Frailty and ageing phenotypes among older people living with HIV across high- and low-income settings: a comparison of the HASA and GEPPO cohorts

Giovanni Guaraldi[1], Grace Banturaki[2], Phoebe Mbabazi[2], Emanuele Focà[1], Judith Amutuhaire[2], Agostino Riva[1], Joseph Musaazi[2], Stefano Calza[1], Giuseppe Vittorio De Socio[1], Barbara Castelnuovo[2], Andrea Calcagno[1]

1.GEPPO Study Group, Italy 2. Infectious Diseases Institute, Makerere University, Kampala, Uganda;

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BACKGROUND

Older people living with HIV (OPLWH) represent a growing proportion of the global HIV population in both high- and low-income settings. Frailty and geriatric syndromes contribute substantially to morbidity, functional decline, and healthcare complexity in this population. Although viral suppression is increasingly achieved worldwide, it is unclear whether ageing-related vulnerability presents similarly across different socioeconomic contexts. Comparative clinical data between settings remain limited. We therefore examined frailty and related geriatric domains in two established cohorts from Uganda (HASA) and Italy (GEPPO).

METHODS

We conducted a cross-sectional analysis of two prospective cohorts of older people living with HIV: HASA (Uganda, ≥60 years) and GEPPO (Italy, ≥65 years). Frailty was assessed using the Fried phenotype (≥3 criteria = frail). Data on non-communicable diseases, polypharmacy, cognitive performance, depression, falls, and physical function (SPPB) were collected using standardized tools and harmonized across cohorts to ensure comparability. (**Table 1**) Analyses were performed in the overall population and in a restricted 65–75-year subgroup

RESULTS

The study included 500 HASA and 520 GEPPO participants. GEPPO participants were **older** (65.4 vs 73.7 years; p<0.001), more frequently **male** (51.2% vs 70.4%; p<0.001), and more likely to **live alone** (8.2% vs 47.8%; p<0.001). **Employment** was higher in HASA (63.5% vs 8.5%; p<0.001), whereas secondary education was more common in GEPPO (34.5% vs 58.6%; p<0.001).

Virological suppression was high in both cohorts (92.2% vs 96.9%; p=0.003), with comparable **current CD4 counts** (median 645 vs 622 cells/µL; p=0.200).

Multimorbidity (≥3 NCDs) (6.2% vs 14.6%; p<0.001) and **polypharmacy** (1.6% vs 30.6%; p<0.001) were markedly more frequent in GEPPO. **Hypertension** (50.1% vs 71.9%; p<0.001), **diabetes** (14.0% vs 23.9%; p<0.001), and **cancer** (1.0% vs 20.8%; p<0.001) were more prevalent in GEPPO, while **chronic kidney disease** was more common in HASA in the 65–75 subgroup (37.9% vs 27.0%; p=0.014).

Overall **frailty prevalence** differed (8.4% vs 13.3%; p<0.001) but was similar in the **65–75 subgroup** (8.5% vs 6.3%; p=0.658).

Domain-specific vulnerability patterns in the age-restricted subgroup are shown in **Figure 1**

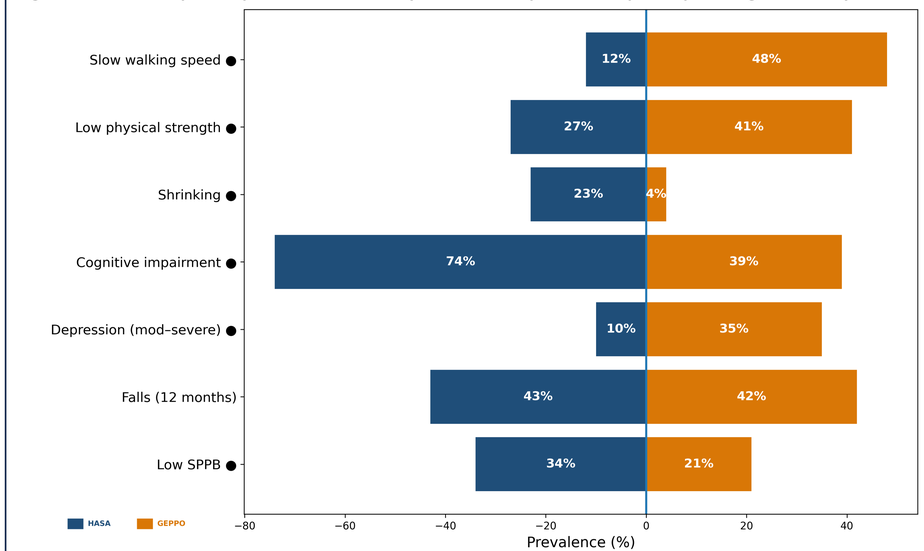
Frailty prevalence was comparable in the 65–75 age group across settings, yet the domains underlying vulnerability differed markedly. In Uganda, frailty was primarily characterized by shrinking and cognitive impairment, whereas in Italy it was driven by mobility limitation, reduced strength, and depressive symptoms.

These findings indicate that frailty in people ageing with HIV represents a multidimensional, context-shaped condition rather than a uniform biological phenotype.

Table 1. Geriatric syndrome and tools used for evaluation

	HASA	GEPPO	Categorization
Frailty	Fried Frailty Phenotype: Involuntary weight loss, weakness, exhaustion, low physical activity and slowness(24)	Fried Frailty Phenotype: Involuntary weight loss, weakness, exhaustion, low physical activity and slowness(24)	≥3 criteria: frail; 1 or 2: pre-frail, 0 criteria: non-frail.
Cognitive function	Montreal Cognitive Assessment (MOCA)(25).	Mini Addenbrooke Cognitive Examination test (MACE)(8)	Impaired: MACE: ≤ 25 MOCA: ≤24 (lowered from 26 to account for cultural differences)
Functional impairment	Short Physical Performance Battery (SPPB): gait speed, a balance test and a chair stand test(26)	Short Physical Performance Battery (SPPB):gait speed, a balance test and a chair stand test(26)	SPPB:10 to 12 High function,7 to 9 Moderate function,0 to 6 Low function
Depression	Patient Health Questionnaire PHQ2 and PHQ9(28)	Center for Epidemiologic Studies Depression (CES-D questionnaire)(29)	Minimal depression: PHQ: 0 to 1 or CES-D: 0 to <15 Mild to moderate: PHQ:2 to 3, CES-D: ≥15 to ≤21 Severe depression: PHQ:4, CES-D: ≥22 to ≤60
History of falls	History of fall questionnaire (a standard 17-item Questionnaire)(30)	History of fall	Any fall in the past 12 months
Quality of life	World Health Organization QOL - OLD questionnaire (WHOQOL-OLD)(31)	EQ-5D-5L(32)	Both scores were normalized from 0 to 100 for easy interpretation.

Figure 1. Domain-specific prevalence of frailty-related components in participants aged 65–75 years.



Diverging bar chart showing the prevalence (%) of selected frailty-related domains in the HASA (Uganda) and GEPPO (Italy) cohorts. ● indicates statistically significant differences between cohorts ($p < 0.05$).

CONCLUSIONS

Despite comparable **virological suppression and CD4 recovery**, ageing trajectories differed substantially across settings. In the 65–75 age group, overall frailty prevalence was similar, yet the **domains driving vulnerability** were distinct. HASA participants showed greater **nutritional decline and cognitive impairment**, whereas GEPPO participants exhibited higher **mobility limitation, multimorbidity, polypharmacy, and depressive burden**.

These patterns likely reflect the interaction between **biological ageing, ART exposure, comorbidity burden, and social context**. In GEPPO, higher rates of cardiovascular risk factors and polypharmacy may contribute to mobility impairment and mood vulnerability, while in HASA, nutritional factors, chronic kidney disease, and contextual determinants may shape frailty expression differently.

Our findings support a **biopsychosocial and context-adapted approach** to ageing with HIV. Frailty in people living with HIV should not be regarded as a uniform biological entity, but as a **multidimensional and setting-sensitive condition**, requiring tailored strategies for screening, prevention, and integrated care across diverse healthcare environments.

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PLAIN LANGUAGE SUMMARY

Older people living with HIV in Uganda and Italy had similar overall levels of frailty, but the way frailty presented was different. In Uganda, weight loss and memory problems were more common, while in Italy reduced physical strength, mobility limitations, and depression were more frequent, highlighting the need for care strategies adapted to local contexts