# New Book on Advanced Topics in MOST With Linda Collins and Kari Kugler

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Aaron Wagner:

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Aaron Wagner:

Welcome to Methodology Minutes. This is a companion podcast to podcast number 31. In that podcast, Linda Collins talks about the book she authored, Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multi-Phase Optimization Strategy (MOST). That podcast provides a general introduction to the multi-phase optimization strategy. This podcast introduces a companion volume titled, Optimization of Behavioral, Biobehavioral, and Biomedical Interventions, Advanced Topics.

Aaron Wagner:

In this podcast, we are going to discuss the advanced topics that are covered in that book. Linda will discuss several of the chapters and her co-editor, Methodology Center Affiliate, Kari Kugler, will discuss the two chapters that she authored. Linda and Kari, congratulations on the books and welcome to both of you.

Kari Kugler:

Thank you.

Linda Collins:

Thank you. Great to be here, as always.

Aaron Wagner:

Great to have you. So Linda, to get started, how was the book on MOST that you edited, different from the book that you authored?

Linda Collins:

Well, the most obvious difference is that one is an authored book and the other is an edited book. But the reason why I felt so strongly that we needed an edited book is that, I wrote about what I knew when I wrote the the first volume. And it became clear to me while I was writing it, that there were a lot of important topics that should be covered, and I wasn't necessarily the right person to cover those topics, that other people had much more expertise in those areas. And so finally, it occurred to me that I could also edit a book and invite those people to write chapters. So now we have an edited book with chapters by a lot of really smart people. So I'm very happy about that.

Aaron Wagner:

Great. And Kari, why do you think the book was needed?

Kari Kugler:

Yeah. I think over the last probably five plus years working with Linda and chatting with other intervention scientists, there came to be a point where we had some advanced topics that we needed to discuss. Some things related to some of the technical aspects with new types of research questions that were emerging, in addition to some practical aspects related to implementation of interventions using MOST.

Aaron Wagner:

Great, thank you. So one of the critical components of the preparation phase of MOST, and again, if you don't know what that is, go back and listen to podcast 31, is to develop a conceptual model. Can you explain what you mean by conceptual model?

Kari Kugler:

Absolutely. So a conceptual model is a theoretically driven model that explicitly delineates how we anticipate the candidate components of our potential intervention, how they are supposed to have an impact on the mediators and corresponding outcomes.

Aaron Wagner:

So this is the first chapter in the book as it is kind of fundamental to shaping your thinking about how the project will proceed. Talk about what you did with that chapter, please.

Kari Kugler:

Absolutely. So you know, as the conceptual model is a big part of the preparation phase of MOST, and I'll talk about in just a minute about how it can also shape other phases of MOST. But what we did in this chapter was showed how we used and developed a conceptual model specifically to look at the intersection of alcohol and sex among college kids.

Kari Kugler:

And so we walked through our team's process of how we went about using the empirical literature, using theory, and even using the little aspects of conjecture to really help understand and articulate how we think our intervention components as they are designed are intended to have an impact on the corresponding mediators on outcome.

Kari Kugler:

And so that's what we talk about in this chapter and we illustrate how we propose to use an experimental design to test each of the components, see which ones are moving the needle on the intended mediators, and then make revisions to that conceptual model based on our outcomes, that then we can go back and do it again.

Kari Kugler:

And so it's showing an iterative process of how we are using the conceptual model to guide the intervention, and the decision about what experimental design we use, what our outcomes are that we are measuring, and then walking through the process of how we would use the results from that experiment, and then make revisions to the conceptual model to then go back forward and test again.

Aaron Wagner:

So it sounds like the conceptual model is your idea of the map of how you get from the intervention to the outcome you want, but then you do the experiment and that reinforms the map all over again.

Kari Kugler:

Absolutely, absolutely. And it lends itself to the continuous optimization principle that is outlined in the companion volume.

Aaron Wagner:

Thank you. Linda, you included a chapter about factorial experiments in the real world. What is a factorial experiment?

Linda Collins:

A factorial experiment, it's one of the most commonly used designs in the optimization phase of MOST, and it's an experiment in which several different components are manipulated at the same time. It's a very efficient type of experimental design that enables you to look at the main effects of a set of components using a relatively small sample size. I don't mean that it's necessarily small in absolute terms, but much smaller than you would need if you were going to look at each one individually. And also, it enables you to look at whether the effect of one component depends in part on the presence or absence of another component, for example. So it really gives you a lot of excellent scientific information.

Aaron Wagner:

So most behavioral scientists and probably a lot of the audience is trained primarily in the randomized controlled trial. Why does MOST try and introduce, or not rather, but include different types of experimental designs?

Linda Collins:

It's really important to use different kinds of experimental designs in the optimization phase. Because optimization poses different kinds of scientific questions than evaluation. The RCT is perfect for the evaluation phase most of the time, but it's rarely what's called for in the optimization phase. A lot of different kinds of experimental designs can be used in the optimization phase, but very often, because of its economy and scientific yield, people end up landing on a factorial experiment.

Aaron Wagner:

And a factorial experiment can in some instances have a relatively high number of experimental conditions. Is that right?

Linda Collins:

Absolutely. Yeah. And certainly if your kind of base is the RCT, which typically only has two or three experimental conditions, you're going to think that a factorial experiment has a lot of conditions. Because typically, a factorial experiment would have 16 or 32 or even more experimental conditions, which is many more than intervention scientists are accustomed to dealing with. I emphasize though, that the sample size requirements are relatively modest in factorial experiments.

Aaron Wagner:

So what have you learned about running these experiments in the real world? Can you run all these conditions at the same time?

Linda Collins:

Intervention scientists are often hesitant when they see the requirements of factorial experiments in terms of number of experimental conditions. A lot of times, if an intervention scientist has spent their entire career doing two arm RCTs, and I come along and say, "Well, you want to think about conducting an experiment that has 16 experimental conditions," they often say, "I just don't see how I can do that."

Linda Collins:

And that's why I thought it was so important to include chapter two in this book, which is written by Megan Piper and her coauthors. There's really no one better than this group at Wisconsin better at implementing large factorial experiments in the field. They were the first ones to do it, they've done it so well, and they really know, I would say pretty much all there is to know about it. So I'm really thrilled that they agreed to include a chapter in this book.

Linda Collins:

And they talk about conceptual and practical aspects of conducting factorial optimization trials in real world settings, that they've conducted numerous factorial experiments in ordinary healthcare settings. Just doctor's offices like the ones that our listeners would go to if they had a sore throat or needed an inoculation or something like that. So I think that chapter's going to be very useful to people.

Aaron Wagner:

Fantastic. There's also a chapter on multilevel factorial designs. How do those differ from the factorial experiments you just described?

Linda Collins:

It's not that they're different so much that there's an additional consideration, which is some kind of nesting structure in the data. So there's several different kinds of nesting structures can affect a factorial experiment. One important one is if you have to do cluster randomization because your subjects are presented to you in clusters. For example, maybe you're doing a school based study and you need to assign entire classrooms or even entire schools to experimental conditions.

Linda Collins:

There's another kind of clustering that we call experimental induced clustering. That's when, for example, you're examining an intervention where one of the components is delivered in a group setting. There, the experimenter is randomly assigning people to groups. So here, the subjects don't come clustered in groups that experimenter is establishing the groups himself or herself, but you still have to take that dependence into account. The subjects may not know each other at the outset of the study, but after they've been in a group together for eight weeks or so, they will know each other very well. And so their responses to whatever outcome variable you have are going to be related. So it's important to take that into account.

Linda Collins:

So Nahum Shani and Dziak contributed a chapter talking about how you handle that in terms of experimental design and then statistical analysis later after you've collected the data.

Aaron Wagner:

Thanks. So adaptive interventions which are interventions that include rules to enable them to change in response to patient need are also addressed in this book. How is most relevant for researchers who are working on developing adaptive interventions?

Linda Collins:

MOST is just as relevant for researchers who are developing adaptive interventions as it is for researchers who are developing more fixed interventions. But a different kind of optimization trial is needed. Chapter four, which is written by Danny Almirall and his coauthors talks about the sequential multiple assignment randomized trial, or SMART, that is a special experimental design for optimization trials that are aimed at optimization of an adaptive intervention, a certain type of adaptive intervention.

Linda Collins:

Adaptive interventions vary in their intensity. And by intensity, I'm talking about how frequently they can be adapted. SMARTs are for situations where the intervention being optimized is a relatively low intensity intervention. So that means it would be adapted relatively infrequently, maybe once or twice over its course, or maybe once a month or something like that. You can compare that to more intensively adaptive interventions, which actually is the topic of the next chapter.

Aaron Wagner:

Thank you very much. And so related to that, you have a chapter on control systems engineering. How does that relate to MOST?

Linda Collins:

Control systems engineering is a great approach to conducting an optimization trial for an intensively adaptive intervention. Intensively adaptive interventions are interventions where the adaptation can occur very frequently. It can occur several times a day, even many times a day over a period of days or weeks or months even, or even indefinitely.

Linda Collins:

In-health interventions are a great example of intensively adaptive interventions. Where participants can carry around perhaps a smartphone and they monitor their behavior over the course of the day. And there can be many opportunities for the intervention to, for example, push out an encouraging message, or make a slight change in the dosage of an intervention component, or perhaps activate a component that hasn't been active up until that point.

Linda Collins:

So you can see how intense that can be, in terms of the structure of the intervention and the rules that are used to adapt it. So control engineering is a great approach to that. You can build a controller for an adaptive intervention in much the same way you would build a controller to control a manufacturing process, or a supply chain, or a climate control system, a cruise control on your car. Those are all examples of controllers, and that basic technology can be applied to interventions and involving humans. And Daniel Rivera is a control engineer, he's a chemical engineer by training, an expert in developing controllers. And he is the primary author of chapter five.

Aaron Wagner:

It's fascinating the way that the engineering keeps coming in like that.

Linda Collins:

It's so interesting. Yeah.

Aaron Wagner:

So Kari, getting back to you, when scientists analyze data from a factorial experiment, there is a difference between using what is called dummy coding and what is called effect coding. What is the distinction between these two types of coding, and why does it matter?

Kari Kugler:

Oh, great question. And I would just like to preface this with, when I first met Linda, she probably gave me a data set from a factorial experiment. And I, like many other behavioral interventionists was trained in dummy coding. So it's a way to provide a numerical value to a categorical variable, and most often with dummy coding you have ones and zeros.

Kari Kugler:

And so had I been given data from a factorial experiment for instance, and had to try to analyze it and come up with a definition of, what is the main effect of a particular component, I would have not known what to do. Because as I was trained with dummy coding, you never interpret a main effect in the presence of interactions. Well based on data from a factorial experiment, you would have interactions in addition to main effects coded in your actual analysis.

Kari Kugler:

And so, it became very important in writing this chapter that we needed to make clear that a lot of people are trained in dummy coding which uses ones and zeros, and it doesn't give you a straightforward answer as you would want it to be in one you want to estimate the effects of main effects and interaction effects. And so needed to make sure that we introduced the concept of effect coding, which is just simply now ones and minus ones, but it has an important impact, in terms of giving you the actual estimates that you are most interested in when you're wanting to analyze data from a factorial experiment,

Aaron Wagner:

Yeah, the little things matter.

Linda Collins:

Well, it seems like such a little thing, zero one, versus minus one [crosstalk 00:15:18] minus one and one. But one thing Kari does in her chapter and I think is really interesting, is she shows the same small dataset analyzed with using dummy coding and analyzed using effect coding, and you get different results. You would draw different conclusions. And neither approach is right or wrong. It's just important for data analysts to know which approach they're using, so that they can draw the appropriate conclusions.

Aaron Wagner:

Yeah, absolutely. I suppose I should say details matter, not little things.

Kari Kugler:

Yeah, details matter. [crosstalk 00:15:51] And so thank you Linda for following up on that, because that's exactly, I mean I think that that was the great example of walking through the difference between them.

Aaron Wagner:

So Linda, why did you decide to include a chapter on cost effectiveness? And what role do you see cost-effectiveness playing in most in the future?

Linda Collins:

John Dziak was kind enough to write an excellent chapter on where we are today at this writing with the use of cost effectiveness analysis in MOST. There's a lot of open questions and he makes it very clear in the chapter that it's mostly about a summing up of the state of the art and kind of a call to action for there to be more work in this area. There's a lot of open questions there.

Linda Collins:

Cost-effectiveness though, I think is going to be increasingly important as we go forward. Intervention scientists are not accustomed to thinking that way. But I think once they do become accustomed to thinking that way, they're going to see how valuable it is to develop interventions, so that they achieve a certain level of cost effectiveness, which using MOST is completely possible.

Linda Collins:

The cost effectiveness of interventions traditionally, has been assessed after the fact. So an intervention is developed, it's evaluated in an RCT and then it's implemented and its cost effectiveness is evaluated. Well at that point, the intervention is a done deal. You can't go back and change it.

Aaron Wagner:

Right.

Linda Collins:

Whereas using MOST, it's possible to optimize to achieve a certain level of cost effectiveness. We're not quite there yet. I have to say that today, and I know John would agree with me, we don't know exactly how to do that, but the pieces are all there. And I think that in the future, the very near future, that's going to be worked out. That's very high in my to do list.

Aaron Wagner:

Yeah. And I imagine that as far as funding these things, getting the most bang for our buck is only going to make our ability to take intervention science and distribute it much further and have a much greater impact on people's lives, which can be a critical part of that.

Linda Collins:

Well, absolutely. And that's one reason why a lot of NIH project officers are very enthusiastic about MOST, because they see the potential there for development of better interventions, and really to get more progress for the taxpayer's money.

Aaron Wagner:

Yeah, that's really exciting. So there is also a chapter about mediation analysis. How does a factorial experiment allow researchers to examine mediation?

Linda Collins:

Very exciting new direction. In a mediation analysis, there's a treatment that impacts the mediator, which in turn impacts an outcome. That's kind of the shorthand approach. Of course, more complicated than that, but that's the basic idea. And the treatment is traditionally just an on-off treatment or treatment control. So it's based on usually a two arm RCT.

Linda Collins:

In chapter eight, Smith, Coffman and Zhu talk about how you can do analysis where the treatment is actually a factorial experiment. So now, you are modeling the mediation of main effects in a factorial experiment, and interestingly, you also can model the mediation of interactions. So interactions knock over, so to speak a mediator, which then knocks over the outcome. So it really opens up the idea of mediation analysis.

Aaron Wagner:

Wow. You don't have to be ready to do that to start reading the first volume? [crosstalk 00:19:35].

Linda Collins:

No, and in fact, I'm glad you asked that question, because I would recommend that that people read the authored book before reading the book we're talking about here. Because this book is about, as the title implies, advanced topics. The authored book provides a comprehensive introduction to MOST, and that background is going to be helpful for most people in understanding these chapters.

Aaron Wagner:

So just to kind of wrap things up, what do you see as the future of MOST?

Linda Collins:

Methodologically, there's a lot of interesting research to do on MOST. And I'm kind of in the process of regrouping, now that these two books are out and seeing what the new directions are going to be. But I'm seeing MOST catching on. A lot of intervention scientists are interested in using it. And of course that was mainly why I wanted to produce these two books, to get the information out there so that intervention scientists would find it straight forward to use MOST in their work. And I'm hoping that rather than sole reliance on the RCT, that people will start thinking more in terms of optimizing before they take an intervention to an evaluation and an RCT.

Linda Collins:

And maybe we can I get to a point where we're seeing steady incremental improvement and behavioral interventions over time, and also where we're getting to a point of immediate scalability. So that once an intervention has been optimized and evaluated, it's ready to go and it can be implemented without the need for any ad hoc modifications.

Aaron Wagner:

Whoa. That's a fantastic vision. Thanks for sharing it with us. And Kari and Linda, thank you both for being here to talk with us today.

Kari Kugler:

Thank you.

Linda Collins:

It was our pleasure.

Aaron Wagner:

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