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A pilot multisite study of patient navigation for pregnant women with opioid use disorder

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ABSTRACT

The opioid crisis continues to affect pregnant and postpartum women the United States, with the number of pregnant women diagnosed with opioid use disorder (OUD) quadrupling over the last decade. The associated increase in morbidity and mortality among mother and baby warrants prompt, targeted intervention efforts that improve engagement, linkage of care, and treatment retention. Patient navigation (PN) is a chronic care intervention that can directly address this need by helping women identify medical, behavioral, and psychosocial care goals. Moreover, PN can assist women in preparing for, engaging in, and maintaining patient participation in necessary services. Specifically, PN includes strengths-based case management, 1-1 clinical support, motivational interviewing, and addiction-relapse prevention programming. The objective of this article is to present the study protocol of a pilot multisite randomized clinical trial, entitled: Optimizing Pregnancy and Treatment Interventions for Moms 2.0 (OPTI-Mom 2.0; NCT03833245). In this study, we build upon a proof-of-concept study, employing evidence-informed frameworks for protocol and intervention expansion in order to construct a PN intervention tailored for pregnant women with OUD in central Utah and southwestern Pennsylvania. Our protocol provides an initial framework of a potentially impactful intervention and may guide development of future programs. Importantly, this study further establishes the evidence-base—with potential to ameliorate serious adverse opioid-related outcomes and improve health for women and their children.

1. Introduction

The opioid epidemic in the United States continues to result in serious health consequences for pregnant and postpartum women. From 1999 to 2014, the prevalence of pregnant women diagnosed with opioid use disorder (OUD) at delivery quadrupled [1]. OUD during pregnancy is associated with adverse maternal and neonatal health outcomes, such as preterm birth, low birthweight, and neonatal opioid withdrawal syndrome (NOWS), which are associated with substantial expenditures of health care resources [2–7]. This escalation in morbidity and mortality due to opioid use during pregnancy and postpartum period [8] calls for rapid and targeted intervention efforts designed to engage, link, and retain pregnant women in OUD treatment.

OUD, like any addiction, is a chronic disease that can be managed and treated successfully with appropriate, evidence-based care [9]. Thus, OUD among pregnant women requires interventions that last beyond the pregnancy episode and take into account the full milieu of potential needs. Standard care for pregnant women with OUD involves medication assisted treatment, with methadone or buprenorphine, combined with additional behavioral health services [10,11]. Recent data has demonstrated that 44% of pregnant women do not receive

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medication-assisted treatment with either methadone or buprenorphine and less than one-third receive behavioral health services [12]. Owing to the manifold challenges faced by pregnant women with OUD that result in low retention in treatment [13], patient navigation (PN) works to reduce barriers to healthcare engagement by guiding patients through the complex and often fragmented healthcare and social service systems [14,15]. PN is a chronic care intervention [16] that can be used to link and retain pregnant women with OUD in treatment. Specifically, PN has the potential to aid pregnant women with OUD to identify needs; determine behavioral health, medical, psychosocial care goals; and collaboratively prepare for, engage in, and maintain activity in these necessary services and thus ameliorate threats to maternal and neonatal health and wellbeing. Previous research that has employed motivational incentives (i.e., contingency management) among pregnant women has shown up to a 3-fold increase in study retention [17], 4–6 weeks longer substance treatment retention [18,19], and a 6 fold increase in retention for substance treatment-related activities [19] compared to controls. However, PN and behavioral and physical health care linkage/retention for pregnant women with OUD has not been documented in the literature previously.

The objective of this article is to report the study protocol of a pilot multisite randomized clinical trial, entitled: Optimizing Pregnancy and Treatment Interventions for Moms 2.0 (OPTI-Mom 2.0; NCT03833245). This study is testing a PN intervention for pregnant women with OUD and assessing linkage/retention in care. Importantly, this study builds upon a proof-of-concept project among 21 pregnant women with who were provided the PN intervention that utilized a one-group repeated measures design [20].

2. Materials and methods

2.1. Study design

To plan the current study, our team's first step was to transform our previous protocol into a two-group, single-blind, multi-site, randomized clinical trial using the guide provided by Chung et al. [52] for planning multisite trials. Specifically, we utilized face-to-face exercises for trial planning, which employed the Nominal Group Method [52] and included an unstructured/critical topical discussion, question/answer session, and consensus building [52,53]. Due to differences in the geographic location of the investigative team members (southwestern Pennsylvania and central Utah), planning sessions were held via web conference [21,22]. Decisions made by the group during these web planning meetings have been applied to the study protocol and procedures manuals for this project. The following design reflects many of the decisions made during this process.

2.2. Participant recruitment and assessment

Pregnant women with OUD who present to one of two academic health centers located in Southwestern Pennsylvania or Central Utah are approached for potential participation. Project investigators are faculty within these two health systems and have track records of clinical investigation and service provision within these settings. The two health care systems within this project are large, tertiary care, academic medical centers that serve urban, suburban, and rural patients in their respective regions. Both systems provide a full complement of general and specialty maternal and neonatal healthcare services, including perinatal addiction care. Pregnant women from each system are identified through clinic-based outreach, electronic health records (automated electronic data warehouse identification and advertisement as well manual searches), and outreach and advertisements to local organizations that serve this population. Women identified are contacted to provide a study overview and a screening invitation by study coordinators via face-to-face communication if present within the clinical settings or by mailed letter if not present. Following identification, screening is carried out by study research staff. Women not interested in screening are asked to provide their reason for not screening.

Study screening identifies if women are: pregnant, ≥18 years, English speaking, plan to carry their babies to delivery, and meet *Diagnostic Statistical Manual-V* [23] criteria for OUD. Women excluded are those with a psychotic or a manic episode in the last 30 days documented in their medical record or through self-report. Self-report psychosis assessment is performed using the subscale from the Behavior and Symptom Identification Scale [24], and self-reported mania is assessed using Altman Self-Rating Mania Scale [25]. Women beyond the 32nd week of gestation are also excluded to allow up to 8 weeks for prenatal intervention delivery. Those who cannot provide contact information for themselves, collateral contact information of 2 persons, or who plan to move from the area within 2 months after their delivery are also excluded from the study. Finally, women who have been enrolled in a medication-assisted treatment program for > 6 weeks are excluded to eliminate potential participants who are already actively engaged in OUD treatment. Participants with symptoms of intoxication (e.g., slurred speech, dozing off) are only consented after these are resolved; the consent document also includes a consent quiz to ensure comprehension of key elements of study participation.

Eligible women who express interest in the study are asked to provide signed informed consent for study participation. The informed consent process is carried out by study research staff and complies with all ethical and procedural requirements approved by a single Institutional Review Board (IRB) approved at both institutions, with the University of Utah acting as the single IRB. Participants also sign a release of medical information that authorizes research team members to review prenatal care, treatment program records, and neonates' medical records.

Following consent and recruitment, all participants are provided with a baseline assessment. Participants are also assessed at 14-weeks following the baseline survey (after completion of the prenatal navigation sessions for PN participants) and at 2 and 6 months postpartum. Assessors are blinded to participant intervention condition. In both study arms, women receive $30 for completing the baseline assessment, $40 for the second assessment, $50 for the third assessment, and $75 for the final assessment. Patients who complete all 4 assessments are given a completion bonus of $50. Women in both arms also may be reimbursed $10 for transportation/parking costs for each study-related visit. Following the baseline assessment, participants are randomized to standard care or the PN intervention. Randomization is stratified by hospital site and performed in blocks of 6 to ensure an even distribution of participants at the medical centers in PN and standard care groups. All screening and outcome data are captured on encrypted tablet devices via REDCap surveying software [26,27] and are stored centrally. The study randomization list and subsequent condition assignment for both sites are also housed and operated within the REDCap platform [26,27].

2.3. Intervention conditions

2.3.1. Standard care

The standard care condition within the two health systems includes brief case management, referral, and limited follow up. Brief case management involves the participant speaking to the clinic or hospital social worker who conducts an assessment for behavioral health and social service needs. All women are referred to OUD pharmacotherapy and any identified behavioral health or social service needs. The southwestern Pennsylvania site offers resources for an onsite inpatient initiation to methadone with continued methadone maintenance provided by federally licensed community methadone treatment programs. The southwestern Pennsylvania site also offers outpatient initiation to buprenorphine (mono-product), with maintenance provided by an onsite outpatient buprenorphine treatment program or through

community partners. Patients in central Utah are offered in-patient initiation to buprenorphine (buprenorphine-naloxone product) onsite or from community partners. Methadone services are offered by referral, which are provided by federally licensed methadone treatment programs within the community. To avoid influence of the compensatory equalization of treatments bias (i.e., increased service provision by social workers delivering standard care that would compete with PN), we have not exposed social work staff to the PN intervention protocol/training, and these staff are regularly encouraged by project investigators to continue to provide services as usual. Our team also conducted interviews with social work staff before study initiation to capture what standard care involves at each medical center in order to characterize details of these services.

2.3.2. Patient navigation

The PN intervention is delivered by the study navigator, who, in this study, is a master's level research clinician. Fig. 2 contains an overview of the PN intervention. The *prenatal portion* of the PN intervention includes delivery of up to 10 sessions. The *postnatal portion* of the intervention is delivered as 4 sessions over 8 weeks. Women who complete the prenatal portion of the intervention before delivery receive regular calls/texts until delivery when the navigator encourages and reinforces abstinence and treatment retention.

Our PN model is based on the work of Parker [28] and the recently completed Project HOPE study (Hospital Visit as Opportunity for Prevention and Engagement for HIV-Infected Drug Users [29,30]). The study navigators underwent a two-day training in motivational interviewing tailored to the study intervention manual. The navigators also received a half-day training in the intervention protocol by study investigators. Intervention fidelity checking occurs throughout the study by audio recording all PN sessions, which are selected at random for fidelity assessments and feedback. Fidelity assessments cover intervention protocols, case management, and motivational interviewing.

The primary goal of the current PN intervention is linking participants before and after delivery to treatment/psychosocial care and clinical support for participants' retention in those services. All PN participants are referred to a medication-assisted treatment program by the study navigator. A major challenge for pregnant women with OUD within these two health systems is linking to services for ongoing medication treatment for OUD and subsequently being retained in care before and after delivery. Women are encouraged to work with their providers to choose the opioid pharmacotherapy, buprenorphine or methadone, which will best meet their needs, and continue with this treatment throughout pregnancy and the postpartum period. The PN intervention also encourages engagement with prenatal and postpartum healthcare and effective transition of newborns into pediatric care.

The PN intervention specifically encompasses two complementary and necessary services: strengths-based case management (SBCM) and 1-to-1 clinical support (see Table 2). PN sessions last 45–60 min. Due to challenges keeping pregnant women with OUD engaged in care, the intervention emphasizes community outreach. For example, the navigator can visit participants' neighborhoods to meet social and family networks to empathically encourage and support engagement with health, social services systems, and recovery support (i.e., narcotics anonymous, alcoholics anonymous) if she becomes disengaged in care or follow up.

SBCM is an evidenced-based component of the PN model that has been demonstrated to help individuals with substance use disorders and chronic health conditions engage in needed care [31,32]. Navigators apply the specialized skills of SBCM to link individuals to ongoing medication treatment for OUD and guide participants to active engagement in health and social services. SBCM gives patients responsibility for, and ownership of, their recovery [32] and has been shown to have a variety of positive effects, particularly treatment retention [33] and linkage with community services [34]. SBCM utilizes patients' strengths for goal setting and developing a working alliance [32] between providers and patients. Specific elements the navigators focus on include: helping patients obtain and complete paperwork; accessing and engaging in drug/mental health counseling/treatment/mutual support, social services uptake, medication treatment for OUD linkage/retention; and engagement in pre/post-natal care and pediatric/developmental care for newborns.

One-to-one clinical support is an essential PN component for identifying, establishing, and retaining health behavior improvement goals. One-to-one clinical support is designed to motivate and assist participants in recognizing and overcoming internal/external barriers to care, including: emotional support, decision support, lifestyle change support, monitoring outcomes of screening/diagnostics, health behavior, and HIV and Hepatitis C virus (HCV) prevention education, which addresses needle sharing and unsafe sex [28]. Participants receive support and verbal reinforcement for completion of paperwork, engaging in drug/mental health treatment, social services uptake, agonist adherence, and engaging in pediatric/developmental care for their infants. One-to-one clinical support is delivered using motivational interviewing skills [35]. Motivational interviewing is an evidence-based approach for promoting health behavior change in healthcare settings [35,36]. Navigators collaborate with participants to resolve ambivalence toward change by guiding them to establish their own goals and strategies, which enables women to take increased ownership in outcomes while also building self-efficacy and increasing the likelihood of achieving abstinence and pharmacotherapy for OUD retention goals. Motivational Interviewing is particularly valuable in aiding and empowering women to resolve barriers to continued care that may come as a result of having discouraging experiences within health care, treatment, or social service systems.

2.4. Intervention augmentation

To expand our intervention approach from our proof-of-concept study to include greater relapse prevention capabilities, we utilized Marlatt and Gordon's relapse prevention model [37,38]. This model posits that both immediate determinants and covert antecedents predict and precede substance use relapse [37]. To systematically infuse relapse prevention into the postnatal PN sessions, we employed the ADAPT-ITT framework (Assessment, Decision, Administration, Production, Topical Experts, Integration, Training, and Testing, Table 1; [39]). ADAPT-ITT was originally designed as a framework for adapting evidence-based HIV interventions.

Our application of the ADAPT-ITT framework resulted in relapse prevention content delivery as the initial task of sessions 2-13 and is called the “Relapse Prevention Check-Up.” Within the Check-Up, the participant is shown a card that contains 6 topics: (1) managing cravings, (2) recognizing and challenging thinking errors, (3) coping with emotions, (4) structuring time and avoiding boredom, (5) engaging with positive social support, and (6) developing healthy habits and self-care practices. Should PN sessions occur over the phone, the navigator verbally relates these topics to the participant. The navigator, following principles of motivational interviewing, asks the participant if there are any of the topics she knows about and/or would like to talk about. After the participant relates what she knows or would like to know more about, the navigator asks permission to share more specific information on topics from the card. The patient navigator then provides education on the topic based on the Marlatt et al. model [37,38]. The navigator employs a Relapse Prevention Plan Worksheet, developed in this phase, to summarize the discussions and the information shared during sessions where relapse prevention is discussed. The navigator provides the summary sheet to the participant during the final prenatal and final postnatal intervention sessions as a record and for reference (or mails the sheet to the participant if the session occurs telephonically).

Table 1
ADAPT-ITT framework (Assessment, Decision, Administration, Production, Topical Experts, Integration, Training, and Testing.

Assessment	Provided relapse prevention written materials to the project coinvestigators with the assignment to read and mark up the materials. Completing this task, investigators attended a 2-h web conference where they: (1) received a presentation on relapse prevention among substance using populations, and (2) provided brief verbal summaries of their assigned reading materials to one another in the group.
Decision	Following the presentation and summaries, the web conference involved roundtable discussion, eliciting suggestions regarding needed intervention components.
Administration	Meeting participants provided specific recommendations on how to incorporate the identified components into the PN manual.
Production	Concluding the web conference, handwritten notes and comments recorded during the Decision phase were requested by the project leader. Once received, this information and the identified relapse prevention content was infused into the PN intervention.
Topical Experts	Adapted intervention sessions materials were circulated to the project coinvestigators for review and comment.
Integration	Comments and edits from the review of the sessions were returned for finalization and incorporation into the intervention manual.
Training	The project leader authored instructions for the adapted sessions on how navigators are to become familiar and proficient in the relapse prevention content, and how navigators are trained.
Testing	Navigators trianed in the relpase prevention infused study materials deliver this materials througout the study.

Table 2
Study measures.

Outcome	Domain	Name	Source	Screen	Baseline	14 weeks	2 months	6 months
Primary/secondary	Tx [a] linkage/retention	Treatment Services Review [59]	Self-Report		X	X	X	X
Primary/secondary	Substance use	Timeline Follow Back [60,61]	Self-Report		X	X	X	X
Primary	Tx linkage/retention	Substance use treatment visits	Medical record		X	X	X	X
Primary	Tx linkage/retention in Tx	Psychiatric care visits	Medical record		X	X	X	X
Primary	Substance use	Urine toxicology	Medical record/ patient	X	X	X	X	X
Primary	Tx linkage/retention	Social service visits	Agency records		X	X	X	X
Secondary	HIV/Hepatitis-C risk behaviors	Risk Behavior Assessment [62]	Self-Report		X	X	X	X
Secondary	Social impact	Maternal Social Support Index [63]	Self-Report		X	X	X	X
Secondary	Social impact	Parenting Stress Index-Short Form [64]	Self-Report				X	X
Secondary	Social impact	Maternal Attachment Inventory [72]	Self-Report				X	X
Secondary	Tx linkage/retention	Adequacy of Prenatal Care Utilization [65–68]	Medical record				X	
Secondary	Tx linkage/retention	Pre/post maternal care visits	Medical record		X	X	X	X
Secondary	Tx linkage/retention	Pediatric visits	Medical record		X	X	X	X
Secondary	Substance use	Neonatal abstinence syndrome	Medical record				X	
Secondary	Tx linkage/retention	Pre/post maternal care visits	Medical record		X	X	X	X
Secondary	Tx linkage/retention	Pediatric visits	Medical record				X	X
Covariate	Substance use	Drug Abuse Severity Test 10 [69–71]	Self-Report		X	X	X	X
Covariate	Alcohol use	Alcohol Use Disorder Identification Test	Self-Report		X	X	X	X
Covariate	Substance use	Fagerstrom Test for Nicotine Dependence [72]	Self-Report		X	X	X	X
Covariate	Physical health	Short Form 36 [73]	Self-Report		X	X	X	X
Covariate	Mental health	Patient Health Questionnaire [74–77]	Self-Report		X	X	X	X
Covariate	Opioid use disorder	DSM 5 for Opioid Use Disorder	Self-Report	X	X	X	X	X

[a] Tx = Treatment.

2.5. Measures

Table 2 lists the measurement domain, the instrument itself, the source, and timing during the study when the measurement is captured. Primary outcomes for this study will capture information on: OUD and other substance use disorder (SUD) treatment linkage/retention, opioid abstinence, adherence to MAT, and linkage/retention in psychosocial services for participants before randomization compared through 6-months post-delivery. Secondary outcomes involve capturing prenatal care, HIV/HCV risk behaviors, and depression and anxiety for participants before randomization compared through 6-months post-delivery; and child/mother indicators following delivery through 6-months. In addition to examining the effect of treatment condition on the above outcomes, covariates that will be collected in this study will assess behavioral, physical, and psychosocial domains (Table 2). Demographic domains are also assessed and include age, race, education level, employment status, marital status, number of other children, and health insurance status.

2.6. Sample size

Given that this project is designed as a pilot study to test an expanded intervention and associated protocols and procedures, our sample size is not based on a power estimate. Rather, our sample size is based on estimates of how many patients can be screened and consented within the study timeframe, an appropriate method for pilot studies [40]. Based on medical record examination, we anticipate an average of 199 potential recruits each year between both medical centers during timeline of recruitment across 15 months. If approximately 70% are eligible and interested, and of those, 70% provide informed consent; we will recruit 122 participants in this study who will be randomized to the PN (n = 61) or standard care conditions (n = 61, Fig. 1).

Definitive estimation and hypothesis testing are not the aim of this pilot study. However, the target sample size will allow estimation of odds ratios (for comparisons of linking participants before and after delivery to treatment/psychosocial care and clinical support and for participants' retention in those services) along with 95% confidence intervals comparing outcome rates in the treatment and control arms, while accounting for within site clustering. The lower bounds of these confidence intervals will differ from the odds ratio estimates by a factor of 1/3 to 1/2 and the upper bounds will differ by a factor of 2 to 3 for a broad range of overall rates and true odds ratios for each site. In particular, this estimation accuracy requires that outcome rates be in the range 12–88% and true odds ratios be in the range 1/50 to 50 for each site. The pilot study will allow detection of strong signals of preliminary benefit and provide suggestions of benefit for subtler signals.

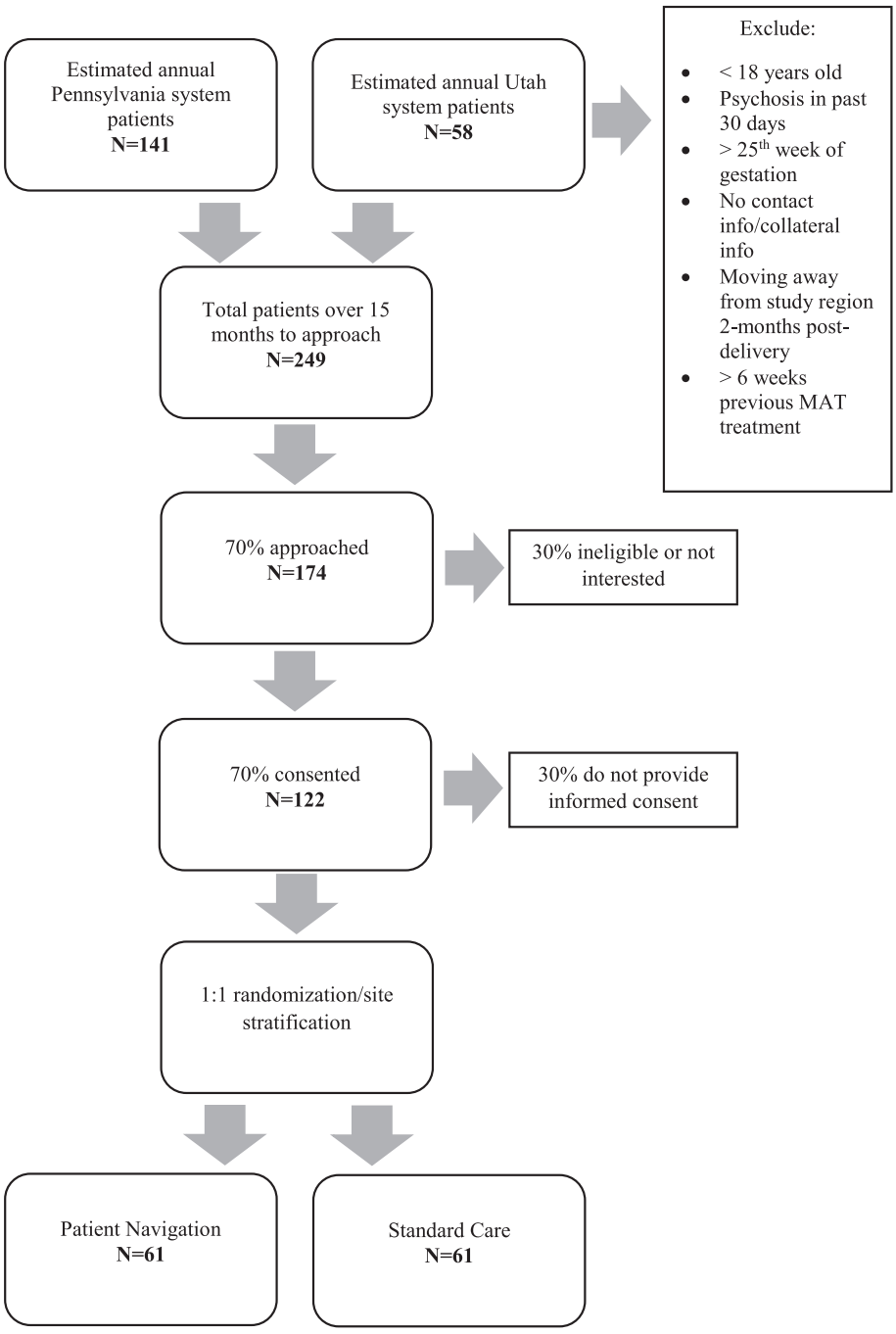

Fig. 1. Anticipated study recruitment.

2.7. Analyses and hypotheses

We will employ descriptive statistics to summarize central tendency, frequencies, and proportions for patient demographics and substance use, health, social, and maternal/neonatal indicators. *t*-tests and χ^2 tests will be used to assess mean and proportion differences between baseline and outcome variables by study group at each time point. We will also develop a series of multilevel models to examine treatment, time, and covariate effects associated with our primary and secondary study outcomes [41,42]. In particular, outcomes will be compared between the study arms in the context of logistic mixed effects models with random effects over time within subject and fixed effects for time trends within each study arm, as well as site and covariates including demographics, substance use, health, social, and maternal/neonatal indicators. Importantly, this multilevel perspective accommodates both overall time-trends and patient-specific time-trends. The multilevel framework allows for flexible treatment of time where change as a putative outcome may be nonlinear, accelerate, or decelerate at different rates across time. The framework also accommodates unequal numbers of observations and unequal spacing of observations across participants (i.e., missing data patterns). All multilevel models will be adjusted for site, demographics, and participant session completion.

Employing the above described multilevel modeling framework, we hypothesize (H), H1: PN recipients will have superior linkage and retention in: (a) OUD and other substance use disorder treatment, (b) psychosocial services, and (c) pre/postnatal care compared to standard care, and H2: a larger portion of PN patients will be (a) adherent to medication treatment for OUD and (b) drug abstinent compared to

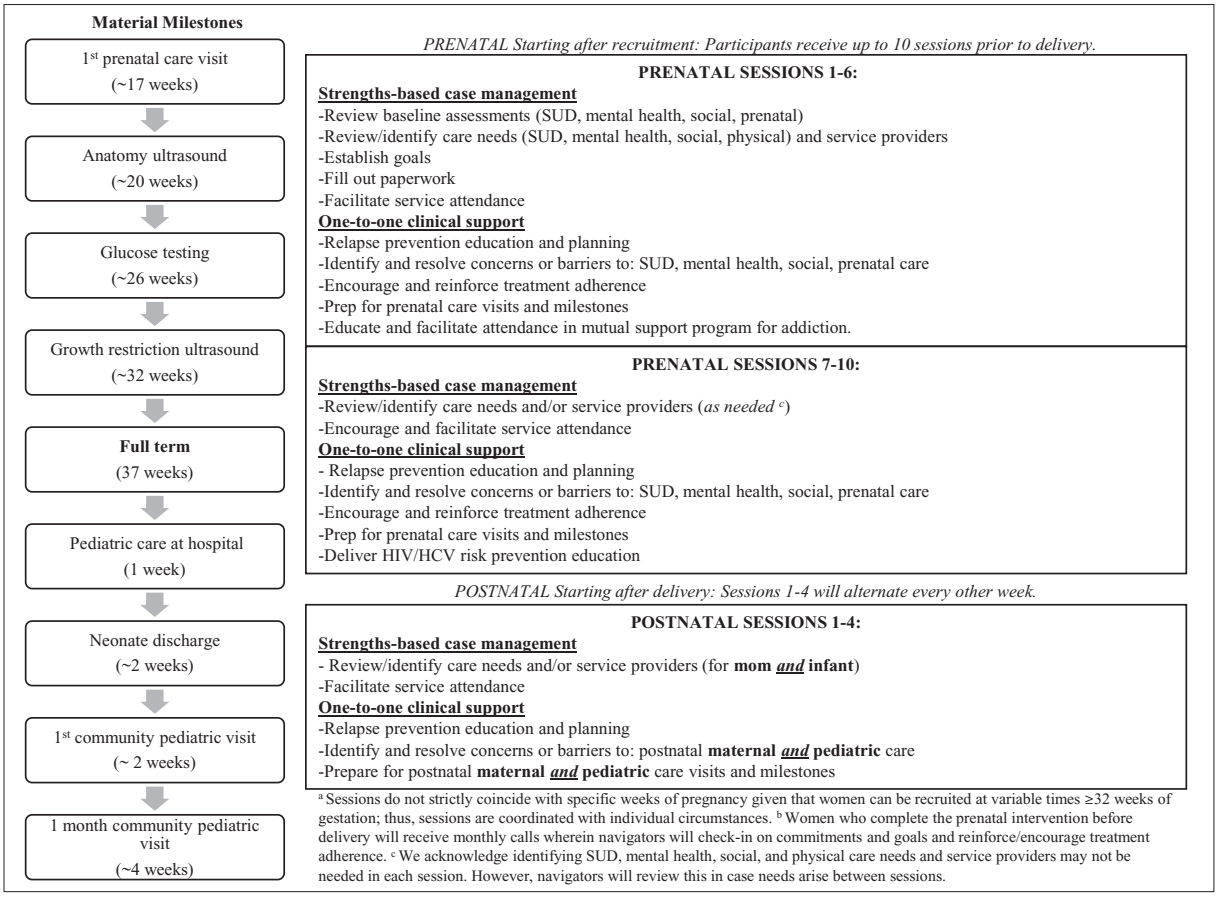

Fig. 2. PN intervention outlining session objectives.

standard care.

3. Discussion

OUD is a treatable chronic condition and pregnancy is an optimal time for behavior change among women [43–50]. Medication for OUD treatment (i.e., methadone or buprenorphine) is key in the care of pregnant women with OUD, but it must also be combined with additional behavioral health services that target psychosocial aspects of addiction [10,11].

Operating within a chronic care paradigm, PN attempts to break down barriers that prevent individuals with OUD from not only accessing medication-assisted treatment (i.e., methadone or buprenorphine), but also from engaging with health, psychiatric, social, and family services that are often not provided through medication-assisted treatment programs [14,15,28,51–53]. To address barriers such as fear/anxiety, communication, transportation, finances, the medical system, and lack of information [14,51,53], navigators develop 1-to-1 relationships to provide personalized support focusing on individual needs [14,15,51,53]. However, PN has only recently begun to be researched in relation to behavioral health problems [29,54–56], such as smoking cessation improvements [57], HIV management [58] and our team's proof-of-concept study that demonstrated intervention feasibility among pregnant women with OUD.

Specifically, our proof-of-concept study findings demonstrated promising initial results for women in a number of behavioral and physical health domains, including improvements in opioid/substance use, mental health, and prenatal care outcomes [20]. This multisite pilot trial study expands upon this previous PN intervention to further establish the internal and external validity of these findings and the potential value of the PN intervention for pregnant women with OUD. Methods for intervention and protocol expansion followed evidence-informed frameworks that facilitated systematic and objective steps. The study intervention also includes added content to prevent drug use relapse among participants, and the protocol has established methods/procedures necessary for conducting a multisite randomized clinical trial to pilot test the PN intervention across two health systems.

3.1. Strengths and limitations

This study includes several strengths. PN is an evidence-based practice that has demonstrated efficacy for a number of other chronic health conditions. Further, unlike most studies that provide medication and/or behavioral/psychosocial interventions during pregnancy, our current study collects outcome information after delivery, for approximately 2 months postpartum. This study likewise advances the field by building upon our preliminary findings by expanding its design to a multisite randomized trial within two regional health systems.

This study also possesses limitations. Recruitment for this study is limited to a convenience sample within the catchment areas of the two tertiary care health systems in urban settings, and thus findings are likely limited in terms of their external validity beyond these regions. We look forward to utilizing what is learned in this study to extend this model of care to larger geographic areas and broader population in future research to strengthen generalizability. We also recognize there may be a broad spectrum of severity of OUD among recruited participants, resulting in varying levels of needs. This variability, combined with limitations of availability of health/social services for participants living outside of urban areas with greater resources, may results in some participants having greater needs, access to treatment, and support than others. We anticipate adjusting outcome analyses for level of engagement in services as well as urbanicity of dwelling.

Notwithstanding these limitations, PN represents a significant potential for aiding pregnant women with OUD to locate, engage, and remain engaged in OUD treatment during pregnancy and the postpartum period.

4. Conclusion

Pregnant women with OUD face a number of significant health and social challenges during pregnancy and following delivery. Interventions designed to collaboratively address and support recovery from this chronic health problem are paramount. Thus, the results of this study testing PN compared to standard care will produce and evaluate necessary protocols/procedures and pilot data preparatory to a large scale, fully-powered, multisite randomized trial. Importantly, this study further establishes the evidence-base—with the potential to ameliorate serious adverse opioid-related outcomes and improve health for women and their children.

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Declaration of Competing Interest

None

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