

Vincent Wietlisbach, Giovanna Meystre-Agustoni,  
Jean Martin

*Institute of Social and Preventive Medicine, University of Lausanne*

## Methadone treatment and risk of HIV infection in drug users without legal access to clean injection equipment

### Summary

The particular situation of the Swiss canton of Vaud (population 550 000) provides favourable observational conditions to assess the efficacy of a methadone treatment scheme in reducing the risk of human immunodeficiency virus (HIV) infection among drug users. On the one hand, the canton has a long tradition of methadone treatment dispensed by medical practitioners. On the other hand, no legal access to clean injection equipment was provided up to 1989. For the 754 drug addicts having entered at least one course of treatment at the end of 1988, HIV status was assessed through two surveys conducted at mid-1986 and at end 1988 among the private practitioners and in the screening centers, hospitals, medico-social institutions and prisons. The overall annual HIV seroconversion rate shifted only slightly from 13% in the first study period (1984 to mid-1986) to 11% in the second period (mid-1986 to end 1988). In both periods, patients no longer on treatment, mostly stable abstainers, were the less exposed to HIV infection with a relative risk of 0.65 ( $p < 0.05$ ). For those still on treatment, the risk of infection was associated directly ( $p < 0.001$ ) with the frequency of courses and inversely ( $p < 0.001$ ) with the duration. Between patients with more than 18 months spent on treatment and those with less than 6 months, the relative risk gradient was 0.8 and 1.4 before mid-1986 and widened out to 0.3 and 2.1 later on. This is mainly due to an increasing HIV incidence among newcomers into treatment. In conclusion, methadone treatment has contributed to a significant risk reduction both through successful detoxication processes and in long-term maintenance, but facilitated access to sterile injection equipment is needed urgently for patients with poor attendance or new to treatment.

In Europe<sup>1</sup> as in Switzerland<sup>2</sup>, intravenous drug users represent the population group in which the HIV (human immunodeficiency virus) spread out the most rapidly

over these last years. Facilitating the access to drug abuse treatment, especially to methadone treatment, and increasing the availability of sterile injection equipment have

been the most commonly suggested means for slowing down this epidemic<sup>3</sup>. The two methods have been associated with lower frequencies of risk-taking behaviours such as needle sharing<sup>4-6</sup> and long-term methadone treatment proved to lead to reduced HIV seroprevalence rates<sup>7-9</sup>. However, as both policies are often implemented in parallel, it is difficult to disentangle their independent effects<sup>5-6,10</sup> and there are still limited relevant data to assess whether these two strategies reinforce each other or detract from each other<sup>11</sup>.

The particular situation of the Swiss canton of Vaud (population 550 000) provides favourable observational conditions to assess for itself the efficacy of a methadone treatment scheme in reducing the risk of HIV infection. On the one hand, no needle distribution program has been implemented in the region and selling of injection equipment over-the-counter was illegal up to 1989. On the other hand, the canton has a long tradition of methadone treatment dispensed by medical practitioners with 130 physicians and 750 drug addicts involved at the end of 1988. Furthermore, a large amount of information have been gathered through two important surveys conducted separately on metha-

done treatment patients and on HIV-infected persons. The present study was carried out for linking together and extending these two data sets in order to investigate the relationship between treatment modalities and the risk of HIV infection.

## Material and methods

Substitution of methadone for heroin was introduced in the 1960s and is aimed at achieving and maintaining abstinence from illicit drug use. In the canton of Vaud, methadone is administered under medical surveillance mostly by private practitioners. Usual admission criteria consist of being 20 years old, a two-year drug addiction history and a failure in another detoxication attempt. The opiate addicts are free to choose their attending physician and to resume treatment after dropout. For each course of treatment, the doctor in charge has to address to the Cantonal Medical Officer an authorization form containing the personal characteristics of the patient, a summary of his medical and drug use history and the proposed therapeutic modalities. The duration of the treatment has to be specified and any prolongation needs to be granted. Patient files are kept up-to-date and enable long-term follow-up of the drug addicts even if they change physicians.

### Study periods

The study extends from 1984 to 1988 and is divided into two observation periods of equal length, each one ending with the realization of either survey. The first period up to mid-1986 corresponds to the emergence of the HIV epidemic among Swiss drug users, the second to the implementation of the first preventive measures. The STOP-AIDS nationwide informa-

tion campaign has been launched in March 1986<sup>12</sup>.

### Survey on methadone patients

At mid-1986, an exhaustive survey was conducted on the 562 opiate addicts who had entered at least one course of methadone treatment<sup>13,14</sup>. Data were gathered by questionnaire and interview from the physicians in charge and by consulting the files of the penal and medico-social institutions. The study included also an assessment of the current clinical and drug dependence status of the subjects. Among many other variables, gender, date of birth, year of first drug injection, calendar of the methadone episodes and HIV status (if known) have been recorded. A complementary study consisted in collecting and updating this limited set of information through the review of the patient files at the Medical Cantonal officer's service for the 461 patients, including 193 newcomers, who followed treatment courses between mid-1986 and the end of 1988.

### Survey on prevalence of HIV infection

By the end of 1988, a retrospective survey was carried out in order to evaluate the cumulative incidence of HIV in the canton<sup>15</sup>. Major hospitals, screening centers, prisons, drug abuse treatment centers and a sample of medical practitioners took part in the study. For each reported case of seropositivity, date of the information, gender and date of birth of the infected person, as well as the suspected route(s) of infection, were written down on an anonymous form. The survey resulted in the collection of 995 such forms corresponding to 725 seropositive persons after elimination of multiple counts. Its degree of completeness has been estimated at about 60%.

### Assessment of the HIV status

The 754 methadone patients were traced back to possible HIV infection in two ways. On the one hand, for 223 of them, a positive HIV status has been found through the mid-1986 survey or its extension to the second study period. On the other hand, 213 were identified as one of the 725 HIV-infected persons reported by the 1988 survey with gender, date of birth and, if necessary, other information as matching keys. In total, 223 methadone patients turned out to be HIV-infected among whom 149 both times. As the two methods of investigation are independent of each other, the overall probability of missing a seropositive patient may be estimated by multiplying their rates of reciprocally undetected cases, respectively 33% (74/223) and 30% (64/213), and amounts to about 10%.

### Risk assessment

Out of the 754 methadone patients, 31 are excluded from the study because they were already seropositive at entry into treatment. The 723 others are considered at risk for HIV infection from their first course of treatment until they become seropositive, die or escape otherwise from follow-up. As determination of current status was part of the mid-1988 survey, nearly all patients of the first study period stay under observation up to the end. To correct for the absence of such a survey in the second period, all subjects lost for follow-up at mid-1986, as no subsequent event (treatment episode, death or seroconversion) has been reported for them, are considered as if they were followed up as alive and uninfected until end 1988.

Within each study period, the risk of HIV infection is supposed to be constant. Under this simplifying assumption, the best estimator of the annual incidence rate in case of

censored follow-up is given by the function  $h \exp(-h)$ , where  $h$  is the ratio of HIV seroconversions to person-years of exposure in the period. Formulas for confidence intervals and tests are taken from the statistical literature<sup>16</sup>. The relative risk of HIV infection prevailing in a particular group will be expressed by the ratio of the incidence rate in that group to the overall incidence rate for the study period.

## Results

Table 1 gives the distribution of the 723 methadone patients according to the year of entry into treatment

and up to the year of end of follow-up. Seroconversions and escapes from observation understandably concentrate on mid-1986 and end 1988, when the surveys providing most of the information have been conducted.

In the first study period, the 397 methadone patients under observation at the beginning and the 143 newcomers were at risk of HIV infection. These 540 subjects have been followed-up for a mean duration of 2.2 years and 159 (29%) of them became seropositive. In the second period, the persons at risk amount to 506, 188 already present at start and 152 new to treatment. To them are added the 166 seronegative subjects lost for follow-up at

mid-1986 for reasons explained previously. In total, these 506 methadone patients were followed-up in the period for 1.6 years on average and 96 (19%) contracted the HIV infection in the meantime. This clear drop in the proportion of methadone patients becoming HIV-infected, from 29% to 19%, is mainly due to a concomitant increase in the proportion of recent entries into treatment, and to the resulting shortening of the duration of exposure from 2.2 years on average to 1.6 years. By contrast, according to the calculation presented in the method section, the annual HIV incidence rate has shifted only slightly from 13% to 11%.

Year	Under observation <sup>A</sup>	Entries into treatment <sup>B</sup>	Ends of follow-up Lost <sup>C</sup>	Dead <sup>D</sup>	HIV+	
1976	0	33	0	0	0	
1977	33	17	0	1	0	
1978	49	24	0	3	0	
1979	70	24	1	0	0	
1980	93	52	1	1	0	
1981	143	108	3	2	0	
1982	246	94	3	2	0	
1983	335	76	10	3	1	
1984	397	65	8	8	1	Spread of HIV epidemic
1985	445	50	5	3	11	1st period
1986 <sup>1</sup>	476	28	166	3	147	Survey on methadone patients
1986 <sup>2</sup>	188	20	13	1	1	
1987	193	60	41	5	33	2nd period
1988	174	72	181	3	62	Survey on HIV prevalence
total		723	432	35	256	

<sup>A</sup> at the beginning of the time interval.  
<sup>B</sup> start of the 1st course of methadone treatment.  
<sup>C</sup> survivals with no mention of HIV infection.  
<sup>D</sup> deaths with no mention of HIV infection.  
<sup>1</sup> 1st semester.  
<sup>2</sup> 2nd semester.

**Table 1.** Description of the study population. Switzerland, Canton of Vaud, 1976–1988, methadone treatment patients with no mention of HIV infection at start of the first course of treatment.

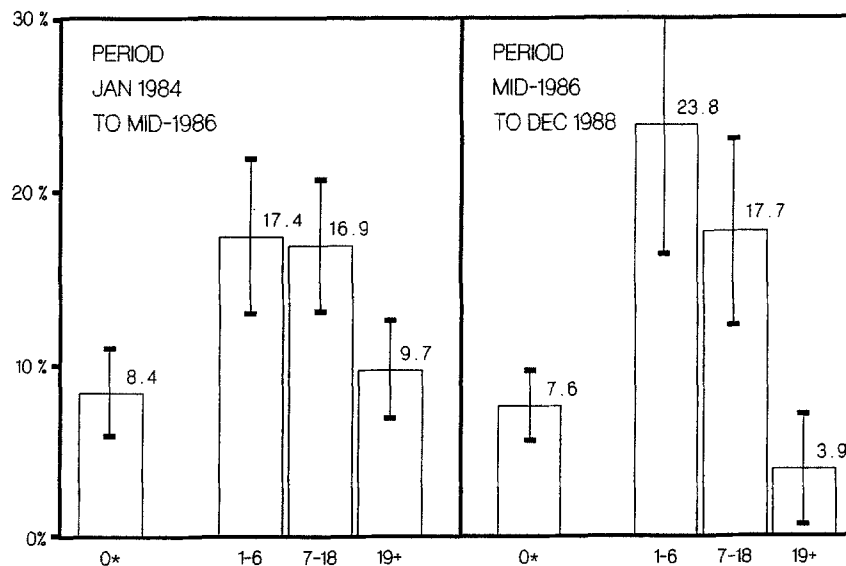
Period	Beginning of 1984 to mid-1986			Mid-1986 to end of 1988		
	no. HIV+/ no. cases	Mean expos years	Relative risk Value 90 %-CI	no. HIV+/ no. cases	Mean expos years	Relative risk Value 90 %-CI
Total	159/540	2.2	1.00 (reference)	96/506	1.6	1.00 (reference)
Gender			<i>P</i> = 0.578			<i>P</i> = 0.622
Male	100/350	2.2	0.97 0.81–1.13	59/324	1.6	0.96 0.76–1.17
Female	59/190	2.2	1.06 0.83–1.29	37/182	1.6	1.06 0.77–1.35
Year of birth			<i>P</i> = 0.247			<i>P</i> = 0.160
< 1956	33/134	2.3	0.80 0.57–1.03	15/106	1.8	0.68 0.39–0.97
1956–1960	83/256	2.3	1.04 0.85–1.23	45/195	1.8	1.07 0.80–1.33
> 1960	43/150	1.9	1.12 0.84–1.41	36/205	1.3	1.13 0.82–1.44
Age at 1st inj.			<i>P</i> = 0.640			<i>P</i> = 0.970
< 18	62/194	2.1	1.09 0.86–1.33	32/161	1.7	1.00 0.71–1.30
18–20	62/218	2.2	0.95 0.75–1.15	41/203	1.7	1.02 0.76–1.28
> 20	35/128	2.1	0.94 0.68–1.21	23/142	1.4	0.96 0.63–1.29
Duration* of drug use			<i>P</i> = 0.713			<i>P</i> = 0.113
0–2	36/135	2.2	0.88 0.64–1.13	17/130	1.8	0.64 0.39–0.90
3–4	52/158	2.2	1.10 0.85–1.36	31/146	1.5	1.23 0.86–1.59
5–7	42/145	2.2	0.97 0.72–1.22	28/132	1.7	1.06 0.73–1.39
> 7	29/102	2.0	1.05 0.73–1.37	20/98	1.5	1.12 0.70–1.53

\* from the first injection to the first course of methadone treatment  
*p* test of equality of the relative risks.

**Table 2.** Relative risk of HIV infection in one year of exposure, according to gender, year of birth, age at first drug injection and duration of initial drug use. Switzerland, Canton of Vaud, 1984–1988, methadone patients with at least one course of treatment before or during the period considered.

Table 2 presents the risk of HIV infection according to gender of the patient, year of birth, age at first drug injection, and duration of initial drug use. None of these variables shows a strong association with the risk. Patients born before 1975 or with more than ten years since drug use initiation, as well as those starting rapidly a methadone treatment, have a significant lower risk.

Associations between methadone treatment modalities and risk of HIV infection are examined in detail in Table 3. Risk of HIV infection is independent from the drug user's age at entry into methadone treatment, but increases with a more recent year of entry. The latter trend becomes significant in the second study period with a dramatic



**Figure 1.** Annual incidence rate of HIV infection and 90% confidence interval according to the number of months on methadone treatment. Switzerland, canton of Vaud, 1984–1988. (\*no longer having treatment during the period.)

Period	Beginning of 1984 to mid-1986			Mid-1986 to end of 1988		
	no. HIV+/ no. cases	Mean expos years	Relative risk Value 90%-CI	no. HIV+/ no. cases	Mean expos years	Relative risk Value 90%-CI
Year of 1st course			$P = 0.159$			$P = 0.033$
<1980	21/87	2.4	0.74 0.47–1.02	7/58	2.2	0.48 0.18–0.79
1980–1982	75/236	2.5	0.95 0.77–1.13	36/149	2.0	1.01 0.73–1.28
1983–1985	61/189	1.9	1.21 0.95–1.47	27/121	2.0	0.98 0.66–1.29
1986–1988	2/28	0.4	1.37 0.00–2.86	26/178	0.8	1.44 0.99–1.89
Age at 1st course			$P = 0.895$			$P = 0.822$
<21	33/102	2.2	1.06 0.76–1.37	18/87	1.7	1.06 0.65–1.48
21–25	84/292	2.2	0.97 0.80–1.15	49/264	1.7	0.94 0.72–1.17
>25	42/146	2.1	1.01 0.75–1.27	29/155	1.5	1.07 0.74–1.39
Frequency <sup>#</sup> of courses			$p < 0.001$			$p < 0.001$
0*	27/138	2.4	0.62 0.42–0.82	36/212	2.2	0.67 0.49–0.86
0.1–0.6	73/226	2.5	0.96 0.77–1.15	18/74	2.2	0.93 0.57–1.30
0.7–1.2	49/118	2.1	1.44 1.10–1.78	21/83	1.5	1.41 0.91–1.91
>1.2	10/58	0.6	1.93 1.01–2.86	21/137	0.5	2.50 1.69–3.32
No. months in treatment			$p < 0.001$			$p < 0.001$
0*	27/138	2.4	0.62 0.42–0.82	36/212	2.2	0.67 0.49–0.86
1–12	45/135	1.7	1.40 1.05–1.75	28/143	0.8	2.06 1.44–2.68
13–18	55/141	2.1	1.33 1.03–1.63	28/106	1.4	1.60 1.11–2.08
>18	32/126	2.5	0.77 0.54–0.99	4/45	2.2	0.35 0.06–0.64

\* no longer having treatment during the period.  
<sup>#</sup> average number of methadone courses per year.  
 $p$  test of equality of the relative risks.

**Table 3.** Relative risk of HIV infection in one year of exposure, according to different modalities of the methadone treatment. Switzerland, Canton of Vaud, 1984–1988, methadone patients with at least one course of treatment before or during the period considered.

upswing of the risk for drug users entering their first course beyond mid-1986. In either study period, patients no longer having treatment are at low risk although their duration of exposure covers nearly the whole time interval. Most of them have given up drug use, as it can be inferred from the drug dependence assessment of the mid-1986 survey. Among 146 patients with no new course of methadone in the first period, 77 (53%) were considered as stable abstainers at its end and 85% of them did not resume treatment in the second period.

For patients still on treatment, the risk of HIV infection is highly correlated with the number of courses

and with the time spent on treatment. The risk rises rapidly with the frequency of courses, that is with the number of instances in which the patient interrupts the treatment and resumes it later, often after an intervening episode of drug abuse. Inversely, the danger of contamination drops steadily with the duration of the treatment and this effect is clearly reinforced in the second period as shown in Figure 1.

### Discussion

According to recent reviews of literature<sup>8,11,17</sup>, there are only a limited

number of published works investigating the association between modalities of methadone treatment and the risk of HIV infection. Various enrolment techniques have been used in these studies with different resulting participation rates and potential selection biases. Most of the studies are cross-sectional, subjects being screened for HIV antibodies. Such design is not relevant for causal inference and may distort the comparison between treatment categories, the observed HIV seroprevalence rates serving as risk indicator and not correcting for the duration of exposure<sup>18</sup>.

The present study offers two advantages in comparison. It is exhaustive, as all drug addicts at least once on methadone treatment before the end of 1988 are included, and it is incidence-based given its longitudinal approach. On the other hand, the assessment of the HIV status is more debatable since it was obtained indirectly by consulting several sources of information. Nevertheless, the proportion of seropositivity cases missed is estimated at less than 10%.

Our study suggests that the administration of methadone reduces the risk of HIV infection significantly in different ways. On the one hand, the low incidence rate observed in patients having given up treatment for a long time, mostly stable abstainers, can be attributed to a large extent to successful detoxication methadone processes. On the other hand, the substantial drop in the risk of HIV infection with longer time spent in treatment supports than methadone maintenance is effective in progressively reducing the opiate addict's need to inject drug. This protective effect of the treatment duration has been found in many other investigations<sup>4,7,9</sup>. Two extensive reviews of existing studies<sup>8,11</sup> conclude that this treatment modality is the most consistent predictor of a low risk of HIV infection.

Another interesting observation is that, between 1984 and 1988, the risk gradient of treatment duration has widened out in both directions, patients longer on treatment becoming less exposed and inversely patients with shorter duration of treatment (mainly newcomers beyond mid-1986) becoming more at risk. Therefore, it is likely, as suggested for other regions<sup>19,20</sup>, that the epidemic spread rapidly through clusters of promiscuous needle sharers to whom patients new to treatment or with poorer attendance are more susceptible to belong.

Rates of new HIV infections among attenders to drug dependence treatment centers have been reported for New York<sup>21</sup>, Amsterdam<sup>22</sup>, Northern Italy<sup>23</sup> and Rome<sup>24</sup>. In all these places, the annual incidence rate came down or stabilized at levels between 5% and 7% in the years 1984–1988. In comparison, the seroconversion rate observed in our study remains high despite a modest decrease from 13% to 11% per year. The concurrent drop from 29% to 19% in the overall proportion of methadone patients becoming infected provides a second clue for a rapid spread of the epidemic

in particular subgroups of drug users.

The results of this study show that methadone treatment under medical surveillance is associated with a significant reduction in the risk of HIV infection even when no legal access to injection equipment is provided. However, in patients with poor attendance or recently admitted on treatment, an increase in the seroconversion rate has been observed. A greater availability of clean needles and syringes emerges from this background as a necessary and complementary policy to better protect from infection the drug addicts who start or continue to inject.

### Zusammenfassung

#### **Methadonbehandlung und HIV-Infektionsrisiko bei Drogenabhängigen ohne Zugang zu sterilem Injektionsmaterial**

Die Wirksamkeit der Methadonbehandlung der Drogenabhängigen in Bezug auf die Prävention der Infektion mit HIV muss gezielt evaluiert werden. Der Schweizer Kanton Waadt (550 000 Einwohner) erlaubte vor 1989 keinen erleichterten Zugang zu sterilem Injektionsmaterial, hingegen waren seit 1976 von den Hausärzten verordnete Methadonkuren zulässig. Von 754 Drogenabhängigen, die vor 1989 mindestens eine Methadonkur absolviert hatten, wurde in zwei Erhebungen (Mitte 1986 und Ende 1988) bei Ärzten, Spitälern, sozialmedizinischen Einrichtungen und Strafanstalten der HIV-Status erhoben. In den beiden Beobachtungsperioden (Anfang 1984 bis Mitte 1986, Mitte 1986 bis Ende 1988) betrug die Serokonversionsraten 13%, bzw. 11% pro Jahr. Diejenigen, die nicht mehr in einer Methadonbehandlung waren, es handelte sich meist um Langzeitabstinente, hatten in beiden Perioden ein relatives Infektionsrisiko von 0,65 ( $p < 0,05$ ). Für die behandelten Patienten nahm das Infektionsrisiko mit der Anzahl Kuren zu ( $p < 0,001$ ) und es war mit der gesamten Dauer der Behandlung negativ assoziiert ( $p < 0,001$ ). In der ersten Periode war das relative Infektionsrisiko 0,8 für jene, die mindestens 18 Monate in Kur waren und 1,4 für Patienten, die weniger als 6 Monate behandelt wurden. In der zweiten Periode waren die entsprechenden Risiken 0,3 und 2,1. Die zunehmende Diskrepanz ist durch eine hohe Serokonversionsrate der Patienten bedingt, die in der zweiten Periode erstmals zur Behandlung kamen. Aus den Studienresultaten darf man darauf schliessen, dass die Methadonbehandlung durch den definitiven Entzug und durch langfristige Substitution wesentlich zur Reduktion des HIV-Infektionsrisikos beigetragen hat. Hingegen ist der erleichterte Zugang zu sterilen Spritzen für Drogenabhängige, die erst am Anfang ihrer Behandlung stehen, eine notwendige Begleitmassnahme.

**Résumé****Traitement à la méthadone et risque d'infection VIH dans une population de toxicomanes sans accès légal à du matériel d'injection stérile**

L'efficacité du traitement à la méthadone comme mesure de prévention de l'infection VIH parmi les toxicomanes doit faire l'objet d'évaluations spécifiques. En Suisse, le canton de Vaud (550 000 habitants) constitue une région d'étude intéressante par le fait qu'aucune facilité d'accès à du matériel d'injection stérile n'existait avant 1989, mais que les cures de méthadone auprès d'un médecin praticien sont autorisées depuis 1976. Pour les 754 toxicomanes ayant suivi au moins une cure avant 1989, le statut sérologique VIH a été recherché par le biais de deux enquêtes (mi-1986 et fin 1988) auprès des médecins, hôpitaux, institutions médico-sociales et prisons. Le taux annuel de séroconversion a passé de 13% entre début 1984 et mi-1986 à 11% entre mi-1986 et fin 1988. Dans chacune de ces périodes, les personnes qui ne sont plus en traitement, essentiellement des abstinents stables, sont les moins exposées à l'infection VIH, avec un risque relatif de 0.65 ( $p < 0.05$ ). Pour les patients traités, le risque d'infection VIH est associé directement avec la fréquence des cures ( $p < 0.001$ ) et inversement avec la durée passée sous méthadone ( $p < 0.001$ ) dans chaque période. Cependant, le gradient de risque s'est accru d'une période à l'autre entre les patients qui ont passé respectivement plus de 18 mois et moins de 6 mois en cure, avec des risques relatifs de 0,8 et 1,4 avant mi-1986, de 0,3 et 2,1 après mi-1986. Ce phénomène s'explique par une forte hausse du taux de séroconversion chez les nouveaux patients. Ces résultats soutiennent l'hypothèse que le traitement à la méthadone permet de réduire le risque d'infection VIH à la fois par des processus de sevrage réussis et par des maintenances à long terme. Cependant, la mise à disposition de seringues stériles s'impose comme une mesure complémentaire urgente auprès des toxicomanes qui commencent les cures de méthadone ou les suivent de manière intermittente.

**References**

- 1 *Stimson GV*. The prevention of HIV infection in injecting drug users: recent advances and remaining obstacles. The Newsletter The International Working Group on AIDS and Drug Use 1991; 5(2-4): 14-19.
- 2 Anonymous. SIDA-information. Bulletin de l'Office fédéral de la santé publique 1992; 7:82.
- 3 *Des Jarlais DC, Friedman SR, Choopanya K, Vanichseni S, Ward TP*. International epidemiology of HIV and AIDS among injecting drug users. AIDS 1992; 6: 1053-1068.
- 4 *Ball JC, Lange WR, Myers CP, Friedman SR*. Reducing the risk of AIDS through methadone maintenance treatment. J Health Soc Behav 1988; 29:214-226.
- 5 *Hartgers C, Buning EC, van Santen GW, Verster AD, Couthino RA*. The impact of the needle and syringe-exchange programme in Amsterdam on injecting risk behaviour. AIDS 1989; 3:571-576.
- 6 *Calsyn DA, Saxon AJ, Freeman G, Whittaker S*. Needle-use practices among intravenous drug users in an area where needle purchase is legal. AIDS 1991; 5:187-193.
- 7 *Schoenbaum EE, Hartel D, Selwyn PA et al*. Risk factors for human immunodeficiency virus infection in intravenous drug users. N Engl J Med 1989; 321:874-879.
- 8 *Cooper RC*. Methadone treatment and acquired immunodeficiency syndrome. JAMA 1989; 262: 1664-1668.
- 9 *Novick DM, Herman J, Scott C, et al*. Absence of antibody to human immunodeficiency virus in long-term, socially rehabilitated methadone maintenance patients. Arch Intern Med 1990; 150:97-99.
- 10 *Robert CF, Déglon JJ, Wintch J, et al*. Behavioural changes in intravenous drug users in Geneva: rise and fall of HIV infection, 1980-1989. AIDS 1990; 4:657-660.
- 11 Congress of the United States, Office of Technology Assessment. The effectiveness of drug abuse treatment: implications for controlling AIDS/HIV infection. Washington, DC: US Government Printing Office; 1990. GPO 052-003-01210-3.
- 12 *Lehmann P, Hausser D, Somaini B, Gutzwiller F*. Campaign against AIDS in Switzerland: evaluation of a nationwide educational programme. Br Med J 1987; 295: 1118-1120.
- 13 *Meystre-Agostoni G, Wietlisbach V, Martin J*. Methadone treatment in medical private practice: outcome according to the number of courses followed. Br J Addic 1990; 85: 537-545.
- 14 *Meystre-Agostoni G, Martin J, Haller-Maslov E, Calanca A, Cereghetti A*. Le devenir des toxicomanes pris en charge à l'aide de méthadone dans le canton de Vaud (1976-1986). Rev Med Suisse Romande 1988; 108:231-256, 501-519.
- 15 *Meystre-Agostoni G, Van Melle G, Chave JP, et al*. Epidémie VIH: une étude parmi les praticiens vaudois. Schweiz Med Wochenschr 1990; 120:1390-1393.
- 16 *Gross AJ, Clark VA*. Estimation and inference in the exponential distribution. In: Survival distributions: reliability applications in the biomedical sciences. New York: J Wiley, 1975; 49-96.

- 17 Hahn RA, Onorato IM, Jones S, et al. Prevalence of HIV infection among intravenous drug users in the United States. *JAMA* 1989; 261:2677–2681.
- 18 Kleinbaum DG, Kupper LL, Morgenstern H. *Epidemiological research: principles and methods*. New York: van Nostrand Reinhold, 1982.
- 19 Robertson JR, Skidmore CA, Roberts JJ. HIV infection in intravenous drug users: a follow-up study indicating change in risk-taking behaviour. *Br J Addict* 1988; 83:387–391.
- 20 Vlahov D, Munoz M, Anthony JC, Cohn S, Celentano DD, Nelson KE. Association of drug injection and patterns with antibody to human immunodeficiency virus type 1 among intravenous drug users in Baltimore, Maryland. *Am J Epidemiol* 1990; 132:847–856.
- 21 Des Jarlais DC, Friedman SR, Novik DM, et al. HIV-1 infection among intravenous drug users in Manhattan, New York City, from 1977 through 1987. *JAMA* 1989; 261:1008–1012.
- 22 Van Haastrecht H, Van der Hoek J, Bardoux C, Leentvar-Kuypers A, Coutinho R. The course of the HIV epidemic among intravenous drug users in Amsterdam, the Netherlands. *Am J Public Health* 1991; 81:59–62.
- 23 Nicolosi A, Correa Leite ML, Musicco M, et al. Parenteral and sexual transmission of human immunodeficiency virus in intravenous drug users: a study of seroconversion. *Am J Epidemiol* 1992; 135 (3):225–233.
- 24 Zaccarelli M, Rezza G, Giradri E, et al. Monitoring HIV trends in injecting drug users: an Italian experience. *AIDS* 1990; 4:1007–1010.

---

**Address for correspondence**

Vincent Wietlisbach  
Institut universitaire de médecine  
sociale et préventive  
17, rue du Bugnon  
CH-1005 Lausanne