# *Clonal Hematopoiesis and HIV Infection are Associated with Geriatric Outcomes: the ARCHIVE Study*

839

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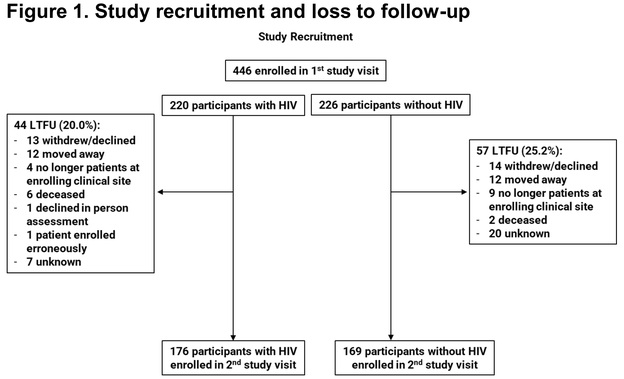
## BACKGROUND

- People living with HIV have accelerated biological aging and a higher prevalence of aging-related comorbidities and geriatric outcomes.
- **Clonal hematopoiesis (CH)**, the clonal expansion of stem cells driven by somatic mutations that increase with age, is linked to adverse clinical outcomes and is increased in people living with HIV [1].
- Here we evaluated geriatric outcomes in older adults with and without HIV to determine whether HIV or CH is associated with geriatric outcomes.

## METHODS

- ***Study population***: Participants were enrolled from the ARCHIVE study, a prospective observational cohort of adults with and without HIV >55 years, and in this analysis, were evaluated for CH and geriatric outcomes.
- ***Geriatric outcomes***: Frailty was measured by the FRAIL questionnaire, which categorizes individuals as frail, pre-frail and robust [2]. Multimorbidity was defined as having 2 or more comorbidities. Phenotypic age acceleration (PAA) was defined as the difference between phenotypic age, measured by nine biochemical and blood cell characteristics, and chronological age [3]. Quality of life (QoL) was measured by the CASP-19 scale [4].
- ***Statistical analysis***: Descriptive statistics compared baseline characteristics across HIV. Multivariable logistic and linear regression evaluated for associations between HIV and CH, and geriatric outcomes.

**Figure 1. Study recruitment and loss to follow-up**



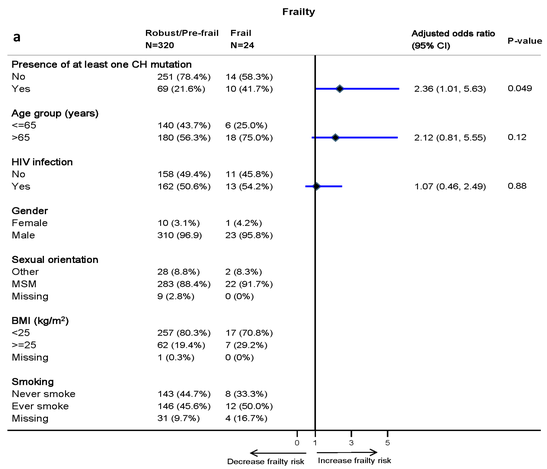

**References**: 1. Dharan, N. Nature Med 2021; 2. Kehler, D. S. BMC Geriatr 2022; 3. Liu, Z. PLoS Med 2018; 4. Hyde, M. Aging Ment Health 2003.

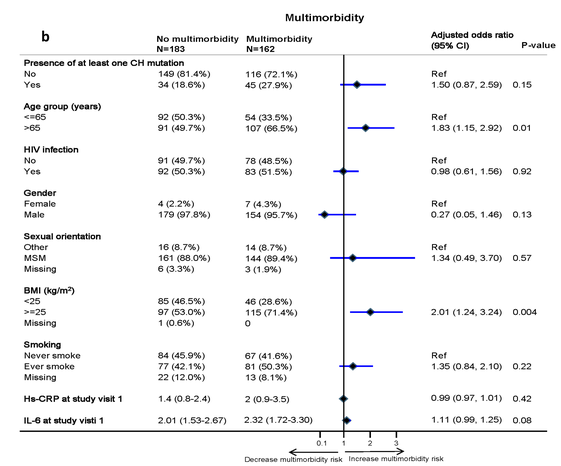
In the ARCHIVE study, HIV infection was independently associated with **increased phenotypic age acceleration.** Clonal hematopoiesis was independently associated with **reduced quality of life** and being **frail** (vs. pre-frail/robust).

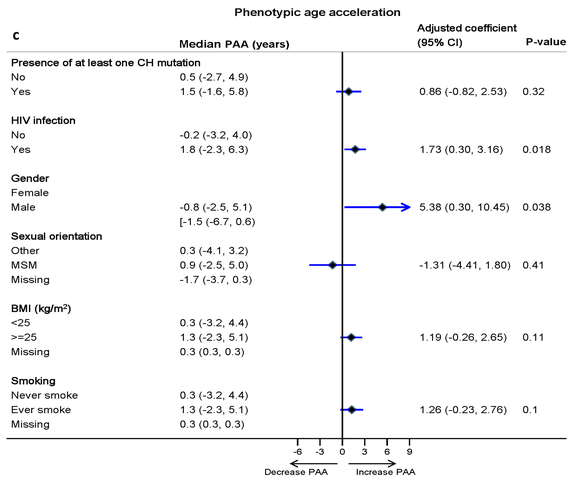
**Figure 2. Associations between clonal hematopoiesis, HIV infection and geriatric outcomes**

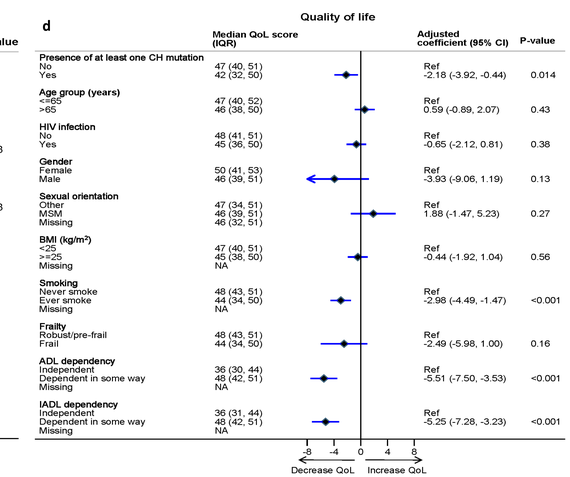
CH, clonal hematopoiesis; PAA, phenotypic age acceleration; QoL, quality of life; hs-CRP, high-sensitive C reactive protein; IL-6, interleukin-6; ADL, Activities of Daily Living; IADL; Instrumental Activities of Daily Living

Logistic regression was used to calculate the adjusted odds ratio for the outcomes: multimorbidity (a) and frailty (b). Linear regression was used to calculate the adjusted coefficients for PAA (c) and QoL (d). (a) For frailty, we adjusted for the presence of any CH mutation, age group and HIV status. (b) For multimorbidity, we adjusted for the presence of any CH mutation, age, gender, HIV status, whether the participant had ever smoked and for MSM status and inflammatory markers (hs-CRP and IL-6). (c) For PAA, we adjusted for the presence of any CH mutation, HIV status, gender, sexual orientation, BMI, and smoking status. (d) For QoL, we adjusted for the presence of any CH mutation, HIV status, gender, sexual orientation, BMI, smoking status, frailty, ADL and IADL dependency.




## RESULTS

- Of 345 participants, 176 adults with HIV and 169 without HIV (**Figure 1**). The median (interquartile range; IQR) age was 67 (62,72) years, 97% identified as male (89% MSM), 61% had a body mass index >25 kg/m$^2$, 41% reported ever smoking, and 54% reported being diagnosed with cardiovascular disease.
- Overall, 23% had at least one CH mutation (27% of those with HIV and 18% of those without HIV; p=0.045), 7% were frail, the median (IQR) PAA was 0.6 years (-2.5,5.0), and the median (IQR) QoL score was 36 (29,39) out of 57.
- Participants with HIV had a median (IQR) duration of HIV of 27 (18,33) years and a median (IQR) CD4 nadir of 246 (143,372) cells/mm$^3$; all but one participant had a suppressed viral load.
- In adjusted regression analyses (**Figure 2**), HIV infection was independently associated with PAA (coefficients 1.73, 95% confidence interval [CI] 0.3-3.16, p=0.02) and CH was independently associated with reduced QoL (coefficients -2.18, CI -3.92, -0.44, p=0.01) and being frail (vs. pre-frail/robust; odds ratio 2.36, CI 1.01-5.63, p=0.049).

## CONCLUSIONS

- In the ARCHIVE cohort, HIV infection was associated with PAA and CH, and CH was associated with frailty and reduced QoL.
- While our results warrant further exploration, they suggest that CH may be used as a biomarker for geriatric outcomes that may prioritize individuals for interventions designed to reduce geriatric outcomes and promote healthy aging.

## ADDITIONAL KEY INFORMATION

**#These authors contributed equally**

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