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ORIGINAL ARTICLE

Budget impact of a set-dose combination of efavirenz-emtricitabine-tenofovir in the treatment of patients infected with HIV-1

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KEYWORD
Budgetary impact;
Efavirenz;
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HIV-positive patients

Abstract
Objective: Estimate the budgetary impact of using a set-dose combination of efavirenz-emtricitabine-tenofovir for the Spanish health care system's treatment of patients infected with HIV-1, while evaluating repercussions for each autonomous community in 2008.
Methods: We developed a budgetary impact model with pharmacological costs for the different currently available treatment options, based on GeSida's recommended guidelines for treating HIV-positive patients. The model defines 5 possible scenarios in which various possibilities for substituting different drug cocktails with the efavirenz-emtricitabine-enofovir combination are contemplated.
Results: The investment per patient on a national level amounts to €7989 in the base scenario (without considering the availability of the efavirenz-emtricitabine-tenofovir combination) and to €7997, €8424, €7830, €8375, and €8527 for scenario 1 (substitution of recommended drugs with efavirenz, emtricitabine, and tenofovir or efavirenz, lamivudine, and tenofovir); scenario 2 (substitution of recommended drugs with efavirenz); scenario 3 (substitution of recommended drugs with tenofovir); scenario 4 (substitution of recommended drugs with tenoforvir or zidovudine); and scenario 5 (total substitution), respectively. Compared with the base scenario this means increments of 0.11%, 5.45%, -1.99%, 4.83%, and 6.73% for scenarios 1, 2, 3, 4, and 5.
Conclusion: Use of a set combination of efavirenz, emtricitabine and tenofovir to treat adult patients with the HIV-1 virus would lead to slight surpluses or even budgetary savings by decreasing the number of daily doses, which could increase patients' quality of life and help them stay on the treatment properly.

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PALABRAS CLAVE
Impacto presupuestario;
Efavirenz;
Emtricitabina;
Tenofovir;
Pacientes infectados por el VIH

Impacto presupuestario de una combinación a dosis fija de efavirenz-emtricitabina-tenofovir para tratamiento de pacientes infectados por el virus de la inmunodeficiencia humana tipo 1

Resumen
Objetivo: Estimación del impacto presupuestario de la utilización de la combinación fija de efavirenz-emtricitabina-tenofovir en el tratamiento de pacientes infectados por el virus de la inmunodeficiencia humana tipo 1 (VIH-1) para el Sistema Nacional de Salud en España, y evaluación de la repercusión para cada comunidad autónoma en el año 2008.
Métodos: Se ha desarrollado un modelo de impacto presupuestario con los costes farmacológicos de las alternativas terapéuticas actualmente disponibles, a partir de las pautas recomendadas por GeSida para el tratamiento de la infección por el VIH-1. En el modelo se han definido 5 posibles escenarios en los que se asumen diferentes posibilidades de sustitución de las distintas asociaciones terapéuticas por la combinación efavirenz + emtricitabina + tenofovir.
Resultados: La inversión por paciente en el ámbito nacional supone un coste de 7.989 € en el escenario base (sin considerar disponibilidad de la combinación efavirenz-emtricitabina-tenofovir) y de 7.997, 8.424, 7.830, 8.375 y 8.527 € para los escenarios 1 (sustitución de pautas con efavirenz, emtricitabina, tenofovir o efavirenz, lamivudina, tenofovir), 2 (sustitución de pautas con efavirenz), 3 (sustitución de pautas con tenofovir), 4 (sustitución de pautas con tenofovir o zidovudina) y 5 (sustitución total), respectivamente, lo que se traduce en incrementos respecto al escenario base del 0,11, 5,45, −1,99, 4,83 y 6,73 % para los escenarios 1, 2, 3, 4 y 5, respectivamente.
Conclusión: La utilización de la combinación fija de efavirenz-emtricitabina-tenofovir en el tratamiento de pacientes adultos infectados por el VIH-1 conllevaría ligeros incrementos o incluso ahorros presupuestarios, con disminución del número de tomas diarias, lo que podría mejorar la calidad de vida de los pacientes, el cumplimiento y la adherencia al tratamiento.

Introduction

Human immunodeficiency virus (HIV) is a virus of the lentivirus family, genus retrovirus, that is classified in 2 types: HIV type-1 (HIV-1) and HIV type-2 (HIV-2). It is the cause of acquired immunodeficiency syndrome (AIDS), a severe immunodepression unleashed as a consequence of infection in the cells of the immune system.[1] HIV-1 is the cause of a world pandemic and, in Spain, is responsible for one of today's major health problems.[2]

The annual incidence of AIDS cases increased in Spain until the mid-1990s. At that time, its progress stopped, probably due to the reduction in HIV transmission and the spread of antiretroviral (ARVT) and highly active antiretroviral therapies (HAART).[3] According to the latest data from the Epidemiological Monitoring System of the Carlos III Health Institute, 1464 cases of AIDS were reported in Spain in 2007. This figure signifies a decrease of 78% compared to those reported in 1996. Even so, in spite of this reduction, Spain remains one of the countries with the highest incidence of AIDS in western Europe.[4]

The AIDS Study Group, GeSida, belonging to the Spanish Society of Infectious Diseases and Clinical Microbiology, together with the Spanish AIDS Plan (PNS) coordinated by the Spanish Ministry of Health and Consumer Affairs, are in agreement on annual recommendations on ARVT in Spain.[5] At present, the treatment of choice for HIV infection, called HAART, is based on combinations of at least 3 drugs which include 2 nucleoside analogues, a protease inhibitor booster or a non-nucleoside analogue.[5,6]

Atripla® (Bristol-Myers Squibb and Gilead Sciences) is the first combination with 3 antiretrovirals available in a daily dose of a single tablet. It is a fixed-dose combination of efavirenz (EFV) (600 mg), emtricitabine (FTC) (200 mg), and tenofovir disoproxil fumarate (TDF) (245 mg), sold in 30 tablet packages.[7,8] The fixed-dose combination of EFV-FTC-TDF has proved its bioequivalence against the individual administration of its components. The EFV + FTC + TDF regimen (administered separately, not as a fixed-dose combination) has been shown to be superior in terms of virological suppression compared to other antiretroviral regimens.[9,10]

Thanks to ARVT, in recent years, AIDS related mortality has dropped and the health related quality of life of patients has shown improvement.[11,12] On the other hand, partly due to the increase in available options and the change from monotherapy/bitherapy to HAART, ARVT has been associated with a considerable increase in direct health costs indicating a significant investment from overall pharmaceutical spending.[13] However, several studies have shown that, in spite of their elevated price, ARVTs reduce and may even save some of the overall costs associated with patients infected with HIV.[14]

In the midst of limited and scarce resources, investment must be rationalised to combine patient treatment with adequate budget management.[5,15] With

that in mind, budget impact studies are tools which provide fundamental information to price regulation and financing decision-makers, as is the inclusion of the drugs in clinical practice and hospital drug therapy guidelines. The objective of this analysis, therefore, is to estimate the budget impact on the Spanish National Health System of the use of co-formulated EFV-FTC-TDF in the treatment of patients infected with HIV-1 and, at the same time, evaluate the repercussions for each autonomous community in 2008.

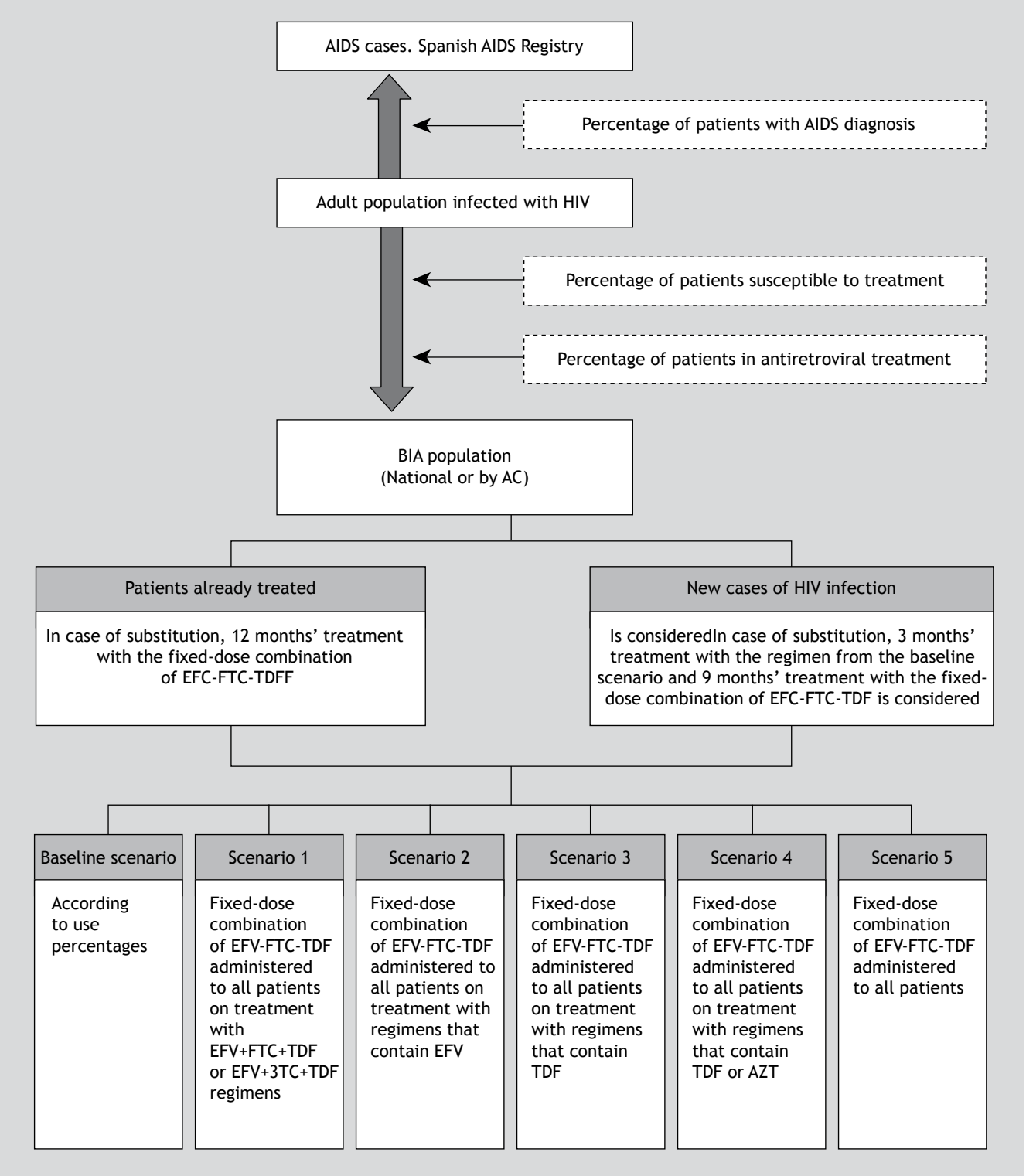

Figure 1. Flowchart for the calculation of target population of the budget impact analysis (BIA). AC indicates autonomous communities; AZT, zidovudine; EFV, efavirenz; FTC, emtricitabine; HIV, human immunodeficiency virus; TDF, tenofovir; 3TC, lamivudine.

Methods

Model

The economic model employed for calculating the budget impact of co-formulated EFV-FTC-TDF was developed with Microsoft Excel 2003 and is structured into the following sections: calculation of target population, characteristics of alternative treatments, and budget impact analysis, based on international recommendations for the development of this kind of analysis.[16,17]

Population

The target population of the analysis consists of adult patients (15 years and over) infected with HIV-1 undergoing treatment with ARVT. This population was obtained from the national registry of AIDS cases, which has gathered cases accumulated across the country, by autonomous community and age group since 1981,[4] the year the AIDS epidemic was recognised.[18]

From the data in the latest hospital survey of HIV/AIDS patients, it was assumed that this population would make up 42.9% of the total number of cases of HIV infection.[19] By applying this percentage, the total cases of HIV infection was established and consequently corrected with the HIV/AIDS mortality figures for 2005.[20]

National and international guidelines on the treatment of HIV patients recommend starting ARVT in patients with lymphocyte counts of CD4 <350 cells/μL.[5,21] According to the results of the hospital survey of HIV/AIDS patients published in 2007, 60.6% of those patients have had counts of CD4 <200 cells/μL.[19] From the group of patients susceptible to treatment, and assuming that 83.2%[19] are actually receiving ARVT, the target population was defined for the budget impact analysis.

The rate per million inhabitants of new cases of HIV/AIDS infection (69.13%)[22] applied to the population of 15 years of age and over for 2008, published by the Spanish Institute of Statistics,[23] allows us to calculate the proportion of new cases within the target population for the analysis. Figure 1 shows the flowchart for the calculation of the target population.

Table 1. Treatment alternatives. Description of regimens considered in the analysis

Regimen number	Drug A	Drug B	Drug C
1	TDF	FTC	EFV
2	TDF	3TC	EFV
3	TDF	FTC	LPV/r
4	TDF	3TC	LVP/r
5	TDF	FTC	FPV/r
6	TDF	3TC	FPV/r
7	TDF	FTC	SQV/r
8	TDF	3TC	SQV/r
9	ABC	FTC	EFV
10	ABC	3TC	EFV
11	ABC	FTC	LPV/r
12	ABC	3TC	LPV/r
13	ABC	FTC	FPV/r
14	ABC	3TC	FPV/r
15	ABC	FTC	SQV/r
16	ABC	3TC	SQV/r
17	AZT	3TC	EFV
18	AZT	3TC	ÑPV/r
19	AZT	3TC	ABC
20	ddI	3TC	EFV
21	TDF	FTC	ATV/r
22	TDF	FTC	NVP
23	ABC	3TC	ATV/r

ABC indicates abacavir; ATV/r, atazanavir with low dose ritonavir; AZT, zidovudine; ddI, didanosine; EFV, efavirenz; FPV/r, fosamprenavir with low dose ritonavir; FTC, emtricitabine; LPV/r, lopinavir with low dose ritonavir; NVP, nevirapine; SQV/r, saquinavir with low dose ritonavir; TDF, tenofovir; 3TC, lamivudine.

Alternative treatments

The treatment regimens considered in the analysis are those defined as preferred regimens in the latest recommendations for the treatment of HIV patients produced by GeSida, which are supported by data from a large number of long duration clinical trials.[5] Furthermore, it was decided to include a selection of the regimens defined as alternative regimens in the GeSida recommendations, which have demonstrated their efficacy in clinical trials, but with fewer patients or for a shorter time; several market studies have shown that, in spite of not being classified as preferred regimens, they are still found among the most frequently used by HIV positive patients in Spain. Table 1 specifies the 23 regimens considered and Table 2, the possible combinations with the medications available that can be adapted to each regimen, with their corresponding percentage use obtained from market studies.[24] Each association is identified with a code in which the first figure indicates the regimen number it refers to and the second figure, the sequential number of pharmacological association.

Budget impact analysis

The model considers a total of 6 scenarios which could represent the treatment situation in Spain of adult patients infected with HIV-1:

a) Baseline scenario: does not consider availability of co-formulated EFV-FTC-TDF in treatment resources.
b) Scenario 1: considers that patients treated in the baseline scenario with EFV + FTC + TDF or EFV + lamivudine (3TC) + TDF regimens, would replace their treatment with a fixed-dose combination of EFV-FTC-TDF.
c) Scenario 2: patients treated in the baseline scenario with any regimen containing EFV would replace the drug association with co-formulated EFV-FTC-TDF.
d) Scenario 3: establishes that patients assigned in the baseline scenario to regimens with TDF would replace their treatment with co-formulated EFV-FTC-TDF.
e) Scenario 4: patients treated with TDF or zidovudine (AZT) would be treated with co-formulated EFV-FTC-TDF.
f) Scenario 5: considers that all patients would be treated with co-formulated EFV-FTC-TDF.

Table 2. Combinations considered. Cost and percentage of use of each combination

Association number	Drug A	Drug B	Drug C		Percentage of use	Cost/day, €
1.1	Truvada		Sustiva		21	23.26
1.2	Viread	Emtriva	Sustiva		0	23.37
1.3	Atripla				3	23.37
2	Viread	Epivir	Sustiva		7	23.37
3.1	Truvada		Kaletra		0	27.76
3.2	Viread	Emtriva	Kaletra		0	27.87
4	Viread	Epivir	Kaletra		0	27.87
5.1	Truvada		Telzir	Norvir	3	26.48
5.2	Viread	Emtriva	Telzir	Norvir	0	26.60
6	Viread	Epivir	Telzir	Norvir	0	26.60
7.1	Truvada		Invirase	Norvir	3	20.99
7.2	Viread	Emtriva	Invirase	Norvir	0	21.10
8	Viread	Epivir	Invirase	Norvir	0	21.10
9	Ziagen	Emtriva	Sustiva		0	21.27
10.1	Kivexa		Sustiva		11	20.69
10.2	Ziagen	Epivir	Sustiva		0	21.27
11	Ziagen	Emtriva	Kaletra		0	25.77
12.1	Kivexa		Kaletra		3	25.19
12.2	Ziagen	Epivir	Kaletra		0	25.77
13	Ziagen	Emtriva	Telzir	Norvir	0	24.50
14.1	Kivexa		Telzir	Norvir	0	23.91
14.2	Ziagen	Epivir	Telzir	Norvir	0	24.50
15	Ziagen	Emtriva	Invirase	Norvir	0	19.00
16.1	Kivexa		Invirase	Norvir	0	18.41
16.2	Ziagen	Epivir	Invirase	Norvir	0	19.00
17.1	Retrovir	Epivir	Sustiva		3	19.00
17.2	Zidovudina CombinoPharm	Epivir	Sustiva		0	17.69
17.3	Combivir		Sustiva		9	18.51
18.1	Retrovir	Epivir	Kaletra		0	23.50
18.2	Zidovudina CombinoPharm	Epivir	Kaletra		0	22.19
18.3	Combivir		Kaletra		6	23.01
19.1	Retrovir	Epivir	Ziagen		0	17.69
19.2	Zidovudina CombinoPharm	Epivir	Ziagen		0	16.38
19.3	Combivir		Ziagen		0	17.20
19.4	Trizivir				13	16.34
20	Videx	Epivir	Sustiva		7	18.89
21.1	Viread	Emtriva	Reyataz	Norvir	0	30.59
21.2	Truvada		Reyataz	Norvir	4	30.47
22.1	Viread	Emtriva	Viramune		0	19.68
22.2	Truvada		Viramune		4	19.57
23.1	Ziagen	Epivir	Reyataz	Norvir	0	28.49
23.2	Kivexa		Reyataz	Norvir	3	27.90

Outlook and perspective

The budget impact analysis has been created from a hospital perspective. As a result, the only costs included were pharmaceutical costs from the considered drug associations. The results obtained are derived from 1 year of treatment and, therefore, no discount rates were applied.[25]

Costs

In line with the hospital perspective of the analysis, the only pharmacological costs included were those of the medications necessary for the possible drug combinations to fulfil the regimens under consideration.

The analysis is calculated in terms of the laboratory sales prices of the medications evaluated. Table 2 specifies the daily treatment costs of each treatment combination. All costs were valued in Euros as of 2008.

Premises

The following premises have been considered in the analysis:

- The ARVT of all patients undergoing treatment consists of triple therapy (a combination of 3 pharmacological agents).
- The budget impact considers the authorised dosage of each medication for maintenance treatments, without considering dose adjustments. Where different packaging is available, the one with the lowest number of tablets/day was chosen.
- A percentage of cases corresponding to new HIV positive patients have been calculated on the ARVT population (over which the analysis calculations are made). Given that co-formulated EFV-FTC-TDF has no indications in patients not treated before, 3 months' treatment with the original regimen has been assumed for this subgroup, and 9 months' treatment with co-formulated EFV-FTC-TDF.
- The substitutions considered imply full replacement for all patients assigned to each treatment regimen.

Sensitivity analysis

In order to test the robustness of the model, a series of univariate sensitivity analyses were conducted. The value of the most uncertain parameters (percentage of patients diagnosed with AIDS, percentage of patients susceptible to treatment, percentage of patients with ARVT, percentage of patients in treatment with co-formulated EFV-FTC-TDF 1 full year, and rate per million of new cases of HIV infection) was modified with a 20% increase or decrease in order to study the effect on final outcomes.

Results

Baseline case

Table 3 shows the results of the total pharmacological cost to the National Health System of each of the evaluated scenarios. On a national level, the investment per patient implies €7,988.74 for the baseline scenario, €7997.17; €8424.00; €7829.74; €8374.83; and €8526.53 for scenarios 1, 2, 3, 4, and 5, respectively, which translates to a respective increase to the baseline scenario of 0.11%, 5.45%, -1.99%, 4.83%, and 6.73% for scenarios 1, 2, 3, 4, and 5, respectively.

Table 4 shows the results of the budget impact analysis by autonomous community.

Table 3. Total annual budget impact of baseline case. Results in Spain

	Baseline scenario	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
Overall budget impact	€499 537 157.34	€500 064 362.10	€526 753 777.96	€489 594 766.26	€523 679 038.00	€533 165 091.36
Budget increase against baseline cenario		€527 204.76	€27 216 620.62	€–9 942 391.08	€24 141 880.66	€33 627 934.02
Increase, %		0.11%	5.45%	-1.99%	4.83%	6.73%
Budget increase against scenario 1			€26 689 415.86	€–10 469 595.84	€23 614 675.90	€33 100 729.26
Increase, %			5.34%	–2.09%	4.72%	6.62%
Budget increase against scenario 2				€–37 159 011.70	–3 074 739.96	€6 411 313.40
Increase, %				–7.05%	–0.58%	1.22%
Budget increase against scenario 3					€34 084 271.74	€43 570 325.10
Increase, %					6.96%	8.90%
Budget increase against scenario 4						€9 486 053.36
Increase, %						1.81%
Budget impact per patient	€7 988.74	€7 997.17	€8 424.00	€7 829.74	€8 374.83	€8 526.53

Table 4. Total annual budget impact of baseline case. Results by autonomous community

otal annual impact, €	Baseline scenario, €	Scenario 1, €	Scenario 2, €	Scenario 3, €	Scenario 4, €	Scenario 5, €
Andalusia	71 408 623.26	71 483 986.96	75 299 227.55	69 987 362.70	74 859 694.79	76 215 722.06
Aragon	9 564 243.83	9 574 337.81	10 085 338.99	9 373 884.71	10 026 469.37	10 208 091.35
Asturias	8 746 336.08	8 755 566.85	9 222 868.63	8 572 255.95	9 169 033.37	9 335 123.54
Balearic Islands	15 131 293.35	15 147 262.71	15 955 701.83	14 830 132.09	15 862 566.03	16 149 904.53
Canary Islands	13 383 345.33	13 397 469.94	14 112 519.19	13 116 973.85	14 030 142.32	14 284 287.83
Cantabria	4 254 439.50	4 258 929.58	4 486 237.00	4 169 762.51	4 460 050.17	4 540 840.64
Castilla y León	18 218 235.49	18 237 462.77	19 210 831.93	17 855 634.19	19 098 695.46	19 444 654.01
Castilla-La Mancha	8 878 256.69	8 887 626.68	9 361 976.75	8 701 550.91	9 307 329.50	9 475 924.80
Catalonia	103 247 661.18	103 356 627.36	108 872 973.29	101 192 701.68	108 237 465.59	110 198 106.18
Comunidad Valenciana	39 840 022.58	39 882 069.20	42 010 653.47	39 047 078.40	41 765 431.05	42 521 980.53
Extremadura	7 070 944.41	7 078 406.98	7 456 195.45	6 930 209.94	7 412 672.53	7 546 947.54
Galicia	23 976 569.88	24 001 874.43	25 282 901.55	23 499 359.27	25 135 321.50	25 590 629.01
Madrid	118 497 683.07	118 622 743.92	124 953 872.43	116 139 199.24	124 224 498.14	126 474 731.84
Murcia	10 144 694.49	10 155 401.07	10 697 414.74	9 942 782.55	10 634 972.34	10 827 616.90
Navarra	5 553 857.45	5 559 718.92	5 856 452.02	5 443 317.88	5 822 267.04	5 927 733.05
The Basque Country	35 216 205.39	35 253 372.10	37 134 913.72	34 515 289.99	36 918 151.72	37 586 896.37
La Rioja	3 251 842.90	3 255 274.85	3 429 015.26	3 187 120.80	3 408 999.59	3 470 751.06
Ceuta	1 075 152.93	1 076 287.63	1 133 731.21	1 053 753.94	1 127 113.45	1 147 530.27
Melilla	540 874.48	541 445.31	570 343.31	530 109.34	567 014.13	577 285.17

Sensitivity analysis

Table 5 shows the results of the univariate sensitivity analysis. The analysis guarantees the robustness of the model. From these results, it can be deduced that the parameter with greatest influence on the model is the number of patients with ARVT: obviously in all scenarios the budget impact increases alongside the number of patients treated. On the other hand, neither the percentage of patients in treatment with co-formulated EFV-FTC-TDF during the full year, nor the rate per million inhabitants of new HIV cases affects the total budget impact. In Figure 2 this sensibility analysis is shown as a tornado diagram.

Discussion

It is common to find publications in the bibliography of economic evaluations of antiretroviral drugs which demonstrate a cost-effective and/or cost-utility relationship below the threshold of efficiency normally accepted in each country.[26,27] However, the introduction of new medications often implies additional funding which does not always ensure the maximisation of health benefits. For this reason, decision-makers need to have access to complementary information of the pharmacological impact on the budget.[28]

This work, through an economic model, provides data on the budget impact in Spain, nationally and by autonomous community, of a new combination of antiretroviral drugs. The model developed for this study has been structured into 2 parts, the calculation of the target population and the budget analysis, which can be managed independently ensuring its simplicity and flexibility. Furthermore, considering only the direct pharmacological costs should be interpreted as an assurance of the transparency of the tool, since the results it provides are not camouflaged by any factor other than the pharmacological budget cost.

The results show that in the baseline scenario, an estimation of the impact of the treatment of HIV-1 infection in Spain, the annual cost per patient is €7988.74. The substitution carried out in scenario 1, in which the administration of co-formulated EFV-FTC-TDF to patients undergoing treatment with EFV + FTC + TDF or EFV + 3TC + TDF, means a treatment modification in 24% of patients, and implies a budget increase of €8.43/patient/year (annual cost/patient of €7997.17). The substitution in scenario 2 would affect 54% and would imply the administration of co-formulated EFV-FTC-TDF to all patients under treatment with any regimen that contains EFV. This modification would cause an increase in the baseline scenario of €435.26/patient/year, with an annual cost per patient of €8424.00. Scenario 3 foresees substitution by co-formulated EFV-FTC-TDF in patients treated with any regimen which includes TDF. This scenario would affect 45% of patients and generate a saving of €159/patient/year, with an annual cost per patient of €7829.74. In scenario 4, which poses replacement by co-formulated EFV-FTC-TDF in patients treated with regimens that include TDF or AZT, this change would affect 76%, and cause a cost increase in relation to the baseline scenario of €386.09/patient/year (annual cost/patient of €8374.83). The last situation, scenario 5, is an extreme situation that assumes the administration of co-formulated EFV-FTC-TDF to 100% of patients, with an increase of €537.79/patient and an annual cost per patient of €8526.53.

The results by autonomous community are proportional to relative weight at population level. The 3 most populated communities, therefore, (Madrid, Catalonia, and Andalusia) assume 59% of the total budget impact of HIV in Spain. However, although the HIV/AIDS infection

Table 5. Total annual budget impact. Sensitivity analysis

Parameter	Value, %	Baseline scenario, €	Scenario 1, €	Scenario 2, €	Scenario 3, €	Scenario 4, €	Scenario 5, €
Percentage of patients diagnosed with AIDS							
Baseline case	42.9	499 537 157.34	500 064 362.10	526 753 777.96	489 594 766.26	523 679 038.00	533 165 091.36
Min. value	34.3	674 731 570.44	675 443 673.02	711 493 426.70	661 302 248.82	707 340 334.00	720 153 274.11
Max. value	51.5	382 740 881.94	383 144 821.49	403 594 012.14	375 123 111.22	401 238 174.00	408 506 302.86
Percentage of patients susceptible to treatment							
Baseline case	60.6	499 537 157.34	500 064 362.10	526 753 777.96	489 594 766.26	523 679 038.00	533 165 091.36
Min. value	48.5	399 629 725.87	400 051 489.68	421 403 022.37	391 675 813.01	418 943 230.40	426 532 073.09
Max. value	72.7	599 444 588.81	600 077 234.52	632 104 533.56	587 513 719.51	628 414 845.60	639 798 109.63
Percentage of patients in antiretroviral treatment							
Baseline case	83.2	499 537 157.34	500 064 362.10	526 753 777.96	489 594 766.26	523 679 038.00	533 165 091.36
Min. value	66.6	399 629 725.87	400 051 489.68	421 403 022.37	391 675 813.01	418 943 230.40	426 532 073.09
Max. value	98.8	599 444 588.81	600 077 234.52	632 104 533.56	587 513 719.51	628 414 845.60	639 798 109.63
Percentage of patients in treatment with fixed-dose combination of EFV-FCT-TDF one full year							
Baseline case	97.6	499 537 157.34	500 064 362.10	526 753 777.96	489 594 766.26	523 679 038.00	533 165 091.36
Min. value	78.1	499 537 157.34	500 038 556.54	525 421 581.91	490 081 425.29	522 497 343.97	531 519 075.07
Max. value	100	499 537 157.34	500 067 575.56	526 919 670.98	489 534 164.57	523 826 189.61	533 370 063.15
New cases of HIV infection. Rate per million inhabitants							
Baseline case	69.13	499 537 157.34	500 064 362.10	526 753 777.96	489 594 766.26	523 679 038.00	533 165 091.36
Min. value	55.30	499 537 157.34	500 064 362.10	526 753 777.96	489 594 766.26	523 679 038.00	533 165 091.36
Max. value	82.96	499 537 157.34	500 064 362.10	526 753 777.96	489 594 766.26	523 679 038.00	533 165 091.36

EFV indicates efavirenz; FTC, emtricitabine; HIV, human immunodeficiency virus; TDF, tenofovir.

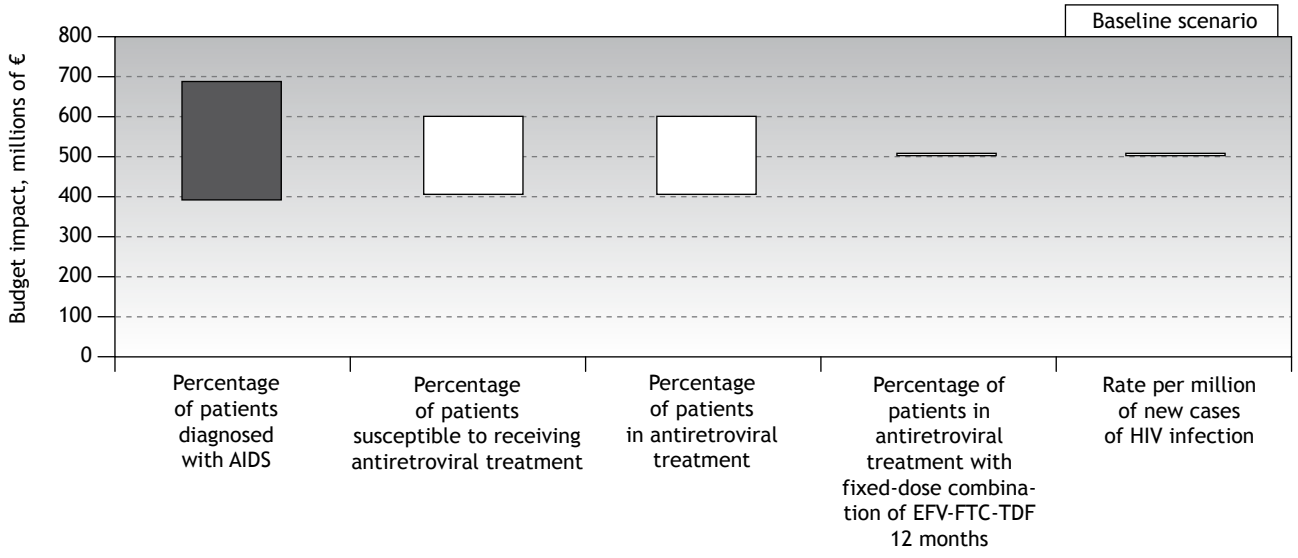

Figure 2. Total annual budget impact. Graphic representation of the sensibility analysis using a tornado diagram (baseline scenario). EFV indicates efavirenz; FTC, emtricitabine; HIV, human immunodeficiency virus; TDF, tenofovir.

has spread throughout Spanish provinces and autonomous communities, the different times at which the HIV infection broke out, sociodemographic characteristics and the degree of penetration in the distinct life-styles of each location, have contributed to identifying important geographical differences in the incidence of this disease. Such is the case of the Basque Country, Ceuta, and the Balearic Islands, communities with a high incidence of AIDS and in which investment in treatment for HIV infection assumes a value of €19.11, €18.79, and €17.72 per capita, respectively, in the baseline scenario, higher than Catalonia's €17.24 per capita and surpassed only by Madrid's €23.13 per capita.

The economic results of the model are based on the prior estimation of the number of patients taken into account.

The sensitivity analysis shows that the parameter with most influence on the results is the percentage of patients diagnosed with AIDS. Despite the importance of the HIV/AIDS epidemic in Spain, which during the 1990s kept Spain in the lead of countries with greatest incidence of the disease;[3,29] it is not easy to determine a reliable and widely accepted value that estimates the proportion of cases infected by HIV that meet the criteria for being diagnosed with AIDS, being this difficulty the main limitation of our work. Even so, the resulting figure of 124 021 surviving HIV patients from the interactive model calculation falls within the range of 110 000 to 150 000 cases estimated by the Spanish Epidemiology Centre.[30] Likewise, the estimation of 2600 new HIV cases per year across Spain is similar to the 2300 new cases in 2000 reported by the same centre,[3] which attests to the soundness of the model in spite of the limitations mentioned above.

Another possible limitation of this model is the assumption of substitution in all of the patients under a given regimen, which may not be completely representative of reality since not all patients assigned to regimens susceptible to modification would change their usual treatment for the fixed-dose combination of EFV-FTC-TDF. This situation would lead to intermediate results falling somewhere between the baseline scenario and those of the scenario in question.

Furthermore, the model analyses only the budget impact by pharmacological cost of the treatment for HIV infection, but it should not be forgotten that other specific aspects of the different treatment alternatives, such as the adverse events profile and aspects related to clinical follow-up, may require the consumption of different resources and, therefore, influence the overall budget impact.

Moreover, the use of a fixed-dose combination implies a simplification of the ARVT, understanding this as the change from one treatment with which absolute virologic suppression is achieved to another, simpler treatment which maintains that suppression. It has been demonstrated that treatment simplifications not only improve patients' quality of life but also their treatment adherence, as they reduce the number of tablets and frequency of administration, eliminate dietary restrictions, improve current toxicity and/or reduce the risk of interactions.[5,31]

In this case, the fixed-dose combination of EFV-FTC-TDF signifies a reduction in the number of tablets and the frequency of administration with respect to the original regimens, and, being equally effective, has been shown to be the preferred choice of HIV patients.[32]

To conclude, the use of co-formulated EFV-FTC-TDF in the treatment of adult patients infected with HIV-1 may generate slight increases, or even decreases, in the overall budget. Furthermore, this new formulation would be associated with a reduction in the number of doses on the part of the patient, which would translate to a better quality of life, compliance and adherence to treatment.

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