Online Resource

This online resource has been provided by the authors to give readers additional information about their work.

Supplement to: Bousmah, M.-a.-Q., Nishimwe, M.L., Tovar-Sanchez, T., Lanteche Wandji, M., Mpoudi-Etame, M., Maradan, G., Ongba Bassega, P., Varloteaux, M., Montoyo, A., Kouanfack, C., Delaporte, E., Boyer, S., for The NAMSAL ANRS 12313 Study Group. (2020). Cost-utility analysis of a dolutegravir-based versus low-dose efavirenz-based regimen for the initial treatment of HIV-infected patients in Cameroon (NAMSAL ANRS 12313 trial).

Contents:

Page 3: Members of the NAMSAL Study Group

Page 4: Table 1. List of 35 perceived HIV symptoms and treatment-related side-effects

Page 5: Fig. S1. Flow chart of the study population

Page 6: Table 2. Unit costs (US dollars, year 2016 value) used to value healthcare resources

Page 7: Treatment of missing data
   Table 3. Sample sizes and the incidence of missing data

Page 8: Incremental estimates of costs and QALYs in the base-case analysis
   Table 4. Results of the generalised linear regression models (GLM) used to obtain the multivariate-adjusted incremental estimates of costs and QALYs (NAMSAL ANRS 12313 trial, n=575)

Page 9-12: Markov cohort simulation: model inputs
   Table 5. Distribution of the study population in the health states at model entry
   Table 6. Comparison of the main characteristics of patients who switched to second-line in the 2LADY ANRS 12-169 trial and in the NAMSAL ANRS 12313 trial
   Table 7. Estimated 3-month transition probabilities according to health states and arm
   Table 8. Healthcare costs (US dollars, 2016) and quality-adjusted life years (QALYs) per 3-month cycle according to health state and arm

Page 13-15: Table 9. Patient-Reported Outcomes, weight and sample size over time in both arms

Page 16: Fig. S2. Baseline and evolution over follow-up of the number of perceived HIV symptoms of at least mild severity

Page 17: Fig. S3. Baseline and evolution over follow-up of the number of perceived HIV symptoms of at least moderate severity

Page 18: Fig. S4. Baseline and evolution over follow-up of the number of perceived HIV symptoms of at least important severity

Page 19: Fig. S5. Baseline and evolution over follow-up of the number of perceived HIV symptoms of very important severity

Page 20: Fig. S6. Baseline and evolution over follow-up of the proportion of patients with at least mild depression (based on the DASS-21 depression score)

Page 21: Fig. S7. Baseline and evolution over follow-up of the proportion of patients with at least mild anxiety (based on the DASS-21 anxiety score)

Page 22: Fig. S8. Baseline and evolution over follow-up of the proportion of patients with at least mild stress (based on the DASS-21 stress score)
Page 23: Fig. S9. Baseline and evolution over follow-up of the Physical Component Summary (PCS)

Page 24: Fig. S10. Baseline and evolution over follow-up of the Mental Component Summary (MCS)

Page 25: Fig. S11. Baseline and evolution over follow-up of the SF-6D utility score

Page 26: Table 10. Unadjusted mean costs ($, year 2016 values) and QALYs per patient over first 96 weeks (NAMSAL ANRS 12313 trial, n=575)

Page 27: Fig. S12. Cost-effective price thresholds for DTG and EFV400 strategies at the threshold of $1,392/QALY

Page 28: Fig. S13. Cost-effectiveness plane and cost-effectiveness acceptability curve for the analysis over 5 years

Page 29: Fig. S14. Cost-effectiveness plane and cost-effectiveness acceptability curve for the analysis over 10 years

Page 30: Table 11. Clinical outcomes at week 96 in the study population (NAMSAL ANRS 12313, n=575)

Page 31: References
Members of the NAMSAL Study Group

TransVIHMI, University of Montpellier-IRD-INSERM, Montpellier, France:
A Ayoubá, A Agholeng, C Butel, A Cournil, E Delaporte, S Eymard-Duvernay, B Granouillac, S Izard, A Lacroix, S Leroy, M Peeters, S Perrineau, L Serrano, J Reynes, T Tovar-Sanchez, N Vidal

Central Hospital of Yaoundé, Yaoundé, Cameroon:
PJ Fouda, C Kounfack, R Mougnoutou, J Olinga, V Omgba, SC Tchokonte Ngandé, B Ymele

Military Hospital of Yaoundé, Yaoundé, Cameroon:
A Kambi, CD Epoupa Mpacko, M Mpoudi-Etamé, M Fotso, R Moukoko, T Nké

Cité Verte Hospital, Yaoundé, Cameroon:
A Akamba, S Lekelem, P Omgba Bassega, SB Tongo Fotack, S Ngono, M Tanga

CREMER, Yaoundé, Cameroon:
E Ebong, G Edoul Mbesse, M Tsongo, E Mpoudi-Ngolé

Cameroon ANRS site, Yaoundé, Cameroon:
T Abong, L Ciaffi, S Koulla-Shiro, M Lantché Wandji, G Manirakiza, ED Mimbé, D Tetsa Tata, M Varloteaux

SESSTIM, Aix-Marseille University-INSERM-IRD, Marseille, France:
S Boyer, MQ Bousmah, G Maradan, ML Nishimwe, B Spire

Pharmacology-Toxicology Unit, INSERM-University of Paris Diderot, Paris, France:
MP Lê, G Peytavin

ANRS, Paris, France:
A Diallo, I Fournier, A Montoyo, N Mercier, C Rekacewicz

UNITAID, Geneva, Switzerland:
C Perez Casa

Data Safety Monitoring Board:
C Charpentier (University Hospital Bichat, Paris, France), N Clumeck (University Hospital Saint-Pierre, Bruxelles, Belgium), P Flandre (INSERM, Paris, France), F Ngom Gueye (Fann Hospital, Dakar, Senegal), L Weiss (chair, University Hospital Pompidou, Paris, France)

Trial Steering Committee:
A Calmy (University Hospitals Geneva, Geneva, Switzerland),
C Kounfack (University of Dschang, Cameroon), A Hill (University of Liverpool, UK), J Reynes (University of Montpellier), E Delaporte (University of Montpellier)

Funding:
UNITAID and the French National Agency for AIDS Research funded NAMSAL trial; study drugs were paid by UNITAID.
| Perceived HIV symptom | Neuro-sensorial symptoms related to efavirenz | Proportion of patients who experienced this symptom with at least mild severity |
|-----------------------|---------------------------------------------|--------------------------------------------------------------------------------|
|                       | DTG arm | EFFV400 arm | Difference | Standard error of the difference | p-value | DTG arm | EFFV400 arm | Difference | Standard error of the difference | p-value |
| 1. Vivid dreams       |          |             | 0.29       | 0.24 | 0.06 | 0.04 | 0.13 | 0.08 | 0.08 | 0.00 | -0.02 | 0.94 |
| 2. Fever              |          |             | 0.29       | 0.31 | -0.03 | 0.04 | 0.51 | 0.21 | 0.26 | -0.05 | -0.04 | 0.22 |
| 3. Loss of balance    |          |             | 0.29       | 0.25 | 0.04 | 0.04 | 0.30 | 0.07 | 0.08 | -0.02 | -0.02 | 0.43 |
| 4. Chills or sweats   |          |             | 0.34       | 0.30 | 0.04 | 0.04 | 0.31 | 0.27 | 0.26 | 0.01 | -0.04 | 0.86 |
| 5. Disturbed sleep    |          |             | 0.29       | 0.25 | 0.04 | 0.04 | 0.30 | 0.14 | 0.13 | 0.01 | -0.03 | 0.86 |
| 6. Fatigue or loss of energy | 0.55 | 0.5 | 0.00 | 0.04 | 0.95 | 0.30 | 0.30 | -0.01 | -0.04 | 0.88 |
| 7. Nightmare          |          |             | 0.21       | 0.18 | 0.02 | 0.03 | 0.46 | 0.20 | 0.22 | -0.02 | -0.04 | 0.50 |
| 8. Cough              |          |             | 0.34       | 0.37 | -0.03 | 0.04 | 0.40 | 0.25 | 0.28 | -0.03 | -0.04 | 0.41 |
| 9. Dizziness          |          |             | 0.33       | 0.28 | 0.05 | 0.04 | 0.24 | 0.17 | 0.20 | -0.03 | -0.03 | 0.39 |
| 10. Cold-like symptoms|        |             | 0.33       | 0.29 | 0.04 | 0.04 | 0.37 | 0.26 | 0.25 | 0.01 | -0.04 | 0.71 |
| 11. Headache          |          |             | 0.42       | 0.51 | -0.08 | 0.04 | 0.055 | 0.43 | 0.47 | -0.04 | -0.04 | 0.37 |
| 12. Vomiting          |          |             | 0.05       | 0.07 | -0.01 | 0.02 | 0.55 | 0.05 | 0.04 | 0.01 | -0.02 | 0.70 |
| 13. Frequently waking during the night | 0.22 | 0.25 | -0.03 | 0.04 | 0.33 | 0.10 | 0.09 | 0.01 | -0.03 | 0.68 |
| 14. Diarrhoea         |          |             | 0.18       | 0.23 | -0.05 | 0.03 | 0.13 | 0.11 | 0.09 | 0.02 | -0.03 | 0.48 |
| 15. Strange dreams    |          |             | 0.11       | 0.10 | 0.01 | 0.03 | 0.81 | 0.04 | 0.07 | -0.03 | -0.02 | 0.13 |
| 16. Abdominal pain    |          |             | 0.29       | 0.29 | 0.01 | 0.04 | 0.89 | 0.25 | 0.22 | 0.03 | -0.04 | 0.39 |
| 17. Feeling like the room is spinning | 0.07 | 0.02 | 0.04 | 0.02 | **0.013** | 0.02 | 0.02 | 0.00 | -0.01 | 0.82 |
| 18. Articular pain    |          |             | 0.26       | 0.26 | 0.00 | 0.04 | 0.91 | 0.26 | 0.23 | 0.03 | -0.04 | 0.51 |
| 19. Hangover-type feeling | 0.05 | 0.06 | -0.02 | 0.02 | 0.41 | 0.10 | 0.07 | 0.03 | -0.03 | 0.30 |
| 20. Nausea            |          |             | 0.16       | 0.15 | 0.01 | 0.03 | 0.81 | 0.12 | 0.15 | -0.03 | -0.03 | 0.40 |
| 21. Intense dreams    |          |             | 0.07       | 0.08 | -0.01 | 0.02 | 0.74 | 0.06 | 0.07 | 0.00 | -0.02 | 0.88 |
| 22. Breathlessness    |          |             | 0.25       | 0.29 | -0.04 | 0.04 | 0.31 | 0.26 | 0.29 | -0.03 | -0.04 | 0.42 |
| 23. Unsteady walking  |          |             | 0.12       | 0.09 | 0.03 | 0.03 | 0.19 | 0.02 | 0.03 | -0.01 | -0.01 | 0.65 |
| 24. Not feeling well  |          |             | 0.15       | 0.14 | 0.02 | 0.03 | 0.57 | 0.07 | 0.07 | -0.01 | -0.02 | 0.76 |
| 25. Feeling light-headed |          |             | 0.05       | 0.05 | 0.00 | 0.02 | 0.94 | 0.05 | 0.04 | 0.01 | -0.02 | 0.70 |
| 26. Wheezing          |          |             | 0.16       | 0.15 | 0.01 | 0.03 | 0.73 | 0.17 | 0.10 | 0.06 | -0.03 | **0.043** |
| 27. Difficulty falling asleep | 0.28 | 0.33 | -0.05 | 0.04 | 0.17 | 0.25 | 0.23 | 0.03 | -0.04 | 0.51 |
| 28. Skin rash         |          |             | 0.19       | 0.21 | -0.01 | 0.03 | 0.69 | 0.10 | 0.07 | 0.03 | -0.02 | 0.22 |
| 29. Scary dreams      |          |             | 0.08       | 0.09 | 0.00 | 0.02 | 0.91 | 0.05 | 0.03 | 0.02 | -0.02 | 0.30 |
| 30. Bronchitis        |          |             | 0.01       | 0.02 | -0.01 | 0.01 | 0.56 | 0.01 | 0.00 | 0.00 | -0.01 | 0.52 |
| 31. Feeling like head is spinning | 0.06 | 0.10 | -0.03 | 0.02 | 0.13 | 0.05 | 0.03 | 0.02 | -0.02 | 0.26 |
| 32. Sore throat       |          |             | 0.11       | 0.09 | 0.02 | 0.03 | 0.36 | 0.05 | 0.05 | 0.00 | -0.02 | 0.83 |
| 33. Feeling faint     |          |             | 0.11       | 0.12 | -0.01 | 0.03 | 0.80 | 0.07 | 0.06 | 0.00 | -0.02 | 0.83 |
| 34. Flu-like symptoms |          |             | 0.28       | 0.27 | 0.01 | 0.04 | 0.77 | 0.20 | 0.19 | 0.01 | -0.04 | 0.77 |
| 35. Other symptoms or feelings | 0.09 | 0.08 | 0.01 | 0.02 | 0.74 | 0.02 | 0.02 | 0.00 | -0.01 | 0.91 |

Notes: Differences are computed as proportion(DTG) - proportion(EFFV400). Abbreviations: DTG=dolutegravir. EFFV400=efavirenz 400mg.

Two-sample test for proportion differences between the two arms.
Fig. S1. Flow chart of the study population

800 participants were assessed for eligibility

204 were excluded
67 did not have HIV-1 group M infection
43 had received antiretroviral therapy previously or had viral load <1000 copies/ml
24 were lost to follow-up at day 0
20 had hemoglobin level <10 g/dl
13 had opportunistic infections
10 withdrew consent
7 were pregnant
6 had elevated liver function results
5 had renal clearance
5 had thrombocytopenia
4 had geographic incompatibility with planned follow-up visits

616 underwent randomization

310 were assigned to DTG-based regimen
310 received trial regimen

310 were included in the ITT analysis

306 were assigned to the low-dose EFV-based regimen
303 received trial regimen
3 did not receive trial regimen

303 were included in the ITT analysis

32 had protocol deviations (excluding 15 treatment interruptions > 15 days):
2 antiretroviral treatment errors (EFV400 instead of DTG)
1 delay of treatment initiation < 15 days
32 switches to EFV600 (including 2 errors related to switch to EFV400)

3 had protocol deviations (excluding 14 treatment interruptions > 15 days):
1 wrongly included (pregnancy)
2 baseline resistance

275 were included in the modified PP

5 died
20 were lost to follow-up

250 were still in care at week 96

300 were included in the modified PP

9 died
23 were lost to follow-up

268 were still in care at week 96

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. ITT=intention to treat. PP=per protocol.
### Table 2. Unit costs (US dollars, year 2016 value) used to value healthcare resources

|                         | Cost (US$, year 2016 value) | Source and year          |
|-------------------------|------------------------------|--------------------------|
| **ARV (unit cost per patient per year)** |                              |                          |
| Dolutegravir/Lamivudine/Tenofovir 50/300/300mg (FDC) | 62.7                         | Global Fund, 2020 [1]    |
| Efavirenz/Lamivudine/Tenofovir 400/300/300mg (FDC) | 65.0                         |                          |
| Lamivudine/Zidovudine 150/300mg | 59.3                         |                          |
| Atazanavir/Ritonavir 300/100mg | 145.8                        |                          |
| Abacavir/Lamivudine 600/300mg | 104.0                        |                          |
| Lopinavir/Ritonavir 200/50mg | 210.7                        |                          |
| Lamivudine/Tenofovir 300/300mg | 38.4                         |                          |
| **Biological tests (unit cost)** |                              |                          |
| Western blot            | 39.5                         | Centre Pasteur du Cameroun, 2020 [2] |
| HIV RNA                 | 26.3                         |                          |
| CD4/CD8                 | 21                           |                          |
| AST/ALT                 | 9.9                          |                          |
| Creatinine              | 2.2                          |                          |
| CBC                     | 6.6                          |                          |
| HbA1c                   | 2.2                          |                          |
| Total cholesterol       | 2.2                          |                          |
| HDL cholesterol         | 6.6                          |                          |
| LDL cholesterol         | 6.6                          |                          |
| Triglycerides           | 4.4                          |                          |
| Glycaemia               | 2.2                          |                          |
| Urine test strip        | 13.2                         |                          |
| HBV serology            | 46                           |                          |
| Urine pregnancy test    | 6.6                          |                          |
| **Clinical consultation costs (unit cost)** |                              |                          |
| Specialist consultation | 5.9                          | Yaoundé Central Hospital, 2016-2019 |

Notes: Unit costs of concomitant treatments applied in the Cameroonian health system throughout 2016-2019 were taken from the relevant national source [3]. The cost of outpatient consultations (including non-routine visits) and hospitalizations were directly collected from their respective bills and reflected the entire follow-up period (2016-2019).

Abbreviations: ARV: Antiretroviral drugs; CBC: Complete Blood Count; FDC: fixed-dose combination.

Unit prices of antiretroviral drugs obtained from the Global Fund Pooled Procurement Mechanism Reference Pricing, which provides prices at which the Global Fund aims to deliver the health products at or below. Mean price of one year of antiretroviral drugs treatment were calculated for each of the regimens prescribed in the NAMSAL trial.
**Treatment of missing data**

With respect to the data on health-related quality of life (HRQOL), the incidence of non-monotone missing data (i.e., intermittent missing responses) was very low, with a maximum of 3% at Week 72 (17 intermittently missed visits for 575 patients). This is presented in Table 3 below. We implemented a random-effects logistic panel regression for the non-monotone missingness of the HRQOL data, controlling for the treatment arm, gender, age and time-dependent HIV RNA load. Results showed that none of the covariates were significantly associated with missingness, indicating that we can reasonably assume that the HRQOL data were missing at random (MAR) [4]. In cost-utility analyses conducted alongside randomized clinical trials, performing a complete case analysis may yield biased estimates in the presence of MAR outcome data [5]. As we showed that patients with missing values did not differ systematically from those with complete data based on observed characteristics (including the treatment arm), we performed single imputation with predictive mean matching of the missing intermittent data. With regard to monotone missing data patterns (i.e., patients lost to follow-up), Table 3 below indicates that their incidence was relatively low, with 7.5% (43 out of 575) of patients lost to follow-up over the first 96 weeks. A logistic regression for the probability of being lost to follow-up, which controlled for the treatment arm, gender, age and baseline HIV RNA load, showed that only age was significantly (and negatively) associated with dropout (OR=0.96, p<0.01). Missing data were therefore imputed using the last utility score carried forward [5]. With respect to the data on costs, for each cost category, individual healthcare resources used during follow-up were extracted from the standardized case report forms, and then multiplied by their respective unit cost. Such prospective collection through clinical report forms is the preferred method to ensure accuracy and completeness of the cost measurement [5,6]. Furthermore, in the case of intermittently missed clinical visits, costs were calculated through the clinical report forms which were filled out retrospectively. Therefore, we can reasonably assume that the risk of missing cost data was minimized. In the case of missing cost data pertaining to patients lost to follow-up, we performed single imputation with predictive mean matching of the missing data.

Table 3. Sample sizes and the incidence of missing data

|                      | Day 0 | Week 12 | Week 24 | Week 48 | Week 72 | Week 96 |
|----------------------|-------|---------|---------|---------|---------|---------|
| **Whole sample (n=575)** |       |         |         |         |         |         |
| In care              | 575   | 556     | 549     | 538     | 527     | 518     |
| Intermittent missing values (HRQoL) | 3     | 5       | 3       | 7       | 17      | 13      |
| Lost to follow-up    | 0     | 13      | 4       | 8       | 10      | 8       |
| Deaths               | 0     | 6       | 3       | 3       | 1       | 1       |
| **DTG arm (n=275)**  |       |         |         |         |         |         |
| In care              | 275   | 267     | 263     | 261     | 256     | 250     |
| Intermittent missing values (HRQoL) | 2     | 3       | 1       | 5       | 8       | 8       |
| Lost to follow-up    | 0     | 5       | 2       | 2       | 5       | 6       |
| Deaths               | 0     | 3       | 2       | 0       | 0       | 0       |
| **EFV400 arm (n=300)** |       |         |         |         |         |         |
| In care              | 300   | 289     | 286     | 277     | 271     | 268     |
| Intermittent missing values (HRQoL) | 1     | 2       | 2       | 2       | 9       | 5       |
| Lost to follow-up    | 0     | 8       | 2       | 6       | 5       | 2       |
| Deaths               | 0     | 3       | 1       | 3       | 1       | 1       |

Abbreviations: HRQoL=health-related quality of life.
Incremental estimates of costs and QALYs in the base-case analysis

Adjusted-mean costs and QALYs per patient and adjusted-incremental costs and QALYs were obtained using generalised linear models (GLM) taking into account the arm effect while adjusting for any imbalance in baseline characteristics (the latter being selected \textit{a priori}). A modified Park test on the raw scale residuals had been performed to choose the most appropriate variance function (Gaussian). The following baseline covariates were included in the costs and QALYs regressions: gender, age, CD4 count, viral load and utilities. Results of the GLM are presented in Table 4 below.

\begin{table}
\caption{Results of the generalised linear regression models (GLM) used to obtain the multivariate-adjusted incremental estimates of costs and QALYs (NAMSAL ANRS 12313 trial, n=575)}
\centering
\begin{tabular}{lcc}
\hline
 & Costs ($, year 2016 values) & QALYs \\
\hline
\textbf{Treatment: DTG (base category=EFV400)} & -27.772 (-1.25) & 0.000 (0.03) \\
\textbf{Gender: women (base category=men)} & 71.740** (3.15) & -0.008 (-0.44) \\
\textbf{Age (continuous, in years)} & -1.581 (-1.50) & -0.001 (-0.77) \\
\textbf{CD4 count (continuous, in cells/mm3)} & 0.049 (0.89) & 0.000 (1.06) \\
\textbf{HIV RNA level (continuous, in copies/ml)} & 0.000 (1.16) & 0.000 (0.69) \\
\textbf{SF-6D utility score (continuous)} & -49.237 (-0.53) & 0.489** (6.93) \\
\textbf{Constant} & 1010.488 (12.21) & 1.024*** (16.16) \\
\hline
\end{tabular}
\end{table}

Notes: Results are presented as coefficient estimates ($t$-statistics).

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. QALY=quality-adjusted life-year.

\* $p<0.05$, ** $p<0.01$, *** $p<0.001$.  


Markov cohort simulation: model inputs

Table 5 below describes the distribution of the study population in the model’s health states (HS) at model entry. Patients still alive were classified into one of the model’s HS according to their clinical outcome at week 96 (or at their last visit for patients lost to follow-up at week 96): i) 96.7% were still on first-line treatment (4.8% had CD4 count <201 cells/mm³, 18.5% % and 23.9% had CD4 count between 201-350 and 351-500 cells/mm³ and 49.6% % had CD4 count >500 cells/mm³); ii) 3.2% had switched to second-line treatment (0.4% had CD4 count <201 cells/mm³; 0.9% and 0.9% had a CD4 count between 201-350 and 351-500 cells/mm³ and 1.1% had CD4 count >500 cells/mm³).

Table 5. Distribution of the study population in the health states at model entry

|                  | DTG arm (n=270) | EFV400 arm (n=291) | Total (n=561) |
|------------------|----------------|-------------------|--------------|
| **1st line ART** |                |                   |              |
| <201 CD4 cells/mm³ | 9 (3.3%)      | 18 (6.2%)        | 27 (4.8%)    |
| 201-350 CD4 cells/mm³ | 44 (16.3%)   | 60 (20.6%)       | 104 (18.5%)  |
| 351-500 CD4 cells/mm³ | 71 (26.3%)   | 63 (21.6%)       | 134 (23.9%)  |
| >500 CD4 cells/mm³ | 144 (53.3%)  | 134 (46.0%)      | 278 (49.6%)  |
| **2nd line ART** |                |                   |              |
| <201 CD4 cells/mm³ | 0             | 2 (0.7%)         | 2 (0.4%)     |
| 201-350 CD4 cells/mm³ | 0             | 5 (1.7%)         | 5 (0.9%)     |
| 351-500 CD4 cells/mm³ | 1 (0.4%)     | 4 (1.4%)         | 5 (0.9%)     |
| >500 CD4 cells/mm³ | 1 (0.4%)     | 5 (1.7%)         | 6 (1.1%)     |

Table 6 below presents the comparison of the main characteristics of the patients who switched to second-line in the NAMSAL ANRS 12313 trial and in the 2-LADY ANRS 12-169 trial which has been used to estimate transition probabilities between second-line HS in the modelling.

Table 6. Comparison of the main characteristics of patients who switched to second-line in the 2-LADY ANRS 12-169 trial and in the NAMSAL ANRS 12313 trial

|                                | 2-LADY population who had EFV (n=181) | NAMSAL population who switched to 2nd line ART (n=20) | p-value* |
|--------------------------------|--------------------------------------|------------------------------------------------------|----------|
| Male, n (% )                  | 73 (40.3%)                           | 6 (33.3%)                                            | 0.563    |
| Mean (95% CI) Age             | 41.6 (40.1 – 43.0)                   | 34.1 (29.1 – 39.1)                                   | 0.007    |
| Mean (95% CI) CD4 count       | 165 (146 – 184)                      | 272 (170 – 375)                                      | 0.043    |
| HIV viral load                |                                       |                                                      |          |
| Mean (95% CI) VL log10        | 4.7 (4.5 – 4.8)                      | 5.3 (5.0 – 5.5)                                      | 0.000    |
| HIV viral load > 5 000 copies | 159 (87.8%)                          | 18 (100%)                                            | 0.117    |
| HIV viral load >= 10 000      | 149 (82.3%)                          | 18 (100%)                                            | 0.052    |
| HIV viral load >= 100 000     | 63 (34.8%)                           | 14 (77.8%)                                           | 0.000    |

Abbreviations: ART=antiretroviral treatment, DTG=dolutegravir, EFV=efavirenz.

Estimations of transition probabilities, and of costs and QALYs according to both HS and arm, are presented hereafter in Table 7 and Table 8, respectively.
## Table 7. Estimated 3-month transition probabilities according to health states and arm

|                | <201 CD4 cells/mm$^3$ | 201-350 CD4 cells/mm$^3$ | 351-500 CD4 cells/mm$^3$ | >500 CD4 cells/mm$^3$ | 1st line ART Failure | <201 CD4 cells/mm$^3$ | 201-350 CD4 cells/mm$^3$ | 351-500 CD4 cells/mm$^3$ | >500 CD4 cells/mm$^3$ | 2nd line ART Failure | Death |
|----------------|------------------------|---------------------------|--------------------------|------------------------|----------------------|------------------------|---------------------------|--------------------------|------------------------|----------------------|-------|
| **DTG arm**    |                        |                           |                          |                        |                      |                        |                           |                          |                        |                      |       |
| <201 CD4 cells/mm$^3$ | 0.725894              | 0.239638                  | 0.026884                 | 0.006740               | 0.000443             | 0.000000               | 0.000334                  | 0.000061                 | 0.000003               |                      | 0.000004 |
| 201-350 CD4 cells/mm$^3$ | 0.024647              | 0.787828                  | 0.150674                 | 0.031169               | 0.002200             | 0.000000               | 0.002709                  | 0.000709                 | 0.000045               |                      | 0.000018 |
| 351-500 CD4 cells/mm$^3$ | 0.005301              | 0.052826                  | 0.735764                 | 0.205774               | 0.000097             | 0.000000               | 0.000073                  | 0.000013                 | 0.000001               |                      | 0.000151 |
| >500 CD4 cells/mm$^3$ | 0.001427              | 0.005666                  | 0.059901                 | 0.931659               | 0.000000             | 0.000000               | 0.000000                  | 0.000000                 | 0.000000               |                      | 0.001329 |
| 1st line ART Failure | 0                      | 0                          | 0                        | 0                      | 0.110793             | 0.000000               | 0.581466                  | 0.281266                 | 0.026099               |                      | 0.000376 |
| <201 CD4 cells/mm$^3$ | 0                      | 0                          | 0                        | 0                      | 0.697866             | 0.227282               | 0.021442                  | 0.002180                 | 0.043000               |                      | 0.008229 |
| 201-350 CD4 cells/mm$^3$ | 0                      | 0                          | 0                        | 0                      | 0.033176             | 0.765383               | 0.142927                  | 0.013760                 | 0.043000               |                      | 0.001754 |
| 351-500 CD4 cells/mm$^3$ | 0                      | 0                          | 0                        | 0                      | 0.002029             | 0.081978               | 0.768950                  | 0.102836                 | 0.043000               |                      | 0.001207 |
| >500 CD4 cells/mm$^3$ | 0                      | 0                          | 0                        | 0                      | 0.001314             | 0.007578               | 0.060854                  | 0.886221                 | 0.043000               |                      | 0.001033 |
| 2nd line ART failure | 0                      | 0                          | 0                        | 0                      | 0.973000             | 0.027000               |                           |                          |                      |                      |       |
| **EFV+d4T arm** |                        |                           |                          |                        |                      |                        |                           |                          |                        |                      |       |
| <201 CD4 cells/mm$^3$ | 0.775641              | 0.170252                  | 0.015831                 | 0.001583               | 0.017562             | 0.003632               | 0.004833                  | 0.002000                 | 0.005610               | 0.000135             | 0.002920 |
| 201-350 CD4 cells/mm$^3$ | 0.029421              | 0.789833                  | 0.144856                 | 0.019997               | 0.007609             | 0.001543               | 0.002052                  | 0.000848                 | 0.002383               | 0.000057             | 0.001400 |
| 351-500 CD4 cells/mm$^3$ | 0.001231              | 0.065361                  | 0.756417                 | 0.169387               | 0.002944             | 0.000543               | 0.000719                  | 0.000295                 | 0.000837               | 0.000019             | 0.002246 |
| >500 CD4 cells/mm$^3$ | 0.000122              | 0.007339                  | 0.049252                 | 0.932776               | 0.005094             | 0.001020               | 0.001356                  | 0.000560                 | 0.001574               | 0.000038             | 0.000870 |
| 1st line ART Failure | 0                      | 0                          | 0                        | 0                      | 0.191693             | 0.146567               | 0.203891                  | 0.094776                 | 0.229062               | 0.008139             | 0.125873 |
| <201 CD4 cells/mm$^3$ | 0                      | 0                          | 0                        | 0                      | 0.697866             | 0.227282               | 0.021442                  | 0.002180                 | 0.043000               |                      | 0.008229 |
| 201-350 CD4 cells/mm$^3$ | 0                      | 0                          | 0                        | 0                      | 0.033176             | 0.765383               | 0.142927                  | 0.013760                 | 0.043000               |                      | 0.001754 |
| 351-500 CD4 cells/mm$^3$ | 0                      | 0                          | 0                        | 0                      | 0.002029             | 0.081978               | 0.768950                  | 0.102836                 | 0.043000               |                      | 0.001207 |
| >500 CD4 cells/mm$^3$ | 0                      | 0                          | 0                        | 0                      | 0.001314             | 0.007578               | 0.060854                  | 0.886221                 | 0.043000               |                      | 0.001033 |

**Note:** Probabilities represent the estimated transition probabilities for different health states and arms. The table outlines the probabilities for different health states (e.g., <201 CD4 cells/mm$^3$) and health transitions (e.g., 1st line ART Failure) across different arms (DTG and EFV+d4T).
## Table

|                | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0.973000 | 0.027000 |
|----------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|----------|----------|
| **2nd line ART failure** | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0.973000 | 0.027000 |
| **Death**      | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0        | 1        |

**Abbreviations:** ART= antiretroviral treatment. DTG=dolutegravir. EFV400=efavirenz 400mg.
Table 8. Healthcare costs (US dollars, 2016) and quality-adjusted life years (QALYs) per 3-month cycle according to health state and arm

| Health State & Health Failure | QALYs per 3-month cycle | Total costs per 3-month cycle | Antiretroviral drugs | Outpatient consultations (including non-routine visits) | Laboratory tests | Concomitant drugs | Hospitalizations |
|-------------------------------|-------------------------|-------------------------------|----------------------|--------------------------------------------------------|-----------------|-----------------|-----------------|
| DTG arm                       |                         |                               |                      |                                                         |                 |                 |                 |
| HS1                           | 0.169                   | 112.6                         | 14.2                 | 8.3                                                    | 77.1            | 5.8             | 7.3             |
| HS2                           | 0.174                   | 93.06                         | 14.1                 | 7.0                                                    | 68.8            | 1.7             | 1.4             |
| HS3                           | 0.173                   | 101.5                         | 14.1                 | 7.2                                                    | 73.3            | 3.1             | 3.7             |
| HS4                           | 0.180                   | 93.7                          | 14.1                 | 6.8                                                    | 70.4            | 2.0             | 0.4             |
| HS5                           | 0.174                   | 99.0                          | 14.0                 | 6.9                                                    | 71.8            | 3.1             | 3.2             |
| HS6                           | 0.169                   | 135.9                         | 46.0                 | 7.5                                                    | 68.1            | 5.0             | 9.4             |
| HS7                           | 0.174                   | 126.4                         | 49.5                 | 7.0                                                    | 64.2            | 5.7             | 0.0             |
| HS8                           | 0.173                   | 131.5                         | 53.5                 | 5.8                                                    | 71.7            | 0.4             | 0.0             |
| HS9                           | 0.180                   | 128.4                         | 52.3                 | 7.7                                                    | 68.4            | 0.0             | 0.0             |
| HS10                          | 0.174                   | 130.6                         | 50.3                 | 7.0                                                    | 68.1            | 2.8             | 2.3             |
| EFV400 arm                    |                         |                               |                      |                                                         |                 |                 |                 |
| HS1                           | 0.183                   | 103.5                         | 14.7                 | 8.2                                                    | 74.1            | 3.6             | 2.9             |
| HS2                           | 0.175                   | 100.2                         | 14.6                 | 7.3                                                    | 73.3            | 2.1             | 2.3             |
| HS3                           | 0.176                   | 98.9                          | 14.6                 | 7.2                                                    | 72.0            | 2.7             | 3.6             |
| HS4                           | 0.179                   | 99.7                          | 14.7                 | 7.1                                                    | 71.7            | 2.8             | 2.9             |
| HS5                           | 0.178                   | 101.7                         | 46.0                 | 9.6                                                    | 71.8            | 2.8             | 2.9             |
| HS6                           | 0.183                   | 135.9                         | 49.5                 | 7.5                                                    | 68.1            | 5.0             | 9.4             |
| HS7                           | 0.175                   | 126.4                         | 53.5                 | 7.0                                                    | 64.2            | 5.7             | 0.0             |
| HS8                           | 0.176                   | 131.5                         | 52.3                 | 5.8                                                    | 71.7            | 0.4             | 0.0             |
| HS9                           | 0.179                   | 128.4                         | 7.7                 | 7.7                                                    | 68.4            | 2.8             | 2.3             |
| HS10                          | 0.178                   | 130.6                         | 7.0                 | 7.0                                                    | 68.1            |                 |                 |

Note: Because of the small number of observations in the second-line health states in the DTG arm, the mean healthcare costs and number of QALYs per 3-month cycle were estimated by pooling both arms. We therefore assumed that medical resource use and QALYs gained while on second-line treatment depended on the health state (described by CD4 cell count and treatment failure) and not on the arm (as patients benefited from the same treatment and care in both arms).

Abbreviations: ART=antiretroviral treatment. DTG=dolutegravir. EFV400=efavirenz 400mg. HS= Health State; QALY=quality-adjusted life-year.
Table 9. Patient-Reported Outcomes, weight and sample size over time in both arms

|                         | Day 0 | Week 12 | Week 24 | Week 48 | Week 72 | Week 96 |
|-------------------------|-------|---------|---------|---------|---------|---------|
|                         | Mean (SD) | n     | Mean (SD) | n     | Mean (SD) | n     | Mean (SD) | n     | Mean (SD) | n     | Mean (SD) | n     |
| **Perceived HIV symptoms and treatment-related side-effects** | | | | | | | | | | | | |
| DTG arm                 | 7.1 (5.4) | 6.1 (4.8) | 6.0 (5.1) | 4.9 (4.3) | 4.1 (4.0) | 4.7 (4.8) | <0.0001 |
| EFV400 arm              | 7.1 (5.2) | 6.3 (5.0) | 6.2 (4.7) | 4.9 (4.2) | 4.3 (4.5) | 4.7 (4.5) | <0.0001 |
| Difference              | -0.0 | -0.2 | -0.2 | -0.0 | -0.2 | -0.0 | -0.0 |
| p-value                 | 0.99 | 0.58 | 0.61 | 0.98 | 0.67 | 0.91 | |
| **Mean (SD) number of symptoms of at least moderate severity** | | | | | | | | | | | | |
| DTG arm                 | 2.8 (3.6) | 2.4 (3.1) | 2.2 (3.4) | 1.8 (2.7) | 1.5 (2.2) | 1.8 (3.1) | 0.0001 |
| EFV400 arm              | 2.7 (3.3) | 2.3 (3.2) | 2.4 (3.1) | 2.0 (1.5) | 1.5 (2.7) | 2.0 (3.1) | <0.0001 |
| Difference              | 0.1 | 0.1 | -0.2 | -0.2 | -0.1 | -0.1 |
| p-value                 | 0.81 | 0.72 | 0.30 | 0.34 | 0.78 | 0.61 | |
| **Mean (SD) number of symptoms of very important severity** | | | | | | | | | | | | |
| DTG arm                 | 1.5 (2.4) | 0.9 (1.9) | 0.8 (1.8) | 0.5 (1.2) | 0.5 (1.2) | 0.7 (1.8) | <0.0001 |
| EFV400 arm              | 1.2 (2.1) | 0.8 (1.8) | 0.8 (1.7) | 0.7 (1.8) | 0.6 (1.4) | 0.6 (1.6) | <0.0001 |
| Difference              | 0.1 | 0.1 | 0.0 | -0.2 | -0.1 | 0.0 |
| p-value                 | 0.53 | 0.42 | 0.91 | 0.10 | 0.43 | 0.98 | |
| **Neuro-sensorial symptoms related to efavirenz** | | | | | | | | | | | | |
| DTG arm                 | 0.4 (1.3) | 0.2 (0.7) | 0.1 (0.5) | 0.1 (0.3) | 0.1 (0.4) | 0.1 (0.5) | <0.0001 |
| EFV400 arm              | 0.3 (1.0) | 0.2 (0.8) | 0.1 (0.6) | 0.0 (0.2) | 0.0 (0.2) | 0.0 (0.2) | <0.0001 |
| Difference              | 0.1 | -0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| p-value                 | 0.51 | 0.64 | 0.68 | 0.48 | 0.52 | 0.11 | |
| **Mean (SD) number of neuro-sensorial symptoms of at least mild severity** | | | | | | | | | | | | |
| DTG arm                 | 2.4 (2.3) | 2.1 (2.1) | 2.1 (2.2) | 1.7 (1.8) | 1.4 (1.6) | 1.5 (2.0) | <0.0001 |
| EFV400 arm              | 2.4 (2.2) | 2.3 (2.2) | 2.2 (2.1) | 1.8 (1.9) | 1.5 (1.8) | 1.6 (1.8) | <0.0001 |
| Difference              | -0.0 | -0.2 | -0.2 | -0.1 | -0.1 | -0.1 |
| p-value                 | 0.96 | 0.39 | 0.38 | 0.55 | 0.56 | 0.66 | |
| **Mean (SD) number of neuro-sensorial symptoms of at least moderate severity** | | | | | | | | | | | | |
| DTG arm                 | 1.0 (1.5) | 0.9 (1.5) | 0.8 (1.5) | 0.6 (1.1) | 0.5 (1.0) | 0.7 (1.5) | 0.0001 |
| EFV400 arm              | 1.0 (1.5) | 0.9 (1.5) | 0.9 (1.4) | 0.7 (1.3) | 0.6 (1.2) | 0.7 (1.4) | <0.0001 |
| Difference              | -0.1 | 0.1 | -0.0 | -0.1 | -0.0 | -0.0 |
| p-value                 | 0.68 | 0.60 | 0.35 | 0.79 | 0.39 | 0.93 | |
| **Mean (SD) number of neuro-sensorial symptoms of at least important severity** | | | | | | | | | | | | |
| DTG arm                 | 0.5 (1.0) | 0.4 (0.9) | 0.3 (0.8) | 0.2 (0.6) | 0.2 (0.8) | 0.3 (0.9) | <0.0001 |
| EFV400 arm              | 0.5 (1.0) | 0.3 (0.8) | 0.3 (0.7) | 0.3 (0.8) | 0.2 (0.7) | 0.3 (0.8) | 0.0013 |
| Difference              | 0.0 | 0.1 | -0.0 | -0.1 | 0.0 | -0.0 |
| p-value                 | 0.88 | 0.11 | 0.76 | 0.088 | 0.86 | 0.84 | |
| **Mean (SD) number of neuro-sensorial symptoms of very important severity** | | | | | | | | | | | | |
| DTG arm                 | 0.1 (0.5) | 0.1 (0.4) | 0.0 (0.2) | 0.0 (0.1) | 0.0 (0.3) | 0.0 (0.2) | 0.0001 |
| EFV400 arm              | 0.1 (0.5) | 0.1 (0.4) | 0.0 (0.3) | 0.0 (0.1) | 0.0 (0.2) | 0.0 (0.2) | 0.0002 |
| Difference              | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| p-value                 | 0.71 | 0.65 | 0.62 | 0.91 | 0.53 | 0.77 | |
| **Mean (SD) depression score** | | | | | | | | | | | | |
| DTG arm                 | 5.9 (7.6) | 4.7 (7.0) | 4.1 (6.4) | 3.0 (5.0) | 2.5 (4.9) | 2.2 (4.4) | <0.0001 |
| EFV400 arm              | 6.1 (7.6) | 4.6 (6.3) | 4.3 (6.3) | 3.1 (4.6) | 2.5 (3.7) | 2.5 (4.0) | <0.0001 |
| Difference              | -0.2 | 0.1 | -0.2 | -0.1 | -0.0 | -0.4 |
| p-value                 | 0.80 | 0.86 | 0.78 | 0.77 | 0.98 | 0.35 | |

Depression, Anxiety and Stress (DASS-21)
| Proportion (SE) of patients with at least mild depression | Day 0 | Week 12 | Week 24 | Week 48 | Week 72 | Week 96 | Change between day 0 and week 96 (p-value) |
|----------------------------------------------------------|-------|---------|---------|---------|---------|---------|-------------------------------------------|
| DTG arm                                                   | 0.233 (0.025) | 0.164 (0.022) | 0.149 (0.022) | 0.075 (0.017) | 0.057 (0.015) | 0.062 (0.016) | <0.0001 |
| EFV400 arm                                                | 0.231 (0.024) | 0.164 (0.022) | 0.137 (0.020) | 0.098 (0.018) | 0.057 (0.014) | 0.065 (0.015) | <0.0001 |
| Difference                                               | 0.0073 | -0.0000 | 0.0124 | -0.0023 | -0.0000 | -0.003 | -0.003 |
| p-value                                                  | 0.83 | 0.99 | 0.69 | 0.34 | 0.99 | 0.88 | |
| Mean (SD) anxiety score                                  | DTG arm | 4.5 (5.7) | 3.4 (4.9) | 3.2 (4.6) | 2.6 (3.7) | 1.9 (3.0) | 2.1 (3.8) | <0.0001 |
| EFV400 arm                                                | 4.3 (4.7) | 3.4 (4.6) | 2.9 (3.9) | 2.4 (3.5) | 2.1 (3.3) | 2.4 (4.2) | <0.0001 |
| Difference                                               | 0.2 | 0.1 | 0.3 | 0.2 | -0.03 | -0.03 | -0.03 |
| p-value                                                  | 0.66 | 0.83 | 0.44 | 0.50 | 0.37 | 0.44 | |
| Proportion (SE) of patients with at least mild anxiety    | DTG arm | 0.231 (0.025) | 0.130 (0.021) | 0.126 (0.021) | 0.122 (0.021) | 0.065 (0.016) | 0.074 (0.017) | <0.0001 |
| EFV400 arm                                                | 0.231 (0.024) | 0.164 (0.022) | 0.123 (0.020) | 0.098 (0.018) | 0.092 (0.018) | 0.104 (0.019) | 0.0002 |
| Difference                                               | 0.010 | -0.035 | 0.003 | 0.024 | -0.027 | -0.029 | -0.029 |
| p-value                                                  | 0.77 | 0.25 | 0.91 | 0.38 | 0.27 | 0.25 | |
| Mean (SD) stress score                                   | DTG arm | 5.1 (5.9) | 4.4 (5.2) | 4.3 (5.4) | 3.5 (4.5) | 3.0 (4.5) | 3.4 (5.0) | 0.0001 |
| EFV400 arm                                                | 5.7 (5.9) | 4.5 (5.3) | 4.5 (4.9) | 3.3 (4.1) | 3.0 (3.6) | 3.5 (5.2) | <0.0001 |
| Difference                                               | -0.6 | -0.4 | -0.2 | 0.2 | 0.0 | -0.1 | -0.1 |
| p-value                                                  | 0.23 | 0.43 | 0.58 | 0.61 | 0.92 | 0.89 | |
| Proportion (SE) of patients with at least mild stress     | DTG arm | 0.070 (0.015) | 0.046 (0.013) | 0.042 (0.012) | 0.020 (0.009) | 0.020 (0.009) | 0.045 (0.013) | 0.24 |
| EFV400 arm                                                | 0.077 (0.015) | 0.052 (0.013) | 0.039 (0.011) | 0.018 (0.008) | 0.008 (0.008) | 0.033 (0.012) | 0.054 |
| Difference                                               | -0.007 | -0.007 | 0.003 | 0.002 | 0.013 | 0.007 | 0.007 |
| p-value                                                  | 0.74 | 0.72 | 0.84 | 0.90 | 0.22 | 0.70 | |

Health-related quality of life (MOS SF-12 2nd version)

| Mean (SD) Physical Component Summary (PCS) | DTG arm | 46.2 (11.0) | 50.5 (8.7) | 51.5 (7.4) | 51.9 (7.1) | 51.9 (6.6) | 51.7 (6.6) | <0.0001 |
| EFV400 arm                                                | 47.8 (10.4) | 51.2 (8.4) | 51.5 (7.8) | 52.2 (6.6) | 52.4 (6.5) | 52.1 (7.4) | <0.0001 |
| Difference                                               | -1.6 | -0.8 | 0.1 | -0.3 | -0.5 | -0.5 | -0.5 |
| p-value                                                  | 0.077 | 0.28 | 0.91 | 0.36 | 0.37 | 0.46 | |

| Mean (SD) Mental Component Summary (MCS) | DTG arm | 45.1 (9.8) | 47.3 (8.9) | 47.5 (7.7) | 47.9 (7.4) | 48.4 (6.7) | 48.7 (6.9) | 0.0001 |
| EFV400 arm                                                | 44.2 (9.5) | 46.8 (9.0) | 47.2 (8.2) | 48.9 (6.6) | 48.3 (6.9) | 47.5 (7.5) | <0.0001 |
| Difference                                               | 0.9 | 0.3 | 0.4 | -1.0 | 0.1 | 1.2 | 1.2 |
| p-value                                                  | 0.27 | 0.50 | 0.60 | 0.12 | 0.83 | 0.072 | |

| Mean (SD) SF-6D utility score                            | DTG arm | 0.725 (0.127) | 0.776 (0.114) | 0.793 (0.104) | 0.789 (0.104) | 0.805 (0.098) | 0.809 (0.096) | 0.809 (0.098) | <0.0001 |
| EFV400 arm                                                | 0.728 (0.111) | 0.781 (0.113) | 0.784 (0.103) | 0.812 (0.085) | 0.809 (0.092) | 0.795 (0.100) | <0.0001 |
| Difference                                               | -0.003 | -0.005 | 0.009 | -0.023 | -0.004 | -0.015 | -0.015 |
| p-value                                                  | 0.77 | 0.61 | 0.29 | 0.0045 | 0.67 | 0.097 | |

| Mean (SD) Body-Mass Index                                | DTG arm | 23.8 (3.8) | 24.7 (4.1) | 25.3 (4.6) | 26.0 (4.1) | 26.4 (4.5) | 26.5 (4.6) | <0.0001 |
| EFV400 arm                                                | 23.5 (4.1) | 23.9 (4.1) | 24.3 (4.1) | 24.9 (4.6) | 25.1 (4.8) | 25.1 (4.7) | <0.0001 |
| Difference                                               | 0.3 | 0.7 | 0.9 | 1.1 | 1.4 | 1.3 | 1.3 |
| p-value                                                  | 0.42 | 0.034 | 0.012 | 0.005 | 0.0005 | 0.0012 | |
|                  | Day 0       | Week 12     | Week 24     | Week 48     | Week 72     | Week 96     | Change between day 0 and week 96 (p-value)* |
|------------------|-------------|-------------|-------------|-------------|-------------|-------------|------------------------------------------|
| **Proportion (SE) of patients with obesity** |             |             |             |             |             |             |                                         |
| DTG arm          | 0.066 (0.015) | 0.084 (0.017) | 0.138 (0.021) | 0.195 (0.025) | 0.223 (0.026) | 0.234 (0.027) | <0.0001                                  |
| EFV400 arm       | 0.080 (0.016) | 0.080 (0.016) | 0.087 (0.017) | 0.123 (0.020) | 0.141 (0.021) | 0.155 (0.022) | 0.0055                                   |
| Difference       | -0.014      | 0.004       | 0.051       | 0.072       | 0.082       | 0.079       |                                          |
| p-value*         | 0.52        | 0.87        | 0.059       | 0.023       | 0.015       | 0.023       |                                          |
| **Proportion (SE) of patients with overweight or obesity** |             |             |             |             |             |             |                                         |
| DTG arm          | 0.370 (0.029) | 0.433 (0.031) | 0.481 (0.031) | 0.533 (0.031) | 0.558 (0.031) | 0.552 (0.032) | <0.0001                                  |
| EFV400 arm       | 0.303 (0.027) | 0.354 (0.028) | 0.381 (0.029) | 0.458 (0.030) | 0.437 (0.030) | 0.449 (0.031) | 0.0003                                   |
| Difference       | 0.067       | 0.079       | 0.100       | 0.075       | 0.121       | 0.103       |                                          |
| p-value*         | 0.092       | 0.057       | 0.019       | 0.085       | 0.0059      | 0.019       |                                          |

**Sample sizes**

|                  | Whole sample (n=575) | DTG arm (n=275) | EFV400 arm (n=300) |
|------------------|----------------------|-----------------|--------------------|
|                  | 572 (99.5)           | 273 (47.5)      | 299 (52.0)         |
|                  | 548 (95.3)           | 262 (45.6)      | 286 (49.7)         |
|                  | 545 (94.8)           | 261 (45.4)      | 284 (49.4)         |
|                  | 529 (92.0)           | 254 (44.2)      | 275 (47.8)         |
|                  | 506 (88.0)           | 245 (42.6)      | 261 (45.4)         |
|                  | 502 (87.3)           | 242 (42.1)      | 260 (45.2)         |

**Abbreviations:** DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.

Notes: Values are presented as mean (standard deviation, SD) or proportion (standard error, SE). Differences are computed as mean(DTG) - mean(EFV400) or proportion(DTG) - proportion(EFV400). The Depression, Anxiety and Stress Scale (DASS-21) is a 21-item instrument using a 4-point ordinal severity/frequency scale to rate the extent to which participants have experienced each state described over the past week [7]. The DASS-21 includes three 7-item subscales of depression, anxiety, and stress, whose scores were calculated by summing and doubling the scores for the relevant items. The three scores thus range between 0 and 42 (with higher values corresponding to poor outcomes), which are then divided into five severity/frequency categories (none, mild, moderate, important, and very important), allowing to compute the proportion of patients in each category.

* Wilcoxon rank sum test and McNemar's chi-squared test for median and proportion change between day 0 and week 96, respectively.

§ Independent group t-tests and two-sample tests of proportions for mean and proportion differences, respectively, between the two arms at each visit.

** Values are presented for the sample sizes as n (percentage of the whole sample of n=575).
Fig. S2. Baseline and evolution over follow-up of the number of perceived HIV symptoms of at least mild severity

Legend: the figure shows the evolution over follow-up of the number of perceived HIV symptoms of at least mild severity in both arms (DTG and EFV400) for:

- The whole sample (Fig. S2a): no significant differences between arms at any time point. The decrease of the number of perceived HIV symptoms of at least mild severity between baseline and week 96 was significant in the DTG arm (p<0.0001) and in the EFV400 arm (p<0.0001).

- Men and women (Fig. S2b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point. The decrease of the number of perceived HIV symptoms of at least mild severity between baseline and week 96 was significant for all four arm-gender subgroups.

- Patients with obesity versus patients without obesity (at each study visit) (Fig. S2c): no significant differences between weight groups and between arms at any time point, except at week 48 in the DTG arm with a higher number of perceived HIV symptoms of at least mild severity for patients without obesity compared with patients with obesity (5.2 ± 4.4 versus 3.5 ± 3.4, p=0.0085).

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Fig. S3. Baseline and evolution over follow-up of the number of perceived HIV symptoms of at least moderate severity

Legend: the figure shows the evolution over time of the number of perceived HIV symptoms of at least moderate severity in both arms (DTG and EFV400) for:

- The whole sample (Fig. S3a): no significant differences between arms at any time point. The decrease of the number of perceived HIV symptoms of at least moderate severity between baseline and week 96 was significant in the DTG arm (p=0.0001) and in the EFV400 arm (p<0.0001).
- Men and women (Fig. S3b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point, except a lower number of perceived HIV symptoms of at least moderate severity at week 12 for men in the EFV400 arm compared with women in the EFV400 arm (1.7 ± 2.3 versus 2.6 ± 3.6, p=0.025) and with men in the DTG arm (1.7 ± 2.3 versus 2.8 ± 3.6, p=0.013). The decrease of the number of perceived HIV symptoms of at least moderate severity between baseline and week 96 was significant only for the subgroups of women. No significant evolution was observed for the subgroups of men (p=0.23 in the DTG subgroup and p=0.11 in the EFV400 subgroup).
- Patients with obesity versus patients without obesity (at each study visit) (Fig. S3c): no significant differences between weight groups and between arms at any time point.

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Fig. S4. Baseline and evolution over follow-up of the number of perceived HIV symptoms of at least important severity

Legend: the figure shows the evolution over time of the number of perceived HIV symptoms of at least important severity in both arms (DTG and EFV400) for:

- The whole sample (Fig. S4a): no significant differences between arms at any time point. The decrease of the number of perceived HIV symptoms of at least important severity between baseline and week 96 was significant in the DTG arm (p<0.0001) and in the EFV400 arm (p<0.0001).

- Men and women (Fig. S4b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point, except a lower number of perceived HIV symptoms of at least important severity at week 12 for men in the EFV400 arm compared with women in the EFV400 arm (0.5 ± 1.3 versus 1.0 ± 1.9, p=0.046) and with men in the DTG arm (0.5 ± 1.3 versus 1.2 ± 2.2, p=0.016). The decrease of the number of perceived HIV symptoms of at least important severity between baseline and week 96 was significant for all arm-gender subgroups, except for men in the DTG subgroup (p=0.10).

- Patients with obesity versus patients without obesity (at each study visit) (Fig. S4c): no significant differences between weight groups and between arms at any time point.

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Fig. S5. Baseline and evolution over follow-up of the number of perceived HIV symptoms of very important severity

Legend: the figure shows the evolution over time of the number of perceived HIV symptoms of very important severity in both arms (DTG and EFV400) for:

- The whole sample (Fig. S5a): no significant differences between arms at any time point. The decrease of the number of perceived HIV symptoms of very important severity between baseline and week 96 was significant in the DTG arm (p<0.0001) and in the EFV400 arm (p<0.0001).

- Men and women (Fig. S5b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point, except a lower number of perceived HIV symptoms of very important severity for women in the EFV400 arm compared with men in the EFV400 arm at baseline (0.3 ± 0.7 versus 0.5 ± 1.4, p=0.016) and at week 72 (0.0 ± 0.2 versus 0.1 ± 0.3, p=0.035). The decrease of the number of perceived HIV symptoms of very important severity between baseline and week 96 was significant for all arm-gender subgroups.

- Patients with obesity versus patients without obesity (at each study visit) (Fig. S5c): no significant differences between weight groups and between arms at any time point, except at week 48 in the EFV400 arm with a higher number of perceived HIV symptoms of very important severity for patients with obesity compared with patients without obesity (0.1 ± 0.4 versus 0.0 ± 0.2, p=0.013), and at week 96 in the DTG arm with a higher number of perceived HIV symptoms of very important severity for patients with obesity compared with patients without obesity (0.2 ± 0.9 versus 0.0 ± 0.2, p=0.010).

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Fig. S6. Baseline and evolution over follow-up of the proportion of patients with at least mild depression (based on the DASS-21 depression score)

Legend: the figure shows the evolution over time of percentage of patients with at least mild depression (based on the DASS-21 depression score) in both arms (DTG and EFV400) for:

- The whole sample (Fig. S6a): no significant differences between arms at any time point. The decrease of the proportion of patients with at least mild depression between baseline and week 96 was significant in the DTG arm (p<0.0001) and in the EFV400 arm (p<0.0001).

- Men and women (Fig. S6b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point, except at baseline in the DTG arm with a higher proportion of women with at least mild depression compared with men (0.270 ± 0.035 versus 0.155 ± 0.034, p=0.025), and at week 12 in the EFV400 arm with a higher proportion of women with at least mild depression compared with men (0.210 ± 0.029 versus 0.066 ± 0.026, p=0.0022). The decrease of the proportion of patients with at least mild depression between baseline and week 96 was significant for all four arm-gender subgroups.

- Patients with obesity versus patients without obesity (at each study visit) (Fig. S6c): no significant differences between weight groups and between arms at any time point, except at week 48 in the DTG arm with a lower proportion of patients with obesity with at least mild depression compared with patients without obesity (0.000 ± 0.000 versus 0.094 ± 0.020, p=0.026).

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Fig. S7. Baseline and evolution over follow-up of the proportion of patients with at least mild anxiety (based on the DASS-21 anxiety score)

Legend: the figure shows the evolution over time of percentage of patients with at least mild anxiety (based on the DASS-21 anxiety score) in both arms (DTG and EFV400) for:

- The whole sample (Fig. S7a): no significant differences between arms at any time point. The decrease of the proportion of patients with at least mild anxiety between baseline and week 96 was significant in the DTG arm (p<0.0001) and in the EFV400 arm (p=0.0002).
- Men and women (Fig. S7b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point, except at week 12 in the EFV400 arm with a higher proportion of women with at least mild anxiety compared with men (0.205 ± 0.029 versus 0.077 ± 0.028, p= 0.0064). The decrease of the proportion of patients with at least mild anxiety between baseline and week 96 was significant for all arm-gender subgroups, except for men in the EFV40 subgroup (p=0.15).
- Patients with obesity versus patients without obesity (at each study visit) (Fig. S7c): no significant differences between weight groups and between arms at any time point.

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Fig. S8. Baseline and evolution over follow-up of the proportion of patients with at least mild stress (based on the DASS-21 stress score)

Legend: the figure shows the evolution over time of percentage of patients with at least mild stress (based on the DASS-21 stress score) in both arms (DTG and EFV400) for:

- The whole sample (Fig. S8a): no significant differences between arms at any time point. The decrease of the proportion of patients with at least mild stress between baseline and week 96 was not significant in the DTG arm (p=0.24) and in the EFV400 arm (p=0.054).

- Men and women (Fig. S8b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point. The decrease of the proportion of patients with at least mild stress between baseline and week 96 was not significant for all four arm-gender subgroups (p=0.51 for men in the DTG subgroup, p=0.32 for men in the EFV400 subgroup, p=0.33 for women in the DTG subgroup, and p=0.098 for women in the EFV400 subgroup).

- Patients with obesity versus patients without obesity (at each study visit) (Fig. S8c): no significant differences between weight groups and between arms at any time point.

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Fig. S9. Baseline and evolution over follow-up of the Physical Component Summary (PCS)

Legend: the figure shows the evolution over time of the mean Physical Component Summary (PCS) in both arms (DTG and EFV400) for:

- The whole sample (Fig. S9a): no significant differences between arms at any time point. The PCS increased by 11.9% (p<0.0001) in the DTG arm and by 9.0% (p<0.0001) in the EFV400 arm.
- Men and women (Fig. S9b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point, except a lower PCS score at baseline for women in the DTG arm compared with women in the EFV400 arm (45.4 ± 11.0 versus 47.7 ± 10.0, p=0.042). The increase in PCS scores between baseline and week 96 was significant for all four arm-gender subgroups.
- Patients with obesity versus patients without obesity (at each study visit) (Fig. S9c): no significant differences between weight groups and between arms at any time point.

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Fig. S10. Baseline and evolution over follow-up of the Mental Component Summary (MCS)

Legend: the figure shows the evolution over time of the mean Mental Component Summary (MCS) in both groups (DTG and EFV400) for:

- The whole sample (Fig. S10a): no significant differences between arms at any time point. The MCS increased by 8.0% (p=0.0001) in the DTG arm and by 7.5% (p<0.0001) in the EFV400 arm.
- Men and women (Fig. S10b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point, except a higher MCS score at baseline for men in the DTG arm compared with men in the EFV400 arm (46.3 ± 10.1 versus 42.9 ± 9.7, p=0.013). The increase in MCS scores between baseline and week 96 was significant for all four arm-gender subgroups, except for men in the DTG arm (p=0.087).
- Patients with obesity versus patients without obesity (at each study visit) (Fig. S10c): no significant differences between weight groups and between arms at any time point, except a higher MCS score at week 96 for patients without obesity in the DTG arm compared with patients without obesity in the EFV400 arm (48.8 ± 7.0 versus 47.4 ± 7.1, p=0.047).

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Fig. S11. Baseline and evolution over follow-up of the SF-6D utility score

Legend: the figure shows the evolution over time of the mean SF-6D utility score in both arms (DTG and EFV400) for:

- The whole sample (Fig. S11a): no significant differences between arms at any time point, except at week 48 with a lower score in the DTG arm (0.789 ± 0.098 versus 0.812 ± 0.085, p=0.0045). The SF-6D utility score increased by 11.6% (p<0.0001) in the DTG arm and by 9.2% (p<0.0001) in the EFV400 arm.

- Men and women (Fig. S11b): no significant differences between gender (men versus women in each arm) and between arms (men in the DTG arm versus men in the EFV400 arm, and women in the DTG arm versus women in the EFV400 arm) at any time point, except a lower SF-6D utility score at week 48 for men in the DTG arm compared with men in the EFV400 arm (0.790 ± 0.096 versus 0.822 ± 0.083, p=0.017), and at week 72 for women in the DTG arm compared with men in the DTG arm (0.793 ± 0.096 versus 0.823 ± 0.093, p=0.012). The increase in SF-6D utility scores between baseline and week 96 was significant for all four arm-gender subgroups.

- Patients with obesity versus patients without obesity (at each study visit) (Fig. S11c): no significant differences between weight groups and between arms at any time point, except a lower SF-6D utility score at week 48 for patients in the DTG arm without obesity compared with patients in the EFV400 arm without obesity (0.783 ± 0.100 versus 0.809 ± 0.086, p=0.0035).

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. W=week.
Table 10. Unadjusted mean costs ($, year 2016 values) and QALYs per patient over first 96 weeks (NAMSAL ANRS 12313 trial, n=575)

|                        | EFV400-based regimen (n=300) | DTG-based regimen (n=275) | Two-sample t-tests p-value |
|------------------------|-------------------------------|---------------------------|---------------------------|
| **Total costs per patient** | 938.5 ± 171.2                 | 913.9 ± 161.9             | 0.077                     |
| Antiretroviral drugs   | 125.9 ± 36.0                  | 116.3 ± 19.8              | 0.0001                    |
| Outpatient consultations (including non-routine visits) | 70.0 ± 11.6                  | 69.4 ± 12.5               | 0.54                      |
| Laboratory tests       | 664.7 ± 81.4                  | 657.1 ± 83.1              | 0.27                      |
| Concomitant drugs      | 51.4 ± 84.5                   | 52.1 ± 89.3               | 0.92                      |
| Hospitalizations       | 26.4 ± 111.5                  | 18.9 ± 85.0               | 0.37                      |
| **QALYs per patient**  | 1.368 ± 0.204                 | 1.367 ± 0.212             | 0.97                      |

Notes: Data are presented as mean ± standard deviation. The mean total costs were not significantly different in both arms though they were slightly lower in the DTG arm ($913.9 ±161.9 versus $938.5 ±171.2, p=0.077). Although current (3rd quarter 2020) generic prices for FDC are nearly equivalent for both combinations ($5.2/month and $5.4/month for the DTG- and EFV400-based regimen, respectively), ARV drugs were the only cost category significantly different between both arms ($116.3 ±19.8 versus $125.9 ±36.0 in the DTG and EFV400 arm, respectively, p=0.0001). Unadjusted mean QALYs per patient were also very similar in both arms (1.367 ±0.212 DTG versus 1.368± 0.204 EFV400, p=0.97).

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. QALY=quality-adjusted life-year.
Fig. S12. Cost-effective price thresholds for DTG and EFV400 strategies at the threshold of $1,392/QALY

Legend: Cost-effective price thresholds for DTG and EFV400 strategies indicating which strategy would be preferred at the threshold of one times the Cameroonian per capita GDP in 2016 ($1,392/QALY), and for any price combination of DTG and EFV400 FDC. The price combinations on the hollow circle line would make DTG cost-effective with a probability of 95%. Any price combination on the solid triangle line would make EFV400 cost-effective with a probability of 95%. The solid circle line depicts the price combinations for which both strategies have the same probability of being cost-effective: \( \text{Prob(DTG:CE)=Prob(EFV400:CE)=50\%} \).

Abbreviations: CE=cost-effective, DTG=dolutegravir, EFV400=efavirenz 400mg, FDC=fixed-dose combinations, GDP=gross domestic product, Prob=probability.
Fig. S13. Cost-effectiveness plane and cost-effectiveness acceptability curve for the analysis over 5 years

Legend: **Fig. S13a** Cost-effectiveness plane depicting the 1,000 simulated pairs of incremental costs and QALYs of DTG versus EFV400 at the $500 threshold over 5 years. **Fig. S13b** Cost-effectiveness acceptability curve showing the probability of DTG being cost-effective compared with EFV400 at various thresholds ranging from 0 to $10,000/QALY over 5 years. In both panels, the plain red line indicates the cost-effectiveness threshold of $500 per QALY gained.

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. QALY=quality-adjusted life-year.
Fig. S14. Cost-effectiveness plane and cost-effectiveness acceptability curve for the analysis over 10 years

Legend: **Fig. S14a** Cost-effectiveness plane depicting the 1,000 simulated pairs of incremental costs and QALYs of DTG versus EFV400 at the $500 threshold over 10 years. **Fig. S14b** Cost-effectiveness acceptability curve showing the probability of DTG being cost-effective compared with EFV400 at various thresholds ranging from 0 to $10,000/QALY over 10 years. In both panels, the plain red line indicates the cost-effectiveness threshold of $500 per QALY gained.

Abbreviations: DTG=dolutegravir. EFV400=efavirenz 400mg. QALY=quality-adjusted life-year.
Table 11. Clinical outcomes at week 96 in the study population (NAMSAL ANRS 12313, n=575)

|                              | DTG arm (n=275) | EFV400 arm (n=300) | Total (n=575) | p-value* |
|------------------------------|-----------------|--------------------|---------------|----------|
| **Number (%), mean (95% CI) or median [IQR]** |                 |                    |               |          |
| Death                        | 5 (1.8%)        | 9 (3.0%)           | 14 (2.4%)     | 0.36     |
| Lost to follow-up            | 20 (7.3%)       | 23 (7.7%)          | 43 (7.5%)     | 0.86     |
| In care                      | 250 (90.9%)     | 268 (89.3%)        | 518 (90.1%)   | 0.53     |
| **Switch to second line ART and HIV drug resistance mutations over the first 96 weeks** | 2 (0.7%)        | 16 (5.5%)          | 18 (3.2%)     | 0.001    |
| HIV drug resistance mutations | 0               | 15 (5.2%)          | 15 (2.7%)     | <0.0001  |
| **Immunological and virological outcomes (n=561**  |                 |                    |               |          |
| Mean (95% CI) CD4 count at 96 weeks | 568 (538 – 598) | 535 (504 – 566)   | 551 (529 – 573) | 0.057    |
| Mean increase (95% CI) in CD4 count from baseline (3 missing) | 238 (217 – 259) | 227 (208 – 247)   | 233 (218 – 247) | 0.13     |
| **CD4 count range (4 categories)** |                 |                    |               |          |
| Whole range                  |                 |                    |               | 0.051    |
| <201 CD4 cells/mm³           | 9 (3.3%)        | 20 (6.9%)          | 29 (5.2%)     |          |
| 201-350 CD4 cells/mm³        | 44 (16.3%)      | 65 (22.3%)         | 109 (19.4%)   |          |
| 351-500 CD4 cells/mm³        | 72 (26.7%)      | 67 (23.0%)         | 139 (24.8%)   |          |
| >500 CD4 cells/mm³           | 145 (53.7%)     | 139 (47.8%)        | 282 (50.6%)   |          |
| **HIV viral load at 36 weeks** |                 |                    |               |          |
| HIV viral load<40 copies/ml  | 221 (81.9%)     | 233 (80.1%)        | 454 (80.9%)   | 0.59     |
| HIV viral load<50 copies/ml  | 224 (83.0%)     | 241 (82.8%)        | 465 (82.9%)   | 0.96     |
| HIV viral load<200 copies/ml | 252 (93.3%)     | 267 (91.8%)        | 519 (92.5%)   | 0.48     |
| HIV viral load<1000 copies/ml| 257 (95.2%)     | 276 (94.9%)        | 533 (95.0%)   | 0.85     |

Abbreviations: ART=antiretroviral treatment. DTG=dolutegravir, EFV400=efavirenz 400mg.
* χ² test for categorical variables and Wilcoxon rank sum test for continuous variables.
** n=270 in the DTG arm and n=291 in the EFV400 arm.
References

1. Global Fund. Pooled Procurement Mechanism Reference Pricing: ARVs (version: quarter 3 2020) [Internet]. 2020. Available from: https://www.theglobalfund.org/media/5813/ppm_arvreferencepricing_table_en.pdf

2. Centre Pasteur du Cameroun (CPC). Ensemble des examens biologiques réalisés au Centre Pasteur (catalogue 2016). Yaoundé, Cameroon: CPC; 2016.

3. Centrale Nationale d’Approvisionnement en Médicaments et Consommables Médicaux Essentiels (CENAME). Grille des prix des produits pharmaceutiques dans le secteur public (version 11, août 2014). Yaoundé, Cameroon: CENAME; 2014.

4. Little R, Rubin D. Statistical analysis with missing data. New York, NY: Wiley and Sons; 1987.

5. Hunter RM, Baio G, Butt T, Morris S, Round J, Freemantle N. An educational review of the statistical issues in analysing utility data for cost-utility analysis. PharmacoEconomics. 2015;33:355–66.

6. MacNeil Vroomen J, Eekhout I, Dijkgraaf MG, van Hout H, de Rooij SE, Heymans MW, et al. Multiple imputation strategies for zero-inflated cost data in economic evaluations: Which method works best? Eur J Health Econ. 2016;17:939–50.

7. Henry JD, Crawford JR. The short-form version of the Depression Anxiety Stress Scales (DASS-21): construct validity and normative data in a large non-clinical sample. Br J Clin Psychol. 2005;44:227–39.