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Implementation and evaluation of Missouri's Medication First treatment approach for opioid use disorder in publicly-funded substance use treatment programs^{*,**,***}



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ABSTRACT

Background: Leaders of Missouri's State Targeted Response to the opioid crisis (STR) grant have prioritized increasing access to treatment medications for opioid use disorder (MOUD) through a "Medication First" approach. This conceptual framework prioritizes rapid, sustained, low-barrier access to MOUD for optimal impact on decreased illicit drug use and mortality. Medication First principles and practices were facilitated through state-level structural changes and disseminated to participating community treatment programs via a multipronged, multi-disciplinary approach. In the first nine months of STR, 14 state-contracted treatment agencies operating 38 sites used STR funding to implement the Medication First model.

Methods: We utilized state billing and service data to make comparisons before and during STR on the following outcomes: MOUD utilization, timely access to MOUD, amount of psychosocial services delivered, treatment retention at 1, 3, and 6 months, and monthly price of treatment. We conducted follow-up analyses examining differences across MOUD types (no medication, methadone, buprenorphine, oral naltrexone, mixed antagonist + agonist, and extended release naltrexone).

Results: During STR, MOUD utilization increased (44.8% to 85.3%), timeliness of MOUD receipt improved (Median of 8 days vs. 0 days), there were fewer psychosocial services delivered, treatment retention improved at one, three, and six month timeframes, and the median cost per month was 21% lower than in the year prior to STR. All differences were driven by increased utilization of buprenorphine.

Conclusions: Findings suggest Medication First implementation through STR was successful in all targeted domains. Though much more work is needed to further reduce logistical, financial, and cultural barriers to improved access to maintenance MOUD, the steps taken through Missouri's STR grant show significant promise at making swift and drastic transformations to a system of care in response to a growing public health emergency.

1. Introduction

1.1. SAMHSA funding to address the opioid overdose crisis

Over the past decade, the U.S. has witnessed an exponential rise in opioid overdose deaths, with record numbers of Americans dying each year (National Institute on Drug Abuse, 2018). The diffusion of highlypotent illicit fentanyl in the Midwest and other parts of the country has contributed to the steep increase in fatalities. To address this crisis, the Substance Abuse and Mental Health Services Administration (SAMHSA) awarded funds in the form of State Targeted Response (STR) grants in May of 2017 to all states and territories. Missouri's first STR priority was to expand access to evidence-based medications for Opioid Use Disorder (MOUD) (Stringer, 2018; Winograd et al., 2019). This paper

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focuses on the treatment outcomes associated with Missouri's "Medication First" (MedFirst) approach, developed and implemented through STR to expand rapid and sustained access to MOUD.

1.2. Unmet need for OUD treatment and health disparities in Missouri

Buprenorphine (including buprenorphine-naloxone), methadone, and extended-release (XR) naltrexone are the three medications for opioid use disorder (MOUD) approved by the U.S. Food and Drug Administration (U.S. Food & Drug Administration Center for Drug Evaluation and Research, 2018). Maintenance pharmacotherapy. meaning use beyond the withdrawal period, with buprenorphine or methadone are the most effective treatments available to people with OUD (Amato, Minozzi, Davoli, & Vecchi, 2011; Mattick, Breen, Kimber, & Davoli, 2014). Buprenorphine, a schedule III substance under the Controlled Substances Act, is an increasingly preferred treatment option because of its greater accessibility relative to methadone, which is a schedule II medication limited by strict federal regulations (Fiscella, Wakeman, & Beletsky, 2018; Nosyk et al., 2013), and ease of initiation relative to XR naltrexone, which requires a lengthy abstinence period prior to initiation (Lee et al., 2018). Buprenorphine and methadone in particular reduce fatal opioid overdose rates by 50-70% (Sordo et al., 2017), reduce illicit drug use, increase treatment retention, and improve psychosocial outcomes (Connery, 2015; Fiellin et al., 2014; Weiss et al., 2015). However, XR naltrexone can be effective in preventing relapse for those who are able to overcome the induction hurdle (Lee et al., 2018).

Utilization of MOUD in Missouri prior to STR funding was low in 2016, despite the state ranking in the top half of the nation for opioid overdose fatalities (19th) (Henry J Kaiser Family Foundation, 2019). According to data from the Missouri Department of Mental Health (MODMH), only 17% of uninsured individuals with OUD receiving care in the public substance use disorder (SUD) treatment system were prescribed buprenorphine, and of those, 78% received fewer than five prescriptions.

Health disparities across race and socioeconomic status are also evident in Missouri. Although rates of fatal opioid overdoses are higher among Whites nationally, Missouri is one of eight states exhibiting higher rates of fatal overdose among non-White individuals, a disparity that has been increasing annually since 2015 (Henry J Kaiser Family Foundation, 2019). This disparity is most pronounced among Black males in Missouri, whose overdose death rate is nearly three times that of White males (19.5 vs 6.7) (Bureau of Vital Statistics Missouri Department of Health and Senior Services, 2018). Missouri is one of 14 states without Medicaid expansion, and the existing Medicaid eligibility requirements are among the most stringent in the country (Brooks, Touschner, Artiga, Stephens, & Gates, 2015). Consequently, according to MODMH data, 9% of the adult population, and approximately 60% of those with OUD in the MODMH specialty SUD treatment system, are uninsured. SUD services for the uninsured are primarily funded through SAMHSA block grants awarded to the MODMH and distributed to SUD agencies in annual allocations.

MODMH and contracted university-based partners developed Missouri's MedFirst treatment approach, financial incentives, and implementation guidelines to expand uninsured client access to MOUD. MedFirst was designed for implementation in Missouri's publiclyfunded SUD treatment programs. Twenty-five of these SUD agencies operate 190 sites state-wide and treat upwards of 6000 uninsured individuals with OUD each year. These agencies were targeted for STR funding and MedFirst implementation because of their existing contractual relationships with MODMH, their considerable experience providing comprehensive care to uninsured clients, and their statewide reach. The MedFirst approach has required agencies which historically provided "drug free" psychosocial treatment (Hubbard, Craddock, & Anderson, 2003) to integrate maintenance buprenorphine therapy into their treatment model. MODMH has sought ongoing improvement in the implementation of MedFirst principles by soliciting feedback from providers and clients and by formally evaluating key MedFirst treatment outcomes.

1.3. The medication first approach

The MedFirst treatment approach for OUD is analogous to the Housing First model for chronic homelessness (Winograd et al., 2019). In a randomized controlled trial of a housing first model, participants who received housing contingent upon participation in SUD treatment spent more time homeless and less time stably housed than participants who received housing without contingencies (i.e., Housing First); notably, substance use outcomes did not differ between the groups (Tsemberis, Gulcur, & Nakae, 2004). Missouri's MedFirst approach is based on the observation that clients often discontinue buprenorphine therapy involuntarily due to strict program requirements, leading to preventable client relapse (Bentzley, Barth, Back, & Book, 2015). The MedFirst principles prioritize and protect client access to pharmacotherapy independent of other service participation.

The four key principles of the Medication First approach are:

- 1) Clients receive pharmacotherapy as quickly as possible, prior to lengthy assessments or treatment planning sessions;
- Maintenance pharmacotherapy is delivered without arbitrary tapering or time limits;
- 3) Individualized psychosocial services are offered but not required as a condition of pharmacotherapy.
- Pharmacotherapy is discontinued only if it is worsening the client's condition.

The MedFirst principles are consistent with the treatment guidelines of SAMHSA (2018), the American Society of Addiction Medicine (Kampman & Jarvis, 2015), and the World Health Organization (2009): these guidelines emphasize the need to treat OUD clients with MOUD as quickly as possible and for as long as it is beneficial. Nationally, low barrier/low-threshold treatment has been promoted in primary care and other office-based medical settings to expand client access to buprenorphine treatment as widely as possible (Korthuis et al., 2017). Success with interim methadone and buprenorphine programs, in which people with OUD receive MOUD while on waiting lists, demonstrates the value of timely access to medications even if the client receives no other services (Schwartz et al., 2006; Sigmon et al., 2016). Indeed, the foundation of MedFirst is low-barrier/low-threshold access, but MedFirst principles were distinctly developed to help traditionally psychosocial-only treatment programs (as opposed to medical settings) implement pharmacotherapy in accordance with best clinical practices. Importantly, the emphasis of MedFirst is also on chronic, uninterrupted maintenance MOUD care, and not merely low-barrier entry into MOUD treatment.

1.4. Concerns about the MedFirst approach

Critics of MedFirst contend a low-barrier approach to MOUD delivery offers superficial symptom management without addressing core issues. In particular, the MedFirst principle (#3) that psychosocial services should be offered *but not required* leads critics to interpret the approach as "Medication Only" (Knopf, 2018). MODMH and the STR team have worked to challenge this interpretation by highlighting that if medication comes *first*, it is implied that other services will follow. We underscore that agencies should continue to offer, promote, and even assertively encourage psychosocial services as appropriate for individual clients – just not make continued MOUD contingent upon participation in those services. We also stress how sessions with nurses, physicians, and other medical professionals can themselves be therapeutic and are valuable for more than just the medication provided, as pharmacotherapy facilitates rather than obstructs mutual support, engagement, and psychosocial rehabilitation (Parran et al., 2010). However, we also note in our messaging that some clients might be unwilling or unable to participate in counseling or other non-medical visits, particularly early in their recovery. For these individuals, Med-First could entail "Medication Only" temporarily or for their entire course of treatment; providers should continue to prescribe MOUD and offer appropriate psychosocial services where clinically indicated – nothing more, nothing less.

Another criticism of low-threshold treatment approaches such as MedFirst is the potential for increased diversion of buprenorphine. However, research suggests the secondary harm resulting from buprenorphine diversion has been negligible, as illicit buprenorphine is most often used to self-treat withdrawal (Cicero, Ellis, & Chilcoat, 2018). Concerns about diversion are further mitigated when they are weighed against the astronomical societal costs of untreated OUD (Hospital Industry Data Institute, 2018).

1.5. Provider, organization, and system interventions to overcome barriers to implementing the medication first approach

Our objectives in the creation and dissemination of the MedFirst approach were to develop a digestible and actionable clinical OUD treatment framework that could be adopted quickly and be sustained post-STR funding. Thus, STR leaders developed several implementation strategies (large and small trainings, webinars, technical assistance, consultation, written implementation guidelines, etc.) meant to help clinical and administrative staff overcome anticipated barriers. Barriers to buprenorphine utilization commonly described in the literature are also found in Missouri, including provider-level attitudinal barriers (e.g., perceptions that use of MOUD is not "real" recovery) and knowledge barriers (e.g., providers are unaware of treatment medications and/or their uses) (Aletraris, Edmond, Paino, Fields, & Roman, 2016: Huhn & Dunn, 2017: Rieckmann, Kovas, McFarland, & Abraham, 2011; Roman, Abraham, & Knudsen, 2011), agency-level barriers such as the administrative burden of MOUD delivery (Hutchinson, Catlin, Andrilla, Baldwin, & Rosenblatt, 2014; Knudsen, Abraham, & Oser, 2011), and systemic, structural barriers such as federal- and state-instituted regulations limiting the ability to widely prescribe MOUD (Haffajee, Bohnert, & Lagisetty, 2018; Huhn & Dunn, 2017; Knudsen & Abraham, 2012). To effect significant change in the SUD treatment system, STR leaders prioritized reducing barriers at all three levels.

1.6. Training and consultation to address provider-level knowledge and attitudinal barriers

Treatment provider favorability towards methadone and buprenorphine is associated with the extent of provider training on the medications (Aletraris et al., 2016; Knudsen, Ducharme, Roman, & Link, 2005; Knudsen, Knudsen, Ducharme, & Roman, 2007; Rieckmann et al., 2011). Thus, to address gaps in knowledge about MOUD and, indirectly, reduce attitudinal barriers to MOUD, STR leaders developed a multimodal, multidisciplinary training curriculum (called Opioid Crisis Management Training [OCMT]) in collaboration with consulting physicians, nurses, counselors, social workers, and people who use drugs and/or are in recovery. The training curriculum includes a content lecture on the role of brain chemistry in opioid addiction, the science of MOUD, the role of the counselor in treating OUD, a panel of individuals sharing how MOUD has helped them achieve recovery, and profession-specific breakout sessions to promote dialogue and problemsolving about MedFirst implementation. Preliminary evaluation shows OCMTs improve knowledge and attitudes surrounding MOUD and serve as an opportunity to connect with providers and encourage utilization of our ongoing training and consultation services. OCMTs are approximately four hours, with subsequent training, webinars, consultation, and clinical shadowing opportunities ranging in length, format, and content based on the needs of requesting providers.

1.7. Steps to address agency-level barriers

To support MedFirst implementation, STR leaders and expert consultants assessed program readiness through "Environmental Scans" and site visits, hold bi-monthly, statewide open "Office Hours" calls to discuss administrative and clinical questions, and provide data-driven, program-specific "Treatment Barometers" comparing data from Pre-STR and STR timeframes. Many state-contracted SUD agencies are in rural areas where transportation and access to waivered prescribers are limited. Thus, to increase access to care and reduce frequency of canceled or "no-show" appointments, STR funds were used to purchase telemedicine equipment and reimburse agencies for client transportation. Additionally, cross-agency collaboration was facilitated to increase prescriber capacity.

1.8. Process, policy, and procedural changes to address structural and systemic barriers

STR leaders anticipated several structural and systemic barriers to implementing MedFirst. These included: 1) State billing procedure requirements for formal, comprehensive assessments during intake; 2) buprenorphine prior authorizations and step-down dosing requirements in Missouri's Medicaid program; 3) over-utilization of group services, non-medical detoxification, and residential services; 4) high administrative burden coupled with low reimbursement rates for medical services; and 5) a dearth of buprenorphine waivered providers in Missouri (Pearson & Brantley, 2018). To address Barrier #1, MODMH altered State billing requirements to allow 30 days for completion of STR client assessments, facilitating faster client access to medical providers. Regarding Barrier #2, through collaboration with the Missouri Medicaid program, prior authorizations for initial buprenorphine prescriptions were removed, as were requirements for step down dosing and tapering plans. (Though uninsured individuals were the target of STR treatment funds, STR leaders also worked simultaneously to remove barriers in the Medicaid system.) Over utilization of group services, non-medical detoxification, and residential services (Barrier #3) was addressed by removing these from the STR services menu and only allowing for their reimbursement through existing agency allocations. To begin to remedy Barrier #4, MODMH increased the provider administrative payments on medical services from 7% to 15% for the STR program. Last, STR leaders addressed Missouri's lack of buprenorphine prescribers (Barrier #5) by offering state-sponsored DATA 2000 trainings and a \$500 reimbursement to medical providers who obtained their waiver. These system-level changes, coupled with the provider- and agency-focused efforts, aimed to incentivize best practice and remove as many obstacles to MedFirst implementation as possible.

1.9. Study objectives

We compared treatment delivery and outcomes prior to and during STR funding among participating agencies. We anticipated clients whose treatment was supported by STR would have increased access to MOUD. Consistent with research on low-barrier/low-threshold models of care (e.g., Bhatraju et al., 2017; Korthuis et al., 2017), we predicted that MedFirst would improve key aspects of OUD treatment, including time to MOUD, utilization of mandated psychosocial services, treatment retention (Mattick et al., 2014; Timko, Schultz, Cucciare, Vittorio, & Garrison-Diehn, 2016), and monthly cost of treatment (Dunlop et al., 2017; Vashishtha, Mittal, & Werb, 2017).

To test these hypotheses, we compared five outcomes of interest in publicly-funded SUD treatment agencies before and during STR. These outcomes were: 1) rate of receipt of MOUD; 2) time between the first billable service and the first MOUD prescription; 3) hours per day of psychosocial services in the first month of treatment; 4) rates of retention in treatment at one, three, and six months; and 5) cost per month of treatment.

2. Material and methods

2.1. Participating programs

Treatment programs were approved for STR funding on a rolling basis after demonstrating readiness to implement MedFirst through a written "Environmental Scan," a site visit from STR and MODMH personnel, and an analysis of previous and current MOUD billing data.

As of March 31, 2018, 38 treatment sites across 14 agencies had been awarded access to STR funding (see full map and list here: https:// missouriopioidstr.org/treatment). To effectively execute the MedFirst approach, programs were encouraged to develop core competence in the medical management of OUD, which includes training staff, restructuring clinical protocols, and collaborating with medical providers in the community who are waivered to prescribe buprenorphine. The long-term goal was sustainable statewide implementation, so that programmatic and policy changes occur regardless of whether a program had access to STR funds, and continue after the STR funding period has ended. Therefore, to achieve long-term sustainability, all state-contracted agencies had access to STR-funded technical assistance and consultation, trainings, and community provider education and events.

2.2. Data source

The dataset used for analyses was structured at the episode of care (EOC)-level, inclusive of all services received by an individual beginning at the time of enrollment. This dataset combines data from the following four State-level datasets, which included information collected and/or provided by treatment agencies and managed by the MODMH: 1) The State-level SUD billing records dataset, which includes billable treatment service entries for clients with OUD in publiclyfunded SUD treatment programs in Missouri; 2) Client-level diagnosis data; 3) Client-level demographic data collected for the federally-required Treatment Episode Data Set (TEDS); and 4) Missouri Medicaid data provided to MODMH that includes all pharmacy claims billed through Medicaid for clients with OUD in the MODMH system. Because agencies have differing policies regarding when clients are officially "discharged" in their system, we standardized the definition of EOCs across agencies to enable accurate comparisons. For our study, if there was a 45-day gap in services, the EOC was deemed over on the date of the last billable service. New EOCs were defined as a treatment episode beginning at least 45 days after the last billable service. The University of Missouri, St. Louis IRB approved this study to conduct secondary data analysis.

2.2.1. Sample inclusion criteria

EOCs were compared as either Pre-STR EOCs (i.e., treatment as usual) or STR EOCs. Pre-STR EOCs were included in the analytical dataset if they met the following criteria: 1) they occurred at one of the 14 STR-funded SUD treatment agencies (to enable within-agency comparisons to STR EOCs); 2) they began in the first nine months of the year prior to STR implementation (i.e., during the 2017 fiscal year, July 2016 through March 2017); 3) they involved clients who, based on the MODMH diagnoses dataset, had any active (i.e., not in remission) diagnosis of opioid abuse, opioid dependence, opioid withdrawal, or OUD.

STR EOCs were included in the analytical dataset if they met the following criteria: 1) they were STR-funded (i.e., treatment services were billed to the STR grant); 2) they occurred at one of the 14 STR-funded SUD treatment agencies; 3) the first billable service for the EOC fell between July 1, 2017, aligning with the start of STR-funded treatment, and 9 months later, March 31, 2018, 4) they involved clients who, based on the MODMH diagnoses dataset, had any diagnosis of opioid abuse, opioid dependence, opioid withdrawal, or OUD; 5) they involved clients who, if they transferred to a different, non-STR funded

program (including transferring between program types within a single agency), had at least two weeks of STR-billed services before transferring. The last criterion was chosen due to the MedFirst approach theoretically having the largest impact in the first month of treatment. We included EOCs with start dates in equivalent nine-month periods for Pre-STR and STR to ensure we had an equal amount of data for each timeframe (up to 12 months of services).

2.2.2. Exclusion criteria

Because our target population was uninsured individuals, we identified and excluded all clients with any medications or services paid by Medicaid during the timeframe (i.e., Pre-STR or STR) of their EOC. Additionally, we identified clients who had a concurrent Medicaid pharmacy claim for any medication during the identified Pre-STR or STR study timeframes, and excluded all of their EOCs. This exclusion criteria did not apply across fiscal years. Thus, if an individual with a Pre-STR EOC did not have a Medicaid pharmacy claim during that fiscal year, but had a Medicaid pharmacy claim in the subsequent fiscal year, they would still be included in the Pre-STR sample.

Additionally, to ensure that Pre-STR EOCs represented treatment as usual in the year prior to STR implementation, we excluded any Pre-STR EOC that had billable services through specialized federal grant programs or initiatives that were specifically designed to incentivize medication utilization (e.g., through the Medication Assisted Treatment-Prescription Drug and Opioid Addiction grant, awarded to two Missouri agencies). We also excluded EOCs that included concurrent services from non-STR and STR programs.

Due to the nature of defining an EOC as the unit of analysis, some unique clients were represented in multiple EOCs (2185 of 2502 [87%] clients have only one Pre-STR EOC; 1186 of 1298 [91%] unique clients have only one STR EOC) as well as be present in both the Pre-STR and STR groups (n = 150). Of the individuals involved in multiple episodes, most were involved in two EOCs (91% of individuals with > 1 EOC pre-STR and 92% of individuals with > 1 EOC during STR).

2.3. Pre-STR and STR outcomes

2.3.1. Medication prescribed

We examined the frequency of specific types of MOUD across EOCs by creating the following medication groups: (1) no medication, (2) oral naltrexone, (3) extended-release (XR) naltrexone, (4) buprenorphine + naltrexone, (5) buprenorphine, and (6) methadone. Thus, we refer to "buprenorphine EOCs," "XR naltrexone EOCs" etc. Approximately 8.6% of EOCs (367 of 4251) involved more than one medication. If the multiple medications prescribed within an EOC shared a mechanism of action, then the EOC was categorized with the medication that is generally associated with greater length of treatment retention. Specifically, if an EOC involved both oral naltrexone and XR naltrexone, it was grouped with XR naltrexone as this is the more effective of the two medications in treatment retention (Connery, 2015; Minozzi et al., 2011; Morgan, Schackman, Leff, Linas, & Walley, 2018). If an EOC involved both methadone and buprenorphine, it was grouped with methadone due to its superior retention rates (Timko et al., 2016).

There were 161 (97 Pre-STR, 64 STR) buprenorphine + naltrexone EOCs, which involved both antagonist (XR naltrexone or oral naltrexone) and agonist (all but one involving buprenorphine) medications, meaning an individual switched from one medication to another. Sixty-one percent of both Pre-STR (n = 59) and STR (n = 39) buprenorphine + naltrexone EOCs involved buprenorphine *followed by* naltrexone, while 18% of Pre-STR EOCs (n = 17) and 16% of STR EOCs (n = 10) involved naltrexone *followed by* buprenorphine. The remainder of the EOCs involved alternating prescriptions between buprenorphine and naltrexone products. Finally, one Pre-STR EOC involved oral naltrexone followed by methadone. These "mixed" EOCs are grouped separately due to heterogeneity in mechanism of action.

2.3.2. Time to medication access

The MedFirst approach calls for rapid access to MOUD for individuals seeking OUD treatment. Therefore, we assessed how quickly medications were prescribed in Pre-STR EOCs compared to STR EOCs. Time to medication access was defined as the number of days between the first billable service and the first billable medication prescription. We report overall mean and median days to medication for all EOCs, and days to first medication within each MOUD group. Because the focus of Missouri's STR funding was to expand maintenance MOUD in outpatient programs, and to deter overutilization of detoxification programs, our analysis of time to medication excluded medications prescribed in a detoxification setting.

2.3.3. Receipt of psychosocial services

We examined the mean and median number of hours of psychosocial services received per day in the first 30 days of a treatment episode. Psychosocial services were defined using billable service codes and included all types of individual counseling, group counseling, group education (even though group services were not reimbursed through STR they may still have been provided and paid from other funding sources), family counseling, community support, case management, and peer support services. Additionally, since opioid treatment programs (OTPs), which provide methadone, have historically provided less intensive psychosocial services than traditional SUD treatment programs, we compared group differences in the receipt of psychosocial services during the first month of treatment separately for OTPs and non-OTPs.

2.3.4. Treatment retention

We report overall treatment retention for Pre-STR and STR EOCs. Treatment retention is dichotomous and was defined based on whether there were continued billable services one, three, and six months after the first billable service. We then compare Pre-STR and STR treatment retention at each of these time points by MOUD group. Cutoff dates for included services and the start date of a treatment episode determine whether treatment retention could be assessed for any given EOC. Treatment retention estimates at one and three months were available for 100% of Pre-STR and STR EOCs. Treatment retention at six months was able to be determined for 64% of Pre-STR EOCs and 56% of STR EOCs.

2.3.5. Treatment cost per month

The median cost per month of treatment services was calculated by creating an adjusted cost of services, dividing the total price per EOC (based on summing all prices of billed services in the MODMH dataset) by length of the treatment episode in months. To determine the extent to which overall cost differences were driven by different MOUDs, we compared cost per month between Pre-STR and STR treatment episodes for each medication group.

2.4. Analysis plan

Data were analyzed at the group level (Pre-STR vs. STR), with EOCs from all agencies combined. Group comparisons on categorical variables (i.e., medication utilization and treatment retention) were assessed using chi-squares. For variables with multiple categories (e.g., utilization of each medication type), pairwise comparisons using the conservative Bonferroni correction to adjust *p*-values at a significance level of < 0.05 were employed. Cramer's V estimates are provided as a measure of effect size for chi-square analyses. Generally, a Cramer's V effect size of 0.1 indicates a small effect, 0.3 indicates a medium effect, and 0.5 indicates a large effect (McHugh, 2013; University of Cambridge MRC Cognition and Brain Sciences Unit, 2018). Group comparisons with non-normally distributed, interval variables (i.e., time to medication, hours per day of psychosocial services, and price per month) were conducted using the non-parametric Mann-Whitney *U*

test, which uses mean ranks to compare the likelihood that a randomly selected score from one group will be greater than or less than a randomly selected score from another group, makes fewer distributional assumptions than parametric tests, and is robust to non-normality. Given minimal overlap between Pre-STR and STR individuals (150 clients of 3800 total), we used tests that assume independence of observations. Both the chi-square tests and the Mann Whitney U are tests for independent, rather than paired, samples.

The Vargha-Delaney A (VDA) was calculated as a measure of effect size for the non-parametric group comparisons. Effect sizes range from 0 to 1 with a value of 0.5 indicating no difference. As presented, the VDA estimate indicates the probability than an observation in the Pre-STR group will be larger than an observation in the STR group. Vargha and Delaney identify small, medium, and large effects as over 0.56, 0.64, and 0.71, respectively (Vargha & Delaney, 2000). Chi-square tests and Mann Whitney *U* tests were conducted in SPSS version 24 and the VDA was calculated using R.

We examine Pre-STR vs. STR differences in outcomes first in aggregate and for follow-up analyses by MOUD group, when applicable, to determine which MOUD group(s) may be driving a given effect. Given the heterogeneity of the buprenorphine + naltrexone group, which includes varying orders in which these medications were prescribed, we include this group of EOCs in analyses of the aggregate findings but exclude it from time-to-medication follow-up analyses, which are designed to examine group differences across MOUD types.

3. Results

3.1. Participating agencies

Fourteen agencies (with 38 sites) were granted access to STR funds during the first nine months of STR. Of these, two were OTPs providing methadone. Two of the largest SUD treatment agencies accounted for 58% of all EOCs. Among the Pre-STR EOCs, 8.5% (242 of 2840) occurred at more than one agency, indicating a transfer of care. Among STR EOCs, 5.1% of EOCs (72 of 1411) occurred at more than one agency.

3.2. Characteristics of the treatment samples

The sex, race, and ethnicity of individuals served in Pre-STR EOCs and STR EOCs are presented in Table 1. (As the dataset was structured at the EOC-level rather than the individual-level, there are fewer unique clients than EOCs.) Demographic characteristics of individuals in STR treatment were similar to those served in the year prior to STR. Clients were predominantly non-Hispanic, and a majority of individuals in

Table 1

Demographics of individuals receiving services at 14 SUD treatment agencies in Missouri, Pre-STR and during STR.

Total served	Pre-STR N = 2502		STR N = 1298	
	n	%	n	%
Sex				
Male	1599	64.6	865	66.6
Female	876	35.4	433	33.4
Race				
White	1782	72.0	922	71.0
Black or African American	604	24.4	337	26.0
Other	89	4.8	39	2.8
Ethnicity				
Non-Hispanic	2451	99.1	1287	99.1
Hispanic	24	0.9	11	0.9

Note: Demographic information was missing for 27 individuals in the Pre-STR group. Proportions are calculated out of 2475.

Table 2

Episodes of care involving medications for OUD before and after STR funding with medication first implementation.

	Pre-STR (<i>N</i> = 2840)		STR/Medication First (<i>N</i> = 1411)	
	n	%	n	%
No medication ^a	1567	55.2	208	14.7
Oral Naltrexone ^a	119	4.2	29	2.1
Extended Release Naltrexone ^a	216	7.6	61	4.3
Buprenorphine + Naltrexone	97	3.4	64	4.5
Buprenorphine ^a	784	27.6	827	58.6
Methadone ^a	57	2.0	222	15.7

^a Indicates statistically significant difference at p < .05 between Pre-STR and STR medication categories.

treatment were White. However, consistent with opioid overdose fatality patterns in the state (Bureau of Vital Statistics Missouri Department of Health and Senior Services, 2018), Black individuals and males were overrepresented in the treatment population relative to their state population.

3.3. Medication first outcomes

3.3.1. Medication prescribed in EOCs

Rates of medication utilization in EOCs are presented in Table 2. Overall, MOUD utilization was higher during STR than Pre-STR (85.3% vs. 44.8%; χ^2 [4, N = 4251] = 893.23, p < .0001), with a medium to large effect size (Cramer's V = 0.458). Differences were also found regarding use of specific MOUD types. Relative to Pre-STR EOCs, STR EOCs were less likely to involve oral naltrexone or XR naltrexone and were more likely to involve buprenorphine or methadone. (However, the increase in methadone was likely due to increased proportional representation of OTPs in STR.)

3.3.2. Time to medication for OUD in EOCs

Medications for OUD were prescribed significantly faster in STR EOCs relative to Pre-STR EOCs (Pre-STR Mean (SD) = 21.16 (36.37) days; Mdn = 8 days; STR Mean (SD) = 4.93 (11.86) days; Mdn = 0 days; U = 341,062, p < .001). A VDA estimate of 0.682

Table 3

Treatment retention.

indicates a medium effect size. This effect was largely driven by the large volume of buprenorphine EOCs, for which the median time to MOUD decreased from two days to zero days ((Pre-STR Mean (SD) = 17.21 (34.94) days; Mdn = 2 days; STR Mean (SD) = 4.40 (10.70) days; Mdn = 0 days; U = 152,442, p < .001).

The largest magnitude of reductions in median time to medication was for the oral naltrexone and XR naltrexone EOCs. The median time to first medication among oral naltrexone EOCs decreased from 18 to 5 days ((Pre-STR Mean (SD) = 33.94 (44.08) days; Mdn = 18 days; STR Mean (SD) = 21.52 (31.08) days; Mdn = 5 days; U = 1143, p = .005). The median number of days to first MOUD among XR naltrexone EOCs decreased from 16.5 to 6 days (Pre-STR Mean (SD) = 29.05 (36.27) days; Mdn = 16.5 days; STR Mean (SD) = 7.97 (10.81) days; Mdn = 6 days; U = 4875.5, p < .001). Finally, median time to methadone during both timeframes was zero days (Pre-STR Mean (SD) = 3.43 (8.28) days; Mdn = 0 days).

3.3.3. Receipt of psychosocial services

On average, STR EOCs involved significantly fewer hours per day of psychosocial services during the first 30 days of treatment relative to EOCs at the same agencies in the first nine months of the year prior (Pre-STR: Mean (SD) = 1.28 (1.96) hours/day; Mdn = 0.25 h/day; STR: Mean (SD) = 0.41 (1.00) hours/day; Mdn = 0.10 h/day; U = 1,494,273.5 p < .001, VDA = 0.624). (Note, there was an *increase* in psychosocial services at OTPs during STR equivalent to one minute per day. Due to the lack of clinical significance of this finding we do not report on it further.)

3.3.4. Treatment retention

Overall, treatment retention improved among STR EOCs compared to Pre-STR EOCs (Table 3). Retention increased at one month from 49.0% to 68.6% (χ^2 [1, N = 4251] = 147.00, p < .001, Cramer's V = 0.186), at three months from 27.3% to 46.9% (χ^2 [1, N = 4251] = 161.67, p < .001, Cramer's V = 0.195), and at six months from 14.2% to 32.9% (χ^2 [1, N = 2609] = 120.71, p < .001, Cramer's V = 0.215). There were small-to-medium effects at each time point. Significant increases in overall retention were driven by increased retention among buprenorphine EOCs, which increased between 18% and 24% in each time period, and to a lesser extent by the

	Pre-STR		STR		Effect Size	Significance	
	n	%	n	%	Cramer's V	Chi-Square	p-value
1 month treatment retention	1391	49.0	968	68.6	0.186	147.00	< .001
No Medication	646	41.2	55	26.4	0.097	16.80	< .001
Oral Naltrexone	75	63.0	20	69.0	0.049	0.358	.550
XR Naltrexone	169	78.2	55	90.2	0.126	4.37	.037
Buprenorphine + Naltrexone	85	87.6	62	96.9	0.161	4.15	.042
Buprenorphine	363	46.3	581	70.3	0.243	95.18	< .001
Methadone	53	93.0	195	87.8	0.066	1.22	.270
3 month treatment retention	776	27.3	662	46.9	0.195	161.67	< .001
No Medication	302	19.3	16	7.7	0.097	16.75	< .001
Oral Naltrexone	41	34.5	9	31.0	0.029	0.122	.727
XR Naltrexone	112	51.9	41	67.2	0.128	4.54	.033
Buprenorphine + Naltrexone	65	67.0	48	75.0	0.085	1.18	.278
Buprenorphine	213	27.2	389	47.0	0.205	67.89	< .001
Methadone	43	75.4	159	71.6	0.034	0.33	.565
6 month treatment retention	259	14.2	259	32.9	0.215	120.71	< .001
No Medication	78	7.7	1	1.1	0.072	5.80	.016
Oral Naltrexone	18	21.2	1	5.3	0.159	2.63	.105
XR Naltrexone	38	29.2	8	27.6	0.014	0.031	.860
Buprenorphine + Naltrexone	30	46.9	21	60.0	0.126	1.561	.212
Buprenorphine	67	13.7	141	31.4	0.213	42.50	< .001
Methadone	28	68.3	87	54.4	0.113	2.58	.108

Note: Treatment retention at 6 months could be determined for 64% of Pre-STR EOCs and 56% of STR EOCs due to the start date of the treatment episode.

relatively higher proportion of methadone EOCs during STR. By 6 months, only buprenorphine EOCs have significantly greater retention during STR (13.7% Pre-STR vs 31.4% during STR, χ^2 [1, N = 938] = 42.5, p < .0001; Cramer's V = 0.213).

Given the robust evidence of methadone treatment yielding the highest retention rates (Timko et al., 2016), we assessed group differences in treatment retention separately for OTPs and non-OTPs. Among non-OTPs, group differences in treatment retention favored STR at each time point, with STR EOCs exhibiting 1.4 times greater retention at 1 month (48.2% Pre-STR vs 66.1% STR, (χ^2 [1, N = 3930] = 107.19, p < .001, Cramer's V = 0.165), 1.6 times greater retention at 3 months (26.4% Pre-STR vs 43.3% STR, (χ^2 [1, N = 3930] = 1409.76, p < .001, Cramer's V = 0.167), and 2.16 times greater retention at 6 months (12.8% Pre-STR vs 27.7% STR, (χ^2 [1, N = 2381] = 73.18, p < .001, Cramer's V = 0.175).

Among OTPs, STR EOCs also generally showed higher retention, but the differences were much smaller and were only statistically significant at one month (71.1% Pre-STR vs 81.7% STR, (χ^2 [1, N = 321] = 4.48, p = .034, Cramer's V = 0.118)) and three months (53.6% Pre-STR vs 66.1% STR, (χ^2 [1, N = 321] = 4.48, p = .034, Cramer's V = 0.118)). Six-month retention at OTPs was 51.5% Pre-STR and 53.1% during STR (χ^2 [1, N = 228] = 0.046, p = .829, Cramer's V = 0.014).

3.3.5. Costs per month

There was a 21% decrease in monthly cost for STR EOCs compared to Pre-STR EOCs (\$1620.56 Pre-STR vs. \$1274.41 STR; U = 1,751,433.50, p < .001); however, the effect size was small (VDA = 0.541). There was a negative correlation between the cost per month and the length of the treatment episode (r = -0.42, p < .001) due to the non-linearity of service costs over the course of a treatment episode. Specifically, there are several sizable upfront costs (intake services and initial assessments) that contribute to the tendency for costs to be higher in the first week of treatment compared to subsequent weeks. Because cost per month was calculated based on average monthly costs, this leads to shorter EOCs with concentrated costs on the "front end" inflating estimates of overall monthly costs.

The overall difference in cost per month was driven by buprenorphine EOCs; the cost per month among buprenorphine EOCs in STR was less than the cost per month among buprenorphine EOCs the year prior (Mdn Pre-STR EOC = 2273.64 vs. Mdn STR EOC = 1410.99, U = 249,984, p < .001) (see Fig. 1). There were no other significant differences in cost per month across Pre-STR and STR EOCs for the other MOUD groups. Data associated with hospital visits, criminal justice involvement, mortality, and other factors affecting the global cost effectiveness of STR was unavailable and therefore not included in these analyses.

4. Discussion

The MedFirst approach supports ongoing access to MOUD without arbitrary tapering or mandatory psychosocial services. The four principles begin with an imperative to provide medication first, chronologically; medical stabilization facilitates client retention and reduces client risk for continued opioid use. The subsequent three principles support medication as the first priority throughout the course of maintenance care. Both rapid and sustained access are critical to address our current overdose crisis, but each comes with its own sets of barriers. Missouri's dearth of buprenorphine waivered providers (Pearson & Brantley, 2018), workforce and capacity shortages, large rural population, and variable pharmacy policies serve as barriers to rapid access to MOUD and are largely practical or logistical in nature. In contrast, many of the barriers to sustained MOUD access, such as provider and staff preference, clients' internalized stigma, widespread misinformation, and housing and employment policies, are more attitudinal in nature. Through development and dissemination of MedFirst, STR leaders attempted to mitigate both logistical and attitudinal barriers to improve initial and sustained access to MOUD.

Our early findings are promising. When comparing across equivalent time periods prior to and during STR, participating SUD treatment agencies more than doubled the proportion of treatment episodes involving MOUD and six-month retention rates through STR funding. An increase in buprenorphine utilization and the increase in retention among buprenorphine treatment episodes, specifically, was the driving contributor to these overall improvements. Additionally, individuals received MOUD earlier in treatment, likely helping them stabilize during a period typically marked by high attrition. Along with improved treatment retention, the median monthly cost of STR treatment episodes was 21% less than the monthly cost of episodes prior to STR. STR episodes were more expensive in the first month than Pre-STR episodes, but were less expensive on average. Because of the high costs of care associated with the earliest treatment visits, this difference was driven by STR clients demonstrating longer retention, thus making the care episode of care more financially efficient overall. Importantly, methadone episodes were similar across Pre-STR and STR, evidencing consistently high retention rates and the lowest monthly price, consistent with prior research showing greater retention in patients receiving methadone (Mattick et al., 2014; Timko et al., 2016). The



Fig. 1. Six-month treatment retention and price per month for pre-STR and STR episodes of care, by medication group.

"mixed" buprenorphine + naltrexone group demonstrated the highest retention rates during STR, which is not necessarily predicted by the literature. We attribute this finding to several possible reasons: first, an individual receiving multiple addiction medications within a given treatment episode is potentially indicative of more engaged care (e.g., a provider listened to a patient's concerns and shifted the treatment approach), which might itself predict greater retention; second, specialty SUD treatment facilities in Missouri are more familiar with prescribing naltrexone due to prior statewide efforts to expand its utilization to treat alcohol use disorder (Schmidt et al., 2012) and opioid use disorder (Substance Abuse and Mental Health Services Administration, 2015). Providers familiar with prescribing buprenorphine and naltrexone consecutively might have learned to predict which patients are most likely to stay engaged with this treatment protocol. Third, and perhaps most notably, some clients intended to start treatment with buprenorphine and subsequently transition to naltrexone, as 61% of those in this "mixed" group did. However, if they left treatment prior to starting naltrexone, perhaps during the period of opioid abstinence required before initiation, their data would be captured in the "buprenorphine" group and not the "mixed" buprenorphine + naltrexone group. This would serve both to artificially deflate the buprenorphine retention figures and inflate the "mixed" group figures because of inherent selection bias for higher-functioning individuals who were able to persist through the period of abstinence required prior to initiating naltrexone.

MedFirst is distinct from implementation models such as Massachusetts' Office-Based Opioid Treatment Collaborative Care (or nurse care manager) model (e.g., Alford et al., 2011) or Vermont's "hub and spokes" model (Brooklyn & Sigmon, 2017), primarily because these are standardized models developed for primary care or office-based settings led by prescribers. The unique contribution of MedFirst is that it was specifically developed to address common treatment practices in publicly-funded specialty SUD treatment programs. Not only have most of these programs traditionally eschewed the use of medications to treat OUD, but they often did not have a prescriber on-site or as a collaborator in the community. Existing practices, such as lengthy initial assessments or mandatory high-intensity psychosocial service engagement, often result from institutional inertia that needed to be directly addressed. The four principles of MedFirst were developed to do just that, and to provide guidance to these facilities as they made the transition to MedFirst. More broadly though, MedFirst is not itself a formal treatment model, complete with protocols or specific step-bystep guidelines. Rather, it is a treatment approach, framework, or even philosophy that is compatible with any low-barrier model of OUD care. To our knowledge, we are not aware of other states implementing the MedFirst approach by name, but lively discussions with experts across the country, in-person, at conferences, and on national listservs, have helped us disseminate MedFirst concepts, address concerns, improve our framing, and hone our messaging.

4.1. Sustainability

In Missouri, STR leaders used STR funds to pilot the MedFirst approach but imposed no new constraints on agencies' annual block grant allocations. Rather, STR leaders financially incentivized best practice treatments (maintenance MOUD) and dis-incentivized practices with a weaker evidence-base (e.g., group services). However, agency leaders have reported fiscal challenges with the MedFirst approach; the decrease in psychosocial service utilization and increase in medical service utilization resulting from this incentive structure have likely reduced these programs' operating margins for STR treatment episodes. Expanding and sustaining the MedFirst approach will require optimization of financial incentives to reduce fiscal challenges to programs. Policy options include increased reimbursement for medical services, capitated rates, outcomes-based payments, and increased Medicaid reimbursement rates for MOUD (Hinde, Hayes, Mark, Bernstein, & Karon, 2017).

Neither time-limited STR funds nor promotion of the MedFirst concept can solve the workforce, capacity, or financial obstacles to broad MOUD access. Overcoming these obstacles will require federal and state regulatory changes beyond the scope of Single State Agency administrators or OUD subject matter experts. Nevertheless, STR leaders seized the opportunity provided by STR to catalyze rapid change in the publicly-funded SUD treatment system with the goal of increasing MOUD access and reducing OUD-related illness and death in Missouri.

4.2. Future directions

STR leaders have submitted grant applications to support the development of an Interdepartmental De-identified Data Repository (IDDR) to help determine the impact of MedFirst implementation on outcomes other than retention such as non-fatal overdose, hospital visits, incarceration, and mortality. The IDDR will also help us determine the extent to which the MedFirst initiative had "spillover" effects in the concurrently enrolled, non-STR clients, such as the Medicaid population. Positive spillover effects would lend additional support for the beneficial and sustainable impact of the MedFirst initiative and the state-level prioritization of increasing MOUD access.

Most of our training efforts have focused on changing provider attitudes and practices, but many people with OUD have their own biases and barriers to maintenance MOUD including medication stigma, fear of potential painful withdrawal, criminal justice involvement, and program structure (Fox et al., 2015; Truong et al., 2019). In the behavioral healthcare field, we promote the importance of client choice but guidance on how to understand and manage choices that conflict with best practice is sparse. More work is needed to better understand the nuances of client preferences and perceptions.

Finally, future studies should investigate the clinical pathways and outcomes of individuals who receive both agonist and antagonist medications during a care episode. Receiving XR naltrexone following an extended course of buprenorphine, for example, may be optimal for a subset of clients, but we do not know who they are. Researchers should explore the factors predicting both success and attrition among individuals receiving more than one class of MOUD to ensure clients and providers have empirically-based information about as many treatment pathways as possible.

4.3. Limitations

Though this study has many strengths and our findings are encouraging, we acknowledge the presence of four primary limitations. First, we cannot examine the extent to which demonstrated improvements among STR agencies could be due to secular changes we would have seen without MedFirst dissemination. To test this, we would need access to similar administrative data, ideally from neighboring states, to conduct a difference-in-difference analysis. Indeed, the observational nature of this data precludes us from determining which clinical mechanisms contribute to our findings. Unlike randomized control trials (RCTS), we could not infer treatment intention, nor do we know exactly how STR efforts have worked to change clinical decision-making. Because our results point to improvements in MOUD utilization and retention – the primary goals of MedFirst – we believe the rollout of this approach and its associated principles is at least partially responsible for these improvements.

Second, our estimates of treatment retention for buprenorphine are lower than what has been highlighted in empirical literature, where sixmonth retention is often close to 60% (e.g., Bhatraju et al., 2017). In addition to the 'voltage drop' that occurs when a treatment moves from the controlled environment of RCTs to real-world settings (Chambers, Glasgow, & Stange, 2013), this is likely also due to limitations in our ability to identify the subset of EOCs involving buprenorphine in which the intention was to transition to naltrexone, as mentioned above. Specifically, if clients left treatment early while being tapered off buprenorphine, their data would be reflected in the buprenorphine category (not the "mixed" buprenorphine + naltrexone category). Thus, our buprenorphine retention figures may be less than what we would find by looking only at care episodes in which maintenance buprenorphine was the intended treatment path.

Third, we use treatment retention as a proxy for clinical outcomes. Though this is frequently done (e.g., Hser et al., 2016), in the future we hope to also examine more holistic outcomes such as employment, familial relationships, and well-being, as well as health and societal outcomes such as subsequent incarceration, hospitalization, and mortality. Last, we defined the time to access MOUD as the difference between an individual's first date of service and the date they received MOUD, though in reality, a more appropriate start date would be the day the individual first called or presented for services, even if they were not enrolled at that time. We know not all agencies are able to admit clients immediately, but we have no way to track initial calls or onsite requests for services, which may have occurred days before the recorded start date. Given this, our assessment of the time to access MOUD should be viewed as a likely underestimate, with a 'zero day' value as not necessarily indicative of 'on-demand' access.

Last, the four principles do not comprehensively address the multiple, potentially complicating, factors associated with real-world delivery of MOUD treatment - particularly diversion of buprenorphine and how providers should handle diversion in the event that it happens. We acknowledge the medical and legal need for providers only to prescribe medication to their patients - not their patients' families, friends, or associates who are not in their care. Thus, though diversion is rarely an all or nothing phenomenon, in the event a client's drug screens are consistently negative for buprenorphine and attempts to understand and re-engage the client with peer support and other clinical strategies have been tried and failed, the Med First clinical consultant team acknowledges discontinuation of the prescription is a legitimate clinical option. Specifically, if the client is not using their prescribed buprenorphine, then the risks typically associated with discontinuing it are not present. However, in contrast to our other principles for which there is clear clinical evidence to guide prescribers (i.e., timely, noncontingent, maintenance access to medication is critical to stabilizing clients and saving lives), there is not a strong evidence base that diversion is a clinical problem, even if it is a legal problem for prescribers. Indeed, regarding the clinical risks of buprenorphine diversion itself, evidence thus far suggests the fears might be limiting access unnecessarily (Doernberg, Krawczyk, Agus, & Fingerhood, 2019). Buprenorphine-involved overdoses are exceedingly rare among unintentional drug overdose fatalities (Paone et al., 2015) - especially compared to the mortality risk associated with discontinuing buprenorphine (Dupouy et al., 2017; Hickman et al., 2018). Thus, the clinical risk associated with discontinuing buprenorphine for an individual client is much greater than the risks to people who are obtaining buprenorphine on the street. Finally, it is worth considering why buprenorphine is diverted, and what policy changes could reduce the size of this illicit market. Clients have a variety of motivations to share or sell their medications, but empathy with their friends or loved ones is the most common; half of those who have been prescribed buprenorphine share it with others who are "dope sick," while only 28% sell it to make money (Kenney, Anderson, Bailey, & Stein, 2017). Moreover, individuals who enter treatment and have prior experience using diverted buprenorphine actually demonstrate better treatment retention than those who are buprenorphine naïve (Cunningham, Roose, Starrels, Giovanniello, & Sohler, 2013), which suggests that on an epidemiological level diversion might even be beneficial. Of course, experience with diverted buprenorphine is not the ideal way to increase eventual treatment retention - rather, treatment should be more timely and accessible, with fewer non-evidence-based requirements, which is the basis of the four Med First principles.

4.4. Conclusion

Missouri's STR-funded efforts have prioritized increased access to MOUD as the primary driver of reductions in illicit opioid use and mortality. STR leaders have changed practice and policy through the development and dissemination of our Medication First treatment approach, which stresses the importance of fast and uninterrupted use of MOUD through the removal of certain treatment requirements. Evaluation of MedFirst implementation is promising: Missouri has seen increases in MOUD utilization, faster connection to medical services, and improved treatment retention, all at costs lower than the standard of care. Through MedFirst, STR leaders aim – first – to save lives through MOUD. STR leaders also promote well-rounded and meaningful recovery as attainable and ideal, while simultaneously communicating the realistic and necessary message that such a thriving recovery can only be achieved if one is first alive to achieve it.

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R.P. Winograd, et al.

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