Title: Replication of an emergency department-based recovery coaching intervention and pilot testing of pragmatic trial protocols within the context of Indiana's Opioid State Targeted Response plan

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Highlights

- This project leverages Indiana's Opioid State Targeted Response efforts.
- Pilot work demonstrates the necessity of flexibility in pragmatic trial design.
- All three milestones were reached and implementation of protocols was successful.
- Data access, recruitment, and identification of hospitals required refinements.
- The subsequent pragmatic trial will help inform ED-based peer supports much faster.

Abstract

Solving the opioid crisis requires immediate, innovative, and sustainable solutions. A number of promising strategies are being carried out by U.S. states and territories as part of their Opioid State Targeted Response (STR) plans funded through the 21st Century Cures Act, and they provide an opportunity for researchers to assess effectiveness of these interventions using pragmatic approaches. This paper describes a pilot study of Project Planned Outreach, Intervention, Naloxone, and Treatment (POINT), the intervention that served as the basis for Indiana's STR-funded, emergency department (ED)-based peer specialist expansion that was conducted in preparation for a larger, multisite pragmatic trial. Through the pilot, we identified, documented, and corrected for challenges encountered while implementing planned study protocols. Per the project's funding mechanism, the ability to move to the larger trial was determined by the achievement of 3 milestones: (1) successful replication of the intervention; (2) demonstrated ability to obtain the necessary sample size; and (3) observe a higher level of engagement in medication for addiction treatment in the POINT group compared to standard care. Overall implementation of the study protocols was successful, with only minor refinements to proposed procedures being required in light of challenges with (1) data access, (2) recruitment, and (3) identification of the expansion hospitals. All three milestones were reached. Challenges in implementing protocols and reaching milestones resulted in refinements that improved the study design overall. The subsequent trial will add to the limited but growing evidence on ED-based peer supports. Capitalizing on STR efforts to study an already scaling and promising intervention is likely to lead to faster and more sustainable results with greater generalizability than traditional, efficacy-focused clinical research.

Key words: Social emergency medicine, recovery coach, peer support, opioid use disorder, medication assisted treatment, pilot study, 21st Century Cures, Opioid State Targeted Response

1.1. Introduction[1]

Signed into U.S. law in December of 2016, the 21st Century Cures Act authorized $1 billion in funding to support prevention and treatment initiatives to curb the opioid epidemic (Bonamici, 2016). Allocation of these funds to U.S. states and territories occurred over 2 years through the State Targeted Response (STR) to the Opioid Crisis grant mechanism managed by the U.S. Substance Abuse and Mental Health Services Administration (SAMHSA, 2016). Thirty-one abstracts from the 57 awarded STR grants mention some form of peer services—i.e., supports provided by paraprofessionals with lived experience in recovery—as being central to their plans (SAMSHA, 2017). Furthermore, 6 of these abstracts specifically highlight plans to implement peer recovery specialists in emergency department (ED) settings. Diffusion of this practice through STR funding presents an excellent opportunity to assess the effectiveness of ED-based peer services. In this paper, we describe a pilot study that leveraged Indiana's opioid STR efforts to lay the groundwork for a pragmatic trial of Project Planned Outreach, Intervention, Naloxone, and Treatment (POINT), an ED-based peer support intervention aimed at connecting people with OUD to medication for addiction treatment (MAT; in the context of OUD treatment, this refers to the use of any of three evidence-based medications: methadone, buprenorphine, or naltrexone). Our experiences conducting this work emphasize the value of flexible research designs when seeking to take advantage of real-world research opportunities such as those presented by the STR funds.

[1] Abbreviations used in this article: emergency department (ED), medication for addiction treatment (MAT), opioid use disorder (OUD), peer recovery coach (PRC), Planned Outreach, intervention, Naloxone, and Treatment (POINT), prescription drug monitoring program (PDMP), standard care (SC), State Targeted Response (STR)

Indiana received approximately $22 million in STR funding to implement its plan to combat the opioid epidemic within its borders. One of the primary components of this plan is the Recovery Coach and Peer Support Initiative (RCSI). The goal of this initiative is to insert peers into the ED setting to engage with patients who present after an opioid overdose and connect them to MAT. The logic underlying this approach is that, given it is a frequent point of contact people living with OUD have with the formal healthcare system (Masson et al., 2002; Mor, Fleishman, Dresser, & Piette, 1992; Sohler et al., 2007), the ED is in a unique position to identify, develop, and implement solutions to improve outcomes for this population (Anderson, Hsieh, & Alter, 2016; Duber et al., 2018). There is indeed burgeoning evidence supporting ED-based interventions for OUD (Hawk & D'Onofrio, 2018), as prior studies have demonstrated feasibility of and patient receptiveness to opioid education and naloxone distribution (Dwyer et al., 2015) and positive outcomes for patients who begin buprenorphine treatment within the ED setting (Berg et al., 2007; D'Onofrio et al., 2017, 2015; Johns, Bowman, & Moeller, 2018). Separate literature demonstrates promising and growing evidence that peers can improve recovery-oriented outcomes for OUD (Bassuk, Hanson, Greene, Richard, & Laudet, 2016; Reif et al., 2014), and these improvements are largely viewed as an effect of peers' ability to better connect with patients than clinicians who do not have lived recovery experience (Powell, Treitler, Peterson, Borys, & Hallcom, 2019; Salzer, 2002; White & Evans, 2014). However, while prior programs have demonstrated some success in implementing peers in ED settings and achieving encouraging service-related outcomes (The Providence Center, n.d.; Powell et al., 2019; Waye et al., 2019), there is no current evidence supporting their effectiveness for improving treatment or recovery outcomes for people living with OUD.

Developed by the second author (KB), POINT is the intervention Indiana drew partial inspiration from when developing the RCSI. Started as a quality improvement initiative at Indianapolis's Eskenazi Hospital in 2016, POINT employs an intensive outreach and follow-up approach facilitated by peer recovery coaches (PRCs) who are trained and certified to assist individuals in addiction recovery (ICAADA, n.d.; Doukas, 2015; Sightes et al., 2017). A member of the POINT team (i.e., a PRC or care coordinator with specialized training) meets vulnerable patients in the ED after opioid overdose and offers them an array of harm reduction-informed services (e.g., risk assessment, HIV and HCV testing, and a naloxone kit) and treatment referrals with follow-up to either a MAT provider, detoxification services, or an inpatient treatment setting. Close collaboration with MAT providers ensures POINT patients have their first assessment within 1-2 business days of ED discharge. After this point, PRCs provide phone or in-person support to navigate barriers to the recovery process, focusing special attention on patients undergoing transitions of care. The entire care transition process takes between 2 weeks and several months, and POINT leaves the door open so patients can re-engage at any time they require help overcoming recovery barriers. POINT also provides supports to patients who are not ready for treatment for the purposes of building a relationship that could lead to MAT linkage at a time when the patient is more accepting of services. At this time, POINT does not initiate MAT within the ED due to health care system and political barriers, which, despite evidence for effectiveness, have prevented the uptake of ED-initiated buprenorphine within much of Indiana and the nation (Lowenstein, Kilaru, Perrone, Hemmons, Abdel-Rahman, Meisel, & Delgado, 2019).

At the end of its first year, the Eskenazi POINT program achieved some notoriety within Indiana due to its early accomplishments. For instance, of 97 patients seen by POINT staff from February to December of 2016, 85% (n =82) agreed to participate in services. Of these, 44% (n = 37) were verified as attending at least one scheduled follow-up appointment and 50% (n =19) of those who made it to their first appointment were still engaged in treatment at 6-month follow-up. Despite these positive early results, POINT and ED-based peer support interventions more generally lack rigorous evidence (i.e., randomized-controlled trials) required to be considered "evidence-based practices." While supporting state-wide implementation of an intervention without demonstrated efficacy could be considered unwise, the reality is that community stakeholders often make decisions to adopt or implement interventions based on factors other than the empirical evidence underlying them. Meanwhile, the gravity of the opioid epidemic requires innovative and promising solutions that can be rapidly scaled, an approach that is incompatible with the traditional research-to-practice pipeline (Office of Science and Technology, 2018; Bonell, Fletcher, Morton, Lorenc, & Moore, 2012; Bowen & Zwi, 2005; Brownson, Royer, Ewing, & McBride, 2006; Milat et al., 2014; Volkow & Collins, 2017). What is required in cases such as this is a more pragmatic practice-to-research approach that can establish an evidence-base for interventions as they are being rolled-out under real-world conditions (Geng, Peiris, & Kruk, 2017; Westfall, Mold, & Fagnan, 2007). As such, the current study seeks to develop the evidence-base for POINT through a pragmatic, multisite clinical trial, a useful approach for making causal inferences within the context of real-world programmatic scale-up (Cheng et al., 2013; Geng et al., 2017). Indeed, this work is supported by a unique funding mechanism from the National Institute on Drug Abuse that recognizes the need for

such approaches, as it only supported projects with strong researcher-state government collaborations that could leverage opportunities made available by STR funding to test approaches to expanding and/or linking clients to MAT (National Institutes of Health, 2017). The government partner in this project is the Indiana Division of Mental Health and Addiction, which is the state entity overseeing STR implementation.

The funding mechanism specifically supports one year of start-up and pilot activities followed by a larger 3-year study. This paper focuses specifically on the 6-month pilot conducted within the first year of funding to prepare our team for a full-scale clinical trial. In the Material and Methods section, we provide an overview of the larger trial as it was conceptualized at the start of the pilot phase before providing specific details related to the pilot. Our results focus on the accomplishment of our pilot goals and necessary adjustments to the proposed design prior to the full trial as determined through challenges encountered related to the implementation of our research protocols and the attainment of 3 pre-identified milestones.

2.1. Material and Methods

This is a 6-month pilot designed to lead to a larger, multi-site cluster randomized trial. As pilots are a scaled-down version of a larger study, all protocols and procedures implemented reflected those we aimed to employ in the subsequent trial, and we therefore describe the methods proposed for the full trial before detailing the approach taken in the pilot.

2.1.1. Proposed clinical trial

Based on the original proposal, the subsequent larger trial was to be conducted at 3 Indiana hospitals comprising the pilot site and two additional hospitals receiving RCSI funding to

be identified at a later date. The trial has two arms: (1) POINT and (2) standard care (SC), consisting of referral to an addiction treatment provider. Time-based cluster randomization happens at the shift-level, with the work day being divided into two shifts (8am-3:59pm and 4pm-11:59pm) so there is always one POINT and one SC shift scheduled each day. Cluster randomization such as this is preferable within the context of a pragmatic trial since it is not practical or ethical to expect ED staff to take time away from care to assign patients to a treatment arm (Bonell et al., 2012; Boutron, Ravaud, & Moher, 2016; Ford & Norrie, 2016; Plaisance et al., 1999; Touzet et al., 2014).

At the time of funding, proposed study eligibility criteria for patients included being: (a) 18 or older; (b) presenting to the ED during the hours of the day the study was running (i.e., 8am to 11:59pm); (c) revived from a non-fatal opioid overdose; and (d) medically stable. Patients were excluded if they were cognitively incapable of providing consent as determined by an ED provider. Eligible patients were to be identified by an emergency medical services alert indicating they had been given naloxone (an opioid-overdose cure) prior to arriving by ambulance to the hospital, and assignment to a study arm determined by the time of ED admission.

Consent for the POINT arm was to be collected by a POINT PRC when they approached the patient for services (PRC services are still offered if the patient does not consent to study enrollment). A waiver of informed consent was sought for the SC arm, as all data were to be deidentified by a third party before transfer to the researchers. In addition, it was determined unfeasible to have ED staff collect consent from patients during the course of care, nor was it ethical for SC consent to be requested by PRCs since asking them to interact with patients and

not provide services might have a negative impact on their personal recovery. All post-ED admission data were to be obtained through secondary sources including: the Indiana Network for Patient Care (i.e., a health information exchange covering a large portion of the state); Medicaid claims; state-level opioid prescribing, as well as criminal justice, child welfare, and county-level coroner data. Together, these sources will help us measure a variety of health-related (e.g., MAT engagement, duration of MAT treatment, subsequent overdose, hospital admissions, and mortality) and social outcomes (e.g., child welfare and criminal justice involvement). This proposed study design, which was tested in the pilot, was approved by the Indiana University Institutional Review Board.

2.1.2. Pilot setting

The setting for the pilot was Indiana University Health Methodist Hospital, a Level I Trauma Center located in downtown Indianapolis, Indiana. Methodist was chosen as the pilot site because: (a) the hospital leadership had already expressed interest in adopting and implementing POINT; (b) Indianapolis EMS has a high rate of overdose encounters, with more than 1,855 people reported to have received naloxone on an EMS run in 2017 (Watson et al., 2018); and (c) it was in close proximity to the research team, allowing for easy identification and correction of issues that might arise related to protocols and procedures.

2.1.4. Pilot measures

As is appropriate for a pilot study (Arain, Campbell, Cooper, & Lancaster, 2010), our focus was largely on **identifying, documenting, and correcting for challenges encountered** that were likely to impede the success of the resulting clinical trial. Additionally, the funding

mechanism required 3 researcher-defined milestones that were to be obtained in order to demonstrate readiness to move from the pilot to the larger study.

Milestone 1 focused on the **successful replication of POINT** at Methodist, defined as successfully implementing 75% of POINT elements that were determined critical through observations of the original Eskenazi program. These 13 elements include: (1) a multi-method system to alert PRCs to ED opioid overdose admissions; (2) dedicated ED office space for POINT staff; (3) initial patient engagement occurs in the ED; (4) PRC-based services; (5) PRCs have lived experience with opioid use; (6) PRCs are philosophical and logistically supported by ED staff; (7) patient choice in services/treatment; (8) transportation provided to initial service/treatment appoints; (9) formal relationship between POINT program and a MAT provider (e.g., specialized referral process, provider involved in POINT administration); (10) walk-in hours for POINT patients established at a *primary* MAT provider; (11) relationships developed with *alternative* treatment providers ; (12) financial support for non-billable services; and (13) naloxone education and distribution.

The goal of **Milestone 2** was to **demonstrate our ability to obtain the necessary sample size** for the resulting trial. The sample size for the subsequent larger trial is n = 712 participants (n = 356 in each arm), which is necessary to provide enough patients to obtain a full year of follow-up data to detect a minimum 6% reduction in subsequent overdose (measured as subsequent ED overdose admissions combined with overdose mortality) at 80% power assuming a 12% rate of subsequent overdose for the SC arm at the 5% significance level (a conservative calculation based on observed subsequent overdose rates at Eskenazi and Indianapolis-wide EMS). We based the sample size on subsequent overdose since it was a

required outcome stated in the funding mechanism and the most distal and difficult of all our outcomes to obtain. Consequently, we should be able to detect a difference in all other variables of interest. To reach the required sample size would require each hospital to enroll average of 4 patients per arm for each month of the larger study. Because Methodist has one of the highest overdose admission rates for the state, we set our recruitment goal for the milestone at n = 30 POINT patients (an average of 5 patients a month over the pilot). We assumed reaching this number would guarantee our ability to also reach sufficient enrollment for SC patients since the proposed waiver of informed consent meant we would not have to worry about refusals in this arm.

Finally, we proposed for **Milestone 3** that there would be **a higher level of MAT engagement in the POINT group**. We defined this as detecting a 10% higher rate in the number of POINT patients who initiated MAT compared to SC. Our focus on MAT initiation, rather than subsequent overdose (the focus of our sample-size calculation), is because it was unlikely we would be able to detect a difference in overdose in just 6 months, whereas MAT initiation would ideally occur relatively soon after ED admission.

3.1 Results

Formal implementation of the program at Methodist began in November of 2017. All PRCs were hired and fully trained by January 20, 2018, and we began offering POINT services on January 12, 2018. Our first patient was enrolled into the study on February 13, 2018. The official end of the pilot was August 31, 2018.

3.1.1. Identified challenges and responses

Overall implementation of the study protocols went smoothly, with only minor refinements to proposed procedures being required in light of specific challenges. These challenges and adjustments fall under three categories: (1) data access, (2) recruitment, and (3) identification of the expansion hospitals.

3.1.1.1. Data access. The first challenge we encountered was learning we would be unable to access methadone treatment data without signed health information releases from study participants per the State of Indiana's interpretation of the 42 Code of Federal Regulations, the legislation pertaining to confidentiality of behavioral health treatment information (e-CFR, n.d.). As such, we were unable to use the proposed waiver of informed consent for the SC arm. In response to this challenge, we hired research assistants to enroll patients on the SC shifts and to provide them with a list of referral resources and information about naloxone use and access (resources are provided regardless of the patient's study consent). While the change requires more staffing and activities, it will allow us to both access the methadone treatment data and to obtain detailed baseline data from SC patients. As such, we constructed a detailed structured interview that included, among other things, questions pertaining to: detailed sociodemographics, social support, living arrangements, substance use patterns and behaviors, context of the current overdose, past overdose experience, treatment history, physical and mental health, and adverse childhood experiences. We also offered patients a $10 gift card as an incentive to complete baseline data collection.

We also experienced a delay in formalizing our relationships with all agencies necessary for obtaining secondary data needed for assessing outcomes. While the agreements were not completed, the process of establishing them was started with every state-level agency

necessary (e.g., Division of Mental Health and Addiction, Office of Medicaid Policy and Planning, and Department of Child Services) except for the state's prescription drug monitoring program (PDMP). The PDMP data were our proposed primary source of identifying subsequent opioid prescribing and engagement in buprenorphine-based MAT. However, we were able to identify an alternate source of obtaining prescribing data through the Surescripts dataset, which is managed by the same organization that manages the Indiana Network for Patient Care, and it includes dispensation data for several large insurance companies. While the dataset is not comprehensive, combining it with Medicaid claims should provide sufficient information for our purposes. As an added benefit, the Surescripts dataset contains information on naltrexone-based MAT, which we would have not been able to detect given our original plan since naltrexone is not a controlled substance and its prescribing is thus not recorded in the PDMP.

3.1.1.2. Recruitment. We faced two specific challenges related to recruitment. The first was that less patients were being admitted to Methodist for opioid overdose than expected. While the reason for this is not clear, it is possible EMS considered Eskenazi to be the *de facto* hospital for overdose runs since they had been providing POINT services for close to 2 years and it was in close enough proximity to Methodist (less than one mile) that distance was likely not a consideration for EMS personnel during patient transport. To account for this and improve enrollment, we broadened our study eligibility criteria to include any individual seeking care for opioid-related issues (e.g., abscess, withdrawal symptoms, endocarditis, opioid intoxication) through the ED and to follow-up and try to recruit patients admitted overnight when staff were not scheduled—this entailed adding the overnight shifts to our randomization procedure. By the end of the pilot, we had recruited a total of 70 participants, 25 were enrolled based on the

new eligibility criteria (e.g., 3 opioid intoxication, 5 endocarditis, 6 opioid withdraw, 11 abscess).

The second challenge was that the ED workflow did not map well to our shift randomization procedures. Specifically, patients were often not ready to be formally approached for study enrollment until 3 or more hours after they were admitted. This posed a problem since a patient admitted during a POINT shift might not be discharged until the SC shift when the PRC was already gone for the day. Because of this, we changed our protocol so that eligibility now depends on the time a person is ready for discharge, rather than the time of ED admission. This change also required us to develop a method for communication between shifts so that PRCs could alert research assistants to patients who were awaiting discharge and vice versa.

3.1.1.3. Identifying expansion hospitals. IU Health applied for and received RCSI funding after the pilot began, and we decided it would be optimal to expand to two other IU Health locations since we already had access to their system through the pilot. However, IU Health had decided to use the RCSI funding to implement telehealth PRCs, which did not fit the POINT model. After a series of discussions, IU Health agreed to withhold telehealth implementation at two of its locations so they could be utilized for the clinical trial. Together, we settled on the hospital locations with the second and third highest rates of opioid overdose admissions after Methodist. However, one of the locations had already established a relationship with a community health provider who was providing PRC services as part of the RCSI, and the city was proposing a moratorium on the number of buprenorphine-based MAT providers that could have negatively impacted treatment referrals (and likely the effectiveness of POINT) if passed.

Given this limitation, we decided to expand to only one hospital and to employ PRCs and research assistants to recruit patients on the overnight shifts to ensure we would be able to meet our numbers.

3.1.2. Milestone attainment

We successfully met all the proposed milestones by the end of the pilot. Regarding **Milestone 1** (i.e., successful POINT replication), Methodist had successfully implemented 10 (77%) of the identified critical elements. Table 1 displays which elements were present and how they were implemented in the Methodist setting.

Table 1

POINT's identified critical ingredients and their implementation at the Methodist site

Identified critical ingredient	Ingredient present at Methodist	Implementation of critical ingredient at Methodist
1. Multimethod admission alert system	Yes	(1) POINT alerted to admission through electronic health record and (2) ED staff can call dedicated line to request POINT staff.
2. Dedicated ED office space	No	POINT space is on behavioral health unit.
3. Patient engagement in ED	Yes	Patients are seen in the ED; however, patients admitted to hospital are followed up with on inpatient unit.
4. PRC-based services	Yes	Two certified PRCs were hired by the hospital for the project.
5. PRCs have lived opioid use experience	Yes	Both PRCs had opioid use experience.
6. ED staff support of PRC	Yes	ED staff demonstrated buy-in by requesting POINT services for patients and cooperating with POINT staff during researcher observations.
7. Patient choice in treatment/services	Yes	Patients are offered information and assistance related to a wide variety of MAT (e.g., methadone, buprenorphine, naltrexone) and non-MAT treatments/supports.
8. Transportation provided to patients	Yes	Bus cards are provided to patients to make initial appointments.
9. Formal relationship with primary MAT provider	No	Relationship with provider who can offer injectable naltrexone is established, but this is not the primary MAT referral source.

10. Walk-in hours with MAT provider	No	Not present
11. Relationships with alternative MAT providers	Yes	PRCs established relationships with 2 methadone clinics and a buprenorphine clinic.
12. Financial support for non-billable services	Yes	Current funding was being provided through research funding.
13. Naloxone education and distribution.	Yes	The pharmacy developed a protocol to ensure naloxone prescribed to POINT patients is billed to the project.

Concerning **Milestone 2** (i.e., obtaining the necessary sample size), Of the 70 patients recruited for the pilot, 46 were enrolled in the POINT arm, which exceeds our original goal of 30 patients. While not a focus of the milestone, it is important to note a total of 26 and 17 of eligible patients declined study participation for POINT and SC arms respectively. Furthermore, 23 eligible patients left the ED before they could be approached and enrolled in the study (reasons for this included patient elopement, fast discharge by ED staff, staff was enrolling another patient), Additionally, a handful of eligible patients were missed because the previous shift for various reasons: 4 were not identified by research staff monitoring admissions; 2 were missed because the research staff was enrolling another patient; and 1 was missed because the days data collection cancelled due to research staffing shortage.

We had to redefine measurement of **Milestone 3** (i.e., higher MAT engagement in POINT arm) given we were unable to obtain secondary data necessary to detect a higher rate of MAT engagement within the POINT group. Instead, we were only able to account for those POINT patients who we knew a PRC had connected with MAT, which was a total of 7 (15%) POINT patients. Given the data limitations, we assumed none of the SC patients successfully engaged in MAT during the pilot, an assumption we were comfortable making since data from the original POINT quality improvement initiative at Eskenazi demonstrated 9% of POINT

patients engaged in MAT compared to < 1% of patients eligible for POINT who did not receive services. In light of this information, we determined Milestone 3 to be accomplished.

4.1 Discussion

One approach to overcoming the slow development and imperfect uptake of scientific evidence for improving OUD outcomes is the use of pragmatic trials to study promising interventions with pre-attained community buy-in while they are being implemented. Such trials require a flexibility not possible in traditional and highly controlled trials (Haff & Choudhry, 2018; Maclure, 2009), and this flexibility often requires a greater focus on external over internal validity (Godwin et al., 2003). The pragmatic trial described above specifically aims to take advantage of Indiana's STR-funded RCSI initiative to understand the benefit of providing ED-based peer supports to people with OUD, a practice that is scaling at a pace faster than the evidence base is developing. Our pilot results demonstrate the necessity of flexibility in pragmatic trials and how required compromises have impacted the design of the larger trial to follow. While challenges are often thought of in a negative light, our identification and ability to address them through alternative solutions is an indicator of our pilot's success.

Challenges encountered and lessons learned resulted in **two major adjustments that will improve the larger trial**. While the consent requirement for accessing state-level methadone data requires more labor in that we have to staff SC shifts with research assistants, we are now obtaining valuable baseline data from patients that will improve our final analyses. We have also expanded our inclusion criteria to anyone entering the ED for an opioid-related issue. This is also considered a strength since broad inclusion criteria are recommended for pragmatic trials to ensure a sample that is more reflective of the type of patient likely to receive

services in real clinical practice (Godwin et al., 2003; Roland & Torgerson, 1998; Ware & Hamel, 2011). Additionally, it provides an opportunity for OUD intervention prior to a person experiencing a potentially fatal overdose.

We also encountered several challenges that have resulted in limitations to our original plan. Our inability to establish and agreement with the PDMP could lead to holes in the data despite our identification of the Surescripts database and ability to obtain Medicaid billing data, the PDMP includes all prescriptions dispensed within Indiana, where the other two databases will only provide information for people with specific types of private insurance and Medicaid. Despite this, we are confident that the majority of opioid prescriptions will be captured due to the large number of patients enrolled in the pilot with Medicaid or Medicaid eligibility (approximately 85%) and the high rate of Medicaid enrollment among those with a substance use disorder in general (Buck, 2011). Despite having access to these other data sources, we are in contact with and continuing to try and establish a data sharing agreement with the PDMP. We are hopeful this can be accomplished before data are required for the final analyses. While accessing the PDMP data would be an improvement, missing data is an unfortunate fact of working with administrative systems that we will need to account for. While the use of secondary data sources is a key limitation of the study overall, unobtrusive data collection methods are preferred in pragmatic trials because remove the burden and artificial aspects of data collection follow-up (Ford & Norrie, 2016). Furthermore, the other secondary data sources we are utilizing will provide a rich array of data on a wide variety of health and social outcomes that are just as important for demonstrating benefits of POINT to stakeholders, which is a key goal of pragmatic trials (Glasgow, 2013; Maclure, 2009; Roland & Torgerson, 1998). Finally, the

change in the admission to a discharge time eligibility indicator could be considered problematic if ED staff are able to hold off a patient discharge during a control shift so that the patient can receive PRC services. However, this is unlikely considering ED staff are not fully aware of the trial procedures that determine eligibility, whether a POINT or SC arm is running recruitment, or what the differences between the two arms are in terms of patient treatment.

The reduction from three to two hospitals harms the generalizability of the subsequent trial by reducing the number of locations from which our sample will be drawn (Roland & Torgerson, 1998; Ware & Hamel, 2011). Moreover, decreasing the number of hospitals will reduce our ability to learn from these modifications and how they might impact patient outcomes. Adaptation is the rule rather than the exception when it comes to program implementation (Aarons et al., 2012; Allen, Linnan, & Emmons, 2012), and Milestone 1's results demonstrate adaptation of POINT is likely to occur at each location in order to ensure an optimal fit within its specific context. While these unplanned adaptations are likely to improve generalizability of the results, we must ensure the hospitals are delivering an intervention that is recognizable as POINT in both locations. To ensure this, we will be conducting fidelity reviews throughout the subsequent trial, documenting deviations and providing guidance for course correction when necessary.

Also concerning Milestone 1, there is a possibility that the inability to replicate three of the 13 identified critical ingredients of the original POINT program (see Table 1) might negatively impact the intervention's resulting effectiveness. For instance, lack of dedicated ED office space could lead to weaker relationships between POINT and ED staff that could benefit care provided. Furthermore, lack of a formal relationship and walk in hours with a MAT

provider means coaches will be required to invest more of their time into health system navigation. And, this will in turn limit time available to provide encouragement and support, which is a central function of their profession (Sightes et al., 2017; White & Evans, 2014). While coaches do have access to a provider of injectable naltrexone, it is likely very few patients will be ready for or accepting of this option because, unlike methadone or buprenorphine, it requires they go through a painful detoxification process prior to administration (Sigmon, Bisaga, Nunes, O'Connor, Kosten, & Woody). That said, at the time of this writing, we are in the process of establishing a formal referral process to a local buprenorphine provider that could potentially ease this issue.

While we met Milestone 2's recruitment goal, we did not include SC patients as a target, and we were low on enrollment in that arm. This has resulted in **three additional modifications** to protocols for the resulting trial. We have (1) modified our SC recruitment script in reaction to these low numbers, and we have seen an improvement in recruitment interactions as a result. To ensure we are better able to identify and engage these patients, we will be (2) conducting in-services with ED staff and (3) receiving weekly ED admission reports (previous data were based on staff recognition and tracking) to analyze and correct for any recognizable patterns of missed patients (e.g., change in staffing, re-training of research staff, ED staff re-education of POINT services).

Finally, the inability to obtain secondary data to assess Milestone 3 was perhaps the most significant challenge encountered in the pilot, as these data would have been useful for predicting POINT's ability to connect patients to MAT—the intervention's primary goal. Typically, this type of pilot information might be used to adjust the sample size for the resulting

trial (Lancaster, Dodd, & Williamson, 2004). However, our sample size calculation was based on the subsequent overdose, which is a more distal outcome. As such, we will likely be able to detect a difference in the groups if it exists given the data indicating the early successes of the original Eskenazi program used to assess Milestone 3.

5.1 Conclusions

The pilot described in this paper has laid the groundwork for a large pragmatic trial of POINT. If successful, this trial will support the evidence-base for the novel and growing practice of ED-based peer support services for connecting people living with OUD to MAT. The pragmatic approach we are taking was made possible by capitalizing on opportunities presented by STR funding, and it is likely to lead to faster and more sustainable results with greater generalizability than a traditional clinical trial would. Researchers seeking to make an impact on the opioid crisis should consider taking advantage of similar opportunities that will become available as subsequent opioid-related funding is inevitably released.

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