Predicting cause-specific mortality with the VACS Index 2.0 among persons with HIV

1058

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BACKGROUND

- The Veterans Aging Cohort Study (VACS) Index 2.0 is a composite score including age and routine clinical lab measurements; intended to capture physiological frailty among persons with HIV (PWH).
- The VACS Index 2.0 is well validated to predict all-cause mortality among PWH.
- Predicting cause-specific mortality among PWH could facilitate targeted care to improve survival.
- We assessed discrimination of the VACS Index 2.0 in predicting cause-specific mortality among PWH on antiretroviral therapy (ART) in Europe and North America.

TABLE 1: Characteristics at follow-up start, N=59741

Characteristic	# missing values	N (%)
Male	0	47842 (80%)
Age (years, mean)	0	43
Hep C virus	0	5193 (9%)
AIDS at ART initiation	0	10679 (18%)
Probable route of HIV acquisition	0	
Sex between men		31287 (52%)
Sex between men and women		19745 (33%)
Injecting drug use		5485 (9%)
Transfusion, other, unknown		3224 (5%)
Race/Ethnicity	0	
Non-Hispanic White		45666 (76%)
Non-Hispanic Black		7787 (13%)
Hispanic		3114 (5%)
Other		2351 (4%)
Unknown		823 (1%)
Viral load (copies/ml)	1785 (3%)	
<101		52294 (90%)
101-1000		2271 (4%)
1001-10000		1147 (2%)
>10000		2244 (4%)
CD4 count (cells/mm^3, mean)	20772 (35%)	605.2
BMI (kg/m^2, mean)	10885 (18%)	24.8

METHODS

- Data were from 12 cohorts contributing to the Antiretroviral Therapy Cohort Collaboration

This study found that the **VACS Index 2.0 can be used to predict cause-specific mortality**. Its highest discrimination was for AIDS, liver related and respiratory causes of death, and lowest discrimination for suicide/accidental death.

METHODS

- VACS Index 2.0 was calculated for PWH who initiated ART between 2000 and 2018, around a randomly selected visit date within the period 1 year after ART initiation to last visit.
- Missingness in VACS 2.0 variables was addressed through multiple imputation.
- We estimated associations between VACS 2.0 and specific causes of death using Cox models
- Model discrimination was evaluated using Harrell's C-statistic.
- Absolute mortality risks were modelled with flexible parametric survival models.

VACS INDEX 2.0 COMPONENTS

Age, sex at birth, body mass index (BMI), CD4 count, creatinine, HIV-1 RNA viral load, haemoglobin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), platelet count, white blood cell count, albumin, and hepatitis C infection.

TABLE 2: VACS Index 2.0 at follow-up start and association with causes of death, using multiple imputed data

Cause of death (N)	Mean VACS Index 2.0 (95% CI)	Hazard ratio (95% CI)	C-stat
All-cause (2425)	68 (67-68)	1.84 (1.81-1.87)	0.83
AIDS (455)	78 (76-80)	2.14 (2.06-2.23)	0.91
Liver (including HCC) (148)	76 (72-80)	2.13 (1.99-2.29)	0.91
Respiratory (99)	72 (68-75)	2.00 (1.83-2.18)	0.89
Non-AIDS infection (141)	72 (68-76)	1.98 (1.85-2.13)	0.87
Non-AIDS-defining cancers (452)	66 (64-68)	1.81 (1.73-1.89)	0.83
Substance abuse (97)	62 (58-66)	1.70 (1.56-1.87)	0.83
Cardiovascular (214)	62 (59-65)	1.66 (1.56-1.77)	0.79
Other (306)	66 (63-69)	1.76 (1.67-1.85)	0.78
Unclassifiable (372)	63 (61-65)	1.70 (1.62-1.78)	0.77
Suicide/accident (141)	50 (46-54)	1.32 (1.20-1.44)	0.65

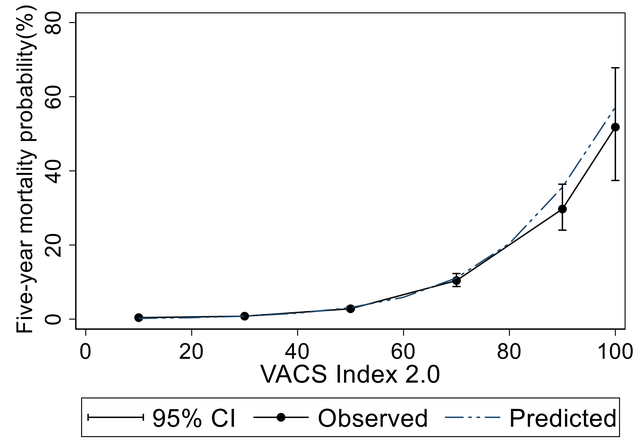
RESULTS

- Characteristics of 59,741 eligible PWH are shown in **Table 1.**
- VACS 2.0 values were measured a median of 3.2 years after ART initiation and ranged from 0 to 129: higher values indicate worse prognosis.

RESULTS

- The mean VACS 2.0 score at follow-up start was 41.0
- There were 2,425 deaths during 168,162 person-years (median follow-up 2.6 years).
- **Table 2** shows that non-AIDS-defining cancers were the most common cause of death, followed by AIDS.
- Discrimination for 5-year all-cause mortality was C=0.83.
- Discrimination for specific causes of death was highest for deaths due to AIDS (0.91), liver-related causes (0.91) and respiratory causes (0.89).
- Discrimination was lowest for suicides/accidental deaths (0.65), unclassifiable causes (0.77), cardiovascular deaths (0.79) and "other" causes (0.78).
- Predicted probabilities of 5-year mortality were low except for PWH with very high (>90) VACS 2.0 values (**Figure 1**)
- The 5-year probability of AIDS death for PWH with VACS 2.0 score 40 was 0.1%, increasing to 7.6% for scores of 90

FIGURE 1: Five-year probability of predicted and observed all-cause mortality



CONCLUSIONS

- The VACS Index 2.0 can be used to predict deaths due to AIDS, liver-related and respiratory causes.
- As expected, discrimination was lowest for causes of death which have contributory factors not included in the calculation of VACS Index 2.0 (i.e. suicide/accident).
- Exploring other indicators of physiological frailty (such as the Charlson Comorbidity Index or indicators of cardiovascular health) are of interest to improve discrimination of the Index for other physiological causes.

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