REDUCTIONS IN MORTALITY RISK AFTER STARTING ART IN 2010-19 VERSUS 1995-2003

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BACKGROUND

Estimates of prognosis for mortality among people with HIV (PWH) are important to guide clinical decision making and preventive care. In 2007 we reported prognostic models estimating 3- and 5-year all-cause mortality risk for PWH who started ART between 1995 and 2003, but these are unlikely to be calibrated to the modern treatment era. These models were based on CD4 count, HIV viral load, transmission risk group, CDC disease stage, age and sex: prognostic accuracy may be improved by considering additional risk factors.

METHODS

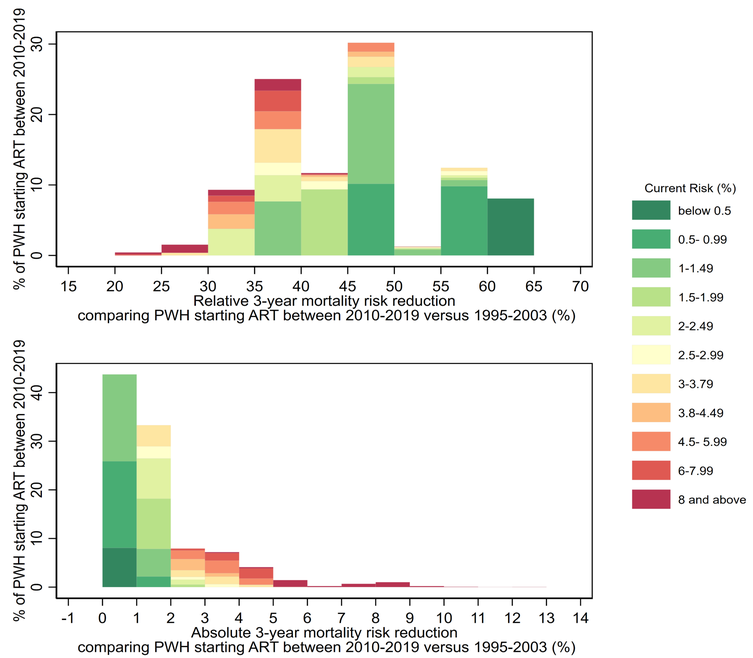
- We analysed data on PWH included in 20 European and North American cohorts (ART Cohort Collaboration [ART-CC]).
- Eligible PWH were aged >16 years, started ART during 2010-19, and had no missing values in the predictors included in the 2007 model (Table).
- Flexible parametric survival models were used to estimate mortality risk from ART start (baseline) and from 6 months after ART start.
- To compare mortality rates between PWH starting ART during 1995-2003 with those starting during 2010-19 among risk groups defined by different combinations of covariates, we calculated both the relative risk reduction (RRR) and absolute risk reduction (ARR).
- We considered additional covariates previously included in the VACS Index 2.0: haemoglobin, FIB4, EGFR, albumin, white blood cell count, BMI and HCV status.
- Effects of numerical predictors were modelled using cubic splines.
- We evaluated models' discrimination using C-statistics, which were calculated in the sample of individuals with no missing values in any of the predictors included in the 2021 model.

Table. Prognostic variables included in different models, and corresponding C-statistics

Models	Predictors	C-statistic
ART-CC 2007	CD4, HIV viral load, transmission risk group, CDC disease stage, age and sex	0.79 from ART start, 0.79 from 6 months after ART start
VACS 1.0 (Justice AC and Tate JP et al, 2010&2013)	CD4, HIV viral load, age, Haemoglobin, FIB4, EGFR and HCV	0.79 from 1 year after ART start
VACS 2.0 (Tate JP et al,2019)	CD4, HIV viral load, age, Haemoglobin, FIB4, EGFR, HCV, Albumin, BMI and White blood count	0.81 from 1 year after ART start
ART-CC 2021	CD4, HIV viral load, transmission risk group, CDC disease stage, age, sex, Haemoglobin, FIB4, EGFR, HCV, Albumin, BMI and White blood count	0.82 from ART start, 0.83 from 6 months after ART start

After adjusting for risk factors at the time of starting ART, the 3- and 5-year mortality risk among PWH starting ART during 2010-19 was substantially lower than for those starting ART during 1995-2003. RRRs ranged from 20% to 65% and ARRs from 1% to 13%. RRRs were generally lowest, but ARRs were generally highest, among those with highest current 3-year mortality risk (**Figure 1**).

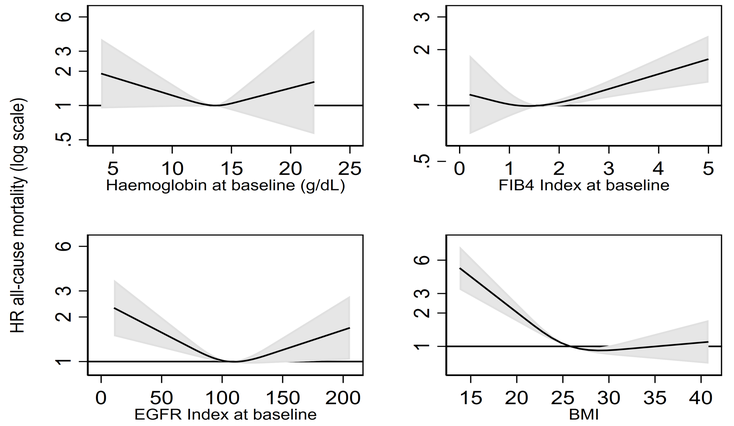
Figure 1. Distributions of estimated 3-year relative and absolute mortality risk reductions, comparing PWH starting ART during 2010-2019 versus 1995-2003, by current (2010-2019) mortality risk. Analyses were based on 85995 included PWH, and risk factors included in the 2007 ART-CC prognostic model (see Table)



References

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Figure 2. Adjusted HR (log scale) with 95% CI for haemoglobin, FIB4, EGFR and BMI at ART start, based on the updated (2021) ART-CC model (n=10945)



RESULTS

- Among 85,995 PWH starting ART between 2010 and 2019, 2517 died.
- The ART-CC 2007 model had excellent discrimination for predicting mortality in patients starting ART during 2010-19.
- Discrimination was improved in the updated 2021 model, based on 10945 PWH with no missing values in any predictor variable (**Table**).
- There were U-shaped associations of mortality with haemoglobin, FIB4, EGFR and BMI, at ART start (**Figure 2**) and 6 months.
- Associations with haemoglobin and EGFR were weak at ART start but stronger at 6 months.

CONCLUSIONS

Reductions in mortality risk among PWH treated with ART since its widespread introduction in 1996 are attributable both to risk profiles having improved over time (through earlier diagnosis and treatment), and to lower mortality among people with the same risk profile. Inclusion of additional risk factors improved discrimination of prognostic models. The updated ART-CC models are useful for predicting mortality risk in PWH up to 5 years after ART start in high-income countries in the current treatment era.

Notes

1. FIB4=Age (years)×Aspartate aminotransferase (U/L)/[Platelet count(10^9/L)× Alanine aminotransferase ^1/2 (U/L)].
2. EGFR=186 × serum creatinine(mg/dL)^(-1.154) × Age(years)^(-0.203) ×0.742[if female] × 1.210 [if black].
3. ART-CC derives HCV status based on patients' HCV antibody test, HCV antigen test and HCV RNA test results.
4. BMI=weight (lb) / [height (in)]^2*703

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