Achieving the Goals of Translational Science in Public Health Intervention Research: The Multiphase Optimization Strategy (MOST)

The National Institutes of Health (NIH) invests billions of dollars annually in basic research designed to increase scientific understanding of social, behavioral, biological, and biomedical factors that cause illness, affect recovery, and facilitate health. Because the ultimate goal of this basic research is to improve human health and well-being, translational science, the process by which basic research findings inform prevention and treatment practice, is critical. Two types of translational science are universally identified (although more complex translational frameworks exist[1]). One is translation of basic science discoveries into new approaches for prevention, diagnosis, or treatment. The other is translation of these new approaches into a form amenable to widespread adoption and implementation.[2,3]

Francis Collins, the current director of the NIH, has called for a "comprehensive, systematic, and creative approach to revolutionizing the science of translation."[4(p1)] Here we introduce the multiphase optimization strategy (MOST),[5,6] an engineering-inspired framework for development, optimization, and evaluation of multicomponent behavioral, biobehavioral, and biomedical interventions, and show how it offers a novel approach to translational science.

CLASSICAL TRANSLATIONAL SCIENCE APPROACH

The classical approach to translation of basic science into interventions typically involves identifying a set of intervention components informed by basic research findings, assembling them into a multicomponent treatment package, and immediately evaluating the effectiveness of the package in a randomized controlled trial (RCT). This approach cannot provide certain information that would be valuable in the translation process. For example, it does not enable evaluation of the performance of individual components, making it difficult to determine whether a component should be removed because it is ineffective or the magnitude of its effect does not justify its cost. Such shortcomings perhaps contribute to how long it takes (an estimated 13 years on average) for a basic research finding to be translated into an intervention.[4]

If a significant treatment effect is detected, the RCT may be followed by subsequent translational research to examine how well the intervention performs under real-world circumstances in the intended setting (e.g., school, hospital, community). Here the ultimate in successful translation would be an intervention of sufficiently high quality to maintain the level of effectiveness observed in the evaluation RCT. The classical approach to translational research typically is to implement the intervention in a sample of the intended settings and model the observed variation in implementation fidelity. If the treatment package was originally developed with little consideration of cost, complexity, or burden, these factors may influence implementation. For example, if the treatment package is too complex, staff may remove components in an ad hoc fashion.

MULTIPHASE OPTIMIZATION STRATEGY

MOST differs fundamentally from the classical approach to translational science because it inserts a phase of optimization of an intervention prior to its RCT evaluation for effectiveness. Optimization is the process through which an intervention is identified that produces the best expected outcome obtainable within key constraints. These constraints are imposed by the need to achieve not only effectiveness but also efficiency, economy, and scalability. One example is a constraint on implementation costs; for example, it may be necessary to implement the intervention for less than $400 per person.

Another example is a constraint on complexity; for instance, it may be determined that more than four intervention components will produce an intervention too complex to be scalable. Then the objective is to produce the intervention with the best outcome that can be obtained with a cost of less than $400 per person, or an intervention consisting of no more than four components. Thus, a scientist working within the MOST framework considers scalability from the beginning of intervention development rather than seeing it as something to be achieved in a separate step following an RCT.

In MOST, intervention components directly informed by basic science advances are

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organized in a theory-driven conceptual model that clearly specifies the mechanisms through which each component is expected to affect the desired outcome.[5] The effects of individual components are subsequently evaluated through efficient experimental designs, such as a factorial experiment (including special cases of the factorial experiment, e.g., the sequential, multiple assignment randomized trial[7]) in an optimization trial. On the basis of the results of the optimization trial, the investigator assesses whether each component affects the desired outcome and how the components interact with one another. From there, the investigator can identify the combination of components that produces the best outcome without exceeding the relevant key constraints.

CLASSICAL APPROACH VS MOST

Imagine two intervention scientists, both of whom wish to start with a particular set of basic science findings about nicotine dependence and conduct the research necessary to arrive at a smoking cessation intervention that maintains an acceptable level of effectiveness in ordinary primary care settings. Dr. C will use the classical approach, and Dr. M will work within the MOST framework. As a starting point, say both scientists have identified the same set of intervention components and pilot tested them.

Dr. C combines all of the components into a treatment package and evaluates the package in an RCT. The package demonstrates a statistically significant effect on tobacco use, so Dr. C conducts a subsequent study in which the intervention is implemented in a sample of primary care practices. The results indicate that insurers are unwilling to pay more than $400 per patient for the intervention, but the intervention costs much more than that. Dr. C has to remove some components to make the intervention cheaper and therefore scalable, but which ones? Without information about the performance of individual components, Dr. C does not know how to make the intervention cheaper without risking loss of some of the very elements that were responsible for the effects observed in the original RCT.

By contrast, consider Dr. M's approach. Early in the process, Dr. M discusses costs with a sample of primary care practices and learns that insurers will not pay more than $400 per patient for a smoking cessation intervention. Instead of immediately combining the components into an intervention package, Dr. M conducts an optimization trial to assess whether each component has a detectable effect on tobacco use and whether there are interactions between components. While conducting this trial, Dr. M also collects data on cost. This information enables Dr. M to identify the subset of components that produces the lowest tobacco use while not exceeding a $400 implementation cost. This subset of components is then evaluated in a standard RCT, assuming the results of the optimization trial suggest that this treatment package is likely to demonstrate a statistically and clinically significant effect in an adequately powered experiment.

The treatment package is immediately scalable because it has been designed to cost less than $400 to implement. If a subsequent implementation trial is deemed desirable and suggests that the intervention must be shortened, decisions about removal of components can be based on the results of the optimization trial.

CONCLUSION

We suggest that MOST offers a novel and practical framework for translational science, one that has the potential to hasten the progress of bench to bedside translation in the long run and ultimately help improve the public health impact of multicomponent behavioral, biobehavioral, and biomedical interventions. AJPH

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CONFLICTS OF INTEREST

No conflicts of interest.

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