



Effect of sociodemographic factors on survival of people living with HIV

Sophie Abgrall^{a,b} and Julia del Amo^{c,d}

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Purpose of review

The purpose is to describe and understand the sociodemographic determinants of survival in people living with HIV within high-income countries in the context of the current recommendation of universal antiretroviral therapy for all HIV-infected persons, irrespective of their CD4 cell count.

Recent findings

Survival rates in people living with HIV have experienced remarkable increases in the last decade because of more efficacious and well tolerated treatments. Still, these improvements are unevenly distributed between regions across the world as well as within regions. HIV outcomes are heavily influenced by what are known as the 'social determinants' of health which have traditionally encompassed the gender, race/ethnicity, and socioeconomic axes. The evidence that these social determinants are now more important than before (more and earlier interventions are now available), has become stronger in the last 2 years.

Summary

Because antiretroviral therapy is now recommended for all HIV-infected persons, sociodemographic factors limiting access to testing, treatment, and retention in care will undoubtedly jeopardize the UNAIDS aspirational objective to end AIDS by 2030. Innovative interventions targeting individuals with social vulnerability are urgently needed to ensure that social inequalities do not continue to be linked with higher mortality.

Keywords

gender, HIV infection, migrant, mortality, socioeconomic determinants

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INTRODUCTION

HIV/AIDS is still one of the top 10 causes of premature death worldwide, with substantial differences between high, middle, and low-income countries. Worldwide, HIV/AIDS is associated with health inequality in all age groups but differences are more marked in the 20–40 years band [1]. The post2015 global health agenda focuses on universal health coverage to meet basic healthcare needs to achieve the target of zero disease for HIV/AIDS, along with tuberculosis and malaria [2]. However, even in a context of universal health care, populations' health outcomes are heavily influenced by social, cultural, environment, and economic factors, known as the 'social determinants of health'. Those determinants, conceptualized in the gender, race/ethnic, and socioeconomic axes, influence the life course of a person with HIV infection from the moment of HIV acquisition, and will jeopardize the success of the 90:90:90 UNAIDS initiative which aims to end AIDS by 2030 through the diagnoses of 90% of all persons living with HIV/AIDS

(PLWHA), through the linkage to care of 90% of those diagnosed and through the achievement of viral suppression in 90% of the later [3].

The benefits of early antiretroviral therapy (ART) at the individual and the population level, which have led to remarkable increases in life expectancy and healthier lives, rely on equitable access and successful lifelong treatment retention [4–8]. However, although the life expectancy of many HIV-infected individuals on cART with restored CD4 cell count is similar to the general populations in countries where HIV care is free and treatment is

^aCESP, Inserm, Univ Paris-Sud, Université de Paris-Saclay, Le Kremlin-Bicêtre, ^bHôpital Antoine Bécère, Clamart, ^cNational Center for Epidemiology and ^dCIBERESP, Ciber of Epidemiology and Public Health, Institute of Health Carlos III, Madrid, Spain

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Correspondence to Sophie Abgrall, CESP, Inserm, Univ Paris-Sud, Université de Paris-Saclay, F94276 Le Kremlin-Bicêtre, France. Tel: +00 33 1 45 37 41 51; e-mail: sophie.abgrall@aphp.fr

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Curr Opin HIV AIDS 2016, 11:000–000

DOI:10.1097/COH.0000000000000301

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KEY POINTS

- Worldwide, HIV/AIDS is associated with inequality in health in all age groups. Even in a context of universal healthcare, the health outcomes of populations are heavily influenced by social, cultural, environment, and economic factors known as 'social determinants' of health.
- Risk factors for late presentation and delayed ART initiation are male sex, older age, particularly people older than 50, IDU, heterosexual transmission, and migrant origin – particularly from sub-Saharan Africa or Latin America. A lower socioeconomic position is associated with late presentation in most studies.
- After ART initiation, although retention into care is lower in PWID and migrants, similar or lower mortality rate are reported in migrants from sub-Saharan Africa or Latin America when compared with native populations, consistent with 'healthy migrant effects', though heterogeneity within migrant groups is observed.
- In high-income countries, differences in mortality rates between HIV-infected people living in Europe and in North America are substantial with higher mortality in socially disadvantaged racial groups than in native white populations, and in women than in men in North America but not in Europe. Such results are explained by differences in socioeconomic status and access to care.

provided universally, some vulnerable and key populations still suffer from excess mortality [9,10]. Indeed, even in contexts of universal health care, barriers to healthcare access, to engagement, and retention in care do exist. Some key populations are particularly affected; persons who inject drugs (PWID), sex workers, transgender individuals, MSM, women, and/or migrants, and some of them belonging to several key groups and thus adding layers of vulnerability. Barriers to access HIV testing and optimal HIV care are multiple and include unstable housing, low socioeconomic status, marginalization, and/or exposure to extreme violence [11]. Further, sexual partnerships with fear of HIV disclosure, stigma, loneliness, and the burden of child care activities are additional factors to be considered in women [12,13]. Special situations arise in migrants [10,14], which relate to the conditions of migration, employment insecurity, exposure to difficult or oppressive work environments, separation from family and friends and mechanisms, and motivations for migrating. For newly arrived migrants, particularly the undocumented, barriers to access health services because of administrative barriers, unfamiliarity with the host environment

and poor communication skills do matter too [15,16]. Nevertheless, even for people accessing to and compliant with ART, social disadvantage is associated with excess of mortality because of non-AIDS causes which are also present in HIV-negative populations of lower socioeconomic status.

In addition, in high-income countries, differences in mortality rates between HIV-infected people living in Europe and North America are substantial. The higher mortality rates of PLWHA in North America compared with Europe's are attributable to a myriad of different factors, including behavioral characteristics and comorbidities, but mostly because of the higher representation of socially disadvantaged patients; African-American and Hispanics in the United States and the First Nations populations in Canada [17]. The ART Cohort Collaboration reported lower mortality after ART initiation in HIV-positive migrants living in Europe and Canada compared with native populations supporting 'healthy-migrant' effects, and showed higher mortality in First Nations in Canada and African-Americans and Hispanics in the United States compared with largely white study participants [18]. Furthermore, the higher mortality of First Nations in Canada was explained by higher non-AIDS mortality rates attributable to substance use and underlying socioeconomic inequalities, and the lower mortality rates in migrants was attributable to lower rate of non-AIDS defining conditions, associated to healthier lifestyles.

In various European studies, HIV-infected women have higher life expectancy than HIV-infected men [19–21] reflecting the life expectancy patterns of the general population which ART has rendered visible. In North America, though, life expectancy in women is lower than men's, as the women living with HIV in North America, largely the United States, have a poorer socioeconomic status to start with, given that their epidemic is driven by past or current drug use, racial, and socioeconomic disadvantage [22,23,24]. So, differences in cohort demographics and healthcare access and utilization can explain such discrepancies between European and North American women, bearing in mind that Canada, unlike the United States, has a universal healthcare system.

It is undoubtable that lifestyle factors such as smoking, excessive alcohol intake, and drug use account for large and preventable differences in mortality. However, survival upon HIV infection is dependent on early diagnosis and timely treatment, followed by linkage to and retention in care, coupled with adherence to medications.

IMPACT OF LATE HIV DIAGNOSIS AND DELAYED TREATMENT ON MORTALITY AND SOCIODEMOGRAPHIC FACTORS

In Europe, where health care in general is universal in most countries, late HIV diagnosis and delayed ART initiation are major prognostic factors [19]. Up to 50% of individuals throughout Europe present late to care in the course of HIV infection, that is, with CD4 lower than 350/ μl or with an AIDS-defining event [25,26[■]], and this is associated with premature elevated mortality because of HIV/AIDS within the first 6 months to 1 year after entry into care [25,27,28]. The excess risk of mortality of persons diagnosed late can persist until 4 years after diagnosis though, after 4 years, differences become nonsignificant, numbers of deaths decrease and causes of death change to liver-related conditions and non-AIDS malignancies [28]. In the last 10 years, although percentages of late presenters have declined from 54–57 to 40–50%, the reduction is mainly significant in MSM, and is still insufficient [25,28]. Risk factors for late presentation and delayed ART initiation are male sex (for transmission routes other than MSM), older age, particularly people older than 50, injecting drug use (IDU), heterosexual transmission, and migrant origin, particularly from sub-Saharan Africa or Latin America [25,28,29[■],30[■],31[■]]. Although late presentation has shown to be deleterious for all PLWHA [25,27,28], disease progression appears to be more rapid among older individuals, and the effect of delaying ART from 500 to 350 or 200/ μl on survival is the most detrimental in oldest persons [19,32].

The relationship between socioeconomic position and late presentation has been approached in different ways. Given that socioeconomic status is very hard to measure, several proxies have been used such as individual educational level and individual income or neighborhood socioeconomic position. Low education attainment (primary school or less and lower secondary school compared with university) is an independent predictor of late presentation [28], and is associated with lower median CD4 cell count at ART initiation. In large multicenter European cohort collaboration, the gradient of the association between educational attainment and late HIV diagnosis was more pronounced among men than women [33[■]]. This pattern was attributable to universal HIV-testing programs targeting all pregnant women for prevention of mother-to-child transmission in Europe, which *de facto* bends HIV testing toward a more general testing approach rather than to high-risk approach. Residence in neighborhoods of low socioeconomic position is also associated with late HIV

presentation [34[■]]. However, in one study in the North of Europe where PWID were not included, educational attainment was not associated with late presentation to care or time to ART initiation [35[■]].

RESPONSES TO ANTIRETROVIRAL THERAPY: KEY POPULATION AND SOCIOECONOMIC FACTORS

After entry into care and ART initiation, sustained virological response and CD4 cell count recovery determine survival. These outcomes are conditioned by drug adherence [36] and retention into care. Overall, PWID, especially men, have the worst survival and MSM have the best [20,21]. Older people, PWID and migrants have poorer virological and immunological responses to ART in various contexts [22,24,29[■],37]. The underlying reasons for these poorer outcomes is their lower retention in the successive stages of the HIV continuum of care cascade, including higher rate of losses to follow-up, particularly soon after entry [22,24,38]. However, in a study of people retained in care and on ART for more than 6 months, the only factors associated with viral replication were social deprivation and younger age [39].

These findings need to be contextualized to the settings where they took place. Thus, the relative importance of some of the sociodemographic factors versus others may vary across the different studies and contexts. For example, while the race/ethnicity axis is very relevant in studies from the United States, this is less of an issue in Western European countries, where the socioeconomic axis is more relevant.

Comparable or lower mortality rates have been reported in migrants from sub-Saharan Africa or Latin America with that of native populations'. This has been recently reported in studies from Spain and France, though it has to be acknowledged that migrants experience poorer virological and immunological responses to ART and an increased risk of AIDS [37,40]. This discrepancy between lower mortality and higher AIDS is consistent with lower non-AIDS mortality and higher tuberculosis incidence in migrants [18,41]. The COHERE Collaboration has recently shown no significant differences in mortality by geographical origin among MSM, highlighting the heterogeneity within migrant groups once large datasets are examined [27,31[■]]. In heterosexual populations, most migrant men had a mortality rate which is lower than or equal to that of native HIV-positive men, whereas no group of migrant women had mortality lower than that of native women. High mortality is identified in

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heterosexual men from Latin America and heterosexual women from the Caribbean [31[■]]. Sociocultural determinants were not assessed in these studies [27,31[■],37,40].

The ART Cohort Collaboration reported lower mortality after ART initiation in HIV-positive women in Europe compared with men's, with larger between-sex differences among heterosexually infected patients than among injecting drug users, and larger between-sex differences in non-AIDS than in AIDS mortality [42[■]]. The lower mortality in women was largely because of non-AIDS-related causes: non-AIDS infections, liver-related death, cardiovascular diseases, and non-AIDS malignancies, where the causal role of smoking has been proven. Consistent with previous studies, no differences in all-cause or cause-specific mortality between men and women were found in Canada and in the United States. In the United States, after adjustment on demographic factors, AIDS and neighborhood poverty, black men and women had higher mortality compared with non-Hispanic whites [23[■],43], as have people born in the United States and people living in area of high poverty [43]. Such results may be because of differences in socioeconomic status and access to care. Indeed, in a study on Medicaid-enrolled HIV/HCV coinfecting patients on ART, lower adherence (but not sex neither race/ethnicity) is associated with survival [44].

In the context of universal free HIV care, when socioeconomic status is investigated in people on treatment, results are conflicting. Overall, in Europe, lower educational level – a good proxy for socioeconomic status – is associated with worse virological and immunological responses to ART and lower survival, after adjustment for sex, age, HIV transmission group, geographical origin, AIDS, CD4, and viral load at ART initiation [45]. In Switzerland, residence in neighborhoods of low socioeconomic position is associated with lower response to ART but not with mortality [34[■]]. In Spain, people with lower education have worse survival than people with university education but no differences are found according to district household income [20]. In France, social vulnerability, measured by a composite indicator using education (having a high-school certificate), employment (being employed) and housing (stable housing, comfortable housing), is a major independent mortality risk factor [46[■]]. In Denmark, outside the context of PWID, though low educational attainment is not associated with viral suppression following ART, the mortality rate ratio is higher in HIV-infected people with low education attainment compared to people with medium and high education attainment, consistent with the mortality patterns in the general population. In this

study, low education is associated with lifestyle-related mortality, mainly smoking and alcohol-related deaths, but not with AIDS-related mortality, suggesting that increased mortality in HIV-infected patients with low education can be because of risk factors unrelated to HIV [35[■]].

CONCLUSION

Socioeconomic factors explain a substantial proportion of the differences in late access to HIV testing, HIV care, and HIV-related outcomes following ART in PLWHA, though the relative importance of some factors versus others varies across the different studies and contexts. Ensuring free and universal access to health care to all people is pivotal – but not enough – to ensure expansion of HIV testing, HIV transmission control, early access to ART, adherence to ART, retention in care, and increase in survival. The fact that social disparities lead to differences in prognosis of HIV even in countries with free access to HIV health care highlight the need of additional efforts with interventions adapted to the specificities of each HIV key populations, as well as policies that fight inequality at the macroeconomic and social level.

Acknowledgements

None.

Financial support and sponsorship

The work has been partially funded by the RD12/0017/0018 project as part of the Plan Nacional R p D p I and cofinanced by ISCIII-Subdireccion General de Evaluacion and the Fondo Europeo de Desarrollo Regional (FEDER).

Conflicts of interest

There are no conflicts of interest.

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Apart from educational level, this study explores the association between a composite indicator of social vulnerability and instability and, death in HIV infection. This global indicator of social vulnerability includes education, employment, and housing stability and comfort. After adjustment on lifestyle factors, psychosocial characteristics (depression, drug using) and known biomedical factors, this indicator remains associated with mortality in HIV-infected people.

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