No variability across centers in adherence and response to HAART in French hospitals: results from the ANRS-EN12-VESPA study.

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Abstract

Objective

Because a centre effect can sometimes exist in HIV treatment, we sought to measure the heterogeneity of French hospital departments delivering HIV care and to test the presence of such an effect on adherence and response to HAART.

Methods

The ANRS-EN12-VESPA study is a nationally representative two-stage cross-sectional survey conducted in France in 2003 and covering 102 hospital departments providing HIV care. Each department described its HIV care activities and care provision. Analyses of adherence and four indicators of treatment outcome were restricted to the 699 patients diagnosed from 1996 onwards and treated with HAART for at least 6 months. The variability between departments was assessed with random-effect models for binary outcomes.

Results

The departments delivering HIV care proved to be somewhat heterogeneous in numerous respects, including their size and their onsite provision of consultancies and other services, as well as the characteristics of their patient population. Mean observed adherence was 63.3%, and the means of the different treatment failure indicators ranged from 6.1% to 59.8%. The departments showed some variability for these outcomes, but no significant centre effect was detected.

Conclusions

Despite the heterogeneity of the specific types of medical services offered by the hospitals providing HIV care, the nationwide treatment results appear homogeneous. This homogeneity could be attributed to the widespread and consistent application of therapeutic guidelines, which are regularly updated by consensus.

Introduction

Since the advent of AIDS, equality and non-discrimination in access to prevention and treatment have been major issues, because so high a percentage of patients belongs to stigmatised or disadvantaged groups, such as drug users, ethnic minorities, immigrants or women. Disadvantaged groups have been shown to have less access to zidovudine treatment [1] and pneumocystis carinii pneumonia (PCP) prophylaxis [2]; they also start HAART later [3]. Aside from the barriers to health care due to patients' financial situation and educational level, physicians' anticipation that patient compliance will be poor [4 ,5] has been shown to explain delayed initiation of HAART. Moreover, several US studies, conducted mainly before the advent of HAART, identified physician experience as a determinant of progression to AIDS and survival [6 ,7 ,8 ,9 ,10].

Since a very high level of adherence is required to fully benefit from HAART, a multidisciplinary approach to HIV care is need to support patients and help them deal with the practical, social and emotional dimensions of living with HIV [11 , 12]. Hospitals and health care centres should provide comprehensive HIV care with a range of medical and social services to achieve the best possible outcomes. Rapid progress in clinical research necessitates the regular updating of treatment recommendations. Physicians should update their practice

regarding treatment so that all patients can benefit from the most recent scientific advances. Such rapid changes might vary according to physician characteristics, type of setting and size of HIV caseload.

The purpose of this paper is to describe the heterogeneity of the hospital HIV treatment provided in France and its effect on treatment outcome.

Material and methods

Study design

This analysis used data from the 2003 ANRS-EN12-VESPA study, a large nationally representative two-stage cross-sectional survey, aimed at studying the social situation of HIV-infected persons in France. The study design has been detailed elsewhere [13]. 85 hospitals providing HIV care were randomly selected among the 143 French hospitals with a HIV caseload greater than 60 patients, stratifying on geographic location and size of HIV caseload. As some large hospitals had several departments serving patients with HIV, the 85 hospitals were composed of 102 departments providing HIV care. Doctors in each of these departments randomly recruited a sample of outpatients (representing about 5% of their caseload) among those with the following eligibility criteria: having been diagnosed with HIV-1 infection for at least 6 months, aged 18 or older, and, if not a French citizen, having lived in France for at least 6 months. Patients who understood French very poorly were excluded. The study design and informed consent procedures complied with the ethical and statutory requirements of the French Data Protection Authority (Commission Nationale Informatique et Libertés).

Information collected

Information was collected for each hospital department and for each individual patient. In each department, a clinical research assistant completed an information sheet on the current HIV patient caseload, department capacity (number of physicians, of inpatient beds, of day hospital beds, and of weekly outpatient appointments), participation in research activities (cohort studies and clinical trials), onsite provision of a range of specialised consultations and care (nutrition, hepatolology, dermatology, drug treatment liaison team, psychiatry etc.), promotion of treatment adherence (group or individual education, leaflets, pillbox provision etc.), and the onsite presence of PLWHA groups.

Information was collected on the following characteristics for all eligible patients: sex, age, employment status, mode of transmission and last known CD4 cell count and viral load. This data allowed for the assessment of participation bias.

Participating patients answered a questionnaire administered in a face-to-face interview. Detailed information was collected on socio-demographic characteristics and on a wide range of social conditions (health care access and use, health behaviour, occupational status, income, housing, social support, HIV disclosure, discriminations encountered, sexual activity and reproductive life). Physicians recorded for each patient the mode of HIV acquisition, disease characteristics, and treatment information (date of diagnosis, date of HAART initiation, clinical stage, CD4 count and viral load at diagnosis, at HAART initiation and last known values).

Variables of interest

The heterogeneity of the departments delivering HIV care was studied for adherence and various measures of treatment outcome.

Adherence to HAART was assessed with a dichotomous outcome (high versus moderate or poor adherence) validated in previous cohort studies [14 ,15]. First, participants were asked about their compliance with HAART in the prior 7 days. They had to choose among the following items, each corresponding to a level of adherence: 'I have followed scrupulously my treatment' (=high adherence), 'I have followed my treatment despite some small lapses' (=moderate adherence), 'I have frequently modified doses or time schedule', 'I have almost never complied with prescription instructions', 'I have stopped treatment' (=poor adherence). Then, participants were asked whether or not they had missed at least one dose during the previous week-end, whether they had taken the whole daily dose in only one take in the previous 7 days, or whether they had failed to respect the time schedule for at least one dose during the same period. Participants previously ranked as highly adherents but who had answered 'yes' to one of these three questions were reallocated to the 'moderate adherence' category.

Treatment outcome was assessed using four different indicators, three defining failure and one denoting success:

- Immunological response was defined as the absence of an increase of ≥100 CD4 cells/mm^3 between HAART initiation and data collection. This threshold was chosen on the basis of the review by May and colleagues [16], showing a median 100 cells increase in CD4 cell count in the first 6 month on HAART, which was here the minimum duration.

- Virological failure was defined as having detectable HIV-RNA (<400 copies/ml) at data collection;

- Immunovirological failure was defined as the combination of a CD4 cell count ≤200/mm^3 and detectable HIV-RNA at data collection;

- Lastly, immunovirological success was defined as the combination of a CD4 cell count ≥ 500/mm³ and undetectable HIV-RNA at data collection. [17]

Population of interest

The VESPA study included 2932 participants from 102 different departments. For the present analysis, we included only the 699 participants (of 97 different departments) who had been diagnosed in 1996 or later and had received HAART for at least 6 months at the time of the study. The medical history of patients diagnosed before and after the HAART era is indeed too different to be pooled in an analysis on this topic. Furthermore, the much higher mortality before 1996 indicates much greater selection bias among the patients diagnosed before that year. A minimum of 6 months is assumed necessary before the treatment can be judged effective and thus classified as a success or failure.

Statistical methods

For each of the five outcomes, the existence of a centre effect was assessed by testing the department as a random variable in a binary mixed model, without any other covariate. If this random variable appeared to be significant, the next step of the analysis was to include in the models covariates measured at the individual level (age, sex, sexual orientation, immigration status, education, HCV coinfection, time since HAART initiation, CD4 cell count at HAART initiation, addictive behaviour, current trial participation, side effects, and adherence, when relevant). If the random variable was no longer significant, then the previously found effect was due only to differences in population structure and a given patient had the same chance of treatment outcome regardless of facility.

Because including centres with very few subjects could result in a lack of robustness, we performed a sensitivity analysis by restricting the analysis to departments with at least five participating patients and then with at least 10 participants. All statistical analyses were performed using SAS 9.1.

Results

Characteristics of departments regarding service provision

Among the 102 departments, the median size of the HIV caseload at data collection was 400 (IQR: [230–750]). The median number of physicians providing HIV care per department was 3 (IQR: [2 –6]), and the median number of outpatient appointments per week was 7 (IQR: [5 –10]). Half of these departments specialised in infectious diseases, a quarter in internal medicine, and the others in haematology, dermatology, pneumonology or hepatology. Internal medicine departments tended to provide a wider range of consultant services than the others. These most often included nutrition (85%), followed by dermatology (55%) and psychiatry (53%). More rarely offered were hepatology (36%), addiction liaison service (39%), endocrinology (32%), neurology (29%) and gynaecology (28%). Individual sessions on adherence education were provided in 83% of the departments, and PLWHA organisations offered an onsite presence in 41%. Most departments participated in clinical research, such as clinical trials (83%) or cohort studies (79%).

Characteristics of participants

The median age of these patients was 42 years (IQR: [35–51]); men accounted for 75% of the sample; 39% self-identified as homo- or bisexual men, 6% were IDU (4% men, 2% women), 29% were French-born heterosexuals with no IDU history (19% men, 10% women) and 26% were immigrant heterosexuals with no IDU history (13% men and women). Most of the heterosexual immigrants came from sub-Saharan Africa (72% of the men and 86% of the women). Late diagnosis (defined either as symptoms of clinical AIDS or CD4 cell count <200/mm³ during the year following diagnosis) was observed in 43% of this population diagnosed in or after 1996. At HAART initiation, 49% had a CD4 cell count < 200 cells/ml.

Structure of departments' population

As shown in Table 1 , these different categories of participants were not uniformly distributed among the hospital departments: the structure of the patient population appeared quite heterogeneous across centres. The median proportion of immigrants was 20%, with an IQR from 0% to 40%. While men constituted a majority of patients, with a median proportion of 75%, this rate varied substantially (IQR: [60%–90%]). The median proportion of patients under 40 was 43% (IQR: [20%–50%]), and the median proportion of patients with late diagnosis was 40% (IQR: [29%–57%]). Few departments treated patients with an IDU history: the median proportion of these patients was 0 and the upper quartile 12.5%.

For the analysis population, the mean number of participants per department was 7.2 and the median 6 (IQR: [1 – 10]).

Adherence and treatment outcomes

Table 2 shows the distribution of adherence and treatment outcomes measured for each hospital department and the related tests for centre effects. The mean percentage of highly adherent participants was 63.3%. The heterogeneity between departments was rather large:

the IQR varied from 50% to 80%, with a median adherence rate of 62%. However, the existence of a centre effect was rejected when we tested the department as a random variable (p = 0.275).

The overall rate of immunological failure was 22.6%, with a departments' median of 20% and an IQR of 0% to 40%. No centre effect existed here either (p = 0.215). The overall rate of virological failure was 12.5%, with a median rate of 7.7%. Only a quarter of the departments had rates above 20%, and 44.3% had no virological failures. Again, no centre effect was detected (p =0.098).

The mean immunovirological failure was 6.1%. Three quarters of the departments had a failure rate under 12.5%, and 61% had no participants in immunovirological failure. The existence of a centre effect was rejected with a p-value of 0.181.

The criteria defining immunovirological treatment success, i.e. a CD4 count over 500/ml and undetectable HIV-RNA, were met by 40.2% of patients. The median department success rate was 36.3%: a quarter had rates only below 13.3%, and another quarter had rates above 50%. The random variable appeared to be significant (p=0.026) for this indicator. A centre effect thus existed, at least when tested for the entire population analysed. Nevertheless, the random term was not significant when a covariate measured on the individual level was introduced, such as the patient CD4 cell count≤200/mm^3 at HAART initiation (p=0.094) or the patients' immigration status (p=0.200).

Our sensitivity analysis consisted in rerunning these models with restricting the analysis population first to the 601 patients of the 60 departments that had at least five participating patients, and secondly to the 378 patients of the 26 departments that had at least ten participating patients.

For adherence, as for the three first indicators of treatment failure, the absence of a centre effect was confirmed. Concerning immunovirological success, the random variable was still significant in the first restriction (p=0.030) and almost still significant in the second restriction to departments with at least 10 patients (p=0.053). Adjusting on covariates measured on the individual level returned as previously a non-significant random term.

Discussion

This study used data from a large random sample of hospitals providing HIV care, both representative at the national level and very diverse in terms of size, region, localisation in either metropolitan areas or medium-sized cities, activity, and specialisation. We observed a significant variation in the size of the HIV caseload, the provision of consultant services offered onsite, patient education to increase adherence, and support from PLWHA organisations. Nonetheless no centre effect was identified, either for adherence to treatment or in HAART outcomes: in France, regardless of where HIV patients are treated for their infection, treatment success or failure depends upon individual determinants. In a previous study of this population, we found that aside from the well-established determinants (such as age, time on HAART, history of interruption in HIV care, suboptimal adherence, HCV co-infection, CD4 cell count and HIV-RNA level and AIDS at HAART initiation), immigrant status and continuing IV drug use were associated with a greater risk of treatment failure [13].

Because of the cross-sectional design of the VESPA study, treatment failure might have been underestimated: deaths that occurred between diagnosis and data collection were not taken into account in the calculation of failure rate. In the HAART era, mortality remains much higher among patients diagnosed with advanced infection than among patients diagnosed before reaching the criteria for treatment initiation [18]. In the former group, the physician's experience may play a critical role [4 ,6 ,8 ,9 ,10].

Our study considered only hospitals caring for a substantial number (60 or more) of persons with HIV. Patients followed in smaller HIV-oriented services are not included although they might have different HIV outcomes. However, the hospitals included provided care for an estimated 90% of the HIV patient population followed in hospitals.

Random sampling ensured the representativeness of each hospital department caseload, but differential participation was related to individual patient characteristics, including lower CD4 cell counts. Participation bias might thus explain the absence of centre effects, especially if patients with poor treatment outcomes had tended to participate less in the hospitals with the poorest outcome rates. As last known CD4 cell count and viral load were available for every eligible patient, we were able to verify that this was not the case, using a mixed binary model which explained the participation of eligible patients by their health status and the treatment outcome rate of their hospital department.

Despite a low number of participants in some departments, we believe that the absence of an observed centre effect is unlikely to be due to lack of power. The assumptions of the random coefficient model we use seem appropriate here, and neither the estimates nor p values changed substantially when the analysis was restricted to the two subsamples with the hospital departments reaching either five or 10 patients with at least 6 months on HAART.

The data were collected in 2003, and could perhaps not reflect the current situation. The treatment practices and the structure of the patient population have evolved. However, since the context of high innovation and frequent improvements in treatment practices is the same today as it was from 1996 to 2003, it is plausible that the observed homogeneity still applies today.

With these limitations, adherence and response to HAART appeared not different across treatment sites despite the diversity in medical care provision. These findings contrast with studies in the US during the 1980s and early 1990s [1 ,2 ,3 ,4]. The very high effectiveness of the current combinations of antiretroviral drugs, when accessible to all who need them, may well be acknowledged as the principal factor for the observed results. The frequent updating of treatment guidelines (at least every two year) may also contribute to the improvement of treatment practices. Moreover, in France, HIV care has been coordinated at the local level since 1988, to facilitate scientific communication, availability of the range of treatment services and care coordination. Dissemination of recent scientific findings among HIV specialists may be facilitated by their participation in clinical research: 83% of the departments included participate in clinical trials and 79% in cohort studies. Such participation provides the opportunity of frequent contacts between HIV experts at national and international levels.

Two decades after the advent of AIDS, at country level, HIV care has become a lay medical specialty. The HIV medical community has remained relatively small, while becoming closely networked. The pioneers have not yet started to retire [19]. These factors, combined with the experience acquired, may account for the relatively homogeneity of good care that could explain the results we observed in the VESPA study. International goals for 2010 include universal antiretroviral treatment for all who need it [20], including in countries with a scarcity of skilled human resources. Studies show that when treatment is provided at no charge, its efficacy reach the same levels in southern countries as it does in northern countries [21]. Accessibility will require that antiretroviral treatment be provided through medical facilities in the community. Long-term networking and training of HIV care providers to improve and maintain high standard skills should be planned to ensure the equal outcomes that should accompany truly equal access to effective treatment.

Ackowledgements:

References:

- 1 . Stein MD , Piette J , Mor V . Differences in access to zidovudine (AZT) among symptomatic HIV-infected persons . J Gen Intern Med . 1991 ; 6 : 35 - 40
- 2 . Easterbrook PJ , Keruly JC , Creagh-Kirk T . Racial and ethnic differences in outcome in zidovudine-treated patients with advanced HIV disease. Zidovudine Epidemiology Study Group . JAMA . 1991 ; 266 : 2713 - 8
- 3 . Wilson IB , Landon BE , Ding L . A National Study of the Relationship of Care Site HIV Specialization to Early Adoption of Highly Active Antiretroviral Therapy . Med Care . 2005 ; 43 : 12 - 20
- 4 . Wong MD , Cunningham WE , Shapiro MF . Disparities in HIV treatment and physician attitudes about delaying protease inhibitors for nonadherent patients . J Gen Intern Med . 2004 ; 19 : 366 - 374
- 5 . Escaffre N , Morin M , Bouhnik AD . Injecting drug users' adherence to HIV antiretroviral treatments: physicians' beliefs . AIDS Care . 2000 ; 12 : 723 - 30
- 6 . Kitahata MM , Koepsell TD , Deyo RA . Physicians' experience with the acquired immunodeficiency syndrome as a factor in patients' survival . N Engl J Med . 1996 ; 334 : 701 - 6
- 7 . Kitahata MM , Van Rompaey SE , Dillingham PW . Primary care delivery is associated with greater physician experience and improved survival among persons with AIDS . J Gen Intern Med . 2003 ; 18 : 95 - 103
- 8 . Laine C , Markson LE , McKee LJ . The relationship of clinic experience with advanced HIV and survival of women with AIDS . AIDS . 1998 ; 12 : 417 - 24
- 9 . Cunningham WE , Tisnado DM , Lui HH . The effect of hospital experience on mortality among patients hospitalized with acquired immunodeficiency syndrome in California . Am J Med . 1999 ; 107 : 137 - 43
- 10 . Bennett CL , Adams J , Gertler P . Relation between hospital experience and in-hospital mortality for patients with AIDS-related Pneumocystis carinii pneumonia: experience from 3,126 cases in New York City in 1987 . J Acquir Immune Defic Syndr . 1992 ; 5 : 856 - 64
- 11 . Sherer R , Stieglitz K , Narra J . HIV multidisciplinary teams work: support services improve access to and retention in HIV primary care . AIDS Care . 2002 ; 14 : (Suppl 1) S31 - 44
- 12 . Hammer SM , Saag MS , Schechter M . Treatment for adult HIV infection: 2006 recommendations of the International AIDS Society--USA panel . JAMA . 2006 ; 296 : 827 - 43
- 13 . Dray-Spira R , Spire B , Heard I . Heterogeneous response to HAART across a diverse population of people living with HIV: results from the ANRS-EN12-VESPA Study . AIDS . 2007 ; 21 : (Suppl 1) S5 - 12
- 14 . Carrieri MP , Raffi F , Lewden C . Impact of early versus late adherence to highly active antiretroviral therapy on immunovirological response: a 3-year follow-up study . Antivir Ther . 2003 ; 8 : 585 - 594
- 15 . Peretti-Watel P , Spire B , Schiltz MA . Vulnerability, unsafe sex and non-adherence to HAART: evidence from a large sample of French HIV/AIDS outpatients . Soc Sci Med . 2006 ; 62 : (10) 2420 - 2433
- 16 . May MT , Sterne JA , Costagliola D . HIV treatment response and prognosis in Europe and North America in the first decade of highly active antiretroviral therapy: a collaborative analysis . Lancet . 2006 ; 368 : 451 - 8
- 17 . Lewden C , Chene G , Morlat P . HIV-infected adults with a CD4 cell count greater than 500 cells/mm3 on long-term combination antiretroviral therapy reach same mortality rates as the general population . J Acquir Immune Defic Syndr . 2007 ; 46 : (1) 72 - 7
- 18 . Mauskopf J , Kitahata M , Kauf T . HIV antiretroviral treatment: early versus later . J Acquir Immune Defic Syndr . 2005 ; 39 : 562 - 9
- 19 . Lert F , Chastang JF , Castano I . Psychological stress among hospital doctors caring for HIV patients in the late nineties . AIDS Care . 2001 ; 13 : 763 - 78
- 20 . WHO, UNAIDS, UNICEF . Towards universal access: Scaling up Priority HIV/AIDS Interventions in the Health Sector: Progress Report . April 2007 ; World Health Organization ; Geneva, Switzerland

- 21 . Braitstein P , Brinkhof MW , Dabis F . Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries . Lancet . 2006 ; 367 : 817 - 24

- 21 . Braitstein P , Brinkhof MW , Dabis F . Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries . Lancet . 2006 ; 367 : 817 - 24

Table 1

Description of departments' care provision, activities and HIV patient population (n=102)

Department characteristics	
	Percent
Onsite provision of consultant services	
Hepatology	36.3
Endocrinology/metabolism	32.4
Dietetic/Nutrition	85.3
Gynaecology	27.5
Dermatology	54.9
Ophthalmology	24.5
Neurology	29.4
Psychiatry	52.9
Pain	28.4
Alcohol addiction	21.6
Addiction liaison service	39.2
Mobile palliative care team	56.9
Pain treatment	66.7
HIV Activities	
Participation in clinical research activities	83,3
Participation in cohorts	79,4
Other activities	
Individual education on adherence	42.2
Onsite presence of PLWHA organisations	41.2
Onsite presence of other organisations	20.6
	Median [IQR]
Size of current HIV caseload	400 [230–750]
Number of physicians	3 [2–6]
HIV patient population	
Proportion of migrants	20% [0%–40%]
Proportion of men	75% [60%–90%]
Proportion of patients under 40 years	43% [20%–50%]
Proportion of patients with late diagnosis	40% [29%–57%]
Proportion of patients with IDU history	0% [0%–12.5%]

Table 2

Distribution of adherence and treatment outcomes among the departments and tests of centre effects

	All departments				Departments with at least 5 patients			Departments with at least 10 patients		
	Nd= 97				Nd=60			Nd=26		
	Np=699				Np=601			Np=378		
	Mean	**Median**	**IQR**	**p-value**[*]	**Median**	**IQR**	**p-value**[*]	**Median**	**IQR**	**p-value**[*]
Adherence	63.3%	61.5%	50%–80%	0.275	60.0%	51%–79%	0.225	58.6%	50%–69%	0.885
Immunological failure[1]	22.6%	20%	0%–40%	0.215	20.0%	14%–32%	0.285	19.4%	15%–30%	0.312
Virological failure[2]	12.5%	7.7%	0%–20%	0.098	14.3%	0%–20%	0.176	10.6%	5%–19%	0.081
Immuno-virological failure[3]	6.1%	0%	0%–12.5%	0.181	6.3%	0%–14%	0.177	7.7%	0%–13%	0.136
Immuno-virological success[4]	40.2%	36.4%	13.3%–50%	0.026	36.6%	29%–47%	0.030	36.6%	30%–47%	0.053
Adjusted for CD4 cell count at HAART initiation:				0.094			0.092			0.170
Adjusted for immigration status:				0.200			0.192			0.280

Nd: Number of hospital departments

Np: Number of patients

[*] Hospital department entered as a random variable

[1] Less than 100 CD4 increase since HAART initiation

[2] HIV-RNA > 400 copies

[3] CD4 < 200 and HIV-RNA > 400 copies

[4] CD4≥500 and HIV-RNA<400 copies