For joining our CMIPS seminar.

It’s really a pleasure to have you all and most importantly, a pleasure to have Dr. Brian Mittman, who we’ve been talking about bringing over here to CMIPS and Yale for quite some time. Dr. Mittman is a distinguished longstanding implementation scientist, I might even say one of the founders of implementation science as a formal discipline. He is a research scientist in the Department of Research and Evaluation with additional affiliations at the US Department of Veteran Affairs, another place where a huge amount of some of the best implementation science, thinking and research has emanated over the years, the University of Southern California and the University of California Los Angeles, where he co-leads the UCLA Clinical and Translational Science Institute.

And I find that very interesting that the implementation and improvement science are linked in the same name, also something we at CMIPS are very interested
in the kind of continuum between implementation science and improvement science, quality improvement, and what are the commonalities and differences and where does one end and the other begin. So I don’t know if that’s something Dr. Mittman is gonna touch upon in his talk today.

He chaired the planning committee that launched the journal, "Implementation Science," which now has a sort of spinoff journal, I forget its name, but now there’s two of them. He served as co-editor in chief of that journal from 2005 to 2012. He was a founding member of the US Institute of Medicine Forum on the science of quality improvement and implementation and chair at the National Institutes of Health Special Emphasis Panel on Dissemination and Implementation Research in Health. He was a founding member of the US Institute of Medicine Forum on the science of quality improvement and implementation and chair at the National Institutes of Health Special Emphasis Panel on Dissemination and Implementation Research in Health. He was a founding member of the US Institute of Medicine Forum on the science of quality improvement and implementation and chair at the National Institutes of Health Special Emphasis Panel on Dissemination and Implementation Research in Health. He was a founding member of the US Institute of Medicine Forum on the science of quality improvement and implementation and chair at the National Institutes of Health Special Emphasis Panel on Dissemination and Implementation Research in Health.
54 00:02:29.280 --> 00:02:30.330 But if you’re interested,
55 00:02:30.330 --> 00:02:32.490 maybe write to me later and we can figure that out.
56 00:02:32.490 --> 00:02:33.750 because it’s very important.
57 00:02:33.750 --> 00:02:37.740 for our implementation dissemination science applications
58 00:02:37.740 --> 00:02:39.720 to NIH here at Yale.
59 00:02:39.720 --> 00:02:41.040 Dr. Mittman directed
60 00:02:41.040 --> 00:02:44.340 the VA’s Quality Enhancement Research Initiative
61 00:02:44.340 --> 00:02:47.100 from 2002 to 2004.
62 00:02:47.100 --> 00:02:50.130 His research examines innovative approaches
63 00:02:50.130 --> 00:02:52.740 to healthcare delivery and improvement
64 00:02:52.740 --> 00:02:55.830 and efforts to strengthen learning healthcare systems,
65 00:02:55.830 --> 00:02:59.490 another area in which we’re very interested in CMIPS.
66 00:02:59.490 --> 00:03:01.890 and many others at Yale are as well.
67 00:03:01.890 --> 00:03:04.920 So today, Dr. Mittman is gonna talk to us
68 00:03:04.920 --> 00:03:08.040 about Addressing Heterogeneity and Adaptability
69 00:03:08.040 --> 00:03:10.380 and Multi-Component Implementation
70 00:03:10.380 --> 00:03:12.360 and HIV Interventions:
71 00:03:12.360 --> 00:03:14.640 Emerging Frameworks for Research
72 00:03:14.640 --> 00:03:16.380 on Complex Health Interventions.
73 00:03:16.380 --> 00:03:18.510 And actually, I wanted to say one thing
74 00:03:18.510 --> 00:03:21.940 before I turn it over to him.
75 00:03:21.940 --> 00:03:23.510 He also serves as a consultant
76 00:03:23.510 --> 00:03:25.110 for our R3EDI Hub,
77 00:03:25.110 --> 00:03:27.670 which is a technical support hub
78 00:03:28.770 --> 00:03:30.780 that supports seven projects
79 00:03:30.780 --> 00:03:33.870 devoted to ending the AIDS epidemic.
80 00:03:33.870 --> 00:03:38.280 under a general coordinating center based in Illinois.
81 00:03:38.280 --> 00:03:40.140 And it’s been a pleasure to have Brian
82 00:03:40.140 --> 00:03:42.720 as a part of our R3EDI Hub team as well.
83 00:03:42.720 --> 00:03:44.970 So without any further ado now,
84 00:03:44.970 --> 00:03:47.700 I will turn things over to Dr. Mittman.
85 00:03:47.700 --> 00:03:49.500 <v ->Great, thank you, Donna,</v>
86 00:03:49.500 --> 00:03:50.970 both for the kind introduction
87 00:03:50.970 --> 00:03:55.170 as well as more importantly the opportunity
to present
88 00:03:55.170 --> 00:03:58.811 and to meet with some of your colleagues today
and tomorrow.
89 00:03:58.811 --> 00:04:01.173 As we were saying before we started,
90 00:04:01.173 --> 00:04:03.540 my hope is to have the opportunity
91 00:04:03.540 --> 00:04:06.720 to join you in person at some point down the
line,
92 00:04:06.720 --> 00:04:08.010 but I know we all share that hope
93 00:04:08.010 --> 00:04:10.560 for lots of in-person gatherings.
94 00:04:10.560 --> 00:04:13.350 You touched on several of my favorite topics,
95 00:04:13.350 --> 00:04:16.590 including implementation science, improvement
science.
96 00:04:16.590 --> 00:04:19.050 I’ll mention that I think very briefly
97 00:04:19.050 --> 00:04:21.450 as well as other topics.
98 00:04:21.450 --> 00:04:24.270 And I’m glad to schedule follow-up talks
99 00:04:24.270 --> 00:04:25.710 to speak about them.
100 00:04:25.710 --> 00:04:28.713 One quick comment on some of your kind
remarks.
101 00:04:30.030 --> 00:04:32.340 I always counsel junior colleagues
102 00:04:32.340 --> 00:04:35.610 to pick a very small field that’s likely to grow
103 00:04:35.610 --> 00:04:37.290 and get in on the ground floor
104 00:04:37.290 --> 00:04:39.210 because it makes you look important.
105 00:04:39.210 --> 00:04:42.660 That’s sort of the big fish, small pond kind of
idea.
But also, the fact that I spend much more of my time advocating and helping to develop and expand fields that I'm interested in sometimes rather than actually doing the research, although I do have a research portfolio. So implementation science is a field that I was able to, again, get in on the ground floor and help to wave the flag, promote interest and advocate at NIH, at PCORI and many other places. And used to spend a lot of time traveling between different facilities and institutions as well as in planes trying to advocate and promote interest in implementation science. But the implementation science field, in my view, is well established. There are many of us who are interested and have active research portfolios. I don’t know that I have that much to offer at this point as far as new ideas, but I have a different view about the field of complex health interventions where I think there is a need to continue to think hard and promote some of the newer emerging frameworks and point out that as researchers are tasked
in studying complex health interventions is a bit different from our tasks and studying other kinds of interventions. I think my most important focus lately in my research is trying to help, again, advocate and share information on some of these emerging frameworks and encourage more development. One more comment in terms of the truth in advertising. I actually won’t spend much time at all talking about specific implementation science or HIV/AIDS intervention examples, but I think it’ll be very clear as to how and why the comments that I will make are directly relevant to both of those bodies of activity. So let me move on and I try to remember which button allows me to advance. So let me start with a very high-level question, and that is ask us all to think a little bit about what we as researchers do in addition to producing scientific generalizable knowledge, what we do to support policy decision makers and practice decision makers questions. And much of the research that’s conducted in medical schools and on other health-related institutions pursues these questions.
Does it work or is it effective?

The FDA of course would like to know if a new drug should be approved.

CMS and others would like to know if it should be funded and promoted.

Should it even be mandated?

Within health systems, P&T committees have decisions to make about inclusion of new drugs in a formulary.

And frontline practicing clinicians need to know whether they should use a new drug or another intervention.

So much of the questions here in the guidance that we endeavor to provide to our policy and practice decision maker colleagues is a set of answers to these questions.

Does it work?

Is it effective?

In the case of comparative effectiveness research, is intervention A better than B?

And of course, we focus on outcomes and impacts when we try to answer this yes/no question. We often have the sample size and the funding and the ability to examine heterogeneity and subgroup effects and so on, and whether contextual factors influence the effects and outcomes.
And of course, our gold standard research method of RCTs and similar experimental methods where we randomize and measure outcome differences, that’s how we go about conducting this research.

But again, the focus is on impact and outcomes. Are the outcomes better for those in the intervention group versus the control group? And if the answer is yes, then the intervention is effective, it’s approved by the FDA, it’s promoted, it’s reimbursed and it’s used. And there are in fact many examples of magic bullets or very strong robustly effective drugs for which we can produce a clear answer to that question.

Yes, this drug is very effective.

Precision medicine, of course, is leading us down the path for drugs and interventions for which there isn’t a clear answer where there are high levels of heterogeneity.

And we do need to tailor the interventions and that’s really the theme of this talk. When we think about complex interventions or complex health interventions, I’ll define them more formally in a minute, but health promotion programs, HIV/AIDS prevention,
treatment programs, implementation strategies,

there are some examples of highly robust,

highly effective complex health interventions

for which we can produce a strong answer.

Yes, this intervention tends to be effective

across multiple settings

and in multiple sets of circumstances.

But by and large, for most complex health interventions,

when we ask the question, is it effective?

The answer that comes out of our research

is sometimes or it depends.

The heterogeneity,

I'll sometimes use the term extreme heterogeneity,

is just so great that the impacts vary considerably

and it’s impossible to produce a simple answer,

yes or no, it is effective or it’s not effective.

So there is no formal established definition

of complex health interventions at this point,

but here are some of the key features

that tend to be mentioned in most discussions

of complex health interventions.

The fact that there are multiple components

and those components interact.

The intervention, the multi-component inter-

vention

tends to target multiple levels,

not always, but certainly multiple entities.

So we have interventions that target patients
and family caregivers and other peers
as well as clinicians and other health system
staff,
as well as in many cases,
communities and even regulatory levels.
These interventions tend to be highly adapt-
able.
They’re not fixed.
So unlike a drug that comes from the factory
in a very consistent chemical formulation
with a high degree of consistency and homo-
genity,
these interventions adapt.
And that’s the case even when we try to
achieve fidelity
to the manualized intervention
and prevent adaptations and modifications,
and that’s another theme I’ll come back to.
Because of all of these features,
the interventions tend to achieve their effects
through multiple pathways
and they tend to be mediated.
So it’s not a drug that has a direct impact
on a physiologic process,
but instead an intervention
that changes attitudes or beliefs,
those changes in attitudes and beliefs
lead to changes in knowledge and intentions.
Those changes in knowledge and intentions
eventually lead to changes in behavior.
But those behaviors are influenced by multiple
factors.
So it’s not only the patient’s own beliefs and knowledge and attitudes, but peer influence, clinician influence, social influence from key opinion leaders and a number of others. So the causal pathways tend to be very complex and I’ll illustrate that in a few minutes. So when we think about a comparison between simple interventions like drugs versus complex interventions, these are some of the key dimensions where there are differences. The difference between a single fixed and highly stable and homogeneous drug that targets a single stable physiologic process to achieve a simple goal such as reducing blood pressure in patients that are not always homogeneous. There are differences, but the argument is that patients, despite genetic profile differences, achieve a different goal such as reducing blood pressure and other physiologic, as well as clearly socioeconomic status in neighborhood and contextual differences, those differences tend to be somewhat smaller than the differences we see across communities and organizations. And again, we can argue that point, but these are the key distinctions between these two categories of interventions.
And the consequences, of course, or the implications for research are that, when we study drugs, oftentimes, not always, but oftentimes we do see a relatively high level of homogeneity with very consistent and often strong, easily detected main effects. Whereas again, with complex interventions, we get the answer along the lines of it depends or sometimes. We see lots of complexity, instability and heterogeneity. And the average effects, because of the heterogeneity, tend to be very weak. We have many subjects or targets in the intervention that do very well, others that do very poorly, but on average, an average effect size estimates that are close to zero. One key point, and that is, this is not a dichotomy, but instead of a continuum. There are elements of complexity in all interventions. The key question is, when is an intervention sufficiently complex that we can’t study it through an RCT with a focus on average effect sizes, but instead need to use the more complex kinds of approaches that I’ll talk about over the next several minutes.
So getting back to this question, does it work, is it effective? And the answer being sometimes or it depends, that answer, of course, is not at all useful for decision makers. So we need to think about a different way of designing, conducting our studies and a different type of evidence or a set of insights and findings that we need to produce for science, but also for policy and practice. So let me back up and illustrate some of the challenges that we face when we deal with complex health interventions. So this is a pattern of results from a hypothetical study that could be a guideline implementation study. We are attempting to improve adherence to evidence-based clinical practice guidelines. In the blue sample, the blue bars in this histogram shows that all of the sites in the intervention group did very well. Our intervention managed to significantly improve rates of adherence among all the intervention physicians or clinics or hospitals, whereas the sites in the yellow or light green are all scattered around zero.
So on average, we saw no change in adherence levels among the usual care comparison sites, although some of course did better and some did worse. It’s just because of random variation. I don’t know that we’ve ever seen findings from any implementation study that resembled this kind of pattern or anything close to it. This clearly would be "New England Journal" or "Lancet" caliber work if we had a strong finding of this sort, but that’s what we would hope to see with our interventions, that we would find or design an intervention and see very robust, very significant effects. This is what we tend to see more often when we study complex health interventions. There’s almost complete overlap between the blue and the light green yellow sites. If you are an intervention site, you are almost as likely to show reduced rates of adherence as you are increases. And similarly, the usual care sites, many of them did show rates of improvement that are comparable to those in the intervention site. So when you have a pattern of results like this, you can’t say to decision makers,
my complex health intervention, my HIV/AIDS prevention program or my implementation strategy or quality improvement program is highly effective, I would advise you to use it. As a decision maker, if I know I’m almost likely to end up spending a lot of money and staff time and disruption and end up with decreased performance, obviously, I’m not going to be interested in this program. So what is our goal then as a researcher? Our goal, of course, is to understand who ended up on the right hand side of this distribution, what the factors were that led to those improvements for both intervention as well as control sites, and what can we do to counsel decision makers to allow them to end up on the right hand side rather than the left hand side of the distribution. So when we think about finding or designing developing complex health interventions that are effective, one position that we could take is our goal as researchers is to develop and generate the evidence showing that our interventions are highly effective.
that assumes that those interventions exist.

Hang on one second, I will be right back.

While he’s out, I can say if people have questions or comments, why don’t you put them in the chat as we go along.

and then at the end of Brian’s talk,

I’ll pose some of the questions and comments to him.

Go ahead, Brian. Thank you.

Yeah, so my apologies.

For those who joined earlier, we were talking about the renovations underway.

My wife was stuck outside because I forgot to open the door for the second pathway into the kitchen because the main path is covered with paint paraphernalia.

So again, because complex health interventions tend not to be robust and we tend not to have the ability to find or develop the needle in the haystack or they don’t exist at all, that a robust complex health intervention is a mythical beast, we need to take a different strategy and a different approach in designing and conducting research and supporting health decision makers.

So rather than pursuing questions
such as is it effective or does it work
or which is more effective,
we need to be thinking about deriving
and developing insights and guidance for practice,
such as how does it work, why does it work?
Where, when and for whom,
the realistic evaluation key questions,
but also how can we enhance its effectiveness?
Which again gets back to this issue of adaptability.
We’d have very few degrees of freedom
to enhance the effectiveness of a drug.
We can obviously titrate the dose
and we can prescribe supportive interventions,
but we can’t modify the chemical formulation of the drug.
We can modify the so-called chemical formulation
of a complex health intervention.
So our goal and our task as researchers
is to guide that tailoring and that adaptation.
So we should strive to support decision makers
as they try to answer these questions.
How do I choose an appropriate complex health intervention?
How do I implement or deploy that program
and tailor it to increase its effectiveness?
But also how do I modify or manage the organization?
Oftentimes just as we can improve health outcomes
by changing diet and exercise
and changing the social surroundings of our patients, we can certainly improve outcomes for complex health interventions by modifying the organization. So again, another task for researchers. But back to the key questions. We need to understand and develop insights and provide guidance regarding how, when, why and where do these interventions work and how can we modify them to make them work. So the focus here instead of on impact in simply asking, does intervention A produce a greater impact or outcome than intervention B, we need to instead focus on the black box. We need to understand the mediators and the moderators, the mechanisms of effect. We need to explicitly study adaptation and we need to study context and how to manage context. So again, another point related to the key theme of different types of research, not a focus on measuring impact, but instead to focus on understanding and studying process. So again, rather than thinking about evidence-based practice.
and generating or producing an estimate of effect sizes,

to me, research on complex health interventions should focus on deriving or developing insights and guidance. So it’s insights and guidance rather than evidence in the way that we typically think of evidence. So, getting back to the features or the characteristics of complex health interventions and why they tend to have such weak average effect sizes and such extreme heterogeneity, we know as I argued that, or I would assert that the intervention targets and settings are much more heterogeneous. Communities differ, individuals differ, and the same behavioral approach that we use or the same implementation strategy for one hospital is not likely to be effective or to work in the same way as in another hospital.

Differences in hospital leadership and culture and staffing patterns and resources and so on all mediate and moderate the effects of the intervention. If we think about health psychology and patient behavior change, and one of the topics that we’re studying.
in Kaiser Southern California, which is HPV vaccination,

we know that clinician brief interventions are likely to be effective for some patients and parents who retain respect for their physicians and will follow their advice.

But for other patients, that physician brief intervention can in fact be counterproductive because it reinforces a patient’s or parent’s op priori belief that these vaccines are poison or my physician is sort of an agent of the drug company trying to enhance profits.

So again, lots of heterogeneity in the targets in the settings.

We also know that the underlying pathologies, their etiology, their root causes differ. And again, the vaccine example is a good one. When we’re dealing with low vaccination rates in a set of clinics or hospitals where patients tend to be respectful and responsive to brief interventions, we can suspect that the reason for low rates of adherence don’t relate to patient resistance, but instead, physicians and staff or the systems not necessarily optimizing their activities.

Whereas in other parts of Kaiser Southern California,
we know that the hospitals and the clinics and the organizational policies and the clinicians are doing everything in their power to improve vaccination rates. The reason for low vaccination rates is patient and parent resistance that is tied to their own beliefs. So understanding differences in the root causes of low adherence rates or quality or outcomes or poor patient behavior and recognizing the heterogeneity, again, is important. And that’s one of the reasons for the highly variable effects of interventions because they sometimes address the root causes and solve the problem, but other times the same intervention does not. And then finally, as I’ve said, the interventions themselves tend to be highly variable and irrespective of our efforts to achieve adherence to a manualized intervention and achieve high rates of fidelity, we know that we won’t always see that intervention be delivered the same way across sites. There’s drift over time, there are local adaptations,
but again, more importantly, we shouldn’t try to achieve fidelity because one version of intervention that does match local circumstances in one setting is not likely to be effective and match local circumstances elsewhere. So the adaptability of interventions, their heterogeneity across place, but also across time is a challenge. But we should view it as a strength that we need to embrace and use to our advantage. So some of you who are in my generation or have kids because I believe this game is still sold, will recognize the image in the upper right hand corner. And this is the way that I often think about complex health interventions, that if we were to watch the very beginning of the mouse trap contraption where we drop the marble and then focus only on the very end and whether the trap falls or not, sometimes it will, sometimes it won’t. But that set of empirical observations doesn’t help us at all in improving the performance of this mouse trap. We need to follow every step in the causal chain and understand which part of the contraption
was not built correctly or where things are going wrong.

So again, the question is not, is it effective, but how does it work? And we need to shine our spotlight, our flashlight and our research attention in terms of data collection analysis on the mechanisms of effect.

As I’ve said, we need to, rather than try to ignore adaptations or suppress them, we need to embrace them. We need to study and guide those adaptations. The concept of a manualized intervention, I think for a complex health intervention requires rethinking.

My favorite example here is a story that I believe is accurate of one of the sites in one of the patient self-management studies where the patient self-management program had a highly detailed manualized intervention, including a very clear script for the leader of a patient self-management education group to use in educating members of the group. And the story is that members of the study team were observing a leader deliver the patient self-management program in an African American church in Baltimore.
And the leader of that program was not following the script. She was making up the comments and the educational content as she went along and the research assistants who were observing came up to her afterwards and congratulated her on a successful session, but said, "I noticed that you were deviating from the script. Why is that?

Don’t you know that this is an evidence-based intervention? And if you follow the manual and follow the script to the letter, you’re guaranteed to see positive outcomes, but if you deviate from it, we don’t know what sort of outcomes you will observe.”

And the leader of the church group said, "Well, as you know, your manual and your script was written in Stanford English. We don’t speak Stanford English here. So I was using language and concepts and ideas and examples that I felt were more suitable for my local circumstances. So that’s a somewhat extreme example, of course, but it does point out that a manualized intervention typically was developed from a study.
at a specific point in time in a specific region, in a specific set of settings. And the details of that intervention might in fact be highly optimal for that particular setting, but are not likely to be feasible and certainly not optimal for other settings. So again, we have to rethink the concept of manualized interventions. Similarly, we have to rethink the concept of core components and the term, core components, that concept is used relatively broadly, but oftentimes it talks about the intervention activities, the scripts, the tools, the protocols, the procedures. And again, those tend to be highly idiosyncratic and often optimized and developed by and for a specific set of settings in target audiences. So the alternative to the concept of core components is to specify a set of core functions in a menu of forms. And I'll talk through that in a few minutes. But let me just briefly point out that in the implementation field, and again using guideline adherence as an example, as I said, we often have very complex,
multi-path, mediated and highly moderated sorts of causal pathways.

And a typical multi-component guideline adherence program targeting physicians has to worry about the physician’s attitudes and norms and try to address them as well as their knowledge and skill, as well as their motivation of their activation. And many of these are influenced by, again, multiple mediated pathways, but also some of those causal effects are highly moderated.

We know that a financial incentive to follow the guideline that consists of a $20,000 bonus is likely to be highly effective for a junior family physician with an income in the $150,000 range. But for the senior surgeon with a multimillion dollar income who knows how to practice and doesn’t need the guidelines, that bonus is not likely to have much effect.

So again, highly heterogeneous effects in complex causal pathways that we need to understand.

So let me again, as an aside, briefly present the PCORI method standards for complex health interventions.

I actually won’t talk about these,
but there is both a PCORI methodology report that provides some supportive detail as well as an article that came out in JGIM several months ago that discusses each of these in more detail. But it’s the issue of core functions that I wanted to talk about for a bit. And again, the underlying motivation is the fact that complex interventions can be adapted. They will be adaptive irrespective of our efforts to achieve fidelity, but more importantly they should be adapted. Now I’ll often say adaptation happens. We should embrace it and study it and ultimately guide it. We should not be trying to ignore or suppress it. So the concepts of core functions and forms were introduced by Penelope Hall a good 15 years ago without a whole lot of attention. and follow-up activity in the intervening years until relatively recently where researchers who study complex health interventions, implementation strategies, began to realize that they have a lot of relevance and value. And this is a short list of publications. There actually are many more
just within the last year or two that have applied concepts of core functions and forms.

So forms are the specific detailed activities. So if we think about physical activity as a broad category, walking, running, swimming are all examples of physical activity. And the argument is that our manualized intervention should not specify 20 minutes of walking, but instead should specify physical activity. In the case of patient education, the underlying core function again is to educate patients and their parents. The different forms we can use are listed here. And again, selecting a form that matches the particular features of the target audience is important in increasing fidelity. So we should not be providing a script, a strict script, but instead laying out the goals of the education and providing a menu of different strategies for achieving those goals through different kinds of forms. So I won’t spend a lot of time on this, but encourage those of you interested to both look at the articles as well as these slides in more detail. But the general approach that we advocate is to think about, again, a set of core functions.
and think through all the different kinds of forms that might be available to operationalize those core functions. And then, also think about how to decide which form to select, and that’s the purpose of research. In addition to identifying and describing the core functions, also to provide guidance for the local tailoring, which item from the menu is optimal for particular setting. Now we know that if we think only about core components or activities, we often can go down the route of modifying those forms or components in what appears to be a very minor way, but in fact completely eliminate achievement in one of the core functions. So if you think about drug detailing or academic detailing, that academic detailing interaction conveys information and education and knowledge, but also conveys professional norms. So that’s an activity or a form that actually operationalizes two core functions. Audit and feedback is another example. Audit and feedback conveys information, but it also conveys professional norms and leadership expectations.
And if you’re focused only on the information function,
you could easily decide, rather than convey the audit and feedback information in a departmental meeting, to convey that information via memo. If you do that, you weaken the professional norm function. One of the advantages of an audit and feedback session that’s conducted in the departmental meeting is the physicians have an opportunity to talk about the guideline, the performance metrics or benchmarks and the variation of performance, and ideally help convince each other that maybe there is room for improvement. Whereas if you receive your own performance via a memo, you’re not likely to be influenced in quite the same way.

One final example, that is quality improvement collaboratives where we know that having a multidisciplinary team and ensuring that the collaborative that’s focusing, for example, on high contamination rates in the OR, the QI team needs not only surgeons and nurses, but also members of the housekeeping staff because they collectively will develop
a better understanding of the root causes of those infection rates of contamination than the physicians alone. But the other core function of that multidisciplinary team is the focus on acceptability of the findings and the recommendations. If a QI team consisting only of surgeons comes out and says that the high infection rates are due to the fact that the housekeeping staff are not wiping down the walls properly, you can be sure that the housekeeping staff are going to discount that because they know that they do their job properly and in their minds the problem is that the hand washing practices of the surgeons are deficient. So again, it’s a single component or feature of intervention that operationalizes two different core functions. And understanding those core functions allows us to avoid making mistakes when we modify the intervention activity in a way that we think may be minor, but again can completely eliminate its ability to successfully carry out one of the core functions. So I think I’ve covered each of these already, but let me walk through them quickly.
Again, the way that we typically think of a manualized intervention is highly detailed, is in fact more likely to do harm in many cases than value. Core components should be replaced by core functions.

There are many implications of that rethinking, one of which of course is that a measurement of fidelity is not a measurement of whether you followed the script, but instead whether you successfully operationalized.

I've already talked about the fact that main effect estimates are not very helpful in evidence as we typically think of it. And again, it gets back to the point I've made a couple of times on the need to rethink the purpose of our research.

So let me wrap up with just a few more slides that list some of the kinds of analytic approaches and research approaches that we need to be leveraging in order to, again, shine our flashlight.

These are some of the quantitative methods, qualitative comparative analysis is becoming more popular.

There are also, of course,
a number of qualitative methods as well.
Process evaluation, theory-based evaluation and the continued emergence of illustrations of approaches to adaptation.
Here are some examples of publications that are now quite dated that illustrate and talk about some of these approaches for measuring and taking into account context for examining moderator effects and mediator effects. Here’s some examples of implementation studies that have embraced and studied adaptation rather than suppressing it or ignoring it. Theory-based evaluation, realistic evaluation, again, are relatively new approaches in the qualitative realm to study mechanisms of effect. There’s still a lot of development work to be done, in my view, in these methods to get to the level of transparency and reproducibility that we need. but valuable approaches. And then, if we look outside the typical conventional toolkit to some of the other approaches such as statistical process control that are implemented. I’m sorry, our improvement science colleagues use
as well as others, these represent other approaches. So just to wrap up, when we study complex health interventions, again, we need to begin by identifying the core functions and developing the menu of forms. Ideally, our research would validate our list of core functions or allow us to revise it so that we understand all the functions that need to be included and also provide evidence that guides the local tailoring. It would be documented in a set of adaptation or tailoring algorithms. And the bottom line, again, is a goal of understanding how complex interventions achieve their effects and how to modify them rather than pursuing the simpler question of whether they are effective. So I will stop there and open up for what I hope will be some robust discussion and comments and questions. That was a really kind of interesting and important talk at sort of the cutting edge of where implementation science is today, and with a lot of information packed in and concepts and things like that.
for us to think about and potentially absorb into our own work. So maybe I might start with this first question which is...

Actually, I’ll even integrate something else that probably is worth both of us mentioning, which is that Brian is actually the co-founder and director of the Multilevel Training Institute that’s offered every year in collaboration with NCI.

And Raul Hernandez-Ramirez, who’s one of our CMIPS primary faculty is a graduate of that institute.

And I’m actually one of the instructors teaching about the analysis of multilevel interventions.

But the question is, my thought and I think a lot of us out here think that the reason, sort of the opposite of what you said, that the reason we like multilevel interventions is because it seemed like the medical model of isolating one component, like what we would’ve said before in the past and maybe right now you might say function and studying it and holding everything else constant, these sorts of implementation studies have been disappointing.

And so, the thought was that actually,
First of all, it’s totally unrealistic in real life. You don’t just have one thing. All of these public health interventions are complex, whether we choose to study them or not. And so, the idea then evolved to that it might make sense to intervene on an entire, sometimes we might say package of components, which now you’re kind of redefining as package of forms maybe. Or maybe it’s package of functions and then the forms are the specific ways that functions are implemented. If I caught all of that very quickly, I think I did, and I think we’re somewhat familiar with this idea in our center as well. So that would strengthen the ability to see an impactful intervention and allow us to translate into practice evidence-based interventions as a whole. But now you’re saying that because of the adaptations and the variability and the heterogeneity, actually these kinds of approaches also are giving weak results. So I’m just wondering if you can comment on that.
Sure.

No, I would concur with everything that you’ve said and I think the main point is that, it’s really that the argument that one size doesn’t fit all. But to begin with, I do agree that, for most of these kinds of problems, the barriers are multi-component and multi-level, and we definitely need multi-level, multi-component complex health interventions.

The simple example goes back to the studies in the 1970s and 1980s of CME as a method for improving physician practices. And the dominant finding from that body of research was physician knowledge and education changed and sometimes physician attitudes changed, but practices didn’t change at all because the practices are held in place by multiple barriers. And if you don’t provide the equipment or the staff support or the time as I said, work on the patient resistance, no amount of educating physicians is likely to lead to the outcomes that we want. And in the causal diagram, the diag that I showed again is an example of that.
If we focus on only one of those causal pathways, believe the other's untouched. So the point though is that we absolutely do need multi-component, often multi-level interventions. The issue though is the need to adapt and tailor them and the same mix of components or the same mix of forms and activities that is highly effective in one setting is not likely to be effective elsewhere. And when we take a complex health intervention and we try to scale it and spread it, or we move from efficacy research to effectiveness research, we are often disappointed in the findings. And that is because of the erroneous belief that one size fits all and that an so-called evidence-based practice is going to be evidence-based and robust and effective across multiple settings. It has to be tailored and we as researchers have to guide that tailoring.

I have lots of questions, but I don’t wanna hog the time. So we have lots of people on here. Do others have any questions they’d like to ask?
I think you can simply unmute yourself and ask your question.

Sure, thank you for the wonderful talk.

I am an investigator working a lot in low and middle income countries and I was interested at the beginning of your talk when you were using the term impact. I think it’s often used as a synonym for effectiveness.

But I think sometimes with public health or even population health interventions, we’re thinking about numbers of people that can be served. And so, I guess that’s sort of a very general question, just curious if you’ve encountered that.

But maybe the more specific question related to your research would be, if volume then is kind of really important if you think about communicable diseases because there may be indirect benefits for addressing that.

And so, I guess that’s sort of a very general question, just curious if you’ve encountered that.

But maybe the more specific question related to your research would be, if volume then is kind of really important if you think about communicable diseases because there may be indirect benefits for addressing that.

Are we looking at sort of the contextual factors related to understanding the fidelity?

Related to how many people are served maybe when we pilot an intervention, but when we think about taking it to scale,
what are some of the considerations about kind of understanding the impact of volume on fidelity and adaptation?

Thank you so much.

Yeah, so first of all, I'm a strong fan of the REAM framework and I think to think about the different dimensions of impact and how they relate to one another is critically important,

that we focus only on effectiveness and ignore the other issues. The ultimate societal impact that we are seeking will not be seen. And I think the heterogeneity may apply differently across different outcomes may apply differently across different outcomes.

in the kind of approach that we need in order to engage a high volume and a high proportion of the target audience versus the approach that we need to use to ensure that the intervention is effective across a large proportion of the target audience which does have its own heterogeneity in subgroups.

Those may be different.

And this may or may not be an answer, but at least this is the way that I would think about it.

the vast majority if not all of these studies, we need to begin with REAM
and explicitly think about all the different dimensions that contribute to the overall impact and outcomes.

And then, we need to recognize and anticipate and explicitly address the heterogeneity across all of those different dimensions and know that as we again scale up and spread and adapt and tailor interventions from one setting to another, that tailoring and adaptations are likely to be needed in different ways and different facets of the intervention in order to ensure that we maximize outcomes and success across all the REAM dimensions.

So again, it’s just a very different way of thinking about research and interventions compared to the typical evidence-based practice that we develop an intervention, we can describe it very simply and we can deploy it anywhere and we will see the same kinds of results. And that’s the case, both because we can’t deploy the interventions as we were designed elsewhere, and that’s especially true of course. And we take US-designed interventions,
try to deploy them in low resource settings within the US and elsewhere, but even if we could deploy them in the same way and implement them, the effectiveness is likely to vary considerably.

Thanks so much, that’s really interesting.

Okay, thank you.

That was a good answer.

Luke, do you have a follow-up question?

Yeah, I mean I would be curious

maybe just to think a little bit about operationalizing some of these things.

Obviously, you work with one of the premier organizations about thinking about how to answer these questions.

In terms of Kaiser, very large health system, many different units, however you’d wanna define those, whether those are sites or providers and so on so forth.

I know I’m just curious about how you think about integrating quantitative and qualitative data with respect to certain types of problems of this nature.

Maybe if there’s any examples that you might be able to share from your work in Kaiser.

So I think that integration is critical.
And this actually relates to the point that Donna raised about implementation science and improvement science. So the improvement science folks do accept and anticipate and address the heterogeneity and the whole issue of rapid cycle implementation where you do something and you sort of see what the impacts are and then you refine it. That’s a form of tailoring. So I think they do recognize the heterogeneity and that’s one way of dealing with it. But I think that rapid cycle evaluation, any kind of evaluation, and understanding the mechanisms of effect we can only learn so much through mediation analysis and other quantitative methods. And if our goal is ultimately to understand how the world works and to understand causal pathways and causal relationships, we do have to mix the quantitative and qualitative. And I think all of our projects at Kaiser that are embedded research projects that are a synthesis of quality improvement activity and approaches where we’re trying to improve things in the near term.
and implementation science and scientific approaches

where we’re trying to generate scientific knowledge,

I think we almost invariably combine quantitative and qualitative as a way of, again, trying to understand how the world works,

try to design the intervention, deploy it, evaluate it early and often in order to refine it and tailor it

and ultimately generate the summative evaluation findings as well.

And I think we all need more guidance and more examples of how this is done because there are a lot of moving parts and a lot of different factors to think of,

not only the REAM multiple dimensions, but the different kinds of data and the different ways of understanding and tracking the mechanisms of effect and the intermediate or proximal outcomes in addition to the distal outcomes.

So lots of challenges, but lots of opportunity for innovation and creativity.

Anyone else that wants to ask you questions?

While we’re waiting to see, I have another question.

So you’re probably familiar, Brian, with Linda Collins’ MOST approach
to developing and assessing or testing interventions

and her focus is also with complex multilevel interventions

where there are the three phases.

But in the third phase,

the third phase is kind of a traditional,

fixed.

You call it manualized,

it doesn’t necessarily have to just be a manual,

it could be other things,

but fixed set of components at certain levels

and that’s kind of tested in a standard RCT-type approach.

And I’m wondering if you think

that the MOST design is useful in certain settings

or do you think that maybe that kind of approach

has kind of seen its better days

because of the fact that it doesn’t take into account

sort of the contextual aspects and the need for adaptation.

But I know among other circles,

the MOST design is very popular

and even we’ve had training in our center in MOST

and I’m currently discussing

a possible grant application with some investigators here

who’d like to use MOST.
So I’m just wondering what your thinking is about that.

Yeah, so I think that approach I think is highly valuable.

As our standard RCTs, as long as we recognize that they need to be augmented with additional kinds of data collection analysis activities that try to understand the mechanisms of effect.

But certainly and when I say that RCTs and a focus on impact and outcomes are not what we should be doing, that’s probably too extreme. I think we obviously need to measure outcomes and we need to use traditional quantitative methods, but we need to augment them and have an equal, in some cases greater focus, on the mechanisms of effect.

And certainly, to try to get a handle on some of the heterogeneity and some of the factors using MOST and other approaches that Linda and others have developed and advocated I think is quite important and valuable. I just think that they’re incomplete and we need to make sure we, again, have the accompanying process evaluation.
1206 00:54:19.680 --> 00:54:21.753 and mediation analysis and others.
1207 00:54:23.010 --> 00:54:23.973 <v ->That makes sense.</v>
1208 00:54:26.220 --> 00:54:27.183 Anyone else?
1209 00:54:28.338 --> 00:54:30.663 Okay, so we have a question in the chat.
1210 00:54:33.180 --> 00:54:34.710 What are some other frameworks
1211 00:54:34.710 --> 00:54:36.930 you would consider reviewing
1212 00:54:36.930 --> 00:54:39.720 when considering a multi-component and
multi-level study?
1213 00:54:39.720 --> 00:54:44.580 So presumably this question is other than
REAM.
1214 00:54:44.580 --> 00:54:45.570 <v ->Sure.</v> <v ->I'm guessing</v>
1215 00:54:45.570 --> 00:54:48.180 and if the person who asked it would like to
elaborate
1216 00:54:48.180 --> 00:54:50.250 or if this is totally clear to you,
1217 00:54:50.250 --> 00:54:51.153 Brian. <v ->Yeah,</v>
1218 00:54:51.153 --> 00:54:52.530 let me give it a quick shot
1219 00:54:52.530 --> 00:54:54.990 and then you can elaborate if I'm missing a
point.
1220 00:54:54.990 --> 00:54:57.630 But I think that CFIR of course,
1221 00:54:57.630 --> 00:55:00.520 which continues to be the go-to high level
framework
1222 00:55:01.650 --> 00:55:03.090 is a way of identifying
1223 00:55:03.090 --> 00:55:05.370 all the different categories of factors.
1224 00:55:05.370 --> 00:55:08.400 So multi-component, multi-level interven-
tions
1225 00:55:08.400 --> 00:55:13.050 address multiple sources of barriers and fac-
tors
1226 00:55:13.050 --> 00:55:15.797 that influence the outcomes that we’re inter-
ested in.
1227 00:55:15.797 --> 00:55:18.990 And CFIR is, in my mind, the best organizing
framework
1228 00:55:18.990 --> 00:55:22.080 that gives us that sort of 50,000 foot level.
1229 00:55:22.080 --> 00:55:23.490 Then when we’ve identified
1230 00:55:23.490 --> 00:55:26.790 the different categories of factors,
we may need to bring in accompanying frameworks.

So, behavior change wheel, theoretical domains framework is quite useful in identifying some of the physician-level behavioral factors.

So I think it does depend on what CFIR tells us. If many of the barriers and influences are regulatory or community, then we may need to bring in political science frameworks or other bodies of theory.

But we start with CFIR to get sort of the lay of land and then we identify frameworks for subsets of factors.

And to me, REAM and I think to most of us is more of an evaluation framework.

It doesn’t really give us the theory, but it directs our attention to the different categories of outcomes that we need to take into account and measure and attempt to improve.

Great, that was a very clear answer.

Thank you so much. And we’re at time, so I think we’ll just thank our speaker.

Hopefully we’ll see him again in person sometime in the near future.
and we look forward to some of our one-on-one meetings today.

and in a few of the subsequent days.

So thank you so much, Dr. Mittman.

Okay, thank you all. Bye everybody.

Okay, bye-bye.