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EDITORIAL

The full translational spectrum of prevention science: facilitating the transfer of knowledge to practices and policies that prevent behavioral health problems

Diana H. Fishbein, Ph.D,[1] Ty A. Ridenour, Ph.D,[2] Mindy Stahl, Ph.D,[2] Steve Sussman, Ph.D[3]

[1]The Pennsylvania State University, 302 Biobehavioral Health Building, State College, 16841, PA, USA
[2]RTI International, Research Triangle Park, Durham, NC, USA
[3]University of Southern California, Los Angeles, CA, USA

Correspondence to: D Fishbein
dfishbein@psu.edu

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Abstract

A broad-span, six-stage translational prevention model is presented, extending from the basic sciences—taking a multi-level systems approach, including the neurobiological sciences—through to globalization. The application of a very wide perspective of translation research from basic scientific discovery to international policy change promises to elicit sustainable, population-level reductions in behavioral health disorders. To illustrate the conceptualization and actualization of a program of translational prevention research, we walk through each stage of research to practice and policy using an exemplar, callous-unemotional (CU) traits. Basic science has identified neurobiological, psychophysiological, behavioral, contextual, and experiential differences in this subgroup, and yet, these findings have not been applied to the development of more targeted intervention. As a result, there are currently no programs considered especially effective for CU traits, likely because they do not specifically target underlying mechanisms. To prevent/reduce the prevalence of conduct disorder, it is critical that we transfer existing knowledge to subsequent translational stages, including intervention development, implementation, and scaling. And eventually, once resulting programs have been rigorously evaluated, replicated, and adapted across cultural, ethnic, and gender groups, there is potential to institutionalize them as well as call attention to the special needs of this population. In this paper, we begin to consider what resources and changes in research perspectives are needed to move along this translational spectrum.

INTRODUCTION

Despite exciting advances in our knowledge of the biological, social, and environmental underpinnings of behavioral health problems, the translation of original research to routine public or mental health practice takes at least one or two decades, sometimes longer. The reasons for this protracted gap between research findings and the implementation of evidence-based strategies and practices are complex, related to difficulties in communication across research and practice disciplines, as well as logistical and political considerations [1]. To more effectively reduce the burden caused by behavioral health problems, more comprehensive translational processes that facilitate the cycle of moving basic research findings to actionable practice and policy are needed. These processes must consider multiple and integrated stages of knowledge transfer that join discovery, intervention creation, evaluation, scaling, policy reform, and public support for prevention science as a holistic process. There are also weighty scientific gaps and logistic, cost, and political barriers that may delay the application and acceptance of science-based practices and policies in settings where they are most needed and can exert the broadest benefits [2]. The fundamental characteristics that define quality behavioral health services –effective, efficient, contemporary, and timely– with potential to improve or save lives cannot be achieved without careful attention to the translational practices that transform basic science discoveries into institutionalized practice and policy. Such work is especially imperative in prevention science given the burden of human suffering as well as the fiscal costs associated with neglect for early detection and intervention of mental, emotional, and behavioral disorders.

Intrinsic to translational research is the communication of scientific discoveries across a "nomological network" to facilitate the acquisition of new knowledge and new applications of that knowledge [1]. Several frameworks have been used to describe translation of research from basic to applied science in the biomedical field, e.g., the NIH Five-Phase Model, the Flay Eight-Phase Model, Classification for Application Model, Program Development Models, Diffusion of Innovations, and Type 1 and Type 2 Translation [1, 2]. Few of these existing models, however, apply specifically to the prevention sciences, and they do not necessarily reflect a system-oriented, transdisciplinary approach incorporating back translation nor do they span the full spectrum from basic discovery to global change in attitudes and systems.

An important element of our proposed translational framework is its emphasis on transdisciplinary collaborations within and across six stages of knowledge transfer. Translational research does not simply involve an additive approach to distinctly different stages but demands a synergistic perspective that values varied expertise and capabilities and requires communication among different programmatic and scientific roles and perspectives within and across stages. These roles may involve persons from rather different academic backgrounds that create a consensual model of inquiry (i.e., transdisciplinary approach) to be able to engage in effective, inclusive translation. Such collaboration may run contrary to a traditional system of scientists tending to work in their own domains and not communicating well or often with those working in other domains [3]; these research silos constitute a barrier to true translation. What is most needed to accelerate translational research and advance the practice of prevention is an integration–not compartmentalization–of thought/theory and approach/methodology applied in an effective and scientifically sound manner.

Another essential characteristic of our translational typology is its incorporation of a system approach [4]. Conceptualizing the etiology of problematic behaviors and the translational paradigm needed to transform this understanding into prevention programming that incorporates or is based on a complex system approach has potential to improve efforts to prevent behavioral health problems in youth and subsequently in adulthood [5, 6]. Although there is no common definition, a complex system is typically thought of as an entity composed of many different parts that are interconnected in such a way that the characteristics of the system as a whole cannot be anticipated from analyzing its components alone. Many factors can contribute to this complexity including interrelated components with bidirectional "feedback" loops, non-linear relationships among some components (e.g., threshold or ceiling effects), impacts stemming from multiple levels of influence, or heterogeneous and often long time delays between cause and effect. Prevention science as a whole may be characterized as a complex system of inquiry. Prevention of behavioral health problems must consider the *dynamic interplay between factors at multiple levels* including *individual* (e.g., genetics, neurobiological factors, and personality characteristics), *micro-social* (e.g., parental role modeling, social network characteristics, and social norms), and *macro-social* (e.g., school systems, advertising campaigns, agricultural initiatives, political parties, and political action [7]). Unfortunately, numerous system-level barriers exist, including scientific funding constraints, as well as political decision-making and institutional disincentives. These realities impede the transfer of basic science knowledge to development of multi-level interventions, despite extensive research indicating that such interventions are necessary and effective in addressing the complex pathways to behavioral disorders.

A new generation of *transdisciplinary* research grounded in a system approach now highlights the many complexities of behavioral health problems that arise from interactions across multiple levels and domains of innate but dynamic individual characteristics, experiences, exposures, and contexts. Emerging prevention research demonstrates that individual differences in risk for behavioral health problems can only truly be understood by recognizing that an individual's orientation to and processing of environmental inputs rely highly upon genetic and neurobiological mechanisms. These underlying mechanisms, in turn, interact with the quality of an individual's psychosocial and environmental exposures and protective factors to alter trajectories either toward or away from poor overall outcomes. A parallel body of research further suggests that neural dysfunction underlying behavioral disorders, regardless of its origins, may be malleable and, relatedly, that compensatory mechanisms can be strengthened with indicated psychosocial (e.g., life skills and socio-emotional learning) or biomedical (e.g., pharmacologic and neurofeedback) manipulations. And of particular intrigue for prevention science is the potential for environmentally induced epigenetic change in one generation to alter outcomes in subsequent generations [8]. Consideration of the interplay of these factors–both causative (impoverished environments) and consequential (effects of adversity on neurodevelopment)–presents new and exciting possibilities for prevention science. These scientific discoveries only await replication and then translation to interventionists, policy-makers, and the public to exert their greatest preventative impact.

TRANSLATIONAL TYPOLOGIES

This emerging body of transdisciplinary research has extraordinary potential for preventing behavioral health disorders and promoting resilience. There are at least two aspects of research in prevention of behavioral health problems that are plagued by deep gaps in translation. First, much of the emerging research on the brain and behavior has not yet been integrated into a holistic model of prevention research or used to inform development of new and innovative practices. And, as mentioned, research silos, communication challenges across disciplines, and narrow funding streams create barriers to such integration. Second, translation science has not done enough to facilitate knowledge transfer through to the end stages of translation including wide-scale dissemination and institutionalization. Certainly, important work has been completed on diffusion and scaling-up of innovations [1]. However, much end stage application typically relies on soft money strategies (i.e., temporary support), is limited by the language or origin of programming (e.g., by the delivering agency), and the means to update and sustain programming generally are not available. A better understanding of exactly how to best institutionalize programming, translate programming globally, and contribute to international policy reform (e.g., in education, mental, and public health) requires a great deal more attention.

These limitations highlight the need for a more refined, interpretable, and consensual model of translational prevention science. We refer to our model as the *full translational spectrum of prevention science* and provide six basic stages of translational research as shown in Table 1 and Fig. 1. Each stage describes the

Table 1 | Full translational spectrum of prevention science: research stages

Type	Type 0 Translation (T0)	Type 1 Translation (T1)	Type 2 Translation (T2)
Definition	The fundamental process of discovery, where findings from the social, behavioral, and biomedical sciences (animal and human) are translated into applied research with human subjects. Includes study of analogous processes and phenomena via field- or lab-based investigations using human subjects that could be applied to preventive intervention.	Moving the research from bench to bedside location. Includes the translation of applied theory to development of methods (measures and analysis) and programs.	Moving from bedside to practice. Involves the translation of program development to implementation (i.e., efficacy trials with emphasis on internal validity and effectiveness trials with emphasis on internal and external validity).
Example	A parallel study with forward and back translation to understand the impact of early environmental adversity on brain development and mechanisms that subsequently confer risk.	Development of measures, methodologies, and interventions that focuses on self-regulatory processes subserved by prefrontal-limbic connections. Includes the initial development of the Good Behavior Game and Promoting Alternative THinking Strategies (PATHS).	Randomized clinical trials of preventive interventions to establish the size of outcomes that can be attributed to the programs (controlling for alternative influences), followed by rigorous testing with well-defined populations.
Type	Type 3 (Translation) (T3)	Type 4 Translation (T4)	Type 5 Translation (T5)
Definition	The practice-oriented phase involving research to test the degree to which efficacy and effectiveness trial outcomes can be replicated under real-world settings. Focuses on adoption, adaptation, and dissemination.	Research focused on "scaling-up." Wide-scale implementation, adoption, and institutionalization of new guidelines, practices, and policies.	Translation for application in global communities. Involves fundamental and universal change in attitudes, policies, and social systems.
Example	Study of parameters of adaptation of highly replicated programs and interventions with strong positive effects across time and context.	Research on scaling of the evidence-based programs in multiple school districts within and across counties.	Policies based on acceptance of science-based practices such as laws instituting juvenile justice reforms and programs providing wide-scale educational innovations.

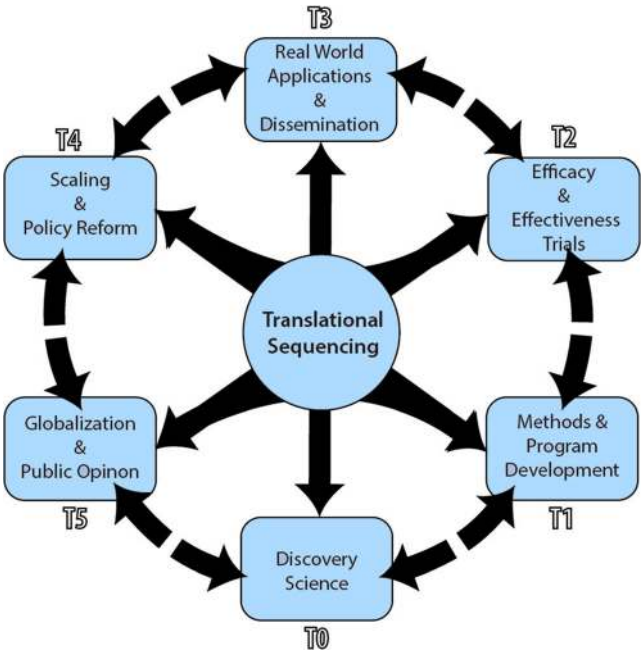

Fig. 1 | The full translational spectrum of prevention science model showing the following six basic stages of translational research: *T0* **Discovery Science,** *T1* **Methods and Program Development,** *T2* **Efficacy and Effectiveness Trials,** *T3* **Real-World Applications and Dissemination,** *T4* **Scaling and Policy Reform, and** *T5* **Globalization and Public Opinion**

results of one activity being translated to an activity in the next stage of translation along the pathway. Research methodologies that are ideal in one stage (e.g., randomized control trials used for Type 2 Translation) often cannot be employed for other stages of translation (e.g., institutions and states often cannot be randomized, per se). Thus, the *full translational spectrum of prevention science* model recognizes the need for rigorous research methods specifically adept to address research questions of each translation type [e.g., 9–11].

Below, we describe each of the six stages starting with Type 0 Translation (T0, Discovery Science). T0 is the basic process of scientific discovery [2]. It is at this most fundamental stage where replicated findings from many areas of basic research from animal and human subject studies, including molecular, cellular, biological, and psychological lab-based or field-based research, with individuals or groups, and incorporating environmental influences are translated to inform the next stage of applied research with human subjects. We refer herein to discoveries that have import to the development of preventive interventions that more directly target mechanisms underlying a behavioral problem, as described in the next stage. Most often, discovery scientists do not consider their work relevant to prevention, e.g., neurotransmitter systems implicated in drug reward that are alterable to some extent with targeted intervention.

Type 1 Translation (T1, Methods and Program Development) refers to the transfer of knowledge from the basic sciences to the applied sciences with the translational outcome being applied methods and theory-based program development. Accomplishments in Types 0 and 1 Translational Research advance our understanding of the underlying mechanisms in behavioral health disorders and, further, of the malleable mechanisms of behavioral change that can be targeted in intervention development. Translation of findings on etiological underpinnings of behavioral health leads to a better understanding of the significant reciprocal impacts of the cognitive/affective processes and the social and physical environment with neurogenetic systems in ways that will, in turn, optimize development of both universal processes for adaptation and *personalized prevention* approaches. This pivotal stage moves us forward on the translational continuum toward actionable impact.

Type 2 Translation (T2, Implementation and Effectiveness) embraces the applied strategies generated by T1 and aims to facilitate, in part, preparation for testing and establishing evidence-based or scientifically validated interventions. For the T2 process to succeed, most prevention scientists require evidence for intervention's *efficacy* (i.e., its degree of benefit under high internal validity conditions and evaluating outcomes attributable to the program) and *economy* (i.e., benefits eventually exceeding its costs) with large defined populations. Although T2 is currently receiving increased attention, the reality remains that many interventions found to be efficacious fail to achieve *effectiveness* (i.e., replicating outcomes from efficacy trials in "real-world" settings, deliverers, and recipients, also using rigorous research designs), do not reach those most in need, or are so poorly implemented that their potential for impact suffers. Likewise, even after evidence has accumulated that demonstrates a program lacks efficacy, a protracted period of time often elapses before such interventions are discontinued due to institutional

inertia or misguided understanding of intervention mechanisms.

These are only a few of the factors that illustrate the importance of T2 implementation research and the processes that support effective practices in real-world conditions [9]. The goal is that individuals in population groups for whom interventions are developed in the "lab" may engage positively and achieve long-term success across multiple domains of functioning. However, without complete implementation evaluation, many others for whom more personalized or culturally tailored approaches are needed never receive the services or "dosages" required, respond less favorably, and thus exhibit a trajectory toward onset and escalation of behavioral maladjustments. And in spite of growing community-level enthusiasm for prevention in concept, key players including funding agencies, political and agency leaders, and frontline service providers often lack the knowledge base and capacity to implement, evaluate, and refine potentially impactful programs. Challenges involving whether or not efficacy and effectiveness outcomes apply to much less well-controlled settings (i.e., real world) are addressed in the Type T3 Translation.

Translational Research (T3, "Real-World" Applications) responds to the further need for the application of an integrative and comprehensive translational research agenda that prioritizes the transfer of research findings from earlier stages in the research process to T3. T3 moves practices developed through T2 research beyond the academic research environment into applied settings where adoption and adaptation of evidence-based practices occur with a goal to systematically reduce individual- and population-level behavioral health disorders. A myriad of different implementation strategies and research designs might be utilized to help understand and maximize T3 translation. Unfortunately, community stakeholders, practitioners, policy-makers, and even scientists across disciplines are not fully aware of the wealth of rigorous and replicated research findings generated by the prevention sciences that have been demonstrated to operate across varying environmental contexts [10]. As a result, there is a serious gap between development of evidence-based programming and program application leading to a lack or inconsistent schemes of systematic and sustainable adoption of evidence-based practices for prevention and insufficient feedback for appropriate fine-tuning of programming across contexts. Further, there is a void in this stage of translation where emerging knowledge in genomics/epigenetics that may inform personalized medicine approaches and advanced knowledge in ethnology could be integrated to ensure personal and cultural adaptations for optimal effectiveness. Hence, more critical and strategic thinking is needed to address the multitude of investigator-level, institutional, and environmental factors that impede the translation of relevant findings across stages of the translational spectrum in a recursive fashion, involving implementation science, wide-scale adoption and adaptation to various settings and cultures, sustainability on a population level, and eventually institutionalization. Remedies include consideration of the foundational findings and delineating transdisciplinary applications of system science and innovative research techniques in the implementation and evaluation sciences. Also important is to enhance communication between researchers and communities (e.g., practitioners and policy-makers) necessary for eventual acceptance and rigorous adoption [4, 9–12].

Type 4 Translation (T4, Scaling and Policy Reform) serves to formally acknowledge and categorize research to understand how to move effective prevention programs into a stage in which they can be *safely* applied in clinical, non-research-oriented contexts and subsequently become self-sustaining in terms of fiscal subsidization, professional servicing, and infrastructure maintenance and support. There is very little research in T4 prevention science translation, possibly because the need to integrate health behavior research with system science and business methodologies, among other disciplines, stretches collaborative networks into uncharted territories needed to move forward. Please see Rohrbach et al. and Spoth et al. [13, 14] for excellent reviews of existing frameworks.

There have been a few evidence-based practices, however, that have reached the doorstage of this T4 stage in terms of greater adoption and some degree of institutionalization. For example, Triple P (https://www.pfsc.uq.edu.au/research/evidence/) has evolved into a system of interventions that are provided in multiple sites across the USA and has been scaled up in Canada and 25 other countries [15]. Parts of the system or unique configurations of the system have been adapted for various jurisdictions. Chamberlain and colleagues have reported in a series of papers the results, vagaries, and successes of scaling the Multidimensional Treatment Foster Care (MTFC) and other interventions at the T4 stage [16]. Forgatch and DeGarmo have applied a "full transfer model" with direct observation and random assignment using the national Norwegian implementation of Parent Management Training-Oregon Model (PMTO™), an empirically supported treatment for families of children with behavior problems [17]. In this work, second-generation teams are trained and then train their own therapists, achieving effects comparable to those in the original efficacy trials with sustained fidelity and cross-cultural generalizability. Also, PROmoting School-community-university Partnerships to Enhance Resilience (PROSPER) is a delivery system that provides evidence-based programs for middle school youth and their families. PROSPER has a three-tiered structure that includes teams from the community, prevention coordinators, and a state management team that facilitates the receipt of ongoing proactive technical assistance based on need assessments of any given community [18–20]. And finally, the well-known Communities that Care (CTC) prevention service delivery

system develops local infrastructures and coalitions of community stakeholders to improve the behavioral health of young people [21, 22].

These programs and systems have achieved widespread implementation, maintenance, and documented successes. However, most are not part of official governmental systems, which would more fully characterize them in the realm of T4 translation. Soft money contracts and grants often fund them, which is limiting and can threaten sustainability and full infiltration. The Evidence-based Prevention and Intervention Support Center (EPISCenter) differs somewhat in this regard. It represents a collaborative partnership between the Pennsylvania Commission on Crime and Delinquency (PCCD) and the Bennett Pierce Prevention Research Center at the Pennsylvania State University. Funding comes from the Pennsylvania Commission on Crime and Delinquency (PCCD) and the Pennsylvania Department of Human Services (DHS). The EPISCenter supports the dissemination, quality implementation, sustainability, and impact assessment of a menu of proven-effective prevention and intervention programs and conducts original translational research to advance the science and practice of evidence-based prevention.

In general, T4 efforts are rife with challenges and system transformation needs that are unmet by the program purveyor alone. There is a need for growing professional capacity to support effective implementation and scale-up within service systems and agencies. A transdisciplinary science of implementation that has been coalescing through the emergence of this new field of implementation, and the application of this science, much like the application of an evidence-based practice (EBP), requires skillful practice to make use of it in context. We manage, plan, and react to the service system or agency in front of us, just as a practitioner does with patient or family in front of them. Science alone cannot fully solve implementation and scale-up issues; they can only be resolved by the application of the science through skillful professional practice. The science needs to continue to accelerate, of course, but it only has its impact at scale through practice.

Type 5 Translation (T5, Globalization and Public Opinion). In concept, the eventual achievement of T4 practice results at the local and national levels in altering our universal (worldwide generalizable) understanding of the key determinants of behavioral health and well-being, constituting stage T5 in this typology. T5 involves translation to global communities, pertaining to ways in which global policies and environmental change can effectively target relevant health conditions across multiple cultures and societies. In effect, this stage addresses international behavioral health priorities as set by international agendas, thus impacting large-scale population-level shifts in well-being. The ultimate goal is to reform universal social systems to become more responsive to human needs based on sound and well-tested scientific evidence, taking into account global political, economic, and cultural variations. Possibly, one recent example approaching the T5 stage is the Framework Convention on Tobacco Control (FCTC) [6] which provides an international model for policies that focus on the many consequences of tobacco consumption. However, although the framework has been accepted to some extent, behavioral health change has not yet occurred on a global level. There are virtually no living examples of T5 in the prevention sciences.

Back translation

Back translation, an iterative part of the process, occurs at every stage in a translational process or continuum in a recursive fashion. This activity incorporates bidirectional exchange across all stages, contributing to constant modifications and refinements, as needed. If the results of a trial are negative or unexpected findings occur, for example, they likely inform knowledge that had been culled during prior translational stages and may require further assessment and refinement. To illustrate, a randomized clinical trial is in essence also an etiology experiment in which specific environmental factors are manipulated while all others are controlled.

Back translation allows us to continuously address outstanding questions posed by persistent or emerging findings of individual- or group-level differences in intervention outcomes. Thus, with ongoing development, implementation, and refinement of the science-based interventions in different populations, cultures, and settings, knowledge regarding etiological underpinnings of high-risk behaviors grows more universal and yet provides for a more comprehensive and confirmatory assessment of underlying mechanisms of therapeutic outcomes for subgroups or individuals as well. The ultimate goal is that, through a transfer of knowledge from etiology to practice and back to etiology, clinical and public health policies will be increasingly responsive, applicable, and effective, thereby exerting greater reductions in psychopathology.

Back translation generally has been neglected in traditional models and will be addressed as a critical component of the bidirectional and recursive translational model in this special issue of *Translational Behavioral Medicine* [11]. Accordingly, this stage is proposed as critical to recognize the necessity for back translating real-world observations to continually confirm and inform etiology and basic biopsychosocial research. Early in the translational process of advancing knowledge from one stage to another, any adaptations could be considered groundbreaking as well as preliminary. Ideally, pilot studies and beta testing would be used prior to large-scale research; Ridenour et al. describe and illustrate rigorous techniques for conducting within-subject (which could consist of persons, clinical settings, and states) experiments for pilot testing of preventive intervention [11].

To optimize the societal benefits of prevention science, the ultimate goal of this translational process is to

determine *what prevention/clinical practices work best for whom (moderation), why (mediation), and under what circumstances (contextual, experiential, and implementation qualities).* In other words, how do individual-level genetic, neurobiological, and psychological mechanisms interact with the psychosocial and physical environment to promote or, alternatively, interfere with improvements in behavior in response to intervention? The premise behind such a program of research is that tailored, targeted interventions will be most effective when psychosocial and pharmacologic manipulations are "mapped" to an individual's unique constellation of social, psychological, and biological attributes, thereby reinforcing more adaptive and normative phenotypes. And in a translational fashion, information gleaned from this transdisciplinary, integrated approach can foster synergistic opportunities to apply prevention science results to protect individuals and communities from harm and foster systematic ways that researchers, practitioners, and policymakers can work together to support improved interventions for more individuals, families, and communities.

Below, we review the full translational spectrum using an exemplar from research focused on a subclass of conduct disorder, an isolating and disruptive behavioral health disorder. This example allows us to stage through the translational process in a largely theoretical framework but based on solid scientific findings. We highlight ways in which understanding the mechanisms, triggers, and developmental progression of a specific conduct disorder subtype may have important implications for the translational processes needed to effectively develop and adopt evidence-based strategies for prevention and treatment.

EXEMPLAR PHENOTYPE: CALLOUS-UNEMOTIONAL TRAITS

The potential utility of a transdisciplinary approach across all six stages of the translational spectrum is exemplified in a futuristic manner by the foregoing discussion of research on callous-unemotional (CU) traits in children. This phenotype was selected due to a new and growing body of discovery research implicating distinct neurobiological and cognitive interactions in and differences between children with and without CU traits.

T0–Youth with conduct problems are characterized by heterogeneous subgroups with disparate environmental risk factors, individual level vulnerabilities, and ultimately behavioral trajectories [23, 24]. The presence of CU traits represents a specific subtype of conduct problems [25] that is characterized by callousness (deficiencies in empathy or remorse), unemotionality (fearlessness and blunted emotions), and uncaring attitudes and behaviors (aggression and difficulty maintaining relationships) [26]. Children with CU traits are at elevated risk of developing more severe, persistent, and treatment-resistant conduct problems compared to children with conduct disorder without CU traits [27]. In fact, characterizing CU traits has emerged as a reliable means of dissociating subsets of youth with conduct problems at highest risk for detrimental outcomes.

During this basic process of discovery, studies are reporting that CU traits are measurable by age six [27] and are highly stable [28]. Of great relevance, children with these traits are also distinctive–psychologically, neurobiologically, and cognitively–from those with other traits and conditions predictive of externalizing problems (e.g., aggression and substance abuse), such as conduct disorder (CD), oppositional defiant disorder (ODD), anxiety, and attention deficit hyperactivity disorder (ADHD). Basic research has shown that, in general, children with conduct problems often exhibit deficits in reinforcement processing in tasks measuring reward-based decision-making [29], passive avoidance learning [30], operant extinction [31–33], and reversal learning [34]. Youth with CU traits, however, also appear to derive positive rewards from deviant behavior (e.g., social status from bullying [35]) and fail to encode outcomes that violate societal expectancies [36, 37]. In addition, youth with CU traits show significant disruption in processing punishment information [38, 39]. This evidence suggests that high CU youth are more likely to initiate early, escalate, and/or persist in deviant behaviors because they are less mindful of its negative consequences [40–44].

T0 research has further shown that these deficits are neurally subserved by abnormalities in the "motivational network" (mesocorticolimbic dopamine pathways) that mediates reward-based decision-making [30, 45]. Neuroimaging studies have related the decision-making impairment in CU youth to reduced representation of expected value within the ventromedial prefrontal cortex (how much reward/ punishment is associated with a response choice) and prediction error signaling within caudate (signaling the difference between the reward expected and that received) [39]. These data suggest a neurobiological mechanism that may explain why CU youth would exhibit poorer and slower learning of reinforcements associated with objects and actions. Thus, typical alterations in corticolimbic systems that predispose adolescents to high-risk behaviors appear to function differently in those with CU traits and in a manner that may further contribute to behavioral dysregulation. And as in all complex human behaviors, there are also environmental exacerbators or triggers (e.g., maltreatment and stress) that interact with these neural factors and, thus, play a role in the ultimate outcome for children with CU traits [46–48]. These behavioral and brain findings support the development of a transdisciplinary, system-based conceptual model that maps impairments in punishment- and reward-based decision-making and dysfunction in underlying neural circuitry leading to psychopathological outcomes of CU traits. This information, applied by prevention scientists, holds great potential to guide the future of translational research.

T1–Transfer of this basic knowledge about the pathophysiology of CU traits to inform the development of

research methods and intervention programs–with the goal to exert an impact on the phenomenon under study–constitutes T1 translation in this example. Success in early risk assessment, prevention, and treatment can only occur if the mechanisms, triggers, and developmental progression of CU traits are understood. Importantly, CU traits predict long-term negative prognosis [49]. This program of research is highly significant given the burden to children, their families, and society of their difficulties in social relationships and oftentimes dangerous behavior. Thus, it is critical that this basic science information be used to guide development of interventions that target these mechanisms and, in turn, determine their role as mediators and moderators of program effects.

In T1, an intervention is developed (conceptually) with components that map specifically to the array of etiologic features of CU psychopathology as putative mediators of effect. First, near-future program development efforts might consider making use of the six-stage "chain model" to develop a prevention curriculum targeting CU [50]. According to this model, a theory of program mediation should first be developed to address CU. Based on discovery of mechanisms underlying CU (T0), strategies might involve, for example, instruction in amygdala-related stimulation protocols (e.g., pharmacotherapy) or environmental stimulation that plausibly addresses CU traits. A targeted intervention activity should alter in some way the functional basis and unfolding of CU and its influence on later antisocial behavior.

Second, there is a need to systematically pool and warehouse promising activities for new uses. The theory of program mediation developed in the prior stage leads one to search for promising interventions to test, from the pharmacological to the psychosocial. Third, there is a need to systematize a set of perceived efficacy studies that can screen among promising program activities or component ideas gathered in the last stage for additional program development work. This could be viewed as a program activity screening stage. There are numerous activities one may screen from. These activities might be adapted from existing programs shown to be effective with this subtype of conduct problems or may be novel, new directions to facilitate youth development and may target individuals or subgroups. Fourth, there is a need to systematize a set of immediate impact studies that can provide a means of determining workability, acceptability, and developmental appropriateness of individual program components. Fifth, there is a need to systematize program construction and pilot testing of a complete program. Rules of construction should be addressed, including a consideration of program content and process sequencing, along with a consideration of pragmatics of testing a complete program. For example, instruction in the topography of CU and self ratings of CU traits would be completed prior to activities designed to alter CU traits or their expression. And finally, in the T1 stage, there is a need to refine a set of immediate posttest/postintervention activity set measures that predict longer-term outcomes relative to short-term measures. Such measures are not overly lengthy or difficult to implement. Pilot testing outcome measures are likely to be able to predict not only target population receptivity but also longer-term behavior.

Given that CU traits significantly compromise typical intervention efforts for conduct problems, approaches informed by neurobiological knowledge regarding subtypes of youth promise to be vastly more effective than non-specific interventions directed toward a heterogeneous population [27, 51]. One way to approach this need is to design interventions around regulatory processes that are potentially malleable, such as those cited above which have been implicated in CU traits [52–54]. For example, pharmacological or psychosocial therapies designed to stimulate activity of the amygdala and its connections (e.g., akin to deep brain stimulation in depression [55]) and reinforce prefrontal inhibitory controls may normalize cognitive and emotional regulatory deficits seen in CU youth. Another intriguing possibility is the potential preventive effect of educating caregivers, educators, and public health policy-makers regarding approaches that may address differential developmental pathways in CU youth. For example, early enrichment, tactile stimulation, stress reduction, and other environmental enhancements early in life may strengthen prefrontal cognitive controls and enlarge the striatum, possibly reducing the novelty seeking and emotional dysregulation associated with CU [56]. Current therapeutic inefficiencies arise because treatment methods do not map program components to underlying etiologies and developmental progression [26, 57]. Targeting program components to subgroups that confer differential vulnerability to conduct problems and that are likely to influence responsivity to a given intervention may substantially improve outcomes and cost-effectiveness. Thus, within the full translational prevention spectrum, studies are needed to link basic understanding of mechanisms to the translation of effective intervention strategies that take into account the specific etiological underpinnings, the interactions between individual and environmental factors, and contextual considerations of intervention implementation (e.g., assessments to inform clinical case conceptualization for CU youth).

In our current example, few interventions have been successful in remediating or redirecting CU traits. Perhaps, application of knowledge from T0 and T1 regarding aberrations in neurobiological, cognitive, and emotional regulatory processes might be suitable targets for intervention; this approach has yet to be undertaken. One existing intervention that may bear fruit is mindfulness-based stress reduction (MBSR). MBSR is predicated on basic research showing significant improvements in cognition, neural activation in regions of interest, and normalization in physiological stress indices [58]; all appropriate targets given basic research implicating deviations in these processes in children with CU traits. Another intervention–emotion recognition training (ERT) [59]–has been used to

address complex issues in CD and found to specifically work well with children and adolescents exhibiting higher level of CU traits. This intervention targets skills that are underpinned by the neural substrates implicated in CU; thus, there are theoretical and empirical reasons to predict a favorable response. Interestingly, this positive effect on children with higher level of CU traits was independent of diagnosis. Also, those children with CU traits who experienced the treatment-as-usual condition exhibited an exacerbation of their behavioral problems. Thus, it is critical to identify appropriately targeted interventions and not programs used more universally or for other "targets" that do not address known specific underlying mechanisms of a given problem. Further, at this stage, translational scientists must develop measures sensitive to individual differences in change in outcomes and subtype specific mediating mechanisms.

T2–The next stage in this translational process–T2–is to implement the adapted or novel intervention(s) on a larger scale, with all due attention rigor in research design, program receptivity, implementation rigor (e.g., fidelity), cultural sensitivities, and potential sustainability. T2 involves translation of program development to implementation with an emphasis on randomized controlled trials (RCTs) under ideal conditions or quasi-experimental trials with large defined populations. At this stage, CU youth would be randomized to two conditions, e.g., standard care preventive intervention or other attentional control and a novel specifically targeted approach. A wait-list control design might be considered unethical given that as CU youth age, the more entrenched CU traits and their cognitive and neurobiological functional corollaries become. Data should be collected at multiple intervals from various perspectives to validate intervention effects. General issues regarding implementation rigor, cultural sensitivity, developmental appropriateness, overall acceptability, and potential sustainability apply to this exemplar in the same way they are considered in more traditional intervention approaches; i.e., they should be attended to irrespective of the mechanistic underpinnings and targeting strategies described up to this point. However, attention to implementation rigor is particularly critical when testing mediation models, thus calling for carefully constructed implementation studies to fully capture process evaluation data.

Additional issues that are particularly relevant to our example may also apply to other specific populations (e.g., juvenile justice-involved or behaviorally and emotionally disturbed youth). One such issue is how to engage children/adolescents with CU traits and their families in programs, both those that involve highly controlled settings and those under more usual conditions. Individuals with these traits (e.g., both youth and adults with psychopathy) are known to "contaminate" other recipients in group settings and often actually perform worse with certain types of interventions than controls [60]. They have tendencies to be resistant, oppositional, and undeterred by threats of punishment. Program components must, then, be stimulating, compelling, novel, and incentivizing to promote full engagement. And it may be more effective to deliver the intervention on an individual basis or in tightly controlled and structured groups of similar peers. Also critical is the involvement of caregivers and other family members given the challenges they often experience in dealing with CU youth and based on strong evidence that parents often have similar conduct problems. Family involvement is key to successful intervention outcomes–yet, these families are often very difficult to recruit and retain. Consideration must be given to family dynamics that are counterproductive or even damaging as CU youth appear to be particularly susceptible to adversity and trauma, in effect exhibiting greater CU traits and destructive behaviors under these conditions [61]. Although these issues are relevant throughout all translational stages, they are particularly critical at the T2 stage when interventions are implemented and evaluated in naturalistic settings where external validity is paramount.

Given that youth with CU traits are often identified by teachers and administrators as being troublesome, prone to classroom disruptions, difficult to teach, and lacking in certain social skills, schools are ideal environments for screening and intervention, especially in the form of clinical referrals. Other venues for the resulting EBPs targeting CU youth are juvenile justice and child welfare systems where these youth are overrepresented. Not only do interventions need to be specifically structured for these distinctive settings but they must not cause undue burden to providers and outcomes should be easily observed and measured and sellable to political leaders. It is helpful when ways to gauge outcomes are consistent with procedures (e.g., intake and exit assessments) already used by the system or setting for easier implementation and sustainability. Both T1 and T2 stages grapple with the contexts and cultures within which to develop programming (family, school, and welfare system, setting where individuals of color may be disproportionately represented) and provide rigorous implementation and impact research designs for testing.

T3–Once success has been achieved in the implementation in controlled settings–which is, again, specifically targeted to underlying mechanisms discovered in T0–this stage of translation (T3) involves dissemination, replication, and scaling-up in real-world settings. Similar to T2, all the same considerations are relevant here regardless of the intervention. A determination must be made of what populations to target, in which settings (e.g., community, school, and clinical), and with what program components that specifically target underlying mechanisms in the problem one is attempting to prevent (e.g., CU traits). Attention to potential mediators and moderators of effects will help to discern who–individuals or groups–responds best to the intervention and why, thus providing opportunities for potentially revising the intervention. In CU youth, knowledge about the role of contextual factors (e.g., trauma, family dynamics, and peer groups) and individual-level factors (e.g.,

aggressiveness, cognitive functioning, and emotion regulation) will help identify potential moderators of effects and suggest potential intervention adaptations needed for greater efficacy. Change in neurobiological indicators may help to identify subgroups more or less likely to respond favorably to any given intervention. Developmental and cultural issues are again addressable at this stage. CU youth may differ in their development in terms of cognitive function and sociability in ways that are likely highly relevant for intervention adoption. Community buy-in issues should be considered at the beginning of the T3 stage involving adoption of CU prevention programming, as well as a means to minimize stigmatizing persons who fall along relative extremes on CU. Effective modes of communication are important to convey the need for the intervention to non-research audiences and to increase palatability to potential recipients, their families, funding agencies, and social systems, all of which may differ for addressing the needs of CU youth. Focusing on the preferences of consumers tends to translate more effectively into eventual behavior change [45].

T4–T4 translation then focuses on scaling up and examining the potential for "true" institutionalization of evidence-based interventions for CU youth that have produced positive outcomes and are accepted by recipients and their families. In general, very few EBPs in the behavioral and mental health fields are scaled at this magnitude, even the few that are based on T0 discovery science. A major reason pertains to the funding sources for this level of research. Many interventions are developed with federal grant dollars and when grants expire, both the research and the funds to support the program conclude. As a result, despite any advances, positive outcomes, and enthusiasm by providers and recipients, there is no scaffolding to sustain the momentum. Without adequate attention to T4, any real progress in preventing the emergence or escalation in the phenomenon under study occurs slowly and without fanfare.

To maximize the opportunities for EBP adoption and scaling across usual practice settings, schools, communities, and public service systems, several stages need to be taken as outlined by Chamberlain and Saldana [62, 63]. In our exemplar, it is important that the intervention is amenable to the setting in which it would be implemented. Universal approaches generally do not directly target CU mechanisms, which means an individual-based program is often necessary. Adoption and scaling, in this case, may be seen as less appropriate given that CU youth are such a minority; however, once effective programs have been developed, school systems should have knowledge of and access to them for ready screening and referral. An intriguing possibility, though, is that there is potential for some universal interventions to also influence CU youth, even though not directly targeted. For example, mindfulness or socio-emotional learning programs *may* produce positive outcomes for *all* children and have a residual effect on improving CU traits. Thus, institutionalizing EBPs may increase resilience universally with a goal to influence (protect or buffer) those at particularly high risk, making these individuals more amenable to additional selective or indicated interventions.

T5–At T5, there is a global shift in mindset given a new and more widespread understanding of CU traits, their underpinnings, manifestations, and potential solutions. There is now greater understanding of the needs of these children based on knowledge of their differences and how existing deficits may be remediated. There is also a much quicker and more effective response given the greater awareness of poor individual outcomes and public safety implications without interventions. Policies are in place at this stage to invoke early detection strategies and a smooth transition to targeted interventions and services. The global nature of this new understanding and response strategy further requires sensitivity and adaptations to accommodate country- and cultural-level differences given the impact of this level of translation on program development, implementation, evaluation, and dissemination. In a sense, it may be best to consider translation as involving some reinvention to be adaptable to country-level differences and their structural and political manifestations. These differences may be surface-level (e.g., any name exemplars, slang terms, and language nuances) or deep-level (e.g., cultural differences in how behavioral health problems are viewed and social structural differences which need to be imparted into the programming). It may also be wise to think in terms of financial support for research and sustainability of programming in a particular country, as well as subjective "ownership" of programming in that country. Again, most translational prevention research in the behavioral sciences does not rise to this level; however, this special issue of *Translational Behavioral Medicine* and similar works may motivate this process through wide-scale policy and mindset change.

Back translation–Back translation comes into play at each stage of the translational process. In this exemplar, one possible finding might be a lack of positive intervention effects in a subgroup of CU youth. They may be distinguishable from other CU youth by some set of particular characteristics that CU youth who respond more favorably do not possess. Interventionists would then turn back to the basic scientists to explore mechanisms that underlie these subgroup characteristics on the basis of any number of potential factors: neurobiological, trauma history, family dynamics, learning challenges, cultural differences, and so forth. Another example of back translation might occur when educational policies are reformed to institute screening techniques, based on T0 knowledge, for early detection of CU traits. Poor predictability or validity may also lead administrators to turn back to either T0 scientists or intervention developers to provide further guidance. Further, failures to adopt or institutionalize proven practices may need more research in translational stages relating to dissemination and persuasion.

This exemplar served the purpose of illustrating how science regarding etiological underpinnings of a problem to be prevented can move through the

translational spectrum from knowledge to the practice of prevention and policy reform. For CU traits and many other behavioral problems, this full route has not been taken; prevention science focuses a great deal of attention to T1-T2 and at times T3, according to our typology, but rarely T4 and, to date, never the T5 stage. And very recently, T0 and T1 are receiving some renewed attention given emerging findings that environmental factors impact epigenetic and neurophysiological states in ways that can focus innovative prevention strategies to target these malleable, developmental processes. The hope is for this discourse to stimulate collaborations across disciplines that speak to each stage of translation to facilitate the transfer of knowledge relevant to prevention science and its actionable outcomes. Children with CU traits (like many other behavioral health problems) are at such very high risk for a whole variety of problems that interfere with their own development and success and potentially threaten public safety. Thus, we recommend that prevention science take heed of these findings by designing intervention studies that map program components to potentially malleable neurobiological markers.

CONCLUSIONS

This manuscript introduced six (T0 through T5) stages of translation, extending the scope of translation from basic science to globalization and institutionalization of programming and promoting a "prevention mentality" whereby proactive approaches are prioritized. It is our hope that this scheme will assist in (1) formulating recommendations for the transfer of scientific information across the spectrum of translation, i.e., from basic research on "mechanisms of behavioral change" for practice and policy impact; (2) confronting the real-world challenges in applying a translational approach with recommended innovations to overcome existing obstacles; and (3) coming full circle to develop methods and processes for effective prevention programs to be self-sustaining and use back translational evidence to inform basic sciences.

To accomplish the goals of this model, perhaps researchers should not simply convey data-driven results but rather engage in telescopic thinking based on outstanding questions in their program of research and the next logical translational stages in the agenda. We need greater discussion about what is needed to move the research to a future point across the translational spectrum and to identify the means to facilitate the application and eventual adoption of replicated results. In particular, we need to confront the obstacles that currently impede the transfer of results to their application and adoption in the real world. From an individual scientist perspective, it is not possible to be familiar enough with multiple fields to be capable of conducting more than one to two stages of translation; successful investigators often collaborate with others in similar fields, and thus, research is not transferred to the next stage. Engaging in translation requires extra stages that can be taxing or stretch any given researcher's purview. A flexible, dynamic, and collaborative approach is necessary to connect scientists across stages. And there are many other obstacles beyond those that are scientific, including narrowly focused review processes, difficulty in obtaining funding, tendencies to silo, and others described by Czajkowski et al. [2]. It is time to consider new translational approaches to address the multitude of obstacles. The challenge is to think beyond our own research and consider how transdisciplinary approaches can produce transformative research and practical applications. Ultimately, our hope is that this model will highlight how a transdisciplinary translational approach to prevention research can improve children's and adolescent's chances for growing up healthy and being afforded the opportunities for healthy development and ultimately success in multiple domains of life.

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