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Brief Report: Gender Differences Among Persons Entering Medication Treatment for Opioid Use Disorder in the Community

Angela Di Paola, PhD[1], **Noor Taweh**[1,2], **Breanne E. Biondi, MPH**[3], **Ariadna Foray, MD**[4], **Cynthia A. Frank, PhD, RN**[1], **Albert Shaw, MD, PhD**[1], **Sandra A. Springer, MD**[1,5]

[1]Department of Internal Medicine, Section of Infectious Diseases, AIDS Program, Yale School of Medicine, New Haven, CT

[2]University of Connecticut, Storrs, CT

[3]Department of Health Law, Policy, and Management, Boston University School of Public Health, Boston, MA

[4]Department of Psychiatry, Yale School of Medicine, New Haven, CT

[5]Center for Interdisciplinary Research on AIDS, Yale University School of Public Health, New Haven, CT

Abstract

Background and Objectives: We evaluated gender differences among persons initiating medications for opioid use disorder (MOUD).

Methods: Analyses of baseline assessments for a study evaluating the impact of MOUD on outcomes included: demographics, DSM-5 diagnoses, depression severity, quality of life (QoL), and medication history (N=125).

Results: When compared to men, women had a greater prevalence of generalized anxiety and post-traumatic stress disorders; and worse psychological QoL. Women were less likely to be prescribed psychiatric medications.

Discussion and Conclusions: Women may benefit from tailored multi-disciplinary programs with MOUD.

Scientific Significance: This study identified that women with OUD seeking MOUD in the community had greater sedative hypnotic non-prescribed medication use and psychiatric comorbidity than men, all of which can contribute to poorer retention in MOUD and higher risk of morbidity and mortality. Thus, concurrent psychiatric disorder screening and treatment integrated with MOUD may improve retention on MOUD, opioid relapse and overdose for women

Keywords

Opioid Use Disorder; Medication for Opioid Use Disorder; HIV; Gender; Pre-exposure prophylaxis (PrEP)

Contact Author: Sandra A. Springer, MD, Address: Department of Internal Medicine, Section of Infectious Disease, Yale AIDS Program, 135 College Street, Suite 323, New Haven, CT 06510, Fax: 203-737-4051, Phone: 203-687-6680, Sandra.springer@yale.edu.

Introduction

There has been a substantial increase in the number of individuals with opioid use disorder (OUD) over the past decade, particularly among women.[1] Historically, men have reported higher rates of OUD, however the increase in OUD among women has increased to rates that are closer to the OUD diagnoses rates in men, therefore reducing the gender gap among those with OUD.[2,3] From 1999–2017, the rate of overdose deaths among women aged 30–64 increased by 1,634% for synthetic opioids and 915% for heroin.[4] Women have a higher prevalence of pain syndromes and different response to analgesic drugs than men,[5] contributing to higher rates of women being prescribed opioid pain medications than men.[6] Furthermore, multiple studies have suggested that women progress from time to initial prescription opioid use to problematic use and seek-treatment faster than men, but this is not true for heroin use.[7,8] This information warrants a more in-depth understanding of this population.

Medication treatment for OUD (MOUD; e.g., buprenorphine, methadone, and extended-release naltrexone) are effective in reducing opioid use, risk of overdose, and all-cause mortality.[9] Despite these benefits, a low proportion of women enter treatment.[10] Women face unique barriers when initiating OUD treatment due to mental health conditions, past traumas, and stigma,[11] yet research continues to overlook critical gender differences in demographics, drug use severity, psychopathology, and other clinical characteristics among persons initiating MOUD.[12] Women initiating MOUD have higher rates of co-morbid depression and anxiety,[13] report greater psychiatric severity and higher levels of functional impairment compared to men.[14,15] Therefore, the aim of this manuscript is to explore the gender-specific differences in clinical characteristics including current and past psychiatric and substance use disorder diagnoses, depression and anxiety symptoms, quality of life (QoL) and reported drug use among a cohort of persons with OUD initiating MOUD.

Methods

Study Design

Project MAT BIO (Medication-Assisted Therapy and BIological Outcomes) is a prospective cohort NIH-funded study of persons with Diagnostic and Statistical Manual of Mental Disorders (DSM-5) diagnosed moderate to severe OUD living with and without HIV who are initiating treatment with methadone or buprenorphine. Participants were screened and enrolled when they began MOUD with biological and self-report measures obtained at baseline, days 7 and 14, and months 1, 3, and 6 post-initiation of MOUD. Study protocol and procedures were approved by Yale Internal Review Board and previously published.[16] Differences in demographic and clinical characteristics were assessed by self-reported gender at baseline. Chi-squared and Fisher’s exact test assessed differences in dichotomous variables, and T-test assessed differences in continuous variables. Data was analyzed using Stata®, version 17 software.

Results

Of the 125 participants enrolled from March 2017 to August 2021, 33 (26.4%) identified as women, 90 (72.0%) as men, and 2 (1.6%) as transgender women based on current gender identity. The persons who identified as transgender women were included in the women grouping of the analyses. Items regarding sex were not collected in this project. Study research assistants who were trained and certified to administer all of the study instruments conducted interviews. All participants were seeking MOUD with 45.6% of men and 45.5% of women starting methadone, and 54.4% of men and 54.3% of women starting buprenorphine. Approximately one third of participants were homeless and three-quarters were not currently in a controlled environment (e.g., prison or inpatient treatment center) in the month before baseline assessment. When compared to men, women were significantly younger, more likely to be White non-Hispanic, identify as a member of the LGBTQ+ community, and have a lower mean lifetime number of months of incarceration (see the table). There were no significant differences in employment status, mean income, HIV or hepatitis C status, or their history of OUD treatments.

Psychiatric disorders

As depicted in the table, women and men had similar prevalence of DSM-5 psychiatric disorders on the Mini-International Neuropsychiatric Interview (MINI)[17] at baseline for major depressive, bipolar disorders, and generalized anxiety disorder. Nine participants did not complete the MINI. However, women had a significantly higher prevalence of post-traumatic stress disorder (PTSD). Although not significant, women also had a higher prevalence of moderate to severe depressive symptoms as per the Patient Health Questionnaire (PHQ-9)[18]. Women were also more likely to be told they should be taking psychiatric medications by a medical professional, but there was no statistical difference in 'currently prescribed psychiatric medications'.

Quality of Life (QoL)

Women had poorer health-related World Health Organization QoL-Bref[19] means scores across all domains (physical, psychological, social relationships, and environment), although only the psychological scores were significantly different.

Substance Use

There was no difference in the types of substances used in the three months prior to the baseline assessment. However, when exploring DSM-5 substance use disorder diagnoses at baseline as per the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)[20] non-prescribed sedative/sleeping pill (31.4% of women vs. 7.8% of men; $p<0.001$) and hallucinogens (14.3% of women vs. 2.2% of men; $p=0.02$) use was statistically significantly different.

Based on the timeline followback (TLFB), the majority of participants reported approximately 19 days of any opioid use in the 30 days before baseline, no significant difference between genders. When exploring the type of opioid used, 94 participants (81.1% of men and 60.0% of women) reported heroin use in the 30 days before baseline ($p=0.01$).

Statistical analyses could not be performed on other opioid use (morphine, fentanyl, oxycodone, and oxycontin) due to the small number of participants (1–4 per type of opioid) who reported use.

Discussion

This is a cross-sectional analysis of gender differences of baseline characteristics of a cohort of persons with OUD seeking MOUD. Women had a higher prevalence of DSM-5 generalized anxiety disorder and PTSD, and greater depression severity as compared to men. Prior research indicates that participants with an anxiety disorder are more likely to meet OUD criteria,[21] and opioid relapse is more likely in women with co-occurrence of affective and anxiety disorders.[10] Women had poorer psychological QoL compared to men in this study which aligns with previous research on those seeking MOUD,[15,22,23] and may be associated with worse MOUD retention and outcomes.[24] Concurrent psychosocial treatment and MOUD are associated with improved outcomes indicating that psychiatric comorbidity is a critical treatment target.[25] Our findings reflect that women were significantly more likely to be told by medical providers that they should be prescribed medications for their mental health conditions, however they were less likely to be currently prescribed these medications as compared to men.

In this study, women reported higher rates of non-prescribed hallucinogen and sedative/sleeping pill use. This is important given among those on MOUD, sedative use has been associated with poorer MOUD retention.[26] In addition, sedative (benzodiazepine) misuse is implicated in 40–80% of methadone deaths[27,28] and up to 80% of buprenorphine-related deaths.[29,30] Given the age of our sample and that maternal mortality involving opioids doubled between 2007 and 2016,[31] with overdose as a leading cause,[32] the results from this analysis highlights the importance of addressing sedative misuse with MOUD particularly among reproductive-age women.

These findings are relevant in the context of treatment outcomes; programs for women may benefit from a multi-disciplinary approach that addresses psychiatric comorbidities as suggested by the American Society of Addiction Medicine[33] compared to traditional siloed care. To combat this risk for relapse for women, concurrent psychiatric therapy may help manage symptoms that emerge with MOUD initiation. Women-specific programming may be beneficial as mixed-gender treatments often fail to address their needs, including childcare assistance, pregnancy care, parenting, domestic violence, sexual trauma, psychiatric comorbidity, housing, income support, and social services.[10,34,35] Furthermore, our results support the need for integrated HIV harm-reduction services, although women were significantly less likely to be diagnosed with HIV, their injection drug use behavior did not differ. This may be due to the younger age of the women. Therefore, engaging women in harm reduction services before they seek treatment including syringe exchange, access to pre-exposure prophylaxis (PrEP) for HIV, and increased HIV testing are essential.

This analysis is subject to limitations including only gathering information on current gender identification, items regarding sex at birth were not collected. The sample had a small number of women participants, which is typical of most analyses of MOUD treatment

studies.[36–40] Although untreated/undertreated ADHD is associated with substance use,[41,42] items regrading ADHD were not asked in this project. Additionally, information collected on psychiatric medications was based on self-report, rather than medical records, which may have introduced recall bias and under/over-reporting. Nevertheless, among this population, we found similar results to other studies of gender differences among persons with OUD initiating MOUD.[1,13–15,23] Analyses included in this manuscript report differences among baseline characteristics of this on-going project. Future analysis will explore gender differences over the six-month study period.

Conclusion

This evaluation provides insights into gender differences in persons with OUD seeking MOUD that may help develop women-specific OUD treatment. More prospective research is required to understand these gender differences in baseline characteristics and how they may affect MOUD initiation and retention, as well as other outcomes including reduction in relapse, opioid overdose, and death among women.

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Declaration of Interest:

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Table.

Participant characteristics by gender, bivariate results

	Women (n=35) n (%)	Men (n=90) n (%)	Test statistic	P value
Demographic related variables				
Age (mean, SD)	37.4 (12.7)	44.1 (12.3)	2.69	**0.008** *
Race and Ethnicity			11.642	**0.007** *
Hispanic	5 (14.3)	33 (36.7)		
White non-Hispanic	23 (65.7)	31 (34.4)		
Black non-Hispanic	5 (14.3)	23 (25.6)		
Other non-Hispanic	2 (5.7)	3 (3.3)		
Homeless	11 (31.4)	28 (31.1)	0.001	0.97
Marital Status			2.833	0.24
Married/Living with a partner	4 (11.4)	21 (23.3)		
Separated/Divorced/Widowed	8 (22.9)	23 (25.6)		
Never Married	23 (65.7)	46 (51.1)		
Sexual Orientation			17.095	**0.001** *
Heterosexual or straight	23 (65.7)	82 (91.1)		
Homosexual, gay, queer, lesbian, or same sex loving	5 (14.3)	7 (7.8)		
Bisexual	7 (20.0)	1 (1.1)		
High School Diploma/GED or higher	30 (85.7)	69 (76.7)	1.252	0.26
Has health insurance	34 (97.1)	89 (99.0)	0.488	0.49
Actively working	4 (11.4)	21 (23.3)	2.232	0.14
In a controlled environment in the past 30 days	10 (28.6)	23 (25.6)	0.118	0.73
Lifetime months incarcerated (mean, SD)				
Months incarcerated	35.3 (69.4)	79.3 (104.2)		
Log transformation	3.0 (1.8)	4.0 (1.3)	2.679	**0.009** *
On probation or parole	7 (20.6)	20 (22.2)	0.039	0.84
Living with HIV	8 (22.9)	37 (41.1)	0.056	0.06
Hepatitis C infection	18 (51.4)	57 (63.3)	1.488	0.22
Mental health and quality of life related variables				
Moderate to severe depressive symptoms per PHQ-9 (score 10+)	21 (60.0)	41 (45.6)	2.103	0.15
Quality of Life (WHOQoL-Bref; mean, SD)				
Physical Health	12.6 (3.5)	13.4 (3.6)	1.061	0.29
Psychological	12.0 (3.4)	14.0 (3.1)	3.123	**0.002** *
Social Relationships	12.5 (3.5)	13.6 (3.9)	1.488	0.14
Environment	12.8 (2.8)	13.4 (2.9)	0.955	0.34
Met DSM-5 criteria for Mental Health Condition (MINI) (n=116)				
Major Depressive Disorder	15 (48.4)	33 (38.8)	0.857	0.36
Bipolar Disorder	9 (29.0)	18 (21.2)	0.785	0.38

	Women (n=35) n (%)	Men (n=90) n (%)	Test statistic	P value
Post-Traumatic Stress Disorder	9 (29.0)	12 (14.1)	3.408	0.07
Generalized Anxiety Disorder	6 (19.4)	4 (4.7)	6.188	**0.01** *
Two or more conditions	12 (34.3)	23 (25.6)	0.953	0.33
Told they should be on medication for mental health issue	25 (71.4)	44 (48.9)	5.177	**0.02** *
Currently prescribed medication for mental health issue	14 (40.0)	23 (25.6)	2.523	0.11
Substance use and treatment related variables				
History of treatment for opioid use disorder (lifetime)				
Received inpatient detoxification	12 (34.3)	29 (32.2)	0.049	0.83
Received outpatient treatment	23 (65.7)	52 (57.8)	0.661	0.66
Prescribed any medication for OUD	20 (57.1)	49 (54.4)	0.074	0.79
Prescribed Methadone	16 (45.7)	31 (34.4)	1.364	0.24
Prescribed Buprenorphine	8 (22.9)	21 (23.3)	0.003	0.96
Prescribed Naltrexone	1 (2.9)	0 (0.0)	2.592	0.28
Referred to a support group	14 (40.0)	37 (41.1)	0.013	0.91
Medication for opioid use disorder to be started			0.000	0.99
Buprenorphine	19 (54.3)	49 (54.4)		
Methadone	16 (45.7)	41 (45.6)		
Reported substance use in past 3 months per ASSIST				
Tobacco	28 (80.0)	78 (86.7)	0.869	0.35
Alcohol	12 (34.3)	46 (47.8)	1.862	0.17
Cannabis	22 (62.9)	49 (54.4)	0.727	0.39
Cocaine	21 (60.0)	40 (44.4)	2.441	0.12
Hallucinogens	5 (14.3)	2 (2.2)	6.937	**0.02** *
Amphetamines	3 (8.6)	2 (2.2)	2.646	0.13
Inhalants	2 (5.7)	1 (1.1)	2.280	0.19
Sedatives or sleeping pills	11 (31.4)	7 (7.8)	11.436	**<0.001** *
Opioids	31 (88.6)	78 (86.7)	0.082	0.78
ASSIST criteria for hazardous use in the past 3 months (score 4+)				
Tobacco	30 (85.7)	83 (92.2)	1.230	0.27
Alcohol (score 11+)	6 (17.1)	17 (18.9)	0.051	0.82
Cannabis	20 (57.1)	43 (47.8)	0.884	0.35
Cocaine	18 (51.4)	47 (52.2)	0.006	0.94
Hallucinogens	3 (8.6)	4 (4.4)	0.812	0.31
Amphetamine	2 (5.7)	5 (5.6)	0.001	0.63
Inhalants	1 (2.9)	2 (2.2)	0.043	0.63
Sedatives or sleeping pills	8 (22.9)	7 (7.8)	5.426	**0.02**
Opioids	34 (97.1)	86 (95.6)	0.165	0.68
Injected drugs within the past 3 months	15 (42.9)	40 (44.4)	0.026	0.87

	Women (n=35) n (%)	Men (n=90) n (%)	Test statistic	P value
Number of days used opioids in past 30 days per TLFB (mean, SD)	17.6 (14.2)	19.5 (12.5)	0.719	0.47
Reported heroin use in past 30 days per TLFB (yes/no)	21 (60.0)	73 (81.1)	6.022	**0.01** *

SD=standard deviation; PHQ-9=Patient Health Questionnaire-9. WHOQoL-Bref=abbreviated World Health Organization Quality of Life; OUD=opioid use disorder; ASSIST=Alcohol, Smoking and Substance Involvement Screening Test; TLFB=Timeline followback

* indicates variables significant at p<0.05