Introduction

The 2015 UNAIDS Fast-Track targets are a call to action to protect the health of the roughly 19·8 million people globally with no access to antiretroviral therapy (ART). The targets stipulate that by 2020, 90% of people with HIV know their status, 90% of people who know their status are on ART, and 90% of people on ART have suppressed viral loads. However, to reach these ambitious

Differences in health-related quality of life between HIV-positive and HIV-negative people in Zambia and South Africa: a cross-sectional baseline survey of the HPTN 071 (PopART) trial

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Summary

Background The life expectancy of HIV-positive individuals receiving antiretroviral therapy (ART) is approaching that of HIV-negative people. However, little is known about how these populations compare in terms of health-related quality of life (HRQoL). We aimed to compare HRQoL between HIV-positive and HIV-negative people in Zambia and South Africa.

Methods As part of the HPTN 071 (PopART) study, data from adults aged 18–44 years were gathered between Nov 28, 2013, and March 31, 2015, in large cross-sectional surveys of random samples of the general population in 21 communities in Zambia and South Africa. HRQoL data were collected with a standardised generic measure of health across five domains. We used β-distributed multivariable models to analyse differences in HRQoL scores between HIV-negative and HIV-positive individuals who were unaware of their status; aware, but not in HIV care; in HIV care, but who had not initiated ART; on ART for less than 5 years; and on ART for 5 years or more. We included controls for sociodemographic variables, herpes simplex virus type-2 status, and recreational drug use.

Findings We obtained data for 19750 respondents in Zambia and 18941 respondents in South Africa. Laboratory-confirmed HIV status was available for 19330 respondents in Zambia and 18004 respondents in South Africa; 4128 (21%) of these 19330 respondents in Zambia and 4012 (22%) of 18004 respondents in South Africa had laboratory-confirmed HIV. We obtained complete HRQoL information for 19637 respondents in Zambia and 18429 respondents in South Africa. HRQoL scores did not differ significantly between individuals who had initiated ART more than 5 years previously and HIV-negative individuals, neither in Zambia (change in mean score −0·002, 95% CI −0·007 to 0·003; p=0·767) nor in South Africa (−0·002, −0·007 to 0·003; p=0·396). However, scores did differ between HIV-positive individuals who had initiated ART less than 5 years previously and HIV-negative individuals in Zambia (−0·006, 95% CI −0·008 to −0·004; p<0·001), and in South Africa (−0·002, −0·004 to 0·000; p=0·003). A large proportion of people with clinically confirmed HIV were unaware of being HIV-positive (1768 [43%] of 4128 people in Zambia and 2026 [50%] of 4012 people in South Africa) and reported good HRQoL, with no significant differences from that of HIV-negative people (change in mean HRQoL score −0·001, 95% CI −0·003 to 0·001; p=0·216; and 0·001, −0·001 to 0·001; p=0·997, respectively). In South Africa, HRQoL scores were lower in HIV-positive individuals who were aware of their status but not enrolled in HIV care (change in mean HRQoL −0·004, 95% CI −0·01 to −0·001; p=0·010) and those in HIV care but not on ART (−0·008, −0·01 to −0·004; p=0·001) than in HIV-negative people, but the magnitudes of difference were small.

Interpretation ART is successful in helping to reduce inequalities in HRQoL between HIV-positive and HIV-negative individuals in this general population sample. These findings highlight the importance of improving awareness of HIV status and expanding ART to prevent losses in HRQoL that occur with untreated HIV progression. The gains in HRQoL after individuals initiate ART could be substantial when scaled up to the population level.

Funding National Institute of Allergy and Infectious Diseases, National Institute on Drug Abuse, National Institute of Mental Health, President’s Emergency Plan for AIDS Relief, International Initiative for Impact Evaluation, the Bill & Melinda Gates Foundation.

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Evidence before this study
We searched MEDLINE, PubMed, and Embase on Feb 9, 2016, for studies published between Jan 1, 1995, and Dec 31, 2015, published in English, that compared the health-related quality of life (HRQoL) of people living with HIV with that of the general population across all World Bank income groups. We used the search terms “HIV”, “AIDS”, “quality-of-life”, and “population”. We excluded studies that focused exclusively on the health of HIV-positive individuals without comparison with the health of HIV-negative individuals or the general population, and studies that evaluated a specific health aspect (eg, depression) and not quality of life across all dimensions, that focused on specific populations (eg, pregnant mothers, diamond miners), or patients with adverse events, particular comorbidities, or co-infections. We identified five studies: three from high-income countries and two from South Africa. One study was published in 2014, and the others were at least 12 years old (one was from 2004, two from 2000, and one from 1996). HIV-positive patient populations differed between studies; two studies comprised 2864 and 3258 patients at all stages of disease, two studies focused on 72 and 134 patients at earlier disease stages (exclusion criterion CD4 cell count <200 per µL or acute or terminal illness), and one study focused on 123 patients with advanced disease (exclusion criterion CD4 cell count >200 per µL). All studies found that HRQoL was lower in HIV-positive individuals than in the general population. The two studies from South Africa found that HRQoL was compromised across all dimensions. The three studies from high-income countries found that HRQoL was most affected by emotional functioning. One study found that physical functioning was worse for patients with AIDS, but not for patients with asymptomatic disease. Almost all previous studies evaluated HRQoL in HIV patients who attended a clinic, participated in a clinical study, or were receiving health care. Because these individuals sought care, their health could have been compromised and they were therefore not representative of the general HIV-positive population.

Added value of this study
This study is one of the most extensive and robust analyses of differences in HRQoL among HIV-positive and HIV-negative individuals in a random sample of the general population in sub-Saharan Africa since the rapid scale up of antiretroviral therapy (ART). HIV status was determined from blood samples taken during the survey and confirmed with laboratory testing. We did a direct comparison of HRQoL between HIV-positive people and HIV-negative people. Furthermore, our study design enabled adjustment for confounders that were collected for both groups in the same way. The data are a random sample of the general population, thus giving an estimate of the HRQoL of all people living with HIV, not just the most ill. The study provides a rare insight into the HRQoL of HIV-positive individuals at different stages of engagement with HIV care, even those who were not aware of their status or who were aware but not in HIV care.

Implications of all the available evidence
Our results can be used to estimate how many quality-adjusted life-years could be gained with HIV treatment because of reductions in morbidity. This is crucial information for policy makers to comprehensively assess the societal worth of HIV interventions aimed at increasing the number of individuals receiving treatment.
District of the Western Cape Province of South Africa and 12 in Zambia, spread across four provinces and six districts (appendix p 2).

The data used in this paper were taken from the baseline survey of the population cohort done between Nov 28, 2013, and March 31, 2015, and the laboratory-confirmed HIV status of all participants. In each of the 21 trial communities, a random sample of households was selected and visited by field staff who enumerated all adults aged 18–44 years. From this list, one adult from each household was randomly selected and provided informed consent to participate in the population cohort. Next, the entire population cohort survey was administered in the respondent’s preferred language by trained field workers. The HRQoL questions were embedded as a section in the population cohort survey. From each respondent, detailed information was gathered about HIV testing, self-reported HIV status, sociodemographics, health, and economic and behavioural aspects. Respondents self-reported their HIV status. If they self-reported being HIV-positive, they were asked whether they were in HIV care, and whether and for how long they had been on ART. After completion of the survey, a research nurse offered all respondents an on-the-spot HIV rapid test with pretest and post-test counselling. HIV status was confirmed by testing of blood samples drawn from consenting participants (appendix p 3).

HRQoL information was gathered in South Africa with the certified translation of the EuroQol five dimensions, five levels questionnaire (EQ-5D-5L).5 Since no certified translation of the EQ-5D-5L was available for Zambia, the study team translated the questionnaire into regional Zambian dialects. The EQ-5D-5L measures HRQoL in five separate domains (mobility, self-care, ability to do daily activities, pain, and anxiety or depression) and each domain is measured with five levels (no problems, slight, moderate, severe, or unable to; appendix pp 3–4). Because the questions are not disease specific, the measured HRQoL of HIV-positive and HIV-negative people can be directly compared—an important feature for this study, EQ-5D has been used previously to study HRQoL in the general population and in people living with HIV in LMICs and high-income countries,6,7 and it is an appropriate generic tool for measuring HRQoL in patients with HIV/AIDS.9

A full ethics review of the trial protocol was done by the ethics committees of the University of Zambia, Stellenbosch University, the London School of Hygiene & Tropical Medicine, Imperial College London, and the US Centers for Disease Control and Prevention.

Statistical analysis
We used multivariate β regression models to evaluate the effect of HIV status and ART on HRQoL scores. We selected complementary log–log link functions over logit, probit, and log–log alternatives on the basis of the model that minimised Bayesian information criterion.10 Two defining properties of the HRQoL utility score guided selection of the regression model. First, it has truncated support (ranging between 0 and 1). Second, as in the case of other studies,7 it was negatively skewed with a spike at the upper end of the scale. Such models have been widely applied in analysing variables that are constrained between 0 and 1 and are either positively or negatively skewed.11–13 β regressions are more robust than other commonly used approaches in estimating covariate effects on HRQoL.14 We used the betareg routine in Stata (version 14). Results are presented as marginal effects, whereby a negative effect represents the magnitude of reduction in the score. With HIV-negative individuals as the base case, the model included people with HIV in five categories: HIV positive and unaware of status (those reporting being negative or unaware of their status, but confirmed self-reporting being HIV-positive in the survey).

### Table 1: Sample demographics

|          | Lithuania (n=19 750) | Zambia (n=19 750) | South Africa (n=18 941) |
|----------|----------------------|-------------------|-------------------------|
| Age (years) | 27 (7 2)              | 29 (7 4)          |                         |
| HRQoL score | 0 88 (0 1)            | 0 89 (0 03)       |                         |
| Sex        |                       |                   |                         |
| Male       | 5428/19 733 (28%)     | 5816/18 612 (31%) |                         |
| Female     | 1405/19 733 (72%)     | 12796/18 612 (69%)|                         |
| Ethnic group |                    |                   |                         |
| 1          | 582/19 750 (30%)      | 12 048/18 941 (64%)| Xhosa                   |
| 2          | 2453/19 750 (12%)     | 480/18 941 (25%)  | multiracial              |
| 3          | 1547/19 750 (8%)      | 526/18 941 (3%)   | Afrikaner                |
| 4          | 1404/19 750 (7%)      | 1564/18 941 (8%)  |                         |
| 5          | 8519/19 750 (43%); other |                 |                         |
| Christian  | 19 479/19 680 (99%)   | 15 140/18 270 (83%)|                         |
| Educational level |               |                   |                         |
| School education less than grade 8 (primary school) | 5544/19 668 (28%) | 1472/18 466 (8%) |
| School education between grades 9 and 12 (secondary school) | 12 808/19 668 (65%) | 15 947/18 466 (86%) |
| College, university, or other higher education | 1316/19 668 (7%) | 1047/18 466 (69%) |
| HSV-2-positive | 8117/19 234 (42%) | 8870/17 857 (50%) |                         |
| Use recreational drugs | 480/19 629 (2%) | 689/18 432 (4%) |                         |
| Alcohol consumption† | 970/19 732 (5%) | 1145/18 770 (6%) |                         |
| HIV-negative | 15 202/19 330 (79%) | 12 992/18 004 (79%) |                         |
| HIV-positive† | 4128/19 330 (21%) | 4012/18 004 (22%) |                         |
| HIV-positive, unaware of status | 1768/4128 (43%) | 2026/4012 (50%) |                         |
| HIV-positive, aware of status, not in HIV care§ | 487/4128 (12%) | 350/4012 (9%) |                         |
| HIV-positive, in HIV care, not yet on antiretroviral therapy§ | 177/4128 (4%) | 173/4012 (4%) |                         |
| HIV-positive, on antiretroviral therapy§ | 1585/4128 (38%) | 1236/4012 (31%) |                         |
| Status unknown | 111/4128 (3%) | 227/4012 (6%) |                         |

Data are mean (SD), n (%), or n/N (%). HRQoL=health-related quality of life. HSV-2=herpes simplex virus type 2.

†All other ethnic groups varied between 0·03% and 6·69%. §Numbers based on laboratory confirmed test results. ¶Numbers based on responses by those who actually drink alcohol.

https://www.hptn.org/sites/default/files/2016-05/HPTN%20Protocol%20071%20V.3.0%2016%20Nov%202015%20Final%20%281%29.compressed.pdf
as positive from the laboratory tests); HIV positive and aware of status, but not in HIV care; HIV positive and in HIV care, but not yet on ART; HIV positive and on ART initiated within the last 5 years; and HIV-positive people who initiated ART 5 or more years previously. The model included the adjustment variables age, sex, education, religion, ethnic group, herpes simplex virus type 2 status, and use of recreational drugs. We also included trial cluster dummy variables to capture community-level unobservable differences. We ran models separately for Zambia and South Africa. The appendix provides results for alternative specifications.

We analysed the five domains of HRQoL to determine which domains contributed to the observed effects on HRQoL. We used seemingly unrelated ordered probit regressions to take into account that an individual’s responses in each of the five domains might be correlated. For example, individuals reporting problems with mobility might also be more likely to report problems completing daily activities. This approach is a generalisation of the standard ordered probit regression model allowing for the error terms of each individual’s responses in the five domains to be correlated. In this case, we had five ordered probit equations (one for each domain) with error terms correlated across the five models. Negative marginal effects show the reduction in the probability of reporting no problems in the specific domain of health. We did the analysis with the `cmp` routine in Stata (version 14).

We used the results of the HRQoL score regressions to quantify the average quality-adjusted life-years (QALYs) that might be gained from treatment. For example, assuming each untreated HIV-positive individual has 10 remaining years of life, irrespective of current age or disease stage, and those on ART have remaining years of life according to life tables by country, age, and sex, we

| Table 2: Five health domain classifications for Zambia and South Africa |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Zambia          | South Africa    | p value for     | Zambia          | South Africa    | p value for     |
|                 | HIV-negative    | HIV-positive    | difference†     | HIV-negative    | HIV-positive    | difference†     |
|                 | (n=15,145)*     | (n=4102)*      |                 | (n=13,648)*     | (n=38,98)*      |                 |
| Mobility        |                 |                 | p=0.0001        |                 |                 | p=0.25          |
| No problems     | 14,727 (97%)    | 3,905 (95%)    |                 | 13,415 (98%)    | 3,847 (99%)     |                 |
| walking around  | Slight or       | 389 (3%)       |                 | 199 (2%)        | 48 (1%)         |                 |
|                 | moderate         | 169 (4%)       |                 |                 |                 |                 |
|                 | problems         |                 |                 |                 |                 |                 |
| Severe problems | 29 (<1%)        | 28 (<1%)       |                 | 14 (<1%)        | 3 (<1%)         |                 |
| unable to walk  |                 |                 |                 |                 |                 |                 |
| Self-care       |                 |                 | p=0.0001        |                 |                 | p=0.18          |
| No problems     | 14,810 (98%)    | 3,922 (96%)    |                 | 13,407 (98%)    | 3,842 (99%)     |                 |
| washing and     | Slight or        | 320 (2%)       |                 | 235 (2%)        | 53 (1%)         |                 |
| dressing myself | moderate         | 156 (4%)       |                 |                 |                 |                 |
|                 | problems         |                 |                 |                 |                 |                 |
| Severe problems | 15 (<1%)        | 14 (<1%)       |                 | 6 (<1%)         | 3 (<1%)         |                 |
| unable to wash  |                 |                 |                 |                 |                 |                 |
| or dress myself |                 |                 |                 |                 |                 |                 |
| Daily activities|                 |                 | p=0.0001        |                 |                 | p=0.38          |
| No problems     | 14,608 (97%)    | 3,860 (94%)    |                 | 13,337 (98%)    | 3,801 (98%)     |                 |
| doing my usual  | Slight or        | 516 (3%)       |                 | 301 (2%)        | 91 (2%)         |                 |
| activities      | moderate         | 226 (6%)       |                 |                 |                 |                 |
|                 | problems         |                 |                 |                 |                 |                 |
| Severe problems | 21 (<1%)        | 16 (<1%)       |                 | 10 (<1%)        | 6 (<1%)         |                 |
| unable to do    |                 |                 |                 |                 |                 |                 |
| my usual        |                 |                 |                 |                 |                 |                 |
| activities      |                 |                 |                 |                 |                 |                 |
| Pain            |                 |                 | p=0.0001        |                 |                 | p=0.12          |
| No pain or      | 13,204 (87%)    | 3,425 (85%)    |                 | 11,035 (96%)    | 3,210 (95%)     |                 |
| discomfort      | Slight or        | 1,860 (12%)    |                 | 504 (4%)        | 181 (5%)        |                 |
|                 | moderate pain    | 640 (16%)      |                 |                 |                 |                 |
| or discomfort   | Severe or        | 94 (<1%)       |                 | 12 (<1%)        | 7 (<1%)         |                 |
|                 | extreme pain     |                 |                 |                 |                 |                 |
| or discomfort   |                 |                 |                 |                 |                 |                 |
| Anxiety or      |                 |                 | p=0.0001        |                 |                 | p=0.02          |
| depression      | Not anxious or   | 13,873 (92%)   |                 | 13,069 (96%)    | 3,699 (95%)     |                 |
|                 | depressed        | 3,642 (89%)    |                 |                 |                 |                 |
|                 | Slightly or      | 1,186 (8%)     |                 | 540 (4%)        | 188 (5%)        |                 |
| moderately      | moderately       | 424 (10%)      |                 |                 |                 |                 |
| anxious or      | anxious or       |                 |                 |                 |                 |                 |
| depressed       |                    |                 |                 |                 |                 |                 |
| Anxious or      | 86 (<1%)        | 36 (<1%)       |                 | 39 (<1%)        | 11 (<1%)        |                 |
| depressed       |                 |                 |                 |                 |                 |                 |
| HRQoL score     | 0.88 (0.04)     | 0.88 (0.06)    |                 | 0.89 (0.03)     | 0.89 (0.04)     |                 |

Data are n (%), n/N (%), or mean (SD), unless otherwise stated. HRQoL=health-related quality of life. *Numbers based on complete responses to the five dimensions of HRQoL and laboratory-confirmed HIV status. †p value (Wilcoxon rank-sum test) for the difference between HIV-negative and HIV-positive groups.
Role of the funding source
The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. RT and KH had full access to the data in the study. RT had final responsibility for the decision to submit for publication.

Results
The full sample included responses from 19750 (83%) of 23676 randomly selected individuals in Zambia and 18941 (88%) of 21568 randomly selected individuals in South Africa. HIV status from laboratory-tested blood samples was available for 19330 (98%) participants in Zambia and 18004 (95%) participants in South Africa. 4128 (21%) of these 19330 respondents in Zambia and 4012 (22%) of 18004 respondents in South Africa had laboratory-confirmed HIV. 19637 (99%) participants in Zambia and 18429 (97%) participants in South Africa had complete EQ-5D-5L information.

Prevalence of HIV in the trial communities was similar in both countries (table 1). A large proportion of HIV-positive participants were unaware of their status (table 1). Of HIV-positive participants aware of their HIV status, more reported being on ART in Zambia than in South Africa (table 1). Both countries had lower proportions of male respondents than female respondents (table 1). The unadjusted results show that HIV-positive people in Zambia reported lower levels of HRQoL than HIV-negative people, particularly in the domain of pain, which had a 4 percentage-point difference between the two groups (table 2). Except for a significant difference in the domain of anxiety or depression, there was no difference in HRQoL between HIV-positive and HIV-negative individuals in South Africa. Mean HRQoL score in HIV-positive and HIV-negative people was 0·88 in Zambia and 0·89 in South Africa (table 2).

Regression results show that, in Zambia, individuals who initiated ART less than 5 years previously reported significantly lower HRQoL scores than HIV-negative participants (table 3). Results for South Africa show that HRQoL did not differ between HIV-positive individuals on ART and HIV-negative individuals (table 3). Compared with HIV-negative individuals, small reductions in HRQoL were reported by HIV-positive individuals who were aware of their status but not enrolled in HIV care and those in HIV-care but not yet on ART (table 3). Although significant, these magnitudes are again unlikely to represent meaningful reductions (table 3).

When we analysed the five domains of HRQoL, results for Zambia showed that HIV-positive individuals who had initiated ART less than 5 years previously were less likely than HIV-negative individuals to report no problems across all five domains (table 4). In both

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countries, HIV-positive individuals on ART for at least 5 years had a similar HRQoL to HIV-negative individuals across all five domains (table 4). In South Africa, individuals in HIV care who had never taken ART were less likely than HIV-negative individuals to report no problems with mobility, self-care, and daily activities (table 4). In both countries, individuals aware of their HIV-positive status but not in HIV care were significantly less likely to report no anxiety or depression than were HIV-negative individuals (table 4).

We estimate that, on average, each HIV-positive individual on ART would gain 26·24 QALYs in South Africa and 26·20 QALYs in Zambia, compared with an untreated individual. If we project these data to the UNAIDS 2016 estimates of 3·64 million individuals not yet on ART in South Africa, treating 90% of these individuals would equate to a gain of roughly 86 million QALYs as a direct benefit. Similar estimates for Zambia would mean 10·4 million QALYs could be gained from reaching 90% of the 0·44 million HIV-positive individuals not yet on ART.

**Discussion**

To our knowledge, this is the first and largest study to evaluate the differences in HRQoL between HIV-positive and HIV-negative individuals since the expansion of ART in LMICs with high HIV burden. Unlike most previous studies, which compared the HRQoL of HIV patients at clinics (who are often at advanced disease stages) with the HRQoL of the general population, this study is the first to evaluate HRQoL by awareness of infection and ART status in a random sample from the general population, using laboratory-confirmed HIV status. We estimated several multivariable models with different categorisations of HIV status. We did analyses separately for Zambia and South Africa. Although a multicountry analysis provides valuable added insight, the two countries have very different population and health-system characteristics; therefore, we refrained from a direct comparison of results between countries.

38% of HIV-positive individuals in Zambia and 31% in South Africa were receiving ART, and receipt of treatment raised their HRQoL to that of HIV-negative individuals. The only exception was individuals in Zambia who had initiated ART less than 5 years previously, who reported a lower HRQoL score than HIV-negative individuals; however, the difference was very small. Roughly 4% of HIV-positive people in both countries were in care and had not started ART. In South Africa, these individuals had lower HRQoL than HIV-negative individuals. This finding was due to the dimensions of mobility, self-care, and problems in doing daily activities, but differences in scores were small when compared with HIV-negative people. 12% of HIV-positive people in Zambia and 9% of those in South Africa were aware of their status but not linked to care. In both countries, these individuals were more likely to report
being anxious or depressed than people without HIV. A high proportion of HIV-positive individuals were unaware of their status (43% in Zambia, 50% in South Africa). In both countries, these individuals reported the same HRQoL as HIV-negative individuals, possibly representing the asymptomatic nature of HIV infection in its earlier stages.

Modelling estimates for KwaZulu-Natal suggest that it would take an average of 4.9 years for 50% of HIV seroconverters to be linked to care. Our findings support the observation that, at any one time, most HIV-positive people do not receive care and are not even aware of their status, but report good health. Overall, our estimates of differences are small and possibly not clinically relevant at the individual level. However, when scaled up to population level, they constitute a substantial loss in QALYs. Our calculations suggest that nearly 100 million QALYs could be gained across the two countries if 90% of currently untreated individuals are on ART, but most of these gains are due to extension in length of life. Other research has shown that early mortality rates among adults accessing ART are high in the first year of ART in sub-Saharan Africa, and that many people enter care at an advanced stage of disease and with clinically significant comorbidities. Our findings call for strategies to avoid losses in HRQoL that occur before individuals receive ART, by aiming at early diagnosis, timely initiation of ART, and improvement of adherence. Delays in health-systems initiation of ART must be minimised, especially in patients who present with advanced immunodeficiency.

Previous studies from high-income countries and LMICs found that average HRQoL of HIV-positive individuals was overall lower than that of HIV-negative individuals. However, evidence is contradictory as to whether HIV-positive individuals with asymptomatic disease or viral suppression have the same or lower HRQoL than HIV-negative people. We found smaller magnitudes of differences in HRQoL, by contrast with previous studies that compared clinical cohorts with the general population. In our sample from the general population, almost 60% of HIV-positive people belonged to one of two groups—either unaware of their status and potentially still in good health, or stable on ART for over 5 years and therefore also in relatively good health. Therefore, comparison of our findings with previous studies is problematic. Additionally, all but one of these studies was done before access to testing and treatment was accelerated. Most previous studies also sampled patients enrolled in HIV care, who were likely to be at a more advanced stage of disease and not representative of the overall population of people living with HIV.

The main strengths of this study are that data were gathered recently, covered a large sample of the general population, comprised both HIV-negative and HIV-positive people from two countries, and enabled adjustment for several confounders that were collected for both groups in the same way. This approach allowed us to provide a rare insight into the HRQoL of HIV-positive individuals at different stages of engagement with HIV care, including those who were not aware of their status or who were aware but not in HIV care. As the largest survey of HRQoL in these countries, our survey findings provide an important resource of quality-of-life estimates for future studies.

Our study has limitations. Blood samples from respondents were tested for their HIV status, but no information about disease stage was available. Therefore, we could not differentiate HRQoL by confirmed disease stage. However, evidence shows that in sub-Saharan Africa, mean CD4 cell count at ART initiation has remained at about 152 per µL in the past decade. The group of individuals on ART in our study is thus likely to have been in more advanced clinical stages of HIV at treatment initiation, with associated lower HRQoL. Our results suggest that, with ART, average HRQoL scores recover to levels in the general population, a finding corroborated by clinical studies. We relied on self-reports of ART initiation, which might have been affected by recall bias. Men were under-represented in the sample because the survey was done during the day and fewer men were available at home for interviews. This imbalance might have biased results if there were systematic differences in reported HRQoL between sexes. Results from previous studies have suggested that women might report lower HRQoL than men at similar disease stages, but these studies used a different instrument. Although we adjusted for a large number of possible confounders, some could have been unobserved and could have affected results if they differed systematically by HIV status. We had to use the health state valuations for Zimbabwe because valuations were not available for South Africa or Zambia. Stigma has been shown to substantially affect mental health of HIV-positive individuals, but this influence could be captured by the anxiety or depression dimension of the EQ-5D-5L.

The unique design of our study allowed us to identify the success of ART in reducing inequalities between the HRQoL of HIV-infected individuals and the HIV-negative population. But our findings are also a call to step up efforts to extend these benefits to the millions of people not yet on ART. Improved access to ART is considered the main reason for the marked increase in overall life expectancy in sub-Saharan Africa over the last decade. Additionally, ART can reduce rates of sexual transmission of HIV and substantial reductions in incidence, with associated savings in future treatment costs, have been predicted. However, the beneficial effect of ART on the HRQoL of HIV-positive individuals is often not the focus of attention. This noteworthy and direct benefit of treatment could provide important additional support to international advocacy efforts for the UNAIDS Fast-Track targets. Policy makers should remember the purpose of medical treatment is to add years to life, and life to years.
Contributors

RT and KH both developed the research idea. RT developed and led on the statistical analysis and contributed to writing the Article. KH took the lead on writing and revising the Article. All other authors commented on the Article and approved the final version.

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Declaration of interests

RH, RT, HA, SFI, KH, SF, AH, SK, NV, PB, NB, and NM report grants from National Institutes of Health (NIH), the President’s Emergency Plan for AIDS Relief (PEPFAR), and the International Initiative for Impact Evaluation (3ie), during the conduct of the study. DD reports personal fees from 3ie and the Bill & Melinda Gates Foundation during the conduct of the study. In addition, RH receives royalties for a textbook on Cluster Randomised Trials. RT reports personal fees from the International Decision Support Initiative, outside of the submitted work; KH reports personal fees from International Decision Support Initiative and personal fees from KPMG, outside of the submitted work; HA reports personal fees from Gilead and the Global Fund for AIDS, Tuberculosis and Malaria, outside of the submitted work. PCS reports personal fees from the International Decision Support Initiative, WHO, Inter-American Development Bank, World Bank, European Commission, Finnish Ministry of Social Affairs and Health, and Health Foundation, outside of the submitted work. RB reports grants from South African National Research Fund Health Career Advancement fellowship during the conduct of the study.

Acknowledgments

We are grateful to all members of the HPTN 071 (PopART) Study Team and to the study participants and their communities for their contributions to this research. HPTN 071 is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) under Cooperative Agreements U1AI068619, U1AI068617, and U1AI068613, with funding from PEPFAR. Additional funding is provided by 3ie with support from the Bill & Melinda Gates Foundation, as well as by NIAID, the National Institute on Drug Abuse (NIDA), and the National Institute of Mental Health (NIMH), all part of NIH. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIAID, NIMH, NIDA, PEPFAR, 3ie, or the Bill & Melinda Gates Foundation. KH was also partly funded by the National Institute for Health Research Health Protection Research Unit in Modelling Methodology at Imperial College London in partnership with Public Health England, and by the MRC Centre for Outbreak Analysis and Modelling (funding reference MR/K001074/1B).

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