965 (39.7)	Agree a bit	146 (6.0)
Very big risk	1413 (58.1)	526 (21.6)	Missing answer	56 (2.3)	Completely agree	73 (3.0)
Unknown	54 (2.2)	55 (2.3)			Unknown	30 (1.2)

Table 7. Opinions about sex and STI, N=2430, unpublished data from Internet survey of MSM in 2007.

Level of agreement	Opinion on specific claims			
	a. Use of a condom at an Internet-date is less important than use of a condom in the dark room or sauna, N=2430 (%)	b. Sex is best without a condom N=2430 (%)	c. Now that there are better HIV medicines, I do not need to be worried as much	d. It is important for me to find sexual partners with an HIV status, similar to mine
Disagree completely	1917 (74.3)	455 (18.7)	1893 (77.9)	279 (11.5)
Disagree a bit	136 (5.3)	176 (7.2)	218 (9.0)	73 (3.0)
Neither agree or disagree	167 (6.5)	445 (18.3)	122 (5.0)	371 (15.3)
Agree a bit	133 (5.2)	528 (21.7)	123 (5.1)	276 (11.4)
Completely agree	71 (2.7)	762 (31.4)	47 (1.9)	1392 (57.3)
Unknown	155 (6.0%)	64 (2.6)	27 (1.1)	39 (1.6)

4.2   Burden of sexually transmitted infections among men who have sex with men in Norway
       (paper II – IV)

Increasing trends in STI among MSM in Norway have been observed for several years (Figure 3, updated with unpublished data). The cases of MSM outnumber (domestic) heterosexual transmission of gonorrhoea, HIV and syphilis in Norway and thus seem to be currently most at risk population for these STI.

While a large majority of MSM report to have been infected by a casual partner, infection by a steady partner was not unusual (paper II-IV). Compared to heterosexual transmission however, commercial sex workers were very rarely mentioned as a source of infection among MSM (paper (II-IV).

Figure 3. Number of newly diagnosed gonorrhoea, syphilis and HIV cases in Norway among men who have sex with men, N= 4421, 1993-2013. Unpublished data marked with indicators.
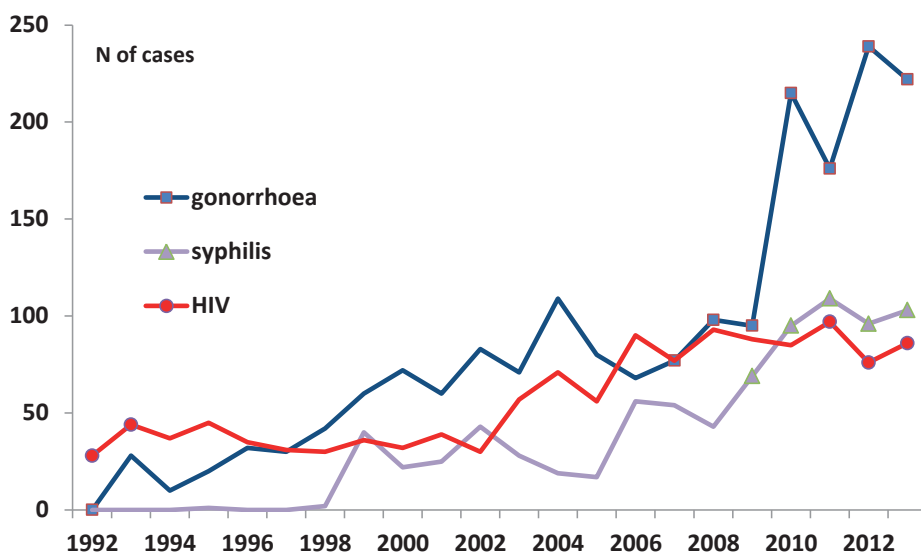
4.2.1   The trends of gonorrhoea among MSM (paper II)

The main findings reported in paper II were:

- Number of homosexually acquired gonorrhoea infections increased more than tenfold from 1994 to 2004.
- While heterosexually infected men mostly acquired their infection abroad (56%), MSM did so in Norway, predominantly in Oslo (73).
- Two thirds of MSM reported in 2003-7 had been infected by a casual partner and only one case reported being infected by a commercial sex worker (CSW)
- Quinolone resistance in gonorrhoea cases increased from 3% in 1995 to 47% in 2007.

MSM represent a smaller proportion of the male population, yet they have surpassed cases of gonorrhoea, reported among heterosexual men (Figure 4). Compared to heterosexual men, median age of cases of MSM was consistently lower.

Figure 4. Number of reported gonorrhoea cases in Norway among men by sexual transmission route, N= 4838, 1993-2013. Updated with unpublished data for the period 2008-2013.
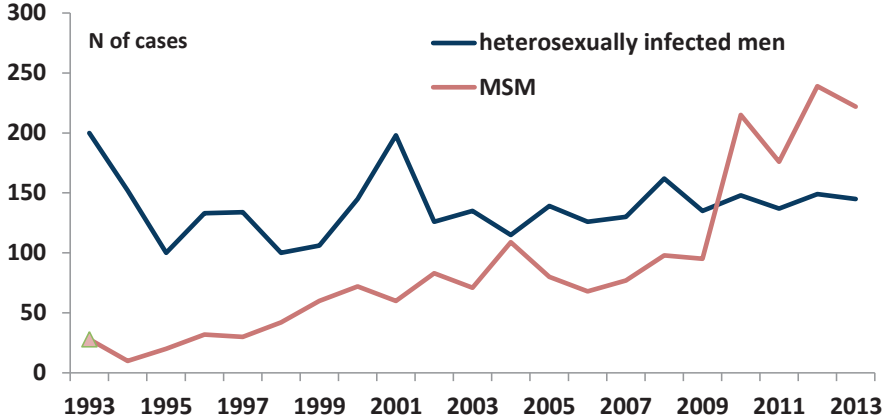
By indications for testing, heterosexual men were mainly tested because they experienced symptoms (98%), predominantly due to urethral gonorrhoea (98%) with their general practitioner conducting majority of positive tests (59 %). In comparison, MSM had more diverse reasons for testing, had samples positive from other and multiple anatomical sites than urethra alone and were predominantly diagnosed at a specialized STI clinic (66%). From 1993 to 2013, an increased number of MSM positive for gonorrhoea from several anatomical sites is observed, Figure 5, unpublished data.

Figure 5. Number of reported gonorrhoea cases in Norway among men who have sex with men by anatomical site positive, N= 1887, 1993-2013. Unpublished data.
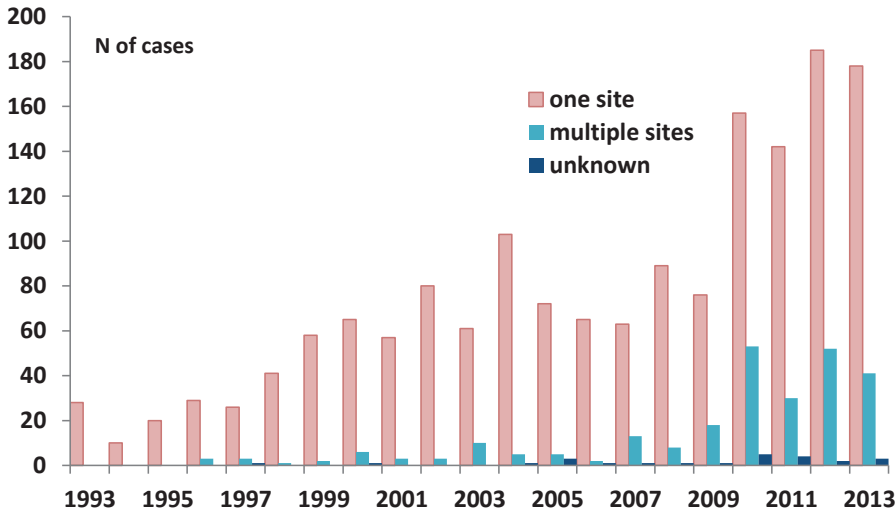
The increase of gonorrhoea among MSM may have been affected by changes in testing, not only by testing multiple anatomical sites, but also with the widespread introduction of NAAT testing in this period (paper II and Figure 6).

Figure 6. Testing methods used to diagnose gonorrhoea in men who have sex with men in Norway, 1993-2013, N= 1887. Unpublished data.
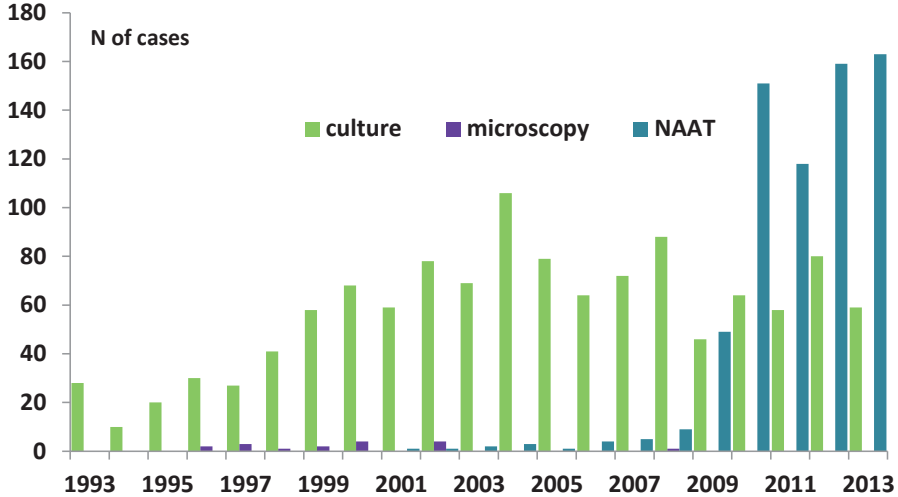
Furthermore, the NAAT diagnosed cases have affected our ability to test for gonorrhoea microbial resistance, a known and widespread emerging problem (paper II, Figure 7).

Figure 7. Number of resistant *Neisseria gonorrhoeae* isolates from men who have sex with men in Norway, N=1887, 1995-2013 (primary axis, line graph) and all MSM infected in this time period (secondary axis, bars). Updated with unpublished data from 2008-2013.
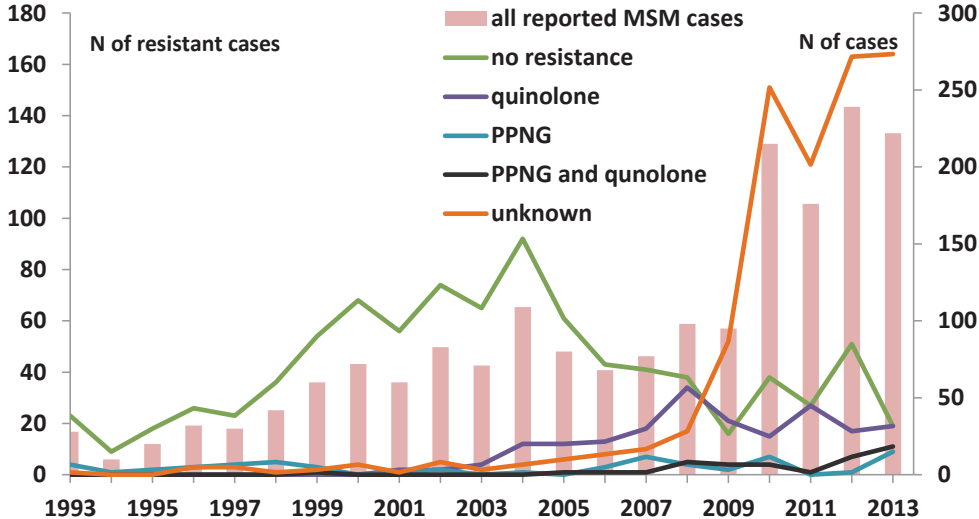
There is an increase of coincidental STI among MSM with gonorrhoea. Since 2009, between 14,7 and 17,2% of MSM diagnosed with gonorrhoea were also infected with HIV, while other concurrent STI (excluding HIV) increased to 12,6% in 2013 (Figure 8, unpublished data). From 2009-2013, more than half (83 out of 153) of MSM diagnosed with gonorrhoea and with coincident HIV had at least one sample for gonorrhoea positive from the rectum (unpublished data), the rest either from pharynx or urethra.

Figure 8. Total number of reported gonorrhoea cases in Norway among men who have sex with men (red line) and cases with concurrent HIV or STI (columns), N= 1887, 1993-2013. Unpublished data.
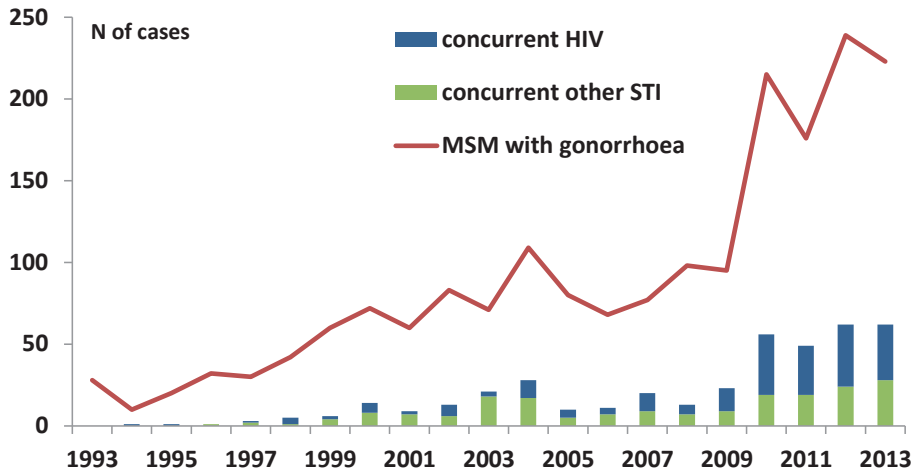
4.2.2 The trends of early syphilis among MSM (paper III)

The main findings reported in paper III were:

- In the entire Norwegian population, the incidence of reported syphilis ranged from 0.05 (1992) to 1.50 (2002) per 100 000 person-years.
- The proportion of those, infected homosexually increased from 0 (1992-1994) to 77% (2008).
- The majority of MSM reported being infected by a casual partner (73%) and in the municipality of Oslo (72%).
- The proportion of HIV co-infection among homosexually infected increased over time and reached 39% in 2008.

While heterosexual men were predominantly diagnosed in primary stage of early syphilis (55.3%), most of MSM were diagnosed in the secondary stage (42.6%). Contrary to MSM, number of infections among heterosexual men remained relatively stable (Figure 9).

Figure 9. Number of early syphilis cases in Norway among men by stage of disease for MSM (columns) and total number for heterosexually infected men, N=1034, 1992-2013. Unpublished data.
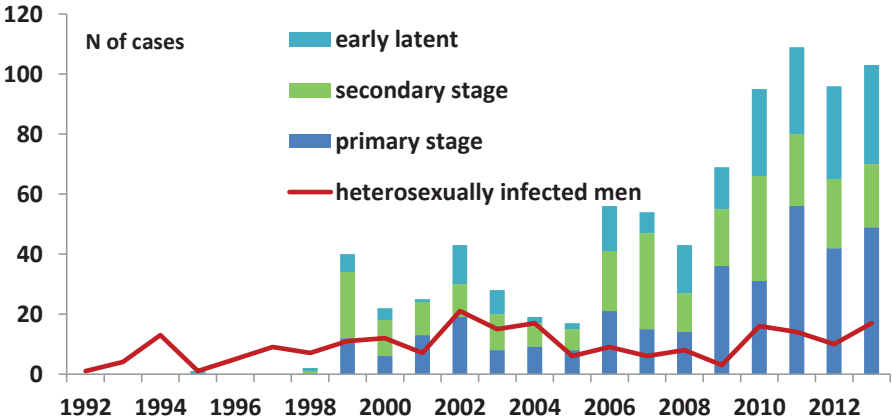
More than a half (61%) of infected MSM was older than 34 years. From 2000-2013, median age of cases of MSM was 38, the highest among STI monitored in MSIS (unpublished data).

The increase in syphilis cases among MSM is observed among those, already infected with HIV. Since 2007, more than 30% of MSM with early syphilis had coincident HIV infection and this proportion increased up to 46.9% in 2012 (unpublished data, Figure 10).

In our study (paper III), HIV positive MSM, diagnosed with syphilis, were more likely to be residents of Oslo and were more likely to have been diagnosed with syphilis later in the course of disease (primary vs. secondary or early latent) and in a hospital compared to HIV negative syphilis infected MSM (bivariate comparison).

Figure 10. MSM, infected with syphilis (bars) and coincident infections with: 1. HIV (red line) or 2. other STI (blue line), 1995-2013, N=822. Updated with unpublished data for the period 2009-2013 (marked with indicators).
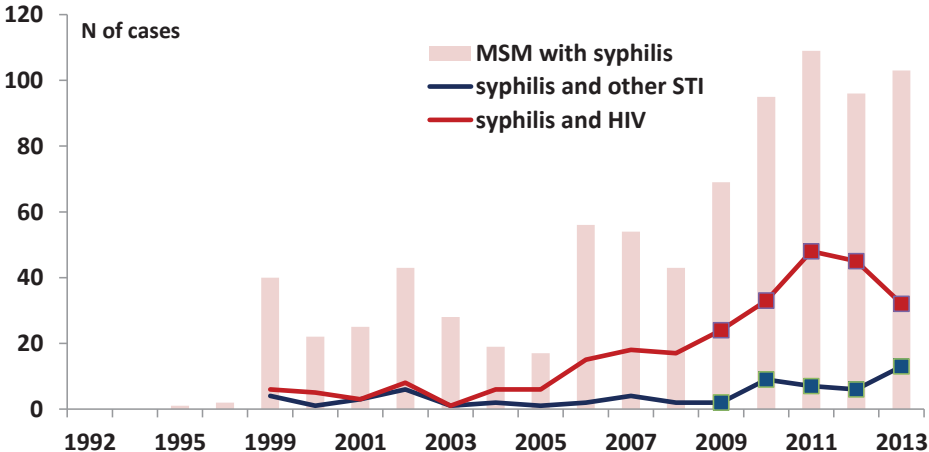
The main findings reported in paper IV were:

- In the years 1995-2002, 30 to 45 MSM were newly diagnosed with HIV each year, while in the years 2003-2011 this increased to between 56 and 97 cases.
- No significant trends over time in overall median age (36 years) were observed.
- Most of the MSM (51%) were infected in Oslo and a casual partner was a source of infection in 590 cases (60%).
- An overall increase of syphilis co-infected cases was observed (p for trend <0.001).

After 2002, a steep increase in reported cases of HIV among MSM has been observed (paper IV, Figure 11).

Figure 11. Number of MSM diagnosed with HIV infection in 1995-2013 in Norway, by year of diagnosis and time interval between the diagnosis year and the estimated year of infection ("yeargap"), N= 1154. Paper IV, updated with unpublished data for 2012 and 2013.
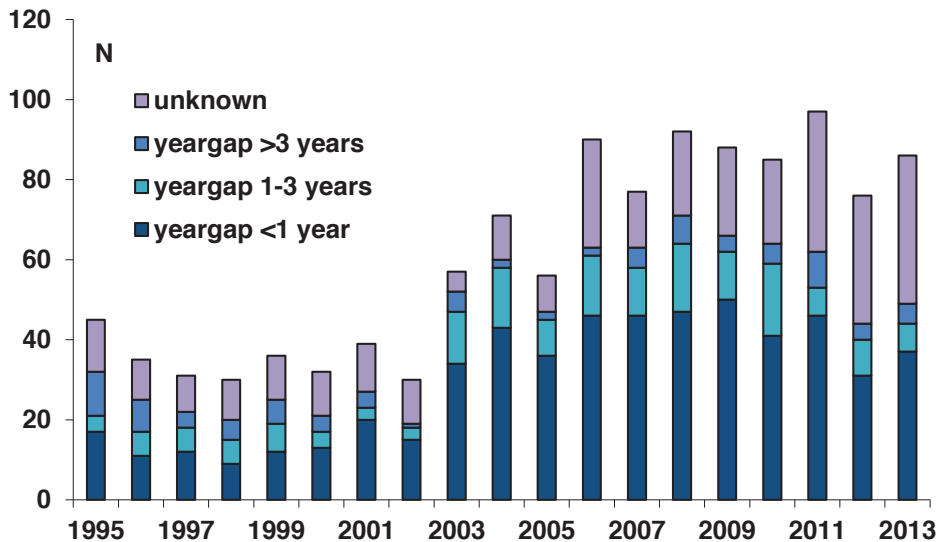
From 2000 to 2013, median age of cases of MSM was 37 (unpublished data) and no apparent trend in median age was observed since 2002. Since 1999, the number of cases of MSM diagnosed at the stage of AIDS is below 10 per year. An increase in coincident STI was observed among cases, predominantly due to cases with HIV and syphilis (Figure 12).

Figure 12. Number of MSM, diagnosed with HIV infection in 1995-2013 in Norway, by year of diagnosis and coincident other STI (red line), N=1154. Unpublished data.
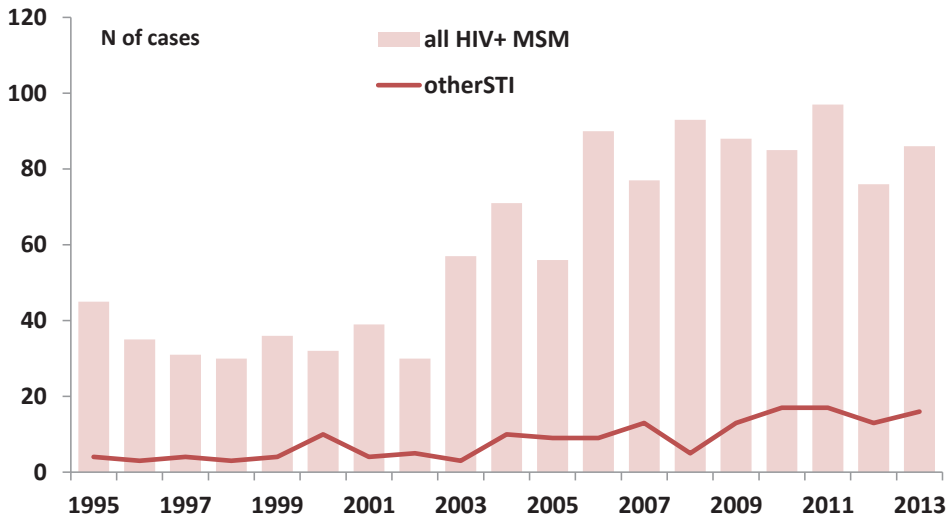
4.2.4 Prevalence estimate of STI among MSM in 2007 (paper I)

Logged in members of the Norwegian MSM oriented website (N=2430) reported STI diagnosed in the past 12 months. Chlamydia was most frequently reported (5.2%), followed by HIV (1.7%), followed by gonorrhoea (1.4%) and syphilis (0.7%). In addition, 26 (1.1%) respondents reported being diagnosed with HIV prior to the past 12 months.

4.3 Risk factors for STI among Norwegian MSM (paper I)

The main findings reported in paper I were:

- Having had Chlamydia during the past 12 months was associated with non-western background (PR 2.8 [1.4-5.7]), number of lifetime male partners (p-trend < 0.001), unsafe sex under the influence of alcohol (PR 1.8 [1.1-2.9]) and with younger age (p-trend = 0.002).
- Having had gonorrhoea during the past 12 months was associated with unrevealed ethnic background (PR 5.9 [1.3-26.3]), having more than 50 lifetime male partners (PR 4.5 [1.3-15.6]) and more than 5 partners in the past 6 months (PR 3.1 [1.1-8.8]), while mid-range income was protective (PR 0.1 [0.0-0.6]).
- Having been diagnosed with HIV in the past 12 months was associated with residing in Oslo or Akershus county (PR 2.3 [1.2-4.6]), non-western background (PR 5.4 [1.9-15.3]), unrevealed income (PR 10.4 [1.5-71.4]), number of lifetime male partners (p-trend < 0.001) and being under the influence of selected drugs during sex in the past 12 months (PR 5.2 [2.7-11.4]). In addition, the frequency of feeling drunk more than four times in a given month was reversibly associated with HIV.
- Having been diagnosed with syphilis was associated with residence in Oslo or Akershus county (crude PR 3.1[1.5-6.3]), non-western background (crude PR 8.5 [2.0-36.5]), having

more than 10 sexual partners in the past 6 months (crude PR 4.4 [1.2-13.8]) and having an anonymous or casual partner in the last 6 months (crude PR 8.7 [1.1-65.3]).

The majority of MSM with a reported STI were residents of Oslo.

Compared to heterosexual single men in general population in Norway (7), members of the Norwegian MSM oriented website (N=) reported more sexual partners in life in 2007.

Table 8. Number of sexual partners in life reported by non-cohabitating MSM (2007) and heterosexual single men (2002).

Nr. of sexual partners in life	General population: men who never had sex with a person of same sex and currently do not live with a partner, 2002, %	MSM Internet study: men, who currently do not live with a partner of any gender, (paper I), 2007, N=1721, %
1	9.9	3.2
2-5	31.7	15.1
6-10	25.0	16.1
>10	33.4	65.6

Other results among members of the Norwegian MSM oriented website suggest that 23.7% had UAI with either anonymous or a casual partner in the last 6 months, 43.9% reported a practice of threesome or group sex, 3.2% reported receiving payment for sex and 4.9% paying for sex in the previous 12 months, 38.0% reported feeling drunk more than four times in a typical month and 26.4% reported unsafe sex under the influence of alcohol in the past year.

Not surprisingly due to the sampling method, as many as 90.9% reported they ever had a date in reality with someone they met on the Internet. When asked how Internet changed their sexual practices, 46.5% reported an increase in number of dating partners and 21.5% an increase in anonymous sex (unpublished data).

Further results of this study suggest that MSM, who reported any selected STI in the past year, represent different demographic groups and groups with different risk behaviours.

In the study sample, poppers, marijuana or hashish, Viagra and cocaine were most frequently used substances in the past 12 months. Poppers and Viagra were also among most frequently reported substances used in connection to sex. While other drugs were in general not very frequently used, all of them had been, by some MSM, used also in connection to sex, Table 9, unpublished data.

Table 9. Use of drugs among MSM, N=2430, unpublished data from Internet survey of MSM in 2007.

N=2430	Frequency of substance use in the past 12 months					Used the substance in connection to sex (N = if the substance was claimed to have been used in the past 12 months)		
Substance use	Never	Once	2-10 times	>10 times	Missing	Yes	No	Missing
Smoked hashish or marijuana, N (%)	1814 (74.6)	233 (9.6)	239 (9.8)	114 (4.7)	30 (1.2)	166 (28.3)	419 (71.5)	1 (0.2)
Gotten high on medicines, N (%)	2224 (91.5)	59 (2.4)	64 (2.6)	41 (1.7)	42 (1.7)	31 (18.9)	132 (80.5)	1 (0.6)
Ecstasy (XTC), N (%)	2294 (94.4)	38 (1.6)	46 (1.9)	9 (0.4)	43 (1.8)	39 (41.9)	53 (57.0)	1 (1.1)
LSD, N (%)	2367 (97.4)	4 (0.2)	4 (0.2)	8 (0.3)	47 (1.9)	3 (18.7)	13 (81.2)	0
Gamma-hydroxybutyrate (GHB), N (%)	2327 (95.8)	27 (1.1)	23 (0.9)	12 (0.5)	41 (1.7)	41 (66.1)	21 (33.9)	0
Cocaine, N (%)	2198 (90.4)	77 (3.2)	82 (3.4)	32 (1.3)	41 (1.7)	62 (32.5)	129 (67.5)	0
Heroin, N (%)	2367 (97.4)	8 (0.3)	5 (0.2)	8 (0.3)	42 (1.7)	4 (19.0)	17 (80.9)	0
Amphetamine, N (%)	2241 (92.2)	42 (1.7)	66 (2.7)	37 (1.5)	44 (1.8)	68 (46.9)	77 (53.1)	0
Methamphetamine, N (%)	2341 (96.3)	11 (0.4)	9 (0.37)	13 (0.5)	56 (2.3)	12 (36.4)	21 (63.6)	0
Poppers, N (%)	1733 (71.3)	190 (7.8)	285 (11.7)	186 (7.6)	36 (1.5)	566 (85.6)	92 (13.9)	3 (0.4)
Viagra, N (%)	2109 (86.8)	82 (3.4)	149 (6.1)	51 (2.1)	39 (1.6)	263 (93.3)	19 (6.7)	0

50

5   DISCUSSION

"Find what you love and let it kill you."
Charles Bukowski

This work emphasizes the importance of STI surveillance and control in a high-risk population of men, who have sex with men in Norway.

Increasing number of gonorrhoea, syphilis and HIV cases among MSM in Norway were observed in the surveillance data in study years, paralleled with increasing trends in co-existing (concurrent) STI. Considering MSM represent a much smaller population, compared to heterosexual men, MSM seem to be disproportionally affected with STI (papers II-IV). High STI burden among Norwegian MSM is an important public health problem, as a significant proportion of MSM in Norway reported a concurrent steady relationship with a woman in our study. Thus, this concentrated epidemic could potentially spread to the rest of the population.

In addition, our study has suggested worrisome prevalence of high risk behaviours among Norwegian MSM, such as: high number of sexual partners, concurrent sexual relationships, substance use related to sex, prevalent UAI, not revealing their sexual orientation to their physicians, early sexual debut and poor awareness of current increasing STI trends in Norway.

Important gaps in STI surveillance and knowledge of STI transmission among MSM in Norway, as well as relative inefficiency of prevention efforts, targeted at them, have also been identified.

5.1   Demographic and behavioural overview of men who have sex with men in Norway

This work has provided some baseline information on a large sample of 16-74 year old MSM from all municipalities in Norway, their socioeconomic status, education, cohabiting status, use of healthcare services and sexual practices.

Majority of MSM with an STI lived in Oslo and also acquired their infection here (papers II-IV). This corresponds to other surveys that suggest higher STI prevalence among MSM in capital cities compared to the general population (28, 42). This finding, however, is not surprising considering several studies suggested that MSM are also more likely to live in big cities, where the heterosexual norm might not be as strong (136).

Though the majority of infected MSM was born in Norway (paper I-IV), the results suggest higher STI prevalence (and a higher risk for Chlamydia and HIV) among immigrants with non-western background (paper I). Cultural barriers associated with homosexuality may put immigrant MSM at a greater risk for STI, as they may suffer from discrimination in employment, housing, earning power and educational opportunities, which may lead to lower level of socioeconomic status (42). Due to a language barrier, it may be particularly difficult for non-western MSM to acquire knowledge and information and access healthcare services.

The fact that younger age was identified as a risk factor for Clamydia in 2007 may represent a testing bias, as younger men are more likely to get tested for this infection in Norway; however MSM, younger

than 25 years, did not seem to be overrepresented among syphilis, gonorrhoea and HIV cases, reported to MSIS. In 2007, similar demographics (mean age, proportion living in Oslo, (high) education, employed) was observed as in the online survey in 2010 (32.8, SD11.8)(135). Demographic results of a Swedish online survey of MSM (N=4273) from 2008 are likewise very similar, apart from slightly higher average age 34 years, with 63% of participants living in one of the Swedish three biggest cities and about a half having high education (136).

In this work, the Internet was confirmed as a popular low threshold meeting place to find a date, despite the fact that the majority (61.4%) of survey participants revealed they are in a steady relationship, (paper I). Almost 10% of these current steady relationships accounted for a relationship with a woman, who may not be aware that they belong to a bridge group. Of interest, about 20% of the participants in the Swedish 2008 survey of MSM (N=4273) reported a sexual intercourse with a woman in the previous year (136).

Little is known about men who have sex with both men and women (MSMW) in Norway. While the proportion of MSM reporting sex with women in a country will largely depend on social and legal constraints, some studies have suggested that 67–85% of MSMW do not disclose their same-sex behaviour to their female sexual partners (or friends and family) and thus use specific strategies, for example, avoiding typical gay sexual venues in their pursuit of same-sex encounters (137). Some studies reported higher rates of HIV risk behaviours (such as transactional sex and substance use with sex) in MSMW compared to men, who have sex with men only (138).

An important proportion of sexually active MSM has never been tested for HIV and among those, who tested HIV positive; more than a third has never been tested before (paper IV). Alternatively, 27.9% were never tested in our 2007 online survey and one third did not know their HIV status in 2010 survey (139). Only 56 % have tested themselves for an STI in the previous year (139). In comparison, in Denmark, between 23-21% MSM have never been tested for HIV (2000-2009) and, in Sweden, between 15-17% (among older than 25 years - vs. 50% of those younger 25 years) (136, 140).

Our results are consistent with findings from a similar 2010 Internet survey and raise concerns about a possible delay in diagnosis and treatment of HIV among MSM in Norway (141). Low testing proportions are a global problem, as fewer than one third of MSM are reported to have been tested in the past 12 months in Western and Central Europe and South and South-East Asia, where MSM play a substantial role in national HIV epidemics (28).

The 2010 survey suggested that those MSM in Norway, who have never been tested for HIV were more likely to: be younger, closeted about same sex attractions, had low HIV transmission and testing knowledge, did not believe that HIV testing is free or affordable in Norway, never took an STI test and did not engage in sex abroad in the past year (141). Similarly, the Swedish survey of MSM suggested that "never-testers" were younger, lived outside of bigger cities and were often single. In addition, those, who did not know where to be tested for HIV, were younger or were more likely to have had sex with a woman in the last year (136).

Tikkanen proposes it may be difficult for some Swedish MSM to ask their dedicated physician for a test, as questions on the reasons might follow (136). This may also apply to Norwegian MSM, who are

admittedly reserved with discussing their sexual practices with their dedicated physician, which may consequently affect healthcare services they are offered. As our unpublished results suggest, some MSM postpone the HIV test due to fear of the consequences of being positive or deem the test unnecessary. Nonetheless, the knowledge of HIV testing sites could be improved.

While those who reject testing are more likely to be HIV positive (142), awareness of one's HIV status is generally an important measure of HIV transmission prevention, as most persons reduce their risk behaviours, after learning they are infected. It was estimated that if all the infected persons have been made aware of their HIV infection, a significant reduction (modelled as 31% in this study) in number of new infections would occur (143).

Studies abroad report increasing social acceptance of same sex partnerships (111), however no recent population estimates of either social acceptance or homosexual practices are available in Norway. Most recent estimates (1987, 1992, 1997 and 2002) on a random population sample have, however, detected an increase in men, reporting sexual intercourse with a man (from 3.6 in 1987 to 10.7 in 2002). In particular, this proportion increased among young men 18-24 years (5.8-14.1 %) (7).

5.2   Burden of sexually transmitted infections among men who have sex with men in Norway

Gonorrhoea has been said to be an "indicator" disease for recent risky sexual behaviour (144) due to its high transmissibility and acute presentation of symptoms. Reported gonorrhoea cases are worrisomely high among MSM in Norway and likely reflect high risk behaviour. Other countries in Europe have observed similar increasing gonorrhoea rates among MSM. In 2009, the highest gonorrhoea rates among MSM in Europe (in 15 countries with available information) were reported by the Netherlands, followed by the UK (42). A high burden among MSM and predominant domestic transmission compared to heterosexual men, who get frequently infected abroad, has also been described in Sweden (145). Abandoned sensitivity testing of *N. gonorrhoeae* to antimicrobials may lead to treatment failures and persistence of gonorrhoea in the population (paper II).

Parallel to the increase in gonorrhoea cases among MSM, increasing trends of early syphilis and HIV, were observed in Norway. In the previous decade, Denmark, Czech Republic and the UK observed the highest proportional increase in syphilis cases among MSM with the highest rates reported by Denmark and the Netherlands (42). In addition, increases in co-infections with other STI have been observed in MSM in Norway with gonorrhoea, syphilis and HIV, suggesting high risk behaviour, particularly among HIV positive. A Danish study revealed a substantial risk for HIV or syphilis among men, diagnosed with one of these STI, or a second (recurring) syphilis infection (146). Worrisome high proportions of (syphilis and HIV) co-infections among MSM have also been reported in Northern Ireland, England and Belgium (42).

Interestingly, the Danish HIV epidemic among MSM exhibits a very similar curve to Norwegian, with a stable incidence on "new high levels" after 2004 in spite of the HIV prevalence increase among MSM and increases in reported risk behaviour (140). While the authors suggest that the "stabilization" of the HIV epidemic among MSM in Denmark is due to prevalent cART treatment and thus lower infectivity of HIV positive, the observed increase in UK in spite of high cART coverage is a stark reminder that a battle against HIV is not won with medication alone and that undiagnosed men might largely contribute to new

infections (147). Even when a high proportion of HIV-infected men is receiving cART and have undetectable viral load, the per-contact probability of HIV transmission due to UAI may be similar to estimates reported in the pre-HAART era (71, 72). Thus, escalated efforts with higher testing activity, cART at diagnosis and promotion of condom use may be needed to prevent further increases in new HIV infections among MSM (147).

Established prevalence rates among 2289 MSM attending two STI clinics in Oslo were much higher than reported STI in our Internet study in 2007: 136 (6%) were positive for gonorrhoea (using two NAAT tests), 228 (10%) were positive for Chlamydia (7% had LGV) and 91 (5.1%) for *M. genitalium* (148). The observed differences could be explained by selection bias.

5.3   Risk factors for STI and behavioural resilience

In the 2007 Internet survey, more than a quarter (25.8%) reported having more than 5 sexual partners in the last 6 months and threesome or group sex, was reported by a high proportion (43.9%), suggesting high degree of partner concurrency and non-monogamous sexual relationships in the study population.

From 1987 to 1992 (in "pre-cART era"), a decrease in number of male partners reported per year was (from a yearly median of 1 to 0.3) observed in Norway among men with current homosexual experience (6), however no recent population estimates are available. Our 2007 study has identified sexually active population of MSM reporting non-monogamous steady relationships and a high sex partner turnover among those most at risk for STI. More than a half reported having more than three sexual partners in the past 6 months.

Condoms were very rarely used for oral sex and inconsistently for insertive or receptive anal intercourse. The 2010 survey showed that 30% of Norwegian participants did not use a condom at their most recent intercourse with a casual partner (139). The proportion was even higher among HIV positive. A perception that sex is best without a condom was shared by the majority of sexually active MSM, asked in 2007 Internet study. The perceived pleasure loss associated with condoms may be a key deterrent for their use (149).

While we did not explore these practices further, rimming, associated with a risk for gastro-intestinal infections in addition to STI, was a relatively frequent practice. It is worrisome that about 20% also reported occasionally engaging in risky practice of fisting, associated with trauma of the rectal mucosa, bleeding and HCV infection (150). Rimming and fisting were also frequently reported in 2010 survey and were found to be associated with UAI with non-primary partners in crude analysis (135). The practices of having sex with CSW are assumed to be rare among MSM, however as much as 4.9% of study participants reported paying for sex in the previous year.

In multivariable analyses, high numbers of sexual partners, threesome or group sex, unsafe sex during the influence of alcohol or selected drugs have been identified as most important behavioural predictors of STI. Prevalent UAI with anonymous or casual partner in the previous 6 months and alcohol abuse in this population are a cause of concern. The 2010 study corroborated widespread use of alcohol and illicit drugs, particularly among HIV positive MSM (139).

Due to aforementioned complexity of alcohol influence on risks for STI, our seemingly puzzling results are not completely unexpected. We identified unsafe sex under the influence of alcohol as a risk factor for Chlamydia infection and, while not statistically significant; the estimates for gonorrhoea and HIV were also towards increased risk. On the other hand, reporting feeling drunk more than four times a month was inversely associated with HIV infection. While we could speculate chronic alcohol consumption may have detrimental effect on sexual function, several studies suggested potential beneficial effect of alcohol consumption on erectile dysfunction (151, 152). It may be that the unexpected direction of this association is a consequence of counselling and behavioural changes after HIV diagnosis in the previous year.

A study in genitourinary clinics in London confirmed that MSM may be more likely, compared to other (non-MSM) men, to use illicit drugs, while alcohol use was similar (153). Before the study in 2007, no data on illicit drugs use among Norwegian MSM were available. At the time, Norwegian MSM reported relatively high proportions of poppers, cannabis and cocaine use in the previous 12 months. If compared to the 2007 UK Gay Men's Sex Survey, in which 85% of men reported using alcohol in the last year, 42% had used poppers, 21% had used Ecstasy, and 21% had used cocaine, the reported proportions substance use among Norwegian MSM are lower, however the results are not entirely comparable due to different sampling methods (154). Among Scottish MSM, sampled in 17 gay commercial venues in 2011, similar proportions of poppers (36.3%9) and Viagra (14.1%) use were reported than among MSM in our study (99).

Taking erection enhancing drugs to treat erectile dysfunction, particularly among older MSM who do not practice additional STI risk behaviour, may improve overall satisfaction with their sex life and general well-being (92). Nonetheless, some research has showed that, when taken recreationally and in combination with other drugs, Viagra alone can be a predictive factor of HIV infection and insertive anal sex (94). While Viagra was not among our selected drugs studied in paper I due to existing controversy at the time, this drug was a potential predictor of UAI with nonprimary partners (and party drugs a significant one) in crude analysis of the 2010 study (135).

In 2007, almost a third of MSM reporting a date on the internet knew the internet partner's HIV status and slightly less than a half of those, who practiced UAI. Almost 70% agreed that it is important to them to find a sexual partner with similar HIV status. The 2010 survey suggested prevalent serosorting among Norwegian MSM (135). The practice of serosorting (choosing partners according to their HIV status in order to practice UAI) is a hazardous one and, as it is highly dependent on (the probability of) assuming the correct HIV status of a partner, may lead to transmission of both STI and HIV (71, 155).

5.4   Methodological considerations

The work presented in this thesis is based on observational data with inherent limitations. Limitations of cross-sectional study design include no evidence of a temporal relationship between exposure and outcome. For example, HIV infection was not associated with number of sexual partners in the last 6 months, but it was strongly associated with number of lifetime sexual partners, indicating that there is likely a change in the behaviour of MSM following the diagnosis of HIV.

In the MSIS surveillance data, the numbers of infected MSM might be underreported due to asymptomatic and undiscovered cases or misclassification in sexual transmission group as MSM may not be open about their sexual practices with their physician (Table 5).

Numbers identified in surveillance data depend on testing activity. With exception of (aggregated) Chlamydia reporting (with no behavioural details), no details of STI testing activity (number of negative tests) are currently available in Norway in order to supplement interpretation of the surveillance data. Furthermore, no yearly survey of STI prevalence exists. This is particularly limiting for interpretation of HIV surveillance data, as HIV is a long lasting infection and may be asymptomatic for years.

Due to their inherent dependency on testing activity and other factors (case misclassification), the surveillance data may provide low level of evidence. However, compared to long term prospective cohort studies, which are complex and expensive, surveillance data is a simplified approach to STI monitoring. When complimented with additional STI monitoring approaches (prevalence monitoring, behavioural surveillance, population based surveys and health services) these data may provide the best possible evaluations for STI trends and identification of risk groups.

It is not completely clear whether the observed increases in STI correspond to actual increases in population of MSM. Predominant detecting methods for gonorrhoea have changed in our study time (Figure 6), which could have affected the total numbers (156). Testing positive from several anatomical sites has increased over the years, likely indicating better adherence to recommendations from 2005 (157), as well as increased sensitivity of NAAT tests, as cultures from anorectum and oropharynx may fail (148). The use of NAAT tests is, however, controversial, due to potential cross-reactivity with commensal *Neisseria* species, more common at nongenital anatomical sites (158). When applied to nongenital anatomical sites, the positive predictive value of NAAT may be very low (in a community based sample of 1427 HIV-negative MSM in Australia, only 30.4% for oropharyngeal samples and 73.7% for anorectal samples) (158). These considerations could partially explain the observed increase in gonorrhoea; however they cannot explain the increasing syphilis rates.

False positive results may lead to adverse social, sexual, and economic consequences because of the requirements of partner notification, claims of infidelity, unnecessary clinic visits and pathology tests, and unwarranted treatment (158). US and Australian guidelines recommend a culture for *N. gonorrhoeae* testing from the pharynx or anorectum samples (158), however the cultures from these sites are more likely to fail. In Sweden, it is recommended that NAATs test results are confirmed using other method or a NAAT targeting different genetic marker (145).

Enhanced testing of MSM (particularly in specialized clinics) could also result in the seemingly increasing trends of STI and a higher proportion of infections detected compared to heterosexual men. The fact that heterosexual men and MSM likely use different diagnostic sites (with STI clinics preference among MSM) could also make surveillance data difficult to compare among two groups of men. Nonetheless, the heterosexual men are more likely to present with urethral gonorrhoeal infection, which is frequently symptomatic. Interestingly, syphilis seems to be discovered later in MSM compared to heterosexual men.

Since the surveillance case reporting of gonorrhoea, HIV and syphilis is anonymous, a chance for double reporting exists. Given the quality control at NIPH, where potential duplicates are double-checked with the reporting laboratory or the physician, the chance of double reporting for acute STI such as gonorrhoea and syphilis is small. The probability of HIV double reporting, however, is increasing with increasing prevalence in the Norwegian population of MSM.

Increased HIV testing activity would likely result in increase of the cases' median age (159), however no such increases in the median age of MSM in Norway were observed, suggesting a stable testing activity during the study time. While the majority of cases were likely infected within 3 years before the diagnosis, the amount of cases with unknown time of infection remains high, making surveillance data less reliable for public health recommendations.

In 2012, Norway was one of the remaining 10 (out of 30) EU/EEA countries, who did not have $CD4^+$ cell counts levels of newly HIV diagnosed cases available for HIV surveillance (160). The proportion of cases detected below the thresholds of $CD4^+$ <200 and <350 is a process indicator for testing performance (161). In addition, this information, stratified by population groups, is informative for decision makers to identify where the HIV testing needs to be strengthened in order for cases to be detected earlier and limit the further spread of the infection.

The sample from the Internet survey is likely not representative of the Norwegian population of MSM due to sampling bias (Norwegian gay oriented website including dating services). It has also been proposed that internet samples might overestimate the extent of intentional UAI (barebacking), as MSM will tend to use the internet to find sexual partners for these activities (90), however other studies showed no differences or even more consistent condom use in online samples (162). Knowing Norwegian language was necessary to complete the questionnaire in 2007. While non-Norwegian speaking participants were thus omitted, participants from all Norwegian counties were represented, Table 1. It is important to remember that offline and online samples of MSM may differ in age of participants, gay identification, (sex) behavioural patterns, HIV testing etc. (162, 163). Demographic characteristics, such as ethnicity or level of education vary with recruitment website (162). Even though the results cannot be generalised to the entire population of MSM, one would, however, expect this to be a sample of sexually active population, where the STI are actively transmitted.

6   MAIN CONCLUSIONS, PROPOSED ACTIONS AND FURTHER STUDIES

"To burn with desire and keep quiet about it is the greatest punishment we can bring on ourselves."
Federico García Lorca, Blood Wedding and Yerma

6.1   What is new from this study

This study has provided the following knowledge on STI among MSM in Norway:

- STI among MSM constitute an important and increasing public health problem in Norway

- Compared to the rest of the population, MSM are disproportionally affected by STI

- Surveillance data suggest worrisome increases in the incidence of gonorrhoea, syphilis and HIV among MSM in Norway

- The majority of MSM with STI are infected in Oslo

- Several behavioural risk factors for an STI have been identified in this population

- Concurrent sexual relationships including women may lead to further spread of STI in the population

- There is a need for an improvement of STI and sexual behaviour surveillance in Norway

- There is an urgent need to enhance prevention efforts

The identified behavioural risk factors in this study include high number of sexual partners and prevalent non-monogamous relationships, inconsistent condom use with anonymous or casual partners and having sex under the influence of alcohol or selected drugs. The STI spread among MSM is further facilitated by epidemiological synergy of concurrent infections, particularly HIV together with syphilis or gonorrhoea. Our study suggests that the HIV epidemic among MSM is likely being driven by non-recognised HIV infections in Norway. Given the burden of HIV among MSM in Norway, HIV testing might have insufficient coverage and uptake.

In addition, this work provides further insights into demographics, sexual practices, STI prevalence, risk factors for STI (including alcohol use and illicit drug use), perceptions and STI transmission knowledge in a large online sample of MSM.

6.2   Proposed actions

Early STI diagnosis and treatment, accessibility of healthcare services and effective behavioural interventions, targeting risk behaviours among MSM, should be a part of strengthened national strategy to improve sexual health among MSM in Norway. In 2012, the Norwegian Health Directorate launched a testing campaign «Bedre å vite» (*Best to know*) with free, low threshold rapid testing for HIV, aimed towards MSM, including CSW. The National competence center for STI Olafiaklinikken prepared detailed procedures for rapid HIV testing, including counselling and supplementary testing for other STI. Rapid testing is since available at many different venues in Oslo and in other bigger cities in Norway (164).

Success with STI testing, counselling and HBV vaccination from a similar, low threshold clinic based in Copenhagen, Denmark, has been reported (165).

Though crucial in combating HIV, increased HIV testing and high cART coverage might not be sufficient to influence the incidence (147). Among pharmacological interventions available, PrEP (to be taken by high risk HIV negative MSM) seems to create many ethical dilemmas, as well as compliancy and viral resistance issues. Many scholars however support early initiation of cART in all HIV-infected MSM as one of the important actions to reduce HIV transmission in this population (146, 166).

As many Norwegian MSM reported different obstacles in deciding to be tested for HIV, novel effective approaches for STI testing recruitment could be explored: utilisation of smartphone applications, advertising at STI clinics or specific websites, social networking, geotagging of existing STI clinics, testing sites and counselling venues. For high risk MSM, identified at STI clinics, SMS reminders for regular testing and check-up appointments could be used. Many of these novel approaches have been implemented in Australia, including enabling the anonymous notification of sex partners following a diagnosis through a website and prompts in patient information systems to remind clinicians to offer STI testing to MSM (167).

Increasing difficulties in interpreting Norwegian surveillance data, particularly for gonorrhoea and HIV, are suggesting that the MSIS system should be thoroughly revised. In order to improve our understanding of the trends, collecting information on testing activity for other STI, apart from chlamydia, should be considered. Increasing prevalence and survival of HIV positive MSM increases the likelihood of duplicate HIV reports. Modernisation of HIV reporting, adding a unique non-identifiable code (for example, utilizing a phonetic algorithm derived from a surname, such as Soundex, or social security number, as in Sweden and Denmark (146, 168)) could provide important improvements to guide decision making in STI prevention work. HIV surveillance could be additionally improved by reporting CD4+ cell counts levels in newly diagnosed cases, which enables an estimate whether the infection was detected early or late and consequently provides more accurate estimate of HIV incidence (166). In 2012, Norway was not among 30 countries (out of 51) in the WHO European Region, including majority of EU/EEA countries, which were able to report CD4+ counts at the time of diagnosis of HIV cases (160). On the other hand, the need for traditional (and identifiable) reporting of AIDS, which is with widely accessible cART no longer a problem in Norway (121), could be re-evaluated.

Establishing a systematic national *N. gonorrhoeae* sensitivity testing (for example, with sentinel sites) is recommended. There seems to be a need to establish clear national guidelines on NAAT testing in Norway in order to increase accuracy of detection, as well as improve antimicrobial sensitivity monitoring.

In order to reverse the STI trends among MSM, significant efforts need to be made. Existing recommendation of yearly testing for STI among sexually active MSM and more frequent testing for those with several partners could be further specified, for example the Australian guidelines suggest at least four tests form different anatomical sites per year (comprehensive STI testing) and more frequent testing for HIV-positive men (incorporated in their routine HIV monitoring), men who have unprotected anal intercourse or more than 10 partners in the previous 6 months, participate in group sex or use recreational drugs during sex (167). The need to concurrently test for multiple blood-borne viruses and

STI is strongly emphasized, as many clinicians may not use the opportunity to expand the testing beyond a single STI.

Anal screening for atypia and management of precancerous lesions should be offered to MSM engaging in anal intercourse, particularly HIV positive (1, 55). In addition to HBV and HAV vaccination being currently offered to MSM in Norway (164), the HPV vaccine is about to be approved in the EU (and hence in Norway) to combat anal cancer, meaning it will be accessible for both genders at their dedicated physician.

It is important to be aware that the above healthcare services remain unavailable to those MSM, who do not reveal their sexual practices to their dedicated physician and do not attend specialized clinics. Physicians should be encouraged to talk about sexual health openly, however following yearly testing guidelines might be challenging. Initiatives to target MSMW online and at other non-gay venues should be made, as these men might be more comfortable attending specialized STI clinics rather than their dedicated physicians for STI screening.

Current knowledge suggests that some specific subgroups (MSM with non-western background, MSMW, young MSM) could be lacking crucial knowledge to help them make informed choices about their sexual health, including accessing specialized healthcare services, STI testing, knowledge of STI and current STI trends in Norway. However, the sole knowledge of safe sex practices does not effectively prevent risk behaviour, particularly when alcohol or drugs are used before or during sex. Thus, more complex and widespread interventions to stop STI transmission are likely necessary in Norway. Education should focus on prevalent practices (including risk reduction practices such as serosorting), "party drugs" and alcohol use in relation to sex, as well as increasing STI trends among MSM. Any STI testing provides an opportunity for counselling on sexual risk behaviour, which should not be missed.

6.3 Further studies

Data on reporting coverage, STI testing activity among MSM (number of positive and number of total tests conducted) and health services accessibility (including knowledge of them), especially for vulnerable populations such as immigrants with non-western background, are lacking in Norway. There is a need for regular evaluation of behavioural trends, STI prevalence (either in voluntary studies or implementing unlinked anonymous testing) and knowledge among MSM.

In order to monitor the risks related to STI transmission and provide information for planning and public health interventions, current STI surveillance in Norway should be supported by regular behavioural studies using agreed core set of indicators, targeted particularly at MSM in Oslo, where most STI infections occur. Our work suggests that internet may be an inexpensive and rapid option for conduction of behaviour studies. Combined analysis of both behavioural surveillance data and data from biological surveillance of STI forms a "second generation surveillance", as defined by The Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organisation (WHO) (169). Behavioural surveillance paired with monitoring of comprehensive STI testing trends among MSM yielded very good results in Australia and provided good information to guide recommendations (167).

Estimates of undiagnosed HIV infections are lacking in Norway. Since CD4+ cell counts are not reported in MSIS, little is known about how early infections are detected on average. The data on true HIV prevalence among MSM, which would include undiagnosed HIV infections, could be for example obtained by unlinked anonymous testing (UAT) in the STI clinics in Oslo, frequented by population of MSM, in order to provide an estimate of STI (HIV and/or HCV) prevalence in (a high risk) population in regular time intervals. Voluntary anonymous testing or UAT could be also offered using saliva tests to attendees of gay venues. The extensive linked study, done on MSM (2009-2011) to evaluate prevalence of gonorrhoea, chlamydia and *M. genitalium* (148), suggest more regular STI prevalence monitoring is potentially feasible.

Effective methods to reduce risk behaviour, including alcohol and substance use, should be further explored. In a recent study in California, a 6 months follow up of a personalized cognitive counselling intervention with rapid HIV testing was associated with abstaining from alcohol and lower frequency of alcohol intoxication, abstaining from marijuana and erectile dysfunction drugs, and reduced number of UAI under the influence of methamphetamine (170). Further studies about MSMW, who might not be associated with typical gay venues or targeted by preventive measures, are recommended.

Many challenges remain to be addressed, including finding effective novel ways in targeting MSM with STI prevention measures. More research is needed to identify effective and long-lasting prevention measures, which should target risk behaviours and enhance testing and treatment in order to lower STI prevalence and transmission among MSM in Norway, particularly in Oslo. Potential language and cultural obstacles should be taken into account, in order to target MSM with non-western background.

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8   APPENDICES

Papers I-IV

BMC
Infectious Diseases

RESEARCH ARTICLE   **Open Access**

Self-reported sexually transmitted infections and their correlates among men who have sex with men in Norway: an Internet-based cross-sectional survey

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Abstract

Background: The incidences of reportable sexually transmitted infections (STI) among men who have sex with men (MSM) have increased since the late 1990 s in Norway. The objectives of our study were to assess factors, associated with recent selected STI among MSM, living in Norway in order to guide prevention measures.

Methods: We conducted a cross-sectional Internet-based survey during 1-19 October 2007 among members of a MSM-oriented Norwegian website using an anonymous questionnaire on demographics, sexual behaviour, drug and alcohol use, and STI. The studied outcomes were gonorrhoea, syphilis, HIV or Chlamydia infection in the previous 12 months. Associations between self-reported selected STI and their correlates were analysed by multivariable Poisson regression. P value for trend (p-trend), adjusted prevalence ratios (PR) with 95% confidence intervals [] were calculated.

Results: Among 2430 eligible 16-74 years old respondents, 184 (8%) reported having had one of the following: syphilis (n = 17), gonorrhoea (n = 35), HIV (n = 42) or Chlamydia (n = 126) diagnosed in the past 12 months. Reporting Chlamydia was associated with non-western background (PR 2.8 [1.4-5.7]), number of lifetime male partners (p-trend < 0.001), unsafe sex under the influence of alcohol (PR 1.8 [1.1-2.9]) and with younger age (p-trend = 0.002). Reporting gonorrhoea was associated with unrevealed background (PR 5.9 [1.3-26.3]), having more than 50 lifetime male partners (PR 4.5 [1.3-15.6]) and more than 5 partners in the past 6 months (PR 3.1 [1.1-8.8]), while mid-range income was protective (PR 0.1 [0.0-0.6]). Reporting HIV was associated with residing in Oslo or Akershus county (PR 2.3 [1.2-4.6]), non-western background (PR 5.4 [1.9-15.3]), unrevealed income (PR 10.4 [1.5-71.4]), number of lifetime male partners (p-trend < 0.001) and being under the influence of selected drugs during sex in the past 12 months (PR 5.2 [2.7-11.4]). In addition, the frequency of feeling drunk was reversibly associated with HIV.

Conclusions: Our study demonstrates different associations of demographic and behavioural factors with different STI outcomes in the study population. Number of lifetime male partners was the most important potential predictor for Chlamydia and HIV. The STI prevention efforts among MSM should focus on Oslo and Akershus, promote safe sex practices and tackle sex-related drug and alcohol use.

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Background

Since the mid-1990 s, sexually transmitted infections (STI) among men who have sex with men (MSM) have been reported to be on the rise in many European countries [1] and worldwide [2,3]. Increasing numbers of HIV infections, gonorrhoea and syphilis among men, infected by other men, have been also observed in the Norwegian surveillance system for communicable diseases [4-6]. Chlamydia is the most common reportable STI in Norway [7] and although MSM-specific data are not available, the rate among Norwegian men in 2007 was as high as 368/100 000 person-years. The STI transmission mainly occurs in the capital Oslo and neighbouring Akershus county, where the MSM population is concentrated [5,8]. The surveillance system collects only limited information on STI patients and specific knowledge about sexual risk behaviour among MSM living in Norway is very limited.

The MSM population is frequently referred to as "hidden" [9,10] due to its unknown size and difficulties to reach. Internet websites have been shown to be convenient cost-effective tools for recruitment of MSM [11]. In 2007, 78% of all households in Norway had Internet access and 88% of men between 16-74 years old have used it recently [12]. Sampling on the Internet may be also more convenient to attract those men, who may be less likely to self-identify as MSM [9].

The objective of this study was to assess the associations between selected factors and self-reported STI in the past 12 months among MSM, living in Norway.

Methods

Participants and Recruitment

An Internet cross-sectional survey was initiated by the Norwegian Institute of Public Health, in cooperation with "Gay and Lesbian Health Norway". Participation was offered to logged-in members of the Norwegian MSM-oriented website from 1 October 2007 to 19 October 2007. This is the leading website for the MSM-net-community in the Norwegian language with more than 31 000 member profiles. The site has about 50 000 visits each week and provides news items, a chat-community, a discussion forum, an events calendar, links and other information. When clicking on the study banner, the participants were guided to an introduction, where the aims and structure of the study were explained. Anonymity of the participants was assured and contact persons for the study from collaborating institutions were provided. The participation was voluntary. Respondents, who answered that they were women, younger than 16 years, had never had sex with a man or were living abroad, were excluded from the analysis.

Selected outcomes

We focused our analysis on MSM, who reported being diagnosed with any of the following STI in the previous 12 months: gonorrhoea, syphilis, HIV or Chlamydia infection ("selected STI"). To check if selected exposures are differently associated with a specific STI, we performed multivariable analyses for Chlamydia, gonorrhoea and HIV infection as separate outcomes (Table 1), but due to the low number of cases, this was not possible for syphilis.

Pilot study

An offline and online testing of the questionnaire was conducted by 15 MSM, who provided a detailed feedback on the content, functionality and the questionnaire layout.

Data collection

Data were collected using the online survey tool Questback and harvested in Excel format.

Measures and data presentation

Demographic characteristics and sexual behaviour were initially classified as presented in Tables 2 and 3; however some categories within variables were merged in multivariable analysis as presented in the Table 4. The variables health region and residing in Oslo/Akershus county were created from the "county of residence" variable. The variable "drugs before sex" was created based on reports of using any of the following drugs before sex: marihuana, prescription drugs, ecstasy, LSD, GHB, cocaine, heroine, amphetamines or methamphetamines.

Statistical analyses

We used Stata 9.0 for the analyses. Associations between reported recent selected STI and categorical independent variables with and without adjustment for potential confounders were studied by Poisson regression with robust variance estimates [13]. Crude and adjusted prevalence ratios (PR) with 95% confidence intervals (CI) were calculated. Three separate multivariable models were generated (Table 1) and they included variables, associated with the outcome at $p < 0.15$ [14] in crude analysis as well as variables, previously shown as predictors of STI. Where the unknown or missing were statistically different in the crude analysis from the rest of the categories within a variable, they were entered in multivariable analysis as a separate category, as presented in the Table 4, otherwise they were excluded. The variable "ever had a date in reality with a partner from the Internet" was not included in the multivariable analysis with gonorrhoea as an outcome due to a zero variance of this potential predictor. Variables health region and residing

Table 1 Overview of the multivariable models, their outcomes and comparison groups in the Internet-based cross-sectional MSM study

Model	Outcome*	Comparison group
1.	Chlamydia, NO selected STI	respondents not reporting any selected STI
2.	gonorrhoea or gonorrhoea AND any selected STI	respondents not reporting any selected STI
3.	HIV infection or HIV infection AND any selected STI**	respondents not reporting any selected STI

* all outcomes diagnosed in the past 12 months
**selected STI - syphilis, gonorrhoea, HIV or Chlamydia in the past 12 months

in Oslo/Akershus were created from the same original variable and, due to our study question, only the latter was selected for multivariable analysis.

In each multivariable model, we excluded those, who did not report an outcome of interest, but were infected with another selected STI - as presented in the Table 1. In addition, we also excluded those, reporting Chlamydia and selected STI in the past 12 months, from the model, where Chlamydia was a sole outcome. Those with another STI were included in the outcomes of the other two corresponding models to represent more at risk populations.

Participation in the study was of no direct benefit to the respondents. The study was approved by the Regional Committee for Medical and Health Research Ethics, Southern Norway, and by the Norwegian Data Inspectorate.

Results

Out of 2598 respondents, 2430 were included in the study after application of our exclusion criteria. The median age of respondents was 31 years, ranging from 16 to 74 years. The respondents were from all regions of Norway, although half of them lived in Oslo or neighbouring Akershus county (Table 2). Most respondents reported being ethnic Norwegians (93%) and having university education (58%). Most men stated their sexual orientation as homosexual (86%), 68% reported more than 10 male sexual partners in their life and 65% reported having had intercourse with an anonymous or casual partner in the last 6 months, of which more than a third reported having unprotected anal intercourse (UAI), (Table 3). We identified 184 (8%) MSM, infected with a selected STI in the past 12 months: 17 (0.7%) reported being diagnosed with syphilis, 35 (1.4%) with gonorrhoea, 42 (1.7%) with HIV and 126 (5.2%) with Chlamydia. In addition, 26 (1.1%) respondents reported being diagnosed with HIV prior to the past twelve months.

Having unsafe sex in the past 12 months under the influence of alcohol was reported by 26.4%. Those who reported feeling drunk four times and more in an average month, represented 38.0% and those who used selected drugs (marihuana, prescription drugs, ecstasy, LSD, GHB, cocaine, heroine, amphetamines or methamphetamines) in connection to sex represented 9.9% of the participants (Table 3).

Crude analyses indicated no associations between a selected STI and age, with the exception of those above 45 years, who were less likely to report Chlamydia (Table 2). Compared to those in health region East (which includes Oslo), those living in health region West in Norway had a lower prevalence ratio for HIV infection and those in the North for Chlamydia. In crude analysis, residing in Oslo or Akershus county was associated with all selected STI. Those with non-western background were more likely to be recently diagnosed with Chlamydia, HIV and syphilis; and those, who did not want to reveal their ethnic background, with gonorrhoea. Education did not seem to be associated with any selected STI in crude analysis, while yearly income, higher than 300 000 Norwegian crowns, as well as unrevealed income, seemed to increase the prevalence ratio for HIV. Conversely, an income of 300-500 thousand Norwegian crowns per year seemed to be protective for gonorrhoea (Table 2).

Among possible sexual exposures, having more than 10 male partners in life was associated with Chlamydia in crude analysis, but it did not seem to be important for other selected STI (Table 3). Number of partners in the past six months was, on the other hand, more important for Chlamydia, gonorrhoea and syphilis, but not for the HIV infected. Selected STI were not associated with sexual orientation, choosing partner on the Internet and steady relationship with either a man or a woman, while many other risk behaviours were associated with all or at least two of the selected STI (Table 3).

In the multivariable model, a decreasing linear trend between Chlamydia and age was observed (p for trend = 0.002), (Table 4). Compared to those without selected STI, HIV infection was more prevalent among residents of Oslo or Akershus county, while the results on residence were inconclusive for gonorrhoea (p = 0.082) and Chlamydia (p = 0.068). Immigrants with non-western background were more likely to report HIV and Chlamydia infection. While unrevealed income was associated with HIV, income did not seem to be relevant for Chlamydia and was, in the category of 300-500 thousand Norwegian crowns per year, protective for gonorrhoea. A positive linear trend between the number of male sexual partners in life and the prevalence of Chlamydia and

Table 2 Demographic characteristics of MSM respondents in the Internet-based cross-sectional study

Demographic characteristics	respondents N = 2430 (%)	Chlamydia* N= 101 (%)	Crude PR Chlamydia [95% CI]	gonorrhoea N = 35 (%)	Crude PR gonorrhoea [95% CI]	HIV N = 42 (%)	Crude PR HIV [95% CI]	Syphilis N = 17 (%)	Crude PR syphilis
age groups (years)									
16-25	768 (31.6)	37 (36.6)	ref. group	16 (45.7)	ref. group	7 (16.7)	ref. group	3 (17.6)	ref. group
26-35	769 (31.6)	35 (34.6)	0.9 [0.6-1.5]	8 (22.9)	0.5 [0.2-1.2]	15 (35.7)	2.1 [0.9-5.2]	6 (35.3)	2.0 [0.5-8.0]
36-45	551 (22.7)	22 (21.8)	0.8 [0.5-1.4]	8 (22.9)	0.7 [0.3-1.6]	11 (26.2)	2.2 [0.8-5.6]	5 (29.4)	2.3 [0.6-10.0]
≥ 46	342 (14.0)	7 (6.9)	0.4 [0.2-0.9]	3 (8.6)	0.4 [0.1-1.4]	9 (21.4)	2.9 [1.1-7.7]	3 (17.6)	2.2 [0.4-11.1]
health region of residence									
East	1415 (58.2)	70 (69.3)	ref. group	26 (74.3)	ref. group	36 (85.7)	ref. group	15 (88.2)	ref. group
West	369 (15.2)	16 (15.8)	0.9 [0.5-1.5]	5 (14.3)	0.7 [0.3-1.9]	1 (2.4)	0.1 [0.0-0.8]	0	0
South	254 (10.4)	7 (6.9)	0.6 [0.3-1.2]	2 (5.7)	0.4 [0.1-1.8]	2 (4.8)	0.3 [0.1-1.3]	2 (11.8)	0.7 [0.2-3.2]
Mid-Norway	236 (9.7)	7 (6.9)	0.6 [0.3-1.3]	2 (5.7)	0.5 [0.1-1.9]	1 (2.4)	0.2 [0.0-1.2]	0	
North	151 (6.2)	1 (1.0)	0.1 [0.2-0.9]	0	0	2 (4.8)	0.5 [0.1-2.1]	0	
unknown	5 (0.2)	0		0	0	0	0	0	
residing in Oslo/Akershus county									
no	1200 (49.4)	38 (37.6)	ref. group	11 (31.4)	ref. group	10 (23.8)	ref. group	4 (23.5)	ref. group
yes	1225 (50.4)	63 (62.4)	1.6 [1.1-2.4]	24 (68.6)	2.1 [1.0-4.3]	32 (76.2)	3.1 [1.5-6.3]	13 (76.5)	3.1 [1.5-6.3]
unknown	5 (0.2)	0		0	0				
ethnic background:									
Norwegian	2265 (93.2)	95 (94.1)	ref. group	30 (85.7)	ref. group	37 (88.1)	ref. group	13 (76.5)	ref. group
western background	90 (3.7)	1 (1.0)	0.3 [0.0-1.9]	2 (5.7)	1.7 [0.4-6.9]	1 (2.4)	0.7 [0.1-4.9]	1 (5.9)	1.9 [0.2-14.6]
non-western background	41 (1.7)	5 (4.9)	2.9 [1.2-6.8]	1 (2.9)	1.8 [0.3-13.2]	3 (7.1)	4.5 [1.4-13.9]	2 (11.8)	8.5 [2.0-36.5]
unknown	34 (1.4)	0		2 (5.7)	4.4 [1.1-17.8]	1 (2.4)	1.8 [0.2-12.7]	1 (5.9)	5.1 [0.7-38.1]
education									
primary school or less	121 (5.0)	6 (5.9)	ref. group	2 (5.7)	ref. group	1 (2.4)	ref. group	1 (5.9)	ref. group
secondary school	903 (37.2)	36 (35.6)	0.8 [0.3-1.9]	16 (45.7)	1.1 [0.3-4.6]	15 (35.7)	2.0 [0.3-15.1]	5 (29.4)	0.7 [0.1-5.7]
high school/university	1401 (57.6)	59 (58.4)	0.8 [0.4-1.9]	17 (48.6)	0.7 [0.2-3.1]	26 (62)	2.2 [0.3-16.4]	11 (64.7)	0.9 [0.1-7.3]
unknown	5 (0.2)	0		0	0	0	0	0	
income before tax in 1000 NOK** in 2005									
< 150	670 (27.6)	24 (23.8)	ref. group	12 (34.3)	ref. group	5 (11.9)	ref. group	4 (23.5)	ref. group
150-299	573 (23.6)	22 (21.8)	1.1 [0.6-1.9]	11 (31.4)	1.1 [0.5-2.4]	8 (19.0)	1.9 [0.6-5.7]	4 (23.5)	1.2 [0.3-4.6]
300-500	854 (35.3)	37 (36.6)	1.2 [0.7-2.0]	3 (8.6)	0.2 [0.1-0.7]	18 (42.9)	2.8 [1.0-7.6]	4 (23.5)	0.9 [0.2-3.2]
> 500	323 (13.3)	18 (17.8)	1.5 [0.9-2.8]	8 (22.9)	1.4 [0.6-3.3]	10 (23.8)	4.1 [1.2-12.0]	5 (29.4)	2.6 [0.7-9.6]
unknown	10 (0.4)	0		1 (2.9)	5.6 [0.8-38.9]	1 (2.4)	13.4 [1.7-104.5]	0	

* only those, who reported Chlamydia as a single STI infection in the past 12 months, were included in this group

** NOK - Norwegian crowns

Proportion of MSM, reporting Chlamydia, gonorrhoea, HIV infection or syphilis in the previous 12 months and their crude associations

Table 3 Sexual behaviour of MSM respondents in the Internet-based cross-sectional study

Sexual behaviour	respondents N = 2430 (%)	Chlamydia a* N= 101 (%)	Crude PR Chlamydia [95% CI]	gonorrhoea N = 35 (%)	Crude PR gonorrhoea [95% CI]	HIV N = 42 (%)	Crude PR HIV [95% CI]	Syphilis N = 17 (%)	Crude PR syphilis [95% CI]
sexual orientation									
homosexual	2088 (85.9)	89 (88.1)	ref. group	30 (85.7)	ref. group	37 (88.1)	ref. group	15 (88.2)	ref. group
bisexual	225 (9.3)	8 (7.9)	0.8 [0.4-1.7]	4 (11.4)	1.2 [0.4-3.5]	3 (7.1)	0.7 [0.2-2.4]	1 (5.9)	0.6 [0.1-4.7]
heterosexual	77 (3.2)	3 (3.0)	0.9 [0.3-2.8]	1 (2.9)	0.9 [0.1-6.5]	2 (4.8)	1.5 [0.4-6.0]	1 (5.9)	1.8 [0.2-13.5]
unsure	40 (1.6)	1 (1.0)	0.6 [0.1-4.1]	0		0		0	
N of male sexual partners in life									
1	68 (2.8)	0		1 (2.9)	ref. group	1 (2.4)	ref. group	1 (5.9)	ref. group
2-5	334 (13.7)	3 (3.0)	ref. group	0		0		0	
6-10	383 (15.8)	6 (5.9)	1.7 [0.4-6.9]	3 (8.6)	0.5 [0.1-5.0]	1 (2.4)	0.2 [0.0-2.8]	0	
11-50	868 (35.7)	40 (39.6)	5.1 [1.6-16.5]	11 (31.4)	0.9 [0.1-6.6]	9 (21.4)	0.7 [0.1-5.5]	5 (29.4)	0.4 [0.0-3.3]
51- > 500	777 (32.0)	52 (51.5)	7.4 [2.3-23.7]	20 (57.1)	1.7 [0.2-12.8]	31 (73.8)	2.7 [0.4-19.6]	11 (64.7)	1.0 [0.1-7.3]
N of male sexual partners in the past 6 months									
0	175 (7.2)	2 (2.0)	ref. group	0		3 (7.1)	ref. group	0	
1-2	978 (40.2)	21 (20.8)	1.9 [0.4-8.1]	6 (17.1)	ref. group	12 (28.6)	0.7 [0.2-2.5]	5 (29.4)	ref. group
3-5	649 (26.7)	29 (28.7)	4.0 [1.0-16.5]	9 (25.7)	2.3 [0.8-6.3]	9 (21.4)	0.8 [0.2-3.0]	4 (23.5)	1.2 [0.3-4.5]
6-10	383 (15.8)	24 (23.8)	5.6 [1.3-23.3]	11 (31.4)	4.7 [1.7-12.6]	6 (14.3)	0.9 [0.2-3.7]	3 (17.6)	1.5 [0.4-6.4]
> 10	242 (10.0)	25 (24.8)	9.2 [2.2-38.3]	9 (25.7)	6.1 [2.2-16.9]	12 (28.6)	2.9 [0.8-10.3]	5 (29.4)	4.4 [1.2-13.8]
unknown	3 (0.1)	0		0		0		0	
anonymous/casual partner in the last 6 months									
no	853 (35.1)	20 (19.8)	ref. group	6 (17.1)	ref. group	12 (28.6)	ref. group	1 (5.9)	ref. group
yes	1572 (64.7)	81 (80.2)	2.2 [1.3-3.6]	29 (82.9)	2.6 [1.1-6.3]	30 (71.4)	1.3 [0.7-2.6]	16 (94.1)	8.7 [1.1-65.3]
unknown	5 (0.2)	0		0		0		0	
UAI** with anonymous/casual partner in the last 6 months									
no	1848 (76.0)	52 (51.5)	ref. group	19 (54.3)	ref. group	24 (57.1)	ref. group	10 (58.8)	ref. group
yes	576 (23.7)	49 (48.5)	3.0 [2.1-4.4]	16 (45.7)	2.7 [1.4-5.2]	18 (42.9)	2.4 [1.3-4.4]	7 (41.2)	2.2 [0.9-5.9]
unknown	6 (0.2)	0		0		0		0	
practice of threesome or group sex									
no	1270 (52.3)	32 (31.7)	ref. group	14 (40.0)	ref. group	13 (30.9)	ref. group	7 (41.2)	ref. group
yes	1068 (43.9)	66 (65.3)	2.4 [1.6-3.7]	21 (60.0)	1.8 [0.9-3.5]	27 (64.3)	2.5 [1.3-4.8]	9 (52.9)	1.6 [0.6-4.1]
unknown	92 (3.8)	3 (3.0)	1.3 [0.4-4.1]	0		2 (4.8)	2.1 [0.5-9.3]	1 (5.9)	2.0 [0.2-15.9]
received money for sex in the last year									
no	2343 (96.4)	93 (92.1)	ref. group	29 (82.9)	ref. group	40 (95.2)	ref. group	16 (94.1)	ref. group
yes	78 (3.2)	7 (6.9)	2.3 [1.1-4.7]	6 (17.1)	6.2 [2.7-14.5]	2 (4.8)	1.5 [0.4-6.1]	1 (5.9)	1.9 [0.2-14.0]
unknown	9 (0.4)	1 (1.0)	2.8 [0.4-17.9]	0		0		0	

Table 3 Sexual behaviour of MSM respondents in the Internet-based cross-sectional study (Continued)

paid for sex in the last year								
no	2305 (94.9)	90 (89.1)	ref. group	29 (82.9)	ref. group	39 (92.9)	ref. group	16 (94.1)	ref. group
yes	118 (4.9)	11 (10.9)	2.4 [1.3-4.3]	5 (14.3)	3.4 [1.3-8.5]	3 (7.1)	1.5 [0.5-4.8]	1 (5.9)	1.2 [0.2-9.1]
unknown	7 (0.3)	0		1 (2.9)	11.3 [1.8-72.2]	0		0	
how many times feeling drunk in a given month								
< 1	487 (20.0)	8 (7.9)	ref. group	2 (5.7)	ref. group	10 (23.8)	ref. group	4 (23.5)	ref. group
1	416 (17.1)	14 (13.9)	2.0 [0.9-4.8]	9 (25.7)	5.3 [1.1-24.2]	12 (28.6)	1.4 [0.6-3.2]	4 (23.5)	1.2 [0.3-4.6]
2-3	588 (24.2)	27 (26.7)	2.8 [1.3-6.1]	12 (34.3)	5.0 [1.1-22.1]	12 (28.6)	1.0 [0.4-2.3]	3 (17.6)	0.6 [0.1-2.8]
≥ 4	923 (38.0)	52 (51.5)	3.4 [1.6-7.2]	12 (34.3)	3.2 [0.7-14.1]	8 (19.0)	0.4 [0.2-1.1]	5 (29.4)	0.6 [0.2-2.4]
unknown	16 (0.7)	0		0		0		1 (5.9)	7.6 [0.9-64.3]
unsafe sex under the influence of alcohol in the past 12 months								
no	1729 (71.1)	49 (48.5)	ref. group	18 (51.4)	ref. group	27 (64.3)	ref. group	11 (64.7)	ref. group
yes	641 (26.4)	51 (50.5)	2.8 [1.9-4.1]	17 (48.6)	2.5 [1.3-4.9]	15 (35.7)	1.5 [0.8-2.8]	6 (35.3)	1.5 [0.5-4.0]
unknown	60 (2.5)	1 (1.0)	0.6 [0.1-4.2]	0		0		0	
under the influence of selected drugs* during sex in the past 12 months**								
no	2106 (86.7)	81 (83.2)	ref. group	25 (71.4)	ref. group	25 (59.5)	ref. group	14 (82.3)	ref. group
yes	240 (9.9)	17 (16.8)	1.8 [1.1-3.0]	10 (28.6)	3.6 [1.8-7.5]	16 (38.1)	5.6 [3.0-10.4]	3 (17.6)	1.9 [0.5-6.5]
unknown	84 (3.5)	3 (3.0)	0.9 [0.3-2.9]	0		1 (2.4)	1.0 [0.1-7.3]	0	
current steady relationship with a woman								
no	2113 (86.9)	89 (88.1)	ref. group	28 (80.0)	ref. group	36 (85.7)	ref. group	13 (76.5)	ref. group
yes	236 (9.7)	10 (9.9)	1.0 [0.5-1.9]	4 (11.4)	1.2 [0.4-3.6]	5 (11.9)	1.2 [0.5-3.1]	3 (17.6)	2.1 [0.6-7.2]
unknown	81 (3.3)	2 (2.0)	0.6 [0.1-2.3]	3 (8.6)	2.8 [0.9-9.0]	1 (2.4)	0.7 [0.1-5.2]	1 (5.9)	2.0 [0.3-15.1]
current steady relationship with a man								
no	1492 (61.4)	65 (64.4)	ref. group	19 (54.3)	ref. group	26 (61.9)	ref. group	8 (47.1)	ref. group
yes	936 (38.5)	36 (35.6)	0.9 [0.6-1.3]	16 (46.7)	1.3 [0.7-2.6]	16 (38.1)	1.0 [0.5-1.8]	9 (52.9)	1.8 [0.7-4.6]
unknown	2 (0.1)	0		0		0		0	
ever had a date in reality with an Internet partner								
no	190 (7.8)	3 (3.0)	ref. group	0	no variance	2 (4.8)	ref. group	1 (5.9)	ref. group
yes	2209 (90.9)	97 (96.0)	2.8 [0.9-8.7]	35 (100)		40 (95.2)	1.7 [0.4-7.1]	16 (94.1)	1.4 [0.2-10.3]
unknown	31 (1.3)	1 (1.0)	2.0 [0.2-19.0]	0		0		0	

* only those, who reported Chlamydia as a single STI infection in the past 12 months, were included in this group

**UAI - unprotected anal intercourse

***selected drugs included: marihuana, prescription drugs, ecstasy, LSD, GHB, cocaine, heroine, amphetamines, methamphetamines

Proportion of MSM, reporting Chlamydia, gonorrhoea, HIV infection or syphilis in the previous 12 months and their crude associations

Table 4 Associations of potential risk factors with three different STI outcomes among MSM respondents of the Internet-based cross-sectional study

Potential risk factors	Chlamydia N = 101		gonorrhoea N = 35		HIV N = 42	
	Adjusted PR [95% CI]	p for trend	Adjusted PR [95% CI]	p for trend	Adjusted PR [95% CI]	p for trend
age groups (years)		0.002		0.255		0.932
16-25	ref. group		ref. group		ref. group	
26-35	0.6 [0.4-1.1]		0.5 [0.2-1.6]		1.4 [0.6-3.2]	
36-45	0.4 [0.2-0.9]		0.7 [0.2-2.3]		0.8 [0.3-2.1]	
≥ 46	0.3 [0.1-0.7]		0.6 [0.1-2.2]		1.5 [0.6-3.8]	
residing in Oslo or Akershus county						
no	ref. group		ref. group		ref. group	
yes	1.4 [1.0-2.1]		1.9 [0.9-4.1]		2.3 [1.2-4.6]	
ethnic background:						
Norwegian	ref. group		ref. group		ref. group	
immigrant with western background	0.3 [0.0-1.8]		1.5 [0.4-6.1]		0.4 [0.0-3.0]	
immigrant with non-western background	2.8 [1.4-5.7]		1.8 [0.5-6.1]		5.4 [1.9-15.3]	
unknown	not included		5.9 [1.3-26.3]		not included	
education		0.568		0.987		not calculated
primary school or less	ref. group		ref. group		merged with ref. group	
secondary school	0.6 [0.3-1.2]		1.7 [0.2-16.1]		ref. group	
high school/university	0.5 [0.3-1.1]		1.6 [0.1-16.5]		0.8 [0.5-1.5]	
annual income before tax in 1000 NOK* in 2005		0.204		0.380		0.102
< 150	ref. group		ref. group		ref. group	
150-299	1.1 [0.6-1.9]		1.0 [0.4-2.5]		1.0 [0.4-2.7]	
300-500	1.2 [0.6-2.1]		0.1 [0.0-0.6]		0.8 [0.3-1.9]	
> 500	1.3 [0.6-2.9]		1.0 [0.3-2.9]		1.5 [0.6-4.3]	
unknown	not included		not included		10.4 [1.5-71.4]	
N of male sexual partners in life:		< 0.001		0.056		< 0.001
1-10	ref. group		ref. group		ref. group	
11-50	4.0 [1.8-8.8]		2.4 [0.7-7.6]		3.0 [0.7-13.2]	
51-> 500	4.4 [1.9-10.3]		4.5 [1.3-15.6]		13.9 [3.5-55.8]	
N of male sexual partners in the past 6 months		0.308		0.065		0.544
0-2	ref. group		ref. group		ref. group	
3-5	1.2 [0.6-2.2]		1.7 [0.6-4.9]		0.6 [0.2-1.8]	
6-10	1.2 [0.7-2.3]		3.1 [1.1-8.8]		0.4 [0.1-1.5]	
> 10	1.6 [0.8-3.2]		3.4 [1.0-11.3]		0.7 [0.2-2.3]	

Table 4 Associations of potential risk factors with three different STI outcomes among MSM respondents of the Internet-based cross-sectional study (Continued)

practice of threesome or group sex			
no	ref. group	ref. group	ref. group
yes	1.5 [1.0-2.3]	0.8 [0.4-1.7]	1.0 [0.5-2.1]
received money for sex in the last year			
no	ref. group	ref. group	ref. group
yes	0.9 [0.3-2.2]	2.3 [0.7-8.4]	1.9 [0.4-8.3]
paid for sex in the last year			
no	ref. group	ref. group	ref. group
yes	1.6 [0.8-3.2]	1.2 [0.3-3.9]	0.6 [0.1-2.2]
unknown	not included	5.5 [0.4-82.7]	not included
how many times feeling drunk in a given month	0.409	0.283	< 0.001
< 1	ref. group	ref. group	ref. group
1	1.6 [0.7-4.0]	3.9 [0.9-16.8]	1.1 [0.4-2.7]
2-3	2.0 [0.9-4.5]	3.3 [0.8-12.9]	0.6 [0.2-1.3]
≥ 4	1.6 [0.7-3.5]	1.3 [0.3-5.0]	0.1 [0.0-0.3]
unsafe sex under the influence of alcohol in the past 12 months			
no	ref. group	ref. group	ref. group
yes	1.8 [1.1-2.9]	1.9 [0.9-4.3]	1.5 [0.7-3.4]
under the influence of selected drugs** during sex in the past 12 months			
no	ref. group	ref. group	ref. group
yes	0.8 [0.5-1.5]	1.7 [0.8-3.9]	5.2 [2.7-11.4]
ever had a date in reality with Internet partner			
no	ref. group	not included	ref. group
yes	1.6 [0.5-5.0]	not included	1.4 [0.4-4.6]
UAI*** with a casual or anonymous partner in the last 6 months			
no	ref. group	ref. group	ref. group
yes	1.5 [0.9-2.4]	1.0 [0.5-2.2]	2.0 [0.9-4.6]

* NOK - Norwegian crowns

**selected drugs included: marihuana, prescription drugs, ecstasy, LSD, GHB, cocaine, heroine, amphetamines, methamphetamines

*** UAI - unprotected anal intercourse

Results represent three separate multivariable models with self-reported STI as outcomes. Different exclusion criteria were applied in these models, as described in the text and presented in the Table 1.

HIV was observed (p for trend < 0.001), while only the category above 50 lifetime partners was associated with gonorrhoea. Number of male sexual partners in the past six months was not important correlate for Chlamydia and HIV, but was, above counts of 5, important for gonorrhoea. The practice of group sex could be a potential risk factor for Chlamydia (p = 0.069). Receiving money or paying for sex was not important for any of the outcomes. The frequency of feeling drunk in an average month was inversely associated with HIV (p for trend < 0.001), while reporting unsafe sex under the influence of alcohol in the past 12 months was correlated to Chlamydia. Being under the influence of selected drugs during sex in the past 12 months was associated with HIV infection. Results for having a date with a partner whom they met on the Internet, and UAI with a casual or anonymous partner in the last 6 months, were inconclusive.

Discussion

This is the first Internet study on sexual risk behaviour among MSM in Norway. Our predominantly well-educated study population frequently used the Internet for dating, reported prevalent partner exchange including recent casual or anonymous partners, and alcohol use. MSM, being diagnosed with Chlamydia, HIV, gonorrhoea or syphilis in the past year represented 8% of our respondents.

Our results suggest that MSM, who reported any selected STI in the past year, represent different demographic groups and groups with different risk behaviours. Younger age, non-western background, number of lifetime male sexual partners and unsafe sex under the influence of alcohol in the past 12 months were factors associated with Chlamydia. Similarly, non-western background was also associated with HIV infection, as well as residence in Oslo or Akershus county, unrevealed income, more than 50 lifetime male sexual partners and being under the influence of selected drugs during sex in the past 12 months. HIV infection was decreasingly associated with the frequency of feeling drunk in a given month. Gonorrhoea was associated with unrevealed ethnic background, more than 50 lifetime male sexual partners and having more than 5 male sexual partners in the past 6 months. Reporting a mid-range income category seemed to be protective.

Collecting data with no human interviewers and without any personally identifying information might have been grounds for more revealing answers on behaviour. Our study has received considerable public attention and was well-known among MSM. Thus, we were able to collect data from relatively large numbers of respondents from all health regions in Norway. High Internet coverage and almost universal computer literacy in Norway made our study widely accessible. Since our questionnaire took

about 45 minutes to complete, we assume double entries were rare.

Representativeness and generalization of the results to the entire MSM population in Norway might not be feasible, as Internet sampling is subject to selection bias, misrepresentation as a member of the sampled population, repeated participation, missing data, inability to gather biological specimens etc. [9]. Those with an STI in the past year might have been more likely to be aware of the past risk behaviour (recall bias) - thus over-estimating the effect size - and to respond as we posted the banner inviting respondents to "help prevent HIV infection" (selection bias). Using self-reporting to estimate STI prevalence could introduce measurement error. The prevalences of self-reported STI in the past year are likely to be an underestimation in our study, as some MSM might not be aware of their (sometimes asymptomatic) current infection or refuse to be tested [15], which could decrease the associations, found in our study. Similarly, respondents with an STI, which was not selected as an outcome, could also decrease these associations. To estimate the frequency of alcohol consumption, we used a rather subjective "feeling of being drunk". We did not specifically ask whether some drugs were injected, however such HIV transmission is rare in Norway due to effective harm reduction programmes: in total, 10 men were reported being infected with HIV due to injecting drugs in Norwegian surveillance system for communicable diseases in 2007 and 7 in 2006 [4]. Since no adjustment for multiple comparisons was made, some of the significant associations might appear due to chance. Despite the large number of participants, we were not able to show statistically significant effects for rare exposures (such as not having a date with Internet partner and paying or receiving money for sex), when the effect size is small. Gonorrhoea as an outcome was rare, which limited our power to detect factors associated with infection. Nonetheless, we believe the study provides an important insight into current MSM behaviour in Norway.

Comparing the findings of our study with other studies is of limited value, as there are notable differences in recruitment sites, inclusion criteria, methodology (including definitions) and STI epidemiology among MSM.

An Internet study from USA, focusing on a six-month period in 2001, reported 0.3% being newly diagnosed with syphilis, 1.8% with gonorrhoea and 1.1% with Chlamydia; while total HIV prevalence of the participants, including non-recent infections, was 7.2% [16], similar to a Danish study from 2006 with 8% [17].

More than a half (57.6%) of our respondents reported finishing high school or university, which was high compared to corresponding Norwegian male population

(24.5% in January 2008) [12], but similar findings (55%) were reported from Danish study recruiting MSM at different venues and online [17]. Immigrants with non-western background seemed underrepresented in our sample (1.7% compared to 6.3% males in Norwegian population [18]); perhaps due to language, cultural barriers or lower proportion of self-identified MSM among them.

A case-control study of MSM from Chicago and Los Angeles found recent HIV seroconversion to be associated with low income, UAI with HIV positive partners, and using Viagra and poppers [19]. In a longitudinal American study, HIV acquisition was found to be related to ethnicity (Black race), use of alcohol or drugs before sex, receptive UAI, insertive UAI with HIV positive partners, use of alcohol or drugs before sex, reporting 4 or more male partners in the last 6 months, amphetamines and heavy alcohol use [20].

In a prospective study in Australia, urethral gonorrhoea and Chlamydia in MSM were associated with these common risk factors: younger age, contact with gonorrhoea or Chlamydia infected sexual partner and a higher number of casual partners in the past 6 months. In addition, gonorrhoea was associated with UAI with HIV positive casual partners, and urethral Chlamydia with more frequent insertive oral sex with ejaculation with casual partners. When no receptive UAI was reported, anal infections with Chlamydia and gonorrhoea were associated with a variety of non-intercourse-receptive anal practices with casual partners [21].

MSM were previously identified as a population with high prevalence of alcohol use [22]. A review article by Woolf and Maisto concluded heavy episodic drinking among MSM is related to HIV infection, while history or frequency of consumption might not be [22].

Our results suggest Norwegian MSM share some similarities in risk behaviour with MSM around the world, perhaps due to sharing popular culture and ideas on the Internet and an increase in international travel [3].

Chlamydia, syphilis and HIV infection may be present for a long time before being noticed or diagnosed, contributing to the fact that relevant exposures, leading to the infection, might have happened a long time ago and behaviour might have changed during this time or, particularly, after the diagnosis and counselling. We can see that some potential risk factors, limited to the past 6 or 12 months before the study, were not important for these infections. Number of lifetime male sexual partners seemed to be more important for HIV and Chlamydia than number of male sexual partners in the past 6 months. In addition, pharyngeal infections result from oral sex practices, potentially decreasing the importance of UAI in transmission of Chlamydia [23], gonorrhoea and syphilis.

The inverse association of Chlamydia and age was expected due to diminishing testing activity and prevalence after age 40 [7]. Chlamydia is geographically-widespread infection in Norway [24] and clustering of MSM cases in Oslo or Akershus, as previously described for gonorrhoea and syphilis [5,6] and as suggested also for HIV infection, might be less emphasized. Nonetheless, most MSM in our study do come from Oslo or Akershus and engaging in sex with multiple and casual partners is likely adjacent to the urban lifestyle.

Although reported by only 1.7% of MSM in our study, non-western background was consistently identified as a risk factor for Chlamydia and HIV. Immigrants from areas with a generalised HIV/STI epidemic could be more likely to know their status as they are offered HIV testing upon arrival to Norway; but these were not likely to answer our questionnaire as it was in Norwegian. Specific reasons for vulnerability of immigrant MSM for STI in Norway could be a subject of further research.

Alcohol might influence the STI transmission by behaviour, sexual arousal, adverse effects on the immune system or perhaps a third, confounding variable (e.g., "sensation-seeking") [25]. MSM may drink to achieve a "cognitive escape", for example to avoid "being worried about HIV/AIDS" [22,26]. Although not significant, prevalence ratio estimates were highest among "moderate drinkers" (groups feeling drunk once or up to three times in an average month) among gonorrhoea and Chlamydia cases. This might imply drinking in social situations and venues (e.g., bars), connected to sensation- and partner-seeking [22]. Our reverse association between the increasing frequency of feeling under the influence of alcohol and HIV infection is puzzling; however drugs seem to be a more important correlate than alcohol in this group. The importance of alcohol in STI transmission is on the other hand emphasized by "unsafe sex under the influence of alcohol in the past 12 months" associated with higher prevalence ratio for Chlamydia. Thus, alcohol use in sexual risk behaviour remains "a controversial topic with mixed findings" [27].

Being under the influence of selected drugs during sex was associated with reported HIV infection in the last year, but not with Chlamydia or gonorrhoea. Drugs may be used before or during sex to enhance sexual pleasure, but their use may have complex and harmful physiological or cognitive side-effects, enhancing the likelihood of frequent partner change and unprotected anal sex with HIV positive partners or partners of unknown serostatus [19]. Further research is needed on the importance of specific drugs in HIV transmission among MSM in Norway.

Conclusions

This first Internet study on sexual risk behaviour of MSM in Norway has reached a large and active online MSM community, thus the possibility of Internet based

health interventions could be further explored. Our study demonstrates different associations of demographic and behavioural factors with different STI outcomes in the study population. The number of male sexual partners and ethnic background seem to be the most important predictors for Chlamydia, gonorrhoea and HIV. Additional research is needed to analyse the association of STI with specific drug and alcohol use. To evaluate time trends and the effectiveness of preventive measures, behavioural studies among MSM in Norway should be repeated regularly.

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Authors' contributions
IJ drafted the manuscript. BS, EK and PA took part in the planning of the study. BS helped with data collection. IJ, AMG, BS, EK and PA contributed to the study design, analysis and interpretation. All authors critically reviewed and approved the final version of this paper for publication. PA is the guarantor.

Competing interests
The authors declare that they have no competing interests.

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The epidemiology of gonorrhoea in Norway, 1993–2007: past victories, future challenges

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Abstract

Background: Gonorrhoea, a bacterial infection caused by *Neisseria gonorrhoeae*, has been increasing in several European countries, particularly among men who have sex with men (MSM) and teenagers. We describe the epidemiology of gonorrhoea in Norway in the recent 15 years in order to guide recommendations on the diagnosis, treatment and prevention of gonorrhoea. An evaluation of the Norwegian Surveillance System for Communicable Diseases (MSIS) in 1994, involving GPs and microbiological laboratories, suggested that the system has a high coverage, capturing over 90% of patients diagnosed with gonorrhoea.

Methods: Using MSIS data on gonorrhoea cases we analysed specific trends by route of transmission, age, gender, anatomical sampling site, antimicrobial resistance and travel history from 1993–2007 and, to focus on more recent trends, from 2003–2007. MSM and heterosexual cases were defined by route of transmission.

Results: From 1993 to 2007, 3601 gonorrhoea cases were reported. MSM cases increased from 10 in 1994 to 109 cases in 2004. From 2003–2007, the incidence of gonorrhoea was 5.4/100,000 person-years (95%CI: 4.9–6.0). Over these five years, MSM accounted for an average of 80 cases per year, of which 69% were infected by casual partners. In the same period, 98% of heterosexually infected had a positive swab from urethra only and only two (0.3%) from the pharynx. Only one woman (0.5%) was positive from the rectum. From 1993 – 2007, antimicrobial resistance results were reported for 3325 *N. gonorrhoeae* isolates (98% of cultured samples). The proportion resistant to quinolone has risen from 3% in 1995 to 47% in 2007, with 81% of the latter isolated from patients infected in Asia.

Conclusion: The overall incidence of gonorrhoea in Norway remains low, but the increasing number of MSM cases calls for new, more effective approaches to prevention. Infections originating from abroad represent a constant risk of importing antimicrobial resistant *N. gonorrhoeae*. Due to the prevalence of quinolone resistant *N. gonorrhoeae* in Norway, third-generation cephalosporins should replace quinolones as the first choice in treatment guidelines. We advocate antimicrobial susceptibility testing for all cases and recommend taking samples for culture from all exposed anatomical sites.

Background

Gonorrhoea, a bacterial infection caused by *Neisseria gonorrhoeae*, is a highly communicable [1] sexually transmitted infection (STI) and, due to a short incubation period, may serve as an indicator of recent risky sexual behaviour in symptomatic cases [2]. Since the seventies, when gonorrhoea was at its peak, the number of cases has decreased dramatically in many European countries [3,4]. Nevertheless, this preventable and treatable infection has been reported to be on the rise in several European countries [3,5] since the late nineties, particularly among men who have sex with men (MSM) [6-10] and teenagers [3,6,8].

Patients with gonorrhoea may experience symptoms such as purulent discharge and dysuria. The majority of heterosexual men (95% and more) are symptomatic, whereas up to 60% of women may be asymptomatic carriers of the disease for as long as 12 months [1]. Pharyngeal and rectal infections, which are mostly asymptomatic [1], may be important in gonorrhoeal transmission among MSM [11]. The risk of acquiring pharyngeal gonorrhoea by oral-genital heterosexual contact has been reported to be 14% for men and 31% for women [12]. Clinical trials reported pharyngeal gonorrhoea to be self-limiting within three months [13,14]. Untreated genital gonorrhoea may lead to serious late complications such as pelvic inflammatory disease, fistula formation and urethral strictures [1]. Furthermore, gonorrhoea increases susceptibility to HIV and HIV shedding in HIV positive patients [15].

Since the mid seventies, when penicillinase producing *N. gonorrhoeae* (PPNG) was first reported [1], treating gonorrhoea has presented an ongoing challenge around the world. In a sentinel surveillance study from 2004, significant proportions of *N. gonorrhoeae* isolates from 12 Western European countries were resistant to azithromycin, ciprofloxacin, penicillin or tetracycline and as much as 22% were resistant to more than one of these antimicrobials [16].

In Norway, under the Infectious Disease Control Act, all clinicians and laboratories are legally obliged to notify gonorrhoea cases to the Norwegian Institute of Public Health (NIPH). Using data from the Norwegian Surveillance System for Communicable Diseases (MSIS), we describe the epidemiology of gonorrhoea in Norway in the last 15 years (including specific trends by route of transmission, age, gender, antimicrobial resistance, place of infection and anatomical sampling sites) in order to develop targeted recommendations for the diagnosis, prevention and treatment of gonorrhoea [17].

Methods

Cases fulfilling any of the following criteria should be reported to MSIS: 1. the patient has clinical symptoms compatible with gonorrhoea and is epidemiologically linked to another case; 2. *N. gonorrhoeae* was proven in the patient's sample by culture, antigen testing or nucleic acid amplification technique (NAAT) or 3. direct Gram-stained smear for microscopy shows intracellular diplococci. The case definition did not change during the study period. All clinicians and all of the approximately 20 clinical microbiology laboratories in Norway report to the system [18]. The Norwegian population during the study period was approximately 4.5 million.

Upon confirmation of a case of gonorrhoea, the laboratory sends a notification to the NIPH and a blank reporting form to the patient's clinician. The clinician fills the form with additional clinical and epidemiological data about the patient and sends it to the NIPH. All reports are anonymous and linked with a unique non-identifying number. NIPH uses laboratory reports to identify and remind clinicians if they fail to report on a case. The system achieves coverage of about 90% [18,19] and the data is of high quality; missing variables are rare. Most of the cases are initially reported by the laboratories; however, a minority of cases is reported directly from two venereal disease clinics and clinicians if direct microscopy of Gram-stained smear is used for establishing the diagnosis.

Among the key data collected by the surveillance system are: sex of the patient, date of sampling, month and year of birth, country of residence, country of birth, country of infection, reporting laboratory, type of diagnostic test used, anatomical sampling site, susceptibility of *N. gonorrhoeae* to antimicrobials, reasons for testing, transmission route and relation to the source person.

For the purpose of this study, we defined MSM cases as men who acquired gonorrhoea infection from another man (homosexual transmission). Similarly, we defined heterosexual cases as persons who acquired gonorrhoea infection from a partner of the opposite sex.

Reporting of PPNG was introduced in MSIS in 1993, while reporting of quinolone resistance started in 1995. No other resistance is currently reported in MSIS. Laboratories test all strains for penicillinase (betalactamase) production and for susceptibility to the most relevant antimicrobials, but the methods may vary by laboratory.

We analysed the data on all cases reported to MSIS from 1993 to 2007 by using Microsoft Excel and Stata 9.0. To describe more recent trends, we analysed data over a five year period from 2003 to 2007. We described cases according to demographic characteristics and various risk factors, including self-reported travel history and transmission route. The annual incidence with a 95% confidence interval (CI) was calculated using yearly population estimates by Statistics Norway http://www.ssb.no. We used Prais-Winsten autoregression to evaluate linear

trends in all studied data over time, taking into account autocorrelation.

Results

From 1993 to 2007 NIPH received 3601 reports of gonorrhoea cases diagnosed in Norway (Figure 1). The number of diagnoses decreased from a high in 1993 of 346 cases (8.0 per 100,000 population) to a low in 1998 of 166 cases (3.8 per 100,000 population). Cases peaked again in 2001 with 327 reports, of which 290 (89%) were diagnosed by culture and 35 (11%) by the newly available NAAT. The mean incidence in the recent five-year period (2003–2007) was 5.4 per 100,000 person-years (95% CI: 4.9–6.0). The sexual transmission route was reported for 3578 (99.4%) cases from 2003 to 2007 (Table 1).

Demographic data and groups by transmission route

In the years 2003 to 2007, among teenagers (10 to19 years) females represented the majority of heterosexually transmitted cases (Table 1). Between 1993 and 2007, the number of cases among all teenage cases did not increase

significantly (p = 0.100); however we did observe a concurrent increase among those aged 45 years and older in all transmission groups (p = 0.001), from 13 cases in 1993 to 48 cases in 2007. The median age among heterosexually infected men and women has increased since the early nineties (p < 0.001 for both), while the median age of MSM has remained relatively stable at around 29 years (p = 0.043) (Figure 2).

The majority of cases occurred in those born in Norway, although cases among migrants and visitors from other European countries and Asia are represented, especially among heterosexuals (Table 1).

In the period from 1993 to 2007, 842 MSM were diagnosed with gonorrhoea; from a low of 10 (4% of all cases) in 1994 to a high of 109 cases (41% of all cases) in 2004 (Figure 1). We observed a linear increase in the number of cases (p < 0.001) in this group during the study period, with an average of 80 cases per year since 2003. The majority resided in Oslo city and acquired their infection
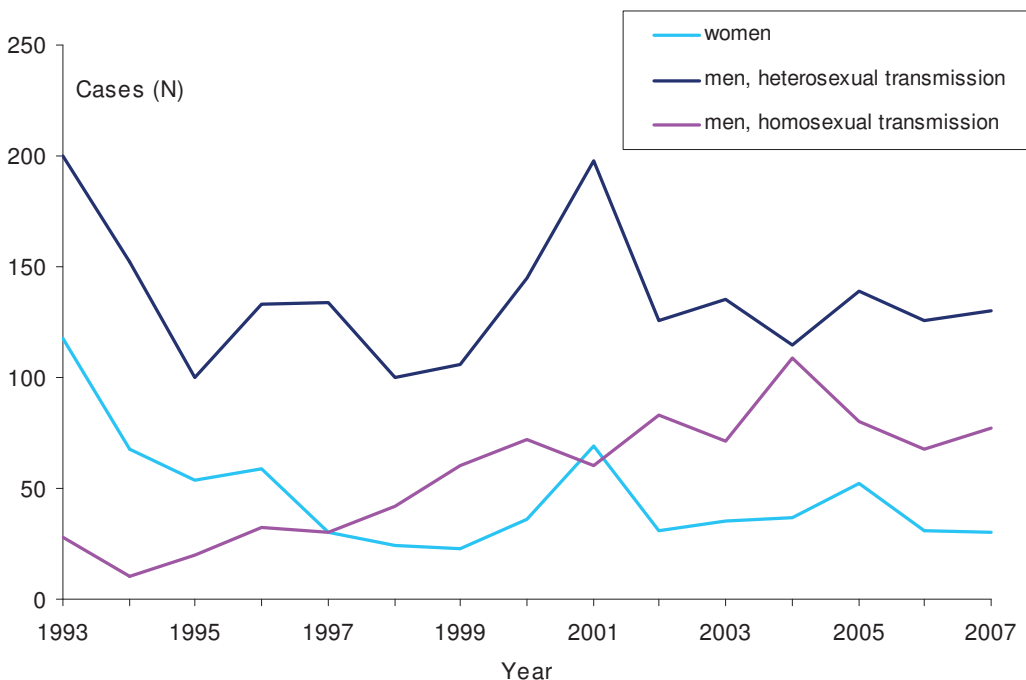
Figure 1
Number of gonorrhoea cases by major transmission routes in Norway (N = 3578), 1993–2007.

Table 1: Selected characteristics of sexually infected gonorrhoea cases reported to the Norwegian surveillance system for communicable diseases (N = 1257), 2003–2007.

Characteristic	Selected categories	Sexual transmission route			
		Heterosexual		Homosexual	Unspecified
		Women n = 185 (%)	Men n = 645 (%)	Men n = 405 (%)	Men n = 22
Age	Median age in years	27	34	31	41
	10–19 years	32 (17)	25 (4)	20 (5)	0
	20–24 years	42 (23)	80 (12)	64 (16)	1
	25–34 years	59 (32)	216 (33)	160 (39)	5
	35–44 years	33 (18)	188 (29)	110 (27)	7
	≥ 45 years	19 (10)	136 (21)	51 (13)	9
Residence	Oslo city	64 (35)	229 (35)	310 (76)	13
	Other	121 (65)	416 (65)	95 (23)	9
Origin by birthplace	Norwegian	131 (71)	505 (78)	350 (86)	21
	European, other	16 (9)	51 (8)	32 (8)	0
	Asian	23 (12)	60 (9)	8 (2)	0
	African	6 (3)	22 (3)	5 (1)	1
	Other	9 (5)	7	10 (2)	0
Reason for visiting Norway	Temporary visit to Norway	15 (8)	19 (3)	13 (3)	0
	First generation immigrant	16 (9)	65 (10)	22 (5)	1
	Other, including permanent residents	154 (84)	561 (87)	370 (91)	21
Place of infection	Infected abroad	55 (30)	364 (56)	62 (15)	2
	- In Thailand	14 (8)	155 (24)	3 (7)	0
	Infected in Norway	124 (67)	274 (43)	341 (84)	15
	- In Oslo	47 (2)	145 (22)	294 (73)	13
	Unknown	6 (3)	7 (1)	2 (0.5)	5
Source partner	Steady partner	74 (40)	90 (14)	81 (20)	3
	Casual partner	84 (45)	388 (60)	280 (69)	4
	Prostitute	0	109 (17)	1 (0.2)	0
	Other	8 (4)	14 (2)	19 (5)	0

Table 1: Selected characteristics of sexually infected gonorrhoea cases reported to the Norwegian surveillance system for communicable diseases (N = 1257), 2003–2007. *(Continued)*

	Unknown	18 (10)	44 (7)	24 (6)	15
Indications for testing	Symptoms	114 (62)	631 (98)	331 (82)	20
	Contact tracing	34 (18)	10 (1)	26 (6)	0
	Own request	14 (8)	2 (0.3)	13 (3)	0
	Blood donor	1 (0.5)	1 (0.2)	0	0
	Pregnancy	1 (0.5)	/	/	/
	No specific reason	21 (11)	1 (0.2)	35 (8)	2
Diagnosed by	General practitioner, private specialist	90 (49)	384 (59)	119 (29)	21
	STI clinic	51 (28)	215 (33)	267 (66)	0
	Hospital	24 (13)	13 (2)	5 (1)	0
	Youth clinic	12 (6)	15 (2)	6 (1)	0
	Other	8 (4)	18 (3)	8 (2)	1

there (Table 1). In these five years, the proportion infected by casual partners varied from 60 to 80%.

Since 1996, the ratio of heterosexual men to women, infected with gonorrhoea in Norway, remained above 2 (Figure 3). Since 1993, symptoms were a reason for testing in 61% of infected women compared to 93% in men. The median duration of symptoms before sampling was four days for men and eight days for women. Between 2003 and 2007, 40% of the women got infected by steady partners compared to 14% of heterosexual men (Table 1).

Anatomical locations of positive samples
From 1993 to 2007, 2677 (75%) of all cases were positive from a urethral swab. Of 91 patients diagnosed from a pharyngeal swab, 70 (77%) were MSM, 13 were women and eight were heterosexually infected men. Of 190 cases diagnosed from a rectal swab, 171 (90%) were MSM and 19 were female; among the females four had samples positive both from rectal and endocervical swabs. The number of positive rectal swabs in women has declined to one or less per year since 2001. From 2003–2007, no heterosexually infected man had gonorrhoea confirmed from more than one anatomical site (Table 2).

Antimicrobial resistance
From 1993 to 2007, 3399 cases (94%) were diagnosed by culture. In 2001, culturing was used in 89% of the cases, the lowest proportion in the entire period. Antimicrobial resistance was reported for 3325 (98%) of all cultured *N.*

gonorrhoeae isolates. From 2003 to 2007, there has been a marked increase in the number of isolates reported to be quinolone resistant only, or both PPNG and quinolone resistant (Figure 4). Quinolone resistance is mainly found in isolates from patients infected in Asia. Among these patients, the proportion of quinolone resistance rose from 8% in 1998 to 81% in 2007.

Imported gonorrhoea
In the early nineties, 70% of the cases reported acquiring their infection in Norway. This proportion decreased to around 60% in 2005 and 2006. Patients that reported unsafe sex during a recent travel to a foreign country prior to diagnosis, i.e. "imported gonorrhoea", were predominantly heterosexual men (80%). In 1993, 26% of the heterosexual infections among men were acquired outside Norway, compared to 62% in 2007. From 2003 to 2007, between 30 and 45 cases have been imported from Thailand to Norway every year. In 2003, 29% of all heterosexual male cases had been infected in Thailand. Other cases originated from around the world, with up to eight cases per year per country acquired in Pakistan, the Philippines, Brazil, Spain and Indonesia. Among those infected abroad, travellers aged 45 years and older represented 21% and those in the age group 35–44 years represented 30% in the period from 2003 to 2007.

Discussion
The incidence of gonorrhoea in Norway from 2003 to 2007 (5.4 per 100,000 person-years) is similar to Sweden,
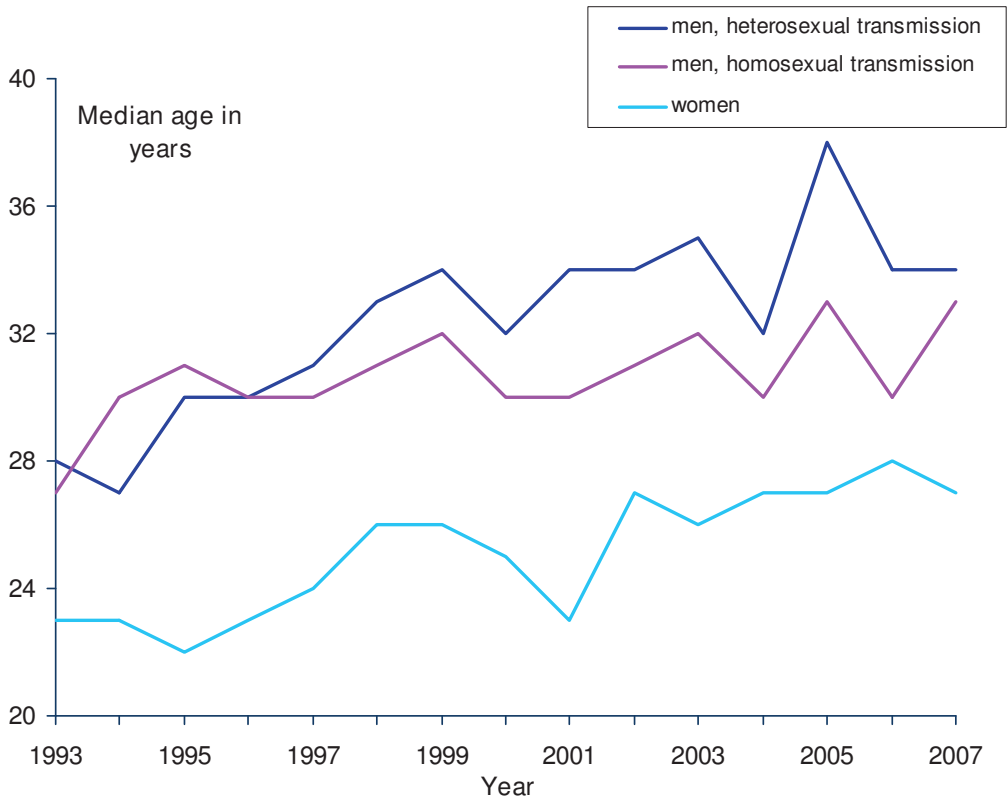
Figure 2
Median age of patients with gonorrhoea in Norway by major transmission routes (N = 3578), 1993–2007.

Finland and Denmark and much lower than in the UK [20], making gonorrhoea a rare disease in Norway. However, several important challenges remain to be faced.

The majority of gonorrhoea cases are among heterosexual men, but because we lack a population denominator to calculate the incidence among MSM, it is not possible to conduct a proper comparison among the transmission groups. Nevertheless, we can conclude that MSM are currently the most vulnerable population to gonorrhoea infection in Norway and that preventive measures against STIs [21] among MSM are failing in Norway, similar to observations in other countries [8-10,22,23]. The rising trend of gonorrhoea among MSM is of particular concern as the proportion of cases infected through a casual part-ner is high, indicating increased risk for other STIs, including HIV. The majority of MSM get infected with gonorrhoea in the capital Oslo; therefore, preventive measures should be particularly focused on this area.

Among heterosexual cases, the median age is increasing. This may be due to the increasing age of the same risk group over time or the fading effect of preventive programmes primarily targeted at the young. Middle-aged men may be more able and willing to afford sex tourism in the areas of the world where gonorrhoea is still prevalent (see below). Based on similar observations of an increasing trend in reported gonorrhoea infections among people 45 years old and older, the need for interventions, aimed specifically at this group, has also been emphasised in the UK [24].
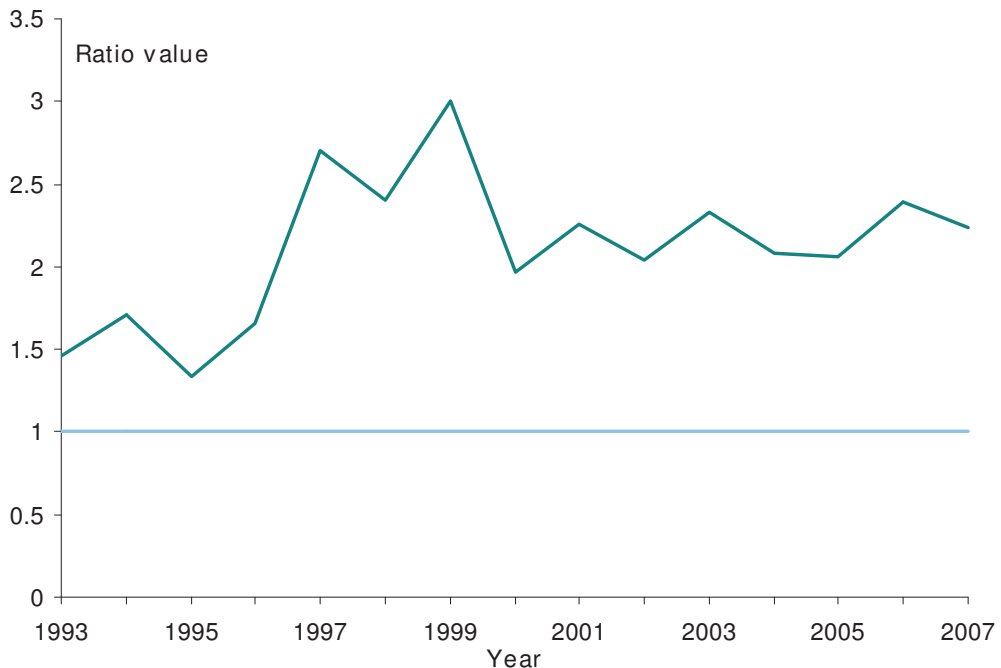
Figure 3
Ratio of heterosexual men to heterosexual women, infected with gonorrhoea; domestic cases only (N = 1637), Norway, 1993–2007.

Among 21 European countries with diverse surveillance systems, Norway had the eighth highest men to women ratio of gonorrhoea cases in 2006 [20]. Among heterosexually acquired domestic cases, the number of males diagnosed is 2 to 3 times greater than females, similar to reports from other countries [6,9]. Reasons for this gender disparity may include: behaviour differences (promiscuity, visiting prostitutes, partner notification etc.), biological differences in developing symptoms, duration of infection and a pool of undiagnosed cases among asymptomatic women. Since women are more susceptible to infection [1] and frequently experience an asymptomatic course of infection, the persistence of endemic gonorrhoea in Norway might be fostered by undiagnosed women. The gender ratio implies that a more thorough approach to contact tracing is warranted; however this is limited by the frequency of infections in heterosexual men associated with casual partners or prostitutes (Table 1), making partner notification difficult. Since symptoms were stated as a reason for testing in only 60% of women,

we can conclude that asymptomatic cases are being diagnosed with gonorrhoea as well.

While gonorrhoea has become rare in Norway, it should still be considered as a diagnostic option. When making decisions for testing, clinicians should be aware that many women in Norway, similar to reports from other countries [9,25], acquire their infection from a steady partner, having no obvious risk-factors for gonorrhoea in their medical history. Furthermore, belated diagnosis might lead to severe health complications as we experienced in a recent gonorrhoea outbreak in Norway in 2008 [26].

The number of samples tested with a negative result in Norway is unknown. There is little evidence whether sampling from several anatomic sites increases the diagnostic sensitivity [27], but studies among MSM show that sampling from the urethra only may lead to a significant proportion (up to 40%) of missed cases [22,28,29]. Regardless of the exposure, rectal co-infection with cervical

Table 2: Anatomical sites of *N. gonorrhoeae* isolates, reported to the Norwegian surveillance system for communicable diseases (N = 1257), 2003–2007.

| *N. gonorrhoea* isolated from*:	Sexual transmission route			
	Heterosexual		Homosexual	Unspecified
	Women n = 185 (%)	Men n = 645 (%)	Men n = 405 (%)	Men n = 22
Urethra	8 (4)	631 (98)	276 (68)	22
Cervix	143 (79)	/	/	0
Rectum	0	0	68 (17)	0
Pharynx	7 (4)	2 (0.3)	20 (5)	0
Urethra, rectum and pharynx	1 (0.5)	0	4 (1)	0
Urethra and pharynx	0	0	7 (2)	0
Rectum and pharynx	0	0	8 (2)	0
Rectum and urethra	0	0	15 (4)	0
Cervix and pharynx	1 (0.5)	/	/	0
Cervix and urethra	19 (10)	/	/	0
Other, unspecified	3 (2)	4 (0.6)	1 (0.2)	0
Unknown	3 (2)	8 (1)	6 (1)	0

* the categories are mutually exclusive

gonorrhoea has been reported in up to 30% of infected women [1], therefore the low number of women who recently tested positive from the rectum (Table 2) may suggest that rectal samples from women are rarely taken. In a study in France, a prevalence of 6% of pharyngeal gonorrhoea among heterosexual men with urethral gonorrhoea has been reported from 1999 to 2001 [23]. To tackle the possible undiagnosed reservoir of infection, it is important that sampling is carried out according to the exposures rather than the presence of symptoms; although some patients might be reluctant to provide the details of their exposure (see "Unspecified" group, Table 2).

Antimicrobial resistant *N. gonorrhoeae* is an increasing problem in Norway, exacerbated by a large proportion of imported infections from Asia. Following their importation into Norway and subsequent onward spread within the population, infections originating abroad are not easily identifiable [26]. Recently reported travel is not a reliable tool to guide treatment choices. More than 40% of infections in 2006 and 2007 were quionolone resistant, regardless of whether they were acquired domestically or abroad (Figure 4), which implies that third generation cephalosporins should replace quinolones as the first choice empirical treatment for gonorrhoeal infections in the Norwegian treatment recommendations [30]; similar to recent recommendations in other countries [31,32]. As resistance to third generation cephalosporins is already emerging [16], improved surveillance of *N. gonorrhoeae* resistance, involving reporting resistance to any relevant antimicrobial, using nationally standardized methods, is necessary for the timely review and revision of national treatment guidelines. This may help to ensure that the most clinically effective empirical treatments, ideally achieving a cure rate of over 95% [33], will be used in the future. This is feasible in Norway due to the prevalent practice of diagnosing gonorrhoea with culture and a high coverage of reporting to MSIS.

Although travellers who got infected with gonorrhoea represent a diverse group, some studies identified demographic factors such as male sex, single status and age of <20 years [34] as associated with a higher frequency of casual sexual intercourse abroad, while others identified
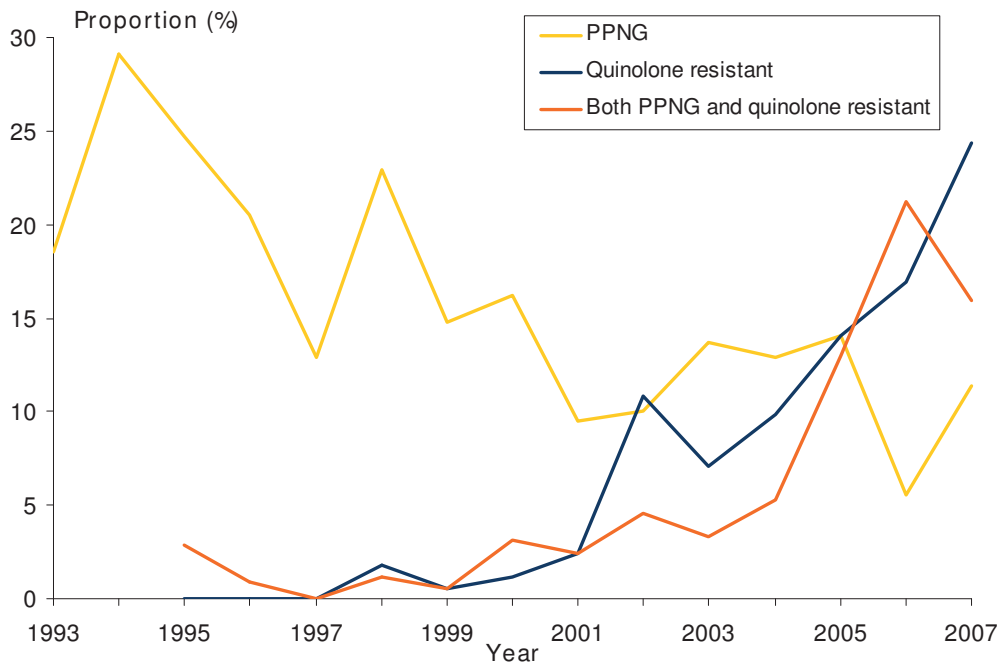
Figure 4
Proportion of PPNG and quinolone resistance of 3399 cultured isolates of *N. gonorrhoeae* Norway, 1993–2007.
PPNG surveillance started in 1993 and quinolone surveillance in 1995.

middle-aged and married travellers [35] as high-risk groups. It is therefore interesting to note that male travellers, older than 45 years, represent a significant proportion among our cases and that as much as half of the infected travellers are older than 34 years.

Among all the infections acquired outside of Norway, Thailand, a known sex tourism destination [34] remains the most prominent country associated with the acquisition of gonorrhoea since the nineties [36], especially among heterosexual men. A similar situation has been described in Denmark and Sweden [6,9]. Due to the high prevalence of HIV infection in Thailand, the rise of imported gonorrhoea is a stark reminder of the high-risk sexual behaviour of some Norwegian travellers. Asymptomatic travellers who had casual sex abroad rarely present at the doctor's office, therefore screening for STIs might not be possible [34].

We identified some potential limitations and weaknesses of our study. The evaluation of the STIs reporting coverage

to MSIS was done more than a decade ago. All behavioural data in the system are self-reported. As the spectrum of collected variables in Norway is rather broad, some missing data were noted. We defined MSM and heterosexual cases according to the reported route of transmission. This definition provides no insight into the actual sexual orientation, behaviour or sexual practices of the patients and is only related to a single exposure, at which patients got infected. Culturing of *N. gonorrhoeae*, a method most frequently used for laboratory confirmation of gonorrhoea in Norway, has specificity of 99% and sensitivity of 60 to 70% [37], which might be further affected by transport conditions. Therefore, a negative laboratory sample does not exclude gonorrhoea. Patients with negative tests should still be reported, providing they experience clinical symptoms compatible with gonorrhoea and are epidemiologically linked to another case. In this scenario, reporting should arise from the clinicians' initiative; however no such cases were reported during the entire period from 1993 to 2007. This could indicate that a small proportion of gonorrhoea infections in Norway remain unreported.

Although clinicians are strongly encouraged to obtain a sample for culturing, some may skip reporting of cases diagnosed with direct microscopy. Nevertheless, we consider MSIS a representative and reliable source of data on gonorrhoea cases in Norway.

The observed peak incidence in heterosexual cases in 2001 was partially influenced by the decision of one laboratory to screen samples collected for Chlamydia testing, with NAAT for both Chlamydia and gonorrhoea. In 2001, this laboratory reported 46 cases in total – much higher than in the previous (4 cases) and the following year (17 cases). Using NAAT for screening in low prevalence populations has been associated with lower positive predictive value [38] and some of the reported cases might have been false positive. This laboratory continued to use NAAT in the following years and reported it as the diagnostic method in 75% of cases. Nevertheless, the peak in 2001 remains prominent even after excluding the cases diagnosed with NAAT, and is largely due to heterosexual cases infected in Norway. No increase in HIV and syphilis was observed in this group at the same time or a year later [17].

Conclusion

The overall incidence of gonorrhoea in Norway is low. Heterosexual transmission is fairly stable, while there is a worrisome increase among MSM. Since most of the MSM report getting infected in Norway (Oslo), prevention efforts at local MSM venues should continue. Further research is necessary to identify more effective prevention measures and reasons for the resurgence of STIs among MSM Europe-wide. Gonorrhoea is frequently brought to Norway from abroad with a higher risk of imported cases being resistant to antimicrobials. As the link to the foreign country might be lost soon after the introduction to Norway, the widespread practice of culturing which enables antimicrobial susceptibility testing should be further encouraged. There is a need for standardisation of national laboratory methods for susceptibility testing and for improving the surveillance of antimicrobial resistance to enable rapid revision of treatment guidelines when necessary. We recommend taking samples for culture of *N. gonorrhoeae* from all exposed anatomical sites.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

IJ performed the data analysis and drafted the manuscript, KB assisted in the interpretation of data and drafting of the manuscript, PA participated in data analysis and drafting of the manuscript. All authors read and approved the final manuscript.

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Syphilis epidemiology in Norway, 1992-2008: resurgence among men who have sex with men

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Abstract

Background: In recent years, the number of syphilis cases has stabilised in many countries of Western Europe, however several countries have reported increases among men who have sex with men (MSM). The aim of this article was to describe the epidemiology of early syphilis in Norway in 1992-2008.

Methods: Cases of early syphilis and congenital syphilis reported to the Norwegian Surveillance System for Communicable Diseases (MSIS) 1992-2008 were described by route of transmission, gender, age, birthplace, stage of disease, HIV co-infection, source partner and place of infection.

Results: The incidence of reported syphilis ranged from 0.05 (1992) to 1.50 (2002) per 100 000 person-years. Of 562 cases reported to MSIS during the study period, 62% were men infected by another man. The proportion of those, infected homosexually increased from 0 (1992-1994) to 77% (2008). Most of them were Norwegians (83%). The proportion of HIV co-infection among homosexually infected increased over time and reached 39% in 2008. The majority reported being infected by a casual partner (73%) and in the municipality of Oslo (72%). Of 152 heterosexually infected men 64% were Norwegians; 51% were infected by casual contacts and 20% by commercial sex workers; 73% were infected abroad. Among 56 women, 57% were Norwegians, 57% were infected by a steady partner and 40% were infected abroad. Almost half (46%) were diagnosed in the early latent stage. Four cases had congenital syphilis, two of whom were adopted from abroad.

Conclusions: Syphilis is rare in Norway, but MSM represent almost two thirds of cases. The increase of HIV co-infected cases among MSM may enhance transmission of both infections. We recommend sexually active MSM to be tested for syphilis 2-4 times a year. Due to its variable clinical course, syphilis might be difficult to recognise at an early stage among women in a low-prevalence population. We estimate current practice of prenatal screening in Norway as sufficient.

Background

Following increases in the early 2000s in Western European countries, the number of reported syphilis cases has recently stabilised; however many countries reported a high proportion of homosexually acquired syphilis (France, Denmark, Ireland, Germany, UK, Sweden, Netherlands) [1]. Increases among men who have sex with men (MSM) have been reported worldwide [2] and a significant proportion of them have been found to be co-infected with HIV [3,4].

Infectious stages of syphilis are primary, denoted by a painless ulcer in about one third of patients, and second-

ary, with diverse symptoms. Patients in the latent stage are seemingly unaffected, but about 25% may experience relapses to secondary syphilis during the early latent stage (i.e. less than a year since infection) [4,5]. Vertical transmission may result in congenital syphilis, difficult to recognise in seemingly asymptomatic newborns [6]. Untreated, syphilis may result in death and serious disability [4,5], however effective penicillin-based treatment is inexpensive. Testing and treatment are free of charge in Norway.

Serological tests for syphilis lack sensitivity and though some may be helpful in assessing the stage of infection, they are unreliable [7]. In determining the stage, particularly in asymptomatic patients, clinicians thus rely on previously documented syphilis tests, anamnesis (i.e. most likely time of exposure, data from contact tracing,

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known previous treatment) and clinical evaluation. Uncertain stage in asymptomatic patients with unknown duration of infection is an important limitation of early syphilis (i.e. primary, secondary and early latent syphilis) surveillance.

Using data from the Norwegian Surveillance System for Communicable Diseases (MSIS), we describe the epidemiology of early syphilis in Norway from 1992-2008.

Methods

Under the Infectious Disease Control Act, syphilis is a mandatory notifiable disease, therefore all clinicians and laboratories in Norway must notify all cases of newly diagnosed syphilis anonymously to the MSIS, based at the Norwegian Institute of Public Health (NIPH). Contact tracing and notification, mandatory by the same act, is the responsibility of the clinicians. Previously mandatory screening of pregnant women in Norway became optional in 1995; however, virtually all pregnant women are still tested. If a patient has a positive syphilis test, screening for other sexually transmitted infections (STIs) is recommended.

Upon a positive syphilis test, all 22 local laboratories in Norway send their notification to both NIPH and the clinician involved. Both of these notification forms carry the same unique non-identifying number for an individual patient. Having received notification from the laboratory, clinicians fill out the corresponding clinical report on the stage of the disease, patient's demographic data, symptoms, co-existing STIs, risk behaviour (including most likely transmission route and time of exposure) and their source partner, and send it to the NIPH. There, only one co-existing STI can be entered into the MSIS database. If the patient is reported to have an HIV infection, HIV is always entered.

At NIPH, only newly recognised cases with early syphilis, defined as laboratory confirmed, primary, secondary or early latent syphilis (less than a year since infection) are entered into the MSIS database. The reports on a single patient from laboratories and clinicians are merged using the unique non-identifying number. Every reported case is individually evaluated at NIPH and clinicians can be contacted if the stage of syphilis is unclear or if they failed to report on a case, notified by laboratory only.

We used the following key variables from the reports: route of transmission, gender, month and year of birth, birthplace (country and continent), place of residence, reason for being in Norway, indications for testing, duration of symptoms, stage of disease, co-existent STI, relation to the source person, place of infection and the type of clinical practice where the diagnose was made. We also studied differences between HIV co-infected and HIV negative men, infected with syphilis homosexually. The data were analysed in categories as presented in Table 1.

The data on all cases of early or congenital syphilis were obtained from MSIS. The size of population used for calculating incidence rate for each year was obtained from Statistics Norway [8] and was about 4.5 million. We used Stata 9.2 software (STATA Corp., TX, USA) for the analysis. Simple linear regression analysis was used to estimate trends over time. Given that the data between subsequent years may be correlated and the variability between the years may not be constant over time, the regression coefficients and their 95% confidence intervals (CI) were calculated using the Newey-West procedure. Bivariate comparisons between groups were performed using Pearson's chi squared test. Due to different mode of transmission, cases of congenital syphilis were described separately.

Results

From 1992 to 2008, 562 cases of syphilis diagnosed in Norway were reported to MSIS, including four congenital cases.

The incidence rate in the study period was 0.7 per 100 000 person-years (95% CI: 0.06-1.0); varying from 0.05 per 100 000 person-years in 1992 to 1.2 per 100 000 person-years in 2008. A peak was observed in 2002 with a rate of 1.5 per 100 000 person-years (Figure 1). On average, there was an increase of 3.8 cases each year (95% CI: 2.8-4.8, p for trend < 0.001). No sexually infected case was younger than 15 years. Of the 502 (89%) men who were infected sexually, 350 (70%) were MSM.

Men, infected homosexually

One man, infected homosexually in 1995, and 2 in 1998 were followed by a marked increase of 40 cases in 1999, representing 75% of all reported cases (Figure 1). More than a half (61%) of the total 350 cases were older than 34 years. The majority (76%) resided in Oslo and 83% were born in Norway. Before testing, 71% had symptoms. The largest proportion of cases was diagnosed in a secondary stage (43%). Almost one quarter of these men were also HIV positive (Table 1). The proportion of those co-infected with HIV increased over time (p for trend < 0.001) and reached 39% in 2008 (Figure 2). This increasing trend remained significant even if calculated from 1999, when HIV co-infected were first reported (p for trend = 0.009). Most homosexually infected men were infected by a casual partner (73%) and in Oslo municipality (72%), (Table 1). Among 69 infected abroad, 18 (5% of all cases) were infected in Spain.

Men, homosexually infected with syphilis, who were also HIV positive, were more likely to be residents of Oslo (p = 0.001), being diagnosed with syphilis later in the course of disease (primary vs. secondary or early latent, p = 0.006) and in a hospital (p < 0.001) than HIV negative,

Table 1: Selected characteristics of sexually infected cases with early syphilis reported to the Norwegian surveillance system for communicable diseases, absolute numbers, (N = 558), 1992-2008.

Characteristic	Selected categories	Sex			P1*	P2*
		Women n = 56 (%)	Men			
			Heterosexual transmission n = 152 (%)	Homosexual transmission n = 350 (%)		
Age	Median age in years	26	37	37	/	/
	15-24 years	22 (39.3)	8 (5.3)	33 (9.4)	0.222	< 0.001
	25-34 years	16 (28.6)	56 (36.8)	103 (29.4)		
	35-44 years	13 (23.2)	47 (30.9)	119 (34.0)		
	≥ 45 years	5 (8.9)	41 (27.0)	95 (27.1)		
Residence	Oslo municipality	16 (28.6)	55 (36.2)	266 (76.0)	< 0.001	0.304
	Other	40 (71.4)	97 (63.8)	84 (24.0)		
Birthplace	Norway	32 (57.1)	97 (63.8)	290 (82.8)	< 0.001	0.773
	Europe, other	8 (14.3)	20 (12.7)	28 (8.0)		
	Asia	11 (19.6)	24 (15.8)	12 (3.4)		
	Africa	3 (5.3)	9 (5.9)	6 (1.7)		
	Other	2 (3.6)	2 (1.3)	14 (4.0)		
Reason for being in Norway	Temporary visit	0	2 (1.3)	9 (2.6)	0.546	0.644
	First generation immigrant/adopted	5 (8.9)	16 (10.5)	30 (8.6)		
	Other, including permanent residents	51 (91.1)	134 (88.1)	311 (88.9)		
Indications for testing	Symptoms	15 (26.8)	121 (79.6)	248 (70.8)	< 0.001	< 0.001**
	Contact tracing	17 (30.3)	12 (7.9)	29 (8.3)		
	Own request	1 (1.8)	5 (3.3)	25 (7.1)		

Table 1: Selected characteristics of sexually infected cases with early syphilis reported to the Norwegian surveillance system for communicable diseases, absolute numbers, (N = 558), 1992-2008. (Continued)

		Routine testing of an immigrant	6 (10.7)	6 (3.9)	0		
		Pregnancy	13 (23.2)	/	/		
		No specific reason/ other	4 (7.1)	8 (5.3)	48 (13.7)		
Median duration of symptoms in days*** (interquartile range)			23 (19-47)	22 (10-56)	22 (9-44)	/	/
Stage of early syphilis		Primary	18 (32.1)	84 (55.3)	125 (35.7)	< 0.001	< 0.001
		Secondary	12 (21.4)	43 (28.3)	149 (42.6)		
		Early latent	26 (46.4)	25 (16.4)	76 (21.7)		
Other reported STI****		none	52 (92.8)	140 (92.1)	239 (68.3)	< 0.001	0.959
		HIV	1 (1.8)	2 (1.3)	85 (24.3)		
		Chlamydia	1 (1.8)	4 (2.6)	16 (4.6)		
		gonorrhoea	0	0	3 (0.9)		
		herpes	0	2 (1.3)	3 (0.9)		
		hepatitis B	1 (1.8)	2 (1.3)	3 (0.9)		
		other	1 (1.8)	2 (1.3)	1 (0.3)		
Source partner		Steady partner	32 (57.1)	20 (13.1)	56 (16.0)	< 0.001	< 0.001
		Casual partner	11 (19.6)	78 (51.3)	254 (72.6)		
		Commercial sex worker	0	31 (20.4)	0		
		Other/Unknown	13 (23.2)	23 (15.1)	40 (11.4)		
Place of infection	Abroad	Total abroad	23 (41.1)	111 (73.0)	69 (19.7)		
		Europe, other	8 (14.3)	43 (28.3)	57 (16.3)	< 0.001*****	0.001*****
		- In Russia	3 (5.4)	20 (13.1)	1 (0.3)		

Table 1: Selected characteristics of sexually infected cases with early syphilis reported to the Norwegian surveillance system for communicable diseases, absolute numbers, (N = 558), 1992-2008. (Continued)

		Asia	9 (16.1)	34 (22.4)	4 (1.1)		
		Africa	3 (5.4)	11 (7.2)	2 (0.6)		
		South/Mid America	2 (3.6)	18 (11.8)	4 (1.1)		
		Other	1 (1.8)	5 (3.3)	2 (0.6)		
	Norway	Total Norway	31 (55.4)	33 (21.7)	270 (77.1)		
		- In Oslo	7 (12.5)	17 (11.2)	244 (69.7)		
	Unknown		2 (3.6)	8 (5.3)	11 (3.1)		
Diagnosed by		General practitioner, private specialist	32 (57.1)	71 (46.7)	85 (24.3)	< 0.001	0.440
		Hospital	7 (12.5)	18 (11.8)	55 (15.7)		
		Youth/STI clinic	15 (26.8)	59 (38.8)	210 (60.0)		
		Other	2 (3.6)	4 (2.6)	0		

*P-values for heterogeneity, using Pearson's chi squared test; P1 comparing homosexually and heterosexually infected men, P2 comparing women and heterosexually infected men
**Women diagnosed during pregnancy were excluded for comparison
*** Data available for 19 women, 109 men, infected heterosexually, and 199 men, infected homosexually
**** Only one co-infection can be recorded into the system: if reported, HIV is always recorded
***** Seven categories were compared, including: Norway, Europe-other, Asia, Africa, South/Mid America, other (abroad), and unknown

but they did not differ by age, birthplace, indications for syphilis testing, source partner and place of infection.

Men, infected heterosexually
During the study period, 152 men were infected heterosexually. No obvious time trend was observed (p for trend = 0.158). More than half (57%) were older than 34 years. Most (64%) were Norwegian, with a notable proportion reporting a birthplace in Asia (16%). The majority (80%) reported symptoms and their infection was mostly discovered in the primary stage. Two men were HIV positive. Casual contacts and commercial sex workers (CSW) were the source of infection in 71%. Most acquired their infection abroad (73%) (Table 1); predominantly in Russia (13%), Pakistan (10%), Brazil (7%) and Thailand (6%). Most Norwegians were infected abroad, mainly in other countries of Europe (36%), Asia (18%) and South and Mid America (16%). Immigrants were mainly infected during travels back to their continent of birth.

Women
Among 56 women reported to be infected with syphilis from 1992-2008, 68% were younger than 35 years. Most of the cases were Norwegian (57%) and 55% acquired their infection in Norway. However, out of 31 infected in Norway, 14 reported their male partner had been infected abroad. Contact tracing was the predominant cause for testing in women (30%), followed by symptoms (27%) and pregnancy (23%). Almost half (46%) of all cases were discovered in the early latent stage of disease. STI co-infections were rare (Table 1). Women reported a steady partner as the source of infection in 57%.

Children with congenital syphilis
The age of the four patients with congenital syphilis at the time of diagnosis ranged from one to five years, one of them was a boy. Two of these children were adopted from abroad. The biological mother of one child was born in Norway, but acquired her infection abroad, while the mother of the other child was infected in Norway and

tested positive with her second pregnancy in 2003, when the affected child was five years old.

Discussion

Syphilis is a rare disease in Norway. However, since 1999, there has been a resurgence among MSM, disproportionately affecting HIV positive men. The epidemic among MSM is mainly concentrated in the capital Oslo. Up to 73% of heterosexual men and 41% of women reported being infected abroad. Compared to men, women seem to be more frequently diagnosed as late as the early latent stage and are diagnosed predominantly by contact tracing. Men infected heterosexually reported being infected by casual partner or a CSW in 71% of cases, as opposed to women, who appear to be mostly infected by their steady partners.

One of the strengths of our study is a probable high coverage of diagnosed patients in MSIS [9,10] due to double notifications from both laboratories and clinicians and a long tradition of reporting among the latter. A large set of variables on each patient is available; allowing for demographic and behavioural insight.

Our study is subject to several limitations. Due to the clinical course of this disease, some infected may stay undiagnosed. Others, discovered by routine testing and possibly asymptomatic, need to be evaluated by a clinician for stage. We cannot completely exclude, however, that some patients, reported as "early latent syphilis" may have been infected longer than a year. This would particularly affect data on women in our study. Contrary to this, every year, about hundred cases are only lab-reported. Clinicians are aware we only include new cases of early syphilis in the database, as we publish this information in a yearly national MSIS report [11]. Contrary to our experience with gonorrhoea with high reporting from both laboratories and clinicians [9], clinicians may opt out from sending in their part of the reporting form for syphilis, if the person has been infected for more than a year or has been known to have a positive test from before. If the stage is unknown or in cases, only reported by the laboratories, internal evaluation at NIPH includes the testing sites (asylum centres), the immigrant status and unknown date of exposure of most of these cases, to determine the likelihood of late syphilis, however it may happen there are some missed early cases among them. Clinicians may also be contacted by NIPH to verify information. Furthermore, behaviour data is subject to response and recall bias. Data in a few variables are frequently missing, including co-infection data. We believe, however, that reporting is reliable on HIV co-infection. Capacity for entering several co-infections at a time should be improved in MSIS. The fact that hardly any cases were reported as homosexually acquired until 1999 cannot be explained by changes in the notification system

or improved sexual behaviour reporting as in comparison, 10-42 cases of homosexually acquired gonorrhoea per year were reported in the same time period and in the same surveillance system [12].

Among European countries with various systems of syphilis surveillance, the highest incidence rates for early syphilis in 2007 (per 100 000 person-years) were reported from: the UK (4.4, primary and secondary stages only), Czech Republic (4.0), Sweden (2.6, less than two yeas since infection), Germany (2.5) [1,13]. At NIPH, no total counts of reported syphilis cases are kept, but late latent probably represent a majority (more than 50%). In the period from 2002-2007, late cases represented 50-73% of all reported cases in Czech Republic, 35-51% in Germany and 24-50% in Slovenia [1].

Compared to infected women in our study, heterosexual men were older, more likely to be diagnosed in a primary stage and to report symptoms, and less likely to be diagnosed through contact tracing. Similar findings were reported from a London-based study [14]. Men are more likely than women to report having been infected abroad, which resembles the situation in Sweden, however women in Sweden acquired their infection abroad more frequently and had a higher median age (33 years) than women in Norway [13]. A prevalence of HIV co-infection among heterosexuals, much higher than in our study (from 6-13%), has been reported from London and France [14,15]. Compared to London with 12% of heterosexual men reporting being clients of CSW [14], a higher proportion of men in Norway used commercial sex services, however they did so mostly abroad.

Similar to many other European countries [16], the epidemics among MSM in Scandinavia are mainly concentrated in men above 30 in metropolitan areas [13,17]. A high, but stable proportion of syphilis and HIV co-infections among MSM in several countries has been ascribed to serosorting, practice of oral sex and compromised immune system [14,17,18]. While information on co-infection is not always available, others have also reported a simultaneous increase of HIV and syphilis among MSM from 2000-2005 [19,20]. HIV positive MSM were also less likely to be in the primary stage of syphilis when diagnosed as reported from London Enhanced Syphilis Surveillance programme (2001-2004) [14].

The increase of pharyngeal, frequently asymptomatic STIs among MSM has been associated with the practice of unprotected oral sex, which is perceived as low risk for HIV transmission [12,18,21]. This might explain the differences in syphilis stage at the time of diagnosis between homosexually and heterosexually infected men, as initial painless lesion ("chancre"), appearing in the oropharynx (as well as the rectum) may pass unnoticed among MSM. Differences in syphilis stage between serodiscordant homosexual men may be explained by potentially asymp-

tomatic disease among the HIV positive [19] and a possible overlap of the primary and secondary stage [4]. Genital ulcers, including syphilitic chancre, can facilitate HIV acquisition and transmission [22], which may, together with frequent partner exchange, explain a simultaneous increase of both infections among MSM.

Compared to official population data, foreign-born people are over-represented among syphilis cases in Norway [23]. The reason could be opportunistic testing of immigrants originating from countries with higher syphilis prevalence. Occasional increases of syphilis cases, linked to CSW, refugees/asylum seekers, immigrants from the eastern Europe, especially Russia, or travelling to these regions, were reported by several countries (Czech Republic, Slovenia, Finland, UK) [24-26]. In Norway, only sporadic syphilis cases related to Russia with limited secondary transmission were noted [27]. It needs to be emphasized, however, that sexual contact abroad is a key risk factor for heterosexually-acquired syphilis in Norway.

Whether or not a proportion of reported cases with late syphilis represents a public health problem we should further focus on in Norway, is debatable. As noted, the majority of these cases are immigrants from countries with high syphilis prevalence and were infected in countries of their origin many years ago. On the other hand,

mild, unspecific and painless syphilis symptoms make it difficult to diagnose the disease early, especially in women or MSM, who may not notice initial lesions in difficult-to-visualise areas [4]. The rarity of the disease in Norway makes it a diagnostic challenge. It is therefore important to focus diagnostic efforts on specific population groups such as MSM and immigrants and, to find women cases, to conduct thorough contact tracing.

An evaluation of the recommendations for yearly syphilis testing of HIV positive MSM in the Netherlands revealed up to third of infections were asymptomatic and only discovered by screening [19]. Clinical care of HIV positive MSM, such as CD4 T cell count or HIV viral load, can conveniently include syphilis testing [28]. We recommend that the epidemic of syphilis among MSM, concentrated in Oslo, be tackled by enhanced syphilis testing for sexually active MSM, whenever they present at the STI clinic or at a general practitioner, ideally 2-4 times a year [29].

The evidence for cost-effectiveness of prenatal screening policy in a very low-risk population (< 1%) seems to be contradictory [30] and universal screening does not prevent mothers from being infected later in the pregnancy. We estimate current recommendations and practice in Norway as sufficient.
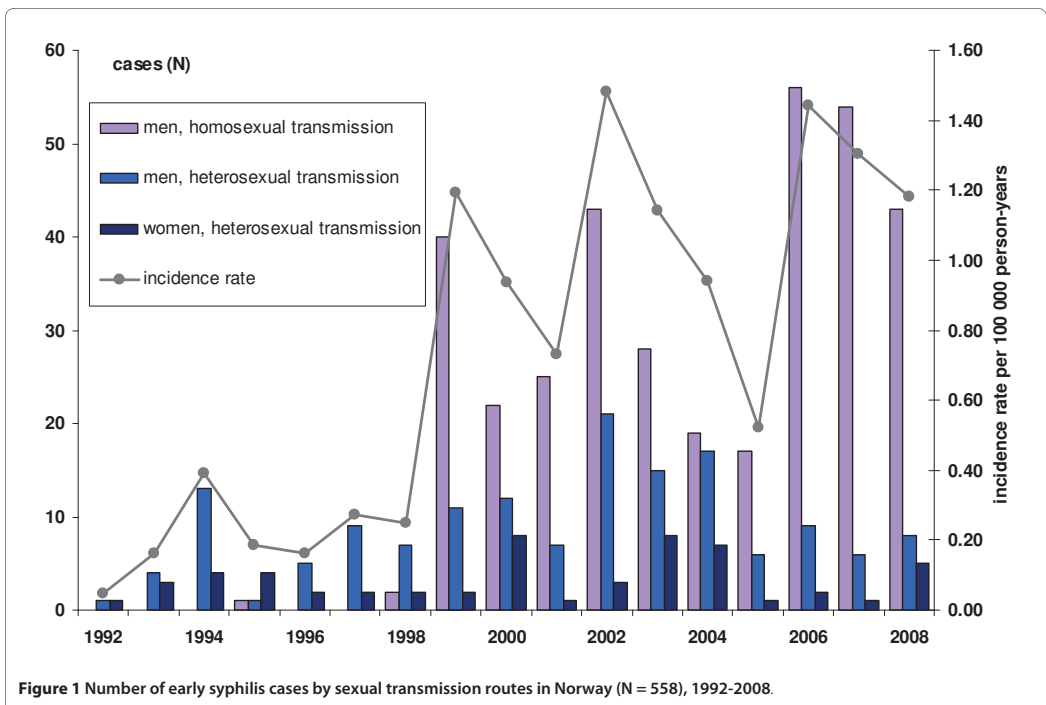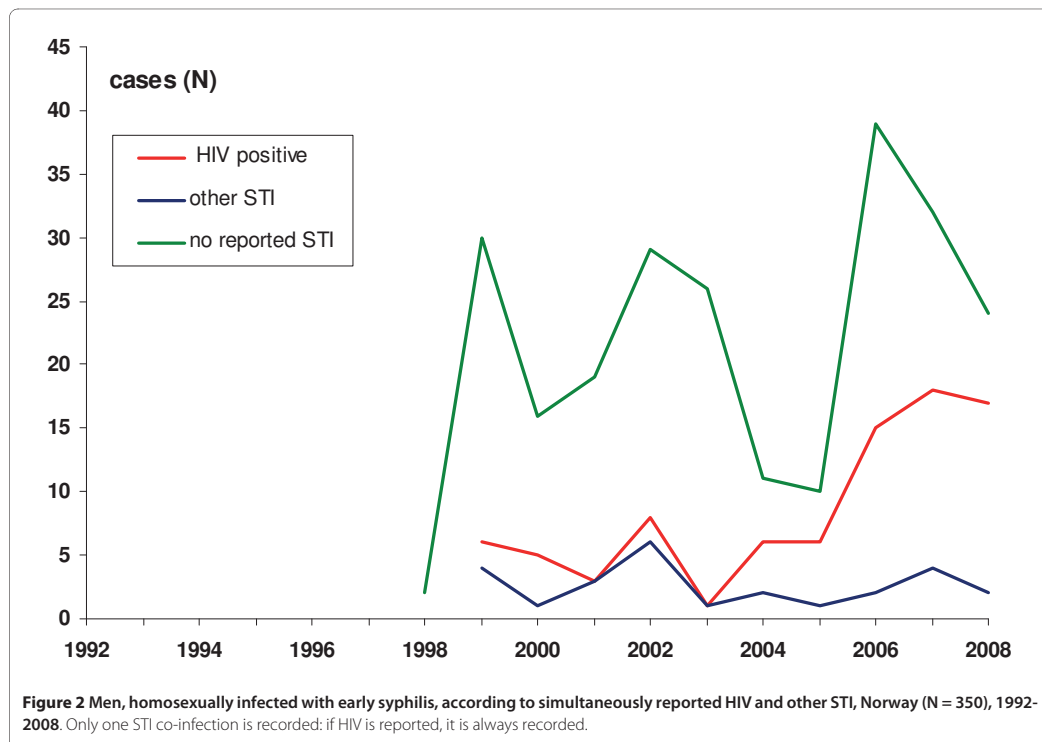

Figure 1 Number of early syphilis cases by sexual transmission routes in Norway (N = 558), 1992-2008.

Figure 2 Men, homosexually infected with early syphilis, according to simultaneously reported HIV and other STI, Norway (N = 350), 1992-2008. Only one STI co-infection is recorded: if HIV is reported, it is always recorded.

Conclusions

In summary, syphilis in Norway is mainly transmitted among MSM in Oslo. Increasing co-infection with HIV in this group underlines the need for enhanced screening and prevention programmes. We recommend sexually active MSM to be tested 2-4 times a year. Among heterosexuals, coincidental import from other countries has been observed, but further spread in Norway was limited.

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Trends in HIV infection surveillance data among men who have sex with men in Norway, 1995-2011

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Abstract

Background: Recent reports on the growing HIV epidemic among men who have sex with men (MSM) in the EU/EEA area were accompanied by an increase of reported HIV among MSM in Oslo, Norway in 2003. Our study with data from 1995 to 2011 has described the recent trends of HIV among MSM in Norway and their socio-demographic and epidemiological characteristics.

Methods: The data were collected from the Norwegian Surveillance System for Communicable Diseases. Cases were described by age, place of infection, clinical presentation of HIV infection, STI co-infection and source partner. We used simple linear regression to estimate trends over time.

Results: During the study period, 991 MSM, aged from 16 to 80 years, were newly diagnosed with HIV. No significant trends over time in overall median age (36 years) were observed. Most of the MSM (505, 51%) were infected in Oslo. In the years 1995-2002, 30 to 45 MSM were diagnosed with HIV each year, while in the years 2003-2011 this increased to between 56 and 97 cases. The proportion of MSM, presenting with either AIDS or HIV illness, decreased over time, while asymptomatic and acute HIV illness increased (p for trend=0.034 or less). STI co-infection was reported in 133 (13%) cases. An overall increase of syphilis co-infected cases was observed (p for trend <0.001). A casual partner was a source of infection in 590 cases (60%).

Conclusions: Though the increases described could be attributed to earlier testing and diagnosis, no change in the median age of cases was observed. This indicates that it is likely that there has been an increase in HIV infections among MSM in Norway since 2003. The simultaneous increase in STI co-infections indicates risky sexual behaviour and a potential to spread both HIV and other sexually transmitted infections.

Keywords: HIV infection, Men who have sex with men, Epidemiology

Background

Increases in HIV transmission among men who have sex with men (MSM) have recently been reported from several continents [1], including Europe. Data from 13 Western European countries suggested an increase of almost 100% from 1999 to 2006 [2]. In 2008, sex among MSM was the predominant mode of transmission of HIV infection in the EU/EEA area, when persons, infected in and originating from countries with generalised HIV epidemics were excluded [3].

HIV infection has been a notifiable disease in Norway since 1986 [4]. In the 1990s, the numbers of newly reported HIV infections were relatively stable, but Norway has experienced an increase in the number of HIV infected since then. Up to the 31st December 2011, heterosexual transmission was reported in 52% of all reported cases and homosexual in 32% [5]. During this time, immigration to Norway has greatly increased [6] and immigrants, infected heterosexually in their country of origin before arriving to Norway, now represent 36% of all reported cases [5]. When it comes to transmission of HIV in Norway, MSM have thus been the most vulnerable population in the past decade. The first steep increase of HIV infections among MSM in Oslo was noticed in

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2003, when 70% of the MSM cases diagnosed in 2003 were infected that same year or the year before [7].

Over the past few years, we have observed that MSM with newly diagnosed gonorrhoea or syphilis in Norway are increasingly co-infected with HIV [8]. This is particularly worrisome, as sexually transmitted infections (STI) might increase both susceptibility to HIV infection and enhance HIV transmission from HIV positives [9].

In order to gain a better insight into the development of the HIV epidemic among MSM in Norway, we aimed to describe the HIV diagnosed MSM over a seventeen year period, using demographic and epidemiological data. Due to an increase in HIV diagnosed MSM in 2003 [7], we were especially interested to find the differences between those MSM infected before 2003 and those infected after 2003.

Methods

Free HIV testing is available at various settings including general practitioners, hospitals, youth clinics and STI clinics in Norway and any HIV positive test has to be confirmed through a reference laboratory. All five reference laboratories are obliged, by law [10] to report positive results anonymously to the Norwegian Institute of Public Health (NIPH) [4] when a new HIV diagnosis in Norway is confirmed. Then, a laboratory fills out a two-part reporting form with a unique reference number. The laboratory sends one part of the form to NIPH and the other part, carrying the same reference number, to the referring clinician, who provides more detailed data, including epidemiological data of the patient to the NIPH. Clinicians are also obliged by law [10], to conduct contact tracing for HIV. NIPH contacts the clinicians who fail to submit their part of the form within a month or who send an incomplete report [4].

This study is based on the Norwegian Surveillance System for Communicable Diseases database, managed at NIPH. From the database, we extracted reports on males, who reported being infected by another man (hereafter MSM cases) and were diagnosed in the years 1995 - 2011. Demographic data on each patient include gender, month and year of birth, county of residence and country of birth. A variety of epidemiological data are collected in addition, such as: presumed transmission route, time and place of infection, indications for HIV test, date of a previous (most recent) negative HIV test, clinical presentation (AIDS was defined according to the 1993 European AIDS definition in the study population, [11]), relationship to the source partner, place of infection, diagnostic site and STI infections, concurrently existing with HIV infection diagnosed (STI co-infections).

For our analyses, we grouped categories of source partner "husband or cohabitant" (58 cases) and "steady partner" (108 cases) into a common category of steady partners. Age was grouped into four categories and county of residence into four health regions. Immigrant background was

assigned to first and second generation immigrants and those, adopted from abroad.

Among several potential co-existing STIs, only one is recorded at NIPH, using hierarchical criteria (1. syphilis, 2. gonorrhoea etc.). A HIV positive patient, who was also positive for Chlamydia and early syphilis (primary, secondary and early latent stage), will thus only have early syphilis recorded in addition to HIV.

A date of infection is estimated from laboratory results, previous negative tests and patients' information. If a previous negative HIV test date is the only information available, date of infection is assigned as the midpoint of the period between that test and the first positive test [4].

Cases with "probable" year of infection had been diagnosed within three years and fulfilled the following criteria: 1. exact date of infection was known, or 2. clinical presentation as an acute HIV infection, supported by either laboratory evidence (sero-conversion) or anamnestic data, or 3. a negative test, no older than three years, was available, or 4. a clinician evaluated the anamnestic data on time of infection to be reliable. If these additional criteria were not fulfilled, but a date of infection was estimated, the cases had "uncertain" year of infection.

Among 252 cases, where the available information did not allow an estimate of the year of infection, we used clinical presentation at diagnosis, assigning 10 years to those with AIDS (median AIDS incubation time, N=53) and 3 months to those with acute HIV (N=1) [12], assigning all these to the "uncertain" year of infection group. The remaining 198 cases with asymptomatic HIV and HIV illness were excluded from estimates of time gap between year of infection and year of diagnosis.

We performed statistical analyses with Stata/SE 11.1 (Stata Corp., TX, USA). We calculated frequency distribution for descriptive analyses. We used linear regression analysis to estimate the trends over time (for STI co-infection this was only possible for syphilis). Given that the data between subsequent years may be correlated and the variability between the years may not be constant over time, the regression coefficients and their 95% confidence intervals (CI) were calculated using the Newey-West procedure.

In order to understand the differences between MSM, infected with HIV earlier in our study period compared to the period after the increase in 2003, we studied factors associated with "diagnosed in the period 2003-2011" (compared to diagnosed in the period 1995-2002) by Poisson regression with robust variance estimates. Crude and adjusted prevalence ratios (PR) with 95% CI were calculated. If there was zero variance in a category, we excluded this category from the analysis.

Results

In the period 1995-2011, 991 men, infected by another man, were newly diagnosed with HIV infection in Norway.

While no significant trend among cases was observed until 2002, the 2003-2011 period had a significant increasing trend of HIV diagnoses among MSM (p for trend <0.001, Figure 1).

The MSM were from 16 to 80 years old when diagnosed. Overall median age was 36 years (range 33-38.5 years) and interquartile range 30 – 44 years. No apparent trend in median age was observed, except for the period 1997 – 2002 (Figure 2).

Men with immigrant background represented 21% (205), and men on a temporary visit to Norway, represented 4% (37). Thus, a large majority were permanent residents of Norway, mostly residents of Oslo municipality (666, 67%), born in Norway (Table 1). The two other most frequent countries of birth were Sweden (3%) and Thailand (3%). Just above half of the cases (505, 51%) were infected in Oslo and 140 (14%) in the rest of Norway.

For those who were infected abroad (248, 25%), predominant countries of HIV acquisition were Thailand (34 cases), Spain (33), USA (26 cases) and Germany (23 cases). Some (109, 11%) could not identify where the infection was acquired. Among those infected abroad, 39 had tested positive prior to arrival in Norway. Among 251 MSM, born abroad, 105 acquired HIV infection abroad, compared to 143 out of 740 MSM, born in Norway. Their median age at diagnosis was lower than for Norwegian born men (31 years vs. 38 years).
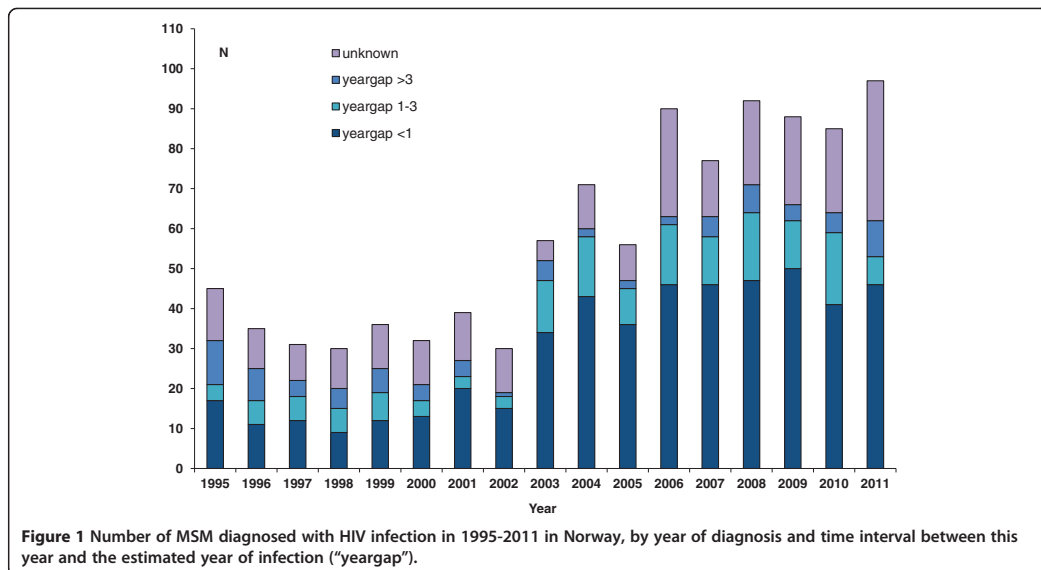
Half of the cases were infected less than a year prior to being diagnosed (Table 1, Figure 1). The increase in infections in 2003 and 2004 (Figure 1) coincides 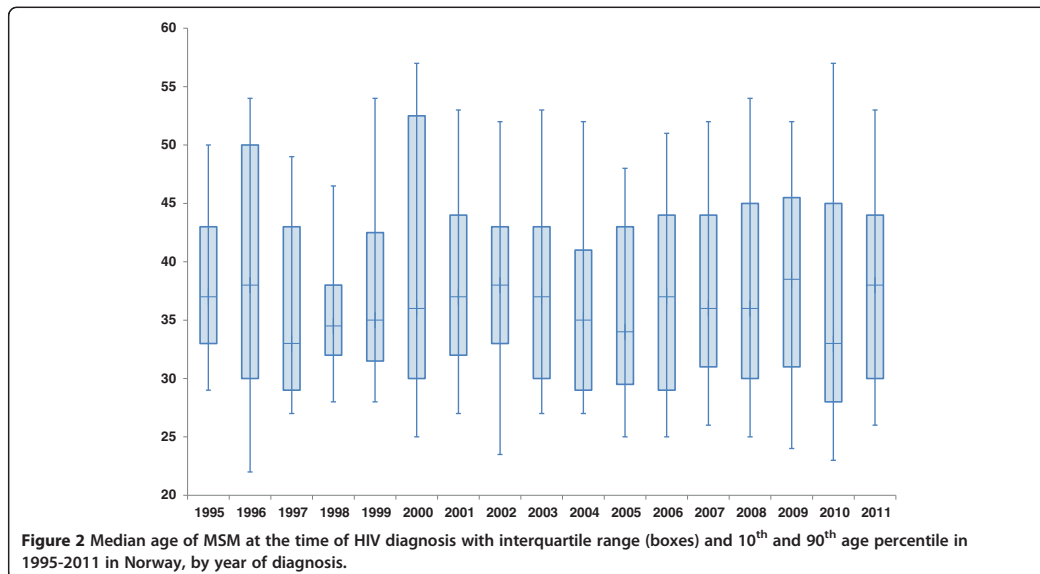with an increase of cases, infected by a casual partner (p for trend <0.001) (Figure 3). The majority of cases were asymptomatic at the time of diagnosis (597, 60%, Figure 4). Furthermore, the proportion of MSM presenting with either AIDS or HIV illness, decreased over time, however, the proportion of both asymptomatic and those with acute HIV illness increased (all with p for trend=0.034 or less).

Of the 133 (13%) cases with concurrent HIV and STI infections, syphilis was reported in 50 (3%). Among the remaining 83, 29 had gonorrhoea. Of those 54, who had neither syphilis or gonorrhoea, 21 had hepatitis B, 16 had Chlamydia, 6 had genital warts, 5 had genital herpes and 6 had "other, unspecified STI".

From 1995 to 1999, one HIV and syphilis co-infection among MSM was reported (in 1998). In 2000, a year after an outbreak of syphilis among MSM in Norway [8], 5 cases (15.6% of all HIV MSM cases that year) with co-infection were reported. From 2001, the numbers of HIV and syphilis co-infected MSM vary (0-9 cases, 0-9% of all HIV cases), but there is an overall increase of syphilis co-infected cases (p for trend <0.001). The number of MSM with any other STI co-infection (excluding syphilis), also increased in time (p for trend = 0.016, lowest 2 in 1998, highest 13 in 2010).

In the crude analysis, MSM diagnosed in the years 2003-2011 were more likely to live in Mid-Norway, were tested at their own request (compared to contact tracing) when found positive, and were more likely to have been tested before compared to those, diagnosed in 1995-2002. MSM diagnosed in 2003-2011 were also less likely to have been diagnosed more than 3 years since infection, to have an unknown year of infection and to be tested at a hospital or

Figure 1 Number of MSM diagnosed with HIV infection in 1995-2011 in Norway, by year of diagnosis and time interval between this year and the estimated year of infection ("yeargap").

Figure 2 Median age of MSM at the time of HIV diagnosis with interquartile range (boxes) and 10th and 90th age percentile in 1995-2011 in Norway, by year of diagnosis.

outpatient clinic (compared to a general practitioner's office). After adjustment for other factors (all listed in the Table 1), findings were similar, and in addition, MSM diagnosed in 2003-2011 seemed to be more likely born abroad compared to those, diagnosed in 1995-2002. The results were significant for MSM from Asia and suggested similar effect for MSM from other countries of Europe (p=0.051), Africa (p=0.055) and North America (p=0.090).

A "probable" year of infection was available for 479 (48 % of total sample) cases and an "uncertain" year of infection for a further 314 (32 %) cases (Figure 5). The number of HIV infections increased markedly in 2003 and remained higher afterwards. The mean time between diagnosis and infection for these 793 (80%) of cases was 7.1 months (interquartile range 2.7 - 23.2). In 2003, the number of cases infected more than doubled compared to a year before (from 27 to 63) and remained at high levels afterwards.

Discussion

We have observed an increase in number of HIV diagnoses among MSM in Norway in recent years, particularly after 2002. The majority of MSM were infected in Oslo and they were of Norwegian origin. Although HIV is diagnosed mainly in asymptomatic MSM, our results suggest that most of the cases diagnosed after 2002, have been infected less than a year before being diagnosed. We observed a simultaneous increase of STI co-infections, which is worrisome, as there is a potential for spread of both HIV and other STI.

The possibility for NIPH to send a reminder to the diagnosing clinicians, if they fail to report a newly identified HIV infection, contributes to a high completeness of information [4]. There were no changes in the reporting system in our study period and reporting delays are rare in Norway [4]. Due to anonymous reporting, cases could be reported twice if they are re-tested; however, laboratories do check for duplicates in the same region before submitting a report and further efforts to detect and remove duplicates are done at NIPH [4]. It is worth emphasizing that all risk behaviour data, obtained by clinicians from their patients, such as, for example, presumed transmission route, HIV infection source partner and other risk factors for HIV transmission (for example, injecting drug use), may be subject to recall and reporting biases. Since some MSM might not be open with their doctor about the way they were infected, we may have missed some cases which have been classified in other transmission groups. As the system records any infection not reported previously, the HIV positive person who immigrated to Norway is also included, if they were tested in Norway (44 in our study population). Merging STI into a common outcome has its limitations, as some STIs might be recent (acute) and others, such as hepatitis B, could be chronic with different risk factors.

The HIV surveillance data monitor the incidence of new *diagnoses* rather than new *infections* and will be thus largely influenced by HIV testing uptake. Since specific tests to distinguish between the early and late infection [13] are not yet routinely applied in HIV diagnostics and reporting in Norway, it is difficult to distinguish between the current

Table 1 Selected characteristics of HIV positive MSM who were diagnosed in Norway in 1995-2011, and factors associated with having been diagnosed in the years 2003-2011 compared to 1995-2002

Demographic, epidemiological and other possibly associated factors	Total sample N=991 (%)	Diagnosed in the years 2003-2011 N= 713 (%)	Diagnosed in the years 1995-2002 N= 278 (%)	Comparison of diagnosed in the years 2003-2011 vs. diagnosed in 1995-2002		
				Crude PR* [95% CI]	Adjusted PR** [95% CI]	p for trend
Age groups (years)						
16-24	73 (7.4)	56 (7.8)	17 (6.1)	ref. group	ref. group	0.418
25-34	362 (36.5)	266 (37.3)	96 (34.5)	1.0 [0.8-1.1]	1.0 [0.9-1.1]	
35-44	323 (32.6)	221 (31.0)	102 (36.7)	0.9 [0.8-1.0]	1.0 [0.8-1.1]	
≥ 45	233 (23.5)	170 (23.8)	63 (22.7)	0.9 [0.8-1.1]	1.1 [1.0-1.3]	
Place of birth						
Norway	740 (74.7)	523 (73.3)	217 (78.1)	ref. group	ref. group	
Africa	23 (2.3)	18 (2.5)	5 (1.8)	1.1 [0.9-1.4]	1.3 [1.0-1.6]	
Asia	64 (6.5)	50 (7.0)	14 (5.0)	1.1 [1.0-1.3]	1.2 [1.0-1.4]	
Europe, other	92 (9.3)	71 (10.0)	21 (7.6)	1.1 [1.0-1.2]	1.1 [1.0-1.3]	
North America	13 (1.3)	11 (1.5)	2 (0.7)	1.2 [0.9-1.5]	1.2 [1.0-1.6]	NA
South/Mid America	59 (5.6)	40 (5.6)	19 (6.8)	0.9 [0.8-1.1]	1.0 [0.8-1.2]	
Health region of residence in Norway						
South-East***	842 (85.0)	602 (84.4)	240 (86.3)	ref. group	ref. group	NA
West	86 (8.7)	58 (8.1)	28 (10.1)	0.9 [0.8-1.1]	0.9 [0.8-1.2]	
Mid-Norway	39 (4.0)	35 (4.9)	4 (1.4)	1.2 [1.1-1.4]	1.3 [1.1-1.5]	
North	24 (2.4)	18 (2.5)	6 (2.2)	1.0 [0.8-1.3]	1.0 [0.8-1.3]	
Year gap****						
< 1 year	498 (50.2)	389 (54.6)	109 (39.2)	ref. group	ref. group	0.001
1-3 years	157 (15.8)	118 (16.5)	39 (14.0)	1.0 [0.9-1.1]	1.0 [0.8-1.1]	
>3 years	84 (8.5)	41 (5.7)	43 (15.5)	0.6 [0.5-0.8]	0.6 [0.5-0.8]	
Unknown	252 (25.4)	165 (23.1)	87 (31.3)	0.8 [0.8-0.9]	0.7 [0.6-0.9]	
Reason for HIV test						
Contact tracing	109 (11.0)	68 (9.5)	41 (14.8)	ref. group	ref. group	NA
Own request	328 (33.1)	261 (36.6)	67 (24.1)	1.3 [1.1-1.5]	1.3 [1.1-1.5]	
Blood donor	1 (0.1)	0	1 (0.4)	excluded	excluded	
Immigrant	11 (1.1)	7 (1.0)	4 (1.4)	1.0 [0.6-1.6]	1.0 [0.6-1.7]	
Symptoms	347 (35.0)	249 (35.0)	98 (35.3)	1.1 [1.0-1.3]	1.2 [1.0-1.4]	
Unspecified	195 (20.0)	128 (18.0)	67 (24.1)	1.1 [0.9-1.3]	1.1 [0.9-1.3]	
Source partner						
Steady	166 (16.7)	117 (16.4)	49 (17.6)	ref. group	ref. group	NA
Casual	590 (59.5)	442 (62.0)	148 (53.2)	1.1 [1.0-1.2]	1.1 [1.0-1.2]	
Commercial sex worker	3 (0.3)	3 (0.4)	0	excluded	excluded	
Other/unknown	232 (23.4)	151 (21.2)	81 (29.1)	0.9 [0.8-1.1]	1.0 [0.9-1.2]	

Table 1 Selected characteristics of HIV positive MSM who were diagnosed in Norway in 1995-2011, and factors associated with having been diagnosed in the years 2003-2011 compared to 1995-2002 *(Continued)*

Diagnosed by						
GP or private specialist	412 (41.6)	315 (44.2)	97 (34.9)	ref. group	ref. group	NA
Youth/STI clinic	320 (32.3)	329 (32.1)	91 (32.7)	0.9 [0.9-1.0]	0.9 [0.9-1.0]	
Hospital/ outpatient dept.	247 (24.9)	163 (22.7)	85 (30.6)	0.9 [0.8-0.9]	0.9 [0.8-1.0]	
Other	12 (1.2)	7 (1.0)	5 (1.8)	0.8 [0.5-1.2]	0.8 [0.5-1.3]	
Previous negative test						
No previous test	336 (33.9)	221 (31.0)	115 (41.4)	ref. group	ref. group	NA
Tested before	588 (59.3)	425 (59.6)	163 (58.6)	1.1 [1.0-1.2]	0.9 [0.9-1.0]	
Unknown	67 (6.8)	67 (9.40)	0	excluded	excluded	
STI co-infection						
None reported	858 (86.6)	617 (86.5)	241 (86.7)	ref. group	ref. group	NA
Any	133 (13.4)	96 (13.5)	37 (13.3)	1.0 [0.9-1.1]	1.1 [0.9-1.2]	

* PR – prevalence ratio.
** adjusted for all the factors, listed in the Table.
**includes Oslo.
***time between infection and diagnosis in years.

increase in HIV transmission and a backlog of cases, undiscovered in the previous years.

While no systematically collected data on testing activity among MSM in Norway in our study period exist, some data suggest satisfactory testing rates. In a 2003 study where MSM were approached at several gay venues in Oslo, 87% have answered they had ever been tested for HIV (76% in 1990, 80% in 1998) [14]. In a 2007 survey in Norwegian language that recruited respondents among visitors to a gay Internet site [15], 69% of 2598 responding MSM reported that they had been tested for HIV at least once and the proportion who tested positive was 4% (data not published). In a more recent internet based cross-European MSM survey from 2010, 67% of responding MSM in Norway reported having received the HIV test result at least once, of which 3.5% were positive [16]. A third has received the result of their HIV test in the last 12 months in 2010 survey [17] and 37% in 2007 survey (data not published). We can conclude testing rates among MSM in Norway are satisfactory, though we should be aware the test uptake is likely lower among those who are infected [18].
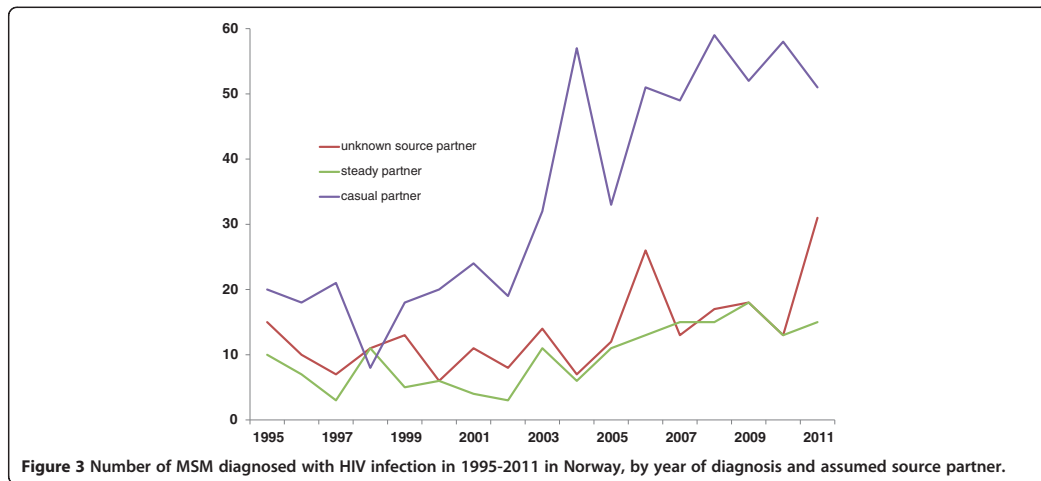
Though information on time of infection is subject to bias, the assumption that there is an actual increase in recently infected cases is supported by the median age showing no significant increase over time [19]. Furthermore, results from the internet based behavioural survey in 2010 have revealed worrisome risky behaviour, as 54% of MSM respondents who had engaged in sex with a non-steady partner had had anal intercourse without a condom in the past year and more than 30% said they did not use a condom the last time they had anal sex with a casual partner [16].

In order to clarify the described increasing trends, our findings call for improvements in HIV monitoring in Norway. Regular monitoring of HIV prevalence using anonymous unlinked studies, as well as monitoring testing trends and MSM behaviour in Norway are recommended. Introduction of CD4 count in surveillance data and approaches to reduce potential double-reporting (such as Soundex code) should be considered, as more and more MSM live with HIV in Norway and the risk of double reporting after re-testing is increasing.

We aimed to estimate year of infection from the information available, though important limitations (see above) with this approach exist, since for 20% of diagnosed cases the year of infection could not be estimated. Thus, our time intervals between infection and first diagnosis are underestimated as those excluded 20% are likely to have an interval longer than 7 months. A French study based on surveillance data from 2004-2007 reported much longer time (median 25 months, interquartile range 5-55) [12]. Had we assigned an overestimate of 10 years to the remaining 20% of cases, our median would increase to 12 months, indicating MSM in Norway are on average being diagnosed earlier than French.

The surveillance systems of new HIV diagnoses in European countries have varying characteristics, which makes it difficult to compare our results, however; similar increasing trends in diagnoses of HIV infections among MSM of all age groups have recently been reported in Belgium (1999-2008) [20], Germany (1999-2005) [21] and

Figure 3 Number of MSM diagnosed with HIV infection in 1995-2011 in Norway, by year of diagnosis and assumed source partner.
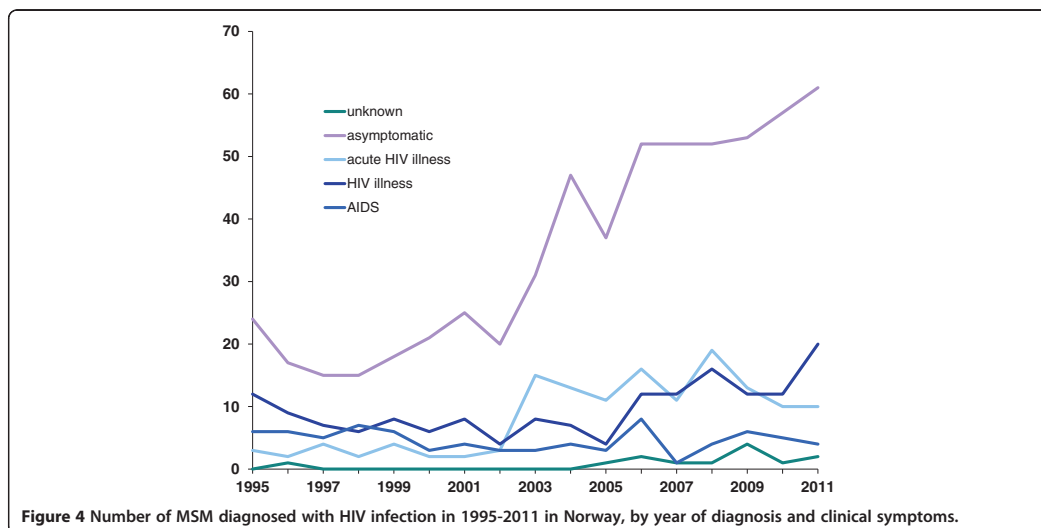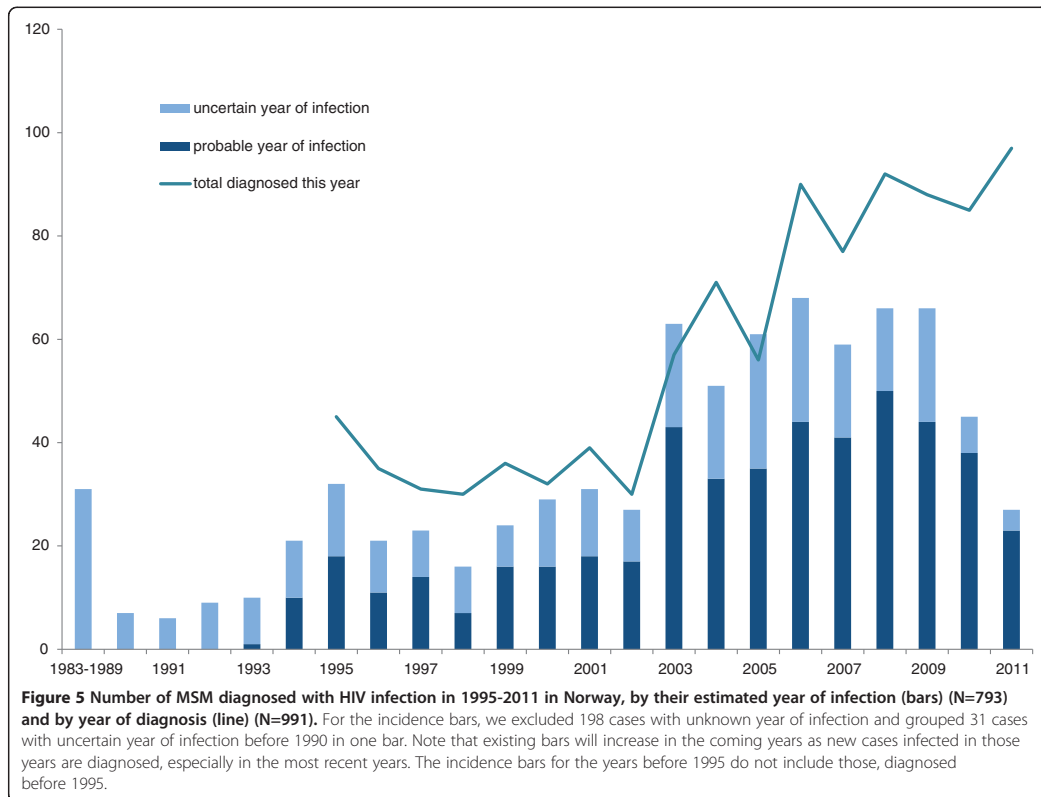
the UK outside of London (1997-2004) [22]. Contrary to this, data from London and the Amsterdam STI clinic (1991-2004) suggested that an increase in HIV incidence was observed specifically among MSM aged 35 years and older [22,23]. Median age in our study seemed to be similar to the one in Belgium and Denmark (1990-2005) [24] with median age 37.

Similar to our findings, in Belgium, 11% of HIV positive MSM had an STI co-infection in 2008 (data provided by participating AIDS Reference Centers) [20]. In the period 2003-2007, as many as 31% of the 1462 newly HIV diagnosed MSM in Spain (data from 19 HIV/STI

clinics) were diagnosed with a concurrent STI [25]. An increase from 5% (2001) to 7% (2003) in concurrent syphilis and HIV was reported from Germany [26]. Syphilis outbreaks including HIV positive MSM were described in metropolitan areas of Western Europe (London, Paris, Dublin, Hamburg) with MSM who were mostly aware of their HIV status [27].

HIV was the most frequently reported STI among MSM in Norway in 2006 [8,28]. With rising HIV prevalence, MSM are more likely to have sex with an HIV positive man than a man with any other acute STI [29]. In addition, the prevalence of STI, which may increase the risk of HIV

Figure 4 Number of MSM diagnosed with HIV infection in 1995-2011 in Norway, by year of diagnosis and clinical symptoms.

Figure 5 Number of MSM diagnosed with HIV infection in 1995-2011 in Norway, by their estimated year of infection (bars) (N=793) and by year of diagnosis (line) (N=991). For the incidence bars, we excluded 198 cases with unknown year of infection and grouped 31 cases with uncertain year of infection before 1990 in one bar. Note that existing bars will increase in the coming years as new cases infected in those years are diagnosed, especially in the most recent years. The incidence bars for the years before 1995 do not include those, diagnosed before 1995.

transmission, is now higher, and per-contact probability of HIV transmission has been evaluated as similar to that of the pre-HAART era [30]. Primary HIV infection may have a larger role in the dynamics of HIV transmission than previously assumed, due to a higher viral load and higher infectiousness [31]. Our results suggest similar trends in Norway.

HIV transmission is predominantly affecting domestic-born MSM [20,24,32], however, similar to other Western countries, immigration has more than doubled in Norway since 2000[33] and foreign born MSM are becoming more represented in the recent years. Foreign born MSM are a "difficult to reach", heterogeneous and vulnerable population, likely diagnosed younger than domestic-born MSM [32]. According to guidelines issued by the Norwegian Directorate of Health, immigrants from high HIV prevalent areas should be offered a free confidential HIV test [34] and support and treatment, if found positive. Nonetheless, less than 1% of MSM were diagnosed due to immigrant screening in our study, which is low compared to the group of heterosexuals, infected before arrival to Norway, who represent more than a third of all newly diagnosed HIV cases in Norway [16]. General practitioners should be aware that some men might be reluctant to provide details of their sexual behaviour to their clinician, particularly if they originate from cultures, where such behaviour is not acceptable. Specific preventive and testing measures, targeted at foreign born MSM, should be evaluated.

Those diagnosed in the years 2003-2011, were more likely to be tested at their own request compared to contact tracing and less likely to be diagnosed at hospital or outpatient clinic than by their general practitioner. With a simultaneous decrease of AIDS and HIV illness, this might have been the effect of a 2005 recommendation to general practitioners for annual HIV and STI testing of MSM in Norway [35] and other MSM targeted public health campaigns, encouraging HIV testing. Thus, risky behaviour among MSM, might have been accompanied by improved awareness on importance of testing and early capture of infections. We concur with the recommendations from 2005 and emphasize the need to target MSM with immigrant background, as well as to conduct thorough partner notification in the general practitioner's setting.

Similar increasing HIV trends are described among MSM around Europe and a coordinated approach in HIV monitoring, prevention and control, should be complemented with identification of new prevention strategies. In the light of failing preventive measures (such as promotion of safe sex practices and condom use), pre-exposure prophylaxis is a promising biomedical intervention, however still controversial due to possible side effects on healthy men, poor adherence among HIV negative, costs, change in sexual behaviour and resistance issues to name a few [36,37]. Further studies are on the way to evaluate the effectiveness of this approach [37]. Effectiveness of male circumcision on HIV transmission among MSM remains unknown [38].

Reasons why those living in Mid-Norway are more frequent among cases from 2003-2011 are not clear. Recently, rapid testing has become available countrywide, in both health centers and specialized clinics, as well as in outreach centers. In the latter, this is an assumed low threshold offer that might increase testing uptake among high risk MSM. It remains unanswered if current healthcare services are sufficiently targeting foreign born MSM with testing and information on STI prevention, though this low threshold offer could make a difference.

Conclusions

Our data suggest continuing spread of HIV among MSM in Norway. On average, MSM are being diagnosed early after infection, however an increasing proportion are co-infected with an STI. This calls for prompt and effective preventive measures as many past preventive efforts seem to have been insufficient or failing. At the same time, current monitoring of HIV infections among MSM has many limitations. In the light of the increase in HIV diagnoses among MSM, this calls for urgent improvements and more research on HIV prevalence, regular testing activity and risky behaviour in this population.

Authors' contributions
IJ drafted the manuscript. ØN collected and entered data and contributed with interpretation. IJ, AG, PA and HB contributed to the design of the study, analysis and interpretation. All authors critically reviewed and approved the final version of this paper for publication.

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Scheme 1: De-identified report on infectious disease for laboratories

Veiledning for laboratoriet

Skjemanummer
12651

Denne slippen rives av og fylles ut av laboratoriet og sendes til MSIS, Folkehelseinstituttet Postboks 4404 Nydalen 0403 Oslo. Skjemaet sendes sammen med det positive prøvesvaret til rekvirenten.
Ved HIV-infeksjon sendes skjema ved funn av en **ny** (for dette laboratoriet) HIV-positiv pasient. Dersom referanselaboratoriet ikke kjenner rekvirentens navn og adresse, sendes **hele** skjemaet (inkludert denne slippen) til primærlaboratoriet som fyller ut og sender på samme måte.

Opplysninger om pasienten

Født:

Mnd.   År

Kjønn: Mann   Kvinne

HIV-1 infeksjon   HIV-2 infeksjon

Dersom pasienten tidligere er testet HIV-negativ, oppgi dato for siste negative prøve:

Dato

Gonore   PPNG (penicillinaseprod.)

Kinolonresistent

Syfilis

Rekvirentens navn, adresse og telefon

Laboratoriets navn

Sendt dato   Signatur

Riv av slippen før utfylling

Scheme 2: De-identified report on infectious disease for diagnosing physician
(next page)

73

Side 1: Sendes MSIS, Nasjonalt folkehelseinstitutt
Postboks 4404 Nydalen 0403 Oslo
Side 2: Sendes kommunelegen der pasienten bor
Side 3: Arkiveres i pasientens journal

Skjemanummer
12651

folkehelseinstituttet

MSIS-melding
Avidentifisert melding om smittsom sykdom

☐ **HIV-infeksjon**

Evt. tid og sted for tidligere positiv prøve

☐ **Gonore**

Lokalisasjon (Urethra, cervix, anus, hals etc.)

☐ **Syfilis**

Ved tidligere behandlet tilfelle av syfilis settes kryss her ☐ og skjemaet sendes inn uten videre utfylling.

Hvis meldt tidligere, fra hvem

Evt. antibiotikaresistens:

Stadium av syfilis vurderes som:

☐ Primær   ☐ Sein latent

Evt. tid og sted for siste negative prøve

☐ PPNG (penicillinaseprod.)

☐ Kinolonresistent

☐ Sekundær   ☐ Tærtiær

☐ Tidlig latent   ☐ Ukjent stadium, men behandles

Født: ☐ ☐   Mann ☐ Kvinne ☐ Ukjent ☐
Mnd. År

Pasientens fastlege

Bostedskommune   **Fødeland**

Mors fødeland   **Fars fødeland**

Hvis født utenlands, angi årsak til opphold i Norge

Tid i Norge etter innvandring   **Evt. dato for reist fra Norge**

Prøvetakingsdato   **Innsykningsdato**

Påvisningsmetode

Laboratorium

Indikasjon for undersøkelse

☐ Symptomer/tegn ☐ Smitteoppsporing ☐ Helseus. av innvandrer

☐ Pas. eget ønske ☐ Helseus. av gravid ☐ Annen rutineus.

Annet

Klinisk bilde   Evt. dødsdato

Dersom pasienten nå har annen seksuelt overført inf. angi hvilke(n)

Antatt smittetidspunkt

Antatt smittested (Kommune eller land)

Ved smitte i utlandet, angi årsak til utenlandsopphold

☐ Smittet før innvandring til Norge

☐ Besøk i eget eller foreldres tidl. hjemland

☐ Forretningsreise   ☐ Turistreise

☐ Arbeid/studie/langtidsopphold   ☐ Ukjent

Annet

Anntatt smittemåte

☐ Heteroseksuell   ☐ Sprøyter/brukerutstyr

☐ Homoseksuell   ☐ Mor til barn

☐ Sex, uspesifisert   ☐ Stikkskade/annen blodkontakt

☐ Blod/blodprodukter   ☐ Annet/ukjent

Beskriv evt. smittesituasjonen nærmere

Anntatt smittekilde

☐ Ektefelle/samboer   ☐ Prostituert

☐ Annen fast partner   ☐ Annen person

☐ Tilfeldig kontakt   ☐ Ukjent

Utfyllende opplysninger om smittekilden
(Nasjonalitet, smittemåte og smittested)

Har pasienten fått personlig smittevernvelledning?

☐ Ja   ☐ Nei   ☐ Ukjent

Hvilke smitteverntiltak er igangsatt?

Melders navn, adresse og telefonnummer

Dato

NB! Husk gjennomskriften. Bruk kulepenn og skriv hardt.

Sendes MSIS, Postboks 4404 Nydalen 0403 Oslo.

Errata list

Abbreviations for different types of corrections:

Abb – abbreviation added

Cor – correction of language
Fct – change of factual error, not affecting the meaning or content of the thesis

Fig – language correction of figure title or figure labels

Tab – language correction of table title

Type of correction: page/line	Original text	Corrected text
Cor: III/22	in an MSM focused project	in a project, focused on MSM
Cor: III/23; VII/3-4; 15/6; 21/6; 54/16; 56/13; 56/40; 57/12; 56/22; 61/5 **Tab:** 34;	MSM population(s)	population(s) of MSM
Cor: VI/2; 9/19; 13/22; 18/7; 21/2; 22/35; 29/17; 57/11,	disease(s) / infectious diseases	infection(s)
Cor: VI/5; VI/11; XI/27; 28/19; 44/1; 51/7; 58/11; 60/31-32; **Fig**: 47	STI infection(s)	STI
Cor: VI/8;	MSM behaviour	behaviour of MSM

20/11		
Cor: VI/23	ethical background	ethnic background
Fct: 6/24-27	As many as 201 out of 600 syphilis positive men in the study were deliberately infected for the purposes of the study. All 600 were left untreated for decades and thus the researchers passively permitted the infection to spread to the family members of these men.	At the time of enrolment in the study, 399 men were infected with syphilis and 201 were considered not infected (ref. 1). Regardless of the outcome during the study, all 600 men were left untreated for decades. While the researchers passively permitted the infection to spread to the family members of men in Tuskegee study, over one thousand individuals enrolled in Guatemala experiment were intentionally exposed to, or inoculated with, *T. pallidum*, *N. gonorrhoeae*, or *Hemophilus ducreyi* between 1946 and 1948 (ref. 1). 1. Ref: Cuerda-Galindo E, Sierra-Valenti X, González-López E, López-Muñoz F. Syphilis and Human Experimentation From World War II to the Present: A Historical Perspective and Reflections on Ethics. Actas Dermo-Sifiliográficas. 2014;105(09):847-53.
Abb: VIII	N.A.	STD sexually transmitted diseases
Cor: 3/24	the MSM criteria of inclusion	the criteria for inclusion of MSM
Cor: 5/37; 11/8	infection(s)	disease(s)
Cor: 8/23, 20/31, 20/33	STI	STD
Cor: 8/24-28	Worldwide, the eight most prevalent STIs are infections with: syphilis, gonorrhea, chlamydia, trichomoniasis, genital herpes, HIV, hepatitis B virus (HBV), and human papillomavirus (HPV); all of which represent,	Worldwide, the eight most prevalent STI are infections with: *Treponema pallidum*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, genital herpes simplex virus, HIV, hepatitis B virus (HBV), and human papillomavirus (HPV); all of which cause,
Cor: 17/29-30	in a MSM sexual practices study	in a study of sexual practices of MSM

Cor: 20/21	MSM transmission	transmission among MSM
Cor: 21/8-9	increases in MSM STI rates	increases in STI rates among MSM
Cor: 23/20-21	the MSM community	the community of MSM
Cor: 24/9	MSM recruitment	recruitment of MSM
Cor: 24/34	among MSM visitors of STI clinics	among MSM visiting STI clinics
Tab: 32	of MSM respondents in the	of MSM responding to the
Cor: 33/20;	MSM Internet survey participants	MSM participating in the Internet survey
Tab: 35; 37; 39; 40; 49;	MSM Internet survey	Internet survey of MSM
Tab: 37	Revealing MSM practices to	Revealing sex with men to
Cor: 41/5; 42/3; 45/6; 46/15; 46/16	MSM cases	cases of MSM
Fig: 41; 42; 42; 43; 43; 44; 45; 45; 46; 47	N.A.	*figure labels for x axis* *colour contrast Figure 9*
Cor: 52/4	MSM online survey	online survey of MSM
Cor: 52/11; 52/34 **Tab:** 36	MSM survey	survey of MSM
Cor: 53/27	MSM syphilis cases	syphilis cases among MSM
Cor: 54/6	MSM attendees of two STI clinics	MSM attending two STI clinics
Cor: 57/24	MSM samples	samples of MSM

Night of Sleepless Love

The night above. We two. Full moon.
I started to weep, you laughed.
Your scorn was a god, my laments
moments and doves in a chain.

The night below. We two. Crystal of pain.
You wept over great distances.
My ache was a clutch of agonies
over your sickly heart of sand.

Dawn married us on the bed,
our mouths to the frozen spout
of unstaunched blood.

The sun came through the shuttered balcony
and the coral of life opened its branches
over my shrouded heart."

Federico García Lorca

Translated by Martin Sorrell in Selected poems, 2007. Original title *Noche del amor insomne.*