**Appendix**

|  |
| --- |
| **Supplementary Table 1: Frailty phenotype criteria**  |
| **Criterion** | **Definition** |
| **Unintentional weight loss** | Self-report of unintentional loss of ≥4.5 kg in prior year or ≥ 2.3 kg in prior 6 months |
| **Low physical activity** | Participants answering 'yes, limited a lot’ when asked whether their health limits vigorous activities such as running, lifting heavy objects, participating in strenuous sports. |
| **Exhaustion1** | Participants answering 'occasionally' or 'most of the time’ to either one of the two statements below:During the last week, how often have you felt that:1) Everything you did was an effort?2) I could not 'get going’ |
| **Decreased grip strength2** | Maximum grip strength out of 3 measurements, using dominant hand. Criterion considered present if participant’s strength was in lowest 20% by sex per BMI stratum of combined cohort. |
|  | Male BMI (kg/m2) | ≤22.6 | Female BMI (kg/m2) | ≤22.3 |
| Male BMI (kg/m2) | 22.7-24.4 | Female BMI (kg/m2) | 22.4-24.5 |
| Male BMI (kg/m2) | 24.5- 26.6 | Female BMI (kg/m2) | 24.6-28.1 |
| Male BMI (kg/m2) | ≥26.7  | Female BMI (kg/m2) | ≥28.2 |
| **Slow gait speed** | Walking time per 4.57m (15 feet) at usual walking speed. |
|   | Maximum walking time out of 2 measurements. Criterion considered present if participants time fell in lowest 20% by sex per height stratum of combined cohort.  |
|   | Male height (cm) | ≤180 | Female height (cm) | ≤165 |
|   | Male height (cm) | >180 | Female height (cm) | >165 |
| 1: two questions included in the Center for Epidemiologic Studies Depression scale questionnaire 2: maximum grip strength was assessed using Jamar handheld dynamometer (Jamar Plusþ Digital Hand Dynamometer, Jamar, USA), the maximum value of three consecutive measurements of the dominant hand was used for analysis.  |
|  |  |
|  |  |

|  |
| --- |
| Supplementary Table 2: Characteristics of participants at the index-visit of the visit pair from the transition to frailty analysis.  |
|   | **Robust-robust** | **Transition to frailty** |
|  | **n = 682 visit pairs** | **n = 60 visit pairs** |
|   | **n (%)****or median (IQR)****or mean (SD)** | **n (%)****or median (IQR)****or mean(SD)** |
| Sociodemographic |  |  |
| HIV-infection | n = 265 (38.9%) | n = 35 (58.3%) |
| Age, years | 52.8 (48.8-58.1) | 57.2 (52. 0-62.9) |
| Risk groupMSM maleNon-MSM maleFemaleMissing | 507 (74.3%)104 (15.3%)71 (10.4%)0 (0%) | 39 (65%)10 (16.7%)11 (18.3%)0 (0%) |
| EthnicityNon-white ethnic descentWhite ethnic descentMissing | 30 (4.4%)652 (95.6%)0 (0%) | 7 (11.7%)53 (88.3%)0 (0%) |
| EducationHigher educational attainment1Lower educational attainmentMissing | 374 (54.8%)299 (43.8%)9 (1.3%) | 21 (35.0%)33 (55.0%)6 (10.0%) |
| Behavior |  |  |
| Smoking statusNeverFormerCurrentMissing | 245 (35.9%)275 (40.3%)156 (22.9%)6 (0.9%) | 19 (31.7%)15 (25.0%)22 (36.7%)4 (6.7%) |
| Pack years(if ever smoked) | 13.2 (3.0-27.0) | 31.5 (12.6-47.8) |
| Heavy-daily alcohol use past 6 months2 | 37 (5.4%) | 4 (6.7%) |
| Binge drinking 3 | 182 (29.1%) | 12 (22.2%) |
| Injection drug use (ever) | 9 (1.3%) | 1 (1.9%) |
| THC use during last 6 months | 37 (5.6%) | 5 (10.4%) |
| Physically active4 | 386 (56.6%) | 25 (41.7%) |
| Body composition |  |  |
| Waist-circumference, cm | 91.5 (9.9) | 92.8 (11.2) |
| Hip-circumference, cm | 98.5 (6.2) | 97.3 (8.4) |
| Waist-to-hip ratio | 0.93 (0.07) | 0.95 (0.08) |
| Body-mass index, kg/m² | 24.7 (3.1) | 24.5 (4.1) |
| Comorbidities5 |  |  |
| Number of age-associated comorbidities01≥2 | 395 (57.9%)210 (30.8%)77 (11.3%) | 19 (31.7%)22 (36.7%)19 (31.7%) |
| Hepatitis B virus DNA positive | 16 (2.4%) | 2 (3.3%) |
| Hepatitis C virus RNA positive | 2 (0.3%) | 1 (1.7%) |
| Cytomegalovirus IgG positive | 555 (81.4%) | 52 (86.7%) |
| Depressive symptoms6CES-D ≤ 8CES-D > 8 < 16CES-D ≥16Missing | 515 (75.5%)100 (14.7%)47 (6.9%)20 (2.9%) | 20 (33.3%)17 (28.3%)13 (21.7%)10 (16.7%) |
| Biomarkers |  |  |
| hsCRP, mg/L | 1.0 (0.6-2.0) | 1.6 (0.7-5.4) |
| D-dimer, mg/L | 0.2 (0.2- 0.4) | 0.3 (0.2-0.5) |
| IL-6, pg/mL | 1.8 (1.1-3.1) | 1. 8 (1.2-2.9) |
| sCD14, ng/mL | 1478 (1176-1869) | 1562 (1347-1940) |
| sCD163, ng/mL | 257 (189-354) | 275 (211-368) |
| I-FABP, ng/mL | 1.4 (0.9-2.1) | 1. 7 (1.0-3.3) |
| HIV-positive participants only |  |  |
| Years since HIV- diagnosis | 12.6 (6.8-17.8) | 12.8 (6.6-17.1) |
| CD4 cell countNadir CD4 count, cells/µLMean CD4 in 12 months prior to enrolment, cells/µLCumulative duration of CD4 count <200 cells/µL (years)CD4/CD8 ratio at enrolment | 180 (80-260)553 (438-713)0.0 (0.0-0.5)0.8 (0.6-1.1) | 170 (100-260)630 (540-760)0.1 (0.0-0.6)0.8 (0.6-1.3) |
| History of CDC-class C AIDS defining diagnosis | 64 (24.2%) | 12 (34.3%) |
| Using cART at enrolment | 252 (95.5%) | 34 (87.1%) |
| Cumulative exposure to ART, years | 10.8 (4.8-15.4) | 10.7 (4.7-15.5) |
| ART-experienced before starting cART | 44 (17.5%) | 10 (29.4%) |
| Having used zalcitabine | 23 (8.7%) | 7 (20.0%) |
| Duration of zalcitabine use (years)7 | 0.7 (0.4-1.8) | 0.8 (0.3-2.3) |
| Having used didanosine | 74 (28.0%) | 10 (28.6%) |
| Duration of didanosine use (years)8 | 2.5 (0.9-5.1) | 2.4 (0.8-7.8) |
| Having used stavudine | 95 (36.0%) | 13 (37.1%) |
| Duration of stavudine use (years)9 | 3.9 (1.9-6.4) | 5.4 (2.7-7.3) |
| Having used zidovudine | 144 (54.6%) | 20 (57.1%) |
| Duration of zidovudine use (years)10 | 3.8 (0.8-7.2) | 2.6 (0.8-5.7) |
| HIV-RNA <200 c/mL in year prior to enrolment11 | 240 (95.2%) | 33 (97.1%) |
| cumulative duration of HIV-RNA <200c/mL, years11 | 6.8 (2.5-11.1) | 5.5 (2.9-9.8) |
| Abbreviations: MSM, men who have sex with men; THC, Tetrahydrocannabinol CES-D, Center for Epidemiologic Studies Depression scale; hsCRP, high sensitive C-reactive protein; IL-6, interleukin-6. sCD14, soluble CD14; sCD163, soluble CD163; I-FABP, intestinal fatty acid-binding protein; ART, antiretroviral therapy; cART, combination antiretroviral therapy; CDC, Centers for Disease Control and Prevention; IQR, inter quartile range1Higher education; attained at least a bachelor’s degree 2Heavy daily alcohol defined as >5 alcohol units almost daily for a man and >4 units almost daily for a woman during the last 6 months3Binge alcohol defined as >6 alcohol units a day, minimally once per month during the last 6 months4Being hysically active was defined following the Dutch guidelines for healthy physical activity (“Combinorm”): at least 5 days per week at least 30 minutes of moderate physical activity or at least 3 days per week at least 20 minutes of heavy physical activity5Comorbidities included are chronic obstructive pulmonary disease or asthma (defining obstruction as having an FEV1/FVC-ratio z-score <-1.64 using Global Lung Initiative reference calculations), diabetes (HbA1c ≥ 48 mmol/mol and/or elevated blood glucose (non-fasting ≥ 11.1 mmol/L or fasting ≥ 7.0 mmol/L) or on antidiabetic medication), hypertension (use of antihypertensive medication or measured grade 2 hypertension following European Guidelines (systolic blood pressure > 160 mmHg and/or diastolic blood pressure > 100 mmHg in all 3 measurements), decreased kidney function (eGFR <60 mL/min/1.73 m2) based on Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation), osteoporosis (having a T score of -2.5 SD or lower, in men aged <50 years and premenopausal women; a Z score of -2 SD or lower in men aged ≥50 years and postmenopausal women), self-reported and validated heart-failure, non-AIDS associated cancer (excluding non-melanoma skin cancers), cardiovascular disease (myocardial infarction, angina pectoris, peripheral artery disease, ischemic stroke and/or transient ischemic attack). 6CES-D scale, with two questions used in the frailty scale excluded from CES-D score calculation. 7for those who had used zalcitabine8 for those who had used didanosine9 for those who had used stavudine10 for those who had used zidovudine11 if currently on cART+ Pearson’s chi-squared test; ++ Kruskal-Wallis test; +++ ANOVA |

|  |
| --- |
| Supplementary Table 3: Association between variables and transition to frailty: results of univariate and multivariable logistic regression models with generalized estimating equations  |
|   | **Univariate****OR (95%CI)** | **p-value** | **Multivariable Model A****OR (95%CI)** | **p-value** | **Multivariable Model B****OR (95%CI)** | **p-value** | **Multivariable Model C****OR (95%CI)** | **p-value** | **Multivariable Model D****OR (95%CI) \*** | **p-value** |
| Sociodemographic |
| HIV status | 2.19 (1.28-3.75) | 0.004 | 2.05 (1.16-3.63) | 0.014 | 1.82 (0.97-3.39) | 0.060 | 1.57 (0.83-2.97) | 0.164 | 1.27 (0.65 -2.50) | 0.482 |
| Age, per 10yr increase | 2.42 (1.66-3.52) | <0.001 | 2.82 (1.88-4.23) | <0.001 | 2.67 (1.76-4.07) | <0.001 | 2.38 (1.54-3.68) | <0.001 | 2.55 (1.62-4.01) | <0.001 |
| Sexual risk groupMSM malenon-MSM maleFemale | ref1.26 (0.61-2.61)2.01 (0.98-4.12) | 0.5320.056 | ref1.13 (0.52-2.44)1.94 (0.80-4.71) | 0.7530.142 | ref1.09 (0.51-2.37)2.36 (0.89-6.26) | 0.8180.084 | ref1.12 (0.52-2.45)2.42 (0.91-6.49) | 0.7710.078 | ref1.09 (0.48- 2.50)2.46 (0 .87- 6.95) | 0.8350.088 |
| Non-white ethnic descent | 2.83 (1.18-6.76) | 0.02 | 1.72 (0.57-5.17) | 0.337 | 1.80 (0.60-5.40) | 0.298 | 1.72 (0.57-5.22) | 0.337 | 1.67 (0.54- 5.18) | 0.379 |
| High-education | 0.51 (0.29- 0.90) | 0.02 | 0.63 (0.35-1.15) | 0.132 | 0.65 (0.36-1.19) | 0.162 | 0.64 (0.35-1.19) | 0.158 | 0.77 (0.40-1.46) | 0.420 |
| Body composition |
| Waist-to-hip ratio, per 0.1 increase | 1.57 (1.09-2.24) | 0.015 |  |  | 1.24 (0.80 -1.94) | 0.338 | 1.15 (0.74-1.78) | 0.547 | 1.21 (0.75-1.95) | 0.426 |
| Comorbidities |
| Number of comorbidities 01≥2 | ref1.72 (0.91- 3.23)4.80 (2.47-9.31) | 0.095<0.001 |  |  |  |  | ref1.55 (0.80-3.03)2.90 (1.37-6.15) | 0.1940.005 | ref1.54 (0.77-3.10)2.80 (1.27-6.15) | 0.2250.011 |
| Depression aCES- D < 8CES- D ≥8 < 16CES- D ≥16 | ref2.97 (1.59-5.55)4.85 (2.37-9.90) | 0.001< 0.001 |  |  |  |  | --- |  | ref3.83 (1.83-8.01)7.20 (3.14-16.58) | <0.001<0.001 |
| Body-composition |
| Waist circumference, per cm increase | 1.01 (0.99-1.04) | 0.361 |  |  |  |  |  |  |  |  |
| Hip circumference, per cm decrease | 1.03 (0.99-1.08) | 0.159 |  |  |  |  |  |  |  |  |
| Body-mass index  | 0.99 (0.90-0.06) | 0.621 |  |  |  |  |  |  |  |  |
| Behavior |
| Heavy daily drinking during last 6 months | 1.23 (0.43- 3.51) | 0.704 |  |  |  |  |  |  |  |  |
| Binge drinking during last 6 months | 0.70 (0.36- 1.36) | 0.294 |  |  |  |  |  |  |  |  |
| Smoking statusNever Ever Current  | ref0.70 (0.35-1.42)1.81 (0.95-3.46) | 0.3290.072 |  |  |  |  |  |  |  |  |
| Tetrahydrocannabinol use during last 6 months | 1.94 (0.73-5.15) | 0.186 |  |  |  |  |  |  |  |  |
| Former injection drug use | 1.39 (0.17- 11.18) | 0.755 |  |  |  |  |  |  |  |  |
| Being physically active | 0.56 (0.33-0.94) | 0.029 |  |  |  |  |  |  |  |  |
| Biomarkers |
| Per 1.0 unit in crease in log transformed soluble CD14 a, ng/mL | 1.64 (0.81-3.30) | 0.167 |  |  |  |  |  |  |  |  |
| Per 1.0 unit increase in log transformed soluble CD163 a, ng/mL | 1.34 (0.78-2.31) | 0.290 |  |  |  |  |  |  |  |  |
| Per 1.0 unit increase in square root transformed I-FABP a, ng/mL | 2.13 (1.32-3.44) | 0.002 |  |  |  |  |  |  |  |  |
| Per 1.0 unit increase in log transformed hs-CRP a, mg/L | 1.69 (1.28 -2.21) | < 0.001 |  |  |  |  |  |  |  |  |
| Dichotomized IL-6 (>10 pg/mL) a | 1.25 (0.54- 2.86) | 0.605 |  |  |  |  |  |  |  |  |
| Dichotomized D-dimer (> 1 mg/L) a | 4.26 (1.33- 13.64) | 0.015 |  |  |  |  |  |  |  |  |
| Hepatitis B virus DNA positive | 1.42 (0.32- 6.38) | 0.643 |  |  |  |  |  |  |  |  |
| Hepatitis C virus RNA positive | 5.42 (0.48-60.65) | 0.170 |  |  |  |  |  |  |  |  |
| Cytomegalovirus IgG positive | 1.48 (0.68- 3.19) | 0.322 |  |  |  |  |  |  |  |  |
| Model A: adjusted for socio-demographics. Model B: adjusted for variables associated with transition towards frailty or variables attenuating the association between HIV status and transitioning to frailty. Model C: the final multivariable model without adjusting for level of depression. Model D: the final multivariable model adjusting for level of depression. Abbreviations: OR, odds ratio: CI, confidence interval; MSM, men who have sex with men; CES-D, Center for Epidemiologic Studies Depression scale; hsCRP, high sensitivity C-reactive protein; IL-6, interleukin-6; I-FABP, intestinal fatty acid-binding protein; a Variables were transformed, dichotomized or categorized appropriately to fit the linearity assumption of the logistic regression model. Variables that were excluded from the model in the forward selection process were smoking status, tetrahydrocannabinol, physical activity, soluble CD14, I-FABP, hs-CRP, D-dimer and Hepatitis C virus RNA positivity.  |

|  |
| --- |
| Supplementary Table 4: Association between variables and transition towards robustness (from frail to prefrail/robust): results of univariate and multivariable logistic regression models with generalized estimating equations  |
|   | **Univariate****OR (95%CI)** | **p-value** | **Multivariable Model A****OR (95%CI)** | **p-value** | **Multivariable Model B****OR (95%CI)** | **p-value** | **Multivariable** **Model C****OR (95%CI)** | **p-value** | **Multivariable Model D****OR (95%CI) \*** | **p-value** |
| Sociodemographic |
| HIV status | 2.49 (0.96-6.46) | 0.060 | 2.25 (0.84-6.03) | 0.107 | 2.05 (0.76-5.55) | 0.157 | 2.92 (0.96-8.83) | 0.058 | 2.73 (0.90-8.30) | 0.076 |
| Age, per 10yr increase | 0.47 (0.28-0.82) | 0.007 | 0.47 (0.27-0.82) | 0.008 | 0.49 (0.28-0.86) | 0.013 | 0.57 (0.32-1.03) | 0.064 | 0.51 (0.28-0.93) | 0.029 |
| Sexual risk groupMSM malenon-MSM maleFemale | ref1.74 (0.34-8.77)2.04 (0.60-6.93) | 0.5050.254 |  |  |  |  |  |  |  |  |
| Non-white ethnic descent | 3.69 (0.67– 20.29) | 0.133 |  |  | 2.03(0.36-11.52) | 0.424 | 2.01(0.35-11.39) | 0.432 | 2.25(0.39-12.96) | 0.365 |
| High-education | 2.31 (0.84-6.33) | 0.105 |  |  |  |  |  |  |  |  |
| Body composition |
| Waist-to-hip ratio, per 0.1 increase | 0.79 (0.46-1.34) | 0.382 |  |  |  |  |  |  |  |  |
| Comorbidities |
| Number of comorbidities 01≥2 | ref0.79 (0.32-1.98)0.28 (0.09-0.90) | 0.6190.032 |  |  |  |  | ref0.56 (0.20-1.60)0.22 (0.06-0.81) | 0.2810.023 | ref0.59 (0.42-1.75)0.29 (0.08-1.10) | 0.3440.068 |
| Depression aCES- D < 8CES- D ≥8 < 16CES- D ≥16 | ref0.86 (0.59-1.26)0.60 (0.40-0.89) | 0.4410.008 |  |  |  |  |  |  | ref1.93 (0.42-8.91)0.53 (0.17-1.68) | 0.3990.279 |
| Body-composition |
| Waist circumference, per cm increase | 0.95 (0.67-1.35) | 0.791 |  |  |  |  |  |  |  |  |
| Hip circumference, per cm decrease | 1.07 (0.68-1.69) | 0.768 |  |  |  |  |  |  |  |  |
| Body-mass index  | 1.04 (0.95-1.14) | 0.401 |  |  |  |  |  |  |  |  |
| Behavior |
| Heavy daily drinking during last 6 months | 0.64 (0.13-3.09) | 0.577 |  |  |  |  |  |  |  |  |
| Binge drinking during last 6 months | - | - |  |  |  |  |  |  |  |  |
| Smoking statusNever Ever Current  | Ref0.41 (0.13-1.27)0.53 (0.18-1.59) | 0.1210.258 |  |  |  |  |  |  |  |  |
| Tetrahydrocannabinol use during last 6 months | 0.24 (0.02-2.78) | 0.254 |  |  |  |  |  |  |  |  |
| Former injection drug use | 4.05 (0.29-56.78) | 0.299 |  |  |  |  |  |  |  |  |
| Being physically active | 1.62 (0.61-4.31) | 0.332 |  |  |  |  |  |  |  |  |
| Biomarkers |
| Per 1.0 unit in crease in log transformed soluble CD14 a, ng/mL | 0.34 (0.11-1.08) | 0.068 |  |  |  |  |  |  |  |  |
| Per 1.0 unit increase in log transformed soluble CD163 a, ng/mL | 0.57 (0263-1.25) | 0.160 |  |  |  |  |  |  |  |  |
| Per 1.0 unit increase in square root transformed I-FABP a, ng/mL | 0.73 (0.35-1.51) | 0.397 |  |  |  |  |  |  |  |  |
| Per 1.0 unit increase in log transformed hs-CRP a, mg/L | 0.87 (0.57-1.33) | 0.516 |  |  |  |  |  |  |  |  |
| Dichotomized IL-6 (>10 pg/mL) a | 1.38 (0.31-6.17) | 0.670 |  |  |  |  |  |  |  |  |
| Dichotomized D-dimer (> 1 mg/L) a | - | - |  |  |  |  |  |  |  |  |
| Hepatitis B virus DNA positive | 1.62 (0.16-16.26) | 0.680 |  |  |  |  |  |  |  |  |
| Hepatitis C virus RNA positive | 4.08 (0.29-56.71) | 0.295 |  |  |  |  |  |  |  |  |
| Cytomegalovirus IgG positive | 0.55 (0.11-2.67) | 0.456 |  |  |  |  |  |  |  |  |
| Model A: adjusted for age. Model B: adjusted for variables associated with transition towards frailty or variables attenuating the association between HIV status and transitioning to frailty. Model C: the final multivariable model without adjusting for level of depression. Model D: the final multivariable model adjusting for level of depression. Abbreviations: OR, odds ratio: CI, confidence interval; MSM, men who have sex with men; CES-D, Center for Epidemiologic Studies Depression scale; hsCRP, high sensitivity C-reactive protein; IL-6, interleukin-6; I-FABP, intestinal fatty acid-binding protein; a Variables were transformed, dichotomized or categorized appropriately to fit the linearity assumption of the logistic regression model. Univariate models regarding bingedrinking and dichotomized D-dimer did not converge.  |

|  |
| --- |
| Supplementary Table 5: Association between variables and transition to frailty: results of univariate and multivariable logistic regression models with generalized estimated equations-HIV-positive participants only |
|   | Univariate OR (95%CI)  |  p-value | Multivariable Model AOR (95%CI)  |  p-value | Multivariable Model BOR (95%CI) \* |  p-value |
| Age, per 10yr increase | 1.95 (1.17-3.24) | 0.010 | 1.78 (0.98-3.21) | 0.056 | 1.84 (1.00 -3.40) | 0.051 |
| Waist-to-hip ratio | 1.10 (0.67-1.79) | 0.712 | 0.73 (0.42-1.27) | 0.266 | 0.73 (0.41-1.31) | 0.295 |
| Number of comorbidities 0 1≥ 2 | ref2.21 (0.89-5.52)4.50 (3.78-11.36) | 0.0850.001 | ref2.06 (0.82 -5.19)3.27 (1.19- 8.99) |   0.1250.021 | ref2.15 (0.81-5.69)3.51 (1.21-10.17) | 0.1230.020 |
| Depression +aCES- D ≤ 8CES- D >8 < 16CES- D ≥16 | ref1.99 (0.88-4.52)4.09 (1.58-10.54) | 0.100.004 | ---- | ---- | ref2.90 (1.14-7.29)5.92 (2.05-17.11) | 0.0240.001 |
| Square root transformed duration of zalcitabine use, yearsa | 2.21 (1.08-4.52) | 0.030 | 2.15 (1.02- 4.54) | 0.045 | 2.33 (1.05-5.21) | 0.038 |
| Hip circumference, per cm decrease | 1.06 (1.00-1.11) | 0.033 |  |  |  |  |
| Waist circumference, per cm increase | 0.98 (0.95-1.01) | 0.237 |  |  |  |  |
| Square root transformed duration of know HIV-infection, yearsa | 1.01 (0.72-1.42) | 0.967 |  |  |  |  |
| Square root transformed cumulative exposure to ART, yearsa | 1.05 (0.74-1.49) | 0.781 |  |  |  |  |
| Cumulative duration of CD4 count <100/µL (years) | 1.30 (0.86-1.97) | 0.211 |  |  |  |  |
| Cumulative duration of CD4 count <200/µL (years) | 1.15 (0.92-1.44) | 0.216 |  |  |  |  |
| Cumulative duration of CD4 count <350/µL (years) | 1.05 (0.94-1.18) | 0.345 |  |  |  |  |
| Nadir CD4 cell count, per 100 cells/ µL increase | 1.00 (0.76-1.32) | 0.994 |  |  |  |  |
| Mean CD4 in 12 months prior to enrolment | 1.10 (0.93-1.30) | 0.258 |  |  |  |  |
| CD4/CD8 ratio at enrolment | 1.04 (0.48 -2.28) | 0.915 |  |  |  |  |
| History of CDC class C AIDS defining diagnosis | 1.63 (0.76-3.47) | 0.208 |  |  |  |  |
| Using cART at enrolment | 0.63 (0.08-5.08) | 0.668 |  |  |  |  |
| ART-experienced before starting cART | 0.50 (0.22-1.13) | 0.096 |  |  |  |  |
| Having used zalcitabine | 2.63 (1.03-6.75) | 0.044 |  |  |  |  |
| Having used didanosine | 1.02 (0.47- 2.24) | 0.954 |  |  |  |  |
| Square root transformed duration of didanosine use, yearsa | 1.01 (0.68-1.48) | 0.975 |  |  |  |  |
| Having used stavudine | 1.06 (0.51-2.21) | 0.880 |  |  |  |  |
| Square root transformed duration of stavudine use, yearsa | 1.13 (0.82-1.56) | 0.452 |  |  |  |  |
| Having used zidovudine | 1.12 (0.54-2.28) | 0.764 |  |  |  |  |
| Square root transformed duration of zidovudine use, yearsa | 0.97 (0.72-1.32) | 0.854 |  |  |  |  |
| HIV-RNA <200 c/mL in year prior to enrolment | 1.67 (0.38-7.44) | 0.499 |  |  |  |  |
| Cumulative duration of HIV-RNA <200c/mL, years | 0.98 (0.91-1.06) | 0.595 |  |  |  |  |
| Abbreviations: OR, odds ratio; CI, confidence interval; CES-D, Center for Epidemiologic Studies Depression scale; ART, antiretroviral therapy; cART, combination antiretroviral therapy; CDC, Centers for Disease Control and Prevention+ excluding two questions which were also used in the frailty scoreavariables transformed or categorized to fit the linearity assumption of the logistic regression model  |