

Original Research

Determining factors of observance of antiretroviral treatments in Cameroon during the start-up period (2000-2002)

Christophe COMMEYRAS, Jean Loup REY, Stéphanie BADRE-SENTENAC, Claudine ESSOMBA-NTSAMA.

ABSTRACT*

Objective: highlight the socioeconomic and environmental determining factors of long-term observance to antiretroviral treatments in developing countries.

Method: The regularity of antiretroviral prescriptions renewal at the central pharmacy of the Yaounde Central Hospital (Cameroon) was measured through analysing the medical and pharmaceutical files of 230 patients over the 21 month start-up period. 99 patients were also interviewed during the last six months. The determining factors were analysed according to various socio-economic criteria, linked with the longitudinal study of treatment observance.

Results: The huge price decrease of HIV treatments during the start-up period was conducive to an increase in new treatments by a factor 5.76. In this context of an exploding demand, the paper shows that observance is firstly dependent on quality information about illness and treatment protocols, while longer term adherence is partly dependent on financial capability, and includes the strong influence of living conditions and behaviours.

Conclusion: The paper recommends the introduction of free treatment as an objective in national sector policies and the organisation of a long term following-up of patients. In the African context of poverty and actual decentralisation of healthcare, the question of the availability of human resources is profoundly enhanced.

Keywords: Acquired Immunodeficiency Syndrome. Patient Compliance. Cameroon.

RESUMEN

Objetivo: Destacar los factores socioeconómicos y ambientales determinantes del cumplimiento a largo plazo de los tratamientos antiretrovirales en países en vías de desarrollo.

Métodos: Se midió la regularidad de la renovación de prescripciones de antiretrovirales en la farmacia central del Hospital Central de Yaounde (Camerún) mediante el análisis de los ficheros médicos y farmacéuticos de 230 pacientes durante el periodo de iniciación de 21 meses. También se entrevistó a 99 pacientes durante los últimos seis meses. Se analizaron los factores determinantes de acuerdo a los diversos criterios socio-económicos, unidos con el estudio longitudinal de cumplimiento terapéutico.

Resultados: El enorme descenso de precio de los tratamientos VIH durante el periodo inicial condujo a un aumento de nuevos tratamientos en un factor de 5,76. En este contexto de demanda explosiva, el artículo demuestra que la adherencia es primero dependiente de la calidad de la información sobre la enfermedad y el protocolo del tratamiento, mientras que el cumplimiento a largo plazo es parcialmente dependiente de la capacidad financiera e incluye una fuerte influencia de las condiciones de vida y de actividad.

Conclusión: El artículo recomienda la introducción de tratamiento gratuito como objetivo en las políticas nacionales y la organización de un seguimiento a largo plazo de pacientes. En el contexto de pobreza africana y actual descentralización de la sanidad, la cuestión de la disponibilidad de los recursos destaca profundamente.

Palabras clave: Síndrome de inmunodeficiencia adquirida.. Cumplimiento terapéutico. Camerún.

(English)

INTRODUCTION

Observance is a major challenge for antiretroviral (ARV) access programs because inobservance brings on the one hand an inefficiency of treatment and on the other hand resistant strains of HIV. These negative effects appear as soon as 95% of the treatment is not correctly observed. It is then clear that observance will become a major stake for the coming years, especially in Africa where the spread of resistant strains may destroy the weak treatment programs. Even though observance and

* Christophe COMMEYRAS, Pharmacy Department, University of Montpellier 1, Montpellier, France.
Jean Loup REY. Réseau Médicament et Développement, Paris, France.
Stéphanie BADRE-SENTENAC, Pharmacy Department, Hotel-Dieu Hospital, Paris, France.
Claudine ESSOMBA-NTSAMA, Yaounde 1 University, Yaounde Central Hospital, Cameroon.

the determining factors are well documented in northern countries there has been very little discussion in the African context and then only very recently.¹⁻⁷ Although focus has been made on non-observance factors.^{8,9}

Cameroon is a central African country of 16 million inhabitants, with an HIV prevalence of around 10%.¹⁰ The Central Hospital of Yaounde (HCY) started in early 2000, for the first time in the public sector, a pilot program for ARV drug delivery linked to specific prescriptions, and ARVs were sold at cost-price by the central pharmacy. A socioeconomic inquiry was systematically made before inclusion to ensure that the patient could afford the treatment costs. A psychosocial service ensured the follow-up. The initial price of a monthly tri-therapy, from April to December 2000, was around 240,000 CFA Francs (365 Euros). Between January 2001 and the end of the study in January 2002, thanks to the national purchasing centre who introduced generic drugs and negotiated with pharmaceutical companies, the price for a monthly treatment had been reduced to between 22,000 and 70,000 CFA Francs (33 to 107 Euros), depending on the drugs administered.

The objective of this study was to highlight the socioeconomic and environmental determining factors of long-term observance to antiretroviral treatments in developing countries.

METHODS

The prescription renewal ratio is a simple and good early warning indicator, for patient as well as for health centres following-up.¹¹ After the validation of this method in the actual context¹² we found it useful to apply some quantitative information regarding the conditions for a regular prescription renewal, crossed with a qualitative analysis of the observance determining factors through a six month longitudinal enquiry. The study took place from April 2000 to January 2002. It included all patients over the age of 15 who had had an open file at the central pharmacy of the HCY for at least 4 months. It excluded accidental exposures to HIV (blood or sex), mother to child prevention (observance is not questioned), patients registered in other hospitals or who had been in HCY for less than four months (regular prescription renewal is not questionable).

A/ Regularity of the prescription renewal at the central pharmacy of the HCY was measured by the coefficient $r = \text{number of delivered prescription} / \text{number of months since the treatment initiation}$.

- The "R" patients had regularly renewed their treatment ($r > 0,9$);
- The "Lost-R" were "R" until they disappeared from HCY (death, home change, abandoned treatment, etc.);
- The "I" patients had irregularly renewed their treatment ($r < 0,9$);
- The "Lost-I" were "I" until they disappeared from HCY;

The regularity of prescription renewal was analysed according to the age of inclusion (4 to 6 months, 7

to 12 months and over 12 months) and various socioeconomic criteria.

B/ Observance was evaluated through a longitudinal enquiry conducted during the last six months of the period while prescriptions were delivered. The questionnaire was anonymous and screened for socioeconomic criteria as well as for problems encountered with illness and/or medication. Observance was measured with two questions relating to eventual delays of one or more than one day of interruption in the medication. The measurements were completed by a doctor's evaluation based on a remaining pills calculation. The statistical analysis was made with epi-info software, using either the Fischer or the Kruskal Wallis test for proportional comparisons and the Anova test for average comparisons.

RESULTS

1832 prescriptions were delivered to 669 patients during the whole period, 441 of whom were registered and treated in the HCY. The well documented role of economic factors in health care utilisation is again highlighted in this study, where the number of included patients is reversely proportional to the treatment price (figure 1). In relation to the inclusion criteria, 230 patients were studied with an average age of 39.75 and a sex ratio of 1.05, 23 had previous experience of ARV treatment when included and the average period since inclusion was 11.12 month.

75 of the 230 included patients which were lost during the period. 46 of them were regular (R) in their treatment renewal until they disappeared. After the 21 months the proportion of R patients was 73% (R + Lost-R, table 1).

	R	Lost R	I	Lost I	Total
Patients	122	46	33	29	230
Percentage (%)	53	20	14	13	100%
- The "R" patients had regularly renewed their treatment ($r > 0,9$);					
- The "Lost-R" were "R" until they disappeared from HCY (death, home change, abandoned treatment, etc.);					
- The "I" patients had irregularly renewed their treatment ($r < 0,9$);					
- The "Lost-I" were "I" until they disappeared from HCY;					

99% of the patients treated for 4 to 6 months regularly renewed their treatment, but 20% of them had already abandoned the HCY central pharmacy. From 7 to 12 months after treatment initiation 77% patients were R, and 31% of were lost. Only 32% of the patients included for over a year were still R; and 39% of them were lost (table 2). The duration from treatment initiation was twice as high in the 62 irregular patients, lost or not, as in the 168 regular ones (Table 2).

Even if the sex-ratio of the 155 patients in the active file (R or I) was 0.94 compared to 1.27 for the lost 75 ones, who were also the youngest (table 3), regularity does not appear to have been statistically linked to the individual characteristics of the patient.

Treatment duration	n	Relative Regularity (R + Lost R)		Absolute Regularity (R)	
13 – 21	56	18	32%	11	19,6%
7 – 12	100	77	77%	53	53%
4 – 6	74	73	98,6%	58	78,4%
TOTAL	230	168	73%	122	53%

Regularity is not either statistically linked to economic characteristics such as income, accommodation or residential property. However, together the results draw a better picture comparing the active patients with the lost ones who were the youngest with a lower income and alone in paying for their treatment (table 3).

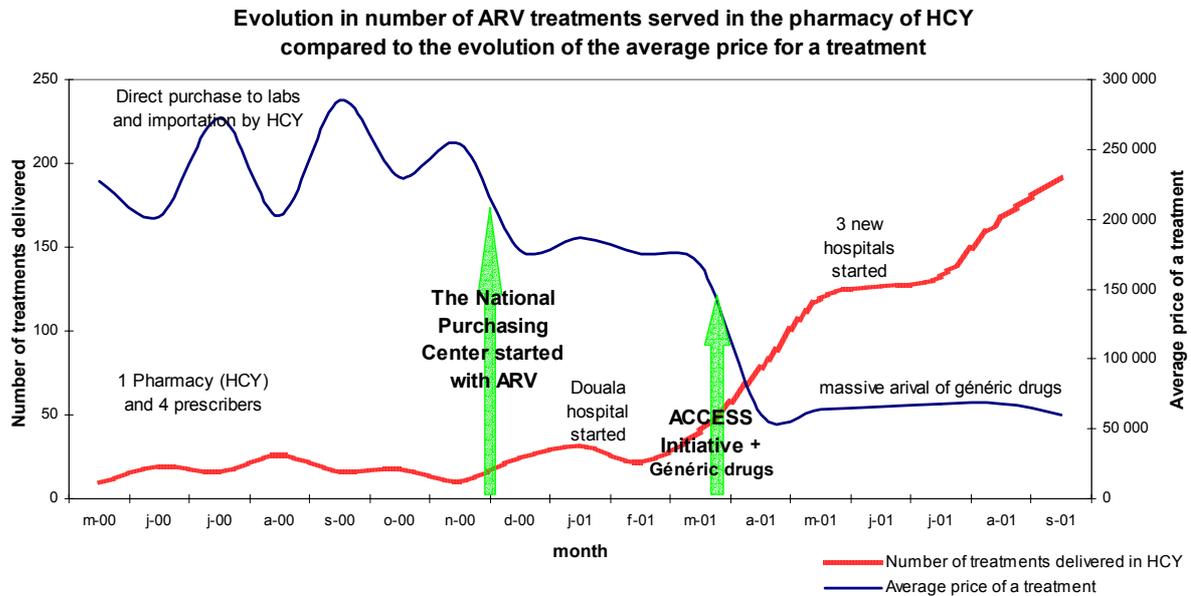


Figure 1: Number of treatment deliveries in relation to treatment price evolution

	R (n=122)	PV R (n=46)	I (n=33)	PV I (n=29)	p (N=230)
Average treatment duration (month)	8,23	10,37	17,18	17,55	11,12
Men	64	24	15	9	0,2
Women	58	22	18	20	
Living in Yaounde	52	14	14	6	0,5
Living outside Yaoundé	52	14	16	13	
Living in couple	122	3	0	0	10 ⁻⁵
Living alone	0	42	31	16	
Accommodation score 0	25	7	8	0	0,2
1	26	4	9	2	
2	19	2	3	0	
3	12	2	0	0	
4	4	0	2	0	
Condom +	121	4	0	0	10 ⁻⁵
Condom +/-	0	41	23	0	
One or Less partner	122	25	0	0	10 ⁻⁵
Over one partner	0	20	12	0	
Circle information +	116	0	0	0	10 ⁻⁵
Circle information -	5	45	16	0	
Known serology	41	45	8	0	0,3
Unknown serology	81	1	0	0	
Income >= 100 kFcf	49	5	9	0	0,07
50 >Income<100 kFcf	6	1	6	0	
Income < 50 kFcf	35	8	8	1	

Regularity is statistically linked to living conditions and behaviour (table 3). The 89 patients who lived alone were very significantly more often irregular (76%) or lost (91%) than those who lived with a partner (7 and 0%, $p=10^{-5}$). The 125 patients who regularly used condoms were more often regular

(74%) than those who didn't use them very often (37%, $p=10^{-5}$). The 116 patients who had informed their family and colleagues about their status were more often regular (69%) than those who hadn't informed anyone (25%, $p=10^{-5}$). The 32 who had more than one partner were more often irregular

(18.5%) than those who had a maximum of one (0%, $p=10^{-5}$).

99 patients out of the 230 were interviewed (43%). Their average age was 41.16 years, out of whom 46 were women aged 37.2 +/- 9 and 53 were men aged 44.6 +/- 8. The Sex-ratio was 1.15, this was close to the reference population's (1.05) and men being older than women ($p=0.0002$). Half lived in Yaounde, 29 lived over 200 km away of which 12 lived over 500 km away. 18 had a primary level education, 45 a secondary and 41 a higher level. 91 were Christians of which 51 were Catholics. 6 were Muslim and 2 were Animists.

16 lived alone, these more often women (69%) than men who were more often with a partner (73%, $p=0.007$). The average monthly income was 128,798 CFA Francs (196 Euros) and the average number of economic dependants was of 6.3 +/- 3. Women had a lower income 91,196 CFA Francs (139 Euros) than men 163,566 CFA Francs (249 Euros, $p=0.0002$). 36 were householders, 38 were renting and 26 were without accommodation. Men were more often householders and women more often without accommodation ($p=0.01$). 68 lived in a villa, 95 had water and 97 an electricity subscription; 66 had a fridge.

The sample was then more urban, better off, older and with more Christians than the general population. There were also more males, with a sex-ratio of 1.15 against 0.98 in the general population.^{13,14}

The average treatment duration was of 11.4 +/- 4, this being very close to the reference population.

The HIV test had been voluntary for 33 patients, related to illness symptoms for 59 and due to relationships for 16. 74 had informed their family, 52 a partner, 25 a friend and for only 13 a colleague. Most women had informed their partner ($p=0.001$).

86 patients found that information on their illness was insufficient. Counselling was also felt to be insufficient by 65 patients and sufficient by 9. ARV had highly increased the quality of life for 73 patients and relatively for 21, even if 15 said they had recourse to traditional medicine.

The average monthly declared health expenditure was 95,000 CFA Francs (145 Euros). It was 59,000 CFA Francs (90 Euros) for ARV, 60,500 CFA Francs (92 Euros) for examinations and 20,500 CFA Francs (31 Euros) for "other health expenditures". 89 patients found ARV to be expensive, 68 declared paying for their treatment themselves, with 35 declaring that they were supported by their family and 10 by someone else. The family is solicited more often by women ($p=0.0005$).

48 patients acknowledged medicating late and 24 acknowledged at least one interruption during their treatment. While doctors counted 18 patients with a bad observance record. The interviews showed that weaknesses in the counselling which followed the huge increase in demand had a greater role in irregular medicating during this period. This was confirmed by the prescription renewal analyses, which showed that patients who had been treated

for more than one year had most of their treatment ruptures at the beginning of that period. These patients declared that they had initially not understood that ARV medicating had to be very closely respected.

However, patients who declared a good comprehension of their pathology had more delays in medication (89% against 44%, $p=0.006$). Those whose treatment was self-financed were judged to be more observant by doctors (87%) than others (61%, $p=0.01$). The declared causes for late prescription renewal were economic for 26 patients (46%), 6 cited transport difficulties, 6 were travelling, 4 gave professional reasons, 2 side effects, 3 shortages at the pharmacy and 10 others. The declared causes for interruption were forgetting (6 cases), travelling (8), adverse effects (2), others (10).

Observance indicators were not statistically linked to the illness's characteristics such as information on status, acceptance or rejection, the patients own opinion of the illness, recourse to traditional healthcare, health expenditure or the person responsible for payment. But the patients who made a voluntary test were felt to be more observant by doctors (75% versus 60%, $p=10^{-4}$) and the longer the treatment duration the higher the rate of delayed medications and the more negative medical staff notation ($p=0.04$ and $p=0.003$, respectively).

Socio-demographic factors were rarely linked to observance indicators, neither were life status indicators ($p=0.06$ for monthly income). However patients with an informal activity were less observant and had later renewals ($p=0.03$ and $p=0.02$). Retreated were also later ($p=0.001$). Moreover, patients with late renewals had more economic dependants (9.9 +/- 3) than others (4.9 +/- 2, $p=0.001$) and are more often lived in rented accommodation (39%) than others (17%, $p=0.001$). The patients judged to be inobservant by doctors were more often in rented accommodation than others ($p=0.02$).

DISCUSSION

There is no referenced method for quantitative observance evaluation in Africa. The most accessible sources of information are the patient's own declarations during inquiries and the accounting of remaining pills. In this study, the qualitative enquiry concerned the patients and did not permit a representative questioning of the lost ones or an analyses of the cause of disappearance (death, financial break-off, side effects, moving, etc).

The population in the study is predominately urban, older, male and wealthy. It is representative of the first included group, especially in Cameroon and Gabon. The curve of included patients follows the decrease in the cost of ARV, which once again shows that financial accessibility is one of the first criteria for access to health commodities.

The regularity of prescription renewal can be seen as being quite correct if we consider the conditions for counselling and delivery (counselling was only

given by doctors during the first prescription and subsequent drug delivery was made without any pharmaceutical counselling and with immediate payment). However it dropped sharply during the second year. Moreover the loss-ratio was very high, and over the whole period only 53% of all included patients had renewed their prescription regularly at the central pharmacy of HCY. The cause has to be looked for both in the quality of the counselling and in the patient's lifestyle and economic situation.

In regard to the population of 230 medical files analysed, the sample of 99 interviewed patients was slightly older because the lost patients that could not be interviewed were younger. It was however quite representative with regard to other criteria such as the sex-ratio, average treatment duration and income.

With regard to the method, the two questions on skipped and delayed medication were efficient and complemented the observance evaluation. They were also more sensitive than medical estimations based on the counting of the remaining pills.

During the structured interviews, the main reasons given to explain late or skipped medication were linked to the patient's misunderstanding the medication, and to situations such as out of stock at the pharmacy, travels or forgetfulness or to the treatment's side effects. Afterwards, better counselling improved the situation and lifestyle factors became determinants. Moreover, even if there was no direct relationship between observance and economic situation, there was one with the profession, the number of economic dependants and the type of habitation. These indirect links between observance and material conditions lead us to think that many patients are heavily investing in their treatment, need to seek out financial support, and finally cannot support the treatment expenditure for very long. These

interpretations confirm those coming from other treatment centres in Yaounde where indirect costs seem to be of higher importance than treatment costs for patients.¹⁵

Finally, the quality of both counselling and following-up of the patients, as well as their social behaviour and long term financial capacity, has to be questioned.

CONCLUSION

The huge price decrease of HIV treatments during the start-up period was conducive to an increase in new treatments by a factor 5.76. In this context of an exploding demand, the paper shows that observance is firstly dependent on quality information about illness and treatment protocols, while longer term adherence is partly dependent on financial capability, and includes the strong influence of living conditions and behaviours.

These results show the importance of a regular following-up of the patients and the organisation of an early detection of individual problems and drawing the patient's attention to the high importance of long-term permanent financing of their treatment, either through insurance policies or independent payment. Preserving the ARV dispensing service in agreed medical centres, where professional and educated personnel can be found, is an indisputable condition of these objectives, especially in the actual widespread of these centres throughout the country.

In regard to these questions, free treatment should be an objective of national policy. Moreover they highlight the pre-eminent question of the shortage of qualified human resources.

References

1. Oyugi, J.H., J. Byakika-Tusiime, E.D. Charlebois, et al., Multiple validated measures of adherence indicate high levels of adherence to generic HIV antiretroviral therapy in a resource-limited setting. *J Acquir Immune Defic Syndr* 2004. 36(5):1100-2.
2. Gourvellec, G., X. Anglaret, S. Toure, et al., Compliance in HIV infected adults. Study of opportunistic infection prophylaxis with cotrimoxazole in Ivory Coast. *Presse Med*, 2004. 33(9 Pt 1):595-600.
3. Laurent C, Diakhate N, Gueye NF, Toure MA, Sow PS, Faye MA, et al., The Senegalese government's highly active antiretroviral therapy initiative: an 18-month follow-up study. *AIDS* 2002. 16(10):1363-70.
4. Lanièce I. L'observance et ses principaux déterminants. Analyses quantitatives, in L'ISAARV, Aspects sociaux, observance et impact sur le système médical. Rapport intermédiaire, IRD, Editor. 2001, IRD: Montpellier. p. 59-74.
5. Lanièce I. Sénégal: la démonstration d'une forte capacité d'adaptation au traitement. in Atelier de Gorée. 2001. Sénégal.
6. Ciss M, Lanièce I, Diop K. Observance des ARV au Sénégal: Intérêt des traitements simplifiés et peu coûteux. in XIIème Conférence Internationale sur le SIDA et les MST en Afrique. 2001. Ouagadougou, Burkina Faso.
7. Ba-Gomis F, Chenal H, Nguyen VK. Etude de l'observance des antirétroviraux à Abidjan: enquête auprès de 84 patients du CIRBA. in XIIème Conférence Internationale sur le Sida et les MST en Afrique. 2001. Ouagadougou, Burkina Faso.
8. Flick U., La perception quotidienne de la santé et de la maladie. 1992, Paris, France: L'Harmattan. 400.
9. Desclaux A. Une combinaison de facteurs et d'acteurs. in Atelier de Gorée. 2001.
10. Document de Stratégie de Réduction de la Pauvreté (DSRP). 2002, Gouvernement de la République du Cameroun: Yaoundé. p. 75.
11. Coulibaly M, Laymond K, Malkin J, et al., Utilisation des factures des médicaments ARV pour le suivi d'un programme de traitement. exemple d'Abidjan Côte d'Ivoire. *Bull Soc Path Exot* 2006;99:41-2.
12. Badré-Sentenac S, Essomba C, Commeyras C, et al., Utilisation du renouvellement des ordonnances d'antirétroviraux comme indicateur d'observance à Yaoundé. *Journal de Pharmacie Clinique* 2005. 24(décembre 2005):225-31.

13. Recensement Général de la Population et de l'Habitat. 1987, République du Cameroun, Ministère des Finances, Direction de la Statistique et de la Comptabilité Nationale: Yaoundé.
14. Conditions de vie des populations et profil de pauvreté au Cameroun en 2001 (ECAM II). 2002, Ministère de l'Economie et des Finances, Direction de la Statistique et de la Comptabilité Nationale: Yaoundé, Cameroun. p. 80.
15. Ollivier F, N'Kam M, Midoungue C, et al., Etude de l'observance des traitements ARV au Centre hospitalier universitaire de Yaoundé (Cameroun). *Santé publique*, 2005(17):559-68.