

Incidence and risk factors for suicide, death due to substance use, and violent/accidental death in persons living with HIV

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Abstract

Objective: Deaths due to suicide, substance use and violence/accidental may reflect similar risk factors and be overlapping in their classification. This study aimed to investigate incidence and risk factors of mortality among people living with HIV (PLWH) due to these three related causes

Design: Prospectively collected data from PLWH ≥ 18 years old and under active follow-up in the EuroSIDA study from 2007–2019 were analyzed.

Methods: Cause-specific Cox regression analysis was used to assess risk factors.

Results: A total of 17,881 participants were included, comprising 149,327 person-years of follow-up (PYFU). Forty participants died by suicide (IR [95%CI]: 0.3/1000 PYFU [0.2, 0.4]), 93 from substance use (IR [95%CI]: 0.6/1000 PYFU [0.5, 0.8]), and 57 by violence/accident (IR [95%CI]: 0.4/1000 PYFU [0.3, 0.5]). An AIDS diagnosis within the last 12 months was associated with nine-fold increased risk of suicide vs. no history of AIDS (adjusted hazard ratio [aHR]: 9.06; 95%CI: 2.07, 39.7). Male gender was associated with double the risk of violent/accidental death (aHR: 2.28; 95%CI: 1.09, 4.78). PLWH in Eastern Europe and those

who acquired HIV by injection drug use (IDU) demonstrated a greater risk of death due to substance use or violence/accident.

Conclusions: The association between a recent diagnosis of AIDS and suicide highlights a critical period for intervention. HIV infection acquired through IDU demonstrated an expected relationship with death due to substance use and violent/accidental deaths. Increased risk of death due to substance use and violence/accident in Eastern Europe demands investigation into specific differences that may drive that association.

Key Words: HIV, mortality, suicide, substance use, violent/accidental death

Introduction

Following widespread access to combination antiretroviral therapy (cART), rates of suicide among people living with HIV (PLWH) were significantly reduced^[1, 2]. However, suicidal ideation and suicidal behaviour remains prevalent among PLWH^[3-6]. Rates of suicide among PLWH are higher than in the general population, with observational cohorts in Switzerland from 2009–2017 and the U.K. from 1997–2012 finding suicide rates among PLWH two to three times higher than in the general population^[6, 7]. These higher rates of suicide may be related to several risk factors, including behavioural factors, comorbidities, and exposure to certain antiretroviral drugs (ARVs)^[1, 8-11].

Deaths due to both substance use and violence/accident have also been shown to be more prevalent among PLWH compared to the general population^[7]; these causes of mortality may reflect similar risk factors. Risk-taking behaviours have been linked to suicidal behaviour, especially in adolescents and young adults^[12-14], as well as violent behaviours^[15], and impulse control disorders^[16]. In the general population, people who die an accidental death have also been shown to share a common set of risk factors with those who die by suicide^[17]. Deaths by suicide may also be misclassified as violent, accidental, or with the cause of death being unknown^[18]. Death due to substance use may reflect an intersection of risk-taking behaviours, suicidality, and accidental death. These three causes of death can be understood as having a similar set of drivers: risk-taking, mental illness, and other stigmatising demographic and socio-cultural factors.

Given their similarities and the relative rarity of these outcomes, this study aimed to report the incidence rates of suicide, death due to substance use, and violent/accidental death in a heterogenous, pan-European population of PLWH^[19] and to investigate their associated risk factors.

Methods

Study population and data collection

EuroSIDA is a prospective observational cohort utilizing demographic, clinical, biological, and therapeutic data that have been systematically collected for over 23,000

PLWH in 35 European countries, Israel, and Argentina since 1994 [20, 21]. Data collection is performed at 6-month intervals (12-month intervals since 2016) and includes details and dates of ART regimens, CD4 and viral load measurements, laboratory data, and clinical (both AIDS and non-AIDS) events. Analyses and a priori predictors were approved by an internal EuroSIDA study group before starting analysis.

Causes of death were established using the Coding Causes of Death in HIV Project (CoDe) methodology [22, 23], implemented in EuroSIDA from 2007 onwards. All participants at least 18 years old at enrollment, under follow-up between 2007–2019, with at least one CD4 cell count measurement were considered for inclusion. Follow-up was defined as at least one recorded clinic visit, HIV viral load, CD4 cell count, or ART start date. Loss to follow-up date was defined as eighteen months after last data collection. Participants with gender missing or recorded as “other” were excluded due to low numbers. Baseline was defined as the latest of date of enrollment into the cohort or 1/1/2007, and participant follow-up continued until death, loss to follow-up, or 31/12/2019.

Immediate and underlying causes of death were both used to classify deaths as suicide, substance use, or violent/accidental. Due to the potential for overlapping risk factors and misclassification, a composite outcome defined as death due to any of the three outcomes of interest was also investigated. We therefore investigated four outcomes: 1) Deaths due to suicide; 2) Deaths due to substance use; 3) Deaths due to violence/accident; 4) Composite Outcome: Deaths due to suicide, substance abuse, or violence/accident. Deaths due to violence/accident included all violent deaths that were not suicide, e.g. automotive crashes, interpersonal violence, accidental falls, and drowning.

Variable Selection

Key variables of interest were selected as risk factors a priori. Baseline variables included gender, mode of HIV transmission (injection drug use [IDU], men who have sex with men [MSM], heterosexual contact, or any other/unknown), region of Europe [19] (North; South, including Israel and Argentina; Central West; Central East; East) and time-updated variables included age, calendar year of follow-up, recent AIDS diagnosis, and current use of an efavirenz containing regimen, classified at baseline and updated monthly thereafter.

AIDS diagnosis was defined as the first clinical diagnosis of a CDC-C AIDS-defining illness [24]. The recent AIDS diagnosis risk factor was classified as: no prior AIDS diagnosis, within 12 months after AIDS diagnosis, or more than 12 months after AIDS diagnosis. Variables associated with an outcome in univariate analyses ($p < 0.1$), were included in multivariable models.

Demographic variables age, gender, and region of Europe were chosen based on their associations with suicide, substance use death, or violent/accidental death in the general population [25-27] and PLWH [6, 7]; mode of HIV transmission was also selected due to mortality associations in other studies of PLWH [6, 28]. Recent AIDS diagnosis was included based on

evidence from both the pre-cART [29, 30] and cART era [1, 31]. Calendar year was included to investigate risk over time. Efavirenz use was included a priori due to its known association with suicide [10], but not considered a main risk factor due to limited power to fully investigate any potential associations observed. Ethnicity was not analyzed due to very few non-white participants with the outcomes of interest. The set of covariates was intentionally limited due to the relatively small number of outcomes.

Statistical Analysis

Crude mortality rates with Poisson 95% confidence intervals were calculated for all-cause and cause-specific mortality. Age, gender, race, region, and mode of HIV transmission were compared between included and excluded participants using t tests and chi squared tests. Cause-specific Cox proportional hazard regression analysis was used to investigate factors associated with each cause of death and the composite mortality outcome, with deaths due to all other causes treated as competing events.

Time-updated age was analyzed in univariate analyses as both a continuous variable and categorical (by quartiles) to investigate non-linear associations. Where time-updated quartile age is a significant predictor and there is no linear association with age per 10 years, quartile age was included in multivariable analysis. Otherwise, time-updated age per 10 years was included in multivariable analysis. To investigate the impact of competing risks, sensitivity analyses using the Fine and Gray [32] method were also conducted, treating deaths due to other causes and loss to follow-up as competing events. Chi square tests were performed to assess regional differences in proportion of deaths with unknown/missing causes. To assess risk factors for unknown or missing causes of death, logistic regression was performed only on participants who died during follow-up. Analyses were conducted using SAS software version 9.4 (SAS Institute Inc., Cary, North Carolina, USA).

Results

Of 23,974 participants enrolled in EuroSIDA, 18,050 were under active follow-up from 2007 through 2019. Participants were excluded due to being younger than 18 years at enrollment (n=46), no CD4 measurement (n=109), or “other” or missing gender (n=7). Thus, 17,881 participants followed for a median of 8.07 (inter-quartile range (IQR) 4.94-13.00) years were included in the analysis. Baseline characteristics are shown in Table 1. There were 1,807 deaths during 149,327 person-years of follow up (PYFU) resulting in a crude mortality rate of 12.10 per 1,000 PYFU (95% confidence interval (CI) 11.56, 12.67). Suicide was reported as an immediate or underlying cause in 40 (2%) of deaths, substance use in 93 deaths (5%), and violence/accident in 57 (3%) deaths. One death was classified as both substance use and violence/accident and one as both substance use and suicide; 186 deaths were included in the composite outcome.

Excluded participants were of similar race and gender as those included, but younger at baseline (median age 34; IQR 26–41 vs 43; IQR 35–50) ($p < .0001$), more likely to

be from Eastern Europe (76.1% of excluded vs. 17.1% of included, $p < .0001$), and more likely to have acquired HIV by IDU (49.7% vs. 28.6%) or other/unknown route of transmission (13.9% vs. 6.9%) ($p < .0001$).

Suicide

The crude mortality rate for suicide was 0.27 per 1,000 PYFU (95%CI 0.20, 0.37). After adjustment, recent AIDS diagnosis was associated with a nine-fold increased risk of suicide (adjusted hazard ratio (aHR) 9.06, 95%CI 2.07, 39.7), compared to participants without a prior AIDS diagnosis (figure 1). However, there was no difference in the rate of suicide between participants more than twelve months after an initial AIDS diagnosis and those without prior AIDS (aHR 1.35, 95%CI 0.68, 2.70). No other factors were associated with suicide in multivariable analysis.

Deaths due to substance use

The crude mortality rate for death due to substance use was 0.62 per 1,000 PYFU (95%CI 0.51, 0.76). Univariate analysis found older age to be associated with a decreased risk of death due to substance use (HR per 10 years age: 0.68, 95%CI: 0.56, 0.83). After adjusting for other risk factors, particularly region of Europe, this was no longer significant (aHR 0.93, 95%CI 0.72, 1.20).

In multivariable analysis (figure 2), participants in Eastern and Northern Europe were found to have similar risk of death due to substance use (East vs. North aHR 1.25, 95%CI: 0.64, 2.46). Risk of death by substance use was statistically significantly greater in Eastern Europe compared to all other regions (vs. Central West aHR 2.48, 95%CI 1.21, 5.07; vs. Central East aHR 2.49, 95%CI 1.26, 4.89; vs. South aHR 10.08, 95%CI 3.79, 26.78), but risk in Northern Europe was only statistically significantly different from Southern Europe (aHR 8.05, 95%CI 2.97, 21.81). Participants in Southern Europe (including Israel and Argentina) demonstrated much lower risk of death due to substance use compared to all other regions.

Death due to violence/accident

The crude mortality rate for death due to violence/accident was 0.38 per 1,000 PYFU (95%CI 0.29, 0.49). Recent AIDS diagnosis was excluded from analyses as no violent/accidental deaths occurred within twelve months after AIDS diagnosis. In multivariable analysis (figure 3) including quartile age, calendar year of follow-up, gender, region, and mode of HIV transmission, male participants had more than twice the risk of violent/accidental death than females (aHR 2.28; 95%CI 1.09, 4.78). A higher rate of violent/accidental death was observed in Eastern Europe compared to all other regions: vs. Central West aHR 3.54, 95%CI 1.42, 8.84; vs. Central East aHR 3.23, 95%CI 1.26, 8.25; vs. Southern aHR 4.84, 95%CI 1.95, 12.00; vs. Northern Europe aHR 2.77, 95%CI 1.09, 7.06. Participants who acquired HIV by IDU showed more than double the risk of

violent/accidental death compared to MSM (aHR: 2.34; 95%CI: 1.11, 4.94). Associations with age and calendar year of follow-up were nullified after statistical adjustment.

Composite outcome (death due to suicide, substance use, or violence/accident)

The crude mortality rate for the composite outcome was 1.26 per 1,000 PYFU (95%CI 1.09, 1.45). In multivariable analysis, gender, region, and mode of HIV transmission remained significantly associated with the composite outcome (figure 4). Gender associations followed the trends in cause-specific analyses; male participants demonstrated nearly double the risk of death (aHR: 1.84; 95%CI: 1.24, 2.73). Mortality risk was higher in participants from Eastern Europe, lower in participants from Southern Europe, and higher among participants who acquired HIV through IDU, similar to the strong associations in analyses of deaths due to substance use or violence/accident.

Time-updated efavirenz use was not significantly associated with any outcome in univariate analyses and was therefore not included in any multivariable analyses. All results were consistent between cause-specific and Fine and Gray methods treating deaths due to other causes and loss to follow-up as competing events.

Unknown/missing cause of death

Of all deaths during follow-up, 389 (22%) were classified as unknown/missing cause (unknown n=387, missing n=2). The proportion of unknown/missing cause of death varied significantly between regions ($p < 0.0001$), from 14.7% in Eastern to 27.5% in Central West Europe. Univariate and multivariable logistic regressions were conducted in the 1807 participants who died during follow-up to investigate risk factors of unknown/missing cause of death. In multivariable analysis including age at death, calendar year of death, and region as covariates, later dates of death were associated with increased odds of unknown/missing cause (per 1 year adjusted odds ratio (aOR): 1.09; 95%CI: 1.06, 1.13). Participants who died in Central West and Northern Europe had approximately 50% greater odds of an unknown/missing cause compared to Eastern Europe (North vs. East aOR: 1.49; 95%CI: 1.07, 2.08; Central West vs. East aOR: 1.55; 95%CI: 1.10, 2.18). Age at death was not associated with unknown/missing cause of death.

Discussion

In this study we investigated rates of death from suicide, substance use, and violence/accident in PLWH across Europe, Israel, and Argentina. To our knowledge, no previous studies have investigated these causes of death among PLWH in an international, prospective observational context.

The suicide mortality rate in this pan-European cohort (0.27 per 1,000 PYFU; 95%CI 0.20, 0.37) was lower than reported by other large observational cohorts in Switzerland (1.11 per 1,000 PYFU; 95%CI: 0.96, 1.27) (Ruffieux et al. ^[6]) and France (0.47 per 1000 PYFU) (Hentzien et al. ^[33]), but on par with one in the United Kingdom (0.21 per

1,000 PYFU; 95%CI 0.18, 0.26) (Croxford et al. [7]), all over similar time periods to the current analysis. While it is beyond the current scope of this manuscript to rigorously compare suicide rates to the general population, the age-standardized suicide rate among the general population in the WHO European region in 2016 was 0.13 per 1,000, indicating higher rates of suicide among PLWH [34]. The rates in this study for death due to substance use (0.62 per 1,000 PYFU; 95%CI 0.51, 0.76) and violence/accident (0.38 per 1,000 PYFU; 95%CI 0.29, 0.49) were both higher than those found in a U.K. cohort (Croxford et al. [7] accidental death: 0.21 per 1,000 PYFU; 95%CI 0.17, 0.26; substance use death: 0.27 per 1,000 PYFU; 95%CI: 0.23, 0.32).

Participants in Eastern Europe and those who acquired HIV by IDU demonstrated a greater risk of both death from substance use and violent/accidental death. Male gender was associated with higher risk of violent/accidental death, reflecting trends in the European general population [25]; there was no gender association with suicide or substance use deaths. Recent AIDS diagnosis was strongly predictive of suicide. Median age at death for the three causes of interest were between four and ten years lower than for all-cause mortality. However, after controlling for other risk factors, particularly region, no significant trends with age or calendar year of follow-up were observed in the rates of any cause of death.

We did not observe any statistically significant differences in the rate of death from suicide between geographic regions or by mode of HIV transmission. Along with lack of power due to few outcomes, differential loss-to-follow-up between regions may also have influenced this finding, as previous EuroSIDA studies have found higher rates of loss-to-follow-up reported by clinics in Eastern Europe as compared to the rest of Europe [35, 36]. There is conflicting evidence from other cohorts whether suicide rates are associated with mode of HIV transmission. MSM and IDU HIV transmission groups have demonstrated higher risk of death from suicide compared to PLWH who acquired HIV by other routes of transmission in some observational cohorts [6], but others have found no association [7, 33].

There was also no significant association observed between suicide and either gender or age. Suicide rates among white men in high income countries peak at middle and old age [26, 27]. In our sample of PLWH with a large proportion of white men in high income countries, we observed no such age association. In the general population a higher rate of suicide is observed in males compared to females in high income countries [26, 27]. However, among PLWH there is conflicting evidence, with some large prospective studies finding a similar gender association to the general population [6, 7], and some reporting no association [33].

The association between suicide and a recent first diagnosis of AIDS is particularly interesting, especially well after the introduction of cART. A link between AIDS diagnosis and suicide was well described in the pre-cART era, but usually explained by despair over a so-called “terminal diagnosis” [29, 30]. There is support in the literature for a greater risk of suicide following HIV diagnosis in the cART era [1, 31], and some evidence for

a greater risk of suicide, substance use, or violent/accidental deaths among participants with any history of AIDS diagnosis [37].

There was significant variation in the risk of death by substance use and violent/accidental death across regions and HIV transmission groups. Participants who acquired HIV by IDU were at greater risk of death by substance use and violent/accidental death. Although current drug use information is unavailable in this dataset, increased mortality due to substance use and violent/accidental death would be expected among this group due to more prevalent injection drug use and other risky behavior [38]. Participants in Eastern Europe were also at greatest risk of death due to substance use or violence/accident, even after statistically controlling for mode of HIV transmission. There were too few events to assess interaction between region and HIV transmission group.

These associations between region and death by both substance use and violence/accident are likely multifactorial. Active IDU is more prevalent in Eastern Europe than other regions, and the mortality rate due to overdoses in the general population are highest in Northern Europe [39, 40]. In Eastern Europe, rates of active IDU may be higher than other regions due to poorer access to opioid substitution therapy and other treatments [41]. Lower quality and access to care for PLWH in Eastern Europe [35, 42-44] and higher suicide rates in the general population [34] are also important to consider. The lower risk of death by substance use in Southern Europe is less readily explained and may be due to unmeasured differences in current drug use. The inverse relationship between age and risk of death due to substance use in univariate analysis was attenuated after controlling for covariates, and pairwise analyses indicated that higher risk among younger participants was mostly driven by regional differences.

There are some limitations to this study. Information regarding risk factors mentioned in the introduction that may link the causes of death of interest (risk-taking behavior, mental illness, and social stigma) are not collected in this study and cannot be analyzed. Other key risk factors were not collected or collected inconsistently across centers, such as socioeconomic information, diagnosed mental illnesses and associated medication, alcohol, and substance use. Further, this study was not powered to investigate associations between mortality and specific antiretrovirals. Efavirenz use was included in the analysis as a potential confounder and, while we did not observe any association with mortality, this result should be interpreted with caution.

Other limitations include deaths with missing/unknown causes and the low number of outcomes, which precluded some statistical tests, e.g. interaction, stratification, or more complex multivariable models, and led to some estimates with wide confidence intervals. Under-ascertainment of outcomes due to loss to follow-up is a concern, especially given the outcomes under analysis. Previous work in this cohort has found quite low LTFU rates (under 4 per 100 person-years [36]), and the inclusion of three cause-specific analyses as well as a composite outcome are additionally meant to alleviate this. As the proportion of deaths with unknown/missing causes is associated with later years of follow up, this may be

due in part to delays in reporting. Since these deaths with unknown/missing causes were not evenly distributed across regions, apparent regional differences may be attenuated if unknown/missing classification was non-random. The number of excluded subjects was relatively small but could represent a population with lower engagement with medical care, as has been shown among transgender^[45] and younger PLWH^[46], leading to higher risk of mortality. This may lead to a small underestimate in deaths but should have little effect on the observed associations or conclusions.

This study also has several strengths. The CoDe methodology is a validated method for ascertaining cause of death, which leads to more accurate classification compared to other methods^[22]. The prospective study design analysing an international, pan-European cohort represents an improvement over case-control studies drawn from national registries^[1, 11, 47] and observational cohorts in only one country^[6, 7, 33, 48], and analyses of suicidal ideation or other suicidal behaviour^[4, 5, 49, 50] instead of validated mortality outcomes.

These findings indicate that Eastern Europe should be an area of focus for preventing death due to substance use and violence/accident among PLWH, as regional differences appear to be independent from known associations with mode of HIV transmission^[38]. It is important to investigate and identify what specific drivers of mortality differ between regions and address those inequities. Suicide represents a preventable cause of mortality in PLWH and hence calls for efforts centered around diagnosis and management of mental health issues in PLWH that could lead to suicide. HIV care has historically focused on viral control, immunological restitution, and treating opportunistic infections. However, care guidelines, e.g. those of the European AIDS Clinical Society, have been shifting recently to recommend frequent mental health screening^[51]. Our results indicate a need for further clinical focus on mental health and research on mental health effects directly following an initial AIDS diagnosis.

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Conflicts of interest

There are no conflicts of interest.

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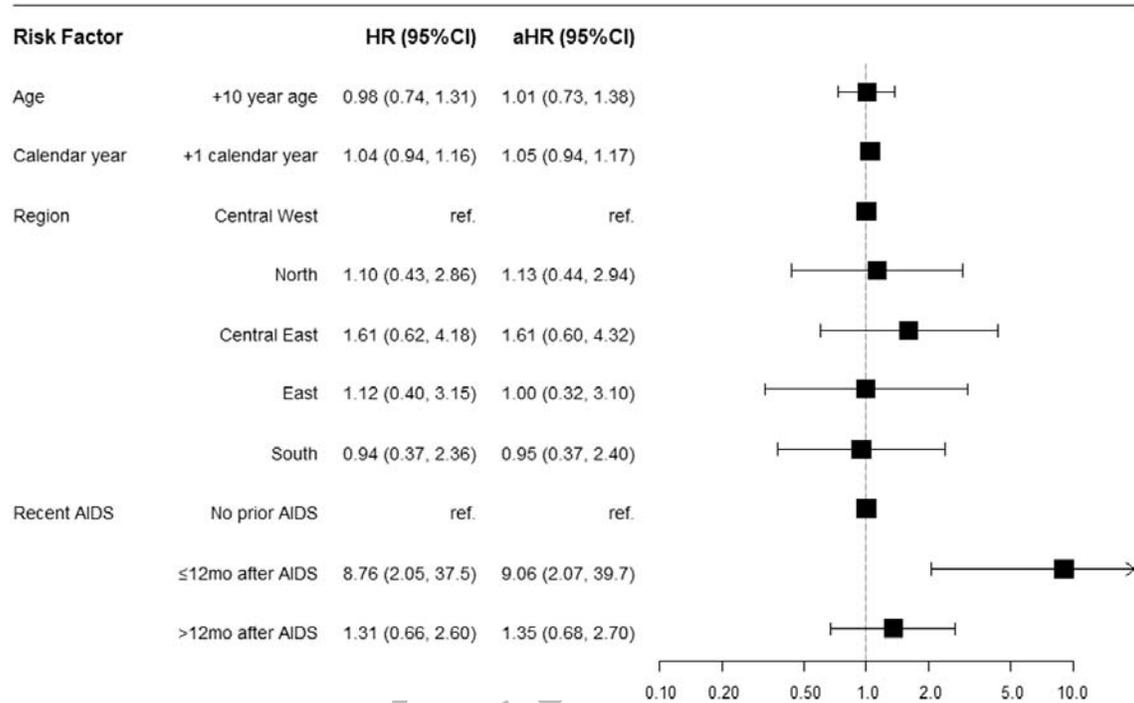
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Figure 1. Hazard ratios from univariate and multivariable Cox regressions investigating factors associated with suicide

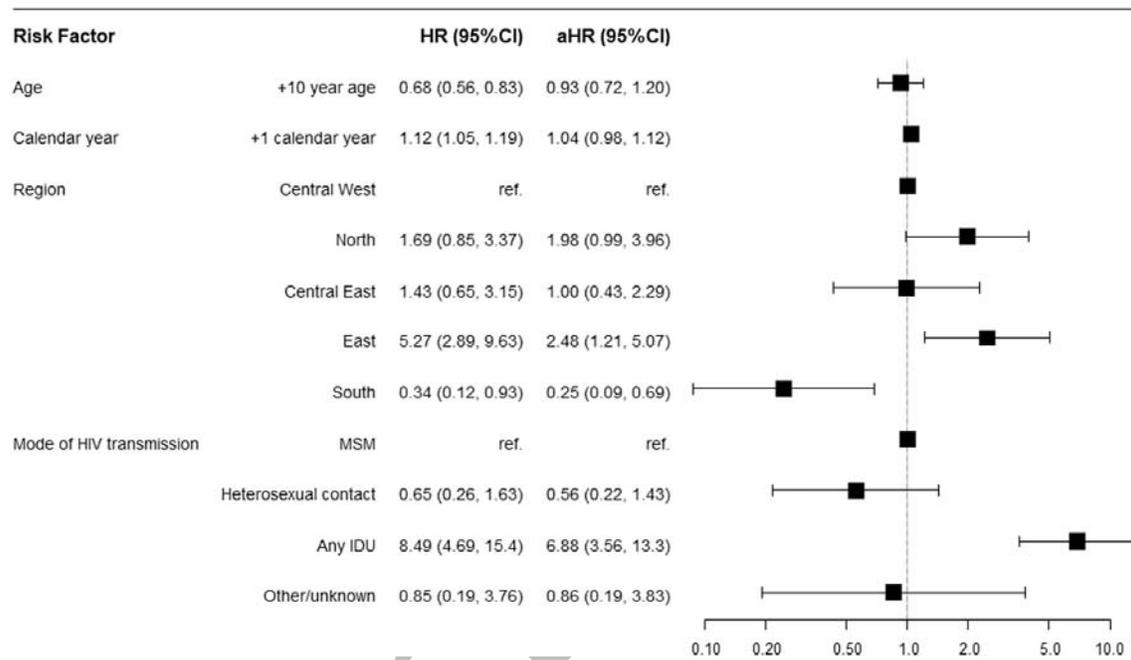
Caption: Univariate and multivariable Cox regressions predicting suicide mortality includes age (per 10 years older, time-updated), calendar year of follow-up (per one year later, time-updated), region, and recent AIDS diagnosis. Only adjusted hazard ratios are drawn.



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Figure 2. Hazard ratios from univariate and multivariable Cox regressions investigating factors associated with deaths from substance use

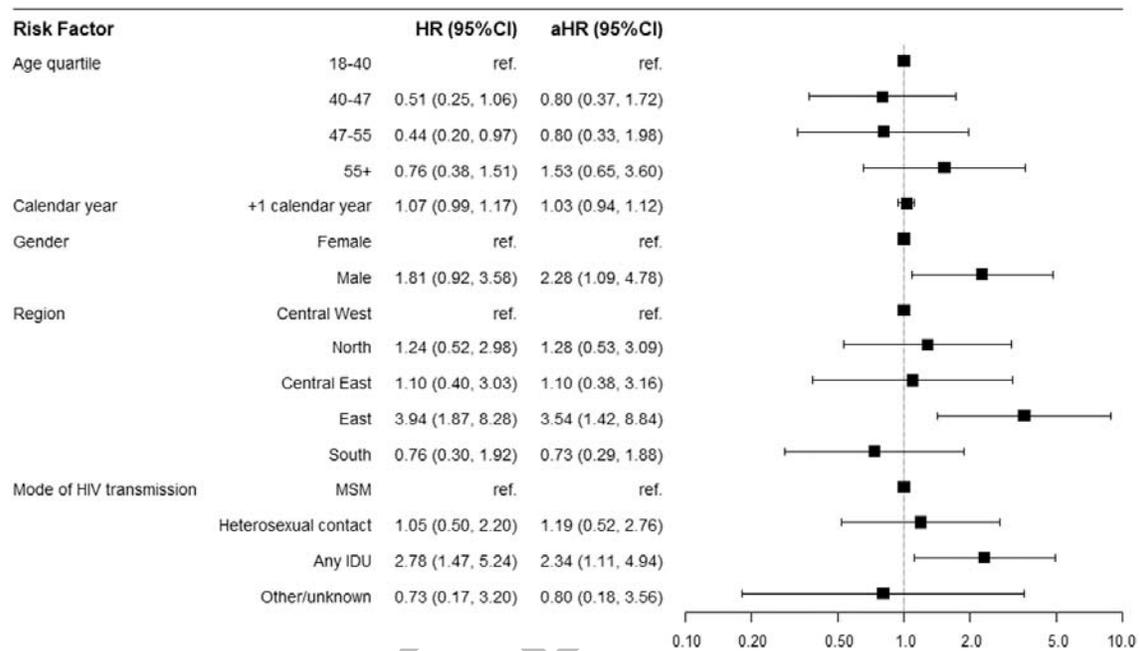
Caption: Univariate and multivariable Cox regressions predicting substance use mortality includes age (per 10 years older, time-updated), calendar year of follow-up (per one year later, time-updated), region, and mode of HIV transmission. Only adjusted hazard ratios are drawn. Abbreviations: MSM – Men who have Sex with Men; IDU – Injection drug use.



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Figure 3. Hazard ratios from univariate and multivariable Cox regressions investigating factors associated with violent/accidental death

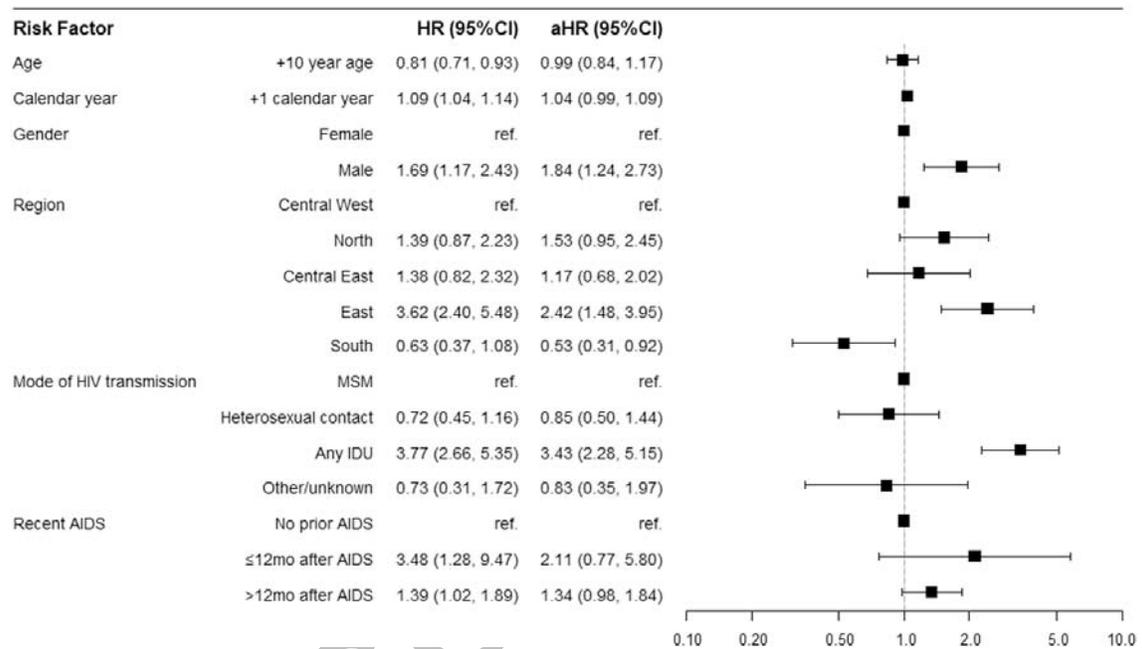
Caption: Univariate and multivariable Cox regressions predicting violent/accidental mortality includes age quartile (time-updated), calendar year of follow-up (per one year later, time-updated), gender, region, and mode of HIV transmission. Only adjusted hazard ratios are drawn. Abbreviations: MSM – Men who have Sex with Men; IDU – Injection drug use.



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Figure 4. Hazard ratios from univariate and multivariable Cox regressions investigating factors associated with the composite outcome: death from suicide, substance use, or violence/accident

Caption: Univariate and multivariable Cox regressions predicting composite outcome (suicide, substance use, or violent/accidental mortality) includes age (per 10 years older, time-updated), calendar year of follow-up (per one year later, time-updated), region, mode of HIV transmission, and recent AIDS diagnosis. Only adjusted hazard ratios are drawn. Abbreviations: MSM – Men who have Sex with Men; IDU – Injection drug use.



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Table 1. Participant characteristics by outcome group: All-cause and cause-specific mortality during follow-up

	All Participants (N=17881)	Did not die (n=16074)	Died, all causes (n=1807)	Suicide (n=40)	Substance use death (n=93)	Violent / accidental death (n=57)
Age at baseline [median (IQR)]	43 (35-50)	42 (35-49)	46 (38-55)	41.5 (34.5-46.5)	38 (32-44)	40 (32-51)
Age at death [median (IQR)]	-	-	52 (42-60)	45.5 (40-51.5)	41 (35-49)	45 (36-55)
Gender						
Male	12957 (72.5%)	11564 (71.9%)	1393 (77.1%)	33 (82.5%)	74 (79.6%)	47 (82.5%)
Female	4924 (27.5%)	4510 (28.1%)	414 (22.9%)	7 (17.5%)	19 (20.4%)	10 (17.5%)
Ethnicity						
White	15416 (86.2%)	13759 (85.6%)	1657 (91.7%)	37 (92.5%)	90 (96.8%)	55 (96.5%)
non-White/unknown	2465 (13.8%)	2315 (14.4%)	150 (8.3%)	3 (7.5%)	3 (3.2%)	2 (3.5%)
Region						
Central West	4391 (24.6%)	4013 (25%)	378 (20.9%)	9 (22.5%)	14 (15.1%)	10 (17.5%)
North	3285 (18.4%)	2850 (17.7%)	435 (24.1%)	8 (20%)	19 (20.4%)	10 (17.5%)
Central East	2434 (13.6%)	2227 (13.9%)	207 (11.5%)	8 (20%)	11 (11.8%)	6 (10.5%)
East	3063 (17.1%)	2674 (16.6%)	389 (21.5%)	6 (15%)	44 (47.3%)	23 (40.4%)
South	4708 (26.3%)	4310 (26.8%)	398 (22%)	9 (22.5%)	5 (5.4%)	8 (14%)
Mode of HIV transmission						

MSM	6299 (35.2%)	5784 (36%)	515 (28.5%)	17 (42.5%)	13 (14%)	15 (26.3%)
heterosexual contact	5232 (29.3%)	4794 (29.8%)	438 (24.2%)	8 (20%)	7 (7.5%)	13 (22.8%)
IDU	5118 (28.6%)	4372 (27.2%)	746 (41.3%)	13 (32.5%)	71 (76.3%)	27 (47.4%)
other, sex unspecified, unknown	1232 (6.9%)	1124 (7%)	108 (6%)	2 (5%)	2 (2.2%)	2 (3.5%)
First AIDS event during follow-up	704 (3.9%)	506 (3.1%)	198 (11%)	1 (2.5%)	9 (9.7%)	6 (10.5%)
Any EFV regimen during follow-up	5415 (30.3%)	4912 (30.6%)	503 (27.8%)	11 (27.5%)	26 (28%)	20 (35.1%)

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