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ORIGINAL PAPER

Determinants of health care costs of HIV-positive patients in the Canary Islands, Spain

Juan Oliva-Moreno · Julio López-Bastida · Pedro Serrano-Aguilar · Lilisbeth Perestelo-Pérez

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Abstract The aims of this study were to estimate medical expenditures on human immunodeficiency virus (HIV) treatment and to identify significant associated variables. We performed a retrospective multi-centre study in the Canary Islands using a sample of 569 patients recruited at outpatient visits. The study examined demographic and clinical variables, health-related quality of life (HRQOL), and health care resources. Clinical data was obtained from medical records and patient interviews. Several empirical models for identifying the relationship between health care costs and independent variables were developed. The greatest expense came from pharmaceutical expenditure (82.1% of direct costs), while hospital costs only represented 4.6% of total expenditure. The data showed a statistically significant association between health care costs and the CD4 count of the previous year. HRQOL was also a significant variable. Therefore, CD4 cell count can be used to predict health care costs in patients. Policymakers could use this information to help guide their decisions in allocating limited health care resources to HIV treatments.

Keywords HIV/AIDS · Health care costs · Health-related quality of life · Observational multi-centre study

J. Oliva-Moreno
Department of Economic Analysis and Finances, University of Castilla la Mancha (UCLM), Toledo, Spain

J. Oliva-Moreno
CIBERESP-CIBER in Epidemiology and Public Health, Toledo, Spain

J. López-Bastida · P. Serrano-Aguilar · L. Perestelo-Pérez
CIBERESP-CIBER in Epidemiology and Public Health, Santa Cruz de Tenerife, Spain

J. López-Bastida · P. Serrano-Aguilar · L. Perestelo-Pérez
Evaluation and Planning Service, Canary Islands Health Service (SCS), Santa Cruz de Tenerife, Spain
e-mail: lperperr@gobiernodecanarias.org

J. López-Bastida
University Hospital Nuestra Señora de la Candelaria, Canary Islands Health Service, Santa Cruz de Tenerife, Spain

J. Oliva-Moreno (✉)
Facultad de Ciencias Jurídicas y Sociales de Toledo Análisis Económico y Finanzas Cobertizo de San Pedro Mártir s/n, Toledo, España
e-mail: Juan.OlivaMoreno@uclm.es

Introduction

Since its discovery at the beginning of the 1980s, human immunodeficiency virus (HIV) has become one of the greatest health challenges in the world [15]. HIV/AIDS places an ever increasing burden on the population's state of health as well as contributing to significant socio-economic difficulties for individuals, families, communities and governments in many countries [8, 51].

The large number of cases and the high cost of providing services related to HIV infection is a major concern addressed by health policy in countries across the globe, regardless of their economic status. Spain is among the countries with the highest AIDS incidence rates in Western Europe [51]–almost 4.2 cases per 100,000 inhabitants in 2005, after adjusting for reporting delays. Since the beginning of the AIDS epidemic, a total of 72,099 new AIDS cases have been reported in Spain, with the number of deaths ranging between 50,000 and 55,000. Even though Spain does not have an official register for HIV positive cases, the prevalence of HIV-infected people was estimated

to range between 2.4 and 3.6 per 1,000 inhabitants (120,000–150,000 people) [11, 45].

Advances in medicine have yet to find a definitive cure for HIV/AIDS, although new therapies—ranging from zidovudine monotherapy to highly active antiretroviral treatment (HAART)—have represented a new era in therapeutic management that has increased life expectancy rate and offered improvement in the quality of life of HIV-patients [2, 24]. The high cost of such therapies makes measuring health care costs and breaking them down by type of treatment or services extremely important. For instance, it is not clear whether the HAART therapy has increased the annual treatment cost per patient [4, 50], although it seems that the lifetime health care costs for patients are much higher, which is due primarily to the increased life expectancy of HIV+ patients. On the other hand, it is clear that the distribution of health care spending has changed as a result of the introduction of new prescription drugs [6–8, 17, 33, 42, 46, 49, 50], with an increase in the ratio of pharmaceutical expenditures to costs associated with inpatient care.

In spite of Spain's relatively high HIV rate, there have been no recent studies on HIV-related costs. The aim of the present study was to calculate the total annual health care costs of people living with HIV/AIDS in Spain, as well as to provide a breakdown of spending on the following items: hospital admissions, outpatient visits, tests, rehabilitation services, emergency services and drugs. In addition, we aimed to identify significant variables associated with health care costs that might help predict costs in HIV patients.

Methods

Study design

A cross-sectional, retrospective study of people diagnosed with HIV/AIDS receiving outpatient care was conducted. Patients were recruited according to disease severity from four hospital outpatient clinics in the Canary Islands, Spain. The 1993 classification scheme proposed by the Centre for Disease Control and Prevention (CDC) in the United States to divide the disease into HIV-asymptomatic, HIV-symptomatic and AIDS stages [1] was used to establish the severity of HIV infection. All patients were informed about the study objectives and the confidentiality of the data and were asked to show their agreement with, and their understanding of, the study conditions by signing a declaration of consent form. The study was approved by the ethics research committee of University Hospital Nuestra Sra. de la Candelaria. The fieldwork was carried out between January and December 2003. Demographic and clinical data were collected for people previously diagnosed with HIV/AIDS. The patients recruited were at least 18 years old and were treated in outpatient clinics. Incarcerated HIV patients were not included in the analysis. Also, some patients were excluded from the final analysis if the information gathered was incomplete.

A total of 569 medical records from HIV+ adult patients were reviewed. Based on data provided by Castilla and de la Fuente [11], we estimated that the sample size represented 23% of all people with HIV/AIDS in the Canary Islands. Medical records were used to obtain data on age, age when HIV transmission was confirmed, gender, most likely cause of transmission and CD4 cell count for the current and previous year (CD4+ counts within cells mm^{-3}). In addition, patients were asked to fill out the general questionnaire, EQ-5D [48]. The EQ-5D identifies five health categories: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and three degrees to describe state of health: no problems, mild problems and severe problems. Additional information about the use of health care resources (emergencies, rehabilitations and outpatient visits) was obtained from a specific questionnaire.

Costs

We estimated health care costs from a National Health System perspective, following a bottom-up approach, assigning a monetary value to the health care resources used by each patient on a case-by-case basis. All costs are expressed in Euros in the base year (2003). Information about the number of hospital admissions, tests and use of prescription drugs for problems related to HIV/AIDS in the 12 months prior to the interview were obtained from medical records. Unit costs were obtained from a number of sources. The cost of inpatient care was based on Diagnosis Related Groups (DRGs) public prices. The unit costs for tests were obtained directly from hospitals in the Canary Islands. Drug costs were calculated based on the official selling prices to hospitals in the Canary Islands. Additional information about the use of health care resources was obtained from a specific questionnaire. Information obtained from questionnaires completed by HIV+ patients was used to determine the number of emergencies, rehabilitation sessions and outpatient visits related to HIV/AIDS. The average cost of a single emergency visit, rehabilitation session and medical appointment were obtained from the SOIKOS healthcare unit cost database [44]. This is the most complete database available in Spain for health care unit costs. The sources of the unit costs are published articles, reports, hospital accounting systems, etc. The figures are updated every year.

Analytical framework

Ordinary least squares regression was used to estimate the determinants of annual costs. We used the Eicker–White

covariance matrix estimator [19], so that inference is valid in the general case where the variance of the error term is not constant across respondents. We used a range of between 519 and 545 valid cases for the analysis.

Models 1, 2 and 3 used the same dependent variable: the direct health care cost. Model 1 has a number of exogenous variables: age, age-squared, gender, time since diagnosis, most likely cause of transmission and CD4 cell count 12 months before interview [low (CD4/μl < 200); medium (200 < CD4/μl < 500) and high (CD4/μl > 500)]. Model 2 incorporates the hospital where the patient received his/her treatment as an explanatory variable. This variable was included as a means to control potential heterogeneity in clinical practice among different centres. We added health-related quality of life (HRQOL; EQ-5D) as an independent variable in Model 3. In the face of potential collinearity problems between the objective health variables (CD4 cell count) and the self-perceived HRQOL levels, a series of Spearman tests was performed on the objective and subjective variables relating to state of health. Although the results were in line with what was expected (there was a statistically significant relationship between CD4 count and quality of life), the correlation coefficient was low. For this reason, both are included simultaneously in Model 3. We also tested Model 3 for problems of multi-collinearity. The variance inflation factor and tolerance were used to assess potential multi-collinearity (for more details, see Greene) [19]. The values obtained were located below critical values.

Models 4 and 5 are identical to Model 2 and 3, respectively, insofar as the independent variables used. However, there were differences for the dependent variable "drugs costs" (Model 4). We analysed this item because it represents the greatest portion of health care costs.

Results

The average age of the sample group of patients was 40.6 years, and the average age at which HIV transmission was confirmed was 32.7. Our sample group was comprised mostly of males (84.2%). The most likely cause of transmission was homo/bisexual contact (46.4%), following by heterosexual contact (20.0%) and intravenous drug use (19.9%). The most likely cause of transmission was not provided (unknown) by 12.8% of the patients questioned. Information about CD4 cell count was obtained for a period before data collection had begun. Patients were divided into three groups based on their CD4 count: low CD4 cell count (CD4/μl < 200), medium CD4 cell count (200 < CD4/μl < 500), and high CD4 cell count (CD4/μl > 500). Twelve months before the interview (year 2002), the CD4 count for 10.5% of the patients questioned was low, 35.6% had a medium CD4 count, and 53.9% had a high count. The average visual analog scale (VAS) score for HRQOL was 0.7581 out of 1. The average time trade-off (TTO) score for HRQOL was, 0.8104 out of 1 (Table 1).

Average health care costs were €8,231 per patient (SD 4,291). The most important item in health care costs was drugs costs, with an average value of €6,752 (SD 3,031). The second highest costs were tests, with an average of €740 (SD 359). Differences in cost by stage of disease are listed in Table 2 and illustrated in Fig. 1.

The results of the statistical models show that time since diagnosis (year 2003 minus the year when HIV transmission was diagnosed), CD4 cell count 12 months before interview, HRQOL, and the hospital are significant variables that help explain health care expenditure (Models 1–3). On the other hand, age, gender and most likely cause of transmission do not appear to be significant variables. When explaining the expenditure for prescription drugs (Models 4 and 5), time since diagnosis, CD4 cell count 12 months before interview, HRQOL and hospital are significant variables. In all the regressions performed (Table 3), the

Table 1 Description of independent variables

	N	Average (SD)/%
Age in December 2003	569	40.6 (8.2)
Time since HIV diagnosis (years)	569	7.9 (4.7)
Gender	569	
Males		84.2%
Females		15.8%
Hospital	569	
Hospital 1		21.1%
Hospital 2		20.2%
Hospital 3		34.3%
Hospital 4		24.4%
Most likely mode of transmission/risk group	569	
Intravenous drug use		19.9%
Homo/bisexual transmission		46.4%
Heterosexual transmission		20.0%
Others (patients with haemophilia and unknown)		13.7%
CD4 count in $t-1$	545	
<200 (low)		10.5%
200–500 (medium)		35.6%
>500 (high)		53.9%
Health-related QOL among surviving patients (EQ-5D)	538	
TTO score		0.8104 (0.2465)
VAS score		0.7765 (0.2132)

HIV Human immunodeficiency virus, *QOL* Quality of life, *VAS* visual analog scale, *TTO* time trade-off

Table 2 Health care costs by stage of disease

All patients ($N = 569$) Type of expenditure	Average	SD	Minimum	Maximum
Medical visits	296	230	0	1,634
Emergency care	59	173	0	1,960
Rehabilitation	1.43	16.4	0	258
Tests	740	359	0	2,701
Drugs	6,752	3,031	0	18,238
Hospital admissions	382	2,330	0	32,136
Total health expenditure	8,231	4,291	280	41,637
Asymptomatic patients ($N = 268$)				
Medical visits	241	143	0	1,158
Emergency care	45	179	0	1,960
Rehabilitation	0.5	5.9	0	86
Tests	645	253	0	2,318
Drugs	6,184	3,054	0	14,792
Hospital admissions	26	422	0	6,909
Total health expenditure	7,140	3,218	310	16,579
Symptomatic patients ($N = 141$)				
Medical visits	329	250	78	1,404
Emergency care	50	113	0	686
Rehabilitation	0	0	0	0
Tests	792	348	120	2,031
Drugs	7,040	3,126	0	18,238
Hospital admissions	264	1,217	0	6,909
Total health expenditure	8,475	3,751	280	20,600
AIDS patients ($N = 160$)				
Medical visits	359	299	44	1,634
Emergency care	90	201	0	1,176
Rehabilitation	4,3	29,8	0	258
Tests	854	464	56	2,701
Drugs	7,451	2,727	0	16,101
Hospital admissions	1,084	4,131	0	32,136
Total health expenditure	9,842	5,599	783	41,637

Values in 2003 Euros

Snedecor F is higher than the critical value and, consequently, explanatory variables are jointly significant.

The results of Models 1 and 2 can be compared with the results of Model 3, and the results of Model 4 can be compared with the results of Model 5. In Model 3, we began with a base case having an annual health care cost of €5,757. Age, gender and mode of transmission were not statistically significant variables. On the contrary, the health care costs for a person with a low CD4 count during year $t-1$ are €4,365 higher the following year (t) compared to a person with a high CD4 count during year $t-1$. With a medium CD4 count ($200 < \text{CD4}/\mu\text{l} < 500$), health care expense will increase by €1,046 in year t compared to a patient with a high CD4 count during the previous year. As for time variables, each additional year since diagnosis means an additional €106 spent on health care. HRQOL is inversely related to health care costs (the better the quality of life, the less the health-care costs). For instance, a person with a low HRQOL (TTO scores lower than 0.75) costs €1,376 more than a person with a high HRQOL (TTO score higher than 0.75). Finally, there were significant differences in the cost of treatment among the four hospitals included in this study. Hospital 3 had a significantly higher cost per patient (€1,670) than Hospital 4 (when the rest of factors were controlled). Hospital 2 had a significantly lower cost per patient (€1,086) than Hospital 4. Hospital 1 did not present significant differences in costs when compared to Hospital 4.

In Model 5, we began with a base case in which annual spending on pharmaceuticals reached €5,205. Age, gender and mode of transmission were not significant explanatory variables for drugs costs. On the contrary, for a person with a low CD4 count during year $t-1$, the drugs costs will be €1,592 in the following period compared to a person with a high CD4 count in $t-1$. With a medium CD4 count ($200 < \text{CD4}/\mu\text{l} < 500$), health care expense will increase by €571 during the t period as compared to a patient with a high CD4 count during the previous period. As regards time variables, each additional year from time of diagnosis means an additional €132 expense on drugs. The HRQOL is inversely proportional to the costs on prescription drugs (the better the quality of life, the less the drugs costs). A person with a low HRQOL (TTO scores lower than 0.75) incurs a cost which is €488 higher than a person with a high HRQOL (TTO score higher than 0.75). Finally, there were significant differences in drugs costs per patient at the four hospitals under consideration. Hospital 3 had a significantly higher cost of drugs per patient of €749 than Hospital 4 (when the rest of factors were controlled). Hospital 2 had a significantly lower pharmaceutical cost per patient (€1,001) than Hospital 4. Hospital 1 had pharmaceutical costs that were comparable to those at Hospital 4.

Discussion and conclusions

International sources documenting HIV/AIDS show that health care costs vary greatly from country to country. At the present time, however, it is not clear if the annual cost of treatment per patient has increased since the introduction of HAART. There is agreement in the literature that annual antiretroviral drug costs have increased, but some studies have found that this fact is balanced by a reduction in the annual costs of inpatient, outpatient and even home care costs. There is less doubt that, in a lifetime context, the overall cost of treating a HIV patient has clearly increased

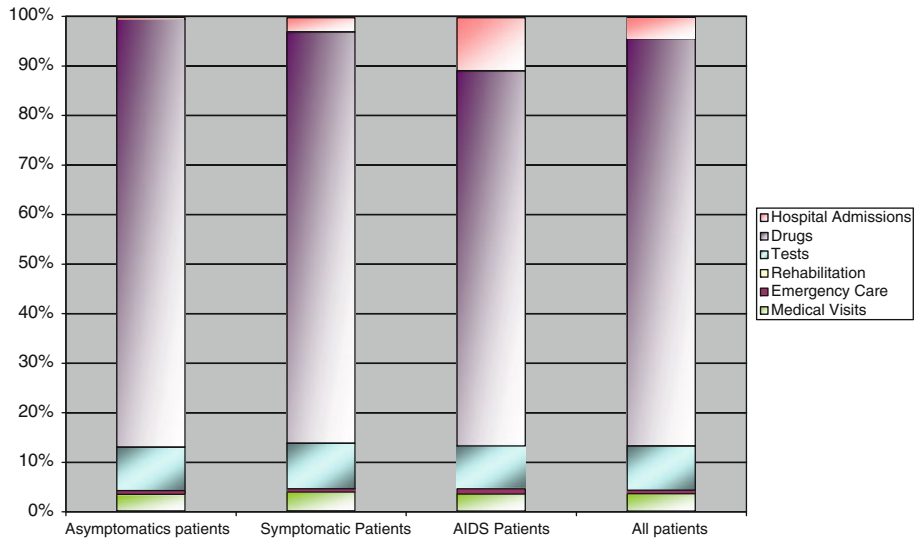

Fig. 1 Distribution of health care costs by stage of disease

in comparison with the early 1990s. This may be explained by the fact that HIV patients live with and require treatment for the virus for approximately 20 years [3–5, 10, 12, 16, 18, 20, 21, 23, 25–30, 32–34, 37, 39, 41, 45, 47, 50].

In Spain, our data for annual treatment costs are lower than the costs previously reported by Antoñanzas et al. [3] and Mompo et al. [34]. A possible explanation for this difference might be the increase in the number of patients with the advanced disease (AIDS) since earlier studies in Spain, which had far fewer AIDS patients in their sample groups. We have tried to increase the reliability of our data by recruiting a larger sample of HIV-positive patients with a sample group distribution similar to that of the AIDS patients in the population. The international trend of reducing the use of inpatient services from 1995 to 2003 is similarly observed in our study. Antoñanzas et al. [3] found that 85% of total health care costs for seropositive patients were for the use of inpatient services, and antiretroviral therapy represented only 8.7%. Our more recent data show a dramatic increase in drugs costs (more than 80% of total health care costs) and a reduction in other items. By contrast, hospital admissions are the third most costly item, with an average cost of €382. In fact, only the 4.2% of patients included in our sample were admitted to hospital in the 12 months prior to the interview.

Our data suggest that, after 1 year, a patient with a low CD4 cell count will incur €4,300–4,600 more in health care-related expenses than patients with higher CD4 cell counts, due to the need for more expensive medication (see Model 5) and intensive use of additional health care resources. In sum, we found that a low CD4 cell count is a good predictor of intensive health care utilisation (more expensive drugs and inpatient services) the following year. These results are in line with previous findings from Krentz et al. [30] for "late presenters". Patients' age, gender and mode of transmission are not significant variables for explaining costs. In the case of age, this is no surprise. Less than 3% of the study sample is older than 60 years of age, and the majority of the patients are closer to 40. Contrary to other studies [12], we have not discovered any differences in cost by sex (due to intolerance and adverse effects). The similarity between the figures for men and women would also suggest that there are no gender inequalities in access to treatment. This finding also hints that there are no inequalities in access to treatment based on the different risk factors involved in the transmission of the disease.

The Canary Islands Health Service consider that information on HRQOL, together with other information sources such as epidemiological and socioeconomic information, plays a key role in priority setting and resource allocation between different health problems in the health care planning [10]. In recent decades, quality of life has increased in importance as a key health status indicator. As Sullivan [47] notes, "Medicine's epidemiological transition from acute to chronic disease is thus prompting an epistemological transition from primarily objective to primarily subjective evidence of health and health care effectiveness. Now some of the most important patient outcomes, like patient choices before them, are valid because they are subjective". Additionally, some studies reveal that bad HRQOL is associated with high mortality [22, 25, 28, 39, 40] and a greater use of health-care services [13, 40, 43]. A relevant result of this study is that, after adjusting for a significant clinical variable such as CD4 cell count, HRQOL is inversely and significantly associated with health care expenditure. Although this result seems to associate HRQOL with health care costs, one must be careful when attributing coincidental effects to this variable. More specifically, the nature of the data (a cross-section) requires caution to be exercised before

Table 3 Determinants of health care costs

	Health care costs Model 1	Health care costs Model 2	Health care costs Model 3	Costs of drugs Model 4	Costs of drugs Model 5
Time since diagnosis (years)	112.51**	100.82**	105.86**	130.63**	132.23**
	(39.59)	(40.33)	(42.23)	(27.88)	(29.32)
Low CD4 count (CD4 < 200) in previous year	4,327.08**	4,623.96**	4,364.57**	1,773.79**	1,591.67**
	(1093.36)	(1072.91)	(1144.21)	(449.15)	(474.83)
Medium CD4 count (200 < CD4 < 500) in previous year	837.13**	1,133.92**	1,045.55**	639.78**	570.87**
	(322.15)	(323.40)	(330.25)	(261.86)	(271.30)
EQ-5D (TTO)			−2,650.13**		−877.56*
			(760.02)		(477.84)
Hospital 2		−1,006.30**	−1,085.88**	−1,012.17**	−1,001.32**
		(466.99)	(482.96)	(360.04)	(380.55)
Hospital 3		1,698.71**	1,669.93**	697.31**	749.28**
		(454.97)	(453.10)	(325.39)	(331.14)
Intercept	2,999.38	3,651.25*	5,757.34**	4,273.46**	5,205.36**
	(2,283.20)	(2,168.41)	(2,201.47)	(1,704.32)	(1,786.76)
N	545	545	519	545	519
R^2	0.1134	0.1721	0.1906	0.1185	0.1207
F	4.99	5.83	5.90	5.36	4.77

Values in euros (standard deviation in brackets). Base patient is a male with a high CD4 cell count the year before the study (CD4/μl > 500), who was infected through heterosexual contact and was receiving treatment at Hospital 4. Some explanatory variables e.g. age, gender, most likely mode of transmission and the dummy variable "Hospital 1" were not statistically significant. Their coefficients have been excluded from the table

* Significant variable: CI = 90%; ** Significant variable: CI = 95

attributing a causal relationship. Future research that delves further into the relationship between HRQOL and costs could provide us with further support.

The multi-centre nature of our study increased reliability and enabled us to observe significant differences in overall costs among the participating hospitals. This fact needs to be considered when analysing data coming from a single health care institution. In fact, an important point of the analysis is the inclusion of hospitals as an explanatory variable. Hospital 3 shows a cost per patient €1,670 higher than the base hospital (Hospital 4) after controlling for other factors. Hospital 3 has a higher hospitalisation rate than the rest, which influences the total amount of the corresponding costs, and also presents a higher medication expense per patient than the hospital used as a reference. It is possible that patients treated in this hospital are at greater risk than those in the other hospitals, but this is reflected neither in the socio-demographic variables (age, gender, time since infection and cause of infection), nor in the clinical history (CD4 count), nor in the self-perceived state of health, when the effects of these variables are controlled for statistically.

Also worth noting is the fact that the cost per patient at Hospital 2 is lower than the base hospital. In this instance, comparison of Models 3 and 5 reveals that the lower cost per patient is due almost entirely to the lower medication expense per patient. A number of causes might be found for this lack of homogeneity. In the first place, the profiles and risks of the patients under treatment in the four centres might differ, which was not reflected in the variables analysed. Secondly, variability could result from the use of different clinical practices in the different centres, not only in the prevention of opportunist infections, but also in the types of antiretroviral treatment chosen. It is not possible to determine these elements with the available information, but it would, without doubt, be of interest to Canary Island decision-makers to know the cause of these differences. Finally, it should be mentioned that this study is limited to analysing the costs associated with the treatment of HIV+ patients. It does not include information on the quality of the treatment each patient receives. This will remain a pending question for future research on whether higher costs stem from improvements in the quality of care or from the use of more innovative medicines that cost more.

Some limitations of the study should be pointed out. First at all, our results are limited by the type of data used. More precisely, a cross-sectional survey is not the most appropriate design for studying causal relationships between variables. A prospective, longitudinal study would be a more appropriate design for this purpose. This is especially relevant in the study of the cause-effect relationship between HRQOL and costs. Secondly, in spite of low R^2 values

commonly found in empirical models with data on individuals, most of the variance is not explained by the models. Consequently, the results should be interpreted with caution. Thirdly, more research is needed to explain the lack of homogeneity in costs among hospitals after controlling for other explanatory variables. We have not considered data on intolerance and the adverse effects of medications such as transaminites, hepatoxicity, hyperglycaemia, lipodystrophy, insulin resistance, accelerated bone loss, dyslipidaemias, nausea and vomiting, headache, anaemia, depression and sleep disturbances [20]. The clinical records used did not treat these problems in a similar manner, and it is not clear if failure to mention them means those interviewed did not suffer adverse effects or if they should be interpreted as missing values. Finally, we consider only health care costs in the analysis. However, the vast majority of HIV+ patients are of working age. As several studies have shown [9, 14, 18, 31, 35, 36, 38] CD4 cell count is a significant variable for explaining labour participation. Thus, CD4 cell count in the $t-1$ period might be a significant variable for predicting labour participation of HIV+ patients.

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