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Addictions treatment mechanisms of change science and implementation science: A critical review

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Abstract

This manuscript aims to contribute to the next phase of mechanisms of behavior change (MOBC) science on alcohol or other drug use. Specifically, we encourage the transition from a basic science orientation (i.e., knowledge generation) to a translational science orientation (i.e., knowledge application or *Translational MOBC Science*). To inform that transition, we examine MOBC science and implementation science and consider how these two research areas can intersect to capitalize on the goals, strengths, and key methodologies of each. First, we define MOBC science and implementation science and offer a brief historical rationale for these two areas of clinical research. Second, we summarize similarities in rationale and discuss two scenarios where one draws from the other—MOBC science on implementation strategy outcomes and implementation science on MOBC. We then focus on the latter scenario, and briefly review the MOBC knowledge base to consider its readiness for knowledge translation. Finally, we provide a series of research recommendations to facilitate the translation of MOBC science. These recommendations include: (1) identifying and targeting MOBC that are well suited for implementation, (2) use of MOBC research results to inform broader health behavior change theory, and (3) triangulation of a

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more diverse set of research methodologies to build a translational MOBC knowledge base. Ultimately, it is important for gains borne from MOBC science to affect direct patient care, while basic MOBC research continues to be developed and refined over time. Potential implications of these developments include greater clinical significance for MOBC science, an efficient feedback loop between clinical research methodologies, a multi-level approach to understanding behavioral change, and reduced or eliminated siloes between MOBC science and implementation science.

Keywords

causality; health behavior change; mediation; moderation; science of behavior change

INTRODUCTION

Beginning in the 1990s, there was a marked increase in the number of randomized clinical trials targeting interventions for alcohol or other drug use (AOD), and the result was numerous manualized treatments deemed evidence-based (McCrady, 2000; Miller & Wilbourne, 2002). However, large-scale reviews and modality-specific meta-analyses (e.g., Imel et al., 2008; Lundahl et al., 2010; Magill et al., 2019; Ray et al., 2020) rarely designate a single, uniquely efficacious treatment. One could call this an *embarrassment of riches*, where many good options exist, but there is no clear guidance on what constitutes optimal frontline care. This observation has been made in the child and adolescent psychotherapy literature (Chorpita et al., 2005), and other scholars have drawn similar conclusions in adult psychotherapy and mental health (Wampold, 2001; Wampold & Imel, 2015). In the addictions, Longabaugh (2007) called this phenomenon a *plateau* in the knowledge base. To have many evidence-based treatments is a positive result of the clinical trials era of the 1990s to present. Nevertheless, even among prominent evidence-based behavioral and pharmacological AOD treatments, effect sizes for treatment response tend to be in the small-to-moderate at early follow-up and small for treatment-related maintenance of change (Ray et al., 2019).

Mechanisms of behavior change science

By the early 2000s, modest and variable treatment effects became the impetus for clinical researchers and research funding bodies to turn their attention to understanding more about how the process of change occurred and for whom certain evidence-based treatments may work best. These questions translate statistically to mediators and moderators, respectively, and the former and to a lesser extent, the latter, became key methods in what is now known as mechanisms of behavior change (MOBC) science. MOBC science is an area of research in the addictions, but its emphasis is consistent with trans-behavioral efforts at the National Institutes of Health's Science of Behavior Change initiative (SOBC; Nielsen et al., 2018), and both efforts draw from conceptual frameworks and methodologies in psychotherapy, mental health, and medicine.

At the National Institute on Alcohol Abuse and Alcoholism (NIAAA), there was a concerted effort to promote MOBC science, starting in 2004 with a satellite meeting held at the annual conference of the Research Society on Alcoholism. Subsequent milestones included the

publication of special issue monographs in *Alcoholism: Clinical and Experimental Research* (Huebner & Tonigan, 2007) and the *Journal of Studies on Alcohol and Drugs* (Mechanisms of Behavior Change Satellite Committee, 2018), the development of an MOBC statement within the NIAAA Strategic Plan (2009, 2017), the formation of an MOBC work group within NIAAA, and calls for MOBC research to extramural applicants (RFA AA-07-005; PA 13-160-162; PAR AA-14-051-053). The overall goal of these efforts was to move beyond questions of behavioral and pharmacological treatment efficacy to consider questions of process, and specifically—the processes through which addictive behavior change occurs. With this knowledge, the quality of direct patient care could be improved by (a) enhancing existing treatment efficacy and efficiency, (b) informing providers of how to best match evidence-based treatments to specific patient sub-populations, (c) improving general approaches to training and supervising AOD providers, and (d) providing knowledge on the essential elements of effective treatments to streamline the process of implementation in the community. These implications fall into the broad domain of implementation science.

Implementation science

Predating the emergence of MOBC science, the field of dissemination and implementation science evolved via efforts to ensure a return on substantial public investment in biomedical research. Scholars became increasingly interested in how knowledge, tools, and other scientific products spread within systems (Bauer & Kirchner, 2020). Despite the availability of evidence-based guidelines and treatments, the central problem was a lack of translation to medical, public health, and other specialty-care settings (Bauer et al., 2015). As a result, science on dissemination and implementation became a way to build a cohesive knowledge base on how to ensure that gains borne out of research would be experienced by the public who both funded them and needed them. Therefore, the goal of dissemination and implementation science is consistent with the goal of MOBC science—to improve the quality of direct care to individuals and communities.

Dissemination and implementation science distinguish among three types of knowledge translation. *Diffusion* is defined as the passive and untargeted spread of research-based knowledge and/or practices while *Dissemination* is active and targeted (Rabin et al., 2008). In contrast, *Implementation Science* is the study of the integration, adoption, and/or sustainment of a research innovation (e.g., an evidence-based treatment) within a specific setting (Rabin et al., 2008). For the current manuscript, the latter type of knowledge translation is of primary interest. The overall goal of implementation science is not only to ensure public benefit from scientific innovation but also to produce a body of knowledge about the processes through which these systemic changes occur. In the addictions, efforts to implement evidence-based treatments are in their infancy, and researchers have lamented the lack of research base for many practices that occur in community AOD treatment programs (Carroll, 2012; Louie et al., 2021; McGovern et al., 2013).

Purpose and aims

Greater emphasis on implementation science is one way to move MOBC science to its next level and accelerate the pace of translation of MOBC-based knowledge and products to direct care settings. Accordingly, the overarching goal of this manuscript is to inform

a transition toward a translational science orientation for MOBC research or what we refer to as—*Translational MOBC Science*. To do so, we examine MOBC science and implementation science, and how these two research areas can intersect to capitalize on the goals, strengths, and key methodologies of each. We briefly discuss Scenario One of the intersection, which is a movement in implementation science toward greater attention to mechanisms of implementation strategy effects. We then discuss Scenario Two, implementation science on MOBC, which is the focus of this critical review. We review the MOBC knowledge base to consider its readiness for translation and implementation. Finally, we provide a series of research recommendations to facilitate Translational MOBC Science. The current review emphasizes MOBC knowledge derived from clinical trials of evidence-based treatments targeting adult AOD. However, we acknowledge the importance of work on adolescent populations as well as MOBC knowledge derived from studies of behavior change occurring outside the context of formal treatment (for recent discussion of the latter, see Witkiewitz et al., 2022).

MOBC SCIENCE AND IMPLEMENTATION SCIENCE

In this section we consider the intersections of MOBC science and implementation science. At their core, MOBC science and implementation science are concerned with improving the care of individuals, groups, and communities suffering from a given health condition (e.g., AOD). Both are also concerned with the process of change. For MOBC, this is typically individual-level behavior change (i.e., patients), and increasingly, the MOBC field recognizes that many change mechanisms (e.g., motivation, self-efficacy, coping skills, and social support) are likely operative regardless of whether a person is receiving professional treatment, mutual aid, or engaging in naturalistic change (Witkiewitz et al., 2022). The individual-level change process is highly complex, including multiple potential mechanisms that are more or less important at various change stages (e.g., initial decision-making, taking action to change, and maintenance of change) and with individual- or contextual-level factors that might determine the effectiveness of a given mechanism at a given point in time (Hallgren et al., 2018). For implementation science, there may be individual-level change when targeting providers, but there may also be change to entire programs or systems of programs (i.e., organization-, system-, and policy-level change; Williams, 2016). As a result, the implementation science change process is more likely to target multiple levels simultaneously than MOBC, but as we will discuss later, this multi-level emphasis is one way implementation science considerations could expand the translational capacity of MOBC.

MOBC science and implementation science—Two scenarios

Scenario one—Mechanisms of implementation strategy effects—The implementation science field has recently challenged itself to demonstrate empirical support for the mechanisms through which implementation strategies (i.e., implementation science interventions) produce their effects. In fact, the call to understand implementation strategy mechanisms arose out of a similar critique to that resulting in the emergence of MOBC science. Specifically, the implementation science field saw a proliferation of theories, frameworks and research, and yet implementation effectiveness continued to be modest

at best (Damschroder et al., 2009; Powell et al., 2014). While implementation science did not suffer from a lack of options, what was missing was an understanding of the causal mechanisms of those options, which could enable their refinement and thus enhance their efficacy, consistency, and transportability across implementation settings. In 2017, the Society for Implementation Research Collaboration convened its 4th annual meeting, and the theme was "Implementation Mechanisms: What Makes Implementation Work and Why?" A 26-member workgroup was subsequently assembled and titled the Mechanisms Network of Expertise. The goal of these efforts was to generate priorities for a research agenda to guide the future study of mechanisms in implementation science.

In a 2018 position paper, members of the workgroup outlined a four-step validation process for identifying mechanisms of implementation strategy effects, and as we will demonstrate, this process is consistent with what occurs in MOBC science on evidence-based treatments. The four-step process begins with a clearly defined target intervention—*the specific implementation strategy* (Lewis et al., 2018). For MOBC science, this is similar to the specification of a treatment via manualization and fidelity assessment. However, Lewis et al. (2018) argue that the implementation strategy should be specified at the smallest unit of analysis (i.e., not a complex package of multiple strategies). Second, the possible *mechanisms* through which an implementation strategy is expected to affect a targeted outcome are identified. Some of these purported mechanisms could be the same as those targeted in MOBC science on evidence-based treatments, such as individual-level knowledge acquisition, behavior change intentions, or personal self-efficacy. Other implementation science mechanisms may be more relevant to systems, such as changes in organizational climate around innovation (see e.g., Aarons et al., 2010).

The third step in the validation process is identification of proximal and distal outcomes. A *proximal outcome* is the most immediate outcome of the purported mechanism, whereas the *distal outcome* is related to the overarching goal of the implementation strategy. For example, an agency-wide training on a new treatment (an implementation strategy referred to by Powell et al., 2015 as Conduct Educational Outreach Visits) is designed to affect provider knowledge and attitudes. These cognitive mechanisms among trainees may relate to increases in use of the treatment with service recipients (i.e., proximal outcome) and ultimately, adoption of the treatment at an agency level (i.e., distal outcome). In MOBC science, mechanisms, proximal and distal outcomes are highly relevant constructs when articulating the causal process of an evidence-based treatment. For example, a cognitive behavioral intervention may change a patient's knowledge and self-efficacy around specific coping skills (i.e., two mechanisms), which may predict coping skill enactment (i.e., proximal outcome) and ultimately, reductions in AOD behaviors (i.e., distal outcome). Finally, in the fourth step of the Lewis et al.' (2018) approach there are *effect modifiers*, which are predictors or moderators that might impact the implementation strategy's causal process. Taking our implementation science and MOBC science examples a step further, perhaps some agency staff have existing attitudes about evidence-based treatments that will limit the influence of the agency-wide training. For MOBC of a cognitive behavioral intervention, client motivation or self-efficacy may influence compliance with the prescribed activities of the treatment; both of these examples result in a scenario where provider or

patient characteristics, respectively, influence the causal processes that ultimately affect the outcomes of the intervention.

Thus far we have summarized a movement in the implementation science field toward greater articulation of the causal process through implementation strategies may produce their effects. We have additionally shown that this four-step process is similar to what occurs in MOBC science on evidence-based treatments. This is Scenario One as depicted in Figure 1, where the direction of study moves from implementation to mechanism (i.e., mechanisms of implementation strategy outcomes). What about the reverse? Figure 1 also shows Scenario Two, where the direction of study moves from the mechanism to implementation (i.e., implementation of MOBC or implementation science on MOBC).

Scenario two—Implementation science on MOBC—The original call of MOBC science was to impact direct patient care via empirically validated causal process models that would lead to specific improvements in evidence-based treatment delivery (NIAAA, 2009, 2017). While MOBC knowledge generation has been robust and there is more basic knowledge to acquire, we propose that now also is the time for translation. We argue that MOBC science findings are a unique fit for implementation because the procedure or product to be implemented will be more targeted and less complex than the implementation of an evidence-based treatment. The target of the intervention derived from MOBC science can be both singular and proximal (e.g., to enhance self-efficacy for using specific coping strategies), which is analogous to the requirement above in Scenario One that states the implementation strategy will have an optimal causal impact only if it is first reduced to its simplest level and when its targeted outcome is pre-specified (Lewis et al., 2018). It is this singularity and proximity that we believe make the output of MOBC science such a natural fit for implementation. In other words, a key barrier to implementing packaged, evidence-based treatments is their complexity while interventions, procedures, or quality improvement protocols targeting a specific MOBC could offer reduced burden at the implementation stage.

We provide a typology of examples that characterize Scenario Two, but this should be considered an emerging typology, as many other types of MOBC knowledge translation are likely possible. The first type is to *implement the mechanism itself* (i.e., an intervention targeting the mechanism) into a direct practice context. The typical evidence-based treatment consists of multiple strategies, often to be enacted in a predetermined order, that target multiple mechanisms, but what if the intervention targeted a single mechanism or a concise set of two or three? A recent example of this is a technology-facilitated measurement-based care intervention delivered as an adjunct to usual care in a community AOD program. Patients self-reported how often they used a specific mechanism (e.g., coping strategies for avoiding AOD use) at regular intervals via a smartphone, and their data was fed back to both patients and providers to help monitor treatment progress and guide clinical discussion. There was a relatively low burden shift to how usual services were delivered, and in this case, the patients and providers showed good engagement, and had positive views on intervention usability and clinical utility (Hallgren et al., 2022).

A second type of MOBC implementation is *changes to supervision and other quality control methods based on MOBC science*. Here, knowledge on a given mechanism can affect how evidence-based supervision is delivered, the content of supervision sessions, and the types of clinician behaviors or therapeutic processes that are assessed in quality control efforts. An example of this is client language about behavior change in motivational interviewing. Specifically, client statements related to making a change in behavior are a proposed mechanism of motivational interviewing (Miller & Rose, 2009), they are a potential marker of shifting motivation over the course of a motivational interviewing session (pro-change statements relative to anti-change statements; Magill & Hallgren, 2019), and have demonstrated statistical mediation effects in the motivational interviewing literature (Houck et al., 2018; Moyers et al., 2007). Over time, this MOBC knowledge has resulted in changes to methods of training motivational interviewing (Motivational Interviewing Network of Trainers (Mint), 2014) and fidelity assessment (Moyers et al., 2016), and there are current efforts to facilitate measurement of this mechanism at a scalable level via artificial intelligence technology (Atkins et al., 2014). In both examples, there is translation of knowledge on a proposed mechanism that resulted in changes in the way care is delivered in the community.

A third type of MOBC implementation is *refinements to existing evidence-based treatments or development of new evidence-based treatments* by making changes to the design, dissemination, and implementation of AOD interventions based on findings from MOBC science. Granted, this type does not reduce the burden inherent to implementing evidence-based interventions, but there would be greater confidence in the necessity of that complexity. In this type, it is not sufficient to feed back MOBC knowledge into subsequent intervention design. Rather, these MOBC-informed treatments must complete the journey to implementation, adoption, and sustainment in the community. At these points in the translational continuum, new information is obtained about successes and failures that occur once intersection with community program needs and resource constraints become apparent.

The NIH Stage Model of Behavioral Intervention Development (Onken et al., 1997, 2014) provides a visual for conceptualizing Scenario Two's third type of MOBC knowledge translation. As can be seen in Figure 2 (reprinted with permission), the model shows that possible paths to follow from an efficacy study are numerous and include further intervention refinement (Stage 1) and effectiveness or hybrid effectiveness (Stages 3 and 4). The model further shows that the outcomes of any implementation effort (Stage 5) should inform subsequent basic research (Stage 0) and intervention development and refinement (Stage 1), which in this case includes refinement to any of the treatment's components and their relation to hypothesized MOBC. The aims of this critical review harken back to Onken et al. (2014) original vision "…that incorporates basic science questions of mechanisms into every stage of clinical science research," which is "…intended to unify various aspects of clinical science toward the common goal of developing maximally potent and implementable interventions" (p. 22). Following this vision can additionally avoid siloed specialties, where clinical trialists abandon their treatments at the efficacy stage and implementation scientists must take the helm and bring the intervention to the community. With more integrated efforts, we might see a future where the time between stage zero through two to five of the NIH Stage Model can be abbreviated. With these three types of

translational MOBC in mind, we move onto the next section and provide a brief review of the MOBC knowledge-base and relevant research recommendations to move Translational MOBC Science forward.

AN OVERVIEW OF THE CURRENT MOBC KNOWLEDGE BASE

Statistical mediators of AOD treatment effects

To facilitate a translational emphasis for MOBC science, there must be MOBC that are appropriate for translation, dissemination, and implementation. To begin this discussion, we should first distinguish between a mediator and a mechanism of behavior change. The two terms often are used interchangeably in the literature, but there are essential technical differences between them that several authors have described (e.g., Kazdin, 2006, 2007; Tryon, 2018). A *mediator* is an intervening variable, and mediation is a statistical result that is necessary but not sufficient to demonstrate that a variable is a mechanism of behavior change. A *mechanism* is a process or event that causes change. To provide support that a variable is a mechanism, researchers must show evidence that there is a causal connection between the variable in question and a given outcome. As Tryon (2018, p. 626) noted, “mediation is to mechanism as correlation is to causation.”

Specifying these definitions lays the foundation for discussion of what constructs might meet empirical criteria as AOD treatment MOBC and thus are candidates for translation and implementation. If mediation is a necessary, but not sufficient criterion for a construct to be a mechanism, then a logical first step is to search the literature to find variables that have empirical support as mediators of AOD treatment effects. There have been numerous studies done in the last two decades on evidence-based treatments, their hypothesized mediators, and health-related outcomes (e.g., Carey et al., 2019; Hagger et al., 2020; Hammerton & Munafò, 2021). The overall result of this work is the identification of many candidate mechanisms with evidence grounded in mediation studies of behavioral, and to a lesser extent pharmacological, treatment clinical trials. The addictions treatment literature reflects parallel growth during this period, and multiple reviews in recent years summarize and integrate these findings. Accordingly, Maisto and Moskal (2019, 2022) did a systematic review of these reviews to synthesize what we know to date about statistical mediators in the AOD treatment literature. To be included in the sample, a review had to be a systematic or nonsystematic review on one or more AOD treatment approaches that included information about empirically-tested mediators. Overall, the most robust (i.e., frequently tested and supported) mediators across nine reviews were client language about behavior change (tested primarily in the motivational interviewing literature), self-efficacy about behavior change, social support for abstinence or moderation of consumption, and enacted coping skills.

Evidence for statistical mediators is growing, but this does not equate evidence for MOBC

The earliest and arguably most influential discussion of empirical criteria for validating an MOBC in the AOD treatment literature is Kazdin and Nock’s (2003) extension of Hill’s (1965) criteria for causality to the subject of statistical mediators in child and adolescent psychotherapy research. This work was followed and applied directly in a concept paper

in the addictions by Nock (2007) and has been extended and elaborated upon in recent publications in the addictions and in general health (Byrne, 2020; Hagger et al., 2020; Witkiewitz et al., 2022). However, the title of a chapter that Kazdin (2006) later published stated "Mechanisms of change in psychotherapy: Methods, breakthroughs, and cutting-edge research (doesn't yet exist)." Therefore, a key figure who led the charge for translating statistical mediators into validated mechanisms did not appear optimistic. The observation was similarly made in Maisto and Moskal's (2019) review and other authors have concluded that Kazdin's lament is relevant to MOBC in health outcome research as well (e.g., Byrne, 2020).

When there is evidence for statistical mediators of AOD treatment effects, but limited evidence suggesting these mediators rise to the status of MOBC, there are clear implications for the implementation of knowledge on MOBC to affect direct care. Specifically, if it is held that empirical support is a necessary condition for implementation, then it would follow that implementation of information about AOD treatment MOBC would be delayed until that empirical base is available. However, the field is poised and perceives a clear need for translation of the evidence base that has been generated (e.g., NIAAA Notice of Special Interest 20–022). In the context of what might appear to be competing knowledge and clinical priorities, we propose that it is important and practical to continue building the evidence for validated MOBC while also considering what constructs or processes have 'good enough' evidence for implementation currently. In other words, this is a rare case in which the field can *eat their cake and have it too*. This means prioritizing research designs and scientific directions that yield high impact and precise information on MOBC with immediate or imminent implications along the translational continuum.

THE TRANSLATIONAL MOBC RESEARCH AGENDA

Kazdin and Nock (2003) proposed seven recommendations that would yield a cohesive knowledge base for empirically supported MOBC. These recommendations, along with brief definitions, are reproduced in Table 1 (Kazdin & Nock, 2003; Table 1, p. 1125). As noted, the Kazdin and Nock (2003) criteria have been extremely influential in guiding MOBC science in AOD treatment research, and in health-related behavior change research in general. However, the resulting literature has relied on recommendations for designing clinical trials that incorporate tests for statistical mediation, and as a result recommendations one through three and five have been prioritized. Specifically, in the context of clinical trials of intervention efficacy the standards of *correlational association*, *specificity of association*, *gradience of association*, and *temporality of association* can be efficiently addressed in a single study. Moreover, the expectation that clinical trials should consider tests of causal mechanisms was communicated clearly by funding bodies, such as within NIH strategic plans and specific institute program announcements (e.g., PAR AA-14-051-053). We argue that the next direction for AOD treatment MOBC involves an emphasis on criteria four, six, and seven. We begin our discussion with criterion seven, which is essentially concerned with the use of theory in evolving the science of MOBC, and by extension, moving MOBC toward greater translation.

Use research to refine behavior change theory

We discuss theory first, because use of theory can be viewed as affecting each of the preceding Kazdin and Nock (2003) recommendations. As can be seen from the brief definition in Table 1, *plausibility and coherence* (criterion seven) relate to a reasonable explanation of cause. In the AOD treatment literature, MOBC research has been guided primarily by theoretical models that are the bases of evidence-based treatments tested within clinical trials. In this sense, theory has played a major role in AOD treatment MOBC research, but the use of theory could be expanded in ways that would advance the accumulation and utilization of evidence over time. For example, we can prioritize the use of general health behavior change theories (e.g., social cognitive theory) over theories grounded in a specific psychopathology or a specific-modality treatment. This approach is consistent with a more transdiagnostic and transtheoretical approach to MOBC research than has occurred to date. Findings on tests of hypothesized MOBC should also feed back into theory and modify it accordingly. The health behavior change literature is instructive in providing a model for the proposed feedback loop. Specifically, Michie et al., 2017; also see Carey et al., 2019 designed and implemented a system that links health behavior change interventions and/or intervention components with specific MOBC that is accessible online (https://theoryandtechniquetool.humanbehaviourchange.org/tool) and evolving, in real time, with knowledge accumulation. The website is interactive, and investigators can enter the results of relevant MOBC studies into the system. Contributions from addiction science to this system are needed, but a potential barrier is that AOD MOBC research has reflected a clear preference for testing hypotheses that are modality-specific despite growing evidence that such hypotheses are not supported (Maisto & Moskal, 2019, 2022). There has been a long-standing and energetic debate in general psychotherapy in this regard (Wampold & Imel, 2015), and we suggest the use of broadly applicable theoretical models is warranted. Alternatively, if theories proposing treatment-specific MOBC become more precise, support for unique causal mechanisms might emerge. Given that possibility, we do not frame this as an either–or question, and instead as a need for a more balanced emphasis.

Prioritize experimental designs with clear implications for translation

The clinical trial *experiment* (criterion four) is the modal research design in published AOD treatment MOBC research. This is not surprising, given the causal chain that has guided MOBC, which is that an intervention causes change in one or more theoretically derived mechanisms, which in turn cause change in one or more health-related outcomes. In this sense, AOD treatment MOBC researchers adhere closely to the experimental recommendation, and this research is extremely valuable in advancing our thinking about how AOD treatments work. The experimental evidence, however, is specific to the capacity of an intervention to impact a mechanism while the association between mechanism and outcome is typically observational in nature. Fortunately, there are variants of classical randomized clinical trial design that can be both cost efficient and well-suited to testing hypotheses about MOBC. Table 2 presents a range of these designs, a brief description of each, an example of each design's application in the AOD treatment literature, and a description of how these designs may further translational MOBC. It is noteworthy that these kinds of studies require interventions or intervention components that follow the tenets of *singularity and proximity* noted earlier, which can facilitate a clear, feasible, and

testable path to a hypothesized MOBC and implementation. We argue these designs are under-represented in the AOD literature, and their increased use in conjunction with ongoing development and refinement of relevant theory would accelerate knowledge and knowledge translation of MOBC.

Consistency across sources of evidence for MOBC translation

While experimental design has much to offer and has contributed to the identification of promising AOD treatment mediators, eating your cake and having it too involves utilization of the evidence we have right now as well as use of a range of research designs that build that evidence over time. Kazdin and Nock's (2003) recommendation of *consistency* (criterion six) is relevant to this aim. Here, non-experimental supplements to the previously described experimental designs, as well as knowledge synthesis frameworks, have a place in furthering translational MOBC. The additional study designs may not involve random assignment of participants to experimental conditions and other considerations for internal validity but have greater ecological validity and generalizability. Two such designs that seem particularly relevant are the natural experiment (e.g., Crane et al., 2020) and the longitudinal observational study (e.g., Reichardt, 2019). Such designs can be used not only to identify MOBC of policy effects or other system-level interventions, but they can also be used for studies of naturalistic change, which is an area that is underdeveloped in the MOBC literature. If studies using these design approaches are added to the MOBC science repertoire, an awareness of their respective biases that impede inferences about causality is necessary. As Rohrer (2018) noted, addressing limitations in non-experimental research is difficult, but the cumulative yield in knowledge from investigators' skilled use of multiple research designs could be substantial.

Currently, there are no specific guidelines or a gold standard that would allow objective determination of MOBC that have met the needed criteria to warrant translation and implementation. Relevant to this task is a process of triangulation, which refers to reaching conclusions from diverse sources of data. In the social and behavioral sciences, using triangulation for making valid causal inferences from research data became prominent with the publication of Campbell and Stanley's (1963) book on causal inference and the application of experimental and quasi-experimental research designs. Although the term is to some degree controversial and its utility has been questioned, triangulation remains a widely used process in social and behavioral science and in health-related research (Munafò & Smith, 2018). As Morgan (2019) noted, three outcomes of triangulation have been considered: convergence, complementarity, and divergence. *Convergence* is highly relevant to this discussion and by far, has received the most emphasis in the literature. When convergence is met, differently designed and independently conducted studies produce similar results. For example, the results of experimental and non-experimental studies, or quantitative and qualitative research, may be considered. The ultimate goal of triangulation in advancing AOD MOBC knowledge is to draw conclusions about causality that are not attributable to any particular study method, but rather to the true relations among variables in question.

The question remains of how to synthesize the findings from a set of research studies following diverse designs. Probably the most common way is via subjective evaluation, and Kazdin and Nock's (2003) seven recommendations assume this approach (also see, e.g., Hammerton & Munafò, 2021; Rohrer, 2018). Along these lines, descriptive categories that characterize the accrued evidence for causality are helpful. One such classification was presented in a report that the Institute of Medicine (IOM) published in 2008. This classification system includes five categories that are ranked in descending order of credibility, including Sufficient Evidence of a Causal Relationship, Sufficient Evidence of an Association, Limited/Suggestive Evidence of an Association, Inadequate/Insufficient Evidence to Determine Whether an Association Does or Does Not Exist, and Limited/Suggestive Evidence of No Association (Samet & Bodurow, 2008, Table 8–2). For example, Sufficient Evidence for a Causal Relationship in this scheme includes sufficient evidence for an association as well as satisfaction of other criteria that are used to assess causality, such as strength and consistency of that association. Regardless of the selected framework, the key point is the importance of diverse sources of knowledge and systematic knowledge synthesis methods that work in concert to build the case for specific MOBC that can be targeted for implementation.

SUMMARY AND IMPLICATIONS

This work explored MOBC science and implementation science, considering areas of compatibility and the potential for *Translational MOBC*. We argue that knowledge about change in AOD use and related consequences and its application to clinical practice would be accelerated by greater use of implementation science principles and methods, and offer a research agenda toward that end. We conclude with a discussion of five ways that integrating MOBC science with implementation science can move the content and course of MOBC research forward.

Greater emphasis on clinical significance

Mechanisms of behavior change research designs that consider immediate or imminent clinical impact can result in findings with greater clinical significance, and greater clinical significance will likely appeal to community providers. In a study by Miller and Manuel (2008), the authors surveyed clinicians participating in the NIDA Clinical Trials Network about the magnitude of change in different patient outcomes (e.g., percentage of days abstinent, legal consequences of AOD use, and biomarker data, such as liver enzymes) that they would find clinically meaningful and would justify their learning new evidence-based practices. The study showed that the clinicians identified specific thresholds of clinical significance for different outcomes rather than placing weight on statistical significance. Part of prioritizing research with immediate or imminent clinical impact is understanding what types of findings matter most to potential research consumers, which is a perspective that has been part of the implementation science ethos for quite some time. This means MOBC researchers should consider partnering with persons with lived experience, treatment providers, and other community program stakeholders early in the research design process. We do not argue that this has not occurred to date, but that it can occur more and should be considered central to every stage of clinical AOD research.

Feedback of implementation results to earlier stages

As noted by Onken et al. (2014) (Figure 2), the paths between basic science (e.g., MOBC science, Stage 0), efficacy trials (Stage 1), and implementation (Stage 5) should be taken with caution. However, with greater translation of MOBC science, feedback among various knowledge generation stages could be enhanced. For example, review data suggest self-efficacy to abstain/moderate AOD is a common mediator across a range of EBTs (Maisto & Moskal, 2019, 2022). Such information would support pursuing implementation of these findings in clinical practice as part of the proposed research agenda. Naturally, the venue of implementation could vary, such as targeting self-efficacy in treatment development, targeting a clinical emphasis on self-efficacy in supervision, or training providers specifically on how to work with self-efficacy as a mechanism. According to the NIH stage model, the outcomes of such implementation efforts would directly feed back into the design of basic research on self-efficacy as a mechanism of behavior change as well as on clinical trials that may be designed subsequently to test the application of new implementation knowledge generated.

Consideration of moderators

With greater attention to clinical significance, implementation potential, and other methods of MOBC translation may come greater attention to considerations of *what works for whom*. In Lewis et al. (2018) work on mechanisms of implementation strategy outcomes, effect modifiers are a part of the standard process model, and this is understandable given the role of context, barriers and facilitators in determining implementation success metrics (e.g., adoption and/or sustainment). In AOD treatment clinical trials, attention to effect modifiers has occurred, but just as with statistical mediators, population-level moderators are often relegated to secondary and even, tertiary aims. There are pragmatic reasons for this, such as the large sample size needed to test moderators with small or medium effect sizes, but failing to attend to moderators could limit the clinical impact of research findings. For example, there may be moderators that reduce treatment effectiveness for some subgroups, which would limit the treatments' broad utility when implemented in the community. This has also been identified as a gap in the general health literature on behavioral interventions (Alcántara et al., 2020; Byrne, 2020). Designing MOBC research with attention to implementation requires consideration of possible moderating variables (e.g., characteristics of persons, their environments, implementation contexts) and is best captured by Michie et al. (2017) extension of the famous quote by Gordon Paul (1967) "what works, compared with what, how well, with what exposure, with what behaviors (for how long), for whom, in what settings, and why?" (p. 4).

Multi-level orientation to behavior change

The implications noted thus far lend themselves to a multi-level orientation to behavior change (e.g., the individual, group, and system). This contextual emphasis is already influential in implementation science, which can be contrasted with MOBC science's more common emphasis on the individual. An excellent example of this orientation is Pfadenhauer et al.' (2017) Context and Implementation of Complex Interventions framework. In this framework, context, implementation, and setting interact among themselves and with the

intervention in question. Following this or similar frameworks increases the complexity of the MOBC researcher's task substantially but is important to achieving the clinical significance and ecological validity that holds the best chance of having lasting influence on the care of individuals in the community.

Bring MOBC and implementation researchers together

Our proposed research agenda for Translational MOBC Science and how attention to implementation might influence it leads ultimately to the conclusion that the best and most significant MOBC research in the future will be done by multi-disciplinary teams of investigators who have knowledge, skills, and experience in both MOBC and implementation science. Such a recommendation seems in line with other initiatives such as the Science of Behavior Change that attempt to break down siloes of knowledge generation and instead produce information relevant to a range of public health outcomes. In Translational MOBC Science, the ideal future will involve investigators versed in both areas of study. Moreover, recent program announcements and Notices of Special Interest demonstrate this is a force in motion because both the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism have identified translational priorities (e.g., RFA-DA-24-010; RFA-DA-23-013; NOT-AA-20-022).

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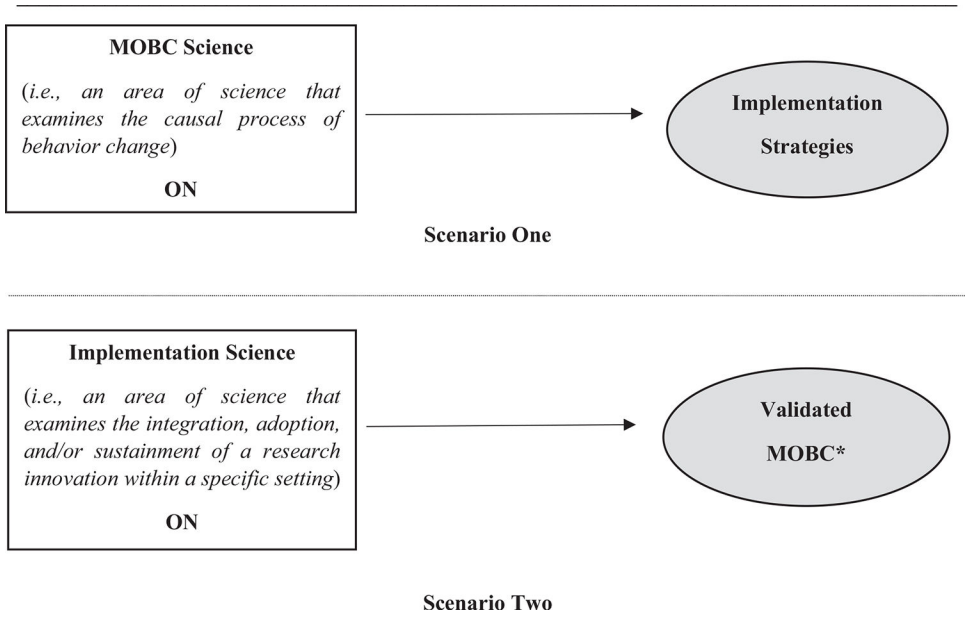

FIGURE 1.
Two scenarios for the intersection of mechanisms of behavior change and implementation science.

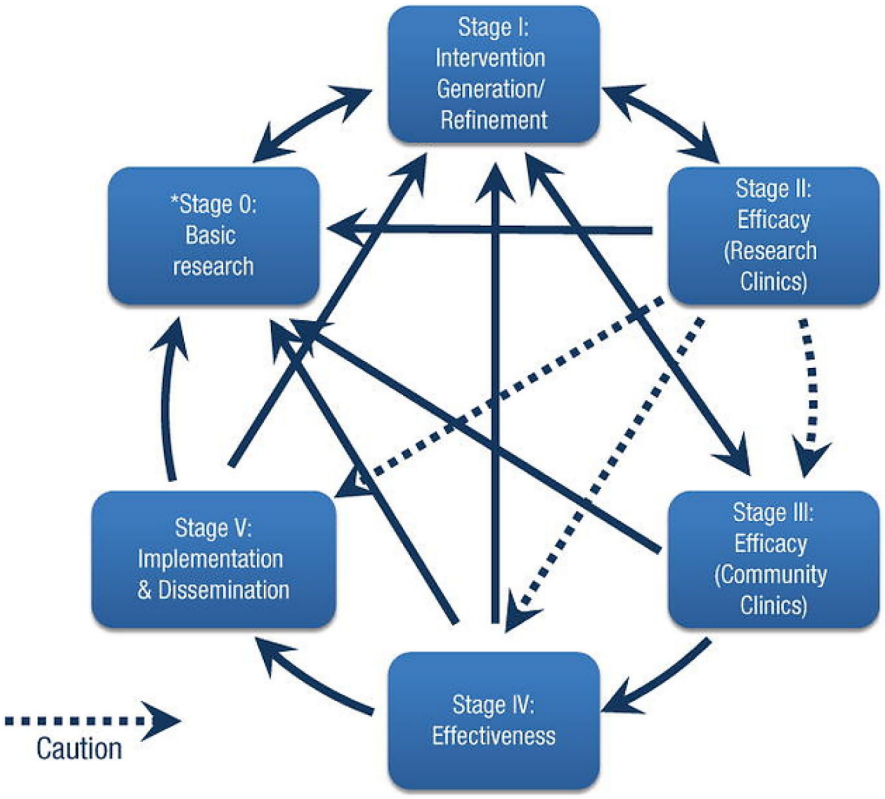

FIGURE 2.
The NIH stage model of intervention development.

TABLE 1

Kazdin and Nock (2003) Criteria for establishing a mechanism of behavior change.

Criteria	Recommendations for research
1. Strong Association	Include measures of potential mechanisms of change in psychotherapy studies.
2. Specificity	Assess more than one potential mechanism, as well as possible confounding.
3. Gradient	Assess whether greater changes in proposed mechanisms are related to subsequent, greater changes in outcomes.
4. Experiment	Intervene to change the proposed mechanism of change.
5. Temporal Relation	Establish a timeline by using continuous measurement of proposed mechanisms *and* outcomes of interest.
6. Consistency	Replicate observed effects in different studies, samples, and conditions (e.g., naturalistic and laboratory settings).
7. Plausibility and Coherence	Use theory as a guide to select potential mechanisms for focus of study, as well as to explain observed effects and integrate them into the broader knowledge base.

Note: Reprinted with Permission, Kazdin and Nock (2003).

TABLE 2

Experimental designs suited to translational MOBC.

Design	Description	Example in disseminated AOD treatment research	Application to translational MOBC
Dismantling Design	Can be used to determine the unique contribution of a component in a multi-component treatment (Guidi et al., 2018)	Morgenstern et al. (2017)	An experimental test of a specific component will isolate the additive effect of that component. This design should allow for specification of a singular and proximal causal chain where the mechanism associated with the component is absent in the observed process model of the comparison condition.
Micro-intervention Design	Investigation of a specific therapeutic technique guided by a theoretical model of change process (Strauman et al., 2013)	Holzhauer et al. (2021)	Similar to above, this type of design allows for the specification of an MOBC that is tied to the technique. If supported, implementation implications include subsequent implementation of the technique, changes to supervision and training, and/or intervention development/refinement
Multiphase Optimization Strategy (MOST; Optimization Phase)	A series of experiments to determine the performance of each component of a multicomponent intervention (Collins et al., 2007)	Windsor et al. (2018)	In this case, all components of a multi-component intervention are empirically validated, providing optimal justification for community implementation.
Micro-randomized Design	Intervention or intervention components are randomly assigned at specific decision points in real time. Design has been used mainly to test just-in-time adaptive interventions (Klasnja et al., 2015)	Carpenter et al. (2020)	This design accommodates patient heterogeneity and provides an evidence-based, stepped care approach. This design is well-suited for the *for whom* questions of Translational MOBC Science.
Hybrid Designs	A clinical trial with outcomes relevant to intervention effectiveness and implementation (Type 1–3; Curran et al., 2012)	Mello et al. (2018)	The design is well-suited to Translational MOBC Science because mechanisms can be specified for both effectiveness and implementation aims.
Single Subject Experimental Design and Mediation	Adding mediation analysis to single case experimental design (Valente et al., 2022)	None identified	This design has implications for practice-based MOBC research where providers in community settings track intervention effectiveness via one or more specific MOBC.

Abbreviations: AOD, alcohol or other drug; MOBC, Mechanisms of Behavior Change.