Correction to: Factors Associated with Mood Disorder Diagnosis Among a Population Based Cohort of Men and Women Living With and Without HIV in British Columbia Between 1998 and 2012

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Published online: 9 December 2019

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Abstract

Using data from the Comparison of Outcomes and Service Utilization Trends (COAST) study we examined factors associated with mood disorder diagnosis (MDD) among people living with HIV (PLHIV) and HIV-negative individuals in British Columbia, Canada. MDD cases were identified between 1998 and 2012 using International Classification of Disease 9 and 10 codes. A total of 491,796 individuals were included and 1552 (23.7%) and 60,097 (12.4%) cases of MDD were identified among the HIV-positive and HIV-negative populations, respectively. Results showed HIV status was associated with greater odds of MDD among men and lower odds among women. Among PLHIV, MDD was significantly associated with: identifying as gay, bisexual or other men who have sex with men compared to heterosexuals; higher viral load; history of injection drug use; and concurrent anxiety, dysthymia, and substance use disorders. Findings highlight the need for comprehensive and holistic HIV and mental health care.

Keywords HIV · Mood disorders · Canada · Mental health

Correction to: *AIDS and Behavior* (2018) 22:1530–1540
<https://doi.org/10.1007/s10461-017-1825-3>

This article has previously been corrected, via an erratum here: <https://link.springer.com/article/10.1007%2Fs10461-017-1858-7>.

Additionally, the original article unfortunately contained an error in Tables 1, 2, Fig. 1 and added one more reference.

These additional errors have been corrected with this erratum, which represents a fully-corrected version of the article.

The original article can be found online at <https://doi.org/10.1007/s10461-017-1825-3>.

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Introduction

With advancements in combination antiretroviral therapy (cART), the life expectancy of people living with HIV (PLHIV) is increasing, necessitating a further examination of the comorbidities that impact their quality of life and well-being [1, 2]. Mood disorders (including depression and bipolar disorders) are one of the most common comorbidities affecting PLHIV [3–6]; on average, 40% of PLHIV are diagnosed with some form of a depressive disorder in their lifetime [5]. Mood disorders are defined as disturbances of a person's emotional state, can signify distress, create functional impairment, and lead to poor health outcomes among affected populations [7]. Globally, depressive disorders are

the primary cause of disability-adjusted life years (DALYs), warranting increased efforts and cost-effective strategies to reduce incidence rates among disproportionately affected individuals, including PLHIV [8].

Despite the known impact of mood disorders, there is a paucity of data examining incidence of mood disorder diagnoses (MDD) within Canada, and specifically amongst men and women living with HIV. As of 2014, there were an estimated 75,500 Canadians living with HIV [9]. According to the Public Health Agency of Canada, it is estimated that approximately 12.6% of Canadians will ever experience a MDD, with approximately 11.3% of Canadians having major depression, and 2.6% having bipolar disorder [10]. Within the province of British Columbia (BC), it was estimated in 2014 that a total of 348,442 individuals, 7.5% of the total provincial population, were living with a MDD, of which 58.7% were female [11]. To our knowledge there has been no previous study that examines sex differences in incidence of MDD between those living with and without HIV in a Canadian setting where cART is universally available.

The low surveillance of MDD among PLHIV is concerning as mood disorders have been found to negatively impact adherence to cART [4], which may increase risk of viral transmission and increase HIV progression [5, 12]. Previous research suggests that substance use, as well as injection drug use (IDU), is associated with development of MDDs, HIV transmission and coping with HIV diagnosis and concurrent mental health disorders (e.g. anxiety disorders) [3, 6]. As PLHIV have higher prevalence of substance use disorders and IDU compared to the general population [13], concurrent MDD and HIV infection may have significant implications for treatment and healthcare utilization among PLHIV in BC [14].

Given the paucity of population level research available to examine differing trends in MDD among PLHIV and HIV-negative men and women within the Canadian context, we aimed to determine the incidence and correlates of MDD among PLHIV and HIV-negative individuals and explore sex differences in trends in MDD over time. In examining predictors of incidence of MDD, this analysis aims to fill critical gaps by identifying how HIV status and sex may predict differential pathways to incidence of MDD among a large sample of BC residents accessing medical services from 1998 to 2012.

Methods

Study Population

This study uses data from the Comparative Outcomes And Service Utilization Trends (COAST) study, a population-based retrospective cohort study examining health outcomes

and service use of PLHIV and the general population in BC from 1996 to 2013. Details of the COAST study design have been previously described in detail [15]. In short, PLHIV and HIV-negative participants were identified through a unique linkage of de-identified data from the BC Centre for Excellence in HIV/AIDS' (BC-CfE) Drug Treatment Program (DTP) and Population Data BC. The DTP collects information on demographic, immunological and virologic outcomes for HIV-positive individuals who have ever accessed antiretroviral therapy (ART) [16], while Population Data BC provides individual-level de-identified data including information on physician billing and hospitalization utilisation using *International Classification of Disease, Ninth Revision* (ICD-9) and *Tenth Revision* (ICD-10) codes [17].

Ethical approval for this study was obtained from the University of British Columbia/Providence Health Care (#H09-02905) and Simon Fraser University (#2013s0566) research ethics boards.

Inclusion and Exclusion Criteria

We examined the incidence of MDD between 1998 and 2012 among a population-level sample of PLHIV as well as a 10% representative sample of BC residents aged 19 years or older within COAST. In order to assess incidence of MDD, individuals from the COAST study were included in this analysis if they did not have a mood disorder diagnosis prior to 1998 (to ensure we are not capturing prevalent cases). PLHIV were included if they had ever initiated cART, meaning those who were contained in the DTP registry, and had a CD4 count at baseline. Figure 1 shows the exclusion/inclusion breakdown for this analysis.

Outcome and Explanatory Variables

The outcome variable, MDD, and explanatory variables Injection Drug Use (IDU) diagnosis, anxiety, dysthymia, somatoform and substance use disorder used for this analysis were developed using case definitions and ICD-9 and -10 codes consistent with existing literature [18, 19] and derived from Population Data BC hospitalization and medical service plan (MSP) datasets within the COAST study [20–24] (refer to Table 1).

For the purposes of this analysis, MDDs were defined as any two of the following criteria over a 12-month period: one or more hospitalization or physician billing code with an ICD-9 or -10 code for episodic mood or depressive disorder.

Demographic variables included sex and age at baseline/entry into cohort (19–29, 30–39, 40–49, 50–59 and ≥60). The presence of a concurrent mental health disorder, including anxiety, dysthymia, somatic symptom disorder, substance use disorder, and IDU were controlled for within PLHIV and total sample models due their potential to be

Fig. 1 Exclusion criteria for MDD incidence analysis among total COAST sample ($n = 528,859$). *PLHIV*, people living with HIV; *cART*, combination antiretroviral therapy; *MDD*, mood disorder diagnosis

Table 1 Case finding algorithms for outcome and explanatory variables

Disease	ICD-9 and -10 Codes
Mood disorder diagnosis	Dataset Discharge abstract (DAD) database: ICD-9: 296.0–296.9, 311.0–311.9 ICD-10: F31.x, F32.x, F33.x, F38.0, F38.1 Medical Services Plan (MSP) Dataset: ICD-9: 296.0–296.9, 311.0–311.9
Anxiety diagnosis	Dataset Discharge abstract (DAD) database: ICD-9: 300.00–300.39 ICD-10: F40.x, F41.x, F41.9, F42.x, F43.x- Medical Services Plan (MSP) Dataset: ICD-9: 300.00–300.39
Substance use disorder diagnosis	Dataset Discharge abstract (DAD) database: ICD-9: 291.x, 292.x, 303.x-, 304.x, 305.x ICD-10: F10.x, F11.x, F12.x, F13.x, F14.x, F15.x, F16.x, F17.x, F18.x, F19.x Medical Services Plan (MSP) Dataset: ICD-9: 291.x, 292.x, 303.x-, 304.x, 305.x
Somatic symptom disorder diagnosis	Dataset Discharge abstract (DAD) database: ICD-9: 300.7, 300.8 ICD-10: F45.x Medical Services Plan (MSP) Dataset: ICD-9: 300.7, 300.8
Dysthymia diagnosis	Dataset Discharge abstract (DAD) database: ICD-9: 300.4 ICD-10: F34.1 Medical Services Plan (MSP) Dataset: ICD-9: 300.4
Injection drug use	Dataset Discharge abstract (DAD) database: ICD-9: 292.0, 292.1, 292.2, 304.0, 304.1, 304.2, 304.4, 304.5–304.9, 305.3–305.9 ICD-10: F19.9, F11.2, F13.2, F14.2, F15.2, F16.2, F19.2, F16.1, F13.1, F11.1, F14.1, F15.1, F18.1 Medical Services Plan (MSP) Dataset: ICD-9: 292.0, 292.1, 292.2, 304.0, 304.1, 304.2, 304.4, 304.5–304.9, 305.3–305.9 Drug Identification Number (DIN) for Methadone or Buprenorphine

risk factors in development of a mood disorders and high prevalence among PLHIV within Canada [3, 18, 25].

For PLHIV, we also included explanatory variables: HIV exposure group (heterosexual, IDU, gay, bisexual and other men who have sex with men [GBM], “other” [e.g. GBM and IDU, or heterosexual and IDU], or unknown) plasma viral load (pVL) at MDD or most recent pVL for those without MDD (continuous, reported per log₁₀ increase), CD4 count at MDD or most recent visit for those without MDD (0–199, 200–349 vs. ≥ 350), AIDS diagnosis at baseline (entry into the COAST cohort), and adherence to cART within the first year of follow-up (≥ 95 vs. $< 95\%$, defined using pharmacy prescription refill information). Adherence data was not available for individuals who initiated cART outside of BC.

Statistical Analysis

Differences in demographic, social, and clinical characteristics between PLHIV and HIV-negative populations by sex were assessed using Chi squared and Kruskal–Wallis tests for categorical and continuous variables, respectively, and were reported in the results where significant at $P < 0.001$ unless otherwise specified. Three explanatory logistic regression models were built to identify which characteristics were more influential in the development of a MDD in our entire sample stratified by sex (male/female) as well as a subset corresponding to PLHIV-only individuals. Variable selection was performed using an AIC-based stepwise backward elimination technique and all estimates controlled for differences in follow-up time (per 1 year). To account for differences in follow-up time (per 1 year) among PLHIV and HIV-negative cohorts, we computed age-standardized incidence rates of MDD by year which were directly age-standardized using the 2000 BC sex-stratified population estimates as reference. Tests for statistical significance were 2-sided with $P < 0.05$ as threshold. All analyses were performed using R $\times$ 64 3.2.2 [26].

Results

In total, 491,796 (93.0% of the original COAST study) individuals were included in this analysis, of whom 485,250 (98.7%) were HIV-negative and 6546 (1.3%) were PLHIV. The median age at entry into the study was 37 (interquartile range [Q1–Q3]: 31–44) and 35 (Q1–Q3): 23–49) among PLHIV and HIV-negative individuals, respectively. At entry, men living with HIV were significantly older than HIV-negative men (38 [Q1–Q3: 32–45] vs. 35 [Q1–Q3: 23–49], $P < 0.001$), while women living with HIV were significantly younger than HIV-negative women (33 [Q1–Q3: 27–39] vs. 36 [23–51], $P < 0.001$).

In order to only include individuals who were antiretroviral treatment (ART) naïve with no prior MDD, we excluded 5778 people living with HIV (PLHIV) who did not initiate cART and who had a MDD diagnosis in the first two years after baseline (41.5%). We further excluded 1543 individuals with missing CD4 or viral load data, and 40 with unknown sex, who had less than one year of follow-up, and who entered the COAST study after December 31st, 2012. The final sample of PLHIV for the MDD incidence analysis was 6546, representing 47.1% of the total PLHIV sample in COAST. Among the HIV-negative sample, we excluded 25,193 individuals if they had an MDD diagnosis in the first two years following baseline, and 4509 if they had unknown sex, less than one year of follow-up, or entered the COAST study after December 31st, 2012. The final HIV-negative sample included in this MDD analysis was 485,250, representing 94.2% of the HIV-negative COAST sample (see Fig. 1).

Results from our 14-year incidence analysis found 1552 (23.7%) cases of MDD among PLHIV and 60,097 (12.4%) cases of MDD among HIV-negative individuals. Table 2 depicts the demographic and clinical characteristics of participants included within this analysis by HIV status stratified by sex. Among PLHIV and HIV-negative groups, respectively, 15.7 and 48.9% of individuals included were female. Compared to the HIV-negative sample, men and women living with HIV were significantly more likely to have a MDD (23.7 vs. 9.2%, $P < 0.001$, for men and 23.5 vs. 15.8%, $P < 0.001$, for women), to have a history of IDU (27.9 vs. 2.0% for men and 51.7 vs. 1.3 for women, $P < 0.001$), to have concurrent anxiety diagnosis (6.9 vs. 1.7% for men and 8.5 vs. 2.9% for women, $P < 0.001$), dysthymia diagnosis (3.1 vs. 0.2%, for men and 3.1 vs. 0.3% for women, $P < 0.001$), somatoform disorder diagnosis (1.9 vs. 0.9% for men and 3.2 vs. 1.8% for women, $P < 0.001$), and substance use disorder (39.0 vs. 8.2% for men and 59.0 vs. 4.4% for women, $P < 0.001$).

Figure 2 depicts the incidence rates of MDD by year for both HIV-negative individuals and PLHIV by sex. Incidence trends show that, from 1998 until 2006, men living with HIV had the highest proportion of new MDD. Starting in 2007, new cases of MDD among women living with HIV surpassed men. Among HIV-negative individuals, women consistently had higher incidence of MDD from 1998 to 2012.

The average age-standardized incidence rate of MDD during our study period was 27.1 and 13.9 cases per 1000 person-years (PY) for PLHIV and HIV-negative individuals respectively. This translates to PLHIV having 1.95 (95% confidence interval [95% CI]: 1.82–2.10) times the rate of MDD compared to HIV-negative individuals. Men living with HIV had a MDD incidence rate ratio (RR) of 2.61 (95% CI: 2.40–2.84) times higher compared to HIV-negative men

Table 2 Characteristics and sex differences of PLHIV (n = 6546) and HIV-negative individuals (n = 485,250) included in the MDD incidence analysis in COAST

Variable	Total (n = 491,796)	Males (n = 253,283)		P-value*	Females (n= 238,513)		P-value*
	No. (%)	HIV-Negative (n = 247,765) No. (%)	PLHIV (n = 5518) No. (%)		HIV-Negative (n =237,485) No. (%)	PLHIV (n = 1028) No. (%)	
HIV-status							
PLHIV	6546 (1.3)						
HIV-negative	485,250 (98.7)						
Mood disorder				<0.001			<0.001
No	430,147 (87.5)	225,102 (90.9)	4208 (76.3)		200,051 (84.2)	786 (76.5)	
Yes	61,649 (12.5)	22,663 (9.2)	1310 (23.7)		37,434 (15.8)	242 (23.5)	
Age at entry into study (median Q1, Q3)	35 (23–49)	35 (23–49)	38 (32–45)	<0.001	36 (23–51)	33 (27–39)	<0.001
Age at entry into study				<0.001			<0.001
19–29	186,221 (37.9)	95,428 (38.5)	828 (15.0)		89,603 (37.7)	362 (35.2)	
30–39	101,579 (20.7)	51,300 (20.7)	2301 (41.7)		47,560 (20.0)	418 (40.7)	
40–49	81,896 (16.7)	42,254 (17.0)	1639 (29.7)		37,834 (15.9)	169 (16.4)	
50–59	49,675 (10.1)	25,467 (10.3)	568 (10.3)		23,591 (9.9)	49 (4.8)	
≥ 60	72,425 (14.7)	33,316 (13.5)	182 (3.3)		38,897 (16.4)	30 (2.9)	
IDU				<0.001			<0.001
No	481,658 (97.9)	242,778 (98.0)	3977(72.1)		234,406 (99.7)	497 (48.4)	
Yes	10,138 (2.1)	4987 (2.0)	1541(27.9)		3079 (1.3)	531 (51.7)	
Anxiety diagnosis				<0.001			<0.001
No	480,387 (97.7)	243,604(98.3)	5137 (93.1)		230,705 (97.1)	941(91.5)	
Yes	11,409 (2.3)	4161(1.7)	381 (6.9)		6780 (2.9)	87 (8.5)	
Dysthymia diagnosis				<0.001			<0.001
No	490,314 (99.7)	247,258 (99.8)	5346 (96.9)		233,324 (98.2)	996 (96.8)	
Yes	1482 (0.3)	507 (0.2)	172 (3.1)		771 (0.3)	32 (3.2)	
Substance use disorder diagnosis				<0.001			<0.001
No	458,164 (93.2)	227,349 (91.8)	3366 (61.0)		227,027(95.6)	422 (41.1)	
Yes	33,632 (6.8)	20,416 (8.2)	2152 (39.0)		10,458 (4.4)	606 (59.0)	
Somatic symptom disorder diagnosis				<0.001			<0.001
No	485,177 (98.7)	245,442 (99.1)	5416 (98.1)		233,324 (98.3)	995 (96.8)	
Yes	6619 (1.3)	2323 (0.9)	102 (1.9)		4161 (1.8)	33 (3.2)	
HIV exposure group				N/A			N/A
Heterosexual		N/A	295 (5.4)		N/A	188 (18.3)	
Injection drug use		N/A	766 (13.9)		N/A	300 (29.2)	
GBM		N/A	1771 (32.1)		N/A	2 (0.2)	
Other		N/A	1159 (21.0)		N/A	230 (22.4)	
Unknown		N/A	1527 (27.7)		N/A	308 (29.96)	
First cART Initiation				N/A			N/A
1996–1999		N/A	2352 (42.6)		N/A	343 (33.4)	
2000–2003		N/A	894 (16.2)		N/A	220 (21.4)	
2004–2007		N/A	913 (16.5)		N/A	214 (20.8)	
2008–2012		N/A	1359 (24.6)		N/A	251 (24.4)	
CD4 at mood disorder (or most recent visit)				N/A			N/A
≥ 350		N/A	3271 (59.3)		N/A	560 (54.47)	
200–349		N/A	1022 (18.5)		N/A	196 (19.07)	
0–199		N/A	1225 (22.2)		N/A	272 (26.46)	

Table 2 (continued)

Variable	Total (n = 491,796) No. (%)	Males (n = 253,283)		P-value*	Females (n = 238,513)		P-value*
		HIV-Negative (n = 247,765) No. (%)	PLHIV (n = 5518) No. (%)		HIV-Negative (n = 237,485) No. (%)	PLHIV (n = 1028) No. (%)	
AIDS diagnosis at baseline							
No		N/A	4666 (84.6)		N/A	913 (88.8)	
Yes		N/A	852 (15.4)		N/A	115 (11.2)	
cART adherence in first year of follow-up				N/A			N/A
< 95%		N/A	2153 (39.0)		N/A	618 (60.1)	
≥ 95%		N/A	3122 (56.6)		N/A	402 (39.1)	
Missing		N/A	243 (4.4)		N/A	8 (0.8)	
Viral load at mood disorder (log10) (or most recent visit) median (Q1–Q3)		N/A	1.69 (1.69–2.84)	N/A		1.69 (1.69–3.86)	N/A

Bold estimates indicate statistically significant variables ($p < 0.05$)

PLHIV people living with HIV; Q1, Q3 quartile 1, quartile 3; IDU injection drug use; cART combined antiretroviral therapy; N/A not applicable

Fig. 2 Age-adjusted incidence rates of mood disorder diagnosis by year among HIV-negative and PLHIV by sex in COAST from 1998 to 2012

(26.4 per 1000 PY vs. 10.1 per 1000 PY) and women living with HIV in our sample had a MDD incidence RR 1.51 (95% CI: 1.25–1.84) times higher compared to HIV-negative women (27.0 per 1000 PY vs. 17.9 per 1000 PY).

Table 3 presents the univariable and multivariable factors associated with MDD incidence by sex. Overall, after adjusting for socio-demographic and concurrent mental health and HCV seropositivity, men living with HIV had higher odds (adjusted odds ratio [aOR]: 1.89, 95% CI: 1.75–2.04) of MDD incidence compared to HIV-negative males. At the univariable level, women living with HIV had higher odds

of MDD compared to HIV negative women (OR: 2.18, 95% CI: 1.87–2.54), however after controlling for age, concurrent mental health disorders and IDU, the adjusted results found that women living with HIV had reduced odds of MDD during the study period (aOR: 0.60, 95% CI: 0.50–0.71).

Among PLHIV specifically (Table 4), adjusted models found that those over 60 years of age had reduced odds of MDD compared to those 19–29 years old (OR: 0.43, 95% CI: 0.24–0.76). Concurrent mental health disorders including anxiety (aOR: 1.74, 95% CI: 1.38–2.18) and dysthymia (aOR: 1.96, 95% CI: 1.43–2.69) were significantly

Table 3 Univariable and multivariable factors associated with MDD among males (n = 253,283) and females (n = 238,513) within the total sample (PLHIV and HIV-negative)

	Males n = 253,283		Females n = 238,513	
	uOR (95% CI)	aOR (95% CI)	uOR (95% CI)	aOR (95% CI)
HIV status				
HIV–	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
HIV+	3.71 (3.47–3.97)	1.89 (1.75–2.04)	2.18 (1.87–2.54)	0.6 (0.5–0.71)
Age at entry into study				
19–29	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
30–39	1.06 (1.02–1.1)	1.01 (0.97–1.05)	0.94 (0.91–0.97)	0.95 (0.92–0.98)
40–49	0.96 (0.93–1)	0.98 (0.94–1.02)	0.84 (0.82–0.87)	0.88 (0.85–0.91)
50–59	0.82 (0.78–0.86)	0.88 (0.83–0.92)	0.66 (0.64–0.69)	0.69 (0.66–0.72)
60+	1.06 (1.02–1.11)	1.19 (1.13–1.24)	0.84 (0.81–0.87)	0.87 (0.84–0.90)
IDU				
No	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Yes	6.97 (6.6–7.35)	4.2 (3.93–4.49)	6.29 (5.86–6.75)	4.88 (4.49–5.30)
Anxiety				
No	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Yes	3.63 (3.4–3.88)	2.67 (2.49–2.86)	2.18 (2.07–2.3)	1.86 (1.76–1.97)
Dysthymia				
No	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Yes	11.12 (9.47–13.06)	5.57 (4.68–6.62)	7.16 (6.16–8.32)	5.06 (4.33–5.91)
Substance use disorder				
No	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Yes	2.53 (2.45–2.63)	1.45 (1.38–1.51)	2.15 (2.06–2.25)	1.33 (1.27–1.41)
Somatic symptom disorder				
No	1.00 (REF)	1.00 (REF)	1.00 (REF)	Not significant
Yes	1.44 (1.29–1.61)	1.20 (1.07–1.35)	1.18 (1.09–1.27)	Not significant

Odds ratio adjusted for follow-up time, previous mental health diagnoses, and IDU

Bold estimates indicate statistically significant variables

IDU injection drug use

associated with MDD incidence during our study period. GBM (aOR: 1.64, 95% CI: 1.22–2.20) and ‘other’ HIV exposure groups (aOR: 1.67, 95% CI: 1.23–2.27) experienced disparate levels of MDD when compared to heterosexual individuals. In a sub-analysis where unknown HIV exposure groups were removed, the only effect on the model was that IDU exposure group remained significant in the adjusted model. Incidence of MDD for PLHIV was also positively associated with missing adherence data (aOR: 1.71, 95% CI: 1.26–2.32), having a CD4 count at MDD (or most recent visit) of 200–349 versus $\geq 350\text{cell}/\mu\text{l}$, and increased viral load at MDD or most recent visit (aOR: 1.72/log10 increase, 95% CI: 1.62–1.83).

Discussion

Our study demonstrated that both men and women living with HIV had significantly higher incidence rates of MDD compared to HIV-negative individuals accessing medical services in BC between 1998 and 2012. Results revealed

that concurrent mental health conditions, including anxiety, dysthymia and substance use disorders, as well as IDU may be predictive of MDD. Our findings suggest that GBM and those with dual HIV-exposure risk (e.g. sexual and IDU) may have higher MDD incidence. Moreover, PLHIV who have higher viral loads and initiated cART outside of BC, and thus have missing adherence data, had higher odds of MDD.

Our work corroborates existing evidence of higher rates of MDD among PLHIV compared to HIV-negative individuals [5, 27]. During our study period, nearly 25% of men and women living with HIV were diagnosed with a MDD, demonstrating a significant public health issue that should be further addressed. These results show men living with HIV may have significantly higher odds of MDD compared to HIV-negative men [28]. Concurrent mental health and addiction issues may be higher among PLHIV who face multiple intersecting stigmas such as GBM and people who inject drugs, compared to HIV-negative individuals [29]. Multiple concurrent mental health concerns among PLHIV, particularly key populations (e.g. GBM and IDU) may be

Table 4 Univariable and Multivariable Model of Factors Associated with Incidence of Mood Disorder Among PLHIV (n = 6,546)

	uOR (95% CI)	aOR (95% CI)
Age at entry into study		
19–29	1.00 (REF)	1.00 (REF)
30–39	0.88 (0.75–1.04)	0.92 (0.77–1.09)
40–49	0.76 (0.63–0.91)	0.89 (0.73–1.08)
50–59	0.62 (0.48–0.8)	0.84 (0.63–1.11)
60+	0.29 (0.17–0.51)	0.43 (0.24–0.76)
Sex		
Female	1.00 (REF)	N/S
Male	0.95 (0.80–1.12)	N/S
Anxiety		
No	1.00 (REF)	1.00 (REF)
Yes	1.73 (1.40–2.14)	1.74 (1.38–2.18)
Dysthymia		
No	1.00 (REF)	1.00 (REF)
Yes	2.63 (1.95–3.54)	1.96 (1.43–2.69)
Substance use disorder		
No	1.00 (REF)	1.00 (REF)
Yes	1.52 (1.34–1.72)	1.13 (0.96–1.32)
Somatic symptom disorder		
No	1.00 (REF)	N/S
Yes	1.23 (0.83–1.82)	N/S
First HAART date		
1996–1999	1.00 (REF)	N/S
2000–2003	0.88 (0.75–1.04)	N/S
2004–2007	0.83 (0.70–0.99)	N/S
2008–2012	0.58 (0.47–0.71)	N/S
HIV exposure group		
Heterosexual	1.00 (REF)	1.00 (REF)
IDU	2.15 (1.60–2.88)	1.38 (0.99–1.91)
GBM/MSM	1.80 (1.36–2.37)	1.64 (1.22–2.20)
Other	2.18 (1.65–2.88)	1.67 (1.23–2.27)
Unknown	1.25 (0.93–1.68)	1.10 (0.81–1.5)
Adherence		
<95%	1.00 (REF)	1.00 (REF)
≥95%	0.68 (0.60–0.77)	1.02 (0.88–1.17)
Missing	1.45 (1.09–1.93)	1.71 (1.26–2.32)
CD4 at mood disorder		
350+	1.00 (REF)	1.00 (REF)
200–349	1.81 (1.55–2.11)	1.34 (1.14–1.59)
0–199	1.85 (1.58–2.18)	0.83 (0.69–1.01)
AIDS at baseline		
No	1.00 (REF)	1.00 (REF)
Yes	0.78 (0.65–0.93)	0.83 (0.69–1.01)
Viral load at mood disorder (log10)	1.71 (1.63–1.80)	1.72 (1.62–1.83)

Odds Ratio adjusted for socio-demographic, differences in follow-up time, previous mental health diagnoses, IDU, and HIV treatment and outcome variables

Bold estimates indicate statistically significant variables

IDU, injection drug use; GBM/MSM, gay, bisexual and other men who have sex with men; ART, antiretroviral therapy; N/S, not significant

influenced by high levels of societal stigmatization, discrimination, as well as increased risks of criminalization associated with using drugs, being a sexual minority, and living with HIV [6, 27, 29]. This association should be further explored as concurrent depression and problematic substance use—especially among key populations—has been found to influence increased risk taking behaviour, such as syringe sharing, inconsistent condom use, and worse HIV treatment outcomes [13].

In line with the current literature, we found that IDU was associated with elevated incidence of MDD within our sample, overall, by sex and HIV status [30]. It is important to note that IDU is a common route of HIV transmission in Canada [31]. It is likely that IDU and substance use disorders amongst PLHIV plays a role in concurrent mental health diagnosis, or vice versa [30, 32]. Previous research has found that individuals with HIV who have a history of illicit drug use are at an increased risk for experiencing depressive symptomology [32]. This may be particularly important among women living with HIV in BC [25], of which over half have a history of IDU and or have been diagnosed with a substance use disorder.

We found that the ratio of MDD incidence among women living with HIV on treatment in BC was higher than women living without HIV. In the final adjusted model, however HIV-negative women had higher odds of a MDD. These findings indicate that the high prevalence of co-occurring mental health disorders, such as substance use disorders as well as history of IDU may better explain the extra burden of MDD among women living with HIV in this sample. Our results corroborate a growing body of evidence that suggests a higher proportion of women living with HIV in Canada are faced with elevated socio-structural inequities compared to men living with HIV and women not living with HIV [25, 30, 33]. For example, previous work has highlighted that, compared to men, women living with HIV are more likely to have a history of IDU [33], and those that do are more likely to experience depression [30].

The combination of clinical symptoms, treatment side effects, addictions stigma, discrimination, and criminalization faced by PLHIV may mask symptoms of depression [27], and create barriers to accessing mental health services, making identifying and diagnosing MDDs difficult [35]. This has serious implications for quality of life amongst PLHIV. Untreated mental health conditions have been associated with increased substance abuse, suicide [36, 37], reduced adherence to cART and poorer treatment outcomes (e.g. higher pVL) [4, 12, 14], highlighting a critical need for HIV care providers to be educated in identifying mental health concerns at earlier stages [35].

Despite no significant difference in odds of MDD between men and women living with HIV, nearly a quarter of women living with HIV were diagnosed with a mood disorder during

the study period. MDD incidence among women living with HIV increased between 2004 and 2010, while declined among men living with HIV. Thus, our results highlight the need for further research to explore gendered factors contributing to elevated incidence of mental health disorders, such as depression, experienced by women living with HIV who face multiple intersecting inequities and barriers to both HIV and mental health care [33]. In a systematic review published in 2011, Sherr and colleagues found that only 6% of interventions for depression were specific to women, with the majority being conducted among women in sub-Saharan Africa [38]. Critical efforts and research are needed to promote improved uptake and rollout of integrated mental health services for women living with HIV in North America [39].

These results indicate that milder forms of depression, generalized anxiety and problematic substance use are likely predictors of more serious forms of depression and bipolar disorders. Efforts should be taken to address and identify mental health concerns and substance use early on, in order to improve treatment outcomes, and the overall well-being of PLHIV as well as individuals in the general BC population. Increasing access to mental health and addiction services among PLHIV has been shown to be a cost-effective strategy and an important intervention for improving treatment outcomes and overall mortality [12]. Previous work found that interventions targeted towards the care and treatment of PLHIV have not been as effective among those with concurrent problematic drinking, mood disorder and/or anxiety disorder diagnosis [32]. This is concerning as our results and previous research have found that harder-to reach individuals that experience multiple intersecting mental health, addiction and drug use issues are more likely to have a MDD [6]. Further research should examine the impact of community-based integrated care for PLHIV, such as the Dr. Peter's Centre in Vancouver [40], which includes multi-levelled comprehensive mental health, addiction and infectious disease treatment services and supports under one roof. Efforts should support community-based organizations working to integrate mental health supports for PLHIV as well as those at highest risk of HIV and MDD incidence (e.g. IDU and GBM).

The unique linkage between the DTP and Population Data BC allows for comparisons in MDD among a large sample of PLHIV and HIV-negative individuals, an area that has not been widely explored within Canada. Furthermore, the use of administrative data may be more sensitive to estimating population level MDD of PLHIV compared to self-reported scales, as the use of validated scales, such as the Centre for Epidemiology Studies Depression (CES-D) scale, may overestimate rates of depression among PLHIV [41].

However, caution should be taken in interpreting these results as they rely on physician billing records, which only reflect the captured (possibly more severe) cases of

MDDs [42]. Future work that triangulates administrative data with self-reported health measures, such as Patient-Reported Outcomes Measurement Information System (PROMIS) tools [43], may be useful for capturing mental health issues before the development of more severe cases of MDD. Limitations for this analysis exist as some variables (e.g. sexual orientation) were only available among PLHIV. As previous research indicates that GBM experience disproportionate levels of mood disorders, further research should examine factors associated with MDD among GBM living with and without HIV [44]. Furthermore, the socio-demographic variables available in COAST do not capture factors that have been found in previous research to be associated with mood disorders, such as sex work status, refugee status, military service history, incarceration experiences, and specific details on alcohol and drug use [3], which may mediate our results.

In conclusion, we found disparities in MDDs experienced by PLHIV, which necessitates further attention and increased efforts to address mental health issues in this population. Given that prior mental health disorder diagnosis was associated with increased odds of MDD overall, especially among PLHIV, this could provide important information on opportunities for intervention for physicians in BC. Increasing access to addiction treatment and psychotherapy at earlier stages may help to reduce population level MDDs as well as improve treatment outcomes for PLHIV, particularly those belonging to HIV exposure groups at high-risk for concurrent mental health disorders such as GBM and IDU, as well as women living with HIV. Furthermore, comprehensive mental health, addiction and concurrent infectious disease treatment should be included as standard care within the treatment of HIV in BC, Canada and globally.

Acknowledgements Author Contributions Study concept and design: K.C., C.O., S.K., D.M.S., O.E., J.S.G.M. & R.S.H. Statistical Analysis: C.F.V. & S.J. Drafting of the manuscript was conducted by K.C., C.O., S.K. & D.M.S., with critical revisions from all authors. The principal investigator (R.S.H.) takes responsibility for the integrity and accuracy of the data, and has the final decision in the submission of the manuscript. In addition, we would like to thank Dr. Jeannie Shoveller, Dr. Kate Salters and other COAST team members and support staff for ongoing support and feedback during the preparation of this manuscript. The authors would like to thank the COAST study participants, the BC Centre for Excellence in HIV/AIDS, the BC Ministry of Health, and the institutional data stewards for granting access to the data, and Population Data BC for facilitating the data linkage process. The COAST study members and investigators include: Rolando Barrios, Guillaume Colley, Oghenowede Eyawo, Nada Gataric, Richard Harrigan, Robert Hogg (PI), Mark Hull, Scott Lear, Viviane Dias Lima, Julio Montaner, David Moore, Bohdan Nosyk, Jeannie Shoveller, Danielle Smith, Sam Wiseman, and David Whitehurst.

Disclaimer All inferences, opinions, and conclusions drawn from this manuscript are those of the authors and do not reflect the opinions or policies of the Data Stewards or the funders.

Compliance with Ethical Standards

Conflicts of interest RSH has received funding from Canadian Institutes of Health, through a Foundation Award, to support this research study; RSH has held grant funding in the last 10 years from the National Institutes of Health, Canadian Institutes of Health Research, Health Canada, Merck, and the Social Sciences and Humanities Research Council of Canada. JSGM is supported with grants paid to his institution, from Abbvie, Bristol-Myers Squibb, Gilead Sciences, Janssen, Merck, and Viiv Healthcare.

Ethical Approval Ethical approval was obtained from the University of British Columbia/Providence Health Care (#H09-02905) and Simon Fraser University (#2013s0566) research ethics boards.

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