HIV Incidence and Use of Pre-Exposure Prophylaxis Among a Large, National Cohort of People with Bipolar Disorder

AT THE FOREFRONT
UChicago Medicine

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Background

- Bipolar disorder (BD) is a severe, chronic mental illness characterized by alternating periods of mania/hypomania and depression[1]
- Affects approximately 2% of the global population (~8 million people in the U.S.)[2]
- Both the manic and depressive phases of BD have been linked to increased risk of HIV acquisition[3]
  - Mania characterized by impulsivity, hypersexuality, increased or uncharacteristic substance use, and euphoria[1]
- Social determinants and a fragmented healthcare system further exacerbate HIV diagnosis and poor outcomes among people with BD[4]
- Daily antiretroviral medication as HIV pre-exposure prophylaxis (PrEP) up to 99% effective but under-utilized[5,6]
- Use of PrEP for HIV prevention among people with BD is largely unknown with only a single study investigating prescription, finding < 1% of people with BD *or* schizophrenia prescribed PrEP between 2013-2018 but did *not* stratify by diagnosis[7]
- The unique needs of people with mental illnesses including BD are identified as priorities for national and international HIV prevention research and policy agendas
- Minimal research has investigated opportunities for HIV prevention care or the unique needs of PLWMI for HIV prevention in the healthcare system
- Administrative claims datasets are ideal for population-level investigation of rare outcomes like HIV[8]

Methods

- Claims-based analysis using the MarketScan commercial claims database of fully-adjudicated medical and pharmacy claims for privately insured Americans
- Data years 2010-2022. Cohort entry at any year.
- Inclusion Criteria:
  - Two outpatient claims on different dates or one inpatient claim for BD diagnosis code (Type I or II)[9]
  - Age ≥ 14 years old
  - At least 6-months of continuous medical and prescription drug coverage prior to index date
- **Index date** (inclusion in cohort): Date of second outpatient or first inpatient claim with BD diagnosis code
- Exclusion Criteria:
  - Two outpatient claims or one inpatient claim for an HIV diagnosis code *prior* to index date
  - >28 days of HIV treatment regimen; single 28-day prescription assumed post-exposure prophylaxis (PEP) *prior* to index date
  - Hepatitis B diagnosis as oral PrEP regimens also approved for HepB treatment, creating a possible confounding effect
- Covariates:
  - Demographic: Marital status, gender (male/female), age, geography and region of residence, relation to primary policy holder
  - Clinical: STI encounters, follow-up outpatient care (psychiatry, primary care [OBGYN included with primary care for females]), psychiatric hospitalizations, use of long-acting injectable (LAI) antipsychotics/anti-cravings, substance use (stimulant, opioid) disorders
- **Primary Outcomes:**
  - New HIV diagnosis: Two outpatient claims or one inpatient claim with HIV diagnosis code *and/or* >30 days of antiretrovirals for HIV treatment (excluded PEP)
  - PrEP Prescription (≥1mo): At least 30 days of oral PrEP *without* concurrent prescription of a third antiretroviral
  - PrEP Prescription (≥3mo): At least 90 days of oral PrEP *without* any other antiretrovirals
- Logistic regression model for each outcome fully adjusting for all relevant clinical and demographic covariates

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Results

- 333,867 enrollees with BD in cohort (Table 1) between 2010-2022
- Total of 435 *new* HIV diagnoses
- 1,337 people with BD prescribed ≥1mo of PrEP (0.40%)
- 909 (0.27%) prescribed ≥3mo of PrEP
- Mean cohort duration of 3.02 years

Table 1. Sample demographics, outcomes, and logistic regression results.

	Sample	HIV			Any PrEP (≥1 mo.)			Sustained PrEP (≥3 mo.)		
Married	*n* (%[a])	*n* (%[b])	aOR (95%CI)	*p*	*n* (%[b])	aOR (95%CI)	*p*	*n* (%[b])	aOR (95%CI)	*p*
No	226,951 (68.0)	352 (0.16)	*Ref.*		1,150 (0.51)	*Ref.*		779 (0.34)	*Ref.*	
Yes	106,916 (32.0)	83 (0.08)	0.39 (0.29, 0.53)	**<.001**	187 (0.17)	0.45 (0.37, 0.55)	**<.001**	130 (0.12)	0.40 (0.32, 0.50)	**<.001**
Sex										
Female	206,642 (61.9)	101 (0.05)	*Ref.*		217 (0.11)	*Ref.*		47 (0.02)	*Ref.*	
Male	127,225 (38.1)	334 (0.26)	5.36 (4.27, 6.72)	**<.001**	1,120 (0.88)	11.5 (9.89, 13.4)	**<.001**	862 (0.68)	43.6 (32.3, 58.8)	**<.001**
Age Group (years)										
13-24	99,254 (29.7)	122 (0.12)	*Ref.*		507 (0.51)	*Ref.*		285 (0.29)	*Ref.*	
25-34	74,304 (22.3)	109 (0.15)	0.99 (0.63, 1.56)	.97	397 (0.53)	0.82 (0.64, 1.04)	.11	287 (0.39)	0.79 (0.58, 1.07)	.13
35-44	68,529 (20.5)	94 (0.14)	0.98 (0.61, 1.58)	.93	259 (0.38)	0.69 (0.53, 0.89)	**.01**	199 (0.29)	0.72 (0.52, 0.99)	**.04**
45-54	56,385 (16.9)	77 (0.14)	1.02 (0.63, 1.66)	.94	144 (0.26)	0.52 (0.39, 0.69)	**<.001**	113 (0.20)	0.56 (0.40, 0.80)	**.001**
55+	35,395 (10.6)	33 (0.09)	0.80 (0.46, 1.39)	.43	30 (0.08)	0.20 (0.13, 0.31)	**<.001**	25 (0.07)	0.25 (0.15, 0.41)	**<.001**
Geography										
Urban	277,654 (83.2)	390 (0.14)	*Ref.*		1,205 (0.43)	*Ref.*		820 (0.30)	*Ref.*	
Rural	40,554 (12.2)	27 (0.07)	0.52 (0.35, 0.78)	**.001**	63 (0.16)	0.47 (0.36, 0.61)	**<.001**	40 (0.10)	0.45 (0.32, 0.63)	**<.001**
Missing	15,659 (4.69)	18 (0.11)	0.93 (0.55, 1.58)	.80	69 (0.44)	0.71 (0.54, 0.93)	**.01**	49 (0.31)	0.71 (0.51, 0.98)	**.04**
Region										
Northeast	52,569 (15.8)	78 (0.15)	*Ref.*		286 (0.54)	*Ref.*		185 (0.35)	*Ref.*	
North Central	72,281 (21.7)	75 (0.10)	0.74 (0.54, 1.02)	.07	213 (0.29)	0.50 (0.41, 0.60)	**<.001**	131 (0.18)	0.47 (0.37, 0.60)	**<.001**
West	143,943 (43.1)	204 (0.14)	1.08 (0.83, 1.41)	.57	546 (0.38)	0.66 (0.57, 0.77)	**<.001**	387 (0.27)	0.72 (0.59, 0.87)	**.001**
South	61,961 (18.6)	76 (0.12)	0.87 (0.63, 1.20)	.40	287 (0.46)	0.98 (0.82, 1.17)	.84	203 (0.33)	1.09 (0.88, 1.35)	.44
Unknown	3,113 (0.93)	2 (0.06)	0.53 (0.12, 2.35)	.40	5 (0.16)	1.04 (0.41, 2.66)	.93	3 (0.10)	1.33 (0.40, 4.41)	.64
Plan Type										
Fee-for-service	230,321 (69.0)	281 (0.12)	*Ref.*		883 (0.38)	*Ref.*		604 (0.26)	*Ref.*	
High Deductible Plan	52,223 (15.6)	73 (0.14)	1.17 (0.90, 1.53)	.24	250 (0.48)	0.94 (0.81, 1.10)	.44	169 (0.32)	0.92 (0.76, 1.11)	.39
Managed Care	39,684 (11.9)	72 (0.18)	1.40 (1.07, 1.82)	**.01**	182 (0.46)	1.31 (1.10, 1.55)	**<.001**	123 (0.31)	1.33 (1.08, 1.64)	**.01**
Unknown	11,639 (3.49)	9 (0.08)	0.73 (0.37, 1.43)	.36	22 (0.19)	0.78 (0.50, 1.22)	.28	13 (0.11)	0.69 (0.38, 1.24)	.22
Relation to Policyholder										
Self (employee)	163,441 (49.0)	260 (0.16)	*Ref.*		788 (0.48)	*Ref.*		601 (0.37)	*Ref.*	
Spouse	77,861 (23.3)	66 (0.08)	1.15 (0.84, 1.58)	.38	110 (0.14)	0.82 (0.65, 1.03)	.09	76 (0.10)	0.84 (0.64, 1.11)	.23
Child/Other Dependent	92,565 (27.7)	109 (0.12)	0.50 (0.32, 0.79)	**.003**	439 (0.47)	0.46 (0.36, 0.59)	**<.001**	232 (0.25)	0.33 (0.24, 0.44)	**<.001**
High-Risk Sexual Behavior Claim[c]										
No	326,882 (97.9)	397 (0.12)	*Ref.*		872 (0.27)	*Ref.*		538 (0.16)	*Ref.*	
Yes	6,985 (2.09)	38 (0.54)	2.67 (1.85, 3.85)	**<.001**	465 (6.66)	16.8 (14.6, 19.3)	**<.001**	371 (5.31)	24.1 (20.4, 28.4)	**<.001**
STI Encounters										
0	320,193 (95.9)	357 (0.11)	*Ref.*		964 (0.3)	*Ref.*		625 (0.2)	*Ref.*	
1	2,979 (0.89)	11 (0.37)	2.82 (1.53, 5.19)	**.001**	49 (1.64)	3.07 (2.24, 4.22)	**<.001**	36 (1.21)	3.37 (2.30, 4.94)	**<.001**
2	2,155 (0.65)	13 (0.6)	4.30 (2.44, 7.55)	**<.001**	35 (1.62)	2.59 (1.78, 3.78)	**<.001**	24 (1.11)	2.43 (1.52, 3.90)	**<.001**
3	1,568 (0.47)	8 (0.51)	3.48 (1.70, 7.11)	**.001**	43 (2.74)	3.99 (2.81, 5.65)	**<.001**	34 (2.17)	4.60 (3.05, 6.95)	**<.001**
≥4	6,972 (2.09)	46 (0.66)	4.02 (2.87, 5.62)	**<.001**	246 (3.53)	4.69 (3.95, 5.56)	**<.001**	190 (2.73)	5.15 (4.19, 6.32)	**<.001**
Outpatient Follow Up Care										
Primary Care Only	114,438 (34.3)	127 (0.11)	*Ref.*		393 (0.34)	*Ref.*		273 (0.24)	*Ref.*	
Psychiatry Only	24,921 (7.46)	43 (0.17)	1.58 (1.10, 2.27)	**.01**	62 (0.25)	0.73 (0.56, 0.97)	**.03**	39 (0.16)	0.74 (0.52, 1.05)	.09
Psychiatry & Primary Care	159,168 (47.7)	195 (0.12)	0.86 (0.68, 1.09)	.20	811 (0.51)	1.37 (1.20, 1.56)	**<.001**	555 (0.35)	1.44 (1.22, 1.69)	**<.001**
Other Providers	35,340 (10.6)	70 (0.20)	2.23 (1.64, 3.04)	**<.001**	71 (0.20)	0.67 (0.52, 0.87)	**<.001**	42 (0.12)	0.63 (0.45, 0.88)	**.007**
Psychiatric Hospitalizations										
0	275,315 (82.5)	339 (0.12)	*Ref.*		1,072 (0.39)	*Ref.*		766 (0.28)	*Ref.*	
1	7,471 (2.24)	25 (0.33)	2.29 (1.51, 3.48)	**<.001**	38 (0.51)	0.96 (0.68, 1.36)	.82	27 (0.36)	1.00 (0.65, 1.52)	.99
2	6,669 (2.00)	10 (0.15)	1.02 (0.54, 1.92)	.96	34 (0.51)	0.97 (0.67, 1.41)	.88	23 (0.34)	0.94 (0.59, 1.49)	.79
3	6,638 (1.99)	11 (0.17)	1.16 (0.63, 2.14)	.63	26 (0.39)	0.77 (0.51, 1.16)	.21	15 (0.23)	0.66 (0.39, 1.14)	.14
≥4	37,774 (11.3)	50 (0.13)	0.92 (0.67, 1.26)	.59	167 (0.44)	0.88 (0.73, 1.05)	.16	78 (0.21)	0.61 (0.47, 0.79)	**<.001**
LAI Agent Use[d]										
No	330,499 (99)	426 (0.13)	*Ref.*		1304 (0.39)	*Ref.*		887 (0.27)	*Ref.*	
Yes	3,368 (1.01)	9 (0.27)	1.15 (0.47, 2.86)	.76	33 (0.98)	1.19 (0.72, 1.95)	.50	22 (0.65)	1.14 (0.59, 2.19)	.71
Comorbid Stimulant Use Disorder										
No	321,236 (96.2)	380 (0.12)	*Ref.*		1,198 (0.37)	*Ref.*		824 (0.26)	*Ref.*	
Yes	12,631 (3.78)	55 (0.44)	2.56 (1.85, 3.53)	**<.001**	139 (1.10)	1.39 (1.12, 1.73)	**<.001**	85 (0.67)	1.35 (1.03, 1.78)	**.03**
Comorbid Opioid Use Disorder										
No	317,444 (95.1)	402 (0.13)	*Ref.*		1,250 (0.39)	*Ref.*		866 (0.27)	*Ref.*	
Yes	16,423 (4.92)	33 (0.20)	0.77 (0.52, 1.15)	.20	87 (0.53)	0.65 (0.50, 0.84)	**<.001**	43 (0.26)	0.47 (0.33, 0.68)	**<.001**
Follow Up Duration (yrs)	-	-	1.14 (1.10, 1.18)	**<.001**	-	1.18 (1.15, 1.21)	**<.001**	-	1.23 (1.19, 1.27)	**<.001**

Regression analyses control for year of cohort entry (2010 – 2022).

a. Column percentage; b. Row percentage; c. Z-codes; d. LAI agents included LAI antipsychotics and LAI anti-craving agents.

- HIV more frequent among males (aOR = 5.36, $p < .001$) and those with comorbid stimulant use disorder (aOR = 2.56, $p < .001$)
- People with BD following up only with psychiatrists *more* likely to acquire HIV (aOR = 1.58, $p = .01$) compared to those following up with psychiatry and a primary care provider & *less* likely to receive at least 1 month of PrEP (aOR = 0.73, $p = .03$)
- Among those with ≥4 encounters for STIs, 3.53% ($n = 246$) were prescribed any PrEP and 2.73% ($n = 190$) were prescribed ≥3 months of PrEP

Conclusions & Future Directions

- PrEP use among people with BD was < 1%, below the already low national percentage of 36% of indicated patients[6]
- Even among those people with BD and multiple encounters for STIs, PrEP prescription was < 4%, despite STI encounters being an indication for PrEP prescription
- Receiving follow-up care from a psychiatrist *only* was associated with greater odds of HIV incidence and reduced odds of PrEP prescription
- Concerted efforts are needed to identify HIV-risk among people with BD and to initiate PrEP prescription
- PrEP care continuum has multiple points of overlap with routine psychiatric care which may serve to reduce barriers to access through co-located psychiatric care and PrEP prescription

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