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Health Care Consumption, Psychiatric Diagnoses, and Pharmacotherapy 1 and 2 Years Before and After Newly Diagnosed HIV: A Case-Control Study Nested in The Greater Stockholm HIV Cohort Study

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ABSTRACT

Objective: We compare individuals with newly diagnosed HIV with sex-, age-, and socioeconomic status–matched HIV-negative controls, with the aim of studying the frequency of health care visits, the types of clinics visited, registered diagnoses, and psychopharmacotherapy.

Methods: The data were collected through the Stockholm Region administrative database (Stockholm Regional Health Care Data Warehouse) for men and women (people) living with newly diagnosed HIV (PLWH) in their medical records (930 men, 450 women) and controls. The odds ratios (ORs) with 99% confidence intervals (CIs) for psychiatric comorbidities and relevant pharmacotherapies were calculated during the 2011–2018 period.

Results: Substance use disorder was higher in PLWH than in controls, before and after newly diagnosed HIV in men (OR = 1 year before 4.36 [99% CI = 2.00–9.5] and OR = 1 year after 5.16 [99% CI = 2.65–10.08]) and women (OR = 1 year before 6.05 [99% CI = 1.89–19.40] and OR = 1 year after 5.24 [99% CI = 1.69–16.32]). Health care contacts and psychiatric disorders were more common in cases than controls 1 and 2 years after diagnosis, particularly for depression in men 1 year after HIV (OR = 3.14, 99% CI = 2.11–4.67), which was not found in women (1 year OR = 0.94, 99% CI = 0.50–1.77).

Conclusions: Before newly diagnosed HIV, PLWH have the same level of psychiatric diagnoses as their controls, except for substance use disorder. Psychiatric problems are more common in PLWH than in their controls after newly diagnosed HIV.

Key words: administrative databases, general population, mental illness, psychotic disorders, bipolar disorders, depression, anxiety disorders, trauma-related disorders, drug dependence disorders, psychotropic medication.

INTRODUCTION

Psychiatric illness has been proposed to be a risk factor for acquiring human immunodeficiency virus (HIV) (1–4), and persons admitted for severe psychiatric illness have been shown to have a higher HIV prevalence than the general population (5,6). Depression is of particular importance in people living with HIV (PLWH), and the prevalence of a diagnosis of depression in PLWH is three times higher in men (10%) and 40% higher in women (8.5%) than in the general population of Stockholm (7). Depending on methodology used and population studied in the world, the prevalence of depressive symptoms in PLWH has been shown to range from 12.8% to 78%, and in a review, no significant differences were noted by country income group (8).

Mental health is of importance in PLWH. Concomitant psychiatric illness may contribute to poor adherence to medication and safe sex practices in PLWH (4,9–11). Both adherence to combination antiretroviral therapy (ART) and adherence to psychotropic drugs are affected by the mental health. In fact, psychiatric illness may affect PLWH in all stages of disease, including disclosure of HIV diagnosis through the whole process related to ART, readiness to start treatment, and lifelong adherence to medication (12,13). Psychological distress after HIV diagnosis is common and has been associated with the stigma that still exists toward PLWH and worries for HIV complications (1,3,4,14). The stigma in PLWH has been shown to be associated with anxiety, depression, and suicide ideation in studies from all over the world (15). In addition, there is a biological explanation to the higher levels of depression, cognitive effects, and fatigue in PLWH, as PHLW have been shown to have impaired neurotransmitter biosynthesis, especially tryptophan and phenylalanine (16).

ART = antiretroviral therapy, **CI** = confidence interval, **HIV** = human immunodeficiency virus, **OR** = odds ratio, **PLWH** = people living with HIV, **VAL** = Stockholm Regional Health Care Data Warehouse

SDC Supplemental Digital Content

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We reported in previous studies of "the Greater Stockholm HIV cohort," a cohort that includes all PLWH in Stockholm Region, that, although the prevalence of diabetes, hypertension, and cancer in PLWH is on a par with that of the general population, PLWH more often have psychiatric disorders (7,17).

By matching cases with newly diagnosed HIV to age-matched controls without HIV, we have the opportunity to conduct a case-control study and see how their health care compares in the years before and after the first recorded HIV diagnosis. Do PLWH have psychiatric diagnoses before their HIV diagnosis, or do psychiatric diagnoses follow and consequently occur after the HIV diagnosis?

Accordingly, the aim of this investigation was to study the frequency of health care visits, the types of clinics visited, relevant psychiatric comorbidities, and prescribed and collected psychiatric pharmacotherapies in all individuals with an incident HIV diagnosis compared with matched HIV-negative controls from 2011 to 2018. We hypothesize that there will be differences between PLWH and controls before the time point of HIV diagnosis and that the differences in psychiatric illness between cases and controls will increase after the diagnosis of HIV.

METHODS

"The Greater Stockholm HIV Cohort Study" is an initiative to provide longitudinal information regarding the health of PLWH in comparison to the health of the total population. The Stockholm Region has more than 2.2 million inhabitants, representing more than one-fifth of Sweden's entire population. The region includes the capital city of Stockholm and several other cities and towns, as well as large rural areas and a sparsely populated archipelago. The Stockholm Region is responsible for financing primary and secondary health care, mainly through taxes. Apart from very few private clinics that operate without subsidies in Stockholm, all consultations and diagnoses are recorded and stored in a central regional database, the Stockholm Regional Health Care Data Warehouse (VAL). The link to VAL makes it possible to perform prevalence and incidence studies for different diagnoses for all residents. These databases compile and store data on health care utilization from primary care, specialist open care, hospital inpatient care, and data on collected prescribed medications. As an indication for its accuracy and validity, VAL is used by the Stockholm Region for updating the National Patient Register kept by the Swedish National Board of Health and Welfare, as well as the annual benchmarking reports of the Swedish National Board of Health and Welfare and the Swedish Association of Local Authorities and Regions. Since 1997, diagnoses have been coded according to World Health Organization's *International Classification of Diseases, Tenth Edition*.

Study Population

The studied cohort in the present study was defined as all men and women who resided in the Stockholm Region at some point between January 1, 2011, and December 31, 2018, and subjects were included with their controls when a first diagnosis of HIV was registered during that time frame. Data on all health care consultations in primary care and specialized open care were extracted from the VAL up to 2 years before and after the first HIV diagnosis was registered. Men and women with a newly diagnosed HIV were used as cases. Approximately 10 controls per case, matched for sex, age, and socioeconomic status without e recorded diagnosis of HIV, were used. Each control was only enrolled once, even if matched with more than one of the cases. Therefore, the number of controls is less than 10 times the number of cases.

Sociodemography

We used the Mosaic tool to classify neighborhood socioeconomic status into three levels, that is, high, middle, or low. Mosaic is a tool developed by the marketing company Experian to classify consumers to make sale activities more effective. The mosaic system makes it possible to achieve a nuanced classification of socioeconomic status. It uses multivariate modeling, using more than 400 variables, to group postcodes into different types and aggregate broader groups. Mosaic uses data from 29 different countries and has been shown to be useful for the classification of cohorts in epidemiologic research (18,19).

Design

This was a case-control study in which individuals with newly diagnosed HIV were compared with controls matched for sex, age, and neighborhood socioeconomic status without such a diagnosis. Diagnoses were registered at discharge from hospital or after a consultation 1 year (1–365 days), referred to as *year 1*, and during 1 year before 1 year before (366–730 days), referred to as *year 2*, before the first diagnosis of HIV was recorded. We also studied registered diagnoses with the same variables 1 and 2 years after HIV diagnosis. The following *International Classification of Diseases* codes were used to define the individuals diagnosed with HIV: B20, B21, B22, and B24.

Visits to Health Care and Clinics

The number of visits to doctors was analyzed for the following types of clinics: emergency care, psychiatric care, gynecology (women), other open care (nonprimary care doctors outside hospitals), and primary care. We had no clear information on specific visits to clinics for PLWH only; they are included in the other open care visits. We also analyzed the total number of visits to health care subdivided into physicians; psychologists, therapists, and social workers; and other health care workers (nurses, physiotherapists, and more).

Psychiatric Diagnoses and Pharmacotherapy

To portray the differences in psychiatric illnesses that could be problematic in PLWH between cases and controls, the following comorbid diagnoses were chosen (20): reactions to stress; anxiety disorders (phobic anxiety and generalized anxiety), psychotic disorders (schizophrenia, acute and transient psychotic disorders, schizoaffective disorder, other psychotic disorder not due to a substance or known physiological condition, and unspecified psychosis not due to a substance or known physiological condition), bipolar disorders (mania without psychotic symptoms and bipolar affective disorders), alcohol use disorder, substance use disorders (opioids, cannabis, sedatives, cocaine, other stimulants, hallucinogens, nicotine, inhalants, and multiple drug use and use of other psychoactive substances), depression (depressive episode and major depressive disorder), and self-harm behaviors.

ATC codes were used to identify pharmacotherapy for sleep disturbances and psychiatric disorders: first-generation sedating anti-histamines (R06AD02, N05BB), neuroleptics (N05A), propiomazine (N05CM06)(sleep medication), antidepressant drugs (N06A), hypnotics (N05CF), stimulants(N06BA), and benzodiazepines (N05BA).

Ethics

All data were pseudonymized, and none of the individuals could be identified. Patient consent was nonapplicable because it is mandatory to be included in the registers when in contact with public health care in Sweden. Management and analysis based on VAL is part of a continuous quality control of health care utilization in the Stockholm Region. Ethical approval was obtained from the regional ethical review board in Stockholm to study diseases and their comorbidities with VAL data (permits: 2013/2196-31/2, 2016/638-32).

Statistical Methods

Means and 99% confidence intervals (CIs) were estimated to compare the number of health care visits with all professionals among individuals newly diagnosed with HIV compared with HIV-negative controls. No overlap in the confidence intervals between cases and their controls was considered statistically significant. Conditional logistic regression was used to calculate odds ratios (ORs) with 99% CIs of psychiatric comorbidities and drug prescriptions among individuals newly diagnosed with HIV compared with HIV-negative controls, separated by sex. Multiplicative interactions were tested for possible interactions between sex and diagnoses before and after

newly diagnosed HIV. To reduce the risk of false discoveries due to multiple testing, a p value of less than .01 was considered as significant. All controls were matched for age, sex, and neighborhood socioeconomic status. Statistical analysis and data management were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, North Carolina).

RESULTS

In total, 450 women and 930 men were diagnosed with HIV for the first time during the study period and were matched to 4361 women and 9004 men without a diagnosis of HIV. The age distribution, neighborhood socioeconomic status, and prevalence and pharmacotherapy of psychiatric disorders are shown for men and women (cases and controls) in Table 1. The similarity in characteristics that we matched for indicates that the matching procedure was well performed. Substance use disorder was more common in cases than controls among both women and men before HIV diagnosis; other noteworthy differences were not found.

Interactions for between sex and different diagnoses before and after new HIV diagnosis was tested and revealed significant interactions between sex and depression, 1 and 2 years after HIV diagnosis, $p < .001$ and $p = .004$, respectively. Significant interactions between sex and diagnoses were also found for anxiety and stress 1 year after diagnosis, $p = .009$ and $p = .003$, respectively. All results hereinafter were stratified by sex.

The number of health care visits, types of clinics visited, and the category of health care professionals met on their visits 2 years and 1 year before the first HIV diagnosis and 1 and 2 years after the first HIV diagnosis are shown in Table 2 (women) and Table 3 (men). The results are summarized hereinafter.

Health Care Visits in Women and Men Before the First Registered Diagnosis of HIV

Women with HIV had fewer visits to specialist clinics, to primary care, and to physicians in general 2 years before their HIV diagnosis than their matched controls. Women with HIV also had fewer visits to primary care 1 year before HIV diagnosis than their controls.

Men with HIV visited primary care less 2 years before HIV diagnosis. Men visited all clinics except primary care significantly more than their controls 1 year before HIV diagnosis. Similarly, there was no difference in the contacts with health care professionals 2 years before diagnosis, but men with HIV had significantly more visits to all health care professionals than their controls 1 year before diagnoses.

Health Care Visits in Women and Men After the First Registered Diagnosis of HIV

Women with HIV visited outdoor specialist clinics, gynecologists, and other specialist clinics more than their controls 1 year after HIV diagnosis and visited the same clinics more than their controls

TABLE 1. Baseline Characteristics in Women and Men (Cases and Controls) 1 Year Before HIV Diagnosis

	Women		Men	
	Frequency 1 y Before Diagnosis for Cases (n = 450)	Frequency 1 y Before Diagnosis for Controls (n = 4361)	Frequency 1 y Before Diagnosis for Cases (n = 930)	Frequency 1 y Before Diagnosis for Controls (n = 9004)
Age (mean and standard deviation)	37.17 (12.19)	37.17 (12.29)	39.85 (13.44)	39.93 (13.41)
Neighborhood socioeconomic status, n (%)				
High	110 (24.4)	1069 (24.5)	374 (40.2)	3618 (40.2)
Medium	82 (18.2)	791 (18.1)	173 (18.6)	1651 (18.3)
Low	258 (57.3)	2501 (57.4)	383 (41.2)	3735 (41.5)
Diagnoses, n (%)				
Suicide attempt (X60–84)	2 (0.44)	7 (0.16)	1 (0.11)	3 (0.03)
Substance use disorder (F11–F19)	8 (1.78)	13 (0.30)	16 (1.72)	36 (0.40)
Alcohol use disorder (F10)	6 (1.33)	17 (0.39)	17 (1.83)	100 (1.11)
Depression (F32, F33)	20 (4.44)	224 (5.14)	24 (2.58)	214 (2.38)
Fatigue syndrome (F43.8)	2 (0.44)	51 (1.17)	4 (0.43)	26 (0.29)
Stress (F43)	10 (2.22)	153 (3.51)	6 (0.65)	119 (1.32)
Anxiety (F40, F41)	15 (3.33)	238 (5.46)	27 (2.90)	252 (2.80)
Bipolar disorder (F30, F31)	2 (0.44)	25 (0.57)	2 (0.22)	46 (0.51)
Psychosis (F20, F23, F25, F28, F29)	2 (0.44)	24 (0.55)	5 (0.54)	62 (0.69)
Pharmaceutical drug type, n (%)				
Stimulants (N06BA)	5 (1.11)	51 (1.17)	9 (0.97)	93 (1.03)
Neuroleptics (N05A)	15 (3.33)	89 (2.04)	12 (1.29)	163 (1.81)
Benzodiazepines (N05BA)	13 (2.89)	129 (2.96)	22 (2.37)	179 (1.99)
Tranquilizers (R06AD02, N05BB)	28 (6.22)	256 (6.87)	29 (3.12)	278 (3.09)
Hypnotics (N05CF)	18 (4.00)	238 (5.46)	68 (7.31)	346 (3.84)
Propiomazine (N05CM06)	11 (2.44)	108 (2.48)	24 (2.58)	171 (1.90)
Antidepressant drugs (N06A)	34 (7.56)	483 (11.08)	49 (5.27)	534 (5.93)

HIV = human immunodeficiency virus.

TABLE 2. Number of Health Care Visits and Health Care Professionals Visited With 99% CIs (Women)

Clinics Visited and Professionals Met on the Visit	2 y Before Diagnosis (n = 450), Cases (99% CI)	2 y Before Diagnosis (n = 4361), Controls (99% CI)	1 y Before Diagnosis (n = 450), Cases (99% CI)	1 y Before Diagnosis (n = 4361), Controls (99% CI)	1 y After Diagnosis (n = 450), Cases (99% CI)	1 y After Diagnosis (n = 4361), Controls (99% CI)	2 y After Diagnosis (n = 450), Cases (99% CI)	2 y After Diagnosis (n = 4361), Controls (99% CI)
Clinics visited								
Emergency clinic visits	0.53 (0.24–0.82)	0.47 (0.42–0.52)	**0.85 (0.54–1.16)**	0.50 (0.45–0.54)	1.36 (0.07–2.65)	0.42 (0.38–0.47)	0.64 (0.38–0.90)	0.35 (0.31–0.38)
Outdoor clinic visits	5.79 (2.67–8.91)	7.47 (6.93–8.01)	7.86 (4.52–11.21)	7.72 (7.15–8.28)	**21.73 (17.79–25.68)**	7.18 (6.64–7.72)	**12.06 (8.06–16.07)**	5.78 (5.34–6.22)
Psychiatry clinic	2.87 (0.03–5.77)	1.57 (1.22–1.91)	3.53 (0.46–6.59)	1.56 (1.21–1.90)	4.61 (0.60–8.62)	1.49 (1.13–1.85)	3.58 (0.08–7.08)	1.06 (0.82–1.29)
Gynecological clinic	**0.25 (0.13–0.37)**	0.50 (0.45–0.56)	0.45 (0.26–0.62)	0.58 (0.52–0.65)	**1.00 (0.80–1.20)**	0.50 (0.45–0.56)	**0.78 (0.62–0.93)**	0.42 (0.37–0.47)
Other specialist clinic	**1.87 (1.14–2.60)**	3.32 (3.01–3.63)	2.88 (2.21–3.54)	3.43 (3.11–4.27)	**15.60 (13.44–17.37)**	3.24 (2.95–3.53)	**7.00 (5.37–8.63)**	2.65 (2.38–2.91)
Primary health care	**1.32 (0.80–1.85)**	2.55 (2.38–2.72)	**1.86 (1.44–2.29)**	2.64 (2.46–2.82)	1.88 (1.33–2.42)	2.37 (2.21–2.54)	**1.35 (0.92–1.79)**	2.00 (1.84–2.17)
Professionals met on visits								
Psychologist, therapist, social worker	0.54 (0.12–0.97)	0.79 (0.63–0.95)	0.68 (0.25–1.10)	0.86 (0.70–1.03)	**3.44 (2.72–4.16)**	0.78 (0.64–0.92)	**1.33 (0.75–1.91)**	0.63 (0.51–0.75)
Physician	**2.67 (1.87–3.48)**	3.88 (3.64–4.11)	4.04 (3.09–4.99)	4.05 (3.82–4.23)	**9.04 (7.77–10.30)**	3.67 (3.45–3.88)	**4.70 (4.02–5.39)**	3.01 (2.82–3.20)
Other	3.10 (0.51–5.69)	3.27 (2.94–3.61)	4.00 (1.18–6.82)	3.30 (2.94–3.65)	**10.61 (7.04–14.18)**	3.16 (2.80–3.53)	**6.67 (3.25–10.09)**	2.50 (2.23–2.76)

CI = confidence interval; HIV = human immunodeficiency virus.

Comparisons in all women with new HIV diagnosis compared with matched HIV-negative controls 2 years (366–730 days) and 1 year (1–365 days) before diagnosis and 1 year (1–365 days) and 2 years (366–730 days) after the first registered HIV diagnosis, during the period 2011–2018. Significant differences were defined as no overlap in the 99% CIs between cases and controls at each time point and are shown in bold.

No statistical tests were made. Nonoverlapping 99% CIs were considered significant.

TABLE 3. Number of Health Care Visits and Health Care Professionals Visited With 99% CIs (Men)

Clinics Visited and Professionals Met on the Visit	2 y Before Diagnosis (n = 930), Cases (99% CI)	2 y Before Diagnosis (n = 9004), Controls (99% CI)	1 y Before Diagnosis (n = 930), Cases (99% CI)	1 y Before Diagnosis (n = 9004), Controls (99% CI)	1 y After Diagnosis (n = 930), Cases (99% CI)	1 y After Diagnosis (n = 9004), Controls (99% CI)	2 y After Diagnosis (n = 930), Cases (99% CI)	2 y After Diagnosis (n = 9004), Controls (99% CI)
Clinics visited								
Emergency clinic visits	0.27 (0.20–0.34)	0.34 (0.31–0.38)	**0.71 (0.60–0.82)**	0.35 (0.31–0.38)	**0.56 (0.43–0.70)**	0.31 (0.28–0.34)	**0.40 (0.31–0.50)**	0.26 (0.23–0.28)
Outdoor clinic visits	5.70 (3.53–7.88)	4.14 (3.81–4.47)	**8.35 (6.18–10.52)**	4.32 (3.99–4.65)	**19.99 (17.16–22.82)**	3.93 (3.62–4.24)	**10.64 (8.39–12.90)**	3.30 (3.06–3.54)
Psychiatry clinic	2.74 (0.76–4.73)	1.10 (0.87–1.33)	**3.16 (1.18–5.15)**	1.10 (0.86–1.34)	**4.23 (1.71–6.89)**	1.03 (0.80–1.27)	**2.98 (1.06–4.86)**	0.74 (0.60–0.88)
Other specialist clinic	2.03 (1.36–2.92)	1.58 (1.50–1.74)	**3.84 (3.12–4.55)**	1.73 (1.56–1.90)	**14.70 (13.48–15.46)**	1.53 (1.40–1.65)	**6.72 (5.85–7.59)**	1.34 (1.21–1.47)
Primary health care	**1.12 (0.87–1.36)**	1.76 (1.62–1.90)	1.91 (1.60–2.21)	1.80 (1.68–1.91)	1.73 (1.37–2.09)	1.65 (1.54–1.75)	1.32 (1.04–1.56)	1.45 (1.35–1.56)
Professionals met on visits								
Psychologist, therapist, social worker	0.46 (0.21–0.70)	0.35 (0.29–0.41)	**0.76 (0.53–0.95)**	0.35 (0.29–0.41)	**3.16 (2.68–3.63)**	0.32 (0.27–0.38)	**1.17 (0.86–1.48)**	0.28 (0.22–0.33)
Physician	2.31 (1.73–2.89)	2.34 (2.28–2.52)	**3.88 (3.23–4.53)**	2.44 (2.32–2.56)	**8.09 (7.50–8.68)**	2.20 (2.09–2.31)	**4.28 (3.71–4.84)**	1.91 (1.80–2.02)
Other	3.21 (1.29–5.12)	1.73 (1.46–1.99)	**4.41 (2.51–6.31)**	1.88 (1.62–2.15)	**9.31 (6.76–11.85)**	1.72 (1.47–1.96)	**5.60 (3.67–7.53)**	1.3727 (1.2128–1.5327)

HIV = human immunodeficiency virus; CI = confidence interval.

Comparisons in all men with new HIV diagnosis compared with matched HIV-negative controls 2 years (366–730 days) and 1 year (1–365 days) before diagnosis and 1 year (1–365 days) and 2 years (366–730 days) after the first registered HIV diagnosis, during the period 2011–2018. Significant differences were defined as no overlap in the 99% CIs between cases and controls at each time point and are shown in bold.

No statistical tests were made. Nonoverlapping 99% CIs were considered significant.

2 years after HIV diagnosis. Women visited primary care significantly less than their controls 2 years after HIV diagnosis. Women with HIV visited all health care professionals significantly more than their controls 1 and 2 years after diagnosis.

Men with HIV undertook significantly more visits to all clinics except primary care 1 and 2 years after diagnosis. They also visited all health care professionals more than their controls after diagnosis.

Psychiatric comorbidities and collected drug prescriptions are shown in Table 4 for women and Table 5 for men, and the results are summarized hereinafter.

Psychiatric Comorbidities and Collected Drug Prescriptions in Women and Men Before the First Registered HIV Diagnosis

Suicide attempt was more common in women 2 years before HIV diagnosis than in their controls. Substance use disorder was approximately five times more common in women with HIV than in their controls. Alcohol abuse was significantly more common 1 year before HIV diagnosis, and antidepressant drug use was significantly less common in women 1 year before HIV diagnosis than in their controls.

Mental and behavioral disorders due to drug abuse were three to four times more common before HIV diagnosis in men than in their controls. It was also more common among men with HIV before diagnosis to collect prescriptions of hypnotic drugs than in their controls.

Psychiatric Comorbidities and Collected Drug Prescriptions in Women and Men After the First Registered HIV Diagnosis

Substance use disorder was approximately five times more common in women with HIV than in their controls. The use of neuroleptics was significantly more common in women 1 year after HIV diagnosis, but there were no significant differences between women with HIV and their controls 2 years after HIV diagnosis.

Substance use disorder was significantly more common in men than in their controls after HIV diagnosis. Men had significantly higher rates of stress, alcohol abuse, and depression both 1 and 2 years after HIV diagnosis, as compared with their controls, but anxiety was only significantly different from controls 1 year after HIV diagnosis in men. The use of psychiatric pharmacotherapies, such as hypnotics, propiomazine, tranquilizers, and antidepressants, was also significantly higher in men with HIV than in their controls 1 and 2 years after the HIV diagnosis. Benzodiazepines were only significantly more used 1 year after HIV diagnosis when compared with controls.

Supplementary Results

As a final analysis, we adjusted the psychiatric diagnoses and pharmacotherapies for the number of visits to doctors 1 year after HIV diagnosis (Table S1, Supplemental Digital Content, http://links.lww.com/PSYMED/A862), which reversed the results. PLWH

TABLE 4. ORs for Relevant Psychiatric Comorbidities and Drug Prescriptions of Relevant Pharmacotherapies in Women With HIV Diagnosis Compared With Matched HIV-Negative Controls 2 Years (366–730 Days) and 1 Year (1–365 Days) Before Diagnosis and 1 Year (1–365 Days) and 2 years (366–730 Days) After HIV Diagnosis (2011–2018)

	2 y Before Diagnosis (n = 450), OR (99% CI)	1 y Before Diagnosis (n = 450), OR (99% CI)	1 y After Diagnosis (n = 450), OR (99% CI)	2 y After Diagnosis (n = 450), OR (99% CI)
Diagnoses				
Suicide attempt (X60–84)	**9.75 (1.19–80.18)*****	2.43 (0.32–18.69)	2.78 (0.35–21.99)	1.62 (0.10–26.19)
Substance use disorder (F11–F19)	**5.29 (1.57–17.80)*****	**6.05 (1.89–19.40)*****	**5.24 (1.69–16.32)*****	3.49 (0.91–13.44)
Alcohol use disorder (F10)	1.87 (0.53–6.53)	**3.46 (1.01–11.82)****	2.43 (0.75–7.97)	1.95 (0.55–6.93)
Depression (F32, F33)	0.84 (0.43–1.63)	0.86 (0.46–1.59)	0.94 (0.50–1.77)	1.09 (0.55–2.17)
Fatigue syndrome (F43.8)	0.68 (0.14–3.16)	0.38 (0.06–2.43)	0.41 (0.06–2.64)	0.35 (0.06–2.24)
Stress (F43)	0.52 (0.19–1.43)	0.63 (0.27–1.46)	1.20 (0.624–2.319)	1.52 (0.73–3.13)
Anxiety (F40, F41)	0.59 (0.28–1.26)	0.60 (0.30–1.20)	0.85 (0.47–1.55)	1.14 (0.61–2.12)
Bipolar disorder (F30, F31)	0.40 (0.029–5.60)	0.77 (0.12–5.16)	2.44 (0.70–8.90)	1.95 (0.47–8.03)
Psychosis (F20, F23, F25, F28, F29)	0.39 (0.03–5.36)	0.81 (0.12–5.39)	0.35 (0.03–4.75)	1.12 (0.23–5.41)
Pharmaceutical drug type				
Stimulants (N06BA)	1.33 (0.43–4.10)	0.95 (0.28–3.20)	1.42 (0.50–4.06)	1.43 (0.46–4.43)
Neuroleptics (N05A)	1.17 (0.49–2.80)	1.66 (0.80–3.44)	**2.37 (1.23–4.56)*****	1.68 (0.79–3.57)
Benzodiazepines (N05BA)	0.80 (0.35–1.81)	0.98 (0.46–2.09)	1.27 (0.60–2.70)	0.84 (0.34–2.09)
Tranquilizers (R06AD02, N05BB)	0.77 (0.41–1.44)	1.06 (0.63–1.81)	1.12 (0.66–1.91)	0.95 (0.51–1.79)
Hypnotics (N05CF)	0.77 (0.39–1.48)	0.72 (0.38–1.37)	1.21 (0.71–2.07)	1.22 (0.69–2.17)
Propiomazine (N05CM06)	0.58 (0.19–1.71)	0.99 (0.43–2.25)	1.33 (0.65–2.74)	1.11 (0.44–2.76)
Antidepressant drugs (N06A)	**0.46 (0.26–0.83)*****	0.66 (0.08–1.06)	0.87 (0.57–1.33)	0.76 (0.46–1.24)

OR = odds ratio; HIV = human immunodeficiency virus; CI = confidence interval.

Conditional logistic regression. Significant differences were defined as $p < .01$ and are shown in bold.

** $p < .01$.

*** $p < .001$.

TABLE 5. ORs for Relevant Psychiatric Comorbidities and Drug Prescriptions of Relevant Pharmacotherapies in Men With HIV Diagnosis Compared With Matched HIV-Negative Controls 2 Years (366–730 Days) and 1 Year (1–365 Days) Before Diagnosis and 1 Year (1–365 Days) and 2 Years (366–730 Days) After HIV Diagnosis (2011–2018)

	2 y Before Diagnosis (n = 930), OR (99% CI)	1 y Before Diagnosis (n = 930), OR (99% CI)	1 y After Diagnosis (n = 930), OR (99% CI)	2 y After Diagnosis (n = 930), OR (99% CI)
Diagnoses				
Suicide attempt (X60–84)	—[a]	3.23 (0.17–63.32)	0.97 (0.07–14.45)	2.42 (0.14–43.20)
Substance use disorder (F11–F19)	**2.54 (1.13–5.69)****	**4.36 (2.00–9.51)*****	**5.16 (2.65–10.08)*****	**3.86 (1.65–9.01)*****
Stress (F43)	1.15 (0.50–2.62)	0.49 (0.16–1.43)	**3.12 (1.91–5.12)*****	**3.31 (1.96–5.60)*****
Alcohol use disorder (F10)	1.25 (0.57–2.77)	1.66 (0.84–3.28)	**2.80 (1.51–5.17)*****	**2.33 (1.10–4.90)****
syndrome (F43.8)	1.08 (0.07–16.23)	1.49 (0.37–5.97)	1.76 (0.43–7.17)	—[a]
Depression (F32, F33)	0.91 (0.50–1.68)	1.09 (0.62–1.91)	**3.14 (2.11–4.67)*****	**2.74 (1.73–4.36)*****
Bipolar disorder (F30, F31)	0.66 (0.14–3.08)	0.42 (0.07–2.70)	0.92 (0.24–3.56)	1.10 (0.33–3.72)
Psychosis (F20, F23, F25, F28, F29)	0.64 (0.17–2.40)	0.78 (0.24–2.59)	1.65 (0.65–4.20)	0.97 (0.25–3.75)
Anxiety (F40, F41)	0.55 (0.26–1.19)	1.04 (0.61–1.76)	**1.82 (1.16–2.84)*****	1.64 (0.98–2.72)
Pharmaceutical drug type				
Hypnotics (N05CF)	1.42 (0.95–2.13)	**1.97 (1.39–2.81)*****	**3.58 (2.69–4.77)*****	**2.48 (1.76–3.50)*****
Propiomazine (N05CM06)	1.25 (0.69–2.29)	1.37 (0.78–2.42)	**3.42 (2.20–5.31)*****	**2.59 (1.57–4.29)*****
Tranquilizers (R06AD02, N05BB)	0.98 (0.56–1.69)	1.01 (0.61–1.68)	**2.46 (1.71–3.55)*****	**1.72 (1.07–2.78)****
Stimulants (N06BA)	0.87 (0.31–2.41)	0.94 (0.38–2.31)	1.21 (0.57–2.60)	1.49 (0.69–3.22)
NRLP (N05A)	0.77 (0.36–1.68)	0.71 (0.33–1.54)	1.13 (0.60–2.13)	1.24 (0.64–2.43)
Antidepressant drugs (N06A)	0.72 (0.4622–1.11)	0.8812 (0.5914–1.3110)	**1.87 (1.39–2.52)*****	**1.85 (1.34–2.57)*****
Benzodiazepines (N05BA)	0.69 (0.32–1.50)	1.20 (0.66–2.15)	**2.28 (1.44–3.62)*****	1.55 (0.86–2.78)

OR = odds ratio; HIV = human immunodeficiency virus; CI = confidence interval.

Conditional logistic regression. Significant differences were defined as $p < .01$ and are shown in bold.

**$p < .01$.

***$p < .001$.

[a]There were no suicide attempts registered in people living with HIV 2 years before the HIV diagnosis and no registered fatigue syndromes 2 years after newly diagnosed HIV.

had significantly lower rates of some of the diagnoses and pharmacotherapies after adjustments for the number of doctor visits.

DISCUSSION

Contrary to our hypothesis, psychiatric illness 1 and 2 years before new HIV diagnosis was at the same level as in matched controls for both men and women, except for suicide attempts in women and substance use disorder, which was higher both before and after HIV diagnosis in both men and women. The fact that PLWH have fewer visits than controls before diagnosis may be due to a fear of knowing about the HIV status and could potentially contribute to the spread of HIV. As expected, the rates of psychiatric disorders were markedly higher 1 and 2 years after HIV diagnosis in men. Interestingly, there were no significant differences between women with HIV and their controls 1 and 2 years after the first registered HIV diagnosis, apart from some higher use of neuroleptics in women 1 year after HIV diagnosis.

Comparisons With Other Studies

In an earlier study, we aimed to explore comorbidities and found that PLWH had the same level of cancer, diabetes, and hypertension as the general population, but significantly worse mental health (17). Therefore, we further explored the prevalence of HIV and its association with psychiatric comorbidities. We found that, despite effective ART, many PLWH had impaired mental health and a history of drug abuse, which may threaten the vision of a contained epidemic (7), because PLWH with drug abuse and poor mental health may be more likely to spread HIV. In the present study, a main finding was that substance abuse disorder was more common in PLWH before diagnosis, which was expected, because injecting drugs is still a common way to contract HIV. Substance abuse disorder in PLWH may be treated successfully because interventions have shown promising results (21,22).

It is well documented that PLWH suffer from more psychiatric illnesses, such as psychosis, schizophrenia, substance dependence, substance abuse, bipolar disorder, suicide ideation, and depression, than HIV-negative individuals (23–25). However, we show that, in our population, psychiatric illnesses, apart from what is associated with substance use disorder, was similar or with nonsignificant differences before newly diagnosed HIV. Neuroleptics was significantly more common after newly diagnosed HIV in women, whereas psychosis was not, which may be explained by the fact that a diagnosis may not have been recorded when symptoms have been treated. In men, there were significantly more stress, depression, and anxiety and a higher use of all psychiatric pharmacotherapies that we studied except for stimulants and neuroleptics, reflecting a poor psychiatric health in men after HIV diagnosis.

Potential Explanations for Our Findings

An explanation for the small differences in psychiatric burden between HIV cases and their matched controls before a registered diagnosis of HIV could be that we matched for sex, age, and

neighborhood socioeconomic status. Neighborhood socioeconomic status has been associated with psychiatric and other diagnoses (26–28), and these matching criteria could have eliminated differences in health. The small differences in psychiatric health could also be explained by the detection and diagnosis of HIV being earlier in the disease progression in Sweden today, before the previously described psychiatric symptoms of HIV occur (29–31). Furthermore, the prevalence of HIV in the population of patients with psychiatric illness in Sweden may differ from what is present in other countries (5,6).

After the diagnosis of HIV, visits to primary care decreased, which may, to some extent, be caused by wider medical management by specialized clinics for PLWH. The high number of visits to health care after HIV diagnosis is also possibly explained by the availability and invitations to care specifically for PLWH. A higher level of diagnoses for psychiatric diseases after HIV diagnoses can be explained by more health care visits, but when we adjusted for the number of visits to doctors after HIV diagnosis, lower rates of psychiatric diagnoses and therapy were seen. However, the model with adjustment for number of visits to doctors is a case of overadjustment because many PLWH visit health care after HIV diagnosis with problems, without receiving psychopharmacotherapy or a diagnosis. Furthermore, a visit to a doctor is in the causal pathway to receiving a diagnosis.

The finding that men have a higher psychiatric disease burden after HIV than women is somewhat puzzling, but the sexual minority stress and its associated experience of shame could partially explain this finding, because men with HIV, to a large extent, are men who have sex with men.

In Sweden, individuals diagnosed with HIV obtain optimal ART because Sweden was the first country to reach the 90-90-90 Joint United Nations Programme on HIV/AIDS goals to contain the HIV epidemic (32). Despite optimal ART, PLWH and comorbid psychiatric illness had a significant increase in psychiatric disease burden after knowing their HIV status, especially men. The potential explanations for the higher psychiatric disease burden could be multifactorial, which may include both primary and secondary organic psychiatric disorders (29–31), coping with the infection (33,34), stress factors such as stigmatization (35,36), impaired neurotransmitter biosynthesis of at least tryptophan and phenylalanine (16), burden imposed by lifelong adherence to ART, an impending risk for therapy failure (37), and comparatively high morbidity and mortality rates despite effective ART (38–40).

Clinical Implications

Despite access to ART, comorbid psychiatric illness has been associated with substantial excess mortality in PLWH (41). PLWH with psychiatric disorders have, in previous studies, been shown to have poorer antiretroviral and psychiatric medication adherence (4,9–11), and we found that, at least among men with HIV, the psychiatric illness and therapies were more common than in their controls. We are also pleased to note that pharmacotherapy for psychiatric diagnoses was collected from prescriptions in the present study because PLWH with comorbid psychiatric illness have been shown to have improved quality of life and a reduced disease burden after the reception of individually tailored interventions (42). We warrant future studies of the differences in successful ART in PLWH with and without psychiatric comorbidities, and whether ART is more successful in individuals with both psychiatric diagnoses and psychopharmacotherapy.

Strengths and Limitations

A strength of the study is the use of high-quality Swedish health care registers, with a focus on the Region Stockholm, Greater Stockholm area. These registers include all forms of primary health care, specialists in ambulatory care, and in-hospital care and cover greater than 99% of all health care. A further strength of our study is that individuals diagnosed with HIV in greater Stockholm have free access to optimal ART and monitoring, according to the Swedish Communicable Diseases Act.

Because data on diagnoses depend on coding by physicians, the actual rates of psychiatric illnesses could be underestimated if they are not coded accurately. Underlying psychiatric disorders are not recorded if individuals have not attended a health care setting. We also had to limit the diagnosis groups and psychiatric pharmacotherapies to a selection that we found relevant, to portray the provided care. We believe that it would not be feasible to include the complete pharmacotherapy provided to PLWH in this article.

We only had access to the sex of the individuals in the register, and it is likely that some individuals in our study had changed their sex since birth. There may be differences in sexual orientation between cases and controls, especially among men, where men who have sex with men is a large group among the cases, and it is possible that some of the differences that we see are differences between heterosexual and homosexual men. Ideally, we would have controlled for sexual orientation. However, as seen in Table 1, the differences in psychiatric illnesses between cases and controls are small before HIV diagnosis.

CONCLUSIONS

Psychiatric illness was basically at the same level between cases and controls before HIV diagnosis in both men and women, indicating that the psychiatric problems, apart from what is associated with a higher level of drug use, appear after HIV diagnosis, and especially so in men. The fact that PLWH have fewer visits to health care than controls before diagnosis could, in the long run, contribute to the spread of HIV.

Because possible suboptimal management of psychiatric illness may lead to nonadherence to medications, therapeutic failure, and nonadherence to safe sex, PLWH with comorbid psychiatric illness may require innovative and comprehensive approaches to adhere to their treatment recommendations.

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