

# Risk Factors for Suboptimal Adherence Identified by Patient-Reported Outcomes Assessments in Routine HIV Care at 2 North American Clinics

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**Purpose:** Use of patient-reported outcomes assessments (PROs) can improve patient-provider communication and focus provider attention on current health issues. This analysis examines the association between suboptimal antiretroviral therapy (ART) adherence and factors obtained through PROs among people with HIV (PWH) at 2 North American outpatient clinics.

**Patients and Methods:** Immediately before a clinic visit, PWH completed self-administered PROs. Unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated from logistic regression models to identify sociodemographic and health-related factors (satisfaction with ART, difficulty meeting housing costs, depression, intimate partner violence, risk of malnutrition, smoking status, alcohol use, and substance use) associated with suboptimal adherence (defined as self-reporting <95% or <80% adherence). Multiple imputation was performed to account for missing data in the multivariate analyses.

**Results:** Of 1632 PWH, 1239 (76%) responded to the adherence assessment; of these, 268 (22%) and 106 (9%) reported <95% and <80% adherence, respectively. Of 1580 PWH who responded, 354 (22%) were dissatisfied with their HIV medication. Of responding PWH, 19% reported moderate-to-severe depression, 23% indicated they were at risk of malnutrition, 34% were current smokers, and 62% reported substance use in the past 3 months. Dissatisfaction with ART was significantly associated with <95% and <80% adherence in the unadjusted analysis (unadjusted OR [95% CI], 3.38 [2.51–4.56] and 4.26 [2.82–6.42], respectively) and adjusted analysis (adjusted OR [95% CI], 2.76 [1.91–4.00] and 3.28 [1.95–5.52], respectively); significance remained after multiple imputation. In adjusted analyses, no risk of malnutrition was significantly associated with reduced odds of <95% adherence after multiple imputation (adjusted OR [95% CI], 0.714 [0.511–0.997]); no other factors were associated with <95% or <80% adherence.

**Conclusion:** These results suggest that implementation of PROs evaluating treatment satisfaction may provide value to adherence management in routine HIV care.

**Keywords:** patient satisfaction, antiretroviral therapy, highly active, treatment adherence, implementation science, quality of life

## Introduction

Modern antiretroviral therapy (ART) regimens are highly effective at achieving virologic suppression, thereby reducing HIV-associated morbidity and mortality and increasing health-related quality of life among people with HIV (PWH).<sup>1,2</sup> However, suboptimal adherence to ART is associated with increased rates of virologic failure.<sup>2,3</sup> Therefore, detecting and addressing suboptimal adherence among PWH is critical in HIV clinical care.

Adherence to ART is associated with multiple behavioral, social, and clinical factors.<sup>4–7</sup> However, identifying and addressing all factors potentially contributing to suboptimal ART adherence in individual patients can be challenging for healthcare providers during brief clinic visits.<sup>8</sup> Screening assessments using patient-reported outcomes assessments

(PROs) in routine HIV care can improve patient–provider communication and focus provider attention on symptoms or behaviors that may not otherwise be addressed, such as mental health issues and substance use.<sup>9–14</sup> Information obtained through PROs may also aid providers in identifying barriers to ART adherence among their patients.<sup>15</sup> For example, previous studies have demonstrated that substance use, depression, and dissatisfaction with ART are associated with suboptimal ART adherence among PWH who completed PROs at routine HIV clinic visits.<sup>8,15</sup>

The PROgress study evaluated the implementation of PROs into routine HIV care at 2 outpatient clinics in North America and assessed the added value of PRO implementation for healthcare providers and PWH.<sup>13</sup> In the PROgress study, both healthcare providers and PWH found that PRO administration before clinic visits was useful, facilitated the discussion of sensitive topics, and improved overall patient care. Here we examine the association between socio-demographic and health-related factors obtained through PROs and suboptimal adherence to ART among PWH enrolled in the PROgress study.

## Materials and Methods

### Study Design and Participants

The PROgress study was a prospective, hybrid type 3 implementation-effectiveness study conducted between August 2018 and July 2020 at 2 outpatient clinics: St Michael’s Hospital (SMH) in Toronto, Ontario, Canada, and the Midway Specialty Care Center (MSCC) in Fort Pierce, Florida, USA. Detailed methodology has been previously described.<sup>13</sup> Eligible participants were aged  $\geq 18$  years with a diagnosis of HIV who attended a participating clinic for a routine visit during the study period and could sufficiently speak and understand English, Spanish, and/or Haitian Creole to be able to complete the PRO. Individuals with psychiatric, cognitive, or motor impairment and those visiting the clinic for a non-routine reason (ie, acute illness or injury) or to see a provider other than their primary HIV care provider were excluded.

The study was conducted in accordance with International Conference on Harmonization Good Clinical Practice Guidelines and the principles of the Declaration of Helsinki. The study was approved by the SMH Research Ethics Board and the University of Washington Institutional Review Board for MSCC. All participants provided written informed consent at the time of their visit.

### Study Design and Participants

Participants completed self-administered PROs on-site immediately before a routine care visit. The PROs were administered via a touch-screen tablet using a previously developed PRO platform (<http://cprohealth.org>). Results of completed PROs were scored using automated algorithms, summarized, and then given to the provider immediately before the clinic visit.

Assessments contained instruments evaluating several sociodemographic and health-related domains. Adherence to ART was evaluated using a visual analog scale item asking the percentage of HIV medication taken in the last month (0–100%); suboptimal adherence was defined as self-reported adherence of either  $< 95\%$  or  $< 80\%$ .<sup>16</sup> Satisfaction with ART was assessed using the following 2 items from the HIV/AIDS-targeted quality of life (HATQoL) instrument: in the past 4 weeks, taking my [HIV] medicine has (1) “been a burden” or (2) “made it hard to live a normal life”.<sup>17</sup> Responses were categorized using a 5-point Likert scale; dissatisfaction with ART was defined as a response of “some of the time”, “a lot of the time”, or “all of the time” to  $\geq 1$  item and satisfaction with ART was defined as a response of “a little of the time” or “none of the time” to  $\geq 1$  item. Difficulty meeting housing costs, ie, rent or mortgage, property taxes, and utilities, was assessed with a single question. Depression was assessed using the Patient Health Questionnaire 9, with a total score of  $> 10$  defined as moderate or severe depression.<sup>18,19</sup> Intimate partner violence was evaluated using the Intimate Partner Violence 4 Questionnaire.<sup>20</sup> Risk of malnutrition was assessed using the Canadian Nutrition Screening Tool; individuals who reported weight loss without trying in the past 6 months and eating less than usual for more than a week were defined as high risk.<sup>21</sup> Smoking status was assessed using a single item from the Center for AIDS Research Network in Integrated Clinical Systems Smoking Questionnaire.<sup>22</sup> Alcohol use was evaluated using the Alcohol Use Disorders Identification Test Consumption Questionnaire;<sup>23</sup> individuals who reported having a drink containing alcohol 2 to 3 times

a week or  $\geq 4$  times a week in the past year were defined as high risk. Substance use was assessed using the modified Alcohol, Smoking, and Substance Involvement Screening Test and was defined as any non-medical use of cocaine, methamphetamine, heroin, fentanyl, narcotics, sedatives, sleeping pills, marijuana, stimulants, inhalants, hallucinogens, or anabolic steroids in the past 3 months.<sup>24</sup>

Chart reviews of medical records were performed as part of the wider PROgress study evaluation and were completed for a subset of participants to obtain information on demographic and disease characteristics.

## Data Analyses

Participant demographics and disease characteristics were summarized using descriptive statistics. To identify socio-demographic and health-related factors associated with suboptimal adherence of  $<95\%$  and  $<80\%$ , unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using univariate logistic regression models, and adjusted ORs and 95% CIs were estimated using multivariate logistic regression models. Variables that yielded  $P$  values  $<0.15$  in unadjusted analyses were included in multivariate logistic regression analyses. Additional multivariate logistic regression models were performed using stepwise selection, with a significance level of 0.15 for a variable to enter the model and a significance level of 0.15 for a variable to stay in the model. Each multivariate logistic regression model included either the burden HATQoL item alone, the normal life HATQoL item alone, or both HATQoL items combined as variables. Current smoker and substance use (past 3 months) were not included as variables in the multivariate models due to a large number of missing values. Only participants who responded to the adherence item were included in the univariate and multivariate analyses.

To account for missing data due to non-responses in the multivariate analyses, multiple imputation was performed using the full conditional specification method with 25 imputations.<sup>25</sup> To avoid overfitting, the number of variables was limited to less than  $m/10$ , where  $m$  is the minimum number of adherent or non-adherent participants.<sup>26</sup> Multiple imputed results were compared with those from the full sample of participants who responded to the adherence item.  $P$  values of  $<0.05$  were considered statistically significant for multivariate models. All analyses were performed using SAS<sup>®</sup> software version 9.4 (SAS Institute Inc, Cary, NC).

## Results

### Study Population

Of 1813 eligible PWH asked to participate in the study, 1632 initiated a PRO and were included in this analysis ( $n=600$  from SMH;  $n=1032$  from MSCC). Among 596 PWH who had data for demographic and disease characteristics available from chart reviews ( $n=297$  from SMH;  $n=299$  from MSCC), 69% were male at birth, 43% were Black, 28% were aged  $\geq 60$  years, and 82% had undetectable viral load (Table 1).

### Characteristics of PWH Obtained from PROs

Of 1632 PWH included in this analysis, 1239 (76%) responded to the assessment relating to ART adherence; of these 268 (22%) participants reported  $<95\%$  adherence and 106 (9%) reported  $<80\%$  adherence (Table 2). Response rates for the other PRO instruments ranged from 61% for the substance abuse item to 99% for the risk of malnutrition and alcohol use items. Of 1580 PWH who responded to 1 or both of the HATQoL items “... taking my [HIV] medicine has been a burden” and/or “... taking my [HIV] medicine has made it hard to live a normal life” (response rate, 97%), 354 (22%) reported they were dissatisfied with their HIV medication. For the individual HATQoL items, dissatisfaction with their HIV medication was reported by 18% of respondents for the burden item and 16% for the normal life item. Of responding PWH, 19% reported moderate-to-severe depression, 23% indicated they were at risk of malnutrition, 34% were current smokers, and 62% reported substance use in the past 3 months. Results obtained from PROs were generally consistent across the SMH and MSCC sites, except for the proportion of PWH reporting that they were current smokers (19% at SMH vs 50% at MSCC) and the proportion reporting substance use in the past 3 months (75% at SMH vs 56% at MSCC; Supplementary Table 1).

**Table 1** Demographic and Disease Characteristics of PWH Included in Chart Reviews (SMH and MSCC)

Parameter, n (%)	PWH (N=596)
Age, y	
<30	68 (11)
30 to <40	117 (20)
40 to <50	109 (18)
50 to <60	135 (23)
≥60	165 (28)
Sex at birth	
Male	409 (69)
Female	187 (31)
Race	
Black	254 (43)
White	222 (37)
Asian	24 (4)
Other races/Not specified <sup>a</sup>	86 (14)
Ethnicity	
Hispanic	42 (7)
CD4+ cell count, cells/mm <sup>3</sup>	
≤350	107 (18)
351 to <500	101 (17)
≥500	388 (65)
Viral load	
Undetectable	487 (82)
Detectable	109 (18)
Transmission risk category <sup>b</sup>	
Bisexual (either gender)	43 (7)
Blood product transfusion	17 (3)
Endemic area	54 (9)
Heterosexual	283 (47)
Injection drug user	31 (5)
Men who have sex with men	243 (41)
Unknown	19 (3)

**Notes:** <sup>a</sup>Including aboriginal, First Nations, Middle Eastern, mixed race, and Native American. <sup>b</sup>Categories are not mutually exclusive.

**Abbreviations:** MSCC, Midway Specialty Care Center; PWH, people with HIV; SMH, St Michael's Hospital.

**Table 2** Sociodemographic and Health-Related Characteristics of PWH Obtained from PROs (SMH and MSCC)

Variable	Category	Respondents, n (%) <sup>a</sup>	PWH with Characteristic, n (%) <sup>b</sup>
ART adherence	≥95%	1239 (76)	971 (78)
	<95%		268 (22)
	≥80%		1133 (91)
	<80%		106 (9)
HATQoL burden item <sup>c</sup>	Satisfied	1527 (94)	1255 (82)
	Dissatisfied		272 (18)
HATQoL normal life item <sup>d</sup>	Satisfied	1555 (95)	1312 (84)
	Dissatisfied		243 (16)
Combined HATQoL items	Satisfied	1580 (97)	1226 (78)
	Dissatisfied		354 (22)
Difficulty meeting housing costs	Yes	1539 (94)	978 (64)
	No		561 (36)
Depression	Moderate/Severe	1533 (94)	298 (19)
	Mild/None		1235 (81)
Intimate partner violence	Yes	1295 (79)	120 (9)
	No		1175 (91)
Risk of malnutrition	Yes	1608 (99)	365 (23)
	No		1243 (77)
Current smoker	Yes	1131 (69)	384 (34)
	No		747 (66)
Alcohol use	High risk	1620 (99)	311 (19)
	Low risk		1309 (81)
Substance use (past 3 months)	Yes	988 (61)	615 (62)
	No		373 (38)

**Notes:** <sup>a</sup>Percentage of the total number of PWH included in the analysis (N=1632). <sup>b</sup>Percentage of respondents for each variable. <sup>c</sup>In the past 4 weeks, taking my [HIV] medicine has been a burden. <sup>d</sup>In the past 4 weeks, taking my [HIV] medicine has made it hard to live a normal life.

**Abbreviations:** ART, antiretroviral therapy; HATQoL, HIV/AIDS-targeted quality of life; MSCC, Midway Specialty Care Center; PRO, patient-reported outcomes assessment; PWH, people with HIV; SMH, St Michael's Hospital.

## Association of Suboptimal Adherence with ART Satisfaction and Characteristics of PWH

In the unadjusted analysis, dissatisfaction with ART was significantly associated with suboptimal adherence of <95% and <80% regardless of whether the burden and normal life HATQoL items were assessed individually or combined (Table 3). The significant association between ART dissatisfaction and suboptimal adherence was observed at both the

**Table 3** Unadjusted Odds Ratios for Association with <95% and <80% Adherence to ART Among PWH (N=1239; SMH and MSCC)

Variable	Category	<95% Adherence		<80% Adherence	
		Unadjusted OR (95% CI)	P value <sup>a</sup>	Unadjusted OR (95% CI)	P value <sup>a</sup>
HATQoL burden item <sup>b</sup>	Dissatisfied (vs satisfied)	4.322 (3.141–5.947)	<b>&lt;0.0001</b>	5.245 (3.451–7.970)	<b>&lt;0.0001</b>
HATQoL normal life item <sup>c</sup>	Dissatisfied (vs satisfied)	2.639 (1.873–3.719)	<b>&lt;0.0001</b>	3.663 (2.358–5.691)	<b>&lt;0.0001</b>
Combined HATQoL items	Dissatisfied (vs satisfied)	3.384 (2.510–4.561)	<b>&lt;0.0001</b>	4.258 (2.824–6.420)	<b>&lt;0.0001</b>
Difficulty meeting housing costs	No (vs yes)	0.669 (0.494–0.906)	<b>0.0093</b>	0.714 (0.455–1.119)	0.1418
Depression	Mild/None (vs moderate/ severe)	0.547 (0.394–0.759)	<b>0.0003</b>	0.638 (0.397–1.024)	0.0629
Intimate partner violence	No (vs yes)	0.642 (0.404–1.023)	0.0623	0.599 (0.313–1.145)	0.1207
Risk of malnutrition	No (vs yes)	0.582 (0.425–0.797)	<b>0.0007</b>	0.610 (0.390–0.956)	<b>0.0309</b>
Current smoker	No (vs yes)	0.675 (0.487–0.937)	<b>0.0188</b>	0.579 (0.355–0.947)	<b>0.0295</b>
Alcohol use	Low risk (vs high risk)	1.254 (0.878–1.792)	0.2135	1.297 (0.757–2.223)	0.3442
Substance use (past 3 months)	No (vs yes)	1.120 (0.781–1.604)	0.5385	1.058 (0.595–1.882)	0.8470

**Notes:** <sup>a</sup>Bold values denote *P* values <0.05. <sup>b</sup>In the past 4 weeks, taking my [HIV] medicine has been a burden. <sup>c</sup>In the past 4 weeks, taking my [HIV] medicine has made it hard to live a normal life.

**Abbreviations:** ART, antiretroviral therapy; CI, confidence interval; HATQoL, HIV/AIDS-targeted quality of life; MSCC, Midway Specialty Care Center; OR, odds ratio; PWH, people with HIV; SMH, St Michael's Hospital.

SMH and MSCC sites ([Supplementary Table 2](#)). In the overall population, individuals with no risk of malnutrition and non-smokers were significantly less likely to have <95% and <80% adherence ([Table 3](#)). No difficulty meeting housing costs and mild or no depression were also significantly associated with a reduced likelihood of <95% adherence.

In multivariate logistic regression models that included either the burden HATQoL item alone, the normal life HATQoL item alone, or both HATQoL items combined, dissatisfaction with ART was significantly associated with <95% adherence (adjusted OR [95% CI], 3.36 [2.26–4.98], 2.29 [1.49–3.52], and 2.76 [1.91–4.00], respectively; *P*<0.05; [Table 4](#)) and <80% adherence (adjusted OR [95% CI], 3.83 [2.25–6.53], 3.12 [1.76–5.52], and 3.28 [1.95–5.52], respectively; *P*<0.0001; [Table 5](#)). After multiple imputation, dissatisfaction with ART remained significantly associated with suboptimal adherence of <95% and <80% across all 3 models. After multiple imputation, no risk of malnutrition was significantly associated with reduced odds of <95% adherence in the model that included the normal life HATQoL item alone or both HATQoL items combined but not in the model that included the burden HATQoL item alone ([Table 4](#)). The other participant characteristics included in the multivariate logistic regression models were not associated with <80% adherence in any model ([Table 5](#)).

At the SMH site, dissatisfaction with ART was significantly associated with <95% adherence both before and after multiple imputation in multivariate logistic regression models including the burden HATQoL item alone or both HATQoL items combined and after multiple imputation in the model including the normal life HATQoL item alone ([Supplementary Table 3](#)). At the MSCC site, a significant association between ART dissatisfaction and <95% adherence was observed in each model both before and after multiple imputation. After multiple imputation in all 3 models, significantly reduced odds of <95% adherence were observed among individuals with no difficulty meeting housing costs at SMH but not at MSCC. At SMH, <80% adherence was significantly associated with ART dissatisfaction before and after multiple imputation in the burden HATQoL item model and after multiple imputation in the other 2 models ([Supplementary Table 4](#)); no results from multivariate logistic regression models were available for <80% adherence at MSCC because HATQoL factors were the only variables with unadjusted *P* values <0.15.

In multivariate stepwise selection models that included either the burden HATQoL item alone, the normal life HATQoL item alone, or both HATQoL items combined, dissatisfaction with ART was significantly associated with

**Table 4** Adjusted Odds Ratios from Multivariate Logistic Regression Models for Association with <95% Adherence to ART Among PWH (SMH and MSCC)

Variable	Category	Before Multiple Imputation <sup>a</sup>		After Multiple Imputation <sup>b</sup>	
		Adjusted OR (95% CI)	P value <sup>c</sup>	Adjusted OR (95% CI)	P value <sup>c</sup>
Model 1: HATQoL burden item					
HATQoL burden item <sup>d</sup>	Dissatisfied (vs satisfied)	3.357 (2.263–4.979)	<b>&lt;0.0001</b>	3.795 (2.725–5.285)	<b>&lt;0.0001</b>
Difficulty meeting housing costs	No (vs yes)	0.880 (0.608–1.273)	0.4974	0.902 (0.652–1.249)	0.5357
Depression	Mild/None (vs moderate/severe)	0.875 (0.582–1.317)	0.5226	0.798 (0.553–1.152)	0.2284
Intimate partner violence	No (vs yes)	0.678 (0.398–1.157)	0.1542	0.777 (0.473–1.276)	0.3181
Risk of malnutrition	No (vs yes)	0.704 (0.476–1.042)	0.0792	0.724 (0.516–1.015)	0.0613
Model 2: HATQoL normal life item					
HATQoL normal life item <sup>e</sup>	Dissatisfied (vs satisfied)	2.286 (1.487–3.516)	<b>0.0002</b>	2.248 (1.566–3.228)	<b>&lt;0.0001</b>
Difficulty meeting housing costs	No (vs yes)	0.808 (0.561–1.165)	0.2536	0.832 (0.605–1.145)	0.2587
Depression	Mild/None (vs moderate/severe)	0.759 (0.509–1.131)	0.1757	0.745 (0.519–1.070)	0.1113
Intimate partner violence	No (vs yes)	0.818 (0.481–1.391)	0.4575	0.860 (0.525–1.407)	0.5471
Risk of malnutrition	No (vs yes)	0.711 (0.484–1.046)	0.0836	0.705 (0.506–0.980)	<b>0.0377</b>
Model 3: Combined HATQoL items					
Combined HATQoL items	Dissatisfied (vs satisfied)	2.762 (1.905–4.004)	<b>&lt;0.0001</b>	3.020 (2.207–4.132)	<b>&lt;0.0001</b>
Difficulty meeting housing costs	No (vs yes)	0.871 (0.604–1.255)	0.4571	0.889 (0.642–1.230)	0.4771
Depression	Mild/None (vs moderate/severe)	0.804 (0.538–1.200)	0.2856	0.798 (0.553–1.150)	0.2259
Intimate partner violence	No (vs yes)	0.779 (0.459–1.323)	0.3557	0.858 (0.524–1.404)	0.5418
Risk of malnutrition	No (vs yes)	0.730 (0.495–1.077)	0.1126	0.714 (0.511–0.997)	<b>0.0481</b>

Notes: <sup>a</sup>N=950, N=951, and N=961 in models 1, 2, and 3, respectively. <sup>b</sup>N=1239 in each model. <sup>c</sup>Bold values denote P values <0.05. <sup>d</sup>In the past 4 weeks, taking my [HIV] medicine has been a burden. <sup>e</sup>In the past 4 weeks, taking my [HIV] medicine has made it hard to live a normal life.

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; HATQoL, HIV/AIDS-targeted quality of life; MSCC, Midway Specialty Care Center; OR, odds ratio; PWH, people with HIV; SMH, St Michael's Hospital.

<95% adherence (adjusted OR [95% CI], 4.06 [2.94–5.60], 2.41 [1.70–3.42], and 3.18 [2.35–4.30], respectively;  $P < 0.0001$ ), with each association remaining significant after multiple imputation across all 3 models (Table 6). Before and after multiple imputation in all stepwise selection models, PWH with no risk of malnutrition were significantly less likely to have <95% adherence. No results from stepwise multivariate analyses were available for <80% adherence because the only variables remaining after stepwise selection were HATQoL factors.

At the SMH site, a significant association between ART dissatisfaction and <95% adherence was observed by each stepwise selection model both before and after multiple imputation (Supplementary Table 5); results from stepwise multivariate analyses at the MSCC site were not available because HATQoL factors were the only variables remaining after stepwise selection. Before and after multiple imputation at the SMH site, significantly reduced odds of <95% adherence were observed among PWH with no difficulty meeting housing costs in all 3 models and those with no risk of malnutrition in the normal life HATQoL item model.



**Table 5** Adjusted Odds Ratios from Multivariate Logistic Regression Models for Association with <80% Adherence to ART Among PWH (SMH and MSCC)

Variable	Category	Before Multiple Imputation <sup>a</sup>		After Multiple Imputation <sup>b</sup>	
		Adjusted OR (95% CI)	P value <sup>c</sup>	Adjusted OR (95% CI)	P value <sup>c</sup>
Model 1: HATQoL burden item					
HATQoL burden item <sup>d</sup>	Dissatisfied (vs satisfied)	3.832 (2.250–6.526)	<b>&lt;0.0001</b>	5.005 (3.219–7.783)	<b>&lt;0.0001</b>
Difficulty meeting housing costs	No (vs yes)	0.944 (0.537–1.660)	0.8422	1.071 (0.657–1.747)	0.7820
Depression	Mild/None (vs moderate/severe)	0.892 (0.498–1.597)	0.7015	1.003 (0.590–1.705)	0.9909
Intimate partner violence	No (vs yes)	0.678 (0.321–1.428)	0.3064	0.744 (0.379–1.458)	0.3883
Risk of malnutrition	No (vs yes)	0.696 (0.399–1.212)	0.2002	0.764 (0.472–1.237)	0.2734
Model 2: HATQoL normal life item					
HATQoL normal life item <sup>e</sup>	Dissatisfied (vs satisfied)	3.118 (1.761–5.521)	<b>&lt;0.0001</b>	3.290 (2.052–5.275)	<b>&lt;0.0001</b>
Difficulty meeting housing costs	No (vs yes)	0.895 (0.511–1.568)	0.6993	0.971 (0.599–1.573)	0.9052
Depression	Mild/None (vs moderate/severe)	0.870 (0.485–1.560)	0.6397	0.949 (0.560–1.606)	0.8447
Intimate partner violence	No (vs yes)	0.763 (0.365–1.595)	0.4723	0.859 (0.442–1.669)	0.6534
Risk of malnutrition	No (vs yes)	0.698 (0.402–1.211)	0.2009	0.740 (0.461–1.188)	0.2122
Model 3: Combined HATQoL items					
Combined HATQoL items	Dissatisfied (vs satisfied)	3.278 (1.945–5.524)	<b>&lt;0.0001</b>	4.018 (2.599–6.211)	<b>&lt;0.0001</b>
Difficulty meeting housing costs	No (vs yes)	0.915 (0.522–1.606)	0.7572	1.045 (0.642–1.701)	0.8596
Depression	Mild/None (vs moderate/severe)	0.908 (0.507–1.626)	0.7445	0.998 (0.589–1.690)	0.9926
Intimate partner violence	No (vs yes)	0.763 (0.364–1.601)	0.4748	0.840 (0.432–1.632)	0.6059
Risk of malnutrition	No (vs yes)	0.688 (0.396–1.195)	0.1847	0.742 (0.461–1.195)	0.2201

Notes: <sup>a</sup>N=950, N=951, and N=961 in models 1, 2, and 3, respectively. <sup>b</sup>N=1239 in each model. <sup>c</sup>Bold values denote P values <0.05. <sup>d</sup>In the past 4 weeks, taking my [HIV] medicine has been a burden. <sup>e</sup>In the past 4 weeks, taking my [HIV] medicine has made it hard to live a normal life.

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; HATQoL, HIV/AIDS-targeted quality of life; MSCC, Midway Specialty Care Center; OR, odds ratio; PWH, people with HIV; SMH, St Michael's Hospital.

**Table 6** Adjusted Odds Ratios from Multivariate Stepwise Selection Logistic Regression Models for Association with <95% Adherence to ART Among PWH (SMH and MSCC)

Variable	Category	Before Multiple Imputation <sup>a</sup>		After Multiple Imputation <sup>b</sup>	
		Adjusted OR (95% CI)	P value <sup>c</sup>	Adjusted OR (95% CI)	P value <sup>c</sup>
Model 1: HATQoL burden item					
HATQoL burden item <sup>d</sup>	Dissatisfied (vs satisfied)	4.056 (2.937–5.602)	<b>&lt;0.0001</b>	4.045 (2.933–5.579)	<b>&lt;0.0001</b>
Risk of malnutrition	No (vs yes)	0.656 (0.471–0.913)	<b>0.0125</b>	0.677 (0.487–0.940)	<b>0.0198</b>
Model 2: HATQoL normal life item					
HATQoL normal life item <sup>e</sup>	Dissatisfied (vs satisfied)	2.413 (1.701–3.423)	<b>&lt;0.0001</b>	2.530 (1.790–3.577)	<b>&lt;0.0001</b>
Risk of malnutrition	No (vs yes)	0.660 (0.477–0.914)	<b>0.0124</b>	0.655 (0.475–0.904)	<b>0.0100</b>

(Continued)



**Table 6** (Continued).

Variable	Category	Before Multiple Imputation <sup>a</sup>		After Multiple Imputation <sup>b</sup>	
		Adjusted OR (95% CI)	P value <sup>c</sup>	Adjusted OR (95% CI)	P value <sup>c</sup>
Model 3: Combined HATQoL items					
Combined HATQoL items	Dissatisfied (vs satisfied)	3.181 (2.351–4.304)	<b>&lt;0.0001</b>	3.255 (2.406–4.404)	<b>&lt;0.0001</b>
Risk of malnutrition	No (vs yes)	0.671 (0.484–0.929)	<b>0.0164</b>	0.672 (0.486–0.931)	<b>0.0167</b>

**Notes:** <sup>a</sup>N=1206, N=1208, and N=1225 in models 1, 2, and 3, respectively. <sup>b</sup>N=1239 in each model. <sup>c</sup>Bold values denote P values <0.05. <sup>d</sup>In the past 4 weeks, taking my [HIV] medicine has been a burden. <sup>e</sup>In the past 4 weeks, taking my [HIV] medicine has made it hard to live a normal life.

**Abbreviations:** ART, antiretroviral therapy; CI, confidence interval; HATQoL, HIV/AIDS-targeted quality of life; MSCC, Midway Specialty Care Center; OR, odds ratio; PWH, people with HIV; SMH, St Michael's Hospital.

## Discussion

In this analysis, dissatisfaction with ART was significantly associated with suboptimal adherence for both the <95% and <80% adherence thresholds in multiple multivariate logistic regression models. Individuals who felt that their HIV medicines were a burden and/or made living a normal life difficult were 2.2 to 5.0 times more likely to have suboptimal adherence than those who were satisfied with their ART medications. Similarly, a cross-sectional study in Brazil demonstrated that PWH who self-reported having low or insufficient adherence had lower medication satisfaction as measured by the HATQoL instrument compared with those who self-reported having strict adherence.<sup>27</sup> Consistent with these results, dissatisfaction with interference with daily routine, efficacy, and simplicity of ART was significantly associated with unstable or poor adherence among PWH enrolled in a cross-sectional study in Germany.<sup>28</sup> Overall, these results indicate that dissatisfaction with ART likely contributes to suboptimal adherence in many PWH. Therefore, screening for treatment satisfaction among PWH via use of PROs may be of value in routine HIV care.

High rates of adherence were self-reported by this self-selecting sample of PWH in the PROgress study, with 78% of participants reporting ≥95% adherence and 91% reporting ≥80% adherence. These adherence rates were higher than those reported in real-world observational studies or claims database studies conducted in Canada, which showed that 56% to 67% of PWH had ≥95% adherence using either refill compliance or proportion of days covered to measure adherence.<sup>29–31</sup> Using proportion of days covered, one US claims database study reported that 52% to 64% of PWH had ≥95% adherence, while another reported that 58% had ≥80% adherence.<sup>32,33</sup> By contrast, other Canadian and US claims database studies reported 86% to 93% of PWH had ≥80% adherence using proportion of days covered, similar to the ≥80% adherence rates observed in the present study.<sup>31,32</sup> Thus, adherence rates reported across studies using different adherence measurements vary widely, and comparisons between such studies should be interpreted with caution.

Because the minimum adherence level required to maintain durable virologic suppression is unclear, thresholds for optimal adherence to ART are not well defined.<sup>2</sup> The widely used adherence level of ≥95% is primarily based on a 2000 study of PWH treated with unboosted protease inhibitors (N=81), which showed that PWH with ≥95% adherence had lower rates of virologic failure compared with those with <95% adherence.<sup>3,34</sup> A 2019 systematic review found that >90% and >95% adherence were consistently associated with virologic suppression, with inconsistent findings observed when thresholds of <90% were used.<sup>2</sup> A 2016 meta-analysis of 43 studies found that the odds of virologic failure were not significantly different between studies using optimal adherence thresholds of 98% to 100%, ≥95%, and 80% to 90%.<sup>3</sup> A 2019 real-world database analysis found similar results, demonstrating no significant differences in the odds of virologic suppression for PWH with adherence levels of 80% to <85%, 85% to <90%, and ≥90%.<sup>35</sup> Overall, these recent analyses suggest that the improved efficacy and durability of modern antiretroviral agents may allow for some dose forgiveness, with acceptable levels of virologic suppression occurring with adherence levels as low as 80% for daily oral therapy.

This analysis has some limitations. The PROgress study included a self-selecting sample from 2 clinics in North America, which may limit the generalizability of these findings. Analyses could not be controlled by demographics and disease characteristics because these data were only available for a portion of the study sample. Adherence was self-reported and can at times be overestimated and influenced by recall or reporting bias.<sup>36</sup> In addition, adherence

was assessed at a single time point and does not reflect changes in adherence over time. Dissatisfaction with ART was not assessed in the context of specific regimens in this study; as more data become available from PROs, the association between suboptimal adherence and dissatisfaction with individual ART regimens can be evaluated.

## Conclusion

Use of PROs can provide important information about a patient's adherence and related risk factors to healthcare providers in real-time. In these 2 North American HIV clinics, dissatisfaction with ART was significantly associated with suboptimal adherence among PWH, indicating the potential value of implementing PROs that evaluate treatment satisfaction in routine HIV care.

## Abbreviations

ART, antiretroviral therapy; CI, confidence interval; HATQoL, HIV/AIDS-targeted quality of life; MSCC, Midway Specialty Care Center; PRO, patient-report outcomes assessment; OR, odds ratio; PWH, people with HIV; SMH, St Michael's Hospital.

## Data Sharing Statement

Anonymized individual participant data and study documents can be requested for further research from [www.clinicalstudydatarequest.com](http://www.clinicalstudydatarequest.com).

## Ethics Approval and Informed Consent

The study was conducted in full compliance with International Conference on Harmonization Good Clinical Practice Guidelines, the principles of the Declaration of Helsinki, and the laws and regulations of the countries in which the research was conducted. The study was approved by institutional review boards for the participating clinics. Data handling within the PRO system was in accordance with current US privacy and security regulations governing the storage and transmission of protected health information (<http://tiny.cc/cirgHIPAApolicies>). All study participants provided written informed consent.

## Acknowledgments

We thank the patients, providers, and research staff from the 2 PROgress study clinics, the Midway Specialty Care Center in Fort Pierce, Florida, USA, and St Michael's Hospital in Toronto, Ontario, Canada, for their commitment to this work. This study was funded by ViiV Healthcare. Editorial assistance was provided under the direction of the authors by Megan Schmidt, PhD, and Jennifer Rossi, MA, ELS, MedThink SciCom, and was funded by ViiV Healthcare.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

This study was funded by ViiV Healthcare. The study sponsor had a role in the study design; the collection, analysis and interpretation of data; and the writing of the manuscript. The decision to submit the manuscript for publication was made by the authors.

## Disclosure

DS, XW, TKH, BJ, and YW are employees of ViiV Healthcare and may own stock in GSK. SS has received grants from the Ontario HIV Treatment Network. HMC has received grants from ViiV Healthcare. MR has received personal fees from Gilead, ViiV Healthcare, Janssen, and Merck for speaking engagements and/or consultancies. JBe has received

personal fees from Bristol Myers Squibb, Tibotec, Merck, ViiV Healthcare, and Gilead for advisory board participation. RF, AM, JBa, KAG, and WBL have nothing to disclose.

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