Health-related quality-of-life of people with HIV in the era of combination antiretroviral treatment: a cross-sectional comparison with the general population

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Summary

Background **Combination antiretroviral therapy has substantially increased life-expectancy in people living with HIV, but the effects of chronic infection on health-related quality of life (HRQoL) are unclear. We aimed to compare HRQoL in people with HIV and the general population.**

Methods **We merged two UK cross-sectional surveys: the ASTRA study, which recruited participants aged 18 years or older with HIV from eight outpatient clinics in the UK between Feb 1, 2011, and Dec 31, 2012; and the Health Survey for England (HSE) 2011, which measures health and health-related behaviours in individuals living in a random sample of private households in England. The ASTRA study has data for 3258 people (response rate 64%) and HSE for 8503 people aged 18 years or older (response rate 66%). HRQoL was assessed with the Euroqol 5D questionnaire 3 level (EQ-5D-3L) instrument that measures health on five domains, each with three levels. The responses are scored on a scale where a value of 1 represents perfect health and a value of 0 represents death, known as the utility score. We used multivariable models to compare utility scores between the HIV and general population samples with adjustment for several sociodemographic factors.**

Findings **3151 (97%) of 3258 of participants in ASTRA and 7424 (87%) of 8503 participants in HSE had complete EQ-5D-3L data. The EQ-5D-3L utility score was lower for people with HIV compared with that in the general population (marginal effect in utility score adjusted for age, and sex/sexuality –0·11; 95% CI –0·13 to –0·10; p<0·0001). HRQoL was lower for people with HIV for all EQ-5D-3L domains, particularly for anxiety/depression. The difference in utility score was significant after adjustment for several additional sociodemographic variables (ethnic origin, education, having children, and smoking status) and was apparent across all CD4 cell count, antiretroviral therapy, and viral load strata, but was greatest for those people diagnosed with HIV in earlier calendar periods. Reduction in HRQoL with age was not greater in people with HIV than in the general population ($p_{interaction}$>0·05).**

Interpretation **People living with HIV have significantly lower HRQoL than do the general population, despite most HIV positive individuals in this study being virologically and immunologically stable. Although this difference could in part be due to factors other than HIV, this study provides additional evidence of the loss of health that can be avoided through prevention of further HIV infections.**

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Introduction

Evidence suggests that people diagnosed with HIV in resource-rich countries have a life expectancy that is almost equivalent to that in people without HIV if they receive appropriate treatment with combination antiretroviral treatment (cART).[1] However, despite substantial improvements in clinical prognosis, much less is known about the health-related quality-of-life (HRQoL) of individuals with HIV compared with that in the general population.[2–4] For example, although evidence from studies from the USA show that people with HIV have higher rates of depression than do people without HIV, the effect of HIV status on other domains and overall HRQoL is less clear.[4] HRQoL is a multidimensional concept that incorporates factors such as physical, cognitive, emotional, and social functioning. Insight into HRQoL is essential to understand the effects of HIV as a chronic disease. Moreover, when measured with so-called utility-based instruments, the information can be used in economic evaluations to help to generate quality-adjusted life-years (QALYs), in which one QALY is equivalent to a year of perfect health.[5]

Recent debate has centred around whether people with HIV age more quickly as a result of their HIV status[6–8]—in other words whether they tend to start having ageing-related ill-health and disability at a younger age than do people without HIV, and whether this difference tends to widen with older age. The aim of this study was therefore two-fold: to assess whether individuals with HIV, particularly those who are virologically stable on

suppressive treatment, have similar levels of HRQoL compared with the general population, after adjustment for demographic and socioeconomic variables such as age, sex, and smoking status; and to assess whether the difference in HRQoL between those with HIV and the general population increases with older age.

Methods

Study population and procedures

We merged data from two large cross sectional questionnaire studies. The first, ASTRA (Antiretrovirals, Sexual Transmission Risk and Attitudes study), was mainly designed to investigate present patterns of sexual behaviour in individuals with diagnosed HIV in the UK. Full details regarding the study design are available elsewhere.[9] Briefly, the study includes an unselected sample of 3258 people with HIV recruited from outpatient clinics at eight urban centres in England, between Feb 1, 2011, and Dec 31, 2012; the response rate was 64%. The ASTRA questionnaire was self-completed and available in English and French; information about viral load and CD4 cell count was extracted from clinical records by study personnel. ASTRA includes about 5% of the total population with diagnosed HIV in the UK. Participants of ASTRA were similar to the UK HIV-diagnosed population in terms of age distribution, and the proportion who were currently receiving ART.[9] However, compared with the UK HIV-diagnosed population, ASTRA contains smaller proportions of black African people and women, but includes a higher percentage of men who have sex with men (MSM).[9] Ethical approval was granted by the North West London REC 2 ethics committee (ref 10/H0720/70) and written informed consent was granted.

The second dataset, relating to the general population, was derived from the 2011 Health Survey for England (HSE).[10] The HSE is an annual study designed to measure health and health-related behaviours in people living in a random sample of private households in England; it excludes people who are homeless or living in communal buildings such as nursing homes. Participants are interviewed at home and later visited by a nurse to collect more detailed clinical information. The 2011 survey includes interviews for 8503 people aged 18 or older. The response rate was 66%; but no information about HIV status is recorded. Ethical approval to use the survey data was obtained from the Oxford A Research Ethics Committee (reference number 10/H0604/56). Oral consent was gramted.

For more on **-tpm- routine** see http://econpapers.repec.org/software/bocbocode/s457538.htm

For the **Health Survey for England—2011** see http://www.hscic.gov.uk/catalogue/PUB09300

HRQoL was defined with the generic Euroqol questionnaire (EQ-5D-3L) instrument which was used in both studies.[11] Evidence suggests that this instrument exhibits good psychometric properties in terms of its use in the measurement of HRQoL in the general population[12] and in people with HIV.[13,14] The EQ-5D-3L consists of a classification system that measures current health on five domains (mobility, self-care, ability to do usual activities, pain or discomfort, and anxiety/depression), each with three levels (indicating no, some, or extreme problems). The (3^5=243) combinations of categories can be scored, or valued, with available country specific so-called utility algorithms (EQ-5D-3L$_{utility}$).[15] Utilities are measured on interval scales, for which perfect health (no problems on all five domains) is equivalent to a value of 1 and death is equivalent to a value of 0. These scales are assumed to represent the strength of preference for specific health-related outcomes. For example, a health state with a value of 0·4 is preferred twice as much as a health state with a value of 0·2.

For more on the **EuroQol Group** see http://www.euroqol.org/

Statistical analysis

Responses were included if participants completed all five EQ-5D-3L domain questions and were at least 18 years of age. Unadjusted differences in demographic variables and in EQ-5D-3L domains between the HIV and general population samples were assessed by χ^2 tests for proportions and Wilcoxon rank sum tests for (non-normally distributed) continuous variables. Regression modelling was used to estimate unadjusted and adjusted differences in EQ-5D-3L$_{utility}$ scores compared between the HIV sample and the general population sample.

Provisional inspection of the EQ-5D-3L$_{utility}$ data showed they were non-normally distributed, with a spike at 1·0, indicating a fairly high proportion of individuals reporting perfect health. For this reason, a two-part regression model was used for the multivariable analysis. This analysis involved fitting two regression models, the results of which are combined to produce a marginal effect for every independent variable. First, a logistic regression was done, in which the dependent variable indicated perfect health (yes or no). Generalised linear modelling was then done for the data relating to people with less than perfect health, with a γ distribution and log link because of the left skewed nature of the data; proportionately few individuals indicated particularly poor HRQoL. The modelling was done with the -tpm- routine for STATA v13.1. In this analysis, negative effect estimates indicate poorer health whereas positive values indicate better health.

The choice of which independent variables to include in models was restricted for two reasons. First, they needed to be common to both the ASTRA and HSE datasets. This ruled out for example, variables indicating homelessness, hepatitis C status, and recreational drug use (available only in ASTRA). Second, the possibility of endogeneity was a particular concern. That is, although variables such as employment status might influence HRQoL, there is a plausible loop in causality because HRQoL might also affect employment status (for example poor health could lead to loss of employment). In this sense, such an independent variable could be seen as an outcome of, or proxy measure for, HRQoL as well as a predictor of it, which is problematic in interpretation of the results. Therefore employment status, long-term sickness, and alcohol use were not judged as potential independent

variables in this main analysis. The non-HIV related independent variables included: sex/sexuality (men who have sex with men [MSM], heterosexual man, or woman); age (as a continuous variable); ethnic origin (white or non-white); having children (yes or no); maximum educational qualification as an indicator of socioeconomic status (university degree or higher, A-level, O-level or equivalent, less than O-level or equivalent, other, or none); and smoking status (never-smoker, ex-smoker, light smoker [ten or fewer cigarettes per day], medium smoker [11–19 cigarettes per day], heavy smoker [≥20 cigarettes per day]).

A series of multivariable models were used to assess the effect of study sample on HRQoL after adjustment for potential confounders. In model 1, only study sample (HIV sample compared with general population), age, and sex/sexuality were included. Model 2 divides the HIV sample into two groups (CD4 count greater than 200 cells per μL and 200 cells per μL or less); additional analysis (not shown) showed that including CD4 count bandings at levels greater than 200 cells per μL did not significantly add to the results. Adjustment for smoking status and other demographic variables (age, ethnic origin, sex/sexuality, having children, and maximum educational qualifications) were also included in model 2. Model 3 was identical to model 2 except that the HIV sample was categorised in terms of treatment status and viral load (on ART with viral load ≤50 copies per mL; on ART with viral load >50 copies per mL; stopped ART; never started ART) rather than by CD4 cell count. Model 4 combined the two methods of categorisation of the HIV sample, resulting in eight HIV categories being compared with the general population sample. Model 5 categorised the HIV sample in terms of calendar year of diagnosis. Additionally, all five models were reanalysed to assess whether the effect of age on HRQoL was different in the HIV sample compared with that in the general population sample. That is, the models were rerun including an interaction term between study sample (HIV sample compared with general population) and age (as a continuous variable).

A potential problem of the use of parametric models such as two-part regression models to account for imbalances in covariates is that they can be highly sensitive to the choice of functional form of the regression models (eg, inclusion of higher order terms in the logistic regression model). Recent methodological work has shown the advantages of matching approaches, which aim to create covariate balances between the groups being compared. Application of the parametric models on a well matched dataset is expected to decrease sensitivity to functional form mis-specification.[16] Thus, a sensitivity analysis was done by rerunning model 1 after creation of a one-to-one matched HSE dataset with the genetic matching approach described by Sekhon[17] (full methodological details are available on request). The datasets were matched on age, sex, smoking status, children, ethnic origin, and educational qualifications, but not MSM because there were too few MSM in the HSE dataset. Model 1 was also reanalysed; first, after removal of all MSM and all people who had retired from both datasets, and second, after further removal from ASTRA, of homeless people, those who had taken any recreational drugs in the past 3 months, and everyone who had ever been diagnosed with hepatitis C. Finally, despite concerns about alcohol use as a predictor of HRQoL, the original models 1–5 were rerun with adjustment for heavy drinking, defined as drinking at least 20 units of alcohol per week (yes or no).

Role of the funding source

The funder of the study had no role in the study design or conduct, data collection, analysis, or interpretation, preparation of the report, or the decision to submit for publication. AM had full access to the data and responsibility for the decision to submit the report for publication.

Results

3151 (96·7%) of 3258 participants of ASTRA had complete EQ-5D $3L_{utility}$ data and 7424 (87·3%) of 8503 participants of the HSE. People diagnosed with HIV were significantly younger than those in the general population sample by roughly 4 years (median 45·2 years, IQR 38·9–50·9 *vs* 49·0 years, 35·0–64·0; p<0·0001). People with HIV were also significantly more likely to be MSM and heavy smokers and to have higher levels of education than people without HIV, but they were less likely to be heavy drinkers (table 1). The higher proportion of MSM in the ASTRA study than in the HSE was unsurprising, but particularly noticeable (table 1). About 5% (n=170) of ASTRA participants had a CD4 count less than 200 cells per μL, 12% had never started ART, and overall 75% had a viral load of 50 copies per mL or less (table 1).

The unadjusted results show that, despite being younger, people with HIV recorded lower levels of health compared with the general population on all five EQ-5D-3L domains (table 2). The anxiety/depression domain was the most markedly reduced, with 24% and 8% absolute differences in the proportions of people who reported at least some problems and severe problems in the two samples. The mean EQ-5D-$3L_{utility}$ score was 0·74 for the HIV sample and 0·82 for the general population sample. The unadjusted difference in overall EQ-5D-$3L_{utility}$ score was –0·08 (95% CI –0·09 to –0·07).

Model 1 suggests that people with HIV had significantly lower EQ-5D-$3L_{utility}$ scores than those in the general population after adjustment for differences in age and sex/sexuality (–0·11 [95% CI –0·13 to –0·10]; table 3). Model 2 shows that adjustment for additional factors (ethnic origin, children, education, and smoking status) did not explain any of the difference in EQ-5D-$3L_{utility}$ between the two samples. Of people with HIV, both the group with CD4 counts of 200 cells per

	HIV (n=3151)	General population (n=7424)	p value
Age >50 years	857/3036 (28%)	3478/7424 (47%)	<0·0001
Sex/sexuality			
Heterosexual male	354/3151 (11%)	3189/7424 (43%)	<0·0001
Female	588/3151 (19%)	4177/7424 (56%)	<0·0001
Men who have sex with men	2209/3151 (70%)	58/7424 (1%)	<0·0001
White	2183/3087 (71%)	6782/7418 (91%)	<0·0001
Smoking status			
Never	1224/3122 (39%)	3486/7408 (47%)	<0·0001
Ex-smoker	918/3122 (29%)	2455/7408 (33%)	0·0002
Light smoker	254/3051 (8%)	530/7408 (7%)	0·038
Medium smoker	339/3051 (11%)	610/7408 (8%)	<0·0001
Heavy smoker	316/3051 (10%)	318/7408 (4%)	<0·0001
Heavy drinker	321/3123 (10%)	1366/7305 (19%)	<0·0001
Long term sick	374/3083 (12%)	237/7233 (3%)	<0·0001
Children*	837/3132 (27%)	2145/7424 (29%)	0·024
Education			
No qualifications	350/3079 (11%)	1586/7417 (21%)	<0·0001
O levels or higher	696/3079 (23%)	1564/7417 (21%)	0·085
A levels or higher	612/3079 (20%)	1468/7417 (20%)	0·92
Degree or higher	1288/3079 (42%)	1833/7417 (25%)	<0·0001
Employment			
Full-time	1507/3083 (49%)	3812/7233 (53%)	0·0004
Part-time	293/3083 (10%)	699/7233 (10%)	0·80
Retired	183/3083 (6%)	1946/7233 (27%)	<0·0001
Homeless	33/3095 (1%)	..	..
Recreational drugs†	1222/3122 (39%)	..	..
Ever had hepatitis C	424/3151 (13%)	..	..
CD4 count ≤200 cells per μL	164/3114 (5%)	..	..
CD4 count >200 cells per μL	2950/3114 (95%)	..	..
On ART viral load ≤50 copies per mL	2312/3080 (75%)	..	..
On ART viral load >50 copies per mL	346/3080 (11%)	..	..
Never started ART	358/3080 (12%)	..	..
Stopped ART	64/3080 (2%)	..	..

Data are n (%). All p values relate to χ^2 tests. Denominators may differ from sample size because of missing values. At least 20 units of alcohol per week. *Health Survey for England records whether people aged younger than 16 years are in the household rather than being a parent. †Proportion taking recreational drugs of any type in the past 3 months. ART=antiretroviral treatment.

Table 1: **ASTRA and Health Survey for England sample demographics**

	HIV (n=3151)	General population (n=7424)	p value*
Mobility problems			<0·0001
None	2296 (73%)	5911 (80%)	
Some	850 (27%)	1502 (20%)	
Severe	5 (<1%)	11 (<1%)	
Problems with self-care			<0·0001
None	2754 (87%)	7032 (95%)	
Some	385 (12%)	367 (5%)	
Severe	12 (<1%)	25 (<1%)	
Problems performing usual activities			<0·0001
None	2128 (68%)	5945 (80%)	
Some	936 (30%)	1328 (18%)	
Severe	87 (3%)	151 (2%)	
Pain/discomfort			<0·0001
None	1834 (58%)	4480 (60%)	
Some	1091 (35%)	2576 (35%)	
Severe	226 (7%)	368 (5%)	
Anxiety/depression			<0·0001
None	1563 (50%)	5441 (73%)	
Some	1268 (40%)	1796 (24%)	
Severe	320 (10%)	187 (3%)	

Data are n (%). *p values by χ^2 tests.

Table 2: **EQ-5D-3L health status classifications for ASTRA and Health Survey for England**

mm³ or less and the group with higher CD4 cells counts had significantly lower EQ-5D-3L$_{utility}$ scores than did the general population sample (table 3); the difference between the two CD4 cell count categories was statistically significant (–0·04, 95% CI –0·08 to –0·005). The results from models 3 and 4 were similar in so much that people with HIV consistently recorded lower EQ-5D-3L$_{utility}$ scores than did the general population, across ART, viral load, and CD4 cell count categories (tables 3 and 4). In particular, the difference in EQ-5D-3L$_{utility}$ for people with HIV who were virally suppressed with CD4 counts greater than 200 cells per μL compared with the general population was –0·11 (95% CI –0·13 to –0·09). Model 5 clearly indicates that calendar year of HIV diagnosis was significantly associated with EQ-5D-3L$_{utility}$ scores, people diagnosed more recently had increased HRQoL, even after accounting for age and the other covariates (table 5). In models 2–5, in addition to HIV status, older age, non-white ethnic origin, female sex, not having children, less education, and present and ex-smoking status were also independently associated with reduced EQ-5D-3L$_{utility}$ scores (tables 3–5).

When included, the interaction term between study sample (HIV sample compared with general population) and age was not statistically significant in any of the models (p>0·05 in all instances). In other words, there was no evidence that the difference in EQ-5D-3L$_{utility}$ score between the two population samples became greater or smaller with changing age.

The results form model 1 remained largely unchanged when they were rerun with the matched dataset (adjusted difference between samples: –0·10; 95% CI –0·12 to –0·08). The results were also similar after removal of all MSM and people who had retired from both datasets and after removal of of homeless people, those who had taken any recreational drugs in the past 3 months, and people who had been ever diagnosed with hepatitis C from ASTRA (adjusted difference between samples: –0·08; 95% CI –0·10 to –0·06). Adjustment of models 1–5 for heavy drinking had negligible effects on the results (data not shown).

	Model 1		Model 2		Model 3	
	ME	95% CI; p value	ME	95% CI; p value	ME	95% CI; p value
HIV status						
General population (base)	..	..	..	..	..	..
HIV+	–0·11	–0·13 to –0·10; <0·0001	..	..	..	..
HIV+, CD4 count ≤200 cells per μL	..	..	–0·15	–0·19 to –0·11; <0·0001	..	..
HIV+, CD4 count >200 cells per μL	..	..	–0·10	–0·12 to –0·08; <0·0001	..	..
HIV+, on ART, VL ≤50 copies per mL	..	..	..	..	–0·11	–0·13 to –0·09; <0·0001
HIV+, on ART, VL >50 copies per mL	..	..	..	..	–0·12	–0·15 to –0·09; <0·0001
HIV+, stopped ART	..	..	..	..	–0·14	–0·20 to –0•07; <0·0001
HIV+, never started ART	..	..	..	..	–0·05	–0·08 to –0·02; 0·0017
Age	–0·004	–0·004 to –0·004; <0·0001	–0·003	–0·003 to –0·002; <0·0001	–0·003	–0·003 to –0·002; 0·0037
Sex/sexuality						
Male heterosexual (base)	..	..	..	..	..	..
Female	–0·03	–0·04 to –0·02; <0·0001	–0·03	–0·05 to –0·02; <0·0001	–0·03	–0·04 to –0·02; <0·0001
MSM	–0·008	–0·03 to 0·01; 0·41	0·002	–0·03 to 0·02; 0·84	–0·005	–0·03 to 0·02; 0·65
Ethnic origin						
Non-white (base)	..	..	..	..	..	..
White	..	..	0·02	0·003 to 0·04; 0·02	0·02	0·005 to 0·04; 0·01
Children						
No (base)	..	..	..	..	..	..
Yes	..	..	0·03	0·02 to 0·04; <0·0001	0·03	0·02 to 0·04; <0·0001
Smoking status						
Never (base)	..	..	..	..	..	..
Ex-smoker	..	..	–0·03	–0·04 to –0·01; <0·0001	–0·03	–0·04 to –0·01; <0·0001
Light smoker	..	..	–0·04	–0·06 to –0·02; <0·0001	–0·04	–0·06 to –0·02; <0·0001
Medium smoker	..	..	–0·06	–0·08 to –0·05; <0·0001	–0·06	–0·08 to –0·05; <0·0001
Heavy smoker	..	..	–0·12	–0·14 to –0·10; <0·0001	–0·12	–0·14 to –0·10; <0·0001
Max qualification						
None (base)	..	..	..	..	..	..
O level	..	..	0·06	0·04 to 0·07; <0·0001	0·06	0·04 to 0·07; <0·0001
A level	..	..	0·08	0·07 to 0·10; <0·0001	0·08	0·07 to 0·10; <0·0001
Degree or higher	..	..	0·12	0·10 to 0·13; <0·0001	0·12	0·10 to 0·13; <0·0001
Other	..	..	0·09	0·07 to 0·11; <0·0001	0·09	0·07 to 0·11; <0·0001
Model						
Number of observations	10 078	..	9855	..	9839	..
Logit	..	..	..	..	..	..
Constant	–1·53	..	–1·00	..	–0·99	..
GLM (log link)	..	..	..	..	..	..
Constant	–1·54	..	–1·19	..	–1·17	..
Log pseudo likelihood	–6595	..	–6326	..	–6315	..

For all factors, each category is compared to the base category. Negative utility values indicate poorer health whereas positive values indicate improved health. ME=marginal effect; change in the utility score associated with a change in each of the independent variables. ART=antiretroviral treatment. VL=viral load. GLM=generalised linear model.

***Table 3*: Models 1–3—multivariable analysis of factors associated with health-related quality-of-life**

Discussion

To our knowledge, this is the largest cross-sectional study to compare a standardised measure of HRQoL in people living with HIV in the era of ART directly with the general population, in a setting with universal access to health care, with the ability to simultaneously adjust for multiple potential confounders (panel).[4] Several multivariable models were constructed with different categorisations of HIV status, but they consistently showed that people diagnosed with HIV had reduced HRQoL compared with the general population, across all ART, CD4, and viral load categories. In particular, the difference was apparent even in people who were virally suppressed on ART. Although anxiety/depression levels were the most noticeably affected, all five EQ-5D-3L domains were reduced suggesting that HIV infection continues to have systemic health implications. This effect was greatest in those people diagnosed for the longest time (model 5). Despite

	ME	95% CI; p value
HIV status		
General population (base category)	..	..
HIV+, on ART, VL ≤50 copies per mL, CD4 count ≤200 cells per μL	–0·13	–0·19 to –0·07; <0·0001
HIV+, on ART, VL ≤50 copies per mL, CD4 count >200 cells per μL	–0·11	–0·13 to –0·09; <0·0001
HIV+, on ART, VL >50 copies per mL, CD4 count ≤200 cells per μL	–0·15	–0·21 to –0·09; <0·0001
HIV+, on ART, VL >50 copies per mL, CD4 count >200 cells per μL	–0·11	–0·14 to –0·08; <0·0001
HIV+, stopped ART, CD4 count ≤200 cells per μL	–0·18	–0·34 to –0·02; 0·022
HIV+, stopped ART, CD4 count >200 cells per μL	–0·13	–0·20 to –0·06; 0·0001
HIV+, never started ART, CD4 count ≤200 cells per μL	–0·17	–0·30 to –0·03; 0·015
HIV+, never started ART, CD4 count >200 cells per μL	–0·04	–0·07 to –0·01; 0·014
Age	–0·003	–0·003 to –0·002; <0·0001
Sex/sexuality		
Male heterosexual (base)	..	..
Female	–0·03	–0·05 to –0·02; <0·0001
MSM	–0·007	–0·03 to 0·02; 0·56
Ethnic origin		
Non-white (base)	..	..
White	0·02	0·004 to 0·04; 0·015
Children		
No (base)	..	..
Yes	0·03	0·02 to 0·04; <0·0001
Smoking status		
Never (base)	..	..
Ex-smoker	–0·03	–0·04 to –0·01; <0·0001
Light smoker	–0·04	–0·06 to –0·02; <0·0001
Medium smoker	–0·06	–0·08 to –0·05; <0·0001
Heavy smoker	–0·12	–0·14 to –0·10; <0·0001
Max qualification		
None (base)	..	..
O level	0·06	0·04 to 0·07; <0·0001
A level	0·08	0·07 to 0·10; <0·0001
Degree or higher	0·12	0·10 to 0·13; <0·0001
Other	0·09	0·07 to 0·11; <0·0001
Model		
Number of observations	9830	..
Logit	..	..
Constant	–1·00	..
GLM (log link)	..	..
Constant	–1·18	..
Log pseudo likelihood	–6307	..

For all factors, each category is compared to the base category. Negative utility values indicate poorer health whereas positive values indicate improved health. ME=marginal effect; change in the utility score associated with a change in each of the independent variables. ART=antiretroviral treatment. VL=viral load. GLM=generalised linear model.

Table 4: **Model 4—multivariable analysis of factors associated with health-related quality-of-life**

the overall impact of HIV, we did not find any evidence that the difference in HRQoL between those people living with HIV and the general population sample was greater with older age.

These results can be used to quantify the average loss in HRQoL resulting from each newly diagnosed person with HIV. For example, with the results from model 1, and supposing that life expectancy is for 40 years after HIV diagnosis but is (conservatively) unaffected by it, the loss is equivalent 4·4 (undiscounted) years of perfect health, or QALYs, per infection. This loss would reduce to 2 QALYs if the affect of infection was assumed to be –0·05, which was the utility reduction for people infected between 2010–12 in model 5.

The multivariable analyses showed that in addition to HIV status, factors such as non-white (compared with white) ethnic origin and female (compared with heterosexual male) sex were also independently associated with reduced EQ-5D-3L$_{utility}$ scores. Thus, these demographic groups seem to be among the most disadvantaged in terms of present levels of health.

The major strengths of this study are that it contains a large number of people with HIV in England (>3000, about 5% of all diagnosed patients in the UK), both studies were contemporaneous, had satisfactory response rates, are reasonably representative of the populations of interest, and some major potential confounding factors such smoking status were adjusted for. Additionally, recruitment in both studies took place in a way that would not be expected to select strongly for healthier participants; ASTRA recruited from hospital clinics and participants of HSE were visited in their homes. Further, the studies were done in a setting with universally free health care, which is likely to reduce the potential for confounding by access to health care. Although non-response rates were similar in each study, bias would be introduced if characteristics of non-responders differed between the studies. For example, if people with poorer physical or mental health were less likely to participate in HSE, but this was not the case for participation in ASTRA, the HSE study population would contain people with greater than average levels of health, and the differences in HRQoL we noted would be overestimates.

The proportion of people who participated in HSE or ASTRA who did not complete all five EQ-5D-3L questions, and therefore were excluded from the analyses, was 9% greater in the HSE sample. Although so-called response fatigue could partly explain this difference, because HSE participants were required to answer a much longer set of questions, whether this introduces bias into the analysis or the plausible effect of it is unknown. For example, perhaps people in HSE who had no ill health elected not to complete the instrument, meaning the differences in HRQoL we report are an underestimate. Conversely, people in HSE might have been too ill to complete all the questions, which would lead to an overestimation of differences.

The differences in health that we report might not be a direct result of HIV infection, but could result in part from other unmeasured differences between the ASTRA and HSE populations. Moreover, we did not make multivariable adjustments for all potentially confounding factors, such as homelessness and hepatitis C status, because the information was not available in both datasets. However, adjustments for major potential

confounders such as smoking status and social class (as measured by level of education), did not attenuate the difference in HRQoL between the two cross-sectional samples, neither did the use of a matched dataset to more fully account for differences in most observable factors. Further analyses are planned with the ASTRA sample linked to clinical level data to investigate the effects of health-related factors such as previous non-AIDS and AIDS clinical conditions on HRQoL.

The HSE study included a much lower proportion of self-reported MSM, who could for example, have different levels of psychological wellbeing compared with other men.[18] Although this factor alone does not explain the difference in HRQoL between the two population samples because removal of all MSM from both samples had little effect on the results, the extent to which this issue confounds the results is unknown. Studies comparing HRQoL between HIV-positive and HIV-negative MSM would shed light on this issue.

Although HSE does not record HIV status, and is therefore likely to include people with HIV, we do not deem this to detract from the analysis because HSE participants were randomly selected and the prevalence of HIV infection in the UK is about 1·5 in 1000, meaning that HSE is predicted to contain around ten people with HIV.

Several recent studies have measured HRQoL in people living with HIV,[19–21] but few have directly compared levels with those recorded in the general population.[2,8,22] A large US study[6] of data from 2009 showed that the prevalence of depression was three-times higher in people with HIV than in the general population. Adjustments were made for several potentially confounding factors such as age, sex, and educational levels, but not for factors such as smoking and stage of HIV infection. However, because a third of people living with HIV in the USA are thought not to be accessing regular care,[23] the potential for confounding by access to health care is greater in the USA study.

Previous studies have consistently concluded that individuals diagnosed with HIV have high levels of depression.[4,24,25] Our study noted higher levels of self-reported anxiety/depression in the HIV sample than in the general population, even after adjustment for several other confounding variables such as smoking status and immunological or virological status. This high prevalence of depression among people living with HIV could be because of a range of factors including those related to living with a chronic disease, social circumstances, relationship issues, stigma, or the effects of specific drugs. The extent to which elevated anxiety/depression evident in MSM living with HIV are also apparent in HIV-negative MSM is unknown. Some evidence suggests that a high prevalence of depression exists independently of HIV status in groups such as MSM.[18] Whatever the underlying drivers of the difference in anxiety/depression between those with and without HIV, the findings further emphasise the importance in identification of those people with HIV who have psychological symptoms and in offering appropriate care. The results suggest this is particularly true for people who were diagnosed in the earlier period of the epidemic and have been living with HIV for many years (model 5, table 5); possibly in part

	ME	95% CI; p value
HIV status		
General population (base category)	..	..
HIV+, diagnosed 1980–84	–0·26	–0·36 to –0·16; <0·0001
HIV+, diagnosed 1985–89	–0·19	–0·23 to –0·15; <0·0001
HIV+, diagnosed 1990–94	–0·17	–0·20 to –0·14; <0·0001
HIV+, diagnosed 1995–99	–0·13	–0·15 to –0·10; <0·0001
HIV+, diagnosed 2000–04	–0·11	–0·14 to –0·09; <0·0001
HIV+, diagnosed 2005–09	–0·07	–0·09 to –0·04; <0·0001
HIV+, diagnosed 2010–12	–0·05	–0·08 to –0·02; <0·0001
Age	–0·003	–0·003 to –0·002; 0·008
Sex/sexuality		
Male heterosexual (base)	..	..
Female	–0·03	–0·04 to –0·02; <0·0001
MSM	0·01	–0·01 to 0·03; 0·42
Ethnic origin		
Non-white (base)	..	..
White	0·02	0·006 to 0·04; 0·008
Children		
No (base)	..	..
Yes	0·03	0·02 to 0·04; <0·0001
Smoking status		
Never (base)	..	..
Ex-smoker	–0·02	–0·03 to –0·01; 0·0001
Light smoker	–0·04	–0·06 to –0·02; 0•0001
Medium smoker	–0·06	–0·08 to –0·05; <0·0001
Heavy smoker	–0·12	–0·14 to –0·10; <0·0001
Max qualification		
None (base)	..	..
O level	0·06	0·05 to 0·08; <0·0001
A level	0·09	0·07 to 0·10; <0·0001
Degree or higher	0·12	0·10 to 0·14; <0·0001
Other	0·09	0·07 to 0·11; <0·0001
Model		
Number of observations	9870	..
Logit	..	..
Constant	–0·91	..
GLM (log link)	..	..
Constant	–1·13	..
Log pseudo likelihood	–6039	..

For all factors, each category is compared to the 'base' category'. Negative utility values indicate poorer health whereas positive values indicate improved health. ME=marginal effect; change in the utility score associated with a change in each of the independent variables. ART=antiretroviral treatment. VL=viral load. GLM=generalised linear model.

Table 5: **Model 5—multivariable analysis of factors associated with health-related quality-of-life**

Panel: Research in context

Systematic review

In June, 2014, we searched PubMed, Medline, and Embase for studies that compared the health-related quality-of-life (HRQoL) of people with diagnosed HIV with the general population. We did not apply any language or date restrictions, and used combinations of the search terms "HIV", "AIDS", "quality-of-life", and "population". Studies including people with haemophilia were excluded. The review identified several studies have compared HRQoL between these two population groups,[2–4] one of which was a recent study.[4] All seem to suggest that HIV significantly affects HRQoL on several health domains, but those measuring anxiety/depression seemed to be the most frequently reduced.

Interpretation

Our study is the largest study of its kind in the UK and in a population with universal access to health care. We found that people living with HIV have reduced HRQoL compared with the general population, and that this difference was apparent even for those people with HIV who were on ART and virologically suppressed. Unlike previous studies, we assessed whether the difference in HRQoL between the two population samples differs with older age, and we identified no evidence to suggest this is the case. Although access to modern cART seems to be associated with life expectancy that is almost equivalent to people who are uninfected, HIV continues to affect morbidity. Our findings provides evidence of the loss of health that can be avoided through prevention of further HIV infections.

because such people were diagnosed with the infection at a time when HIV prognosis was particularly poor.

With available treatment, HIV has been transformed into a chronic disease with life expectancy approaching that of the general population. However, although we noted no evidence that the difference in HRQoL between the two population samples becomes greater or smaller with increasing age, HRQoL remains significantly lower in people with HIV, even in those people who are virologically suppressed on ART. A substantial part of the difference in HRQoL is attributable to the higher levels of self-reported anxiety/depression in people with HIV. The British HIV Association has clearly set out guidance for appropriate mental health services for people with HIV, with the aim of detecting early psychological difficulties and providing appropriate therapeutic support for those who require it.[26] There is a well established evidence base on the efficacy of several treatment approaches and such interventions that focus on the psychological needs of people living with HIV should be a priority.

Contributors

All authors were involved in the study conception and study design, and acquisition, analysis or interpretation of the data. AM, FL, and AP drafted the report. All authors critically reviewed the report for important intellectual content. AM, AP, NK, and FL did the statistical analysis. AM, AP, AR, SC, GH, LS, and FL obtained funding. AM, FL, NK, and AP provided administrative, technical, or material support. AM, AP, and FL supervised the study. AS, FL, AR, MF, and JA acquired the data.

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Declaration of interests

NK, AS, AP, FL, GH, SC, and AR declare no competing interests. AM has provided advice to Gilead. MF has received honoraria, support to attend meetings, and lecture fees or research funding from AbbVie, Bristol Myers Squib, Gilead, Janssen, Merck, and ViiV. JA has advised for Gilead, ViiV, and MSD; provided educational activities for Gilead, ViiV, Jansen, MSD, Bristol Myers Squib, and Abbott; has received fees for conferences and travel from Gilead and ViiV; has received research funding from Gilead and Bristol Myers Squib; and is also a trustee/patron of the NAZ Project London, MAC AIDS Fund, Terrence Higgins Trust, and the Sophia Network. LS has received honoraria and support to attend meetings and lecture fees or research funding from Abbott, GlaxoSmithKline, Bristol Myers Squib, and ViiV.

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