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Precision Strategies as a Timely and Unifying Framework for Ongoing Prevention Science Advances

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The purpose of this Special Issue is to encourage prevention scientists to take advantage of the recently actuated precision medicine movement to promote research toward determining what works for whom and under what conditions, also termed treatment matching (Collins and Varmus 2015). This strategy is not new to medicine, behavioral health, or prevention science. Nevertheless, the orchestrated proclamation by President Obama and Director of NIH, Francis Collins, M.D. of the Precision Medicine Initiative (PMI) with its $215M and 1 million participant prospective natural history study reinvigorated these efforts at the NIH and among treatment developers and healthcare providers (Collins and Varmus 2015; PMWC 2018; www.whitehouse.gov/precision-medicine). The 1 million participant prospective study has come to fruition in the form of the *ALL OF US* Research Program (NIH 2019; Sankar and Parker 2017) which emphasizes genetics, environmental factors, social influences, and lifestyle and is thus highly consistent with underlying theories of prevention science (Meagher et al. 2017). Past medical and behavioral clinical trials directed toward treatment matching have yielded mixed results, but overall such studies have played important roles in advancing their respective fields (Broekhuizen et al. 2012; Project MATCH Research Group 1998; Strecher 1999).

August and Gewirtz (2018) discuss recent progress in prevention science targeting internalizing and externalizing outcomes (including substance use) but concluded that the literature "offered few clues as to alternative interventions that might be effective for those who fail to benefit [from existing interventions]" (pp. 1–2). Generally speaking, attempts at intervention matching in prevention science have not yielded sizable improvements over other prevention programs, but there are exceptions (Broekhuizen et al. 2012; O'Leary-Barrett et al. 2016; Strecher 1999). The more common contribution of a study to precision prevention is the discovery of a subpopulation for which an intervention either lacks or provides especially large efficacy as opposed to identification of the optimal treatments for multiple subpopulations (Cho et al. 2016; Glenn et al. 2018; Howe 2018). Moreover, for the purpose of advancing precision prevention science, discoveries about subpopulations for which an intervention fails to work or yields iatrogenic effects can be among the most cited and important studies in terms of experimental insight into the underlying mechanisms of etiology and prevention (Dishion et al. 1999; Tryon 2018). To this end, there are myriad secondary analyses of existing datasets with potential to contribute important insights to prevention medicine.

Precision Medicine

Multiple factors have been described as characterizing precision medicines which are common to precision prevention (Meagher et al. 2017). Examples include the need for novel clinical trial designs; more reliable preclinical testing; developing networks of databases and research resources to support scientists, practitioners, and patients to accelerate the translation of basic science to practice; improving assessment of disease risk; understanding disease mechanisms; treatment matching; and finally understanding how applied uses of knowledge can be of most benefit to the recipients of intervention (Collins and Varmus 2015). Riley et al. (2015) added that two technologies with high potential for advancing precision medicine within behavioral health are intensive prospective data collection using ecological momentary assessment (EMA) and portable devices such as smartphones. Along with rapid advances in biosensors, these three technologies provide venues with high potential for individualized healthcare and prevention including individualized monitoring, detection of high risk for impending medical or behavioral events such as suicide attempt or violence to alert caretakers to prevent such events, and immediate access to professional intervention. Research using adaptive designs illustrates how these

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technologies might be leveraged within prevention science and practice (Luers et al. 2018; Tsai et al. 2007).

Collins and Varmus (2015) highlight certain areas where behavioral health is needed in personalized medicine even for medical outcomes such as cancers including the facts that "behavioral and environmental factors contribute more to premature death than do genetic factors" (Riley et al. 2015, p. 244). Optimal treatment response and matching strategies are likely to involve subgrouping based on behavioral, environmental, and patient preference factors. The dynamic and interactive nature of behavioral and environmental factors is more informative of changes in risk and disease states over time compared to genomic, phenotypic, and health outcome factors. Much of the needed methodological advances will require contributions from a range of professions including statisticians, data scientists, and technology developers.

Precision Prevention

Similar to what PMI has been to coalescing healthcare professionals, precision prevention could lead to a meaningful paradigm shift within prevention science, but it will require concerted efforts from numerous researchers. The manuscripts of this Special Issue demonstrate methods and discoveries that employ precision medicine principles in prevention contexts. They also illustrate the degree to which prevention scientists' advances are informed by the range of translation types discussed by Fishbein and Dariotis (2017) and cross-inform multiple translation types. Their translational framework model acknowledges that the full range of translational studies, from discovery science through globalization, exerts influences at the personal level. To illustrate, the universal preventive intervention fluoridation of public water has its foundations in laboratory studies (Type 0) (Ayoob and Gupta 2006) and the mindfulness preventive interventions being tested in the USA originated in Eastern religions (Type 5) (Baer 2003). The translational types that are most germane to precision prevention are demonstrated in the manuscripts of this Special Issue: discovery science (Type 0), methods and program development (Type 1), efficacy and effectiveness trials (Type 2), and real-world applications and dissemination (Type 3). Also demonstrated by every manuscript in this Special Issue are the interwoven nature of studies from different translation types as well as the need for many scientists to advance our understanding of what works for whom under which circumstances.

Special Issue's Precision Prevention Studies

In this issue's single discovery science translation type, Dishion et al. (2018) demonstrate the rich insights that can be garnered from carefully observing adolescents' brief interactions with friends and parents. Quantifying the content of their conversations and interaction patterns was far more predictive of substance use disorders in early adulthood than traditional self-report measures. The same was true for predicting violent offenses committed in early adulthood, although juvenile court records were more predictive than both social interactions and self-reports. In contrast, compared to social interactions, self-reports of anxiety and depression in adolescence more accurately predicted their early adulthood levels of anxiety and depression, respectively. Dishion et al.' (2018) study also demonstrates novel assessment methodologies (Type 1), techniques that could be useful in real-world applications (Type 3) and efficacy and effectiveness trials (Type 2). This study's implications are more germane to selective/indicated prevention than primary prevention (which was delivered years prior to the reported data collection) because the predictors were measured at ages 16 and 17.

Three of this issue's manuscripts are primarily reports of methods and program development (Type 1). Connor (2017) presents an individualized approach to literacy instruction which takes advantage of computer technology to deliver new lessons only after a student has mastered the skill(s) of a preceding lesson. This approach is convenient for teachers, clearly meeting a real-world need (Type 3) and demonstrates sizable efficacy (Type 2). Howe (2018) presents the logic underlying testing of causal inferences which are perhaps the most fundamental assumptions in research designs to develop and strengthen preventive interventions. He extends this logic to baseline target moderated mediation designs which can inform tailored preventive intervention, one key strategy of precision prevention with clear implications for efficacy testing (Type 2) and real-world applications (Type 3). One example of a baseline target moderated mediation is reported by Glenn et al. (2018). Luers et al. (2018) present standardized effect sizes for micro-randomized trials in which multiple elements of interventions are delivered in a short sequence with each element being randomly assigned. Their methodological innovations include micro-randomized trials, provision of standardized effect sizes specific to those designs, and the mobile health preventive intervention used in their study. Their most direct implications for other study types are for efficacy and effectiveness testing (Type 2).

Two studies reported in this special issue fit the traditional efficacy or effectiveness, Type 2, study. Glenn et al. (2018) report on a personalized adaptation of a traditionally group-administered *Coping Power* intervention, hypothesizing that each version may be more beneficial for different types of youths. Whereas past studies demonstrated that the *Group Coping Power* has efficacy for reducing aggression, the comparative efficacy is greater for *Individual Coping Power*. On the other hand, *Individual Coping Power* is more expensive, requires greater effort from the practitioner, and thus can be

offered to fewer youth than *Group Coping Power*. Discovery science studies suggested that (a) affiliations with deviant peers can increase a youth's own deviant behavior (e.g., potentially an outcome of completing *Group Coping Power* with deviant peers) and (b) having lower inhibitory control may contribute to youths' vulnerability to social contagion risks. Consistent with their hypotheses, Glenn and colleagues reported that sympathetic nervous system measures (heart rate variability, skin conductance) did mediate outcomes of *Individual Coping Power* but in somewhat nuanced ways (interacting with baseline aggression, different outcomes at home versus school). Thus, Glenn and colleagues' study both draws from, and informs, discovery science (Type 0). Moreover, the technologies used to measure sympathetic nervous system and interactions leading to program outcomes both draw from and inform methods and program development (Type 1).

Estrada et al. (2018) tested an internet-delivered adaptation of the evidence-based *Familias Unidas* program to prevent behavioral problems in Hispanic adolescents by improving their families' functioning. This team's prior work on methods and program development (Type 1) resulted in efficacy for reduced drug use and cigarette use as well as improved family functioning (although family functioning did not statistically mediate the substance use outcomes of *eHealth Familias Unidas*). Discovery science may be needed to clarify the program's effects because the mediating mechanism(s) for *eHealth Familias Unidas* were not identified by Estrada et al. (2018). Doing so may elucidate important insights for improving their intervention as well as other prevention strategies. In terms of real-world applications and dissemination (Type 3), the internet-delivered *eHealth Familias Unidas* costs less to deliver and can be offered to far more families than the traditional *Familias Unidas* program, especially if families reside in rural or other hard-to-reach locations.

Both of the real-world application and dissemination (Type 3) studies in this special issue tested novel strategies to improve parental engagement in family-based prevention programs. Gewirtz and colleagues (Gerwitz et al. 2018) tested whether children's behavior problems are improved compared to the traditional randomized clinical trial by giving their parents the choice of three venues via which they would receive a parenting program (group, home-based, or individually at a clinic) or services-as-usual. Children of parents who chose one of the three prevention venues experienced improved hyperactivity/impulsivity (per teacher ratings) at 6 months compared to children of parents who were not able to choose the intervention venue as well as compared to the parents who chose services-as-usual. Additionally, intervention drop out was considerably greater among parents who were not able to choose the venue compared to those able to choose a venue and compared to those who were randomized to services-as-usual. Three implications of these results are that allowing parents to choose how they receive an intervention facilitates a program's efficacy, reduced attrition, and savings in cost and effort of delivering an intervention to individuals who may be unmotivated to assimilate new parenting skills. Gewirtz et al. provide more nuanced discussion with implications for future Type 1 and Type 2 studies.

Garcia-Huidobro et al. (2018) report on a proof-of-concept study of a recruitment strategy designed to encourage fathers' participation in the evidence-based *Padres Informados Jovenes Preparados* program to improve parenting skills and in turn prevent substance use in Latino youths. Using an adaptive design, parents who did not attend group-based intervention were offered one-to-one intervention. Ninety-six percent of participants completed at least ¾ of the intervention. Offering the one-to-one option was clearly impactful for nearly half of the enrolled fathers who completed the entire program in this venue. Although this proof-of-concept study used a relatively small sample, if the findings are replicated it will offer a much-needed technique for encouraging father involvement in family-based prevention (with direct implications for translation study Types 1–3).

Next Steps Toward Personalized Prevention

Ultimately, prevention science aims to equip individuals with knowledge, skills, abilities, and supports that they need to avoid snares in development toward adulthood; cope resiliently with psychopathology; and attain healthy, productive, and satisfying lives (Hussong et al. 2004). Compared to universal prevention strategies, relatively little evidence is available regarding selective/indicated strategies, which by definition would be the handiwork of precision prevention. Howe (2018) demonstrates an analytic approach that could be applied to numerous efficacy or effectiveness studies to test whether interventions yield better outcomes in individuals at high or low levels of a baseline characteristic. Such findings could in turn lead to selective/indicated adaptations of an intervention that are better suited for those individuals. An example of this strategy is Glenn et al.s' (2018) adaptation of the *Group Coping Power* to *Individual Coping Power* and identification of subtypes of youth who are more likely to benefit from each program.

Prevention science has long relied on methods that are designed to test population-oriented hypotheses such as efficacy. More recently, methods have been evolving to intensively investigate intra-individual processes over time (e.g., in response to an intervention) concurrently with interindividual differences (Howe et al. 2010; Ridenour et al. 2017; Voelkle et al. 2014). Such methodologies could permit prevention scientists to carefully identify the mechanisms whereby an intervention is able (or fails) to influence individuals toward

desired outcomes and in turn refine the intervention to attain stronger impacts (Tryon 2018).

To evaluate novel aspects of personalized prevention, innovative assessments will be needed. Technologies that can provide intensive within-person monitoring were mentioned previously. Little if any research has been conducted toward individualized outcomes assessment, in spite of numerous theories recognizing that individuals are predisposed to a range of potential outcomes as opposed to having the potential to experience the entire range of possible human outcomes (Tarter et al. 1999). To illustrate, obtaining a 4-year college degree is not a realistic expectation for individuals born with moderate mental handicaps; yet, research involving academic outcomes has not measured scholastic achievement in terms of how well individuals attain or surpass the achievements that are realistic for their own predispositions. Likewise, for individuals who are highly predisposed to psychopathology either due to genetics or environmental factors, experiencing a mild version of that pathology may be a meritorious accomplishment. According to a precision prevention orientation, gauging individuals' outcomes might be best evaluated with regard to his or her range of potential outcomes rather than in reference to the range of outcomes that occur in the general population.

A daunting challenge facing prevention scientists at this time is monumental reductions in funding for prevention research. Thus, a paradigm shift toward personalized prevention may not only be scientifically strategic and encouraged by the PMI, it may be needed for the continuation of prevention science. Expanding into new settings, adapting to collaborate with professionals and basic scientists with whom we are unaccustomed but share similar aspirations, and refocusing to better understand mechanisms of within-person change (not only statistical mediators) are a few of the possibilities for adapting to the shifting prospects of prevention science. Progress also will likely require innovative approaches and interventions to improve upon the less-than-tantalizing efficacies that have been generated by one-size-fits-all interventions. Under these conditions, personalized prevention is a principal whose time has come.

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Compliance with Ethical Standards

Conflict of Interest The author declares that he has no conflict of interest.

Ethical Approval For a commentary involving no research participants, formal consent is not required.

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