SYRINGE AVAILABILITY AS HIV PREVENTION: A REVIEW OF MODALITIES

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ABSTRACT This review examines recent research into modalities for improving access to sterile syringes for injection drug users (IDUs) as a means to reduce human immunodeficiency virus (HIV) transmission. English language studies with empirical data were collected through Uncover reports and MedLine searches from 1998 to 2000. Although syringe-exchange programs are the most established and well-evaluated means of improving access to sterile syringes, research on alternative modalities—such as pharmacy sale, injector-specific packs, mass distribution, and vending machines—and on coverage of special populations suggests the need to pursue multiple avenues of increasing syringe availability simultaneously and, in particular, to explore modalities other than syringe-exchange programs when HIV incidence is under control. The impacts on HIV transmission of cocaine injection and sex with IDUs need to be explored further. Finally, any evidence of declining hepatitis C incidence among young IDUs might serve as a surrogate for a sharp drop in injection-related HIV risk behaviors in that population.

INTRODUCTION

Efforts to increase the availability of sterile syringes (or needles and syringes) have had the intent of preventing human immunodeficiency virus (HIV) transmission among injection drug users (IDUs) and their sexual partners and offspring. As of May 1998, 129 countries and territories in the world had documented the occurrence of illicit injection drug use, 109 with associated HIV infection (Andrew Ball, World Health Organization, personal communication, April 1999). As of June 1999, 36% of all AIDS cases reported to the US Centers for Disease Control and Prevention were among IDUs, their sexual partners, or their offspring.[1] In 1997, four federal agencies issued an HIV Prevention Bulletin that recommended that, to reduce the risk of infectious disease, IDUs unable to stop using drugs

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should "use a new, sterile syringe to prepare and inject drugs" and should practice safe injection techniques.[2]

While in the US and several other countries, political controversy often limits discussion about improving syringe availability to whether it should or should not be done, researchers have worked with the premise that improved availability of syringes aids in HIV prevention. In recent years, researchers' questions have centered on "How should we?" and "How can we achieve adequate coverage?" Syringe exchange has been the dominant modality for increasing the availability of sterile syringes in most countries. However, other modalities, or a variation on the basic syringe-exchange program (SEP) model, may be more politically feasible or, in some circumstances, more cost-effective HIV prevention. Adaptations on certain modalities may also serve special populations better, such as youth, female sex workers, prisoners, and populations in countries with emerging epidemics, and may be appropriate to respond to changes in a locality's HIV transmission rates. (This review does not address in detail issues such as syringe disposal, impact of SEPs on drug use or drug treatment, etc., because these issues do not pertain directly to reducing injection-related HIV risk behaviors; nonetheless, there are extensive data elsewhere on those subjects.)

METHODS

Survey and analysis of research on the role of syringe availability in prevention of HIV among IDUs were performed. In particular, questions about modalities for improving syringe availability and coverage of special populations were addressed. To obtain relevant research, studies were selected from periodic reviews of monthly Uncover search results in 1998 and 1999, searches of PubMed (MedLine) for papers published from 1989 to 2000, and a survey of postings to the nep@drcnet.org bulletin board. Search terms included "syringe availability," "syringe exchange," and "needle exchange." Papers were extracted in English and reviewed to confirm the reporting of empirical data related to the role of syringe availability in disease prevention among IDUs.

RESULTS

Multiperson use of syringes remains a major route of HIV transmission in most developed and many developing countries. In the US, questions concerning syringe use were added to a drug use questionnaire administered by telephone to 17,747 subjects in 1995 and 18,269 subjects in 1996.[3] Of subjects who had ever injected drugs, 21.9% reported that the last time they injected, someone had used the syringe before; 22.4% reported having passed a used syringe to others; close

to 60% reported obtaining syringes only from unsafe sources (i.e., not a pharmacy or SEP). These figures suggest that efforts to improve syringe availability in the US have yet to affect a significant proportion of IDUs. Multiple modalities for improving syringe availability merit attention.

Syringe Exchange

SEPs are the archetypal modality for improving syringe availability for IDUs. In 1999, there were over 160 SEPs operating in 39 US states, the District of Columbia, the Commonwealth of Puerto Rico, and US Territories (North American Syringe Exchange Network, personal communication, November 1999). Evaluations of SEPs have examined frequency of risky injection behavior (i.e., injecting with previously used equipment) and HIV and hepatitis B (HBV) and C (HCV) viruses[4] seroprevalence and incidence. Studies have also looked at characteristics of IDUs, "user friendliness"[5] and legal status of SEPs, sexual risk behavior, and service provision.[6] In response to early concerns about the possibility of increased drug use, numerous studies examined issues, like prevalence of drug injection in a community, not related directly to disease transmission. These have been reviewed extensively elsewhere.[6,7] Individually, the results of these studies provide only limited evidence of effectiveness, but taken collectively, they provide powerful support.

Many researchers have examined HIV seroprevalence and SEP participation among IDUs. Fuller reviews of these studies are available elsewhere.[6,7] One such study, published in 1991, included 145 IDUs in Amsterdam. Authors found that 3% of SEP "participants" (N = 72) versus 28% of "nonparticipants" (N = 73) possessed drugs, but no clean injection equipment on a daily basis[8]; 9% versus 22% were involved in needle sharing over the previous month; 74% versus 28% used their needle just once. Authors found stable HIV prevalence (30%) from the opening of the SEP in 1986 and decreasing reports of acute HBV in the population (from 26 in 1984 to 5 in 1988). The analysis was based on SEP registration data; statistical significance was not calculated, and authors stressed the role of SEPs as part of a strategy including AIDS information and counseling, psychosocial care, and methadone maintenance treatment.[8]

Since the issuance of the National Academy of Medicine report in 1995,[7] further studies have been published. An international examination of 81 cities (29 with SEPs) found average annual change in seroprevalence to be 11% lower in those cities with SEPs compared to those without (95% confidence interval [CI] 17.6 to −3.9, $P = .004$).[9] A study published in 1997 examined HIV seroprevalence (through fingerprick) and injecting and sexual behaviors (through self-adminis-

tered questionnaire) among all participants in 21 SEPs covering all jurisdictions in Australia over a 1-week period.[10] Data from 1,005 complete sets revealed that HIV seroprevalence was 2.1%, and that 31% of subjects reported injecting with a previously used syringe within the past month. HIV seroprevalence was significantly higher among self-described homosexuals (22.5% vs. 0.7%, $P < .001$), suggesting that SEPs may not address sexual risk factors adequately. A compilation of surveys involving several thousand IDUs in five US cities showed that the average number of injections per syringe declined by at least 50% after the establishment of SEPs in the cities where such an analysis could be made (New Haven, Connecticut; Baltimore, Maryland; and Chicago), and that there were statistically significant increases in the proportion of SEP participants reporting once-only use of syringes in the cities where such an analysis could be made (San Francisco, Baltimore, and Chicago).[11] Limitations include the retrospective nature of the analysis (i.e., none of the studies originally were intended to address these questions). In addition, the San Francisco study was small and cross sectional, the Chicago study involved a single interview and required 3 years of recall, and the Baltimore data extend only 6 months into the establishment of the SEP.[11]

A study of risk behaviors before (N = 302) and after (N = 86 initial, N = 76 follow-up) the closing of the only SEP in Windham, Connecticut, examined the proportion of syringes obtained from "safe" (i.e., pharmacies and SEPs) and "unsafe" (i.e. family/friends, diabetic non-IDU, street source) sources. Results showed (1) a drop in the safe proportion from 86% before closure, to 64% within 11 months of closure, and 3 months later to 49% and (2) a rise in the unsafe proportion from 14% before closure, to 36% within 11 months of closure, and 3 months later to 51%. Data from initial interviews before and after closure were significantly different ($P < .001$),[12] but authors do not address the likelihood that self-reports were influenced by media coverage.

Several studies in 14 localities or regions have measured or estimated HIV seroincidence among SEP participants (see Table I).[13–32] Studies in 12 locations showed similar or lower HIV seroincidence (see top 12 sites listed in Table I) among participants compared to nonparticipants, although several relied on mathematical modeling[16,28] or small sample sizes.[14,15] Three studies in New Haven, Connecticut, tagged syringes distributed through SEPs and based conclusions on mathematical modeling and needle distribution rates, client visit dates, needle circulation times, and the fraction of returned needles that were HIV positive[33]; significant declines in the proportion of returned syringes that tested positive for HIV were observed.[22,23] A meta-analysis of three studies in New York City

TABLE 1 HIV Incidence Estimates Among Needle-Exchange Participants in Selected Cities

City	HIV Prevalence*	Measured HIV Seroconversions†	Estimated HIV Serocoversions‡	Notes
Lund, Sweden (1991)[13]	Low	0		
Glasgow, Scotland (1993)[14]	Low		0–1 (2)	
Sydney, Australia (1993)[14]	Low		0–1 (2)	
Toronto, Canada (1993)[14]	Low		1–2 (2)	
England and Wales (1994, 1998)[15,16]	Low		0–1 (1)	
Kathmandu, Nepal (1995)[17]§	Low	0		Recent, unpublished data show precipitous rise in HIV seroprevalence[18]
Tacoma, WA (1995)[19]	Low	<1		
Portland, OR (1993)[20]	Low	<1		
Amsterdam, The Netherlands (1991)[21]	High	4		More recent data show sharp decline in HIV seroincidence among SEP participants (1992);[22,23] effect levels off (1995)[24]
Chigao, IL (1994)[25]	High	0		3 HIV seroconversions occurred among non-SEP participants
New York, NY (1994)[26]	Very high	2		Meta-analysis shows protective effect of SEPs on HIV seroincidence (1996)[27]
New Haven, CT (1993)[28]	Very high		0 (3)	
Montreal, Canada (1993)[29]	Moderate	13		More recent data show increased risk of HIV seroconversion among SEP participants (1997)[30]
Vancouver, Canada (1997)[31]	Moderate	24		

Source: Adapted from D. C. des Jarlais, Current findings in syringe exchange research: a report to the Task Force to Review Services for Drug Misusers, Department of Health, United Kingdom, 1994, unpublished.

*Low = 0% to 5%; moderate = 6% to 20%; high = 21% to 40%; very high = 41+%.

†Cohort study and/or repeated testing of participants per 100 person-years at risk.

‡Estimated from (1) stable, very low (2%) seroprevalence in area; (2) self-reports of previous seronegative test and a current HIV blood/saliva test; (3) HIV testing of syringes collected at exchange per 100 person-years at risk; and (4) stable or declining seroprevalence.

§Recent data show unexplained rise in HIV prevalence.

(total N = 1,442) found, in a pooled-data, multivariate proportional hazards analysis, that nonparticipation versus participation was associated with a hazard ratio of 3.35 (95% CI 1.29–8.65) for HIV seroincidence.[27] In Amsterdam, follow-up studies found a sharp decline in HIV seroincidence,[18,24] followed by a leveling off of effect.[34] Finally, there has been a resurgence of HIV in Kathmandu, Nepal, attributed to the small size of the program and inadequate coverage of the

population (T. Smits, Asian Harm Reduction Network, personal communication, March 9, 2000; B. B. Karki, Planning Division, Ministry of Health, Nepal, personal communication, April 2000).

This review examines in detail only the two studies showing a relative increase in HIV seroincidence among SEP participants. Canadian studies in Montreal and Vancouver showed increases in HIV seroincidence among SEP participants relative to nonparticipants or frequent versus infrequent attenders. Both studies initially raised the prospect that SEPs might serve as a social meeting place for IDUs, creating new high-risk social networks[35] that might potentiate HIV transmission.[36] In Montreal, 16% of SEP participants were seropositive at the time of enrollment in the study compared with 6% of nonparticipants[30]; thus, the rate of new infection would be expected to be 2.7 times higher for participants than for nonparticipants—the actual difference was 2.5.[36] The management of the Montreal SEP and the methodology of the study have been critiqued.[37] The authors since have followed 739 IDUs in Montreal from 1995 to 1999 to understand better the relationship between SEP attendance and HIV seroconversion. Since 1995, Montreal SEPs removed the limit on number of syringes per participant, changed site location, and attempted to integrate services with outreach and other modes of syringe access. HIV incidence in this study was the same for SEP participants and nonparticipants and was associated highly with cocaine injection (hazard ratio 4.49 for 1–9 injections/month and 9.5 for more than 10 injections/month) and sex with an HIV-positive individual within the past month (5.06).[38]

In Vancouver, 1,006 IDUs were surveyed, and frequent SEP attendance was found to be an independent predictor of HIV-positive serostatus; 257 follow-up interviews showed no protective effect of the SEP, and there was an HIV seroincidence of 18/100 person-years (relative to HIV-negative IDUs; HIV-positive IDUs were more likely to inject cocaine, $P < .001$).[31] The authors of the study performed a follow-up prospective study involving 694 HIV-negative IDUs in Vancouver from 1996 to 1997.[39] At baseline, they found frequent SEP participants to be significantly more likely than infrequent participants ($P < .001$) to have numerous HIV risk factors, including unstable housing, frequent injection, frequent cocaine injection, and recent periods of incarceration. Seroincidence data collected at follow-up did not differ from predictions of several multivariate Cox regression models, and the authors concluded that it was risk behaviors rather than the SEP per se that accounted for infection rates. Risk behaviors declined among frequent SEP participants relative to nonparticipants. Among 36 subjects who reported sharing syringes with a new partner during the study period, only 1 had met that partner at the SEP, evidence against the formation of new networks.

Increased prevalence of cocaine injection may limit the effectiveness of SEPs, such as those in Montreal and Vancouver,[37,38] due to the high number of injections involved. A study published in 1997 compared SEP participants who continued to inject with a previously used syringe (N = 158) with those who stopped (N = 391).[40] From a cohort of randomly recruited subjects, only those who had reported risky injection behavior in the 30 days prior to using the SEP were included. Persistent sharers were more likely to pass used syringes to others ($P < .001$) and to inject cocaine on a daily basis ($P < .001$). SEPs generally have limited hours and, although low threshold, involve a commitment from drug users that may require significantly more effort from them, which may be more difficult to elicit from those who inject cocaine. This issue is addressed tangentially in numerous studies, but the role of cocaine in syringe use practices requires additional study.

Since 1991, eight US government-sponsored reports have reviewed SEPs, concluding that they are effective HIV prevention tools (see Table II) (D. Satcher, personal communication to J. I. Boufford, December 10, 1993; available from the Drug Policy Foundation, 4455 Connecticut Avenue, NW, Suite B-500, Washington, DC 20008).[6,7,41–45]

Special populations Special populations addressed by SEPs include female sex workers, prisoners, populations in transitional or developing states, and street youth.

Those who trade sex and inject drugs are at particularly high risk of HIV. A comparison of female sex workers and non–sex workers at five SEPs in five US cities found that sex workers were significantly more likely to engage in a variety of HIV risk behaviors, including injecting more frequently ($P < .0005$), injecting daily ($P < .005$), injecting cocaine ($P < .005$), injecting speedball ($P < .005$), smoking crack cocaine ($P < .005$), reusing syringes more than twice ($P < .005$), backloading syringes ($P < .005$), attending shooting galleries ($P < .005$), trading used works ($P < .005$), obtaining syringes from non-SEP sources ($P < .05$), and injecting without an alcohol wipe ($P < .005$).[46] Based on these and other data showing, for example, that female sex workers were more likely than other female SEP participants to be under severe emotional distress ($P < .0005$) and to have been homeless within the past 6 months ($P < .005$), the authors concluded that SEPs should offer more referrals and on-site services, engage in syringe exchange in areas where sex workers stroll, encourage alternate routes of administration (sniffing, smoking), and involve sex workers in program design and implementation. These data suggest that sex workers may engage in more injection-related HIV risk behaviors that remain unaddressed by SEPs.

TABLE II Findings of US Government Studies of Efficacy of Syringe-Exchange Programs

Agency	Year Published	Conclusions and Recommendations of Studies: Reduction in HIV Transmission	No Increase in Drug Use	Revoke Federal Funding Ban	Revoke State Prescription and Paraphernalia Laws
National Commission on AIDS	1991[41]	Yes*	Yes	Yes	Yes
General Accounting Office	1993[42]	Yes†	Yes	NA	NA
University of California (for CDC)	1993[6]	Yes	Yes	Yes	Yes
National Academy of Science	1993‡	Yes	Yes	Yes	Yes
Office of Technology Assessment	1995[7]	Yes§	Yes	Yes	Yes
National Institutes of Health Consensus Conference	1995[43]	Yes	Yes	NA	NA
Department of Health and Human Services	1997[44]	Yes	Yes	Yes	Yes
	1998[45]	Yes	Yes	No	NA

Source: Adapted from P. Lurie and E. Drucker, An opportunity lost: HIV injections associated with lack of a national needle-exchange programme in the USA, *Lancet* 1997;349:604–608.

NA = not available because studies reviewed data without making policy recommendations.

*Legal barriers that preclude SE lead to increase HIV transmission.

†Research suggests promise as an AIDS prevention strategy.

‡From D. Satcher note to J. I. Boufford, December 10, 1993; available from the Drug Policy Foundation, 4455 Connecticut Avenue, NW, Suite B-500, Washington, DC 20008.

§Reducing proportion of contaminated syringes in circulation will reduce HIV transmission.

Worldwide, HIV and HCV infection rates are higher among prisoners than the general population.[47] High prevalence of risk behaviors, including drug injection, has been documented among inmates. While in the US this is considered the result of preincarceration risk behaviors, international data suggest intraprison transmission. A questionnaire completed in conjunction with a voluntary anonymous HIV test by 429 inmates in two British prisons showed that 37–42% were IDUs, and among those who had been in prison for more than 4 weeks, 51% had injected heroin a mean of 6.0 times during the previous 4 weeks.[48] Of 4,285 surveyed federal prison inmates in Canada, 11% reported injecting drugs in prison, and many reported having shared a syringe with up to 20 other inmates.[47] Syringes reportedly have been shared by more than 10 inmates and then passed to other wards in Kazakhstan prisons.[49] Although improving syringe availability in prisons has been resisted in most countries, broad efforts in Switzerland since 1990,[50] Canada since 1992,[51] and Australia[52] have resulted in ready and discreet

availability of safer injecting materials, such as bleach, cotton, and syringes. An evaluation of a prison-based SEP for female inmates in Hindelbank, Switzerland, found no increase in heroin or cocaine use by self-report and a precipitous drop in syringe sharing in the prison.[53]

Emerging epidemics of HIV among IDUs in several eastern European and developing states have led public health agencies to begin SEPs, methadone maintenance programs, and outreach programs.[54] In eastern Europe, syringe sharing has been reported in cities, including Moscow, Kaliningrad, Odessa, Poltava, Svetlogorsk, Tblisi, Almaty, Shymkent, and Tashkent.[55] In Tashkent, 94% of IDUs reported having shared injection equipment.[56] The Russian Health Ministry reported that 90% of over 30,000 HIV infections in Russia are among IDUs.[57] Serious concern was raised by numerous reports (from Kaliningrad, Moscow, Odessa, and Shymkent[55] as well as other Russian cities[58]) that human blood was added during drug preparation. If the drugs themselves were fomites of HIV transmission, improved syringe availability might have no beneficial effect. These fears have been allayed somewhat by in-depth ethnography of the drug production process for opiate and amphetamine drugs in several eastern European and central Asian states,[54] and virological tests in which clinical isolates of HIV, briefly incubated in liquid opiate solutions that had been collected in three Polish cities, were unable to replicate when introduced into cultures of stimulated target T cells.[59,60] However, the last study should be replicated for confirmation, preferably on site. Moreover, the means of distribution of drugs in several eastern European states—dealers commonly sell drugs preloaded in syringes or allow buyers to frontload from a larger syringe—complicates HIV prevention efforts.[61]

Data from developing states support SEP-style interventions (see Table III).[62–64,66–72] In the hills of Thailand, multiperson use of syringes was common prior to the introduction of SEPs.[62] Behavior change was well documented from 1993 to 1994, and HIV prevalence remained stable at 33% during that period. The greatest difficulty was encountered in political and community agencies.[62] Interviewing 47 current and former IDUs, researchers in Manipur, India, found fear of arrest and harassment to be the top reason IDUs did not carry their own syringes or bleach.[63] IDUs in Malaysia also reported fear of arrest for paraphernalia possession as the top reason they shared syringes.[64] In addition, and in line with findings from North America,[65] IDUs in both Manipur and Malaysia reported being injected by others for a period of time when they began injecting.[63,64]

A feasibility study suggests SEPs would be appropriate for Vietnam if the involved community development, former IDUs as staff, outreach services in

TABLE III Harm Reduction Evaluations Showing Reduced Risk Behaviors in Developing States

Program	City/Country
Syringe exchange	Kathmandu, Nepal[16,69] Brazil (not yet completed)
Bleach distribution	Churachandpur, India[70]; Manipur, India[69] Kathmandu, Nepal[69]
Community outreach	Bangkok, Thailand[71,72] Churachandpur, India[70] Kathmandu, Nepal[69]

Source: Adapted from K. S. Riehman, *Injecting Drug Use and AIDS in Developing Countries: Determinants and Issues for Policy Consideration.* Geneva: World Bank, Policy Research and Development; October 1996.

lieu of a fixed site, and a plan for retrieving discarded syringes.[67] A total of 586 participants in a SEP in Kathmandu, Nepal, were interviewed one or more times from 1991 to 1994.[66] Data were analyzed based on whether the subject's 1994 interview was the first or subsequent and on the year of first interview (i.e., as a proxy for length of time exposed to SEP). Among those interviewed in 1994, those who had been interviewed previously reported a lower number of times sharing needles in the past month ($P = .06$) and a lower number of people with whom needles had been shared ($P = .024$). The authors reported that, of 195 person-years of follow-up among those interviewed more than once, HIV seroincidence was zero (95% CI 0–0.1). In a sample of 127 SEP participants in Kathmandu, frequency of injecting fell from 24.4 to 17 injections per week in a 1-year period. The number of persons with whom syringes were shared dropped 21%, and the number of times syringes were shared declined 29%. In the mid-1990s, HIV prevalence among IDUs in Kathmandu remained below 2%,[17,66] but recent data suggest a jump in prevalence (T. Smits, Asian Harm Reduction Network, personal communication, March 9, 2000; B. B. Karki, Planning Division, Ministry of Health, Nepal, personal communication, April 1, 2000). Limited resources have restricted severely the type of research necessary in developing countries.

Finally, rapid incidence of HIV, HBV, and HCV, as evidenced by high seroprevalence among drug users with under 1 year of injecting experience (13.9%, 49.8%, 64.7%, respectively),[73] suggests an urgent need to target IDUs early. A survey of "street youths"—those adolescents out of school, unemployed, and runaway or homeless who are often involved in gangs, drug sales, or sex work—in Hollywood, California, found that, among the 30% that had injected drugs, 59% had shared syringes, and only 33% reported using bleach to sterilize injecting equipment.[74] Youths who inject drugs are at particular risk for disease

incidence because they are less likely to have been infected already and, having injected drugs for a shorter period of time, are less likely to know about disease transmission and to practice risk reduction behaviors.[75]

A study published in 1997 involved one-time interviews of participants at a youth SEP in Hollywood (N = 86) and nonparticipants recruited at other locations (N = 106). Researchers found participants less likely to share syringes or other injection equipment, to use other drugs to come down, to need help injecting, or to report sharing a syringe when high or craving; participants were more likely to report easy access to sterile syringes and to engage in booting.[76] Demographic data differed only by race; however, the greater likelihood for participants to "boot" and not to need help injecting suggests more injecting experience and sophistication. Other unmeasured variables, like degree of dependence, income, perceived HIV risk, likelihood and frequency of cocaine or methamphetamine injection, and access to services, may also account for the results of this study.[77] In sum, questions about the effectiveness and safety of SEPs for youth remain unanswered.

Hepatitis C

Several studies have also examined HCV transmission among IDUs. Sexual transmission of HCV is rare.[78] Among IDUs, there is no correlation between HCV status and sex work history.[79,80] Yet, among IDUs in Australia, where HIV seroprevalence is below 3% and incidence is under 1%, HCV prevalence approaches 65% and incidence 15%.[4,81] Among Australian IDUs under 20 years of age, HCV incidence has been recorded as high as 75.6% (N = 31).[82] The ratio of estimated likelihood of becoming infected from needlestick with an HCV versus from an HIV-infected syringe is 50 : 1.[83]

Two studies looking at HCV incidence among syringe-sharing IDUs versus those who reported no syringe sharing found 17% versus 4% incidence,[84] respectively, and 30.2% (N = 80) versus 11.9% (N = 72) incidence, respectively.[82] Self-selection bias in the second study may have drawn in subjects at higher risk for HCV transmission.[82] A community-based, prospective study of 229 young IDUs found an HCV incidence rate of 16/100 person-years; 36.6% were HCV positive at baseline, and seroprevalence was associated independently with reusing a syringe at least one time in the past 6 months (95% CI 1.39–11.00), injecting for the first time with someone 5 or more years older (95% CI 1.43–6.23), or alone and injecting cocaine or speedball exclusively (95% CI 1.53–12.01) or with other drugs (95% CI 2.62–10.64) versus injecting no cocaine in the past 6 months.[85] HCV seroconversion was associated with injecting for less than 2 years (95% CI 1.6–32.8) and continuing to inject at follow-up (95% CI 1.0–19.9).[85]

Studies of the impact in Washington State of SEPs on HBV and HCV transmission among IDUs in Tacoma and Seattle showed conflicting results. The earlier case-control survey of 112 IDUs suggested SEP participation was associated with a six-fold and seven-fold reduction in HBV and HCV risk, respectively.[86] The later prospective study of 647 IDUs found no protective effect.[87] Authors did not find any confounding factors. In sum, because HCV transmission is associated so closely with injection-related risk factors and generally occurs early in the injection career, these data may suggest a need for research into the effect of SEP participation on young IDUs (discussed below). Should such research show a protective effect of SEP participation, HCV incidence rates among participants might prove a powerful indirect measure of the effect of an intervention on injection-related HIV risk factors. (This is in contrast to HBV transmission, which is highly transmissible through sex and has been shown to have little correlation to HIV seroincidence among IDUs.[88]) If, for example, HCV incidence fell, but HIV incidence remained stable, that would be suggestive, although not conclusive, evidence of sexual rather than injection-related transmission of HIV.

Pharmacy Sale

Pharmacy sale of syringes is lower cost and less labor intensive than SEPs because the infrastructure already exists. Having pharmacy access is important because of the sheer number of syringes that would be needed to ensure a sterile syringe for every injection. Based on consultation with experts and a basic formula (Number of IDUs × Average number of injections per day × 365 days), it was estimated that 920 million to 1.7 billion injections of illicit drugs take place in the US each year.[89] Authors recommended widespread sale and distribution of syringes through pharmacies to fulfill more of the demand, as has been the response in much of Europe and in New Zealand and Australia.

The first evidence of HIV prevention effect through pharmacy sale of syringes was provided in 1991. A study of 2,921 IDUs found HIV prevalence to be lower among those with a history of diabetes (9.8%) compared to those with no history of diabetes (24.3%), despite similar duration and intensity of drug use and sexual practices.[90] Diabetic IDUs also reported less sharing of injection equipment and less attendance at shooting galleries. These results likely are related to education on safer injection practices received by diabetics, but nonetheless suggest that ready access to syringes may affect HIV transmission through changed injection practices.

Legal restrictions on sale of syringes (i.e., statutes and local ordinances requiring a prescription for sale and/or possession of syringes) are the most significant barriers to HIV prevention through pharmacy sale. There are 47 US states that

have drug paraphernalia statues; 8 have statutes requiring a prescription for syringe purchase and possession, and 23 have pharmacy regulations or practice guidelines that restrict access.[91]

A law requiring prescriptions for pharmacy sale of syringes, enacted in Massachusetts in 1924, remains the primary barrier to that modality of HIV prevention in the state.[92] That law was modified in 1993 to allow the establishment of SEPs, but a similar drug paraphernalia law has been used to arrest and incarcerate drug users for syringe possession (in 1995, 824 individuals were arrested for syringe possession; 41% were incarcerated) and to restrict pharmacy sale.[93] In contrast, the 1987 drug paraphernalia law adopted by the Oregon legislature specifically excluded syringes based on Oregon Health Division testimony to the HIV prevention value of maintaining and improving access to sterile syringes.[94]

Pharmacy sale of syringes is legal in Maryland (at the discretion of the pharmacist), yet before the implementation of SEPs in Baltimore, only 53.5% of IDUs had obtained any of their syringes through a pharmacy; 51.5% reported regularly obtaining syringes from street dealers or shooting galleries.[95] Likewise, in Rhode Island, which has a prescription statute, a study performed when the first SEP opened in 1995 found that the mean number of times a syringe was reused was 24 (median = 20, N = 477).[96] In Maine, the legislature removed the existing prescription requirement in 1993, but it was not until 1997 that the drug paraphernalia law was changed to permit possession of up to 10 syringes.[3] The change was advocated by the Maine Bureau of Health based on data from 1990 and 1995, which illustrated an increase in incidence of injection-related HIV from 6 cases (11% of total) to 24 cases (18% of total);[97] data from 1992 to 1995, which showed that over 40% of chronic HCV cases were among former or current IDUs[98]; and data from a telephone survey of 208 pharmacists in 1995, which confirmed that only 15% were willing to sell syringes to suspected IDUs.[99] On the federal level, the Mail Order Drug Paraphernalia Act permits enforcement against anyone who knowingly sells or distributes syringes to IDUs.[91]

A second major barrier to improving access to sterile syringes through pharmacy sale has been professional regulations and personal beliefs among pharmacists themselves. Pharmacists in Baltimore are permitted to sell syringes without a prescription and are supportive of SEPs (78.3%, N = 46), yet a smaller majority supported the nonprescription sale of syringes at pharmacies (67.4%), and in practice, 56.5% required a prescription or diabetic identification.[100] This barrier is also prevalent in countries that have prioritized HIV prevention among IDUs: In a postal survey of 2,469 community pharmacies in England and Wales (79% response rate), about 28% currently were selling syringes to IDUs, and three-

fourths were willing to do so, but only 3% participated in local SEPs, and only 4% kept a sharps container on site for syringe disposal. Of those unwilling to sell to IDUs, 90% believed that business would be damaged by the presence of IDUs, compared to 62% of those willing to sell.[101]

A rare opportunity for a prospective examination of the effect of pharmacy sale was provided in 1992, when the Connecticut legislature legalized sale and possession of up to 10 syringes. Two questionnaires were administered through drug treatment centers, correctional settings, and HIV counseling and testing sites in 1992, shortly after the laws went into effect (N = 124), and 7 months later (N = 134).[102] In the later study, a smaller proportion of IDUs reported having shared a syringe previously (68% vs. 52%, $P = .02$), a smaller proportion of those who previously had shared a syringe reported doing so in the past 30 days (52% vs. 31%, $P = .02$), a smaller proportion reported purchasing syringes on the street (74% vs. 28%, $P = .0001$), and a larger proportion reported obtaining syringes from pharmacies (19% vs. 78%, $P = .0001$). Subjects in this study were not selected randomly and were interviewed at unequal interviews, possibly leading to differential recall bias.[102] This and a subsequent study also reported problems with IDUs' continued fears of police harassment and limited syringe sales to IDUs.[103]

According to a mail survey of pharmacy managers in five major Connecticut cities, 31.4% of managers were allowed to sell in all instances, and 18.1% of those permitted to sell at their discretion were willing to sell to suspected IDUs.[104] It was determined that this was related to the reluctance of IDUs to carry 10 or more syringes (the legal limit) and the reluctance of pharmacists to break open the usual packs of 10 syringes. In response, the Connecticut Department of Public Health distributed packs of two syringes and two condoms to selected pharmacies to be distributed free of charge or for up to $1.[105] This program reportedly had no effect on the willingness of pharmacists to stock single syringes, but no problems were reported, and all subjects were willing to continue distributing packets. A survey, published in 1999, of 206 SEP participants in Baltimore found that 19% had purchased syringes at a pharmacy in the past 6 months, and 37% reported being turned down when attempting to purchase syringes at a pharmacy. There were 92% who reported that they would purchase syringes, at a median price of $1 (mean = $0.80) per syringe, at a pharmacy if legal restrictions were lifted; this price well exceeds typical retail prices.[106]

One reason SEPs may be preferable to pharmacy sale is the risk of transmission through other injection equipment (e.g., cotton, cookers, water).[107] Data from interviews administered to 12,323 IDUs from 19 sites in the US showed that, among 3,935 subjects that had shared both syringes and other supplies, 64% of

311,000 potential HIV exposures in a 30-day period were from multiperson use of cookers, water, or cotton. This study did not differentiate between reuse rates for nonsyringe injection equipment and did not inquire about backloading or frontloading of syringes; in addition, the wide standard deviation of the data and difference between mean and median values may represent skewed data, and the lack of knowledge about the relative risk of HIV transmission through nonsyringe injection equipment should be considered when interpreting these data. Nevertheless, the possibility of HIV transmission and the likelihood of HCV transmission through these items further heighten the importance of SEPs, which generally provide cookers, water, and cotton along with syringes. Sale of injector-specific packs that include sterile syringes and other injection equipment may compensate for this presumably SEP-specific benefit, but no formal evaluation has been performed[89] (for more information on injector-specific packs, contact HIT, Cavern Court, 8 Mathew Street, Liverpool L2 6RE, UK; available on-line at http://www.hit.org.uk), notwithstanding the pilot study in Connecticut mentioned above.

Another, perhaps surprising, benefit of SEPs relative to pharmacy sale is positive public opinion. In the US, a 1996 Kaiser Family Foundation poll found 66% popular support. Hart Research polls found 54–55% support from 1995 through 1997 for SEPs, while only about one-third of the public supported syringe deregulation.[109,*] A 1995 household survey of 274 Baltimore residents found that 65% supported establishing SEPs, and 47% supported nonprescription pharmacy sale of syringes.[110]

Finally, pharmacy sale may not provide for the relatively convenient return of used syringes available through SEPs. The opening of SEPs has been associated with no increase[111] or a decrease[6,112] in improperly discarded syringes, with lasting effect.[113] Syringe disposal programs, traditionally implemented for diabetics, may be a useful adjunct to pharmacy sale. A workshop involving staff from 15 disposal programs in the US, Canada, and Australia identified three strategies—puncture-resistant containers discarded in trash, community drop boxes, and sharps containers turned in at local health sites—and the importance of involving pharmacists, physicians, waste disposal authorities, and program participants.[114] An

*A Kaiser Family Foundation survey[109] found that 66% of all Americans are in favor of providing clean needles to IDUs: 66% of those aged 18–29 years, 63% of those over 65 years of age; 56% of Republicans, 67% of Independents, 71% of Democrats; 62% of Evangelicals, 69% of non-Evangelicals, 67% of Catholics. A separate poll found 55% in support of SEPs (Human Rights Campaign poll, conducted April 8–10, 1997, by Tarrance Group and Lake Sosin Snell and Associates). A 1997 poll conducted for the Family Research Council by the Polling Company found 62% opposition to SEPs; that poll, however, presented SEPs and drug treatment as either/or policy choices.

evaluation of a community drop box program in Baltimore found growing public and official support after program implementation and no change in the number of improperly discarded syringes.[115]

Pharmacy sale may reduce risky injecting behavior by up to 40%.[116] Potential barriers to HIV prevention through pharmacy sale include statutes, local ordinances, professional regulations, pharmacists' attitudes, police harassment, and public opinion. Pharmacy sale may also contribute less to behavior change and to contact with other social service agencies, although sale of injector-specific packs and education of pharmacists may overcome many of these problems at a lower cost than SEPs and provide the ability to reach IDUs in places that cannot sustain SEPs.

Other Methods

Prescription of syringes by physicians may be effective in areas lacking SEPs or in states with restrictions on pharmacy sale, and such practice may help establish syringe provision as a medically necessary standard of care.[117] A physician at Providence Hospital in Rhode Island recently began prescribing syringes to IDUs in a program that will be evaluated closely.[118,119]

In over a dozen European and Australian cities, syringes are also available from vending machines (often located in police stations or drug treatment facilities) that provide a sterile syringe when a syringe is deposited.[6,120,121] The first formal evaluation surveyed 343 IDUs at SEPs, pharmacies, and vending machine sites in Marseilles, France, and found that 21.3% reported vending machines as their primary source of syringes. Those subjects were significantly more likely to be under 30 years of age, never to have received maintenance treatment, and to report not sharing injection equipment; they were significantly less likely to live in their own house or to report a positive HIV test. The authors concluded that vending machines might reach young IDUs who are less likely to attend SEPs or pharmacies.[121] Subjects were recruited only from locations that supplied syringes; thus, no information provided is about the proportion of IDUs not attending these sites. A 1995 study in Western and South Australian reported support for vending machines as a complement to other services among IDUs, although subjects expressed concern about risks for noninjecting youth (T. Reeves, Many Needle and Syringe Exchange Program, Australia, personal communication, May 5, 2000). Some Australian SEPs have since offered this service through a standard cigarette machine that dispenses small black disposable containers with syringes, cotton, alcohol wipes, and a spoon.[122]

No formal study has evaluated the modality of "mass distribution"—in which syringes are distributed widely through drug user networks to saturate the

market—although Moving Equipment, an underground SEP in New York City, has developed a rationale and protocol.[123] The number of syringes distributed to a client is based on answers to a series of questions, including "How many works do you need today?" "How many times a day do you inject?" and "When do you plan to get more works?" In response to the concern that IDUs might take extra syringes and sell them, the distribution modality encourages secondary distribution, aiming to minimize the black market profit in syringes through market saturation. If saturation is considered an effective means of preventing HIV among IDUs, changes in the price of syringes purchased on the street may be a good measure of the success of a localized distribution intervention.

Difficult-to-reuse (DTR) syringes (e.g., those in which the needle retracts or the barrel locks after use) have been targeted at prevention programs based on the commonsense notion that, if a syringe cannot easily be reused, the risk of that syringe transmitting HIV is lowered.[124] Assuming that IDUs will utilize DTR syringes (several models obstruct traditional injection techniques[125,126]), it is questionable whether HIV prevention efforts would be served by their development. Probability modeling has been used to demonstrate that, if DTR syringes are introduced to IDUs and lead to a 0.7 proportional decline in the availability of regular syringes, HIV transmission rates are likely to rise (i.e., HIV risk reduction always increases by the addition of a regular syringe rather than a DTR syringe).[124] This analysis presumes that traditional syringes still will be available, and that programs function on limited resources.

A survey of 593 IDUs in seven US cities described the primary barriers to once-only use of syringes as restrictions on the availability of syringes and beliefs and practices of IDUs.[127] Distribution of DTR syringes may help modify the practices of IDUs, as was the case with SEPs, but is less likely to affect the primary concern of legal restrictions on syringe availability. Should a pilot of DTR syringes be launched, it would be prudent to select a locality with few restrictions on syringe access (i.e., exemptions from paraphernalia laws, no prescription requirement, ready access to SEPs).

Finally, an economic analysis of the costs of five different means of increasing syringe availability estimated the cost of providing a portion of the total syringes needed to ensure a new syringe for each injection in the US.[128] While an analysis of New York City, San Francisco, and Dayton, Ohio, determined that there would be a cost savings to increasing syringe availability through any modality in all three cities, the authors determined that SEPs were the most expensive means of increasing syringe availability and pharmacy sale the least expensive (see Table IV). The most intriguing element was the estimated incidence rate and the

TABLE IV Cost of Five Modalities of Increasing Syringe Availability in Three Cities

Program	Cost/Syringe	Minimum Annual Seroincidence for Cost Neutrality (%)
SEP	$0.97	2.1
Pharmacy-based SEP	$0.37	0.8
Pharmacy kit distribution	$0.64	1.4
Pharmacy kit sale	$0.43	0.9
Syringe sale	$0.15	0.3
Total cost of providing 50% of annual need*		
New York City	$6–40 million	
San Francisco	$1–6 million	
Dayton, OH	$30,000–200,000	

Source: Adapted from P. Lurie, R. Gorsky, T. S. Jones, and L. Shomphe, An economic analysis of needle exchange and pharmacy-based programs to increase sterile syringe availability for injection drug users, *J Acquir Immune Defic Syndr Hum Retrovirol* 1998;18(suppl 1):S126–S132.

*Annual need = single syringe for every injection.

type of program rate required for cost neutrality: the data suggest, but do not prove, that as incidence decreases, pharmacy sale may become a more cost-effective means to improve syringe availability. This is particularly interesting in New York City, where HIV incidence has dropped from 4.4/100 person-years in the early 1990s[129] to approximately 0.7/100 person-years in recent years.[130] The authors did not consider other benefits or costs of each modality.

DISCUSSION

Improving syringe availability to prevent HIV transmission is achieved best through multiple modalities and by addressing the issues faced by special populations of IDUs. SEPs do not lead to increased drug use or initiates, but do result in reduced risk of HIV transmission; follow-up studies in Montreal and Vancouver showed a pattern consistent with other research on SEPs. Ecological and prospective research still is lacking for non-SEP modalities; more data are becoming available for pharmacy sale, including acceptability by pharmacists, syringe disposal, and cost-benefit calculations. Vending machines and injector-specific packs are two additional promising modalities that may better reach populations such as street youths, sex workers, and rural, homeless, or incarcerated IDUs. Distribution should also be evaluated, possibly with an economic analysis of black market syringe prices or an ethnographic research design that tracks the life cycle of

tagged syringes. Finally, initial data on physician prescription of syringes should be available soon.

Syringe availability should be considered in the context of a comprehensive approach to HIV prevention among IDUs that includes other prevention and treatment services, as well as efforts to reduce the transmission of other blood-borne infections. In particular, the high incidence of HCV among non-syringe-sharing IDUs combined with data on virus transmission through other injecting equipment (for more information, contact HIT, Cavern Court, 8 Mathew Street, Liverpool L2 6RE, UK; available on-line at http://www.hit.org.uk) highlight both the importance of improving the availability of syringes and the importance of comprehensive SEPs or IDU-specific packs that include cotton, water, alcohol swabs, and cookers. These data also suggest that the effect of efforts to improve syringe availability on HCV transmission among youths may be a powerful proxy for the effect of such interventions on injection-related HIV risk behaviors in the same population.

Finally, different modalities for improving syringe availability are complementary and not competitive; thus, they are likely to be most effective and offer the broadest coverage as part of a comprehensive set of initiatives. For those localities that have reined in an epidemic of HIV among IDUs through SEPs, a cost-benefit analysis suggests that improving pharmacy access to syringes should be a top priority. This conclusion is tempered by concerns about the impact of cocaine injection and sexual risk behaviors, as well as by striking rates of injection-related HIV incidence among young IDUs. A strategy involving multiple, simultaneous modalities is ideal.

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