

The Human Immunodeficiency Virus (HIV) Index: Using a Patient-Reported Outcome on Engagement in HIV Care to Explain Suboptimal Retention in Care and Virologic Control

Katerina A. Christopoulos,¹ Torsten B. Neilands,² Kimberly A. Koester,² John A. Saucedo,² Samantha E. Dilworth,² Michael J. Mugavero,³ Heidi M. Crane,⁴ Rob J. Fredericksen,⁴ Edward R. Cachay,⁵ Kenneth H. Mayer,⁶ Richard D. Moore,⁷ Sonia Napravnik,⁸ and Mallory O. Johnson²

¹Department of Medicine, Zuckerberg San Francisco General Hospital, University of California, San Francisco, San Francisco, California, USA, ²Department of Medicine, University of California, San Francisco, San Francisco, California, USA, ³Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA, ⁴Department of Medicine, University of Washington, Seattle, Washington, USA, ⁵Department of Medicine, University of California, San Diego, San Diego, California, USA, ⁶The Fenway Institute at Fenway Health, Boston, Massachusetts, USA, ⁷Department of Medicine, Johns Hopkins University, Baltimore, Maryland, USA, and ⁸Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

Background. We investigated the prospective association between a brief self-report measure of engagement in human immunodeficiency virus (HIV) care (the Index of Engagement in HIV Care; hereafter “Index”) and suboptimal retention and viral suppression outcomes.

Methods. The Centers for AIDS Research Network of Integrated Clinical Systems cohort study combines medical record data with patient-reported outcomes from 8 HIV clinics in the United States, which from April 2016 to March 2017 included the 10-item Index. Multivariable logistic regression was used to estimate the risk and odds ratios of mean Index scores on 2 outcomes in the subsequent year: (1) not keeping $\geq 75\%$ of scheduled HIV care appointments; and (2) for those with viral suppression at Index assessment, having viral load >200 copies/mL on ≥ 1 measurement. We also used generalized linear mixed models (GLMMs) to estimate the risk and odds ratios of appointment nonattendance or unsuppressed viral load at any given observation. We generated receiver operating characteristic curves for the full models overlaid with the Index as a sole predictor.

Results. The mean Index score was 4.5 (standard deviation, 0.6). Higher Index scores were associated with lower relative risk of suboptimal retention ($n = 2576$; logistic regression adjusted risk ratio [aRR], 0.88 [95% confidence interval, .87–.88]; GLMM aRR, 0.85 [.83–.87]) and lack of sustained viral suppression ($n = 2499$; logistic regression aRR, 0.75 [.68–.83]; GLMM aRR, 0.74 [.68–.80]). The areas under the receiver operating characteristic curve for the full models were 0.69 (95% confidence interval, .67–.71) for suboptimal retention and 0.76 (.72–.79) for lack of sustained viral suppression.

Conclusions. Index scores are significantly associated with suboptimal retention and viral suppression outcomes.

Keywords. HIV; engagement in care; retention in care; viral suppression; patient-reported outcome.

The schematic of the human immunodeficiency virus (HIV) care cascade made a significant impact on HIV treatment and prevention [1]. This framework provides a simple, yet compelling, representation of the successes and challenges in the fight against HIV by laying out estimates of a sequential series of key steps entailed in successful HIV control. The fact that in 2011 only approximately one-quarter of those living with HIV in the United States were thought to be virally suppressed

galvanized a wave of research and programmatic efforts focused on improving this outcome.

As the HIV care cascade became the organizing paradigm to measure the effectiveness of HIV treatment and prevention activities, important discussions ensued over how best to operationalize cascade metrics, particularly retention in care and viral suppression [2–5]. Research sought to compare the performance of various cascade measures, [6] and as this literature expanded, retention in HIV care often came to be used interchangeably with *engagement* in HIV care, even though patients may be retained based on appointment attendance but not engaged with care such that they take or consistently adhere to antiretroviral therapy (ART) or feel particularly connected to their care [7].

While retention and viral suppression may be necessary for engagement, they are not sufficient and may be more accurately viewed as outcomes of care engagement. At the same time, the

Received 30 June 2020; editorial decision 19 December 2020; published online 29 December 2020.

Correspondence: Katerina A. Christopoulos, Department of Medicine, Zuckerberg San Francisco General Hospital, University of California San Francisco, 995 Potrero Ave, Fourth Floor, San Francisco, CA 94110 (katerina.christopoulos@ucsf.edu).

Clinical Infectious Diseases® 2021;73(7):e2175–83
DOI: 10.1093/cid/ciaa1892

cascade paradigm put the onus for progression through its steps on the patient without acknowledging the care-related factors that might affect an individual's journey [8, 9]. As implied by the definition of the word "engaged"—"to attract and hold fast"—engagement is a process that occurs in relation to the provider and the clinic, in that the patient must be held fast by the care experience. Given the absence of a measure of engagement in HIV care, we aimed to develop a scale that incorporated the perspectives of those living with HIV and acknowledged the roles of the provider and the clinic in the engagement process.

We created the 10-item self-reported Index of Engagement in HIV Care (hereafter "Index"), using iterative formative work with HIV patients and providers, researchers of engagement in care, and policy experts [10–12] and performed a cross-sectional validation in the Centers for AIDS Research Network of Integrated Clinical Systems, an observational study of patients in routine HIV care [13]. Our formative work yielded a definition of HIV care engagement as follows: "Engagement in HIV care is the ongoing interaction of patients, their providers, and care settings that is characterized by a patient's sense of connection to and active participation in care." The validation study demonstrated that our scale measured a unidimensional construct of HIV care engagement and that scores correlated with concurrent viral suppression and prior retention in care.

The main objectives of the current analysis were to estimate the prospective association between the Index and 2 outcomes: suboptimal retention in care and failure to achieve sustained viral suppression. A secondary exploratory objective was to investigate the predictive value of the Index with regard to these outcomes.

METHODS

Study Setting and Population

The Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort study integrates electronic medical record data with patient-reported outcomes (PROs) from a regionally diverse network of academic HIV clinics in the United States [14]. Cohort inclusion criteria are age ≥ 18 years and ≥ 2 HIV primary care visits in a 12-month period. The self-administered PRO survey is collected approximately every 4–6 months as part of routine clinical care and consists of validated scales for ART adherence, depressive symptoms, and other psychosocial constructs known to affect HIV outcomes [15].

From April 2016 to March 2017, the Index, consisting of 10 items with 5-point Likert response scales (Table 1), was added to PROs at the following sites: University of Alabama, Birmingham; University of Washington; University of California, San Diego; University of California, San Francisco; Fenway Health; University of North Carolina at Chapel Hill; and Johns Hopkins University. The Index took on average 1 minute

Table 1. Frequencies of the 10 Index Items (N = 3398)

Item	Patients Responding, No. (%)	Mean Index Score (SD) ^a	Response, %				
			Not at all	A little	A moderate amount	A lot	A great deal
How much ...			Not at all	A little	A moderate amount	A lot	A great deal
... do you trust your HIV care provider?	3306 (97)	4.7 (0.7)	0.5	1.3	3.7	20.1	74.3
... does your HIV care provider respect what you have to say?	3314 (98)	4.6 (0.7)	0.8	1.4	4.5	23.4	70.0
... does your HIV care provider really understand you as a person?	3300 (97)	4.4 (0.9)	1.0	2.9	10.2	28.8	57.1
... the clinic help you meet your most important health needs	3325 (98)	4.5 (0.8)	0.8	1.8	6.1	26.5	64.8
How ...			Not at all	Slightly	Moderately	Very	Extremely
... open do you feel you can be with your care HIV provider?	3301 (97)	4.6 (0.7)	0.9	1.2	5.5	26.5	65.9
... well does your HIV care provider explain things in a way that is easy to understand?	3314 (98)	4.6 (0.6)	0.4	1.1	3.5	25.1	70.0
... comfortable do you feel asking questions during your HIV care appointments?	3327 (98)	4.6 (0.7)	1.0	1.5	4.7	26.7	66.2
... well do you follow through on HIV care when things in your life get tough?	3307 (97)	4.2 (1.0)	2.3	4.1	13.2	32.6	47.8
How much of a role do you have in making decisions about your HIV care?			None	Small	Medium sized	Big	Very big
	3349 (99)	4.4 (1.0)	3.2	2.8	6.3	26.5	61.2
How often do you leave your HIV care appointment feeling like you really got good care?			Never	Sometimes	Half the time	Most of the time	Always
	3335 (98)	4.5 (0.9)	2.7	3.3	2.5	23.2	68.3

Abbreviations: HIV, human immunodeficiency virus; Index, Index of Engagement in HIV Care; SD, standard deviation.

^aAn Index score was calculated for 3308 respondents with ≥ 8 nonmissing items.

to complete. Each site has institutional review board approval to send electronic medical record and PRO data to the University of Washington, which conducts quality checks before providing deidentified data.

For the retention analysis, the study population was all patients who completed the Index and had a year of follow-up time. For the viral load analysis, the study population was all patients with suppressed viral load who completed the Index and had a year of follow-up time (we excluded patients with a detectable viral load at the time of the Index because they would already be identified for engagement efforts; the real value of Index would be in identifying those at risk for subsequent virologic failure).

Predictor

The primary predictor was the mean Index score, calculated as the sum of all items without missing responses divided by that number of items. If <75% of the items were answered, the Index score was set to missing.

Outcomes

We hypothesized that higher Index scores would be associated with a lower risk of subsequent suboptimal retention in care and failure to achieve sustained viral suppression. These outcomes were operationalized as (1) not keeping $\geq 75\%$ of scheduled primary care appointments in the subsequent year and (2) viral load >200 copies/mL on any measurement in the year after Index administration.

Covariates

Consistent with published articles on the CNICS cohort, [16, 17] covariates were age, gender identity, race/ethnicity, sexual orientation, length of time in CNICS, and site. Logistic regression models were adjusted for the number of scheduled primary care appointments and the number of viral load measurements for the retention and viral load outcomes, respectively.

Statistical Analysis

Descriptive analyses were conducted using SAS 9.4 (SAS Institute). Preliminary analyses were conducted using *Mplus* 8.3 software (Muthen & Muthen) to fit unadjusted and adjusted logistic regression models of mean Index score and patient characteristic covariates on each of the 2 outcomes. We also used *Mplus* software to fit generalized linear mixed models of appointment attendance and viral load in the year after Index administration to account for correlations among repeated measures within participants, which were addressed via the inclusion of a random intercept term. We used *Mplus* because it allows the inclusion of cases with incomplete data on the predictor, covariates, or outcomes under the assumption of being conditionally missing at random via direct maximum likelihood estimation, enabling comparison of the results with missing data included versus excluded.

For each model, we screened for 2-way interactions of Index score and each patient characteristic covariate. Owing to the large sample size, we used the Bayesian information criterion to determine whether to retain interactions in subsequent modeling. We also conducted sensitivity analyses for both the retention and the viral load outcomes (Supplementary Material). For the logistic regression model with the viral load outcome, we conducted 2 sensitivity analyses: (1) a reprise of the entire model selection process with a sample that included participants with missing viral load at the time of Index; and (2) 2 additional iterations of the interaction screening process, in which individuals with missing viral load data in the year after Index were considered all detectable or all undetectable.

For the logistic regression model for the retention outcome, we repeated the modeling process described above, using a sample that included participants who had no scheduled appointments in the year after Index. The linearity of the association of the continuous Index variable with the log odds of each outcome was evaluated by including restricted cubic splines for the Index variable and by comparing the Bayesian information criterion statistics from a full model with all splines to a nested model in which the nonlinear splines had estimates constrained to zero.

For the final models, we compared results from 2 versions of each model: those in which incomplete data were included versus the same model in which only complete cases were included (Supplementary Material). As there were no substantive differences between the results from each method, in the interest of simplicity, final analyses were conducted with Stata 16 software (StataCorp), using data from complete cases. Because outcomes may not be sufficiently rare for the adjusted odds ratios (aORs) to adequately approximate adjusted risk ratios (aRRs), we report aRRs and their associated 95% confidence intervals (CIs) in the Results; both aRRs and aORs reported in the tables for completeness and to enable comparisons with other aOR effect sizes reported in the literature.

Additional secondary exploratory analyses generated receiver operating characteristic (ROC) curves and areas under the curve (AUCs) with 95% CIs in SAS 9.4 software (SAS Institute) for the retention and viral load outcomes; we display ROC curves for the full model overlaid with the ROC curve for Index as a sole predictor. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and 95% CIs were calculated for models including only the Index as a sole predictor and the outcome; these statistics are reported at the predicted probability cutoff where sensitivity and specificity are both maximized (and are equal). We also report the threshold value of Index evaluated at this predicted probability cutoff.

RESULTS

Just more than half (53%) of the study sample of 3398 patients were ≥ 50 years of age, 19% identified as cis-gender female and

Table 2. Patients in Routine Human Immunodeficiency Virus Care Undergoing Index Assessment as Part of Patient-Reported Outcomes in the Center for AIDS Research Network of Integrated Clinical Systems (N = 3398)

Characteristic	Patients, No. (%) ^a		
	Total Sample	Retention Sample ^b	Viral Load Sample ^c
Site	(n = 3398)	(n = 2680)	(n = 2783)
UCSD	526 (15.5)	519 (19.4)	400 (14.4)
UAB	601 (17.7)	589 (22.0)	515 (18.5)
UW	522 (15.4)	511 (19.1)	447 (16.1)
UNC	517 (15.2)	... ^d	461 (16.6)
FENWAY	338 (10.0)	322 (12.0)	298 (10.7)
JHU	575 (16.9)	568 (21.2)	508 (18.3)
UCSF	319 (9.4)	171 (6.4)	154 (5.5)
Age, y	(n = 3398)	(n = 2680)	(n = 2783)
18–29	614 (18.1)	457 (17.1)	476 (17.1)
30–39	976 (28.7)	757 (28.3)	789 (28.4)
40–49	1128 (33.2)	907 (33.8)	934 (33.6)
≥50	680 (20.0)	559 (20.9)	584 (21.0)
Current gender	(n = 3398)	(n = 2680)	(n = 2783)
Cis-male	2670 (78.6)	2111 (78.9)	2192 (78.8)
Cis-female	649 (19.1)	504 (18.8)	532 (19.1)
Gender minority	79 (2.3)	65 (2.4)	59 (2.1)
Race	(n = 3388)	(n = 2671)	(n = 2773)
Black	1402 (41.4)	1071 (40.1)	1174 (42.3)
White	1500 (44.3)	1201 (45.0)	1239 (44.7)
Latinx	322 (9.5)	268 (10.0)	244 (8.8)
Other	164 (4.8)	131 (4.9)	116 (4.2)
Heterosexual orientation	1134 (33.7) (n = 3368)	892 (33.5) (n = 2664)	950 (34.4) (n = 2765)
On ART regimen	3159 (94.3) (n = 3351)	2483 (93.8) (n = 2646)	2655 (96.7) (n = 2746)
Viral load >200 copies/mL ^e	329 (10.3) (n = 3208)	271 (10.7) (n = 2523)	...
CD4 cell count, median (IQR), cells/μL ^f	585 (385–818) (n = 2332)	569 (375–804) (n = 1757)	610 (415–842) (n = 1902)
Time in CNICS, median (IQR), y	7.1 (3.1–12.3) (n = 3388)	6.9 (3.0–12.1) (n = 2673)	7.3 (3.3–13.0) (n = 2779)
Index items answered, mean (SD), no.	9.8 (1.0) (n = 3398)	9.7 (1.1) (n = 2680)	9.8 (1.0) (n = 2783)
Index score, mean (SD)	4.5 (0.6) (n = 3308)	4.5 (0.6) (n = 2601)	4.5 (0.5) (n = 2708)

Abbreviations: ART, antiretroviral therapy; CNICS, Centers for AIDS Research Network of Integrated Clinical Systems; FH, Fenway Health; Index, Index of Engagement in HIV Care; HIV, human immunodeficiency virus; IQR, interquartile range; JHU, Johns Hopkins University; SD, standard deviation; UAB, University of Alabama at Birmingham; UCSD, University of California, San Diego; UCSF, University of California, San Francisco; UNC, University of North Carolina at Chapel Hill; UW, University of Washington.

^aData represent no. (%) of patients unless otherwise specified.

^bRetention sample included patients with ≥1 scheduled visit and 1 year of follow-up (n = 2680).

^cViral load sample included patients with a suppressed viral load and 1 year of follow-up (n = 2783).

^dThe UNC did not report missed visits during the period under observation, so it was not included in retention analyses.

^eViral load closest to Index measurement, within 365 days prior to Index measurement.

^fCD4 cell count closest to Index assessment, from 180 days before to 90 days after measurement.

2% as gender minority (eg, transgender, nonbinary), 41% were black and 9% Latinx, and about one-third (34%) identified as heterosexual (Table 2). Patients had been in CNICS for a median of 7 years (interquartile range [IQR], 3–12 years). ART use was reported by 94% at the time of Index administration, and 10% had an unsuppressed viral load. The mean Index score was 4.5 (standard deviation, 0.56) and the Cronbach α was .90. Responses by Index item are displayed in Table 1.

Of the 3398 patients, 96% had 1 year of follow-up time with regard to viral load measurements, and 2783 (85%) of these patients had suppressed viral load at the time of Index assessment (Figure 1). One site (University of North Carolina at Chapel Hill) did not report missed visits during the period under observation, so it was not included in retention analyses. Of the remaining

2736 patients with adequate follow-up time, 56 (2%) did not have ≥1 scheduled appointment in the year after Index assessment. The median number of scheduled primary care appointments in the year after Index assessment was 4 (IQR, 2–6), and 70% attended ≥75% of all scheduled appointments. Of those with adequate follow-up time, 93% had an observed viral load measurement. The median number of viral load measurements was 2 (IQR, 1–3), and 19% were unsuppressed at ≥1 measurement.

Results indicated that no interactions were of sufficient import to retain and that the Index score was linearly associated with each outcome, yielding the final main effects models presented in Tables 3 and 4. The mean Index score was significantly associated with each of the outcomes in unadjusted and adjusted analyses (Tables 3 and 4). It was associated with lower

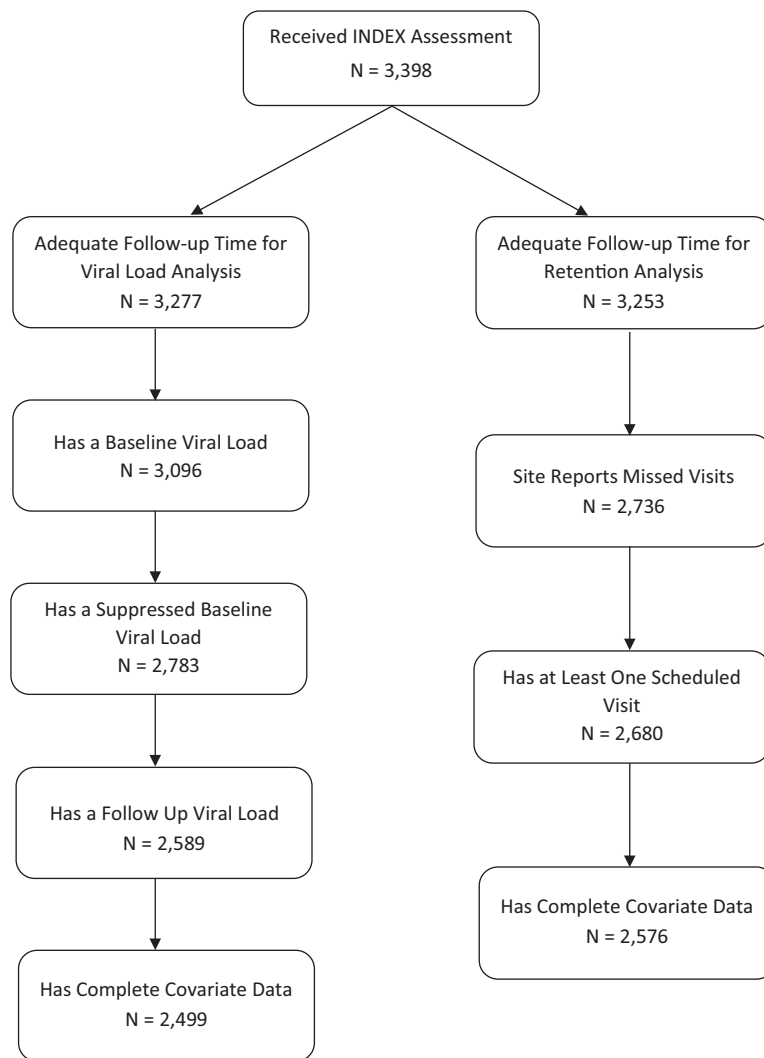


Figure 1. Flowchart of analysis populations in patients assessed using the Index of Engagement in HIV Care score. Abbreviation: HIV, human immunodeficiency virus.

risk of not keeping $\geq 75\%$ of scheduled appointments in the next year ($n = 2576$; aRR 0.88; 95% CI, .87–.88) and having an unsuppressed viral load at any measurement in the next year ($n = 2499$; 0.75; .68–.83). In addition, the Index score was associated with decreased risk of missing any scheduled primary care visit in the next year (aRR 0.85; 95% CI, .83–.87) and decreased odds of an unsuppressed viral load at any subsequent measurement in the next year (0.74; .68–.80). Younger age, black race, and number of scheduled primary care visits were positively associated with subsequent missed visits, while time in CNICS was negatively associated with missed visits. The number of viral load measurements was positively associated with any unsuppressed viral load. The results of sensitivity analyses that address those with missing viral load measurements or scheduled follow-up appointments were comparable with the results presented here ([Supplementary Material](#)).

The areas under the curve for the final model were (Index score plus covariates) was 0.69 (95% CI, .67–.71) for suboptimal

retention and 0.76 (.72–.79) for lack of sustained viral suppression ([Figure 2](#)); AUCs for the Index score as a sole predictor were estimated at 0.58 (.56–.61) for retention and 0.58 (.54–.63), for viral load, respectively. The sensitivity and specificity of the Index score in the viral load model were 0.56 (95% CI, .39–.67) and 0.57 (.50–.72), respectively. The PPV and NPV were 0.08 (95% CI, .08–.09) and 0.95 (.95–.96). For Index score in the retention model, the sensitivity was 0.55 (95% CI, .48–.62), the specificity was 0.57 (.50–.67), and the PPV and NPV were 0.36 (.33–.37) and 0.75 (.75–.76), respectively. The value of the Index score evaluated at the same predicted probability as these statistics was 4.7, indicating that an Index score below this threshold yields a “positive” test result.

DISCUSSION

With adjustment for covariates, scores on the Index explained suboptimal retention and failure to achieve sustained viral

Table 3. Adjusted Risk and Odds Ratios for Suboptimal Retention and Virologic Failure in the Year After Index Assessment: Logistic Regression Analysis

Variable	Not Keeping 75% of Visits ^a						≥1 Unsuppressed Viral Load ^b					
	Unadjusted Analyses			Adjusted Analyses			Unadjusted Analyses			Adjusted Analyses		
	OR (95% CI)	PValue	aRR (95% CI)	aOR (95% CI)	PValue	OR (95% CI)	PValue	aRR (95% CI)	aOR (95% CI)	PValue		
Index	0.61 (.52–.70)	<.001 ^c	0.88 (.87–.88)	0.66 (.57–.77)	<.001 ^c	0.65 (.50–.83)	.001 ^c	0.75 (.68–.83)	0.65 (.50–.85)	.001 ^c		
Age, y												
18–29	2.98 (2.26–3.91)	<.001 ^c	2.06 (1.79–2.37)	3.68 (2.71–4.98)	<.001 ^c	1.14 (.72–1.80)	.57	1.44 (.94–2.20)	1.53 (.92–2.54)	.10		
30–39	1.58 (1.22–2.03)	<.001 ^c	1.52 (1.31–1.77)	2.05 (1.54–2.73)	<.001 ^c	0.69 (.44–1.07)	.10	0.82 (.54–1.28)	0.8 (.49–1.33)	.39		
40–49	1.48 (1.15–1.89)	.002 ^c	1.38 (1.19–1.61)	1.72 (1.31–2.26)	<.001 ^c	0.82 (.54–1.23)	.33	0.87 (.58–1.28)	0.85 (.54–1.33)	.47		
≥50 (reference)		
Race/ethnicity												
White (reference)		
Black	1.46 (1.21–1.74)	<.001 ^c	1.28 (1.10–1.49)	1.49 (1.17–1.91)	.001 ^c	1.75 (1.26–2.42)	.001 ^c	1.03 (.72–1.48)	1.03 (.67–1.58)	.89		
Latinx	1.47 (1.10–1.95)	.008 ^c	1.10 (.91–1.33)	1.17 (.85–1.61)	.33	0.67 (.32–1.42)	.29	0.72 (.36–1.43)	0.69 (.31–1.50)	.34		
Other	1.60 (1.10–2.34)	.02 ^c	1.13 (.88–1.44)	1.21 (.80–1.84)	.36	0.51 (.16–1.64)	.26	0.39 (.10–1.46)	0.34 (.08–1.46)	.15		
Gender												
Cis-male (reference)		
Cis-female	1.17 (.95–1.44)	.15	1.05 (.89–1.25)	1.09 (.83–1.43)	.55	1.93 (1.38–2.72)	<.001 ^c	1.35 (.92–1.98)	1.42 (.91–2.21)	.12		
Gender minority	1.70 (1.03–2.81)	.04^c	2.08 (.78–1.51)	1.14 (.66–1.97)	.65	1.85 (.78–4.39)	.16	1.60 (.76–3.36)	1.75 (.7–4.35)	.23		
Heterosexual orientation	1.09 (.91–1.29)	.35	1.07 (.91–1.25)	1.11 (.86–1.44)	.41	1.58 (1.16–2.16)	.004 ^c	1.11 (.76–1.63)	1.13 (.73–1.76)	.59		
Years in CNICS	0.97 (.95–.98)	<.001 ^c	0.97 (.97–.98)	0.96 (.94–.97)	<.001 ^c	0.97 (.95–1.01)	.06	0.97 (.95–1.01)	0.97 (.94–1.00)	.06		
No. of observations ^d	1.14 (1.11–1.17)	<.001 ^c	1.09 (1.06–1.11)	1.12 (1.09–1.15)	<.001 ^c	1.59 (1.44–1.75)	<.001 ^c	1.53 (1.38–1.70)	1.56 (1.41–1.73)	<.001 ^c		

Abbreviations: aOR, adjusted odds ratio; aRR, adjusted risk ratio; CI, confidence interval; CNICS, Centers for AIDS Research Network of Integrated Clinical Systems; HIV, human immunodeficiency virus; Index, Index of Engagement in HIV Care; OR, odds ratio.

^aFor retention analyses, the sample size was 2576 for adjusted analysis and ranged from 2601 to 2680 for unadjusted analyses

^bFor viral load analyses, the sample size was 2499 for adjusted analysis and ranged from 2522 to 2589 for unadjusted analyses

^cSignificant at $P < .05$.

^dNumber of scheduled appointments and viral load measurements in the year after Index assessment

Table 4. Adjusted Risk and Odds Ratios for Longitudinal Retention and Viral Load Outcomes in the Year After Index Assessment: Generalized Linear Mixed Models

Variable	Kept vs Missed Each Visit ^a			Suppressed vs Unsuppressed Viral Load at Each Measurement ^b		
	aRR (95% CI)	aOR (95% CI)	PValue	aRR (95% CI)	aOR (95% CI)	PValue
Index	0.85 (.83–.87)	0.69 (.61–.77)	<.001 ^c	0.74 (.68–.80)	0.48 (.31–.73)	.001 ^c
Days from Index Assessment	1.00 (1.00–1.00)	1.00 (1.00–1.00)	.13	1.00 (1.00–1.00)	1.00 (1.00–1.00)	.55
Age, y						
18–29	1.94 (1.72–2.19)	2.94 (2.35–3.68)	<.001 ^c	1.43 (.89–2.31)	1.84 (.80–4.19)	.15
30–39	1.53 (1.34–1.73)	1.94 (1.58–2.38)	<.001 ^c	0.85 (.52–1.38)	0.76 (.34–1.69)	.50
40–49	1.35 (1.20–1.53)	1.58 (1.31–1.92)	<.001 ^c	0.86 (.55–1.32)	0.77 (.37–1.60)	.49
≥50 (reference)
Race/ethnicity						
White (reference)
Black	1.31 (1.17–1.48)	1.51 (1.26–1.80)	<.001 ^c	1.23 (.82–1.83)	1.40 (.72–2.74)	.32
Latinx	0.99 (.85–1.15)	0.98 (.78–1.24)	.88	0.71 (.33–1.53)	0.57 (.17–1.90)	.36
Other	1.02 (.82–1.25)	1.02 (.75–1.40)	.89	0.34 (.08–1.34)	0.19 (.03–1.35)	.10
Gender						
Cis-male (reference)
Cis-female	1.12 (.99–1.28)	1.19 (.98–1.45)	.08	1.40 (.92–2.13)	1.76 (.86–3.59)	.12
Gender minority	1.00 (.77–1.29)	1.00 (.68–1.46)	.99	1.36 (.56–3.29)	1.68 (.36–7.77)	.51
Heterosexual orientation	1.12 (.99–1.26)	1.18 (.98–1.42)	.08	1.08 (.71–1.65)	1.15 (.57–2.30)	.70
Years in CNICS	0.98 (.97–.99)	0.97 (.95–.98)	<.001 ^c	0.97 (.94–1.00)	0.95 (.90–1.00)	.05 ^c

Abbreviations: aOR, adjusted odds ratio; aRR, adjusted risk ratio; CI, confidence interval; CNICS, Centers for AIDS Research Network of Integrated Clinical Systems; Index, Index of Engagement in HIV Care.

^aFor retention analysis, the number of cases was 2576 with 11348 observations.

^bFor viral load analysis, the number of cases was 2499 with 5375 observations.

^cSignificant at $P < .05$.

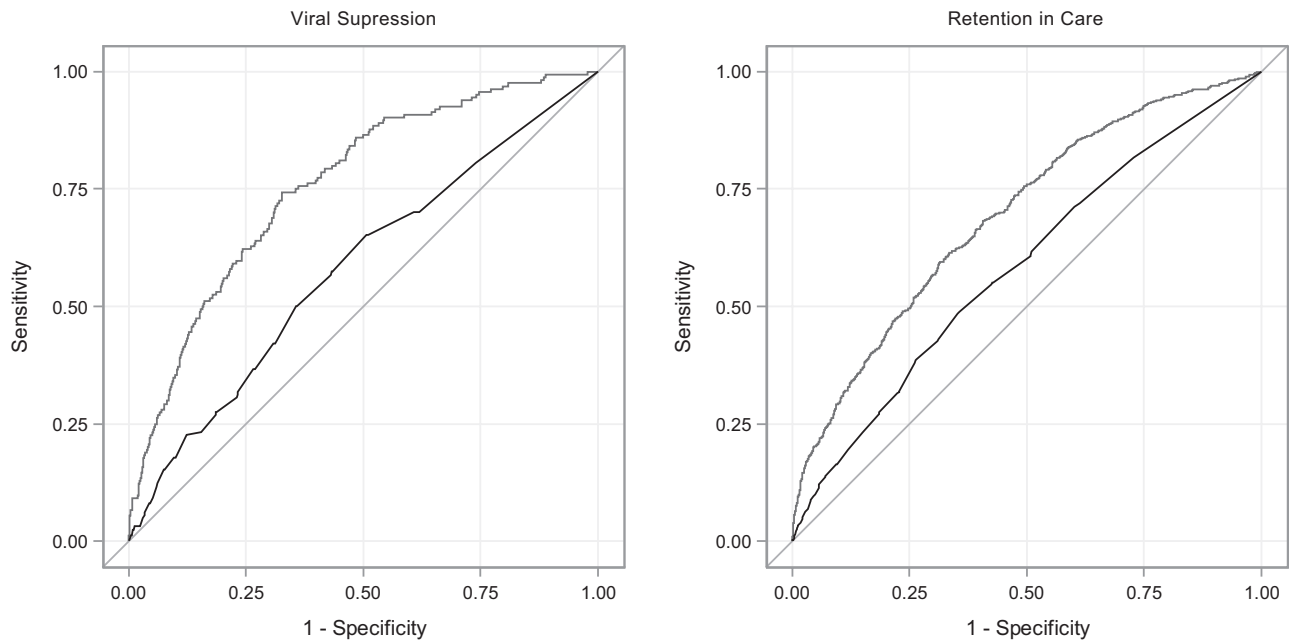


Figure 2. Receiver operating characteristic curves of full models overlaid on the Index of Engagement in HIV Care score as sole predictor. Abbreviation: HIV, human immunodeficiency virus.

suppression in a regionally diverse cohort of patients in routine care in the United States. These findings add to the HIV literature by providing the prospective validation of the first scale to measure patient engagement in care developed for, and in part with, people living with HIV. While healthcare empowerment [18] and patient activation [19, 20] are related concepts and may overlap in part with patient engagement, these measures focus largely on the cognitive-behavioral components of an individual's attitudes and behaviors around healthcare, particularly the confidence and knowledge to take action. Since this study was conceived, researchers in Italy developed a model of healthcare engagement (though not specifically for those living with HIV) that also sees engagement as a multidimensional process “resulting from the conjoint cognitive (think), emotional (feel), and conative (act) enactment of individuals towards their health management,” [21] providing additional face validity of our definition of care engagement. Earlier discourse has also noted the importance of distinguishing patient engagement from patient satisfaction and the patient experience [22].

In our secondary exploratory analysis, the Index and available covariates explained respectable amounts of AUCs, and incorporation of the Index added to the predicted AUCs of these models. However, in busy clinical settings, patient care needs and limited electronic medical record functionality can preclude the use of predictive algorithms that account for multiple covariates, and the results of laboratory measurements such as viral load may not immediately be known. If the only information available to a clinician is the Index score, assuming a sensitivity and specificity of 56%, a score >4.7 would have an NPV

of 95% for not having virologic failure and an NPV of 75% for failing to attend 75% of appointments in the next year.

It is unsurprising that the Index performed better for viral load than for retention because the study population consisted of patients who have been attending clinic appointments—though perhaps suboptimally—over years. However, given that maintenance of viral suppression is a cornerstone of efforts to end the HIV epidemic [23] as well as the principle that undetectable = untransmittable, [24] the Index could contribute meaningfully, in that its high NPV means that clinicians can be reasonably confident that those scoring >4.7 do not require intervention. While the PPV is low, meaning that more of those who score ≤ 4.7 would be targeted for intervention than might need it, the applicable interventions could be worth doing in and of themselves, as they would aim to strengthen a patient's connectedness to care.

Indeed, one key area is the patient's relationship with the HIV primary care provider, particularly around communication and rapport building [25–27]. The patient's perception of the clinic as able to meet health needs is also crucial [28]. Other areas include fostering active participation in one's care and promoting resilience during difficult times or unexpected life events [29]. Strengthening communication, building trust in a provider and clinic, and fostering resilience are all things that could have ancillary benefits for the patient in and of themselves. As health-related quality of life gains traction as the fourth “90” vis-à-vis “90-90-90” targets for HIV, [30] PROs offer a key opportunity to measure and intervene on factors that not only ensure optimal care but also promote well-being [31].

Limitations of the current study include a population that has established HIV care and has relatively high rates of viral suppression and retention. Moreover, scores on the Index were high. The limited range of the Index and the outcomes in this sample could negatively affect the ability of the Index to predict outcomes in AUC analyses; using the Index in a sample with more variability could yield different results. It is worth noting that AUCs for prediction are generally lower than those for diagnostic tests, particularly in the behavioral sciences [32]. In addition, Index items may not be as applicable to those new to care, for whom it is important to identify provider and clinic-related constructs that may predict subsequent disengagement from care. Indeed, as previous research has acknowledged, engagement is a temporal journey involving distinct psychological states occurring from diagnosis to being a person living with a disease [8, 21].

The Index was validated in university-affiliated HIV clinics. Validation of the Index in community clinics and other HIV care settings is an important next step. Although the Index was part of the PROs for almost a year, and many patients should have had an opportunity to complete it, it may not have been administered to patients with very poor retention or those with significant psychosocial challenges (eg, intoxication from substance use). Finally, the Index was administered in English, resulting in the exclusion of the monolingual Spanish-speaking patients. Our team has developed a Spanish-language version of the Index and is working on its validation.

In sum, the Index provides a brief screening tool for patient engagement that has been prospectively validated in a large, diverse cohort of patients in care in the United States. It is a feasible measure to incorporate in investigations of HIV cascade outcomes and has potential applications for intervention research to improve engagement by identifying patient concerns. With further study across diverse samples and settings, the Index could be an effective way to identify patients at risk of viral rebound.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. The authors thank the people living with human immunodeficiency virus who, through their involvement in the Centers for AIDS Research Network of Integrated Clinical Systems cohort, generously contributed to this research.

Disclaimer. The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health (NIH).

Financial support. This work was supported by the NIH (grants R01 MH102198 to K. A. C. and M. O. J., K24 DA037034 to M. O. J., K01 MH113475 to J. A. S., and R24 AI067039) and by the National Center for Advancing Translational Sciences, NIH (through University of California,

San Francisco—Clinical & Translational Science Institute grant UL1 TR001872).

Potential conflicts of interest. Unrelated to this work, K.A. C. and E. R. C. have received investigator-initiated grant support from Gilead Sciences and have served as medical advisory board members for Gilead Sciences; E. R. C. also reports grant support from Merck. H. M. C. reports grant support from ViiV, the NIH, and the Agency for Healthcare Research and Quality. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis* 2011; 52:793–800.
2. Institute of Medicine. Monitoring HIV care in the United States: indicators and data systems. Washington, DC: The National Academies Press. 2012. Available at: <https://doi.org/10.17226/13225>.
3. Mugavero MJ, Amico KR, Horn T, Thompson MA. The state of engagement in HIV care in the United States: from cascade to continuum to control. *Clin Infect Dis* 2013; 57:1164–71.
4. Marks G, Patel U, Stirratt MJ, et al. Single viral load measurements overestimate stable viral suppression among HIV patients in care: clinical and public health implications. *J Acquir Immune Defic Syndr* 2016; 73:205–12.
5. Cole SR, Napravnik S, Mugavero MJ, Lau B, Eron JJ Jr, Saag MS. Copy-years viremia as a measure of cumulative human immunodeficiency virus viral burden. *Am J Epidemiol* 2010; 171:198–205.
6. Mugavero MJ, Westfall AO, Zinski A, et al; Retention in Care (RIC) Study Group. Measuring retention in HIV care: the elusive gold standard. *J Acquir Immune Defic Syndr* 2012; 61:574–80.
7. Christopoulos KA, Olender S, Lopez AM, et al. Retained in HIV care but not on antiretroviral treatment: a qualitative patient-provider dyadic study. *PLoS Med* 2015; 12:e1001863.
8. Christopoulos KA, Massey AD, Lopez AM, et al. “Taking a half day at a time:” patient perspectives and the HIV engagement in care continuum. *AIDS Patient Care STDS* 2013; 27:223–30.
9. Castel AD, Tang W, Peterson J, et al. Sorting through the lost and found: are patient perceptions of engagement in care consistent with standard continuum of care measures? *J Acquir Immune Defic Syndr* 2015; 69(suppl 1):S44–55.
10. Wood TJ, Koester KA, Christopoulos KA, Saucedo JA, Neilands TB, Johnson MO. If someone cares about you, you are more apt to come around: improving HIV care engagement by strengthening the patient-provider relationship. *Patient Prefer Adherence* 2018; 12:919–27.
11. Koester KA, Johnson MO, Wood T, et al. The influence of the ‘good’ patient ideal on engagement in HIV care. *PLoS One* 2019; 14:e0214636.
12. Johnson MO, Koester KA, Wood T, Neilands TB, Pomeranz JL, Christopoulos KA. Development of an index of engagement in HIV care: an adapted internet-based Delphi process. *JMIR Res Protoc* 2017; 6:e224.
13. Johnson MO, Neilands TB, Koester KA, et al. Detecting disengagement from HIV care before it is too late: development and preliminary validation of a novel index of engagement in HIV care. *J Acquir Immune Defic Syndr* 2019; 81:145–52.
14. Kitahata MM, Rodriguez B, Haubrich R, et al. Cohort profile: the centers for AIDS research network of integrated clinical systems. *Int J Epidemiol* 2008; 37:948–55.
15. Crane HM, Lober W, Webster E, et al. Routine collection of patient-reported outcomes in an HIV clinic setting: the first 100 patients. *Curr HIV Res* 2007; 5:109–18.
16. Mugavero MJ, Westfall AO, Cole SR, et al; Centers for AIDS Research Network of Integrated Clinical Systems (CNICS). Beyond core indicators of retention in HIV care: missed clinic visits are independently associated with all-cause mortality. *Clin Infect Dis* 2014; 59:1471–9.
17. Christopoulos KA, Neilands TB, Hartogensis W, et al. Internalized HIV stigma is associated with concurrent viremia and poor retention in a cohort of US patients in HIV care. *J Acquir Immune Defic Syndr* 2019; 82:116–23.
18. Johnson MO, Rose CD, Dilworth SE, Neilands TB. Advances in the conceptualization and measurement of health care empowerment: development and validation of the health care empowerment inventory. *PLoS One* 2012; 7:e45692.
19. Hibbard JH, Stockard J, Mahoney ER, Tusler M. Development of the patient activation measure (PAM): conceptualizing and measuring activation in patients and consumers. *Health Serv Res* 2004; 39:1005–26.

20. Marshall R, Beach MC, Saha S, et al. Patient activation and improved outcomes in HIV-infected patients. *J Gen Intern Med* **2013**; 28:668–74.
21. Graffigna G, Barelo S, Bonanomi A, Lozza E. Measuring patient engagement: development and psychometric properties of the patient health engagement (PHE) scale. *Front Psychol* **2015**; 6:274.
22. Boissy A. Patient engagement versus patient experience. *NEJM Catalyst* **2017**. Available at: <https://catalyst.nejm.org/doi/full/10.1056/CAT.17.0481>.
23. Fauci AS, Redfield RR, Sigounas G, Weahkee MD, Giroir BP. Ending the HIV epidemic: a plan for the United States. *JAMA* **2019**; 321:844–5.
24. Eisinger RW, Dieffenbach CW, Fauci AS. HIV viral load and transmissibility of HIV infection: undetectable equals untransmittable. *JAMA* **2019**; 321:451–2.
25. Flickinger TE, Saha S, Moore RD, Beach MC. Higher quality communication and relationships are associated with improved patient engagement in HIV care. *J Acquir Immune Defic Syndr* **2013**; 63:362–6.
26. Mallinson RK, Rajabiun S, Coleman S. The provider role in client engagement in HIV care. *AIDS Patient Care STDS* **2007**; 21(suppl 1):S77–84.
27. Farrell L, Ingersoll K, Ceperich SD. Enhancing patient adherence: promoting engagement via positive patient-provider relationships in HIV/AIDS care. *Med Encount* **2009**; 23:69–71.
28. Wessinger MH, Hennink MM, Kaiser BN, et al. Retention in HIV care depends on patients' perceptions of the clinic experience. *AIDS Care* **2017**; 29:1212–7.
29. Earnshaw VA, Bogart LM, Dovidio JF, Williams DR. Stigma and racial/ethnic HIV disparities: moving toward resilience. *Am Psychol* **2013**; 68:225–36.
30. Lazarus JV, Safreed-Harmon K, Barton SE, et al. Beyond viral suppression of HIV—the new quality of life frontier. *BMC Med* **2016**; 14:94.
31. Kall M, Marcellin F, Harding R, Lazarus JV, Carrieri P. Patient-reported outcomes to enhance person-centred HIV care. *Lancet HIV* **2020**; 7:e59–68.
32. Rice ME, Harris GT. Comparing effect sizes in follow-up studies: ROC area, Cohen's *d*, and *r*. *Law Hum Behav* **2005**; 29:615–20.