Milken Institute School of Public Health
THE GEORGE WASHINGTON UNIVERSITY

Application of a Claims-Based Frailty Index to Identify Risk of Mortality in an Observational Cohort of Adults with HIV

Morgan Byrne[1], Shannon Barth[1], Megan O'Brien[1], Amanda D. Castel[1] on behalf of the DC Cohort Executive Committee

1: Milken Institute School of Public Health, The George Washington University, Washington, DC.

925

THE DC COHORT

BACKGROUND

- Frailty reflects vulnerability to adverse outcomes, including mortality, and is relevant to an aging population of people with HIV (PWH).
- Routine HIV care rarely includes standardized frailty assessment.
- An adapted Harvard Claims-Based Frailty Index[1] (CFI) offers a scalable, reproducible approach for measuring frailty in HIV cohorts.

OBJECTIVE:
Adapt and apply a CFI in the DC Cohort and estimate the association between frailty categories and all-cause mortality.

METHODS

This analysis includes participants from the **DC Cohort**, an ongoing multi-site observational study of approximately 14,000 PWH receiving care in Washington, DC since 2011 with data linked to the DC Department of Health (DOH)

Inclusion Criteria:
- Age ≥ 40 years
- DC Cohort observation ≥ 24 months following enrollment
- Participants in active care with ≥ 1 HIV outpatient visit confirming ongoing care

Index Date
- Earliest date when age and enrollment criteria were first met, and active care confirmed

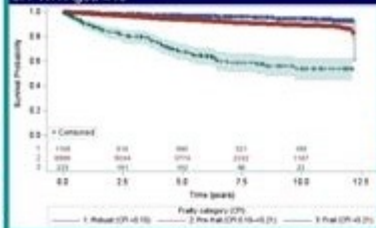
Frailty Measure (CFI):
- Code inputs: ICD-9/10 (diagnoses) and CPT (procedures)
- Weighted scoring: each indicator was weighted using published regression coefficients (Kim et al., 2018) calibrated to approximate a survey-based frailty index
- CFI score: sum of weighted indicators
- The CFI ranges from ~0–1, with higher scores indicating greater frailty burden. Conventional thresholds classify individuals as:
  - Robust (<0.10),
  - Prefrail (0.10–<0.21), or
  - Frail (≥0.21).

Outcome: All-cause mortality identified by DC Cohort and DOH
Time-to-event: follow-up from index date to death; censored at last cohort contact and/or end of study period (2011–2025).

Statistical Analysis:
- Descriptive characteristics summarized by frailty category
- Cox proportional hazards (PH) models estimated hazard ratios (HRs) for all-cause mortality
  - PH assessed using time-varying effects in the full model with log (time) interactions and a resampling-based supremum test
  - Multivariable models adjusted for (race/ethnicity), age (per 5 years), sex at birth, insurance, HIV transmission risk, CD4 (per 50 cells/μl, opportunistic infection history, time since HIV diagnosis [Antiretroviral Treatment (ART) Era], and smoking.

CONTACT: Morgan Byrne; byrne410@gwu.edu

Figure 1. Kaplan-Meier Survival Curves by CFI Category of PWH Aged ≥40



Survival curves diverged by frailty status early. In adjusted models , pre-frailty increased mortality risk by 51% and frailty was associated with four-time higher risk.

RESULTS

Table 1. Baseline Characteristics of PWH Aged ≥40 in the DC Cohort, by CFI Category

Characteristics	Overall (N=7,907)	Robust (N=1,108)	Pre-frail (N=6,566)	Frail (N=233)	p-value
Age at index, median (IQR)	52.3 (45.1-59.0)	50.0 (41.8-56.4)	52.5 (45.4-59.1)	58.5 (52.3-66.0)	**<0.001**
Site type					0.45
Community	4910 (62.1)	700 (63.2)	4067 (61.9)	143 (61.4)	
Hospital	2982 (37.7)	404 (36.5)	2489 (37.9)	89 (38.2)	
Race/ethnicity					**<0.001**
Non-Hispanic Black	6095 (77.1)	783 (70.7)	5111 (77.8)	201 (86.3)	
Hispanic	423 (5.4)	92 (8.3)	321 (4.9)	10 (4.3)	
Non-Hispanic White	1094 (13.8)	170 (15.3)	907 (13.8)	17 (7.3)	
Other/Unknown	280 (3.5)	59 (5.3)	217 (3.3)	4 (1.7)	
Sex at birth					**<0.001**
Male	5689 (72.0)	870 (78.5)	4654 (70.9)	165 (70.8)	
Female	2203 (27.9)	234 (21.1)	1902 (29.0)	67 (28.8)	
Primary insurance					**<0.001**
Public	4967 (62.8)	540 (48.7)	4234 (64.5)	193 (82.8)	
Private	2718 (34.4)	525 (47.4)	2156 (32.8)	37 (15.9)	
Unknown/Other	222 (2.8)	43 (3.9)	176 (2.7)	3 (1.3)	
Smoking status					**<0.001**
Current/Former	4082 (51.6)	420 (37.9)	3492 (53.2)	170 (73.0)	
Never	3052 (38.6)	570 (51.4)	2434 (37.1)	48 (20.6)	
Missing	773 (9.8)	118 (10.6)	640 (9.7)	15 (6.4)	
Alcohol abuse					**<0.001**
Current/Former	1965 (24.9)	191 (17.2)	1666 (25.4)	108 (46.4)	
Never	4293 (54.3)	705 (63.6)	3497 (53.3)	91 (39.1)	
HIV transmission risk					**<0.001**
Male-to-male sexual contact	3047 (38.5)	535 (48.3)	2450 (37.3)	62 (26.6)	
Heterosexual Contact	2765 (35.0)	347 (31.3)	2324 (35.4)	94 (40.3)	
Intravenous Drug Use	597 (7.6)	28 (2.5)	527 (8.0)	42 (18.0)	
Other/Unknown	1498 (19.0)	198 (17.9)	1265 (19.3)	35 (15.0)	
CD4 cells/μl at index, median (IQR)	541 (349-756)	567 (375-764)	539 (346-757)	496 (287-711)	**0.004**
Opportunistic infection history					**<0.001**
Yes	3483 (44.1)	421 (38.0)	2911 (44.3)	151 (64.8)	
Time since HIV diagnosis					**<0.001**
Pre-treatment era (1981-1990)	779 (9.9)	103 (9.3)	639 (9.7)	37 (15.9)	
AZT era (1990-1997)	1549 (19.6)	177 (16.0)	1308 (19.9)	64 (27.5)	
HAART era (1997-2015)	5118 (64.7)	749 (67.6)	4245 (64.7)	124 (53.2)	
cART era (2015-2025)	443 (5.6)	76 (6.9)	359 (5.5)	8 (3.4)	

Footnote (Missing data): Missing categories not displayed; percentages are calculated including missing values. Missing in site type (15), race/ethnicity (15), sex at birth (15), smoking status (773), alcohol abuse (1,449), injection drug use (2,462), ART era (18).

RESULTS (Continued)

- Among **7,907 PWH** (median age 52; 72% men; 77% Black), mean Frailty (CFI) was 0.12 (IQR 0.11-0.15).
- **CFI categories:** 14% robust (<0.10), 83% prefrail (0.10-<0.21), 3% frail (≥0.21)

Table 2. Multivariable Cox Proportional Hazards for All-Cause Mortality Among DC Cohort Participants ≥40 Years, N=7187

	Adjusted HR (95% CI)
Frailty (reference Robust [<0.1])	
Frail (≥0.21)	**4.16 (2.72, 6.36)**
Pre-frail (0.10–<0.21)	**1.51 (1.06, 2.16)**
Age at index, (per 5 years)	**1.06 (1.05, 1.07)**
Site type (Community vs. Academic)	**0.56 (0.47, 0.67)**
Race/Ethnicity, (reference White)	
Hispanic	0.94 (0.52, 1.70)
Non-Hispanic Black	1.13 (0.83, 1.55)
Other/Unknown	0.87 (0.45, 1.68)
Smoking status, (reference Never)	
Current/Former	**1.62 (1.31, 2.01)**
Missing	0.88 (0.54, 1.46)
Insurance status, (reference Private insurance)	
Public insurance	**2.16 (1.63, 2.86)**
Other/Unknown insurance	1.34 (0.58, 3.12)
HIV transmission risk, (reference Heterosexual contact)	
Injection drug use (IDU)	**1.61 (1.26, 2.04)**
Male-to-male sexual contact	**0.72 (0.56, 0.93)**
Other/Unknown	**0.66 (0.50, 0.86)**
Female sex (reference Male)	**0.64 (0.50, 0.81)**
CD4 count (per 50 cell/μL)	**0.97 (0.95, 0.98)**
Opportunistic infection history	**1.34 (1.10, 1.62)**
Time since HIV diagnosis, (reference cART (2015-25)	
HAART (1997-2015)	**2.01 (1.10, 3.68)**
AZT (1990-97)	**2.55 (1.37,4.72)**
Pre-Treatment (1981-90)	**2.31 (1.22,4.39)**

Abbrev: antiretroviral therapy (ART); highly active antiretroviral therapy (HAART). **Footnote:** Cox PH model, adjusted for factors (see Methods). PH diagnostics suggested minor non-proportionality for (age, site type, race). Participants with missing factors were excluded from modelling.

- Pre-frailty (HR:1.51, 95% CI:1.06-2.16) and frailty (HR:4.16, 95% CI: 2.72-6.36) were associated with increased mortality risk in multivariable models.
- Higher mortality risk shown with older age (HR 1.06 per year, 95% CI: 1.05-1.07), public insurance (HR:2.16, 95% CI: 1.63-2.86), IDU (HR 1.68, 95% CI:1.33-2.13), and smoking (HR 1.62, 95% CI:1.31-2.01).

CONCLUSIONS

- CFI identified substantial prefrailty in PWH with both prefrailty and frailty predicting mortality.
- CFI can be automated in EHRs to target patients for functional evaluation.
- EHR-based frailty screening could flag patients for targeted functional and geriatric assessment to identify those in need of additional supportive services.

REFERENCES

1. Kim, Dae Hyun et al. "Measuring Frailty in Medicare Data: Development and Validation of a Claims-Based Frailty Index." The journals of gerontology. Series A, Biological sciences and medical sciences vol. 73,7 (2018): 980-987. doi:10.1093/gerona/glx229

ACKNOWLEDGEMENTS

[illegible]