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## The Benefits of Care: Treated HIV Infection and Health-Related Quality of Life Among Older-Aged People in Uganda

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### Abstract

**Objectives:** To explore how HIV care affects health-related quality of life (HRQoL) among older people in Uganda.

**Methods:** We enrolled older-aged ( > 49 years) people with HIV receiving HIV care and treatment, along with age- and sex-similar people without HIV. We measured health-related quality of life using the EQ-5D-3L scale.

**Results:** People with HIV (n=298) and people without HIV (n=302) were similar in median age (58.4 vs. 58.5 years), gender, and number of co-morbidities. People with HIV had higher

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self-reported health status ( $b=7.0$ ; 95% Confidence Interval [CI], 4.2–9.7), higher EQ-5D utility index ( $b=0.05$ ; 95% CI, 0.02–0.07), and were more likely to report no problems with self-care (adjusted odds Ratio [AOR], 2.0; 95% CI, 1.2–3.3) or pain/discomfort (AOR=1.8, 95% CI, 1.3–2.8). Relationships between HIV serostatus and health-related quality of life differed by gender, but not age.

**Conclusions:** Older people with HIV receiving care and treatment reported higher health-related quality of life than people without HIV in Uganda. Access to primary care through HIV programs and/or social network mobilization may explain this difference, but further research is needed to elucidate the mechanisms.

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## Introduction

There are over 37 million people with HIV (PWH) as of 2020 (WHO, 2020), with 70% of them residing in sub-Saharan Africa (UNAIDS, 2016; WHO, 2020). Due to successful antiretroviral therapy (ART) distribution programs, the life expectancy of PWH has increased significantly in the region, and there has been a sizeable increase in the population of PWH over 50 years of age (Palella et al., 1998) Bhatia et al., 2012; Siedner, 2019). Data, mostly from the global north, indicate that PWH are more prone to aging-related co-morbidities at younger ages compared to people without HIV (PWOH) (Bhatia et al., 2012; Gabuzda et al., 2020). Consequently, HIV infection has historically been associated with reductions in health-related quality of life (HRQoL) (Hays et al., 2000; Miners et al., 2014). Although many of these HRQoL metrics substantially improve after ART initiation, HRQoL among treated PWH remains reduced compared to HIV-negative populations of similar age (Briongos-Figuero et al., 2011).

Less is known about the extent to which HIV infection and access to treatment influence HRQoL among older-age adults in Sub-Saharan Africa (SSA). Importantly, the epidemiology of co-morbidity and the massive investments in HIV care programs may differentially affect HRQoL. For example, in some resource-limited settings, the scale-up of ART is accompanied by additional interventions such as peer support, vocational training, job referrals, clean water, food security, micro-finance training, and access to general health care (Small et al., 2019). So, whereas HIV has historically been associated with lower HRQoL, many of these HIV-related interventions can be expected to counteract or even ameliorate differences that have been historically observed among PWH in the global north.

Understanding the relationship between HIV infection and HRQoL will be valuable for designing the next generation of healthcare programs in the region. To do so, we analyzed data from a cohort of older adults in Uganda to understand the association between treated HIV infection and HRQoL. We aimed to estimate the association between treated HIV and HRQoL among older people in Uganda. We hypothesized that PWH on ART have a similar HRQoL to PWOH due to benefits they receive through their access to clinical care. As a secondary aim, we investigated how demographic factors, such as gender and age, modify the relationship between HIV treatment and HRQoL in Uganda.

## Methods

### Study population and data collection

Data were collected from 10/2020–10/2021 as part of *the Quality of Life and Ageing with HIV in Rural Uganda Study*, a cohort study designed to identify determinants of well-being and interventions to improve quality of life for older PWH in Uganda. Eligible people with HIV (PWH) were selected from a prior longitudinal cohort study (Siedner et al., 2021) and were recruited directly from HIV clinics at the Mbarara Regional Referral Hospital and Kabwohe Clinical Research Centre. We included HIV positive adults aged 49 years or older who had been taking ART for a minimum of 3 years. After each round of recruitment, we used population census data to select age- and sex-similar people without HIV from an ongoing population cohort (Takada et al., 2019) within the clinic catchment area (the participants of which were recruited from their homes). Although the study was initially planned to be conducted in person, during the first year of the COVID-19 epidemic we transitioned to remote, phone-based interviews. Six hundred participants were enrolled: 298 PWH from the parent study (Siedner et al., 2021) and 302 confirmed HIV-negative participants from the population cohort. Of those approached for participation in this study, 100% agreed to participate. All research assistants received training in the ethical conduct of human subjects research. As with study interviews, informed consent procedures were conducted by phone (Reenen et al., 2018).

### Measures

The study questionnaire included questions on sociodemographics, self-reported history of comorbidities including diabetes, high blood pressure, heart attack or heart failure, kidney problems, stroke, cancer, COPD, asthma, pneumonia, high cholesterol, and tuberculosis, and HRQoL. HIV serostatus was the independent variable measured based on verbal confirmation and the test results from the prior study data.

The primary outcomes of interest were HRQoL defined in three ways: 1) The European Quality of Life Vertical Visual Analog Scale (EQ-VAS), wherein respondents rated their overall health on the day of the interview on a scale of a 0–100 (with 0 indicating worst health and 100 indicating best health) (Feng et al., 2014); Karimi & Brazier, 2016). The EQ-5D-3L survey EuroQol Office, 2019) rated participant health status across five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels: no problems, some problems, and extreme problems. The scale has been used extensively to assess HRQoL including in sub-Saharan Africa and among populations of PWH (Herdman et al., 2011). 2) The EQ-5D Index (health utility) was a continuous variable derived from the EQ-5D-3L sub-scale ratings across five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) using time-tradeoff valuations from a prior study in Zimbabwe (Jelsma et al., 2003). The EQ-5D index scores are utilities derived from the respondents' profile across 5 dimensions. The EQ-5D index ranges from 0 to 1 (with 0 denoting death and 1 denoting complete health). Negative values of the EQ-5D index indicate quality of life is worse than death. 3) The EQ-5D-3L Sub-Scale (including Mobility, Self-care, Usual Activities, Pain/Discomfort, Anxiety/Depression) with a report of some problems or extreme problems in each of the

five sub-scale domains was used to create binary variables for each domain (no problem was coded as 1 vs. some or extreme problems were coded as 0).

### Statistical Analyses

We first conducted descriptive analyses of the sample by HIV serostatus using chi-square for the categorical variables and analysis of variance for the continuous variables. To estimate the association between HIV serostatus and HRQoL, we fit linear regression models (for the VAS scale and health valuation or utility score) and logistic regression models (for the five sub-scales of EQ-5D), both with and without the other covariates (age, sex, education, marital status, alcohol consumption, and the number of comorbidities). For the sub-scale analyses of the EQ-5D, each domain was dichotomized as no problems versus some or significant problems, because of the small sample size in the significant problems sub-groups across most of the sub-scales. Specifically, fewer than 5 participants in the HIV serostatus sub-groups reported having extreme problems for mobility, usual care, usual activities, and anxiety/depression. Finally, after finding differences in HRQoL by HIV serostatus, we conducted a post-hoc analysis to assess for effect modification by gender or age (a continuous or binary variable with the cutoff point as 58 years old as the median of the distribution) on the association between HIV and HRQoL. All analyses were conducted with SAS version 9.4 (SAS, 2013).

### Ethical Considerations

The study was approved by the ethics committees at Mbarara University of Science and Technology and Mass General Brigham. We also obtained clearance to conduct the study from the Uganda National Council of Science and Technology. All participants gave verbal consent. Written consent was waived by the review committees due to the COVID-19 epidemic and the infeasibility of obtaining written consent during remote data collection.

### Results

Six hundred participants were enrolled, selected from the 298 PWH, and 302 confirmed HIV-negative participants. PWH and PWOH were similar in terms of age, sex, and educational attainment (Table 1). However, PWH were less likely to be married or cohabitating (54% vs. 80%,  $p<0.001$ ). The total number of comorbidities between PWH and PWOH was similar (mean 0.5 vs. 0.5,  $p=0.71$ ); although PWH had a lower prevalence of high blood pressure (16.8% vs. 25.8%,  $p=0.01$ ), a lower prevalence of high cholesterol (4.4% vs. 8.9%,  $p=0.03$  respectively), and a higher prevalence of prior TB compared to the PWOH group (10.4% vs. 0.3%,  $p<.0001$ ).

Compared with PWOH, PWH had a higher unadjusted mean HRQoL as measured by the VAS-Self Reported Health Status [mean score (SD): 74 (16) vs. 67 (17),  $p<0.0001$ ; Figure 1a] and by EQ 5D Index (utility score) [mean score (SD): 0.82(0.15) vs. 0.78(0.17),  $p<0.001$ ; Figure 1c]. These differences persisted in multivariable models adjusted for potential confounders (Table 2). In addition, we also added a supplementary table (Supplementary Tables 2a and 2b) with the ranges of both the EQ-VAS and the EQ-5D utility index for a normative US population compared to our study population overall

and by age group (Sullivan & Ghushchyan, 2006). PWH were more likely to report not experiencing problems with the self-care and pain and discomfort dimensions of the sub-scale of EQ-5D compared to PWOH (OR=1.96, 95% CI=1.15–3.32; OR=1.83, 95% CI=1.3–2.57 respectively) after adjustment for confounders (Table 2).

Despite a lack of difference in the number of comorbidities between men and women (Supplementary Table 1), we found that the relationship between HIV serostatus and HRQoL differed by gender (Table 2, Figures 1b and 1d). Among women, PWH had higher utility scores and higher EQ-VAS compared to PWOH. Among men, PWH reported better overall EQ-VAS, but similar utility scores compared to PWOH (Table 2). In models including interaction terms, the difference by HIV serostatus and gender was significant for utility scores, but not for overall HRQoL (Supplementary Table 3). For the EQ-5D sub-scales, HIV status was associated with better self-care among women but not men. HIV status was associated with not having problems with pain/discomfort or having problems with anxiety/depression domains among men but not women after adjusting for the covariates (Table 2, Figure 2). We found no effect modification in the relationship between HIV and HRQoL by age (Supplementary Table 3).

## Discussion

In this cross-sectional study of older-age people in rural Uganda, we found that PWH reported better HRQoL than age- and sex-similar PWOH recruited from a population-based sample. This difference was observed in multiple domains, including overall self-reported health, the EQ-5D Utility Index, and the sub-scale dimensions of self-care and pain. While further data are needed to understand the mechanisms underlying these differences, we hypothesize that this finding may be due to improved access to services and resources provided through HIV treatment programs such as those available through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) (Hutchins, 2022).

The results of our study contrast with data from the global north, which have generally shown that older PWH report lower HRQoL than PWOH (Hays et al., 2000; Bing et al., 2000; Miners et al., 2014; Langebeek et al., 2017; Millar et al., 2017). For instance, a cross-sectional survey in the United Kingdom comparing PWH vs. a random sample of private households in the general population found lower HRQoL utility scores among PWH, as well as for all five sub-scale domains of the EQ-5D (Miners et al., 2014). Similarly, in a national probability sample in the United States (Bing et al., 2000) and a cohort study from an outpatient clinic in the Netherlands (Langebeek et al., 2017), PWH reported lower HRQoL in physical and mental health than PWOH. The mean values of HRQoL, measured by both the EQ-VAS and the EQ-5D Utility Index, are slightly lower among the participants in our study compared with US population norms. For example, we found the mean EQ-VAS score was 75.3 among 55–64 year-old PWH and 68.5 among PWOH in our cohort. In contrast, the mean EQ-VAS was 76.9 in an age-similar segment of the US population (Supplemental Table 2a and 2b). The authors hypothesized that the observed differences by HIV serostatus were attributable to higher employment rates, higher educational attainment, and a lower number of comorbidities among HIV uninfected individuals. Compared to the participants in our study, the participants in those studies had similar demographic profiles.

However, in the Netherlands study the study population was slightly younger and was predominantly male.

In contrast to this earlier body of work, data like ours from sub-Saharan Africa are emerging and suggest that PWH in sub-Saharan Africa have higher HRQoL than PWOH (Thomas et al., 2017; Martin et al., 2014; Nyirenda et al., 2012). A large population-based study of a younger study population (18–44 years of age) in Zambia found that the expansion of ART distribution programs reduced the difference in HRQoL between people with and without HIV (Thomas et al., 2017). Another study conducted in central Uganda also reported that PWH on ART had a higher QoL in terms of physical, psychological, and environmental domains than PWOH as measured by the World Health Organization Quality of Life. However, they did not see a difference in QoL in terms of the social domain (Martin et al., 2014). Similarly, a study in South Africa among people ranging from 30–94 years also found that PWH on ART had better functional ability, QoL, and overall health status compared with PWOH (Nyirenda et al., 2012).

The causes of improved HRQoL among PWH in the region are not well understood. Secondary benefits of the HIV care programs might be partially responsible. The PEPFAR program or other HIV implementation programs is often accompanied by additional interventions such as peer support, vocational training, clean water, and access to general health care. We hypothesize that the unique access to primary care supported by such programs – and the resiliency and social support networks that are likely needed for ongoing chronic care maintenance in such settings – may also be a key contributing factor. This hypothesis is supported by data suggesting improved primary health care delivery for PWH in the region, as evidenced by similar or improved cardiometabolic disease indicators in many settings, which was observed in our study, with a lower proportion of high blood pressure and high cholesterol (Gaziano et al., 2017; Manne-Goehler et al., 2017; Niwaha et al., 2021).

Our study found that the association between HIV status and HRQoL was modified by gender. Specifically, the increased HRQoL seen among PWH in terms of health utility, was more evident in women than men. A similar trend was seen with overall self-reported health, although this was not statistically significant. The unequal benefit of HIV care programs on well-being in the region is well known, with men being less likely to access HIV care and remain in care than with women, resulting in a widening mortality gap between the sexes (Marshall & Cahill, 2021; Bor et al., 2015; Tsai & Siedner, 2015; Nardell et al., 2022). These differences have resulted in different life expectancy gains by gender among PWH in the region (Nsanziimana et al., 2015; Johnson et al., 2013; Mills et al., 2011). Men with HIV infection were also more likely to report having problems with anxiety and depression compared to men without HIV infection. Notably, we did not find similar differences in anxiety among women. Our data did not enable us to identify the reasons for this difference, so this finding suggests a need for more research to better understand sex differences in mental health among people with HIV. Given the complex interactions between stigma and norms of masculinity, men with HIV may be more reluctant to seek social support for their mental health problems (Makusha et al., 2020; Fleming et al., 2016; Quinn et al., 2019), making this a particularly difficult public health problem to address. In contrast to the sex

differences in anxiety, we did not find an interaction between HIV and age on HRQOL: both relatively older and younger PWH in our cohort had higher HR-QOL than age-similar PWOH.

The findings of the study should be interpreted with limitations in mind. First, we analyzed cross-sectional data from the first year of a longitudinal study, so it is not possible to draw causal inferences about relationships between HIV status and HRQoL. Second, our outcomes of interest were measured by self-report. In order for the usual biases (e.g., recall bias, social desirability bias) to affect our findings, they would need to be differentiated by HIV serostatus. Third, our findings are also limited to PWH on ART, so they are not representative of those out of care.

Given the study design, our study findings are generally applicable to people living with HIV on treatment in Uganda, and comparable HIV-uninfected, population-based controls. A particular strength of our study was the recruitment of age- and sex-similar people without HIV from the community (rather than from health centers).

## Conclusions

Older PWH on ART in rural Uganda reported higher overall HRQoL and improved self-care and pain or discomfort than PWOH. We also found that this association appears to be driven primarily by women with HIV. Men with HIV seems to have lower HRQoL in the anxiety/depression EQ-5D subdomain. Further work is needed to understand the mechanisms of enhanced HRQoL among PWH and to consider approaches to improve overall wellbeing and healthcare delivery optimization for both female and male in similar rural, resource-limited settings.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Data availability statement.

The data that support the findings of this study are available from the corresponding author, LQ, upon reasonable request.



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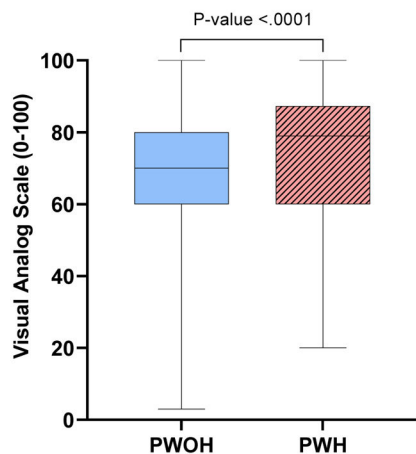
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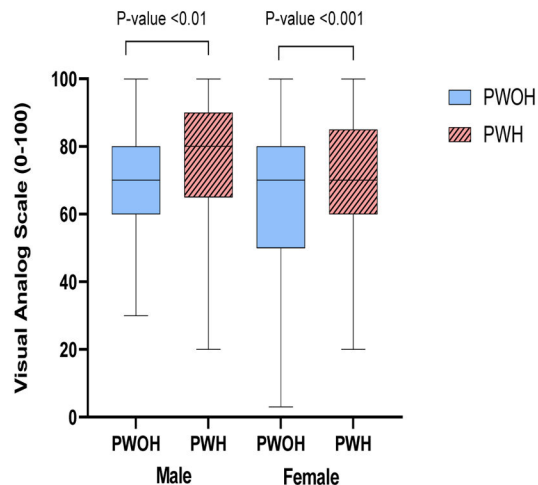
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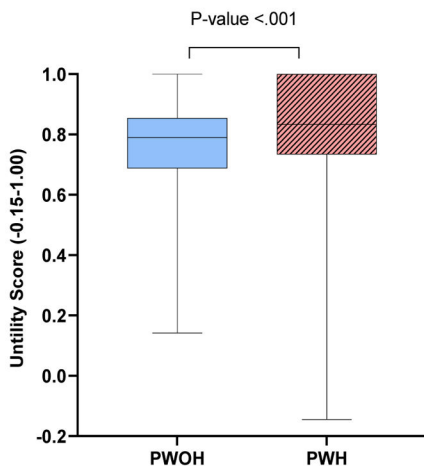
**Figure 1a:** Self-Reported Health Status by PWOH vs. PWH



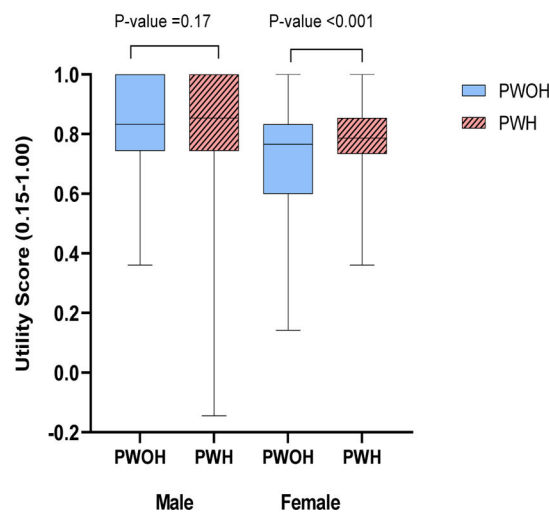
**Figure 1b:** Self-Reported Health Status by Gender and PWOH vs. PWH



**Figure 1c:** EQ-5D Index Score by PWOH vs. PWH



**Figure 1d:** EQ-5D Index Score by Gender and PWOH vs. PWH



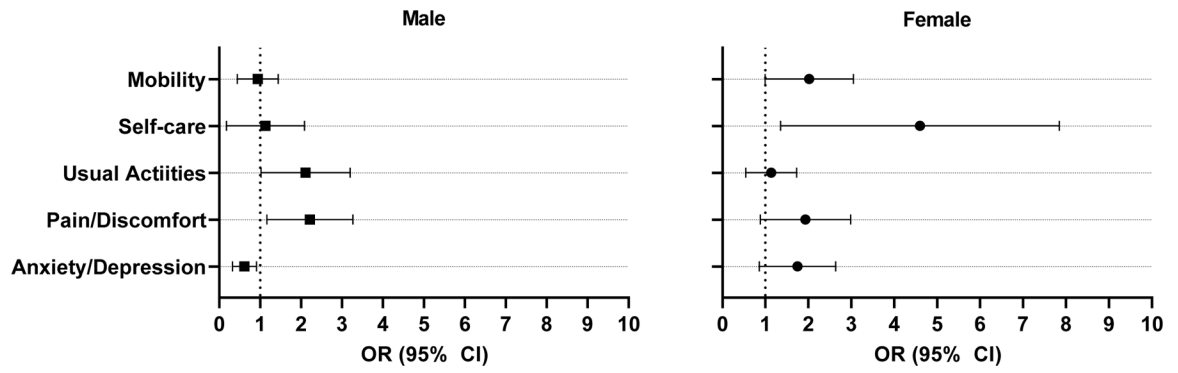
**Figure 1:** Self-Reported Health Status (EQ-VAS) and EQ-5D Utility Score between people without HIV (PWOH) vs. with people with HIV (PWH)

Notes: PWH: People with HIV

PWOH: People without HIV

P-values: represent results of studentized T-test comparing each QoL scale between PWOH vs. PWH

Higher scores = better QoL



**Figure 2:**  
 Association between HIV Status and Health-Related Quality of Life Sub-Scales, Stratified by Gender

Notes: OR: Odds Ratio from logistic regressions with a response of having no problems in each domain as the outcome of interest (i.e. an OR > 1 suggests a greater of odds of not having problems with that sub-scale for PWH vs. PWOH)

CI: Confidence Interval

**Table 1:**

Study Population Characteristics by People without HIV (PWOH) vs. People with HIV (PWH)

	Total Cohort (n=600)	PWOH (n=302)	PWH (n=298)	P-value
Demographics characteristics				
Mean age (mean, SD)	58.4(6.6)	58.5 (6.9)	58.4 (6.4)	0.86
Female (n, %)	295 (49.2)	148 (49.0)	147 (49.3)	0.94
Living with spouse/partner (n, %)	405 (67.5)	242 (80.1)	163 (54.7)	<.0001
Educational Attainment (n, %)				
Primary or less (No school, or P1-P7)	443 (73.8)	226 (74.8)	217 (72.8)	0.93
Secondary (S1-S6)	95 (15.8)	47 (15.6)	48 (16.1)	
Post-secondary	62 (10.3)	29 (9.6)	33 (11.1)	
Lifestyle characteristics				
Alcohol consumption (n, %)	143 (23.8)	82 (27.2)	61 (20.5)	0.05
Self-reported medical history (n, %)				
Diabetes	36 (6.0)	17 (5.6)	19 (6.4)	0.7
High Blood Pressure	128 (21.3)	78 (25.8)	50 (16.8)	0.01
Heart attack or heart failure	9 (1.5)	4 (1.3)	5 (1.7)	0.72
Kidney problems	7 (1.2)	2 (0.7)	5 (1.7)	0.25
Stroke	3 (0.5)	0 (0.0)	3 (1)	0.08
Cancer	2 (0.3)	0 (0.0)	2 (0.7)	0.15
COPD	2 (0.3)	2 (0.7)	0 (0.0)	0.16
Asthma	5 (0.8)	1 (0.3)	4 (1.3)	0.17
Pneumonia	31 (5.2)	13 (4.3)	18 (6.1)	0.33
High cholesterol	40 (6.7)	27 (8.9)	13 (4.4)	0.03
Tuberculosis	32 (5.3)	1 (0.3)	31 (10.4)	<.0001
Mean total comorbidities (0–11)	0.5 (0.8)	0.5 (0.8)	0.5 (0.8)	0.71

Notes: PWH: People with HIV

PWOH: People without HIV

P1-P7: Primary school from grade 1–7

S1-S6: Secondary school from grade 1–6

SD: Standard Deviation

COPD: Chronic obstructive pulmonary disease

**Table 2:**

Association between HIV Status and Health-Related Quality (HRQoL) by Gender

	Overall sample			Men			Women			
	b	95% CI		b	95% CI		b	95% CI		
<u>Overall self-reported health</u>										
EQ-VAS (100-point visual analogue scale)	6.98 <sup>Ω</sup>	4.22	9.73	5.03 <sup>Ω</sup>	1.49	8.58	9.23 <sup>Ω</sup>	4.89	13.57	
<u>EQ-5D-3L Health Valuation</u>										
EQ 5D Index	0.05 <sup>Ω</sup>	0.02	0.07	0.02	-0.02	0.05	0.10 <sup>Ω</sup>	0.06	0.14	
<u>EQ-5D-3L Sub-Scale</u>										
	aOR	95% CI		aOR	95% CI		aOR	95% CI		
Mobility	1.26	0.88	1.79	0.85	0.49	1.48	1.83 <sup>Ω</sup>	1.07	3.13	
Self-care	1.96 <sup>Ω</sup>	1.15	3.32	0.86	0.34	2.19	3.84 <sup>Ω</sup>	1.8	8.16	
Usual Activities	1.29	0.91	1.83	1.92 <sup>Ω</sup>	1.13	3.28	1.03	0.6	1.77	
Pain/Discomfort	1.83 <sup>Ω</sup>	1.3	2.57	2.05 <sup>Ω</sup>	1.26	3.34	1.74	0.99	3.07	
Anxiety/Depression	0.8	0.58	1.11	0.57 <sup>Ω</sup>	0.35	0.93	1.6	0.94	2.7	

Notes:

b: *linear regression coefficient adjusted for age, education, marital status, alcohol consumption and the number co-morbidities*

aOR: *Odds ratios from logistic regressions adjusted for age, education, marital status, alcohol consumption and the number co-morbidities*

<sup>Ω</sup>P-value: <0.05

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