





Factors associated with deaths from suicide in a French nationwide HIV-infected cohort

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Objectives

People living with HIV (PLHIV) are at a higher risk of dying by suicide than the general population. Epidemiological data regarding determinants of suicide in PLHIV are scarce. The aim of this study was thus to study demographic, socio-economic, psychiatric history and immunovirological characteristics associated with death from suicide in the French multicenter Dat'AIDS cohort, from January 2000 to July 2013.

Methods

This was a nested case-control study. All deceased PLHIV during the study period who died by suicide and whose medical files could be checked were included as cases. Controls were selected using incidence density sampling. For each case, up to four controls were selected among all actively followed PLHIV at the index date (date of death of cases). Controls were matched for time from HIV diagnosis (5-year periods) and clinical centre.

Results

Seventy cases and 279 controls were included in the study. By multivariable analysis, the factors significantly associated with death from suicide were: not having children, active or substituted drug consumption, alcohol intake > 20 g/day or history of alcohol abuse, history of depressive disorder and/or of attempted suicide, and psychotropic drug intake. Conversely, age, gender, country of birth, positive HCV serology and HIV-related factors, such as AIDS status, use of combination antiretroviral therapy (cART), nadir and current CD4 counts and HIV viral load, were not significantly associated with the risk of death from suicide.

Conclusions

In the cART era, HIV-related factors are not associated with a higher risk of suicide mortality. Suicide prevention measures should target PLHIV with the psychological morbidities observed in our cohort.

Keywords: Dat'AIDS cohort, suicide, suicide mortality, HIV, psychological morbidity

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Introduction

Although a decrease in the rate of suicide has been reported among people living with HIV (PLHIV) since the advent of combination antiretroviral therapy (cART),

PLHIV nonetheless remain at a higher risk of death from suicide than the general population [1–4]. In Denmark, HIV infection was shown to be associated with a four-fold-increase in the risk of subsequent suicide between 1986 and 2006. This increased suicide risk associated with HIV infection was slightly greater before the introduction of cART in 1997, with a five-fold increase in risk, but the increased risk remained highly significant in the cART era (around three-fold higher risk) [2]. In Switzerland, suicide deaths decreased significantly following the introduction of cART, but they remain above the rate observed in the general population, with a standardized mortality ratio of 3.5 in HIV-infected men and 5.7 in HIV-infected women [1]. In Spain, between 1999 and 2006, the standardized mortality ratio for suicide in the cohort of PLHIV aged 20–59 years was 9.6 [95% confidence interval (CI) 3.8–19.7] [3]. In the European multicohort CASCADE study, 6.4% of all deaths in 2006 were related to suicide [5]. In France, suicide was the sixth most common cause of death in PLHIV, accounting for about 5% of causes of death in 2010, whereas it represented 1.7% of causes of death in the French general population in 2012 [6,7]. Furthermore, suicide was the second most common cause of death among French PLHIV with immunovirological success (with a CD4 count > 500 cells/ μ L and undetectable HIV viral load), accounting for 12.5% of deaths in this population [8].

Epidemiological data regarding the determinants of suicide in PLHIV are scarce [1,9,10]. The aim of this study was thus to study demographic and socio-economic factors, as well as psychiatric history and immunovirological characteristics associated with dying by suicide in the French multicenter Dat'AIDS cohort in the cART era, from January 2000 to July 2013.

Methods

This was a multicenter case–control study nested in the Dat'AIDS cohort. Dat'AIDS is a French multicenter prospective cohort that includes in-patients or out-patients treated in 19 French public hospitals, including French overseas territories. It is based on a computerized medical record that has been used by clinicians in real time during their consultations since 2000 (Nadis[®]; Fédialis Medica, Marly le Roi, France) [11]. It is subject to continuous quality control. By 2013, more than 34 000 patients had been included in the cohort. The Dat'AIDS cohort study is registered with Clinicaltrials.gov under the identifier NCT02898987.

All PLHIV who died by suicide during the study period and for whom the medical files could be checked were included as cases. Death by suicide was recorded if the

death category was identified as 'suicide' or the International Classification of Disease 10th Revision (ICD-10) for death was in the range X60–X84 (intentional self-harm). Date of death was the index date.

Controls were selected using incidence density sampling [12], meaning that patients who were actively followed in the Dat'AIDS cohort at the index date of the case could be selected as controls. For each case, up to four controls were selected. Controls were selected among all PLHIV actively followed at the index date, and were matched for duration of follow-up since HIV diagnosis (in 5-year periods) and clinical centre.

The following variables were extracted from the Dat'AIDS cohort database from the nearest date possible to the index date: date of birth, gender, country of origin, level of education, socio-professional category, marital status, whether the subject had any children, alcohol consumption, smoking status, drug use, risk categories for HIV infection, duration of HIV infection, AIDS status, use of cART, nadir CD4 cell count, CD4 cell count, HIV viral load and hepatitis C virus (HCV) serology. History of anxiety disorder, depression, bipolar disorder, schizophrenia and suicide attempts (at any time in the patient's life) was extracted using the relevant ICD-10 codes.

To increase exhaustiveness, the following data were also cross-checked using the medical files of both cases and controls: country of origin, level of education, socio-professional category, marital status, having one or more children, and history of anxiety disorder, depression, bipolar disorder, schizophrenia, suicide attempts and use of psychotropic drugs (anxiolytics, anti-depressive, neuroleptics and thymoregulators) at the index date.

Mean \pm standard deviation (SD) and number (percentage) were used to describe quantitative and qualitative population characteristics, respectively. Covariates were compared using Fisher's exact test, the χ^2 test, the Mann–Whitney *U*-test or Student's *t*-test, as appropriate. Multiple imputation, which is an established method for handling missing data, was performed using the multiple imputation procedure [13]. We created 30 data sets in which missing data were imputed per each PLHIV's set of available covariates, including all covariates included in the analysis model, and inclusion as a case or a control. Auxiliary covariates were also included in the imputation model. It was decided not to impute the level of education and socio-professional category in view of a very high rate of missing data. Missing data were assumed as missing at random. A fully conditional specification was used to impute missing data [14]. Univariable and multivariable conditional logistic regression models were then constructed for each created data set. Covariates with a *P*-value < 0.20 by univariate analyses were included in

the final multivariable model then selected using a manual backward selection method. Because we used incidence density sampling for control selection, the estimated odds ratios in this study were unbiased estimates of relative risks (RRs) [15]. Thus, the RR, adjusted relative risk (aRR) and 95% CI were generated for each imputed data set, and the results were then aggregated according to Rubin's rule [16].

Statistical significance was considered to have been reached at two-tailed $P < 0.05$. SAS software, version 9.4 (SAS Institute Inc., Cary, NC), was used for all statistical analyses.

This study was performed in accordance with the Declaration of Helsinki and current French legislation relating to biomedical research. All patients were included in the cohort after receiving oral information and giving written consent. All patient information was entered in the database using nonidentifying, coded identification numbers. The cohort was approved by the French national authority for the protection of privacy and personal data (Commission Nationale Informatique et Liberté).

Results

Among the 34 308 PLHIV included in the Dat'AIDS cohort between January 2000 and July 2013, 2438 deaths (7.1%) were reported, of which 99 were suicide (4.1%). The incidence of suicide mortality was 45.9/100 000 patient-years for the period 2000–2006, and 46.5/100 000 patient-years for the period 2007–2013.

This study included a total of 349 patients, of whom 70 died by suicide and 279 were controls (69 cases had four controls, and one case had three controls) for whom the medical files could be checked. A higher rate of men who have sex with men (MSM) was the only significant characteristic varying between the excluded ($n = 29$) and included ($n = 70$) patients (69 vs. 43%, respectively; $P = 0.02$). Detailed characteristics of the patients are presented in Table 1. The median delay between the suicide date and the characteristics collected was < 6 months for alcohol consumption, smoking status, drug use, CD4 cell count and HIV viral load and < 3 years for HCV serology. Patients who died by suicide had a mean (\pm SD) age of 44.9 ± 9.3 years and were mostly men (80%), and less than half were MSM (43%). They were born in France in 91% of cases, were living alone in 73% of cases and had children in 26% of cases. Most of them were receiving cART (83%), with 7% receiving efavirenz (EFV)-based cART. The mean CD4 cell count was > 350 cells/ μ L and HIV viral load was undetectable in 62% of cases. Active or substituted drug consumption was noted in 25% of cases overall. HCV serology was positive in 60.0% of

patients with active or substituted drug abuse, in 71.4% of patients with former drug abuse and in 6.5% of patients with no drug abuse. A history of a previous psychiatric disorder was reported in 53 cases (76%).

In the univariable analysis, being born in France, not having children, living alone, having active or substituted drug consumption (versus never or former), having alcohol intake > 20 g/day or a history of alcohol abuse, having a low CD4 cell count at the index date, and having a history of anxiety disorder, depressive disorder, schizophrenia, suicide attempt or psychotropic drug intake (whatever the class of psychotropic) were associated with death from suicide, whereas age, gender, risk category for HIV infection, tobacco consumption, cART use, AIDS status, nadir CD4 cell count, HIV viral load and positive HCV serology were not (Table 2).

In the multivariable analysis, not having children, active or substituted drug consumption, alcohol intake > 20 g/day or a history of alcohol abuse, a history of depressive disorder and/or of attempted suicide and psychotropic drug intake remained significantly associated with death by suicide (Table 2). As living alone could be related to not having children, we repeated the multivariate analysis including 'living alone' in the multivariable model. This analysis revealed the same independent risk factor for having children (RR 0.27; 95% CI 0.10–0.71; $P = 0.008$).

Discussion

In this nested case-control study performed in a large French cohort of PLHIV in the cART era, we found that most factors associated with suicide mortality among PLHIV were similar to those of the general population [10,17,18]. Not having children and psychological morbidity such as active or substituted drug consumption, alcohol intake > 20 g/day or a history of abuse, a history of depressive disorder and/or of attempted suicide, and intake of psychotropic drugs were significantly associated with death by suicide, whereas age, gender, country of birth, positive HCV serology and HIV-related factors, such as AIDS status, use of cART, nadir and current CD4 counts and HIV viral load, were not found to be associated with an increased risk of suicide.

In the general population, severe mental illness and substance use disorders have previously been associated with excess suicide mortality [17,19]. In a British cohort of 18 201 patients with severe mental illness, the age- and sex-standardized mortality ratio for suicide was seven-fold higher than in the general population [19]. In a cohort of > 4.8 million men and women receiving Veterans Health Administration care in the USA, a current diagnosis of any

Table 1 Baseline characteristics of 70 people living with HIV PLHIV who died by suicide and 279 controls from the Dat'AIDS cohort

	Controls (<i>n</i> = 279)	Missing	Cases (<i>n</i> = 70)	Missing
Age (years)	45.5 ± 10.4	0	44.9 ± 9.3	0
Male gender	192 (68.8)	0	56 (80.0)	0
Level of education				
Primary/secondary school	73 (56.2)	149	8 (34.8)	47
Secondary school diploma or higher	57 (43.9)		15 (65.2)	
Socioprofessional category				
Management, liberal professions	26 (11.4)	51	11 (21.2)	18
Other	202 (88.6)		41 (78.8)	
HIV transmission group				
Heterosexual	116 (41.6)	0	21 (30.0)	0
MSM	105 (37.6)		30 (42.9)	
IDU	38 (13.6)		15 (21.4)	
Other	20 (7.2)		4 (5.7)	
Positive HCV serology	50 (19.9)	28	17 (29.8)	13
Undetectable HIV viral load (< 200 copies/mL)	196 (71.3)	4	43 (62.3)	1
CD4 count (cells/μL)	565 ± 303	0	487 ± 319	0
≥200 cells/μL	244 (87.4)		58 (82.9)	
CD4 nadir < 200 cells/μL	136 (48.8)	0	34 (47.2)	0
On antiretroviral therapy	241 (86.4)	0	58 (82.9)	0
Receiving efavirenz	32 (11.5)		5 (7.1)	
AIDS	66 (23.7)	0	19 (27.1)	0
Time since HIV diagnosis (years)	13.0 ± 6.7	0	13.1 ± 6.7	0
Time since ART initiation (years)	9.6 ± 5.4	22	9.2 ± 5.7	6
Having children	107 (43.0)	30	16 (25.8)	8
Living alone	151 (57.0)	14	50 (73.5)	2
Country of birth, France	212 (76.0)	0	64 (91.4)	0
History of anxiety disorder	62 (22.3)	1	29 (42.0)	1
History of depressive disorder	66 (23.8)	1	44 (63.8)	1
History of bipolar disorder	5 (1.8)	1	3 (4.4)	1
History of schizophrenia	9 (3.2)	1	8 (11.6)	1
History of attempted suicide	11 (3.6)	2	16 (22.9)	0
Number of suicide attempts, if any				
1	9 (90.0)	0	10 (62.5)	0
2	1 (10.0)		3 (18.8)	
3	0 (0.0)		3 (18.8)	
Drug abuse				
No	200 (76.3)	17	38 (60.3)	7
Active or substituted	25 (9.6)		16 (25.4)	
Former	37 (14.1)		9 (14.3)	
Tobacco use				
Never smoked	101 (38.4)	16	22 (36.1)	9
Former smoker	48 (18.3)		6 (9.8)	
Current smoker	114 (43.4)		33 (54.1)	
Alcohol intake				
Non drinker	121 (47.5)	24	21 (36.2)	12
Former drinker	13 (5.1)		9 (15.5)	
Occasional drinker	31 (12.2)		6 (10.3)	
Drinker, ≤ 20 g/day	56 (22.0)		4 (6.9)	
Drinker, > 20 g/day	34 (13.3)		18 (31)	
Psychotropic drug use	48 (17.8)	9	44 (67.7)	5
Antidepressant use	19 (7.6)	10	27 (42.2)	6
Anxiolytic use	30 (11.2)	10	32 (50.0)	6
Neuroleptic use	10 (3.7)	10	11 (17.2)	6
Thymoregulator use	0 (0.0)	10	1 (1.6)	6

Results are expressed as mean (± standard deviation) or *n* (%).

ART, antiretroviral treatment; HCV, hepatitis C virus; IDU, injecting drug user; MSM, men who have sex with men; PLHIV, people living with HIV.

substance use disorder, and the specific current diagnoses of alcohol, cocaine, cannabis, opioid, amphetamine or other psychostimulant, sedative hypnotic and anxiolytic use disorders were all associated with an elevated risk of

suicide in both men and women [17]. Among PLHIV, histories of injecting drug use, psychiatric treatment and suicidal ideation have also been independently associated with suicide mortality [1,9,10,20].

Table 2 Univariable and multivariable analysis of factors associated with dying by suicide among French people living with HIV in the Dat'AIDS cohort from January 2000 to July 2013

	Univariable analysis			Multivariable analysis		
	RR	95% CI	P-value	aRR	95% CI	P-value
Age	0.99	0.97–1.02	0.61			
Gender, male	1.83	0.96–3.47	0.06			
Country of birth, France	3.50	1.44–8.50	0.006			
Having children	0.47	0.25–0.90	0.02	0.26	0.10–0.70	0.008
Living alone	2.01	1.10–3.66	0.02			
HIV transmission group						
Heterosexual versus all	0.58	0.33–1.04	0.07			
Homosexual versus all	1.29	0.73–2.29	0.39			
Other versus all	0.78	0.25–2.41	0.67			
Drug addiction						
No	1	–	–	1	–	–
Active or substituted	3.54	1.63–7.67	0.001	3.29	1.10–9.85	0.03
Former	1.43	0.59–3.45	0.43	1.65	0.50–5.38	0.41
Alcohol intake > 20 g/day	4.33	2.27–8.27	< 10 ⁻⁴	3.56	1.43–8.88	0.007
Tobacco smoking, current	1.56	0.88–2.77	0.13			
Positive HCV serology	1.59	0.80–3.18	0.19			
AIDS	1.19	0.66–2.14	0.56			
On antiretroviral therapy	0.73	0.35–1.56	0.42			
CD4 count, per 50 cells/ μ L increase	0.95	0.91–1.00	0.047			
CD4 count nadir, per cells/ μ L increase	1.01	0.94–1.09	0.79			
HIV viral load < 200 copies/mL	0.63	0.35–1.13	0.12			
History of anxiety disorder	2.60	1.46–4.62	0.001			
History of bipolar disorder	2.89	0.56–14.91	0.21			
History of depressive disorder	7.08	3.71–13.50	< 10 ⁻⁴	3.76	1.49–9.50	0.007
History of schizophrenia	4.40	1.50–12.91	0.007			
History of attempted suicide	10.27	3.72–28.35	< 10 ⁻⁴	5.93	1.58–22.24	0.008
Psychotropic drug intake	13.27	6.18–28.51	< 10 ⁻⁴	6.37	2.56–15.85	< 10 ⁻⁴
Antidepressants	9.55	4.44–20.55	< 10 ⁻⁴			
Anxiolytics	8.72	4.21–18.05	< 10 ⁻⁴			
Antipsychotics	5.11	2.04–12.79	0.0005			
Thymoregulators	3 409 771.69	< 0.0001–> 999.9	–			

aRR, adjusted relative risk; CI, confidence interval; HCV, hepatitis C virus; RR, relative risk.

Between 1990 and 2010, a decrease of > 20% in suicide mortality in the general population was observed in France and in some other European countries [21]. In the multicohort European DAD study among PLHIV, rates of suicide fell by around half between the early cART era (1999–2000) and the 2007–2008 period [22]. In contrast, since 2000, the rate of suicide among PLHIV in France has remained stable, accounting for 4%, 5% and 5% of causes of death in 2000, 2005 and 2010, respectively [23]. Furthermore, in the cART era (2010), the rate of suicide, which was the second leading cause of death among PLHIV with immunovirological success (12.5%), was lower in patients who were not controlled immunologically and in patients with immunovirological failure (2% and 4%, respectively) [8]. Similar results were observed in our cohort, with an incidence of suicide mortality for the periods 2000–2006 and 2007–2013 of 45.9 and 46.5/100 000 patient-years, respectively. The lack of any decrease in suicide mortality since the onset of the cART era could be explained by the high prevalence of

psychiatric morbidity in PLHIV [24,25]. In line with other studies, we found a high prevalence of depressive disorders, drug abuse, psychotropic drug intake, history of suicide attempts and alcohol abuse, both among patients who died by suicide and among controls [9,10,25,26]. A history of depressive disorder was observed in 64% of patients who died by suicide, and in 24% of controls. These results are in line with a study on a representative sample of 2392 PLHIV conducted in France in 2011 in whom the prevalence of a major depressive episode during the previous 12 months was 28.1% [26]. Compared with the general population by sex, regardless of sexual orientation and origin, major depressive episode prevalence was 5.1-fold higher in HIV-infected MSM [95% CI 3.9–6.6], 3.1-fold higher in non-sub-Saharan African (SSA) heterosexual men (95% CI 2.2–4.4), 1.6-fold higher in SSA migrant men (95% CI 0.9–2.6), 2.6-fold higher in non-SSA heterosexual women (95% CI 2.1–3.3), and 1.9-fold higher in SSA migrant women (95% CI 1.5–2.5) [26]. In this same cross-sectional survey, a suicide risk, defined

as having either thought about or planned to commit suicide, or attempted suicide during the previous 12 months was reported by 6.3% of PLHIV [25]. In our study, a history of attempted suicide was reported in 10% of patients overall, but in 23% of patients who died by suicide and 4% of controls. In another cross-sectional survey conducted in France in 2003, among 2932 PLHIV, 22% of participants who completed a face-to-face questionnaire reported having attempted suicide at least once during their life [27]. Furthermore, harmful alcohol consumption, regular benzodiazepine use and polydrug use were reported in 13%, 16% and 6% of participants, respectively, using the CAGE score in the same survey [28,29].

Living alone and/or reporting a feeling of loneliness has been associated with suicide mortality and/or suicide risk among PLHIV [9,25]. In our study, both living alone and not having children were highly prevalent in both patients who died by suicide (73% and 74%, respectively) and controls (57% and 57%, respectively), and were also associated with suicide mortality in univariable analysis. However, only the factor of not having children remained significantly associated with suicide in multivariable analysis, even after adjusting the multivariate model for living alone.

Male sex and age are both independent risk factors for suicide mortality in Western countries, including France [7]. These factors have also been associated with suicide mortality in the Swiss cohort [1]. In line with data on suicide in the general population (73%), as well as in PLHIV (74%), the majority of patients who died by suicide in our study were men (80%) [6,7]. However, although controls were selected among all PLHIV being actively followed at the index date, and compared with patients who died by suicide, matched only for the time since HIV diagnosis (in 5-year periods) and clinical centre, and not for age and gender, we did not find male sex and age to be significantly associated with suicide, possibly because of insufficient statistical power. Nonetheless, male sex was also not found to be associated with suicide in the Canadian HOMER PLHIV cohort [10]. While MSM have been reported to have a higher suicide risk, sexual orientation was not associated with suicide in our study [25].

In Western countries, suicide mortality in the general population has been found to be lower in ethnic minority groups [19,30,31]. Among PLHIV in the Swiss cohort, Swiss nationality was associated with a more than two-fold increase in the risk of suicide [1]. In our study, in which 76% of patients were born in France, this factor was not associated with increased suicide mortality. However, actual ethnicity was not evaluated as such in our study (only the place of birth), because the collection of data regarding ethnicity is not permitted in France.

An association between increased CD4 cell count and a reduced risk of suicide mortality has previously been observed in Swiss and Australian cohorts [1,9]. In contrast, in the Canadian HOMER cohort, having no experience with an AIDS-defining illness was independently associated with suicide mortality [10]. In our study, none of the HIV-related factors were associated with suicide mortality. This could be explained by a high mean duration of HIV infection (> 13 years), and the large proportion of patients with immunovirological control of HIV disease, with CD4 count > 200 cells/ μ L and undetectable HIV viral load in 86% and 68% overall, respectively. Among the antiretroviral drugs widely used in France before 2013, discontinuation of antiretroviral regimens because of neuropsychiatric adverse events was observed almost exclusively with EFV-based regimens [32]. Initial treatment with an EFV-based regimen was reported to be associated with a two-fold increase in the risks of suicidal ideation and attempted or completed suicide compared with a regimen without EFV in four randomized trials [20]. In our study, only 13% of patients overall and 7% of patients who died by suicide were receiving an EFV-based regimen, highlighting clinicians' awareness of EFV's neuropsychiatric side effects, precluding its prescription in patients with psychological morbidity.

The main strength of our study is that it provides data from a large nationwide prospective cohort study of > 33 000 PLHIV followed in routine practice in France. Furthermore, this study evaluated almost all factors potentially associated with suicide. This study included all patients for whom the medical file could be carefully checked, ensuring greater accuracy of the data collected and limiting the number of missing data. However, this study also has a number of limitations that should be underlined. PLHIV frequently have a lower socio-economic status and experience greater social discrimination than the HIV-uninfected population, and such factors have been associated with psychiatric morbidity including suicide [9,12,25–27]. In addition, a higher education level has also been associated with a lower risk of suicide [33,34]. The absence of data relating to material deprivation and experience of discrimination, and a high number of missing data concerning level of education and employment, both in our database and in the patients' medical files, precluded evaluation of these variables. The second limitation concerns the actual number of patients who died by suicide, which may have been underestimated, given that the cause of deaths remained unknown in 19% of all cases in our cohort. Indeed, no data on the autopsy rate are available in our database, although autopsy studies have revealed that 9.4% of deceased PLHIV had committed suicide [35]. Thirdly, patients with a

psychiatric history were identified by the presence of ICD-10 codes, and this assumes that the diagnoses were correctly established by clinicians.

In conclusion, identifying risk factors associated with dying by suicide in PLHIV is necessary to improve quality of care, and may help to identify patients who could benefit the most from interventions aimed at preventing suicide. In the cART era, HIV-related factors are no longer associated with a higher risk of suicide mortality. Suicide prevention measures should target PLHIV with the psychological morbidities identified in our cohort.

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Author contributions

All authors participated in the design of the study protocol and data collection. MH and MD performed the data management and statistical analyses. MH, MD and FBS wrote the first draft of the manuscript. All authors participated in interpretation of the data and writing of the final manuscript and all authors approved the final manuscript. FBS and MD were responsible for the overall supervision of the study.

Appendix: The Dat'AIDS Study Group

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References

- 1 Keiser O, Spoerri A, Brinkhof MWG *et al.* Suicide in HIV-infected individuals and the general population in Switzerland, 1988–2008. *Am J Psychiatry* 2010; **167**: 143–150.
- 2 Jia C-X, Mehlum L, Qin P. AIDS/HIV infection, comorbid psychiatric illness, and risk for subsequent suicide: a nationwide register linkage study. *J Clin Psychiatry* 2012; **73**: 1315–1321.
- 3 Aldaz P, Moreno-Iribas C, Egüés N *et al.* Mortality by causes in HIV-infected adults: comparison with the general population. *BMC Public Health* 2011; **11**: 300.
- 4 Rice BD, Smith RD, Delpech VC. HIV infection and suicide in the era of HAART in England. *Wales and Northern Ireland. AIDS* 2010; **24**: 1795–1797.
- 5 Marin B, Thiébaud R, Bucher HC *et al.* Non-AIDS-defining deaths and immunodeficiency in the era of combination antiretroviral therapy. *AIDS* 2009; **23**: 1743–1753.
- 6 Morlat P, Roussillon C, Henard S *et al.* Causes of death among HIV-infected patients in France in 2010 (national survey): trends since 2000. *AIDS* 2014; **28**: 1181–1191.
- 7 Suicide : connaître pour prévenir. Dimensions nationales, locales et associatives - 2e rapport/février 2016 - Observatoire national du suicide (ONS) - Ministère des Solidarités et de la Santé. 2016. <http://drees.solidarites-sante.gouv.fr/etudes-et-statistiques/la-drees/observatoire-national-du-suicide-ons/article/suicide-connaître-pour-prevenir-dimensions-nationales-locales-et-associatives> (accessed 5 September 2017).
- 8 Goehring F, Bonnet F, Salmon D *et al.* Causes of Death in HIV-Infected Individuals with Immunovirologic Success in a National Prospective Survey. *AIDS Res Hum Retroviruses* 2017; **33**: 187–193.

- 9 McManus H, Petoumenos K, Franic T *et al.* Determinants of suicide and accidental or violent death in the Australian HIV Observational Database. *PLoS ONE* 2014; 9: e89089.
- 10 Gurm J, Samji H, Nophal A *et al.* Suicide mortality among people accessing highly active antiretroviral therapy for HIV/AIDS in British Columbia: a retrospective analysis. *CMAJ Open* 2015; 3: E140–E148.
- 11 Pugliese P, Cuzin L, Cabié A *et al.* A large French prospective cohort of HIV-infected patients: the Nadis Cohort. *HIV Med* 2009; 10: 504–511.
- 12 Protopopescu C, Raffi F, Brunet-François C *et al.* Incidence, medical and socio-behavioural predictors of psychiatric events in an 11-year follow-up of HIV-infected patients on antiretroviral therapy. *Antivir Ther (Lond)* 2012; 17: 1079–1083.
- 13 Lee KJ, Simpson JA. Introduction to multiple imputation for dealing with missing data. *Respirology* 2014; 19: 162–167.
- 14 White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011; 30: 377–399.
- 15 King G, Zeng L. Estimating risk and rate levels, ratios and differences in case-control studies. *Stat Med* 2002; 21: 1409–1427.
- 16 Rubin DB, Schenker N. Multiple imputation in health-care databases: an overview and some applications. *Stat Med* 1991; 10: 585–598.
- 17 Bohnert KM, Ilgen MA, Louzon S, McCarthy JF, Katz IR. Substance use disorders and the risk of suicide mortality among men and women in the US Veterans Health Administration. *Addiction* 2017; 112: 1193–1201.
- 18 Qin P, Agerbo E, Mortensen PB. Suicide risk in relation to socioeconomic, demographic, psychiatric, and familial factors: a national register-based study of all suicides in Denmark, 1981–1997. *Am J Psychiatry* 2003; 160: 765–772.
- 19 Das-Munshi J, Chang C-K, Dutta R *et al.* Ethnicity and excess mortality in severe mental illness: a cohort study. *Lancet Psychiatry* 2017; 4: 389–399.
- 20 Mollan KR, Smurzynski M, Eron JJ *et al.* Association between efavirenz as initial therapy for HIV-1 infection and increased risk for suicidal ideation or attempted or completed suicide: an analysis of trial data. *Ann Intern Med* 2014; 161: 1–10.
- 21 Fond G, Llorca P-M, Boucekine M *et al.* Disparities in suicide mortality trends between United States of America and 25 European countries: retrospective analysis of WHO mortality database. *Sci Rep* 2016; 6: 20256.
- 22 Data Collection on Adverse Events of Anti-HIV drugs (D:A:D) Study Group, Smith C, Sabin CA *et al.* Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D Study. *AIDS* 2010; 24: 1537–1548.
- 23 Lewden C, May T, Rosenthal E *et al.* Changes in causes of death among adults infected by HIV between 2000 and 2005: The “Mortalité 2000 and 2005” surveys (ANRS EN19 and Mortavic). *J Acquir Immune Defic Syndr* 2008; 48: 590–598.
- 24 Mirza RA, Eick-Cost A, Otto JL. The risk of mental health disorders among U.S. military personnel infected with human immunodeficiency virus, active component, U.S. Armed Forces, 2000–2011. *MSMR* 2012; 19:10–13.
- 25 Carrieri MP, Marcellin F, Fressard L *et al.* Suicide risk in a representative sample of people receiving HIV care: Time to target most-at-risk populations (ANRS VESPA2 French national survey). *PLoS ONE* 2017; 12: e0171645.
- 26 Feuillet P, Lert F, Tron L *et al.* Prevalence of and factors associated with depression among people living with HIV in France. *HIV Med* 2017; 18: 383–394.
- 27 Préau M, Bouhnik A-D, Peretti-Watel P, Obadia Y, Spire B. ANRS-EN12-VESPA Group. Suicide attempts among people living with HIV in France. *AIDS Care* 2008; 20: 917–924.
- 28 Michel L, Carrieri MP, Fugon L *et al.* Harmful alcohol consumption and patterns of substance use in HIV-infected patients receiving antiretrovirals (ANRS-EN12-VESPA Study): relevance for clinical management and intervention. *AIDS Care* 2010; 22: 1136–1145.
- 29 Roux P, Fugon L, Michel L *et al.* Determinants of benzodiazepine use in a representative population of HIV-infected individuals: the role of HIV status disclosure (ANRS-EN12-VESPA study). *AIDS Care* 2011; 23: 1163–1170.
- 30 Chang M-H, Moonesinghe R, Athar HM, Truman BI. Trends in Disparity by Sex and Race/Ethnicity for the Leading Causes of Death in the United States–1999–2010. *J Public Health Manag Pract* 2016; 22 (Suppl 1): S13–S24.
- 31 Bauwelincx M, Deboosere P, Willaert D, Vandenheede H. Suicide mortality in Belgium at the beginning of the 21st century: differences according to migrant background. *Eur J Public Health* 2017; 27: 111–116.
- 32 de Boissieu P, Dramé M, Raffi F *et al.* Long-term efficacy and toxicity of abacavir/lamivudine/nevirapine compared to the most prescribed ARV regimens before 2013 in a French Nationwide Cohort Study. *Medicine (Baltimore)* 2016; 95: e4890.
- 33 Han B, Kott PS, Hughes A, McKeon R, Blanco C, Compton WM. Estimating the rates of deaths by suicide among adults who attempt suicide in the United States. *J Psychiatr Res* 2016; 77: 125–133.
- 34 Kimura T, Iso H, Honjo K *et al.* Educational levels and risk of suicide in Japan: The Japan Public Health Center Study (JPHC) Cohort I. *J Epidemiol* 2016; 26: 315–321.
- 35 Catalan J, Harding R, Sibley E, Clucas C, Croome N, Sherr L. HIV infection and mental health: suicidal behaviour—systematic review. *Psychol Health Med* 2011; 16: 588–611.