

## Supplemental text 1. Systematic Review Protocol

### Suicidal ideation, suicide attempts, and suicide deaths in persons with HIV: a systematic review and meta-analysis

#### Background

Since its discovery in the 1980s, Human Immunodeficiency Virus (HIV) continues to carry a significant global burden of disease. While the disease remains incurable, anti-retroviral therapy (ART) has been effective in controlling disease progression, improving quality of life, and prolonging longevity. In 2018, the World Health Organization and United Nations Program on HIV/AIDS (UNAIDS) approximated that globally approximately 40 million people are living with HIV/AIDS (PLWHA). Depression is one of the most common comorbidities of PLWHA, with seropositive individuals reporting higher rates of depression than seronegative counterparts<sup>1-3</sup>. Depression in affected individuals remains cyclical, chronic, poorly-treated and is correlated with poorer clinical outcomes with lack of care retention, higher viral load, and increased mortality rates<sup>1,4</sup>. Unfortunately, untreated depression has led to exceptionally high rates of suicide within this vulnerable population. Data shows that patient suicide rates within the first year of HIV diagnosis exceed that of the general population<sup>5-7</sup>. In this meta-analysis, we sought to explore the relationship between HIV and suicide risk. The primary objective was to examine the incidence of suicide completion in PLWHA and to delineate the associated risk factors. Furthermore, we examined the incidence and prevalence of suicide ideation and attempts within PLWHA. This comprehensive statistical review provides a snapshot of the global health burden associated with the psychosocial effects of HIV on affected patients.

**PROSPERO registration number: CRD42020161501**

#### Objectives

The objective of this review was to ascertain the incidence of suicide ideation, attempt, and completion in PLWHA. Specific aims were:

- (i) To examine the global incidence of suicide completion in PLWHA
- (ii) To examine the global prevalence of suicide ideation, attempt, and completion in PLWHA
- (iii) To delineate risk factors associated with suicide ideation, attempt and completion in PLWHA

#### Search Strategy

##### *Inclusion criteria*

- Reported on the reporting suicide rates in PLWHA
- Published from inception to before February 1, 2020
- Published in any language

##### *Exclusion criteria*

- Not conducted in humans
- Case reports and studies that did not report the incidence of suicide, suicide attempts, or suicide ideations were excluded
- Meeting abstracts, review papers, and commentaries

#### Database searches

The databases searched included:

- PubMed
- MEDLINE
- Cochrane Library

#### Search Terms

Our keyword search was based on Medical Subject Headings (MeSH) with various combinations of “Suicide\*”, OR “Depression\*”, OR “Suicide attempt\*”, OR “Suicidal Ideation\*”, OR “Suicide Completion\*” OR “Mental Illness\*” OR “Anxiety\*”, AND “HIV\*” “Human immunodeficiency syndrome” “AIDS” or “Acquired Immunodeficiency Syndrome”.

### **Title and abstract screening**

We searched the databases listed above. The citations were downloaded into the Endnote software. We excluded duplicate articles. Four reviewers independently screened titles and abstracts and documented, with reasons, studies were excluded from the review.

### **Full-text screening and data extraction**

We extracted data from eligible the papers identified during the abstract screening step. We extracted the following information: country of study, year published, study period, total sample size, number of patients with suicidal ideation, number of patients with suicidal attempt, number of patients with suicidal completion, percent of study sample that was male, mean age, percent of population with HAART, average CD4 count, mean viral load, percent with reported depression and percent of individuals with AIDS.

### **Assessment of Methodological Quality of the Papers**

Four reviewers independently assessed the quality of the papers included in the review using a standardized form.

### **Data Analysis**

We used the `metaprop` function of the *meta*-package in R Statistical Software for analysis. The primary outcome was the overall rate of suicide completion, suicide attempts, and suicide ideation in PLWHA. We extracted rates from each manuscript. The R package was used to create a random-effects model with logit transformation of proportions for pooling of studies. The confidence intervals were calculated using the exact binomial (Clopper-Pearson) interval method. The between-study heterogeneity was assessed using the  $I^2$  statistic, expressed as % (low (25%), moderate (50%), and high (75%)) and Cochrane’s  $Q$  statistic (significance level  $< 0.05$ ). We performed subgroup meta-analyses to look at geographical differences in the suicide risk. We conducted a meta-regression analysis, using study level median age, and study level gender proportions, year of study, the proportion of study population with AIDS, HAART proportions, mean/median CD4 counts and percentage of the study population with depression diagnosis. We report absolute differences (per 1000) in the overall probability of suicide. The Egger’s test and funnel plots were used to assess small sample size bias.

Supplemental Table 1: PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	p.1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	p.3
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	p.4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	p.5
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	S1Text
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	p.6 and p.7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	p.6 and p.7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	p. 6 and p.7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	p. 6 and p.7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	p. 6 and p.7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	p.6 and p.7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	p. 7 and p.8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	p.6 and p.7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.	p.8

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). – not addressed as much in methods – should we add more?	Suppl Fig 2 and 4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	p.7, p.8 and p.11
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened (should be in methods), assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	p.6 p.7 and Fig 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. – this would be all figures correct?	p.8 and S3 Table
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Suppl Table 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Fig 2, Fig 3, Fig 4, Fig 5, Fig 6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	p.9 and p.10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Suppl Figure 2 and 4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	p.7, p.8 and Table 2
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	p. 13, p.14 and p.15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	p.14 and p.15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	p. 13,14 and p.15
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	p. 17

**Supplemental Table 2: Literature search strategy**

Database	Search Terms
<b>MEDLINE</b>	PubMed and OVID (MEDLINE) search terms 1. (("HIV"[Mesh] OR "Acquired Immunodeficiency Syndrome"[Mesh])) 2. (("Suicide"[Mesh] OR "Suicide, Attempted"[Mesh] OR "Suicide, Completed"[Mesh] OR "Suicidal, Ideation"[Mesh]) 3. (("Mental Disorder "[Majr] OR "Depressive Disorders"[Majr])) 4. 1 AND 2 5. 1 AND 3
<b>Cochrane Library</b>	1. (("HIV"[Keyword] OR "Acquired Immunodeficiency Syndrome"[ Keyword])) 2. (("Suicide"[ Keyword] OR "Suicide, Attempted"[ Keyword] OR "Suicide, Completed"[ Keyword] OR "Suicidal, Ideation"[ Keyword]) 3. (("Mental Disorder "[Majr] OR "Depressive Disorders"[Majr])) 4. 1 AND 2 5. 1 AND 3
<b>SCOPUS</b>	1. (("HIV"[Keyword] OR "Acquired Immunodeficiency Syndrome"[ Keyword])) 2. (("Suicide"[ Keyword] OR "Suicide, Attempted"[ Keyword] OR "Suicide, Completed"[ Keyword] OR "Suicidal, Ideation"[ Keyword]) 3. (("Mental Disorder "[Majr] OR "Depressive Disorders"[Majr])) 4. 1 AND 2 5. 1 AND 3
<b>JOANNA BRIGGS INSTITUTE</b>	1. (("HIV"[Keyword] OR "Acquired Immunodeficiency Syndrome"[ Keyword])) 2. (("Suicide"[ Keyword] OR "Suicide, Attempted"[ Keyword] OR "Suicide, Completed"[ Keyword] OR "Suicidal, Ideation"[ Keyword]) 3. (("Mental Disorder "[Majr] OR "Depressive Disorders"[Majr])) 4. 1 AND 2 5. 1 AND 3

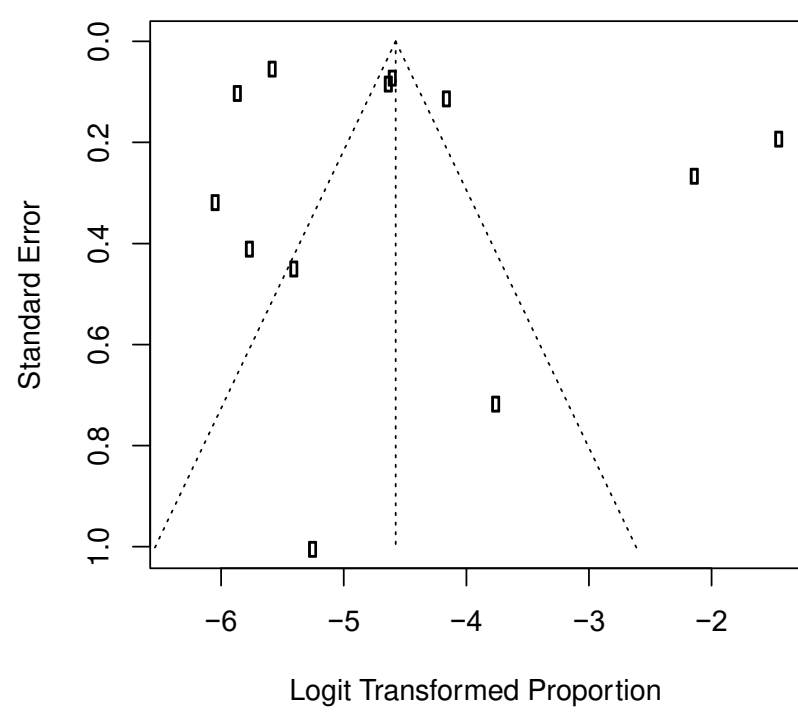
**Supplemental Table 3.** Depicts the quality assessment of studies using the Newcastle-Ottawa Scale and the GRADE quality of evidence. This includes 27 cross-sectional, 7 prospective cohort, 5 retrospective cohort, and 1 nested case-control study.

Author Year of Publication	Type of Study	Sum	Quality	Selection				Comparability	Outcome/Exposure			GRADE QoE
				1	2	3	4	5	6	7	8	
Carrieri 2017	Cross-sectional	9	High (>7)	1	1	1	2	2	1	1	0	Moderate
Cochand 1998	Cross-sectional	6	Moderate (5-7)	0	0	1	2	1	1	1	0	Low
Cooperman 2005	Cross-sectional	7	Moderate (5-7)	1	0	1	2	2	1	0	0	Low
Dannenberg 1996	Prospective	6	Moderate (5-7)	0	1	1	1	1	1	0	1	Moderate
de Almeida 2016	Cross-sectional	7	Moderate (5-7)	1	0	0	2	2	1	1	0	Very low
Ferlatte 2017	Cross-sectional	6	Moderate (5-7)	1	0	1	1	1	1	1	0	Low
Gielen 2005	Cross-sectional	6	Moderate (5-7)	1	0	1	2	1	1	0	0	Low
Grassi 2001	Cross-sectional	7	Moderate (5-7)	1	0	1	2	1	1	1	0	Low
Gurm 2015	Retrospective	6	Moderate (5-7)	1	1	1	0	2	1	0	0	Moderate
Heckman 2002	Cross-sectional	7	Moderate (5-7)	1	1	1	2	1	1	0	0	Low
Hentzien 2018	Nested Case-Control	8	High (>7)	1	1	1	0	2	1	1	1	Moderate
Hsing-Fei Lu 2018	Cross-sectional	8	High (>7)	1	0	1	2	2	1	1	0	Moderate
Jovet-Toledo 2014	Cross-sectional	8	High (>7)	1	1	1	2	1	1	1	0	Moderate
Kalichman 2000	Cross-sectional	4	Low (1-4)	0	0	0	2	1	1	0	0	Moderate
Kalungi 2017	Cross-sectional	7	Moderate (5-7)	1	1	0	2	1	1	1	0	Low
Keiser 2010	Prospective	8	High (>7)	1	1	1	1	2	1	1	0	Moderate
Kelly 1998	Cross-sectional	8	High (>7)	1	0	1	2	2	1	1	0	Moderate
Kreniske 2019	Prospective	4	Low (1-4)	1	1	1	0	0	0	0	1	Low
López 2018	Cross-sectional	7	High (>7)	1	0	0	2	2	1	1	0	Very Low
Malbergier 2001	Cross-sectional	7	High (>7)	0	0	1	2	2	1	1	0	Moderate
Marzuk 1997	Cross-sectional	7	Moderate (5-7)	1	1	0	2	1	1	1	0	Moderate
May 2004	Cross-sectional	9	High (>7)	1	1	1	2	2	1	1	0	Moderate
Paparizos 2017	Retrospective	6	Moderate (5-7)	1	1	1	0	1	1	0	1	Low
Passos 2014	Cross-sectional	9	High (>7)	1	1	1	2	2	1	1	0	Moderate
Preau 2008	Cross-sectional	7	Moderate (5-7)	1	0	1	1	2	1	1	0	Low
Protopoescu 2012	Prospective	6	Moderate (5-7)	1	1	1	1	1	1	0	0	Low
Quintana-Ortiz 2008	Retrospective	6	Moderate (5-7)	1	1	1	0	2	0	0	1	Moderate
Rice 2010	Cross-sectional	7	Moderate (5-7)	1	1	1	2	0	1	1	0	Moderate
Rodriguez 2019	Prospective	4	Low (1-4)	0	1	1	0	1	1	0	0	Low
Roy 2003	Cross-sectional	6	Moderate (5-7)	0	1	1	2	0	1	1	0	Low
Scheer 2001	Cross-sectional	7	Moderate (5-7)	1	1	1	2	0	1	1	0	Moderate
Shim 2018	Cross-sectional	7	Moderate (5-7)	1	0	0	2	2	1	1	0	Moderate
Van Haastrecht 1994	Prospective	5	Moderate (5-7)	0	1	1	1	1	1	0	0	Very low
Walter 2016	Cross-sectional	7	Moderate (5-7)	0	0	0	2	2	1	1	0	Low
Wang 2018	Cross-sectional	6	Moderate (5-7)	1	0	0	2	1	1	1	0	Low
Wang 2019	Cross-sectional	5	Moderate (5-7)	1	0	0	1	1	1	1	0	Low
Yann Ruffieux 2019	Retrospective	8	High (>7)	1	1	1	0	2	1	1	1	Moderate
O'Donnell 2016	Retrospective	7	Moderate (5-7)	1	1	1	0	2	1	0	1	Moderate
Sherr 1995	Prospective	6	Moderate (5-7)	1	1	1	1	0	1	0	1	Moderate
Quinlivan 2017	Cross-sectional	7	Moderate (5-7)	0	0	1	2	2	1	1	0	Moderate

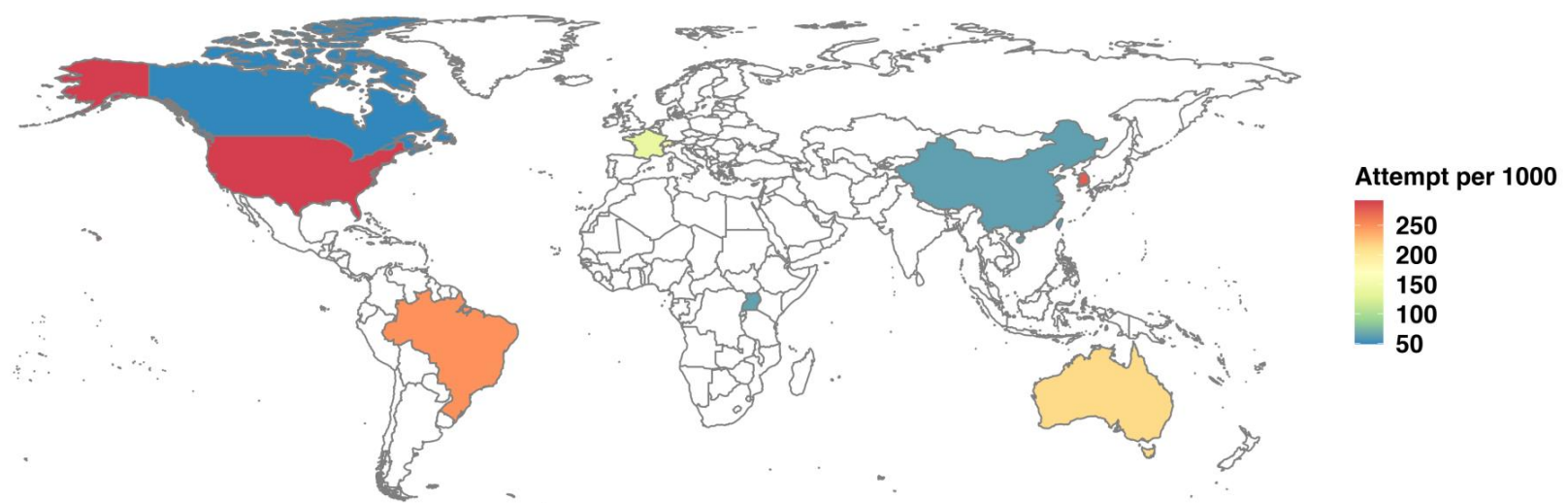
**Supplemental Table 4:** Meta-regression results: Advanced HIV disease (AIDS) was significantly associated with suicide completion.

Study-Level Predictors	Univariate absolute difference (per 1000) (95%CI) in incidence rate of suicide completion	p-value	Univariate absolute difference (per 1000) (95%CI) in prevalence of suicide attempts	p-value
Year of study	-0.8 (-7.5 to 5.9)	0.81	-1.7 (-9 to 5.6)	0.66
Study level-Male Gender (%)	0.25 (-4.2 to 4.7)	0.91	-0.3 (-1.9 to 1.3)	
Study-Level Mean or Median Age (y)	3.4 (-2.7 to 9.6)	0.28	-1.8 (-24.3 to 20.7)	0.88
Mean Age >40 years	2.3 (-1.4 to 4.2)	0.32	3 (-2 to 4.9)	0.43
Study-level AIDS frequency (%)	<b>3.4 (1.3 to 5.5)</b>	<b>0.001</b>	-0.3 (-2.4 to 1.8)	0.77
Study-level HAART (%)	N/A		-13.5 (-48.7 to 21.70)	0.45
Study-level mean CD4 count	-0.3 (-0.9 to 0.3)	0.32	N/A	
Study-level % of depression	N/A		0.94 (-5.7 to 7.5)	0.28
Study-quality, high versus low/medium	2.2 (-1.3 to 3.2)	0.40	1.3 (-2.3 to 4.3)	0.23

**Supplemental Figure 1:** Funnel plot of the studies on suicide completion. There is asymmetry indicative of small study bias.

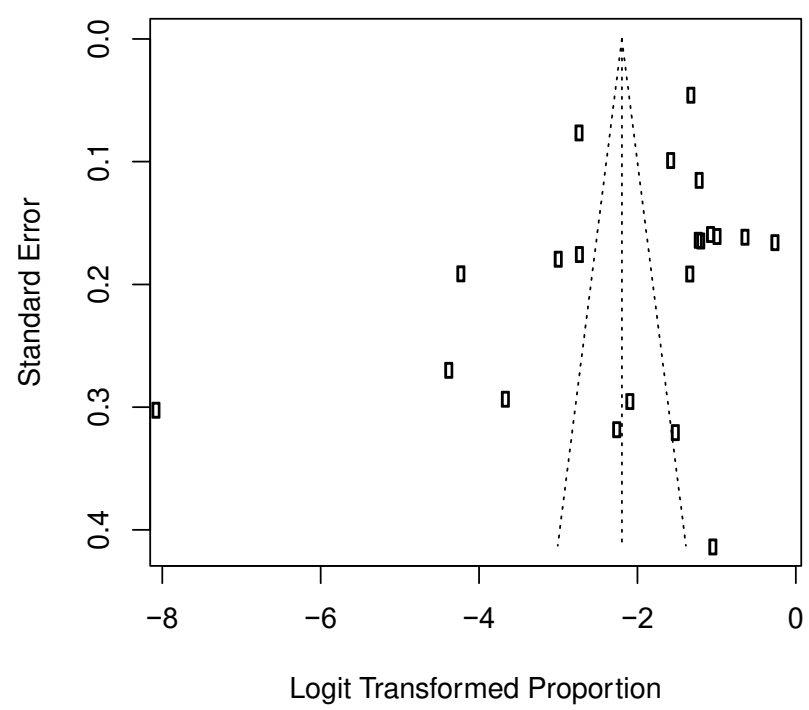


**Supplemental Figure 2:** Country-specific prevalence of suicide attempts in people living with HIV/AIDS.





**Supplemental Figure 3:** Funnel plot of the studies on suicide attempts. There is asymmetry indicative of small study bias



## References

1. Pence BW, Mills JC, Bengtson AM, et al. Association of Increased Chronicity of Depression With HIV Appointment Attendance, Treatment Failure, and Mortality Among HIV-Infected Adults in the United States. *JAMA Psychiatry* 2018; **75**(4): 379-85.
2. Nanni MG, Caruso R, Mitchell AJ, Meggiolaro E, Grassi L. Depression in HIV infected patients: a review. *Curr Psychiatry Rep* 2015; **17**(1): 530.
3. Rabkin JG. HIV and depression: 2008 review and update. *Curr HIV/AIDS Rep* 2008; **5**(4): 163-71.
4. Zuniga JA, Yoo-Jeong M, Dai T, Guo Y, Waldrop-Valverde D. The Role of Depression in Retention in Care for Persons Living with HIV. *AIDS Patient Care STDS* 2016; **30**(1): 34-8.
5. Aldaz P, Moreno-Iribas C, Egúés N, et al. Mortality by causes in HIV-infected adults: comparison with the general population. *BMC Public Health* 2011; **11**: 300.
6. Hentzien M, Cabie A, Pugliese P, et al. Factors associated with deaths from suicide in a French nationwide HIV-infected cohort. *HIV Med* 2018.
7. Jia CX, 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**(10): 1315-21.