

Case Study: METRICAL

Music & MEemory: A Pragmatic TRIal for Nursing Home Residents with ALzheimer's Disease

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Acknowledgements

- METRICAL: Music & MEmory: A Pragmatic TRIal for Nursing Home Residents with ALzheimer's Disease
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- The views and opinions expressed in this presentation are those of the presenter and do not necessarily reflect the official policy or position of the funder.

Background

- Drugs used to manage agitated behaviors in nursing home residents with dementia increase the risk of falls and death
- Reminiscence therapies may reduce agitated behaviors resulting from boredom, social isolation, or sensory deprivation by eliciting long-stored memories
- In Music & Memory, the music a resident preferred when s/he was young is put on a personalized music device (mp3 player) and played at early signs of agitation
- Effectiveness evidence for Music & Memory and other nonpharmacological approaches for managing behaviors is lacking

Research Study

- Music & MEemory: A Pragmatic TRIal for Nursing Home Residents with ALzheimer's Disease (METRIcAL) – R21 / R33 Mechanism
- The purpose of the trial is to assess the real-world effectiveness of a personalized music intervention for management of agitated behaviors in nursing home residents with dementia.
- Examine factors associated with variation in providers' adherence to the implementation of intervention.

Hybrid Design? (A Disclaimer)

- This session focuses on effectiveness-implementation hybrid designs
- This trial was not designed using the hybrid definitions presented, but, rather, using the NIH Stage Model for Behavioral Intervention Development
- However, the trial meets many of the criteria of a pilot hybrid type 2

Landes SJ, McBain SA, Curran GM. An introduction to effectiveness-implementation hybrid designs. *Psychiatry Res.* 2019 Oct;280:112513.

Outline

- Study overview
- Highlight key design features
- Discuss points of alignment with hybrid type 2 trial

METRICAL

- Conducting two cluster-randomized, parallel trials evaluating the effectiveness of a personalized music intervention for agitated behaviors in nursing home residents with dementia
- Each trial enrolled 54 nursing homes (27 treatment, 27 control); ~800 residents per trial
- Both trials have the same primary and secondary outcomes
- Both trials have the same implementation evaluation metrics
- However, the intervention differs between the two trials

Original Trial Design

- Stepped-wedge design with primary outcome measured in the first year in a subset of facilities (parallel design)

	Period 1 (June, 2019 - January, 2020)	Period 2 (April, 2020 - November, 2020)	Period 3 (February 2021 - September, 2021)
Sequence 1 (27 Nursing Homes)	Intervention*† (405 residents)	Intervention* (405 residents)	Intervention* (405 residents)
Sequence 2 (27 Nursing Homes)	Control*† (405 residents)	Intervention* (405 residents)	Intervention* (405 residents)
Sequence 3 (27 Nursing Homes)	Control* (405 residents)	Control* (405 residents)	Intervention* (405 residents)

*Administrative data (MDS, EHR) used to evaluate secondary study outcomes in all periods for all sequences

†Primary outcome data (CMAI) collected in Sequence 1 and Sequence 2 during Period 1 only

About 38% of U.S. Coronavirus Deaths Are Linked to Nursing Homes

By The New York Times Updated October 20, 2020

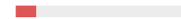
38%

OF ALL U.S. DEATHS
84,000+



7%

OF ALL U.S. CASES
540,000+



The Striking Racial Divide in How Covid-19 Has Hit Nursing Homes

Homes with a significant number of black and Latino residents have been twice as likely to be hit by the coronavirus as those where the population is overwhelmingly white.

Exclusive: Nearly Half of U.S. Nursing Homes Have Staff Infected With COVID-19

An AARP analysis also finds a quarter of facilities are short on workers and PPE

Effect of the pandemic on study design

- We chose the stepped-wedge design because...
 - Need for sequential rollout
 - Desire for all clusters to receive the intervention
 - Likely to be an efficient design for anticipated intra-cluster correlation and cluster size
- BUT... stepped-wedge design is sensitive to confounding by time, particularly when time is correlated with the study outcome due to a secular trend (like increased agitation during a national pandemic)
- LUCKILY...we chose the CMAI as our primary study outcome and we were powered for a stand alone parallel trial (Period 1 Only)

Stepped-Wedge Interrupted by Pandemic

	Period 1 (June, 2019 - January, 2020)	Period 2 (April, 2020 - November, 2020)	Period 3 (February 2021 - September, 2021)
Sequence 1 (27 Nursing Homes)	Intervention*† (405 residents)	Coronavirus pandemic*	Intervention* (405 residents)
Sequence 2 (27 Nursing Homes)	Control*† (405 residents)	Coronavirus pandemic*	Intervention* (405 residents)
Sequence 3 (27 Nursing Homes)	Control* (405 residents)	Coronavirus pandemic*	Intervention* (405 residents)

*Administrative data (MDS, EHR) used to evaluate study outcomes in all periods for all sequences

†Primary data (CMAI) collected in Sequence 1 and Sequence 2 during Period 1 only

Conduct a second parallel trial

	Period 1 (June, 2019 - January, 2020)	Period 2 (April, 2020 - November, 2020)	Period 3 (February 2021 - September, 2021)
Sequence 1 (27 Nursing Homes)	Intervention*† (405 residents)	Coronavirus pandemic*	Intervention* (405 residents)
Sequence 2 (27 Nursing Homes)	Control*† (405 residents)	Coronavirus pandemic*	Intervention*† (405 residents)
Sequence 3 (27 Nursing Homes)	Control* (405 residents)	Coronavirus pandemic*	Control*† (405 residents)

*Administrative data (MDS, EHR) used to evaluate study outcomes in all periods for all sequences

†Primary data (CMAI) collected in Sequence 1 and Sequence 2 during Period 1 only

Second parallel trial

- Already completed recruitment and enrollment
- Sequence 2 & 3 were already balanced at baseline (post-randomization)
- **Opportunity to learn from first trial**
- Cluster-randomized adaptive trial (see protocol)

McCreedy EM, Gutman R, Baier R, Rudolph JL, Thomas KS, Dvorchak F, Uth R, Ogarek J, Mor V. Measuring the effects of a personalized music intervention on agitated behaviors among nursing home residents with dementia: design features for cluster-randomized adaptive trial. *Trials*. 2021 Oct 7;22(1):681. doi: 10.1186/s13063-021-05620-y. PMID: 34620193; PMCID: PMC8496617.

Trial 1

- 8-month intervention (June, 2019 – January, 2020)
- Researchers conducted on-site data collection in 54 nursing homes (27 treatment & 27 control)
- Data were collected at three site visits:
 - Pre-intervention (Baseline)
 - Mid-intervention (4-months)
 - End of intervention (8-months)
- Administrative (MDS and EMR) data was transferred monthly

Trial 1 - Effectiveness

- No effect of the intervention on frequency of agitated behaviors

	Total, n=976	Intervention, n=483	Control, n=493	AME (SE) [95% CI]
Total CMAI score, Mean (SE) Source: Staff Interview Primary outcome	49.65 (1.64) [46.44 , 52.86]	50.67 (1.94) [46.87 , 54.47]	49.34 (1.68) [46.05 , 52.63]	1.33 (1.38) [-1.37 , 4.03]
Total ARBS score, Mean (SE) Source: Minimum Data Set Secondary outcome	0.43 (0.11) [0.22 , 0.64]	0.35 (0.13) [0.10 , 0.60]	0.46 (0.11) [0.25 , 0.67]	-0.11 (0.10) [-0.30,0.08]

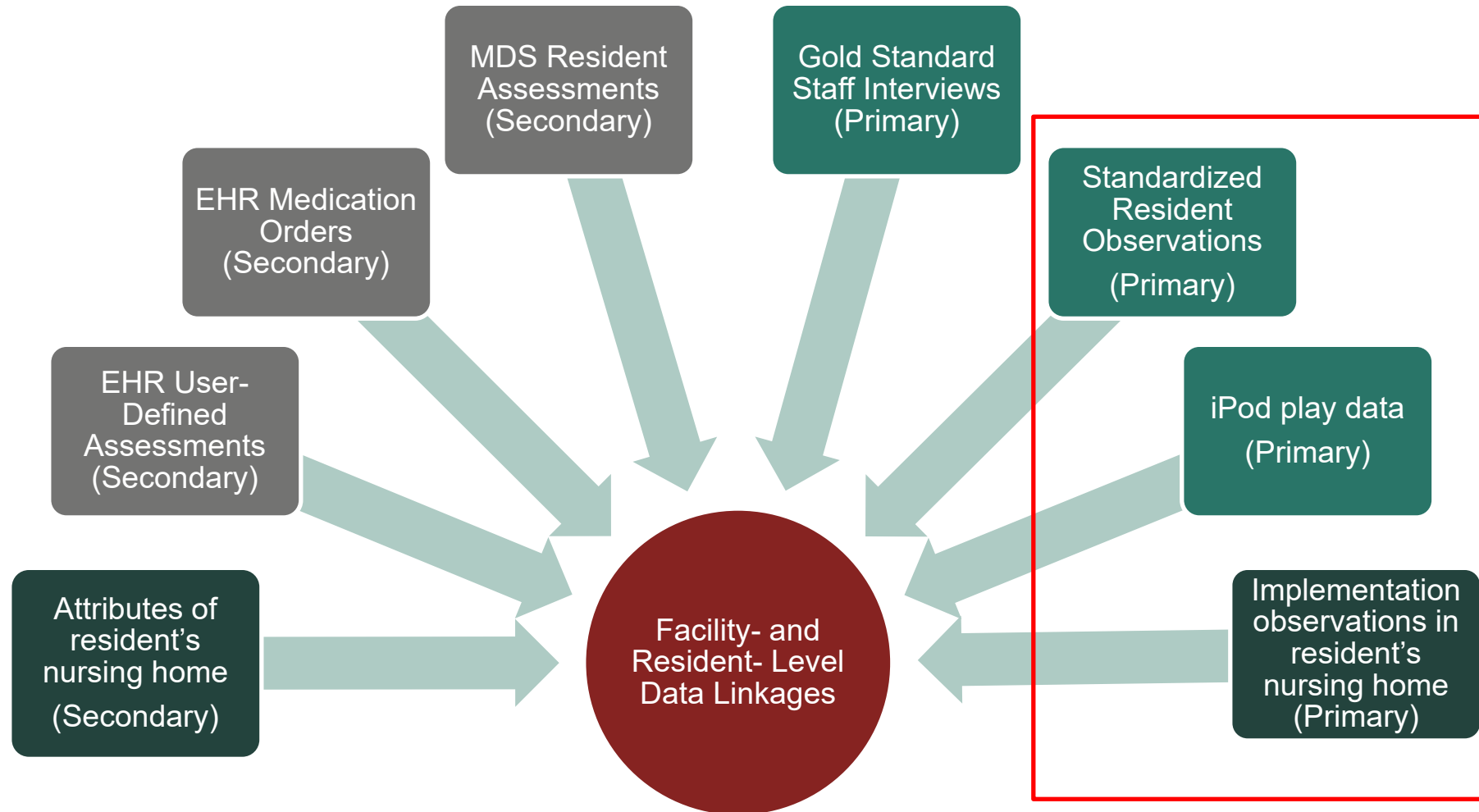
Abbreviations: CMAI, Cohen-Mansfield Agitation Inventory; ARBS, Agitated and Reactive Behavior Scale; SE, standard error; AME, average marginal effect

Trial 1 - Effectiveness

- No statistically significant effects of the intervention on medication use, but near significant findings for antipsychotics

	Total, n=976	Intervention, n=483	Control, n=493	AME (SE) [95% CI]
Proportion of residents with any antipsychotic use in the past week, Mean (SE)	28.1 (1.0) [26.2 , 30.0]	26.2 (1.4) [23.4 , 29.0]	29.6 (1.3) [27.2 , 32.3]	-3.61 (1.85) [-7.22, 0.00]
Proportion of residents with any antidepressant use in the past week, Mean (SE)	58.1 (1.1) [56.0 , 60.3]	57.5 (1.5) [54.6 , 60.5]	58.8 (1.5) [55.8 , 61.7]	-1.26 (2.05) [-5.28, 2.76]
Proportion of residents with any antianxietal use in the past week, Mean (SE)	22.6 (1.2) [20.2 , 25.0]	20.8 (1.5) [17.8 , 23.8]	24.3 (1.7) [20.9 , 27.6]	-3.47 (2.08) [-7.55, 0.06]

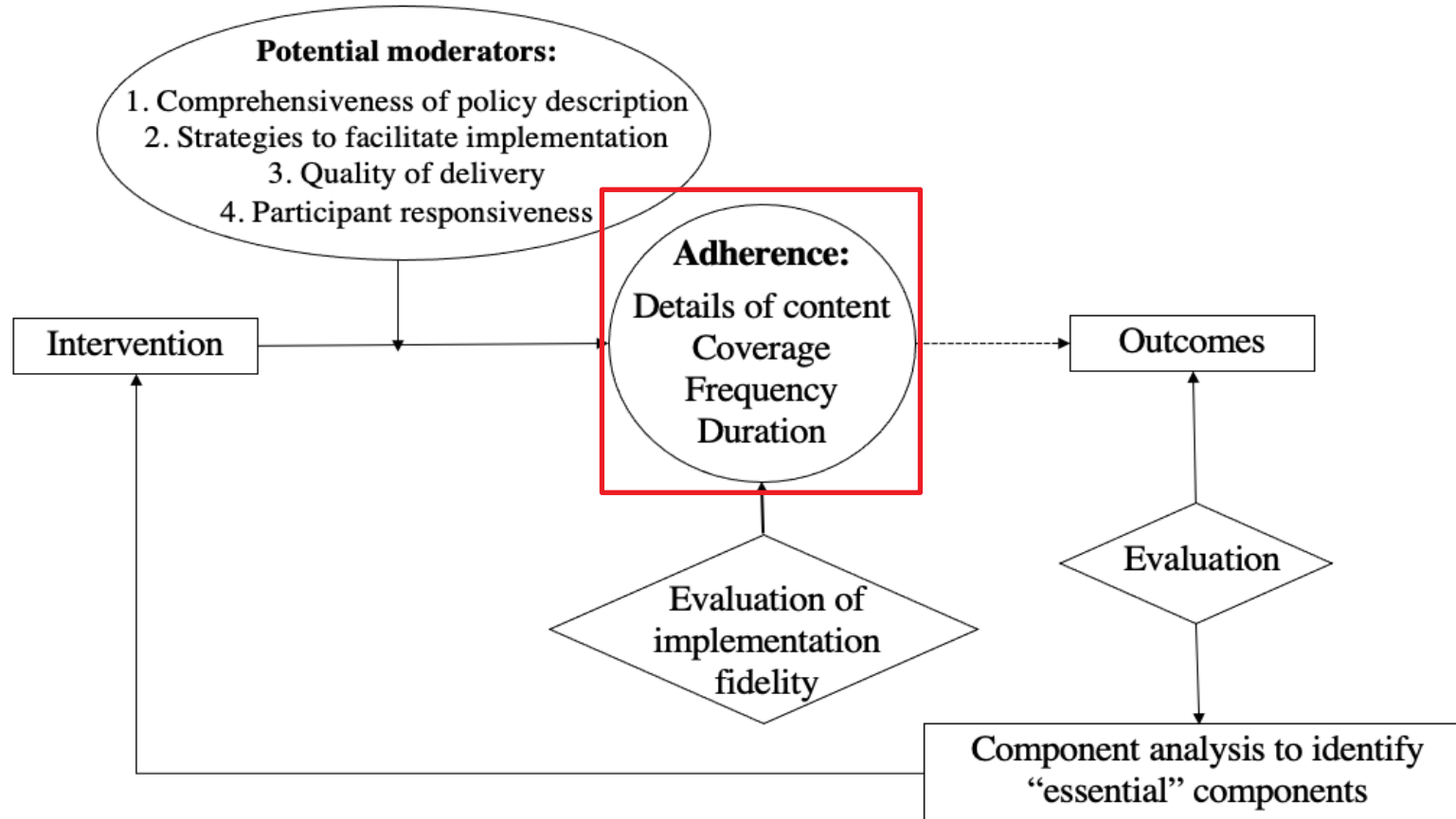
Trial 1 – Implementation Data



Trial 1 - Implementation data

- **iPod play data**
 - Degree of playlist personalization
 - Dose (minutes per day exposed)
- **Structured observations**
 - Complete labeling of individual headphones / iPods
 - Accessibility of iPods by nursing staff
- **Initial use forms**
 - Date music started with resident (used for dose)
 - Reason music used with resident
 - Method and time spent identifying resident preferred music
- **Staff interview**
 - Frequency of nursing staff use of music with resident

Trial 1 – Implementation Fidelity



Trial 1 – Implementation Fidelity

FIF Adherence Dimension	Definition	Distribution
1. Details of content	Adherence to core components of intervention protocol: personalization of playlists, processes for labeling, storing and charging equipment, engaging multidisciplinary team	Range: 7.0–14.0 Mean (SD): 9.6 (2.0)
2. Coverage	Total number of residents exposed intervention	Range: 5.0–19.0 Mean (SD): 13.5 (3.7)
3. Frequency	Proportion of targeted residents with nurses administering the music at least once per week	Range: 0.0–1.0 Mean (SD): 0.4 (0.3)
4. Duration	Median minutes of music per resident exposed day	Range: 0.0–86.9 Mean (SD): 28.5 (23.4)

Trial 1 Learnings

- Process for identifying and loading preferred music for residents with dementia was time consuming and affected coverage
- Music identification process completed by activities staff, intervention never “owned” by nursing
- Intervention being used but lack of clinical targeting
- If want music to be substitute for PRN medication use, need a solution that can be owned by nursing staff from the beginning

McCreedy E, Sisti A, Gutman R, Dionne L, Rudolph J, Baier R, Thomas K, Olson M, Zediker E, Uth R, Shield R, Mor V. Pragmatic Trial of Personalized Music for Agitation and Antipsychotic Use in Nursing Home Residents with Dementia. (Revise and Resubmit)

Olson M, McCreedy E, Baier R, Shield R, Zediker E, Uth R, Thomas K, Mor V, Gutman R, Rudolph J. Measuring Implementation Fidelity in a Cluster-Randomized Embedded Pragmatic Clinical Trial (ePCT): A Complex Intervention Used in US Nursing Homes. (Submitted)

Modifications

	Trial 1	Trial 2
Intervention	<ul style="list-style-type: none">• Resident preferred music identified by activities staff through trial-and-error process• Activities staff load music on iPods	<ul style="list-style-type: none">• Resident “preferred” music predicted using play data from first trial• Research staff load music on iPods before sending to nursing homes
Implementation	<ul style="list-style-type: none">• Study consultants and corporate representatives co-lead training for participating nursing homes• Study consultants and corporate representatives co-lead monthly coaching calls	<ul style="list-style-type: none">• Corporate representatives lead training (no study consultant participation)• Corporate representatives lead monthly coaching calls (no study consultant participation)

Other features of adaptive design

- **Increasing enroll residents who are likely to benefit from the program**
 - Identify resident and clinical characteristics associated with more play time
 - Examine midpoint selection from the first trial
- **Equilibrate researcher-collected measure of agitation to administrative measure**
 - Administrative data subject to under-detection
 - Collecting gold standard measure allows for more complete representation of outcomes, but resource intensive
 - Collecting both types of data in the current study allows us to create an imputation model that may be used in future studies to reduce data collection burden

Hybrid type 2

- Dual focus on the clinical intervention and implementation related factors
- Explicit measurement of implementation outcome (e.g., adoption, fidelity)
- Pilot test an implementation strategy aimed at increasing use and fidelity of the intervention

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- Conducted process evaluation during R21 pilot phase (Type 1)
 - NOT primarily focused on implementation outcomes or directly comparing strategies (Type 3)

Landes SJ, McBain SA, Curran GM. An introduction to effectiveness-implementation hybrid designs. *Psychiatry Res.* 2019 Oct;280:112513.

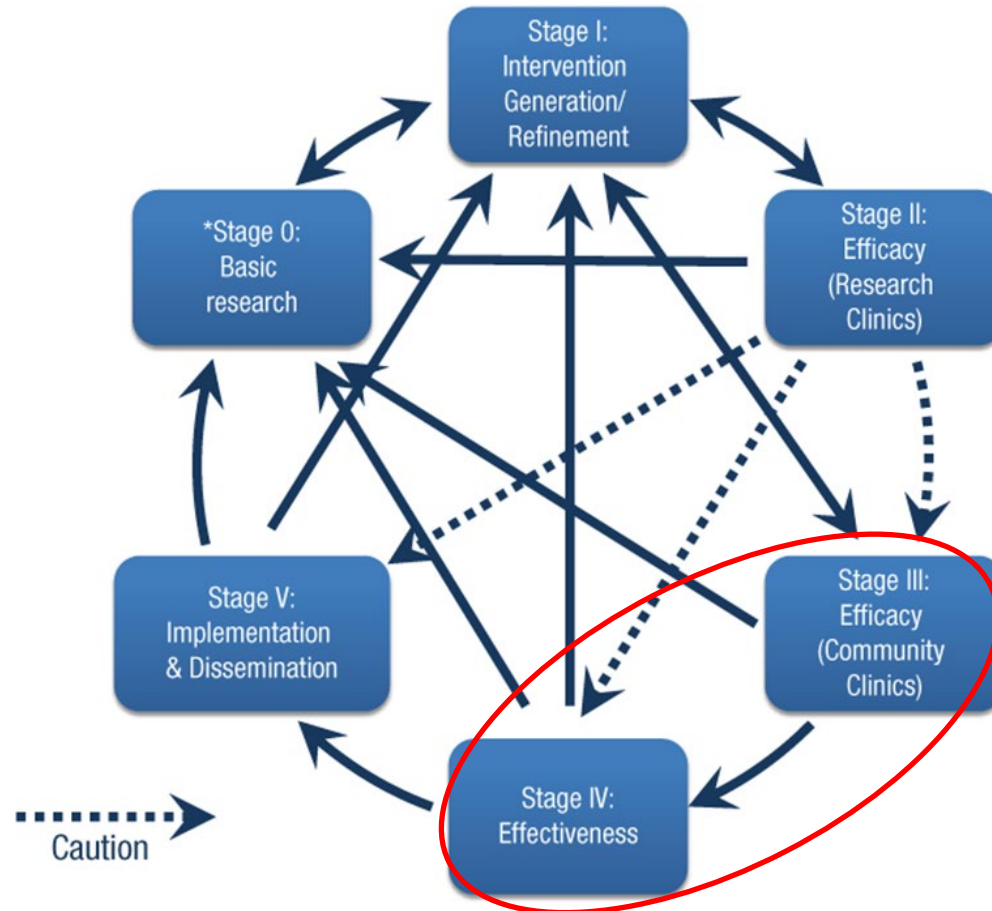
Conclusions

- Rigorous measurement of fidelity guided modifications in intervention and implementation strategies
- Hybrid and adaptive designs may shorten the time to useable evidence
- Don't retrofit -- Plan to use hybrid and/or adaptive designs as part of your next submission!

Extra Slides – NIH Models

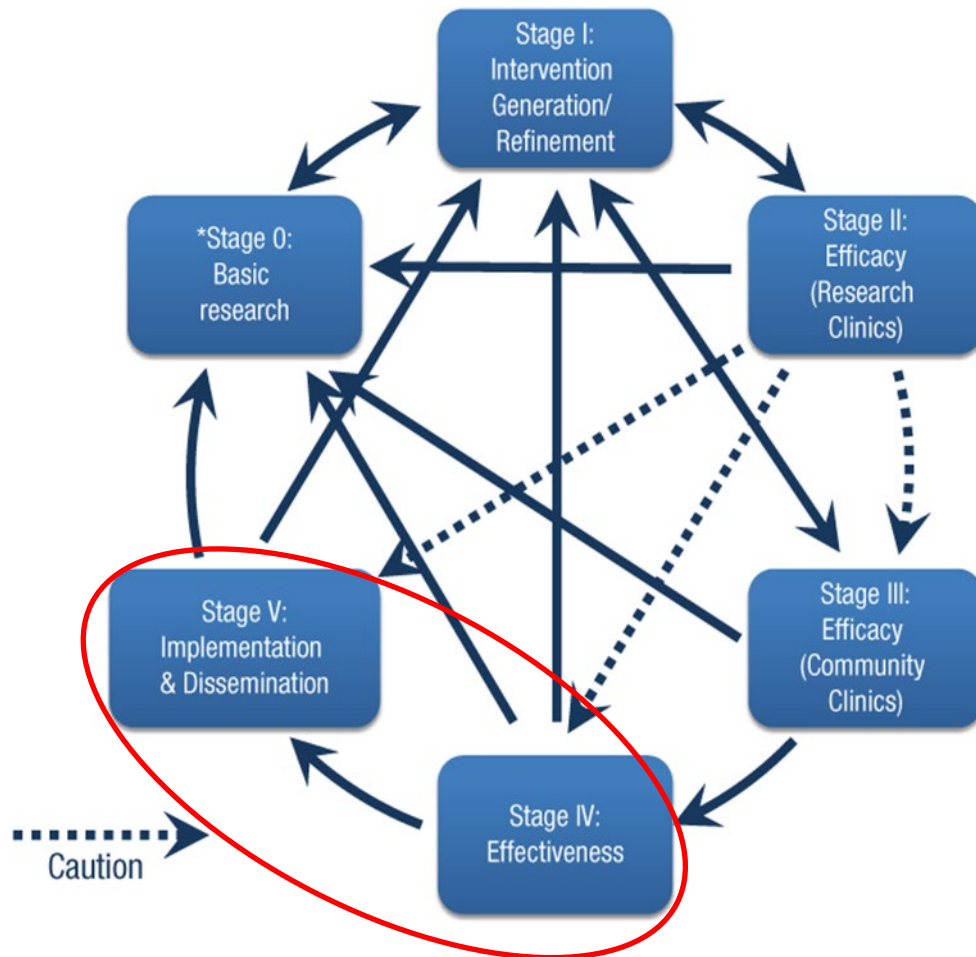


Trial 1: Stage III / IV Hybrid Trial



- Lack of real-world efficacy evidence for intervention
- Opted for less pragmatic outcome ascertainment
- Researcher involved in training and monthly coaching calls

Trial 2: Stage IV / V Hybrid Trial



- Using implementation data from Trial 1, revise intervention
- No researcher involvement in training and monthly coaching calls

R21: Used Pilot Study to Improve Pragmatic Trial Readiness

Element	Key Question	Readiness Score BEFORE Pilot (1 low, 5 high)	Readiness Score AFTER Pilot (1 low, 5 high)
Implementation Protocol	Is the protocol detailed and replicable?	3	5
Evidence	Does the evidence base support efficacy?	3	3
Risk	Is the intervention known to be safe?	4	5
Feasibility	Can the intervention be implemented under existing conditions?	3	4
Measurement	Can outcomes be captured pragmatically?	2	3
Cost	Is the intervention economically viable?	4	4
Acceptability	Are providers willing to adopt the intervention?	5	5
Alignment	Does the intervention align with stakeholders' priorities?	5	5
Impact	How useful will the results be?	4	4

R21 :Under-detection and sensitivity to change

	Administrative Data n=40	Gold Standard Staff Interview n=40
Any physical behaviors directed toward others (baseline %)	5.6	35.9
Any verbal behaviors directed toward others (baseline %)	9.2	40.6
Any other behaviors not directed toward others (baseline %)	10.1	55.5
Average within person % change in behavior frequency (pre-post)	-14.0	-16.0*

*p-value<.01, paired t-test with continuity correction, causality not implied