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## Re-Emergence of HIV Infection and Syphilis Among Men Who Have Sex with Men

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### 1. Introduction

Sexual activity has been shown to be the primary mode of transmission for several important viral and bacterial infections among men who have sex with men (MSM) throughout the world and therefore sexually transmitted infections (STIs) are still one of major public health problem worldwide. Since the earliest days of the human immunodeficiency virus (HIV) epidemic MSM have been profoundly affected by the disease; by the time the first AIDS cases were reported in the early 1980s, HIV had already spread widely among homosexual and drug-user communities. In western Europe, has been estimated that HIV incidence peaked around 1983 among MSM and in 1987-88 among injecting drug users, with 120.000 homosexual/bisexual men infected by 1985, and 144.000 injecting drug users infected by 1989 (Downs et al., 2000). MSM account for a substantial proportion of HIV infections and compose a “bridging group” for transmission to heterosexuals because of the high frequency of reported bisexuality. Widescale behavioural modification in response to the emerging HIV/AIDS pandemic saw dramatic reductions in the incidence of many acute STIs in the late 1980s (WHO, 2007). However, these have not been maintained and many states are now observing increases in rates of diagnosed STIs; then the proportion of homosexual men reporting “unsafe sex”, often measured as unprotected anal intercourse (UAI) with casual partners, has increased since the mid-1990s (Prestage et al., 2005). In western Europe, among MSM, HIV diagnoses increased in 2002 (22%, from 2757 in 2001 to 3371 in 2002) after a slow decline in the previous years. Increased high risk sexual behaviour and migration of HIV-infected people from sub-Saharan Africa have contributed to the rise in the incidence of STIs since 2000 (Hamers & Downs, 2004). On the other hand, antiretroviral treatment, which lowers the viral load, may reduce the likelihood that an HIV infected person infect a partner during unprotected sexual intercourse. Mathematical modelling suggests that the effect of antiretroviral treatment on lowering transmission at the population level could be offset by an increase, even modest, in risk behaviour, and the net effect of these opposing forces on HIV incidence has been much debated (Katz et al., 2002).

This HIV infection increase, in some industrialized countries, has also coincided with several reported outbreaks of syphilis among the MSM population (Couturier et al., 2004); in particular, oral sex between men appears to have been important in the transmission of syphilis in outbreaks reported overseas, probably because among MSM unprotected oral sex is considered a safe practice. Data of literature report that syphilis transmission attributed to oral

sex has been estimated between 20 and 46% (Peterman & Furness, 2007). Syphilis remains a global problem despite the existence of simple and validated screening tests; moreover, it has been described as strongly associated with prevalent HIV infection among MSM thereby playing an important role in the increase of this infection in a susceptible population. The interaction between HIV infection and syphilis is of great interest for the epidemiological and clinical implications that apply to both heterosexuals and MSM (Peterman & Furness, 2007). The World Health Organization (WHO) estimates 12 million new syphilis cases worldwide annually, of which 140,000 in western Europe where the infection has re-emerged both in homosexual men, in particular in HIV-positive gay men, and in heterosexuals (WHO, 2001; Simms et al., 2005; Xu et al., 2011). An increase of cases among MSM has been found in Italy (Istituto Nazionale di Statistica [ISTAT], 2005), Sweden (Velicko et al., 2004), Scotland (Wallace et al., 2005) and in Germany (Marcus & Hamouda, 2004), suggesting that syphilis is now endemic in the MSM population in parts of Western Europe. In the USA, the scenario is similar because an increase in syphilis cases among MSM occurred between 2000 and 2005, characterised by high rates of HIV co-infection and high-risk sexual behaviour (Fenton et al., 2008). As infection is frequently asymptomatic, annual serological screening for syphilis is to recommend in this group of men. Syphilis offers a classic example of the re-emergence of an easily diagnosed and readily treatable STD.

In this report we review the recent epidemiology of HIV infection and syphilis among MSM in the developed and developing world and discuss potential reasons for the emerging trends and their implications for prevention and control.

## 2. HIV /AIDS

HIV infects defense/immune system cells such as CD4+ T cells, macrophages and dendritic cells. After infection HIV uses CD4+ cells as host to make copies and infect other cells, this leads to the reduction of CD4+ cells and immune system totally collapse. The development from HIV to AIDS is checked by decline of CD4+ cells. Two types of HIV has been characterized, HIV-1 and HIV-2. HIV-1 is the most virulent and pathogenic strain; the HIV-2 epidemic remains limited, both in terms of prevalence and with respect to geographic spread because, worldwide, the predominant virus is HIV-1. The relatively uncommon HIV-2 type is concentrated in West Africa (Senegal, Ivory Coast, Guinea Bissau) and other countries characterized by a considerable immigration of people coming from West Africa. The HIV-1 is further divided into 3 groups: 1. group M (main) ; 2. group O (outlier) ; 3. group N (non M - non O). These groups have been identified in their envelop region. The major HIV pandemic is caused by HIV-1 group M strains; groups O and N of HIV-1 are rare and limited to Cameroon in Central Africa (McCutchan, 2006). Group O accounts for less than 10% of HIV-1 infections in Cameroon and has spread little beyond these confines ; only a handful of group N infections have been identified. Within HIV-1 group M, nine subtypes are recognized namely subtypes A, B, C, D, F, G, H, J and K, that represent lineages of HIV and have different geographic location. Many of the HIV-1 group M subtypes are rare and remain at low prevalence. In contrast, subtype B is widespread globally, dominating epidemics in the Americas, Western Europe, and Australia. Subtype C accounts for more than 50% of all infections worldwide, concentrated in Southern and East Africa, and in India; subtype D strains are found principally in East Africa, and to a lesser extent in West Africa. In some parts of the world less information is available about HIV diversity, particularly North Africa, the Middle East, and parts of Central Asia (McCutchan, 2006).

The study and monitoring of the genetic evolution of the HIV-1 represent an essential strategy for controlling the global HIV-1 epidemic and for developing efficient preventive and therapeutic strategies.

## **2.1 The current scenario in developed countries**

The HIV epidemic is resurging in gay communities in developed world. As a consequence, a number of European countries have conducted behavioural surveys among MSM to monitor HIV and STIs risk in this population ; behavioural surveillance provides important information for planning and evaluating prevention interventions (Elford et al., 2009). In Canada (Public Health Agency of Canada, 2007), the United States (CDC, 2007) and Australia (National Centre in HIV Epidemiology and Clinical Research, 2007) MSM represent the risk group diagnosed most frequently with HIV infection. In particular, in the United States, the MSM population accounted for the majority of new HIV infections in 2006. This re-emergence has led some commentators to suggest that HIV prevention in MSM is faltering so president Obama's released National HIV/AIDS Strategy calls for more emphasis on addressing the HIV prevention and care needs of MSM (The White House Office of National AIDS Policy, 2010).

### **2.1.1 European Union and European Free Trade Association countries**

The number of newly diagnosed HIV cases reported among men who have sex with men (MSM) has recently increased throughout European Union (EU) and European Free Trade Association (EFTA) countries. The predominant mode of transmission for HIV infection in EU and EFTA countries is sex between men. In 2006, 7693 newly diagnosed HIV infections among MSM were reported (56.7 per million men aged 15-64 years). In most of the European countries with data for 2000-2006, the number of new HIV diagnoses increased by 86%, the median age at HIV diagnosis remained unchanged (36 years), whereas the proportion of MSM presenting with an AIDS-defining illness at the time of HIV diagnosis declined from 25% in 2000 to 10% in 2006. Basically there is a decrease of cases of AIDS and death in the presence of an increase of HIV infection. (Likatavicius et al., 2008). In general, reported HIV prevalence ranged between 8% and 68% among MSM with sexually transmitted infections, between 10% and 18% among those recruited in community settings, but remained <10% in central Europe and Ireland. Whereas the decreasing rates of AIDS diagnoses and AIDS deaths reflect relatively good access to therapy, the increasing numbers of new HIV diagnoses and relatively high prevalence of HIV among MSM suggest the need for Europe-wide HIV prevention among MSM. Currently, the prevalence of HIV among homosexual and bisexual men is 10-20% in most western European countries; prevalence is usually higher in large cities than elsewhere (Hamers & Downs, 2004). In the below report, there are summarized the results of serological investigations carried out in several European countries, which show the pattern of increasing HIV incidence in these last years. In Madrid, in a study among homosexual and bisexual men who repeatedly attended voluntary HIV testing centres, HIV incidence decreased from 4.7 per 100 person-years in 1988 to 1.1 in 1995, but then increased to 2.2 in 2000. More recently, incidence studies based on the serological testing algorithm for recent HIV seroconversion (STARHS) have been done among homosexual and bisexual men attending sexually transmitted infection clinics in the Netherlands and the UK (Hamers & Downs, 2004). In Amsterdam, an overall incidence of 3.0 infections per 100 person-years during 1991-2001 was noted, with a

significant increase over time. The increase was evident in men older than 34 years but not in younger men. In the UK, the overall annual incidence was 2.4% (3.1% in London, 1.0% elsewhere) with no significant trends in HIV incidence during 1995–2001. However, more recent data showed an increasing trend to 3.5% in 2002 (Hamers & Downs, 2004). Belgium is currently experiencing an alarming upward trend among MSM in the number of new HIV diagnoses that, in the past decade, increased by 228% (from 101 cases diagnosed in 1999 to 332 cases in 2008). The majority of new HIV infections were diagnosed among Belgians citizens (72%), followed by other European nationalities, sub-Saharan Africa and other/unknown nationality (Sasse & Defraye, 2009).

In Slovenia, of a total of 48 newly diagnosed HIV infection cases reported for 2008 (23.5/million population), 34 cases, representing more than two thirds, were MSM. Since 1999, the annual reported rate of newly diagnosed HIV cases in MSM raised from 2.5 to 16.7 per million men 15-64 years old, an increase of more than six times. The overall increase in the number of newly diagnosed HIV cases in Slovenia during recent years has been due almost exclusively to the increase in new diagnoses among MSM (Klavs et al., 2009).

Increases in risky sexual behaviour in a population in which HIV is already highly prevalent, coupled with increases in sexually transmitted infections that enhance the risk of HIV transmission, have the potential to lead to an expansion of HIV transmission among homosexual and bisexual men (Hamers & Downs, 2004).

### 2.1.2 United States / Canada

On June, 5, 1981, MMWR published a report of *Pneumocystis carinii* pneumonia in five previously healthy young men in Los Angeles. These cases were later recognized as the first reported cases of AIDS in the United States; since that time, this disease has become one of the greatest public health in the world. HIV infection and AIDS have claimed the lives of more than 22 million persons worldwide, including more than 500.000 persons in USA (CDC, 2006). Prevention interventions have contributed to a steady decline (from an estimated 8.048 in 2001 to 5.962 in 2004) in new HIV/AIDS diagnoses (CDC, 2005) but despite these successes, several challenges remain. In the United States, in contrast to other risk groups for which HIV/AIDS diagnoses have decreased, cases among MSM increased 8,6% from 2001 up to 72% in 2006 (CDC, 2008a). Among MSM with new infections, 46% were white, 35% were black, and 19% were Hispanic. Among MSM aged 13-29 years, the number of new HIV infections in blacks (5.220) was 1.6 times the number in whites (3.330) and 2.3 times the number in Hispanics (2.300). Among black and Hispanic MSM, most new infections were in persons aged 13-29, whereas, among white MSM, most new infections were in persons aged 30-39 years (CDC, 2008b). In Milwaukee county has been reported a 144% increase during 2000-2008 in black homosexual men aged 15-29 years. Interestingly, an increase in syphilis diagnoses among young black MSM in Milwaukee preceded the increase in HIV diagnoses, which suggests that changes in risk behavior or sexual networks might explain the increase (CDC, 2011).

The Centers for Disease Control and Prevention have documented a dramatic increase in the rates of sexually transmitted diseases among men who have sex with men (MSM) living in major urban centres across the country over the past 10 years (CDC, 2004). The MSM currently represent the group with the largest number of new HIV infections in the USA and its incidence have been increasing consistently since the early 1990s. Based upon national surveillance at sexually transmitted disease clinics, median positivity rates for



gonorrhoea and chlamydia are higher among HIV-infected MSM than among HIV-uninfected or unknown status MSM. Syphilis seroreactivity rates are up to four times greater among HIV-infected MSM than HIV-uninfected or unknown status MSM (<http://www.cdc.gov/STD/stats06/msm.htm> as cited in Mayer et al., 2010). This trend of higher comparative rates of incident sexually transmitted infection (STI) among HIV-infected MSM is also evident in community samples both nationally (Whittington, 2002, as cited in Mayer et al., 2010) and internationally (Dodds, 2007, & Dougan, 2007, as cited in Mayer et al., 2010). Consistent with high rates of STI among HIV-infected MSM, some studies suggest that rates of high-risk sexual behaviors (i.e. anal intercourse without a condom) may be up to three times higher among HIV-infected MSM compared with HIV-uninfected MSM (Mayer et al., 2010).

In Canada at the end of 2005, an estimated 58,000 people were living with HIV infection which represents an increase of about 16% from the 2002 estimate of 50,000. In terms of exposure category, prevalent infections in 2005 were comprised of 29,600 MSM (51%), 9,860 IDU (17%), 8,620 heterosexual/non-endemic (15%), 7,050 heterosexual/endemic (12%), 2,250 MSM-IDU (4%), and 400 attributed to other exposure (<1%). The largest absolute increase was among the MSM exposure category with 3,400 more prevalent infections since 2002 (13% increase) (Boulos et al., 2006). This trend among MSM and MSM-IDU is been associated with increases in risky sexual behavior. The causes of this increase are complex and may include decision-making based on false assumptions about a partner's HIV status, dissatisfaction and difficulties with condom use, feelings of marginalization, depression and the choice to not use condoms as a gesture of commitment to a partner. The scenario is different among Aboriginal persons because the distribution of new cases of HIV in 2005 was 53% IDU versus 10% MSM and 3% MSM-IDU; this highlights the uniqueness of the HIV epidemic among Aboriginal Canadians and underscores the complexity of Canada's HIV epidemic (Boulos et al., 2006). Moreover, an estimated 16,900 persons HIV positives (26% of total prevalent infections) were unaware of their HIV-infected status and this proportion varied from an estimated 19% of HIV-infected MSM, to 25% of HIV-infected people who inject drugs, and 35% of HIV-infected heterosexuals (Yang et al., 2010).

### 2.1.3 Australia

Since 2000 the annual number of new diagnoses of HIV in Australia has increased by 38%. Gay men continue to be the most affected, accounting for 64% of people who were newly diagnosed as having HIV infection in 2004-2008, and 82% of the infections that were determined to have been acquired no more than a year before they were diagnosed (de Wit et al., 2010). Recent trends in new HIV diagnoses differ across Australian jurisdictions (Figure 1), the region with the highest number of HIV diagnoses each year is the state of New South Wales (NSW) with approximately 70% of these cases attributed to homosexual transmission (de Wit et al., 2010). While the population rate of HIV diagnosis doubled in Victoria between 1999 and 2006, increased markedly in South Australia and Western Australia in that period and steadily increased in Queensland since 1999, in NSW over the past decade the rate has remained relatively stable (Guy et al., 2007, as cited in de Wit et al., 2010). Historically, NSW has had the highest HIV infection rate; the apparent stability of the current HIV epidemic in gay men in NSW may reflect testing patterns, HIV status knowledge and disclosure and the well-reasoned use of risk-reduction strategies that this enables. A mathematical model has been used in conjunction with HIV/AIDS data from the Australian National HIV/AIDS

Registry to estimate numbers and ages of Australian men who have sex with men living with HIV infection from 1980 to 2005 (Murray et al., 2009). The average age of HIV-infected Australian MSM is estimated to exceed 44 years of age by the year 2010 and has increased by 1 year of age for each two calendar years since the mid-1980s. HIV-infected MSM over 60 years of age have been increasing in number by 12% per year since 1995. A consequence of successful therapy with subsequent ageing of those infected has meant that from 2001 estimated deaths from other causes exceed AIDS deaths in Australia (Murray et al., 2009). Australian guidelines recommend annual testing for HIV and sexually transmitted infections (STIs) for all men who have sex with men (MSM) and 3-6 monthly testing for those at higher risk as defined by behavioural criteria; a recent study (Guy et al., 2010) showed that there is poor adherence to national guidelines that recommend regular re-testing of MSM for STIs, particularly among those at higher risk who require more frequent testing.

Clinical strategies are urgently needed to encourage more frequent HIV/STI testing among MSM, especially in the higher risk subgroup.

## **2.2 The current scenario in developing / transitional countries**

MSM in developing/transitional countries have a several-fold higher odds of HIV infection compared to the general population, with an 18-fold higher risk in Asia (Baral et al., 2007, as cited in Solomon et al., 2010). MSM in Africa are a highly vulnerable population at risk for HIV infection, in spite of this, the Africa region has documented limited HIV and STDs data on MSM, largely due to stigmatization of homosexual behaviour in the population (Smith et al., 2009). After Asia and sub-Saharan Africa, the region most impacted by HIV infection is Latin America where high rates HIV prevalence have been documented among MSM with no evidence of significant decrease (Halperin et al., 2009).

### **2.2.1 India**

There are more than 39.5 million people living with HIV worldwide, more than 2.5 million live in India where sexual transmission is the predominant mode of HIV transmission and is estimated to be the major risk for about 86% of those infected (National AIDS Control Organization, 2006, as cited in Solomon et al., 2010). The overall HIV prevalence in India is 0.36% ; the high reported HIV prevalence among some high-risk groups such as female sex workers (FSW) and men who have sex with men (above 5%), puts the country in the classification of concentrated epidemic. Protecting India's large population of FSW and MSM from infection is a critical priority and it is also an effective way to protect the remaining population from infection (UNAIDS, 2009, as cited in Gutierrez et al., 2010). A study carried out in Mumbai (formerly known as Bombay) found high rates of unprotected sex, bisexuality and HIV among urban Indian MSM (Kumta et al., 2010); another study conducted in Andhra Pradesh (AP) also found that MSM reported high rates of unprotected anal sex with other men and women. Andhra Pradesh (total population of 76.2 million) is among the six states in India with the highest HIV prevalence; about 10% of all AIDS cases in India are in AP (Dandona et al., 2005).

In India, the first evidence of HIV was described among sex workers in Tamil Nadu (TN) (Simoes et al., 1987, as cited in Solomon et al., 2010), then spreading to monogamous housewives via their husbands (Gangakhedkar et al., 1997, & Newmann et al., 2000, as cited

in Solomon et al., 2010). Since heterosexual transmission was the primary driver of HIV in India, most prevention programs have targeted these individuals; recent evidence suggests that the HIV epidemic is declining among these populations (Arora et al., 2008, & Kumar et al., 2006, as cited in Solomon et al., 2010). By contrast, MSM remain the only high-risk population in India where HIV prevalence is increasing (National AIDS Control Organization, 2007, as cited in Solomon et al., 2010). There are an estimated 2.35 million sexually active MSM in India (National AIDS Control Organization, 2006, as cited in Solomon et al., 2010); historically, MSM in India have been a hidden population because of Section 377 of the Indian Penal Code which criminalizes anal intercourse and Indian culture's requirement of opposite sex marriage (Herget, 2006, as cited in Solomon et al., 2010). Consequently, few studies of HIV epidemiology among MSM in India exist. Most derive from urban sexually transmitted infection (STIs) clinics and few have characterized MSM in rural/semi-urban areas. In a landmark decision on July 2, 2009, the Delhi High Court repealed Section 377 (Nilajana, 2009, as cited in Solomon et al., 2010). While this allows more freedoms for MSM, it is likely that stigma and discrimination will continue and may even increase as MSM become more visible in Indian society. A study conducted across 18 different cities (classified in six urban sites, six semi-urban, six rural) in the south Indian state of Tamil Nadu showed HIV and syphilis prevalence of 9 and 8% respectively among not married MSM and of 14 and 11% among married MSM; HIV infections were not restricted to the large metropolitan cities because several semi-urban and rural settings also had HIV-infected MSM (Solomon et al., 2010).

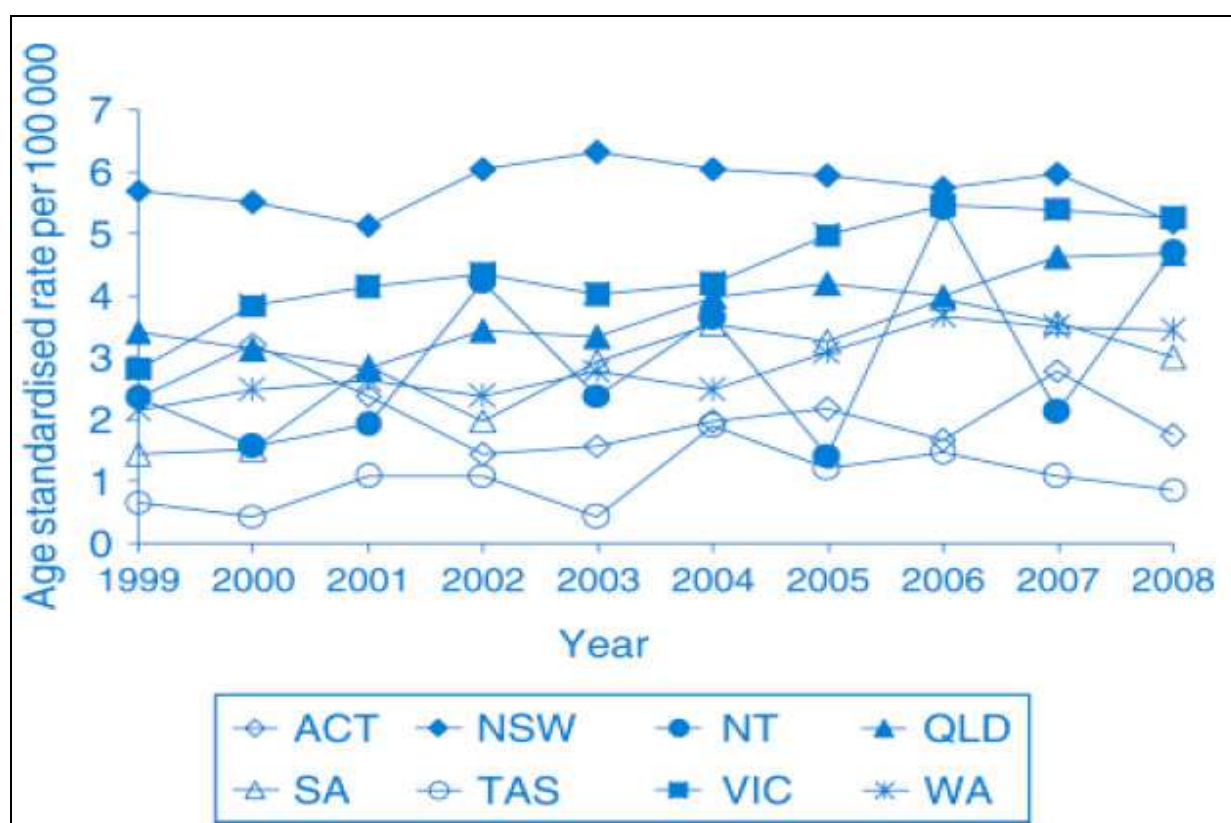


Fig. 1. Newly diagnosed HIV infection, 1999–2008, by year and state and territory, Australia. (Source: de Wit et al., 2010)



### 2.2.2 Sub-Saharan Africa

In sub-Saharan Africa the scenario is similar to that of India because research on MSM was neglected for a long time; most African countries do not include MSM in their HIV surveillance systems. Criminalisation of male-to-male sex, social denial and difficulty in reaching this population were the explanations given for the weak involvement of researchers in this area (Dahoma et al., 2011). However, recently, the assumption that this population could be significantly vulnerable to HIV and STIs has encouraged a growing number of epidemiological studies. Although heterosexual contact remains the main mode of HIV transmission in sub-Saharan Africa, HIV prevalence there has been described to be higher within MSM population than in the general population. In the first epidemiological study conducted on MSM in Senegal, HIV prevalence was 21.5% compared with less than 1% for the general Senegalese population. The high frequency of sexual contact with women reported by this study's participants also suggests that a sexual bridge between MSM and women could contribute to the expansion of the HIV epidemic (Wade et al., 2005). High levels of HIV infection also were reported among MSM in Zanzibar where a survey conducted from April through June 2007 among 509 MSM participants showed HIV prevalence of 12.3% (65/509) (Dahoma et al., 2011). Moreover, the study showed high levels of bisexual activity (70.8% of participants) which in combination with high risk sexual behaviour (i.e. inconsistent condom use) raise concerns about the potential bridging role of MSM in transmitting HIV infection into the general population (Dahoma et al., 2011). In Nigeria results from a survey conducted in Lagos, Kano and Cross River states during 2007 showed that MSM are highly affected by HIV and that condom use in anal sex is low in commercial and non-commercial partnerships. HIV is more established among MSM in Lagos, there were wide variations in HIV prevalence with estimates ranging from 17.4%, to 9.3% and 1.1% in Lagos, Kano and Cross River respectively (Merrigan et al., 2011). Moreover, as previously observed in other African countries, significant proportions of Nigerian MSM had unprotected sex with female partners indicating a potential bridge for HIV transmission between MSM and the general population (Merrigan et al., 2011).

These data suggest that prevention interventions should be systematically implemented within the high-risk group of MSM in the African context.

### 2.2.3 China

In China, men who have sex with men have now become one of the priority populations for prevention and control of HIV pandemic because MSM transmission of HIV is a critical and growing public health problem. The estimated number of people living with HIV in China has also increased markedly from 400,000 in 2007 to 740,000 in 2009. Among new HIV infections reported in China, the proportion of MSM transmission has risen dramatically. According to pooled prevalence estimates from meta-analyses (Chow et al., 2011), the overall national HIV prevalence among MSM in China has increased from 1.3% during 2003-2004 to 2.4% during 2005-2006 and then to 4.7% during 2007-2008; moreover, a significantly positive correlation was observed between HIV and syphilis prevalence among Chinese MSM during 2003-2008 countrywide.

With substantial increases in HIV and syphilis infection, Chow et al. (2011) also observed an increase in prevalent HIV-syphilis co-infections (1.4% during 2005-2006 to 2.7% during 2007-2008) (Figure 2). In 2009, 32.5% of 48,000 new HIV infections was attributed to male

homosexual exposure, which is almost triple the reported level in 2007 (12.2% of 50,000 new cases) (UNGASS, 2010, as cited in Chow et al., 2011). In Shenyang city, the capital of Liaoning Province in northeast China, MSM transmission accounted for 39.6% of new infections in 2009. Epidemiological studies from 2006 suggested that HIV infection among MSM in Shenyang was increasing rapidly, with an HIV incidence density of 5.4/100 person-years (Xu et al., 2010). A 3-year prospective open cohort follow-up survey (from 2007 to 2009) that recruited a total of 1282 MSM (229 in 2007, 598 in 2008 and 455 in 2009) revealed a significant increase in incidence density of HIV from 4.7/100 person-years to 10.2 /100 person years (Table 1). Furthermore, due to a higher transmission probability of HIV associated with penile-anal intercourse and levels of risk related behaviour, Chinese MSM have an approximately 45-fold higher risk of acquiring HIV than other males in the general population (Zhang et al., 2011).

Type of recruited MSM cohorts	Infection rate	Incidence density (95% CI)
Recruited cohort in 2007	5.7 %	4.7/100 person-years
Recruited cohort in 2008	6.2 %	6.1/100 person-years
Recruited cohort in 2009	8.1 %	10.2/100 person-years

Table 1. China. Shenyang city : new infection rates and incidence density of HIV. (Source: Zhang et al., 2011)

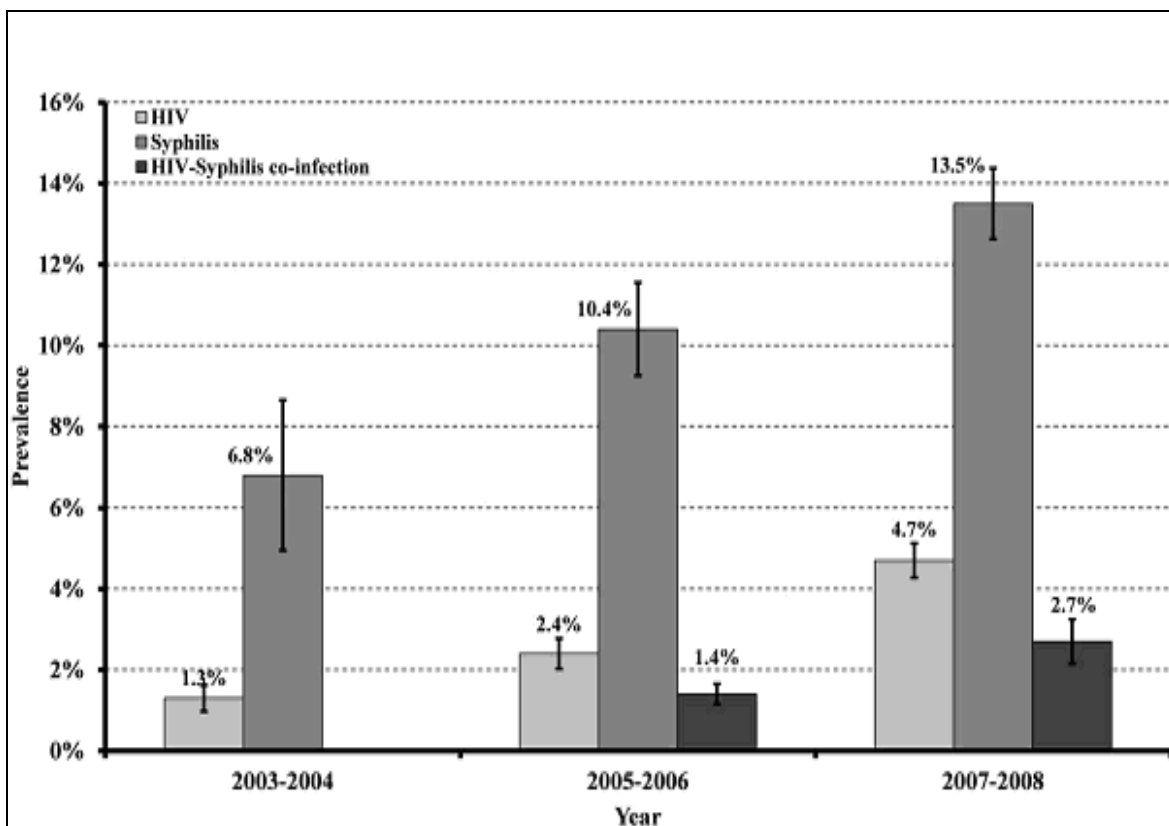


Fig. 2. China : estimated prevalence of HIV, syphilis infection and HIV-syphilis co-infection among men who have sex with men during 2003-2008. (Source : Chow et al., 2011)

### 3. *Treponema pallidum* / Syphilis

Syphilis. The name of this widespread and ancient disease is familiar to health care providers worldwide, it was coined by the Italian physician Girolamo Fracastoro in his tale of the shepherd Syphilus, who contracted the disease after insulting the pagan Sun god.

Syphilis is a genital ulcerative disease caused by the spirochaete *Treponema pallidum* subsp. *pallidum* (Fenton et al., 2008), identified in 1905 by Schaudinn & Hoffmann (Waugh, 2005, as cited in Fenton et al., 2008). The disease is treatable with standard antibiotics (Pao et al., 2002, as cited in Fenton et al., 2008), but in the absence of therapy, gives rise to four sequential clinical stages commonly known as primary, secondary, latent (divided into early and late stages) and tertiary syphilis (Table 2) (Botham et al., 2006). In the initial stages, the infection is highly transmissible and often presents as ulcerative genital lesions. Secondary syphilis results from the multiplication and dissemination of Treponemes throughout the body. The most common manifestation is a disseminated mucocutaneous rash.

The secondary stage occurs up to 6 months after the healing of the primary lesion and lasts for several weeks or months and may reoccur in approximately 25% of untreated patients (Stamm, 1998, as cited in Fenton et al., 2008). The oral cavity is the most common extra-genital site of infection; oral chancres are observed in about 4–12% of patients with primary syphilis and occur at the site of penetration of the organism into the mucosa. Anatomical sites commonly affected are especially the tongue, gingiva, soft palate and lips (Ficarra & Carlos, 2009) (Figure 3). The tertiary or late stage of syphilis is rarely seen today in the era of effective and prevalent antibiotic therapy. Treponemes invade the central nervous or cardiovascular systems, eyes, skin, and other internal organs, producing damage as a result of their invasive properties and inflammation (Fenton et al., 2008). With minor differences, syphilis generally presents similarly in HIV-positive and HIV-negative patients. In primary syphilis, HIV-infected patients may present with more than one chancre (up to 70% of patients) and with larger and deeper lesions. About a quarter of HIV-infected patients present with concomitant lesions of both primary and secondary stages of syphilis at the time of diagnosis. Approximately one-third of patients with early syphilis have invasion of Treponemes in the cerebrospinal fluid (CSF), regardless of their HIV status. However, by contrast with HIV-uninfected patients, most of the new cases of clinical neurosyphilis in HIV-infected individuals are identified early at the initial presentation, suggesting that HIV infection may be associated with an increased risk of developing neurological complications (Zetola & Klausner, 2007).

#### 3.1 The current scenario in developed countries

Rates of syphilis in many developed cities worldwide reached their lowest recorded levels towards the end of the 1990s. Since 1997, however, outbreaks of syphilis among men who have sex with men have been reported in North America and Europe, and those with HIV infection have been disproportionately affected (CDC, 2002). Australia has two distinct patterns of infectious syphilis: a substantially declining occurrence in Indigenous remote communities and an increasing incidence in males residing in urban and regional areas (Ward et al., 2011).

##### 3.1.1 European Union and European Free Trade Association countries

In the early 1990s rates of syphilis infection in Western Europe (WE) were at historically low levels, these decreases were accompanied by marked reductions in the incidence of congenital syphilis and tertiary disease. But **syphilis has re-emerged in western Europe**

since 2000 and a large increase and outbreaks affecting major urban centres in Europe, mainly in MSM, have been reported (Figure 4) (Sullivan et al., 2009). **Changes in sexual behaviour have facilitated the spread of syphilis especially among men who have sex with men and improved surveillance systems and case detection have lead to an increase in the reported numbers of cases.** The first of several outbreaks of syphilis in MSM was observed in Hamburg (Germany) in 1996/1997, and syphilis incidence began to increase nationwide in 2001 (Marcus & Hamouda, 2005); in Germany, for syphilis cases in MSM, 7% in the year 2002 were classified as re-infections.

INFECTIOUS	NON-INFECTIOUS
<p><b>Primary</b> One or more ano-genital or oral ulcers (chancres) are present, which may vary considerably in appearance. Serological tests are reactive.</p> <p><b>Secondary</b> Skin spots or rashes are present, particularly on the trunk, palms and soles, often with generalised lymphadenopathy. The primary chancre may still be present. Non-treponemal (RPR, VDRL) titre 1:4.</p> <p><b>Latent</b> No symptoms of syphilis are present, but treponemal (TPPA, FTA-Abs) tests are reactive and the non-treponemal (RPR, VDRL) tests have increased two titres.</p> <p><b>Early latent</b> Disease acquired within the past two years.</p>	<p><b>Late latent</b> Disease acquired more than two years ago or at an unknown time.</p> <p><b>Neurosyphilis</b> Syphilis of any stage with clinical symptoms of neurosyphilis or raised CSF protein or WCC in the absence of other known causes of these abnormalities.</p> <p><b>Tertiary</b> Characteristic abnormalities of the cardiovascular, skin, bone or other systems.</p> <p><b>Congenital syphilis</b> A condition affecting an infant whose mother had untreated or inadequately treated syphilis at delivery.</p>

Table 2. Classification of syphilis. (Source: Botham et al., 2006 )

This proportion increased to 16% in 2004, in seven cities (Frankfurt, Cologne, Berlin, Mannheim, Munich, Leipzig, Hamburg) with > 100.000 population, with the highest incidence of syphilis in 2004 (>10/100.000), 25% of reported cases in MSM were classified as re-infections. This datum indicates an intense circulation of syphilis in restricted subgroups of MSM in the largest cities (Marcus & Hamouda, 2005). In Denmark an outbreak of syphilis began in 2003 and continued in 2004. Data from the national surveillance system showed that most cases are in men who have sex with men, and that a large proportion of these patients are also HIV positive. The majority of cases were reported from Copenhagen municipality; the outbreak did not seem to be affecting the age group under 20 years. Probably, most of the MSM found with both syphilis and HIV were already HIV positive when they acquired syphilis infection (Cowan, 2004). In the United Kingdom, between 1997 and 2002, diagnoses of primary, secondary, and early latent syphilis made at genitourinary medicine clinics increased by 213% in heterosexual males, 1412% in men who have sex with men (MSM), and 22% in females. These increases were initially observed in larger cities and then progressed to suburban and rural settings (Simms et al., 2005). In 2004, among MSM/bisexual men an alarming increase of 212% as regards 2003 has been observed in



Scotland; most of the diagnoses (91%) were made in the Glasgow and Edinburgh clinics (Figure 5) (Wallace et al., 2005). The Swedish Surveillance system of syphilis is population-based. All health care specialists have the responsibility to notify diagnosed syphilis directly to the national surveillance system SmiNet. Also all laboratories diagnosing syphilis have the responsibility to notify to the SmiNet. From the data obtained through the surveillance system seems that the major contributor to the recent rise in syphilis cases in Sweden is infections among MSM (Figure 6) (Velicko et al., 2008). Among MSM who acquired a syphilis infection in Sweden in recent years, the majority acquired it in big cities, especially Stockholm (up to 96% of all reported cases among MSM); syphilis incidence among MSM was 20-28 times that of males in general in Sweden.



Fig. 3. Secondary oral syphilis: mucous patches covered by *grayish, white* pseudomembranes of the lower vestibular mucosa. (Source : Ficarra & Carlos, 2009).

It can be assumed that MSM to a larger extent choose to live in big cities since they assure more anonymity and less stigmatisation for MSM (Velicko et al., 2008). In contrast to WE countries, in Central and Eastern Europe between 1998 and 2007 there was a general decline in the number of reported syphilis cases (Savage et al., 2009). During the same period the sex ratio was relatively stable at around 1:1, with the exception of Slovenia where the male: female ratio rose to almost 5:1 in 2007 and 39% of male cases were reported to be MSM (Savage et al., 2009). Recent increases in overall early syphilis reported rates in Slovenia (in 2008 increase of 130% compared with 2007), with great majority of cases occurring in men (94%) and among cases in men a substantial proportion of cases among men known to have sex with men (44%) and among those almost one in three with a foreign MSM partner within three months preceding syphilis diagnosis, suggest recent increase in unsafe sexual behaviour among MSM and sexual mixing of Slovenian MSM with MSM abroad (Klavs et al., 2009). Most worrying, two in three early syphilis cases reported in 2008 among MSM were men with known HIV infection, indicating unsafe sexual behaviour among HIV-positive MSM aware of their infection. In the Czech Republic, most cases of syphilis, total of 18.000 were diagnosed after the World War II during the mass screening of the population aged 15 to 40 years in 1951. In the following years, the incidence of syphilis decreased considerably; the absolute number of reported syphilis cases has increased rapidly during the 1990s as a result of geopolitical and socioeconomic changes (Kuklova et al., 2011). The syphilis rate has risen eightfold from 1.6 per 100.000 inhabitants in 1990 to 13.5 per 100.000 inhabitants in 2001 due to high proportion of syphilis cases among immigrants coming mainly from the Ukraine, Moldavia, the Russian Federation and Georgia. After reaching a peak in 2001, the incidence of syphilis has been decreasing but, after 2006, the incidence has increased again. Men, in particular MSM, prevail over women among the infected persons (Kuklova et al., 2011).

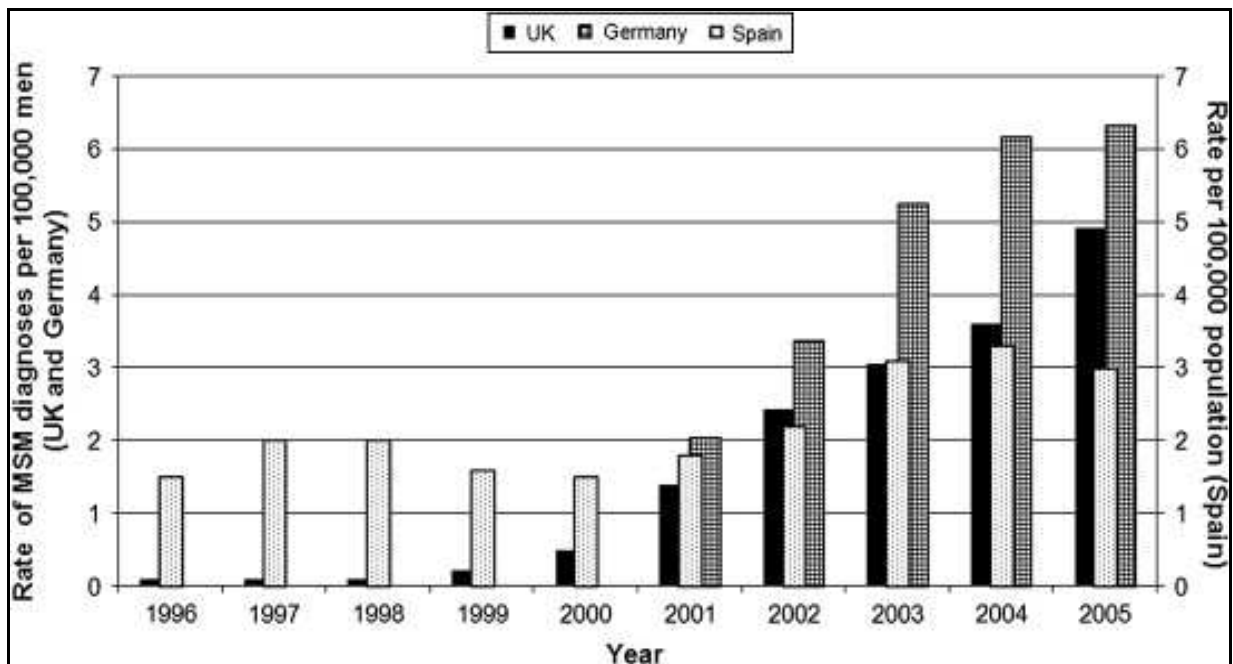


Fig. 4. Primary and secondary syphilis rates in United Kingdom and Germany (rate of diagnoses among MSM per 100,000 men) and Spain (rate per 100,000 population), 1996-2005. (Source: Sullivan et al., 2009).

### 3.1.2 United States / Canada

Although syphilis is uncommon in much of the US population, several groups are disproportionately affected, including African Americans, Hispanics, and men who have sex with men (MSM).

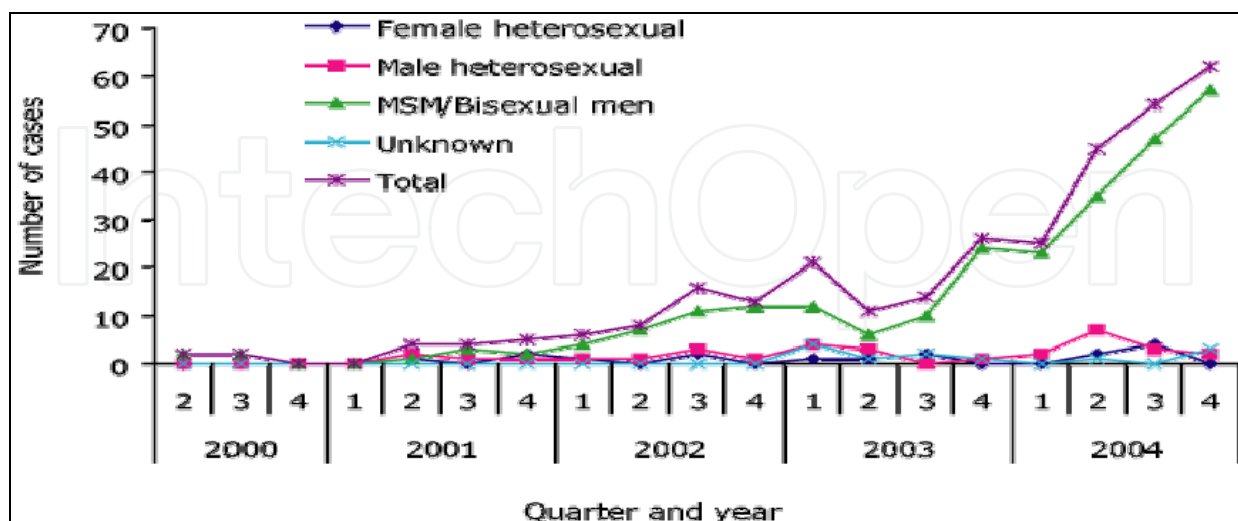


Fig. 5. Number of cases of infectious syphilis diagnosed at STI clinics in Scotland by sexual orientation and quarterly totals, 2000-2004. The majority of cases were diagnosed at sexually transmitted infections (STIs) clinics in Edinburgh (45%) and Glasgow (42%). ( Source : Wallace et al., 2005)

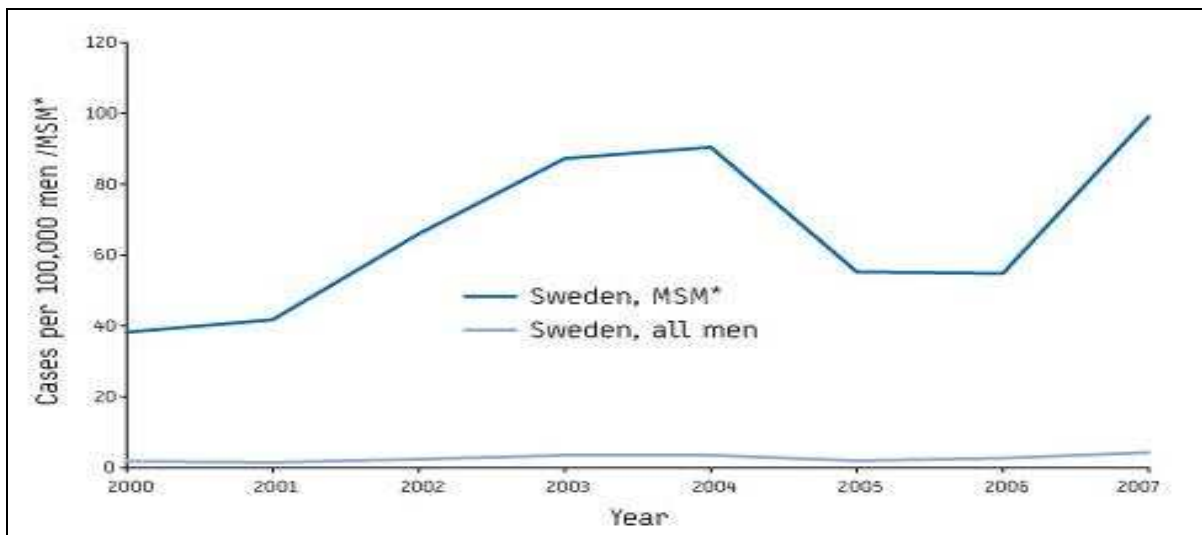


Fig. 6. Estimated syphilis incidence among MSM and observed syphilis incidence among all males, notified cases in Sweden, 2000-2007. (Source: Velicko et al., 2008)

After steady decreases for >1 decade, rates of syphilis in the United States reached their lowest point during 2000, when the rate of primary and secondary syphilis was 2.1 cases per 100,000 persons. By 2005, the rate of primary and secondary syphilis increased to 3.0 cases per 100,000 persons, representing an increase from 5976 to 8724 cases, of which 86% occurred in men. This increase in the rate ratio of male to female patients (from 1.2 in 1996 to 5.7 in 2005) was a reflection of the disproportionate burden of disease among MSM, who accounted for ~65% of all persons with primary and secondary syphilis (Zetola & Klausner, 2007). Large metropolitan communities of MSM have been particularly affected by concurrent epidemics of syphilis and HIV infection; genital ulcers bleed frequently during sexual intercourse, resulting in potential increases in HIV infectiousness. In California more of 60% of MSM with syphilis are HIV infected, and it is estimated that, in major cities, 20-50% of MSM with syphilis have also HIV infection. The increase in the rate of syphilis and other sexually transmitted diseases (STDs) among MSM suggests a decrease in safer sex practices. In this regard, the success of HAART, the use of the Internet to meet sex partners, the increased frequency of serosorting (i.e., finding sex partners with the same HIV serostatus), and the increase in recreational drug use, both illicit (e.g., crystal methamphetamine) and prescribed (e.g., sildenafil citrate), have all likely contributed to increases in the rate of syphilis. In addition, the idea that oral sex is "safer" sex and rarely associated with HIV transmission may explain the role of oral sex in syphilis transmission (Zetola & Klausner, 2007). Recently, considering the high incidence of asymptomatic syphilis in HIV positive MSM, has been stressed the importance of frequent routine syphilis testing in this group of population. In USA, syphilis cases occurring among MSM increased from 441 in 2000 to 4424 in 2003; the estimated percentage of all reported cases occurring among MSM in 2003 was 62% (Table 3) (Heffelfinger et al., 2007). During 2000 through 2003, there was an estimated increase of 2298 cases among white MSM; in contrast, cases among heterosexual men and women decreased 50% (from 5532 to 2753) between 2000 and 2003.

In Canada, a review of infectious syphilis cases carried out in Ottawa, from 2001-2006, showed that rates of syphilis have risen more than tenfold (Leber et al., 2008) and that the majority of cases (83.5%) occurring among men who have sex with men. These individuals

differed from the general MSM population residing in Ottawa in their being older, more likely to be HIV positive, and more sexually promiscuous; inconsistent condom use by MSM engaged in either oral or anal sex was pervasive. Visceral manifestations of syphilis, including neurosyphilis, were more common in persons co-infected with HIV. Multiple sexual partners, unprotected oral sex, and increased age among MSM were the predominant risk factors contributing to this syphilis epidemic (Leber et al., 2008). Co-infection with HIV modified the clinical presentation of syphilis, necessitating a more intensive diagnostic and therapeutic approach. The interconnection of urban sexual networks has likely contributed to the dynamics of local syphilis transmission and suggests that effective interventions will require a coordinated national approach (Leber et al., 2008).

Year	Total No. of cases	Cases among men	Cases among women	Male-Female Case ratio	Cases among MSM	Cases among heterosexual men and women <sup>a</sup>
2000	5973	3528	2445	1.44	441	5532
2001	6100	4132	1968	2.10	1653	4447
2002	6862	5268	1594	3.30	3257	3605
2003	7177	5959	1218	4.89	4424	2753

a. Calculated by subtracting estimated cases among MSM from the total number of cases.

Table 3. Numbers of Primary and Secondary Syphilis Cases Among Different Groups, Along With Male-Female Case Ratios: United States, 2000-2003. (Source: Heffelfinger et al., 2007).

### 3.1.3 Australia

Syphilis appeared to be well controlled in large urban centres in Australia during the 1990s, probably as a result of HIV prevention efforts; an overall decrease in syphilis rate was seen until 2001. Since 2001, enhanced syphilis surveillance has been undertaken in south-eastern Sydney for all new laboratory syphilis notifications. The New South Wales (NSW) surveillance classifications for newly diagnosed adult cases are showed in Table 2. However, in 2002 the overall rates of syphilis increased by 14.1%, possibly related to public health activities such as active testing for STIs at selected sex-on-premise venues (Victoria), a targeted syphilis campaign coinciding with the Gay Games in Sydney in 2002 (New South Wales), and the establishment of a syphilis registry (Queensland) (Yohannes et al., 2004, as cited in Botham et al., 2006). In particular, inner Sydney has recently experienced a rapid increase in infectious syphilis, similar to other developed cities with large gay male populations. During 2001-04, 1275 syphilis notifications were received ; of these notifications 1112 were classified as 361 infectious syphilis, 221 non-infectious syphilis and 530 treated syphilis. The majority of infectious syphilis diagnoses were made in the earlier primary or secondary stages. The enhanced syphilis surveillance program showed infectious syphilis is affecting a defined population in Sydney: men (31:1 male-to-female ratio for 2004), English speaking and Australian born (Botham et al., 2006). The male-to-female ratio for 2004 of 31:1 strongly suggests transmission between men (Botham et al., 2006). The public health response to this epidemic has included work by the Sexually Transmitted Infections in Gay Men Action Group (STIGMA). This group was formed in 2000 and initiated the project for



enhanced syphilis surveillance and also developed and disseminated guidelines entitled *Sexually Transmitted Infection Testing Guidelines for Men who have Sex with Men*. These guidelines recommend annual syphilis serology for all men who have had sex with another man in the previous year; this recommendation, promoted to clinicians and the gay community, may have contributed to the overall increase in syphilis notifications. Data of literature (Jin et al., 2009) showed that in Sydney STIs peak among MSM occurred in the 35-44 year age group, suggesting a decline in sexual “safety” among older gay men, and that syphilis incidence was almost 10-fold higher in HIV-positive than in HIV-negative MSM and it was not related to a CD4 count below 350  $\mu\text{L}$ ; UAI with HIV positive partners was of particular importance in the transmission of syphilis. Within Australia, syphilis has also increased largely in gay men in the Queensland and Victoria (Bourke & Schmidt, 2009).

### **3.2 The current scenario in developing/transitional countries**

Infectious diseases continue to cause an enormous burden of death and disability in developing countries; a relevant role is represented from sexually transmitted infections. Even if the last years have seen a re-emergence of international interest in the role of MSM in STDs epidemics globally, data on their incidence and prevalence, in particular of syphilis, are still poor in most of the developing countries. This is most evident in sub-Saharan Africa, north Africa and the Caribbean, where stigma around homosexuality is still considered appalling. However, even in Asia and Latin America, studies conducted usually lack a clear understanding of these populations and their diverse behaviours (Càceres et al., 2008).

#### **3.2.1 India**

Reports from sexually transmitted disease clinics and single health care institutions in India suggest an increase in genital ulcerative sexually transmitted infections such as syphilis. The little information available on rates of syphilis in India show an incidence rate of 5.4 per 100 person years in a sexually transmitted disease clinic in India from 1993-2000 and prevalence rates as high as 21.9% amongst a convenience sample of long-distance truck drivers in 2000 (Gawande et al., 2000, & Reynolds et al., 2006, as cited in Schneider et al., 2010). A recent study (Schneider et al., 2010) carried out in Andhra Pradesh in the general population (6,235 men and 6,382 women study participants) showed prevalence rates of 2.08% for men and 1.42% for woman; nearly one in four persons surveyed that were seropositive for syphilis were also HIV infected. 85 men, that declared to have sex with men > 6 months ago, showed a syphilis prevalence of 2.4% while other 47, that declared own homosexuality within last 6 months, showed a prevalence of 6.4%. The strong association between syphilis and HIV seroprevalence in this population-based study suggests that acceleration of direct linkages between syphilis testing and HIV counselling and testing would be useful in enhancing the control of STIs and HIV in India; particular attention should be paid to homosexuals men of India that have one of the highest rates of HIV prevalence amongst groups at high risk of sexual transmission of HIV.

#### **3.2.2 Sub Saharan Africa**

In 1999, WHO estimated that were 4 million cases of syphilis among adults in sub-Saharan Africa. In Africa syphilis is endemic and the incidence is high also among

pregnant woman; this is a worrying fact because maternal syphilis has a severe impact on pregnancy outcome and there are significant challenges to implementing syphilis screening programmes in sub-Saharan Africa (Watson-Jones et al., 2005). Many prevalence studies have been conducted in the general population but unfortunately, data on the prevalence of syphilis in MSM are scanty, likely because of stigma and discrimination against homosexuality. Some studies conducted among blood donors have shown a variable prevalence among different sub-Saharan geographical areas: in Burkina-Faso a study (Nagalo et al., 2011) showed that seroprevalence of syphilis (3.96%) was lower than the prevalence of among blood donors in Tanzania (4.6% among HIV negative, 12.1% among HIV positive) (Matee et al., 2006) but higher than the 1.1% observed in Nigeria (Buseri et al., 2009), where recently no syphilis was detected among 879 examined MSM (Merrigan et al., 2011) suggesting a lower prevalence of syphilis in Nigerian population compared to other African populations. A recent study carried out in Ghana in a sample of 1366 prison inmates, including 403 homosexuals men, revealed seroprevalence syphilis rates of 13.7% and 23.3% in heterosexual and homosexual respectively and syphilis seropositivity was significantly associated with HIV seropositivity (Adjei et al., 2008). These results confirm data previously reported and emphasize the need for preventive interventions in areas such as prisons that are known to be high-risk environments for the spread of bloodborne and sexually transmitted infections.

### 3.2.3 China

Syphilis was nearly eradicated in China in 1964 (Cohen et al., 1996, as cited in Chow et al., 2011) but recently it has returned to become one of the top five most reported notifiable diseases. Has been documented a 30-fold increase in syphilis diagnoses from 0.2 cases per 100,000 individuals in 1989 to 6.5 cases per 100,000 individuals in 1999 and a further 3-fold increase over the following decade to 22 cases per 100,000 individuals in 2008 (Tucker et al., 2010, as cited in Chow et al., 2011). Cross-sectional studies have found a high prevalence of syphilis among men who have sex with men in China. Sample representativeness remains one of the challenges in effective STDs surveillance and prevention targeting men who have sex with men worldwide. Although convenience samples are widely used in studies of MSM, previous studies suggested that these samples might not be representative of the broader MSM population. This issue becomes even more critical in many developing countries where needed resources for conducting probability sampling are limited. A study carried out in Beijing during 2009 among four MSM samples using different recruitment methods showed rates of Syphilis infection of 21.8%, 36.2%, 11.8%, and 13.8%; rates of inconsistent condom use were 57%, 52%, 58%, and 38%. Significant differences were found in various socio-demographic characteristics (e.g., age, migration history, education, income, and places of employment) and risk behaviours (e.g., age at first sex, number of sex partners, involvement in commercial sex, and substance use) among samples recruited by different sampling methods (peer outreach, informal social network, Internet, and venue-based) (Guo et al., 2011). Other recent studies (Xu et al., 2011; Zhang et al., 2011) carried out in Shenyang city (in 2009) and Liaoning (from April 2008 to January 2009) showed a syphilis prevalence of 14.9% and 5% respectively. These variable results of seroprevalence confirm the importance of using multiple sampling methods to reach MSM from diverse backgrounds and in different social segments and to improve the representativeness of the MSM samples when the use of probability sampling approach is not feasible.

#### 4. Conclusion

Men who have sex with men, among all races and ethnicities, remain at great risk for HIV infection and syphilis; behavioural prevention remains central to reduce their transmission and can be the key to this process. Sex is life, but we have to be conscious of the fact that safe sex is the first premise. Sexually transmitted diseases (STDs) are among the first ten causes of unpleasant diseases in young adult males in developing countries and the second major cause of unpleasant diseases in young adult women worldwide. In general, STDs are epidemics and present enormous health and economic consequences. The surest way to avoid transmission of sexually transmitted diseases, including syphilis, is to abstain from sexual contact or to be in a long-term mutually monogamous relationship with a partner who has been tested and is known to be uninfected. Avoiding alcohol and drug use may also help prevent transmission of syphilis because these activities may lead to risky sexual behavior (Zetola & Klausner), (Mayer et al. 2010). It is important that sex partners talk to each other about their HIV status and history of other STDs so that preventive action can be taken. An adequate screening for re-emerging STDs should be done on a routine basis in every part of the world, in particular among highly vulnerable subjects at risk for HIV and syphilis as homosexual men; individuals unaware of their infection are a priority for being tested and diagnosed to enable them to take advantage of care services and receive counselling to prevent further spread of HIV and *T. pallidum*. Partner selection based on perceived serostatus could be used as a strategy for risk reduction among MSM but it strategy has some limits since those most recently infected may be most infectious and least likely to know of their status, reliance on partner's awareness and disclosure of their own serostatus may be a risky strategy. Individuals who are infected with STDs are 5-10 times more likely than uninfected individuals to acquire or to transmit HIV through sexual contact. The breaking of the genital tract or trauma of the rectal mucosa creates a portal of entry for HIV, and HIV positive individuals co-infected with other STDs, especially ulcerative infections such as syphilis, are more likely to shed HIV in their genital secretions. The most effective method available for protection against STDs and HIV is the correct and consistent use of condom that is increasing everywhere except in developing countries. In particular, high risk sexual behaviours reported in Africa and in India among MSM and high levels of bisexual activity are of grave concern. Most worrisome is that condom use messages for preventing HIV and STDs do not appear to have penetrated this population given the low proportion of MSM using condom ; three most often repeated reasons for not using condoms with regular partners include non availability, feeling the partner is safe and feeling that condoms do not give sexual pleasure (Kumta et al., 2010). Interestingly, a study carried out in the south-eastern part of India (Andhra Pradesh) showed that one of the primary reasons for low condom usage was that many married MSM did not disclose their sexual orientation to their wives and therefore struggled to explain the necessity of condom use (Gutierrez et al., 2010). This datum suggests that in some parts of the developing world prevention work is handicapped unless it addresses broader issues surrounding sexual identity, stigma and discrimination. Internet is commonly used by MSM to find sexual partners. The net is a relatively safe space where sexuality can be addressed in a frank and honest way because the web allows anonymity and confidentially. In a context where homosexuality is penalised, blackmail and police harassment are common and the media are homophobic, internet may be a way to support and inform men who have sex with men about HIV/STDs and other issues which men ask about (Pebody, 2010). For example, in

Romania, Kovacs used a sexual networking site to build a support network of HIV positive MSM (an extremely marginalised and, until then, invisible group in Romania). In another example, in Thailand, Mplus Organisation works with various groups including men selling sex, transgender people and MSM; the organisation lets their existing contacts know that staff will be present on various social networking sites and MSM Messenger at specific times, where they are available to interact and answer questions (Pebody, 2010). These data suggest that Internet is a double edged sword because on the one hand promotes sexual encounters and promiscuity, on the other hand can help prevent the spread of HIV and other sexually transmitted infections such as syphilis. Interestingly, during a recent syphilis outbreak that involved 7 MSM in San Francisco who met in an online chat, electronic notification of the cluster was provided to hundreds of chat room users. Despite very limited contact information, the Department of Public Health was able to notify and treat 42% of the named sex partners (Klausner et al., 2000). The major challenge for the future is to reduce the rates of new infections in a context of increasingly diverse and complex prevention responses. A key requisite for this development is the occurrence of transformations that tackle homophobic violence and ensure the respect for the human rights of gay men, transgenders and other MSM.

In conclusion, more research is need to further clarify which strategies (i.e. reducing unprotected anal sex, condom distribution, having oral sex instead of anal sex, reducing number of partners, avoiding serodiscordant partners, strategic positioning or reducing anal sex even with condom use) are most effective in reducing sexually transmitted infections transmission among MSM, the messages most effective in promoting preventive behaviours, and the methods and settings in which these messages can be most effectively delivered.

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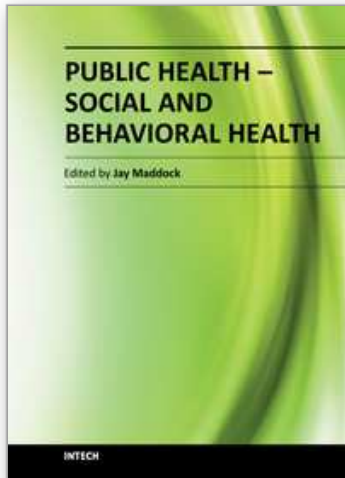
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