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ORIGINAL PAPER

Economic and public health consequences of delayed access to medical care for migrants living with HIV in France

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Abstract In 2013, migrants accounted for 46% of newly diagnosed cases of HIV (human immunodeficiency virus) infection in France. These populations meet with specific obstacles leading to late diagnosis and access to medical care. Delayed access to care (ATC) for HIV-infected migrants reduces their life expectancy and quality of life. Given the reduction of infectivity under antiretroviral (ARV) treatment, delayed ATC for HIV-infected migrants may also hinder the control of the HIV epidemic. The objective of this study is to measure the public health and economic consequences of delayed ATC for migrants living with HIV in France. Using a healthcare payer perspective, our model compares the lifetime averted infections and costs of early vs. late ATC for migrants living with HIV in France. Early and late ATC are defined by an entry into care with a CD4 cell count of 350 and 100/mm^3, respectively. Our results show that an early ATC is dominant, even in the worst-case scenario. In the most favorable scenario, early ATC generates an average net saving of €198,000 per patient, and prevents 0.542 secondary infection. In the worst-case scenario, early ATC generates an average net saving of €32,000 per patient, and prevents 0.299 secondary infection. These results are robust to various adverse changes in key parameters and to a definition of late ATC as an access to care at a CD4 level of 200/mm^3. In addition to individual health benefits, improving ATC for migrants living with HIV proves efficient in terms of public health and economics. These results stress the benefit of ensuring early ATC for all individuals living with HIV in France.

Keywords HIV/AIDS · Migrant populations · France · Access to care · Public policy

JEL Classification I180 · I13

Introduction

In France, migrant populations are considered a risk group for HIV (human immunodeficiency virus). In 2010, 34,500 migrants were considered to be infected with HIV [1]. Migrants account for a large share of the total population living with HIV in France. According to the VESPA 2 (VIH Enquête Sur les Personnes Atteintes) survey conducted in 2011, one-third of people living with HIV (PLHIV) under care in France could be considered as migrants [2]. Moreover, even if the share of new HIV diagnosis among migrants decreased between 2003 and 2007, migrants still accounted for nearly half (46%) of new HIV discoveries in 2013 [3]. The HIV epidemic among migrants in France is heavily concentrated among migrants from sub-Saharan Africa, who accounted for more than three-quarters of the migrants diagnosed with HIV in France in 2011 [2]. Furthermore, 67% of new HIV diagnosis among migrants involved migrants from sub-Saharan Africa in 2013 [3]. Migrant populations are characterized by a significant delay in screening. In the literature, late presenters are defined as HIV-infected people diagnosed

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with a CD4 cell count[1] below 350/mm^3 (below 200/mm^3 for advanced disease presenters). According to the French Hospital Database on HIV (FHDH), almost 50% of migrants diagnosed in France in 2011 were late presenters. Moreover, in 2013, 39% of newly diagnosed male migrants could be classified as advanced disease presenters compared to 25% of all newly diagnosed patients and 17% of newly diagnosed men who have sex with men (MSM) [3]. To sum up, the HIV epidemic is active among migrants in France and the migrant population is characterized by a delayed access to diagnosis and care.

Inequalities of health related to citizenship or migration status have been documented in France [4]. Several studies report barriers to HIV testing among migrants in France. Massari et al. [5] use data including 3023 households representative of the Paris metropolitan area in 2005 to investigate the link between migration origin and HIV testing. The authors show that foreigners or French men with at least one foreign parent were more likely never to have been tested for HIV compared to men with two French parents. In 2005, INPES (Institut National de Prévention et d'Education à la Santé) conducted a KABP (Knowledge Attitudes Beliefs and Practices) survey among 1874 sub-Saharan migrants living in the Paris metropolitan area [6]. In this study, undocumented migrants or migrants with a temporary residence permit had 50% lower odds of having ever been tested for HIV compared to French people of sub-Saharan origin. Structural barriers to HIV testing linked to a restricted access to testing and care have also been reported for migrants in the UK, the Netherlands, the USA, Canada, and Spain [7, 8].

The legal framework regulating access to care (ATC) of migrants is a critical factor for early HIV diagnosis in this population. In France, only legal migrants have access to the standard health insurance system, which guarantees full health coverage for HIV patients. Nevertheless, since 1998 France has set up specific legal provisions and social benefits aimed at providing access to medical care for migrants living illegally in the territory. On the one hand, a regular residence permit may be granted under certain conditions to severe ill non-nationals whose health condition requires medical care that they could not receive in their country of origin. On the other hand, non-nationals without a legal residence permit but who can prove a residency in France for more than 3 months may benefit from a means-tested program called Aide Médicale d'État ("State Medical Aid", AME). AME allows for free access to medical care for these migrants. For undocumented migrants who just arrived in France, the "urgent care" (soins urgents) scheme allows hospitals to be reimbursed for health care provided to them. As long as their administrative status is not stabilized, migrants move between these different coverage schemes. This might deteriorate their ATC and the continuity of health care received. Moreover, even if the different coverage schemes should guarantee universal ATC, obstacles to initial access to the health system for illegal migrants remain [9]. Indeed, by relying on multiple schemes, the system is hampered by its administrative complexity and results in lack of accessibility and reliability for the users. This lack of accessibility is especially relevant for the increased flow of refugees and immigrants who arrived in France since 2015, as these migrants suffer from highly precarious administrative status.

Existing literature has pointed out the ethical issues related to inequalities of ATC, including sexual and reproductive healthcare services, for migrants living in France and in Europe [10, 11]. For HIV-infected migrants, the literature has also underlined the individual health benefits that could occur from earlier access to HIV testing and HIV medical care [5–7]. However, available studies have not investigated the consequences of delayed ATC for migrant PLHIV on public health and healthcare costs. Only one study has discussed the public health and economic consequences that could result from a restricted ATC for migrant PLHIV in Spain [12]. In this article, the Spanish Expert Committee of the AIDS (Acquired Immune Deficiency Syndrome) Study Group argues that a delayed ATC is likely to increase the number of HIV infections and to raise long-term healthcare costs in Spain. However, no in-depth analysis of the consequences of delayed ATC for HIV-infected migrants is undertaken in this article. Our objective is to investigate the public health and economic consequences associated with a delayed ATC for migrants living with HIV in France. Measuring the public health and economic consequences of delayed ATC for HIV-infected migrants is important in order to inform public health authorities. Indeed, if delayed ATC for HIV-infected migrants has negative epidemiological effects as well as negative economic impacts, it would reinforce, beyond ethical concerns, the need to adopt specific public policies aiming to favor early ATC for migrants. We use a simple static model that compares the lifetime costs and averted infections of two ATC strategies for migrant PLHIV in France: an early and a late ATC that are defined by an entry into care with a CD4 cell count of 350 and 100/mm^3, respectively. Given evidence on the preventive effect of antiretroviral (ARV) treatments[2] [13], our model integrates

[1] CD4 cells are a type of white blood cell that fights infection. CD4 count helps tell how strong the immune system is, indicates the stage of the HIV disease, guides treatment, and predicts how the disease may progress. Keeping the CD4 count high reduces complications of HIV disease and extend life expectancy of patients.

[2] Antiretroviral treatments are used to delay progression of the disease and death for HIV-positive patients.

the positive externality of ARV treatments on the prevention of secondary infections. Indeed, taking into account the avoidance of secondary infections is likely to significantly alter the cost-effectiveness of the two studied strategies. The results of our analysis provide evidence on the negative economic and public health impacts of delayed ATC for migrant PLHIV in France. Further research should investigate the effectiveness and cost-effectiveness of specific interventions aiming at increasing ATC in this population.

Methods

This study was commissioned by the French National AIDS Council within the broader work it conducted on the French policy on ATC for illegal immigrants [9]. The objective of our study is to investigate the public health and economic consequences of the observed delayed ATC among migrant PLHIV in France. Therefore, the study does not analyze the cost-effectiveness of a specific intervention that aims to improve ATC among migrants. Our study rather compares the lifetime costs and averted infections of two situations regarding access to healthcare for migrant PLHIV in France: an early and a late ATC that are defined by an entry into care with a CD4 cell count of 350 and 100/mm^3, respectively. Given the fragility of basic epidemiological data on the HIV epidemic among migrants in France, as well the scarcity of behavioral and socio-demographic data for HIV-infected migrants, we use a simple static and deterministic model rather than a Markov-type, a compartment or an agent-based model. We focus on averted infections instead of Quality-Adjusted Life Years (QALYs) to measure health outcomes since averted infections are commonly used as a health outcome in studies related to HIV. In particular, several major studies that investigated the preventive effect of ARV treatments, either at the individual [14] or population level [15], used averted infections or decreases in HIV incidence as the main health outcomes. Averted HIV infections and reduced HIV incidence have also been used as health outcomes in several cost-effectiveness analyses of ARV treatments as prevention [16]. Moreover, measuring health outcomes by QALYs would require making additional (uncertain) hypotheses, as we lack data on mean age at HIV infection and diagnosis among migrants in France. Nevertheless, we provide a rough calculation of QALYs saved by early ATC compared to late ATC in "Appendix B".

Our analysis faces two main difficulties. The first difficulty is the lack of harmonization regarding the definition of the migrant population. Among the various epidemiological sources available, only the data from the VESPA 2 survey strictly distinguish migrant people as persons born in a foreign country as foreign nationals. Other data sources, for various technical and/or legal reasons, do not allow this accuracy. For example, analyses of InVS (Institut de Veille Sanitaire), based in part on the mandatory reporting of HIV, use the criterion of birth place to define a migrant. Given these divergent definitions, we will use the generic term of migrant in this study with an awareness of the limitations related to the lack of consistency in the definition of this population. The second difficulty relates to the size of the hidden HIV epidemic among migrants in France. Existing estimates for hidden prevalence and incidence among this population are obtained through back-calculation. These estimates are marked with uncertainty and raise specific questions in the migrant population where a significant part of infections is imported from home countries of migrants. Therefore we have to correct these estimates in order to take into account the diversity in the place of HIV infection among migrants.

Modeling of strategies

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/mm^3, whereas late ATC is defined as entry into care at time t_2 with a CD4 cell count of 100/mm^3. The average number of secondary infections caused by a person infected with HIV throughout 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 $\overline{r_0}$ 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.

Secondary infections

One key parameter in our analysis is α, the reduction factor for the number of secondary infections once diagnosed and on treatment, 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 secondary infections, we have $\alpha < 1$.

Life expectancy is affected by the timing of treatment initiation: we denote by T_1 the value of T (the remaining life expectancy after infection) 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:

$$R_0 = \overline{r_0} + \sum_{t=2}^{t_1} \underline{r_0} + \sum_{t_1+1}^{T_1} \alpha \underline{r_0}. \quad (1)$$

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

$$\begin{aligned} R_0^2 - R_0^1 &= \overline{r_0} + (t_2 - 1)\underline{r_0} + \alpha(T_2 - t_2)\underline{r_0} \\ &\quad - [\overline{r_0} + (t_1 - 1)\underline{r_0} + \alpha(T_1 - t_1)\underline{r_0}] \\ &= \underline{r_0}[(1 - \alpha)(t_2 - t_1) - \alpha(T_1 - T_2)]. \end{aligned} \quad (2)$$

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:

Costs

For each situation regarding access to care, we compute TC_i, the total treatment costs under access to care $i = 1$ (early ATC) or $i = 2$ (late ATC). 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 ATC is cost-saving if $TC_1 < TC_2$, i.e., if:

$$\begin{aligned} (C_1 - C_2) &< C_1(R_0^1 - R_0^2) \\ &< C_1\underline{r_0}[(1 - \alpha)(t_2 - t_1)] - \alpha(T_1 - T_2)]. \end{aligned} \quad (3)$$

The cost-saving potential of early ATC 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.

Parameter values

Treatment timing and cost parameters

Existing literature on treatment timing and costs in the era of ARV treatments provides confident values for these parameters, which allows us to build a central scenario. The impact of these parameter values on final results will be tested in the sensitivity analysis.

Annual costs of care for early and late-treated patients are estimated by Sloan et al. [17] who simulate the evolution of two cohorts of French patients based on their CD4 level at treatment initiation. Patients enter care with a mean CD4 cell count of 372/mm^3 in the first cohort and 97/mm^3 in the second cohort. A diagnosis at an average level of 97 CD4 cells/mm^3 appears as a pessimistic assumption for migrants in France. However, this hypothesis is not unrealistic given the large share of migrants diagnosed at a late or a very late stage of the disease. Moreover, aiming to treat migrants below a CD4 cell count of 350/mm^3 also seems more realistic than a very early treatment initiation at 500 CD4/mm^3. Indeed, late diagnosis and treatment for migrants in France is partly related to the duration of infection prior to migration. For both cohorts, patients present the same medical and demographic characteristics as new patients diagnosed with HIV in France in 2005 (mean age of 38 at diagnosis and 62% of men).

Data on costs of care adopt a healthcare payer perspective and are, except for ARV treatment and HIV monitoring, stratified by disease stages for both cohorts.

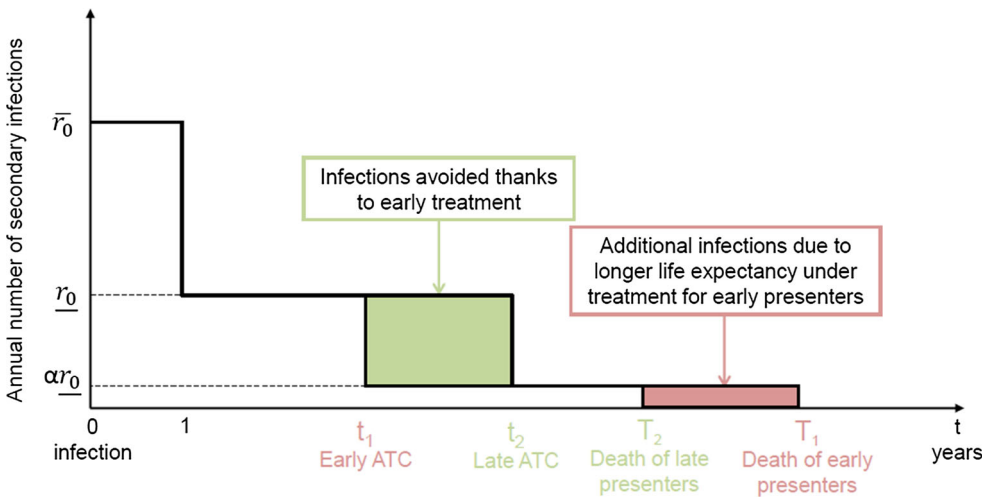

Fig. 1 Comparison of early and late ATC

Four disease stages are considered by the authors: chronic HIV with no history or current AIDS-defining disease (stage 1), occurrence of an acute AIDS-defining disease (stage 2), chronic HIV with a history of AIDS-defining disease (stage 3) and month before death (stage 4). For each of these stages, healthcare utilization is based on data collected from a cohort of 1775 patients treated in the hospital of Tourcoing between January 1998 and December 2005. Costs for each stage of the disease are obtained by multiplying resource utilizations per patient by their unit costs (obtained from different sources). Resource utilizations include inpatient hospitalizations and daycare visits, outpatient visits, laboratory tests, and clinical procedures as well as treatments for hepatitis B, hepatitis C, and metabolic abnormalities. Inpatient visit costs are calculated by assigning the 2004–2005 costs of the French "Echelle Nationale des Coûts" to each diagnosis-related group's inpatient stay. The unit cost of each diagnosis-related group's inpatient stay includes the costs of diagnosis, clinical procedures, laboratory tests, drugs dispensed, and hotel/overhead costs. Outpatient costs are measured using a microcosting approach and include physician fees, drugs, laboratory tests, and clinical procedures. Unit costs for laboratory tests and clinical procedure are drawn from the 2008 French "Nomenclature des Actes de Biologie Médicale" and the 2011 French "Classification Commune des Actes Médicaux", respectively, while drug costs are derived from the 2008 Tourcoing Hospital Pharmacy database and reflect costs throughout France. Antiretroviral drug and HIV monitoring test costs are included separately from stages' costs. The costs of ARV regimens range from €9120 per year for first-line ARV treatment to €30,840 per year for subsequent regimens. Unit costs of CD4 and viral load tests, which are performed every 3 months, are drawn from the 2008 "Nomenclature Générale des Actes Professionnels".

Based on their simulations Sloan et al. [17] calculate an average life expectancy of 26.5 years and an undiscounted lifetime cost of care of €535,000 (€320,700 discounted) for the first cohort of patients. For the second cohort of patients, life expectancy is 23.8 years and the undiscounted lifetime cost of care is €513,200 (€322,500 discounted). In this article, early treated patients only benefit from three additional years of life compared to patients treated later. However, studies available in the literature report higher gains in life expectancy for early treated patients. A study of the "Antiretroviral Therapy Cohort Collaboration" [18], based on 14 cohorts of patients in North America and Europe, found that life expectancy at 35 would be 27, 30, and 37 years, respectively, for patients initiating ARV treatment at a level of less than 100 CD4/mm^3, between 100 and 200 CD4/mm^3, and above 200 CD4/mm^3. Given a mean age at diagnosis of 38 in Sloan et al. [17], a life expectancy of 34 years for early treated patients is assumed. The lifetime cost of care for early treated patients then increases significantly. Extrapolating the results of Sloan et al. [17], the undiscounted lifetime cost of care for early treated patients reaches €686,426 (€411,464 discounted) if life expectancy under treatment is 34 years.

Lodi et al. [19] estimate the median time between seroconversion and CD4 cell counts of 200, 350, and 500/mm^3 from the CASCADE data gathering 25 patient's cohorts in Europe, Australia, Canada, and sub-Saharan Africa. The authors estimate a median of 4.19 and 7.93 years, respectively, between seroconversion and levels of CD4 less than 350 and 200/mm^3. We therefore assume that early and late treatments start 4 and 9 years after infection.

Value of α

Existing literature does not provide a reference value for α, the reduction factor for the number of secondary infections once diagnosed and on treatment. Based on available information, we therefore derive plausible values for α allowing us to simulate different scenarios. The value of α depends on both the reduction of infectivity under treatment and the evolution of preventive behaviors once patients are diagnosed.

Reduction of infectivity under treatment

In 2012, the results of the HPTN (HIV Prevention Trials Network) 052 trial showed a 96% reduction in new transmissions among HIV-discordant couples when the infected partner was on treatment, albeit in a trial where conditions of care and adherence's monitoring were optimal [20]. Observational cohort studies may allow us to get a better approximation for the decline of infectivity under treatment in real-life conditions. Three recent meta-analyses provide results of 92, 91, and 64%, respectively [21–23]. However, the unfavorable result of 64% obtained in the last study can be explained by the inclusion of three studies that took place in China [24], Uganda [25], and Rwanda/Zambia [26], where conditions of care are less favorable than in France and the share of patients experiencing treatment failure much higher.

In France, once HIV-infected migrants are diagnosed and treated, they benefit from efficient antiretroviral treatments and monitoring. Thanks to the frequent monitoring of viral load and the availability of a full range of effective ARV drug combinations, very few patients, even within the migrant population, experience treatment failure in France. As a matter of fact, results of the VESPA 2 survey show that very high levels of virological suppression are obtained in France among migrants once they are treated,

since 94.7% of them have a viral load <400 copies/ml. We therefore think that a reasonable scenario is to assume a 90% reduction in infectivity for migrants under treatment in France.

Evolution of preventive behaviors after diagnosis

Two scenarios for the evolution of preventive behaviors after diagnosis are explored. In a meta-analysis of 11 American studies, Marks et al. [27] find a 53% reduction in the likelihood of having unprotected sex among PLHIV diagnosed compared to those unaware of their HIV status. Therefore, the optimistic scenario assumes a favorable change in preventive behaviors with a 53% decline in the share of unprotected sex acts after diagnosis. In the pessimistic scenario, we assume no change in sexual behaviors following diagnosis.

In short, when sexual behaviors are unchanged, the reduction factor for the number of secondary infections once diagnosed, 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.

Value of $\underline{r_0}$

Existing literature does not provide a reference value for the average number of secondary infections per undiagnosed migrant each year, $\underline{r_0}$. Based on available information we therefore derive plausible values for $\underline{r_0}$ allowing us to simulate different scenarios. In a given year, the value of $\underline{r_0}$ is equal to:

$$\underline{r_0} = \frac{\text{Number of infections caused by undiagnosed migrants in France}}{\text{Number of undiagnosed migrants present in France}}$$

The calculation of value of $\underline{r_0}$ is problematic, as two sources of inaccuracy can be identified. First, incidence should only consider migrants actually infected in France. Assuming that all infections among migrants occur after arrival in France would bias the value of $\underline{r_0}$. Second, the HIV epidemic among migrants in France is not isolated from the epidemic among French nationals. Not taking into account contaminations from migrants to French heterosexuals would also would bias the value of $\underline{r_0}$. As there are no data available to clearly quantify transmissions between migrants and French heterosexuals, we cannot introduce cross-populations HIV transmissions in the calculation of $\underline{r_0}$. We therefore approximate $\underline{r_0}$ 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.

Three types of data are required to calculate the average number of secondary infections per undiagnosed migrant each year, $\underline{r_0}$: 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 reporting of HIV cases. Such estimations raise specific difficulties in the migrant population where a share of infections is imported from home countries of migrants. Thus, we adjust existing estimates for this bias by using available data from the VESPA 2 and ANRS PARCOURS surveys.

Number of new infections among migrants in France each year

Ndawinz et al. [28] estimated that 2469 new transmissions occurred among migrants in France in 2007. However, a significant share of these new infections may have occurred in the birth country of the migrants. Using the ANRS PARCOURS data, Desgrees du Lou et al. [29] estimate the place of HIV infection among respondents by using a method combining life-events and CD4 cell counts data. They find that 49% of migrants from sub-Saharan Africa would have been infected with HIV in France. Assuming a relative stability in incidence for the migrant category since 2007, and given the share of infections in France (49%), the number of new infections among migrants in France each year is estimated to be 1210.

Number of undiagnosed HIV-positive migrants in France

In 2010, 25,000 diagnosed and 9500 undiagnosed migrants were living in France [1]. 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, these estimates might include by anticipation migrants infected in their home country but not yet arrived in France. 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 discussions, we consider that the first group represents 49% of undiagnosed migrants; that is to say 4655 undiagnosed migrants infected in France. Groups 2 and 3 should therefore be constituted by 51% of the 9500 undiagnosed migrants (4845 migrants). The distribution of migrants between these two categories will depend on 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 VESPA 2 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 calculations based on these data, we estimate 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. Details on estimations based on the VESPA 2 data are available in "Appendix A". If we use these estimates as a proxy for the distribution between groups 2 and 3, we can consider that 23.43–47.24% of the 4845 undiagnosed migrants infected abroad are actually in France (1135–2289 migrants infected abroad but already in France). Summing up these estimates to the number of migrants infected in France, there would be between 5790 and 6944 undiagnosed HIV-positive migrants on the French territory.

In an attempt to estimate the place of infection among heterosexual adults born abroad and diagnosed with HIV in the UK between 2004 and 2010, Rice et al. [30] used a similar method to estimate the probable year of infection for migrants. They also estimate the likely year of infection based on the CD4 cell count of migrants at diagnosis. Unlike us, however, they calculate the year of infection based on the rate of CD4 cell count decline before treatment initiation. We could not use this method, as we did not have data on several CD4 cell count measurements prior to the start of antiretroviral treatment.

Share of HIV infections attributable to undiagnosed HIV migrants

Marks et al. [31] developed a calculation method to estimate the share of HIV infections attributable to undiagnosed HIV-infected individuals in the USA. This formula reflects the relative contribution of diagnosed and undiagnosed HIV-infected individuals to sexually transmitted new HIV infections. We adapt this calculation method to the population of migrants in France. The share of HIV infections attributable to undiagnosed HIV migrants can be calculated using the following formula:

$$T_u = \frac{(UN_u \mathrm{SP}_u)}{(UN_u \mathrm{SP}_u) + (bUN_a \mathrm{SP}_a)((1-T)+\varepsilon T)}, \quad (4)$$

where N_a is the number of diagnosed migrants, N_u the number of undiagnosed migrants, SP_a the mean number of sexual contacts of diagnosed migrants per year, SP_u the mean number of sexual contact of undiagnosed migrants per year, U the share of undiagnosed HIV-infected migrants engaging in unprotected sex, b a parameter accounting for the reduction in unprotected sex following HIV diagnosis, T the share of diagnosed migrants under ARV treatment, and ε a parameter that stands for the decrease in infectivity following ARV treatment initiation.

Given previous discussions, N_a is set at 25,000, N_u is set between 5790 and 6944 and ε is set at 0.1. We assume that 70.4% of diagnosed migrants are under ARV treatment such that T is equal to 0.704 [32]. We suppose that the number of sex partners is unchanged after diagnosis such that $\frac{SP_u}{SP_a} = 1$. Finally, as said above for the value of α, two scenarios are considered for the evolution of risk behaviors following the HIV diagnosis leading to two possible values of b (1 or 0.47).

Table 1 summarizes possible values for the share of HIV infections attributable to undiagnosed HIV migrants:

Table 1 Share of HIV infections attributable to undiagnosed HIV migrants

	Preventive behaviors	
Number of undiagnosed migrants (N_u)	53% reduction in unprotected sex acts ($b = 0.47$)	No change in unprotected sex acts ($b = 1$)
5790	57.35%	38.73%
6944	61.73%	43.12%

When no change in sexual behaviors after diagnosis is considered, the share of HIV transmission caused by undiagnosed migrants ranges from 38.73 to 43.12%. The share of transmissions caused by undiagnosed migrants reaches 57.35–61.73% if we integrate a 53% decrease in unprotected sex after diagnosis.

If we consider that 5790 undiagnosed migrants live in France and that these migrants are responsible for 38.73–57.35% of the 1210 new infections each year, we obtain a value of $\underline{r_0}$ ranging between 0.0809 and 0.1199. If we instead assume that 6944 undiagnosed HIV-positive migrants live in France, and that these migrants are responsible for 43.12–61.73% of the 1210 new infections each year, we obtain a value of $\underline{r_0}$ between 0.0751 and 0.1076.

Table 2 summarizes the possible values for the average number of secondary infections per undiagnosed migrant each year ($\underline{r_0}$) depending on the hypotheses on the size of hidden epidemic among migrants and the evolution of risk behaviors following diagnosis:

The highest value of $\underline{r_0}$ (0.1199) is obtained for a low hidden epidemic among migrants and when risk behaviors decrease among treated migrants. Indeed, in this situation,

Table 2 HIV epidemic among undiagnosed migrants in France

	Value of $\underline{r_0}$: Average number of secondary infections per undiagnosed migrant each year	
	Number of undiagnosed migrants (N_u): 5790	Number of undiagnosed migrants (N_u): 6944
53% reduction in unprotected sex acts ($b = 0.47$)	0.1199	0.1076
No change in unprotected sex acts ($b = 1$)	0.0809	0.0751

a low number of undiagnosed migrants will be responsible for a large share of new infections, making the HIV epidemic highly active among undiagnosed migrants. On the contrary, the lowest value of $\underline{r_0}$ (0.0751) is obtained for a high hidden epidemic among migrants and when risk behaviors are not affected after diagnosis of HIV. In this case, a high number of undiagnosed migrants are responsible for a low share of new HIV infections so that the HIV epidemic is less active among undiagnosed migrants.

Parameter values and uncertainty

Table 3 summarizes the model's hypotheses and parameter values:

Given the uncertainty surrounding parameter values, sensitivity analyses will be conducted to test how results change following adverse changes in treatment timing, death dates, and cost parameters. The first sensitivity analysis assumes that the treatment delay for late presenters (t_2–t_1) is reduced from 5 to 4 years ($t_2 = 8$). The second sensitivity analysis assumes that residual life expectancy for early presenters (T_1–t_1) increases from 34 to 36 years (leading to an increase in C_1 to €726,804) and the third that residual life expectancy for late presenters (T_2–t_2) decreases from 23.8 to 22 years (leading to a decrease in C_2 to €474,386). The fourth sensitivity analysis uses discounted values of lifelong costs of care instead of undiscounted ones. As lifelong costs of care are very uncertain, the fifth set of simulations run sensitivity analyses on the values of these costs. We first simulate changes in the lifelong costs of care for early and late presenters (C_1 and C_2) that do not modify the relative value of these costs: we simulate 10/30% increases and decreases in both lifelong costs of care. Then, we simulate the most unfavorable case where the relative value of the lifelong cost of care of early presenters increases compared to that of late presenters. More precisely, we simulate a 10% increase in the lifelong cost of care of early presenters and a 10% decrease in the lifelong cost of care of late presenters. Such an evolution might be seen if the relative cost of ARV treatments increases compared to the costs of hospitalizations, outpatient visits, or opportunistic diseases' treatments, which are more common among late presenters. The next type of sensitivity analysis assumes that the benefit of preventing a secondary infection is reduced to C_2 instead of C_1. The last simulation investigates the case where late presenters start treatment at a CD4 cell count of 200/mm^3 instead of 100/mm^3.

Results

Four scenarios are considered in the analysis depending on the hypotheses on the size of the hidden epidemics and the evolution of preventive behaviors following diagnosis. Table 4 summarizes the results of scenarios analysis.

Results show that early treatment for HIV-infected migrants in France dominates late treatment in all scenarios, whatever the assumptions made on the number of undiagnosed migrants in France or the evolution of preventive behaviors after diagnosis. In the most favorable

Table 3 Summary of the model's hypotheses and parameter values

Parameter	Definition	Value	Reference
C_1 (€)	Lifelong cost of care for early presenters	686,426	[17, 18]
C_2 (€)	Lifelong cost of care for late presenters	523,200	[17]
t_1 (years)	Treatment start date for early presenters	4	[19]
t_2 (years)	Treatment start date for late presenters	9	[19]
T_1 (years)	Death date for early presenters	38	[18]
T_2 (years)	Death date for late presenters	32.8	[18]
α	Reduction factor for the number of secondary infections once diagnosed and on treatment	0.047–0.1	[21–23, 27]
$\underline{r_0}$	Average number of secondary infections per undiagnosed migrant each year	0.0751–0.1199	Author's calculation based on [28, 29, 31, 32]

Table 4 Results of scenarios analysis

Evolution of preventive behaviors after diagnosis	53% reduction in unprotected sex acts ($b = 0.47$)		No change in unprotected sex acts ($b = 1$)	
Number of undiagnosed migrants (N_u)	5790	6944	5790	6944
	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Average number of secondary infections per undiagnosed migrant each year: r_0	0.1199	0.1076	0.0809	0.0751
Reduction factor of secondary infections after HIV diagnosis: α	0.047	0.047	0.1	0.1
Net cost of early ATC (€)	−198,831	−160,663	−47,791	−31,945
Averted infections for early ATC	0.5420	0.4864	0.3220	0.2989
Cost per averted infection for early ATC (€)	Early ATC dominant	Early ATC dominant	Early ATC dominant	Early ATC dominant

Table 5 Results of sensitivity analysis

	Cost per averted infection for early ATC in €			
	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Reduced treatment delay between early and late presenters: t_2–$t_1 = 4$ ($t_2 = 8$)	Early ATC dominant	Early ATC dominant	8781	62,474
Increased life expectancy for early presenters: T_1–$t_1 = 36$ ($C_1 =$ €726,804)	Early ATC dominant	Early ATC dominant	Early ATC dominant	25,646
Reduced life expectancy for late presenters: T_2–$t_2 = 22$ ($C_2 =$ €474,386)	Early ATC dominant	Early ATC dominant	3311	56,580
Discounted values of lifelong costs of care	Early ATC dominant	Early ATC dominant	Early ATC dominant	Early ATC dominant
10% increase in lifelong costs of care for early and late presenters	Early ATC dominant	Early ATC dominant	Early ATC dominant	Early ATC dominant
30% increase in lifelong costs of care for early and late presenters	Early ATC dominant	Early ATC dominant	Early ATC dominant	Early ATC dominant
10% decrease in lifelong costs of care for early and late presenters	Early ATC dominant	Early ATC dominant	Early ATC dominant	Early ATC dominant
30% decrease in lifelong costs of care for early and late presenters	Early ATC dominant	Early ATC dominant	Early ATC dominant	Early ATC dominant
10% increase in lifelong cost of care for early presenters (C_1) 10% decrease in lifelong cost of care for late presenters (C_2)	Early ATC dominant	Early ATC dominant	155,507	225,831
Infection averted valued at lifelong cost of care for late treated patients (C_2) instead of lifelong cost of care for late treated patients (C_1)	Early ATC dominant	Early ATC dominant	24,799	66,349
Late ATC at 200/mm^3 CD4 cell count instead of 100/mm^3 CD4 cell count	Early ATC dominant	Early ATC dominant	Early ATC dominant	Early ATC dominant

case (scenario 1), early ATC generates an average net saving of €198,831 per patient and prevents 0.542 secondary infection. In scenario 2, the early ATC allows an average saving of €160,663 while avoiding 0.486 secondary infection. When no change in risk behaviors is assumed after diagnosis, early ATC remains dominant. In the worst-case scenario (scenario 4), early ATC still generates an average net saving of €31,945 per patient and prevents 0.299 secondary infection. In scenario 3, the early ATC saves an average of €47,791 while avoiding 0.322 secondary infection.

Table 5 presents the costs per averted infection for early ATC resulting from adverse changes in key parameters:

Early ATC remains dominant in scenarios 1 and 2 for all adverse changes in key parameters. Thus, early ATC is always dominant when risk behaviors decrease after diagnosis. Under scenario 3, early ATC remains dominant when the life expectancy of early presenters increases from 34 to 36 years, when the discounted values of lifelong costs of care are used and when proportional increases or decreases in the lifelong costs of care for early and late presenters are considered. Facing other adverse changes in

key parameters, the early ATC in scenario 3 generates a net cost per infection averted that ranges from €3311, when life expectancy of late presenters decreases, to €24,799 when averted infections are valued at C_2 and €155,507 when we consider 10% increase and 10% decrease in the lifelong costs of care for early and late presenters, respectively. Under scenario 4, the early ATC remains dominant when discounted values of lifelong costs of care are used and when we consider proportional increases or decreases in the lifelong costs of care for early and late presenters. However, it becomes more expensive than late ATC in the other situations. In scenario 4, the cost per averted infection ranges from €25,000 when life expectancy for early presenters increases from 34 to 36 years, to €66,000 when averted infections are valued at C_2 and €226,000 if the lifelong costs of care for early and late presenters are increased and decreased by 10%, respectively.

Among sensitivity analyses on parameter values, the highest costs per averted infection are obtained in the case where the gap between the lifelong costs of care of early and late presenters increases. This might happen if the cost of ARV treatments becomes relatively higher compared to the costs of hospitalizations, outpatient visits, and opportunistic infections' management. However, we have no reason to believe that such cost evolution was seen in France in recent years. In "Appendix B" we calculate, for all cases where early ATC is more expensive than late ATC, the cost per QALY of early ATC. We take into account QALYs saved for early presenters compared to late presenters and QALYs saved from averted infections. In the worst-case scenario (scenario 4 with 10% increase in the lifelong cost of care for early presenters and 10% decrease in the lifelong cost of care for late presenters), early ATC would cost €7593/QALY, which is far below usually accepted cost-effectiveness thresholds [33].

In the last sensitivity analysis, we test whether early treatment for migrant PLHIV in France remains dominant if a lower delay in treatment is considered. We therefore define late treatment as an entry into care at a CD4 level of 200/mm^3 against 100/mm^3 in the main analysis. No information is available regarding the lifetime cost of care for patients initiating treatment at a CD4 level of 200/mm^3 in France. Instead, we approximate this cost by multiplying the average annual cost of care for patients initiating treatment at a CD4 level of 350/mm^3 (€20,189) and the life expectancy of patients who initiate treatment at a CD4 level of 200/mm^3. According to a study of the "Antiretroviral Therapy Cohort Collaboration", life expectancy at age 35 is 30 years for patients initiating ARV treatment at a CD4 count level ranging between 100 and 200/mm^3 [18]. If we consider a life expectancy of 27 years for patients initiating treatment at a CD4 level of 200/mm^3 (as the average age at treatment initiation is 38 in the cohort whose cost data are derived from), and given the mean annual cost of care, the total lifetime cost of care for patients initiating treatment at a CD4 level of 200/mm^3 is set to €545,103. Based on data of Lodi et al. [19], we consider a time delay of 3.74 years between early and late entry into care in this case. When late presenters start treatment at a CD4 cell count of 200/mm^3 instead of 100/mm^3, the main results are maintained since the early ATC is dominant in all scenarios.

Discussion

Several studies have pointed out the ethical issues and individual health losses related to late ATC for migrant PLHIV in France and other high-income countries [5–7, 10, 11]. However, no study, either in France or in other developed countries, has investigated the public health and economic consequences of this late ATC. We use a simple static and deterministic model to investigate the economic and public health consequences associated with delayed ATC for migrants living with HIV in France. Our results show that beyond the individual health benefit for infected migrants, reducing the time between HIV infection, screening, and treatment for HIV-positive migrants would prevent secondary infections and thus allow for a better control of the HIV epidemic. Moreover, on top of the public health benefit, earlier diagnosis and treatment for HIV-positive migrants is also desirable from an economic point of view. Indeed, 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 early ATC can offset this extra cost by avoiding future expenditures. Our results are robust to various changes in parameter values. Early ATC remains dominant when late treatment is defined as an entry into care at a CD4 level of 200/mm^3. When more pessimistic values for key model parameters are assumed, early ATC remains dominant in the scenarios involving a decrease of risk behaviors among HIV-infected migrants after diagnosis. In the scenarios that assume a stability of risk behaviors after diagnosis, early ATC remains at least cost-effective following adverse changes in key model parameters.

Our study is specific to France. However, our analysis could easily be adapted to other developed countries where data on HIV lifelong costs of care as well as data on the HIV epidemic among migrants are available. Results of scenario analysis, that considers different values for the average number of secondary infections per undiagnosed migrant each year, show that early ATC for HIV-infected migrants might be dominant even in countries where the

HIV epidemic is less active among undiagnosed migrants. Moreover, results of sensitivity analyses on costs demonstrate that early ATC remains dominant even following large proportional variations in the lifelong costs of care for early and late presenters. Therefore, early ATC for migrant PLHIV might be dominant even in countries where costs of care are lower of higher than in France. However, early ATC might cost more than late ATC in countries where the structure of HIV care costs is different than in France. This is especially the case for countries where the costs of ARV treatments and monitoring is relatively higher compared to the costs of inpatient and outpatient visits.

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 secondary infections. Therefore, the results from the static model tend to underestimate both the number of infections averted and the savings due to earlier treatment of HIV-positive migrants. Despite this limitation, we find that early ATC for migrants living with HIV in France is dominant. Despite the limitations of a static model, it appears difficult to build a dynamic model characterizing the HIV epidemic among migrants in France because of the significant lack of data on this risk group. Indeed, there is very few retrospective epidemiological data on prevalence and incidence for migrants in France. In addition, there are significant uncertainties about the dynamics of infections among migrants in France and contacts in France between migrants and French nationals.

Late ATC for HIV-infected migrants has negative public health and economic consequences. Earlier treatment initiation for migrant PLHIV should be promoted. Then, interventions that favor greater and earlier use of HIV screening by migrants should be adopted. In France, the harmonization of health care provision systems for migrants, which is costless, could constitute such type of intervention. Beyond legally facilitating ATC, further strategies could be adopted to increase HIV testing among migrants. Outreach street-based HIV rapid testing programs have been shown to be effective in reaching vulnerable populations, including migrants [34]. This screening strategy should therefore be developed for migrant populations. The deployment of community health mediators, who act as a prevention relay in migrant's communities, could also favor HIV testing in this population [35]. Fear of stigmatization and confidentiality breach are often cited by migrants as barriers to HIV testing [7, 8]. In this context, HIV self-test kits might also constitute an instrument to increase HIV testing among migrants.

Conclusions

We aimed to measure the economic and public health consequences of delayed ATC for migrants living with HIV in France. We use a simple model that compares the lifetime costs and averted infections of early vs. late ATC for migrants living with HIV in France where early and late ATC are defined by an entry into care with a CD4 cell count of 350 and 100/mm^3, respectively. We show that early treatment for all HIV-infected migrants in France would allow for a better control of the HIV epidemic on the territory by reducing HIV incidence. Moreover, early ATC for all HIV-infected migrants would also allow for a long-term reduction in HIV healthcare costs. Our results hold true, even following adverse changes in treatment timing and cost parameters, if risk behaviors of HIV-infected migrants decrease after diagnosis. When preventive behaviors do not change after HIV diagnosis, early ATC becomes more expensive than late ATC in the long run if we consider a smaller treatment delay for late presenters, a higher life expectancy for early presenter, a lower life expectancy for late presenter or a relative increase in the cost of care for early presenters compared to late presenters. However, even in these cases, our analyses show that early ATC is at least cost-effective.

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Compliance with ethical standards

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Appendix A: share of undiagnosed time spent in France for migrants infected abroad

The calculation of the share of the total undiagnosed time spent in France and in the countries of origin for migrants infected abroad was realized on data extracted from the VESPA2 survey. This survey was conducted in 2011 by researchers from INSERM (Unités 912, SESSTIM,

Marseille et 1018, CESP Villejuif) with the financial support of Agence Nationle de Recherche sur le Sida et les hépatites virales (ANRS). The access to VESPA2 data necessary to this estimation was possible thanks to the help of the Centre de Recherche en Epidémiologie et Santé des Populations (CESP). We are grateful to members of CESP ant to her head of department, France Lert, for allowing us to access these data.

The share of total time undiagnosed spent in France and in the country of origin for migrants infected abroad is calculated to be used as a proxy to determine the share of infected migrants infected abroad but already in France. For this calculation, the following data are used for migrants declaring contamination in their country of origin: date of arrival in France, date of diagnosis, date of first available medical examination related to HIV and CD4 level at this first examination. Several computational steps were performed to obtain the share of total time undiagnosed spent in France for migrants infected abroad from the VESPA2 data.

1 Calculation of the duration of infection at the time of initial medical examination.
Data from Lodi et al. [19] on time from seroconversion to different levels of CD4 cell count are used to estimate the duration of infection at first medical examination. Based on these data, the estimated duration of infection at first medical examination is assumed to be, less than or equal to 4 years if the CD4 cell count is above 350/mm^3 between 4 and 8 years if the number of CD4 is between 200 and 350/mm^3 and greater than or equal to 8 years if the CD4 cell count at examination is less than 200/mm^3. Regarding the latter, an upper bound for the duration of infection is set to twelve years. Indeed, after 12 years of untreated infection patients are assumed to be diagnosed because of symptoms related to the entry into the AIDS stage.
2 Calculation of the year of infection.
The probable year of infection is calculated as the difference between the year of the first medical examination and the probable duration of the infection since the first examination. If the estimated year of infection exceeds the year of arrival in France it is then considered that the year of infection is the same as the year of arrival in France.
3 Calculation of the total time spent undiagnosed, the time spent undiagnosed in France and the share of the total time undiagnosed spent in France.
The total time spent undiagnosed is calculated as the difference between the year of diagnosis and the estimated year of infection. The total time spent undiagnosed in France is calculated using the date of arrival in France and the estimate of the total time spent undiagnosed. It is assumed that, if the year of arrival in France is the same as the year of diagnosis and the year of infection, total time spent undiagnosed is equal to 1 year divided equally between the country of origin and France.
4 Calculation of the share of undiagnosed time spent in France.
The share of the total time spent undiagnosed in France is calculated by dividing the estimated time spent undiagnosed in France by the total time spent undiagnosed.

Appendix B: cost per QALY of early ATC

Compared to late ATC, QALYs saved thanks to early ATC can be divided in two categories, those saved for early treated patients compared to late-treated patients and those saved due to averted HIV infections.

1. QALYs saved for early treated patients compared to late treated patients.
In the main analysis, early and late patients have respective life expectancies of 24 and 34 after ATC. Moreover, early and late-treated patients start treatment 4 and 9 years after infection, respectively. Therefore, life expectancy from infection to death is 38 for early presenters and 33 years for late presenters. At the individual level, 5 years of life after HIV diagnosis are thus saved thanks to early ATC. In the UK, a recent study highlighted a 11% decrease in health-related quality of life (HRQoL) of HIV-infected patients under ARV treatment compared to that of the general population [36]. Thus, if we normalize to 1 the HRQoL of uninfected individuals, each year spent while being HIV-infected is worth 0.89 QALY. As a result, 4.5 (5×0.89) QALYs are saved thanks to prolonged life expectancy for early presenters.
When we consider that the life expectancy of early presenters after treatment initiation increases to 36 years or that the life expectancy of late presenters after treatment initiation decreases to 22 years, early presenters benefit from 7 extra years of life compared to late presenters and the number of QALYs saved for early treated patients compared to late treated patients increases to 6.2 (7×0.89).
2. QALYs saved for averted HIV infections.
In our model, early treated patients initiate treatment at age 38 (given cost data of Sloan al. [17] used) and have a residual life expectancy of 34 years after treatment initiation. Among the general population in France, residual life expectancy is 45 among people aged 38 (data from the Institut National d'Etudes

Table 6 Cost per QALY of early ATC

	QALY saved by early ATC		Additional cost of early ATC		Cost per QALY for early ATC in €	
	Scenario 3	Scenario 4	Scenario 3	Scenario 4	Scenario 3	Scenario 4
Reduced treatment delay between early and late presenters: t_2–$t_1 = 4$ ($t_2 = 8$)	8.16	7.90	2188	14,450	268	1829
Increased life expectancy for early presenters: T_1–$t_1 = 36$ ($C_1 =$ €726,804)	10.70	10.37	−8654	7280	Early ATC dominant	702
Reduced life expectancy for late presenters: T_2–$t_2 = 22$ ($C_2 =$ €474,386)	10.72	10.40	1019	16,148	95	1553
Value of infection averted = C_2 instead of C_1	9.23	8.89	7985	19,832	865	2231
10% increase in lifelong cost of care for early presenters (C_1)	9.23	8.89	50,070	67,500	5425	7593
10% decrease in lifelong cost of care for late presenters (C_2)						

Démographiques). Then, 11 years of life expectancy are won thanks to the avoidance of one secondary infection. If we normalize to 1 the HRQoL of uninfected individuals, 11 QALYs are lost due to shortened life expectancy in case of HIV infection. Besides reduced life expectancy, HIV-infected individuals also suffer from reduced HRQoL compared to non-infected individuals. During their residual life expectancy of 34, early treated patient experience an 11% decrease in HRQoL compared to non-infected individuals. Thus, around 3.7 QALYs (0.11×34) are lost due to decreased HRQoL in case of HIV infection. In total, the loss of 14.7 ($11 + 3.7$) QALYs is thus saved for one averted infection.

3. QALYs saved in early ATC compared to late ATC.
To obtain the total number of QALY saved thanks to early HIV treatment compared to late treatment we need to add QALYs saved for early treated patients compared to late treated patients and QALYs saved for one averted infection weighted by the number of averted infections in each scenario. Table 6 presents the results of sensitivity analyses as cost per QALY in the cases where early ATC is not dominant:

References

1. Supervie, V., Brouard, C.: Cascades et parcours de soins, analyse comparative VIH/VHC.: presented at the XVème congrès de la SFLS. http://invs.santepubliquefrance.fr/content/download/109012/388078/version/1/file/2014_Cascade_VIHVHC_SFLS.pdf (2014)
2. Lert, F., Annequin, M., Tron, L., Aubriere, C., Spire, B.: Situation socioéconomique des personnes vivant avec le VIH suivies a l'hôpital en France métropolitaine en 2011. Premiers résultats de l'enquête ANRS-Vespa2. Bull. Epidemiol. Hebd. **26–27**, 293–299 (2013)
3. Cazein, F., Pillonel, J., Le Strat, Y., Pinget, R., Le Vu, S., Brunet, S.: Découvertes de séropositivité VIH et de sida, France, 2003-2013. Bull Epidemiol Hebd. **9–10**, 152–161 (2015)
4. Jusot, F., Silva, J., Dourgnon, P., Sermet, C.: Inégalités de sante liées à l'immigration en France: effet des conditions de vie ou sélection à la migration? Revue économique **60**(2), 385 (2009)
5. Massari, V., Lapostolle, A., Cadot, E., Parizot, I., Dray-Spira, R., Chauvin, P.: Gender, socio-economic status, migration origin and neighbourhood of residence are barriers to HIV testing in the Paris metropolitan area. AIDS Care **23**(12), 1609–1618 (2011)
6. Lydie, N., Beltzer, N., Fenies, K., Halfen, S., Lert, F., and Le Vu, S.: Les populations africaines d'Ile-de-France face au VIH/sida. Connaissances, attitudes, croyances et comportements. Institut National de Prévention et d'Education à la Sante, Saint-Denis. http://inpes.santepubliquefrance.fr/Barometres/Etude_sida_migrants/pdf/synthese.pdf (2007)
7. Fakoya, I., Reynolds, R., Caswell, G., Shiripinda, I.: Barriers to HIV testing for migrant black Africans in Western Europe. HIV Med **9**(s2), 23–25 (2008)
8. Alvarez-del Arco, D., Monge, S., Azcoaga, A., Rio, I., Hernando, V., Gonzalez, C., Bolumar, F.: HIV testing and counselling for migrant populations living in high-income countries: a systematic review. Eur J Public Health **23**, 1039–1045 (2013)
9. Conseil National du Sida.: Avis sur la protection sociale des étrangers vivant avec le VIH en France et l'intérêt de son évolution vers le droit commun. http://cns.sante.fr/wpcontent/uploads/2015/2013-09-19_avi_fr_politique_publique.pdf (2013)
10. Carrera, S., & Merlino, M.: Undocumented immigrants and rights in the EU. Addressing the gap between social science research and policy-making in the Stockholm Programme? CEPS, Brussels. http://aei.pitt.edu/15103/1/Undocumented_Migrants__Ennstrom_Rpt__by_Carrera__Merlino_eversion.pdf (2009)
11. Keygnaert, I., Guieu, A., Ooms, G., Vettenburg, N., Temmerman, M., Roelens, K.: Sexual and reproductive health of migrants: does the EU care? Health Policy **114**(2), 215–225 (2014)
12. Pérez-Molina, J.A., Ortega, F.P., Comité de expertos del Grupo para el Estudio del Sida (GESIDA) de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC):

Evaluación del impacto del nuevo marco legal sanitario sobre los inmigrantes en situación irregular en España: el caso de la infección por el virus de la inmunodeficiencia humana. Enfermedades Infecciosas y Microbiología Clínica **30**(8), 472–478 (2012)
13. Cohen, M.S., McCauley, M., Gamble, T.R.: HIV treatment as prevention and HPTN 052. Curr Opin HIV AIDS **7**(2), 99–105 (2012)
14. Cohen, M.S., Chen, Y.Q., McCauley, M., Gamble, T., Hosseinipour, M.C., Kumarasamy, N., Godbole, S.V.: Antiretroviral therapy for the prevention of HIV-1 transmission. N. Engl. J. Med. **375**(9), 830–839 (2016)
15. Hayes, R., Ayles, H., Beyers, N., Sabapathy, K., Floyd, S., Shanaube, K., Fraser, C.: HPTN 071 (PopART): rationale and design of a cluster-randomised trial of the population impact of an HIV combination prevention intervention including universal testing and treatment–a study protocol for a cluster randomised trial. Trials **15**(1), 57 (2014)
16. Kahn, G.J., Marseille, A.E., Williams, G.B., Granich, R.: Cost-effectiveness of antiretroviral therapy for prevention. Curr. HIV Res. **9**(6), 405–415 (2011)
17. Sloan, C.E., Champenois, K., Choisy, P., Losina, E., Walensky, R.P., Schackman, B.R., Ajana, F., Melliez, H., Paltiel, A.D., Freedberg, K.A., Yazdanpanah, Y., Cost-Effectiveness of Preventing AIDS Complications (CEPAC) investigators : Newer drugs and earlier treatment: impact on lifetime cost of care for HIV-infected adults. AIDS (London, England) **26**(1), 45–56 (2012)
18. Antiretroviral Therapy Cohort Collaboration: Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. Lancet **372**(9635), 293–299 (2008)
19. Lodi, S., Phillips, A., Touloumi, G., Geskus, R., Meyer, L., Thiebaut, R., Pantazis, N., Amo, J.D., Johnson, A.M., Babiker, A., Porter, K., CASCADE Collaboration in Euro Coord: Time from human immunodeficiency virus seroconversion to reaching cd4 + cell count thresholds 200, 350, and 500 cells/mm3: assessment of need following changes in treatment guidelines. Clin. Infect. Dis. Off. Publ. Infect. Dise. Soc. Am. **53**(8), 817–825 (2011)
20. Cohen, M.S., McCauley, M., Gamble, T.R.: HIV treatment as prevention and HPTN 052. Curr Opin HIV AIDS **7**(2), 99 (2012)
21. Attia, S., Egger, M., Müller, M., Zwahlen, M., Low, N.: Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. AIDS (London, England) **23**(11), 1397–1404 (2009)
22. Baggaley, R.F., White, R.G., Hollingsworth, T.D., Boily, M.-C.: Heterosexual HIV-1 infectiousness and antiretroviral use: systematic review of prospective studies of discordant couples. Epidemiology (Cambridge, Mass.) **24**(1), 110–121 (2013)
23. Anglemyer, A., Rutherford, G.W., Horvath, T., Baggaley, R.C., Egger, M., Siegfried, N.: Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. Cochrane Database Syst Rev **4**, CD009153 (2013)
24. Jia, Z., Mao, Y., Zhang, F., Ruan, Y., Ma, Y., Li, J., Guo, W., Liu, E., Dou, Z., Zhao, Y., Wang, L., Li, Q., Xie, P., Tang, H., Han, J., Jin, X., Xu, J., Xiong, R., Zhao, D., Li, P., Wang, X., Wang, L., Qing, Q., Ding, Z., Chen, R.Y., Liu, Z., Shao, Y.: Antiretroviral therapy to prevent HIV transmission in serodiscordant couples in China (2003–11): a national observational cohort study. Lancet **382**(9899), 1195–1203 (2013)
25. Birungi, J., Wang, H., Ngolobe, M.H.and Muldoon, K., Khanakwa, S., King, R., Kaleebu, P., Shannon, K., Ocha, R., Montaner, J., Mills, E., Laurenco, L., Abdallar, N., and Moore, D.: Lack of effectiveness of art as an hiv prevention tool for serodiscordant couples in a rural art program in Uganda. Oral abstract session: 19th International AIDS Conference (2012)
26. Sullivan, P., Kayitenkore, K., Chomba, E., Mwananyanda, L., Vwalika, C., Conkling, M., Luisi, N., Tichacek, A., and Allen, S.: Is the reduction of HIV transmission risk while prescribed antiretroviral therapy (arvt) different for men and women? Results from discordant couples in Rwanda and Zambia. 5th International AIDS Society Conference on HIV Pathogenesis and Treatment and Prevention. Abstract Number 2009 WEAC101. Cape Town. (2009)
27. Marks, G., Crepaz, N., Sentertt, J.W., Janssen, R.S.: Meta-analysis of high risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. J. Acquir. Immune Defic. Syndr. **39**(4), 446–453 (2005)
28. Ndawinz, J.D.A., Costagliola, D., Supervie, V.: New method for estimating HIV incidence and time from infection to diagnosis using HIV surveillance data: results for France. AIDS (London, England) **25**(15), 1905–1913 (2011)
29. Desgree du Lou, A., Pannetier, J., Ravalihas, A., Gosselin, A., Supervie, V., Panjo, H., Bajos, N., Lert, F., Lydie, N., Dray-Spira, R., and the PARCOURS study group (2015).: HIV acquisition after arrival in France among sub-Saharan African migrants living with HIV in Paris area. Estimations from the ANRS PARCOURS study. Presented at IAS 2015-Vancouver, Canada
30. Rice, B.D., Elford, J., Yin, Z., Delpech, V.C.: A new method to assign country of HIV infection among heterosexuals born abroad and diagnosed with HIV. AIDS (London, England) **26**(15), 1961–1966 (2012)
31. Marks, G., Crepaz, N., Janssen, R.S.: Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS (London, England) **20**(10), 1447–1450 (2006)
32. Supervie, V.: L'épidémie cachée. Communication orale lors des soirées ASLP/COREVIH—Les rencontres VIH en Paca Ouest Corse. http://fr.aphm.fr/sites/default/files/files/Corevih/corevih_vsupervie_epidemiecachee.pdf (2014)
33. McCabe, C., Claxton, K., Culyer, A.J.: The NICE cost-effectiveness threshold. Pharmacoeconomics **26**(9), 733–744 (2008)
34. Belza, M.J., Hoyos, J., Fernández-Balbuena, S., Diaz, A., Bravo, M.J., de la Fuente, L., the Madrid HIV rapid testing group: Assessment of an outreach street-based HIV rapid testing programme as a strategy to promote early diagnosis: a comparison with two surveillance systems in Spain, 2008–2011. Eur. Surveill. **20**(14), 23–33 (2015). **(pii = 21089)**
35. European Centre for Disease Prevention and Control. Migrant health: epidemiology of HIV and AIDS in migrant communities and ethnic minorities in EU/EEA countries. ECDC, Stockholm. http://ecdc.europa.eu/en/publications/publications/0907_ter_migrant_health_hiv_access_to_treatment.pdf (2009)
36. Miners, A., Phillips, A., Kreif, N., Rodger, A., Speakman, A., Fisher, M., Lampe, F.C.: Health-related quality-of-life of people with HIV in the era of combination antiretroviral treatment: a cross-sectional comparison with the general population. Lancet HIV **1**(1), e32–e40 (2014)