

# Characterization of data-driven geriatric syndrome clusters in older people with HIV: a Mexican multicenter cross-sectional study



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## Summary

**Background** As living with HIV has been proposed as a condition that may accelerate aging, the main objective of this work was to estimate the prevalence of geriatric syndromes (GS) among older Mexicans with HIV dwelling in the community. Secondly, to evaluate whether the accumulation of GS could be associated with an adverse HIV-related clinical profile, independent of chronological age.

**Methods** Multicenter, cross-sectional study including 501 community-dwelling people aged  $\geq 50$  years with HIV. The overall prevalence of nine selected GS and their cumulative number were estimated. An Age-Independent Cumulative Geriatric Syndromes scale (AICGSs) was constructed, and correlations between the AICGSs and HIV-related parameters assessed. Finally, k-mean clustering analyses were performed to test the secondary objective.

**Findings** Median age 56 (IQR: 53–61) years, 81.6% of men. Polypharmacy (74.8%), sensorial deficit (71.2%), cognitive impairment (53.6%), physical disability (41.9%), pre-frailty (27.9%), and falls (29.7%), were the more prevalent GS. A significant negative correlation was found between the AICGSs and normalized values of CD4+ nadir cell counts ( $r = -0.126$ ; 95% CI:  $-0.223$  to  $-0.026$ ,  $p < 0.05$ ). Similarly, a significant inverse adjusted association between the CD4+ nadir cells and the AICGSs was observed on linear regression analysis ( $\beta -0.058$ ; 95% CI:  $-0.109$  to  $-0.007$ ,  $p = 0.03$ ). Cluster analysis identified three differentiated groups varying by age, metabolic comorbidities, AICGSs, and HIV-related parameters.

**Interpretation** An elevated prevalence of GS was observed in the studied population. Moreover, the accumulation of GS was associated with adverse HIV-related profiles, independent of age. Thus, early detection and management of GS are crucial to promote healthier aging trajectories in people with HIV.

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**Keywords:** HIV; Geriatric syndromes; Chronic diseases

## Introduction

The population of older people with HIV (OPWH) has kept a continuous and substantial increase in life expectancy over the last two decades worldwide.<sup>1</sup> However, even though people with HIV are living longer due to combination antiretroviral therapy (cART), the

treatment seems not to fully restore the induction of certain biological processes that correlate with the aging process, even when treatment goals are achieved.<sup>2</sup> The aging process is probably being more pronounced in people with longer expositions to HIV viral load, or a history of uncontrolled infection.<sup>3</sup> After the age of 50,

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### Research in context

#### Evidence before this study

Research predominantly conducted in high-income countries has shown a high prevalence of geriatric syndromes in older people living with HIV, as well as an early presentation of these conditions. Consequently, efforts to study this issue in-depth, and to provide better services to a population with specific needs, are already underway. However, in low and middle-income countries, where this phenomenon is probably also occurring, there are very few studies documenting it, and there is insufficient awareness in the social and health services to address it. In this sense, we conducted a PubMed database search without language restriction for studies evaluating geriatric syndromes in people with HIV published between April 1, 2013, and April 1, 2023. The search were terms “geriatric syndromes” AND “HIV” OR “Human immunodeficiency virus”. The search yielded a non-negligible number of studies on the topic, most of which were conducted in high-income countries in North America and Europe. Noteworthy, single-center studies focusing on a specific geriatric syndrome have been published in Brazil and Mexico. However, none of the retrieved articles consisted of a

prevalence estimation of diverse geriatric syndromes in community-dwelling older people with HIV in a Latin American country.

#### Added value of this study

Findings from this work follow the trend of revealing an elevated prevalence of geriatric syndromes in older people with HIV in five clinics from Mexico. There was also an age-independent association between geriatric syndromes and adverse HIV-related profiles. This multi-center collaboration represents the first efforts and results to address the issue of aging in the context of HIV outside of a single specialized clinic in Mexico City.

#### Implications of all the available evidence

The results represent an initial approach to this public health issue in our country and could be used to highlight situations that we are probably overlooking. They should also be used to organize research and policy efforts to create a network of care adapted to local resources and needs.

people with HIV, particularly those who have aged with HIV, appear to exhibit an earlier occurrence or greater incidence of many aging-related conditions compared to HIV-uninfected peers. This is not limited to non-communicable chronic diseases such as cardiovascular diseases, cancer or cognitive impairment, but also, to an earlier-than-expected appearance of specific age-related conditions as geriatric syndromes, even with well-managed HIV care.<sup>4,5</sup>

Geriatric syndromes (GS) are multifactorial conditions that result from deficits in multiple domains including clinical, psychological, and environmental vulnerabilities. Likewise, GS do not fit into a discrete disease category and are highly prevalent in older people.<sup>6,7</sup> Moreover, GS increase morbidity and mortality, tend to accumulate, and are difficult to reverse. Therefore, early recognition and management of GS are crucial in the promotion of healthier aging trajectories as people with HIV grow older.

While the mechanisms contributing to the development of GS in OPWH are multifactorial, a shared mechanism that may have a central role as a substrate for these conditions is immune dysfunction. The negative synergistic effect of aging and HIV on chronic immune activation (particularly monocyte activation) and the development of persistent inflammation despite viral suppression has been widely associated with accelerated aging and deleterious health effects in this population.<sup>8,9</sup>

Due to the above, living with HIV has been described as a condition that accelerates/exacerbates aging, thus

being responsible for the early development of GS. Hence, a geriatrics-focused approach of functional preservation will become increasingly important in caring for OPWH living in the community.<sup>10</sup> However, one remaining concern when evaluating the nature of this earlier appearance of specific syndromes is how to distinguish between the effects of chronological age from the effects of the disease, given the high co-occurrence of GS in advancing chronological age.<sup>11</sup> Therefore, the main objective of the present study was to estimate the prevalence of GS among Mexican OPWH and, secondly, to evaluate whether the accumulation of GS could be associated to an adverse clinical profile related to HIV trails, independently of chronological age.

## Methods

### Design

Multicentric, cross-sectional study including 501 community-dwelling people aged 50 years or older, living with HIV, and all receiving cART. Participants were recruited from five specialized HIV clinics in five different States of Mexico, including Mexico City. All of the included sites were Mexican Ministry of Health clinics with ongoing collaborations and availability of trained evaluators during the study's time frame.

### Setting

Participating sites were in the cities of Cuernavaca, Aguascalientes, León, Nezahualcóyotl (municipality),

and Mexico City, which are in states of the Central and *Bajío* regions of the country. The Nezahualcōyotl and Cuernavaca sites were outpatient clinics from a national network of integrated care for people with HIV. The Aguascalientes and León sites were outpatient clinics in general hospitals, and the Mexico City site was a specialized outpatient clinic within a tertiary care hospital. Descriptive characteristics of the study's participants stratified by site are presented in Supplementary Material—Table S4. For the eligibility criteria, all people aged  $\geq 50$  with HIV were openly invited to participate in this study during their clinical visits; the recruitment period was from August to November 2017. Afterwards, all participants underwent a standardized comprehensive geriatric assessment including socio-demographic characteristics, self-reported comorbidities, and poly-medication. In addition, anthropometrical measurements were obtained, and biochemical parameters recorded. Information concerning participants' ethnicity was not recorded, which precluded the analysis of this variable.

All the information was captured on a specifically designed study form. This study was approved for the Institutional Research Ethics Committee (GER-698-12/12-1) and all participants signed an informed consent.

### Sample size

The sample consisted of individuals who accepted the invitation to participate in the study and who underwent the evaluation at each site.

### Geriatric syndrome assessment

We defined nine GS based on their common definitions and these were: disability for mobility, instrumental (IADL) and basic (ADL) activities of daily living, poly-medication, visual or hearing impairment, cognitive impairment, falls, urinary incontinence, and frailty.<sup>7</sup> Mobility was assessed by the Rosow & Breslau scale: doing heavy housework, walking a half mile, and going up the stairs.<sup>12</sup> For the IADL, participants reported their ability to perform 8 activities of daily living based on the Lawton & Brody scale: using the telephone, having responsibility for one's own medication, managing money, being able to transport oneself, shopping, grooming, doing housework, and doing laundry (The last three items were only considered as disabilities for participants that previously performed them).<sup>13</sup> For the ADL, participants were asked if they needed help for any task for six tasks evaluated by the Barthel ADL index: bathing, dressing, transferring from bed to chair, climbing stairs, toileting, and feeding.<sup>14</sup> For each domain of disability, if participants indicated that they were unable to perform one or more activities without help, they were considered as having mobility, IADL or ADL disability. Poly-medication was defined as participants self-reported taking  $\geq 3$  medications excluding cART. Sensorial deficit syndrome was defined as

patients who self-reported any degree of visual or hearing deficit. Cognitive impairment was defined with a Mini-Mental State Examination (MMSE) score  $< 24$  pts or an International HIV Dementia Scale (IHDS)  $\leq 10$  pts.<sup>15,16</sup> Depressive symptoms were assessed using the 15-item Geriatric Depression Scale (GDS) where a score of  $> 5$  points indicated their presence.<sup>17</sup> Falls syndrome was defined as any auto-reported fall in the last year. Urinary and/or fecal incontinence was determined using the specific item of the Barthel ADL index. In the specific case of urinary incontinence and the presence of falls, the documentation of an event may not necessarily represent the geriatric syndrome, given the relatively younger population. This may be considered as an arbitrary use of the definition. Frailty components were defined according to the phenotype proposed by Fried et al. and previously validated in Mexican population: 1) self-report of unintentional weight loss within the previous year; 2) Exhaustion was defined by two questions from the Center for Epidemiological Studies-Depression (CES-D) scale; 3) Slowness determined by the 4-m gait speed test; 4) Weakness established for hand-grip strength, and 5) Low physical activity was determined by the Spanish version of the Physical Activity Scale.<sup>18</sup> As recommend, those meeting three or more criteria were classified as frail; those meeting one or two were considered prefrail; and those meeting none as non-frail. The cumulative number of geriatric syndromes was extracted for each patient.

### Anthropometric and HIV measurements

Height and weight were recorded, and body mass index calculated [BMI = weight (kg)/height (m)<sup>2</sup>]. HIV assessments included current CD4+ T-lymphocyte cell counts (measured within one month of the clinical evaluation at the latest), which were obtained by means of flow cytometry and treated as a dichotomous variable ( $\leq 200$  or  $> 200$ ); current HIV-RNA levels (viral load, VL), which was treated as a dichotomous variable (suppressed when  $< 40$  copies/mL and not suppressed when  $\geq 40$  copies/mL were found), and current CD4+ cell nadir values (the lowest measure registered).

### Statistical analysis

Continuous data is represented as either means (standard deviation) or medians (interquartile range), based on the distribution determined by the Anderson-Darling normality test. In the case of categorical variables, the absolute frequency and associated percentage are provided. Statistical analyses were carried out using R Studio (Version 4.2.1). We used the mice R Package (Version 3.14.0) to impute continuous missing values, assuming the missing data are at random. The imputation was done using multiple chained equations, and five imputed datasets were created.<sup>19</sup> The imputed datasets were combined using Rubin's rules for a maximum of five iterations. The percentage of missing

values for continuous variables, as well as density histograms and summary statistics for both the original and imputed variables are reported in Supplementary Material—Figure S5. No statistically significant differences between the imputed variables and the original distribution of the missing continuous variables were observed.

#### Prevalence estimation of GS

To estimate the overall prevalence of the nine selected GS and their cumulative number, the Clopper-Pearson method from the *epiR* package (Version 2.0.3) was used. As a sub analysis, we stratified the estimated prevalence of GS within their individual components.

#### Age-independent cumulative geriatric syndrome scale

For the secondary objective, we sought to evaluate the accumulation of GS independently of chronological age. A statistical limitation for this is that most of the geriatric assessment tools do not weight their results based on age. Hence, we used the residual of a fitted Poisson regression model that predicts the accumulative number of GS based on chronological age to mitigate the effect of age on diverse GS. We extracted then, the residuals for every subject and named it the age-independent cumulative geriatric syndrome scale (AICGS). We assessed independence, symmetric distribution, and linearity of residuals as well as the deviance equal to the model variance, as our main assumptions for our Poisson regression model (Supplementary Material).

#### Association of AICGS and HIV assessment

First, to evaluate the correlation of the AICGS scale with the normalized transformation of the last measurement of CD4+, and CD4+ cell nadir counts, the Pearson product-moment correlation coefficient was used. The differences between AICGS scale and the categorized VL were assessed using a Mann–Whitney U test. To visualize the relationship of both variables, we plotted dispersion and boxplots graphs using *ggplot 2* package (Version 3.3.5). Then, to assess an association of our HIV assessment, we fitted linear regression model using the AICGS scale as dependent variable and as our independent variables the normalized values of the last count of CD4+, CD4+ cell nadir along with the VL, sex, education, and the number of comorbidities.

#### K-mean cluster analysis

To test whether the accumulation of GS could be the result of an adverse clinical profile related to HIV trails independently of chronological age, we performed k-mean clustering analysis. Variables for our clustering model were selected on the premise that the AICGS scale along with the current and CD4+ cell nadir counts would help us to better characterize subjects that have

different geriatric syndrome and HIV traits. The cluster analysis was performed using a k-means algorithm with standardized centered values with a mean value of 0 and a SD of 1. The *kmeansruns* function was tested using a k value of 3 and 4 with a 100-run selection from the *fp* package (Version 2.2.9). Then, cluster selection was assessed by resampling the dataset 100 times and computing the Average Silhouette Width and the Calinski-Harabasz criterion. The Jaccard coefficient was used to assess stability and a score >0.70 was considered to be stable. Finally, descriptive characteristics of our variables for all clusters were compared.

#### Role of the funding source

The funding source had no role in the design, analysis, and data interpretation, writing, or reporting of the manuscript.

The study is reported according to the STROBE statement for reporting observational studies.<sup>20</sup>

#### Results

Clinical characteristics of the 501 participants are presented in Table 1. Median age was 56 (IQR: 53–61; range 50–84) years, 409 (81.6%) were men, with median schooling of 12 (IQR: 6–16) years. Dyslipidemia (n = 208, 41.5%), hypertension (n = 120, 23.9%), and diabetes (n = 70, 13.9%) were the most frequent chronic diseases. Median current and nadir CD4+ counts were 479 (IQR: 334–667) and 154 (IQR: 54–183) cells per ml, respectively. Almost ten percent (n = 48, 9.8%) of participants had detectable VL. The comprehensive geriatric assessment, individual components for each geriatric syndrome, and stratification by sex are presented in Supplementary Material—Tables S1 and S2.

#### Prevalence of geriatric syndromes

Polymedication was the most prevalent GS, followed by sensorial deficit, cognitive impairment, any type of disability, either prefrailty/frailty, falls, depressive symptoms, and incontinency. Overall, 26.35% (n = 132, 95% CI: 22.54%–30.44%) had at least three of any GS, 17.6% (n = 88, 95% CI: 14.3%–21.2%) had ≥5 GS, and only 1.6% (n = 8, 95% CI: 0.69%–3.12%) did not have any GS (Fig. 1). Further stratification of the individual components for each GS revealed a higher prevalence of visual impairment (n = 353, 70.6%, 95% CI: 66.4%–74.6%), cognitive impairment assessed by the IHDS scale (n = 255, 54.9%, 95% CI: 50.3%–59.5%), and disability for mobility (n = 177, 35.4%, 95% CI: 31.2%–39.7%) (Supplementary Material—Figure S1). Finally, we assessed differences among current CD4+ counts and CD4+ nadir cells according by types of GS. Those with prefrailty/frailty had lower current CD4+ counts in comparison with nonfrail participants, and persons who reported falls had lower CD4+ nadir cells compared with

Parameter	All-population (n = 501)
Men (%)	409 (81.64)
Age (Years) [median, (IQR)] [range]	56 (53–61) [50–84]
Education (Years) [median, (IQR)]	12 (6–16)
<b>Comorbidities</b>	
No-comorbidities (%)	194 (38.7)
1 comorbidity (%)	142 (28.3)
≥2 comorbidities (%)	165 (32.9)
Diabetes (%)	70 (13.9)
Arterial hypertension (%)	120 (23.9)
Dyslipidemia (%)	208 (41.5)
Cancer (%)	35 (6.9)
Cardiovascular disease (%)	14 (2.7)
COPD (%)	12 (2.4)
Chronic hepatopathy (%)	1 (0.2)
OAD (%)	23 (0.2)
Osteoarthritis (%)	30 (5.9)
Chronic kidney disease (%)	18 (3.5)
Depression (%)	30 (5.9)
Anxiety (%)	19 (3.7)
<b>Clinical and anthropometric profiles</b>	
BMI (kg/m <sup>2</sup> ) [median, (IQR)]	25 (22.69–27.55)
Hemoglobin (g/ml) [median, (IQR)]	15.2 (14–16.2)
Glucose (mg/ml) [median, (IQR)]	94 (87.65–103)
Albumin (mg/ml) [median, (IQR)]	4.4 (4.16–4.7)
Nadir CD4+ T-lymphocytes (cells/ml), [median, (IQR)]	154 (54–183)
Current CD4+ T-lymphocytes (cells/ml), [median, (IQR)]	479 (334–667)
Detectable RNA-HIV copies (%)	48 (9.8)

Abbreviations: COPD, Chronic obstructive pulmonary disease; OAD, Osteoarthritis; BMI, Body mass index.

**Table 1: Sociodemographic, reported comorbidities, clinical and anthropometric characteristics of the population of study.**

those who did not fall (Supplementary Material—[Figure S2](#)).

### Age-independent cumulative geriatric syndrome scale evaluation

Using the cumulative number of GS and chronological age, we extracted the fitted residuals of our Poisson regression models. The distribution and Poisson model assumptions are presented in Supplementary Material—[Figure S3](#). We observed a significant negative correlation with AICGS scale against normalized values of CD4+ nadir cells ( $r = -0.126$ , 95% CI:  $-0.223$  to  $-0.026$ ,  $p < 0.05$ ) but not for current CD4+ counts ( $r = 0.800$ , 95% CI:  $-0.080$  to  $0.098$ ,  $p = 0.80$ ) ([Fig. 2](#)). The adjusted linear regression analysis shows that only CD4+ nadir cells had an inverse association with the AICGS scale ([Table 2](#)).

### Data-driven clustering characterization

Lastly, we performed k-mean clustering to assess the impact of adverse clinical profiles related to HIV trails independently of chronological age. Using the AICGS scale, along with the current and CD4+ cell nadir counts,

we were able to identify three well-differentiated groups among the studied population. The average silhouette width and the Calinski-Harabasz criterion are presented in Supplementary Material—[Figure S4](#). Cluster 1 ( $n = 116$ ; 23.2%) consisted of participants with low CD4+ nadir, and those who had the highest AICGS scale. Cluster 2 ( $n = 189$ ; 37.7%) was characterized as having the lowest CD4+ nadir, current CD4+ cell counts as well as a lower AICGS scale. Finally, Cluster 3 ( $n = 196$ ; 39.1%) was characterized by higher CD4+ nadir and current CD4+ cell counts, as well as the lowest AICGS scale ([Fig. 3](#)). Further characterization of the clusters reveals older age in Cluster 2, followed by Clusters 1 and 3 (Supplementary Material—[Table S3](#)). Finally, a higher proportion of chronic diseases was observed in Cluster 1 compared to the other two clusters.

### Discussion

The objective of this article was to estimate the prevalence of GS among OPWH in Mexico, and to evaluate if a cumulative number of GS could be associated to an adverse clinical profile related to HIV trails

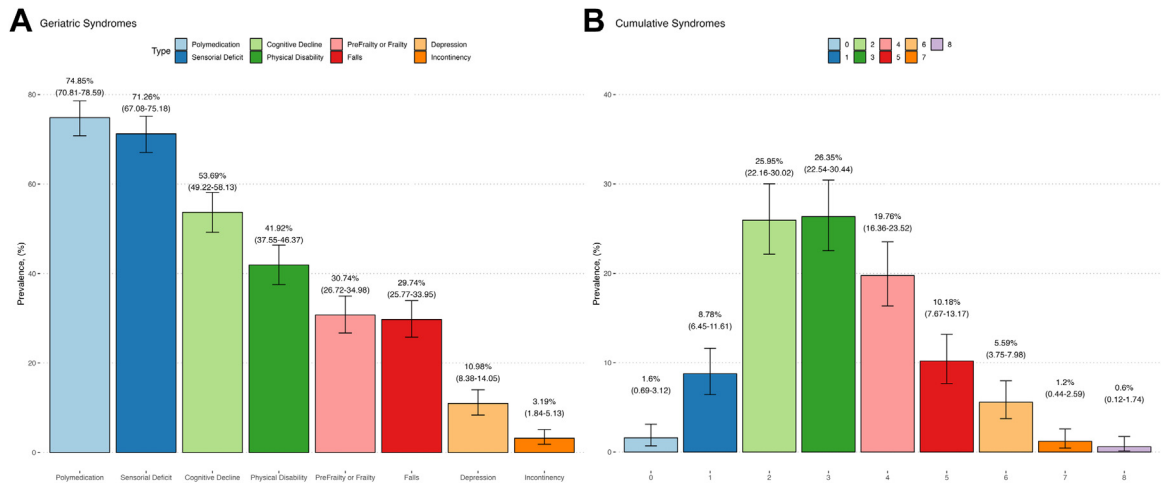


Fig. 1: Unadjusted prevalence of geriatric syndromes by type (A) and its cumulative frequency (B) in our study population.

independently of age. The obtained results show a high prevalence of GS in a relatively young population, with the most frequent syndromes being polypharmacy, visual deficit, cognitive impairment, disability for mobility, and prefrailty. Then, using a k-mean clustering approach it was possible to identify three well-differentiated groups of participants that displayed contrasting clinical profiles related to HIV trials independently of chronological age.

Confronting our results with the existing literature, the observed prevalence of the reported GS is concordant with an elevated prevalence of GS in other studies, with the exception of frailty.<sup>21-23</sup> The observed frailty prevalence in this study is lower in comparison to what is reported by two systematic reviews on the subject: the most recent being by Yamada and collaborators reporting a pooled prevalence of 10.9%.<sup>24,25</sup> However, when contextualizing the observed results, it is important to consider that this comparatively lower prevalence of frailty has already been reported in another Mexican

study.<sup>22</sup> Nevertheless, other findings such as the observed prevalence of disability for mobility, multimorbidity, as well as a very low proportion of participants without any GS, are still remarkable, as this remains a relatively young population. Particularly, the observed prevalence of conditions such as disability for mobility could point to how frailty is being assessed as a partial explanation for its relatively low observed prevalence. Regarding the potential drivers of disability for mobility, it is proposed that several conditions may interact with each other and influence the development of the outcome. For instance, HIV-related factors (chronic viremia), chronic immune activation along with an age-related low-grade inflammation (inflammaging), as well as certain medications and comorbidities may lead to muscle damage, resulting in decline of muscle function.<sup>26,27</sup>

With respect to cognitive impairment, despite the high prevalence observed, the figure remains within the reported range for this condition in middle-aged and

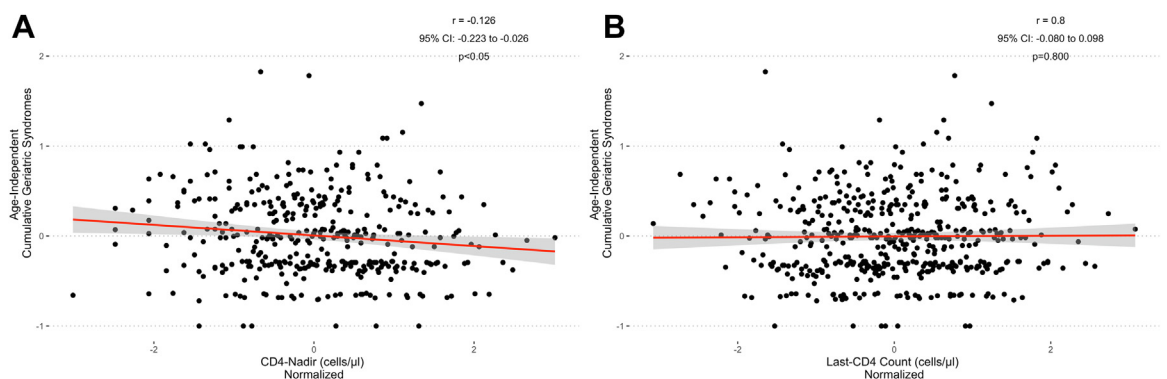


Fig. 2: Scatter plots of CD4-nadir and Last CD4 count against age-independent cumulative geriatric syndromes score.



Model	Parameter	Beta coefficient	95% CI	T value	p value
Age-independent cumulative geriatric syndromes $\chi^2(5) = 4.03$ ( $p < 0.01$ ) $R^2 = 0.06$ AIC: 513.81	CD4+ nadir	-0.058	-0.109 to -0.007	-2.40	0.03
	Current CD4+ counts	0.0148	-0.0368 to -0.0645	0.53	0.59
	Viral load	0.0001	-0.001 to 0.001	0.001	0.99
	Men	0.109	-0.014 to 0.233	2.55	0.08
	Age of school	0.006	-0.001 to 0.0147	0.02	0.13
	Number of comorbidities	0.092	0.056-0.128	5.09	<0.001

CD4-Nadir, CD4-last count, and HIV RNA were transformed using the ordered quantile normalizing equation.

**Table 2: Linear regression models to predict age-independent cumulative geriatric syndromes using CD4+ nadir, current CD4+ cell counts, and viral load adjusted for sex and age of school.**

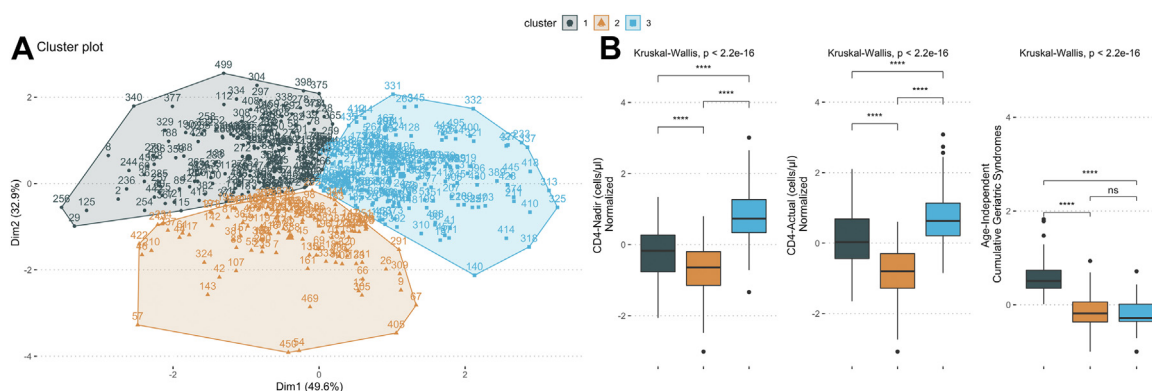
older people with HIV. Cognitive complaints and cognitive impairment remain a relatively frequent condition in the cART era; for instance, the reported prevalence of HIV-associated neurocognitive disorder (HAND) remains in the range of 15–50%. However, mild forms of HAND currently represent the majority of cases.<sup>28</sup>

Moreover, the elevated prevalence of GS in this study would appear to a certain extent, not only independent of chronological age and associated to adverse clinical HIV profiles, but also, associated to a high burden of comorbidities, considering the observed results for the AICGS scores and cluster analyses. If we break down the profiles for the three identified clusters, a major difference between them is the proportion of participants with two or more metabolic diseases. Clusters 1 and 2 evidenced participants with relatively similar HIV-related markers, with different age profiles (although only by approximately two years), but more importantly, with a marked difference in metabolic conditions and had AICGS scores that went in opposite senses. Lower scores observed in the cluster with a lower burden of metabolic diseases (cluster 2), even in the presence of the lowest CD4+ cell nadirs; and the highest AICGS scores observed in the cluster with the highest proportions of metabolic diseases (cluster 1). Cluster 1 even

included relatively younger participants. In the same direction, cluster 3 evidenced younger participants, with fewer comorbidities, better HIV-related markers and low AICGS scores, which could be interpreted as a decreased accelerated aging attributable to a better HIV profile.

These results not only support the existing literature on a higher prevalence, or earlier onset of geriatric syndromes in people with HIV, but may also suggest that to some extent, the presence of metabolic diseases also participates in their development.<sup>9,29</sup> The associations between metabolic diseases, particularly diabetes, and the development of GS such as frailty and dementia, as well as their common metabolic pathways, have been the subject of numerous studies.<sup>30,31</sup>

Finally, another noteworthy finding was that in the performed regressions analyses only the CD4+ nadir, showed an inverse and significant correlation with the AICGS score. This finding keeps pointing to the growing evidence of the potential role that the immune system has on the development of age-related conditions in the context of HIV.<sup>3,32</sup> Perhaps, the point at which we start an intervention (i.e., cART) could also have an effect on the aging trajectory. Potentially being the persons who coexist for longer periods with worse disease markers, the ones who may biologically behave like



**Fig. 3: Cluster characterization using PCA-cluster plot (A) and boxplot of its distribution of cluster components (B).**

older individuals (i.e., a higher proportion of falls in participants with a history of lower CD4+ nadirs) was proposed by other studies.<sup>21,29,33</sup>

The findings of the present study highlight the importance of promoting GS screening in people with HIV, likewise, that an appropriate control of highly prevalent conditions, such as metabolic diseases, could play a role in their prevention. It seems that, regardless of age, there are always interventions available to promote healthier aging trajectories and thus prevent as much as possible prolonged exposures to comorbidities and GS.

The fact that a higher prevalence of GS in older persons with HIV is already described, the cross-sectional design, which precludes establishing causality or risk prediction, the issue of multiple comparisons for some of the results, and the lack of information concerning time since HIV diagnosis, history of poor HIV control (only the nadir of CD4+ cells), antiretroviral drug classes, or the history of tuberculosis (TB), and TB treatment agents can be considered as limitations of this study. These latter factors may contribute, for instance, to low-grade chronic inflammation, and thus may have an impact on the outcomes studied. In terms of external validity, our results might only be comparable with cities with relatively similar socio-sanitary characteristics (e.g. Latin America). Likewise, the results may not be fully representative of the Mexican states nor its cities, as only one site per city was included. Similarly, the five cities are also different in terms of their socio-demographic conditions, and their economic and health indicators are heterogeneous. For example, regarding their population, it ranged from ≈378,000 inhabitants (Cuernavaca) to ≈9.2 million inhabitants (Mexico City) in 2020.<sup>34</sup> Moreover, although the evaluation was conducted in outpatient clinics with similar follow-up programs, each center's infrastructure was not the same (two outpatient clinics, two general hospitals and one tertiary care center), Supplementary Material—Table S4. Finally, convenience sampling can be subject to selection bias, i.e., the inclusion of healthier or more motivated participants.

However, we should emphasize several strengths, such as the sample size, the multi-centric study approach focused on community-dwelling individuals, as well as the robust analyses (data-driven approach) and finally, the fact that this is the first study of its kind in the country. Which is not only a relevant contribution to the local epidemiology of this topic, but also allows the promotion of public health policies on this population, since it evidences a problem that we are probably not addressing.

### Conclusions

This multicentric study of older persons with HIV in Mexico found an elevated prevalence of GS, which continues to support concepts such as an accentuated

aging in this population. One of the main contributions of the study's findings is that an accumulation of GS was associated to adverse clinical profiles related to HIV trails, independently of age, particularly in people with a high burden of metabolic diseases. These results emphasize the importance of integrating strategies for early detection of geriatric syndromes in individuals living with HIV while maintaining a strong focus on metabolic health, healthy aging, and beyond.

### Contributors

VHR and JAAF designed, drafted and revised the manuscript, and directly accessed and verified the underlying data reported in the manuscript.

NEAV performed statistical analysis/data interpretation, and contributed to manuscript drafting and revisions.

BECR, PFBZ, YKV, FB, and HE contributed equally to critical analysis, data interpretation and edition.

### Data sharing statement

The dataset presented in this article is not readily available as it is property of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Requests to access the dataset should be directed to: [alberto.avilaf@incmnsz.mx](mailto:alberto.avilaf@incmnsz.mx). R code is accessible in: [https://github.com/neftalivilla/GS\\_Clusters\\_HIV](https://github.com/neftalivilla/GS_Clusters_HIV).

### Declaration of interests

The authors have no conflict of interest to disclose.

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### Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lana.2023.100502>.

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