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Sustained viral suppression among people with HIV in the era of Undetectable = Untransmittable (U = U) in Australia

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Introduction: In Australia, cross-sectional estimates suggest that over 95% of people with HIV are virally suppressed; however, these measures reflect only the most recent viral load. Sustained viral suppression (SVS) is essential for optimizing health and preventing transmission. This study describes SVS among people with HIV who are engaged in care in Australia and factors associated with SVS.

Methods: We analyzed national data from the ACCESS sentinel surveillance system. Eligible participants attended an ACCESS clinic in 2023, received continuous antiretroviral therapy (ART; ≥1 prescription per calendar year), and had at least two viral load tests in the preceding three years (median:6; IQR: 5–7). SVS was defined as all viral load results less than 200 copies/ml. Multivariable logistic regression identified factors associated with SVS.

Results: Of 6036 eligible participants (95% men; median age 54 years), 5751 (95.3%) achieved SVS, while 99.1% were suppressed based on their last test. Older age (adjusted odds ratio [aOR]: 1.01; 95% confidence interval (95% CI): 1.002–1.03), residence in more socioeconomically advantaged areas (aOR: 1.06; 1.01–1.12), and higher mean $CD4^+$ cell count (aOR: 1.00; 1.001–1.002) were associated with higher odds of SVS. Receiving care at publicly funded sexual health/hospital-based clinics (aOR:0.64; 0.48–0.86), more diagnoses of gonorrhea (aOR: 0.81; 0.67–0.96) or infectious syphilis in the last three years (aOR: 0.85; 0.73–0.98), and co-infection with hepatitis C in the last 3 years (aOR: 0.56; 0.36–0.87) were associated with lower SVS.

Conclusions: More than 95% of people with HIV receiving ART and engaged in ongoing care achieved SVS. Strengthened, person-centered support for groups with lower SVS may enhance clinical outcomes and sustain Australia's progress toward HIV elimination goals.

AIDS 2026, **40**:1152–1160

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Received: 8 December 2025; revised: 5 February 2026; accepted: 11 February 2026.

DOI:10.1097/QAD.0000000000004488

Keywords: antiretroviral therapy, Australia, health service delivery, hepatitis C co-infection, HIV care continuum, HIV viral load, sentinel surveillance, sexually transmitted infections, socioeconomic factors, sustained viral suppression, treatment as prevention, U = U

Introduction

Viral suppression is important not only to improve health among people living with HIV [1] but also to prevent transmission of HIV infection to others (i.e., treatment as prevention [TasP]) [2]. Achieving maximal treatment and prevention effects of antiretroviral treatment (ART) requires sustained viral suppression (SVS) [3], requiring indicators of viral suppression over time as opposed to prevalence of viral suppression at a certain point in time. In all the major studies providing evidence for Undetectable = Untransmittable (U = U) [4–6], people living with HIV were virally suppressed not only at the study entry or fixed points of follow-up, but were consistently virally suppressed throughout their follow-up. A systematic review [7] found that while ART greatly reduces transmission risk, HIV transmission may still occur when viral load is more than 200 RNA copies/ml. These findings highlighted the importance of supporting people living with HIV to sustain viral suppression to maintain the effectiveness of TasP.

Estimating the proportion of the population with viral suppression using the results from the most recent test may overestimate SVS [8]. For instance, in a study of HIV surveillance data from the United States (US), although 82.9% of people with HIV in the cohort had viral suppression based on the last test during the 2-year observation period (2012–2013), only 61.8% of the cohort were consistently suppressed in all tests conducted during this two-year period [3]. Moreover, SVS could vary by age, sex, and race and, for instance, was lower among women, younger participants and African Americans [3,8,9].

Australia endorsed TasP as a tool to virtually eliminate HIV transmission in successive National HIV Strategies [10,11]. In Australia, national cascade indicators show the percentage of people virally suppressed among those taking ART has surpassed 95% [12]. However, these annual indicators are a cross-sectional population level estimate based on the viral load at last test and did not reflect whether the viral load had been consistently suppressed. No studies have determined the level of SVS among people living with HIV in Australia. To address this gap, the objective of this analysis was to identify the SVS rate among Australian people living with HIV on treatment and factors associated with SVS using data from a national sentinel surveillance network.

Materials and methods

Study population

This study used data from the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmissible Infections and Blood Borne Viruses (ACCESS, https://accessproject.org.au/) [13]. ACCESS is a national sentinel surveillance network that includes over 100 health services, including high HIV/sexually transmissible infection (STI) caseload general practices, publicly funded sexual health clinics, pathology laboratories, and community-based services across all states and territories in Australia. ACCESS extracts and collates de-identified routinely collected electronic medical record data from participating health services using automated data extraction software known as GRHANITE. Data from ACCESS are anonymously linked using a highly sensitive linkage algorithm that utilizes probabilistic and de-identifying linkage keys generated from patient identifiers created prior to data being extracted [14]. This means that records of clients visiting any clinic across the ACCESS network can be comprehensively and anonymously linked [14].

Sustained viral suppression definition and eligibility criteria

People living with HIV who met all of the following criteria were included in this analysis: attended a clinic within ACCESS in 2023; had evidence of ART prescription at least once per calendar year for the past 4 years (2020–2023); and had at least one viral load test between 2020–2021 (i.e., first follow-up year) and at least one viral load test between 2022–2023 (i.e., third/last follow-up year) (See Fig. 1). An additional year of ART before the follow-up started was included in the criteria to allow those who had just started ART to achieve viral suppression [15]. Those under 18 years of age in 2023 were excluded from the analysis.

SVS was defined as an individual having a suppressed viral load (<200 RNA copies/ml) in all the tests during the three years preceding their last follow-up date in 2023. A threshold of less than 200 RNA copies/mL was applied in line with the Australian national guideline [16] and because empirical evidence indicates no risk of sexual transmission at viral loads below this level [17]. Duration of unsuppressed viral load was calculated for the period starting from the first test with viral load at least 200 copies/ml to a test with viral load less than 200 copies/ml or the end of follow up (i.e., last visit in 2023). If a person

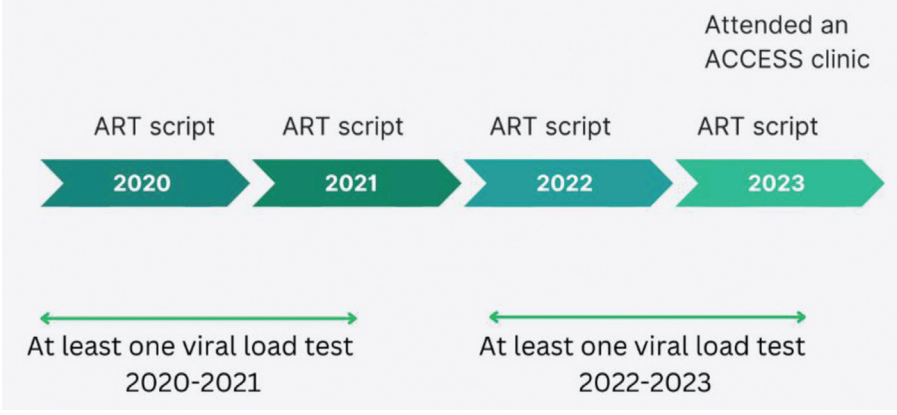

Fig. 1. Inclusion criteria for the participants. All the conditions outlined in the figure have to be met to be included in the study.

had more than one period with unsuppressed viral load in the past 3 years, they were combined.

Covariates

The following variables, which are routinely collected across most services in ACCESS, were considered as a covariate in this study: sociodemographic (age, sex, sexuality, residential postcode, country of birth, and language spoken at home); type of clinic (general practices/publicly funded sexual health services / hospital-based infectious disease clinics); STIs (chlamydia, gonorrhea, and infectious syphilis); co-infections with hepatitis B virus (HBV) and hepatitis C virus (HCV); and HIV-related variables ($CD4^+$ cell count and duration of HIV infection). Gay or bisexual status among men was determined based on reported sexuality, partner sex, or a history of rectal chlamydia or gonorrhea testing [18]. Residential postcode was used to derive two variables: remoteness of the residential area [19] and index of relative socioeconomic advantage and disadvantage (IRSAD), which reflects the economic and social conditions of households in that area; lower scores indicate relatively greater disadvantage [20]. Culturally and linguistically diverse (CALD) background was defined as being born in a non-English speaking country or reporting the use of a language other than English at home.

Analysis

First, we estimated the proportion of people with HIV (PWH) who achieved SVS, defined as a viral load less than 200 RNA copies/ml in all tests over the preceding three years, among those who attended an ACCESS clinic in 2023, received continuous ART ($\geq$1 prescription per calendar year), and had at least two viral load tests in the preceding three years. Second, for those who did not achieve SVS, the highest viral load in the last 3 years was reported along with the estimated duration of unsuppressed viral load. Third, the SVS rate was compared with the viral suppression rate estimated based on the last available viral load test to assess whether the cross-sectional rates reported in cascades and surveillance differ from SVS in the Australian context. Fourth, as a sensitivity analysis, SVS was determined among all PWH regardless of the ART status. Last, univariable and multivariable logistic regression analyses were conducted to identify sociodemographic, clinical, and structural factors associated with SVS. Variables associated with SVS with a P value less than 0.1 in univariable analyses were included in the multivariable analysis. Stata SE Version 17.0 was used for all analyses and P value less than 0.05 was regarded as statistically significant.

ACCESS was approved by the human research ethics committees of the Alfred Hospital (248/17), the Northern Territory Department of Health and Menzies School of Health (08/47), the Aboriginal Health and Medical Research Council (NSW; 1099/15), Central Australian Human Research Ethics Committee (19–3355), ACON (2015/14), the Victorian AIDS Council and Thorne Harbour Health (VAC REP 15/003). Individual patient consent was not required for our analysis because the data is de-identified and collected for the purposes of public health surveillance.

Results

A total of 10 964 people living with HIV attended a clinic participating in ACCESS in 2023. Of these, 4928 did not meet the inclusion criteria (see Fig. 2), leaving 6036 eligible participants (median age: 54 years [IQR: 44–62]). Demographic characteristics of participants included in the analysis were compared with those excluded (Supplementary File 1, http://links.lww.com/QAD/D825). Compared with included participants, those excluded primarily due to incomplete viral load testing or absence of annual ART prescriptions were more likely to be female, nongay or bisexual men (non-GBM),

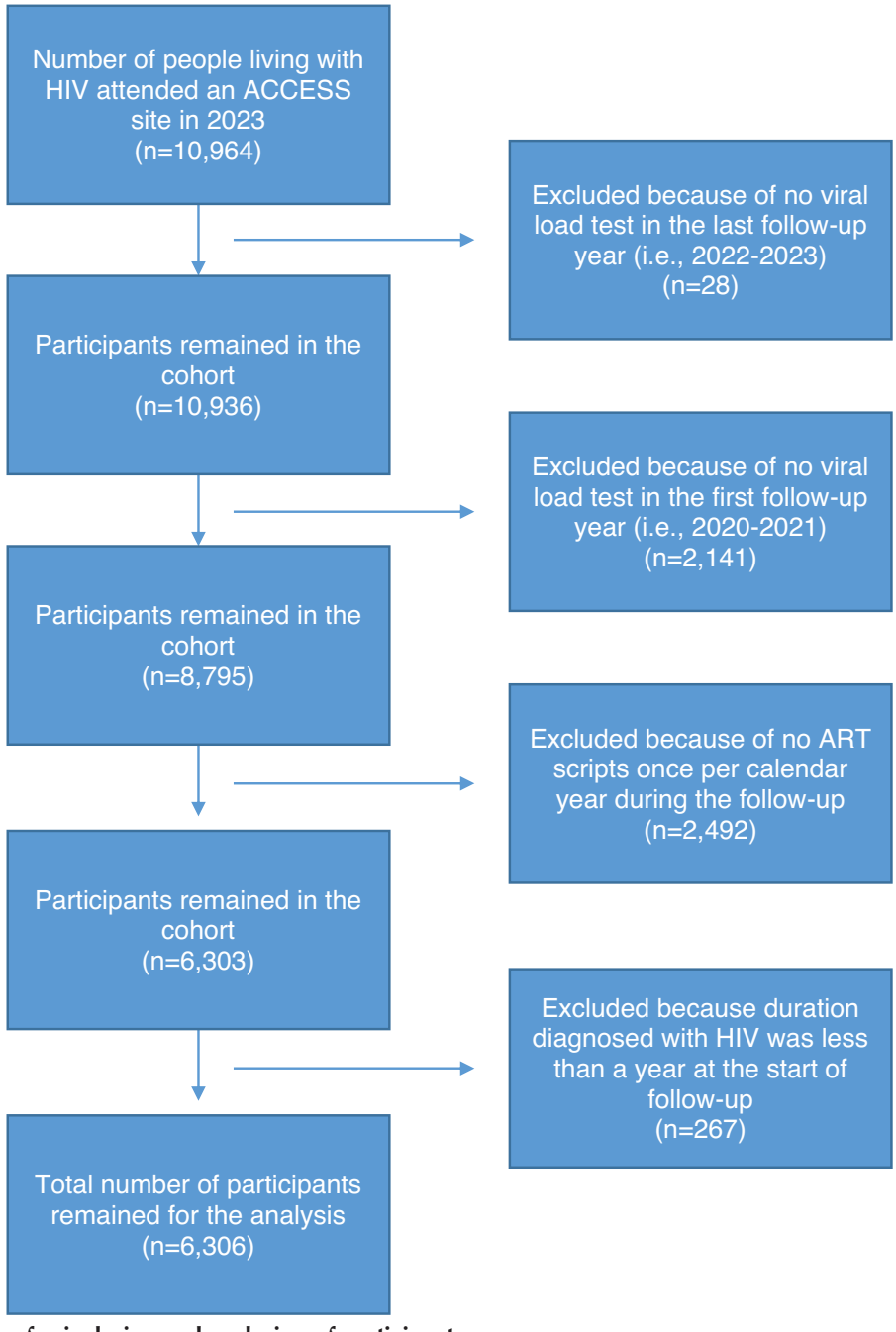

Fig. 2. Flow diagram for inclusion and exclusion of participants.

younger, and to reside in areas of greater socioeconomic disadvantage. Viral suppression based on the most recent viral load test was lower among excluded participants than among those included in the analysis (95.4 vs. 99.1%), consistent with lower engagement in care and treatment continuity in this group.

Table 1 presents characteristics of participants included in the analysis. Most participants were men (95.2%), GBM (85.2%), resided in major cities (79.9%), and lived in areas within the upper 50th percentile of IRSAD (81.7%). About half were born in Australia (52.7%) and 21.8% of were classified as from a CALD background. About 64% of the participants were receiving care at a general practice. During follow-up, 20.0, 17.3, and 11.3% were diagnosed at least once with chlamydia, gonorrhea, and infectious syphilis, respectively. In addition, 5.5% were co-infected with HCV during the follow-up, and 5.7% had been infected with HBV.

A total of 5751 participants (95.3%) were classified as achieving SVS (median number of viral load tests = 6

Table 1. Characteristics of the participants.

	Count/mean	Percentage/SD	Missing
Demographics			
Age in years	53.23	12.08	
Age group			
<25	12	0.2%	
25–34	407	6.7%	
35–44	1127	18. 7%	
≥45	4490	74.4%	
Patient sex (Male)	5746	95.2%	9 (0.2%)
Gay, bisexual, and other MSM	5144	85.2%	
Born in Australia	3179	64.0%	1068 (17.7%)
Culturally and linguistically diverse background	1316	21.8%	1041 (17.3%)
Remoteness of patient's postcode			30 (0.5%)
Major cities of Australia	4823	79.9%	
Inner or outer regional Australia	1156	19.2%	
Remote or very remote	27	0.4%	
Index of Relative Socio-Economic Advantage and Disadvantage			29 (0.5%)
1st quartile	478	7.9%	
2nd quartile	620	10.3%	
3rd quartile	849	14.1%	
4th quartile	4060	67.3%	
Structural factors			
Service type			
General practices	3868	64.1%	
Publicly funded sexual health clinics or hospital-based clinics	2139	35.4%	
Community health services	29	0.5%	
Remoteness of the clinic location			
Major cities of Australia	5511	91.3%	
Inner or outer Regional Australia	525	8.7%	
Medical history			
Infection with chlamydia at least once during the study period	1209	20.0%	
Infection with gonorrhea at least once during the study period	1046	17.3%	
Infection with active syphilis at least once during the study period	684	11.3%	
Co-infection with hepatitis C virus at least once the study period	331	5.5%	
Ever infected with hepatitis B virus	343	5.7%	
Mean CD4 in the past three years	735.64	269.95	
Duration diagnosed with HIV	4402.46	1598.6	

[IQR: 5–7, range: 2–20]). Those who had unsustained viral suppression ($n = 285$) spent an estimated 52 916 of 283 125 follow-up days (19%) with a viral load at least 200 RNA copies/ml. Among these individuals, 45% never exceeded 1000 copies/ml while 20% had peak viral load between 1001 and 10 000 copies/ml, 20% between 10 001 and 100 000, and 15% had more than 100 000 copies/ml (Fig. 3). When viral suppression was calculated based on the last available test result, 99.1% were suppressed. When the SVS was assessed among all PLHIV regardless of the ART status, 92.7% achieved SVS.

Table 2 presents results from the univariable and multivariable logistic regressions. In the univariable analysis, older age (odds ratio [OR]: 1.02, 95% confidence interval (95% CI): 1.01–1.04), residence in areas with higher IRSAD deciles (OR: 1.33, 95% CI: 1.00–1.77), and higher mean $CD4^+$ cell counts over the follow-up period (OR: 1.00, 95% CI: 1.001–1.002) were associated with higher odds of sustained suppression at *P* value less than 0.1. Receiving care at a publicly-funded sexual health clinic or hospital-based clinic (OR: 0.67, 95% CI: 0.53–0.85) (versus general practices), higher number of chlamydia (OR: 0.91, 95% CI: 0.81–1.01), gonorrhea (OR: 0.78, 95% CI: 0.69–0.89) and infectious syphilis (OR: 0.76, 95% CI: 0.67–0.87) diagnoses during the follow-up, and co-infection with HCV at least once during the follow-up (OR: 0.56, 95% CI: 0.37–0.85) were associated with lower odds of SVS at *P* value less than 0.1.

In the multivariable analysis, the following variables remained significantly associated with SVS at *P* value less than 0.05: older age (adjusted OR [aOR]: 1.01, 95% CI: 1.002–1.03), residence in areas with higher IRSAD deciles (aOR: 1.06, CI: 1.01–1.12), receiving care at a publicly-funded sexual health clinic or hospital-based clinic (aOR: 0.64, CI: 0.48–0.86) (versus general practices) higher number of gonorrhea infections during the follow-up (aOR: 0.81, CI: 0.67–0.96), higher number of active syphilis infections during the follow-up (aOR: 0.85, CI: 0.73–0.98), co-infection with HCV at least once during the follow-up (aOR: 0.56, CI: 0.36–0.87), and higher mean $CD4^+$ cell count in the past 3 years (aOR: 1.00, CI: 1.001–1.002).

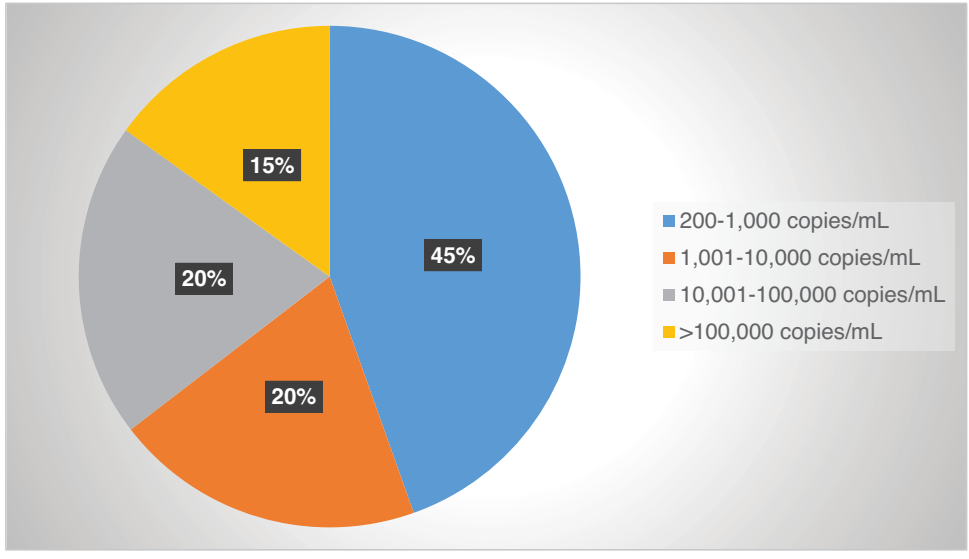

Fig. 3. Distribution of maximum viral load levels among participants with unsustained viral suppression.

Discussion

In the era of U = U where treatment is both a tool to keep people with HIV infection well but also a prevention tool, achieving SVS is critical. Using national surveillance data, this study assessed SVS over a 3-year period among PWH in Australia who remained engaged in care and had consistent evidence of ART use. We found that 95.3% of participants achieved SVS, exceeding the UNAIDS target of 95% and remaining lower than the 99.1% suppression rate based on the most recent viral load test, which reflects the cross-sectional viral suppression rate commonly reported in national HIV surveillance in Australia [21].

Importantly, among the 4.7% who did not achieve SVS, nearly half (45%) had a maximum viral load below 1000 copies/ml, a level considered by WHO as virologically suppressed and associated with minimal risk of

Table 2. Univariable and multivariable regression results determining the association between patients' demographics, structural, and clinical factors with sustained HIV viral suppression.

	Univariate		Multivariate	
	OR	95% CI	OR	95% CI
Patient demographics				
Age	1.02***	1.01, 1.04	1.01*	1.002, 1.03
Patient sex (Male), Ref: Female	1.24	0.74, 2.08		
Gay, bisexual, and other men who have sex with men (Yes), Ref: No	1.00	0.71, 1.39		
Born in Australia (Yes), Ref: No	1.04	0.80, 1.36		
Culturally and linguistically diverse background (Yes), Ref: No	0.95	0.71, 1.26		
Remoteness of patient's postcode (Ref: Major cities of Australia)				
Inner or outer regional Australia	1.20	0.87, 1.66		
Remote or very remote	0.64	0.15, 2.71		
Index of Relative Socio-Economic Advantage and Disadvantage (Decile)	1.07**	1.02, 1.12	1.06*	1.01, 1.12
Structural factors				
Site type (Ref: General practices/community health services)				
Publicly funded sexual health clinics or hospital-based clinics	0.67**	0.53, 0.85	0.64**	0.48, 0.86
Community health services	1.18	0.16, 8.76	1.34	0.17, 10.14
Remoteness of the clinic location (Inner or Outer Regional Australia), Ref: Major cities of Australia	0.99	0.65, 1.51		
Medical history				
Number of chlamydia infection episodes during the last 3 years	0.91†	0.81, 1.01	1.14	0.97, 1.35
Number of gonorrhea infection episodes during the last 3 years	0.78***	0.69, 0.89	0.81*	0.67, 0.96
Number of infectious syphilis infection episodes during the last 3 years	0.76***	0.67, 0.87	0.85*	0.73, 0.98
Co-infection with hepatitis C virus at least once in the last 3 years	0.56**	0.37, 0.85	0.56*	0.36, 0.87
Ever infected with hepatitis B virus	1.72	0.75, 3.93		
Mean CD4 in the past 3 years	1.001***	1.001, 1.002	1.001***	1.001, 1.002
Duration diagnosed with HIV	1.00001	0.99, 1.0001		

CI, confidence interval; OR, odds ratio.
†$P < 0.1$, *$P < 0.05$, *$P < 0.01$, ***$P < 0.001$.

transmission [17,22]. Nevertheless, low-level viremia and intermittent "blips" have been linked to future virological failure and resistance, underscoring the need for continuous support to engage in treatment and care and targeted interventions for these individuals [23,24].

Our study also identified key subgroups less likely to achieve SVS. Younger age, living in lower socioeconomic index areas, repeated STI diagnoses (gonorrhea and syphilis), HCV co-infection, and receipt of care at publicly funded sexual health or hospital-based clinics were all associated with reduced odds of SVS. These findings are consistent with previous research [9,25,26] and point to structural, social and behavioral barriers that may hinder ART adherence and continuity of care [27,28]. These individuals may benefit from comprehensive, tailored support including adherence counseling and drug resistance screening, psychosocial and mental health services, stronger linkage to peer and harm reduction programs, and consideration of long-acting injectable ART for individuals with adherence challenges [29–34]. Clinicians should also address ART-related side effects, which can negatively impact adherence [35,36]. Publicly funded clinics, which often serve more marginalized populations and clinically-ill clients, may require additional resources to provide comprehensive support services and ensure equitable outcomes [37].

Our study observed that those with unsustained viral suppression spent 19% of the observed follow-up days with viral loads at least 200 RNA copies/ml, indicating a potential risk of onward transmission [22]. This is important given our findings suggesting associations between lower SVS and repeated diagnoses of gonorrhea or syphilis, as well as evidence of hepatitis C infection, which may reflect a range of factors, including underlying sexual or social network characteristics, higher partner turnover, inconsistent condom use, and injecting practices [38,39]. These patterns highlight the importance of ensuring that people who may be embedded in networks with elevated HIV acquisition or transmission potential have access to a broad suite of prevention strategies [39,40]. This includes timely HIV testing, linkage to PrEP for HIV-negative partners or networks, access to sterile injecting equipment, and supportive clinical engagement tailored to individuals who may face greater challenges in maintaining SVS [39,41].

Our findings should be interpreted in the context of engagement in care. Approximately 45% of people living with HIV who attended an ACCESS site in 2023 were excluded from the primary analysis because they did not meet eligibility criteria related to viral load monitoring or evidence of ART prescription, both indicators of sustained engagement in care. Additional analyses demonstrated that excluded individuals were more likely to be female, non-GBM, younger, and to live in more socioeconomically disadvantaged areas, and that viral suppression based on the most recent viral load test was lower among excluded participants compared with those included in the analysis. It is therefore likely that SVS would be lower if all people living with HIV attending ACCESS sites were included. Importantly, however, when all people living with HIV were included regardless of ART prescription history in a sensitivity analysis, SVS remained high at 92.7%, indicating that the high level of sustained suppression observed is not solely an artefact of restricting analyses to individuals with optimal engagement in care.

Our SVS rate is higher than those reported internationally with a relatively narrow difference between sustained viral suppression (95.3%) and viral suppression at the most recent viral load test (99.1%), despite a longer follow-up period. For example, a U.S. study of 10 942 people living with HIV reported a SVS rate of 65.9% over 1 year, while 78.5% were virally suppressed based on a single viral load measurement [8]. Another U.S. analysis among GBM receiving care through the Ryan White Program found that 84.4% achieved SVS over 1 year [42]. Similarly, in a nationwide Taiwanese study, 87% achieved sustained viral suppression over a two-year period (2019–2020), whereas 96% were virally suppressed at the most recent viral load test [26]. Furthermore, a study conducted among 533 PWH in Trinidad and Tobago reported that only 31.5% achieved SVS over 1 year [43]. However, such comparisons should be interpreted cautiously. Many international studies include broader populations with less consistent engagement in care, limited ability to ascertain ART continuity, or treatment interruptions, whereas our primary analysis was restricted to individuals with regular viral load monitoring and consistent evidence of ART prescriptions. In addition, healthcare system differences, including Australia's universal access to healthcare and HIV treatment, are likely to contribute to higher sustained viral suppression compared with settings where access to care and treatment is more variable [21].

Our study has important strengths, including the use of a large, nationally representative surveillance dataset and the ability to quantify time spent above key viral load thresholds. However, some limitations must be noted. First, sustained viral suppression estimates primarily reflect PWH who were engaged in ongoing care, as eligibility required regular viral load monitoring and evidence of ART prescriptions; generalizability to all people living with HIV may therefore be limited. Compared with national HIV notification-based estimates [44], participants included in this analysis were less likely to be female (5 versus 13.9%) and more likely to be GBM (85.2 versus 72.4%), while the proportion born in Australia was similar (64 versus 59.8%); these differences likely reflect patterns of engagement in HIV care. Second, duration since HIV diagnosis was estimated from the earliest available positive test or monitoring record, which may underestimate true duration and explain the lack of association with SVS. Lastly, behavioral and structural factors such as substance use, alcohol use, and involvement with the criminal legal

system, which may substantially affect access to care and adherence to ART are not routinely or consistently collected across all ACCESS sites and therefore could not be examined in this analysis.

Conclusion

Using nationally representative surveillance data, we found that over 95% of Australian people living with HIV who were receiving ART achieved SVS over a 3-year period, closely aligning with cross-sectional suppression estimates and reinforcing the effectiveness of Australia's HIV treatment programs. These findings are encouraging as the country pursues TasP and aims for virtual elimination of HIV transmission by 2030. However, a small subset of individuals did not achieve SVS, often facing overlapping behavioral and structural challenges such as younger age, socioeconomic disadvantage, repeated STI diagnoses, hepatitis C co-infection, and care at publicly funded clinics. Addressing these gaps will require comprehensive, person-centered approaches, including adherence support, mental health and psychosocial services, harm reduction strategies, and access to long-acting ART options, alongside strengthened resources for clinics serving priority populations to ensure equitable outcomes and sustained progress toward HIV elimination.

Acknowledgements

The authors acknowledge the contribution of the ACCESS Team members who are not co-authors of this article, including Wayne Dimech, NRL; Alexis Apostolellis, Australasian Society for HIV Medicine; Aaron Cogle, National Association of People with HIV Australia; Rani West, ATLAS; Daniel Coase, Federation of Ethnic Communities' Councils of Australia (FECCA); Dash Heath-Paynter, Health Equity Matters (AFAO); David Lewis, Western Sydney Sexual Health Centre; David Nolan, Royal Perth Hospital; David Templeton, Royal Prince Alfred Hospital; Edward Huddy, Ministry of Health; Emma Sanguineti, Queensland Ministry of Health; Florin Douglas, Deakin University; Janaki Amin, NSW Ministry of Health; Jane Davies, Menzies School of Health Research; Jane Hocking, University of Melbourne; John Didlick, Hepatitis Australia; John G, Australian Injecting and Illicit Drug Users League (AIVL); Jess Doumany, Australian Injecting and Illicit Drug Users League; Jason Ong, Melbourne Sexual Health Centre; Lisa Bastian, WA Department of Health; Mandy Charleton, Ministry of Health; Manoji Gunathilake, Royal Darwin Hospital; Megan Campbell, National Aboriginal Community Controlled Health Organisation (NAACHO); Mish Pony, Scarlet Alliance; Nathan Ryder, Hunter New England LHD; Norm Roth, Prahran Market Clinic; Philip Cunningham, SydPath; Phillip Read, Kirkton Road Centre; Stella Pendle, Australian Clinical Laboratories; Tom Rees, SA Ministry of Health; Stella Lintzeris, Kirby Institute, UNSW Sydney; Thi Nguyen, Burnet Institute; Victoria Polkinghorne, Burnet Institute; Michael Traeger, Burnet Institute; Nyssa Watson, Burnet Institute.

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ACCESS receives core funding from the Australian Department of Health & Aged Care with the aim of monitoring Australia's progress in the control of blood-borne viruses and sexually transmitted infections. In addition, the governments of Victoria and Western Australia provide funding for state-level outcomes. ACCESS also acknowledges past support from the governments of New South Wales, Northern Territory, and the Australian Capital Territory, as well as the National Health and Medical Research Council (NHMRC; APP1082336 and GNT1092852).

E.P.F.C. is supported by a National Health and Medical Research Council Leadership Investigator Grant (GNT2033299). A.C. is supported by a National Health and Medical Research Council Emerging Leadership Investigator Grant (2034148).

Conflicts of interest

There are no conflicts of interest.

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