

Global HIV Cohort Studies among Injecting Drug Users and Future Vaccine Trials

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The author reviewed the most recent data on the global HIV epidemic among Injecting Drug Users (IDUs) and summarized potential cohorts of IDUs that could participate in future HIV vaccine trials. An additional review of molecular epidemiology was described by region for better understanding of the state of the epidemic and potential impact on the development of HIV preventive strategies. From 1980 to mid-2005, increases in the prevalence rate were observed in many countries in Asia, Eastern Europe, Latin America and the Caribbean, and Canada among IDU. The HIV epidemics in some of these countries could rapidly expand if appropriate preventive measures are not undertaken. From cohort studies, high incidence rates were identified in China, Thailand, Canada, and Spain. Several studies also showed high participation and retention rates of injecting drug users that emphasized their potential to be volunteers in future vaccine trials.

Keywords: HIV/AIDS, Incidence, Prevalence, Injecting drug user, IDU, Vaccine, Cohort

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By the end of 2004, the HIV/AIDS pandemic had already spread to more than 60 million people worldwide, and at least 39.4 million were living with HIV/AIDS^(1,2). Around five million people were newly infected and more than 3 million lives were lost to AIDS in 2004. Although we are now in the third decade of the epidemic, there are still new infection cases in virtually every affected country, and HIV's spread continues to occur in new regions, populations and birth cohorts. Recent reports from Joint United Nations Program on HIV/AIDS (UNAIDS) and World Health Organization (WHO) show that the pattern of HIV transmission has been changing in many countries. One of the emerging problems is spread among injecting drug users, which has rapidly increased in many parts of the world since 2003. In Russia, Ukraine, Belarus and the Central Asian Republics of Kazakhstan and Tajikistan, and further east in China, Iran, Malaysia, Indonesia and Vietnam,

the majority of reported HIV infections and AIDS cases in 2001 arose not from sexual transmission but through needle-sharing behaviors among Injecting Drug Users (IDU)^(1,2). Overall, the number of countries reporting HIV infections among IDU to the World Health Organization rose from 52 in 1992 to 114 in the year 2000, underscoring the widening global nature of IDU risk⁽¹⁾. As of 1999, UNDP estimated that there were roughly 20 million injecting drug users in 134 countries⁽³⁾.

In a recent report of UNDCP, it was estimated that the cumulative number of HIV infections among injecting drug users may have reached as high as 3.3 million by the end of 2000⁽⁴⁾.

Even though the HIV epidemic was identified more than 20 years ago, the only public health tools and prevention strategies we have to control the epidemic are education, condom promotion, risk reduction strategies, drugs for prevention of mother to child transmission, and highly active antiretroviral therapy. For prevention of transmission among drug users there are several strategies with sound evidence of efficacy, including drug treatment and substitution therapy for heroin injectors, harm reduction approaches and

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needle and syringe exchange⁽⁵⁻¹⁰⁾. Unfortunately, these prevention strategies have been proven highly politically sensitive in a number of states, and their implementation and use have been much less widespread than the scale and scope of the global IDU HIV epidemic would suggest is warranted^(3,11,12).

All of these measures are definitely effective to control transmission, and some can slow progression of disease in infected cases. But new infections continue, thus, many believe that other additional effective strategies are needed to control HIV epidemics. Most prominent among these are HIV vaccines.

The increasing genetic diversity of HIV-1 is a further challenge to vaccine development. Without evidence of efficacy or a validated correlate of protection or disease amelioration, vaccine research has struggled to understand what components of HIV variability are of import. To make a HIV vaccine to effectively induce both neutralizing antibodies and Cytotoxic T-Lymphocyte (CTLs) is a major obstacle. Other barriers include the possible differences in immune responses to different modes of transmission, and the difficulty of identifying appropriate cohorts for vaccine efficacy trials - both challenges may have particular relevance for IDUs.

Some studies on HIV-1 incidence in IDUs have shown high rates; these include IDU cohorts in Thailand, China, Canada, and some in Europe^(12-20,22-30). These findings not only emphasize the seriousness of the IDU problem but also indirectly alert us to think about the potential of IDUs to act as the volunteers in future research, including vaccine trials. An outstanding example is the IDU cohort that participated in Phase III AIDS VAX trial in Bangkok, Thailand, the first HIV-1 vaccine efficacy trial in a developing country. This cohort had evidence of a high seroincidence rate in the lead-in study, measured at over 5/100PY⁽²⁸⁾, and, after the trial finished, the annual infection rate was estimated to be 3.1% in both placebo and vaccine groups with more than 90% of the volunteers completed their 3-year commitment to the study⁽³¹⁾. Clearly, the more information researchers have on at-risk cohorts, the more chance that global HIV prevention and control can be accomplished.

The present paper attempts to review the information published on the global HIV epidemic among IDUs, and to identify the available data on potential cohorts of IDUs for future vaccine trials.

Material and Method

The author searched the literature in MEDLINE, Journals@Ovid Full Text, and PubMed from 1980

through mid-2005, using the terms HIV, AIDS, Incidence, Prevalence, Epidemiology, injecting drug user, and IDU. Only articles written in English were reviewed. Additionally, the references from each article were reviewed and the unpublished reports and additional data that may have been missed during the research process were identified. The information on global epidemiology of HIV among IDUs were obtained from various sources, including reports by National AIDS Programs, World Health Organization, UNAIDS, UNDP, UNODC, other related agencies and published papers and articles. The most updated data was selected to be used and summarized in this review. Additional information on molecular epidemiology was reviewed and added to complete the understanding on global HIV/AIDS epidemic among IDUs.

For incidence data, the author included the studies that: 1) were conducted in any parts of the world; 2) contained HIV incidence data for IDUs; 3) indicated geographical area and the year of data collection. The author excluded those studies that: 1) had multiple reports from the same results (only the most recent one was selected); 2) only described demographic characteristics without definite data on incidence rate or incidence density.

For those incidence studies, the information extracted from eligible studies consisted of location, year of study, population source, cohort size, seroincidence (per 100 person-year), method of study, retention rate, viral clade represented and principal investigators. Seroincidence was measured as the number of seroconversions per 100 Person-Year (PY) in the follow-up unit. In cases where different units were used, the author recalculated such data into a 100 PY unit.

Prevalence data was reviewed and described in descriptive fashion categorized by region. Molecular epidemiology was also concisely described and summarized only the main characteristics in IDUs specific for each region. Incidence data was tabulated into tables, consisting of studies from US, Canada, Europe, and Asia.

Results

1) Update on global distribution of HIV epidemic in IDUs

a) Asia and the Pacific

More than 1 million people in Asia and the Pacific acquired HIV in 2004, cumulatively bringing to an estimated 8.2 million people currently living with the virus^(1,2). Throughout the region, injecting drug use

accounts for much of the rapid growth of HIV epidemic. More than 50% of IDUs have already contracted the virus in parts of Malaysia, Myanmar, Nepal, Thailand and in Manipur in India^(1,2).

In China, serious HIV epidemics are occurring among IDUs in at least nine provinces, including Beijing Municipality. Of these, the most recent outbreaks of HIV among IDUs have been observed in Hunan and Guizhou provinces, with HIV prevalence rates of 8% and 14% respectively. Additionally, over half of all 25 IDU sites detected HIV infections with the prevalence ranging from 1% to 80% in Yunnan, Xinjiang, Guangxi, and Sichuan provinces. The National Surveillance System has estimated that around 90% of cumulative numbers of HIV infections are related to injecting drug use (up to 70%) and to faulty plasma collection procedures (10-20%)^(1,2,32,33).

In Indonesia, drug injection is now growing in urban areas with 124,000 to 196,000 estimated IDUs, among whom HIV prevalence has risen steeply; from 0% in 1998 to 50% in 2001. National estimates indicate that more than 43,000 IDUs have become HIV infected so far^(1,2).

In Vietnam, a country with more than 78 million citizens, 88% of all reported HIV infections in 2000 were from injecting drug use, with HIV prevalence around 65%. HIV prevalence among IDUs was reported as high as 89% outside urban areas. Recent evidence also revealed a considerable proportion of street-based sex workers associated with drug injection (20-40%)⁽³⁴⁾.

In Myanmar, as of June 2000, a total of 29,636 HIV cases with 4,063 AIDS cases had been reported by the Ministry of Health, and these reports are generally considered to grossly underestimate the actual burden. Recent estimates of 530,000-640,000 persons living with HIV in 2000 are conservative. Nevertheless, 30% of reported HIV cases were from injecting drug use. In 1999, HIV prevalence among IDUs reached 54% that was equivalent to 57% in commercial sex workers. In 2000, with the estimated number of 150,000-250,000 IDUs, the prevalence rate was rising up to 63%⁽³⁵⁾.

In Thailand, rising HIV prevalence was observed in IDUs at the level of 38% in 1996, 42% in 1998, and as high as 50% in 2002^(2,36). Moreover, as of 2002, IDU accounted for 5.25% of cumulative HIV infected cases. It was estimated that 10-20% of 1,270,000 drug users were IDUs⁽³⁶⁾.

In India, there were at least 2,225,000 drug users with 25-30% of them involved in drug injection. HIV prevalence has been reported between 9-64% among IDUs during the past few years. A high preva-

lence rate was found in certain areas such as 80% in Manipur, 45% in Delhi, and 31% in Chennai^(32,33,36).

In Nepal, during the late 1990s, HIV prevalence had been reported at the level of 50% or higher among IDUs⁽⁶⁾. One study in Katmandu has documented prevalence rate rising from 0 to 40% between 1995 and 1997⁽³⁷⁾.

b) Eastern Europe and Central Asia

During the past decade, up to 90% of HIV epidemics in this region have been attributed to injecting drug use^(1,2).

In Russia, 56% of IDUs in Togliatti city were found to be HIV positive in 2001, whereas 33% were detected among needle-exchange attendees in Rostov-Don. In 1999, some estimates suggested that there were 700,000 IDUs in Russia, 20 times higher than in 1990. For female IDU sex workers, limited data shows that HIV prevalence was also very high, ranging from 17% in St. Petersburg to 61% in Togliatti, and 65% in Kaliningrad^(3,38,39).

In the Ukraine, 60% of new infections were from IDUs in 2001, declined from more than 80% in 1997⁽¹⁾. Seropositivity among registered IDUs increased from virtually zero before 1995 to 2% in 1995, and 7% in 1996⁽⁴⁰⁾. In the city of Odessa, there were 35,000-40,000 estimated IDUs at the end of 1999, i.e., 500% up from 1990⁽³⁾.

In Belarus, 67% of IDUs were HIV positive, and 87% of new infections by the end of 1997 were attributed to injecting drug use⁽³⁾.

In Poland, 50% HIV prevalence was reported among IDUs in Szczecin, and 60% in small sample in Lublin⁽⁴⁰⁾.

For other countries such as Slovenia, Czech Republic, Croatia, and Slovak Republic, the results from several surveys showed that HIV prevalence were very low among IDUs⁽⁴⁰⁾.

c) Latin America and the Caribbean

As of 2002, injecting drug use accounted for at least 40% of new infection in Argentina and 28% in Uruguay⁽⁴¹⁾. HIV prevalence study in Buenos Aires city in Argentina was reported at the level of 43.3% with the predominance of B/F recombinant⁽⁴²⁾.

In Brazil, 21.3% of total AIDS cases were from injecting drug use. A survey conducted between 1990 and 1992 in Santos showed 62% seropositivity⁽⁴¹⁾.

In Mexico, sentinel surveillance showed 6% HIV prevalence among IDUs in 1998 with high percentage of needle sharing (around 30%)⁽⁴¹⁾.

d) Middle East and North Africa

Although this region is one of the least affected by HIV/AIDS epidemic, significant outbreaks among IDUs have occurred in about half the countries, especially in North Africa and in the Islamic Republic of Iran. Recent reports indicated that IDUs accounted for 91.7% of total HIV/AIDS cases in Libya in 2001, 73% in Bahrain in 2000, 34% in Tunisia in 1999, and 18.4% in Algeria in 2000⁽³²⁾. In Iran, 1% of the estimated 200,000-300,000 IDUs was believed to be HIV positive, whereas HIV prevalence among imprisoned drug injectors was 12% in 2001⁽²⁾.

e) US and Western Europe

For Western Europe, HIV epidemic among IDUs is most concentrated in the south where IDUs account for 66% of AIDS cases in Spain, 64% in Italy, and 61% in Portugal^(1,2,32). Reported HIV prevalence among IDUs in Spain in 2000 was 20-30% nationwide, while, in France the prevalence rate ranged from 10% to 23%^(1,2). In some countries, increases in HIV prevalence have been identified. In Italy, from 1997 to 2000, HIV prevalence increased among IDUs routinely tested in drug treatment in the regions of Sardinia (20, 22, 24, and 30%), Emilia-Romagna (22, 28, 27, and 33%), Trentino (17, 18, 17, and 23%), and Piedmont (13, 11, 12, and 15%). In the Netherlands, an increase was observed in the city of Heerlen, from 16.5% in 1996 to 21.6% in 1999⁽⁴³⁾.

However, a decrease in HIV prevalence had been observed in studies repeated over time in several countries or cities, including Copenhagen (from 20% in 1985 to 9% in 1990), Stockholm (16% in 1987 to 5% in 1995), Italy (31% in 1990 to 23% in 1993 nationally, and 44% in 1990 to 37% in 1993 in Lombardy), Spain (74% in 1986 to 59% in 1990 in Madrid, and 59% in 1987 to 44% in 1992 in Valencia), Switzerland (38% in 1985 to 3% in 1994, but increased to 6% in 1995), Edinburgh (9% in 1989 to 4% in 1991), and Tayside (Scotland, 3.6% in 1993-1997)^(44,45).

In US, injecting drug use is still a prominent route of HIV infection, accounting for 14% of all reported HIV diagnoses as of 2002. A study in New York, conducted between 1991 and 1996, showed that there was an average 2.67% decline in HIV prevalence among IDUs per year (from 50% in 1991 to less than 30% in 1996). Other studies in various cities also showed a similar trend in HIV prevalence among IDUs⁽¹¹⁾.

In Canada, IDUs accounted for 6.9% of cumulative AIDS cases and 16.4% of cumulative positive HIV test reports up to June 30, 2002. 47% of new infec-

tions in 1996 were also from IDU. Results from Winnipeg Injection Drug Epidemiology (WIDE) study showed that HIV prevalence among IDUs in that city increased from 2.3% from 1986-90 to 12.6% in 1998. A seroprevalence survey among IDUs in Victoria, BC, showed that 21% were HIV positive, higher than the 6% found in 1990s. From the Vancouver Injection Drug Users Study (VIDUS) between 1996 and 2001, the prevalence among IDUs aged 24 years and younger was reported at 17%⁽⁴⁶⁾.

f) Sub-Saharan Africa

Pockets of IDUs have been reported in several countries including Kenya, Mauritius, Nigeria, and South Africa. In Nigeria, a study conducted in Lagos in 2000 revealed that more than 20% of street-based drug users were injecting. The prevalence of 11% among IDUs in the Lagos study was higher than the national average of 5.4% in the same year⁽³²⁾.

HIV and genetic diversity

The main characteristic of HIV epidemic is genetic variation. Multiple subtypes of HIV have been identified and can recombine with each other to be specific recombinant strains that are known as Circulating Recombinant Forms (CRFs). Those CRFs have been found in widespread epidemics. Up to now, there are at least nine genetic subtypes and fifteen CRFs worldwide, each has its own characteristics regarding the prevalence and geographic distribution. Some of them have just been identified among IDUs such as in Thailand (CRF01/B), Argentina (B/F recombinant), and in Spain and Portugal (B/G recombinant). However, HIV pandemic generally composed of four main subtypes with high prevalence and additional two important CRFs that can be summarized as the following^(47,48):

1. Subtype A: mainly in East Africa and the former Soviet Republics
2. Subtype B: The Americas, Western Europe, and Australia
3. Subtype C: Southern Africa, Horn of Africa, and India
4. Subtype D: East Africa
5. CRF01_AE: mainly in Southeast Asia
6. CRF02_AG: West and West Central Africa
7. CRF07_B/C and CRF08_B/C: China and Myanmar

Additionally, most other subtypes (e.g. F, G, H, J, K) and important CRFs are found in Central Africa.

The impact of a growing HIV epidemic among IDUs has definitely been involved with genetic vari-

ability issues. New CRFs have been generated in the past few years by mixing of multiple HIV-1 subtypes. These characteristics have been revealed in several recent IDU epidemics such as Nepal, China, Finland, the former Soviet Republics, Spain, Argentina and Thailand^(47,48). These variants may result in difficulties in “matching” appropriate vaccine candidates to novel subtypes and CRFs. However these findings also emphasize the need for IDUs to be considered as potential volunteers in vaccine trials in multiple regions.

2) Incidence data

The author found a relatively limited number of eligible papers with incidence data in IDU: 10 conducted in the US, 7 in Canada, 6 in Europe, and 5 in Asia, shown in Table 1-4 and Fig. 1-4. HIV incidence varied widely in different settings, and among IDU population characteristics. Several studies were excluded as they were using the same cohort. For HIV incidence in US, a total of nine cities were included in all studies with the incidence rate ranging from 0.38 to 8.4 per 100 PY depending on time and place of the study. All studies showed declining trends of HIV incidence among IDUs. Interestingly, at least three studies reported the data on annual retention rates of IDU cohorts at moderate to high levels, varying from 50% to 94% at 1 year, with one study reporting 88% after 18 months.

Among seven studies in Canada, although the HIV incidence was declining, the evidence of high incidence in some specific cities and populations has been identified such as in Montreal, Vancouver, and among Aboriginal male IDUs. Moreover, the average incidence in Canada has still been shown at the higher level than in US during the same time period. Similarly to the US, a more than 80% annual retention rate was reported in two studies.

In the past decade, six studies of HIV incidence among IDUs were conducted in Europe, including studies in Italy, Germany, Spain and the Netherlands. HIV incidence was highest during 1992-1994 in Rome, Italy at the level of 39.3 per 100 PY. The incidence rate in remaining studies ranged from 0.69 to 8 per 100 PY and one report showed the declining trend.

Five studies were identified in Asia with a strikingly high HIV incidence among IDUs. The studies were conducted in two countries, i.e., 2 in China and 3 in Thailand. In Thailand, the incidence decreased from the range of 11-57 per 100 PY before 1995 to 5.8 (4.8, 6.8) in Bangkok and 7.2 in Chiang Mai after 1995. For Longchuan County in China, the incidence was found

to increase over time from 10 per 100 PY in 1991 to 30 in 1994. A similar picture was seen in Pingxiang City, China, from 2.38 (0.9, 6.44) per 100 PY in 1998 to 6.86 (2.2, 15.6) in 1999. Very high annual retention rates were reported in two studies from Thailand, from 98% at 12 months to 71.2% at 36 months. However, the results from the studies in Asia have released some clues about the probability of new wave of HIV epidemic that may affect the global picture of HIV infection.

Discussion

The results from this review indicate that IDUs are an emerging factor that may determine the HIV situation in many parts of the world. Prevalence data from countries in Asia, Eastern Europe, Latin America and the Caribbean and Canada, shows significant increasing trends. In addition, some countries in Middle East, North Africa and Sub-Saharan Africa have also revealed the rising trend of seropositivity among IDUs. From the incidence studies, although declining trends of HIV incidence have been observed in many papers, some of them still had a high incidence among specific IDU groups or in specific cities such as in China, Thailand, Canada, and Spain.

The difference in prevalence and incidence data observed in these studies may be from many factors. The difference in patterns of drug abuse in each country that may have an impact on HIV transmission such as IDUs in some countries use cocaine (e.g. Argentina), but some countries use heroin (e.g. Asia). This may influence the frequency of injection. Government policies also have direct effects on drug using populations, including such policies as distribution of sterile or clean needles to IDU group, availability of drug treatment, and specifically of substitution therapy for opiate users.

Another dimension of concern is the linkage between IDUs and heterosexual transmission of HIV in some countries such as Brazil since the mid-1980s, more recently in Argentina, Uruguay, and Vietnam^(32,58,59). A large number of AIDS cases are occurring among non-injecting female sex partners of male IDUs. An additional linkage between IDU and heterosexual transmission of HIV lies in the association of injecting drug use in females and their involvement in unprotected sex and in commercial sex, as shown by current field research taking place in Vietnam, Brazil and Argentina^(58,59). While data in Brazil shows a change in IDUs, using safer injecting practices, no such behavioral change seems to be occurring in their sexual practices. Compounding the risk of heterosexual

Table 1. HIV incidence studies among injecting drug users in US

Location	Year	Population Source	Cohort Size	Seroincidence/ 100 PY	Method of Study	Retention Rate	HIV-1 Clade	Author [reference]
Baltimore, MD	1988-1998	HIV negative IDUs	1,532 plus additional 338 in 1994	overall 3.14 (2.78, 3.53) 4.45 in 1988-90 3.35 in 1991-94 1.84 in 1995-98	prospective	1,532 (70%) at 1 yr. 338 (93%) at 1 yr.	B	KE Nelson [49]
Bronx, New York	1985-present	IDUs in methadone maintenance program	622	1.7	prospective	NA	B	Harel DM [50]
Chicago	1988-1992	Out-of-treatment IDUs	641	8.4 in 1988 2.4 in 1992	prospective	NA	B	Wiebel WW [51]
Columbia, NY	July 1997-May 1999	Street-recruited IDUs 15-30 yrs and injecting =5 yrs	226	6.6 (2.2,13.3)	prospective	50% at 12 months	B	Fuller CM [52]
New York	1997-1999	18-30 yrs IDUs	241 IDUs	overall 0.4 (0.0,2.5)	prospective	NA	B	Des Jarlais DC [53]
Nine Cities in US	1995	4892 seronegative IDUs in 15 sites from 9 cities	1,124 IDUs	0.38 in male IDUs 1.24 in female IDUs	prospective	94% at 6 months 89% at 12 months 88% at 18 months	B	Seage GR [54]
Rhode Island	1989-1997	women in prison	1,081 for those reincarcerated	0.6 (0.3,1.1)	prospective	NA	B	Rich JD [55]
San Francisco	1987-1998	Street-recruited IDUs	8,065 IDUs	1.2 (0.7,2.0)	S/LS EIA semisurvey	NA	B	Kral AH [56]
San Francisco	1993-1999	persons with voluntary HIV testing at least twice	2,893 in a county hospital	overall 1.4 (1.2,1.7) IDU 2.0 (1.6,2.4) MSM and IDU 3.8 (2.7,5.1)	retrospective	NA	B	Kellogg TA [57]

NA: Not available; S/LS EIA: Sensitive/Less sensitive Enzyme-linked Immunosorbent Assay

Table 2. HIV incidence studies among injecting drug users in Canada

Location	Year	Population Source	Cohort Size	Seroincidence/ 100 PY	Method of Study	Retention Rate	HIV-1 Clade	Author [reference]
Montreal, Canada	1992-1998	IDUs with at least three visits	833	30.42 for consistent sharers 13.78 for inconsistent sharers 2.51 for non sharers	longitudinal study	NA	B	Brogly SB [13]
Ontario, Canada	1992-2000	persons with voluntary HIV testing at least twice	38,167 repeat testers (IDUs)	0.64 (0.18,1.1) in 1992 0.14 (0.02,0.27) in 2000	Poisson method	NA	B	Calzavara L [14]
Quebec and Ontario,	1999	IDUs in setting other than NEPs	1,386	3.8 (0.5,7.0)	prospective	NA	NA	Hankins C [15]
Vancouver, Canada	1996-2001	13-24 yrs of IDUs	234	Male 2.96 Female 5.69	prospective	NA	B	Miller CL [16]
Vancouver, Canada	1996-2001	HIV negative IDUs	941	Aboriginal Male 19.4 Non-Aboriginal Male 9.2 Aboriginal Female 20.2 Non-Aboriginal Female 9.4	prospective	NA	B	KJP Craib [17]
Vancouver, Canada	May 1996-1997	IDUs	257	18.6 (11.1,26.0)	prospective	83%	B	Strathdee SA [18]
Vancouver, Canada	1996-1998	IDUs in the downtown, eastside of Vancouver	934	11.8 (10.1,13.5) in frequent NEPs 6.2 (4.7,7.7) for non-freq	prospective	694 (80%)	B	Schechter MT [19]

NA: Not available; NEPs: Needle exchange programs

Table 3. HIV incidence studies among injecting drug users in Europe

Location	Year	Population Source	Cohort Size	Seroincidence/ 100 PY	Method of Study	Retention Rate	HIV-1 Clade	Author [reference]
Rome, Italy	Jun 1992- Dec 1994	voluntary HIV testers	709 (12 IDUs)	39.3 for IDUs	retrospective	NA	NA	Giuliani M [20]
Northern Italy	1993-1999	IDUs attending drug dependence treatment center	7,945	overall 0.69 (0.58,0.82) 0.55 (0.44,0.68) for male 1.4 (1.03,1.87) for female	prospective	NA	NA	Sabbatini A [21]
Italy	1989-1996	repeat HIV testers in 47 STD centers	1,950	overall 1.7 (1.2,2.2) Heterosexual IDUs 2.4 (0.1,4.7) homosexual IDUs 13.8 (1.8,29.5)	retrospective	NA	NA	Suligoi B [22]
Valencia, Spain	1987-1996	IDUs	4,023	6.85 (6.04,7.66)	cohort study	NA	B/BF	Hernandez-Aguado [23]
Berlin, Germany	1993-1994	IDUs from multiple agencies	191 IDUs	overall 5.9 (2.7,11)	longitudinal study	65% at least two visits (8-12 months)	B	Stark K [24]
Amsterdam, The Netherlands	1986-1997	IDUs	879	8 in 1986 4 in 1991-1997	prospective	NA	B	van Ameijden EJC [12]

NA: Not available

Table 4. HIV incidence studies among injecting drug users in Asia

Location	Year	Population Source	Cohort Size	Seroincidence/ 100 PY	Method of Study	Retention Rate	HIV-1 Clade	Author [reference]
Longchuan county, China	1991-1994	IDUs	433	10 in 1991 30 in 1994	cohort study	NA	NA	Wu Z [25]
Pingxiang city, China	Feb 1998 - Sep 1999	heroin users	318 through Jan 1999 130 through Sep 1999	2.38(0.9,6.44) till Jan 1999 6.86 (2.2,15.6) till Sep 1999	prospective (Poisson method)	NA	NA	Shenghan L [26]
Bangkok, Thailand	1987-1992	IDUs in drug detox. units	5,974	20 in 1987 57 in 1988 11 in 1991-1992	retrospective	NA	E, B	Kitayaporn D [27]
Bangkok, Thailand	1995-1998	IDUs attending methadone treatment program aged 18-50 years old	1,209	5.8 (4.8,6.8)	prospective	1124 (93%) at least 1 F/U visit 88.2% at 12 months 75.9% at 24 months 71.2% at 36 months	HIV-1 subtype E (79%), B (21%)	Vanichsemi S [28]
Chiang Mai, Thailand	1999-present	IDUs/non-IDUs in DTC	348 IDUs 532 non-IDUs	7.2 for IDUs 2.98 overall	cohort study	98% at 1 yr 96% at 2 yrs	AE CRF01AE/B	Suriyanon V [29, 30]

NA: Not available; DTC: Drug treatment center

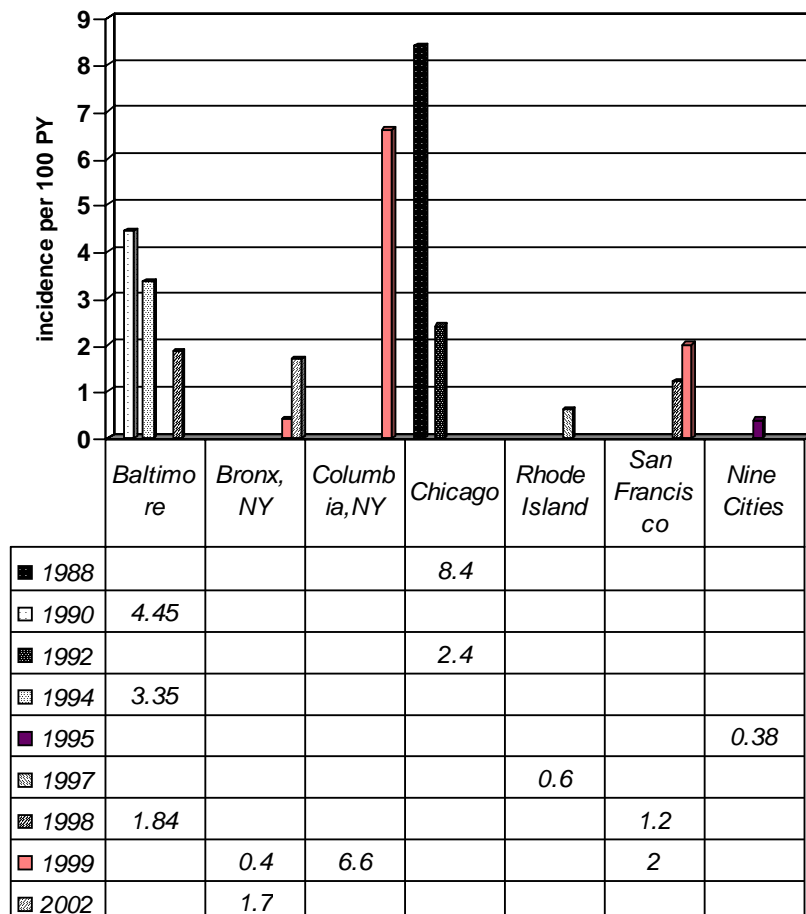


Fig. 1 HIV incidence per 100 person-year (PY) among injecting drug users in US*
 * Details of the studies are in Table 1

transmission, users of illicit drugs have higher levels of HIV infection than non-users according to recent data on blood donors in Rio⁽⁵⁸⁾.

The genetic diversity of HIV remains challenging for those in vaccine research. The variation in subtypes and different recombinants of HIV and their relationship to modes of transmission have also complicated the situation in several countries. When the author compares infections through mucosal transmission and injecting drug route, there may be a higher possibility for injection to transmit higher amounts of viruses directly to newly infected persons. This does not mean only a high rate of transmission, but it also includes the chance for super-infection as well. The injection route could possibly advance the probability of viral mutation and the chance of many types of recombination such as intra-subtype, inter-subtype and inter-group recombination⁽⁴⁷⁾. Conversely, when a

variant spreads among a network of injectors, inter-personal variability can be strikingly low, compared to the diversity seen in sexually propagated outbreaks, which suggests other differences. Understanding the impact of route of transmission on molecular epidemiology will be difficult without more thorough information about the molecular epidemiology of HIV infection among IDU and non-IDU populations and the current epidemic situation where multiple modes of transmission occur.

In the past, many researchers held that IDUs might not be good candidates for vaccine trial due to their high chance of lost-to-follow-up and other limiting factors that could prevent them from participating in studies, such as imprisonment, socio-economic status and education. From the present review, there is evidence suggesting that IDUs can successfully participate in vaccine studies. The results from several

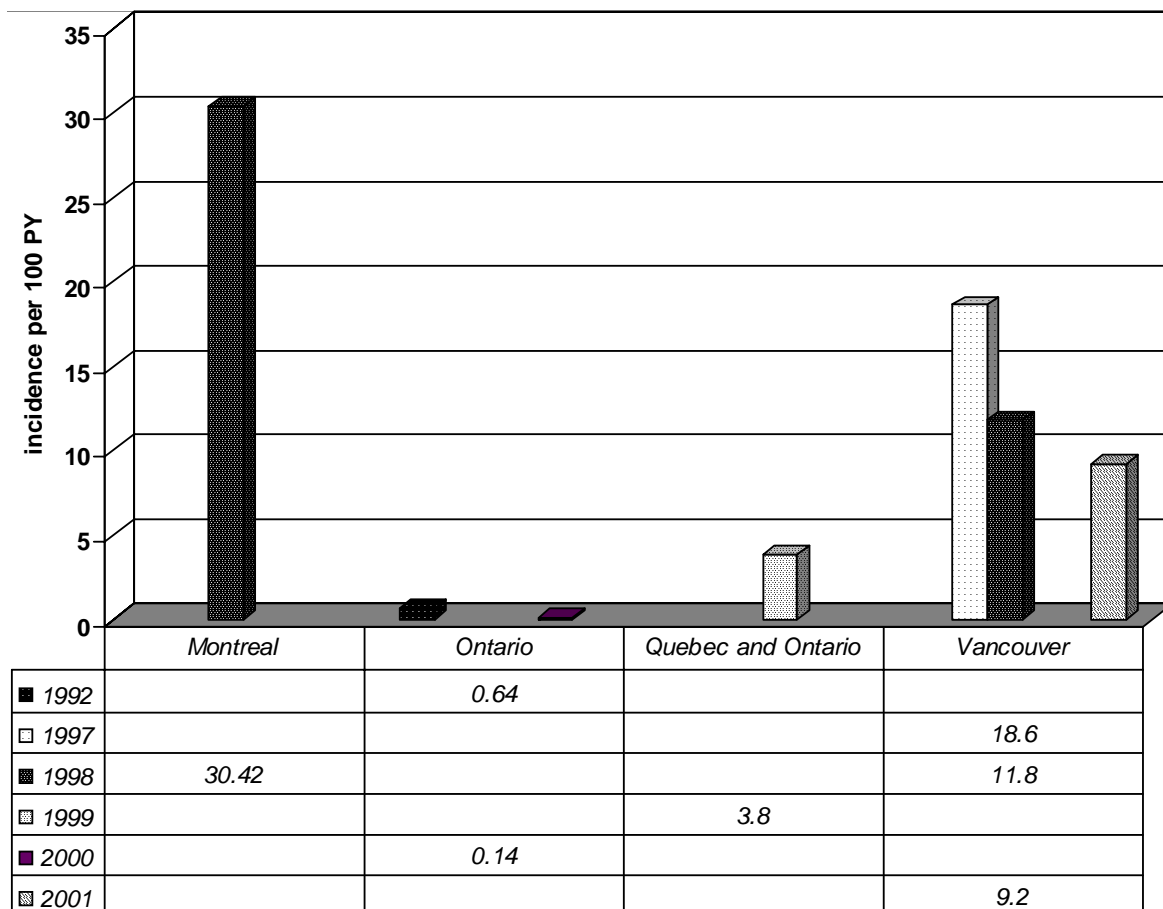


Fig. 2 HIV incidence per 100 person-year (PY) among injecting drug users in Canada*
 * Details of the studies are in Table 2

incidence studies have shown a very high follow-up rate (annual retention rate), especially in high incidence areas such as Thailand, China and Canada. Other countries with high follow-up rate are the US and Germany. Additionally, in the real world, Phase III HIV vaccine study in Thailand has shown that IDUs could be recruited as volunteers with a very high retention rate.

However, the author can observe that most of the studies that were conducted in the past till present had mostly male IDU population. This may be explained by many reasons such as the nature of IDU in some countries is confined mostly in the male population. Some countries (e.g. in Asia) reported that female sex workers also used injected drugs and were summarized in the sex worker group instead of the IDU group.

Other factors that need to be taken into consideration before recruiting IDUs are their population characteristics in specific area, ethical issues and

human rights. For example, the debate may occur if the researchers recruit IDUs only from prisons. Concerns will occur regarding the decision and human rights of the volunteer whether he/she voluntarily participated or not. Although the earlier example is shown as a disadvantage for utilizing IDUs as the volunteers, there may be the possibility to have advantage to use IDUs. In Thailand, some IDUs have their own networks in the community. If one of IDUs participates in the study, there is a high chance that other IDUs in his/her networks may join the study with volunteer's referral or invitation. Moreover, this kind of network could increase the understanding of the study, and also increase the follow-up rate.

Finally, wherever an IDU group is to be considered as a potential volunteer cohort, the survey of interest for participation in the trial should be conducted as well as planning for education about vaccines, the

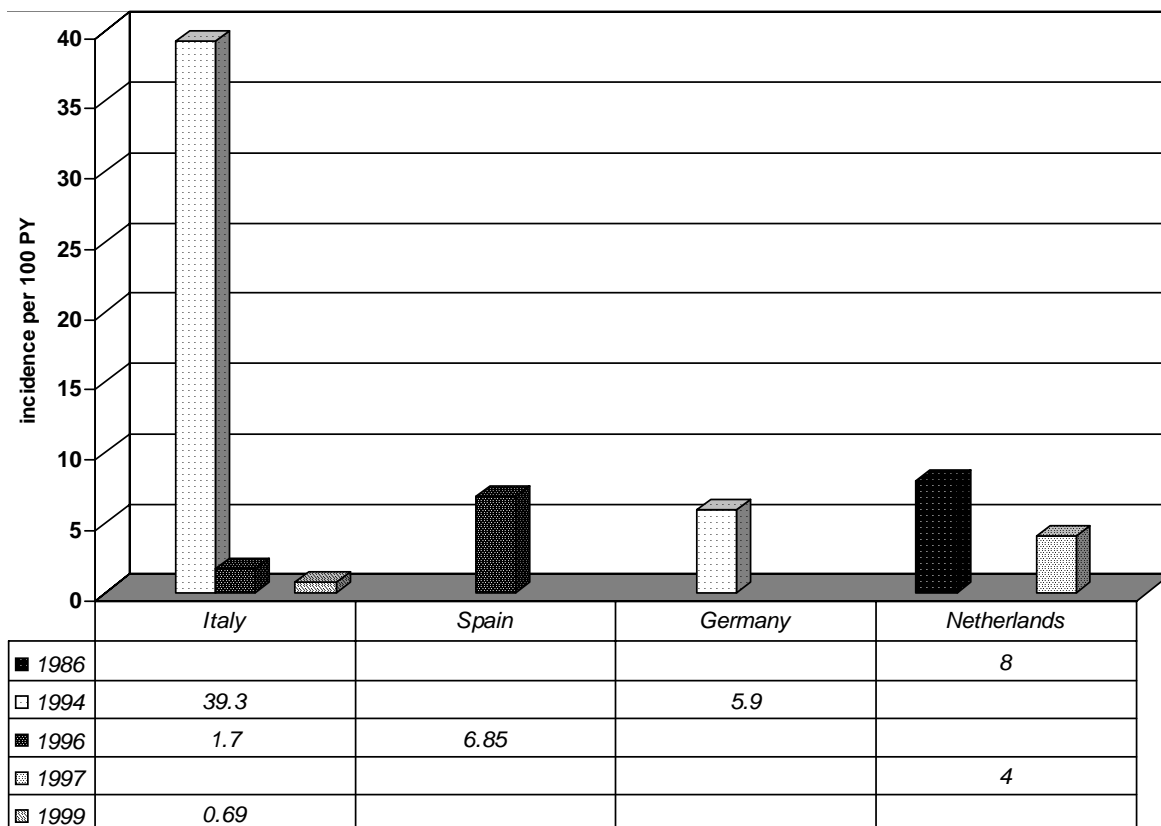


Fig. 3 HIV incidence per 100 person-year (PY) among injecting drug users in Europe*
 * Details of the studies are in Table 3

risks from participation, ongoing communication with the community and responsiveness to community concerns.

Conclusion

Injecting drug use is an emerging problem that could affect the course of the HIV epidemic in many countries. Increases in prevalence rate were observed in many countries in Asia, Eastern Europe, Latin America and the Caribbean and Canada. High incidence rates were identified in China, Thailand, Canada, and Spain. Additionally, several studies have shown that IDUs could be potential cohorts for vaccine study with high follow-up rate.

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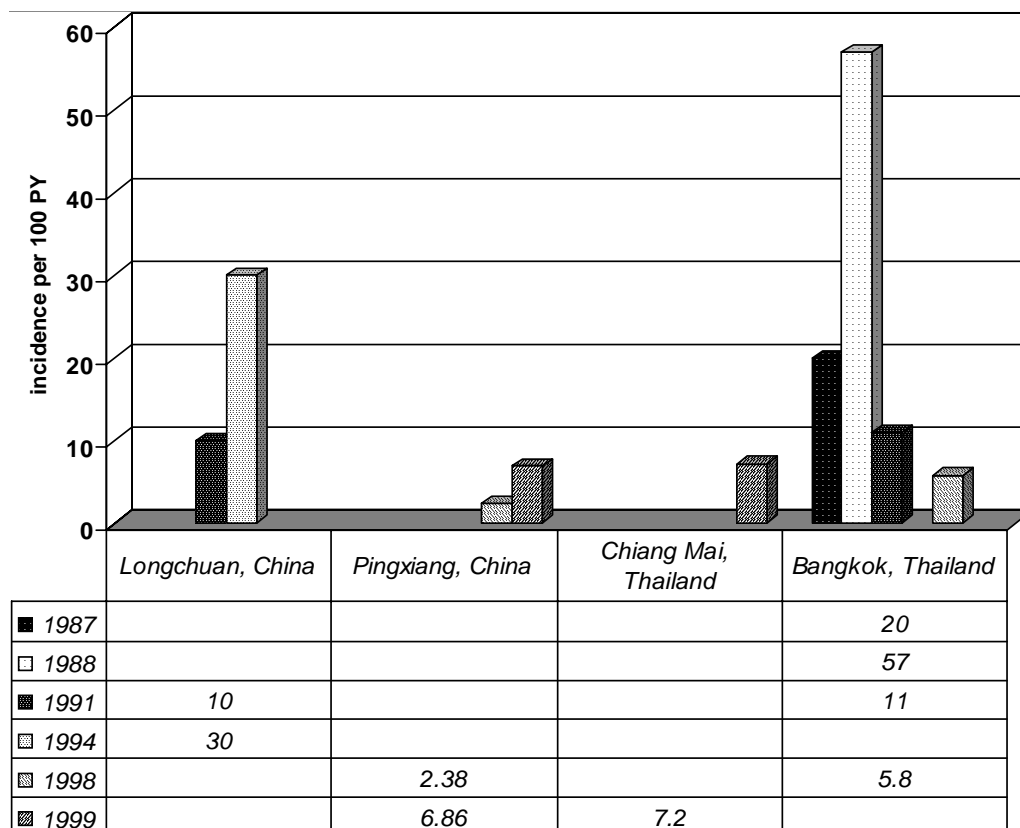


Fig. 4 HIV incidence per 100 person-year (PY) among injecting drug users in Asia*
* Details of the studies are in Table 4

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การศึกษาอุบัติการณ์การติดเชื้อเอชไอวีในกลุ่มผู้ติดยาเสพติดชนิดฉีดทั่วโลกและผลต่อแนวทางการศึกษาวิจัยวัคซีนในอนาคต

ธีระ วรรณรัตน์

ผู้วิจัยได้ทบทวนวรรณกรรมเกี่ยวกับการศึกษาอุบัติการณ์การติดเชื้อเอชไอวีในกลุ่มผู้ติดยาเสพติดชนิดฉีดทั่วโลก และรวบรวมกลุ่มศึกษาที่อาจเป็นกลุ่มสำหรับเข้าร่วมศึกษาวิจัยวัคซีนเอดส์ในอนาคต นอกจากนี้ยังได้ทบทวนสถานการณ์ของระบาดวิทยาในระดับโมเลกุลของเชื้อเอชไอวีในแต่ละภูมิภาค เพื่อให้ทราบสถานการณ์และแนวโน้มการระบาดของโรคเอดส์ และผลต่อการศึกษาวิธีการป้องกันเอดส์ จากการศึกษาตั้งแต่ปี พ.ศ. 2523 ถึง กลางปี พ.ศ. 2548 พบว่ามีอัตราความชุกของโรคเอดส์มากขึ้นในกลุ่มผู้ติดยาเสพติดชนิดฉีด ในหลายประเทศ โดยเฉพาะอย่างยิ่งทวีป เอเชีย ยุโรปตะวันออก ลาตินอเมริกา แอฟริกาใต้ และแคนาดา ซึ่งแสดงถึงแนวโน้มการแพร่ระบาดจะเพิ่มมากขึ้นหากไม่มีมาตรการป้องกันที่ดีพอ นอกจากนี้ข้อมูลจากการศึกษาแบบไปข้างหน้า ในหลายประเทศพบว่ามีอุบัติการณ์ของการติดเชื้อเอดส์สูง เช่น จีน ไทย แคนาดา และสเปน ทั้งนี้ในหลายการศึกษาพบว่ามีอัตราการกลับมาติดตามผลของอาสาสมัครค่อนข้างสูงแสดงว่ามีความเป็นไปได้ที่กลุ่มผู้ติดยาเสพติดชนิดฉีดเป็นกลุ่มที่จะสามารถเข้าร่วมการศึกษาวิจัยวัคซีนเอดส์ในอนาคต
