

# Access to antiretroviral treatment among French HIV infected injection drug users: the influence of continued drug use

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## Abstract

**Study objective**—To determine the influence of continued drug use and its perception by prescribing physicians on access to antiretroviral treatment among French HIV infected injection drug users (IDUs). **Design**—Cross sectional including enrolment data (October 1995–1996) of the cohort study MANIF 2000. Access to treatment is compared in three groups: former IDUs (n=68) and active IDUs whether or not this behaviour remains undetected (n=38) or detected (n=17) by physicians.

**Setting**—Hospital departments for specialist AIDS care in south eastern France and inner suburbs of Paris.

**Patients**—All enrolled patients with CD4<sup>+</sup> cell counts < 400 with detailed clinical history, access to treatment, risk behaviours, and past drug use as reported by both physicians and patients (n=123).

**Main results**—A minority (43.9%) already received an antiretroviral treatment. Active IDUs had worst socioeconomic and psychological conditions but only those detected by physicians were considered as poorly compliant. Logistic regression showed that, with respect to ex-IDUs and independently of clinical stage, active IDUs, whether or not they were perceived as such by physicians, were threefold more likely not to receive antiretroviral treatment.

**Conclusions**—Even among French HIV infected IDUs who have regular access to AIDS specialised hospital care, continued drug use reduced the likelihood of being prescribed antiretroviral treatment. To reduce delays in access to new treatments, specific efforts must be devoted towards both AIDS specialists and IDU patients to overcome current stereotypes of non-compliance associated with continued injection.

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Socioeconomic differences have been observed to be strongly associated with access to newly introduced treatments for a variety of diseases, reflecting non-financial, as well as financial barriers to care. It is well established that injection drug users (IDUs) tend to have less access to care for HIV infection in general and to antiretroviral medication in particular than other groups of transmission.<sup>1-3</sup> Inadequate

health care insurance coverage is of course related with unmet health care needs of HIV infected people,<sup>4,5</sup> but important inequities in utilisation of HIV health care services still exist even when free or low cost public sector care is available.<sup>6,7</sup>

The French Social Security system guarantees health care insurance coverage for the whole population and since 1993, all medical care is totally free of charge as soon as a patient has a diagnosis of HIV infection. Importance of non-financial barriers to HIV care, such as the impact of injection drug use on physicians' judgments about compliance of patients, may therefore be easier to evaluate in the French context.

The MANIF 2000 French cohort study of patients HIV infected through intravenous drug use gave us the opportunity to study the determinants of access to antiretroviral treatment according to perception of patient's drug use by prescribing physicians. The study was carried out before the introduction of new treatments with protease inhibitors in this population, but current recommendations for early initiation of multiple combination treatments<sup>8</sup> create an increased interest for better understanding the potential role of subjective factors in slowing down access of IDUs to any antiretroviral treatments.

## Methods

MANIF 2000 is a prospective study that started in October 1995 whose aim is to assess the effect of persistent misuse of drugs on progression of HIV infection among patients initially infected through injection drug use. The study enrolls patients aged 18 years or more, with CD4<sup>+</sup> cell counts  $\geq$  300/mm<sup>3</sup> in the last visit before enrolment, with no opportunistic infections, in hospital departments of Marseilles, Nice and inner suburbs of Paris (that is, the French geographical areas with the highest proportion of IDUs among AIDS cases—more than 35% of new cases in 1996).

For each eligible patient, data collected at enrolment include a detailed retrospective clinical history based on medical records, and a medical questionnaire filled out by the hospital AIDS specialist at the end of consultation that contains, in addition to clinical information and history of antiretroviral treatment, questions about physician's opinion about current drug use by his patient; physicians' beliefs about their patient's likelihood to comply with appointments and with medications are as-

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Table 1 Demographic, lifestyle, and medical/psychiatric characteristics of injection drug users by injection status (1= former, 2 = active undetected by physicians, 3 = active detected by physicians) in the French IDU cohort study MANIF 2000 (October 1995–October 1996)

	Group 1	Group 2	OR 95%CI	Group 3	OR 95%CI	Total (n=123)
	-- (n=68)	+ - (n=38)		++ (n=17)		
	%	%		%		%
Sex (male)	66.2	68.4	1.1 (0.4, 2.8)	70.6	1.2 (0.4, 5.0)	67.5
Living alone	44.1	71.1	3.1 (1.2, 8.0)	52.9	1.4 (0.4, 4.7)	53.7
Level of education ( $\geq$ high school certificate)	19.1	7.9	0.4 (0.1, 1.5)	17.6	0.9 (0.2, 4.0)	15.4
Living on welfare	51.5	78.9	3.5 (1.3, 9.8)	88.2	7.1 (1.4, 67.1)	65.0
In maintenance drug abuse treatment <sup>1</sup>	11.8	47.4	6.7 (2.3, 20.2)	43.8	5.8 (1.5, 24.1)	27.0
Poor housing conditions	11.8	28.9	3.1 (1.0, 9.5)	35.3	4.1 (1.0, 16.7)	20.3
Has been institutionalised	45.6	60.5	1.8 (0.8, 4.4)	52.9	1.3 (0.4, 4.4)	51.2
Follow up in hospital ( $>5$ y) <sup>1</sup>	50.7	32.4	0.5 (0.2, 1.2)	29.4	0.4 (0.1, 1.4)	42.1
Time from HIV diagnosis ( $>5$ y)	81.0	57.9	0.3 (0.1, 0.9)	58.8	0.3 (0.1, 1.2)	70.7
CDC stage B	44.1	44.7	1.0 (0.4, 2.5)	64.7	2.3 (0.7, 8.5)	47.2
Antecedents of PCP prophylaxis <sup>1</sup>	20.6	18.9	0.9 (0.3, 2.7)	17.6	0.8 (0.1, 3.6)	19.7
Referred to a psychiatrist <sup>1</sup>	6.0	45.9	13.4 (3.7, 59.3)	31.3	7.2 (1.3, 40.9)	21.7
Referred to a social worker <sup>1</sup>	6.0	37.8	9.6 (2.6, 43.1)	37.5	9.5 (1.8, 52.1)	20.0
Poor compliance with medications* <sup>2</sup>	23.1	37.8	2.0 (0.8, 5.4)	93.3	46.7 (5.9, 2011)	36.8
Poor compliance with appointments* <sup>1</sup>	17.9	29.7	1.9 (0.7, 5.5)	82.4	21.4 (4.7, 127)	30.6
Satisfied with relationship to medical staff† *	58.8	71.1	1.7 (0.7, 4.4)	68.8	1.5 (0.4, 6.3)	63.9
Poor compliance with medical prescription† <sup>1</sup>	33.8	43.2	1.5 (0.6, 3.7)	31.2	0.9 (0.2, 3.2)	36.4
Satisfied with current state of health†	83.8	63.2	0.3 (0.1, 0.9)	62.5	0.3 (0.1, 1.2)	74.6
Depressed‡	44.1	84.2	6.8 (2.3, 22.1)	76.5	4.1 (1.1, 18.8)	61.0
Low social support§	31.3	39.4	1.4 (0.5, 3.7)	66.7	4.4 (1.2, 18.1)	38.3

\*Physicians' declaration that patients are "never" or "rarely" compliant. †Patient's self perception that they are "never" or "rarely" compliant. ‡Patients with possible depression (scores  $>17$  in French version of CES-D). §Patients who declare "not at all" or "only a little" support from family members, partners, and friends in everyday life. <sup>1</sup>For these variables, 1–3 patients did not answer the question. <sup>2</sup>6 patients did not answer the question.

essed by means of two questions using a five point scale (never/rarely/sometimes/often/always). In parallel, in depth data about patient's social and psychological characteristics as well as their personal experience with HIV infection and care are obtained by means of a face to face questionnaire administered by a nurse and a self administered questionnaire. This latter questionnaire includes, among different psychometric scales, the French version of the Center for Epidemiological Studies-Depression Scale (CES-D),<sup>9,10</sup> three questions about patient's perceived social support in current daily life by partner, family and friends (using four point scales: not at all/ only a little/ fairly/very important), and patients' self perception of compliance with medical prescriptions (using the same five point scale as in the physician's questionnaire). It also contains 19 questions about HIV related risk behaviours including type of drug use, frequency of injection, and access to drug maintenance treatment during lifetime and the last six months.

To assess the impact of active drug use and its perception by physicians on access to antiretroviral treatment, we examined patients and physicians' answers about current drug use and classified patients into three categories: those who declared that they did not inject any drug in the last six months and were concordantly perceived as abstinent by their physician (group 1); those who acknowledged injecting behaviour during the same period but were discordantly perceived as abstinent by their physician (group 2); those who were considered as active IDUs by physicians (group 3).

A total of 325 patients were recruited in the first year of the study (October 1995–October 1996). Determinants of access to antiretroviral treatment were evaluated in the subset of 129 patients with less than 400 CD4<sup>+</sup> cell counts/mm<sup>3</sup> at enrolment, as it is the subgroup of patients where initiation of antiretroviral treat-

ment has to be considered according to official French clinical guidelines.<sup>11</sup>

Mann-Whitney or  $\chi^2$  tests were used for comparing characteristics of patients in the three groups and for identifying variables likely to be related to access to antiretroviral treatment. Odds ratios and their 95% confidence intervals were calculated to quantify the strength of association. To examine the hypothesis that continued drug use and its perception by physicians influences prescription of antiretroviral drugs, even after adjustment for clinical and psychosocial variables also related to access to treatment in univariate analyses ( $p < 0.05$ ), multiple logistic regression models were performed.

## Results

Among the 129 patients with CD4<sup>+</sup> cell counts  $< 400/\text{mm}^3$ , six could not be classified for current drug use because of missing data and were subsequently excluded from the analysis. The remaining 123 patients were classified as follows: (1) A total of 71 patients declared being abstinent of injection drug use, and only three were discordantly considered as active injectors by the physician. Group 1 (abstinent perceived as such by physicians) therefore includes 68 patients. (2) Another group of 52 patients reported having injected drugs during the last six months. But 38 of them were not considered as such by the physician's judgment and formed group 2 (active IDUs not perceived as active by physicians). (3) Group 3 (patients considered as active by physicians) consisted of 17 patients: 14 patients who acknowledged current injection drug use and three patients who did not. It must be noted that for these three patients, physicians' questionnaires mentioned clinical signs of recent injection drug use.

When comparing medians and interquartile ranges in the three groups of patients (1,2,3), no significant differences were found as far as

age, (32 (30.2–36.0); 33 (30.0–36.0); 34 (30.0–37)) time since last visit before enrolment, (2 months (1–4); 2 (1–5.5); 2 (1–3.5)), CD4<sup>+</sup> cell counts/mm<sup>3</sup> at enrolment (329 (270–358); 321 (290–360); 300 (262–346)), and plasma viral load (log cp/ml) (4.3 (3.4–4.8); 4.2 (3.6–4.8); 4.4 (3.8–4.7)). Patients who stopped injection had shorter periods ( $p < 0.05$ ) of drug use during lifetime (8 years (4–11) *v* 14 (11–17) and 15.5 (6.5–16.7)).

Table 1 shows that the three groups had similar distribution by sex, CDC stage, education level, experiences of imprisonment, years of follow up at the hospital, years from initial HIV diagnosis, and antecedents of pneumocystis carinii pneumonia (PCP) prophylaxis, suggesting that they did not generally differ in terms of access to health care. Table 1 also shows that active IDUs (groups 2 and 3), whether or not they were recognised as such by physicians, had worse socioeconomic conditions, were more depressed and unsatisfied by their current health status than those who had stopped injecting drugs (group 1). Active IDUs were also more likely to have been referred to a specialist for psychiatric or anxiety disorders, and to social workers for support during the last six months. Table 1 also shows that physicians clearly distinguish IDUs that they identify as such (group 3) and the rest of the sample in terms of poor compliance. Physicians' perceptions contrast with patients' declarations about compliance and satisfaction with medical staff, which are similar in the three groups.

A minority ( $n=54$ ; 43.9%) of patients already benefited from a prescription of antiretroviral treatment. Among the 49 treated patients where detailed information about past treatment was available, 30 (61.2%) received a combination therapy with two or more reverse transcriptase inhibitors and 15 (30.6%) had their antiretroviral treatment started during the last 12 months. No significant difference for duration of antiretroviral treatment was observed between treated IDUs and ex-IDUs. At the time of data collection (October 1995–October 1996), no protease inhibitor had yet been prescribed to any patient.

Advanced CDC stage, living in a stable relationship with a partner, and abstinence of drug use were the only variables to be significantly associated with receiving antiretroviral treatment. Multiple logistic regression (table 2) shows that, after accounting for CDC AIDS staging system, former IDUs were three times more likely to receive antiretroviral drugs than

#### KEY POINTS

- Socioeconomic differences have often been observed in access to new treatments and related to financial and non-financial barriers.
- Since 1993, the French social security system guarantees a free of charge access to health care for all HIV infected persons.
- The cohort MANIF 2000 can show how continued drug use among HIV infected persons can influence access to antiretroviral treatment in the absence of financial barriers.
- Results call for actions towards both AIDS specialists and IDUs for overcoming stereotypes of non-compliance associated with continued injection.

active IDUs whether or not the latter were labelled as such by physicians (groups 3 and 2).

#### Discussion

HIV infected IDUs who continue to use drugs tend to have a lower access to medical care, and a lower frequency of clinical encounters than those who stopped injecting behaviour<sup>2,3</sup>; in the US HIV infected IDUs have been found to be more likely to use informal unpaid home care than other patients.<sup>12</sup> As a consequence continued drug use is likely to be associated with lower access to antiretroviral treatment.

The French context allowed us to check the impact of continued drug use on access to antiretroviral treatment when financial barriers to HIV care in general do not exist. Our data strongly show that even among French HIV infected IDUs who had regular access to AIDS specialised hospital care, with similar medical conditions (in terms of clinical stage, levels of CD4<sup>+</sup> cell counts, and plasma viral load) and similar duration of medical follow up, those who continue to inject drugs were less likely to benefit from antiretroviral treatment.

Of course, it cannot be excluded that, in our study, some active IDUs have been offered antiretroviral treatment but have declined this opportunity more often than ex-IDUs. Our data, however, suggest that physicians' perceptions of patients' behaviours influence their decision to start antiretroviral treatment and that continued drug use, whether or not it is explicitly recognised in the patient-physician relationship, is associated with greater physi-

Table 2 Factors associated with access to antiretroviral treatment in HIV infected injection drug users with CD4<sup>+</sup>T-lymphocytes <400/mm<sup>3</sup>. France MANIF 2000 cohort study (October 1995–October 1996) ( $n=123$ )

	% Treated	OR and 95%CI	Adjusted OR and 95%CI
CDC AIDS staging			
stage A	29.2	1	
stage B	51.7	2.59 (1.16, 5.85)	2.84 (1.31, 6.17)
Living in a stable relationship			
No	30.3	1	
Yes	50.9	2.38 (1.07, 5.34)	—
Injection status			
1 Former IDU	47.1	1	
2 Active IDU undetected by physicians	31.6	0.52 (0.21, 1.29)	0.36 (0.15, 0.85)
3 Active IDU detected by physicians	29.4	0.47 (0.12, 1.64)	0.26 (0.08, 0.87)

cian's reluctance to start antiretroviral prescription.

Despite the adherence of physicians to a universal code of ethics, discriminatory attitudes toward HIV infected patients have been well documented among health care professionals,<sup>13 14</sup> and such attitudes are exacerbated where these patients are IDUs.<sup>15-17</sup> However, it is also well established that discriminatory biases quickly decline as health professionals become familiar with treating people with HIV.<sup>18-20</sup> Our data did not report whether or not discriminatory attitudes may have persisted among AIDS specialists in the hospital departments participating in our study.

They show in any case that the subjective judgments of doctors about the poor personal and social environment and anticipation of poor compliance of patients, which may be based on previous experience in clinical interaction, influence their decisions to withhold antiretroviral treatment among HIV infected patients who continue to use drugs.

The fact that active IDUs, who are not seen as active anymore by their physicians, also remain less likely to receive antiretroviral treatment than actual former users, suggest that clinicians tend to make judgments based upon perceived chaotic lifestyles, even in the absence of perceived injection drug use. These judgments are partly based on real conditions: not surprisingly those who continue to use drugs remain in the worst social and psychological conditions, which create additional difficulties for continuity of care.<sup>21-23</sup> Such situations can raise legitimate concerns among physicians about the capacity of patients to comply to treatment, and risks of developing drug resistance that could be harmful for the long term management of the patient himself as well as others in case of HIV transmission.

However, it has also been shown that HIV infected health seeking behaviours are directly influenced by their perception of health care professional attitudes. Recent progress in antiretroviral treatment makes an obligation for professionals to revisit the stereotype of non-compliant and non-reliable IDU patients.<sup>24-26</sup> After all, the extent to which IDUs have already changed their behaviour to reduce risk of AIDS worldwide has been impressive going well beyond what most medical experts in the field would have predicted.<sup>27</sup>

Introduction of protease inhibitors may change this differential access to treatment according to current status toward drug use. But to the extent that non-compliance has been clearly linked to viral resistance and drug failure in the case of antiprotease inhibitors,<sup>28</sup> it is quite possible that persistence of injecting drug use will create a barrier for rapid access to these new treatments, unless specific efforts are devoted for improving the quality of relationships between AIDS specialists and their IDU clients and for increasing appropriate social and psychological support to this group of HIV infected patients.

Successful AIDS/HIV risk reduction intervention among IDUs most usually have several

components including outreach work and peer education targeted for their social networks.<sup>29</sup> Interventions aimed at increasing IDUs access and compliance to multiple combination therapies will certainly have to be based on similar principles, but our study suggests that these types of interventions targeted at IDUs in their social environment could be usefully complemented by other actions towards both AIDS specialists and IDU patients for overcoming current stereotypes of non-compliance associated with continued injection.

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