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Factors influencing the quality of life in persons living with human immunodeficiency virus infection in Almaty, Kazakhstan

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Abstract

The study purpose was to determine the factors associated with health-related quality of life (HRQoL) among people living with HIV (PLHIV) in Kazakhstan. A convenience sample of 531 adult PLHIV registered at the Almaty City AIDS Center was used for this cross-sectional study. HRQoL data were collected with the World Health Organization's Quality of Life HIV brief questionnaire, depression – with Patient Health Questionnaire-9, and clinical data were retrieved from medical records. Multivariate logistic and Tobit censored regressions were used to examine the relationship of socio-demographic, behavioral, and clinical factors with HRQoL and the six specific HRQoL domains: 35.8% of participants did not report good HRQoL. The following variables were identified as independent predictors of poor HRQoL: probable depression (adjusted odds ratio [AOR] 13.42, 95% confidence interval [CI]: 4.56–39.52); history of injecting drug use (AOR 2.10, 95% CI: 1.40–3.14); CD4+ T-cell count $<$200 cells/mm^3 (AOR 2.17, 95% CI: 1.30–3.62); previously married status (AOR 2.23, 95% CI: 1.16–4.28); and co-infection with tuberculosis, syphilis, toxoplasmosis, Chlamydia, herpes simplex, or cytomegalovirus (AOR 1.59, 95% CI: 1.06–2.39). HRQoL of PLHIV in Almaty was independently influenced by several factors. An interdisciplinary approach is needed in planning healthcare and social services addressing improvement of HRQoL among PLHIV.

Keywords

PLHIV, Health related quality of life, Kazakhstan HIV, Asia, epidemiology, AIDS

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Introduction

Significant improvement in the treatment of persons living with human immunodeficiency virus (HIV) infection through the introduction of antiretroviral therapy (ART) has resulted in delayed disease progression and prolonged survival, allowing HIV infection to now be classified as a chronic disease.[1] Consequently, the impact of HIV infection and ART on different dimensions of quality of life (QoL), including physical and emotional well-being, social support systems, and life roles, has emerged as a significant consideration for people living with HIV (PLHIV). Health-related quality of life (HRQoL) refers to aspects of QoL that are specifically affected by and related to one's physical

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and mental health.[2] The determinants reported to be associated with HRQoL among PLHIV were summarized in recent literature reviews[3,4] and included numerous socio-demographic, clinical, psychological, and behavioral factors. In particular, lower socioeconomic status, insufficient social support, advancing HIV stage, lower immunological status, lower adherence to ART, and psychiatric co-morbidities were consistently associated with poorer HRQoL. However, results of past studies have also exhibited conflicting findings for some associations between putative predictors and QoL in PLHIV. Furthermore, given the multi-dimensional nature of QoL reflecting patients' perception of different aspects of well-being, more research is needed to understand the determinants of each specific domain in order to optimize care for this vulnerable group.

Eastern Europe and Central Asia is the only region in the world where the HIV epidemic continues to grow rapidly, with a 30% increase in new HIV infections between 2010 and 2017.[5] The region's epidemic is concentrated predominantly among high-risk groups, especially among people who inject drugs (PWID) and their sexual partners. In Kazakhstan, according to the National AIDS Center data, the estimated number of PLHIV by the end of 2017 was 26,000; 80% of which (20,841) knew their status and 17,958 were registered for care.[6] The prevalence of HIV in Kazakhstan in 2017 was 0.1% among the general population, 0.2% among those aged 15–49 years, and 9.2% among PWID. Since 2011, the heterosexual route of transmission has become predominant among newly diagnosed cases, reaching 62.0% in 2017, while injecting drug use (IDU)-associated transmission decreased to 29.2%. In recent years, the number of PLHIV receiving ART in the country has increased significantly (from 233 people in 2005 to 11,482 people in 2017), and ART coverage reached 55.1% in 2017, with 55% of patients achieving suppressed HIV viral load (VL). The implementation of the WHO's Test and Treat approach for initiating ART was launched in Kazakhstan in 2018 and represented a change from the criteria used in 2012–2013 (CD4 cell count $\leq$350 cells/mm^3); access to ART is free for all patients in the country. As a result of the steady scale-up of ART, there has been a downward trend in mortality from AIDS-related illness (from 16.1 per 1000 PLHIV in 2005 to 10.6 in 2017). However, HIV prevalence varies widely across regions of Kazakhstan (e.g. from 11.0 to 190.3 per 100,000 population in 2013).[7] Among the places with the country's highest HIV prevalence is Almaty, the most populous city in Kazakhstan. In 2013, there were 3093 cumulative HIV cases since 1987 and 1989 PLHIV enrolled in HIV care in Almaty. In 2017, the prevalence of HIV in Almaty had reached 213.9 per 100,000 population.[6]

Data on HRQoL among PLHIV in Eastern Europe and the Central Asian region are relatively scarce.[8–11] Predictors of good QoL among PLHIV in the region include younger age, higher level of education, and being in a relationship (in Croatia)[8]; receiving ART, having high education, CD4 cell count $\geq$200 cells/mm^3 (in Georgia)[10]; and being employed or studying and absence of HIV-related symptoms (in Estonia).[11] People with opioid use disorder and those with highly elevated psychiatric symptoms experienced lower QoL (in Russia).[9] However, QoL among PLHIV and its determinants has not been studied in Kazakhstan.

The objective of this study was to examine HRQoL among PLHIV living in Almaty, Kazakhstan, and to assess the impact of socio-demographic and disease-related factors on overall HRQoL and specific domains of HRQoL in order to facilitate the development of treatment and social care programs and interventions.

Methods

Study design and population

We conducted a cross-sectional study at the Almaty city AIDS Center, 1 of the 16 regional centers in Kazakhstan involved in medical treatment and psychological and social support for PLHIV. A convenience sample of registered adult PLHIV under care (531) was recruited in April–December of 2013 during routine clinical care visits and provided informed consent. Eligible participants were 18 years of age or older, with documented laboratory-confirmed HIV infection, and able to speak Russian; all eligible patients were asked to participate in the study.

Ethical considerations

The Research Ethics Committee of the Kazakh National Medical University approved the original study protocol. Written informed consent was obtained from each participant. The secondary analysis of de-identified data from the 2013 study reported here was deemed exempt from review by the Institutional Review Board of the University at Albany.

Study measures and instruments

HRQoL. The main outcome of interest for this study, HRQoL, was assessed using the validated Russian version of the World Health Organization's Quality of Life HIV brief questionnaire (WHOQOL-HIV-Bref).[12] This is a multidimensional instrument with 31 questions grouped into six domains and two general questions (overall QoL, 'How would you rate your

quality of life?', and general health perception [GHP], 'How satisfied are you with your health?').[13] Each question is rated on a 5-point Likert interval scale and refers to the past two weeks. The mean scores of overall QoL and GHP questions were used as a measure of overall HRQoL and evaluated as a dichotomous variable: those who reported good HRQoL were compared to those who did not report having good HRQoL, including the neutral responses. Specifically, participants with mean scores of >3.0 were categorized as having good HRQoL and their counterparts (mean scores of ≤ 3.0) as having poor HRQoL.[11] The six domains assessed by the WHOQOL-HIV-Bref are physical functioning (e.g. physical pain, HIV infection-related physical problems), psychological functioning (e.g. life enjoyment, ability to concentrate), level of independence (e.g. ability to perform daily living activities), social relationships (e.g. acceptance by others, satisfaction with personal relationships), environment (e.g. feelings of safety in physical environment, financial resources), and spiritual/religious/personal beliefs (e.g. feeling that life has meaning, fearing the future). The summary domain scores were calculated by multiplying the average scores of all items in each domain by four, giving the domain scores ranges of 4–20, with 4 corresponding to the worst result and 20 corresponding to the best one. Internal consistency of the WHOQOL-HIV-Bref was high in the current sample (Cronbach's $\alpha = 0.811$–0.936 for the six domains and overall QoL and GHP) and all item-test correlations were ≥ 0.5 with the exception of the spirituality domain.

Socio-demographic characteristics. Socio-demographic characteristics, including age, gender, ethnicity (Russian, Kazakh, or other), marital status (single, married/cohabiting, separated/divorced/widowed), educational level (university level versus high school or lower), and employment status (employed/student versus not employed), were self-reported.

Clinical characteristics. Clinical HIV infection-related variables retrieved from medical records included WHO clinical stage,[14] time since diagnosis with HIV (in years, divided into <1.5, 1.5–5, and >5 years), most recent CD4+ T lymphocyte cell count (in cells/mm^3, categorized as >350, 200–350, and <200), ART history (categorized as receiving versus not receiving antiretroviral drugs), HIV transmission group (categorized as having history of IDU versus no history of IDU). Most recent HIV-1 VL was categorized as ≥ 500 versus <500 copies/ml (due to sensitivity of available assays) and hepatitis C virus (HCV) was categorized as no versus undetectable VL versus detectable VL. Patients with a current diagnosis of tuberculosis ($n = 21$), toxoplasmosis ($n = 25$), cytomegalovirus infection ($n = 42$), syphilis ($n = 47$), chlamydiosis ($n = 113$), or herpes simplex infection ($n = 40$) were combined into a 'co-infection' group. More than a quarter of patients (58) had two or more different infections.

Major depressive disorder. Major depressive disorder, or depression, symptoms were assessed using the validated Patient Health Questionnaire-9 (PHQ-9), translated into Russian.[15] The PHQ-9 assesses nine symptoms of depression specified in the DSM-IV and scores each criterion based on its frequency over the last two weeks from '0' (not at all) to '3' (nearly every day). Participants who reported being bothered by five or more symptoms (with one symptom being depressed mood or anhedonia) at least 'more than half the days' (score '2') were considered to have major depression. The criterion 'Thoughts that you would be better off dead or of hurting yourself in some way' was counted if present at all, regardless of frequency.

Statistical analysis

SAS 9.4 Software was used for data analysis. Descriptive statistics were calculated for all variables of interest. Bivariate analysis of categorical and continuous variables (using Chi square test, Fisher's exact test, or t-tests, as appropriate) was performed to examine associations between socio-demographic and health-related factors and HRQoL outcomes. A multivariable logistic regression model was fit with HRQoL (poor versus good) as the binary dependent variable and the variables related to HRQoL in the bivariate analyses as the covariates of interest, including participants' socio-demographic, clinical, and risk behavior characteristics. We used a backward elimination strategy to arrive at the final predictive model. Goodness-of-fit test of the final models and the area under the receiver operating characteristic (ROC) curve were used to assess the predictive ability and fit of the model. Multivariable Tobit regression models were used to examine factors associated with each WHOQOL-HIV-Bref domain, due to left and right censoring of domain mean scores, which ranged from 4 to 20.[16] Separate models were run for each domain.

Results

Characteristics of study population

Of the 600 approached patients, 69 refused to complete the survey (88.5% participation rate). No one was excluded because of the language barrier. As shown

in Table 1, of the 531 patients in the resulting study sample, more than half were males. The mean age of the group was 37.4 years. The majority of the participants were of Russian and Kazakh ethnicities, had high school or lower educational level, were legally married or co-habiting at the time of data collection, were not employed, and were diagnosed with HIV between 1.5 and 5 years or more than 5 years prior. Overall, 8.5% of participants met the PHQ-9 criteria for major depressive disorder. Almost half of the study participants were co-infected with hepatitis C; among those, about two-thirds had detectable HCV RNA. A large proportion of patients had a history of current co-infections, including tuberculosis, syphilis, toxoplasmosis, chlamydiosis, herpes simplex, and/or cytomegalovirus. A substantial proportion of the patients were not taking ART, although many of those not on ART were symptomatic (45.3%) or had CD4+ count 350 cells/mm^3 and lower (44.9%), and more than half had detectable ($\geq$500 RNA copies/ml) VL (56.7%) (these data are not presented in the table).

The assessment of QoL

The mean scores for each HRQoL domain and two general questions are presented in Table 2. Overall, scores in the HRQoL domains (range 4–20) were rather high, ranging from 13.01 (Environmental health) to 15.49 (Physical health). Participants with good HRQoL had higher scores in all domains than their counterparts with 'poor' HRQoL.

Bivariate analysis

More than one-third of participants (35.8%) were classified as having poor HRQoL. As shown in Table 1, those with poor HRQoL were older compared to participants with good HRQoL ($p = 0.003$). Participants with poor HRQoL in contrast with their counterparts had lower level of education ($p = 0.009$), lower proportion of married/co-habiting ($p = 0.001$), higher prevalence of major depressive disorder ($p < 0.0001$), and IDU history ($p < 0.0001$). They also had a higher proportion of persons with CD4+ <200 cells/mm^3 ($p = 0.004$), more advanced symptomatic stages of HIV infection ($p = 0.003$), and co-infection prevalence ($p = 0.003$) compared to persons with good QoL. The two groups did not differ by gender, ethnicity, employment status, time since HIV diagnosis, HIV-1 and hepatitis C VLs, and history of ART.

Multivariable regression analysis

In the final multivariable logistic regression model, the presence of major depressive disorder; having a history of IDU; being separated, divorced, or widowed; having CD4+ cell count less than 200 cells/mm^3; and presence of co-infection were independently associated with poor HRQoL (Table 3).

Goodness-of-fit statistics using Pearson's chi square, deviance, and the Hosmer–Lemeshow statistic indicated adequate fit of the predictive model to the data ($p = 0.190$, $p = 0.513$, $p = 0.446$, respectively). The model demonstrated an acceptable ability to discriminate between those subjects who experienced the outcome of interest versus those who did not (the area under the ROC curve was 0.763).

Table 4 shows the results of multivariable Tobit regression models predicting each HRQoL domain score. Major depressive disorder was associated with lower scores in the physical health, level of independence, and social relationships domains, after controlling for other factors. History of IDU was an independent predictor of lower scores in all domains, except for spirituality/beliefs. Lower education level was an independent predictor for lower scores in physical and environmental health, and level of independence domains. Being separated/divorced/widowed significantly predicted poorer reported physical health, and never married status was a strong predictor of poorer social relationships. Older age ($\geq$50 years) was a significant predictor of lower reported scores in independence and social relations. CD4+ <200 cells/mm^3 was a predictor of poorer physical health and level of independence. Patients with longer time since HIV diagnosis (1.5–5 and >5 years) reported significantly higher scores in spirituality/personal beliefs domain. There were significant interactions between depression and several factors in predicting each domain score: age and education level for psychological health, history of ART for level of independence, level of education and marital status for environmental health.

Discussion

In this study of 531 PLHIV in Almaty, Kazakhstan, over one-third of participants (35.8%) were identified as having poor HRQoL. Independent predictors of poor HRQoL included the presence of major depressive disorder, being formerly married, CD4+ <200 cells/mm^3, history of IDU, and the presence of co-infections.

The mean scores for overall QoL and GHP and the six domains of the WHOQOL-HIV-Bref questionnaire in our study are in general agreement with data obtained by other researchers.[17–19] At the same time, the mean scores of overall QoL and GHP for our sample were slightly higher compared to studies from other former Soviet Union countries with the predominant IDU route of HIV transmission, including

Table 1. Socio-demographic and HIV-related characteristics of people living with HIV with good and poor health-related quality of life, Almaty, Kazakhstan, 2013.

	Total (n = 531)		Good HRQoL[a] (n = 341)		Poor HRQoL (n = 190)		
Characteristic	n	%	n	%	n	%	p-value[b]
Socio-demographic							
Gender							0.074
Male	294	55.4	179	52.5	115	60.5	
Female	237	44.6	162	47.5	75	39.5	
Age (years)							0.003
18–35	240	45.2	171	50.2	69	36.3	
36–49	242	45.6	146	42.8	96	50.5	
≥50	49	9.2	24	7.0	25	13.2	
Ethnicity							0.516
Kazakh	146	27.5	97	28.5	49	25.8	
Russian	289	54.4	187	54.8	102	53.7	
Other	96	18.1	57	16.7	39	20.5	
Education							0.009
University	69	13.0	54	15.8	15	7.9	
High school or lower	262	87.0	287	84.2	175	92.1	
Marital status							0.001
Married/co-habiting	377	71.0	256	75.1	121	63.7	
Single	98	18.5	61	17.9	37	19.5	
Separated/Divorced/Widowed	56	10.5	24	7.0	32	16.8	
Employment							0.096
Employed/student	178	33.5	123	36.1	55	28.9	
Unemployed	353	66.5	218	63.9	135	71.1	
Depression[c]							<.0001
No	486	91.5	335	98.2	151	79.5	
Yes	45	8.5	6	1.8	39	20.5	
HIV-infection related							
Time since HIV diagnosis (years)							0.436
<1.5	124	23.4	84	24.6	40	21.1	
1.5–5	207	39.0	135	39.6	72	37.9	
>1.5	200	37.7	122	35.8	78	41.1	
CD4+ T lymphocytes (cells/mm^3)							0.004
>350	224	42.2	157	46.0	67	35.3	
200–350	188	35.4	122	35.8	66	34.7	
<200	119	22.4	62	18.2	57	30.0	
History of injecting drug use							<0.0001
No	276	52.0	200	58.7	76	40.0	
Yes	255	48.0	141	41.3	114	60.0	
WHO clinical stage of HIV infection							0.003
Stage I (Asymptomatic)	214	40.3	156	45.8	58	30.5	
Stage II	117	22.0	69	20.2	48	25.3	
Stage III and IV	200	37.7	116	34.0	84	44.2	
Hepatitis C viral load (RNA copies/ml)							0.723
No hepatitis C	273	51.4	181	53.1	92	48.4	
Undetectable	91	17.1	56	16.4	35	18.4	
Detectable	167	31.5	104	30.5	63	33.2	
HIV viral load (RNA copies/ml)							0.659
<500	251	51.9	160	52.6	91	50.6	
⩾500	233	48.1	144	47.4	89	49.4	
Co-infection[d]							0.003
No	280	57.7	190	62.9	90	49.2	
Yes	205	42.3	112	37.1	93	50.8	

(continued)

Table 1. Continued.

Characteristic	Total (n = 531)		Good HRQoL[a] (n = 341)		Poor HRQoL (n = 190)		p-value[b]
	n	%	n	%	n	%	
ART[e]							0.079
No	245	46.1	167	49.0	78	41.1	
Yes	286	53.9	174	51.0	112	58.9	
Age at HIV diagnosis (years), mean (SD)	37.35 (8.65)		36.44 (8.15)		38.98 (8.28)		0.001

ART: antiretroviral therapy.
[a]HRQoL: Health-related quality of life was assessed using the WHOQOL-HIV-Bref questionnaire. The mean scores of two general questions ('How would you rate your quality of life?', and 'How satisfied are you with your health?'), ranged from 1 to 5. The participants with mean scores of >3.0 were categorized as having good HRQoL, and their counterparts (mean scores of ≤3.0) as having poor HRQoL.
[b]p-value from Chi square test for categorical variables and t-test for continuous variables, $p < 0.05$ considered statistically significant.
[c]Depression: probable major depressive disorder.
[d]Co-infection: presence of at least one of the following infections: tuberculosis, syphilis, toxoplasmosis, chlamydiosis, herpes simplex, or cytomegalovirus infection.
[e]ART: history of antiretroviral therapy.

Table 2. Mean scores for the six domains and overall quality of life and general health of the WHOQOL-HIV-Bref, Almaty, Kazakhstan, 2013.

Health-related quality of life domains and questions	Mean (SD)		
	All (n = 531)	Good HRQoL (n = 341)	Poor HRQoL (n = 190)
Overall QOL	3.56 (0.66)	3.98 (0.21)	2.80 (0.51)
Overall GHP	3.42 (0.72)	3.82 (0.40)	2.69 (0.57)
Physical health	15.49 (2.66)	16.73 (1.69)	13.27 (2.64)
Psychological health	13.57 (2.07)	14.50 (1.43)	11.89 (1.98)
Level of independence	13.95 (2.40)	15.00 (1.69)	12.05 (2.32)
Social relationship	14.10 (2.88)	15.35 (1.92)	11.77 (2.93)
Environmental health	13.01 (1.92)	13.79 (1.45)	11.58 (1.84)
Spirituality/Religion/ Personal beliefs	14.03 (2.64)	14.25 (2.76)	13.63 (2.35)

GHP: general health perception; HRQoL: health-related quality of life; QOL: quality of life; SD: standard deviation.

Table 3. Results of multivariable logistic regression model predicting poor health-related quality of life in people living with HIV, Almaty, Kazakhstan (n = 485).

Variable	Adjusted odds ratio (95% CI)	
Marital status		
Married/Co-habiting	1.00	(ref)
Single	1.08	(0.63–1.84)
Separated/Divorced/Widowed	2.23	(1.16–4.28)
Depression[a]		
No	1.00	(ref)
Yes	13.42	(4.56–39.52)
CD4+ T count (cells/mm^3)		
>350	1.00	(ref)
200–350	1.31	(0.82–2.10)
<200	2.17	(1.30–3.62)
History of injection drug use		
No	1.00	(ref)
Yes	2.10	(1.40–3.14)
Co-infection[b]		
No	1.00	(ref)
Yes	1.59	(1.06–2.39)

[a]Depression: probable major depressive disorder.
[b]Co-infection: presence of at least one of the following infections: tuberculosis, syphilis, toxoplasmosis, chlamydiosis, herpes simplex, or cytomegalovirus infection.

Estonia and Georgia (3.56 ± 0.66 versus 2.9 ± 0.8 and 3.0 ± 0.7, respectively).[10,11] Moreover, mean scores in physical health were also higher in our sample: 15.49 ± 2.66 compared to 13.3 ± 3.2 and 13.3 ± 3.6, respectively. This could possibly be explained by differences in socio-demographic characteristics of study participants, higher prevalence of hepatitis C co-infection, and IDU history in the Estonian study.

Probable major depressive disorder was found to consistently affect HRQoL and three specific HRQoL domains in our participants (physical health, level of independence, and social relationships). These results are similar to those of previous studies showing depression as one of the most common co-morbidities of HIV infection that strongly interferes with daily life and negatively impacts HRQoL.[20–22] However, it is still unclear whether depression is exacerbated by the presence of HIV, or, conversely, it is a manifestation of HIV brain disorder.[21] Moreover, the association between depression and HRQoL in our sample is likely underestimated due to probable underreporting of depression symptoms by study participants. For example, in other settings, the prevalence of major depressive disorder among HIV patients ranged from 14.0 to 27.2%,[21] whereas in our study it was 8.5%.

Table 4. Results of Tobit regression models predicting health-related quality of life in six specific domains among people living with HIV, Almaty, Kazakhstan, 2013.

	Physical health (n = 529)			Psychological health (n = 482)			Level of independence (n = 528)		
Variable	b	SE	p-value	b	SE	p-value	b	SE	p-value[a]
Age, years (ref: 18–35)									
36–49				−0.180	0.188	0.339	−0.332	0.190	0.080
≥50				−0.464	0.323	0.151	−0.667	0.322	0.038
Education level (ref: University)									
High school or lower	−1.127	0.306	<0.001	−0.378	0.264	0.152	−1.019	0.265	<0.001
Marital status (ref: Married/Co-habiting)									
Single	−0.339	0.268	0.205						
SDW	−0.702	0.343	0.041						
Depression[b] (ref: No)									
Yes	−3.563	0.369	<.0001	0.932	1.072	0.384	−2.923	0.692	<.0001
CD4+ T count, cells/mm^3 (ref: >350)									
200–350	0.099	0.234	0.673				−0.011	0.207	0.958
<200	−0.641	0.268	0.017				−0.601	0.234	0.010
Hepatitis C viral load (RNA copies/ml) (ref: No hepatitis C)									
Undetectable							0.035	0.253	0.889
Detectable							0.472	0.213	0.027
History of IDU (ref: No)									
Yes	−0.665	0.208	0.001	−0.497	0.238	0.037	−1.072	0.201	<.0001
History of ART (ref: No)									
Yes							−0.374	0.192	0.051
HIV viral load (RNA copies/ml) (ref: <500)									
≥500				−0.081	0.234	0.729			
Interaction terms									
Depression in HS/L				−2.768	1.003	0.006			
History of ART in PLHIV with depression							−1.600	0.687	0.020
History of IDU in PLHIV with depression							1.308	0.641	0.041
Depression and age (ref: Depression in age 18–35 years)									
Depression in 36–49 years				−0.596	0.697	0.392			
Depression in ≥50 years				−2.931	0.917	0.001			
HIV viral load ≥500 RNA copies/ml in IDUs				−0.685	0.339	0.043			

ART: antiretroviral therapy; IDU: injecting drug use; HS/L: high school or lower education level; PLHIV: people living with HIV; SDW: separated, divorced or widowed.

[a]p-value < 0.05 was considered statistically significant.

[b]Depression: probable major depressive disorder.

In the current study, IDU was found to be an independent predictor of poor HRQoL in general and in all specific domains with the exception of spirituality/beliefs. Illicit drug use has been found to be associated with decreased mental and physical HRQOL in PLHIV in many other settings,[23–27] reflecting the many other socio-economic, psychological, and health challenges faced by this group.[28] Drug use can cause both direct physical deterioration[25] and indirect effects on HRQoL via associated psychiatric conditions.[27] However, not all studies revealed such relations. For example, in Estonian and Georgian patients (with 60 and 34.3% of IDUs in study samples, respectively), the negative association of IDU with HRQoL was not confirmed.[10,11] Given a substantial amount of illicit drug users among PLHIV in Almaty and in the whole country, specific programs targeted to this vulnerable population to improve their HRQoL are needed.

Our findings support the importance of intimate relationships in individual's HRQoL: those who were separated/divorced/widowed had worse scores compared to married/co-habiting in general HRQoL, physical health, and social relationships, and those who were single (never married) had the worst scores in the social relationships domain. A stable family situation and living together as a couple are thought to be contributors to higher HRQoL possibly through social and emotional support for PLHIV.[25,29–31]

In our study, age and educational level were not independent predictors of HRQoL, but were significantly associated with lower scores in several HRQoL domains. Although published findings have been mixed, ours, to some extent, are consistent with those indicating that older patients report worse HRQoL scores.[24,25,32–34] Our findings suggest that older age (≥50 years) is associated with lower scores in level of independence and social relationships; moreover, older

Table 4. Continued.

	Social relationship (n = 525)			Environmental health (n = 521)			SRPB (n = 483)		
Variable	b	SE	p-value	b	SE	p-value	b	SE	p-value[a]
Age, years (ref: 18–35)									
36–49	0.081	0.244	0.740						
≥50	−0.914	0.413	0.027						
Education level (ref: University)									
High school or lower				−0.710	0.236	0.003			
Marital status (ref: Married/Co-habiting)									
Single	−1.496	0.383	<.0001	−0.322	0.211	0.128			
SDW	−0.812	0.295	0.006	−0.316	0.275	0.251			
Depression[b] (ref: No)									
Yes	−3.262	0.412	<.0001	1.443	0.917	0.116	1.181	0.903	0.191
Time since HIV diagnosis, years (ref: <1.5 years)									
1.5–5							0.850	0.310	0.006
>5							1.147	0.320	<0.0001
HIV viral load (RNA copies/ml) (ref: <500)									
≥500							−0.498	0.226	0.028
Injecting drug use (ref: No)									
Yes	−0.966	0.231	<.0001	−0.706	0.157	<.0001			
Interaction terms									
Depression in PLHIV with HS/L				−2.667	0.961	0.006			
Depression and marital status (ref: Depression in married/Co-habiting)									
Depression in single				−1.538	0.667	0.021			
Depression in SDW				−0.797	0.739	0.281			
Depression and time since HIV diagnosis (ref: Depression in PLHIV with HIV diagnosis <1.5 years)									
Depression in PLHIV with HIV diagnosis 1.5–5 years							−2.364	1.121	0.035
Depression in PLHIV with HIV diagnosis >5 years							−2.564	1.074	0.017

HS/L: high school or lower; SDW: separated, divorced or widowed; SRPB: spirituality, religion, personal beliefs.
[a]p-value < 0.05 was considered statistically significant.
[b]Depression: probable major depressive disorder.

age and depressive symptoms jointly account for significantly lower psychological health in patients. Additionally, lower level of education (high school or lower) was significantly associated with worse physical health, level of independence, social relationships, and psychological health among those with depression symptoms. Possible explanation may be that lower education is to some extent a proxy of lower socio-economic status and potentially decreases opportunities for employment and social support, and may also reflect a poorer ability to understand treatment recommendations.[35] In contrast with other findings,[11,29,31,36–38] gender and employment status were not associated with HRQoL in our sample.

Several HIV-related clinical variables were independently associated with HRQoL (CD4+ T-cell count, presence of co-infections) or with some specific HRQoL domains (HIV VL, CD4+ count, time since HIV diagnosis), supporting previous evidence of significant associations between poor clinical parameters and decreased HRQoL.[35,39,40] Recently, some researchers have suggested that the significance of immunological markers and HIV-related clinical variables in predicting HRQoL may disappear in the era of early initiation of ART among relatively healthy patients.[29,41,42] However, for the populations of PLHIV with a higher proportion of patients at advanced clinical stage, as was the case in our study, these criteria continue to be relevant for HRQoL.

When the study was conducted (2013), the criterion used for initiating ART in Kazakhstan was exhibiting CD4 cell count ≤350 cells/mm^3. Our findings on association between poor clinical parameters and patients' poor QoL support treatment initiation at least for people with advanced disease considering that ART should potentially improve patients' HRQoL through suppressing the etiologic agent and gradually restoring their immune system. Moreover, given a large

proportion of immunosuppressed participants (83.8% had $\leq$500 CD4+ cells/mm^3), the positive effect of ART on HRQoL through the expected considerable reduction in plasma HIV RNA and restoration of immunologic function might be significant. WHO's current treatment recommendations are to start treatment even earlier, at the time of diagnosis.[43] Implementation of this approach, started in Kazakhstan in 2018, as well as effective management of co-infections, could improve patients' HRQoL. However, since several diseases with different clinical presentation and severity were combined in one 'co-infections' variable, the association between current co-infections and poorer HRQoL should be explored further to identify the impact of individual diseases and their clinical manifestations on HRQoL.

Overall, our findings related to independent determinants of scores in specific domains could be used as a rationale for complex interventions among PLHIV aimed to improve different dimensions of their HRQoL.

This study had several limitations. Because of the cross-sectional design, the exact direction of the associations between predictor variables and HRQoL cannot be established. The participants were recruited at a single site, so our findings may not be fully representative of all PLHIV in Kazakhstan. In particular, our sample included a lower proportion of men and PLHIV infected through IDU and a higher ART coverage rate and proportion at advanced clinical stages compared to the whole population of PLHIV in Kazakhstan in 2013.[7] Since the data were collected during 2013, the clinical characteristics and treatment experiences of our sample may not reflect current conditions among PLHIV; however, these data can serve as a starting point for comparing the QoL of PLHIV in the region in subsequent studies. Some important variables, such as income, cognitive function, non-AIDS co-morbidities, stigma and discrimination, alcohol abuse, and social support, which have been shown to be predictors of HRQoL in PLHIV in other studies were not included in the analysis because we did not have enough information on them. The relatively high cutoff point (500 copies/ml) used to see the effect of plasma HIV RNA levels possibly influenced our estimates of patients with undetectable VL. In addition, misclassification of ICD-10 diagnoses of depression is a possible source of bias due to the low sensitivity of the PHQ-9 screening tool[44] as well as likely underestimation of this condition given the stigma and cultural peculiarities regarding mental health issues.

Notwithstanding these limitations, the current research is the first with relatively large sample size exploring different categories of determinants (socio-demographic, clinical, psychological, behavioral) to assess the HRQoL and its specific dimensions of PLHIV in Kazakhstan as well as in the Central Asia region. Another strength of our study is that information on clinical data were obtained from medical records, decreasing the possibility of information bias. Lastly, we used an internationally validated instrument to assess HRQoL that allows comparing the findings across countries. Future prospective research should focus on replicating these results among populations of other sites in the country.

Conclusions

Study findings suggest that early initiation of ART, providing integrated HIV/AIDS and substance dependence services, routine assessment for depression and co-infections with effective management, as well as educational interventions are crucial to enhance HRQoL. PLHIV who inject drugs, are depressed, who are older than 50, and who have advanced disease, especially those who are formerly married, require more social and psychological support. Thus, an interdisciplinary approach is needed in planning health care services addressing HRQoL improvement of PLHIV.

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Authors' contributions

BTZ, ZSN, MT, GSB, and JD conceptualized the study and data analysis plan. ZSN and GMA contributed to the acquisition and collection of the data. BTZ analyzed the data and drafted the manuscript. ZSN, MT, GSB, and JD reviewed and commented on the manuscript, which was revised and approved by all of the other authors.

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References

1. Mocroft A, Vella S, Benfield T, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. *Lancet* 1998; 352: 1725–1730.
2. Karimi M and Brazier J. Health, health-related quality of life, and quality of life: what is the difference? *PharmacoEconomics* 2016; 34: 645–649.
3. Degroote S, Vogelaers D and Vandijck DM. What determines health-related quality of life among people living with HIV: an updated review of the literature. *Arch Public Health*. 2014; 72: 40.
4. Gakhar H, Kamali A and Holodniy M. Health-related quality of life assessment after antiretroviral therapy: a review of the literature. *Drugs* 2013; 73: 651–672.
5. UNAIDS. Global AIDS update 2018. Miles to go: closing gaps. Breaking barriers. Righting injustices. Geneva: UNAIDS, https://www.unaids.org/sites/default/files/media_asset/miles-to-go_en.pdf (2018, accessed 11 January 2019).
6. Republican Center for the Prevention and Control of AIDS of the Ministry of Health of the Republic of Kazakhstan. Report on the activities of the AIDS service for 2017, Almaty, 2018 (in Russian) [Отчет о деятельности службы СПИД за 2017 год, Алматы, 2018], http://www.kncdiz.kz/files/00004587.pdf (2018, accessed 11 January 2019).
7. Republican Center for the Prevention and Control of AIDS of the Ministry of Health of the Republic of Kazakhstan. Report on the activities of the AIDS service for 2013, Almaty, 2014 (in Russian) [Отчет о деятельности службы СПИД за 2013 год, Алматы, 2014], http://www.kncdiz.kz/files/00000867.pdf (2014, accessed 11 March 2018).
8. Belak Kovacević S, Vurusić T, Duvancić K, et al. Quality of life of HIV-infected persons in Croatia. *Coll Antropol* 2006; 30: 79–84.
9. Desrosiers A, Blokhina E, Krupitsky E, et al. Psychiatric symptoms, quality of life, and HIV status among people using opioids in Saint Petersburg, Russia. *Drug Alcohol Depend* 2017; 172: 60–65.
10. Karkashadze E, Gates MA, Chkhartishvili N, et al. Assessment of quality of life in people living with HIV in Georgia. *Int J STD AIDS* 2017; 28: 672–678. Jun
11. Rüütel K, Pisarev H, Loit H-M, et al. Factors influencing quality of life of people living with HIV in Estonia: a cross-sectional survey. *J Int AIDS Soc* 2009; 12: 13.
12. WHO. The World Health Organization Quality of Life (WHOQOL)-BREF, https://www.who.int/substance_abuse/research_tools/en/russian_whoqol.pdf?ua=1 (2004, accessed 10 December 2018).
13. Pedroso B, Gutierrez GL, Duarte E, et al. Quality of life assessment in people living with HIV/AIDS: clarifying the WHOQOL-HIV and WHOQOL-HIV-Bref Instruments, http://cdn.intechweb.org/pdfs/22273.pdf (2011, accessed 4 March 2018).
14. WHO. WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva: WHO, http://www.who.int/hiv/pub/guidelines/HIVstaging150 307.pdf (2007, accessed 19 December 2017).
15. Kroenke K, Spitzer RL and Williams J. The PHQ-9. *J Gen Intern Med* 2001; 16: 606–613.
16. Twisk J and Rijmen F. Longitudinal Tobit regression: a new approach to analyze outcome variables with floor or ceiling effects. *J Clin Epidemiol* 2009; 62: 953–958.
17. Liping M, Peng X, Haijiang L, et al. Quality of life of people living with HIV/AIDS: a cross-sectional study in Zhejiang Province, China. *PLoS One* 2015; 10: e0135705.
18. Meemon N, Paek SC, Yenchai D, et al. Application of the WHOQOL-HIV-BREF questionnaire in HIV-infected Thai patients: reliability and validity of the instrument. *J Assoc Nurses AIDS Care* 2016; 27: 698–708.
19. O'Connell K, Skevington S, Saxena S, et al. Preliminary development of the World Health Organisation's quality of life HIV instrument (WHOQOL-HIV): analysis of the pilot version. *Soc Sci Med* 2003; 57: 1259–1275.
20. Jia H, Uphold CR, Wu S, et al. Health-related quality of life among men with HIV infection: effects of social support, coping, and depression. *AIDS Patient Care STDs* 2004; 18: 594–603.
21. Serafini G. Associations among depression, suicidal behavior, and quality of life in patients with human immunodeficiency virus. *World J Virol* 2015; 4: 303.
22. Trépanier LL, Rourke SB, Bayoumi AM, et al. The impact of neuropsychological impairment and depression on health-related quality of life in HIV-infection. *J Clin Exp Neuropsychol* 2005; 27: 1–15.
23. Korthuis PT, Zephyrin LC, Fleishman JA, et al. Health-related quality of life in HIV-infected patients: the role of substance use. *AIDS Patient Care STDs* 2008; 22: 859–867. Nov
24. Liu C, Johnson L, Ostrow D, et al. Predictors for lower quality of life in the HAART era among HIV-infected men. *J Acquir Immune Defic Syndr* 2006; 42: 470–477.
25. Perez IR, Baño JR, Ruz MAL, et al. Health-related quality of life of patients with HIV: impact of sociodemographic, clinical and psychosocial factors. *Qual Life Res* 2005; 14: 1301–1310.
26. Préau M, Vincent E, Spire B, et al. Health-related quality of life and health locus of control beliefs among HIV-infected treated patients. *J Psychosom Res* 2005; 59: 407–413.
27. Sherbourne CD. Impact of psychiatric conditions on health-related quality of life in persons with HIV infection. *Am J Psychiatry* 2000; 157: 248–254. 1
28. Galea S and Vlahov D. Social determinants and the health of drug users: socioeconomic status, homelessness, and incarceration. *Public Health Rep* 2002; 117: S135–S145.
29. Nobre N, Pereira M, Sutinen J, et al. Quality of life of people living with HIV/AIDS: a cross-country comparison study of Finland and Portugal. *AIDS Care* 2016; 28: 873–877.
30. Rao D, Hahn EA, Cella D, et al. The health related quality of life outcomes of English and Spanish speaking persons living with HIV/AIDS from the continental United States and Puerto Rico. *AIDS Patient Care STDs* 2007; 21: 339–346.

31. Worthington C and Krentz HB. Socio-economic factors and health-related quality of life in adults living with HIV. *Int J STD AIDS* 2005; 16: 608–614.
32. Gibson K, Rueda S, Rourke SB, et al. Mastery and coping moderate the negative effect of acute and chronic stressors on mental health-related quality of life in HIV. *AIDS Patient Care STDs* 2011; 25: 371–381.
33. McGowan J, Sherr L, Rodger A, et al. Effects of age on symptom burden, mental health and quality of life amongst people with HIV in the UK. *J Int AIDS Soc* 2014; 17(4Suppl 3): 19511.
34. Préau M, Marcellin F, Carrieri MP, et al. Health-related quality of life in French people living with HIV in 2003: results from the national ANRS-EN12-VESPA Study. *AIDS* 2007; 21: S19–S27.
35. Murri R, Fantoni M, Del Borgo C, et al. Determinants of health-related quality of life in HIV-infected patients. *AIDS Care* 2003; 15: 581–590.
36. Degroote S, Vogelaers DP, Vermeir P, et al. Socio-economic, behavioural, (neuro)psychological and clinical determinants of HRQoL in people living with HIV in Belgium: a pilot study. *J Int AIDS Soc* 2013; 16: 18643.
37. Passos SMK and Souza Ld de M. An evaluation of quality of life and its determinants among people living with HIV/AIDS from Southern Brazil. *Cad Saúde Pública* 2015; 31: 800–814.
38. Rueda S, Raboud J, Mustard C, et al. Employment status is associated with both physical and mental health quality of life in people living with HIV. *AIDS Care* 2011; 23: 435–443.
39. Call SA, Klapow JC, Stewart KE, et al. Health-related quality of life and virologic outcomes in an HIV clinic. *Qual Life Res* 2000; 9: 977–985.
40. Gill CJ, Griffith JL, Jacobson D, et al. Relationship of HIV viral loads, CD4 counts, and HAART use to health-related quality of life. *J Acquir Immune Defic Syndr* 2002; 30: 485–492.
41. Igumbor J, Stewart A and Holzemer W. Comparison of the health-related quality of life, CD4 count and viral load of AIDS patients and people with HIV who have been on treatment for 12 months in rural South Africa. *SAHARA J* 2013; 18: 1–7.
42. Mwesigire DM, Martin F, Seeley J, et al. Relationship between CD4 count and quality of life over time among HIV patients in Uganda: a cohort study. *Health Qual Life Outcomes* 2015; 13: 144.
43. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd ed. Geneva: WHO, http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1 (2016, accessed 19 December 2017).
44. Manea L, Gilbody S and McMillan D. A diagnostic meta-analysis of the Patient Health Questionnaire-9 (PHQ-9) algorithm scoring method as a screen for depression. *Gen Hosp Psychiatry* 2015; 37: 67–75.