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Cost-effectiveness analysis of early access to medical and social care for migrants living with HIV in France.*

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Abstract

Background

In 2011, migrants accounted for 47% of newly diagnosed cases of HIV infection in France, including 70% from Sub-Saharan Africa. These populations meet with specific obstacles leading to late diagnosis and access to medical and social care. Reducing these delays has a proven benefit to patients' health and contributes to a better control of the epidemic by preventing secondary infections.

Methods

The objective of this study is to assess the cost-effectiveness impact of an early access to care (ATC) for migrant people living with HIV (PLHIV) in France. The model compares "early" vs. "late" ATC for migrant PLHIV in France, defined by an entry into care with a CD4 cell count of 350 and 100/mm³ respectively, and integrate the positive externality of treatment on prevention. To evaluate the cost-effectiveness of "early" ATC, incidence and hidden prevalence among migrants in France were estimated.

Findings

Early ATC strategy proved cost-saving, or cost-effective in the worst case scenario. In the most favorable scenario, early ATC generated an average net saving of €198,000 per patient, and prevented 0.542 secondary infection. In the worst case scenario, early ATC strategy generated an average cost of €28,000, a cost-effectiveness ratio of €133,000 per averted infection and prevented 0.211 secondary infection.

Interpretation

In addition to individual health benefit, improving early ATC for migrant PLHIV proves an efficient strategy in terms of public health and economics. These results stress out the benefit of ensuring ATC for all individuals living with HIV in France.

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1 Introduction

The main benefit associated with early treatment of HIV is medical. An early care translates into significant health gains for patients whose life expectancy and quality of life increase. Early treatment of HIV infection also has a double benefit from the economic and public health point of view.

In 2011, the HPTN 052 trial's results proved a 96% reduction in the number of new infections among discordant couples when the infected partner was under ARV treatment.¹ Detection and early treatment of HIV patients would thus avoid secondary infections that would be associated with future costs of care. This collective benefit, or positive externality of treatment, is likely to significantly alter the traditional framework of cost-benefit analysis. On the top of the health benefit for those treated, early treatment of people infected with HIV may not only be cost-effective but also cost-saving.

In France, migrant populations are considered as a risk group for HIV. Indeed, 34,500 migrants were considered to be infected with HIV in 2010 and people from sub-Saharan Africa represent a share of nearly 40% in the new discoveries of HIV since 2003 in France.^{2,3} Unlike others risk groups such as MSMs or IDUs, migrant populations are characterized by a significant delay in screening. According to the French Hospital Database on HIV, almost 50% of migrants diagnosed in France during 2011 had CD4 cell count levels lower than 350. Given these data, the study of the benefits associated with earlier entry into care for the migrant population in France is particularly relevant, especially in the light of the preventive effect of ARVs provided by the results of HPTN 052 trial.

This article assess the cost-effectiveness impact of an early access to care (ATC) for migrant people living with HIV (PLHIV) in France. The model integrates the positive externality of ARV treatments on prevention of secondary infections. Moreover, existing estimates of incidence and size of hidden prevalence among migrants in France were corrected to take into account the specificity of the epidemics among this population which is partly imported. The main results of this study suggest that an earlier entry to care for migrant would constitute a cost-saving or at least a cost-effective intervention even in the scenarios implying the most unfavorable hypothesis. Indeed, even if earlier treatment initiation increases life expectancy and the lifetime total cost of care, the decrease in secondary

infections made possible by this intervention compensate this overspending by suppressing future costs of care.

This article proceeds as follows. Section 2 describes the model used in the analysis, section 3 looks for the values of model parameters, section 4 presents the results and section 5 evaluates their robustness. The last section concludes.

2 Modeling of intervention

2.1 Secondary infections

The model compares “early” (1) and “late” (2) ATC for migrants living with HIV in France. “Early” ATC is defined as entry into care at time t_1 after infection, with a CD4 cell count of 350, whereas “late” ATC is defined as entry into care at time t_2 with CD4 cell count of $100/mm^3$. The average number of secondary infections caused by a person infected with HIV throughout his/her life is denoted by R_0 . It can be decomposed by year as $R_0 = \sum_{t=1}^T r_0^t$, where r_0^t is the average annual number of secondary infections caused by an HIV-infected individual in year t after infection, and T is her remaining life expectancy. Both T and r_0^t depend on the treatment received by the individual. We denote by \bar{r}_0 the value of r_0^t in the first year after infection. Due to the phase of high viral load during seroconversion, this value is larger than \underline{r}_0 , the value of r_0^t after this early stage. Finally, this value is changed into $\alpha \underline{r}_0$ when the individual is under treatment.

One key parameter in our analysis is α , which results from two effects. The first is the reduction in infectivity induced by treatment. The second is the impact that diagnosis may have on risk behaviors. When the net effect is a reduction in disease transmission we have $\alpha < 1$.

Life expectancy is affected by the timing of treatment initiation: we denote by T_1 the value of T for individuals with early ATC, and by $T_2 < T_1$ the corresponding value with late ATC.

Under these notations, the total number of secondary infections of an HIV-infected patient who benefits from a treatment at date t_i is equal to:

$$R_0 = \bar{r}_0 + \sum_{t=2}^{t_i} \underline{r}_0 + \sum_{t=t_i+1}^{T_i} \alpha \underline{r}_0.$$

The number of secondary infections avoided thanks to the early treatment strategy is therefore equal to:

$$\begin{aligned} R_0^2 - R_0^1 &= \bar{r}_0 + (t_2 - 1)\underline{r}_0 + \alpha(T_2 - t_2)\underline{r}_0 \\ &- [\bar{r}_0 + (t_1 - 1)\underline{r}_0 + \alpha(T_1 - t_1)\underline{r}_0] \\ &= \underline{r}_0[(1 - \alpha)(t_2 - t_1) - \alpha(T_1 - T_2)] \end{aligned}$$

The first term represents the decrease in secondary infections thanks to the earlier treatment initiation and the second term stands for the increase in secondary infections due to a prolonged life expectancy for early treated patients.

Figure 1 describes early and late ATC strategies:

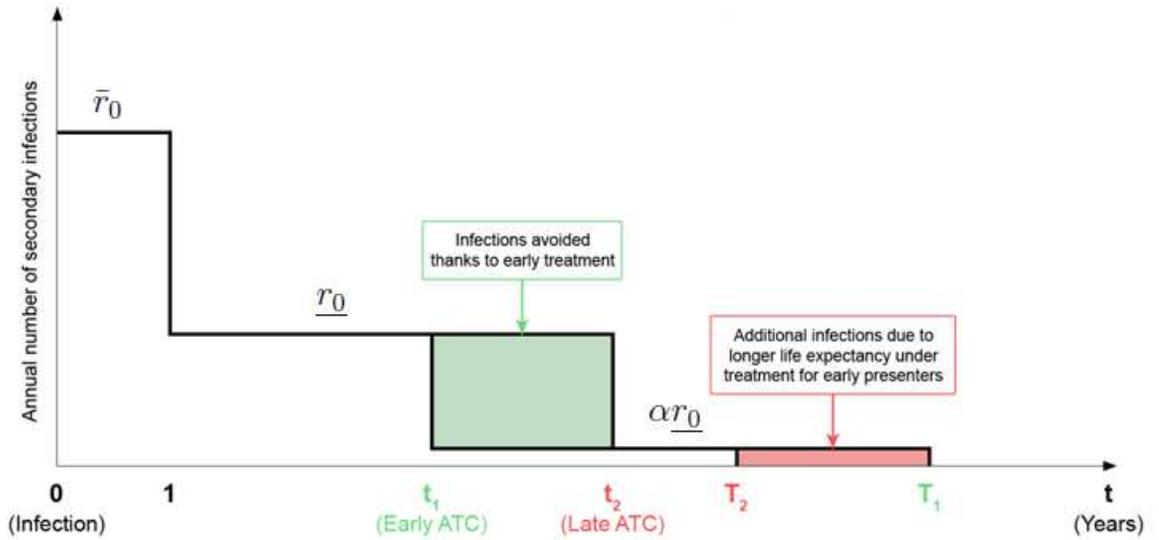


Figure 1: Comparison of early and late ATC

2.2 Costs

For each strategy, we compute TC_i , the total treatment costs under strategy $i = 1$ (early treatment) or $i = 2$ (late treatment). This total cost is defined as the lifelong cost of care once the patient is diagnosed C_i , plus the cost of secondary infections. By convention, we value this cost at C_1 , which corresponds to the assumption that all individuals who are secondarily infected will benefit from early treatment. Under this assumption, we have that $TC_i = C_i + R_0^i C_1$.

Notice that early treatment strategy is cost-saving if $TC_1 < TC_2$, i.e. if:

$$\begin{aligned}(C_1 - C_2) &< C_1(R_0^1 - R_0^2) \\ &< C_1 r_0 [(1 - \alpha)(t_2 - t_1) - \alpha(T_1 - T_2)]\end{aligned}$$

The cost-saving potential of the early treatment strategy depends on the tradeoff between the savings generated by the decrease in secondary infections thanks to early treatment and the extra cost associated with the increase in life expectancy for early treated patients.

3 Parameters value

3.1 Treatment timing and cost parameters

Existing literature on treatment timing and costs in the era of HIV/AIDS provides confident estimates for these parameters which allows us to build a central scenario. The impact of these parameters value on final results will be tested in robustness analysis in section 5.

Annual costs of care for early treated and late treated patients are provided by an article of Sloan, Champenois, Choisy and al. in which the authors simulate the evolution of two cohorts of French patients based on their CD4 level at treatment initiation.⁴ Treatment timings are suggested by Lodi, Philips, Touloumi et al. who estimates the median time between seroconversion and CD4 cell counts of 200, 350 and 500 from the CASCADE data gathering

25 patients' cohorts in Europe, Australia, Canada and sub-Saharan Africa.⁵ Finally, life expectancy under treatment for early and late presenters is based on the results of the ART Cohort Collaboration which synthesizes data on 14 cohorts of patients in North America and Europe.⁶ Table 1 summarizes the parameters values :

	Definition	Value (early treatment)	Value (late treatment)
C_i	Lifelong cost of care	686,426	513,200
t_i	Treatment start date	4	9
T_i	Death date	38	32.8

Table 1: Treatment timing and cost parameters

3.2 Value of α and $\underline{r_0}$

Existing literature does not provide reference values for α and $\underline{r_0}$. Based on available information we therefore estimate plausible values for these parameters allowing us to simulate different scenarios of intervention.

3.2.1 Value of α

The parameter α reflects the change in the annual number of secondary infections for HIV positive migrants who are diagnosed, and its value depends on both the reduction of infectivity under treatment and the evolution of preventive behaviors once patients are diagnosed.

The decline in infectivity of patients receiving ARV treatment is related to the decrease in viral load induced by the treatment and depends in part on patients' adherence. The decrease in infectivity for ARV patients is probably less than the 96% measured in the HPTN 052 trial where the conditions of care and adherence's monitoring were optimal.¹ Observational cohort studies may allow us to get a better approximation for the decline of infectivity under treatment in real life conditions. Three meta-analyzes provide more or less optimistic results ranging from 92% to only 84%.⁷⁻⁹ Following these results, we assume a 90% reduction in infectivity for migrants under treatment in France.

Two scenarios for the evolution of preventive behaviors after diagnosis are explored. Following Marks, Crepaz, Senterfitt and Janssen, the scenario assumes a favorable change in preventive behaviors by a 53% decline in the share of unprotected sex acts after diagnosis.¹⁰ In the pessimist scenario, we assume no change in sexual behaviors following diagnosis.

In short, when sexual behaviors are unchanged, the value of α is equal to 0.1, whereas if we assume a 53% reduction in unprotected sexual acts after diagnosis, the value of α decreases to 0.047.

3.2.2 Value of r_0

No estimation of r_0 is available for migrant populations in France. We therefore approximate it by calculating the annual number of new transmissions in the migrant category which is due to undiagnosed migrants and by dividing it by the total number of undiagnosed migrants in France. Therefore three types of data are required: the number of undiagnosed migrants present in France (1), the number of new infections among migrants in France each year (2) and the share of these new infections caused by undiagnosed HIV infected migrants (3). Available estimations of incidence and hidden prevalence among migrants in France are based on back-calculation from mandatory reportings of HIV cases. Such estimations are marked with uncertainty and raise specific difficulties in the migrant population where a significant part of infections is imported from home countries of migrants. Thus, in the rest of the section we try to adjust existing estimates for this bias.

Ndawinz, Costagliola and Supervie estimated that 2469 new transmissions occurred among migrants in 2007.¹¹ However, a significant share of these new infections may have occurred in the birth country of migrants. An assumption has thus to be made regarding the share of these new transmissions that took place in France. Among migrants interviewed in the VESPA 2 survey conducted in 2011 among PLHIV in France by the ANRS, 32.9% declared a contamination in France. Assuming a relative stability in incidence for the migrant category since 2007, and given the share of infections among migrants occurring in France, the number of new infections among migrants in France each year is assumed to be 812.

Based on ANRS estimates for 2010, 9500 undiagnosed migrants live in France. This

estimation relies on incidence estimates in the migrant population obtained through back-calculation. It therefore tends to overestimate the actual size of the hidden epidemics among migrants in France. As some migrants are infected ante-migration in their home country, ANRS estimates might include by anticipation migrants infected in their country of origin but not yet arrived in France.^{2,3} The estimated 9500 migrants with undiagnosed HIV can be divided into three categories: migrants infected in France (1), migrants infected abroad but present on the French territory (2) and migrants infected abroad but not yet arrived in France (3). According to previous estimates for the share of new infections occurring in France we consider that the first group represents 32.9% of undiagnosed migrants, that is to say 3125 undiagnosed migrants infected in France. Groups (2) and (3) should therefore be constituted by 67.1% of the 9500 undiagnosed migrants (6375 migrants). The distribution of migrants between these two categories will depend on several factors including the time between infection and migration and the timing of diagnosis after arrival in France. One way to approximate the distribution of undiagnosed migrants infected abroad between categories (2) and (3) (present or not present in France) is to rely on the share of the total undiagnosed time spent in France or in the country of origin for migrants infected abroad.

The VESPA2 survey provides data on year of arrival in France, year of diagnosis, year of first medical examination related to HIV and CD4 level at this time for all migrants declaring a contamination in their country of origin. From these data, age of infection at first examination can be estimated based on data of Lodi, Philips, Touloumi et al.⁵ This allows in turn to determine a probable date of infection for each of these migrants. From the supposed year of infection and the year of arrival in France it is then possible to calculate the total time spent undiagnosed and the share of that time spent in France or in the country of origin. From calculations based on VESPA2 data we estimated a share of undiagnosed time spent in France ranging from 23.43% ([18.58, 28.28]) to 47.24% ([40.98, 53.49]) for migrants infected in their country of origin. If we use these estimates as a proxy for the distribution between groups (2) and (3) we can consider that 23.43 to 47.24% of the 6375 undiagnosed migrants infected abroad are actually in France (1494 to 3012 migrants infected abroad but already in France). Summing up these estimates to the number of migrants infected in France, there would be between 4619 and 6137 undiagnosed HIV positive migrants on the French territory.

The share of HIV infections attributable to undiagnosed HIV migrants is calculated following the calculation method developed by Marks, Crepaz and Janssen.¹² As said above for the value of α , two scenarios are considered for the evolution of risk behaviors following the HIV diagnosis.

Table 2 summarizes the possible values for \underline{r}_0 depending on hypothesis on the size of hidden epidemic among migrants and the evolution of risk behaviors following diagnosis:

Preventive behaviors	Hidden epidemics	
	Low	High
Optimist	0.091	0.0778
Pessimist	0.0589	0.0531

Table 2: Possible values of \underline{r}_0

4 Results

Four scenarios are considered in the analysis depending on hypothesis on the size of the hidden epidemics and the evolution of preventive behaviors following diagnosis. Table 3 summarizes the results of scenarios analysis.

Evolution of preventive behaviors	Optimist		Pessimist	
	Low	High	Low	High
Hidden prevalence	Scenario 1	Scenario 2	Scenario 3	Scenario 4
\underline{r}_0	0.091	0.0778	0.0589	0.0531
α	0.047	0.047	0.1	0.1
Net cost of early ATC	-109,152	-68,192	12,313	28,158
Averted infections (AI) for early ATC	0.4114	0.3517	0.2344	0.2113
Cost per AI for early ATC	Cost-saving	Cost-saving	52,532	133,237

Table 3: Results of scenarios analysis

Results show that early treatment for HIV-infected migrants in France is a cost-saving intervention when risk behaviors decrease after diagnosis. In the most favorable case (scenario 1), early ATC generates an average net saving of €109,000 per patient and prevents 0.41 secondary infection. When no change in risk behavior is assumed after diagnosis, the early ATC strategy allows for a reduction in the number of secondary infections but generates a net cost compared to the late treatment strategy. In the worst case scenario (scenario 4), early ATC prevents 0.2 secondary infection but generates an additional cost of €28,000, which leads to a cost-effectiveness ratio of €133,000 per averted infection.

5 Sensitivity analysis

Table 4 presents cost-effectiveness ratios resulting from adverse changes in t parameters. The first situation assumes that the treatment delay for late presenters ($t_2 - t_1$) is reduced from 5 to 4 years. The second one runs the simulation when life expectancy for early presenters ($T_1 - t_1$) increases from 32 to 36 years, and the third one when life expectancy for late presenters ($T_2 - t_2$) decreases from 23.8 to 22 years. The fourth simulation assumes that instead of C_1 , the benefit of preventing a secondary infection is reduced to C_2 . Finally, the last simulation investigates the case where late presenters start treatment later at a CD4 cell count of 200 instead of 350.

	Cost per averted infection in €			
	Scenario 1	Scenario 2	Scenario 3	Scenario 4
$t_2 - t_1 = 4$	Cost-saving	Cost-saving	268,450	372,750
$T_1 - t_1 = 36$ ($C_1 = 726\ 804$)	Cost-saving	Cost-saving	232,603	337,393
$T_2 - t_2 = 22$ ($C_2 = 474\ 387$)	Cost-saving	Cost-saving	260,939	364,420
Value of infection averted = C_2	Cost-saving	Cost-saving	225,750	306,460
Late ATC at 200 CD4 cell count	Cost-saving	Cost-saving	102,841	189,051

Table 4: Results of sensitivity analysis

Early ATC remains cost saving in scenarios 1 and 2. Early initiation strategies thus remain cost-saving when risk behaviors decrease after diagnosis. Under scenarios 3 and 4, which are more pessimistic in terms of sexual behavior evolution, the cost per averted

infection ranges from 104 k€ to 372 k€.

6 Conclusion

When early and late treatment are respectively defined as entry into care at 350 and 100 CD4, reducing the time delay between infection screening and treatment initiation appears to be a cost-saving intervention or at least cost-effective, even in the worst scenarios. If a decrease in risk behaviors is assumed after diagnosis, these results remain robust when late treatment is defined as an entry into care at 200 CD4, or when more pessimistic values of the key model parameters are assumed.

Beyond the medical benefits for treated patients, earlier diagnosis and treatment for HIV-positive migrants is also desirable from an economic point of view. Even if earlier treatment increases life expectancy and therefore the lifetime cost of care of HIV patients, the decrease in the number of secondary infections associated with such an intervention can offset this extra cost by avoiding expenditures in the future.

The main contributions of this article are twofold. This article is the first attempt to integrate the preventive effect of ARV treatments in cost-effectiveness analysis of treatments for the migrant population in France. Moreover, existing estimates of incidence and size of hidden prevalence among migrants in France were corrected to take into account the specificity of the epidemics among this population which is partly imported.

The main limitation of this evaluation is related to the static nature of the model studied. A static model can only take into account infections averted in the first stage while a dynamic model could highlight the cumulative process of avoided secondary infections. In the real world, people whose infection is avoided thanks to the intervention would also have infected other people if they had been infected. The results from the static model therefore tend to underestimate both the number of infections averted and the savings due to earlier treatment of HIV-positive migrants.

The model studied in this paper is simple. Its main benefit is to make explicit all the assumptions under which costs and impact of different strategies are simulated. The simulations shows that earlier treatment initiation for migrants should be promoted, from both economic and public health points of view, even though a part of the benefits associated with this type of intervention cannot be directly taken into account. Thus, it seems that any intervention promoting greater use of screening and better access to care for HIV-positive

migrants should be recommended.

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