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Extended-release naltrexone: A qualitative analysis of barriers to routine use

Kelly Alanis-Hirsch, PhD[1], **Raina Croff, PhD**[2], **James H. Ford II, PhD**[3], **Kim Johnson, PhD**[4], **Mady Chalk, PhD**[5], **Laura Schmidt, PhD**[6], and **Dennis McCarty, PhD**[2]

[1]Duke University School of Medicine

[2]Department of Public Health and Preventive Medicine, Oregon Health & Sciences University

[3]Center for Health Systems Research and Analysis, University of Wisconsin-Madison

[4]Center for Health Enhancement System Studies, University of Wisconsin-Madison

[5]Center for Policy Research and Analysis, Treatment Research Institute

[6]Philip R. Lee Institute for Health Policy Studies and Department of Anthropology, History and Social Medicine, University of California at San Francisco

Abstract

The Medication Research Partnership (a national health plan and nine addiction treatment centers contracted with the health plan) sought to facilitate the adoption of pharmacotherapy for alcohol and opioid use disorders. Qualitative analysis of interviews with treatment center change leaders, individuals working for the manufacturer and its technical assistance contractor, and health plan managers extracted details on the processes used to order, store, bill for, and administer extended-release naltrexone. Qualitative themes were categorized using domains from the Consolidated Framework for Implementation Research (intervention characteristics, outer setting, inner setting, and provider characteristics).

Characteristics of XR-NTX that inhibited use included the complexity of ordering and using the medication; cost was also a barrier. Outer setting barriers reflected patient needs and external health plan policies on formulary coverage, benefit management, and reimbursement. Program structures, the lack of physician linkages, a culture resistant to the use of medication, and unease with change were inner setting elements that limited use of XR-NTX. Patient stereotypes and a lack of knowledge about XR-NTX affected practitioner willingness to treat patients and prescribe XR-NTX. The Consolidated Framework for Implementation Research provided a useful lens to understand and interpret the processes affecting access to XR-NTX.

Corresponding Author: Dennis McCarty, Ph.D., Department of Public Health, Oregon Health & Science University, 3181 SW Sam Jackson Park Road, Portland, OR 97239, 503-494-1177, mccartyd@ohsu.edu.

Disclosures

The other authors reported no conflicts.

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Keywords

naltrexone; extended-release naltrexone; barriers; consolidated framework for implementation research

1.0 Introduction

The Food and Drug Administration (FDA) approved extended-release naltrexone (XR-NTX; Vivitrol®) (an injectable opioid antagonist released over 28 days) for treatment of alcohol dependence (in 2006) and to prevent opioid relapse (in 2010). Oral naltrexone is efficacious (O'Malley et al., 1992; Volpicelli, Alterman, Hayashida, & O'Brien, 1992), and effective when compared to acamprosate (Anton et al., 2006). Studies document the efficacy and tolerability of the extended-release formulation in clinical trials (Garbutt et al., 2005; Lapham, Forman, Alexander, Illeperuma, & Bohn, 2009), effectiveness in primary care for treatment of alcohol dependence (Lee, Grossman, DiRocco, et al., 2010) and use with drunken driving offenders (Finigan, Perkins, Zold-Kilbourn, Parks & Stringer, 2011).

Routine use in clinical practice for alcohol and opioid dependence, however, remains uncommon; a 2007/2008 survey of addiction treatment centers reported that 16% used XR-NTX for some patients (Abraham & Roman, 2010). The 2013 National Survey of Substance Abuse Treatment Services, however, suggests few patients are on the medication; of more than 1.2 million patients in care on March 31, 2013, less than 1% (n = 3,781) received XR-NTX (SAMHSA, 2014). Use for treatment of opioid dependence, moreover, remains stunted despite a randomized placebo controlled trial that demonstrated enhanced opioid abstinence and reduced craving (Krupitsky et al., 2011). In view of the empirical evidence of efficacy and effectiveness, the slow adoption of XR-NTX is disappointing and requires careful assessment of the barriers to routine use.

Medication Research Partnership

Nine addiction treatment centers, a health plan they contract with, and investigators collaborated in the Medication Research Partnership to integrate pharmacotherapies into routine care for alcohol and opioid use disorders. Eight programs were specialty addiction treatment centers providing detoxification and residential rehabilitation and one program provided intensive outpatient and outpatient treatment. When the study began, participating programs routinely used methadone or buprenorphine (n = 8 sites) to facilitate opioid withdrawal (but not as long-term opioid agonist therapy). There was limited use of opioid antagonists primarily for alcohol dependence if patients requested oral naltrexone (5 sites) or XR-NTX (4 sites).

The study sites reported that the approval, ordering, and induction processes for XR-NTX provided unexpected challenges and required development of internal processes and infrastructure to support prior authorization, ordering, receipt and delivery of the medication. To better understand the complexities, we interviewed providers, prescribers, health plan managers and pharmaceutical representatives. Studies on the adoption of medication for the treatment of alcohol and drug use disorder have examined the association of counselor education (Fitzgerald & McCarty, 2009; Fuller, Rieckmann, McCarty, Smith,

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& Levine, 2005), counselor and client attitudes (Rieckmann, Daley, Fuller, Thomas, & McCarty, 2007), organizational characteristics (Knudsen, Abraham, & Roman, 2011; Knudsen, Ducharme, & Roman, 2006)) and financing (Knudsen & Roman, 2012) with use of medications but there is little work on features of the medication and payer systems that can inhibit use.

2.0 METHODS

The Medication Research Partnership tested organizational change strategies to promote enhanced patient access to medications that can support recovery from alcohol and opioid dependence. Because the health plan's headquarters were in the Delaware Valley, the participating providers were drawn from nearby states (Delaware, Maryland, and Pennsylvania). Participating addiction treatment center staff and health plan personnel completed training in organizational change using the NIATx model (Gustafson et al., 2011; McCarty et al., 2007) and received coaching on organizational change, topical webinars, and presentations on the use of medications at four learning sessions.

Transcribed telephone interviews with the change leaders from each study site (n = 39), notes from coaching calls and site visits (n = 75) and program reports during Learning Sessions (n = 23) were reviewed to extract implementation barriers related to XR-NTX. We also interviewed health plan managers (n = 3) and representatives from the pharmaceutical company and its technical assistance contractor (n = 3) to confirm processes for ordering and using XR-NTX. Institutional Review Boards at Oregon Health & Science University, University of California, San Francisco, and University of Wisconsin reviewed and approved the study; Treatment Research Institute deferred to the Oregon Health & Science University review.

2.1 Implementation Support

Learning Sessions—Four Learning Sessions provided an arena for training and cross-collaboration among sites and with the national health plan. The first Learning Session (October 2011), conducted prior to the initiation of change cycles, oriented sites to the project, process improvement strategies, walkthroughs, rapid cycle change projects, and provided tools for tracking action plans and monitoring change. Sites also completed a questionnaire on the services available at the study site and prior experience with medication. In the second Learning Session (May 2012), conducted after completion of the first six-month change cycle, physicians with addiction medicine expertise provided training on the use of medications for alcohol and drug use disorders. Additional presentations addressed strategies for reducing staff resistance and summarized the business case. Participants received copies of papers describing cost-benefits of using pharmacotherapy for treatment of alcohol and opioid dependence. Sites made brief presentations outlining their initial change cycles and plans for the next change cycle. The third Learning Session (December 2012), conducted at the end of the second change cycle, emphasized site presentations and also provided guidance on building partnerships with primary care and sustaining change. The fourth Learning Session (June 2013), conducted following completion of the third and final change cycle, focused on site presentations and

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sustainability plans. The Learning Sessions provided a forum for sites to share their successes and failures and plans for sustaining their successes.

Change Teams—Prior to the initial Learning Session, sites selected an administrator or clinician as a change leader and formed a change team of staff in key positions (e.g., clinic director, chief medical officer, lead counselor, lead nurse) to assist in increasing use of addiction medications. Teams ranged in size from two to five, and met weekly at the beginning of a change cycle. Teams developed and tested organizational changes to support increased use of medications during each six-month change cycle; based on results, they adopted, adapted, or abandoned changes. Change teams determined the method, frequency, and extent to which they promoted the use of medications to agency staff and leadership. Organizational change coaches familiar with the substance abuse field supported change leaders with ongoing assistance through monthly conference calls and a site visit during the second change cycle.

2.2 Interviews

Qualitative interviews were scheduled every seven to nine months; change leaders at four sites completed five of five scheduled interviews, four change leaders completed four interviews and one change leader completed three interviews. The interviews provided qualitative data about site experiences with organizational change and the use of medications. The semi-structured interviews inquired about system changes supporting the integration of medication into addiction treatment, and financial, administrative, and technical barriers to the use of the medication and its sustainability. Interviews were conducted with the change leader at each site to maximize comparability across time. To minimize participation burdens, we did not interview other members of the change teams. Interviews were digitally recorded and professionally transcribed.

Change leader interviews conducted prior to the first Learning Session served as a reference point for agency culture and treatment philosophy prior to receiving implementation support from the Medication Research Partnership. During the 21 month period of change implementation (three 6-month change cycles plus one month to organize and attend Learning Sessions at the end of each change cycle), interviews focused on internal and external barriers to integrating medication into treatment and the strategies utilized to make policy and process changes. In the sustainability period (24 months following the end of the third change cycle) change leader interviews probed internal change processes, involvement of leadership and staff, relationships with the commercial health plan, and strategies to initiate, test, and sustain changes to support use of medications. Overall, the interviews captured transitions in staff and leadership attitudes, level of internal support for changes, the decision-making process, barriers to the use of medication, and the sustainability process to promote continued use of medications.

2.3 Qualitative Analysis

Interview transcripts were coded using Atlas-ti 7.0 software. Standard methods for qualitative analysis were used with a focus on constant comparison to explore similarities and differences across sites (Glaser & Strauss, 1967). Analysis and data collection were

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conducted simultaneously. Four members of the research team coded transcripts that were not from interviews they conducted to allow a wider view of the change challenges and strategies. Coders developed a common coding scheme deductively based on themes from interview guides and inductively from themes repeatedly mentioned during interviews and presentations. The analysts returned to the interview data to confirm and clarify specific themes, collapse similar themes and expand divergent themes. Transcripts were evenly divided among the analysts. Analysts coded the first four transcripts independently to achieve consistency in coding. Repeated iterations of group and individual coding, memo writing, and telephone meetings led to consensus on emergent themes.

Consolidated Framework for Implementation Research—The Consolidated Framework for Implementation Research (CFIR) was developed to facilitate the maturation and standardization of implementation research (Damschroder, Aron, Keith, Kirsh, Alexander, & Lowery, 2009). CFIR's five domains and subdomains (intervention characteristics, outer setting, inner setting, provider characteristics, and the implementation process) provided a structure for the qualitative analysis (Damschroder et al., 2009; Damschroder & Hagedorn, 2011). Because the qualitative analysis focused on the barriers to use of XR-NTX, assessment of the implementation processes (CFIR domain 5) were not included in the analysis. Relevant sub-domains are detailed in the results section but not all sub-domains are essential for implementation of specific technologies. Analysis emphasized features associated with the ordering, shipping, use, and payment of XR-NTX that inhibited use. Quotations and observations from the qualitative interviews illustrate the issues and concerns that contributed to the difficulty of using XR-NTX.

3.0 RESULTS

Four CFIR domains (intervention characteristics, outer setting, inner setting, and provider characteristics) categorized features that affected use of XR-NTX. Specific relevant sub-domains were examined to describe the technological and systemic barriers to routine use of XR-NTX. Some CFIR sub-domains were not apparent in the analysis.

3.1 Intervention Characteristics: Characteristics of XR-NTX

The subdomains for the intervention's characteristics include intervention source, strength of the evidence, relative advantage, trialability, complexity, design and packaging, and cost (Damschroder et al., 2009). In contrast to the simplicity of many oral medications (i.e., write a prescription, fill it at a nearby pharmacy, and swallow a pill as prescribed), XR-NTX is comparatively complex requiring a special ordering process, time for shipping and receipt, and injection process. XR-NTX is also relatively expensive.

Ordering, Packaging and Design—Psychiatry and oncology routinely use medications that require special handling and injection. Medications, however, are used infrequently in treatment for alcohol and drug use disorders, and only XR-NTX requires injection and is ordered through specialty pharmacies. Specialty pharmacies manage delivery and support the distribution of specialty pharmaceuticals; XR-NTX's cold shipping and cold storage requirements include refrigerated warehouses, insulated shipping containers, and temperature data loggers (Edelman, 2004). Because health plans use an assignment of

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benefits for reimbursement, the pharmacy must speak directly to the patient and affirm that the patient requests the medication and authorizes the pharmacy to bill his/her health plan. These requirements increased the time from order to shipping and administration and sometimes reduced the probability of injection.

Specifications around preparing XR-NTX for administration complicated its use. XR-NTX is shipped as a kit containing a vial of dry powder (naltrexone microspheres), a liquid diluent, a syringe, and needles. The kit must be brought to room temperature, approximately 45 minutes, before mixing. Once mixed, XR-NTX must be administered quickly before it becomes unusable. Pharmacies and physicians prefer to mix the medication while the patient waits. Patients were sometimes impatient and left prior to the administration.

Cost—The commercial retail price of XR-NTX (about $1,200 per monthly dose plus physician fees) is relatively expensive. Treatment centers expressed frustration with the expense.

> The clients that I'm talking to want [XR-NTX]. But they can't afford it. No insurance is paying for it, and they can't afford it. ...It's a huge problem right now. Yeah, if it's not [covered by] insurance, we can't refer anybody to [XR-NTX].

Another provider explained that the cost of XR-NTX affected the patient's willingness to use medication to assist in recovery, "If the insurance doesn't pay, ninety-five percent of the people or more are not interested in obtaining medication assisted treatment."

For patients with insurance that included XR-NTX as a benefit, how the medication was covered affected the cost to the patient. As a pharmacy benefit, patients may have a copayment equal to 50% of the medication's retail cost. Because XR-NTX requires a deep muscle injection, however, many health plans cover it as a medical procedure. When classified as a medical benefit, patients may have to pay their medical deductibles before the health plan begins to pay for the medication.

3.2 Outer Setting Domain

The outer setting's subdomains include addressing patient needs, cosmopolitanism (relationships and networking with other corporations), peer pressure, and external policies and incentives. Patient needs and external policies had dominant impacts on the ability to use XR-NTX.

Patient Needs—Use of XR-NTX is more complicated for patients dependent on opioids because naltrexone is an opioid antagonist. If injected prior to the patient being clear of opioids, naltrexone precipitates a withdrawal that can be severe, protracted, and uncomfortable. The package insert recommends that patients be opioid free for seven to ten days prior to the XR-NTX injection. Prolonged detoxification periods increase risk of a return to use. One provider talked about the challenges of keeping someone from using during the critical days before they can be injected safely. This center offered extra support such as daily one-on-one sessions. Despite their efforts, the provider noted that "…many [patients] are lost during those seven days."

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The challenge to induct opioid dependent patients on XR-NTX was compounded by payer changes in the days covered for inpatient detoxification. A program director reported that payers reduced the use of detoxification and inpatient days and told treatment centers to transition patients to intensive outpatient before patients completed seven opioid-free days and could receive an injection. When patients transitioned to outpatient care, some returned to opioid use before they could be medicated. The center felt they were "in a Catch-22" because they were blamed for rapid readmission.

External Policies—Three sets of health plan policies affected treatment centers: 1) health plan coverage (formulary restrictions, cost sharing, and coverage of XR-NTX as a medical or a pharmacy benefit), 2) health plan management (cost-containment policies and preauthorization), 3) claims and reimbursement (billing as a medical benefit or a pharmaceutical benefit).

Health Plan Coverage: XR-NTX is not included on many health plan formularies. As a non-formulary medication the patient must pay for the medication out-of-pocket. Health plans can make formulary exceptions, but this causes increased cost sharing which may be prohibitive to patients. A treatment center change leader expressed frustration at the lack of access to XR-NTX:

> Most HMOs, most other insurances are not paying for [XR-NTX]. It's an expensive medication. And most insurance plans, and government plans, wait until something goes generic before they'll cover it on their formulary. So you've got lots of years down the road to wait before this is going to go generic.

Health Plan Management: Health plan cost-containment policies can deter, complicate, and delay treatments. These processes may not be transparent and may require persistence. Preauthorization processes can inhibit treatment programs and patients from initiating XR-NTX treatment. For specialty treatment providers, navigating the oblique system may take days and delay patient treatment. A residential treatment provider stated,

> …with the whole process of preauthorization, that's a real area of difficulty for me because they, I would have to imagine, intentionally make the process somewhat difficult…I don't want to put my bias, but I think that the insurance companies are hoping that I give up.

His sentiment was not unique. Treatment providers and physicians must document medical necessity and the health plan must concur prior to authorization.

Step therapy can be another health plan barrier. Some health plans require patients to fail at a lower level of treatment or a less expensive medication before approving opioid agonist and antagonist therapy. For XR-NTX, step therapy may require that the patient fail in abstinence-based counseling, and fail with daily dosing of oral naltrexone before authorizing XR-NTX. Fail first requirements increase the risk of return to use, overdose, or death. A provider commented "…for a lot of the commercially insured patients, the payers would ask for a prior [authorization] stating that the person has failed other treatments [before getting]

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[XR-NTX].” He also noted that changes in Medicaid formularies affected patients seeking XR-NTX:

> In March there was a flip-over in [the State’s] managed Medicaid…it cut a lot of the people who were being funded for [XR-NTX] out. Now they’re being required to have failures prior to being able to go straight to [XR-NTX]. … So that’s cut back the amount of people we were able to bring in and put into the [XR-NTX] program.

Health plans may also impose quantity limitations – the maximum allowable quantity of a medication that is covered by one prescription and co-pay. If a prescription is only good for one XR-NTX injection at a time, patients must pay potentially substantial co-pays each month and the complex re-authorization process must be completed each month.

Health Plan Reimbursement—Health plans with restricted access to XR-NTX can require practitioners to “buy-and-bill.” The program or practitioner purchases the medication from a specialty distributor and bills the health plan after a member receives the medication. There is a risk that the claim will be rejected and a risk of storing expensive medication that expires prior to use. Most programs refuse to buy-and-bill because of the financial risks. One residential treatment center addressed this possibility,

> It was also an option for us [the treatment center] to buy [XR-NTX] in bulk and charge the patient, and charge their insurance through the medical [benefit]… But it was like, do we really want to be in the business of holding and dispensing and charging for [XR-NTX]? No, we don’t.

Health plans that have arranged an assignment of benefits use specific specialty pharmacies and allow the pharmacies to assume the patient’s benefit and get reimbursed directly from the health plan. Because the benefits are assigned from the patient, the pharmacy must contact the patient directly and confirm that the medication is desired and that the patient will be able to receive the medication. This confirmation process delayed delivery and when patients were prohibited from receiving telephone calls (as in many residential treatment programs) the inability to speak to the pharmacy prevented the patient from receiving the medication. Although the medication is shipped to a physician’s office, the patient owns the medication and only that patient can receive the medication.

3.3 Inner Setting Domain

Program structure, networks and communications, program culture, and implementation climate reflect the inner setting and affected use of XR-NTX.

Structural Characteristics (Program Structure)—Addiction treatment centers participating in the Medication Research Partnership sometimes struggled with staffing. A large residential program observed that use of XR-NTX required changes in workflow. Nurses required time to educate patients about the medication and secretarial support was necessary to link patients with physicians willing to continue to order XR-NTX in their home communities. The program added a nurse to handle these tasks.

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Change efforts at one small program seemed to halt when staff where out because of vacation or medical leave. The center sought to increase linkages with physicians so patients could continue on XR-NTX. When personnel were out, the center shifted into coverage of basic duties. The change leader explained, "We're a small organization… when staff are out or something happens, it … creates crises." Immediate patient care becomes the priority rather than system change.

Networks and Communications (Linkages to Care)—Residential programs without outpatient services and linkages to primary care physicians found continuity of care challenging. A large treatment center talked about the difficulties in finding aftercare physicians who would continue a patient on XR-NTX. If referrals in the patient's home area could not be located, this site refused to initiate medications. Another residential treatment center surveyed their aftercare resources and reported the difficulty these providers were having finding sufficient referrals to support XR-NTX:

> …most [of our outpatient aftercare providers] do not have physicians that are part of their system to prescribe … or administer [XR-NTX]. Some of them are in the process of finding physicians in the area, particularly like the recovery houses. Like who would be a good physician to send Joe to get his [XR-NTX].

A senior manager at a residential addiction treatment program noted that prior to making a first injection,

> We may have social work call their provider, their family doctor or psychiatrist, whoever, to see if they're able to [provide subsequent injections], because not all physicians are going to do an [intramuscular] injection in their office. And if there's not, the [XR-NTX] website does have a list of people who can do it. There's like injection sites or something. So I might do that. But again, sometimes it's a little further out, so we'll give [patients] the information, [but] we may not necessarily set up that appointment for them.

Finding physicians willing to take XR-NTX patients is even more challenging when that provider must be in the health plan's network.

Once XR-NTX is initiated, many providers believed that the second injection was more important because delays in the medication order, delivery, and coverage process inhibited continuation in care. An outpatient provider said, "[XR-NTX] is going to get you clean for a month. But after that…It's the second month…shot you really need." The second injection is also challenging if patients must make their arrangements to ensure they receive the injection. Lapses in this process were opportunities for the patient to discontinue treatment and return to use.

Program Culture—Four of the nine Medication Research Partnership treatment centers ascribed to abstinence-only philosophies at baseline. A performance improvement director stated that their philosophy was that the ultimate goal of being sober should be to be medication-free and added, "[We're] not going to rush into something because it's the treatment du jour."

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An inpatient program had a problem with staff longevity – staff at all levels of responsibility had worked at the center for decades. These employees were comfortable with the status quo and firmly entrenched in doing things the way "they have always been done". There was little interest in making even small changes.

Another change leader talked about their center's physician culture. For this site, buy-in to use of recovery medications hinged on the endorsement of their physicians. The change team believed that until the physicians accepted and validated the use of medication, they would not be able to focus on any other change projects. "The problem would be is they're not...How do I put this? You can't tell a medical doctor that on day seven you need to prescribe this. You can't do that…."

Implementation Climate (Readiness to Change)—Related to, but separate from, program culture was program readiness for change. Change agents interviewed talked about lack of motivation for change at various levels of their organizations. One site struggled with reticence from the top down. There was no true interest in altering their care model. The change leader at this center was the only staunch advocate for implementing evidence-based medications, but she lacked the power and authority to initiate changes. The center withdrew from the Medication Research Partnership prior to the end of the study.

3.4 Participant (Clinician) Characteristics

Prescriber knowledge and beliefs about the value of XR-NTX, feelings of self-efficacy, individual readiness for change, identification with the organization, and personal attributes contributed to the characteristics that posed barriers to the use of XR-NTX. Limited clinician knowledge and inexperience inhibited self-efficacy and contributed to reluctance to use XR-NTX.

Knowledge and beliefs—Beliefs and stereotypes about patients with alcohol and drug use disorders inhibited the willingness of primary care practitioners to use XR-NTX. A spokesperson for the manufacturer explained that prescribers envision patients that require more time and may be disruptive to their practices. XR-NTX induction, moreover, was perceived as time intensive. He believed that pharmacies were reluctant to get onboard with XR-NTX for similar reasons.

Self-efficacy—In addition to general lack of knowledge about medications, there was insecurity around the medication. Physicians lacked self-efficacy when it came to XR-NTX. A Clinical Director explained that some of the center's physicians were likely to continue a patient on medication that had already been prescribed but would not start patients on recovery medications. This center made it the responsibility of the detoxification physician to initiate XR-NTX and other medications. The other physicians supported this decision and expressed relief at not having to prescribe XR-NTX and induct patients.

4.0 DISCUSSION

CFIR provided a useful lens to categorize and interpret the processes involved in the implementation of XR-NTX in addiction treatment centers contracting with a national health

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plan. Implementing any new technology or evidence-based practice is difficult and complex interventions are more challenging to implement (Rogers, 2003). The obstacles seemed magnified with XR-NTX. Effective use of XR-NTX requires programs to navigate prior authorization processes, learn how to order the medication, network with medical practices to continue injections in the community, and foster an organizational culture that supports its use.

Although our analysis generated a litany of issues and obstacles that inhibit use of XR-NTX, resources to facilitate use are available to treatment providers. The manufacturer of XR-NTX contracts for a service to facilitate insurance approvals, verify reimbursement, route the prescription to the appropriate pharmacy (different plans use different pharmacies), enroll eligible patients in the [XR-NTX] Value Program (coupons to help cover co-pay expenses), and locate a practitioner to provide the injection. The manufacturer's local representatives also assisted treatment centers. One center worked closely with the representative to train staff and develop a system for ordering XR-NTX and linking with physicians:

> The rep came in. We had an education session for the staff, just like why do we use it? What are the statistics on it? What are the side effects? What are the pros and cons? How do you find a provider in your community? … The rep…helped us set up a system you know…the specialty pharmacy and just how to do things. We had her come in to do staff education with the nurses. She was just here to do some staff education with the counselors. And she's committed to coming once a month, for a period of months, to talk to staff, answer any questions and receive any feedback or anecdotal information that staff wants to give her.

Medications to assist in recovery from alcohol- or opioid-use disorders remain under-utilized and struggle to gain ground. Staff members at all levels within organizations were reticent about medications and not seeing their use as "real" recovery. Many were rooted in care as usual and reluctant to change. Physicians were insecure about prescribing medications due to their lack of knowledge and training. Successful patient experiences helped treatment center personnel see the value of XR-NTX for treatment of alcohol and opioid dependence. Treatment centers that were more effective in moving the use of XR-NTX into routine clinical care created an infrastructure to support authorization, ordering, and timely injection. In addition, nurses were trained to provide patient and family education and to encourage patients to include pharmacotherapy in treatment plans.

4.1 Limitations

Study limitations include a small sample of treatment centers and change leaders. Provider interviews were usually conducted with the same change leader at each site. While working with the same respondent over time improved comparability of interview responses for each site during the course of the study, and improved comparability between sites, this strategy may have introduced systematic bias. To the best of their ability, change leaders spoke on behalf of their staff and patients about the barriers, facilitators, and attitudes regarding the use of XR-NTX in recovery, but staff and patient perspectives may have been limited or misconceived. It may be helpful in future studies to capture patients' perspectives from

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patients and to include families' impressions about the use of XR-NTX. The small geographic area (Delaware, Maryland, and Pennsylvania) may also limit the study's generalizability. Finally, the change projects were tailored to each participating program and were not standardized.

4.2 Conclusion

As a specialty medication, XR-NTX poses logistical complications that require coordination among many entities to ensure the injection is delivered appropriately and timely. Systems of care (i.e., specialty pharmacy, treatment center, insurance provider, injection clinician) must work closely to ensure that patients receive their medication in a timely and appropriate fashion. Coordinating care across so many divergent systems with their own internal policies, procedures, and requirements remains a challenge.

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Highlights

- The Consolidated Framework for Implementation Research structured a qualitative analysis of features of extended-release naltrexone that inhibited use for the treatment of alcohol and opioid use disorders.
- The processes of ordering, storing, and using and the cost of extended-release naltrexone were characteristics of the intervention that reduced use.
- Features of the outer setting (environment) that inhibited use included requirements for patients with opioid use disorders to be opioid free for seven to ten days and health plan formulary, benefit management, and reimbursement policies.
- Program cultures, resistance to change, and weak linkages with primary care for ongoing injections also affected routine use of the medication.