

Methods: Mind the Gap  
Webinar Series

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# Deconstruction of the Type 2 Hybrid Effectiveness- Implementation Study Design that Uses Two Randomized Controlled Trials

Presented by:  
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University of North Carolina at Chapel Hill



**DEBATE**

**Open Access**

# Design of a dual randomized trial in a type 2 hybrid effectiveness—implementation study



June Stevens, Sarah Denton Mills, Thomas J. Millett, Feng-Chang Lin and Jennifer Leeman

# Outline



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1. Implementation basics
2. Literature search on Type 2 Hybrids with two RCTs
3. Diagrams explaining DRCT design
4. How implementation strategies and interventions are interrelated
5. Power calculations
6. Take home messages and closing thoughts





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# The oft' quoted statistic:

It takes an average of 17 years for research evidence to reach clinical practice.

Westfall J et al. Practice-based research – “Blue Highways” on the NIH roadmap. *JAMA* 2007;297:403–6

Rogers E et al. *Diffusion of innovations*. 4th edn New York, NY: The Free Press, 1995 [[Google Scholar](#)]

Balas E. et al. Managing Clinical Knowledge for Health Care Improvement. *Yearbook of Medical Informatics*. Stuttgart: 2000:65–70

Grant et al. Basic research and health: a reassessment of the scientific basis for the support of biomedical science. *Res Eval* 2003;12:217–24

Wratschko K. Empirical Setting: The pharmaceutical industry. *Strategic Orientation and Alliance Portfolio Configuration*. New York, NY: Springer, 2009

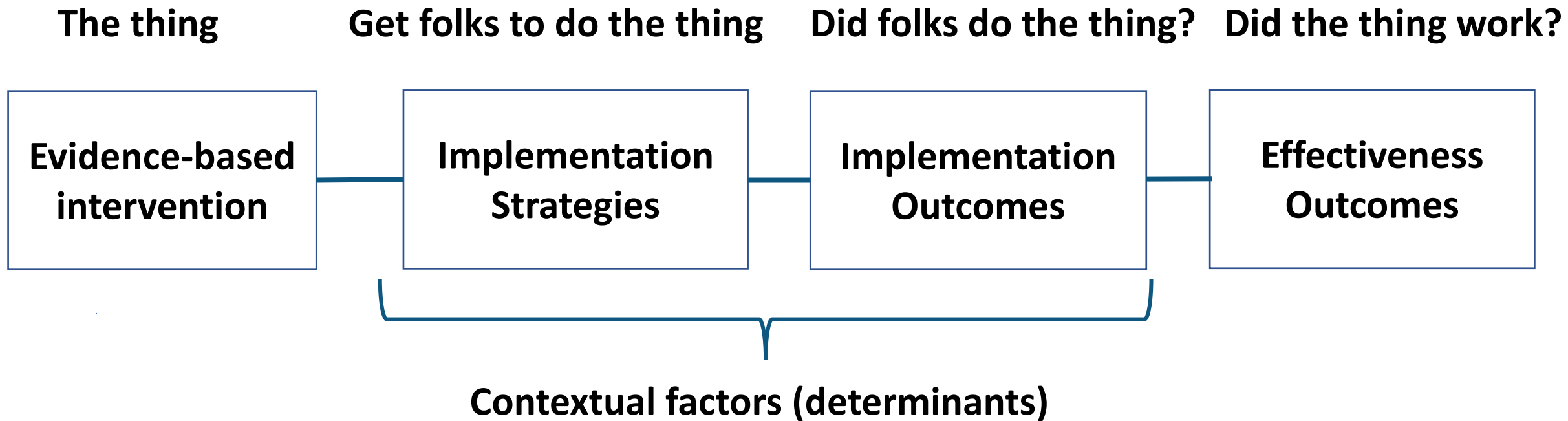


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# Why study implementation?

- Numerous developed health interventions that have been shown to be effective are not contributing to health because they are not being implemented.
- Disparities in health are magnified by a lack of implementation strategies that are effective in diverse populations.
- Therefore, research is needed to identify strategies for reaching diverse populations to increase the uptake of interventions that will improve health.

# Implementation Science (Adapted from Curran, 2020)

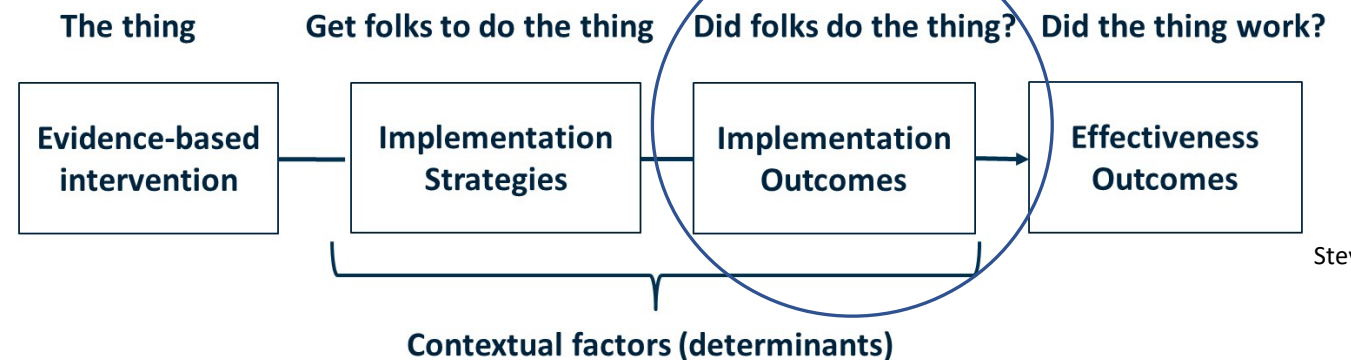


# Implementation Outcomes – Did folks do “the thing”?



- Did the intended population participate (were they **reached**) by the intervention?
- Did settings/providers **adopt** the intervention?
- Did settings/providers **implement** the intervention with fidelity (i.e., as designed)?
- Did settings/providers **maintain** the intervention over time?

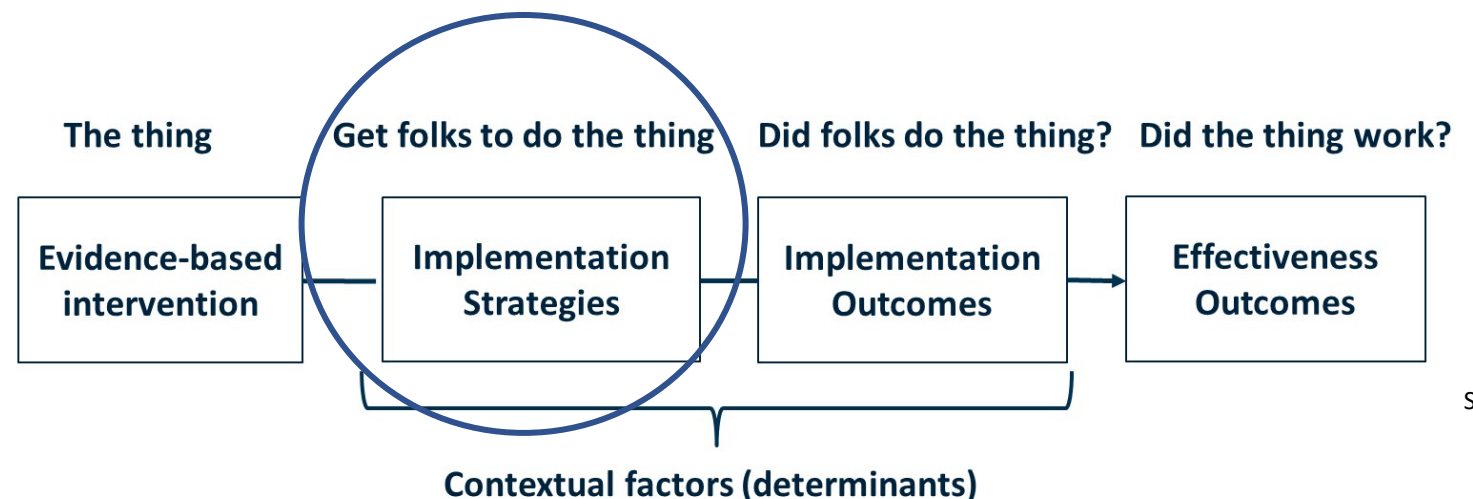
[RE-AIM.org](http://RE-AIM.org)



# Implementation strategies are how we achieve good implementation outcomes



Implementation strategies = “methods or techniques used to enhance the adoption, implementation, and sustainability of a clinical program or practice.” (Proctor, Powell, & McMillen, 2013)





# Hybrid Implementation - Effectiveness Studies



[Geoffrey M. Curran,](#)

“An effectiveness-implementation hybrid design is one that takes a dual focus *a priori* in assessing clinical effectiveness and implementation.”

[Med Care. 2012 Mar; 50\(3\): 217–226.](#)

Also:

Psychiatry Res, Oct 2019

Front. Health Serv., December 2022

# Types of Hybrid-Effectiveness Studies

Type	Implementation	Intervention
I	Secondary focus	Primary focus
II	Dual focus	Dual focus
III	Primary focus	Secondary focus

Source: Adapted from Curran et al., 2012 and Landes, McBain and Curran, 2019



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# DRCT

A kind of Type Two Hybrid

Type	Implementation	Intervention
I		
II	<b>Randomized trial Hypothesis:</b>  <b>The active implementation strategy results in a more favorable implementation outcome compared to control implementation.</b>	<b>Randomized trial Hypothesis:</b>  <b>The active intervention results in a more favorable health outcome compared to control intervention.</b>
III		

# Why do a Type 2 Hybrid Study (instead of a Type 1 or 3)?



- Efficiency of using one study sample to test both implementation and intervention
- Previous research on the intervention may not have been conducted in a pertinent population
- Concerns that adaptation of the intervention may impact its potency
- Previous research on intervention may be lacking or weak

# What is a DRCT?



A DRCT is a type 2 hybrid-effectiveness study that uses 2 RCT's to

- Examine the impact of implementation strategies on implementation outcomes  
*and*
- Examine the impact of an intervention on health outcomes.

# Why do a DRCT?

## i.e., Why use 2 RCT's rather than other study designs?



A well-executed, randomized trial avoids bias and offers the strongest causal evidence with which to determine the truth of a hypothesis.

# Guidance from CONSORT and StaRI

- CONSORT provides expert guidance for preparation of publications that use RCT study designs
- Standards for Reporting Implementation (StaRI) is the CONSORT Extension that addresses implementation research

(available from <http://www.equator-network.org>)



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The StaRI guidelines emphasize the importance of clearly identifying and differentiating implementation strategies and intervention programs.

Pinnock H, Barwick M, Carpenter CR, et al. Standards for reporting implementation studies (stari) statement. *BMJ*. 2017;356:i6795. doi:10.1136/bmj.i6795



# StaRI – “dual strands” of exposures and outcomes



Implementation		Intervention



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# StaRI- “Dual Strands” (1)

## Examples of Types of Exposures

Implementation Strategies		Intervention
Facilitation		Practices
Coaching		Procedures
Education		Products
Identify and prepare champions		Pills



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# StaRI- “Dual Strands” (2)

## Named Intervention Examples

Implementation Exposures (Implementation Strategies)		Intervention Exposures (Intervention)
Facilitation		Kaiser Bundle (NW)
Coaching		IDEAL-Life Goals (Hopkins/Mich)
Education		PACE (NYU)
Identify and prepare champions		SAA/CO-SBAP (Colorado)



# StaRI- “Dual Strands” (3)

## Examples of Outcomes

Implementation Outcomes		Intervention Outcomes
Reach		Smoking Frequency
Acceptability		HTN Control
Adoption		Asthma Attack Frequency
Appropriateness		Asthma Symptom Reduction
Feasibility		Simple 7 score (CVD Health)
Implementation Cost		BMI
Penetration		Weight
Sustainability		Framingham Score



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1. **Implementation basics**
2. **Literature search on Type 2 Hybrids with two RCTs**
3. Diagrams explaining DRCT design
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6. Take home messages and closing thoughts



# 2. Literature Search



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**Thomas Millett, MPH**

**Sarah Mills, MPH, PhD**

# DRCT



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- We searched for type 2 hybrid studies that used 2 RCT's to
  - Examine the impact of implementation strategies on implementation outcomes  
*and*
  - Examine the impact of an intervention on health outcomes.



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# *Limited* Literature Search

- Find examples of published DRCTs and get a rough idea of prevalence and methods
- Chose 4 diverse journals specializing in implementation science and clinical trials that we thought likely to publish type 2 hybrid studies



*Implementation Science*



Implementation  
Research & Practice

*Implementation Research and Practice*

**TRANSLATIONAL**  
BEHAVIORAL  
MEDICINE  
PRACTICE, POLICY, RESEARCH

*Translational Behavioral Medicine*

*Contemporary  
Clinical Trials*

Design, Methods, and Analysis

*Contemporary Clinical Trials*



Articles identified from initial search:

**n=408**

Articles identified as  
Type 2 Hybrid Studies:

n=

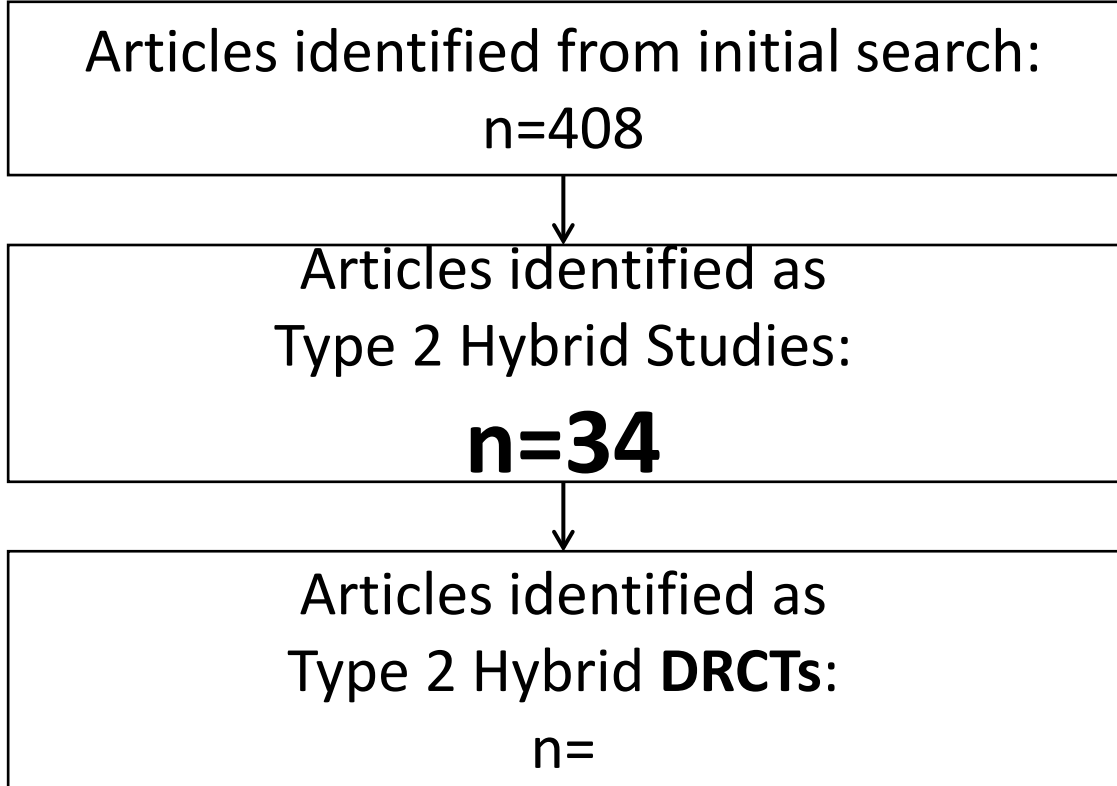
Articles identified as  
Type 2 Hybrid **DRCTs**:

n=

Search strategy limited to previous 6 years and developed with health sciences librarian:

"type II" OR "type II hybrid" OR "hybrid type 2" OR "hybrid type ii" OR "hybrid type II" OR "implementation-effectiveness" or "dual RCT" OR "effectiveness-implementation"

- *Implementation Science* (n=244)
- *Translational Behavioral Medicine* (n=73)
- *Contemporary Clinical Trials* (n=62)
- *Implementation Research & Practice* (n=29)



- Examine both implementation and effectiveness (Curran et al, 2012)
- Not limited to a particular study design (Curran et al, 2022)
- *Implementation Science* (n=22)
- *Translational Behavioral Medicine* (n=1)
- *Contemporary Clinical Trials* (n=9)
- *Implementation Research & Practice* (n=2)



## 6 studies that came close

- Protocols (n=3)
  - Espel-Huynh et al (2019)
  - Iverson et al (2020)
  - Linendoll et al (2023)
- Reporting of qualitative data (n=2)
  - Espel-Huynh et al (2021)
  - Lawson et al (2023)
- Design and analysis issues
  - Garner et al (2020)

Articles identified from initial search:  
n=408

Articles identified as  
Type 2 Hybrid Studies:  
n=34

Articles identified as  
Type 2 Hybrid **DRCTs**:  
**n=0**



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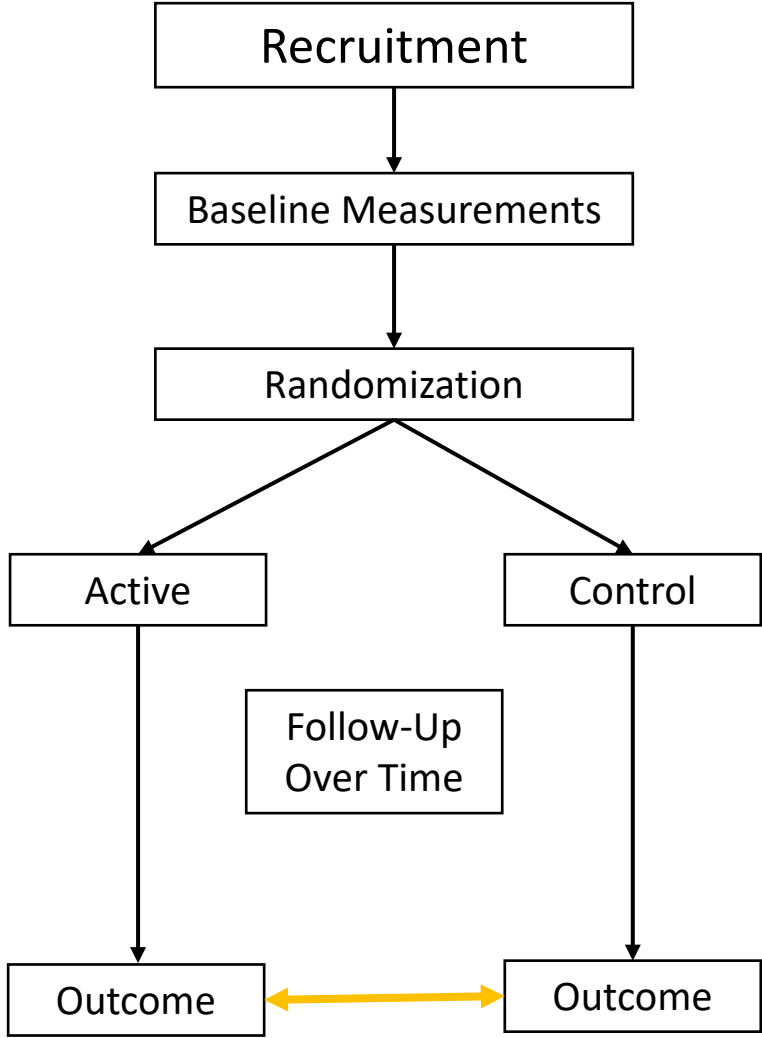
# Outline

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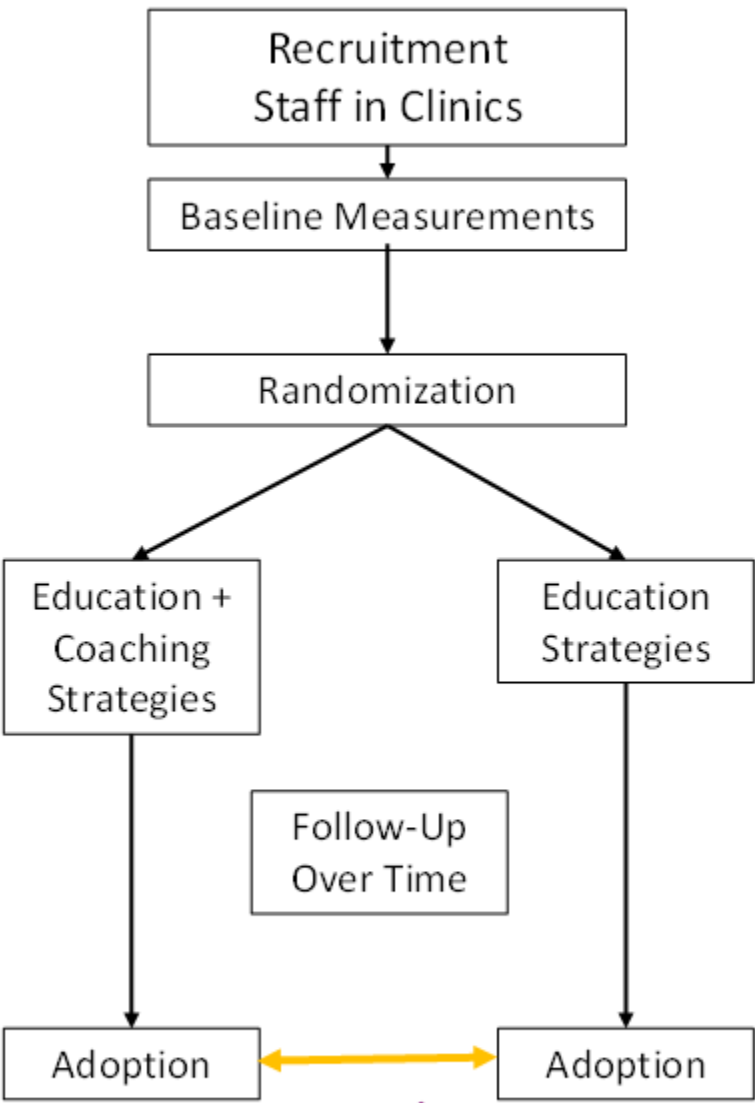
# 3. Classic RCT



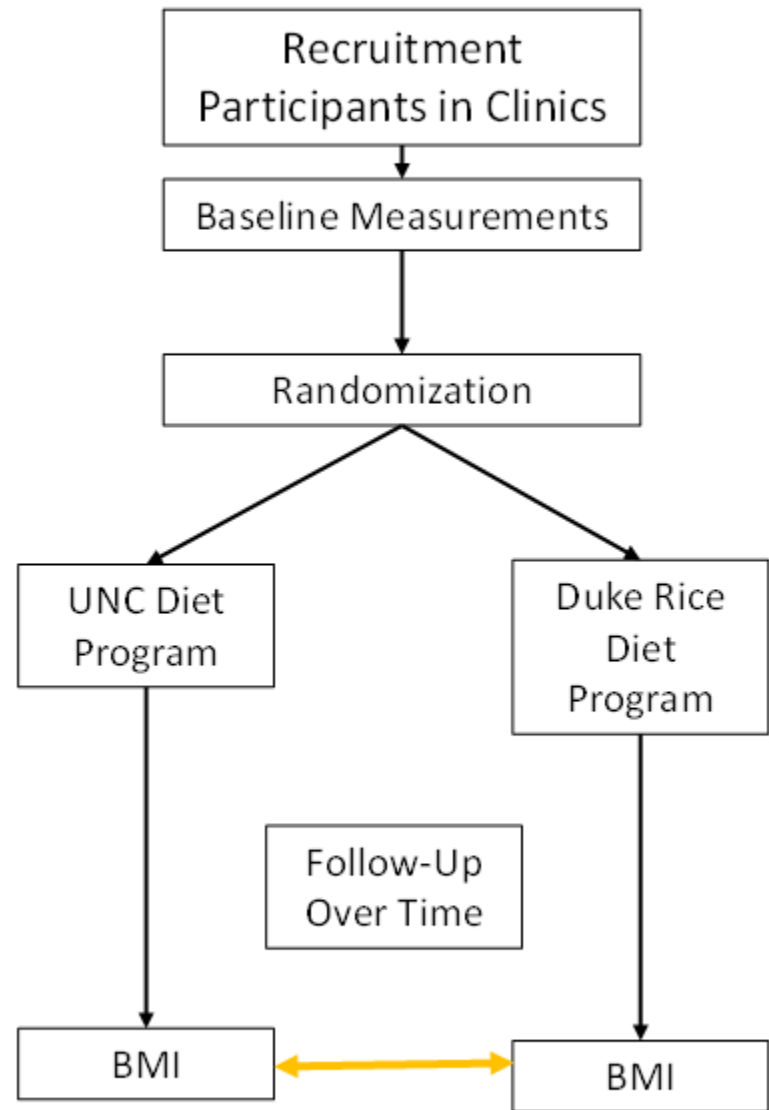


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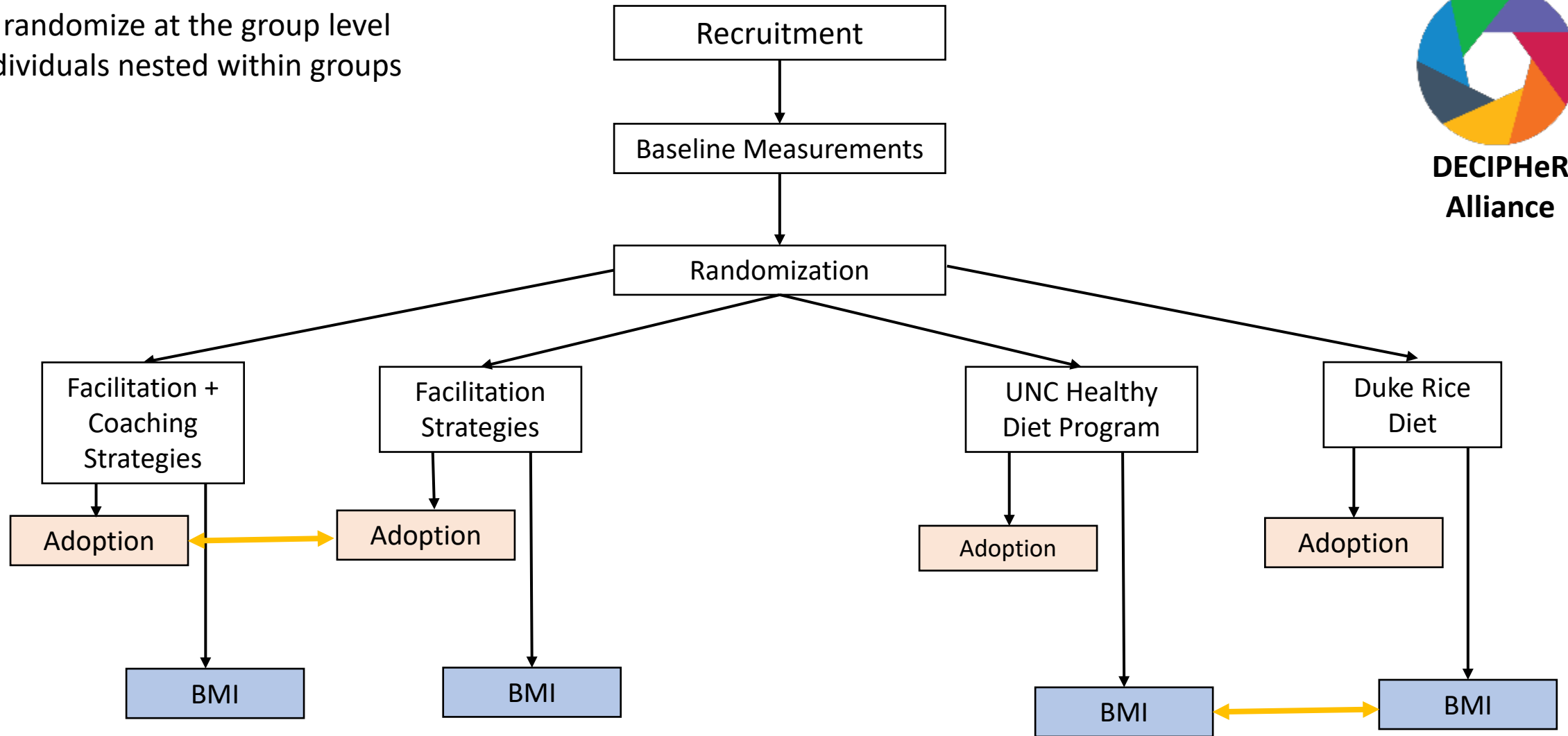
### Implementation

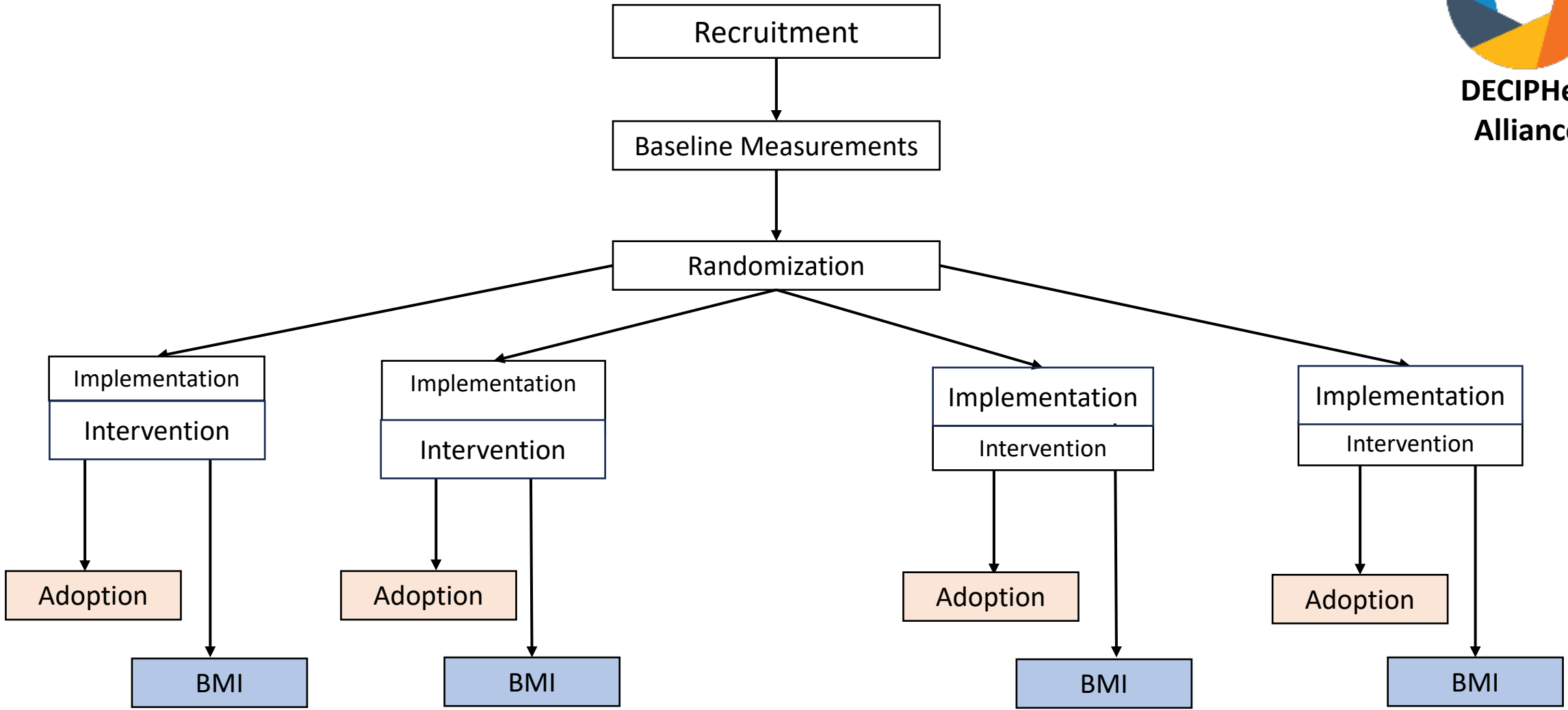


### Intervention



Usually randomize at the group level with individuals nested within groups









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# Introduce new notation

## Exposures

Potential causal factors that can be behaviors, treatments, traits or exogenous factors. Can be naturally occurring or assigned.

S = Implementation **S**trategies

P = Intervention **P**rogram

(Rothman et al. 2008)



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# Introduce new notation (continued)

**Exposures**  
Potential causal factors that can be behaviors, treatments, traits or exogenous factors. Can be naturally occurring or assigned.



**S= Implementation Strategies**

**P = Intervention Program**

<b>7 Ps</b>
<b>1. Programs</b>
<b>2. Practices</b>
<b>3. Principles</b>
<b>4. Procedures</b>
<b>5. Products</b>
<b>6. Pills</b>
<b>7. Policies</b>

Brown et al., 2017



# Exposures are active or control

**Exposures**  
Potential causal factors that can be behaviors, treatments, traits or exogenous factors. Can be naturally occurring or assigned.



$S_a, S_c$  = Implementation **S**trategies

$P_a, P_c$  = Intervention **P**rogram

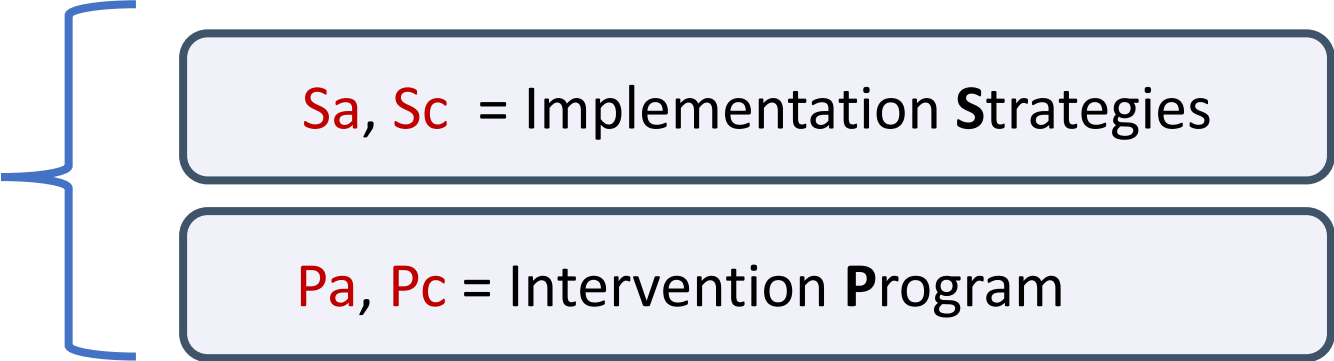
**a = active**

**c = control or comparison**



# DRCT - Study Arms formed by 2 exposures

**Exposures**  
Potential causal factors that can be behaviors, treatments, traits or exogenous factors. Can be naturally occurring or assigned.



**Study arms**

Each arm has S and P pair  
Ex: SaPa is the active **arm**

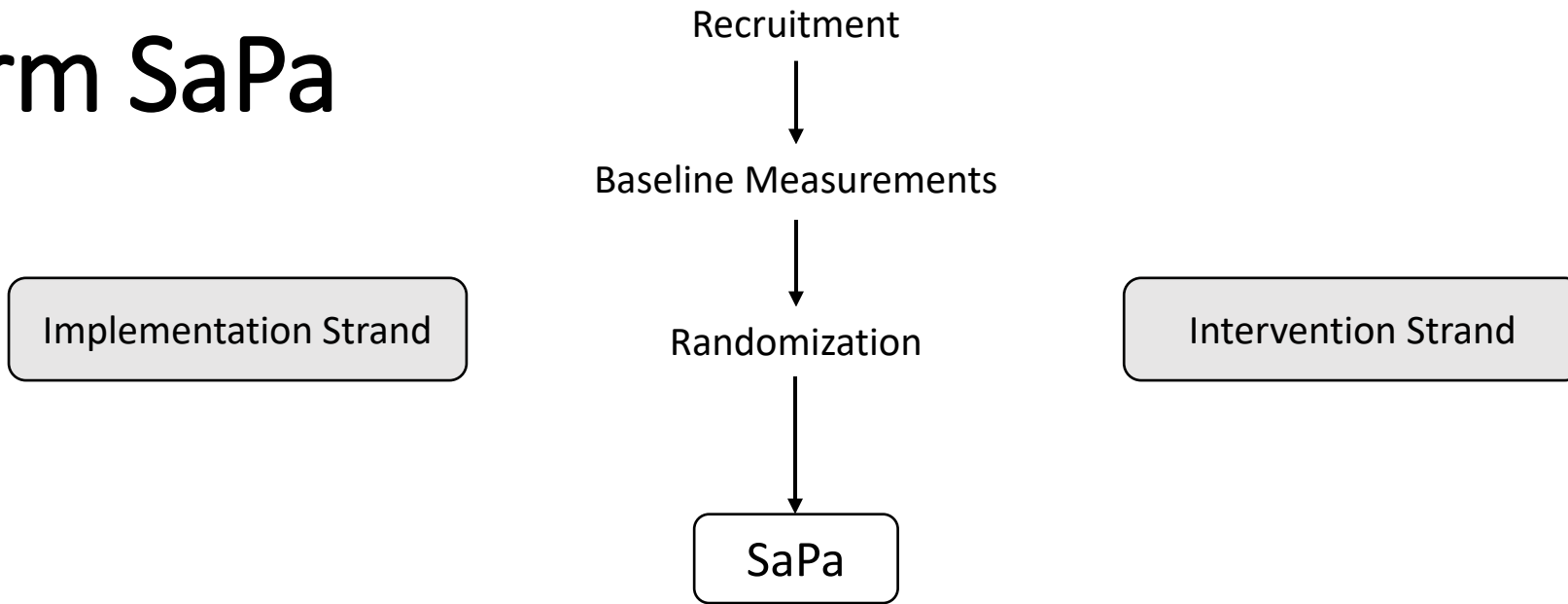


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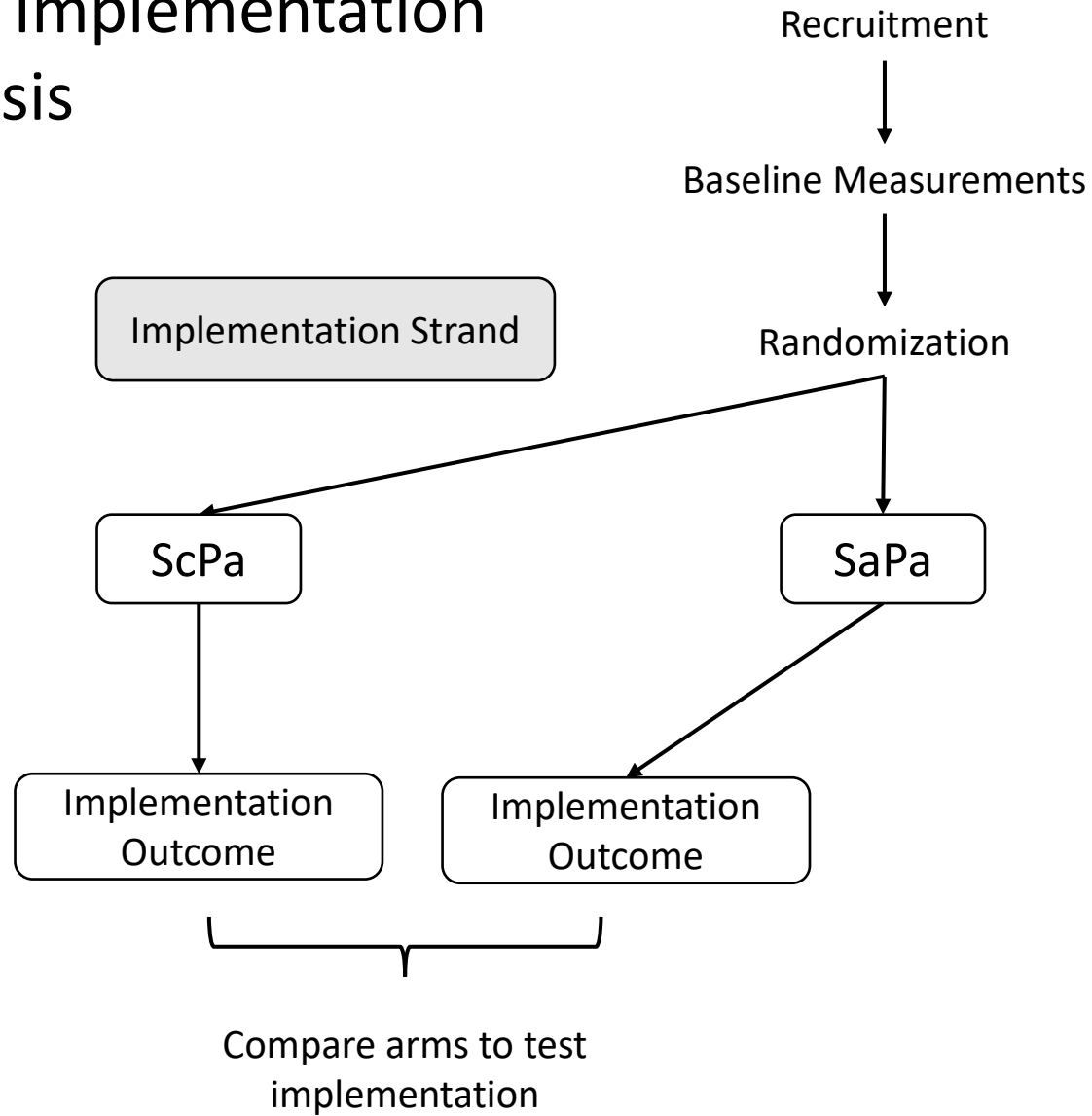
SaPa is the “package” that you hypothesize will give more favorable results and you want to deliver, sustain and spread.

# Active Arm SaPa



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# Examine Implementation Hypothesis





# Implementation strand



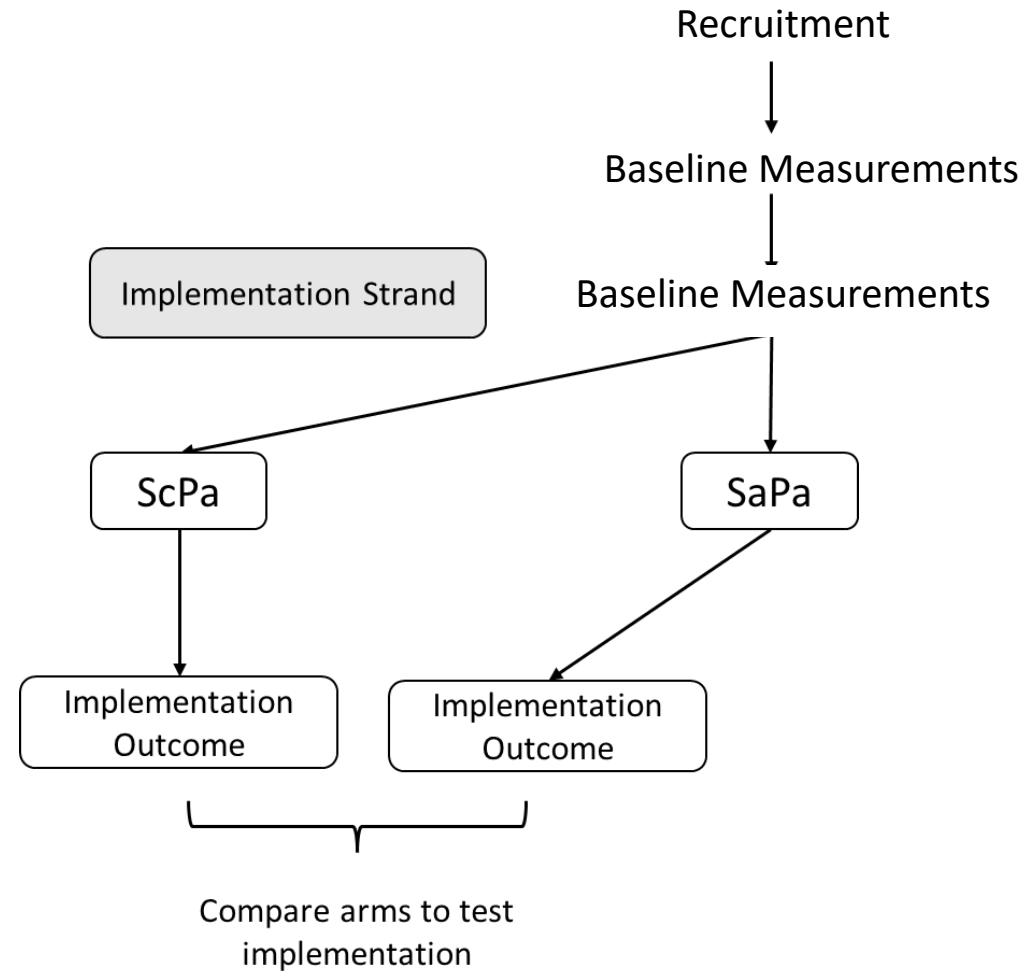
## EXAMPLE

SaPa

- Enhanced education and coaching to support community-based staff in UNC Diet Program (Sa)
- UNC Diet Program (Pa)

ScPa

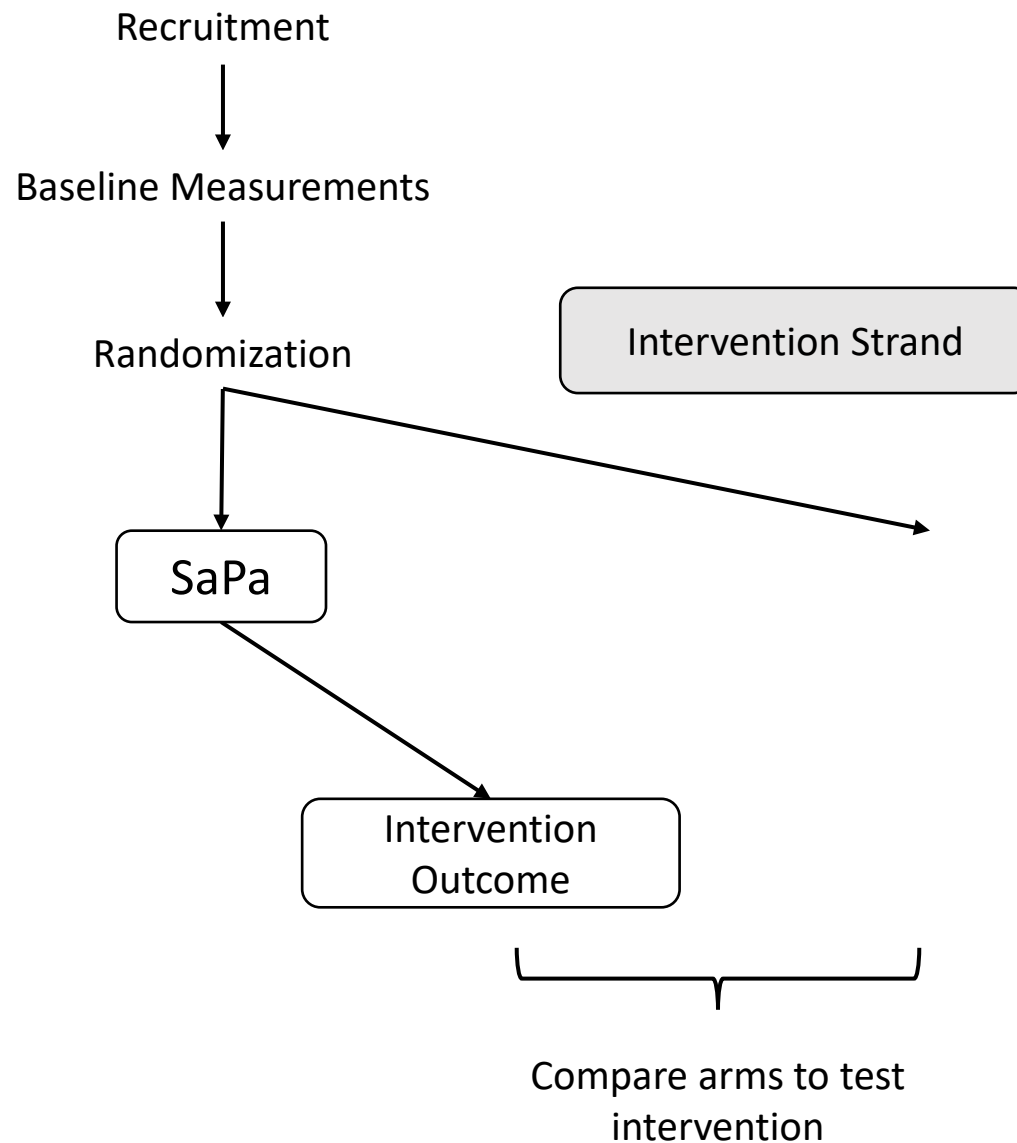
- Routine education to support clinic-based staff in UNC Diet Program (Sc)
- UNC Diet Program (Pa)



# Examine Intervention Hypothesis

Know:  
SaPa is the active arm

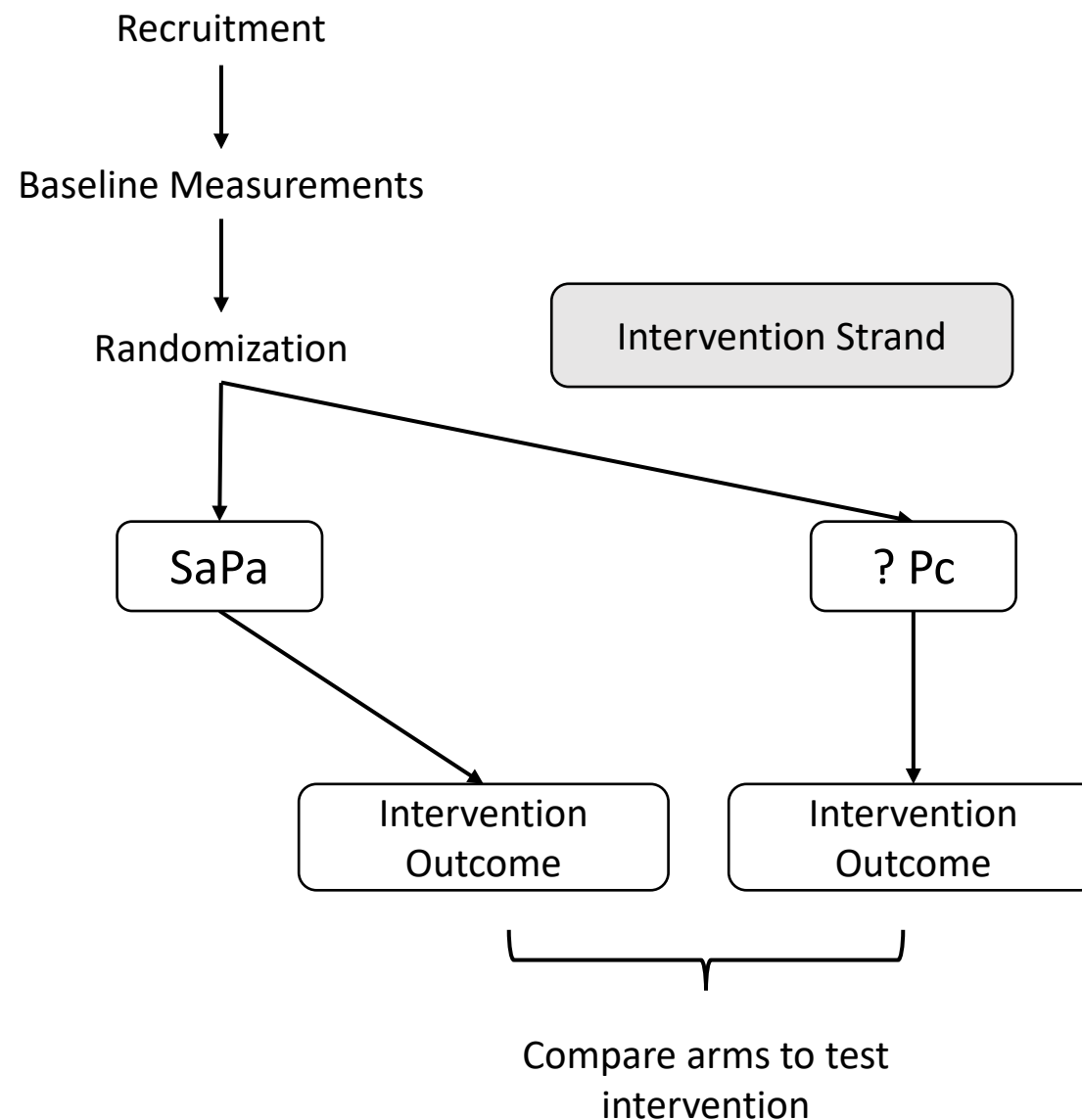
What are the exposures in the control arm?



# Examine Intervention Hypothesis (continued)



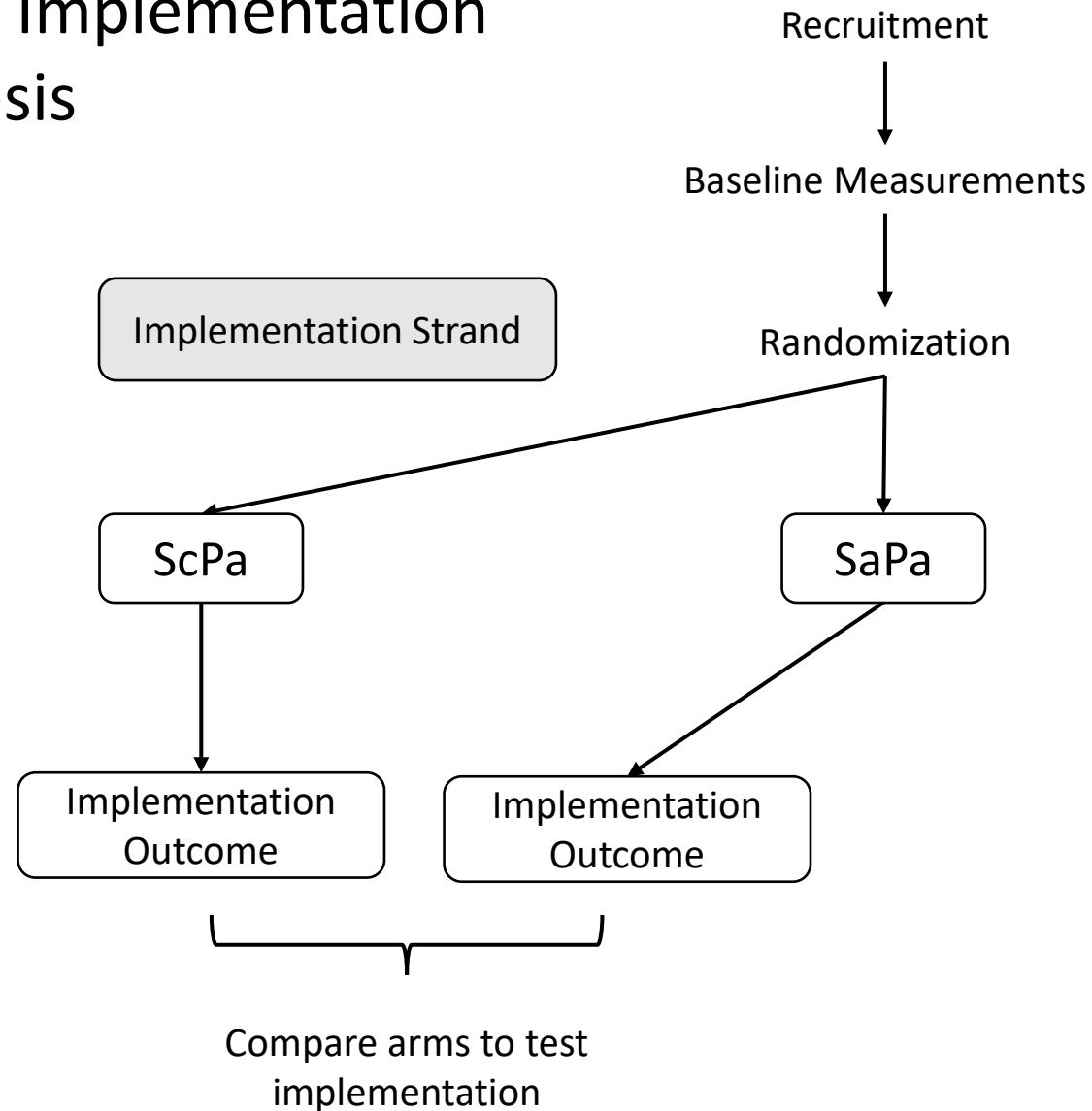
- Want to compare active intervention program Pa to the control program Pc
- Know that ? Addresses barriers and facilitators of the control intervention.



# Examine Implementation Hypothesis



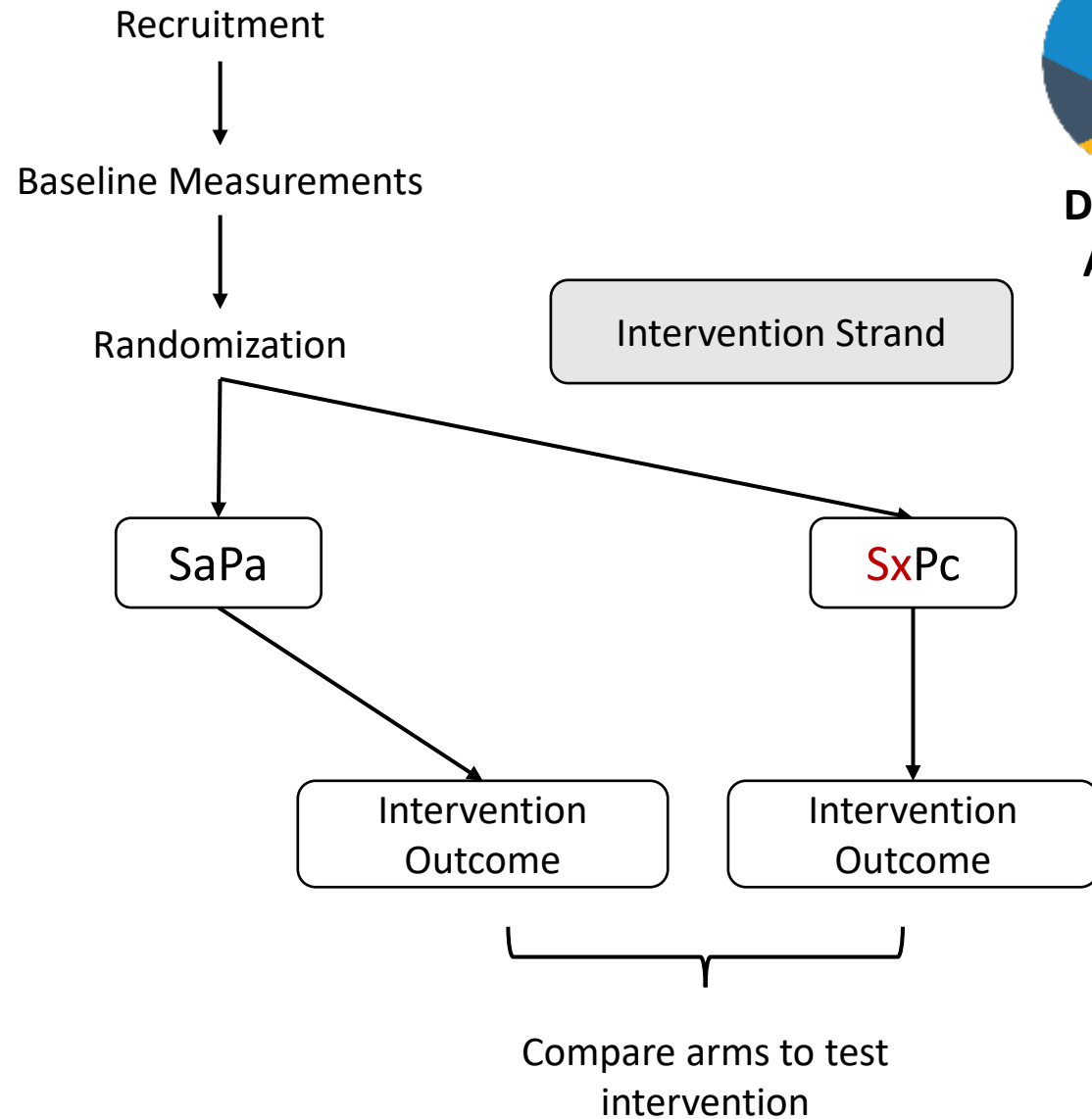
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- Control exposure for the implementation strand cannot be Sc
- Sc addresses uptake of Pa, not Pc
- So need another subscript

# Examine Intervention Hypothesis

- Sx is used to denote the implementation strategy used in the control arm of the Intervention Strand
- We will be addressing Sx in the next 2 sections



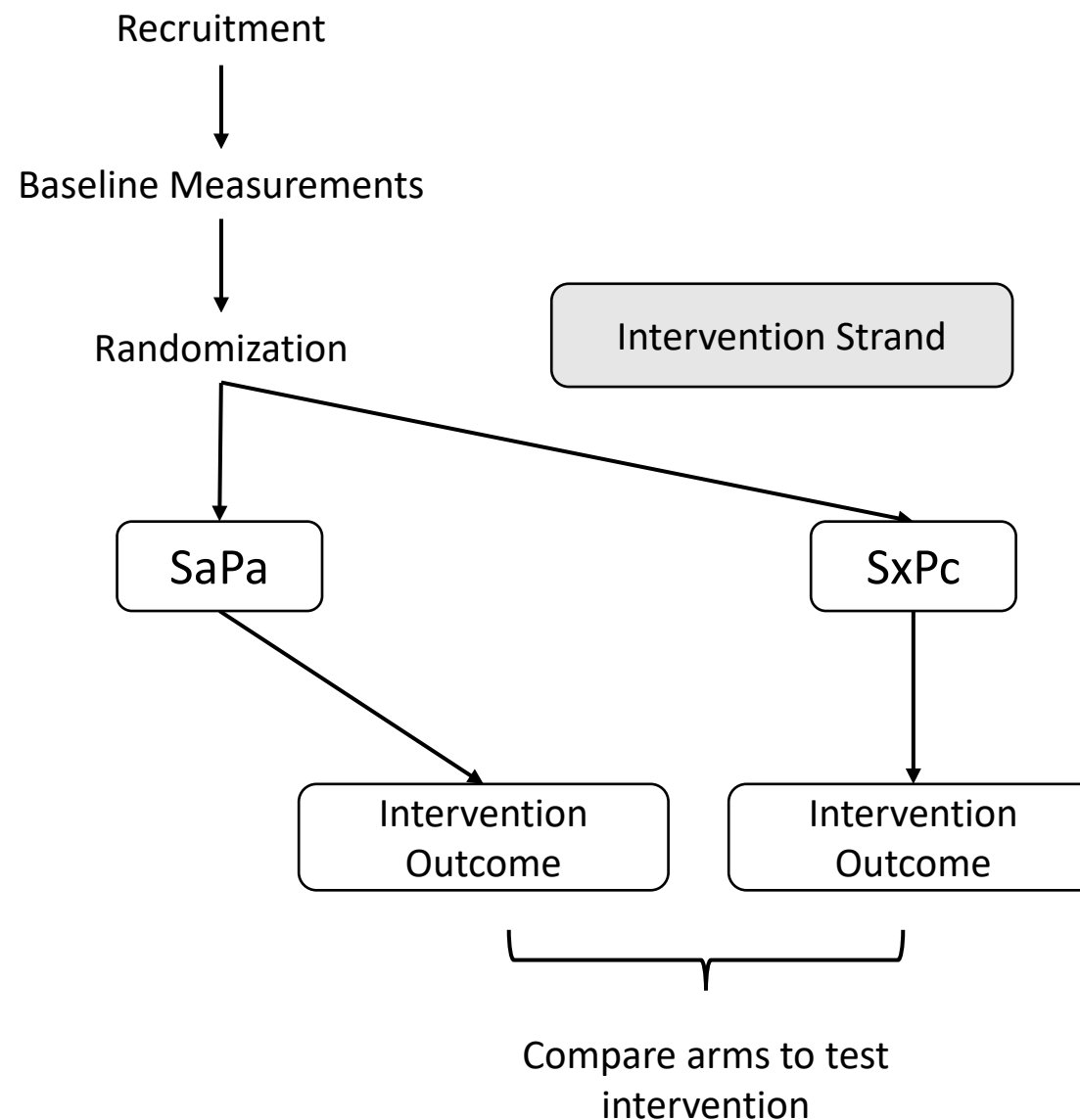
# Intervention Strand

## EXAMPLE

SaPa

SxPc

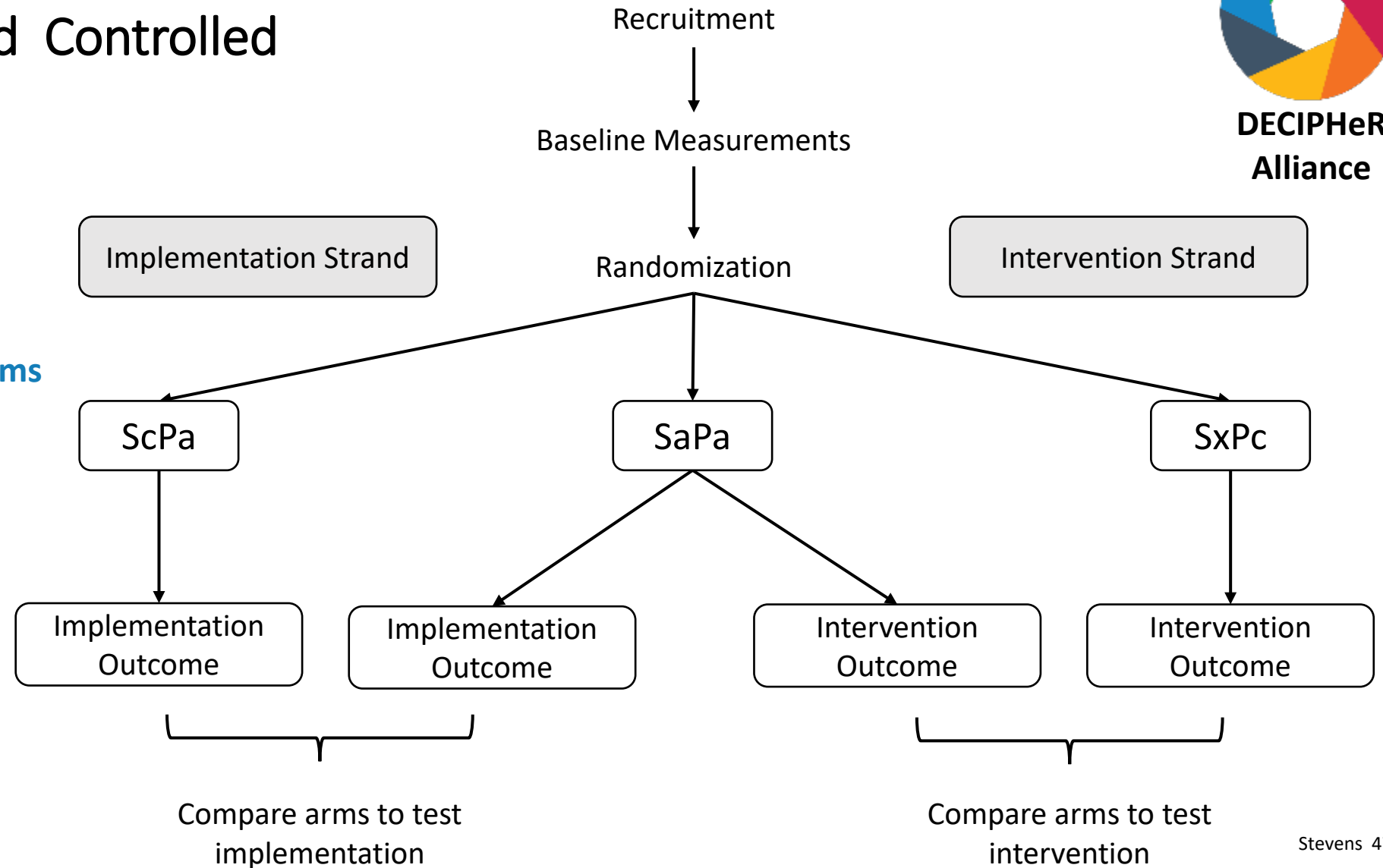
- Enhanced education and coaching to support community-based staff in UNC Diet Program (Sa)
- UNC Diet Program (Pa)
- Enhanced education and coaching to support clinic-based staff in Duke Diet Program (Sx)
- Duke Diet Program (Pc)



# DRCT – Dual Randomized Controlled Trial



1. 3 Arms
2. All outcomes in all 3 arms
3. Levels
4. One randomization





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# Prespecified secondary analyses

- In addition to the 2 analyses required to make DRCT, investigators examine many other secondary hypotheses
- One of these will be the impact of the implementation on the health outcome
  - SaPa vs ScPa on the Health Outcome
- This is a very important analysis but is not a requirement of the DRCT design.





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DRCT =

- SaPa vs ScPa effect on **implementation** outcome  
and
- SaPa vs SxPc on **health** outcome

An Option

Effect of implementation on health outcome=

SaPa vs ScPa effect on **health** outcome

Can do all those comparisons using the design with 3 arms

# Outline



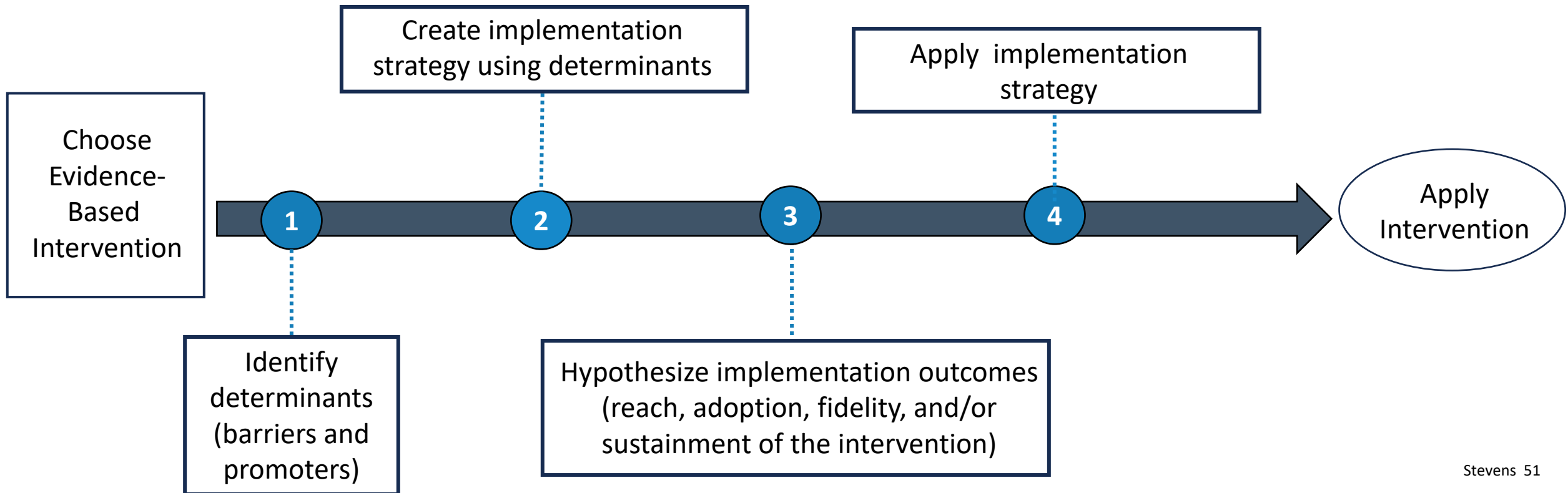
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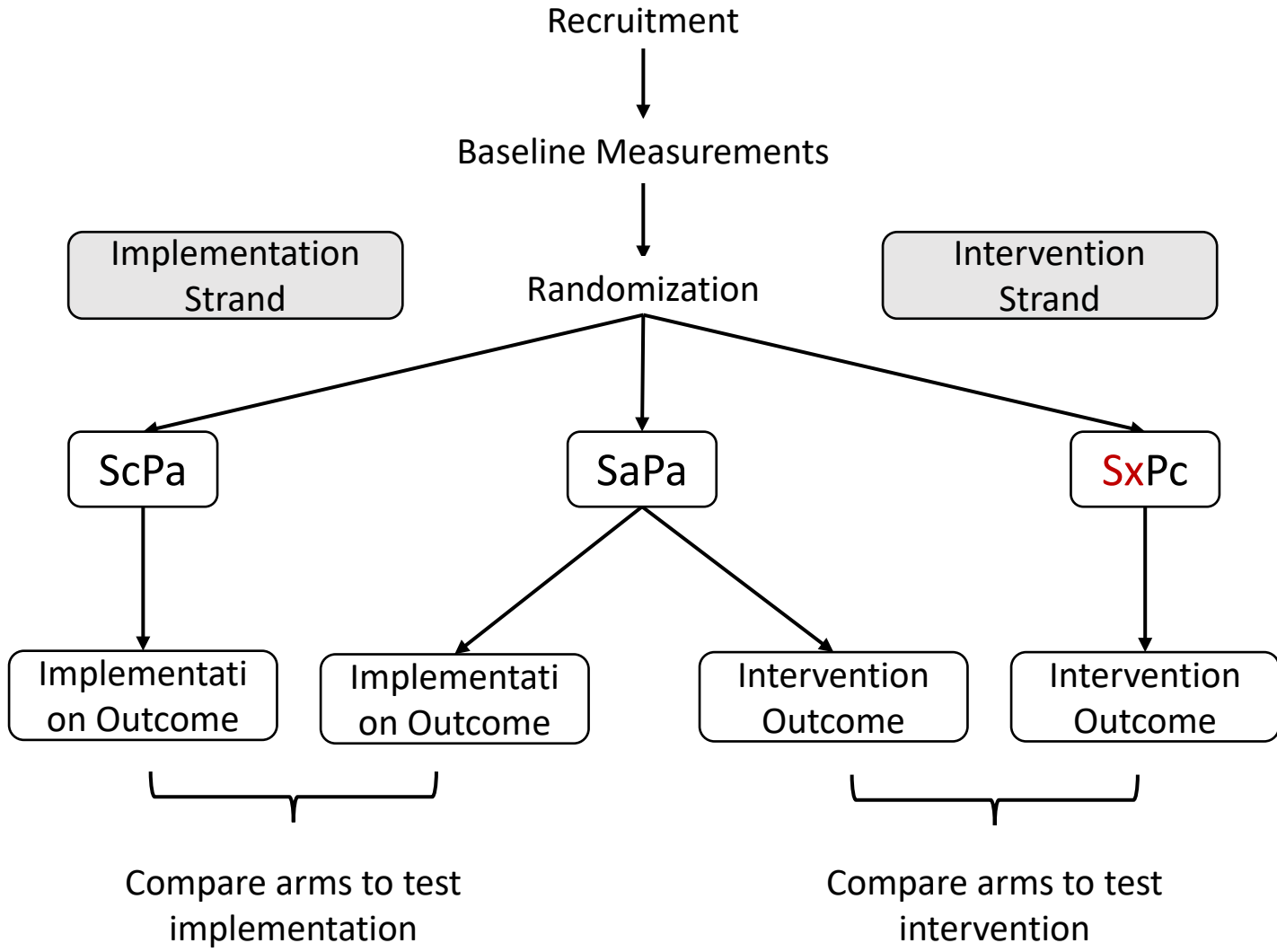
Stevens 50

# Theoretical sequence of implementation study





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Why use Sx instead of Sa or Sc?

Implementation strategies are tailored to the intervention.

### **Pa**

#### **UNC Diet Program**

- One-to-one delivery
- Four online sessions & four booster calls
- Linkage to community care
- Mediterranean diet

### **Pc**

#### **Duke Diet Program**

- Group delivery in specialized clinic
- Eight in-person sessions
- Monitoring of carbohydrate intake
- Low carbohydrate diet

Sc and Sx differ because they are tailored to address barriers distinct to each intervention

## Barriers

### UNC Diet Program

- Engaging public health providers
- Participant confidence
- Health educator beliefs about Mediterranean Diet (e.g., good fats, low sugar)

## Barriers

### Duke Diet Program

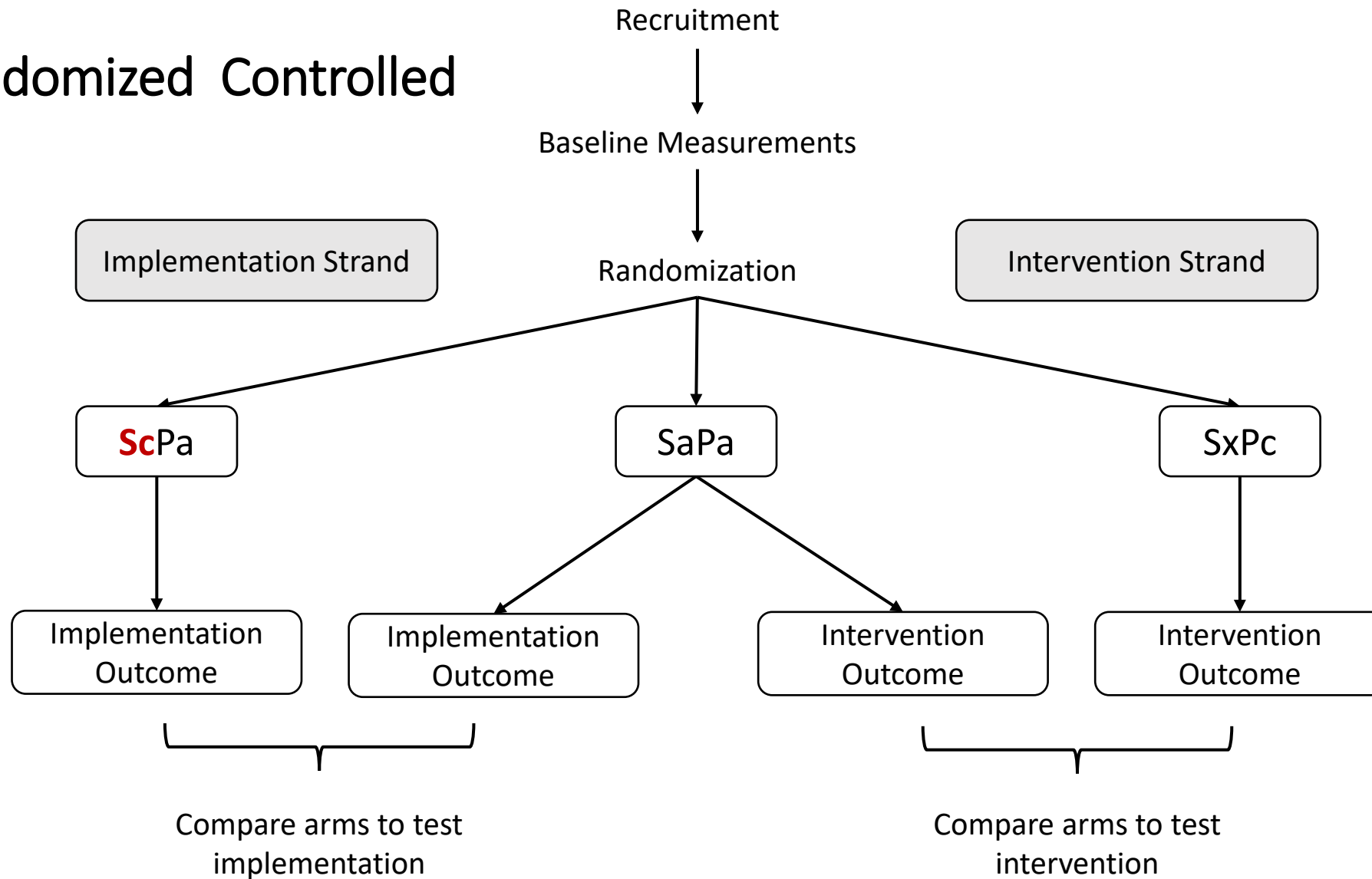
- Transportation
- Child care
- Group dynamics
- Cost of low carb foods



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One more thing about Sc --

# DRCT – Dual Randomized Controlled Trial





## Sc: the control implementation in the Implementation Strand

Generally speaking, **Sc** should **not** be an activity that **is known** will produce (essentially) **no** change in the primary implementation outcome.

Example: An **Sa** strategy is to provide vouchers for a farmers' market to Center Staff and train those staff to distribute the vouchers to participants.

Implementation outcome is % of Center staff who distribute vouchers.

If **Sc** does not include vouchers or training, then the % of Center staff who distribute vouchers **will be** (essentially) zero.

# Conclusion when $S_c$ is likely to produce 0 change in the implementation outcome



- Often is not useful to have control implementation exposure that investigators **already know** is most likely to have no (0) effect on the implementation outcomes.
- Often abandons **equipoise** -- a state of genuine uncertainty on the part of the scientific community regarding the comparative therapeutic merits of each arm in a trial (Freedman 1987) that is key to ethical randomization of participants to treatments (London, 2017).

Why don't we just use a  
factorial design?

# Typical Factorial -- 4 Groups in a 2 X 2



## 1<sup>st</sup> letter

A=Video to discourage smoking

C=Video neutral on smoking

A=nicotine patch

C=placebo patch

## 2<sup>nd</sup> letter

A=nicotine patch

C=placebo patch

		Video	
		A	C
Patch	A	AA	CA
	C	AC	CC

Primary purpose is to determine main effects of each factor and interaction between factors.

**Outcome - Smoking behavior**  
**Same level (participant)**



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# Factorial - 4 Groups in a 2 X 2

Implementation Strategies (S)

		Implementation Strategies (S)	
		A	C
Interventions P	A	SaPa	ScPa
	C	SaPc	ScPc

DRCT  
SaPa vs ScPa  
and  
SaPa vs SxPc



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# 4 Groups in a 2 X 2

Implementation Strategies (S)

		A	C
Interventions P	A	SaPa	ScPa
	C	SaPc	ScPc

DRCT

SaPa vs ScPa  
and  
SaPa vs SxPc

The active implementation (Sa) paired with the control intervention (Pc) results in preparing providers to administer an intervention that is different from the one you want them to administer.



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# 4 Groups in a 2 X 2 (continued)

Implementation Strategies (S)

		Implementation Strategies (S)	
		A	C
Interventions P	A	SaPa	ScPa
	C	SaPc	ScPc

Sc has to make sense with the active intervention, so probably will not make sense with the control intervention.



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# Factorial is not optimal

1. Focus is not on the SaPa the arm the investigator hypothesized is best
2. The links between the implementation and intervention can make some of the implementation and intervention pairs in a factorial not useful.
3. The implementation theoretically comes before the intervention which sets up a potentially causal effect on outcomes
4. Minimum of 4 arms instead of 3 as in the DRCT



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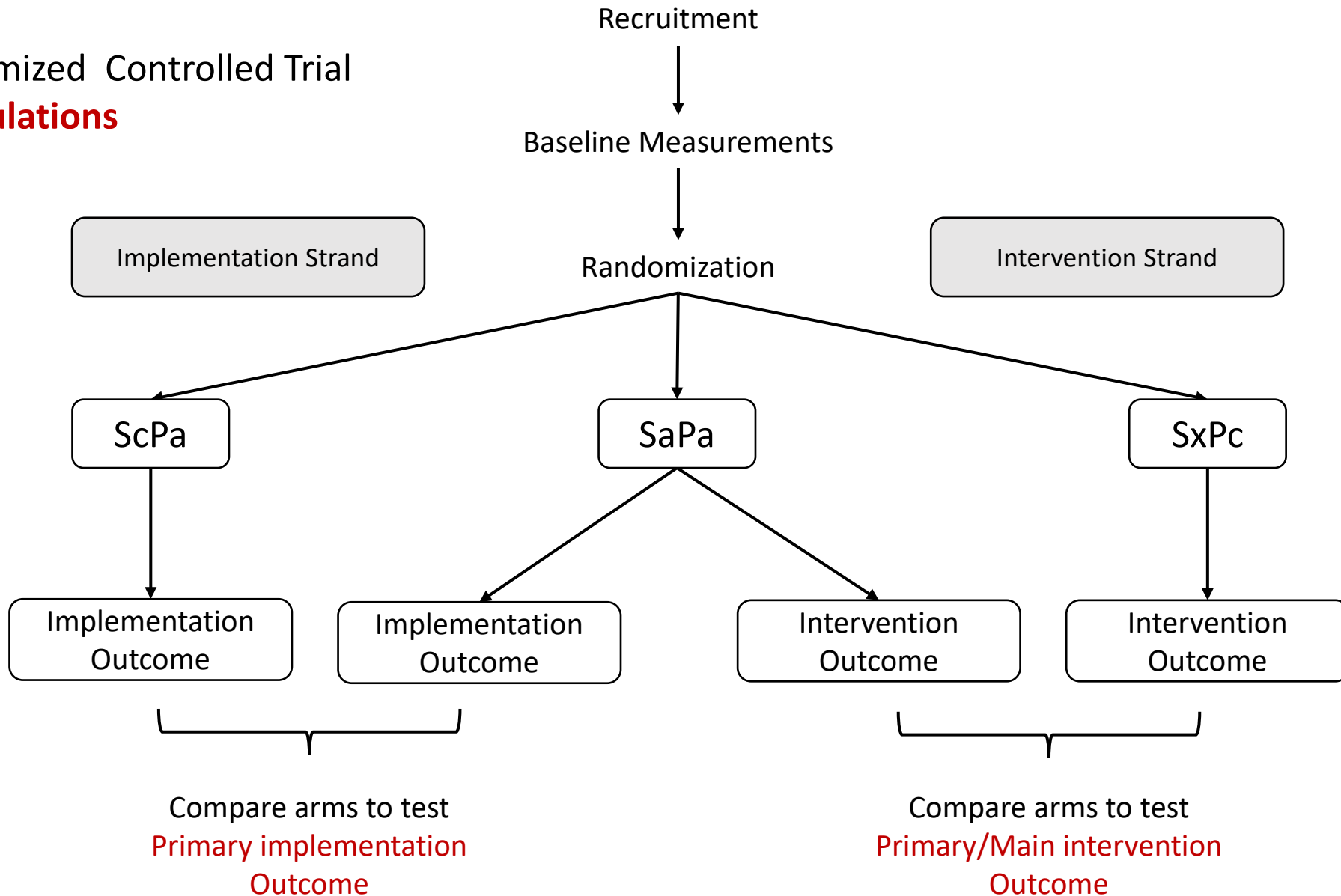
# DRCT –

Dual Randomized Controlled Trial

## Power Calculations



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# Power calculations

- Studies are often (but not always) group or cluster randomized (clinics, schools, churches, community centers etc.)
- The correlations within groups must be accommodated in the statistical analysis
- A group randomized trial often needs to be larger than a trial that randomizes individuals



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# Correction for multiple testing?

- In the power calculation and analysis of a DRCT should the p-value be corrected for multiple comparisons?
- Maduri Raman, Feng-Chang Lin and I are writing a paper on this subject, and I do not want to speak on the topic until the paper is accepted.

# My advice to investigators:



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- Make it a priority to involve a biostatistician in the construction and conduct of the power analysis.

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# Take home messages

- **DRCT is kind of type 2 hybrid study that uses two RCTs: one to examine effects of implementation strategies on implementation outcomes and one to examine effects of the intervention on health outcomes.**
- **A DRCT must have at least 3 arms.**
  - **An active arm**
  - **A control arm for the implementation**
  - **A control arm for the intervention**
- **Each arm has an implementation and an intervention exposure**



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# Take home messages (continued)

- **Important to clearly define and distinguish implementation strategies and outcomes and intervention components and outcomes.**
- **Consider other options for the control exposure ( $S_c$ ) in the control implementation arm ( $S_cP_c$ ) if you have strong certainty that it will cause no change in the implementation outcome.**





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# Take home messages (continued)

- **The implementation strategies must be appropriate to address barriers to the intervention being used**
- **Power the study for both the Implementation and the Intervention primary analyses**

# Closing Thoughts



# For an implementation-focused study, Why do a Type 2 Hybrid Study (instead of a Type 1 or 3)?



- Efficiency of using one study sample to test both implementation and intervention
- Previous research on the intervention may not have been conducted in a pertinent population
- Concerns that adaptation of the intervention may impact its potency
- Previous research on intervention may be lacking or weak



# Why do a DRCT?



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A well-executed, randomized trial avoids bias and offers the strongest causal evidence for finding the truth of a hypothesis.

# Why not do a DRCT?



- Expensive and complicated.
- Sufficient evidence of the effectiveness of the intervention may already be available.
- The study procedures and handling of outcomes that maximizes study goals may result in compromises in RCT methodology that introduce substantial bias.
- The target sample may not find randomization and masking acceptable.

# Guidances



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- Design trials using the CONSORT, StARI and other RCT guidances.
- If your DRCT cannot be in compliance with RCT guidances, consider another study design and/or include a description of the shortfalls in the publication of the work.

Currently,

DRCTs are not often found in the implementation literature.



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**We hope that this work will encourage investigators to use the DRCT design to move forward research on public health practice.**



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U24HL151308



THE UNIVERSITY  
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*at* CHAPEL HILL





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# QUESTIONS