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Sexual orientation, gender identity and virologic failure among people with HIV: a cohort study in all of US research program

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Abstract

Background Sexual and gender minorities (SGMs) are at higher risk of HIV incidence compared to their heterosexual cisgender counterparts. Despite the high HIV disease burden among SGMs, there was limited data on whether they are at higher risk of virologic failure, which may lead to potential disease progression and increased transmission risk. The All of Us (AoU) Research Program, a national community-engaged program aiming to improve health and facilitate health equity in the United States by partnering with one million participants, provides a promising resource for identifying a diverse and large volunteer TGD cohort. Leveraging various data sources available through AoU, the current study aims to explore the association between sexual orientation and gender identity (SOGI) and longitudinal virologic failure among adult people with HIV (PWH) in the US.

Methods This retrospective cohort study used integrated electronic health records (EHR) and self-reported survey data from the All of Us (AoU) controlled tier data, version 7, which includes participants enrolled in the AoU research program from May 31, 2017, to July 1, 2022. Based on participants' sexual orientation, gender identity, and sex assigned at birth, their SOGI were categorized into six groups, including cisgender heterosexual women, cisgender heterosexual men, cisgender sexual minority women, cisgender sexual minority men, gender minority people assigned female at birth of any sexual orientation, and gender minority people assigned male at birth of any sexual orientation. Yearly virologic failure was defined yearly after one's first viral load testing, and individuals with at least one viral load test > 50 copies/mL during a year were defined as having virologic failure at that year. Generalized linear mixed-effects models were used to explore the association between SOGI and longitudinal virologic failure while adjusting for potential confounders, including age, race, ethnicity, education attainment, income, and insurance type.

Results A total of 1,546 eligible PWH were extracted from the AoU database, among whom 1,196 (77.36%) had at least one viral failure and 773 (50.00%) belonged to SGMs. Compared to cisgender heterosexual women, cisgender sexual minority women (adjusted Odds Ratio [aOR] = 1.85, 95% CI: 1.05–3.27) were at higher risk of HIV virologic failure. Additionally, PWH who were Black vs. White (aOR = 2.15, 95% CI: 1.52–3.04) and whose insurance type was Medicaid vs. Private insurance (aOR = 2.07, 95% CI: 1.33–3.21) were more likely to experience virologic failure.

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Conclusions Maintaining frequent viral load monitoring among sexual minority women with HIV is warranted because it allows early detection of virologic failure, which could provide opportunities for interventions to strengthen treatment adherence and prevent HIV transmission. To understand the specific needs of subgroups of SGMs, future research needs to examine the mechanisms for SOGI-based disparities in virologic failure and the combined effects of multi-level psychosocial and health behavior characteristics.

Keywords Sexual orientation, Gender identity, Virologic failure, HIV

Background

Sexual orientation and gender identity (SOGI) disparities in HIV are well documented in the United States (US) through national sexually transmitted infections (STI) surveillance data and population-based studies [1–3]. Due to stigma and minority stress (e.g., internalized homophobia, identity concealment, expectation of rejection, and prejudicial events), sexual and gender minorities (SGMs, i.e., individuals who identify as bisexual, asexual, intersex, gay, lesbian, queer, nonbinary, transgender, or two-spirit) are at higher risk of HIV acquisition and experiencing barriers to comprehensive health care compared to their heterosexual-cisgender counterparts, where cisgender is referred to individuals whose gender identity fully align with their sex assigned at birth [1, 2, 4, 5]. According to the 2021 STI treatment guidelines from the Center for Disease Control and Prevention (CDC), the estimated lifetime HIV infection risk among men who have sex with men (MSM) is one in six, compared with one in 253 among heterosexual women and one in 524 for heterosexual men [1]. A systematic review and meta-analysis estimated that there were nearly 1 million transgender people in the US, and 25-28% of them were HIV positive [2, 6]. Compared to transmen (individuals whose gender identity is man but with the sex assigned at birth being a female: 3.2%), HIV prevalence in transwomen (individuals whose gender identity is woman with the sex assigned at birth being a male: 14.1%) was significantly higher [2]. Additionally, studies have found that transgender individuals are less likely to be retained in HIV care than cisgender men or women [7]. Despite the high HIV disease burden among SGMs, there was limited data on whether they are at higher risk of HIV virologic failure, which occurs when the HIV viral load fails to maintain an undetectable level and is closely related to potential disease progression and increased transmission risk [8].

The Healthy People 2030 and the Institute of Medicine recommended collecting SOGI information in electronic health records (EHR) and federally funded population-level surveys to explore health disparities and meet the needs of SGM population [9, 10]. There is a compelling need to integrate multiple data sources to generate more diverse and large SGM samples, which is important to identify health inequities and design healthcare interventions or services among SGM people with HIV (PWH) [11]. The National Institutes of Health's All of Us (AoU) Research Program is a national community-engaged program aiming to improve health by partnering with one million participants, of whom more than 80% were from historically underrepresented communities in biomedical research in the US [12]. Specifically, the AoU program integrated self-reported survey data (including gender identity, sexual orientation, and sex assigned at birth) with EHR data (including gender dysphoria-related ICD code and medication information), physical measurements, and biospecimens to create a data repository [12]. This allows us to explore SOGI disparities in HIV virologic failure using diverse and large volunteer cohorts from different sources [13].

Integrating multiple datatypes (e.g., self-reported data and EHR data) from AoU, this study aims to compare HIV virologic failure burden between adult SGMs and non-SGMs in the US. We hypothesized that SGM PWH experience higher risk of virologic failure compared to non-SGM PWH.

Methods

Data sources and participants

The AoU Controlled Tier dataset included individual-level basic survey, EHR, wearables, and genomic data. All US adults (age ≥ 18 years old) who are not in prison and could provide consent to participate are eligible for participation in AoU. Participants were recruited online or through partner healthcare practitioner organizations in the US [12]. As of February 4, 2024, there have been more than 100 funded partner organizations and over 860 institutional sites to help collect measurements and samples. More than 762,000 participants have consented to join the program, and over 523,000 participants have completed the initial steps of the program, including completing the first three surveys, donating ≥ 1 biospecimen to the biobank, and providing physical measurements. This longitudinal cohort study analyzed the basic survey, conditions, drug exposures, and labs & measurement data of PWH using the most recent AoU Controlled Tier data, version 7, which includes data collected between May 31, 2017, and July 1, 2022. The protocol of the current study has been previously published [14], and the institutional review board at the University of South Carolina approved this study (Pro00124806) as a non-human Subject study.

Cohort identification

A similar method from a previous study was used to identify the HIV cohort using AoU Controlled Tier data (Version 7) [15]. Participants were identified as PWH if they met any of the following criteria: [1] responded "Yes" to the survey question "Have you ever been diagnosed with the following conditions? – HIV/AIDS" (concept ID: 1384391); [2] had positive response values for HIV screening test results (e.g., "Detected", 'HIV-positive", "Reactive", "Positive", "High", and Abnormal") or viral load test (e.g., numeric values > 200); [3] had records of HIV diagnosis codes (SNOMED Codes or International Classification of Diseases [ICD]-10 codes) in "conditions" domain and records of using HIV-related drugs in the "drug exposure" domain. Detailed information about the process of data extraction and integration for HIV cohort construction in AoU is described elsewhere [15]. Individuals without at least two viral load testing results were excluded from the current analysis because we were not able to identify their virologic failure status longitudinally, which is the primary outcome of this study.

Measures

Sexual orientation and gender identity (SOGI)

Gender identity was assessed using a combination of survey and EHR data [6, 13]. In the survey data, we identified gender minorities using responses to two questions, including [1] "What was your biological sex assigned at birth?" (responses include female and male); and [2] "What terms best express how you describe your gender identity?" (Responses include woman, man, non-binary, transgender, and additional options). Participants whose responses to gender identity were not "woman"/"man" or there were incongruences in their sex assigned at birth and gender identity were considered as "gender minority." To be more specific, participants who responded "female" to question one but didn't respond "woman" to question two and who chose "male" to question one but didn't choose "man" for question two were coded as "gender minority." Otherwise, participants were coded as "cisgender." [16] In the EHR data, we used transgender/gender nonbinary diagnosis code (ICD-9 and ICD-10 codes) in the "condition occurrence" table and gender affirming medications in the "drug exposure" table. All the ICD-9 and ICD-10 codes used to identity transgender/gender nonbinary individuals in AoU were listed in Supplemental Table 1. Based on drug exposure, gender minorities were defined as individuals who: [1] were assigned as male at birth and took estrogens/progestins; [2] were assigned as female at birth and took testosterone; [3] took estrogens/progesterone and spironolactone; and [4] took estrogen/progesterone and finasteride [6]. The process of identifying potential gender minority individuals among PWH is illustrated in Fig. 1.

Sexual orientation was assessed using one survey question: "Which of the following best represents how you think of yourself?" Participants who responded "Straight" were categorized as "heterosexual," and those who responded with other answers (e.g., "bisexual", "Gay", and "Lesbian") were considered as "sexual minority." By combining sexual orientation, sex at birth, and gender identity, we categorized participants' SOGI into six groups, including cisgender heterosexual woman (CHW), cisgender heterosexual men (CHM), cisgender sexual minority women (CSMW), cisgender sexual minority men (CSMM), gender minority people assigned female at birth (GMF) of any sexual orientation, and gender minority people assigned male at birth (GMM) of any sexual orientation.

Other sociodemographic variables

Other sociodemographic variables included in the analysis were age at AoU enrollment (e.g., 18–29, 30–39, 40–49, 50–64, and ≥65 years old), race (e.g., White, Black, and Other/Unknown), ethnicity (e.g., Hispanic, non-Hispanic, and Unknown), highest education attainment (e.g., less than high school degree, high school degree or more, and unknown), insurance type (e.g., private insurance, Medicaid, Medicare, multiple insurance, uninsured, and other insurance/unknown), and annual household income (e.g., < $35,000, ≥ $35,000, and unknown). Specifically, the "Other/Unknow" race group included participants who responded "Asian," "More than one race," "Skip," "Other," and "Prefer not to answer" to the survey question race. All of these variables were identified based on the basic survey questions in AoU. The detailed information of survey questions and responses used in the current study was described elsewhere [17].

Outcome variable

The outcome in the analysis was a binary variable, HIV virologic failure. It was defined yearly after one's first viral load testing, and individuals with at least one viral load test > 50 copies/mL during a calendar year were coded as "1 = virologic failure" at that year [18]. The viral load test results were extracted from the "measurement" domains in the EHR data, and records with numeric values or log transformation equivalents were included.

Statistical analysis

We used count and percentage to describe the sociodemographic and SOGI characteristics among PWH by virologic failure status. The variable distributions between individuals with and without virologic failure were compared using Person's Chi-square test. Generalized linear mixed-effects models were used to explore the association between SOGI and longitudinal virologic failure while adjusting for potential confounders, including

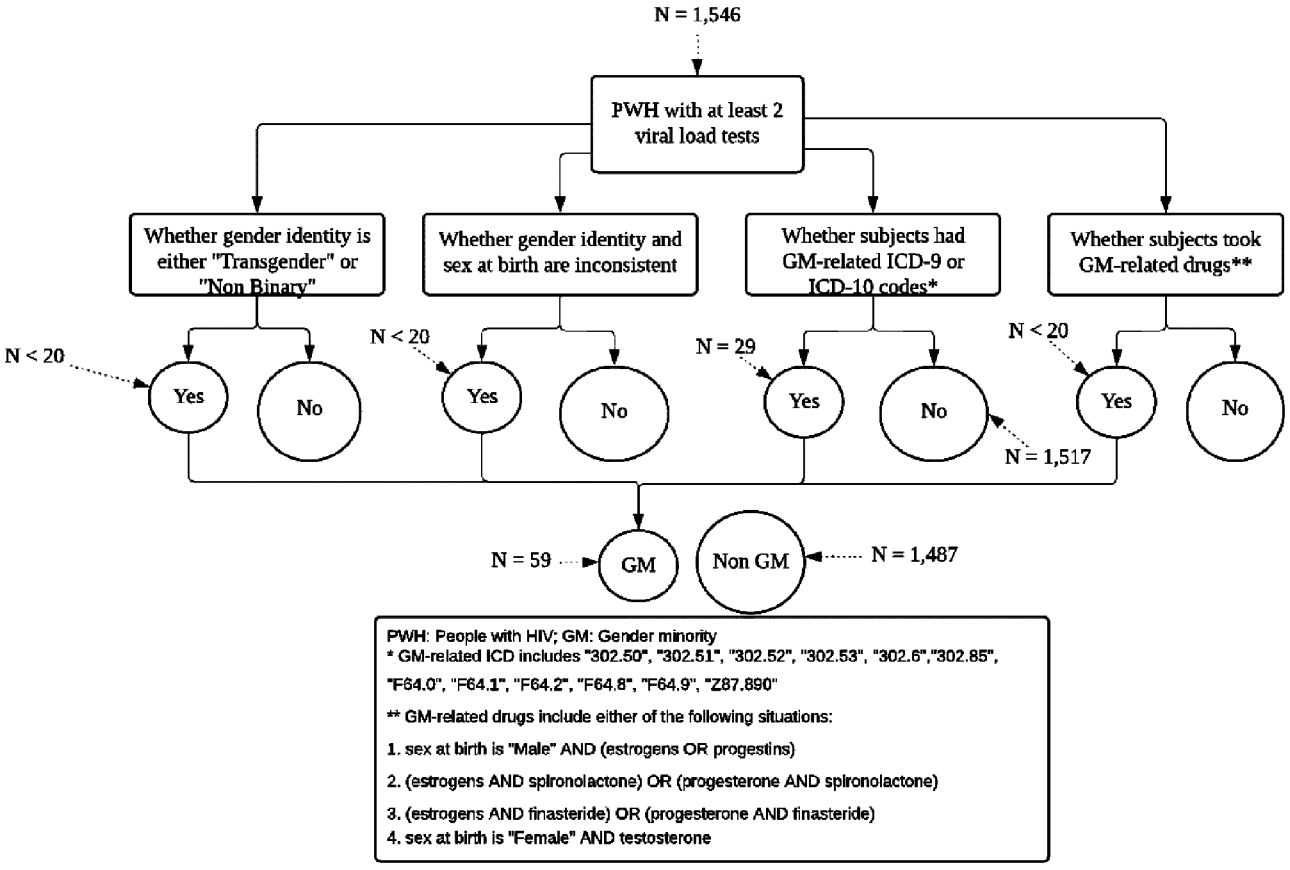

Fig. 1 Pipeline to identify potential gender minority individuals among confirmed HIV cohort in All of Us

age, race, ethnicity, education attainment, income, and insurance status.

Results

A total of 1,546 PWH with at least two viral load testing records and sex at birth being either male or female were identified in the AoU Version 7 Controlled Tier data. Among 1,546 included PWH, the range of their viral load was between 0 and 10,000,000 copies/mL, 1,196 (77.36%) had at least one viral failure, and 773 (50.00%) belonged to SGMs (CSMW, CSMM, GMF of any sexual orientation, and GMM of any sexual orientation) (Table 1). Except for cisgender sexual minority men (41.79%) and cisgender heterosexual women (18.20%), the most selected SOGI was the cisgender heterosexual man (21.80%), followed by cisgender sexual minority woman (4.40%). A total of 59 GMs were identified (31 based on survey questions alone and 29 based on condition domain alone), including 27 GMF of any sexual orientation and 32 GMM of any sexual orientation (Fig. 1). The total number of individuals from three domains were larger than 59 due to the repetition between domains.

Of the 1,546 PWH included in the analyses, 1,015 (65.65%) were assigned as female at birth, 901 (58.28%) were Black, and around half of them (50.19%) were aged 50–64 at enrollment. Most participants had at least a high school education (91.14%) and an income of less than $35,000 (62.55%). For insurance type, the most reported type was Medicaid (40.04%), followed by other insurance/unknown (23.22%), multiple insurance (17.21%), private insurance (9.18%), Medicare (9.18%), and uninsured (1.16%). A higher percentage of Black individuals were found among PWH experiencing virologic failure (60.54% vs. 50.57%, $p<0.001$) (Table 1).

Compared to participants who were aged 18–29 at enrollment, those who were aged 50–64 were less likely to have virologic failure (Crude OR [cOR]=0.43, 95% CI: 0.20–0.92) and the significant difference disappeared after adjusting other variates in the model (adjusted OR [aOR]=0.49, 95% CI: 0.23–1.04). Compared to cisgender heterosexual women, cisgender sexual minority women (aOR=1.85, 95% CI: 1.05–3.27) were at higher risk of HIV virologic failure. However, no significant difference in virologic failure was found between GMs (i.e., GM female [aOR=0.56, 95% CI: 0.25–1.25] and GM male [aOR=1.67, 95% CI: 0.75–3.69]) and cisgender heterosexual women. In addition, PWH who were Black vs. White (aOR=2.15, 95% CI: 1.52–3.04) and whose

Table 1 Characteristics distribution by virologic failure status among people living with HIV in the US from 1997 to 2022

	Overall (*N* = 1,546)[1]	Virologic failure		*p*-value[2]
		No (*N* = 350)[1]	Yes (*N* = 1,196)[1]	
Age at enrollment (years old)				0.022
18–29	40 (2.59)	*	*	
30–39	180 (11.64)	*	*	
40–49	269 (17.40)	51 (14.57)	218 (18.23)	
50–64	776 (50.19)	181 (51.71)	595 (49.75)	
65+	281 (18.18)	78 (22.29)	203 (16.97)	
Sex at birth				0.600
Male	531 (34.35)	125 (35.71)	406 (33.95)	
Female	1,015 (65.65)	225 (64.29)	790 (66.05)	
Sexual identity & orientation				0.400
CHW	436 (28.20)	101 (28.86)	335 (28.01)	
CHM	337 (21.80)	68 (19.43)	269 (22.49)	
CSMW	68 (4.40)	*	*	
CSMM	646 (41.79)	151 (43.14)	495 (41.39)	
GMF of any sexual orientation	27 (1.75)	*	*	
GMM of any sexual orientation	32 (2.07)	*	*	
Race				< 0.001
White	256 (16.56)	91 (26.00)	165 (13.80)	
Black	901 (58.28)	177 (50.57)	724 (60.54)	
Other/Unknown	389 (25.16)	82 (23.43)	307 (25.67)	
Ethnicity				0.600
Hispanic	326 (21.09)	*	*	
Non-Hispanic	1,164 (75.29)	269 (76.86)	895 (74.83)	
Unknown	56 (3.62)	*	*	
Education attainment				0.300
Less than high school degree	73 (4.72)	*	*	
High school degree or more	1,409 (91.14)	321 (91.71)	1,088 (90.97)	
Unknown	64 (4.14)	*	*	
Income				0.006
< $35,000	967 (62.55)	220 (62.86)	747 (62.46)	
>= $35,000	220 (14.23)	65 (18.57)	155 (12.96)	
Unknown	359 (23.22)	65 (18.57)	294 (24.58)	
Insurance type				0.200
Private insurance	142 (9.18)	38 (10.86)	104 (8.70)	
Medicaid	619 (40.04)	130 (37.14)	489 (40.89)	
Medicare	*	*	*	
Multiple insurance	266 (17.21)	71 (20.29)	195 (16.30)	
Uninsured	*	*	*	
Other insurance/ Unknown	359 (23.22)	72 (20.57)	287 (24.00)	

Notes: CHW (Cisgender heterosexual women); CWM (Cisgender heterosexual men); CSMW (Cisgender sexual minority women); CSMM (Cisgender sexual minority men); GMF (gender minority people assigned female at birth), and GMM (gender minority people assigned male at birth)

[1] n (%); Mean (Standard Deviation)

[2] Pearson's Chi-squared test

*Counts less than 20 (and corresponding percentages) cannot be displayed due to NIH All of Us Research Program Data and Statistics Dissemination Policy. Some additional data were collapsed or obscured to prevent secondary calculation of these values

insurance type was Medicaid (aOR = 2.07, 95% CI: 1.33–3.21) or was other insurance/Unknown (aOR = 2.21, 95% CI: 1.40–3.47) vs. Private insurance were more likely to experience virologic failure (Table 2).

Discussion

To the best of our knowledge, this is one of the first studies examining the SOGI disparities in virologic failure among PWH in AoU. Using the large and diverse population-level cohort data from AoU, we found that cisgender sexual minority women disproportionately experienced the burden of HIV virologic failure compared to cisgender heterosexual women. However, no significant difference in virologic failure was found between gender minorities and cisgender heterosexual women. These findings highlight the need to explore and address the specific needs of subgroups within the SGM communities to improve their HIV care outcomes.

No significant difference in virological failure was found between cisgender men and cisgender women in the current study. Prior studies showed mixed results with respect to virologic failure between cisgender men and cisgender women [19–22]. In a survival analysis of nearly 2,800 PWH in the US, Fleming et al. identified that male sex was directly associated with a higher risk of virologic failure than females [23]. This might be due to that men generally are less likely to seek healthcare and have poorer retention in HIV treatment [24]. A population-based study across eight US states and Washington, DC., on the contrary, demonstrated that cisgender women had significantly higher virologic failure rates than men (19% vs. 14%) from year 2010 to 2012 [19]. It was explained that at the interpersonal level, women receive less HIV-related social support and greater HIV stigma than men [25], and at the individual level, there might be more competing priorities that interfere with HIV medical regimens for women than men, such as having significant others to take care of [25]. More research

Table 2 Generalized linear mixed-effects models: factors associated with yearly HIV virologic failure

	Crude OR (95%CI)	Adjusted OR (95%CI)
Age at enrollment (years old)		
18–29	ref	ref
30–39	0.91 (0.4, 2.06)	0.94 (0.42, 2.12)
40–49	0.73 (0.33, 1.62)	0.8 (0.36, 1.75)
50–64	**0.43 (0.2, 0.92)**	0.49 (0.23, 1.04)
65+	0.48 (0.22, 1.06)	0.58 (0.26, 1.3)
Sexual identity & orientation		
CHW	ref	ref
CHM	1.23 (0.9, 1.68)	1.27 (0.93, 1.73)
CSMW	**1.91 (1.08, 3.39)**	**1.85 (1.05, 3.27)**
CSMM	1.08 (0.82, 1.41)	1.27 (0.97, 1.68)
GMF of any sexual orientation	0.49 (0.21, 1.11)	0.56 (0.25, 1.25)
GMM of any sexual orientation	2.13 (0.96, 4.72)	1.67 (0.75, 3.69)
Race		
White	ref	ref
Black	**2.33 (1.71, 3.19)**	**2.15 (1.52, 3.04)**
Other/Unknown	**2.07 (1.46, 2.95)**	**2.16 (1.22, 3.82)**
Ethnicity		
Hispanic	0.93 (0.71, 1.22)	0.83 (0.49, 1.43)
Non-Hispanic	ref	ref
Unknown	1.52 (0.82, 2.81)	1.15 (0.52, 2.56)
Education attainment		
Less than high school degree	ref	ref
High school degree or more	1.09 (0.65, 1.83)	1.01 (0.59, 1.7)
Unknown	1.37 (0.65, 2.91)	0.96 (0.45, 2.06)
Income		
< $35,000	ref	ref
>= $35,000	0.87 (0.63, 1.21)	1.39 (0.95, 2.03)
Unknown	**1.4 (1.07, 1.82)**	**1.39 (1.07, 1.82)**
Insurance type		
Private insurance	ref	ref
Medicaid	**2.03 (1.35, 3.05)**	**2.07 (1.33, 3.21)**
Medicare	1.23 (0.73, 2.07)	1.48 (0.86, 2.54)
Multiple insurance	1.42 (0.9, 2.23)	**1.66 (1.03, 2.69)**
Uninsured	1.42 (0.5, 4.02)	1.18 (0.42, 3.35)
Other insurance/Unknown	**2.24 (1.45, 3.47)**	**2.21 (1.4, 3.47)**

Notes: CHW (Cisgender heterosexual women); CHM (Cisgender heterosexual men); CSMM (Cisgender sexual minority women); CSMM (Cisgender sexual minority men); GMF (gender minority people assigned female at birth), and GMM (gender minority people assigned male at birth); Bold OR (95%CI): the corresponding p-value < 0.05.

is needed to examine the sex disparities in psychosocial characteristics or individual health behaviors among PWH to disentangle the complex factors that put cisgender women or men at increased risk of virologic failure.

Cisgender sexual minority women in the cohort had a markedly increased risk of virologic failure than cisgender heterosexual women, which is consistent with previous research [26, 27]. Sexual minority women might experience intersected stigma from multiple aspects, including HIV-related stigma, sexism, and homophobia. Numerous studies have documented negative associations of the discrimination of HIV-positive status and sexism with the well-being (e.g., mental and physical health) of female PWH [26, 28]. Social norms and stigmatizing communities construct sexual minorities as "demonic" and consider HIV a "gay disease." [29] One systematic review showed that women who have sex with women confronted more violence than their heterosexual counterparts [3]. The convergence of HIV-related stigma and homophobia might result in some enacted stigma, even violent behaviors, which in turn prohibits sexual minority PWH from disclosing their HIV status and seeking HIV-related health care services [30]. Some coping strategies that could help sexual minority women living with HIV include resilience (individual level), social networks (interpersonal level), and HIV- or sexual orientation-related stigma reduction education in healthcare facilities (structural level) [31–33]. More knowledge is needed to understand the barriers that sexual minority women with HIV face in accessing health services and retention in HIV care to improve the health status of SGMs.

This study is subject to several limitations. First, the AoU research program has been recruiting more participants from historically underrepresented populations and relying on convenience sampling, making our findings not representative of the US population. Second, due to the lack of geolocation information in the AoU program, we were not able to account for some regional or socioeconomic factors beyond the individual level (e.g., structural racism and health care accessibility) that might confound our findings. Third, the EHR data are only available for people from AoU-funded healthcare provider organizations, potentially introducing ascertainment bias. Fourth, only self-reported survey data were used to identify sexual orientation, which might lead to the underestimation of sexual minorities. Some individuals, such as those with a sexual orientation being gay, might not disclose their sexual orientation due to fear of stigma, discrimination, or even potential violence. Fifth, a varied number of viral load tests were done among participants, which might introduce bias if a specific group of participants has a consistently larger number of viral load tests, making it hard to draw reliable conclusions from the data. Lastly, the medication data within AoU was inadequate for accurately defining adherence to Antiretroviral Therapy, a critical determinant of virological failure.

Conclusion

This study is one of the few to examine the SOGI disparities in HIV-related health outcomes in combination with birth sex by integrating multiple data sources at the national level. Our computing phenotyping for detecting

SGMs was an extension of previously validated EHR-data-based algorithms by incorporating self-reported survey questions. This enables us to identify cases that would have been missing in the EHR database due to not being linked to healthcare systems. To design tailored interventions for subgroups of SGMs with HIV, further research is needed to examine the mechanisms for SOGI-based disparities in virologic failure and the combined effects of multi-level psychosocial and health behavior characteristics.

Abbreviations

SOGI	Sexual orientation and gender identity
US	United States
STI	Sexually transmitted infections
SGMs	Sexual and gender minorities
CDC	The Center for Disease Control and Prevention
MSM	Men who have sex with men
EHR	Electronic health records
PWH	People with HIV
AoU	All of Us
ICD	International Classification of Diseases
CHW	Cisgender heterosexual woman
CHM	Cisgender heterosexual men
CSMW	Cisgender sexual minority women
CSMM	Cisgender sexual minority men
GMF	Gender minority people assigned female at birth
GMM	Gender minority people assigned male at birth

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-19559-7.

Supplementary Material 1

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Author contributions

FS conceptualized and wrote the first draft and critically revised the manuscript. FS and JZ set up the statistical test design. RC and BH conducted the data analysis, which was reviewed and verified by JZ. FS prepared tables and figures with input from RC and BH. SW provided clinical input. FS, JZ, XY, SW, BO and XL reviewed and edited the manuscript. Authorship was determined using ICMJE recommendations.

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Data availability

The data that support the findings of this study can be accessed via the All of Us Researcher Workbench (https://workbench.researchallofus.org/). The data are not publicly available and cannot be made available by the corresponding author on reasonable request due to privacy or ethical restrictions. At the time of publication, access to the All of Us Researcher Workbench is restricted to researchers whose institution has signed a data use agreement with All of Us (https://www.researchallofus.org/register/).

Declarations

Ethical approval and consent to participant

The study protocol received approval from the institutional review board at the University of South Carolina and relevant SC state agencies (USC IRB number: Pro00124806). Due to the use of secondary data, the USC IRB has granted the planned study a 'non-human subject research designation and has waived the need for informed consent of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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