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DEPRESSION IN HIV INFECTION: RELATED FACTORS AND EFFECTS ON QUALITY OF LIFE

Master's Thesis

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Running head: *Depression in HIV infection*

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Abstract

Having human immunodeficiency virus (HIV) infection means living with a highly stigmatized chronic disease for the rest of one's life. Previous studies have shown that depression rates are three times higher in people living with HIV (PLHIV) than in the general population. Aim of this study was to analyse mental health problems faced by PLHIV, mental health's relation to quality of life and what factors are associated with depressive symptoms. Eight hundred PLHIV participated in the cross-sectional study. Depression, using screening instrument EST-Q2, was identified in 53% of PLHIV, which is considerably higher than reported in other studies. Of those identified as having depression, only 22% were told by their physician that they have depression (indicating high under-diagnosing), and only 14% had taken antidepressants. Thirty-six percent of participants reported having had suicidal ideation. Depression was strongly correlated with anxiety, fatigue and insomnia. Being depressed decreased quality of life in all aspects measured with WHOQoL-HIV BREF. According to stepwise regression analyses, frequency of depressive mood was associated with unemployment, recent and former injecting drug use, having children, age and having completed 9 years of education. No infection related indicators (e.g., CD4 cell count, viral load, antiretroviral therapy), gender or social isolation were found to be statistically associated with depressed mood.

Depressioon HIVi nakatunute seas: seotud tegurid ja mõju elukvaliteedile

Kokkuvõte

Inimese immuunpuudulikkuse viiruse (HIV) kui kroonilise ja väga stigmatiseeritud infektsiooniga elamine on raske. Uuringud on näidanud, et HIVga nakatunute seas on depressioon kolm korda levinum kui tavaelanikkonnas. Käesoleva uurimuse eesmärgiks oli hinnata HIVi nakatunute vaimset tervist, kuidas see on seotud elukvaliteediga ning millised tunnused ennustavad depressiivsust. Läbilõikelises uuringus osales 800 HIVi nakatunut. Kasutades EEK-2, tuvastati depressioon 53% inimestest, mis on märkimisväärselt enam kui paljudes teistes uuringutes leitud. Depressiooniga inimestest vaid 22%-le oli arst öelnud, et tal on depressioon (viidates kõrgele aladiagnoosimisele) ning vaid 14% oli saanud antidepressantravi. 36% osalenutest oli kunagi mõelnud enesetapule. Depressioon oli tugevasti korreleeritud ärevusega, väsimuse ja insomniaga. Depressiivsus halvendas elukvaliteeti kõikides aspektides mõõdetuna WHOQoL-HIV BREF-ga. Töötus, praegune ja endine narkootikumide süstimine, laste olemasolu, vanus ja põhiharidus seostusid depressiivse meeleoluga. Infektsiooniga seotud tegurid (nagu CD4 rakkude hulk, viiruskoormus, antiretroviirusravi), sugu ning sotsiaalne isolatsioon ei olnud statistiliselt seotud depressiivsusega.

Introduction

The Human Immunodeficiency Virus (HIV) targets the immune system and weakens people's surveillance and defence systems against infections and some types of cancer. As the virus destroys and impairs the function of immune cells, by attaching itself and taking control over CD4 T-lymphocytes (CD4 cells), infected individuals gradually become immunodeficient. Immunodeficiency results in increased susceptibility to a wide range of infections and diseases that people with healthy immune systems can fight off. The most advanced stage of HIV infection is Acquired Immunodeficiency Syndrome (AIDS). AIDS is defined by the development of certain cancers, infections, or other severe clinical manifestations in people with HIV. HIV can be suppressed by combination antiretroviral therapy (ART) consisting of three or more antiretroviral (ARV) drugs. ART does not cure HIV infection but controls viral replication within a person's body and allows an individual's immune system to strengthen and regain the capacity to fight off infections. Strict adherence to lifelong ART is crucial for favourable outcomes of ART as only then can the infection be suppressed. With ART, people can live healthy and productive lives. Since the introduction of ART in the 1990s, life expectancy of people living with HIV (PLHIV) has been prolonged (Kaul, 2009).

At the end of 2012, there were 35.3 million PLHIV globally and 2.2 million in Europe (World Health Organization, 2014). It was estimated that in 2012 between 7,200 and 11,000 people were HIV infected in Estonia (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2013). By May 10, 2014 there were 8,816 people in Estonia who were diagnosed with HIV and over 300 new cases are added every year (24.6 new cases per 100,000 people) (Estonian Health Board, 2014). This places Estonia first in Europe in prevalence of HIV per 100,000 people (European Centre for Disease Prevention and Control, 2013).

With the advent of effective treatment and increased life expectancy, HIV infection has become a chronic condition. As with other chronic medical conditions, HIV infection is often complicated by co-morbid depression (Moussavi et al., 2007). Previous studies indicate that the prevalence of depression in HIV-positive people is up to three times higher than among HIV-negative controls (Do et al., 2014). Prevalence rates vary greatly between studies and depend on sample and instruments used. A review article reported it to be as low as 18% and up to 81% (Arseniou, Arvaniti, & Samakouri, 2014). High prevalence of depression among PLHIV exists across countries despite cultural differences, differences in diagnostic criteria, measures used and differences in samples (e.g. PLHIV in care, HIV infected men who have sex with men [MSM], HIV infected injecting drug users [IDU]) (Rabkin, 2008).

Studies show that depression is still greatly under-diagnosed and under-treated among PLHIV (Rodkjaer, Laursen, Balle, & Sodemann, 2010; Asch et al., 2003). Prevalence of depression among PLHIV in Estonia has not been addressed before.

Relationship between the virus and depression is complex. In some people, depression can probably be the result of HIV influencing the central nervous system (CNS). HIV can cross the blood brain barrier (BBB) and reside in brain microglia and macrophages as a "Trojan Horse" (Barreto, Viegas, Ziff, & Konkiewitz, 2014). Although not infecting neurons, HIV can produce synaptodendritic neuron injury and neuron death, leading to damage of a variety of neural systems. ARV drugs are unable to penetrate BBB and therefore CNS can be a reservoir for the virus. The cytokinergic hypothesis of depression posits that depression is caused by the actions of cytokines. As chronic neuroinflammation is a major feature of CNS HIV infection, it seems plausible to assume that cytokinergic mechanisms may play an important role in developing depression amongst PLHIV (Barreto et al., 2014). Biological mechanisms of depression in HIV infection need further studying.

Depression is associated with HIV progression. There is clear evidence that health outcomes of depressed PLHIV are worse compared to non-depressed PLHIV and evidence suggests that it is mediated by ART adherence (Hartzell, Janke, & Weintrob, 2008). The relation between depression and ART-adherence is twofold: ART lowers the risk for developing clinically significant depression (Gutiérrez et al., 2013) and reduced depression is associated with improved ART adherence (Wagner et al., 2011). Evidence suggests that the latter happens through good adherence to antidepressant medication (Bottonari et al., 2012). Inconsistent use of ARV drugs over time partially explains the relationship between depressive symptoms and HIV disease progression (Carrico et al., 2011). A review of longitudinal studies found substantial and consistent evidence that chronic depression, stressful events, and psychological trauma may negatively affect HIV disease progression in terms of decreases in CD4 cells, increases in viral load, and greater risk for clinical decline and mortality (Leserman, 2008).

Majority of PLHIV come from already marginalized groups like MSM or IDU. In the Western world HIV is mostly transmitted through sex between men and in the Eastern Europe injecting drug use is still the main cause of transmission (UNAIDS, 2012). HIV is rarely transmitted through sex between women (Chan et al., 2014).

HIV may be further stigmatized by accumulating stigmas of the aforementioned two behaviours. HIV stigma perceived by PLHIV has been associated in longitudinal studies with symptoms of psychiatric disorders including depression (Hatzenbuehler, O'Cleirigh, Mayer,

Mimiaga, & Safren, 2011). Depression plays the mediating role between perceived stigma and ART non-adherence (Rao et al., 2012). In addition, HIV is a chronic and life-threatening illness and, like other such illnesses, can be stressful to manage. HIV's life-threatening nature may instigate fears of impending mortality. It has been demonstrated that life stress has negative impact for depressed PLHIV and suggest that ART adherence interventions with depressed individuals could be enhanced via development of stress management skills (Bottonari, Safren, McQuaid, Hsiao, & Roberts, 2010).

A review concluded that risk factors for depression are gender (women are more vulnerable), older age, pre-infection history of depression, more severe infection stage, diminished social support, stressful life events, HIV stigma, occupational disability, body image changes, isolation, debilitation, AIDS diagnosis, CD4 cell count, care of children (stressor), low socio-economic status, low education level; but it is not associated with sexual orientation (Arseniou et al., 2014).

Quality of Life (QoL) is defined as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (WHOQOL Group, 1994). This definition reflects the view that QoL refers to a subjective evaluation, which is embedded in a cultural, social, and environmental context.

Asymptomatic HIV-infected people report better QoL in comparison to symptomatic and AIDS patients in all domains of QoL meaning disease progression decreases QoL of PLHIV in general (Rai, Dutta, & Gulati, 2010). Depression in HIV is associated with decreased QoL (Primeau, Avellaneda, Musselman, St. Jean, & Illa, 2013). Most studies looking into depression and QoL have found inverse associations between the two in all or most domains measured in different parts of the world, e.g., in India (Peter, Kamath, Andrews, & Hegde, 2014), USA (Jia et al., 2005), Brazil (Zimpel & Fleck, 2014) and Taiwan (Yen et al., 2004).

Study of QoL of PLHIV in Estonia using WHOQoL-HIV instrument has shown that the poorest QoL was found in Environmental domain (especially with regard to the economical situation) and Personal Beliefs (concerns about the future, spirituality) (Rüütel, Uusküla, Minossenko, & Loit, 2008). In 2005 PLHIV in Estonia infected through sexual transmission reported better QoL than those infected through injecting drug use (Rüütel, Pisarev, Loit, & Uusküla, 2009). As expected, PLHIV with higher income, better health status and biological markers reported better QoL.

One cannot talk of high rates of depression and low QoL without describing

suicidality in this patient group. Suicidal ideation, attempts and completions remain alarmingly common in PLHIV despite a recorded decline in suicide rates since the advent of ART to levels comparable with those of other chronic disease-afflicted populations (Shirey, 2013). Suicide rates remain more than three times higher in PLHIV than in the general population (Keiser et al., 2010). Suicidality is associated with older age, male gender, injecting drug use and advanced clinical stage (Keiser et al., 2010; Kalichman, Heckman, Kochman, Sikkema, & Bergholte, 2000).

Therefore depression has a major impact on PLHIV's life both in the present moment as well as in the long run.

Aim of this study was to explore mental health of HIV infected people in Estonia with regard to factors associated with and outcomes of depression and their effect on health status and quality of life. It was hypothesized that i) prevalence of depression is very high, ii) depression is greatly under-diagnosed, and iii) depression affects all domains of quality of life. Factors related to having more depressive symptoms are variables like age, gender, low education level, having children, being in social isolation, being an IDU and indicators of worse health status (e.g., lower CD4 cell count, higher viral load).

Methods

Participants and procedure

This cross-sectional study was conducted in three infectious diseases outpatient clinics situated in regions around which HIV epidemic is concentrated in Estonia (over 90% of new HIV cases are found) (Rüütel, Trummal, Salekešin, & Pervilhac, 2011): Tallinn, Kohtla-Järve and Narva. Data was gathered between January 2013 and November 2013 using a structured questionnaire filled in by the participant. It included questions on socio-demographic characteristics, quality of life, mental health, substance abuse, sexual behaviour, HIV treatment and usage of services aimed at PLHIV. For completing the survey patients received a €10 supermarket gift voucher. Patients' medical records were queried for pertinent medical information. Study used convenience sampling in which participants were recruited by their infectious disease physician during their regular visits to the clinic (nobody was specifically contacted and invited). All participants gave a written informed consent. All study materials (informed consent, questionnaire) were available in both Estonian and Russian. Participation was anonymous and no personal identifiers were collected. Patient was eligible for participation if he/she was HIV-infected, at least 18 years of age, spoke Estonian or Russian, had been aware of his/her HIV status for at least 3 months, was not pregnant nor under the

influence of drugs or alcohol. The study was approved by Tallinn Medical Research Ethics Committee.

Measures

Data for gender, age, town of the outpatient clinic, ethnicity, employment status, level of education completed, number of people living with, having children, having been in prison, having told anyone about HIV infection, medical insurance status and probable time of infection was examined. Additionally, information on sexual and drug use behaviour, recent history of depression (whether a doctor had told them during previous 12 months they may be having depression) and antidepressant use (whether had they been prescribed antidepressants during previous 12 months), their suicidal ideation and attempts (ever, within past 12 months or never) and probable time of contraction with HIV were analysed. MSM status was defined among men as ever having had a sexual intercourse with a man and/or defining himself as homosexual or bisexual. IDU status was defined as having had injected drugs during one's lifetime. Information on previously mentioned variables is based on patient self-reports. Data on ART, most recent viral load, CD4 cell count and time of HIV diagnosis were extracted from medical records (by physician). When calculating time since contracting with HIV patient reports were taken into account. If patient reported retrospective estimation was very close to the documented date of diagnosis by physician the latter was preferred.

EST-Q2

The Emotional State Questionnaire (EST-Q) is a screening instrument for mental health status (Aluoja, Shlik, Vasar, Luuk, & Leinsalu, 1999). After some modification in 2002 it was improved to EST-Q2 which was used in the current study. EST-Q2 contains subscales of Depression, Anxiety, Agoraphobia-Panic, Fatigue and Insomnia, reflecting symptoms of depression and anxiety disorders according to ICD-10 and DSM-IV. Agoraphobia-Panic measure was not used in this study as depression was of more interest than anxiety disorders. EST-Q2 keeps nonspecific symptoms such as fatigue and insomnia apart from core symptoms of anxiety and depression, which is supposed to improve the discriminative power of the subscales (Aluoja et al., 1999). The EST-Q2 version consists of 28 items. Patients were asked to report how much the various problems had troubled them in the prior four weeks using a five-level item with response options, "not at all = 0" to "all of the time = 4". Maximum possible score for Depression is 32, for Anxiety 24, for Fatigue 16 and for Insomnia 12. Significant differences in subscales between patients and population and also across

diagnostic groups have confirmed the discriminative validity of the instrument (Aluoja et al., 1999; Ööpik, Aluoja, Kalda, & Maaroos, 2006). The cut-off point of ≥12 was used for depression for maximum specificity and lowest false positive rate (Ööpik et al., 2006).

WHOQoL-HIV BREF

The World Health Organization Quality of Life Questionnaire for HIV brief version (WHOQoL-HIV BREF) was used to assess patient's quality of life (WHOQOL HIV Group, 2004). The questionnaire has been adapted into Estonian (Rüütel et al., 2008). Patient is asked to evaluate his/her QoL within the past two weeks. The instrument consists of 31 items, with individual items being rated on a 5 point scale where "1" indicates low, negative perceptions, and "5" indicates high, positive perceptions (or items are later recoded in that direction). Items are distributed into six domains: Physical Health, Psychological Health, Level of Independence, Social Relationships, Environment, and Spirituality/Religion/Personal Beliefs, plus 2 items for evaluating a person's overall view of his/her quality of life and of his/her satisfaction with health. The sum of scores of each domain can range from 4 to 20. Compared to WHOQoL BREF, there are 5 items especially aimed at PLHIV: symptoms of HIV, social inclusion, forgiveness and blame, concerns about the future, death and dying. The questionnaire has been validated and used widely in HIV studies (Skevington, Norweg, Skandage, & WHOQOL HIV Group, 2010).

Data management and statistical analysis

Two data files were compared after double data entry. Discrepancies were resolved by referring to the source documentation or, if the latter was unclear, a decision was made by co-investigators of the project with documenting on the method for data clarification. The sample and results from instruments were described with number of people and percentages for discrete variables and with mean and standard deviation for continuous variables. Spearman correlations were used for evaluating association between WHOQoL-HIV items and EST-Q2 depression scores. To study the relationships between WHOQoL-HIV BREF domains and EST-Q2 subscales, Pearson's correlations were used. Spearman's correlations were used to correlate EST-Q2 subscales with WHOQoL-HIV General QoL and Health Related QoL as the latter two are ordinal items. ANOVA was used for comparison of mean depression score in different groups as well as to evaluate the distinctibility between QoL domains when having depression and when not screening positive for it. To evaluate variable's predictive power multiple stepwise linear regressions were used. Data was analysed using SPSS 21.0.

Results

Sample characteristics

Eight hundred people participated in this study (Table 1).

Table 1

Sample characteristics (N = 800)

	n	%
Gender		
Men	471	58.9
Women	329	41.1
Town of the outpatient clinic		
Tallinn	332	41.5
Kohtla-Järve	318	18.8
Narva	150	39.8
Ethnicity		
Estonian	87	10.9
Russian	676	84.7
Other	35	4.4
Education level completed		
Less than basic	50	6.3
Basic (9 years)	283	35.6
Secondary	150	18.9
Vocational	268	33.8
Higher	40	5.0
Employment status		
Employed	323	40.6
Unemployed	472	59.4
Injecting drug use		
IDU (vs. non-IDU)	534	66.9
Men IDU (vs. men non-IDU)	363	77.1
Women IDU (vs. women non-IDU)	171	52.0
Sexual orientation		
MSM (vs. non-MSM)	48	10.2

Note. N = total sample size*; n* = number of cases.

The mean age of participants was 34.0 (*SD* = 7.6) years and the mean time since contraction with HIV was 3,039 (*SD* = 1,374) days or 8.3 (*SD* = 3.7) years by the time of participation. Mean CD4 cell count was 416.1 (*SD* = 371.9). Mean viral load was 128,992 (*SD* = 755,390) copies/ml; 45.6% (*n* = 364) people had an undetectable viral load. ART was received by 85.9% (*n* = 687).

Of all the participants, 84.6% (*n* = 677) reported having medical insurance, 41.3% (*n* = 330) had been in prison, 13.9% (*n* = 111) were living alone, 70.8% (*n* = 566) had at least one child and 5.6% (*n* = 45) reported having told nobody about his/her HIV infection (social isolation).

Of all men who had had sex with a man 31.0% (*n* = 18) defined themselves as homosexual or bisexual. Some men defined themselves as homo- or bisexual without having had sex with a man.

Of all IDU, 29.6% (*n* = 158) had injected drugs in the previous four weeks (31.1% of IDU men [*n* = 113] and 26.3% of IDU women [*n* = 45]). Mean age of IDU was 32.5 (*SD* = 5.2). Mean duration of IDU was 14.1 (*SD* = 4.5) years.

Prevalence of mental health problems

In this analysis, having depression is referred to when depression subscale score was 12 or more, i.e., screened positive for depression. When referring to having depressive symptoms, overall depression subscale score is kept it mind which measures frequency of depressive mood symptoms.

One hundred twenty-two (15.2%) people were told by his/her physician within the past 12 months that he/she (patient) had depression. Seventy-five (9.3%) reported having taken antidepressant medication within the past 12 months. Seven hundred twenty-nine people (91.1% of total sample) answered to all depression related questions. Mean score in EST-Q2 depression scale was 12.4 (*SD* = 7.7). Using a cut-off point of ≥12, depression was prevalent in 53.1% (*n* = 387) of the participants. Of the people whose EST-Q2 score was above the depression cut-off point, 21.5% (*n* = 82) reported his/her doctor having had said in the previous 12 months that the patient had depression. Only 14.4% (*n* = 54) reported having taken antidepressants in the previous 12 months.

Among people with a history of injecting drug use, 60.3% (*n* = 292) screened positive for depression. On the other hand, among non-IDU only 38.5% (*n* = 94) screened positive for depression. ANOVA showed that the mean score of depression differed significantly between IDU and non-IDU ($F(1, 726) = 41.42$, $p < .001$). Depression was screened among 46.3% (*n* =

19) of MSM and 54.4% (n = 209) of non-MSM. According to ANOVA those two groups didn't differ significantly in mean depression scores ($F(1, 423) = 1.51$, $p = .22$).

Mean score for anxiety was 10.0 (SD = 5.5), for fatigue 7.3 (SD = 4.2) and for insomnia 6.0 (SD = 3.8). Pearson's correlations were significant and strong between different EST-Q2 subscales. Depression score's correlation with fatigue score was $r = .69$, $p < .001$; with insomnia $r = .64$, $p < .001$; and with anxiety $r = .83$, $p < .001$. In addition, correlation between fatigue and insomnia was $r = .70$, $p < .001$; between fatigue and anxiety $r = .72$, $p < .001$; and between insomnia and anxiety $r = .63$, $p < .001$. This indicates that all mental health problems measured here have significant co-morbidity.

Of the total sample, 36.2% (n =288) reported ever having thought about suicide. Of them, for 54.2% (n = 156) the last time they thought about it was less than 12 months ago. Of the total sample, 20.4% (n = 162) had ever attempted to commit suicide. Of those ever having tried it, 24.7% (n = 40) had attempted to commit suicide within the previous 12 months. Only 18 people who had recent (within the past 12 months) suicidal ideation and/or attempts weren't screened positive for depression. All others (n=123; 87.2%) were screened to have depression. PLHIV who had attempted to commit suicide within the past 12 months and had answered to all EST-Q2 depression subscale questions, only 2 out of 33 weren't screened positive for depression.

Table 2

Correlations between WHOQoL-HIV domains and EST-Q2 subscales

	Depression	Anxiety	Fatigue	Insomnia
Physical	-.63***	-.58***	-.71***	-.69***
Psychological	-.76***	-.65***	-.66***	-.59***
Level of Independence	-.59***	-.52***	-.64***	-.54***
Social Relationships	-.64***	-.52***	-.46***	-.49***
Environment	-.56***	-.47***	-.49***	-.47***
Personal Beliefs	-.67***	-.62***	-.49***	-.43***
General QoL[a]	-.57***	-.47***	-.48***	-.48***
Health Related QoL[a]	-.55***	-.48***	-.59***	-.51***

Note. [a] *Spearman correlations*

*** $p < .001$.

WHOQoL-HIV domains: correlations with mental health

The occurrence of symptoms of depression, anxiety, insomnia and fatigue, as detected using the EST-Q2, revealed at least a moderate negative correlation with QoL in all domains of the WHOQoL-HIV indicating that worse mental health relates to lower quality of life (Table 2).

Quality of life in depression

Mean scores of all WHOQoL-HIV items and domains were lower for depressed (screening positive for depression) vs. non-depressed patients (Table 3). Mean scores in different domains of QoL are significantly different between depressed and non-depressed patients. Correlations between depression score and WHOQoL-HIV items are moderate to strong. This indicates that QoL is affected by depression in all aspects observed and the negative effect is moderate to strong.

Table 3

Comparison of QoL between depressed and non-depressed PLHIV (mean scores, ANOVA for QoL domains) and Spearman correlations with depression score

	No depression		Depression			
	M	*SD*	*M*	*SD*	r_S	$F\ (df_1, df_2)$
Physical	15.9	2.6	12.3	3.1		260.8***
Pain and discomfort	4.4	0.8	3.7	1.0	-.41***	(1, 688)
Energy and fatigue	3.6	1.0	2.6	1.0	-.52***	
Sleep and rest	3.5	1.0	2.5	1.1	-.53***	
Symptoms of PLHIV	4.4	0.8	3.5	1.2	-.48***	
Psychological	14.6	2.4	10.6	2.7		410.3***
Positive feelings	3.3	1.0	2.4	1.0	-.49***	(1, 697)
Cognition	3.5	0.8	2.9	0.7	-.50***	
Self-esteem	3.8	0.9	2.6	1.0	-.61***	
Bodily image & appearance	3.8	1.0	2.6	1.2	-.56***	
Negative feelings	3.9	0.7	2.7	0.9	-.72***	

(Continued)

Table 3

(Continued)

	No depression		Depression			
	M	*SD*	*M*	*SD*	r_S	$F(df_1, df_2)$
Level of Independence	14.2	2.9	11.0	3.1		199.2***
Mobility	3.3	1.0	2.7	1.0	-.38***	(1,703)
Activities of daily living	3.7	0.8	2.8	1.0	-.57***	
Treatment dependency	3.6	1.2	3.0	1.1	-.34***	
Work capacity	3.7	0.9	2.6	1.0	-.57***	
Social Relationships	15.3	2.9	11.5	3.5		237.8***
Personal relationships	3.8	1.0	2.8	1.1	-.55***	(1, 690)
Social support	3.9	0.8	3.0	1.1	-.49***	
Sexual activity	3.5	1.2	2.6	1.2	-.42***	
Social inclusion	4.1	1.0	3.2	1.2	-.50***	
Environment	14.5	2.3	12.0	2.5		180.5***
Physical security	3.6	0.8	2.9	0.9	-.48***	(1, 694)
Housing	3.8	0.9	3.1	1.	-.37***	
Financial resources	2.8	1.3	1.8	1.1	-.48***	
Health/social care	3.9	0.8	3.4	1.1	-.28***	
Learning opportunities	4.2	1.0	3.6	1.1	-.31***	
Leisure opportunities	3.1	1.1	2.8	1.1	-.19***	
Physical environment	3.5	0.9	3.0	0.9	-.33***	
Transport	4.0	1.0	3.3	1.2	-.37***	
Personal Beliefs	16.1	2.7	12.3	3.1		278.6***
Spirituality, personal beliefs	3.8	1.0	2.8	1.1	-.52***	(1, 687)
Forgiveness and blame	4.6	0.8	4.1	1.2	-.28***	
Concerns about the future	3.7	1.1	2.6	1.3	-.53***	
Death and dying	3.9	1.2	2.9	1.4	-.45***	
General QoL[a]	3.5	0.7	2.8	0.7	-.57***	
Health Related QoL[a]	3.4	0.9	2.4	0.9	-.55***	

Note. F value from ANOVA when comparing depressed vs. non-depressed in WHOQoL-HIV domains.

*** $p < .001$.

Factors related to depressive symptoms

The relationship of infection related variables like CD4 cell count, CD4 count less than 200 (AIDS indicator), viral load, time since contracting with HIV and receiving ART were analysed in comparison to depression scores with stepwise regression analysis. Only time since being infected turned out to be significantly associated with depression score ($\beta = .14$, $t(724) = 3.86$, $p < .001$). Time since contracting HIV explained merely 2% of the variance in depression scores ($R^2 = .02$, $F(1, 724) = 14.92$, $p < .001$). This indicates that in that model, health status of infection predicts almost nothing in depression scores. Therefore depressive symptoms should be best associated with non-biological factors among this sample.

Socio-demographic variables like age, gender, education, employment status, town, ethnicity, living alone or not, having children or not, having been in prison and social isolation were analysed with stepwise regression analysis. Five models were developed. Variables in the first model explained 6%, second 8%, third 9%, fourth 10% and last model 11% of variance in depression scores. Table 4 gives an overview of model 5 ($R^2 = .11$, $F(5, 722) = 17.13$, $p < .001$).

Table 4

Socio-demographic predictors of EST-Q2 depression score[a]: regression model 5

	t	*B*	*SE(B)*	*β*
(Constant)	5.11	7.78	1.5	
Being employed (vs. unemployment)	-5.84	-3.30	.56	-.21***
Having children (vs. not having children)	4.30	2.58	.60	.15***
Having been in prison (vs. not having been)	2.71	1.55	.57	.10**
Basic education (vs. all other levels of education)	3.18	1.91	.60	.12**
Age	2.25	.08	.04	.08*

Note. Predictors are presented in the order of addition into subsequent stepwise regression analysis models.

[a] Mean depression score = 12.4 (*SD* = 7.7).

*** $p < .001$; ** $p < .01$.

Next IDU, current IDU and MSM status were analysed with stepwise regression. Two models were developed of which first one explained 6% and the second 8% of variance in depression scores. First model included current IDU variable ($\beta = .24$, $t(727) = 6.62$, $p < .001$; $R^2 = .06$, $F(1, 727) = 43.80$, $p < .001$). The second model, already including current IDU ($\beta = .18$, $t(726) = 4.73$, $p < .001$), added lifetime prevalence of IDU ($\beta = .17$, $t(726) = 4.41$, $p < .001$) to

the model (R^2 = .08, F(2, 726) = 32.2, p < .001). Therefore, in addition to depression prevalence among IDUs, IDU status and behaviour was associated with being more depressed. MSM behaviour had no effect on having more depressive symptoms.

Finally, all variables previously studied with regression analyses were added as predictors of depression score (age, gender, education, employment status, town, ethnicity, living alone or not, having children or not, having been in prison, social isolation, CD4 cell count, CD4 count less than 200, viral load, time since getting the infection, ART, lifelong IDU, current IDU and MSM status). Six models were produced. Variables in the first model predicted 6%, second 9%, third 11%, fourth 13%, fifth 14% and sixth 15% of variance in depression scores. Table 5 gives an overview of model 6 (R^2 = .15, F(6, 718) = 20.29, p < .001).

Table 5

Overall predictors of EST-Q2 depression score[a]: regression model 6

	t	*B*	*SE(B)*	*β*
(Constant)	3.20	5.14	1.61	
Being employed (vs. unemployment)	-4.94	-2.76	.56	-.18***
Current IDU (vs. not IDU recently)	3.77	2.74	.73	.14***
Having children (vs. not having children)	4.10	2.41	.59	.14***
IDU (vs. not ever IDU)	3.63	2.32	.64	.14***
Age	3.17	.12	.04	.12**
Basic education (vs. all other levels of education)	2.70	1.6	.59	.10**

Note. Predictors are presented in the order of addition into subsequent stepwise regression analysis models.

[a] Mean depression score = 12.4 (*SD* = 7.7).

*** p < .001; ** p < .01.

Discussion

A cross-sectional study using convenience sampling focusing on health and behaviours of PLHIV in care in Estonia was conducted among 800 participants. It was found that depression is highly prevalent among PLHIV in Estonia decreasing person's quality of life and being associated with other mental health problems measured. Depression is considerably under-diagnosed.

Of all people in the study, 53.1% screened positive for depression. This prevalence is higher than found in a review (Rabkin, 2008). Such high prevalence rate may come from

using a screening instrument (although a cut-off point of the smallest false positive rate was used) and diagnostic interviews would have evaluated the prevalence to be lower. Yet in comparison to studies using a screening instrument as well, depression prevalence has still been found to be lower than in this study (e.g., Gibbie et al., 2006). A rate that high may be the result of a high proportion of IDU in the sample. Jones and colleagues (2010) found that prevalence of depression was higher among IDU (both HIV infected and not infected) than non-IDU. Results of this study show the same: depression prevalence among IDU was 60.3% vs. non-IDU 38.5% with difference in mean depression scores statistically significant between them. History of injecting drug use is a difficult confounding factor to address as substance abuse and addiction are associated with depression regardless of HIV infection. Evidence supports that depression leads to more risky behaviours (including sharing of needles) which can lead to contracting HIV (Stein, Solomon, Herman, Anderson, & Miller, 2003). Reasons behind such high depression rate need further studying for better understanding of difficulties faced by PLHIV in Estonia.

It is alarming that only 21.5% of people who screened positive for depression were told they have depression by his/her physician. As these results should be addressed with some caution, it is clear though that depression has a tendency to be greatly under-reported in Estonia as has been shown to be the case in other countries (e.g., in Denmark [Rodkjaer et al., 2010] and USA [Asch et al., 2003]). Under-reporting of depression may come from the need to treat addiction related symptoms before depression (e.g., in drug dependence treatment) as two thirds of the sample had a history of injecting drug use. It can also be related to short duration of a physician's appointment where lack of time to address concerns about current mood or thoughts can be a problem. As depression has a serious impact on person's QoL, routine screening of depression during a physician's appointment should be implemented. According to a review, both psychotherapy as well as psychopharmacological treatment has been shown to be efficient among PLHIV (Olatunji, Mimiaga, O'Cleirigh, & Safren, 2006). Although only 14.4% reported having taken antidepressants, they may have got further psychological help. Therefore conclusions about under-treating of depression cannot be made based on this study.

Depression was highly correlated with fatigue, insomnia and especially anxiety. Co-morbidity of psychiatric disorders like depression and anxiety are well-known regardless of HIV. The medical sequel of HIV infection, associated opportunistic infections, and side effects of ART can mimic symptoms of depression (i.e., fatigue, concentration problems, somatic symptoms, decreased appetite/weight loss) (Simoni et al., 2011). Therefore it has

been suggested that when measuring depression, instruments that separate somatic symptoms from depressive mood symptoms should be preferred when studying depression among PLHIV (Kalichman, Rompa, & Cage, 2000). Somatic symptoms may skew depression rates unnecessarily.

For example, although fatigue is greater among depressed (vs. non-depressed) PLHIV it can also be related to immunosuppression itself (Millikin, Rourker, Hallman, & Power, 2003). Prevalence of insomnia doesn't differ between PLHIV and HIV uninfected people and among PLHIV is associated with depression but also with bigger waist size (Crum-Cianflone et al., 2012). In this study, correlations between EST-Q2 different mental health subscales were fairly strong. The relation between fatigue on all other variables measured was the strongest though. This indicates that if fatigue was included in measuring depression, it would not have given as specific indicator of depressed mood as was currently possible.

Depression score was most strongly associated with anxiety score indicating that among this population, depressive symptoms alongside symptoms of anxiety are common. Although in order to make any conclusions further studies need to be executed, hypothetically it may come from such high-proportion of IDU in the sample as anxiety is commonly associated with substance abuse.

Although lives of PLHIV have been considerably prolonged thanks to ART, fear of mortality and stigma surrounding the infection can lead to depression and therefore worse health outcomes. Bravo, Edwards, Rollnich, and Elwin (2010) review concluded that PLHIV face three key decisions: (i) whether or not to disclose their diagnosis to others; (ii) decisions about adherence to treatments; and (iii) decisions about sexual activity and desires about parenthood. Problems associated with these decisions often result in isolation and mental illness such as depression and anxiety, lack of access to social support, and refusal to seek treatment. It is important to decrease HIV self-stigma to improve health outcomes on HIV infected individuals. This can also be the reason for such high co-occurrence of depressive and anxiety symptoms.

Lessening that stigma can be beneficial to the society as well. Burden of living with HIV stigma has been shown to lead to depression (Nachega et al, 2012), depression increases risky behaviours (needle sharing, unprotected sex) (Comulada et al., 2010; Perdue, Hagan, Thiede, & Valleroy, 2003) and to ART non-adherence (Gonzalez, Batchelder, Psaros, & Safren, 2011). Good adherence to ART is important as it leads to undetectable viral load (Bonner, Mezochow, Roberts, Ford, & Cohn, 2013) which reduces infectiousness. Therefore not having depression decreases behaviours related with HIV transmission, but even when an

unprotected sexual intercourse occurs, low viral load decreases considerably the possibility of transmitting HIV (Engsig et al., 2010).

It was found that suicidal ideation is unfortunately very common among PLHIV as over a third reported ever having thought of ending one's life, and over half of them thought of doing it even within the past year. Fifth of all the participants had attempted suicide and of those people fourth had tried it within the past year. Almost all suicidal people still screened positive for depression. Badiee and colleagues (2012) also found that lifetime suicidality is associated with current depressed mood and also showed that it was associated with substance abuse. The serious impact of depression on lives of PLHIV can be vast and is needed to address as it can lead to ending one's life.

Improving QoL is a major goal in treating individuals infected with HIV, so it is important to identify which domain of individual's life is most affected by the disease. Depression, fatigue, insomnia and anxiety were all significantly correlated with QoL in all domains of WHOQoL-HIV BREF on a moderate to strong level. This indicates that mental health problems need to be addressed as they impact all aspects of people's life. Impact of mental health on QoL has been shown with many other diseases as well, e.g., in kidney diseases (Abdel-Kader, Unruh, & Weisbord, 2009), and diabetes (Scharm, Baan, & Pouwer, 2009). Although pathways between QoL and depression are hard to evaluate as depressed people may already evaluate QoL poorer because of the decreased mood, results from QoL measurements give a valuable insight to person's current subjective well-being.

In this study it was found that depression significantly affected all domains of QoL when compared to non-depressed peers. Depressive symptoms were especially strongly correlated with satisfaction with one's health in general and in relation to only health, self-esteem, acceptance of bodily image, satisfaction with ability for daily activities, capacity for work, satisfaction with one's personal relationships and frequency of negative feelings. It has been shown that PLHIV report poorer health related QoL than people with other chronic illnesses, including diabetes, multiple sclerosis, and clinical depression (Hays et al., 2000; Korthuis et al., 2008). This study found that being depressed is associated with even more lower health related QoL. As PLHIV generally experience higher rates of psychological distress relative to the general population and, and in some cases, relative to other chronic illness populations as well, psychological factors may represent one pathway to decreased health related QoL (Pence, Miller, Whetten, Eron, & Gaynes, 2006; Ciesla & Roberts, 2001).

One of the aims of this study was to look into factors associated with depression in HIV. Although no causality can be concluded from a cross-sectional study, regression

analysis can still help evaluate factor's predictive power to dependent variable. For this, multiple stepwise regression analyses were executed. The predictive power of a variable depended on the formulated model.

When analysing infection related variables, solely time since contracting HIV appeared to contribute to having more depressive symptoms but explaining merely 2% of the variance in depression scores. In this study none of HIV infection related immunodeficiency markers (CD4 cell count and viral load, AIDS status) were related to depression.

Out of all the observed socio-demographic variables, employment, having children, being in prison, basic education (completed 9 grades) and older age contributed to depressive symptoms. Having a job protected from having many depressive symptoms, all the others contributed to having more of them. It has been shown in other studies among PLHIV as well that having a job protects from and long-term unemployment increases likelihood of depression (Amiya, Poudel, Poudel-Tandukar, Pandey, & Jimba, 2014; Milner, Page & LaMontagne, 2013). Having a job may give a purpose and feelings of being part of the society leading to better mental health.

Having children may be a stressor because it means being responsible for somebody and the burden makes one experience frequent depressive mood (Arseniou et al., 2014). But it can also be because of fear of what other children think or how they act towards his/her child when found out that the parent has HIV infection. It can also be caused by having to be constantly careful and conscious about one's activities to not transmit HIV to the child.

Having been in prison can be a life-long stressor leading to depression. Two fifths of the sample of this study had been in prison. The statistically significant relation to depressive mood should be studied further as the literature trying to explain it among PLHIV is scarce.

Reason for basic educational level's impact may be because with low level of education "mental health literacy" may not be sufficient to aid recognition, management and prevention of depression as suggested by Asch and colleagues (2003).

Age as a predictor has also been found before, e.g., Hinkin, Castellon, Atkinson, and Goodkin (2001) found that in the older cohort depression was more prevalent compared to younger people. In HIV context "old" is commonly referred to people over 49 (Rabkin, 2008) as the virus is mainly transmitted among younger people.

In this sample it was not found that gender is associated with being more depressed although this has been shown in numerous other studies (see Rabkin, 2008; Arseniou et al., 2014). It was also not found that social isolation was a predictor. The latter might have

occurred because of a small sample size as well as not sufficient measurement. Sample and life conditions of PLHIV in Estonia need to be studied further for better comprehension.

Out of behaviours of vulnerable populations, being an MSM was not found to be related to being more depressed. This has been shown in other studies as well (Ciesla & Roberts, 2001). Having recently injected drugs was associated with having more depressive symptoms, and so was lifelong status of IDU. As discussed before, injecting drug use is related to depression in a complex way. This study showed that substance abuse is associated with being more depressed.

Finally, all variables measured (socio-demographic, vulnerable population behaviours, infection related indicators) were analysed. It was found that best predictors were employment status, followed by current IDU, having children, lifetime IDU, and lastly older age and basic education predicting all together 15% of the variance in depressive score. None of the other (e.g., infection related indicators, ART, gender, being in prison) added statistically significant prediction to variance in depressive mood.

Results of this study as well as from previous studies accentuate the need for further structural equation modelling on this topic (e.g., Schuster, Bornovalova, & Hunt, 2012). HIV is an immunodeficiency disease which means there is no universal organ affected by the virus. It is very difficult to make overarching conclusions without analysing pathways between multiple variables simultaneously. Structural equation modelling may shed more light on causal pathways between depression, HIV and factors associated with them.

As this study demonstrated the wide scope of depression among PLHIV and its negative effect on quality of life as well as co-occurrence with other mental health problems, future studies should analyse its impact on ART adherence. Being on ART is very difficult as sometimes medication has to be taken many times a day multiple pills at a time for the rest of one's life. Adjusting to this regime can be difficult. Many studies in other countries have demonstrated that depression can lead to worse ART adherence (e.g., Rao et al., 2012; Hartzell et al., 2008).

Although WHOQoL-HIV BREF is a widely used QoL instrument and has been validated for PLHIV, EST-Q2 is not a mental health screening instrument with a frequent use in scientific literature. To the knowledge of the author, it is the first documented use of EST-Q2 among PLHIV. A lot of depression studies among PLHIV have used Beck Depression Inventory (BDI). A future study could compare depression scores from BDI and EST-Q2 and see their fit with diagnosis according to a clinical interview. This will make interpreting of results from this study with results from other countries and populations more accurate.

As two thirds of the sample had a history of injecting drug use, further understanding of the impact and pathways of current and former substance abuse to depression in PLHIV needs to be developed. Future studies shouldn't be exclusively investigating drug abuse, but should also look into drinking and smoking as they are associated with depression as well (Schuper et al., 2010).

In conclusion, the prevalence of depression seems to be uncommonly high among PLHIV in Estonia. It is being under-diagnosed even though it is strongly associated with one's quality of life. Depression is associated with other mental health problems like fatigue, insomnia and anxiety that too decrease one's quality of life. Best predictors for depressive mood were found to be employment (having a job protects from it), current and former injecting drug use (increases), having children (a stressor), negative effect of older age and low level of education (completion of nine grades). Results of this explorative study point to the need of further future research among this population to better understand and improve the life and services aimed at PLHIV.

Limitations

This study analysed results from PLHIV already in care, they cannot be generalized to all PLHIV living in Estonia as to hard-to-reach populations (e.g., IDU with serious opiate addiction with frequent use) may not be included. Also, being in care may already have a positive impact on QoL and depression as was demonstrated by comparing IDU receiving ART and IDU who did not (Jones et al., 2010). It can only be hypothesized that situation of HIV infected IDU not in care may be even worse. Even though participation was anonymous, the results may still be affected by social desirability bias. Most of data is reported by patients themselves, including assessment of illegal drug use and therefore people may be hesitant to tell the whole truth. Duration of being infected with HIV considered both retrospective estimation by patient as well as documented date of diagnosis by his/her infectious disease physician. As the mean duration of infection was more than 8 years, estimation reported by patient may not be that precise influencing the accurateness of the calculated variable. When talking of under-diagnosing, using results from a screening instrument can already bias real-life situation (as compared to diagnosing with a clinical interview). It is also not known whether or not patient's physician has really considered the patient to be depressed or not (physician's side of the story is not known). Information about co-morbidities not directly relating to HIV wasn't documented and therefore depression and QoL may actually be influenced by confounding factors. When measuring suicidality, it is not known how patient

actually interpreted the questions (some may just wish they were dead, some may actually be planning a suicide).

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