Research Questions and Design Considerations: Effectiveness to Implementation

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Goals for the session

- Discuss some *Whens* and *Hows* of getting into D&I research
- Present older and newer conceptions of the "research pipeline"
  - Efficacy… Effectiveness… D&I
  - We are moving away from "pass the baton" to something more integrated and coordinated
  - Designing for D&I: Thinking ahead for implementation and sustainability
- Discuss the concept of "hybrid designs" which combine elements of clinical/preventive effectiveness and implementation research
  - Type 1: Explore *Implementabilty* of an intervention while we are testing its effectiveness
  - Type 1: Learn what is needed to support implementation in the "real world" (towards implementation strategies)
  - Type 2: Test implementation strategies *during* effectiveness trials (simultaneous look at both)
  - Type 3: Test implementation strategies while also documenting clinical/prevention intervention outcomes (evaluating them as they relate to uptake and fidelity)
- Present examples of hybrid design studies
- Questions

Who am I?

- Sociologist by training (1996)
- Most of the last 20 years in a Department of Psychiatry
  - Last 2 years also in a Department of Pharmacy Practice
- Began doing implementation research in the VA in 1998
  - Quality Enhancement Research Initiative (QUERI)
  - Implement EBPs while studying how best to implement
- NIDA, NIMH, NIDDK, NIMHD implementation research grants
  - Testing implementation strategies in support of adoption of EBPs
- Focus as well on methods and design in implementation research

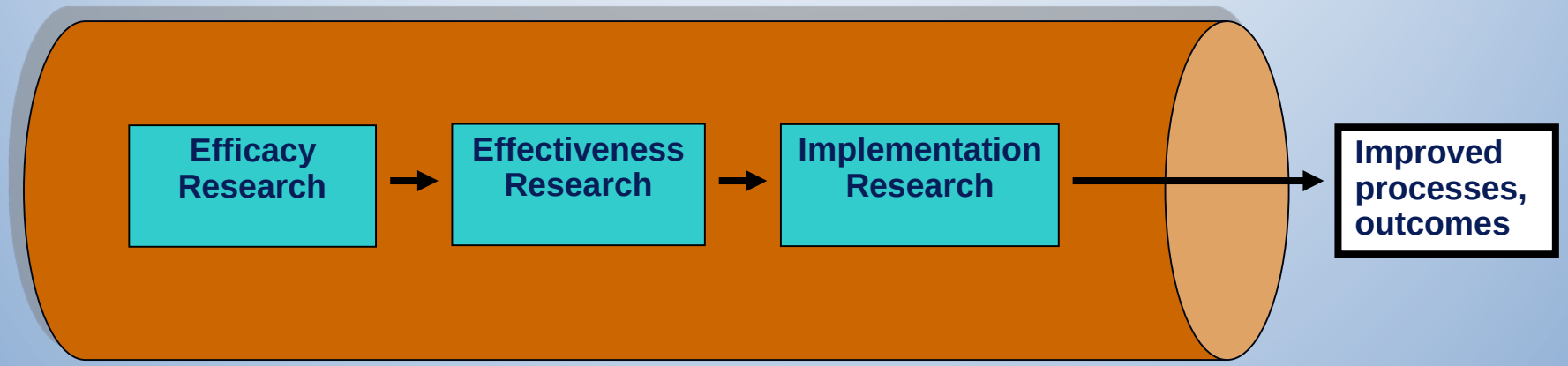
Who are you?

(Based on pre-conference survey and my own guessing…)

- People who have done mostly “clinical research” who are curious about “implementation research”
- People who would like to get their effective clinical interventions into widespread use
- People who want to support implementation of best practices in the real world right now
- People already doing implementation research who want to learn more, take it further, or get a refresher
- People who feel their science is too orderly and boring
- Other?

Traditional Research Pipeline

(when do we do implementation research?)



- "Finish" efficacy research
- "Finish" effectiveness research
- *Then* start implementation research…

Efficacy

Efficacy trial research question(s)

- Does intervention beat control under ideal conditions?
- Is this idea worth pursuing any further?

Efficacy trial design considerations

- Highly controlled conditions
- Highly trained researchers under tight control
- Highly selected sample
- Favors internal validity

Effectiveness

Effectiveness trial key research questions*

- Does intervention beat control under more routine conditions?
- How do interventions compare to each other (and under which circumstances is one better than the other)?
- Can we afford this intervention? Which one is more cost effective?

Effectiveness trial design considerations

- Seek to replicate general practice conditions
- Broader and more complex sample
- Favors external validity (generalizability)

*I'll *revisit* these questions shortly…

D & I

D&I key research questions*

- What barriers and facilitators to implementation exist?
- What implementation strategies are indicated?
- Does implementation intervention/strategy beat control?

D&I research design considerations/options

- Observational “Diagnostic” study of implementation context
- Pilot test of an implementation strategy
- Implementation trial of 1 or more strategies
- Favor internal or external validity depending on evidence, context…

*Focusing here for now on questions and designs associated with preparing for and then testing implementation strategies in support of specific interventions… so ignoring for now, for example, large observational studies of uptake initiated by policy, mandates, etc.)

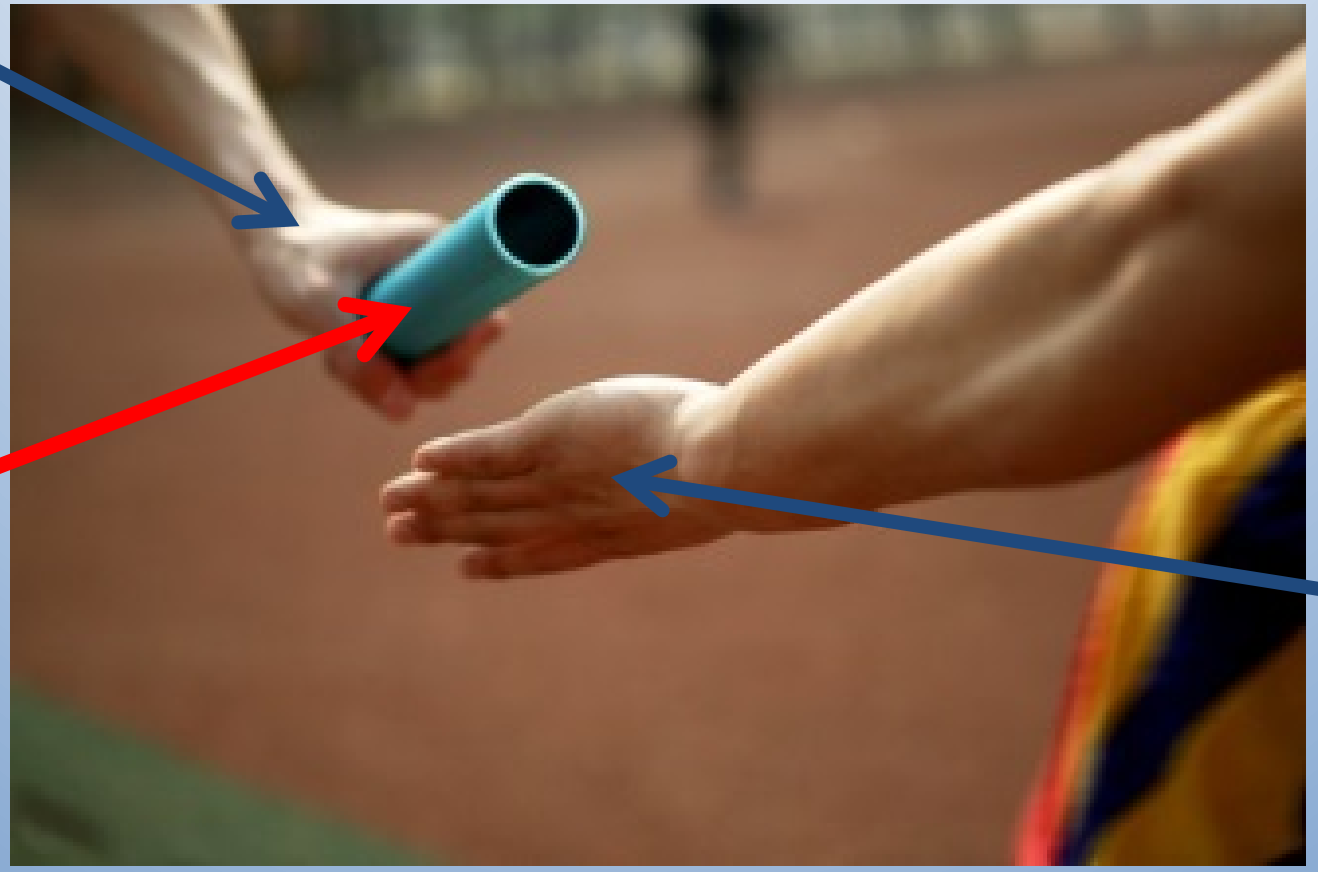
Relay race analogy: “Here… GO! GO! GO!”

“Here… GO! GO! GO!”

Intervention *“ready for”* dissemination and implementation

“Here… GO! GO! GO!”

“Clinical” Researcher



Intervention “*ready for*” dissemination and implementation

“Implementation” Researcher

Early VA QUERI Experience: early 2000's

- QUERI RFA for implementation research
  - Mandated proof of "strong evidence base" for intervention
    - Adaptation for context was OK, but not departing from "core EBPs"
      - No real guidance at this point on *how* to do this…
  - No expectation to collect effectiveness outcomes
- Reflected (and reified) traditional pipeline thinking
- Over time, the RFA was revised to reflect newer IS thinking and realities of VA
  - E.g., VA mandates for practices with "weak" evidence base and wanting research on how best to implement them ("um, we're gonna need a new RFA")

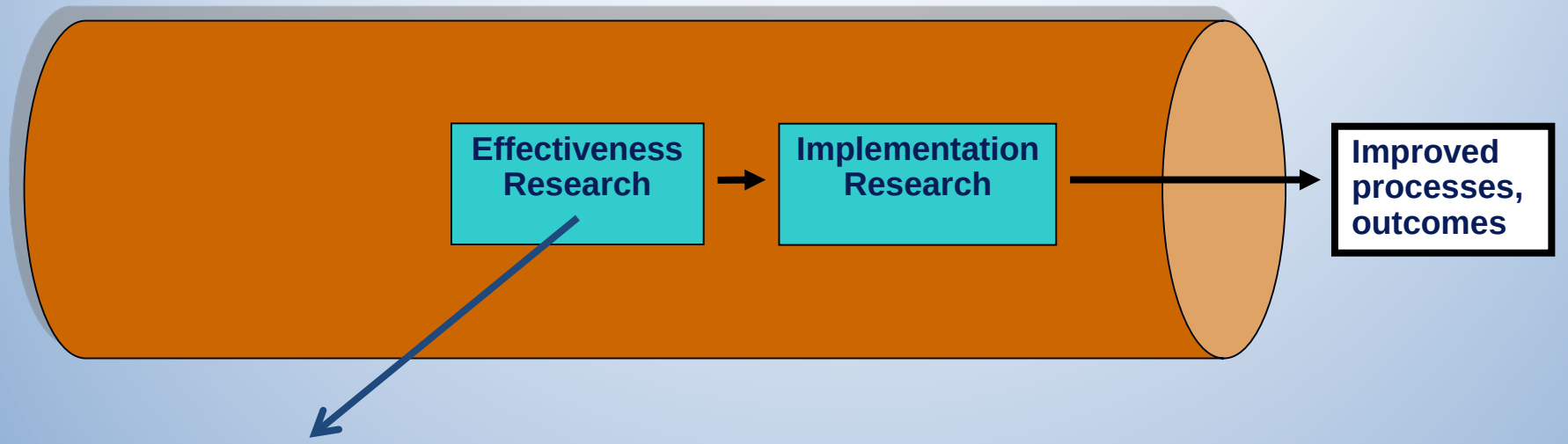
What is it like now?

- **Most agree that efficacy, effectiveness, and implementation research shouldn't be so separate and sequential, and doing so overlooks complexity, leads to some wrong answers, and slows us down…**
  - **Wells (1999) and Glasgow et al (2003) recommend principles/approaches for "closing the gap" between efficacy and effectiveness research**
  - **Green (2006) argued that most of our EBPs are not built on practice-based evidence**
  - **Curran et al (2012) propose "hybrid designs" to combine elements of effectiveness and implementation research**
  - **Brownson et al (2013), Owen et al (2012) offer/summarize principles for "designing [interventions] for dissemination"**
  - **Chambers et al (2013) "Dynamic Sustainability Framework" challenges assumptions of "voltage drop" and "program drift"**
  - **Wiltsey-Stirman et al (2013) propose a framework for modifications and adaptations of EBPs**
  - **Chambers and Norton (2016) argue for a focus on science of adaptation and purposive collection of data on outcomes associated with adaptation *(embrace that we need to fit interventions to settings… a lot)***
- **While I cannot say that the pipeline has been radically altered as of yet, looking around this room shows us that many people are interested in these ideas and want to get in the D&I research enterprise!**

What to do now?

- I will focus most of the rest of the talk on describing hybrid effectiveness-implementation designs
- But, I first want to "plug" and briefly describe the related concept of "designing for dissemination/implementation"
  - Could be a useful initial step into the D&I space for persons who have spent most of their time doing effectiveness research
    - Ross leads a breakout session on this topic at 11:35am today!
  - Bring D&I thinking and planning into what you are already doing
  - This extends the scope of research questions for effectiveness!
  - Also, consider "Re-design" for D&I if your are considering taking an EBP out of its comfort zone…
    - E.g., new type of provider, different setting, different culture

Design for Dissemination-Implementation



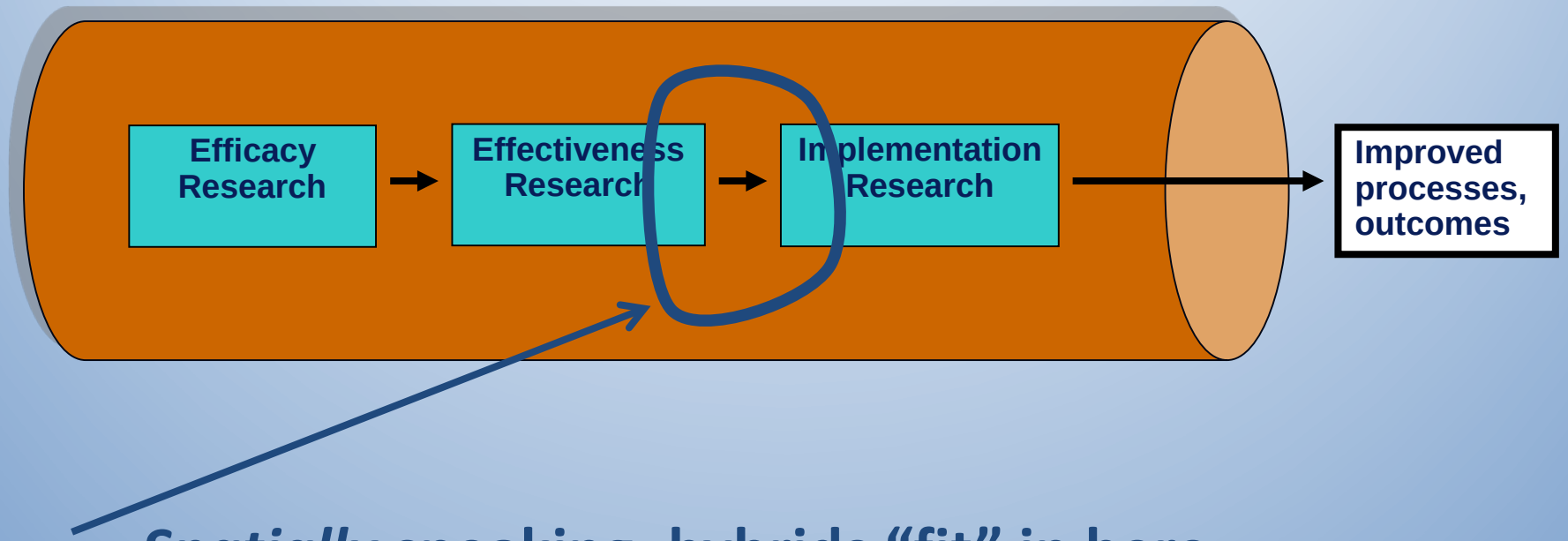
- Build for *implementability* as early as you can
  - -- Or, start there in a new effort to translate a "proven" EBP
- "End-user" input and partnership before trial (PCORI anyone?)
  - -- Better interventions *and* increased buy-in
- Use of *implementation frameworks* in design of components
  - -- See CFIR framework, construct 1 *(trialability, adaptability, complexity, cost…)*
- Focus on service delivery issues– staffing, technology, dose
  - -- What are the hard-to-reach places? Look at underserved locations

Effectiveness research questions revisited for D4D&I

Effectiveness trial research questions

- Does intervention beat control under more routine conditions?
- How do interventions compare to each other (and under which circumstances is one better than the other)?
- Can we afford this intervention? Which one is more cost effective?
- What components can be adaptable for multiple settings?
- What different staffing models can be used to deliver the intervention?
- What technologies could be used to speed uptake, support implementation into new settings?
- How would the intervention need to be specified/changed to be implemented in low resource conditions?
- *And more…*

OK, now on to hybrid designs…



Spatially speaking, hybrids "fit" in here…

Why Hybrid Designs?

- The speed of moving research findings into routine adoption can be improved by considering *hybrid designs* that combine elements of effectiveness and implementation research
- Don't wait for "perfect" effectiveness data before moving to implementation research
- We can "backfill" effectiveness data while we test implementation strategies
- How do clinical/prevention outcomes relate to level of adoption and rate of fidelity?
  - How will we know this without data from "both sides"?

Effectiveness-implementation Hybrid Designs

Combining Elements of Clinical Effectiveness and Implementation Research to Enhance Public Health Impact

Geoffrey M. Curran, PhD, Mark Bauer, MD,† Brian Mittman, PhD,‡ Jeffrey M. Pyne, MD,* and Cheryl Stetler, PhD‡*

Objectives: This study proposes methods for blending design components of clinical effectiveness and implementation research. Such blending can provide benefits over pursuing these lines of research independently; for example, more rapid translational gains, more effective implementation strategies, and more useful information for decision makers. This study proposes a "hybrid effectiveness-implementation" typology, describes a rationale for their use, outlines the design decisions that must be faced, and provides several real-world examples.

Results: An effectiveness-implementation hybrid design is one that takes a dual focus a priori in assessing clinical effectiveness and implementation. We propose 3 hybrid types: (1) testing effects of a clinical intervention on relevant outcomes while observing and gathering information on implementation; (2) dual testing of clinical and implementation interventions/strategies; and (3) testing of an

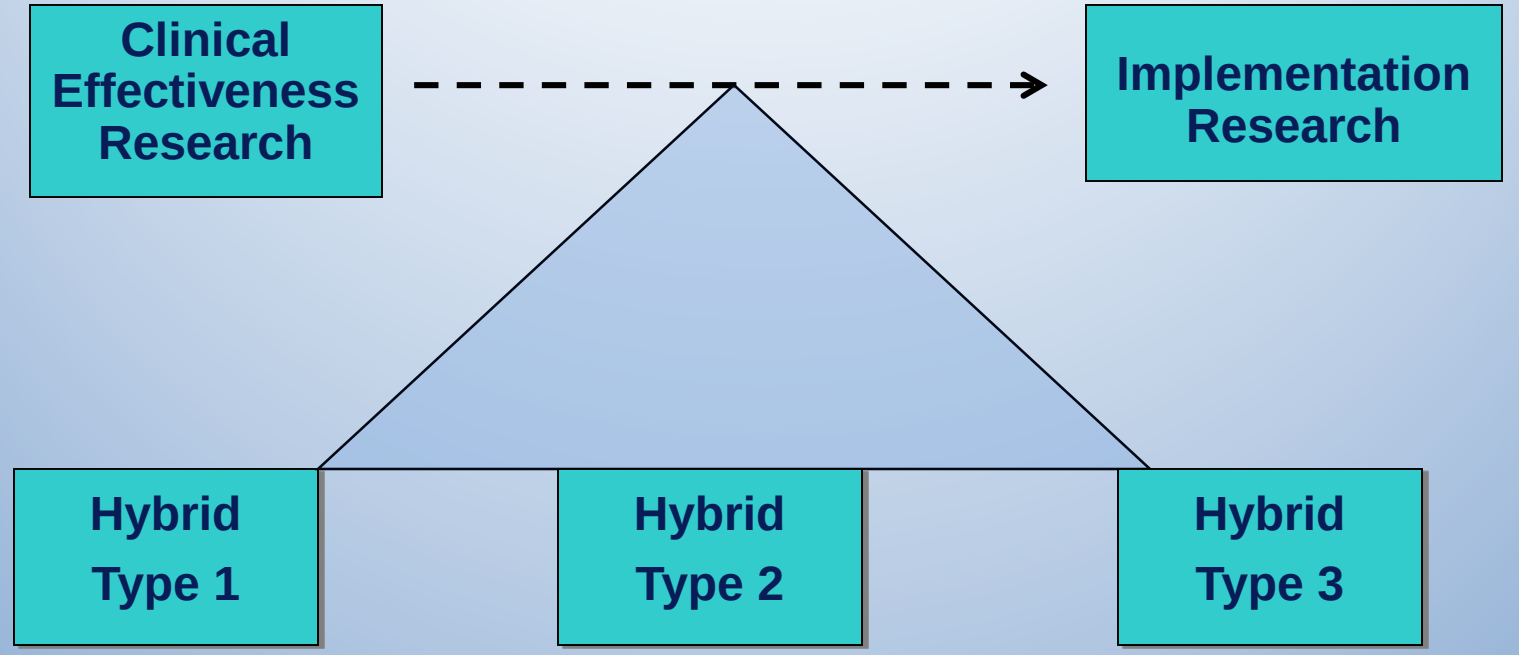
Much has been written about the nature of health care science-to-service gaps both in general[1–3] and relative specifically to health promotion[4] and numerous medical specialties.[5–9] Thus far, the literature indicates that gaps between research and practice can result from multiple factors, including educational/knowledge deficiencies and/or disagreements,[10,11] time constraints for practitioners,[12,13] lack of decision support tools and feedback mechanisms,[13] poorly aligned incentives,[14] and a host of other organizational climate and cultural factors.[2,15,16]

In addition to these provider-level and systems-level barriers to rapid translation, Glasgow et al[4] and others[17–20] argue that the time lag between research discovery and routine uptake is also inflated by the dominant developmental approach; that is, one that encourages delimited, step-wise progressions of research through clinical efficacy research, then

Some terms before we cover the types

- We use the term **intervention** to refer to the *clinical/prevention practice* we have an interest in exploring
- We use the term **strategy** to refer to the *implementation-support activities/tools* we have an interest in exploring
- Both are *interventions* whose *effectiveness* we are interested in, but in the hybrid design context it can get confusing…
- We usually use the term **effectiveness** only when referring to the clinical outcomes.
- We often use the term **impact** to describe the implementation outcomes.

Types of Hybrids



Hybrid Type 1: test clinical/prevention intervention, observe/gather information on implementation

Hybrid Type 2: test clinical/prevention intervention, test/study implementation strategy

Hybrid Type 3: test implementation strategies, observe/ gather information on clinical/prevention outcomes

Research aims by hybrid types

Study Characteristic	Hybrid Type I	Hybrid Type II	Hybrid Type III
Research Aims	***Primary Aim:*** Determine effectiveness of an intervention ***Secondary Aim:*** Better understand context for implementation	***Primary Aim*:** Determine effectiveness of an intervention ***Co-Primary* Aim*:** Determine feasibility and/or (potential) impact of an implementation strategy *or “secondary”…	***Primary Aim*:** Determine impact of an implementation strategy ***Secondary Aim*:** Assess clinical outcomes associated with implementation

Hybrid Type 1 Designs

Definition:

- **Test clinical/prevention intervention and explore implementation-related factors *(80%/20%...)***

Description:

- **Conventional effectiveness study "plus":**
  - **Describe implementation experience (worked/didn't; barriers/facilitators)**
  - **Interview/survey/observe participants regarding implementation experience**
  - **What is needed to support implementation in the real world?**

Indications (circa 2012):

- **Clinical/prevention effectiveness evidence remains limited, so intensive focus on implementation might be premature…BUT**
- **Effectiveness study conditions offer ideal opportunity to explore implementation issues, plan implementation strategies for next stage**

Design Characteristics

- **The original definition of a type 1 emphasized secondary aims/questions and exploratory data collection and analysis preparatory to implementation activity**
- **Current review we are doing indicates that this is the common model of type 1**
- **However, some type 1 studies are doing more intense focus on "implementability"**
  - **E.g., adapting intervention for better presumed uptake before the trial and measuring "implementation potential" as a more equal/central element (if not explicitly measuring uptake and fidelity *[which would be more a type 2…]*)**

Example 1: CALM study

- **Curran et al., 2012, *Implementation Science***
- **Large effectiveness trial of anxiety intervention in primary care**
  - 4 cities, 17 clinics, 1004 patients
  - Care managers using software tool with patients to navigate Tx manual
  - Care managers were local nurses/social workers already working in the clinics
  - Intervention was designed with "future implementation in mind"
- **Qualitative process evaluation alongside trial**
  - 47 interviews with providers, nurses, front office, and anxiety care managers
  - Most interviews done on the phone
  - Interview guide informed by an implementation framework (PARIHS)
    - (these days, that link needs to be very explicit…)

CALM study process evaluation

- **Interview Guide**
  1. What worked and what didn't work?
  2. How did CALM operate in your clinic? Adaptations?
  3. How did CALM affect workload, burden, and space?
  4. How was CALM received by you and others in your site and how did that change over time?
  5. Were there "champions" or "opinion leaders" for CALM and if so, what happened with them?
  6. How did the communication between the care manager, the external psychiatrist, and local PCPs work?
  7. What outcomes are/were you seeing?
  8. What changes should be made to CALM?
  9. What are the prospects for CALM being sustained in your clinic and why/why not?

Example 2: Talking Health study

- **Zoellner et al., 2014, *Contemp Clin Trials***
  - Patient-level RCT of intervention to reduce consumption of sugar-sweetened beverages
  - RE-AIM framework guided evaluation
    - Process evaluation: Reach, implementation
    - Health behaviors evaluation: Effectiveness, maintenance
    - Interviews assessed perceptions of intervention components (small group sessions, personal action plans, drink diaries/exercise logs, teach back call, IVR calls, resources provided)
    - Adoption not measured: research staff delivered intervention

Hybrid Type 2 Designs

Definition:

- **Test clinical/prevention intervention and test/study implementation strategy *(50/50? 60/40? 72/28?)***

Description:

- **Dual-focus study:**
  - **Clinical/Prevention Effectiveness trial within either:**
    - **Implementation trial (so, a comparative effectiveness factorial type design)**
    - **Pilot (non-randomized) study of implementation strategy**

Indications (circa 2012):

- **Clinical/prevention effectiveness data available, though perhaps not for context/population of interest for this trial**
- **Data on barriers and facilitators to implementation available**
- **Implementation momentum in terms of system/policy demands?**

Design Characteristics

- **The original definition of a type 2 described possibilities of dual focused, dual randomized, factorial designs & randomized effectiveness trials nested in pilots of an implementation strategy**
  - **Majority of currently published Type 2s are the latter**
  - **Dual randomized designs used non-complex interventions/strats**
- **When looking at the aims or hypotheses of existing studies, most have primary focus on *intervention outcomes***

Design Characteristics

- **Important to have an explicitly described implementation strategy that is distinct from the intervention**
- **Measure adoption, fidelity…**
- **Important to be clear about intervention components versus implementation strategy components**
  - This isn't always easy to decide
  - E.g., *delivery format…*
    - *Is delivering the intervention over the telephone an intervention component or an implementation strategy?*

Example: Brief CBT with pilot impl strat

- **Cully et al., 2012, *Implementation Science***
  - Clinical trial of brief cognitive behavioral therapy in treating depression and anxiety
  - Patient randomization only; Pilot study of implementation strategy (online training, audit and feedback, facilitation)
  - Intent-to-treat analysis of clinical outcomes
  - Feasibility, acceptability, and "preliminary effectiveness" data collected on implementation strategy
    - Measured knowledge acquisition, fidelity to model
    - Qualitative data on implementability, time spent, etc.
  - Measured sustainability of provision of brief CBT after trial
  - Preparatory to implementation trial of strategy

Example 2: HiTIDES study

- Pyne et al., 2009; Curran et al., 2011
- Patient randomized trial of collaborative care for depression in 3 HIV clinics
- Pilot test of implementation strategies
  - EBQI
  - External facilitation/coaching, audit and feedback, problem solving, etc
- FORMATIVE evaluation before, during, and after implementation

What is EBQI?

- Rubenstien et al., 2006; 2014
- Partnership process to adapt intervention and specify implementation strategy *(pre-implementation)*
  - Local clinicians suggest intervention adaptations for their context and guide/approve implementation strategy selection
  - Clinical experts say go/no go on adaptations
  - Implementation experts recommend implementation strategies
  - Leaders/administrators lead and support
- Builds trust, understanding
- Maintain "evidence-based factors" while locally adapting
- Other similar models out there (see Powell et al., 2015; Stirman et al., 2013)

What is Formative Evaluation (FE)?

- Build the plane while we fly it! (Stetler et al., 2006)
- The first iteration of the adapted intervention and (especially) implementation strategy likely not optimal
- Adapt intervention and implementation strategy based on routine data collection on outcomes, feasibility, satisfaction, recommendations
  - Implementation strategy usually gets adapted more; good time for it as this is a pilot study of the strategy…
- BEGIN with "diagnostic" needs assessment, barriers/facilitators, preferences, etc. before attempting implementation (This bit can also be the last aim of a Type 1…!)

Type 3…?

- We're not really going over this type today…
- BUT
  - These designs primarily compare implementation strategies
  - Randomization usually occurs at provider/clinic/system level
  - Main outcomes are adoption, fidelity, sustainability
  - Secondary outcomes are clinical outcomes (non-randomized…)
  - Works best with "easy" to access clinical outcomes
    - Not so great for MH outcomes that usually require primary data collection
- I am happy to provide more info on these another time…

New thinking on hybrid designs

- New thinking on “lack of fixed-ness” of interventions contributed to changing views on when and why of hybrid-type designs
- **Hybrid type 1** as “default” for effectiveness research?
  - Certainly for comparative effectiveness research
- We expect dual-randomized **type 2** trials to be rare
  - However, stepped-wedge designs (randomization to same strategy by time) can work well with Type 2 and we are seeing these more
- Hybrid **type 3** implementation trials… seek balance
  - When wouldn’t we want clinical/prevention outcomes data?
  - Balance of evidence(s), resources, time, expertise

Challenges for later…

- If we use Formative Evaluation during a study and revise the intervention and/or implementation strategy, how do we know when to measure outcomes? What about power?
- What do we do when we expect sites to need different implementation strategies to succeed?
  - Adaptive designs are fun…!
- When do we start to care about how much implementation strategies cost?

Resources

- http://cancercontrol.cancer.gov/IS/
  - Great website for introductory and advanced help
  - Seminars, tool, publications, grant examples
  - Wonderful team of consultants (David Chambers is lead)
- http://impsci.tracs.unc.edu/
  - "Get informed, get funded, get published…"
  - Lots of grant examples, trainings, tools, theory stuff
- http://www.societyforimplementationresearchcollaboration.org/
  - Measures resources, working groups, conference
- *Implementation Science* journal
  - Just start reading…
  - Searchable by key word

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