The prevalence of mental health disorders in people with HIV and the effects on the HIV care continuum

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Objective: To describe the prevalence of diagnosed depression, anxiety, bipolar disorder, and schizophrenia in people with HIV (PWH) and the differences in HIV care continuum outcomes in those with and without mental health disorders (MHDs).

Design: Observational study of participants in the North American AIDS Cohort Collaboration on Research and Design.

Methods: PWH (≥18 years) contributed data on prevalent schizophrenia, anxiety, depressive, and bipolar disorders from 2008 to 2018 based on International Classification of Diseases code mapping. Mental health (MH) multimorbidity was defined as having two or more MHD. Log binomial models with generalized estimating equations estimated adjusted prevalence ratios (aPR) and 95% confidence intervals for retention in care (≥1 visit/year) and viral suppression (HIV RNA ≤200 copies/ml) by presence vs. absence of each MHD between 2016 and 2018.

Results: Among 122 896 PWH, 67 643 (55.1%) were diagnosed with one or more MHD: 39% with depressive disorders, 28% with anxiety disorders, 10% with bipolar disorder, and 5% with schizophrenia. The prevalence of depressive and anxiety disorders increased between 2008 and 2018, whereas bipolar disorder and

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schizophrenia remained stable. MH multimorbidity affected 24% of PWH. From 2016 to 2018 ($N = 64\ 684$), retention in care was marginally lower among PWH with depression or anxiety, however those with MH multimorbidity were more likely to be retained in care. PWH with bipolar disorder had marginally lower prevalence of viral suppression (aPR = 0.98 [0.98–0.99]) as did PWH with MH multimorbidity (aPR = 0.99 [0.99–1.00]) compared with PWH without MHD.

Conclusion: The prevalence of MHD among PWH was high, including MH multimorbidity. Although retention and viral suppression were similar to people without MHD, viral suppression was lower in those with bipolar disorder and MH multimorbidity.

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Keywords: anxiety, bipolar disorder, depression, HIV, HIV care continuum, mental health, schizophrenia

Introduction

With advances in HIV care, chronic disease management including care for co-occurring mental health disorders (MHDs) among people with HIV (PWH) has become a primary focus of attention [1]. MHDs remain a significant source of morbidity and mortality across the world [2]; however, health outcomes of PWH with MHDs remains under studied, particularly within the Treat All era (≥2015) [3]. At the introduction of highly active antiretroviral therapy (ART) (1996), estimates of 12-month prevalence of MHDs among PWH in the United States found nearly half of PWH screened positive for one or more of: major depression, dysthymia, generalized anxiety disorder, or panic attacks [4]. Studies have reported the prevalence of major depression, anxiety, bipolar disorder (BD), and schizophrenia are more common among PWH compared to the general population [5–13].

MHDs have been associated with adverse outcomes in PWH, including unsuppressed viral load and excess mortality [14–16]. Prior to the Treat All era, adherence to ART in PWH with BD was 48% compared to 91% among PWH without BD [17]. Schizophrenia in PWH has been associated with reduced linkage into care and adherence to treatment [18]. PWH who have effective treatment of their psychiatric symptoms are more successful in their HIV treatment [9,19], underlining the importance of early screening and evidence-based treatment for MHDs among PWH [20].

HIV and depressive disorders are predicted to be the top two leading causes of burden of disease by 2030 [21]. Estimates of the burden of MHDs among PWH are important for guiding policy and programs to ensure access to care, retention in care, viral suppression, and increased wellbeing of PWH. The objective of this study was to describe the prevalence of schizophrenia, anxiety, BD and depressive disorders in PWH in North America, and the relationship of these disorders on HIV care continuum outcomes during the transition to the Treat All era.

Methods

Study population

The North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) is a consortium of HIV cohort studies located throughout the United States and Canada [22]. Participants in contributing clinical cohorts who linked into care (i.e. ≥2 HIV care visits in 12 months) were enrolled in the NA-ACCORD. NA-ACCORD participants have similar demographics to the population of PWH in the United States [23]. Each participating cohort annually submits data in a standardized format to the Data Management Core (DMC, University of Washington, Seattle, Washington, USA). The DMC assesses data quality, harmonizes the data, and securely transfers it to the Epidemiology/Biostatistics Core (EBC, Johns Hopkins University, Baltimore, Maryland, USA). The EBC identifies cohort-specific 'observation-windows' for outcomes to minimize the risk of falsely assuming complete event ascertainment from electronic health records [24]. Each participating cohort has been granted ethics approval by their respective local institutional review boards, as well as by the Johns Hopkins School of Medicine.

The source population for our nested study were PWH (≥18 years) participating in one of 13 NA-ACCORD-contributing clinical cohorts ascertaining anxiety, depression, BD, and schizophrenia diagnoses. Individual-level selection criteria for our study population included those who were observed in care from January 1, 2008 to December 31, 2018 (study period).

Mental health disorders

Many of the NA-ACCORD clinical cohorts have mental health (MH) screening and treatment within their HIV clinics. Cohorts collected inpatient and outpatient MH diagnoses from health records using a list of ICD-9 and ICD-10 codes for depression, anxiety, BD, and schizophrenia (Table 1, Supplemental Digital Content, http://links.lww.com/QAD/C710). Each MHD was defined as having at least one documented diagnosis over the

follow-up period. MH multimorbidity was defined as two or more MHDs (depression, anxiety, BD, or schizophrenia). A diagnosis of BD excluded classification of this participant as having depression; these two diagnoses were considered mutually exclusive [25]. Treatment data for BD and schizophrenia was obtained at the first time an individual met the criteria for a BD or schizophrenia diagnosis and was prescribed a treatment medication (Table 1, Supplemental Digital Content, http://links.lww.com/QAD/C710). Due to the lack of specificity of medications for depression and anxiety, treatment data for these disorders were not included.

HIV care continuum outcomes: retention in care and viral suppression

Retention in care was defined as having at least one HIV primary care visit within a calendar year. Viral suppression was defined as having an HIV RNA less than 200 copies/ml at the patient's last measurement of the year; this cut-off reflected the highest lower limit of quantification among assays used by contributing cohorts.

Covariates of interest

Covariates of interest were included based on review of relevant literature and *a priori* hypotheses of association with HIV care continuum outcomes. Sex was defined as sex assigned at birth. Race/ethnicity was grouped into non-Hispanic white, non-Hispanic Black, Hispanic, and other/unknown. HIV acquisition risk group was determined at enrollment into the NA-ACCORD; using a mutually exclusive hierarchy: injection drug use (IDU); men who have sex with men (MSM); heterosexual sexual contact; other/unknown risk. Cigarette smoking was ever/never use. At-risk alcohol use was ever having an alcohol abuse or dependence diagnosis in the medical record. $CD4^+$ cell count and HIV RNA were measured at baseline (i.e., the closest measurement to study entry, within 9 months prior through 3 months after study entry). ART regimen was also assessed at baseline (i.e. the closest record to study entry, ±6 months) and classified as at least two antiviral drugs from at least one drug class (nonnucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase inhibitors, other/unknown).

Comorbidities were assessed at baseline (i.e., prior to study entry through 9 months after entry) using operationalized definitions for treated hypertension, diabetes mellitus, hypercholesterolemia and stage 3 chronic kidney disease (CKD), which have been described elsewhere [26,27]. Hepatitis B (HBV) and hepatitis C (HCV) infection were parameterized as ever/never (Table 2, Supplemental Digital Content, http://links.lww.com/QAD/C710).

Statistical analysis

Study entry was defined as the date the cohort began observing patients, MH observation-window open date, patient enrollment into the NA-ACCORD, or January 1, 2008, whichever came last. The MH observation-window was specific to the cohort and defined as the calendar years when the cohort was ascertaining diagnoses for all four MHDs. Study exit was defined as the earliest date the cohort stopped observing patients, MH observation-window close date, the date the patient was lost to follow-up (LTFU, defined as 1.5 years with no $CD4^+$ or HIV RNA measurement), date of death, or December 31, 2018, whichever came first.

Pearson chi-square tests and Kruskal–Wallis tests were used to assess the differences in demographic and clinical characteristics by each MHDs. Annual prevalence for each MHDs was estimated among those in care in the year, and trends were evaluated from January 1, 2008 to December 31, 2018, with a log binomial model with generalized estimating equations (GEE) with an independent working correlation matrix (as participants could contribute information to multiple years) that included calendar year as a continuous variable to test the hypothesis that there was no change in prevalence from one year to the next. We estimated MHDs as ever having clinical diagnosis of these conditions (cumulative) which can result in increased prevalence with increasing time; however, given the open cohort design of the NA-ACCORD, individuals can enter and exit care, reflecting PWH in clinical care in any given year.

Retention in care and HIV viral suppression were estimated among those observed in care from January 1, 2016, to December 31, 2018 (the most recent years of available data) and stratified by the four MHDs categories and MH multimorbidity; estimates of HIV viral suppression were further restricted to include only those who initiated ART. In alignment with the trends in prevalence of MHDs analysis, log binomial models with GEE (independent working correlation matrix) estimated crude (PR) and adjusted prevalence ratios (aPR) and associated 95% confidence intervals (CIs) for each MHDs in this 2-year period. As is recommended when investigating disparities, we did not include variables that may be downstream of MHDs so as to avoid inappropriate attenuation of potential MHDs disparities in retention in care or viral suppression; multivariable models included demographic characteristics (age, sex, race/ethnicity, HIV acquisition risk group, and cohort) in addition to the MHDs of interest [28,29]. Subgroup analyses were conducted to evaluate whether having an untreated BD or schizophrenia was associated with a difference on retention in care or viral suppression. A sensitivity analysis defining HIV viral suppression as less than 50 copies/ml was conducted as this was the lower limit of detection across cohorts during the restricted study period (2016–2018) (Table 3, Supplemental Digital Content, http://links.lww.com/QAD/C710). All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina, USA).

Results

Characteristics of the study population

Among 122 896 PWH included in this study between 2008 and 2018, 67 643 (55%) were diagnosed with at least one of the four assessed MHDs: 47 553 (39%) were diagnosed with depressive disorder, 34 219 (28%) with anxiety disorder, 11 716 (10%) with BD, and 5022 (5%) with schizophrenia (Figure 1, Supplemental Digital Content, http://links.lww.com/QAD/C710). In the last two years of observation (2016–2018) ($n = 64\,689$), the prevalence of depression was 43%, anxiety was 35%, BD was 10% and schizophrenia was 5% (Fig. 1). Among the study population, 1494 (1%) were LTFU, of whom 880 (59%) had a diagnosis of one or more MHDs, and 527 (35%) had an unsuppressed viral load.

A greater proportion of those with depression, anxiety and BD were non-Hispanic white PWH, whereas a greater proportion of those with schizophrenia were non-Hispanic Black PWH compared to those without these diagnoses. The median age at study entry was older among those with schizophrenia {51 years [interquartile range (IQR): 44, 57]} compared to those without schizophrenia [46 years (IQR: 37, 54)]. PWH with any of these MHDs were more likely to have a history of IDU as an HIV acquisition risk factor and were more likely to smoke, have HCV coinfection, and hypertension compared to those without these diagnoses. Those with schizophrenia were more likely to have diabetes (Table 1).

PWH with any of these four MHDs were more likely to have initiated ART prior to 2005 compared to PWH without each MHDs (Table 1), suggesting those with longer durations of HIV care may also be more likely to have a diagnosed MHDs. There were no significant differences in $CD4^+$ cell count or HIV RNA levels at study entry between those with and without depression, anxiety, or BD. PWH with schizophrenia were more likely to have missing $CD4^+$ cell count or HIV RNA measurements at study entry and to have never initiated ART (Table 1).

Prevalence of mental health disorders and the effects on the HIV care continuum

Depression

The prevalence of depressive disorder increased from 35.9% (35.5–36.4%) in 2008 to 44.8% (44.0–45.5%) in 2018 ($P = 0.001$ for annual trend) (Fig. 1). Those with depression had a higher annual prevalence of retention in care, and lower annual prevalence of viral suppression, compared with those without depression from 2008–2018 ($P < 0.01$) (Fig. 2a). In adjusted models however, PWH with depression had a 2% (0.97–0.98%) lower prevalence of retention in care and a statistically nonsignificant 1% (0.99–1.00%) lower prevalence of

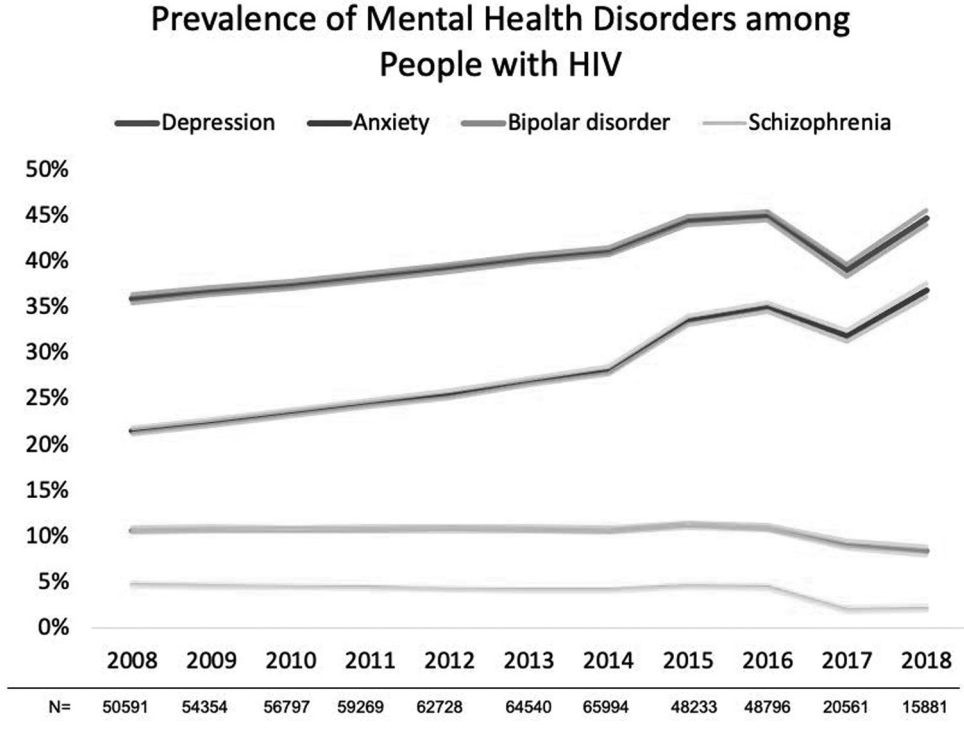

Fig. 1. Prevalence (and 95% confidence intervals represented by the lighter color shade) of mental health disorders, 2008–2018. Trends in annual prevalence for each mental health disorder evaluated with a log binomial model with generalized estimating equations, depressive disorder (*P* for trend = 0.001), anxiety disorder (*P* for trend = <0.001), bipolar disorder (*P* for trend = 0.058), and schizophrenia (*P* for trend = 0.013). Fluctuations in annual prevalence in 2017 and 2018 in mental health disorders may be due to less PWH being observed in our study during this time. PWH, people with HIV.

Table 1. Demographic characteristics at study entry among PWH in the NA-ACCORD and under observation for mental health outcomes between 2008 and 2018 ($N = 122\,896$).

	Overall		Depression				Anxiety				Bipolar disorder				Schizophrenia			
	$N = 122\,896$		No depression $n = 75\,343$		Depression $n = 47\,553$		No anxiety $n = 88\,677$		Anxiety $n = 34\,219$		No Bipolar disorder $n = 111\,189$		Bipolar disorder $n = 11\,716$		No Schizophrenia $n = 117\,874$		Schizophrenia $n = 5022$	
Characteristics	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*N*	%	*n*	%
Age																		
Median (IQR)	46 (37–54)		45 (35–53)		47 (39–55)		46 (36–54)		47 (39–54)		46 (37–54)		46 (38–53)		46 (37–54)		51 (44–57)	
Sex																		
Male	104062	85%	63524	84%	40538	85%	74216	84%	29846	87%	94408	85%	9654	82%	99687	85%	4375	87%
Female	18832	15%	11819	16%	7013	15%	14458	16%	4374	13%	16770	15%	2062	18%	18184	15%	648	13%
Race																		
Non-Hispanic White	44816	36%	**25796**	**34%**	**19019**	**40%**	**29022**	**33%**	**15794**	**46%**	**39626**	**36%**	**5190**	**44%**	**43516**	**37%**	**1300**	**26%**
Non-Hispanic Black	52196	42%	32902	44%	19295	41%	**40677**	**46%**	**11519**	**34%**	47384	43%	4812	41%	**49163**	**42%**	**3033**	**60%**
Hispanic	17651	14%	10938	15%	6713	14%	12557	14%	5094	15%	16382	15%	1269	11%	17100	15%	551	11%
Non-Hispanic Asian	2219	2%	1517	2%	703	1%	1714	2%	505	1%	2125	2%	94	1%	2186	2%	33	1%
Other/unknown	6014	5%	4191	6%	1823	4%	4706	5%	1308	4%	5663	5%	351	3%	5908	5%	106	2%
HIV acquisition risk																		
IDU	21115	17%	**10656**	**14%**	**10459**	**22%**	**12265**	**14%**	**8850**	**26%**	**16487**	**15%**	**4628**	**40%**	**18452**	**16%**	**2663**	**53%**
MSM	42869	35%	**28477**	**38%**	**14392**	**30%**	**32157**	**36%**	**10712**	**31%**	**39954**	**36%**	**2915**	**25%**	**42379**	**36%**	**490**	**10%**
Heterosexual contact	24662	20%	**17061**	**23%**	**7601**	**16%**	**20609**	**23%**	**4053**	**12%**	**22916**	**21%**	**1746**	**15%**	**23987**	**20%**	**675**	**13%**
Other/Unknown	34250	28%	**19149**	**25%**	**15101**	**32%**	23645	27%	10605	31%	**31823**	**29%**	**2427**	**21%**	33055	28%	1195	24%
Smoking																		
Never	26585	22%	15963	21%	10621	22%	18691	21%	7892	23%	24978	22%	1607	14%	**25991**	**22%**	**594**	**12%**
Ever	61191	50%	**32229**	**43%**	**28963**	**61%**	**39501**	**45%**	**21690**	**63%**	**52673**	**47%**	**8518**	**73%**	**57253**	**49%**	**3938**	**78%**
Not assessed	35120	29%	**27151**	**36%**	**7969**	**17%**	**30484**	**34%**	**4636**	**14%**	**33529**	**30%**	**1591**	**14%**	**34629**	**29%**	**491**	**10%**
Hepatitis C infection	25009	20%	**13459**	**18%**	**11551**	**24%**	**16323**	**18%**	**8686**	**25%**	**21006**	**19%**	**4003**	**34%**	**22814**	**19%**	**2195**	**44%**
Hepatitis B infection	7004	6%	4196	6%	2808∗	6%	5084	6%	1920∗	6%	6268	6%	736∗	6%	6681	6%	323∗	6%
Treated hypertension	36543	30%	**19099**	**25%**	**17445**	**37%**	**23625**	**27%**	**12918**	**38%**	**32221**	**29%**	**4322**	**37%**	**34030**	**29%**	**2513**	**50%**
Diabetes	12136	10%	6577	9%	5559	12%	8447	10%	3689	11%	10803	10%	1333	11%	**11209**	**10%**	**927**	**18%**
CKD stage 2 (eGFR <60)																		
No	103064	84%	**61511**	**82%**	**41553**	**87%**	**72926**	**82%**	**30138**	**88%**	**92597**	**83%**	**10467**	**89%**	98721	84%	4343	86%
Yes	7978	6%	4669	6%	3309	7%	5792	7%	2186	6%	7295	7%	683	6%	7547	6%	431	9%
Not assessed	11854	10%	9163	12%	2691	6%	9958	11%	1896	6%	11288	10%	566	5%	11605	10%	249	5%
Hypercholesterolemia	26243	21%	**14206**	**19%**	**12035**	**25%**	**17154**	**19%**	**9089**	**27%**	23286	21%	2957	25%	**24921**	**21%**	**1322**	**26%**
statin use	20674	17%	**11003**	**15%**	**9671**	**20%**	**13625**	**15%**	**7049**	**21%**	18631	17%	2043∗	17%	19608	17%	1066∗	21%
CD4$^+$ cell count (cells/μl)																		
Median (IQR)	431 (251–634)		428 (247–630)		435 (258–643)		421 (240–626)		454 (279–657)		430 (250–629)		439 (265–642)		423 (234–631)		412 (237–612)	
<200	19986	16%	12521	17%	7465	16%	15293	17%	4693	14%	18317	16%	1669	14%	19212	16%	774	15%
≥200	85238	70%	51917	69%	33321	70%	60584	69%	24654	72%	77174	70%	8064	69%	**82142**	**70%**	**3096**	**61%**
Missing	17571	14%	10905	14%	6727	14%	12799	14%	4873	14%	15689	14%	1983	17%	**16519**	**14%**	**1153**	**23%**
HIV RNA (copies/ml)																		
<200	43075	35%	26436	35%	16638	35%	31138	35%	11937	35%	39150	35%	3925	34%	**41604**	**35%**	**1471**	**29%**
≥200	51433	42%	32139	43%	19294	41%	37676	42%	13757	40%	46465	42%	4968	42%	**49448**	**42%**	**1985**	**40%**
Missing	28388	23%	16768	22%	11621	24%	19862	22%	8526	25%	25565	23%	2823	24%	**26821**	**23%**	**1567**	**31%**
Year of ART initiation																		
1996–2004	33820	28%	**17283**	**23%**	**16537**	**35%**	**22135**	**25%**	**11685**	**35%**	**29805**	**26%**	**4015**	**34%**	**31748**	**27%**	**2072**	**41%**
2005–2009	26728	22%	16041	21%	10687	22%	19484	22%	7244	21%	24120	22%	2608	22%	25761	22%	967	19%
2010–2018	48644	40%	**32385**	**43%**	**16259**	**34%**	**36322**	**41%**	**12322**	**36%**	**44853**	**40%**	**3791**	**32%**	**47515**	**40%**	**1129**	**22%**
Not initiate ART	13690	11%	9622	13%	4068	9%	10726	12%	2964	9%	12391	11%	1299	11%	**12835**	**11%**	**855**	**17%**
HIV treatment regimen at ART initiation																		
NNRTI	14770	12%	10107	13%	4663	10%	10841	12%	3929	12%	13655	12%	1115	10%	**14495**	**12%**	**275**	**5%**
PI	6609	5%	3913	5%	2696	6%	4689	5%	1920	6%	6023	5%	586	5%	6408	5%	201	4%
Integrase Inhibitor	42922	35%	25933	35%	16989	36%	30968	35%	11954	35%	39322	36%	3600	31%	**41553**	**35%**	**1369**	**27%**
Other/unknown	44343	36%	**25402**	**34%**	**18941**	**40%**	31021	35%	13322	39%	**39266**	**35%**	**5077**	**43%**	**42029**	**36%**	**2314**	**46%**
Never on HAART	13690	11%	9622	13%	4068	9%	10726	12%	2964	9%	12391	11%	1299	11%	**12835**	**11%**	**855**	**17%**

P-values calculated using chi-squared tests for all categorical or binary variables and *t*-tests for all continuous variables. All *P*-values are <0.001, unless specified with (∗). Due to large numbers of participants statistical significance was common, however clinical significance was considered as a difference in 5% between comparison groups and these differences are bolded. Age, sex, race/ethnicity, and HIV transmission acquisition group are time-fixed variables, measured at enrollment into the NA-ACCORD. IDU, injection drug use; MSM, men who have sex with men; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

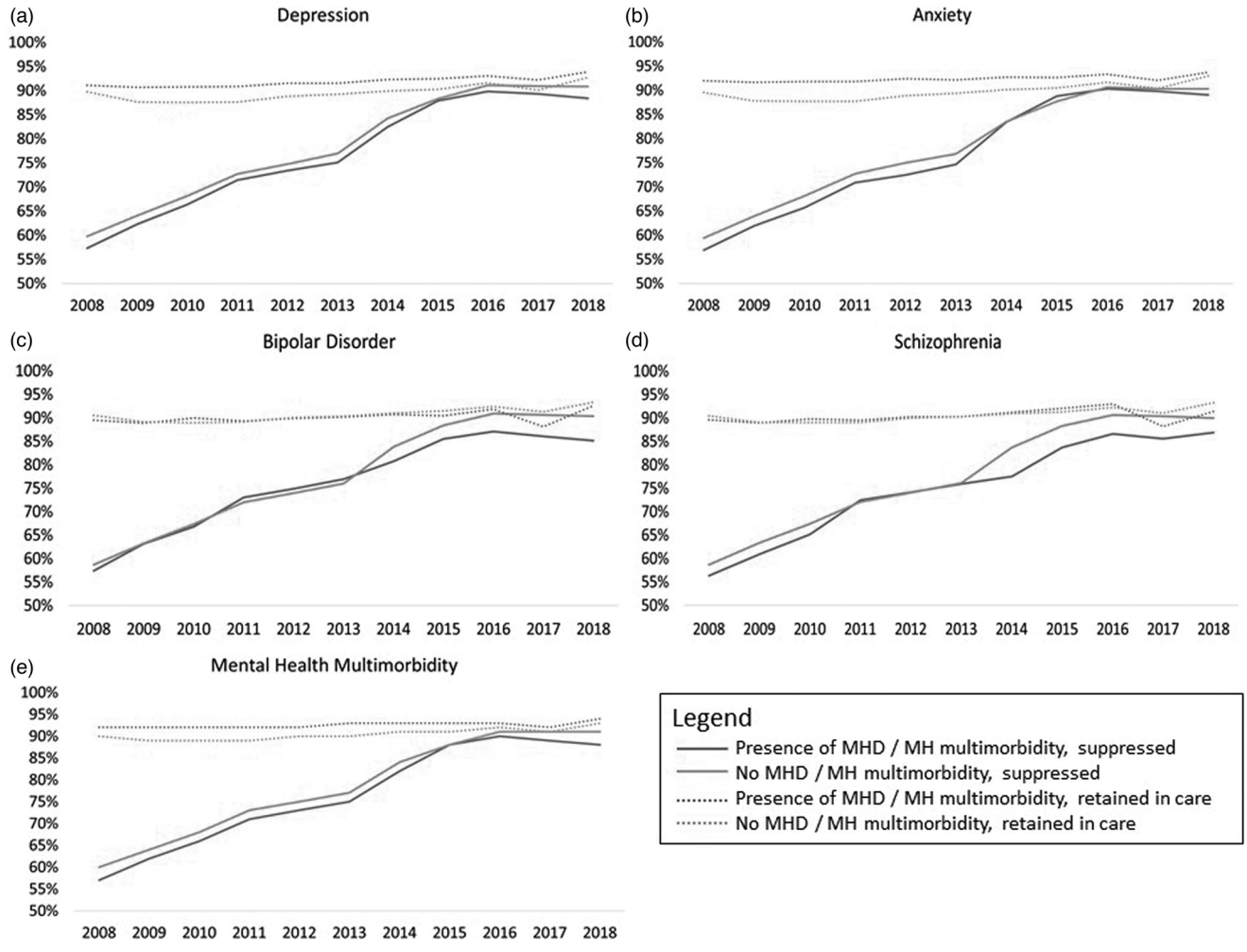

Fig. 2. Trends in retention in care and viral suppression by (a) depression diagnoses, (b) anxiety diagnoses, (c) bipolar disorder diagnosis, and (d) schizophrenia diagnosis, 2008–2018 ($N = 122\ 896$). Retention is defined as two or more HIV care visits between 2016 and 2018. Suppression defined as having a viral load ≤200 copies/ml between 2016 and 2018.

viral suppression than those without depression in recent years (2016–2018) (Table 2).

Anxiety

The prevalence of anxiety disorder increased from 21.5% [21.1–21.8%] in 2008 to 36.9% [36.1–37.6%] in 2018 ($P = 0.001$ for annual trend) (Fig. 1). Those with anxiety had higher annual proportion of retention in care compared to those without anxiety between 2008 and 2017 ($P < 0.01$). From 2008 to 2013, those with anxiety had a consistently lower viral suppression compared to those without anxiety ($P < 0.001$), however viral suppression was similar by anxiety diagnosis from 2014–2018 (Fig. 2b). In adjusted models PWH with anxiety had a 2% [0.97–0.98] lower prevalence of retention in care than those without anxiety in recent years (2016–2018). Those with anxiety had no difference in the prevalence of viral suppression compared to those without anxiety in both crude and adjusted models (Table 2).

Bipolar disorder

Unlike depression and anxiety, the prevalence of BD decreased over calendar time, from 10.7% [10.4–10.9%] in 2008 to 8.4% [7.9–8.8%] in 2018 ($P = 0.058$ for annual trend) (Fig. 1). There was minimal difference in annual trends of the proportions retained in care among those with and without BD from 2008 to 2018. Those with and without BD had similar proportions virally suppressed from 2008 to 2013, but from 2014 to 2018 the proportion suppressed was lower in those with BD compared to those without BD ($P < 0.001$) (Fig. 2c). Those with BD had no difference in the prevalence of retention in care compared to those without (2016–2018) in adjusted models. Those with BD had a 5% [0.94–0.97] lower prevalence of viral suppression than those without BD; however, this changed to a 2% [0.98–0.99] lower prevalence of viral

Table 2. The impact of mental health disorders on the HIV care continuum among PWH on ART (2016–2018).

	n	%	PR[a]	95% CI	aPR[b]	95% CI
Retained in care ($N = 54\ 606$)						
No depression	30463	56%	1.00		1.00	
Depression	24143	44%	**1.03**	**1.03–1.04**	**0.98**	**0.97–0.98**
No anxiety	35068	64%	1.00		1.00	
Anxiety	19538	36%	**1.03**	**1.02–1.03**	**0.98**	**0.97–0.98**
No bipolar disorder	48943	90%	1.00		1.00	
Bipolar disorder	5663	10%	1.01	1.00–1.01	1.00	1.00–1.01
No schizophrenia	52304	96%	1.00		1.00	
Schizophrenia	2302	4%	1.01	1.00–1.03	1.00	1.00–1.01
No MH disorder	20724	38%	1.00		1.00	
One MH disorder	17101	31%	**1.02**	**1.02–1.03**	**1.01**	**1.01–1.01**
MH multimorbidity[c]	16781	31%	**1.04**	**1.04–1.05**	**1.02**	**1.02–1.02**
Suppressed HIV RNA (≤200 copies/ml) ($N = 20\ 231$)						
No depression	12625	62%	1.00		1.00	
Depression	7606	38%	**0.99**	**0.98- 0.99**	1.01	1.00–1.02
No anxiety	13901	69%	1.00		1.00	
Anxiety	6330	31%	1.00	1.00- 1.01	1.00	1.00–1.01
No bipolar disorder	18572	92%	1.00		1.00	
Bipolar disorder	1659	8%	**0.95**	**0.94–0.97**	**0.98**	**0.98–0.99**
No schizophrenia	19865	98%	1.00		1.00	
Schizophrenia	366	2%	**0.96**	**0.93–0.99**	1.00	0.98–1.01
No MH disorder	9136	45%	1.00		1.00	
One MH disorder	6282	31%	**0.97**	**0.97–0.98**	0.99	0.99–1.00
MH multimorbidity[c]	4813	24%	**0.98**	**0.97–0.99**	**0.99**	**0.99–1.00**

ART, antiretroviral therapy; MH, mental health; PWH, people with HIV.
[a]PR = unadjusted prevalence ratio from a log binomial regression model.
[b]aPR = adjusted prevalence ratio from a log binomial regression model, adjusted for decade of age, race/ethnicity (due to small numbers, Asian/PI was collapsed into the other/unknown category), sex, HIV acquisition risk group, and cohort.
[c]Mental health multimorbidity included those with ≥2 MH comorbidities.
Values with $P < 0.05$ are bolded.

suppression among those with BD after adjustment for demographic characteristics (Table 2).

Schizophrenia

The prevalence of schizophrenia declined over time, from 4.7% [4.5–4.9%] in 2008 to 2.1% [1.9–2.3%] in 2018 ($P = 0.013$ for annual trend) (Fig. 1). Those with schizophrenia had similar retention in care to those without from 2008 to 2014, and a higher proportion retained in care in 2015–2016 ($P < 0.01$). Those with and without schizophrenia had similar viral suppression until 2013; from 2014 to 2017 those with schizophrenia were less likely to be virally suppressed compared to those without schizophrenia ($P < 0.001$) (Fig. 2d). In adjusted models PWH with schizophrenia had no difference in the prevalence of retention in care compared to those without schizophrenia (2016–2018). Those with schizophrenia had a 4% [0.93–0.99] decrease in the prevalence of viral suppression compared to those without schizophrenia, and this attenuated to no difference after adjustment for demographic characteristics (Table 2).

Multimorbidity of mental health disorders among people with HIV

From 2008 to 2018, MH multimorbidity prevalence was 24% (29 243/122 896), with 92% of those with schizophrenia ($n = 5022$), 82% with anxiety ($n = 34\ 219$), 69% with BD ($n = 11\ 716$) and 53% with depression ($n = 47\ 553$) having a diagnosis of at least one other MHDs (Fig. 3). Anxiety was the most common MH comorbidity among those with depression, BD, and schizophrenia. From 2008 to 2017, the annual proportion of PWH retained in care was similar but consistently higher in those with (vs. without) MH multimorbidity ($P < 0.001$), whereas viral suppression was similar but consistently lower among PWH with MH multimorbidity ($P < 0.001$), with a gap beginning to widen from 2016 to 2018 (Fig. 2e).

In more recent years (2016–2018), the prevalence of MH multimorbidity was 16% (19 457/64 864) among PWH (Figure 2, Supplemental Digital Content, http://links.lww.com/QAD/C710). Those with MH multimorbidity had a 4% [1.04–1.05%] higher prevalence of retention in care compared to those without MHDs (2016–2018); however, this attenuated to a 2% [1.02–1.02%] higher retention in care after adjustment for demographic characteristics. Those with MH multimorbidity had a 2% [0.97–0.99%] lower prevalence of viral suppression compared to those without MHDs, and this attenuated to a 1% [0.99–1.00%] lower prevalence in viral suppression after adjustment for demographic characteristics (Table 2).

Treated vs. untreated bipolar disorder and schizophrenia

The majority of PWH diagnosed with BD (89%) and schizophrenia (88%) initiated MH treatment. In adjusted analyses there was a statistically nonsignificant 1% lower

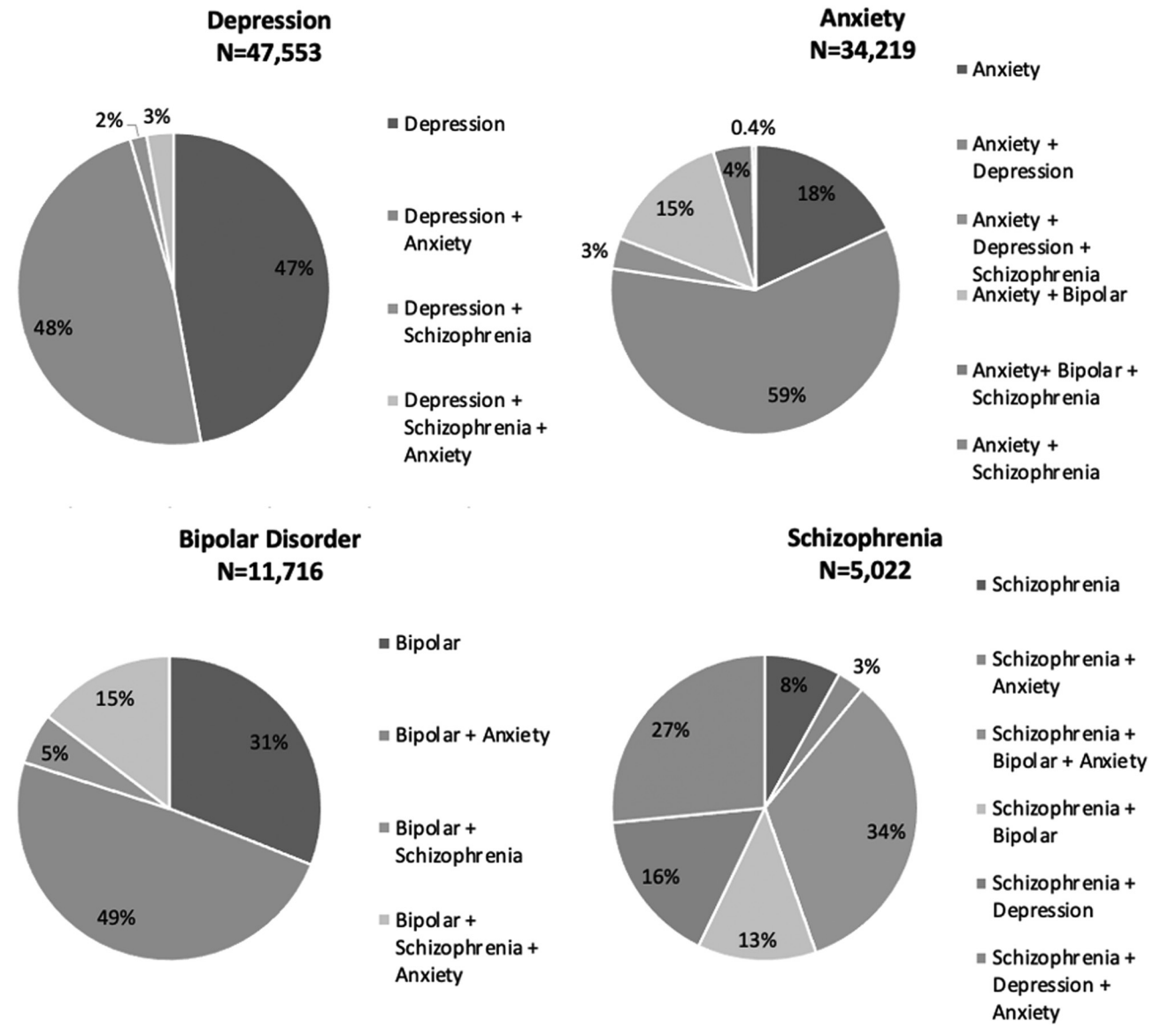

Fig. 3. The percentage mental health multimorbidity, by individual mental health comorbidity, 2008–2018. A diagnosis of BD excluded classification of this participant as having depression; these two diagnoses were considered mutually exclusive. BD, bipolar disorder.

prevalence of retention in care and viral suppression among PWH with untreated BD compared to those without BD. Untreated schizophrenia was associated with a statistically nonsignificant 1% higher prevalence of retention in care and no difference in viral suppression when compared to PWH without schizophrenia (Table 4, Supplemental Digital Content, http://links.lww.com/QAD/C710).

Discussion

MHDs prevalence is high among PWH in North America; many with an MHDs are also MH multimorbid. We found greater prevalence of MHDs in PWH than that reported in other studies of the general US population [30–32]. A nationally representative survey of over 9000 US adults found 46.4% had a lifetime prevalence of any MHD, and 27.7% had two or more disorders [30]. We evaluated just four MHDs and found 55.1% of PWH had a MHDs and 23.8% had ≥2 MHDs. The general population lifetime prevalence of having a major depressive disorder was 16.6%, generalized anxiety disorder 5.7% and BD was 3.9% [30]; in our study population of PWH the estimate was 2.3-fold higher (38.7%) for depression, 4.9-fold higher (27.8%) for anxiety, and 2.4-fold higher (9.5%) for BD. The lifetime prevalence of schizophrenia in US adults is approximately 0.4% [31–33], and >10-fold higher (4.1%) in our study population of PWH.

From 2008 to 2018, the annual prevalence of depression and anxiety increased among PWH in our dynamic study population, which reflects trends in the US general population. [34,35] This increase is likely multifactorial and may be influenced by a greater clinical recognition over time, increased incidence, or increased duration of depression or anxiety disorder due to delayed diagnosis and treatment [35]. BD and schizophrenia remained stable until recent years, when prevalence decreased among PWH in our study population. Studies from the US general population suggest either stable or decreasing prevalence of both BD and schizophrenia [36–40]. Reasons for these trend shown in both our study population and the US general population are unknown, with suggestions that changing diagnostic criteria may be contributory [36–39].

Although prior studies have demonstrated that PWH with MHDs access health services less often and have worse outcomes along the HIV care continuum [1,41–43], we did not identify large differences associated with MHDs or MH multimorbidity on retention in care or viral suppression. However, we did find PWH with depression and anxiety had marginally lower retention in care and those with MH multimorbidity had marginally increased retention in care. Guidance suggests more frequent follow-up visits for PWH with MHDs [44,45], therefore despite small differences observed in retention in care between those with and without MHDs, this may signal greater disparity. We found lower viral suppression among PWH with BD and MH multimorbidity compared to those without these diagnoses. Because of the high prevalence of these MHDs among PWH, it is unlikely 'Ending the HIV Epidemic' viral suppression goals will be reached without interventions tailored to those with MHDs [46].

The proportion of PWH in NA-ACCORD achieving viral suppression increased between 2008 and 2018, however it was lower among those with (vs. without) BD and with (vs. without) schizophrenia. Additionally, retention in care was similar among those with (vs. without) these MHDs. PWH who have BD or schizophrenia experience barriers to viral suppression that exist even when they are successfully retained in care, a gap which has widened during the Treat All era. The explanation for this gap is unknown, however factors of influence may include reduced prescription of ART and/or MH treatment, and decreased adherence to, or drug-drug interactions between, ART and MH treatments [47,48].

Prior studies have found that retention in HIV care and ART adherence was higher among PWH receiving care for their MHDs [49–52]. Combining HIV and MHDs care visits provides added convenience and incentive and may increase access to both types of care. When evaluating PWH with BD and schizophrenia, we found the majority (~90%) had initiated therapy for these disorders. This may explain the minimal differences in HIV care continuum among those with MHDs vs. those without. Our findings highlight the success of HIV care programs to provide PWH with both HIV and MH treatment, but also the ongoing need for improved resources for MH screening, linkage to treatment, and support programs to eliminate the identified gaps. The importance of MH services being integrated into HIV care programs has been emphasized through the COVID-19 pandemic as reports suggest increasing prevalence and worsening symptoms of MHDs [53,54].

One strength of this work is the use of a large, diverse, and representative cohort of PWH who have linked into HIV care in North America. However, enrollment criteria into the NA-ACCORD includes only individuals successfully linked into HIV care. Those who have never linked into care may be more likely to also have MHDs (albeit potentially less likely to have a clinical diagnosis of MHDs) and would not be included in this study population. A second strength lies in the ascertainment for diagnoses to classify PWH as ever having a MHDs, however, underdiagnosis is MHD common in both people with and without HIV.

Limitations include that we did not have sufficient data to evaluate time-varying severity or management of these MHDs and are therefore likely identifying a heterogenous population of MHD severity and treatment among PWH. The generalizability of increased retention in care among PWH with MHDs and multimorbidity may be limited to clinics similar to those contributing to the NA-ACCORD who provide in-clinic MH screening and treatment. MHDs may have been diagnosed prior to or near the time of HIV diagnosis and age at diagnosis was not available. HIV continuum of care outcome definitions allow for comparison of our results to other studies, however the sensitivity of the definitions may be influencing the small differences seen between groups. Retention in care was measured with in-person visits and virtual care visits were not ascertained. Despite this being a large evaluation of MHDs in PWH, we were constrained by a small sample size for certain analyses within a specific MHD. Finally, we could not describe MHDs in PWH by active drug or alcohol use status, socioeconomic status, family history of MHDs or high stress/traumatic life events, which were not measured.

Conclusion

This analysis provides novel insight into the prevalence and HIV care continuum outcomes associated with MHDs and multimorbidity in PWH. Due to the high prevalence of MHDs and multimorbidity among PWH, clinicians must remain vigilant with screening for these disorders and providing effective engagement into MH services when needed. Understanding barriers to viral suppression, and effective interventions to overcome such barriers among PWH with MHDs and multimorbidity

must continue to be a priority to increase the health and well being of PWH.

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Availability of data and materials: Complete data for this study cannot be publicly shared because of legal and ethical restrictions. The NA-ACCORD Principals of Collaboration requires submission and approval of a concept sheet that describes the intended research project for which data are being requested. The NA-ACCORD Executive Committee and the Steering Committee (composed of principle investigators of contributing cohorts) must approve the concept sheet and elect to have their data included for the research project. A signed Data User Agreement is required before data can be released. Guidance for how to obtain NA-ACCORD data are outlined on the NA-ACCORD website (www.naaccord.org/collaboration-policies).

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Conflicts of interest

K.N.A. is a consultant to the All of Us Research Program and serves on the scientific advisory board for Trio Health. M.J.G. has received honoraria for ad hoc participation on National HIV advisory Boards to Merck Gilead and ViiV Health. P.F.R. received honoraria from Gilead and Johnson & Johnson (money paid to individual); funding from NIH/NIAID (money paid to institution). J.E. receives grants and personal fees from ViiV Healthcare, Janssen, and Gilead Sciences and personal fees from Merck, outside the submitted work. All other authors report no relevant conflicts of interest.

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