A randomized comparison of health-related quality of life outcomes of dolutegravir versus efavirenz-based antiretroviral treatment initiated in the third trimester of pregnancy

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Abstract

Introduction: Evidence on health-related quality of life (HRQoL) outcomes is limited for new antiretroviral therapies (ART). Dolutegravir-based treatment is being rolled out as the preferred first-line treatment for HIV in many low- and middle-income countries. We compared HRQoL between treatment-naïve pregnant women randomized to dolutegravir- or efavirenz-based ART in a clinical trial in Uganda and South Africa.

Methods: We gathered HRQoL data from 203 pregnant women of mean age 28 years, randomized to either dolutegravir- or efavirenz-based ART. We used the medical outcomes study-HIV health survey at baseline, 24 and 48 weeks between years 2018 and 2019. Physical health summary (PHS) and mental health summary (MHS) scores were the primary study outcomes, while the 11 MOS-HIV subscales were secondary outcomes. We applied mixed model analysis to estimate differences within and between-treatment groups. Multivariate regression analysis was included to identify associations between primary outcomes and selected variables.

Results: At 24 weeks postpartum, HRQoL scores increased from baseline in both treatment arms: PHS (10.40, 95% CI 9.24, 11.55) and MHS (9.23, 95% CI 7.35, 11.10) for dolutegravir-based ART; PHS (10.24, 95% CI 9.10, 11.38) and MHS (7.54, 95% CI 5.66, 9.42) for efavirenz-based ART. Increased scores for all secondary outcomes were significant at p < 0.0001. At 48 weeks, improvements remained significant for primary outcomes within group comparison. Estimated difference in PHS were higher in the dolutegravir-based arm, while increases in MHS were more for women in the efavirenz-based arm at 24 and 48 weeks. No significant differences were noted for corresponding PHS scores at these time points compared between groups. Differences between arms were observed in two secondary outcomes: role function (1.11, 95% CI 0.08, 2.13), p = 0.034 and physical function outcomes (2.97, 95% CI 1.20, 4.73), p = 0.001. In the multivariate analysis, internet access was associated with higher PHS scores while owning a bank account, using the internet and longer treatment duration were associated with an increase in MHS scores.

Conclusion: We found no important differences in HRQoL outcomes among HIV-positive women started on dolutegravir relative to efavirenz in late pregnancy. Increases in HRQoL in the first year after delivery provide additional support for the initiation of ART in HIV-positive women presenting late in pregnancy.
Introduction
When treatment is initiated in the third trimester of pregnancy, dolutegravir-based antiretroviral therapy (ART) results in greater viral load suppression (less than 50 HIV RNA copies per ml of blood plasma) at delivery compared with pregnant women taking efavirenz-based ART [1]. Dolutegravir-based ART is now a preferred treatment option for HIV infection in mothers, and prevention of perinatal transmission of HIV. However, additional evidence on patient outcomes including health-related quality of life outcomes (HRQoL) is needed for ART regimens in pregnancy.

HRQoL is a patient outcome measure that focuses on addressing multidimensional aspects of health that include patients’ social role, physical status, emotional status, cognitive functioning, and a sense of general satisfaction with life [2, 3]. In addition to commonly used clinical outcomes such as CD4 count and viral load, HRQoL is now an essential outcome in most HIV patient-centered studies [4]. Previous studies found associations between HRQoL outcomes and initiation of antiretroviral therapy among people living with HIV (PLHIV) [5–8]. Some HRQoL evidence exists among HIV patients treated with ART [5–7, 9, 10]. Studies have shown gender differences in HRQoL outcomes among PLHIV for instance, HIV-positive women on ART tend to report poor HRQoL compared with men [11, 12]. However, few studies have examined HRQoL in women and pregnant women living with HIV [13–15]. In addition, pregnancy may lower HRQoL even without HIV infection [16]. Knowledge is scarce on HRQoL in women initiating ART in the third trimester of their pregnancy.

Prolonged use of ART is associated with adverse effects that can potentially impair overall HRQoL [17, 18]. The balance between survival benefits and the adverse effects of using ART on quality of life warrants further research [4, 19]. Adverse events may impair adherence to ART, which in turn could reduce effectiveness for prevention of transmission, and/or prevention of disease progression.

We assessed HRQoL as part of the DolPHIN-2 Study (clinicaltrials.gov registration NCT03249181) that randomized pregnant women initiating ART in the third trimester at the Infectious Diseases Institute and the University of Cape Town in Uganda and South Africa, respectively. We compared the change in HRQoL for women started on dolutegravir- versus efavirenz-based therapy before and after delivery. This knowledge is important to facilitate health policy considerations in programming newer interventions for HIV within sub-Saharan Africa.

Methods
Research participants and setting
This study is part of the DolPHIN-2 clinical trial that focused on the treatment efficacy of dolutegravir-based versus efavirenz-based ART initiated in late pregnancy. DolPHIN-2 was a randomized, open-label trial, that recruited pregnant women in South Africa and Uganda aged at least 18 years, living with HIV but are treatment naïve and an estimated gestation of at least 28 weeks, initiating ART in the third trimester. Participants were randomly assigned (1:1) to dolutegravir-based or efavirenz-based ART between the years 2018 and 2019. 268 treatment-naïve pregnant women were enrolled in the study. Ethical review committees in South Africa, Uganda, and the UK approved the study. Full details of the clinical outcome study are accessible elsewhere [1].

Quality of life measurement
We used the HIV Medical Outcomes Survey (MOS-HIV) to assess HRQoL in trial participants. HRQoL data were collected at three study visits; 4 weeks pre-partum, and at 24 and 48 weeks postpartum. The MOS-HIV is a comprehensive health status measure designed to assess HRQoL in patients living with HIV/AIDS [20, 21]. We used the MOS-HIV 35-item questionnaire that includes eleven dimensions of HRQoL including; general health perceptions (GHP), physical functioning (PH), role functioning (RF), social functioning (SF), cognitive functioning (CF), pain, energy/fatigue, mental health (MH), health distress (HD), quality of life (QoL) and health transition (HT) [22]. We interpreted the survey tool into two local languages of Xhosa and Luganda in South Africa and Uganda respectively. Participant responses to each dimension were aggregated and scores converted to a 0–100-point scale, with 100 indicating the highest achievable health status by a participant [23]. The survey instrument includes two distinct categories of the Physical Health Summary (PHS) and the Mental Health Summary (MHS), based on ten MOS-HIV subscales excluding the health transition dimension [19]. The PHS includes measures of physical functioning, activities, and pain while the MHS includes measures for mental health and psychological functioning [21]. Revicki and others provided evidence from a randomized clinical trial on the reliability and validity of the PHS and MHS scores of the MOS-HIV scales [19, 20, 24].

Keywords: HRQoL, Dolutegravir, Pregnancy, Women, HIV, ART
Statistical analysis

STATA 13 (StataCorp LP, Texas, USA) and SAS 9.4 (SAS Institute) were used for data analysis. Permuted block randomization (block size of 4), stratified by country was employed and baseline variables were balanced as indicated in Table 1, drawn from the primary clinical outcome study [1]. Power calculations were based on the primary clinical trial endpoint (HIV viral load less than 50 copies per mL at birth) published elsewhere [1]. We used available data with valid HRQoL data from the original trial and no formal sample size calculation was performed in this exploratory analysis of HRQoL outcomes. We employed linear mixed models in this study to estimate differences in HRQoL scores between treatment

| Characteristics                        | Dolutegravir (n = 82) | Efavirenz (n = 89) | Total (n = 171) |
|----------------------------------------|-----------------------|--------------------|-----------------|
| Treatment site                         |                       |                    |                 |
| Uganda                                 | 48 (59%)              | 54 (61%)           | 102 (60%)       |
| South Africa                           | 34 (41%)              | 35 (39%)           | 69 (40%)        |
| Married                                |                       |                    |                 |
| Yes                                    | 14 (17%)              | 9 (10%)            | 23 (13%)        |
| No                                     | 68 (83%)              | 80 (90%)           | 148 (87%)       |
| Currently employed                     |                       |                    |                 |
| Yes                                    | 35 (43%)              | 30 (33%)           | 65 (38%)        |
| No                                     | 47 (57%)              | 59 (66%)           | 106 (62%)       |
| Phone financial transactions           |                       |                    |                 |
| Yes                                    | 54 (66%)              | 57 (64%)           | 111 (65%)       |
| No                                     | 28 (34%)              | 32 (36%)           | 60 (35%)        |
| Own bank account                       |                       |                    |                 |
| Yes                                    | 38 (46%)              | 41 (46%)           | 79 (46%)        |
| No                                     | 44 (54%)              | 48 (54%)           | 92 (54%)        |
| Used internet                          |                       |                    |                 |
| Yes                                    | 41 (50%)              | 44 (49%)           | 85 (50%)        |
| No                                     | 41 (50%)              | 45 (51%)           | 86 (50%)        |
| Education level                        |                       |                    |                 |
| Primary                                | 17 (21%)              | 28 (32%)           | 45 (26%)        |
| Secondary                              | 50 (61%)              | 43 (48%)           | 93 (54%)        |
| Higher/university                      | 2 (2%)                | 3 (3%)             | 5 (3%)          |
| Tertiary/vocational                    | 2 (2%)                | 3 (3%)             | 5 (3%)          |
| No education                           | 11 (14%)              | 12 (14%)           | 23 (14%)        |
| Listen to radio                        |                       |                    |                 |
| At least once a week                   | 68 (83%)              | 73 (82%)           | 141 (82%)       |
| Less than once a week                  | 8 (10%)               | 9 (10%)            | 17 (10%)        |
| Not at all                             | 6 (7%)                | 7 (8%)             | 13 (8%)         |
| Watch television                       |                       |                    |                 |
| At least once a week                   | 64 (79%)              | 77 (86%)           | 141 (83%)       |
| Less than once a week                  | 6 (7%)                | 5 (6%)             | 11 (7%)         |
| Not at all                             | 11 (14%)              | 6 (7%)             | 17 (10%)        |
| Age (years)                            | 27.5 (5.1)            | 27.5 (5.0)         | 27.5 (5.0)      |
| Treatment duration (weeks)             | 56.3 (28.4)           | 55.9 (30.1)        | 56.1 (29.2)     |
| Log_{10} viral load (copies per mL)    | 4.0 (1.1)             | 4.2 (0.9)          | 4.1 (1.1)       |
| CD4 at enrollment (cell per µL)        | 514.9 (283.7)         | 456.6 (225.2)      | 484.6 (270)     |
| PHS score                              | 69.9 (11.9)           | 70.7 (9.2)         | 70.3 (10.6)     |
| MHS score                              | 81.2 (16.8)           | 81.5 (15.6)        | 81.4 (16.1)     |

Data are n (%) and mean (SD)

* At enrollment
groups and follow-up visits. During the study, some participants dropped out, resulting in some incomplete observations, and were not imputed but were assumed to be missing completely at random in the mixed model analysis. We specified changes from baseline in HRQoL scores as dependent variables, with baseline measurements included as covariates, treatment arm, visit number, and the interaction between visit and treatment as main effects, and subject as a random effect. For example, for the mixed model analysis of change in PHS from baseline, baseline measurements of PHS are treated as a covariate, treatment arm, visit number, and the interaction between visit and treatment as main effects, and subject as a random effect. Further, multivariate analysis was included to determine individual factors associated with HRQoL in late presenting women living with HIV. PHS and MHS were included as dependent variables in the model and baseline measurements were included as covariates (age, employment status, education, viral load CD4 count, and ART treatment duration) and added into the mixed model separately one by one. We based all hypothesis testing on 2-sided tests.

Results
Baseline characteristics
Two hundred and three HIV-positive pregnant women with HRQoL information were included in this analysis. 84% (171 out of 203) had baseline socioeconomic and demographic data (Table 1). 71% of the women (145 out of 203) had baseline HRQoL scores. Mean age was 27.5 years (SD ± 5.0) in both treatment groups, with secondary level as the highest education level for 50 (61%) and 43 (48%) of women on dolutegravir and efavirenz, respectively.

Difference in HRQoL scores at 24 weeks postpartum
Increased scores from baseline in primary outcomes were observed in both dolutegravir and efavirenz groups; PHS (10.40, 95% CI 9.24, 11.55) and MHS (9.23, 95% CI 7.35, 11.10) in the dolutegravir group while PHS (10.24, 95% CI 9.10, 11.38) and MHS (7.54, 95% CI 5.66, 9.42) in the efavirenz group (Table 2). Changes from baseline were significant for all secondary outcomes with p<0.0001 and p<0.05 for general health perception and cognitive function. There were no significant differences in PHS and MHS when dolutegravir-based ART was compared to efavirenz-based ART (0.16, 95% CI −1.47, 1.79) and (1.69, 95% CI 0.97, 4.35) (Table 3). Overall, no significant differences are observed in primary and secondary HRQoL outcomes when compared between groups, except for role function (1.11, 95% CI 0.08, 2.13) and physical function outcomes (2.97, 95% CI 1.20, 4.73) both with a probability value less than 0.05.

Discussion
We found significant improvements in HRQoL in both treatment groups from the third trimester of pregnancy to 24 weeks postpartum for all primary and secondary endpoints. These HRQoL outcomes persisted over 48 weeks postpartum in terms of PHS and MHS domains in both treatment groups. We are not aware of any previous analysis of HRQoL for HIV-positive women initiating ART in late pregnancy in a similar LMIC setting. A comparable study in Portugal reported better quality of life in HIV-positive women after childbirth than during pregnancy [25]. Another study in South Africa showed that after 6 months of follow-up in a post-caesarean delivery section, HIV-positive women scored significantly lower on quality of life assessment than HIV-negative women [14]. In the general population of PLHIV, studies have shown a positive impact of ART initiation on HRQoL in Africa [6, 26–29] and outside Africa [21, 30, 31].

We found no significant differences in PHS and MHS scores between treatment groups at 24 and 48 weeks postpartum. This may be attributable to the comparable clinical effectiveness of dolutegravir and efavirenz. For instance, a previous study in Botswana included 1729 pregnant women initiated on dolutegravir-based therapy.
and 4593 women initiated on efavirenz-based therapy from government hospitals. Findings showed no statistically compelling difference in the risk for any adverse birth outcome (33.2% vs. 35.0%) and severe birth outcome (10.7% vs. 11.3%) among women using dolutegravir versus efavirenz [32]. Although no significant differences in HRQoL scores were found between treatment groups at 95% CI in the present study, the clinical importance of the small differences is worth considering. A previously published article on the reliability and validity for PHS scores and MHS scores indicated that an over 3-point difference in scores is clinically important [19]. We found no estimated between-group difference equal to or over 3 points for the PHS and MHS at 24 weeks and 48 weeks postpartum.

Between-group differences in secondary endpoints were significant for role function and physical function at 24 weeks postpartum. Participant HRQoL outcomes reflect treatment effectiveness and disease progression [21]. The absence of a significant difference could relate to comparable efficacy between dolutegravir and efavirenz and other non-nucleoside reverse transcriptase inhibitors [33–37].

In the SPRING-1 (phase IIb trial), 205 treatment naïve adult patients were randomized to dolutegravir 10, 25, or 50 mg versus efavirenz 600 mg dose. At 96 weeks, findings revealed that dolutegravir safety profile was more favorable with no dose–response relationship with adverse events; drug tolerance was also generally better with dolutegravir-based dose compared with

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### Table 2
Summary results from mixed model analysis of primary and secondary outcomes (change from baseline in score) at 24 weeks and 48 weeks by treatment group

| Primary and secondary outcomes | Outcomes                | Visit (weeks) | Mixed model analysis |  |
|-------------------------------|-------------------------|--------------|---------------------|--|--|
|                               |                         |              | Dolutegravir        | Efavirenz  |
|                               |                         |              | Difference from baseline (95% CI) | p-value | Difference from baseline (95% CI) | p-value |
| Primary outcomes              | Physical health summary | 24           | 10.40 (9.24, 11.55) | < 0.0001 | 10.24 (9.10, 11.38) | < 0.0001 |
|                               |                         | 48           | 14.32 (13.08, 15.57) | < 0.0001 | 13.90 (12.70, 15.11) | < 0.0001 |
|                               | Mental health summary   | 24           | 9.23 (7.35, 11.10)  | < 0.0001 | 7.54 (5.66, 9.42) | < 0.0001 |
|                               |                         | 48           | 12.50 (10.49, 14.51) | < 0.0001 | 12.63 (10.63, 14.63) | < 0.0001 |
| Secondary outcomes            | Role function           | 24           | 6.87 (6.14, 7.60)   | < 0.0001 | 5.76 (5.04, 6.49) | < 0.0001 |
|                               |                         | 48           | 6.87 (6.48, 7.26)   | < 0.0001 | 6.87 (6.49, 7.26) | < 0.0001 |
|                               | Physical function       | 24           | 16.92 (15.67, 18.17) | < 0.0001 | 13.95 (12.72, 15.19) | < 0.0001 |
|                               |                         | 48           | 18.22 (17.51, 18.93) | < 0.0001 | 18.18 (17.49, 18.88) | < 0.0001 |
|                               | Social function         | 24           | 10.94 (10.15, 11.73) | < 0.0001 | 11.19 (10.41, 11.97) | < 0.0001 |
|                               |                         | 48           | 12.53 (12.04, 13.02) | < 0.0001 | 12.28 (11.80, 12.76) | < 0.0001 |
|                               | Pain                    | 24           | 10.91 (8.87, 12.94) | < 0.0001 | 12.57 (10.54, 14.59) | < 0.0001 |
|                               |                         | 48           | 15.42 (13.69, 17.14) | < 0.0001 | 13.71 (12.01, 15.41) | < 0.0001 |
|                               | General health          | 24           | 1.63 (0.55, 2.72)   | 0.0032 | 1.88 (0.80, 2.96) | 0.0007 |
|                               |                         | 48           | 4.26 (3.36, 5.17)   | < 0.0001 | 4.27 (3.38, 5.17) | < 0.0001 |
|                               | Health transition       | 24           | 12.07 (8.30, 15.84) | < 0.0001 | 12.58 (8.81, 16.35) | < 0.0001 |
|                               |                         | 48           | 11.95 (8.60, 15.30) | < 0.0001 | 9.79 (6.45, 13.12) | < 0.0001 |
|                               | Quality of life         | 24           | 12.36 (9.28, 15.45) | < 0.0001 | 9.76 (6.65, 12.86) | < 0.0001 |
|                               |                         | 48           | 14.89 (12.15, 17.63) | < 0.0001 | 13.59 (10.85, 16.33) | < 0.0001 |
|                               | Health distress         | 24           | 15.10 (12.45, 17.75) | < 0.0001 | 11.99 (9.35, 14.63) | < 0.0001 |
|                               |                         | 48           | 19.33 (17.10, 21.55) | < 0.0001 | 19.93 (17.74, 22.13) | < 0.0001 |
|                               | Cognitive function      | 24           | 2.30 (0.31, 4.29)   | 0.0236 | 4.97 (2.99, 6.95) | < 0.0001 |
|                               |                         | 48           | 6.60 (4.88, 8.33)   | < 0.0001 | 6.50 (4.79, 8.21) | < 0.0001 |
|                               | Energy                  | 24           | 15.49 (13.14, 17.85) | < 0.0001 | 15.86 (13.51, 18.20) | < 0.0001 |
|                               |                         | 48           | 22.90 (20.90, 24.89) | < 0.0001 | 21.43 (19.46, 23.40) | < 0.0001 |
|                               | Mental health           | 24           | 8.57 (6.44, 10.70)  | < 0.0001 | 6.43 (4.32, 8.54) | < 0.0001 |
|                               |                         | 48           | 11.49 (9.70, 13.29) | < 0.0001 | 12.26 (10.50, 14.03) | < 0.0001 |

* P-values for estimated differences in dolutegravir
* P-values for estimated differences in efavirenz
efavirenz-based dose [38]. Primary analysis from the clinical endpoint study (DoIPHIN-2 RCT) showed non-inferior outcomes for dolutegravir compared to efavirenz on clinical indicators directly linked to participant’s HRQoL. For example, fewer drug-related serious adverse events occurred in the dolutegravir-arm compared to the efavirenz-arm (1.5% vs. 3.8%). More rapid viral load suppression before delivery occurred in the dolutegravir arm compared to efavirenz arm [36].

In the multivariate analysis, we found a negative association between CD4 count and MHS scores. This is surprising since we expect HRQoL to rise with the increase in CD4 count. One African study showed that, although CD4 increased, the quantitative impact on HRQoL changes was minimal in PLHIV [8]. We found no similar study discussing this association in late pregnancy. Two studies in Uganda and South Africa reported no association between CD4 count and HRQoL indicators in HIV general population [39, 40].

Using the internet and watching television was associated with better PHS and MHS scores. Qualitative studies in Uganda and Kenya showed that avoidance and distraction were common coping techniques used by youth living with HIV to prevent poor health outcomes, among these included chatting with friends, watching television, and listening to music [41, 42]. A related study in Europe found a significant association between social support and HRQoL among adult PLHIV [43]. Owning a bank account was associated with higher MHS scores. A study in Uganda found that higher income was associated with a better overall quality of life among PLHIV [26]. Other studies outside Africa showed that employment predicted good overall quality of life for PLHIV [43–45] but this was not identified as a predictor in our study.

### Table 3

Summary results from mixed model analysis of primary and secondary outcomes (change from baseline) with repeated measurements at 24 weeks and 48 weeks: between group comparison

| Primary and secondary outcomes | Outcomes                  | Visit (weeks) | n* mean (SD) | Mixed model analysis |
|--------------------------------|---------------------------|---------------|--------------|---------------------|
|                                |                           |               | Dolutegravir | Efavirenz | Difference (95% CI) | p-valueb |
| Primary outcomes               | Physical health summary   | 24            | 86, 11.9 (13.11) | 88, 9.02 (10.88) | 0.16 (−1.47, 1.79) | 0.8466   |
|                                |                           | 48            | 74, 15.41 (11.32) | 79, 12.62 (9.46) | 0.42 (−1.31, 2.15) | 0.6316   |
|                                | Mental health summary     | 24            | 87, 10.56 (15.84) | 86, 6.69 (15.26) | 1.69 (−0.97, 4.35) | 0.2112   |
|                                |                           | 48            | 75, 13.41 (16.74) | 76, 11.16 (14.34) | −0.13 (−2.97, 2.71) | 0.9277   |
| Secondary outcomes             | Role function             | 24            | 89, 5.55 (29.07) | 90, 2.78 (21.67) | 1.11 (0.08, 2.13)  | 0.0348   |
|                                |                           | 48            | 312, 10.90 (30.69) | 324, 3.09 (16.40) | −0.01 (−0.56, 0.55) | 0.9812   |
|                                | Physical function         | 24            | 88, 19.60 (22.53) | 90, 11.39 (21.25) | 2.97 (1.20, 4.73)  | 0.0010   |
|                                |                           | 48            | 308, 20.45 (20.99) | 324, 16.05 (16.89) | 0.04 (−0.96, 1.04) | 0.9441   |
|                                | Social function           | 24            | 88, 12.73 (25.04) | 89, 9.21 (21.33) | 0.25 (−1.36, 0.86) | 0.6612   |
|                                |                           | 48            | 304, 14.47 (25.09) | 320, 10.50 (20.52) | 0.25 (−0.43, 0.94) | 0.4674   |
|                                | Pain                      | 24            | 89, 13.34 (28.00) | 90, 10.69 (22.37) | −1.66 (−4.54, 1.22) | 0.2570   |
|                                |                           | 48            | 312, 17.15 (24.23) | 324, 12.19 (19.37) | 1.70 (−0.72, 4.13) | 0.1686   |
|                                | General health            | 24            | 89, 1.46 (13.04) | 90, 2.67 (12.18) | −0.25 (−1.77, 1.28) | 0.7521   |
|                                |                           | 48            | 312, 3.46 (10.83) | 324, 5.00 (10.76) | −0.01 (−1.28, 1.26) | 0.9900   |
|                                | Health transition         | 24            | 88, 9.94 (25.30) | 88, 15.06 (27.48) | −0.51 (−5.86, 4.63) | 0.8512   |
|                                |                           | 48            | 308, 9.09 (29.90) | 316, 12.97 (31.08) | 2.16 (−2.58, 6.90) | 0.3707   |
|                                | Quality of life           | 24            | 89, 13.48 (24.73) | 88, 9.09 (24.32) | 2.61 (−1.77, 6.99) | 0.2428   |
|                                |                           | 48            | 312, 15.71 (22.00) | 316, 12.66 (19.05) | 1.30 (−2.58, 5.18) | 0.5096   |
|                                | Health distress           | 24            | 88, 17.61 (30.90) | 88, 10.45 (26.19) | 3.11 (−0.64, 6.86) | 0.1035   |
|                                |                           | 48            | 304, 21.51 (30.10) | 315, 17.84 (22.72) | −0.61 (−3.74, 2.52) | 0.7028   |
|                                | Cognitive function        | 24            | 89, 2.58 (18.92) | 90, 4.22 (17.17) | −2.67 (−5.48, 0.14) | 0.0621   |
|                                |                           | 48            | 312, 6.79 (16.53) | 320, 5.94 (17.65) | 0.10 (−2.33, 2.53) | 0.9354   |
|                                | Energy                    | 24            | 88, 17.27 (21.53) | 89, 14.44 (21.60) | −0.36 (−3.68, 2.96) | 0.8309   |
|                                |                           | 48            | 307, 24.59 (18.96) | 320, 19.81 (20.76) | 1.46 (−1.34, 4.27) | 0.3062   |
|                                | Mental health             | 24            | 88, 9.73 (19.17) | 90, 5.96 (19.61) | 2.14 (−0.86, 5.14) | 0.1622   |
|                                |                           | 48            | 307, 12.40 (19.68) | 324, 11.21 (18.05) | −0.77 (−3.29, 1.74) | 0.5472   |

SD standard deviation

*a Number of observations at two visits, each visit compared with baseline

*b P-value for estimated mean differences between treatment groups at different study visits


Most women had lower levels of education and primary level education was negatively associated with MHS in our study. We may attribute this to poor socioeconomic outcomes associated with low education levels, e.g. 62% of respondents reported being unemployed in this study, and employment status influences HRQoL [43, 44].

Table 4  Multivariate analysis of factors associated with health related quality of life

| Variables                  | Comparison            | PHS Coefficient (95% CI) | p-value | MHS Coefficient (95% CI) | p-value |
|----------------------------|-----------------------|--------------------------|---------|--------------------------|---------|
| Age                        | -0.01 (− 0.17, 0.15)  | 0.8974                   |         | 0.00 (− 0.26, 0.27)      | 0.9714  |
| Married                    | Yes (vs. no)          | 0.01 (− 2.25, 2.27)      | 0.9911  | -0.28 (− 3.72, 3.16)     | 0.8725  |
| Currently employed         | Yes (vs. no)          | 0.42 (− 1.15, 1.99)      | 0.6002  | -1.55 (− 4.08, 0.99)     | 0.2291  |
| Phone financial transactions| Yes (vs. no)          | -0.42 (− 2.00, 1.16)     | 0.5988  | 1.00 (− 1.59, 3.58)      | 0.4483  |
| Own bank account           | Yes (vs. no)          | 0.77 (− 0.69, 2.23)      | 0.2962  | 5.23 (2.84, 7.62)        | <0.0001 |
| Study site (SA)            | SA site (vs. UG site) | 0.33 (− 1.15, 1.81)      | 0.6612  | 7.53 (5.31, 9.75)        | <0.0001 |
| Used internet              | Yes (vs. no)          | 1.62 (0.19, 3.05)        | 0.0269  | 6.65 (4.41, 8.89)        | <0.0001 |
| Listen to radio            | At least once a week  | 0.80 (− 2.00, 3.59)      | 0.5728  | 3.24 (− 1.06, 7.55)      | 0.1384  |
| Watch television           | At least once a week  | 0.93 (− 1.37, 3.23)      | 0.4246  | 4.68 (1.09, 8.27)        | 0.0110  |
| Education level            | Higher/university     | -2.16 (− 6.63, 2.31)     | 0.3416  | -1.71 (− 8.90, 5.47)     | 0.6380  |
| Primary                    | -0.85 (− 3.27, 1.56)  | 0.4851                   |         | -5.52 (− 1.94, 1.58)     | 0.0065  |
| Secondary                  | -1.07 (− 3.23, 1.09)  | 0.3280                   |         | -1.47 (− 4.94, 1.99)     | 0.4019  |
| Tertiary/vocational        | 1.46 (− 3.03, 5.96)   | 0.5201                   |         | -0.25 (− 7.82, 7.31)     | 0.9473  |
| No education               | 0.00                   | -                       |         | 0.00                     | -       |
| Viral load                 | 0.00 (− 0.00, 0.00)   | 0.4418                   |         | 0.00 (− 0.00, 0.00)      | 0.3030  |
| CD4 count                  | 0.00 (− 0.00, 0.00)   | 0.3079                   |         | -0.01 (− 0.01, 0.00)     | 0.0052  |
| Treatment duration         | 0.02 (− 0.01, 0.05)   | 0.1376                   |         | 0.09 (0.04, 0.13)        | 0.0003  |

PHS physical health summary, MHS mental health summary, CI confidence interval, SA South Africa, UG Uganda

In conclusion, we found no important differences in HRQoL outcomes among women living with HIV, who were started on dolutegravir-based versus efavirenz-based therapy in the last trimester. Increases in HRQoL scores in the first year after delivery provide additional support for the initiation of ART in HIV-positive women presenting late in pregnancy.

Conclusions

Acknowledgements

Author contributions
SK, ML, LM, CW, DW, and HR designed the main research study. KK, ML, TM established the cohort including participant identification, consenting, and
data collection. PNO and ML designed and performed the sub-study. PNO, TC, and DW analyzed data. PNO wrote the primary draft of the manuscript. All authors contributed to writing subsequent drafts. All authors read and approved the final manuscript.

Funding
The University of Liverpool sponsored the DoiPHIN-2 study with funding from UNITAID under funding agreement number 2016-08-UoL. ViiV Healthcare donated Dolutegravir drug. CW is funded by Wellcome Clinical Research Career Development Fellowship, Award Number: 222075/2/20/Z.

Availability of data and materials
Anonymized de-identified data is available on request to the corresponding author.

Declarations

Ethical approval and consent to participate
Ethics review committees in Uganda, South Africa, and the UK approved the study. Evidence of a personally signed and dated informed consent document indicating that the participant has been informed of all pertinent aspects of the study was part of inclusion criteria.

Consent for publication
We maintained full anonymity of participant’s details throughout this writing. No consent was required.

Competing interests
The authors declare that they have no competing interests.

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Received: 11 January 2021 Accepted: 4 May 2022
Published online: 07 June 2022

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Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

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