

Statistics for Social and Behavioral Sciences

Linda M. Collins

Optimization of Behavioral, Biobehavioral, and Biomedical Interventions

The Multiphase Optimization Strategy
(MOST)

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To John, Matthew, Joy, and Jazeya

Preface

In the United States and worldwide, billions of dollars have been spent to develop behavioral, biobehavioral, and biomedical interventions (hereafter referred to simply as interventions) to prevent and treat health problems, promote health and well-being, prevent violence, improve learning, promote academic achievement, and generally improve the human condition. Numerous interventions are in use that are successful in the sense that they have demonstrated a statistically and clinically significant effect in a randomized controlled trial (RCT). However, many are less successful in terms of progress toward solving problems. In fact, after decades of research, as a society we continue to struggle with the very issues these interventions have been designed to ameliorate. Only very slow progress is being made in many areas; in some, the problem continues to worsen. Let us consider two examples in the public health domain, both from the Healthy People goals set every ten years by the United States Centers for Disease Control and Prevention (CDC).

The first example concerns adult obesity. One of the CDC's Healthy People 2010 goals was to reduce the prevalence of adult obesity from the 2000 baseline of 23% down to 15%. Unfortunately, by 2010 adult obesity had *increased* to 34%. This is a serious issue for American society; according to Finkelstein, Trogon, Cohen, and Dietz (2009), the medical care costs of obesity in the United States are \$147 billion per year (in 2008 dollars). The healthy people 2020 goal is to reduce adult obesity to 30.5%. On the one hand, this would be a 10% reduction from the 2010 prevalence; on the other hand, it is higher than the 2000 base rate.

The second example concerns cigarette smoking. Cigarette smoking remains the leading preventable cause of death in the United States and worldwide (CDC, 2016b). In 2015, the prevalence of adult smoking in the United States was about 15% (CDC, 2016a). This is a marked improvement over the 2000 base rate of 21%. The goal for Healthy People 2020 is to reduce the prevalence of adult smoking to 12%, and there is optimism that this goal can be met. However, there are startling disparities in the prevalence of smoking. For example, in 2015 the prevalence of smoking among adults with a general equivalency degree (GED) certificate (a credential equivalent to completion of high school, earned by taking an

examination) was more than 30%, which is nearly five times the prevalence among adults with a college degree and more than nine times the prevalence among those with a graduate degree.

In my view, there are three primary reasons why progress in areas like obesity and tobacco use, as well as many other areas in which interventions could potentially make a huge difference, has been slower than it ideally could have been.

First, *intervention science is making little progress toward accumulating a coherent base of scientific knowledge* about which intervention components work and which components do not work, which ones work particularly well together, and which components work well for subgroups of individuals with particular characteristics. If an ever-expanding base of scientific knowledge in this area were established, scientists could draw on this established knowledge when developing an intervention, and add to it by investigating new components. Such an approach would enable scientists to keep improving interventions. Instead, most of today's interventions are "black boxes" – it is unclear what the active ingredients are, so the mechanisms that produce any observed effects are poorly understood. This makes it difficult to see the way forward to improve the intervention or to build on what previous studies have accomplished.

Second, *there has not been sufficient emphasis on steady, programmatic, incremental, and measureable improvement of interventions*. It would be helpful if every new intervention were an improvement over its predecessors in specific ways and by specific amounts; in this way interventions would become better and better over time. Think of how much improvement has been made in intervention science in the past 40 years, and compare this to the steady progress made in consumer products, such as the automobile, during this time. It is easy to point to a variety of metrics that can be used to express improvements in the automobile. For example, compared to the cars of 40 years ago, today's cars are more fuel efficient, more comfortable, more reliable, and safer. By contrast, even though new interventions appear regularly in the scientific literature, it is difficult to point to similar metrics to express clear progress over time. Compared to 40 years ago, or last year, are today's interventions measurably more effective? Less expensive? Easier to implement? Less burdensome?

Third, *many evidence-based interventions are too expensive, demanding, or complex to be scalable*. Today there is little expectation that efficiency, economy (in terms of both immediate monetary outlay, and time and other resource demands), and scalability will be given serious consideration while an intervention is being developed and evaluated. It follows that there is little disincentive to develop interventions by including any and all components the investigator believes may boost the treatment effect and produce a significant hypothesis test in the RCT. The thinking is that the first order of business is to demonstrate a significant effect in an RCT; once an effect has been demonstrated, there will be an opportunity to consider the matters of efficiency, economy, and scalability before the intervention is implemented in the intended setting.

This perspective has led to the development of many interventions that have earned the prized designation "evidence-based" but at the same time are difficult or

impractical to implement because they are prohibitively expensive, dauntingly complex, or too time-consuming for staff. Some end up never being implemented broadly; others are implemented broadly only after removal or revision of components to reduce cost or complexity. Because, as mentioned above, the active ingredients of most interventions are unknown, there are no guidelines for which components are essential and which may be removed without a huge sacrifice in effectiveness. As a result, any revisions to the intervention are ad hoc and run the risk of removing what may be an essential element, thereby reducing or even nullifying the intervention's effect. (See Chap. 7 for a more concrete explanation of how ad hoc revisions can backfire.) In any case, once such revisions have been made, the revised intervention no longer merits the designation "evidence-based" because it is not the same as the one that was originally evaluated.

A Vision for the Future

I remain optimistic that society can meet its goals in areas like public health, education, and human well-being. But to accomplish this, I believe better interventions are needed—interventions that are more effective, more cost-effective, more efficient, and more scalable. These interventions will be more practical to implement exactly as designed and evaluated. Imagine a near future in which. . .

. . .only components that positively and demonstrably affect the outcome are eligible for inclusion in an intervention, so no time or money is squandered on useless or counterproductive components.

. . .interventions are built in a principled manner to meet clearly specified standards of effectiveness, efficiency, economy (including cost-effectiveness), and scalability. It is always clearly reported what these standards are and how a particular intervention measures up to them. The standards may vary depending on the needs of the area, resources available, and the environment in which the intervention is to be applied.

. . .key constraints expected to affect scalability, such as constraints on implementation costs, are taken into account from the beginning of intervention development. The objective is to develop an intervention that delivers the best outcome achievable within those constraints and is immediately scalable without the need for any ad hoc modifications.

. . .as findings emerge from basic research, approaches for translating them to components for inclusion in interventions are programmatically tested, and only the approaches that work are added to interventions. Investigators continue to test dramatically new ideas, but must demonstrate specifically how and to what extent they are better than existing alternatives.

. . .every study adds to the knowledge base about which intervention components do and do not work, even if it does not produce an incrementally and materially improved intervention.

. . .as time goes on, a knowledge base grows about what works and how. Scientists developing new interventions build on this knowledge base and keep moving forward. This accelerates the pace of intervention science.

. . .looking back over a period of time, say ten years, it is clearly evident that the interventions in a particular area have steadily become measurably more effective, efficient, cost-effective, and scalable.

How can this future become a reality? *To realize the tremendous potential that interventions have to make the world a better place, it is necessary to start taking a very different approach to their development and evaluation.*

This book and its companion volume (Collins & Kugler, 2018) are about one possible such approach, the multiphase optimization strategy (MOST). MOST is a framework for development, optimization, and evaluation of behavioral, biobehavioral, and biomedical interventions.

A Brief Comparison of the Classical Approach and MOST

MOST integrates perspectives, concepts, and approaches used in engineering, statistics, biostatistics, and behavioral science. The fundamental idea is that *interventions can and should be optimized to meet specific criteria, and only after an intervention has been optimized should it be evaluated in an RCT*. Optimization of interventions and evaluation of interventions are different phases of research, pose different questions, and require different methodological approaches.

As described in detail in this book, MOST consists of three phases: preparation, optimization, and evaluation, in that order. Activities in the preparation phase include selection of the components that are candidates for inclusion in the intervention, and development of a detailed conceptual model of the process to be intervened on. In the optimization phase of MOST, which occurs before an intervention is evaluated in an RCT, steps are taken to optimize the intervention to meet specific criteria established a priori by the investigator. This optimization may take any of a variety of forms, depending on the type of intervention to be optimized. In the evaluation phase of MOST, the effectiveness of the optimized intervention is evaluated in a standard RCT. For the first seven chapters of this book, the emphasis is on fixed interventions—those in which all participants undergo the same treatment. In Chap. 8 adaptive interventions, in which treatment may vary across participants and over time, are discussed. Optimization of adaptive interventions is discussed further in the companion volume in the chapters by Almirall, Nahum-Shani, Wang, and Kasari and Rivera, Hekler, Savage, and Downs.

The classical approach to intervention research has consisted of identifying the components that are to make up the intervention; possibly pilot testing¹ them to ensure that they are implementable, not toxic, etc.; making any necessary revisions based on the pilot testing; immediately combining the components into an intervention package; and testing the efficacy or effectiveness of the package in an RCT. Typically the RCT will have two “arms” (experimental conditions): a treatment arm in which subjects receive the intervention package and a control arm in which subjects receive a suitable control protocol, such as the current standard of care. After data have been collected on sufficient subjects to afford the desired level of

¹See the definition of pilot test in Chap. 2 and in the glossary.

statistical power, the difference between the outcome for the treatment and control groups is estimated. If this difference is statistically significant, then the intervention is said to be efficacious (if the experiment was conducted in a tightly controlled setting) or effective (if the experiment was conducted in a real-world setting).

From the MOST perspective, one major difficulty with the classical approach is its sole reliance on the RCT, to the exclusion of other approaches, for all phases of research. As mentioned above, optimization and evaluation of an intervention are distinctly different phases of research. Optimization refers to identifying the set of components and component levels that will make up the optimized intervention, and evaluation refers to assessing whether the optimized intervention has a statistically and clinically significant effect. The RCT, although eminently well-suited to the primary research question that motivates evaluation—that is, whether an intervention has a significant effect as a package—is poorly suited to addressing the kinds of research questions that come up during optimization of an intervention. An important part of optimization and, over time, ongoing improvement of an intervention, is assessment of the performance of the individual components under consideration for inclusion in an intervention and whether and how the components affect each other's performance. The RCT does not provide this information. Post-hoc analyses on the data from an RCT, such as mediation analyses, can be helpful for testing theories and generating hypotheses for future research, but they are limited in what they reveal about the performance of individual intervention components. In MOST, an intervention is always optimized before evaluation in an RCT, and this optimization is based on experimentation that provides direct information about the performance of individual components and, ideally, how they affect each other. Thus, experimental designs other than the RCT are needed. These ideas are developed in detail in the book.

The RCT has been, and remains, an excellent way to evaluate interventions once they have been optimized, because it provides a direct, straightforward, and sensible way of determining whether a single treatment, or an array of treatments *as a package*, performs better than a control. Some intervention scientists have expressed concern that using MOST implies abandoning the RCT. My response has always been that the RCT is an integral part of the evaluation phase of MOST; this is discussed in Chap. 1. This book does not include a chapter on the RCT per se, because there are already many excellent books on the topic.

How MOST Has Been Developed So Far

MOST emerged from a conversation that took place in 2003 between Susan Murphy and Vijay Nair in a hallway of the Statistics Department at the University of Michigan. Susan Murphy's area is statistical theory and applied methodology pertaining to development of adaptive interventions, and Vijay Nair's area is theoretical and applied statistics related to engineering research. Susan and I had been collaborating for several years on some conceptual aspects of methodology

related to development of adaptive interventions. I had been complaining to Susan repeatedly for some time about how, in my view, intervention science was not making very rapid progress. Susan and Vijay started discussing this perceived lack of progress, and Vijay briefly described to her the way products are developed in engineering, noting the differences from how intervention scientists seemed to develop interventions. Susan, who has always been an outstanding matchmaker of collaborators, immediately phoned me to say I needed to visit Michigan right away to spend a day meeting with Vijay and her, to see how far we could get adapting the engineering approach for use in intervention science. The eventual outcome of that meeting was Collins, Murphy, Nair, and Strecher (2005), the first article on MOST.

Methodological research can be as messy as other areas of science, and there are aspects of research on MOST that have been a bit messy. I would like to take this opportunity to call two messy aspects of research on MOST to your attention. The first is the change in how the phases of MOST are conceptualized. In Collins et al. (2005) we outlined three phases of MOST, namely screening, refining, and confirming. Those phases came straight out of engineering and map very well onto what is done in that field. Numerous publications related to MOST have been structured around those phases. However, after about eight years of working with intervention scientists within the MOST framework, I came to the conclusion that screening, refining, and confirming did not map well enough onto what these scientists needed to do. I then reconceptualized MOST so that it consists of the three phases discussed in this book, namely preparation, optimization, and evaluation, and soon began using the new phases in my speaking and writing. The evaluation phase is simply a renaming of the confirming phase, but the preparation and optimization phases are different from the previous screening and refining phases. For example, the previous screening phase did not include the critically important conceptual model (Chap. 2). The first article using the new framework was Collins, Kugler, and Gwadz (2016). Intervention scientists immediately seemed to be more comfortable with the new framework and to be better able to relate the framework to their own research, so the change had a positive effect overall. However, I regret that the reformulation has created some confusion.

A second aspect of research on MOST that has been messier than I had hoped is the integration of MOST and work related to development of adaptive interventions. After our 2005 publication, Susan Murphy continued to work in the area of adaptive interventions, particularly on the sequential, multiple assignment, randomized trial (SMART), a pioneering experimental design. (More recently, she has been working in the m-health area, pioneering the microrandomized trial.) I continued to develop the MOST framework. Not until some time later did it dawn on us that the SMART is a type of optimization trial, and that Susan's work on adaptive interventions, as well as the work of Daniel Almirall and Inbal (Billie) Nahum-Shani, fit squarely within the MOST framework. I wish we had realized this sooner, partly because now it seems so obvious, and partly because our publications before about 2012 reinforce the mistaken idea that MOST and SMART are two nearly unrelated approaches. I sincerely hope this book and the companion volume help to integrate MOST and SMART in the minds of readers. More work remains to be done on this integration.

I do not claim that all of the ideas in this book are new or original, although I hope some of them will be new to some readers. Previous authors, for example Yeaton and Sechrest (1981), have called for a better understanding of the effectiveness of individual intervention components. The work of Stephen West and Leona Aiken (e.g., West & Aiken, 1997; West, Aiken, & Todd, 1993), including an excellent presentation by Steve West I attended in the mid-1990s, has stimulated my thinking. In particular, West et al. (1993) is the first time I know of that the idea of optimizing behavioral interventions appears in the scientific literature. The MOST framework is adapted from standard operating procedures in wide use in engineering. I have cited Wu and Hamada (2011) many times in this book and other writing, but these citations are an inadequate reflection of how much their book, which I consider a modern classic, has influenced me.

Some readers may find a few of the ideas in this book controversial—for example, the position taken on hypothesis testing when selecting components and component levels for the optimized intervention. My view is that none of the ideas in this book are written in stone, and I would be extremely gratified if in some small way this book helps to stimulate discussion that ultimately will move the science of optimization of interventions forward.

Some Examples of Implementations of MOST

This book will demonstrate that the MOST approach can be implemented without the need for much of an increase in the level of resources that is devoted today to the classical approach. However, a realignment in how those resources are spent, as compared to how resources are typically spent in the classical approach, will be necessary in most cases. The ideas presented in this book and the companion volume have been successfully implemented to develop interventions in a variety of areas and in a variety of settings. In fact, the list of applications of MOST and related ideas to optimize interventions is growing rapidly. I will list a few examples here of studies that have used or are using the MOST framework to develop an intervention.

A team of investigators led by Michael Fiore and Timothy Baker at the University of Wisconsin, and including Megan Piper, Robin Mermelstein (University of Illinois, Chicago), and me, conducted several optimization trials examining components of a clinic-based intervention for adult smoking cessation. More about this project, which was funded by the National Cancer Institute (part of the United States National Institutes of Health), can be found in Baker et al. (2011, 2016), Collins et al. (2011), Cook et al. (2016), Piper et al. (2016), and Schlam et al. (2016).

Connie Kasari at the University of California, Los Angeles, and her collaborators developed an adaptive intervention aimed at improving communication skills in non-verbal schoolchildren. More about this project, which was funded by Autism Speaks, can be found in Kasari et al. (2014).

Linda Caldwell and Edward Smith at Penn State, along with their collaborators, including me, investigated three factors hypothesized to affect the fidelity of delivery

of a school-based intervention aimed at preventing drug abuse and HIV in South Africa. More about this project, which was funded by the National Institute on Drug Abuse (part of the United States National Institutes of Health), can be found in Caldwell et al. (2012).

Bonnie Spring at Northwestern University and I, along with a team of collaborators, conducted an optimization trial examining several components of a weight-loss intervention for overweight adults. More about this project, which was funded by the National Institute of Diabetes and Digestive and Kidney Diseases (part of the United States National Institutes of Health), can be found in Pellegrini et al. (2014, 2015).

Amy Kilbourne, Daniel Almirall, and their collaborators at the University of Michigan developed an adaptive strategy to enhance the implementation of an evidence-based mental health intervention. More about this project, which was funded by the National Institute on Mental Health (part of the United States National Institutes of Health), can be found in Kilbourne et al. (2014).

At this writing, a team of investigators including Kari Kugler, Kate Guastafarro, and me at Penn State, and David Wyrick, Jeffrey Milroy, and Amanda Tanner at the University of North Carolina, Greensboro, are conducting a series of optimization trials to examine components of an online intervention to prevent excessive alcohol use and risky sex in college students. More about this project can be found in the Kugler, Wyrick, Tanner, Milroy, Chambers, Ma, Guastafarro, and Collins chapter in the companion volume.

Also at this writing, a team led by Dr. Marya Gwadz at New York University and I are conducting an optimization trial examining several components of an intervention to persuade HIV-positive individuals who are not currently on antiretroviral therapy (ART) to engage in the healthcare system, start taking ART, and reduce their viral loads. More about this project can be found in Gwadz and colleagues (2017).

These are just a few examples chosen to illustrate several points. First, it is possible to obtain funding to conduct research to optimize interventions, and this funding can be obtained from both government and private sources. Second, interventions in any domain can be optimized. The above examples are in the areas of smoking cessation, weight loss, drug abuse and HIV prevention, mental health, learning disabilities, and health care services; there are projects in many other areas. Third, optimization can be aimed not only at the content of the intervention, but also at participant involvement and adherence or implementation quality and fidelity.

Objective and Chapters

The objective of this book and the companion volume is to provide readers with the background needed to use MOST to develop and evaluate optimized interventions. The present book offers a comprehensive introduction to MOST. It also provides an orientation to what might be called the MOST mindset, which is a perspective on,

and approach to, intervention research that is different from how most of today's intervention scientists have been trained.

Chapter 1 provides a conceptual overview of MOST. In writing this book, my biggest struggle was determining the order in which to present the material. For example, as you may see if you read the book from start to finish (which I recommend), selection of an experimental design for the optimization trial can seem abstract without a sense of how the results are to be used later in decision-making. Yet, decision-making cannot be covered before experimental design, because to discuss decision-making it is necessary to understand what kind of experimental results the decision-making is to be based on. Chapter 1 is my attempt to deal with this dilemma by helping the reader see how the topics covered in this book are pieces that fit together and form a coherent whole.

Chapter 2 covers the first of the three phases of MOST, the preparation phase. This chapter emphasizes the importance of a well-specified conceptual model and discusses how the investigator can specify such a model. This model then guides subsequent decisions that are made in MOST. This chapter also covers the role of pilot testing in MOST and introduces the concept of the optimization criterion.

Chapters 3, 4, 5, 6, and 7 are concerned with the optimization phase of MOST. Chapters 3 and 4 introduce the factorial experiment. Particular care is taken with this introduction, because factorial designs and their close relatives are important tools in the optimization phase of MOST. An appropriately designed factorial experiment can produce a high yield of scientific information in the optimization phase. Yet it has been my experience that there are pervasive misunderstandings among intervention scientists about factorial experiments. For example, some years ago I gave a presentation about MOST at a highly-regarded medical school in the United States, in which I discussed the idea of using a factorial experimental design for the optimization trial. I was invited to have lunch with their junior intervention scientists after the presentation, and gladly accepted. During lunch one of the junior scientists said she was very taken with the idea of MOST and could readily see what it offered her research area, but she would probably never use it. When I asked why, she said her department head had told them all that he would never permit a grant proposal using a factorial experiment to be submitted by anyone in the department, because in his view it is not practical to power factorial experiments. If, like that eminent scientist, you believe this mistaken notion about factorial experiments now, I hope after reading Chap. 3 you are convinced that factorial experiments can be highly efficient when properly conducted and analyzed.

Chapter 4 contains an extensive discussion of the interaction, which is an important feature of factorial experiments. Why include a separate chapter on interactions in this book? Interactions are a complex topic, and in my experience, there is considerable confusion about them. This confusion concerns interpretation of interactions, whether main effects can be interpreted if interactions are present, and whether it is possible to power an experiment so that it has a reasonable chance of detecting an interaction if it is present. Perhaps due to this confusion, some investigators may be reluctant to undertake a factorial experiment and prefer simpler designs that do not involve estimation of interactions. This book takes the opposite

perspective and proposes that to understand what works, why, and for whom, it is necessary to examine interactions. Thus, interactions are critically important in science; in fact, it can be argued that behavioral, biobehavioral, and biomedical science can advance only so far without incorporating the concept of interactions into theory and gathering reliable empirical information on interactions. From this perspective, interactions merit more attention than they have typically received in empirical investigations, particularly in intervention science.

Chapter 5, which is probably the most technical in the book, discusses reduced factorial designs, highlighting the fractional factorial design. Fractional factorial designs can be very economical and efficient in situations where it is desired to reduce the number of experimental conditions that must be implemented. Fractional factorial designs make exactly the same overall sample size requirements as complete factorial designs, but require implementation of fewer experimental conditions—usually half or fewer. The choice of which conditions to include in the design is made solely on statistical grounds, to preserve important properties of the factorial experiment. Fractional factorial designs require certain assumptions that may or may not be plausible in a given situation; these are reviewed in the chapter. Fractional factorial designs are not for every situation, but under the right circumstances they can enable intervention scientists to do more with less, and so they merit consideration alongside other design options.

Chapter 6 discusses how to be a good manager of research resources by selecting the most efficient experimental design that provides the desired scientific information. Different experimental designs make different resource demands. Some require more experimental subjects but fewer experimental conditions; others require fewer experimental subjects but more experimental conditions. Depending on which is more costly, adding subjects or adding experimental conditions, different designs may cost very different amounts. Chapter 6 also covers some practical issues related to implementation of factorial experiments in field settings.

Chapter 7 starts with the premise that an investigator has conducted an optimization trial using a factorial or fractional factorial design, properly analyzed the data, and obtained results. These results are to form the basis for making the necessary decisions about the composition of the optimized intervention. Chapter 7 walks through a suggested decision-making process that starts with experimental results and the optimization criterion, and ends with the optimized intervention.

Chapters 1, 2, 3, 4, 5, 6, and 7 emphasize fixed interventions, that is, interventions in which the design calls for providing all participants with the same intervention. Chapter 8 discusses adaptive interventions. In an adaptive intervention, the intervention is altered at critical decision points, according to pre-specified decision rules. This is done to adapt the intervention so that it responds to characteristics of the individual or setting, or to what amount and kind of progress the individual is making over time. The purpose of Chap. 8 is primarily to introduce optimization of adaptive interventions. As mentioned below, two chapters in the companion volume provide a more advanced and detailed treatment of optimization of adaptive interventions.

Because individual chapters of this book are available for downloading, I tried to make each chapter as self-contained as possible. This resulted in some unavoidable redundancy; for example, most chapters begin with a summary of the hypothetical example that is threaded through the book. I apologize if those who read the book from start to finish find this tedious.

Intended Audiences and How to Use This Book

The intended audience for this book includes scientists who develop and evaluate behavioral, biobehavioral, and biomedical interventions; statisticians, biostatisticians, quantitative psychologists, and other methodologists working in intervention science; and trainees preparing for careers in these areas.

I have tried to keep this book relatively non-technical. This preface, Chap. 1, and much of Chap. 2 have been written for a general scientific audience. The rest of the book has been written to be understandable to anyone who has had graduate training in statistics up through multiple regression. Those with more technical backgrounds, such as statisticians, may find the treatment in this book incomplete and wish to do some additional reading on some topics. Examples include fractional factorial designs and the details of multivariate analysis of data gathered via a factorial experiment. A good starting point would be the reference lists in each chapter.

This book is a suitable textbook for an advanced graduate course, provided students have had the necessary training in multiple regression. Instructors also may wish to assign some or all of the chapters in the companion volume.

Some readers may be wondering whether it is necessary to read every chapter. Of course, I recommend that everyone read the entire book! I particularly make this recommendation to investigators who are planning to write a grant proposal featuring MOST or to lead the optimization of an intervention using MOST. However, it is realistic to assume that, depending on an individual's role in intervention science, some chapters may be of more interest than others. Some scientists work in a team where responsibilities are divided among team members. Those who are primarily responsible for development of interventions from a conceptual perspective may be particularly interested in Chaps. 1, 2, and 8. Team members primarily responsible for the methodological aspects of research may be particularly interested in Chaps. 1, 3, 4, 5, 6, and 7.

Some readers may primarily be looking for an overview of MOST. Examples are program officials at granting agencies, such as the National Institutes of Health in the United States, who field inquiries from prospective grantees who wish to include MOST in their proposals; and senior scientists responsible for mentoring junior scientists who are considering using MOST in their work. These individuals will probably find Chaps. 1 and 2 particularly helpful.

Interventions in Different Domains

There is a single hypothetical example threaded through this book for pedagogical purposes, concerning an intervention aimed at improving adherence to antiretroviral therapy (ART) in HIV+ individuals. This would be classified as a behavioral or perhaps biobehavioral intervention (see definitions in Chap. 1 and the glossary). I selected this example because of my background in these types of interventions. Unfortunately, this means two other types of interventions receive less emphasis in the book. One is biomedical interventions, which consist of pharmaceuticals, surgery, physical therapy, and the like. The other is educational interventions, which are an important subset of behavioral interventions. Everything said in this book also applies directly to optimization and evaluation of both biomedical and educational interventions. Factorial experimentation when cluster randomization is necessary is an important topic for optimization of educational interventions. This is not covered in detail in the present volume, but it is covered in the Nahum-Shani and Dziak chapter in the companion volume.

Additional Resources

Each chapter in the companion volume offers a treatment of an advanced topic, written by experts in those areas. The material in the present book provides a necessary foundation for these chapters. A very brief description of the chapters in the companion volume is provided at the end of Chap. 8.

Additional resources can be found at <http://methodology.psu.edu/ra/MOST>. These resources include material that is supplementary to this book or the companion volume; brief descriptions of applications of MOST in a variety of areas; FAQ in which some of the material in this book is presented in an informal way; suggested readings; and software.

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In this brief acknowledgments paragraph I wish to thank a few people who were directly instrumental in the preparation of this book. Several cohorts of students in my graduate seminar read previous drafts of many of the chapters. These students, along with hundreds of people who have participated in presentations and workshops I have given, have asked questions that stimulated my thinking or helped me to find a better way to explain something. Donna Coffman, David Conroy, John Dziak, Kate Guastaferrero, Kari Kugler, Susan Murphy, and Kelly Rulison gave me extremely helpful comments on an earlier version of the manuscript. John Graham made himself available to talk over some key aspects of the book at critical times. Amanda Applegate's editorial assistance was invaluable throughout the process. Many thanks to all of you.

Concluding Remarks

Above I asked to you imagine a scenario in which interventions are made up exclusively of components of demonstrated effectiveness; interventions are built to meet clearly specified standards and are immediately scalable; translation from basic science into intervention practice is done scientifically and programmatically; every study adds to the knowledge base about what works and how; and interventions become incrementally and steadily more effective, efficient, cost-effective, and scalable over time. In this book I hope to convince you that MOST can help behavioral, biobehavioral, and biomedical scientists make this scenario a reality.

It is my sincere hope that this book and the companion volume will help intervention scientists to think in a new way about development and evaluation of interventions. I hope readers will consider shifting a bit of the focus of their own work away from the evaluation of interventions as a package and toward optimization of interventions to meet specific criteria. I also hope the field as a whole will start to value demonstrable, incremental, and cumulative improvement over time in interventions. My dream is that fifteen years from now, we can all look back to the current state of intervention science and be able to say convincingly, “Today’s interventions are much more effective, efficient, economical, and scalable than those were.”

Finally, to those who see value in the ideas offered in this book, but are hesitant to implement them because they seem to be too radical a departure from business as usual, I offer this quote from Pythagoras (570 BC – 495 BC; quoted in Edwards, 1891, p. 101):

Choose always the way that seems best, however rough it may be, and custom will soon render it easy and agreeable.

University Park, PA, USA
2017

Linda M. Collins

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Chapter 1

Conceptual Introduction to the Multiphase Optimization Strategy (MOST)

Abstract The multiphase optimization strategy (MOST) is an engineering-inspired framework for development, optimization, and evaluation of behavioral, biobehavioral, and biomedical interventions. This chapter provides a conceptual overview of MOST and discusses how it is different from the classical approach. The focus of the classical approach is on developing an intervention a priori and then evaluating it in a randomized controlled trial (RCT). By contrast, the focus of MOST is on a phased approach: first developing and optimizing an intervention and then evaluating the optimized intervention in an RCT. The optimization is based on carefully conducted and fully powered optimization trials. The objective of MOST is to arrive at an intervention that not only demonstrates effectiveness in an RCT but also is efficient, economical, and scalable. Readers are encouraged to read the preface before this chapter, because it provides a rationale for and orientation to the book.

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