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The prevalence of comorbidities and differences in noncommunicable diseases and nonrandom associations of comorbidities between HIV-infected and -uninfected individuals in Guangdong Province, China

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Abstract

Background Globally, uncertainty persists regarding the prevalence of comorbidities in noncommunicable diseases (NCDs) among people living with HIV (PLWH) compared those without HIV. This uncertainty extends to the degree of nonrandom associations between comorbidities in both populations, particularly in resource-limited settings.

Methods This cross-sectional study involved 343 HIV-infected individuals (cases) and 686 HIV-uninfected counterparts (controls), with a 1:2 individual matching ratio. Nonrandom associations between comorbidities were assessed using Somers' D statistic.

Results Comorbidity prevalence was significantly higher in cases (48.7%, 95% confidence interval [CI]: 43.4%-54.0%) than in controls (26.8%, 95% CI: 23.5%-30.1%). Cases exhibited more comorbidities than controls (6 and 4, respectively). Depression, cardiovascular diseases, chronic liver disease, chronic kidney disease, and chronic renal insufficiency were more prevalent among cases (25.7%, 7.9%, 11.1%, 3.5%, 2.0%, respectively) compared to controls. No significant differences were observed in the prevalence of diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and musculoskeletal disorders between the two populations (cases: 7.9%, 12.5%, 0.3%, 6.4%, respectively; controls: 5.1%, 15.6%, 0.1%, 3.9%, respectively). Nonrandom associations between comorbidities were statistically significant in both groups, with Somers' D values ranging from 0.101 to 0.982 in cases and from 0.102 to 0.472 in controls.

Conclusions The HIV-infected population demonstrates a higher prevalence of comorbidities compared to the HIV-uninfected population. Nonrandom associations between comorbidities exist in both populations, with stronger associations observed among PLWH.

Keywords HIV, Noncommunicable diseases, Comorbidities, Prevalence, Nonrandom associations, Guangdong Province, China

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Background

The HIV epidemic landscape has undergone significant transformations across numerous countries and regions [1], including China [2], since the initial spread of HIV and the advent of combination antiretroviral therapy (ART). The efficacy of ART in suppressing HIV replication has led to a marked decrease in mortality and a substantial increase in life expectancy among HIV-infected patients. Consequently, HIV has evolved into a chronic condition, with many patients requiring lifelong ART [3, 4]. In recent years, a notable demographic shift has emerged, with a growing proportion of newly diagnosed HIV patients being over 50 years old in some countries. In China, this group accounts for approximately one-fifth or more of new cases [5]. This trend has resulted in an increase prevalence of age-related noncommunicable diseases (NCDs), also referred to as chronic comorbidities [6] among the aging HIV-infected population. HIV-infected adults tend to develop NCDs at younger ages compared to their counterparts in the general population (HIV-uninfected individuals with similar sociodemographic characteristics) [7]. There remains a paucity of comprehensive data regarding the prevalence of all chronic comorbidities in this population, particularly in low- and middle-income countries, despite the conduct of studies focusing on specific conditions or groups of disorders such as diabetes mellitus, hypertension, and cardiovascular diseases (CVD) in HIV-infected populations with or without ART.

Overall, the global comparison of NCDs prevalence between HIV-infected populations and their corresponding general population remains inconclusive [8–11]. Some studies suggest a higher prevalence of common comorbidities among HIV-infected adults compare to the general population [7, 11]. This disparity may be attributed to the combined effects of persistent HIV-related immune activation, inflammation, and long-term ART exposure, in addition to general factors such as age, sex, behavioral factors, and related diseases [12–15]. However, other studies have reported similar [16] or even lower [17] prevalence of certain comorbidities in the HIV-infected populations, potentially due to methodological factors including unmatched case–control designs [18], limited sample sizes, characteristics of the HIV epidemic, age distribution of newly infected patients, and duration of ART.

Furthermore, HIV-infected adults exhibit a predisposition to certain chronic comorbidities [7, 10, 19, 20], including diabetes mellitus, hypertension, and dyslipidemia. Moreover, there may be nonrandom associations between these chronic comorbidities [21, 22]. Understanding the degree of these nonrandom associations could reveal patterns of high-frequency comorbidities, enabling targeted interventions and informing the development of prevention, treatment, and management strategy for HIV and chronic conditions in countries with disease-oriented health systems. Such insights could contribute to more appropriate condition management and improved health-related quality of life. However, to our knowledge, there are only two studies have explored nonrandom associations between comorbidities in HIV-infected adults.

These research questions are equally pertinent in China, despite the existence of 16 studies (nine in Chinese and seven in English) investigating the prevalence of several common comorbidities. These studies encompass multicenter clinical trials, cross-sectional studies, and a three-year cohort study of HIV-infected adults aged 18 years and older. Notably, there is a dearth of research on comorbidities among HIV-infected individuals from Guangdong province. To address these knowledge gaps in the context of HIV and aging, this cross-sectional study employs a 1:2 individual matching for cases and controls. The primary objectives are to: (1) explore the prevalence of chronic comorbidities among the HIV-infected adults aged 45 years and older; (2) determine whether the prevalence is higher among HIV-infected individuals compared to the corresponding general population; (3) investigate the degree of nonrandom associations between comorbidities in both populations. It is important to note that this study does not explore risk factors for age-related comorbidities in both matched populations.

Methods

Subjects, study design, and sampling methods

This study employed a cross-sectional design with cases and controls (HIV-uninfected individuals). Cases were HIV-infected individuals aged 45 years and older on ART, recruited through convenience sampling from an investigation of chronic conditions at Guangdong Center for Diagnosis and Treatment of AIDS. Controls were selected from the general population through a four-stage stratified random sampling from Guangdong Province, who participated in China's fifth national health service survey (CNHSS) in 2013. The sampling stages included counties (districts), towns, villages and households. We implemented a 1:2 individual matching strategy for cases and controls based on same age, sex and current city of residence. When a match couldn't be found, controls were replaced by subjects from an adjacent city and unrepeated households. Ultimately, we matched 2 controls per case due to the relatively small sample size of controls.

Collection

We initially included 432 cases between February 26 to April 20 and August 6 to September 29, 2021, to investigate the prevalence of chronic comorbidities [6], perceptions of chronic comorbidities and psychosocial conditions. After rigorous quality control measures, 343 cases were included in the final analysis. The quality control process involved excluding cases with incomplete required items (15), illogical matrix responses (27), outliers in significant variables (23), and missing values for most chronic conditions (24, Fig. 1). Importantly, no significant differences were found between the 24 cases and the 343 included cases in the main characteristics (detailed in supplementary table S1). For controls, we analyzed 686 matched individuals. There were selected from 31,795 individuals aged 45 to 79 years (out of 81,859 members in 24,129 households) who participated the fifth CNHSS in 2013. They were matched 1:2 to the 343 cases based on age, sex, and current city of residence, with one member per household selected and matched.

Measures

Comorbidities [6] in cases and controls were primarily self-reported chronic conditions diagnosed by doctors, supplemented by medical records (ICD-10) for consenting cases from the designated hospital. Trained investigators recorded the chronic conditions of controls using a 133-item classification system based on human body systems. We included 22 conditions for cases and 13 for controls. Nonrandom associations were analyzed for 12 conditions, as chronic obstructive pulmonary disease (COPD) was unreported in controls. Case comorbidities were selected based on their impact of functioning, quality of life, and treatment burden [23], as there is no consensus definition for comorbidities among people living with HIV (PLWH). Our primary inclusion criteria for the 22 and 13 conditions were: (1) common NCDs: CVD, metabolic disorders (diabetes mellitus, hypertension, dyslipidemia, kidney diseases), mental health conditions (specifically depression), and cancer; (2) conditions significantly impacting quality of life or with high treatment burden: liver disease, musculoskeletal disorders, and COPD; (3) data availability. We calculated overall prevalence, prevalence of various conditions, and the number of chronic comorbidities among subjects. Somers' D statistic was used to measure nonrandom associations between comorbidities.

Depression in cases was defined using the Geriatric Depression Scale (GDS)-15 [24] with a cut-off value of 5. For controls, depression was assessed through a structured questionnaire item regarding depression or anxiety experienced that day, with response options of no, moderate, or major. Dyslipidemia data was not collected for controls.

Smoking status was categorized as current or previous smoking. Alcohol consumption was a binary variable (yes/no). We calculated ART duration for cases by comparing investigation dates with initial ART treatment dates from China's web-based HIV/AIDS comprehensive response information management system. ART duration (years) was divided into four groups: 0.1–2, 2.1–5, 5.1–10, and 10.1–17 years, based on ART impacts on patients [10, 25] and long-term exposure effects [26].

Statistical analysis

We employed means and standard deviations (SD) for normally distributed quantitative variables, and frequencies and proportions with 95% confidence intervals (CIs) for qualitative variables. For group comparisons, we utilized chi-square or Fisher exact tests for categorical variables, Wilcoxon rank-sum or Kruskal–Wallis tests for ordinal variables, and analysis of variance for quantitative variables. The linear and nonlinear comorbidity trends by age and ART duration were analyzed using Cochran-Armitage test [27]. Associations between comorbidities were assessed using Somers' D statistic [21, 28], with *P*-values calculated through permutation method with 100 permutation iterations [29]. The significance of these Somers' D statistics was evaluated using the Benjamini–Hochberg procedure [30] to control the false discovery rate (FDR) at 0.05. Statistical tests were two-side with $\alpha = 0.05$. Statistical analyses were performed using R version 4.2.3.

To address group imbalances, we implemented a propensity score matching (PSM) based on nine characteristics: age, sex, current city of residence, body mass index (BMI), education, marital status, employment, current smoking, and alcohol consumption. Age, sex, and residence were exactly matched due to their strong correlation with NCDs. Propensity scores were calculated using a logistic model with nearest-neighbor matching (MatchIt package, clipper = 0.05, matching ratio = 1:2). While PSM results (detailed in supplementary tables S2-S6) were comparable to 1:2 individual matching, we selected the latter for main analysis due to its higher precision in prevalence estimate.

We performed sensitivity analysis using multiple imputation (mice package) with 5 imputations based on random forest methodology to assess the impact of missing NCDs data ($n = 24$). Results indicated negligible effects on overall prevalence (S7). Complete methodological details and study timeline are available in the supplementary material.

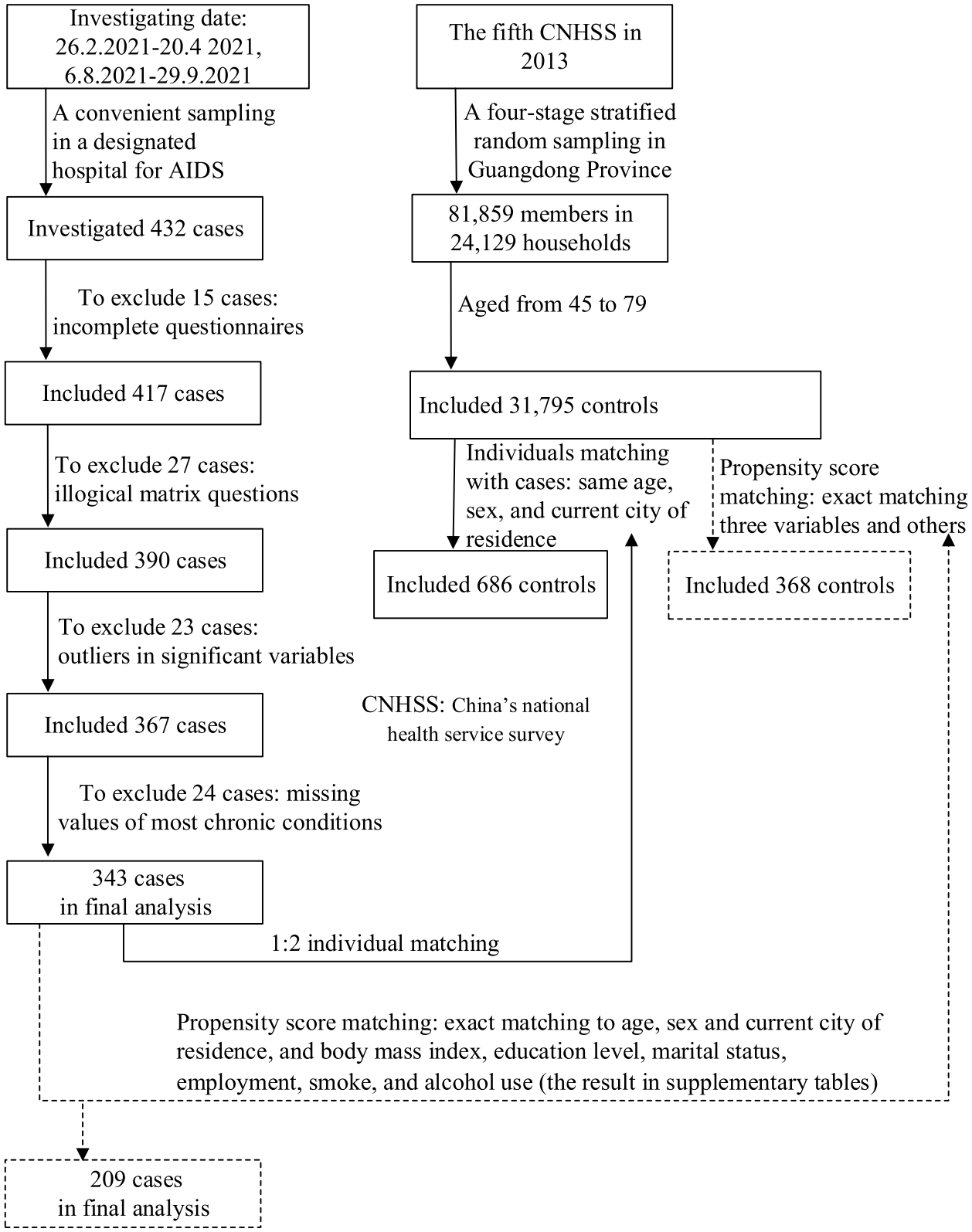

Fig. 1 The flowchart of quality control of the data and individual matching between cases and controls

Results

Population characteristics

The 343 matched cases, aged 45 to 79 years, had a mean (SD) age of 52.9 (7.4) years, with 80.2% male and 60.1% residing in Guangzhou city (Table 1). Significant differences between cases and controls were found in marital status (chi-square = 115.33, $P < 0.001$), education level ($Z = 2.84$, $P = 0.002$), and employment status (chi-square = 20.83, $P < 0.001$), but not in BMI ($F = 2.51$, $P = 0.11$). Cases had lower rates of marriage and employment, but slightly higher education levels. Notably, 22.4% of cases reported no monthly income.

Behavioral characteristics differed in current smoking (chi-square = 6.96, $P = 0.008$) and previous smoking (chi-square = 10.18, $P < 0.001$), but not alcohol consumption (chi-square = 0.38, $P = 0.538$). Current smoking was less prevalent among cases (35.2% vs 44.5%), while ex-smoking was more common (17.6% vs 8.8%). The mean (SD) ART duration was 6.4 (3.8) years, ranging from 0.1 to 17 years.

Prevalence of comorbidities

Table 2 illustrates the prevalence of comorbidities in both populations. Cases exhibited a higher overall prevalence of comorbidities (48.7%, 95% CI: 43.4%−54.0%) compared to controls (26.8%, 95% CI: 23.5%−30.1%), with a greater number of comorbidities (6 vs 4). Among cases, the most prevalent conditions were depression (25.7%, 95% CI: 21.0%−30.2%), dyslipidemia (19.0%, 95% CI: 14.8%−23.1%), hypertension (12.5%, 95% CI: 9.0%−16.0%), chronic liver diseases (CLD, 11.1%, 95% CI: 7.8%−14.4%), diabetes mellitus (7.9%, 95% CI: 5.0%−10.7%), and CVD (7.9%, 95% CI: 5.0%−10.7%). For controls, hypertension (15.6%, 95% CI: 12.9%−18.3%) and diabetes mellitus (5.1%, 95% CI: 3.5%−6.8%) were most prevalent.

Significant differences between cases and controls were observed in the prevalence of depression, CVD, CLD, chronic kidney disease (CKD), and chronic renal insufficiency, with cases showing higher rates. However, no significant differences were found in diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), and musculoskeletal disorders (MD).

Notably, CLD (11.1%, 95% CI: 7.8%−14.4%) and CKD (3.5%, 95% CI: 1.6%−5.4%) were reported among cases but not controls. Depression were markedly higher in cases (25.7%) compared to controls (2.9%) (chi-square = 125.88, $P < 0.001$). Among CVD, a significant difference was found in heart diseases (HD, chi-square = 9.55, $P = 0.002$), but not in myocardial infarction, cerebrovascular conditions, and peripheral vascular conditions. Cancer prevalence was higher in cases (1.7%, 95% CI: 0.4%−3.1%) than controls (0.3%, 95% CI: 0.0−0.7%).

Subgroup analysis

Table 3 presents comorbidity prevalence by age, sex and ART durations. A linear trend was observed between age groups and total comorbidity prevalence in both populations, with cases consistently showing higher rates across all age groups ($Z = -3.12$, $P = 0.001$ among cases; $Z = -6.62$, $P < 0.001$ among controls). Prevalence ranged from 42.5% to 66.6% in cases and 17.3% to 52.8% in the controls across age groups. Both male and female cases had higher comorbidity prevalence than controls (chi-square = 39.13, $P < 0.001$; chi-square = 8.57, $P = 0.003$), with female showing higher rates than male in both populations.

A nonlinear trend was observed between ART duration and comorbidity prevalence ($Z = -3.67$, $P = 0.0002$), ranging from 30.6% to 73.6% across durations. Hypertension prevalence differed significantly between populations in non-smokers (chi-square = 4.12, $P = 0.042$) but not in smokers (chi-square = 0.05, $P = 0.819$). Supplementary Table 8 (S8) shows no significant difference in ART duration distribution by age group (a Kruskal–Wallis test, chi-square = 1.26, $P = 0.738$).

Nonrandom associations between comorbidities

Table 4 and 5 illustrate nonrandom associations between comorbidities in both populations, with Somers' D statistics consistently larger for cases than controls across all nonrandom associations. For cases, which included 22 chronic conditions, the cut-off value was 0.101, with associations ranging from 0.101(chronic kidney insufficiency and fatty liver disease (FLD)) to 0.982 (kidney atrophy and cerebrovascular disease (CBVD)). Notable associations among cases included kidney atrophy and hypohepatia (0.968), dyslipidemia and gout (0.813), and depression with hypertension (0.880) and COPD (0.746). Depression also showed strong associations with metabolic diseases. For controls, which included 12 chronic conditions, the cut-off value was 0.102, with associations ranging from 0.102 (depression and diabetes mellitus) to 0.472 (depression and CKD). Notable associations among controls included CVD with diabetes mellitus, hypertension and depression (Somers' D > 0.300).

Discussion

The prevalence of all comorbidities among PLWH from Guangdong Province, China, was higher than that in the general population matched by same age, sex and current city of residence, and the number of comorbidities was larger in the HIV population. The prevalence of common comorbidities except diabetes mellitus

Table 1 Population characteristics of this cross-sectional case–control study in Guangdong Province, China

Population Characteristics	Cases (HIV-infected) (n = 343)	Controls (HIV-uninfected) (n = 686)	Chi-square/*Z*/*F*	*P* value
Sociodemographic status				
Age (mean ± SD.), n (%)	52.9 ± 7.4	52.9 ± 7.4	-	-
45 to 49	153 (44.6)	306 (44.6)		
50 to 59	132 (38.5)	264 (38.5)		
60 to 69	40 (11.7)	80 (11.7)		
70 to 79	18 (5.2)	36 (5.2)		
Sex, n (%)			-	-
Male	275 (80.2)	550 (80.2)		
Female	68 (19.8)	136 (19.8)		
Current address, n (%)			-	-
Guangzhou	206 (60.1)	412 (60.1)		
Others in Guangdong	137 (39.9)	274 (39.9)		
Marital status, n (%)			115.33	< 0.001
Not married	49 (14.3)	26 (3.8)		
Married	228 (66.5)	634 (92.4)		
Divorced or widowed	49 (14.3)	26 (3.8)		
Others	17 (4.9)	0 (0.0)		
Education level, n (%)			2.84	0.002
Illiterate	8 (2.3)	19 (2.8)		
Primary	61 (17.9)	179 (26.1)		
Secondary	133 (39.0)	238 (34.7)		
High school	74 (21.7)	167 (24.3)		
College or university and over	65 (19.1)	83 (12.1)		
Missing	2	-		
Employment status, n (%)			20.83	< 0.001
No	83 (24.3)	96 (14.0)		
Yes	205 (59.9)	501 (73.0)		
Student	54 (15.8)	89 (13.0)		
Missing	1	-		
Income per month ($), n (%)			-	-
0	77 (22.9)			
0 to 139	13 (3.9)			
140 to 419	73 (21.7)			
420 to 839	114 (33.9)			
840 to 1395	28 (8.4)			
> 1395	31 (9.2)			
Missing	7			
BMI (mean ± SD.), n (%)	22.7 ± 3.0	23.0 ± 2.9	2.51	0.114
< 18.5	21 (6.1)	34 (4.9)		
18.5 to 23	225 (65.6)	421 (61.4)		
24 to 28	75 (21.9)	197 (28.7)		
> 28	22 (6.4)	34 (5.0)		
Health risk behavior				
Current smoking, n (%)			6.96	0.008
No	220 (64.1)	381 (55.5)		
Yes	123 (35.9)	305 (44.5)		
Previous smoking, n (%)			10.18	0.001
No	178 (82.4)	344 (91.2)		
Yes	38 (17.6)	33 (8.8)		

Table 1 (continued)

Population Characteristics	Cases (HIV-infected) (n = 343)	Controls (HIV-uninfected) (n = 686)	Chi-square/*Z*/*F*	*P* value
Alcohol consumption, n (%)			0.38	0.538
No	239 (69.7)	465 (67.8)		
Yes	104 (30.3)	221 (32.2)		
Duration of ART (years, mean ± SD.), n (%)	6.4 (3.8)	-	-	-
0.1 to 2	49 (14.7)			
2.1 to 5	80 (23.9)			
5.1 to 10	147 (44.0)			
10.1 to 17	58 (17.4)			
Missing	9			

BMI denotes body mass index, as classified by the Asian standard. ART denotes antiretroviral treatment. NCDs denote noncommunicable diseases. *Z* denotes the statistic of a Wilcoxon rank-sum test, *F* denotes the statistic of analysis of variance

and hypertension, such as CVD, CLD, CKD, and cancer, in the HIV population was also higher than that of the general population. Furthermore, the prevalence of subgroups including age group and sex were higher in the HIV population, and the prevalence of comorbidities showed a linear trend with age group in both populations. Nonrandom associations between comorbidities were all significant in both populations, were higher for FLD and dyslipidemia with other comorbidities in the HIV population, respectively, and were higher for rheumatism and other comorbidities in the general population.

Our findings align with previous matched studies showing higher comorbidity prevalence in HIV-infected populations [7, 11, 31]. Differences in prevalence among common comorbidities were similar in both populations [25, 32–34] and higher in the HIV-infected group. However, we found no significant differences in the prevalence of hypertension, diabetes mellitus, and COPD in both populations. This result differs from some studies [18, 20, 35] reporting higher prevalence in HIV-infected populations [35] but aligns with others [8, 9, 36]. Older age at HIV diagnosis and long-term ART exposure (> 60% of patients with ART duration exceeding 5 years) may partially explain these findings [25, 26].

Age and sex differences in comorbidity prevalence were observed, with higher prevalence in the HIV-infected population cross all categories. A linear trend of increasing prevalence with age was noted in both populations, consistent with the nature of chronic conditions. Interestingly, females showed higher prevalence than males in both populations, contrary to most studies [4, 37, 38]. This may be due to the relatively small female sample size (68 individuals, 19.8% of cases). Additionally, a nonlinear trend was observed between ART duration and comorbidity prevalence, aligning with studies showing no difference in survival for HIV-infected patients with long-term ART exposure [26].

Nonrandom associations between comorbidities were observed in both populations, with larger Somers' D in the HIV-infected population. This could be attributed to two factors: specific risk factors for chronic comorbidities in HIV-infected adults, including persistent HIV-related inflammation and long-term ART exposure [13, 14, 39–41], in addition to general factors such as age, sex, smoking history, and the greater number of comorbidities among cases compared to controls.

While our results are specific to Guangdong Province, China, we believe that the profile of NCDs among PLWH may be similar in other regions with comparable HIV epidemics. Our study provides three key insights: (1) approximately more than half of PLWH aged 45 years and above are affected by NCDs; (2) NCDs prevalence is higher in PLWH than in HIV-uninfected counterparts; (3) NCDs in PLWH tend to cluster to some extent. These findings have important practical implications for managing HIV in the context of aging: (1) the management of PLWH should transition from a disease-oriented approach to a people-oriented one, with a focus on extending the healthy life expectancy of PLWH; (2) NCDs management of PLWH should integrate into China's National Basic Public Health Services Program [42]; (3) clinical practice should emphasize: enhance screening for NCDs, promotion of healthy lifestyles, and comprehensive care that goes beyond ensuring the effectiveness of ART. By implementing these strategies, healthcare providers and policymakers can address the complex health needs of aging PLWH more effectively, potentially improving their overall quality of life and long-term health outcomes. This holistic approach recognizes the

Table 2 The prevalence of comorbidities with noncommunicable diseases in this study in Guangdong province, China

Comorbidities, n (%, 95% CI)	Cases (HIV-infected) ($n=343$)	Controls (HIV-uninfected) ($n=686$)	Chi-square/Z	P value
NCDs	167 (48.7, 43.4–54.0)	184 (26.8, 23.5–30.1)	48.64	< 0.001
Number of NCDs			7.52	< 0.001
0	176 (51.3)	502 (73.2)		
1	101 (29.5)	137 (20.0)		
2	34 (9.9)	36 (5.2)		
3	21 (6.1)	10 (1.5)		
4	11 (3.2)	1 (0.1)		
Depression			125.88	< 0.001
No	255 (74.3)	666 (97.1)		
Yes	88 (25.7, 21.0–30.2)	20 (2.9, 1.7–4.2)		
Diabetes mellitus			3.10	0.078
No	316 (92.1)	651 (94.9)		
Yes	27 (7.9, 5.0–10.7)	35 (5.1, 3.5–6.8)		
Hypertension			1.72	0.190
No	300 (87.5)	579 (84.4)		
Yes	43 (12.5, 9.0–16.0)	107 (15.6, 12.9–18.3)		
CVD			20.32	< 0.001
No	316 (92.1)	672 (98.0)		
Yes	27 (7.9, 5.0–10.7)	14 (2.0, 1.0–3.1)		
HD	16 (4.7, 2.4–6.9)	10 (1.5, 0.6–2.4)	9.55	0.002
MI	2 (0.6, 0.0–1.4)	2 (0.3, 0.0–0.7)	-	0.604*
CBVD	7 (2.0, 0.5–3.5)	3 (0.4, 0.0–0.9)	-	0.019*
PVD	6 (1.7, 0.4–3.1)	2 (0.3, 0.0–0.7)	-	0.019*
Dyslipidemia		…	-	-
No	278 (81.0)			
Yes	65 (19.0, 14.8–23.1)			
CLD			78.91	< 0.001
No	305 (88.9)	686 (100.0)		
Yes	38 (11.1, 7.8–14.4)	0 (0.0)		
Hypohepatia	12 (3.5, 1.6–5.4)	-		
FLD	15 (4.4, 2.2–6.5)	-		
LC	13 (3.8, 1.8–5.8)	-		
CRI			-	0.0004*
No	336 (98.0)	686 (100.0)		
Yes	7 (2.0, 0.5–3.5)	0 (0.0)		
CKD			-	< 0.001*
No	331 (96.5)	686 (100.0)		
Yes	12 (3.5, 1.6–5.4)	0 (0.0)		
KA			-	0.333*
No	342 (99.7)	686 (100.0)		
Yes	1 (0.3, 0.0–0.9)	0 (0.0)		
MD			3.10	0.078
No	321 (93.6)	659 (96.1)		
Yes	22 (6.4, 3.8–9.0)	27 (3.9, 2.5–5.4)		
Osteoporosis	8 (2.3, 0.7–3.9)	0 (0.0)	-	-
Rheumatism	2 (0.6, 0.0–1.4)	5 (0.7, 0.1–1.4)	-	-
Gout	2 (0.6, 0.0–1.4)	0 (0.0)	-	-
CS	3 (0.9, 0.0–1.9)	0 (0.0)	-	-
LS	7 (2.0, 0.5–3.5)	12 (1.7, 0.7–2.7)	-	-

Table 2 (continued)

Comorbidities, n (%, 95% CI)	Cases (HIV-infected) ($n=343$)	Controls (HIV-uninfected) ($n=686$)	Chi-square/Z	P value
ONFH	2 (0.6, 0.0–1.4)	0 (0.0)	-	-
SP	2 (0.6, 0.0–1.4)	0 (0.0)	-	-
COPD			-	1.000*
No	342 (99.7)	685 (99.9)		
Yes	1 (0.3, 0.0–0.9)	1 (0.1, 0.0–0.4)		
Cancer			-	0.019*
No	337 (98.3)	684 (99.7)		
Yes	6 (1.7, 0.4–3.1)	2 (0.3, 0.0–0.7)		

CI denotes a confidence interval. NCDs denotes noncommunicable diseases. CVD denotes cardiovascular diseases. HD denotes heart diseases. MI denotes myocardial infarction. CBVD denotes cerebrovascular conditions. PVD denotes peripheral vascular diseases. CLD denotes chronic liver disease. FLD denotes fatty liver disease. LC denotes liver cirrhosis. CRI denotes chronic renal insufficiency. CKD denotes chronic kidney disease. KA denotes kidney atrophy. MD denote musculoskeletal disorders. CS denotes cervical spondylosis. LS denotes lumbar spondylosis. ONFH denotes osteonecrosis of the femoral head. SP denotes scapulohumeral periarthritis. COPD denotes chronic obstructive pulmonary disease. Z denotes the statistic of a Wilcoxon rank-sum test. *denotes probability of a Fisher's exact test

Table 3 Prevalence of chronic comorbidities among cases and controls in Guangdong province, China

Characteristics, n (%)	Cases		Controls		Chi-square/Z	P value
	Yes (n = 166, 48.4%)	No (n = 177, 51.6%)	Yes (n = 184, 26.8%)	No (n = 502, 73.2%)		
Age*†, n (%)						
45 to 49	65 (42.5)	88 (57.5)	53 (17.3)	253 (82.7)	33.82	< 0.001
50 to 59	60 (45.5)	72 (54.5)	73 (27.6)	191 (72.3)	12.5	< 0.001
60 to 69	29 (72.5)	11 (27.5)	39 (48.7)	41 (51.3)	6.13	0.013
70 to 79	12 (66.7)	6 (33.3)	19 (52.8)	17 (47.2)	0.85	0.331
Sex‡, n (%)						
Male	129 (46.9)	146 (53.1)	139 (25.3)	411 (74.7)	39.13	< 0.001
Female	37 (54.4)	31 (45.6)	45 (33.1)	91 (66.9)	8.57	0.003
ART duration (year, mean ± SD.) *, n (%)	7.3 (4.1)	5.6 (4.8)	-	-	-3.67	0.0002
0.1 to 2	15 (30.6)	34 (69.4)			6.87	0.032
2.1 to 5	39 (48.7)	41 (51.3)				
5.1 to 10	67 (45.6)	80 (54.4)				
10.1 to 17	42 (72.4)	16 (27.6)				
Missing	3	6				

ART denotes antiretroviral treatment. * denotes the Cochran-Armitage test for trend, including a linear trend or not. There is a linear trend between age and proportions of chronic comorbidities, $Z=-3.12$, $P=0.001$ among cases, $Z=-6.62$, $P<0.001$ among controls. There was a nonlinear trend between the duration of ART and proportions of chronic comorbidities among the cases ($Z=-3.67$, $P=0.0002$; chi-square = 6.87, 2 of a degree of freedom, $P=0.032$) because the chi-square value from a part of nonlinear is also a statistical significance. † denotes a significance level alpha of 0.05/4 by a Bonferroni correction. ‡ denotes a significance level alpha of 0.05/2 by a Bonferroni correction

interconnected nature of HIV and NCDs, paving the way for more integrated and patient-centered care models.

Our study has four main limitations. First, the study design lacks an HIV-infected ART-naïve population to differentiate between the HIV and ART impacts on comorbidities in patients. Second, the inclusion criteria for NCDs was limited due to age and treatment burden considerations, though the impact of excluded NCDs on our findings is minimal. Our inclusion criteria have been carefully designed to capture the most relevant and impactful conditions affecting this population. These criteria ensure that our study captures a range of conditions of NCDs particularly relevant to the HIV-positive population while also considering the practical aspects of data collection. The selected conditions provide a comprehensive representation of the NCDs comorbidity profile among PLWH, particularly in the context of aging.

Third, it is important to acknowledge that the prevalence of NCDs reported in our study may be somewhat lower than the actual rates due to the reliance

Table 4 Somers' D statistics for 22 chronic comorbidities in HIV infections in Guangdong Province, China

NCDs	Depression	Diabetes	Hypertension	HD	CBVD	PVD	Dyslipidemia	Hypohepatia	FLD	LC	CKI	CKD	KA	COPD	Osteoporosis	Rheumatism	Gout	CS	LS	ONFH	SP	Cancer
Depression	0																					
Diabetes	0.124	0																				
Hypertension	0.026	0.025	0																			
HD	-0.007	0.049	0.393	0																		
CBVD	0.176	-0.080	0.164	-0.048	0																	
PVD	0.417	-0.080	0.212	0.292	-0.021	0																
Dyslipidemia	-0.051	0.196	0.129	0.195	-0.048	-0.193	0															
Hypohepatia	-0.007	0.005	0.216	0.038	0.110	-0.036	-0.024	0														
FLD	0.011	0.266	-0.061	0.091	-0.045	-0.045	0.360	-0.045	0													
LC	0.053	-0.002	-0.130	-0.048	0.253	-0.039	-0.117	0.047	0.034	0												
CKI	-0.116	0.357	0.310	0.098	-0.021	0.149	0.244	-0.036	0.**101**	-0.039	0											
CKD	0.080	0.177	-0.044	-0.048	-0.036	-0.036	0.322	-0.036	0.127	0.047	0.402	0										
KA	-0.257	-0.079	-0.126	-0.047	0.982	-0.018	0.813	0.968	-0.044	-0.038	-0.020	-0.035	0									
COPD	0.746	-0.079	-0.126	-0.047	-0.020	-0.018	-0.190	-0.035	-0.044	-0.038	-0.020	-0.035	-0.003	0								
Osteoporosis	0.505	0.047	0.256	0.080	-0.024	-0.024	0.062	0.092	-0.045	-0.039	-0.024	-0.036	-0.023	-0.023	0							
Rheumatism	-0.258	-0.079	-0.126	-0.047	-0.021	-0.018	-0.191	-0.035	-0.044	-0.038	-0.021	-0.035	-0.006	-0.006	-0.023	0						
Gout	0.245	-0.079	0.880	-0.047	-0.021	-0.018	0.312	-0.035	0.459	-0.038	-0.021	-0.035	-0.006	-0.006	-0.023	-0.006	0					
CS	-0.259	0.257	0.210	-0.047	-0.021	-0.018	0.145	-0.035	0.292	-0.038	0.652	0.301	-0.009	-0.009	0.313	-0.009	-0.009	0				
LS	0.176	0.211	0.018	0.098	-0.021	-0.021	-0.048	0.110	0.101	0.107	0.125	0.256	-0.020	-0.020	0.268	-0.021	-0.021	0.316	0			
ONFH	-0.258	-0.079	-0.126	0.456	-0.021	-0.018	0.312	-0.035	0.962	-0.038	-0.021	-0.035	-0.006	-0.006	-0.023	-0.006	-0.006	-0.009	-0.021	0		
SP	0.245	-0.079	-0.126	-0.047	-0.021	-0.018	0.312	-0.035	-0.044	-0.038	-0.021	0.468	-0.006	-0.006	-0.023	-0.006	-0.006	-0.009	-0.021	-0.006	0	
Cancer	0.248	-0.080	0.042	-0.047	0.149	-0.018	-0.023	-0.036	-0.045	0.131	-0.021	-0.036	-0.018	-0.018	0.146	-0.018	-0.018	-0.018	-0.021	-0.018	-0.018	0

HD denotes heart diseases. CBVD denotes cerebrovascular conditions. PVD denotes peripheral vascular conditions. FLD denotes fatty liver disease. LC denotes liver cirrhosis. CKI denotes chronic kidney insufficiency. CKD denotes chronic kidney disease. KA denotes kidney atrophy. COPD denotes chronic obstructive pulmonary disease. CS denotes cervical spondylosis. LS denotes lumbar spondylosis. ONFH denotes osteonecrosis of the femoral head. SP denotes scapulohumeral periarthritis. Bold value denotes a cut-off value from the Benjamini–Hochberg procedure to control the false discovery rate at level alpha

Table 5 Somers' D statistics for 12 chronic comorbidities in the general population in Guangdong Province, China

NCDs	Depression	Diabetes	Hypertension	HD	CBVD	PVD	CKD	Rheumatism	LS	MD	COPD	Cancer
Depression	0											
Diabetes	**0.102**	0										
Hypertension	0.097	0.317	0									
HD	0.173	0.354	0.451	0								
CBVD	0.306	-0.051	-0.157	0.320	0							
PVD	-0.029	-0.051	0.345	-0.015	-0.004	0						
CKD	0.472	-0.051	0.345	-0.015	-0.004	-0.003	0					
Rheumatism	-0.029	0.150	0.246	-0.015	-0.007	-0.007	-0.007	0				
LS	0.225	-0.052	0.181	-0.018	0.317	-0.018	-0.018	-0.018	0			
MD	0.063	-0.052	0.119	-0.016	-0.016	-0.016	-0.016	-0.016	0.075	0		
COPD	-0.029	-0.051	-0.156	-0.015	-0.004	-0.003	-0.003	-0.007	-0.018	-0.016	0	
Cancer	-0.029	0.450	-0.156	-0.015	-0.004	-0.003	-0.003	-0.007	-0.018	-0.016	-0.003	0

HD denotes heart diseases. CBVD denotes cerebrovascular conditions. PVD denotes peripheral vascular conditions. CKD denotes chronic kidney disease. CLD denotes chronic liver disease. LS denotes lumbar spondylosis. MD denote other musculoskeletal disorders, except rheumatism and LS. COPD denotes chronic obstructive pulmonary disease. Bold value denotes a cut-off value from the Benjamini–Hochberg procedure to control the false discovery rate at level alpha

on self-reported comorbidities. Although we supplemented this information with medical records from the designated hospital for PLWH, and implemented a multiple imputation for missing NCDs, there remains a possibility of underreporting and underestimation. Finally, the sample size, while not small, could benefit from including more cases, particularly female cases, to better represent the PLWH population in Guangdong Province.

Future studies should incorporate an HIV-infected ART-naïve control group to distinguish between HIV infection and ART-related effects on comorbidities. We also recommend enhancing data quality through comprehensive medical record review, standardized NCD diagnostic criteria, and larger sample sizes with improved sex representation. These methodological refinements would strengthen the validity and generalizability of findings regarding NCD patterns in HIV-infected populations.

Conclusion

Our study reveals that NCDs are highly prevalent among PLWH in Guangdong Province, with the prevalence significantly exceeding those observed in their HIV-uninfected counterparts. Importantly, we found that these NCDs tend to cluster, suggesting complex interactions between multiple health conditions in this population. Given these findings, we propose a paradigm shift in the management of PLWH towards a more holistic, people-oriented approach. This transition necessitates several key changes in clinical practice: enhanced screening protocols for NCDs, increased emphasis on promoting healthy lifestyles, and implementation of comprehensive care strategies. Our research underscores the need for further investigation into the clustering patterns of comorbidities among PLWH. Such studies could provide valuable insights into the complex interplay between HIV, aging, and NCDs, potentially uncovering new approaches to patient care.

Abbreviations

ART	Antiretroviral therapy
BMI	Body mass index
CBVD	Cerebrovascular disease
CIs	Confidence intervals
CKD	Chronic kidney disease
CLD	Chronic liver diseases
CNHSS	China's fifth national health service survey
COPD	Chronic obstructive pulmonary disease
CVD	Cardiovascular diseases
FDR	False discovery rate
FLD	Fatty liver disease
GDS	Geriatric Depression Scale
HD	Heart diseases
ICD-10	International Classification of Disease, Tenth Revision
MD	Musculoskeletal disorders
NCDs	Noncommunicable diseases
PSM	Propensity score matching
SD	Standard deviations

Supplementary Information

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Supplementary Material.

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Authors' contributions
RY conceptualized the study design, oversaw case data quality control and cleaning, conducted data analysis, prepared results, and drafted the initial manuscript. YZ participated in case collection and data cleaning. JG conceived the case investigation, provided overall study supervision, and revised the initial manuscript. All authors contributed to manuscript development and approved the final version.

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Data Availability
The data that support the study findings are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study used data from the investigation for chronic conditions of HIV-infected individuals aged 45 years and older on ART at Guangdong Center for Diagnosis and Treatment of AIDS and Guangdong Province in China's fifth national health service survey (CNHSS). The investigation of HIV-infected individuals was approved by the Medical Ethics Committee of the School of Public Health, Sun Yat-sen University (No. 2023–056). The data of CNHSS was approved by National Bureau of Statistics.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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