

Socioeconomic and psychosocial factors are associated with poor treatment outcomes in Australian adults living with HIV: a case-control study

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Abstract. *Background:* A substantial minority of patients living with HIV refuse or cease antiretroviral therapy (ART), have virological failure (VF) or develop an AIDS-defining condition (ADC) or serious non-AIDS event (SNAE). It is not understood which socioeconomic and psychosocial factors may be associated with these poor outcomes. *Methods:* Thirty-nine patients with poor HIV treatment outcomes, defined as those who refused or ceased ART, had VF or were hospitalised with an ADC or SNAE (cases), were compared with 120 controls on suppressive ART. A self-report survey recorded demographics, physical health, life stressors, social supports, HIV disclosure, stigma or discrimination, health care access, treatment adherence, side effects, health and treatment perceptions and financial and employment status. Socioeconomic and psychosocial covariates significant in bivariate analyses were assessed with conditional multivariable logistic regression, adjusted for year of HIV diagnosis. *Results:* Cases and controls did not differ significantly with regard to sex (96.2% ($n = 153$) male) or age (mean (\pm s.d.) 51 ± 11 years). Twenty cases (51%) had refused or ceased ART, 35 (90%) had an HIV viral load >50 copies mL^{-1} , 12 (31%) were hospitalised with an ADC and five (13%) were hospitalised with a new SNAE. Three covariates were independently associated with poor outcomes: foregoing necessities for financial reasons (adjusted odds ratio (aOR) 3.1, 95% confidence interval (95% CI) 1.3–7.6, $P = 0.014$), cost barriers to accessing HIV care (aOR 3.1, 95% CI 1.0–9.6, $P = 0.049$) and lower quality of life (aOR 3.8, 95% CI 1.5–9.7, $P = 0.004$). *Conclusions:* Despite universal health care, socioeconomic and psychosocial factors are associated with poor HIV outcomes in adults in Australia. These factors should be addressed through targeted interventions to improve long-term successful treatment.

Additional keywords: antiretroviral therapy, ART failure, finance, HIV cascade.

Received 30 July 2018, accepted 16 April 2019, published online 13 September 2019

Introduction

The HIV treatment cascade is used to model the stages of the HIV care continuum, namely HIV diagnosis, engagement in HIV healthcare, receiving antiretroviral therapy (ART) and achieving and maintaining a suppressed HIV viral load.¹ Based on surveillance data to December 2017, it is estimated that 27 545 people are living with HIV in Australia. Of these, an estimated 89% are diagnosed, 85% are retained in care, 78% are receiving ART and 74% have achieved viral suppression.² The

Joint United Nations Programme on HIV/AIDS (UNAIDS) '90–90–90' targets are that 90% of patients with HIV are diagnosed, 90% of those diagnosed are treated with ART and 90% of those treated are virologically suppressed.³ Public health policies and community organisation campaigns are implemented to improve outcomes at each step of the HIV treatment cascade.

If the goal of successful ART is virological suppression, regression in the treatment cascade at the individual (patient)

level (e.g. from virological suppression to stopping ART) could be considered a poor treatment outcome. For patients who have initiated ART after a confirmed HIV diagnosis, poor outcomes could comprise not being on ART or being on ART but experiencing virological failure (i.e. a detectable HIV viral load). Improving the HIV cascade in Australia requires increasing the number of patients retained in care with sustained viral suppression. Furthermore, attention should be directed towards improving health and quality of life outcomes, a proposed 'fourth 90'.⁴ This refers to the importance of maintaining high quality of life of people with HIV, which could be achieved by preventing progression to AIDS⁵ or the development of a serious non-AIDS event (SNAE).⁶

Although socioeconomic disadvantage has been shown to be associated with suboptimal HIV outcomes, this has primarily been studied in low- and middle-income countries.⁷ In high-income settings, many studies examining the relationship between socioeconomic indicators and virological outcomes were conducted before recommendations of lifelong ART,^{8,9} or before single-tablet ART,^{10–14} and may be less relevant in the current ART era. More recent longitudinal studies in high-income settings have found lower household income to be associated with virologic failure.¹⁵ In addition, some, but not all, studies showed that lower education was related to worse virologic outcomes.^{16,17} Studies examining covariates of adherence or treatment outcomes often limit eligibility to specific groups or populations, for example enrolling only people who inject drugs^{11,12} or women,¹⁵ or excluding men who have sex with men.¹⁷ This may limit the generalisability of findings.

In the contemporary ART era, most studies assessing associations between socioeconomic factors and HIV treatment outcomes have been conducted in the US. The effects of socioeconomic status may be greater in the US than in high-income countries with universal health care.¹⁸ Nevertheless, an Australian single-site cross-sectional survey reported that 30% of patients who had difficulties meeting pharmacy dispensing costs had ceased ART.¹⁹ However, that self-report survey was completed anonymously and could not be linked to clinical endpoints. It remains unknown whether socioeconomic covariates are associated with HIV treatment outcomes in a high-income country with publicly subsidised health care. Therefore, the aim of the present study was to assess associations between socioeconomic and psychosocial variables and poor HIV treatment outcomes in Australia, a high-income setting with subsidised health care.

Methods

We implemented a case-control study of adult participants living with HIV through St Vincent's Public Hospital, Sydney, Australia, from 2014 to 2016. All eligible patients that study staff were aware of (e.g. through hospital admission systems and out-patient clinics) were approached and offered participation in the study. Participants were defined as eligible cases if, at the time of entry, they had one or more of the following: not taking ART, a detectable HIV viral load at ≥ 50 copies mL⁻¹ or hospitalised with an AIDS-defining illness or a new SNAE.⁶ Participants were matched to controls enrolled at the same site in a nationwide cohort study of HIV-infected

adults on ART with an undetectable viral load (<20 copies mL⁻¹) at study entry and on stable ART for at least 3 months.²⁰ Participants were matched for site of enrolment (the controls from the larger cohort were selected from the same site as the cases) and sex.

All participants completed the same study assessments, with participants who were enrolled as cases completing a single study visit that mirrored the baseline visit completed by the controls. The visit consisted of completing a study questionnaire and a cognitive screening test. The participant self-completed questionnaire incorporated a series of measures assessing sociodemographics, financial and employment status, health care and treatment access, physical health, mental health, quality of life, drug and alcohol use, life stressors, social supports, HIV disclosure, HIV stigma, ART regimen (use, side effects and adherence), concomitant medication use and ART-related necessity beliefs and concerns.^{19,21–30} Participants completed a brief neurocognitive screening (CogState).³¹ Data collected by study coordinators included medical and HIV history, SNAEs,⁶ comorbidities, sexually transmissible infections and laboratory data. The study assessments are described in detail elsewhere.²⁰

Human research ethics approval was obtained from the St Vincent's Hospital Human Research and Ethics Committee. All participants provided written informed consent before enrolment. Participants were offered an A\$20 meal voucher in return for participation.

Sample size calculation and statistical analysis

We initially planned for inclusion of 37 cases and 111 controls to enable detection, with 90% power, of an odds ratio (OR) of ≥ 3.5 , with a target ratio of 1 : 3 cases to controls. This was based on the assumption that financial strain (as a marker of socioeconomic disadvantage) would lead to poorer HIV treatment outcomes (as defined) in approximately 29% of cases, based on data derived from a separate sample enrolled at the same site.¹⁹

We purposefully assessed a range of socioeconomic and psychosocial variables identified in the literature, testing these for associations in bivariate analyses comparing cases and controls using a significance level of $P < 0.05$ (two-tailed). The significance of differences in continuous variables normally distributed in each group was analysed using independent samples *t*-tests. The significance of differences in non-normally distributed continuous variables was assessed using the Mann–Whitney *U*-test. The significance of differences in categorical variables was analysed using Chi-squared tests, and ORs were generated with a 95% confidence intervals (CIs). Life stressors and quality of life scores were dichotomised according to their mean and median value respectively.

Socioeconomic and psychosocial variables significantly associated with poor outcomes in bivariate analyses were entered in an initial conditional multivariable logistic regression model. A forced-entry stepwise hierarchical model reduction approach was used to identify independent covariates. Length of time living with HIV (recoded as a binary variable using median split: diagnosed before 1999 vs diagnosed since

1999) was included and retained throughout model reduction. Socioeconomic and psychosocial variables significantly associated with poor outcomes in the final model were considered independently associated with poor HIV treatment outcomes as defined. All statistical analyses were conducted using IBM SPSS Statistics Version 23.0 (IBM Corp., Armonk, NY, USA).

Unless indicated otherwise, data are presented as the mean \pm s.d.

Results

Participants

Thirty-nine cases were enrolled and compared with 120 controls. The characteristics of the cases are presented in Table 1. There were no significant differences between the cases and controls in terms of age (50.3 ± 9.7 vs 51.4 ± 11.6 years respectively) or sex (37 (94.9%) vs 116 (6.7%) male respectively). Significant differences between cases and controls in bivariate analyses were found for financial assistance required for cost-of-living expenses (56.4% ($n = 22$) vs 25.8% ($n = 31$) respectively), receiving income from social benefits (61.5% ($n = 24$) vs 35% ($n = 42$) respectively)

Table 1. Characteristics of cases (i.e. the 39 participants with poor HIV treatment outcomes) at presentation

Data are presented as n (%). ART, antiretroviral therapy; SNAE, serious non-AIDS event

Not taking ART	20 (51.3)
HIV viral load >50 copies mL ⁻¹	35 (89.7)
AIDS-defining illness	12 (30.8)
Hospitalised with a new SNAE	5 (12.8)

and cost being a barrier to accessing HIV care (28.2% ($n = 11$) vs 9.2% ($n = 11$) respectively).

Thirty-five cases (90%) had a viral load >50 copies mL⁻¹ (either not taking ART or on ART with virologic failure). Nineteen of 39 cases (48.7%) had previously recorded viral suppression since ART initiation. No case met all four inclusion criteria; 10 cases (25.6%) met three criteria, 19 (48.7%) met two criteria and 10 (25.6%) only met one criterion. Ten cases (25.6%) were recruited while they were hospital in-patients. No control had an active AIDS-defining illness, although 39 (32.5%) had a history of an AIDS-defining illness. No controls were hospitalised. Seventy controls (58.3%) had a known comorbidity, mostly cardiovascular disease ($n = 33$ (27.5%)).

Multivariable analysis

Ten socioeconomic and psychosocial variables examined were significantly associated with poor outcomes as defined (i.e. with being a case) in bivariate analysis: mode of HIV transmission, not being in a sexual relationship, two or more life stressors in the previous 12 months, quality of life lower than the sample mean, being under- or unemployed, income from social benefits, foregoing necessities for financial reasons, requiring financial assistance for cost-of-living expenses in the previous 12 months, cost as a barrier to accessing HIV care and injection drug use (see Table 2).

Variables significant in bivariate analyses were entered into a multivariable model that was statistically significant ($\chi_{10}^2 = 46.175$, $P < 0.001$), correctly classified 79.9% of cases and explained 37.5% of the variance (Nagelkerke R^2) in poor treatment outcomes. Three covariates were independently associated with poor treatment outcomes: foregoing necessities for financial reasons (adjusted OR (aOR) 3.1, 95% CI 1.3–7.6, $P = 0.014$), cost barriers to accessing HIV

Table 2. Socioeconomic and psychosocial variables associated with cascade failure

P -values were calculated using Chi-squared tests. aOR, adjusted odds ratio; CI, confidence interval; MSM, men who have sex with men; OR, odds ratio; IVDU, intravenous drug use

Variable	No. cases	No. controls	Bivariate analysis		Multivariate analysis	
			OR (95% CI)	P -value	aOR ^A (95% CI)	P -value
Social						
Mode of HIV infection not MSM (e.g. IVDU, unknown, other)	16	27	2.4 (1.1–5.2)	0.024		
Not in a sexual relationship	28	64	2.2 (1.0–4.9)	0.043		
No. life stressors in the previous 12 months higher than sample median of 2.0 ^B	22	33	3.4 (1.6–7.2)	0.001		
Lower quality of life than sample mean	30	39	6.9 (3.0–16.0)	<0.001	3.8 (1.5–9.7)	0.004
Financial						
Under- or unemployed (no work, or would increase work hours if possible)	28	51	3.4 (1.6–7.6)	0.001		
Income from social welfare	24	42	3.0 (1.4–6.3)	0.003		
Required financial assistance for cost-of-living expenses in the previous 12 months	22	31	3.7 (1.8–7.9)	<0.001		
Has foregone necessities for financial reasons in the previous 12 months	23	22	6.4 (2.9–14.1)	<0.001	3.1 (1.3–7.6)	0.014
Cost was a barrier to accessing HIV care	11	11	3.9 (1.5–9.9)	0.003	3.1 (1.0–9.6)	0.049
Drug use: monthly or more						
IVDU	13	17	3.0 (1.3–7.0)	0.008		

^AOnly those variables that remained significant in the multivariate analysis are included here.

^BLife stressors included serious illness, serious accident, mental illness, serious disability, death of family member or close friend, a new relationship, divorce or separation or relationship breakdown, unable to secure employment, alcohol- or drug-related problems, gambling problems, abuse or violent crime, witness to violence, trouble with the police and caring for someone with ill health.

care (aOR 3.1, 95% CI 1.0–9.6, $P = 0.049$) and lower quality of life (aOR 3.8, 95% CI 1.5–9.7, $P = 0.004$).

Discussion

In this study, three socioeconomic and psychosocial covariates were independently associated with poor treatment outcomes: foregoing necessities for financial reasons, cost barriers to accessing HIV care and low quality of life. Importantly, poor treatment outcomes encompassed HIV viraemia, as well as not taking ART or hospitalisation with an AIDS-defining illness or new SNAE.

The association of socioeconomic variables, notably financial strain and cost barriers to accessing HIV care (e.g. pharmaceutical copayments and medical practitioner gap payments), with poor treatment outcomes is consistent with previous Australian findings that patients in a hospital outpatient setting who have difficulty paying for ART-related out-of-pocket expenses are more likely to cease ART and that a smaller subset of these patients also had difficulty meeting travel costs to attend the clinic.¹⁹ Despite the importance of financial constraints, less than 5% of patients in the previous study were asked by healthcare workers whether they had difficulty meeting these expenses.¹⁹ Further attesting to the importance of socioeconomic factors in HIV treatment outcomes, a large cross-sectional study in the UK, a country with a national health system similar to that in Australia, found that virological failure was most likely in participants experiencing the highest rate of financial hardship.¹⁶ In addition, a systematic review found an association between unemployment and virological non-suppression or changes in viral load in four of five included studies.¹⁸

In the present study, 100% of the control participants and 77% of the case participants were enrolled before a state-wide abolition of the pharmaceutical copayment for ART for HIV. Prior to its removal, this was A\$37.70 for full paying patients per medication, capped at A\$1494.90 annually. This policy change may have resulted in a reduction in the cost barriers to accessing HIV care, and further studies since the policy change are required.

Some social disadvantages may contribute to vulnerability to HIV, including social disparities in health (e.g. environmental resources or constraints, socioeconomic position, access to care).³² From our data, it is not possible to tell whether a patient's HIV serostatus contributed to their socioeconomic disadvantage or whether the disadvantage became more pronounced following their HIV diagnosis.

Lower self-reported quality of life was also associated with poor treatment outcomes. As with all associations, we are unable to infer the direction of this association. It may be that as patients become more unwell, with detectable virus and opportunistic infections, there is a decline in quality of life. However, it may also be that those with a lower quality of life are less likely to adhere to treatments or engage in their health care. This further supports the incorporation of the 'fourth 90' (representing good health-related quality of life).⁴ It has been proposed that the 'fourth 90' encompass comorbidities and self-perceived quality of life, a model of person-centred chronic care

acknowledging that virological suppression is not the only measure of successful treatment.⁴

The present study has several limitations. Recruitment was at a single hospital site, and predominantly male patients were enrolled; hence, the findings are not necessarily generalisable to other settings and populations (e.g. women or youth) in Australia or elsewhere in high-income countries. Recruitment was challenging in this patient population, because many potential participants were disengaged from care, unwell or had limited ability to consent to participate because of substance use. This may have compounded the potential for selection bias.

The sample of cases in this study was relatively small ($n = 39$), and this is reflected in wide CIs. Statistical power for the study was set to detect an OR of 3.5, which may have limited the possibility of detecting smaller effects. Future research would benefit from a larger sample size, which would have allowed analysis of the separate components of the composite endpoint encompassing not being on ART, virological failure while on ART or hospitalisation due to an ADC or a new SNAE. In addition, other statistical techniques could be used with a larger sample, notably principle component analysis to examine interitem correlations and establish multi-item scales that contribute a lower risk of multicollinearity.^{33–36} Further, larger studies in other settings are required.

Conclusions

This study found that, in a high-income setting with a universal healthcare system providing highly subsidised health care and pharmaceuticals, socioeconomic and psychosocial variables are associated with poorer treatment outcomes in adults with HIV. Targeted policy and interventions that ensure the provision of financial and social support to those who need it likely contributes to mitigating critical socioeconomic and psychosocial barriers to successful HIV treatment. This, in turn, may contribute to increasing the number of people with HIV who are on ART, promote sustained viral suppression, and reduce hospitalisations due to ADC or new SNAEs.

Conflicts of interest

Krista J. Siefried has received a fellowship grant from Gilead Sciences, travel and conference sponsorships from Gilead Sciences and an Australian Government Research Training Program (RTP) Scholarship. John McAllister has received lecture fees from ViiV Healthcare and conference and travel sponsorships from ViiV Healthcare and MSD. John de Wit has received lecture sponsorship from BMS Australia. Andrew Carr has received research funding from BMS, Gilead Sciences and ViiV Healthcare; consultancy fees from Gilead Sciences and ViiV Healthcare; lecture and travel sponsorships from BMS, Gilead Sciences and ViiV Healthcare; and has served on advisory boards for Gilead Sciences, MSD, and ViiV Healthcare. The remaining authors have no potential conflicts of interest to declare.

Acknowledgements

The authors thank all the study participants for their time. This study was funded by a Gilead Fellowship Grant and The Balnaves Foundation.

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