

**Psychosocial Syndemics Affecting Treatment Outcomes for
Individuals Receiving Medication for Opioid Use Disorder**

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Abstract

Background/Objectives: Successful engagement with and retention in medication treatment for opioid use disorder (MOUD) is an important focus in the fight against the opioid crisis. Gaps in opioid use disorder (OUD) care point to a need for improved understanding of factors that affect MOUD outcomes and how barriers may act as syndemic factors, compounding one another's effects. This study used qualitative methods to solicit feedback about barriers to retention and successful treatment outcomes in methadone maintenance treatment (MMT) and used these findings to build a conceptual framework of interaction.

Methods: This study was conducted at a community-based drug treatment center that serves a low-income population, the majority of whom identify as Black or African American. We recruited patients and staff as well as peer recovery coaches who work in OUD recovery across Baltimore City. Semi-structured interviews and focus groups asked about factors that influence MMT treatment outcomes and how barriers co-occur and interact. We used thematic analysis to examine themes pertaining to our research questions and two independent coders coded each transcript based on identified themes.

Results: Patient participants ($n=20$) had a mean age of 48.4 ($SD=10.0$), 70% male, and 60% Black or African American. Mean reported age of first drug use was 17.7 ($SD=5.1$). Staff and peer recovery coach (PRC) participants ($n=12$) had a mean age of 49.2 ($SD= 0.7$), were 42% male, 75% Black or African American, with an average of 9.6 years working in substance use (SU) treatment. Barriers described by participants fit into several broad themes: individual/self, social, institutional or structural, community or environmental, and stigma. Participants described co-occurrence of these barriers as fueling one another and having a disastrous effect on treatment outcomes.

Conclusions: Understanding barriers to successful MOUD (specifically MMT) outcomes experienced by this vulnerable population and considering the synergistic effect of these barriers may assist with identification and promotion of the types of interventions needed to effectively and efficiently mitigate their impact. The conceptual model developed in the analysis of qualitative results for this study can inform future research, including quantitative analysis to build further support for the syndemic relationships presented in the model.

Keywords: syndemics, methadone, opioid use disorder, treatment outcomes, social determinants of health

Psychosocial Syndemics Affecting Treatment Outcomes for Individuals Receiving Medication for Opioid Use Disorder

The rate of opioid overdose deaths per year in the United States more than doubled between 2010 and 2017 and, in 2018, about 47,000 people died as a result of opioid overdose (Centers for Disease Control and Prevention (CDC), 2020). Such staggering statistics and tremendous loss of life contributed to the declaration of a national public health emergency in 2017 and increased federal allocation of funds for treatment and recovery services for opioid use disorder (OUD) (US Department of Health & Human Services, 2017).

The State of Maryland, and Baltimore City in particular, sits at the center of the US national overdose crisis. Maryland ranks within the top five states for age-adjusted opioid-related fatalities (Kaiser Family Foundation, 2020) and Baltimore City reported a drug overdose fatality rate in 2017 (45.1 per 100,000) that is higher than any other metropolitan county in the country (Baltimore City Health Department, 2018). In 2017, Governor Larry Hogan of Maryland declared a state of emergency in response to opioid-related fatalities (Exec. Order No. 01.01.2017.02, 2017) and, in January 2019, he announced an executive order to study mental and behavioral health as related to substance use disorders (Exec. Order No. 01.01.2019.02, 2019). As the State focuses attention on overdose prevention and access to treatment, understanding the larger picture of determinants of successful treatment for OUD will allow for development of tailored services and modifications of existing programs to address gaps.

Despite the relatively recent federal and state public recognition of the “opioid crisis,” some effective treatment strategies for OUD are well established, dating back to development in the 1960s (Joseph et al., 2000). Medication for OUD (MOUD) includes evidence-based approaches that incorporate prescribed medications (e.g. methadone, buprenorphine, and

naltrexone) and behavioral therapy (National Academies of Sciences, Engineering, and Medicine, 2018). Given the chronic course of OUD, long-term adherence to a regimen and retention in care is crucial to prevent withdrawal symptoms that can precipitate relapse and fatal overdoses. This study investigated psychosocial factors that may impact outcomes of MOUD, specifically methadone maintenance treatment (MMT) and how interaction between these factors can further contribute to poor treatment outcomes.

MMT (like other MOUD options) is employed to relieve withdrawal symptoms and curb cravings by providing a safe and controlled level of medication. Like most current MOUD regimens, MMT involves daily dosing, but is unique in that it usually requires daily observed dosing (i.e., daily medication dispensed at the clinic and taken by patients in front of clinic staff). The necessary length of time on MMT varies on an individual basis, but prior research indicates that three months on treatment is needed to reduce or stop use, and optimal outcomes (long-term prevention of relapse) occur with longer durations of treatment (NIH, 2018). However, fewer than half of the people who initiate MMT are retained in treatment for at least twelve months (Reisinger et al., 2009). People who drop out of MMT experience 3.2 times the rate of all-cause mortality and 4.8 times the rate of overdose mortality compared to people who remain on treatment (Sordo et al., 2017). Thus, there is a serious public health need to identify and evaluate strategies that address barriers to MMT retention.

The factors that interfere with MMT retention cannot be considered in isolation, but rather in the context of other disorders, social factors, and environmental exposures. Patients engaged in MMT frequently live with co-occurring psychosocial problems and stressors. For example, a random sample of women receiving MMT at methadone treatment clinics in New York City included 89.8% report of lifetime intimate partner violence, 37.8% report of childhood

physical abuse, and 28.1% PTSD diagnosis (Engstrom et al., 2012). Other findings from Baltimore, Maryland indicate almost 50% of patients newly admitted to an MMT program met diagnostic criteria for psychiatric disorders (Kidorf, 2018). Psychiatric comorbidity, homelessness, and violent victimization have all been shown to be associated with worse treatment outcomes for people receiving MMT or other treatment for substance use disorders (SUD) (Carpentier et al., 2009; Lo et al., 2018). However, there is little information available on the effect of co-occurrence of such barriers. A comprehensive investigation of the interaction between psychosocial and structural factors affecting MMT outcomes has not yet been conducted.

Syndemics theory is a conceptual model that may be particularly relevant to understanding the interactive effects of these psychosocial and contextual factors on MMT retention. “Syndemics” or “synergistic epidemics,” highlight the interaction between co-occurring illness and other factors that compound the negative effect of one another (Singer, 2009). The syndemics conceptual framework was originally developed in the setting of the early AIDS epidemic and is still commonly employed to understand factors that influence health disparities among people living with HIV (Singer, 1996; Wilson et al., 2014), including HIV transmission risk (Stall et al., 2003) and antiretroviral (ART) adherence (Blashill et al., 2015; Harkness et al., 2018). Although recent work has begun to consider how opioid use may overlap with other epidemics, for instance with HIV, HCV, and suicide (Fornili, 2018; Perlman & Jordan, 2018), to date, research has yet to elucidate the psychosocial and structural syndemic factors that influence important OUD treatment outcomes, such as MMT retention. Building off of prior work that applied the syndemics model to understanding psychosocial influences on ART adherence among people living with HIV, this study aimed to apply the syndemics

framework to consider psychosocial and contextual influences on MMT outcomes and establish a conceptual model on which to build future research.

Therefore, this study employed a qualitative design to better understand syndemic factors that influence MMT outcomes in a community-based opioid treatment program in Baltimore City. Qualitative data, obtained through focus groups and individual interviews, helped identify factors affecting patient-defined MMT outcomes and provided insight into how those factors may co-occur and interact.

Methods

Setting

This study took place at the University of Maryland Drug Treatment Center (UMDTC), a community-based, outpatient substance use treatment center in West Baltimore that has been providing substance use services to individuals living with opioid use disorder since 1972. The program is certified by the Maryland Department of Health and Commission on Accreditation of Rehabilitation Facilities (CARF). Currently, over three hundred patients receive MMT at this clinical site each day. MMT is dispensed daily Monday through Saturday at UMDTC, with a take-home dose given for Sunday. Patients start with an initiation dose (25 or 30 mg) that is increased/titrated by 5mg every other day until patients reach a “blocking dose” at which cravings are curbed (usually around 60 mg per day). After reaching a blocking dose, usually around two weeks after initiation, treatment plans are reviewed every 90 days, with input from the patient, their primary treatment counselor, and other treatment team members. With demonstrated program fidelity (including at least 90 days of consecutive negative toxicology screens for alcohol and illicit drug use), contingency is offered for up to six take-home doses, minimizing clinic visits to one per week. Though abstinence from alcohol and drugs is not

required for treatment, it is a requirement for take-home doses as it is seen as a way to prevent mixing methadone and other substances, which can lead to serious health consequences. Patients work with their counselors and treatment team to decrease or stop use of opiates and other substances. For clinical purposes, if patients miss doses for thirty consecutive days, they are considered to be no longer in treatment and require re-admission to the program.

Participants

Participants for this study ($n=32$) included UMDTC staff ($n=8$), peer recovery coaches (PRCs) working in the greater Baltimore community ($n=4$), and patients currently enrolled in MMT at UMDTC ($n=20$). Demographic and other descriptive characteristics of participants can be found in Table 1. A majority of participants, across patients, staff, and PRCs, identified as male and Black or African American. We recruited UMDTC staff (i.e. drug treatment counselors, case managers, nurses, and physicians) who were purposefully selected based on their roles in patient care and program administration. We also recruited PRCs, individuals with lived SU experience, who work in SU treatment in Baltimore City. PRCs were recruited through networking with a peer research collaborator and other community-based organizations in Baltimore City. As recommended in qualitative analysis, sample sizes are estimates of the number of individuals needed to reach theoretical saturation (Pope & Mays, 2006).

Though qualitative work with staff and PRCs primarily included focus groups, participants were given the option of participating in focus groups or individual interviews to accommodate varying work schedules and personal preference. For the patient focus groups and semi-structured interviews, we recruited patients receiving MMT at UMDTC. In addition to recruitment with flyers and word of mouth, patients were referred by treatment program staff to purposefully sample patients who were both successfully engaged in treatment as well as

struggling with retention, allowing us to receive input from both perspectives. Staff utilized patient dosing records to identify patients who had missed at least five MMT doses in the past two weeks. Staff flagged those patients in the dosing system so they were given information about the study when they arrive for a dose on a day that a member of the research team was on-site to conduct an interview. If interested in learning more about the research opportunity, those patients were introduced directly to a research team member and given the options of a same-day interview or scheduling an interview or focus group participation at a later date.

All focus group and interview participants were provided gift card compensation in the amount of \$25 for their time.

All study procedures were reviewed and approved by the University of Maryland, College Park IRB with Interagency Agreement (IAA) approved by the University of Maryland, Baltimore.

Procedures

We elected to conduct both focus groups and individual interviews to capture the patient, staff, and peer perspectives as fully as possible, recognizing that we may elicit different insights from these two qualitative methodologies. Focus groups allowed for shared ideas across the group and consensus on most common or pervasive barriers to successful treatment outcomes while individual interviews drew on the individual experience and allowed us to capture more specific examples of barrier co-occurrence and interactions. Focus groups included a maximum of six participants in each. Staff, peers, and patients chose to participate in a focus group or individual interview, but could not participate in both. Focus groups were separated such that patients only participated in focus groups with other patients. Staff and community peers participated in focus groups together.

We developed a semi-structured focus group and interview guides informed by syndemics theory to solicit feedback on syndemic factors influencing MMT outcomes in this population. Semi-structured guides were adapted in collaboration with local staff and stakeholders prior to finalizing and further adapted through an iterative process based on feedback from participants. Participants were asked to describe how patients define successful MMT outcomes. Therefore, conceptualization of successful outcomes and recovery were not restricted to treatment retention or MMT dosing-related measures. Open-ended questions inquired about observed barriers to positive/successful treatment outcomes and retention in MMT. Participants were asked if and how they understand these barriers to co-occur and affect one-another. The focus group guide utilized an interactive approach to allow participants to consider and write down their own ideas of most commonly experienced barriers to successful MMT outcomes. Written responses were collected by a focus group facilitator and presented back to the group to facilitate discussion. Focus group participants were then asked to vote on top three barriers. Group-determined top three barriers were used in the follow-up questions about interaction between co-occurring barriers (listing out and specifically inquiring about combinations of barriers).

The individual interview guide similarly asked participants to identify three most common barriers to successful MMT outcomes and the interviewer used that information to ask questions about co-occurrence and how they may affect one another (as with focus groups, listing out and specifically inquiring about combinations of barriers).

Analysis

All recordings were transcribed and all transcriptions were double-checked for accuracy. Using thematic analysis, the coding team iteratively developed separate patient and staff/PRC

codebooks outlining themes, sub-themes, and definitions in the transcripts. These codebooks were modified as new concepts arose (Boyatzis, 1998). Using these established codebooks, two independent coders coded transcripts using Nvivo Version 12. The coders met weekly to discuss and resolve discrepancies in coding. A third person arbiter was involved in these meetings and resolution of coding discrepancies brought to these meetings were made by discussion and consensus. Transcripts were analyzed with thematic analysis (Braun & Clarke, 2006) informed by grounded theory (Glaser & Strauss, 1967) to deductively analyze themes from the interview guide while inductively identifying additional themes. The coders achieved high inter-coder reliability ($\kappa=0.92$) across larger study aims.

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Results

Intersecting themes emerged from the patient and staff/PRC interviews and focus groups, based on our two study aims: to define barriers to MMT retention and successful treatment outcomes, and to identify interactions between specified barriers and their effects on successful treatment outcomes. In development of the conceptual framework and organization of identified barriers, we drew upon the social-ecological framework, originally developed by Bronfenbrenner (1979) and more recently applied to illustrate the dimensionality of the opioid crisis (Bunting et al., 2018; Jalali et al., 2020) and other qualitative research describing syndemics that include substance use (Nydegger & Claborn, 2020).

Barriers to MMT Retention and Successful Treatment Outcomes

When asked about challenges to staying in MMT and achieving successful treatment outcomes, participants described a range of barriers that they have experienced themselves in treatment or that they have observed others experiencing. While participants described MMT as lifesaving and a crucial component of recovery from OUD, every participant (patients, PRCs, and staff) readily shared substantial challenges faced in realizing the full benefit of MMT, and how participants defined successful MMT outcomes varied, including retention in treatment, abstinence from substances, discontinuation of treatment, and improved social relationships. Representative quotes for each of the themes described below can be found in Table 2a. Barriers to successful MMT outcomes, with organization below informed by the social-ecological framework (Bronfenbrenner, 1979), include factors at the individual-level, interpersonal- or social-level, institutional- or structural-level, and community- or environmental-level.

Individual-Level Barriers

Participants shared a number of barriers that can be grouped together at the individual level, including patients describing barriers they themselves experience, and staff/PRCs describing barriers that their patients experience at the individual-level. One staff participant described this idea broadly saying, of patients, “they look at outside things as holding them back when it’s actually them” (Staff Participant, FG1). More specific individual-level barriers included the themes of individual health (mental and physical), motivation for engagement in treatment/recovery, readiness for change, sense of self-worth, and responsibilities or demands on time, which are all elaborated upon below.

Mental and Physical Health. Patient participants explained that they miss doses or have trouble staying in recovery when they feel tired: “sometimes I get depressed and tired and I don't

come” (Patient Participant, 1032) or are experiencing poor physical health, especially chronic pain. Much of what was shared in this theme of individual barriers related to unaddressed or undermanaged mental health concerns. One patient explained his experience this way: “my brain, it’s just the way it works...I’ve ruined it and I’ll never fix it, which is pretty sad” (Patient Participant, 1035). This also reflects an individual sense of hopelessness and low self-worth.

Motivation and Readiness for Change. Participants shared ideas about individual readiness and motivation for change. One staff participant described low motivation as patients not making a commitment to themselves and looking outside themselves for reasons why treatment is not working (Staff Participant, FG1). Similarly, but from a slightly different perspective, patient participants explain the idea of readiness for change, including different levels of engagement with treatment until they felt like they were ready for recovery. Patient participants shared the experience of being in the MMT program to avoid withdrawal symptoms, but not yet being ready for recovery. One patient participant shared, “This the third time I’ve been on the methadone program. The first two I walked off, because I really wasn’t ready” and went on to explain that people start MMT for different reasons (e.g. avoiding withdrawal, looking for help, or court ordered) and readiness for change is an individual experience (Patient Participant, 1029).

Responsibilities and Demands on Time. Another sub-theme that came up at the individual level was responsibilities and demands on time. This idea reflects individual priorities that patients need to attend to for themselves, like sleep, self-care, and self-improvement (as one participant described the challenge of prioritizing her education). With a slightly different perspective, another participant shared her experience of idle or unstructured time as her biggest

barrier to successful treatment outcomes. She explained that she needs productive activities in order to distract her from cravings and triggers that would make her think about using.

I just need something to do with this time of mine, you know what I mean? I get so frustrated with that. I just need something to do to absorb my time. (Patient Participant, 1030)

Meaningful use of time was common across responses. However, the way that MMT and other treatment or recovery activities factor into structuring that time differed between participants.

Interpersonal- and Social-Level Barriers

Social Influences. Many participants described needing to change “people, places, and things” in recovery from OUD. When, for a variety of reasons, they are unable to change the people with whom they spend their time, proximity to other people who use substances presents substantial challenges to modifying their own substance use or maintaining abstinence from substances. As described by one participant, “because of the company that we keep, we don't know how to change our thinking to be really ready to get clean” (Patient Participant, 1029). In addition to other people using drugs, interpersonal conflict and dealing with “negativity” of others can be overwhelming and makes it difficult to focus on recovery (Patient Participant, FG3). While some participants described a social circle that influenced them to use, a lack of healthy social support was another component of how social influences affected substance use in this population. Participants shared that lack of social support in their recovery is a major barrier to successful outcomes. One patient focus group discussion emerged around the idea that a person cannot be successful in recovery by themselves, but many people on MMT do not have family or a reliable support system.

Connection with Care Providers. Another challenge described by some participants was lack of clear communication with MMT providers in a way that they felt like their goals were understood. One patient participant explained that it can be difficult to express needs related to dosing, especially when MMT dose and effectiveness may be affected by other medications, such as antiretroviral medication for HIV. He said that it is hard to get on the same page about trying to feel better. Another patient participant described her goal of tapering off of MMT and said that she did not feel like her counselor shared that goal. Both participants expressed frustration with communicating needs to multiple people and not feeling like they were understood. Furthermore, and supporting what these patient participants described, a staff participant explained their perception of patient non-compliance. That staff participant described the feeling that patients are willfully non-compliant with program policies and emphasized her belief in the importance of discipline and structure (Staff Participant, FG1) while patient participants expressed frustration with staff not understanding the challenges that they face, “they got to learn how to be more understanding” (Patient Participant, FG3).

Responsibilities and Demands on Time. Similar to the individual-level barrier of responsibilities and demands on time, this theme came up at the interpersonal level as responsibilities to other people, especially with employment. Though participants often described responsibilities and work as positive aspects of recovery, they included it as a reason for struggling with treatment when work or family responsibilities conflict with treatment responsibilities (i.e. dosing and meetings with care providers). Specifically, participants shared how it is challenging to balance employment and other interpersonal responsibilities in the context of the restrictive schedule of MMT typically requiring structured, daily dosing six days per week and frequent toxicology testing for recent drug use.

Institutional or Structural-Level Barriers

The institutional and structural barriers that emerged, including coordination of care, program policies and schedule, unstable housing, and transportation, applied to both the treatment program at which the study took place as well as broader institutions, such as public services and other recovery programs.

Coordination of Care. Participants described both the importance of coordinated, integrated services that support retention in MMT and address other health and mental health outcomes, yet also the institutional limitations in coordination of these services. The types of services mentioned included health care, including mental health care, and social services such as housing and financial assistance. Of particular concern among participants was coordination of mental health services with MMT. One patient participant mentioned difficulty finding a new doctor and a new therapist and said that this got in the way of focusing on recovery and MMT attendance. Another participant, when describing services available at the treatment center, said “one social worker, and she can’t see everybody, right? She can only do so much” (Patient Participant, 1030). A staff member also shared his experience that it is not enough to give patients information about available resources, they need to actually help connect them; but frequently counselors do not have the capacity to make those connections. That staff participant said “the most challenging part of it is where you’re unable to get everything that they need in one place” (Staff Participant, FG2).

Program Policies and Schedule. Multiple participants also brought up MMT program policies as barriers. Patient participants explained that assigned dosing times made them feel restricted as did unexpected program requirements when they arrived for dosing. One participant explained:

It seems like every week, there's something that's like holding that stops me. Because sometimes I mean, I have to get to work, and I go up to the window and they're like, 'Oh, well, you gotta go see this person or this person, or this person.' You know? (Patient Participant, 1038).

The same participant described frustration with the policy of needing to have a job in order to qualify for early dosing since his job is “not on the books” but requires him to start work early.

Unstable Housing. Participants described challenges associated with other institutions and programs from which they receive services. The most commonly cited structural barrier was housing services. Several patient participants described their experience with applying for housing assistance and being on the waitlist. One participant said of her experience:

I've been to housing around the corner from here and filled out an application and they said, only thing the lady said to me was 'see you in seven years.' (Patient Participant, 1029)

Another participant living in transitional housing for people in recovery said that she “plans [her] life around the program” because she recognized the importance of stable housing. However, meeting times and other requirements of the transitional housing program made it difficult for her to move forward with job opportunities and other things that she described as important to her independence and growth. Unstable housing and homelessness were the most frequently mentioned challenges in MMT, described as making it difficult to focus on recovery. All but two participants (across patients, staff, and PRCs) brought up housing as a “top three” barrier to successful treatment outcomes.

Transportation. Unstable housing as well as where someone lives can impact engagement with MMT through challenges with transportation. One participant explained:

I've figured the buses out and everything, but it's still not driving. When scheduling is hard as it is already, not having a vehicle makes it even harder (Patient Participant 1036)

Other patient participants echoed this difficulty with relying on buses both due to financial strain and the time that it takes to travel to the treatment program for daily dosing.

Community or Environmental-Level Barriers

Community Violence. Participants shared the idea of community violence and concern about safety as a barrier to treatment. “You have some of those areas where there's [treatment] programs that you just don't want to be” (Patient Participant, 1016) and participants shared that they do not feel comfortable being in or traveling through some areas where there is a lot of violence.

Environmental Triggers for SU. Similarly, some areas or environments were described by participants as triggering cravings. One patient participant shared that he tried to avoid these environmental triggers by staying at the MMT program for as long as he can, until they close, and then he said, “I go home, you don't see me. I don't come out for nothing” (Patient Participant, FG4).

Homelessness. Additionally, as indicated above, homelessness is recognized as a major problem in the community served by this drug treatment center, and lack of affordable housing options can be considered a structural/institutional barrier as well as an environmental barrier. Housing, at the institutional-level was described as a systems barrier such that people are not able to access necessary housing resources as a result of bureaucracy. As a result, the environmental-level barrier of homelessness exists and affects the community such that “90% of everybody that's still on drugs is homeless” (PRC participant, FG2).

Cross-Cutting Barrier: Stigma

Another important barrier to successful treatment that cut across all of the levels described above was stigma. Specifically, participants shared how stigma affects OUD treatment both as stigma that medical providers demonstrate towards people who use drugs as well as stigma that patients perceive around use of MMT. Participants explained how medical providers demonstrate distrust of people who use drugs. One participant, in describing his experience trying to establish a pain management plan after surgery, said:

Now, if doctors see that you're on methadone in any way, you're automatically judged and it should not be like that. (Patient Participant, FG3)

Descriptions of stigma around MMT ranged from stigmatizing remarks by City officials and authority figures to family members believing that being on MMT means someone is still getting high. Participants explained that a common image of people on MMT is nodding off and not able to function and that this idea has been perpetuated at a high level such that the stereotype applies to the entire community and people refer to Baltimore as “the city that nods” (PRC Participant, FG3).

Interrelationships Between Barriers

As described in the methods section, questions about interaction between barriers (or syndemic relationships) were solicited by interviewers using specific questions about what it is like to experience all different combinations of stated barriers together. In response to these questions about how the above described barriers may affect one another, a series of themes were identified that outlined interrelationships. Figure 1 provides a visual depiction of the relationships between barriers, with some acting in a linear manner and others reflecting a multiplicative effect. Table 2b includes representative quotes for each of the identified

relationships. Although participants shared many thoughts on co-occurring barriers, the relationships between barriers reflected here are limited to those for which participants specified a *worsening* effect rather than just co-occurrence, as this was the aim of questions referring to syndemic relationships and in-line with current syndemics theory (Singer et al., 2020).

At a broad level, when asked about the co-occurrence of barriers, participants shared their belief that certain barriers have a multiplicative effect on one another. One participant, when talking about her challenges with getting stable housing said:

Then you have all the other issues in between just set it off like it's a bomb and it just goes off and it just branches out, you know what I mean, in different places. It branches out in different places. (Patient Participant, 1029)

Another participant shared her thoughts on unreliable transportation and responsibilities and demands on her time: “Oh, they just make it worse. Just make it ten times worse” (Patient Participant, 1030).

Table 2b provides representative quotes for eight distinct interrelationships between barriers that were described by participants, and these are summarized more generally below.

Unstable Housing and Mental Health. The interaction between unstable housing and mental health and motivation reflects a relationship in which the barrier of unstable housing worsened the effect of mental health and motivation. Participants described the mental strain and demoralization of applying for and not being able to secure stable housing. One participant shared that her housing situation led to major depression saying about the housing application process “it just sent me over the edge” (Patient Participant, 1030).

Transportation Barriers, Physical Health, Demands on Time. Distance from treatment (and related difficulty with transportation) was described as interacting with poor

physical health or pain and responsibilities and demands on time such that distance from the treatment program worsened the effect of each of those barriers on missed MMT doses. The need to travel far or use unreliable transportation to get to the treatment program worsened the effect that poor physical health and pain have on attending MMT dosing visits. Distance and difficulty with transportation also exacerbated the impact other responsibilities and demands on time had on dosing visit attendance as do program policies and schedule.

Let's say they've got an appointment, my dose is at eight o'clock. But I have an appointment at eight o'clock that I can't miss. I go to my appointment of course, that means I'm not going to be able to get dosed until later in the day, again, you start feeling bad, things start going up in your head, thinking about going and getting something out there to make you feel better. (Patient Participant, 1039)

Another participant remarked that “if I had transportation, I could definitely get here and get out of there quickly and be at work and not have any issues with that” (Patient Participant, 1036).

Community Violence and Distance from Treatment. Community violence and concern about safety also had a syndemic effect on the direct relationship between distance from treatment/transportation and missed MMT doses such that participants reported avoiding neighborhoods or areas that are also necessary to get to the treatment center.

Program Policies and Responsibilities/Demands on Time. Further discussion about program policies and the interaction with other demands included the following statement from a patient.

If you know it's already a problem trying to get here and now you have to get here at a certain time, what if that messes with your schedule? That was a big issue. So, I mean, that was the only thing I can really come up with that was an issue... I've seen people

move you know, because of that schedule issue. Just say ‘screw it,’ not even, you know, end up leaving and they go get high. (Patient Participant 1038)

This experience reflected the effect that program policies, in this case dosing schedule, had on the challenges of other demands on time. The larger context of this participant’s quote was discussion about employment responsibilities and trying to keep a job.

Stigma and Physical/Mental Health. Regarding stigma that medical providers have around SUD and MOUD, participants shared experiences with or beliefs about not being able to get medication for debilitating pain due to stereotypes of people who use drugs. Since pain is a barrier to attending MMT dosing appointments, stigma and inadequate medical care have a worsening effect. Also, participants described the effect that stigma around MOUD had on sense of self-worth and mental health such that “they always felt less than” (PRC Participant, FG2). This can have a compounding effect on low self-worth and pre-existing mental health conditions.

Discussion

This study aimed to develop a preliminary conceptual model of barriers to successful MMT outcomes and the syndemic relationships between these barriers. To our knowledge, this is the first study to apply syndemics theory to understanding treatment outcomes for OUD. Based on qualitative feedback from patients, staff, and PRCs, we developed a preliminary conceptual model that describes syndemic relationships that impact poor MMT treatment outcomes. We utilized the social-ecological framework to organize the levels of barriers that emerged from participant responses (individual, social, institutional, and environmental). This approach allowed us to incorporate patient perspective and voice into how we understand the experience of barriers at these multiple levels. Patient, staff, and PRC participants had complementary responses across themes that reflected similar ideas in response to primary study aims.

The four levels of barriers that were identified in thematic analysis included distinct as well as cross-cutting and interacting factors. At the individual level, participants described barriers related to personal health and readiness for change. At the social level, they shared barriers experienced in the context of social circles that influence substance use as well as lack of social support. At the institutional level, barriers included housing as well as challenges with program policies and schedules, and at the environmental level, barriers included community violence and environmental triggers for substance use. Participant descriptions of the impact of stigma (related to SU and MMT) on treatment outcomes arose across all of the social-ecological framework levels. Importantly, stigma in the context of this analysis was focused on participant descriptions of how they recognized stigma existing and affecting treatment and recovery.

Descriptions of barriers to successful MMT outcomes in this study align with previously published challenges associated with MOUD outcomes. Past studies have demonstrated the association of psychiatric comorbidity (Kidorf, 2018), homelessness (Lo et al., 2018), violent victimization (Lo et al., 2018), and stigma (related to MMT and/or substance use) (Tsai et al., 2019; Woo et al., 2017) with poor MOUD outcomes and treatment discontinuation. The barriers described by participants in this study are consistent with what has been published in the past, both from qualitative and quantitative research. Furthermore, the social-ecological framework is well established for conceptual organization of factors associated with substance use morbidity, recovery, and treatment. A qualitative study looking at barriers to treatment for people with OUD recently released from prison used this framework to describe themes that came out of interviews with clinicians and, similar to our study, reported individual-level motivation, social circle that influences substance use, and over-stretched clinician capacity as examples of individual, social, and institutional barriers to treatment (Bunting et al., 2018). A unique aspect of the current study

is the focus on syndemics theory and the *interaction* between barriers across social-ecological levels.

We distinguished between syndemic relationships and other interrelationships of co-occurring barriers in order to provide clarity in the definition of syndemics. Mere co-occurrence and clustering of disease and adversity does not meet criteria to be defined as a syndemic. Thought leaders on the topic of syndemics have described that the concept is not “synonym of comorbidity” (“Syndemics,” 2017) and must include a proposed mechanism by which the association occurs (Bhardwaj & Kohrt, 2020). Specifically, leaders in the field have critiqued how the concept of syndemics has been inappropriately applied to any clustering of social determinants of health and a “sum score” approach to analysis has proliferated a serious misunderstanding in the literature (Tsai, 2018). The sum score approach to analysis implies additive effects that would suggest very different intervention approaches compared to syndemic *interactions* that have a multiplicative effect. The current analysis identified co-occurrence of many barriers, and the conceptual model detailed in Figure 1 allows for the distinction between the different types of relationships between barriers (i.e., direct effect, interactive relationship). We differentiated between the sequential effect of unstable housing on social circle that influences substance use and other relationships between barriers that seem to interact differently. Thus, future research can test these relationships with intentionality and consider intervention options that most efficiently target the effect of unique relationships between barriers. Furthermore, the levels of barriers in this conceptual model are in-line with methodological recommendations for incorporation of ecological- and individual-level in development of multi-level models of syndemics (Tsai et al., 2017).

Syndemic theory has recently received a lot of attention in scientific literature with a 2017 *Lancet* series bringing together ideas about this framework as a means of understanding disease and health conditions in global populations (“Syndemics,” 2017). Qualitative research to inform mechanisms of syndemic relationships has been undertaken previously, especially in the context of HIV risk and treatment (Gagnon, 2018; Lyons et al., 2013; Quinn et al., 2018). However, qualitative research to inform syndemic factors affecting MMT treatment outcomes has not previously been undertaken but is crucial to allow for further meaningful research in this area, especially informing quantitative analyses. Conceptualization of syndemics in the context of OUD has been limited and has focused on the impact of OUD on other health outcomes, such as suicide (Fornili, 2018) and infectious diseases (Perlman & Jordan, 2018). Our study lays the groundwork for expansion of syndemics theory to better understand barriers of successful OUD treatment outcomes.

The syndemics literature has been cited in recommendations for public health interventions (Hart & Horton, 2017; Willen et al., 2017). As described above, the way that we conceptualize syndemic interactions carries implications for most effective means of intervening on these factors. With the understanding of a multiplicative effect, an intervention targeting one factor would have a greater impact on treatment outcomes than would be expected if no interaction was present (Tsai, 2018). So, we can harness information gathered from syndemics research to promote efficiency in intervention decisions, which is especially important in low-resource settings experiencing high disease burden (such as economically disadvantaged areas of Baltimore City, where this study took place, which are experiencing high mortality in the opioid epidemic).

In recent research, syndemics theory has been used to build transdiagnostic treatment protocols (Safren et al., 2020). Safren and colleagues sought to develop a unified protocol to address mental health and related psychosocial syndemic factors in people living with uncontrolled HIV in Miami, FL. They initially intended to implement a unified protocol with standard content for all patients (based on CBT for adherence and depression), but found that specific barriers to treatment and complex life circumstances described by individual patients were best addressed through a module-based design where content was selected “based on life circumstances and particular set of mental health and social-structural comorbidities” (Safren et al., 2020, p. 3275). Implementation of such a module-based design for people facing challenges in MOUD can be informed by the conceptual model presented in the current study to help select the most efficient strategies to target high-impact barriers (those that have a synergistic effect on other barriers). Safren and colleagues also describe the importance of integrated case management and linkage to wraparound services that holistically address complex social-structural barriers faced by patients in treatment for HIV. Similar recommendations were made by participants in a qualitative study informing implementation of a PRC-delivered intervention (based on Behavioral Activation for substance use) to support linkage to and retention in treatment for SUD (Satinsky et al., 2020). Our research, and future studies elaborating on syndemic barriers to MOUD, should be used to consider similar intervention approaches for people facing challenges in treatment.

Limitations

Findings must be considered in the context of methodological limitations that should be addressed in future research expanding on this topic. First, as a study employing only qualitative methodology, the findings are not intended to be generalizable. Second, though we employed

procedures to reach a diverse sample of patient participants (both consistently and inconsistently attending dosing visits), inclusion criteria necessitated that patient participants be actively enrolled in the MMT program. Therefore, we were unable to get the perspective of patients who discontinued MMT and have not returned to treatment. Participant responses were also limited by narrow staff representation with only one participant representing medical staff in the MMT program. We also recognize the limitations to generalizability given this study recruited patients and staff from just one treatment program and one MOUD modality (MMT versus other options such as buprenorphine or naltrexone). Third, as a result of the scope of the current study, barriers were classified into relatively broad categories, such as mental health and physical health. Though this approach is common in the literature, recent recommendations promote a more granular approach that allows for identification of more specific pathways and processes of interaction (Bhardwaj & Kohrt, 2020). Finally, although we use language describing syndemic factors as *affecting* treatment outcomes based on participant responses regarding their perceptions of these factors, we recognize that we are not able to make substantiated claims about causality using a cross-sectional, qualitative design.

Design Considerations

Several study design considerations are important to note. First, an important aspect of how the interview and focus group guides solicited feedback from participants is the way that successful treatment outcomes were defined. Participants were asked to share their own, personal definitions of successful MMT outcomes. Therefore, there was no pre-set, common definition of successful treatment nor consensus on how ongoing substance use fits into that definition. Thus, substance use was included as a mediator between other barriers and successful treatment outcomes in the conceptual model. However, depending on individual participant beliefs,

substance use may also be conceptualized as an independent barrier affecting treatment outcomes or a component of the definition of poor treatment outcomes. Additionally, this qualitative research was designed to inform quantitative assessment of the syndemic barriers identified. Quantitative data collection progress was delayed by the COVID-19 pandemic, however is in progress and will be an important next step following from this research.

Several program policy changes took place at the treatment center between starting this study and completion of the last interview. Early study participants described challenges associated with assigned dosing times, especially interfering with other responsibilities and demands on time, but the program eliminated dosing times before the final patient interview and now allow patients to attend dosing visits anytime between 7:00 am and 1:30 pm (though earlier time is still reserved for patients who need early dosing and have documented jobs). Although it was not a study aim to get feedback from participants on this particular change, one patient participant shared that it was a good thing that they “finally got rid of [dosing times]” (Patient Participant, 1036).

Although the qualitative data collection was not directly impacted by the global COVID-19 pandemic, it is important to acknowledge several programmatic changes that have resulted from COVID-19. The pandemic and lockdown/social distancing response has affected people living with OUD broadly, likely exacerbating some barriers to treatment described in this study. However, the pandemic has had a unique impact on people receiving MMT as a result of national regulatory modifications to policies around take-home dosing and frequency of in-person visits (SAMHSA, 2020). Some people have been advocating for loosening MMT dosing restrictions and increasing access to take-home dosing before and outside the context of the viral pandemic (Green et al., 2020; Greenblatt et al., 2020). Research is underway to investigate the

impact of these treatment changes, both positive and negative, and understand how they may have affected the interrelationships of barriers identified pre-pandemic (R61AT010799-01S1; PI: Magidson). The proposed conceptual model will be an important guide as we consider the unique vulnerabilities individuals with OUD face in achieving successful OUD treatment outcomes during COVID-19.

Conclusions and Future Directions

This qualitative study, including perspectives from patients and staff of an MMT program as well as PRCs who work in diverse drug treatment settings, is the first to apply syndemics theory to understanding OUD treatment outcomes. As syndemics theory is expanding from its original conceptualization in HIV outcomes to application in other public health contexts, the use of this theory to establish a framework of relationships between barriers to successful MMT outcomes has strong public health implication. Enormous morbidity and mortality in the opioid epidemic must be targeted with intentional interventions that address barriers and their interactions across levels of the social-ecological framework. The conceptual framework of syndemic barriers to successful OUD treatment outcomes can provide a basis for future study and intervention development to enhance outcomes of MMT for people living with complex psychosocial, interpersonal, and structural challenges. We hope this proposed conceptual model will be used to inform future research to further investigate and quantify these syndemic barriers in relation to MOUD outcomes (MMT and more broadly), as well as inform transdiagnostic behavioral interventions based on syndemics theory that address individuals' barriers at multiple levels.

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