



# FEED THE FUTURE

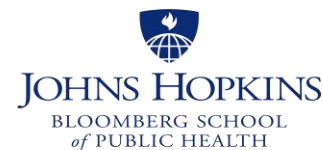
The U.S. Government's Global Hunger & Food Security Initiative

# Research Design – Types of Interventions and Statistical considerations

## Tinku Thomas



**USAID**  
FROM THE AMERICAN PEOPLE



Friedman School  
of Nutrition Science  
and Policy



# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

## U.S. GOVERNMENT PARTNERS





# FEED THE FUTURE

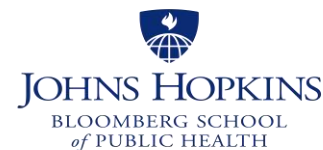
The U.S. Government's Global Hunger & Food Security Initiative

## THIS SESSION WILL COVER

Discuss several aspects of experimental research design

Discuss research design options depending on the research questions/hypothesis

Identify the methods of randomization in intervention studies

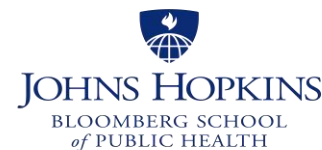


Friedman School  
of Nutrition Science  
and Policy



## EPIDEMIOLOGIC STUDY OBJECTIVES

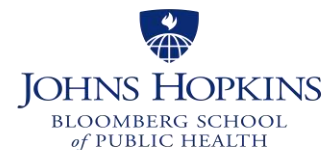
- What are the determinants of health and disease? How common (prevalent) are they?
- How are these determinants arranged –Are there patterns we can discover?
- What is the relationship of the determinant(s) to the health/disease of the people being studied?





## THE ROAD TO CAUSAL PATHWAY

- If we know the **causal pathway** to illness, we can **remove** factors that cause disease (prevention), or better treat disease (treatment) when it occurs.
- Often a string of studies provides proof—
  - Case report or case series
  - Cross sectional studies
  - Cohort or nested case control studies
  - Intervention studies
- These provide descriptions of disease, studies of diet, of environment, behavior of people.
- They form a coherent whole (consistency) despite different study designs.



Friedman School  
of Nutrition Science  
and Policy



# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

## Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies

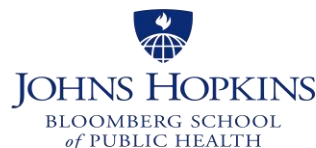
Russell J de Souza,<sup>1,2,3,4</sup> Andrew Mente,<sup>1,2,5</sup> Adriana Maroleanu,<sup>2</sup> Adrian I Cozma,<sup>3,4</sup> Vanessa Ha,<sup>1,3,4</sup> Teruko Kishibe,<sup>6</sup> Elizabeth Uleryk,<sup>7</sup> Patrick Budykowski,<sup>4</sup> Holger Schünemann,<sup>1,8</sup> Joseph Beyene,<sup>1,2</sup> Sonia S Anand<sup>1,2,5,8</sup>

*BMJ* 2015;351:h3978

**Results** For saturated fat, three to 12 prospective cohort studies for each association were pooled (five to 17 comparisons with 90 501-339 090 participants). Saturated fat intake was not associated with all cause mortality (relative risk 0.99, 95% confidence interval 0.91 to 1.09), CVD mortality (0.97, 0.84 to 1.12), total CHD (1.06, 0.95 to 1.17), ischemic stroke (1.02, 0.90 to 1.15), or type 2 diabetes (0.95, 0.88 to 1.03). There was no convincing lack of association between saturated fat and CHD mortality (1.15, 0.97 to 1.36;  $P=0.10$ ). For trans fats, one to six prospective cohort studies for each association were pooled (two to seven comparisons with 12 942-230 135 participants). Total trans fat intake was associated with all cause mortality (1.34, 1.16 to 1.56),



**USAID**  
FROM THE AMERICAN PEOPLE



Friedman School  
of Nutrition Science  
and Policy



# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

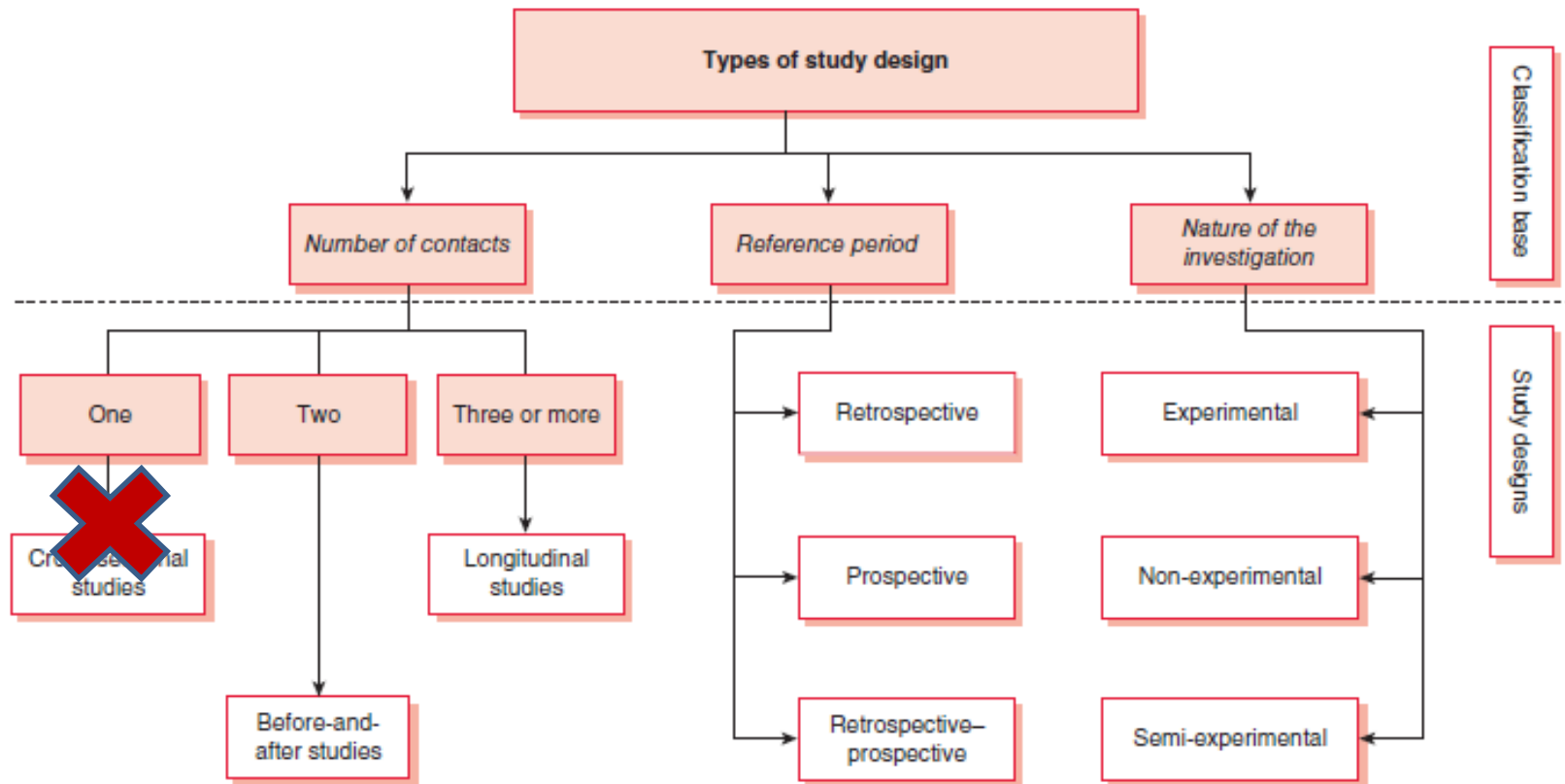


Figure 8.1 Types of study design

Kumar, Ranjit. *Research Methodology: A Step-by-Step Guide for Beginners, 4th Edition*. Sage Publications (UK), 01/2014. [Bookshelf Online].



**USAID**  
FROM THE AMERICAN PEOPLE



**JOHNS HOPKINS**  
BLOOMBERG SCHOOL  
of PUBLIC HEALTH

**Tufts**  
UNIVERSITY

Friedman School  
of Nutrition Science  
and Policy



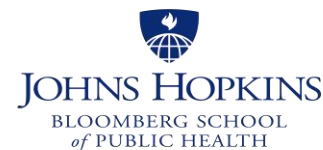


# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

## THE THEORY OF CAUSALITY

- There can be multiple causes for an outcome, modifiable and non-modifiable
- The focus would be on the modifiable/intervenable causes
- Pre-requisite for intervention is establishing causality
- A conceptual framework is helpful to help understand causality
- Appropriate study design help determine and **isolate the impact** of select causes
- Ascertain the impact of causal variables and effect of intervention on outcome validly, objectively and accurately

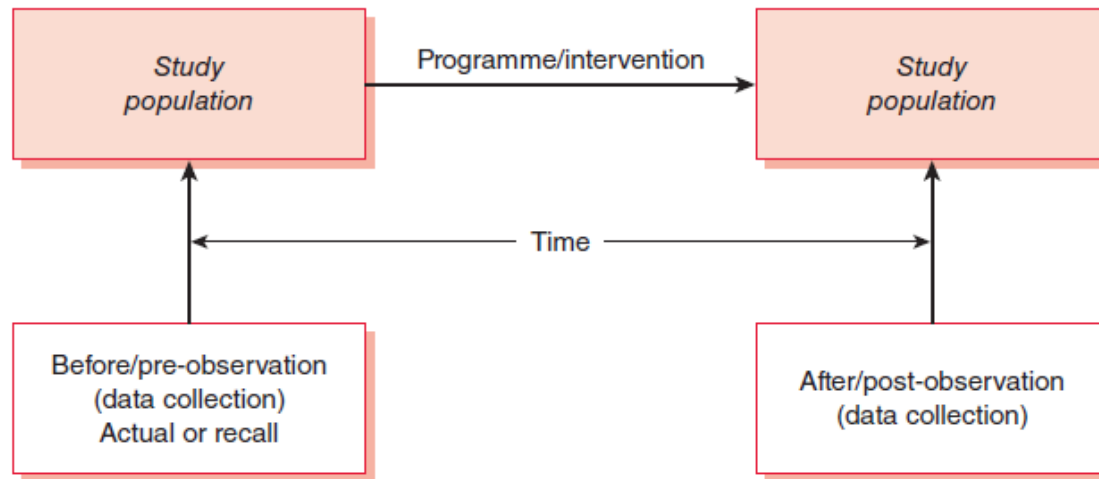


Friedman School  
of Nutrition Science  
and Policy





## Before and after study design



**Figure 8.2** Before-and-after (pre-test/post-test) study design

Kumar, Ranjit. *Research Methodology: A Step-by-Step Guide for Beginners, 4th Edition*. Sage Publications (UK), 01/2014. [Bookshelf Online].



**USAID**  
FROM THE AMERICAN PEOPLE



**JOHNS HOPKINS**  
BLOOMBERG SCHOOL  
of PUBLIC HEALTH

**Tufts**  
UNIVERSITY

Friedman School  
of Nutrition Science  
and Policy



# FEED THE FUTURE

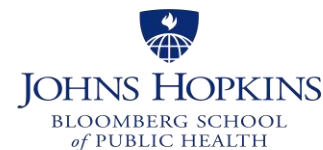
The U.S. Government's Global Hunger & Food Security Initiative

## EXAMPLE: BEFORE AND AFTER STUDY DESIGN

- Intervention: Mandatory iron fortification of salt
- Outcome: Prevalence of anaemia
- Population: Women in reproductive age group



**USAID**  
FROM THE AMERICAN PEOPLE



Friedman School  
of Nutrition Science  
and Policy

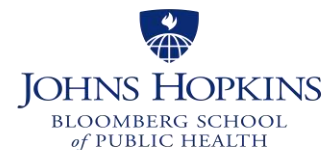


# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

## ADVANTAGES AND DISADVANTAGES

- Measure change in outcome (Eg: Prevalence of anaemia reduced by 10%)
- Measures total change, cannot ascertain whether independent or extraneous variables are responsible for producing change in the dependent variable.
- Because of time-lapse there could be an effect of maturing of the population. This is particularly true for young children.
- Sometimes the instrument itself educates the respondents-reactive effect





# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

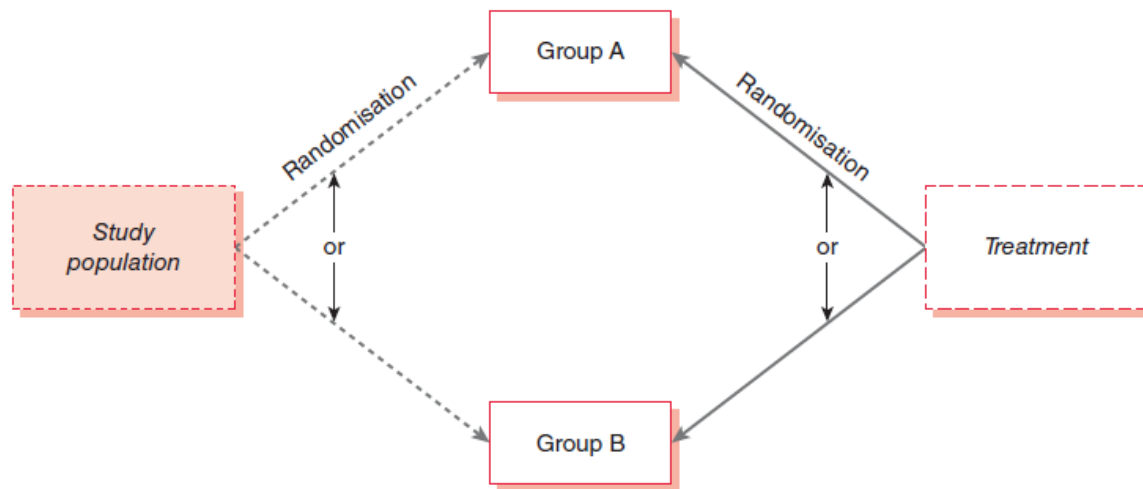


Figure 8.7 Randomisation in experiments

Kumar, Ranjit. *Research Methodology: A Step-by-Step Guide for Beginners, 4th Edition*. Sage Publications (UK), 01/2014. [Bookshelf Online].



**USAID**  
FROM THE AMERICAN PEOPLE



**JOHNS HOPKINS**  
BLOOMBERG SCHOOL  
of PUBLIC HEALTH

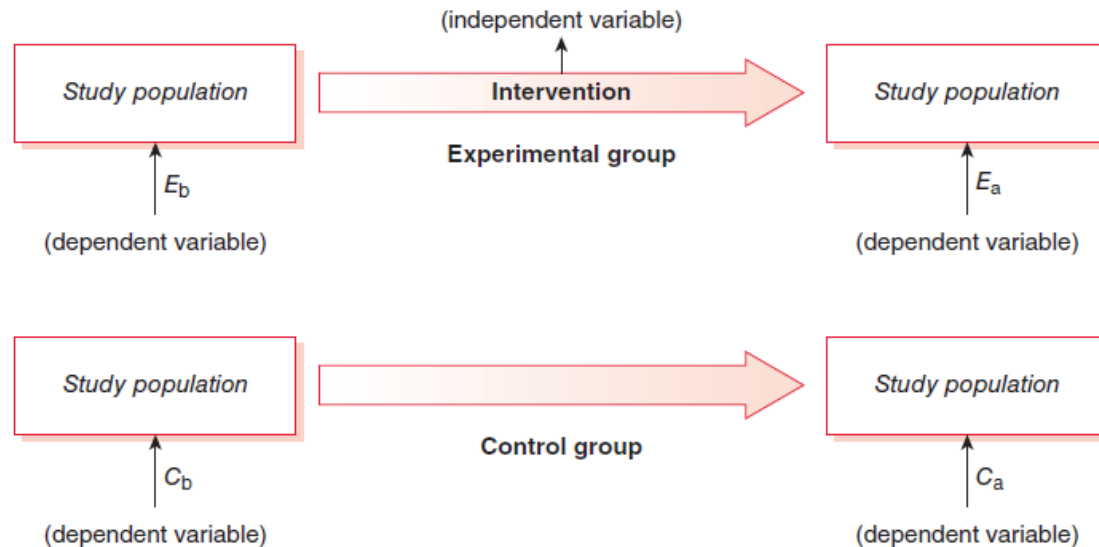
**Tufts**  
UNIVERSITY

Friedman School  
of Nutrition Science  
and Policy



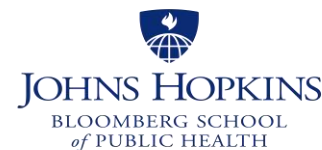
# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative



**Figure 8.10** The control experimental design

Kumar, Ranjit. *Research Methodology: A Step-by-Step Guide for Beginners, 4th Edition*. Sage Publications (UK), 01/2014. [Bookshelf Online].



Friedman School  
of Nutrition Science  
and Policy



# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

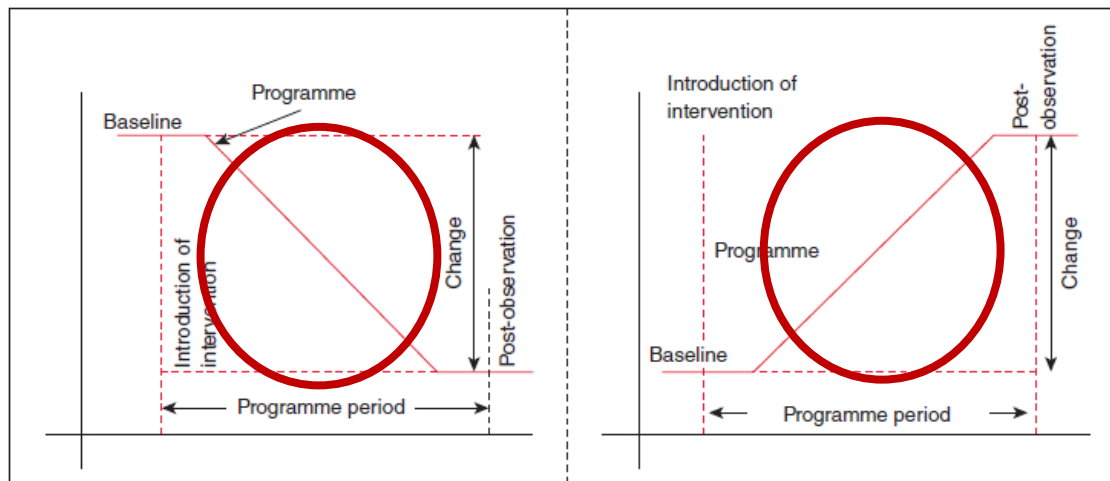
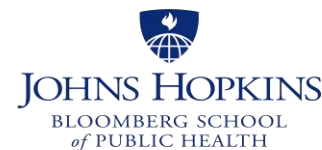


Figure 8.9 Measurement of change through a before-and-after design

- Effect is  
Change=Endline-Baseline  
Efficacy is  
**Difference in change  
between Intervention and  
control**  
Eg: Change in Hb between  
intervention and control  
Efficacy  $Hb_{diff_{int}}$  vs  $Hb_{diff_{cont}}$

Kumar, Ranjit. *Research Methodology: A Step-by-Step Guide for Beginners, 4th Edition*. Sage Publications (UK), 01/2014. [Bookshelf Online].



Friedman School  
of Nutrition Science  
and Policy

# Effect to evaluate

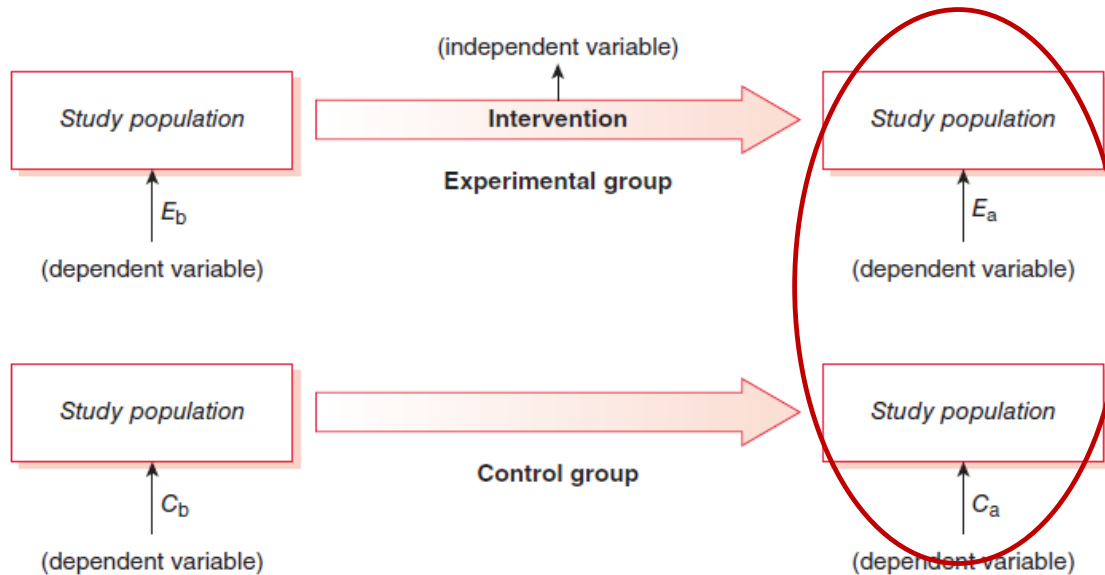


Figure 8.10 The control experimental design

- Effect is **Difference in outcome between Intervention and control**

Eg: Difference in Hb between intervention and control at **Endline**

Eg: Difference in infant cognition between intervention and control after MN intervention for mothers

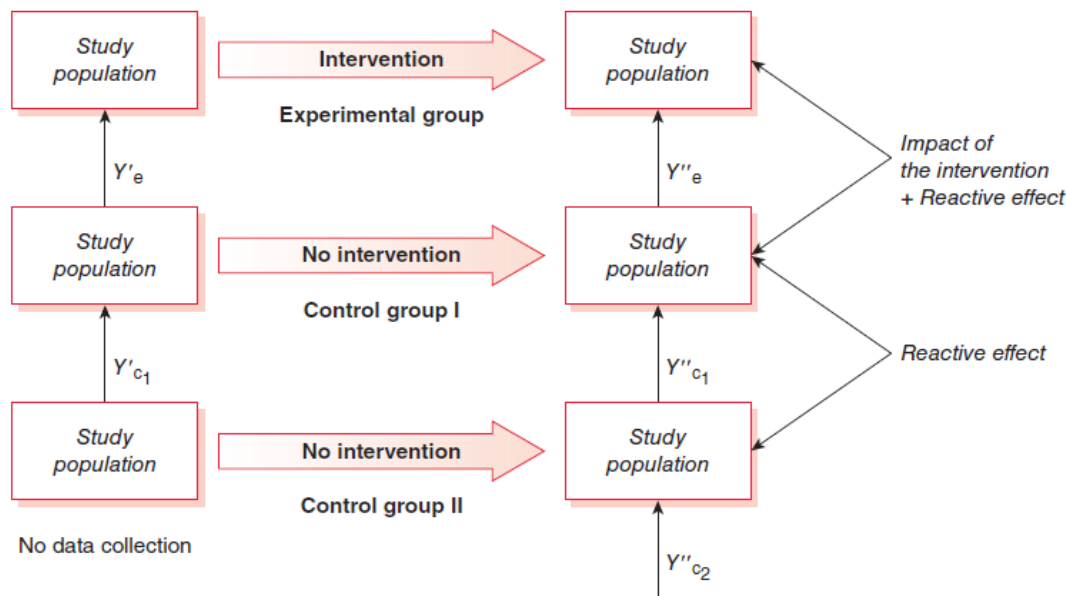
Kumar, Ranjit. *Research Methodology: A Step-by-Step Guide for Beginners, 4th Edition*. Sage Publications (UK), 01/2014 [Bookshelf Online]





# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative



Difference in outcome  
between Intervention group  
and the primary control group

**Eg:** Effect of intervention on  
endurance in children  
Intervention: MN fortified  
drink for school aged children  
Control 1: Isocaloric drink  
Control 2: Nothing

Figure 8.11 Double-control designs

Kumar, Ranjit. *Research Methodology: A Step-by-Step Guide for Beginners, 4th Edition*. Sage Publications (UK), 01/2014 [Bookshelf Online]



**USAID**  
FROM THE AMERICAN PEOPLE



**JOHNS HOPKINS**  
BLOOMBERG SCHOOL  
of PUBLIC HEALTH

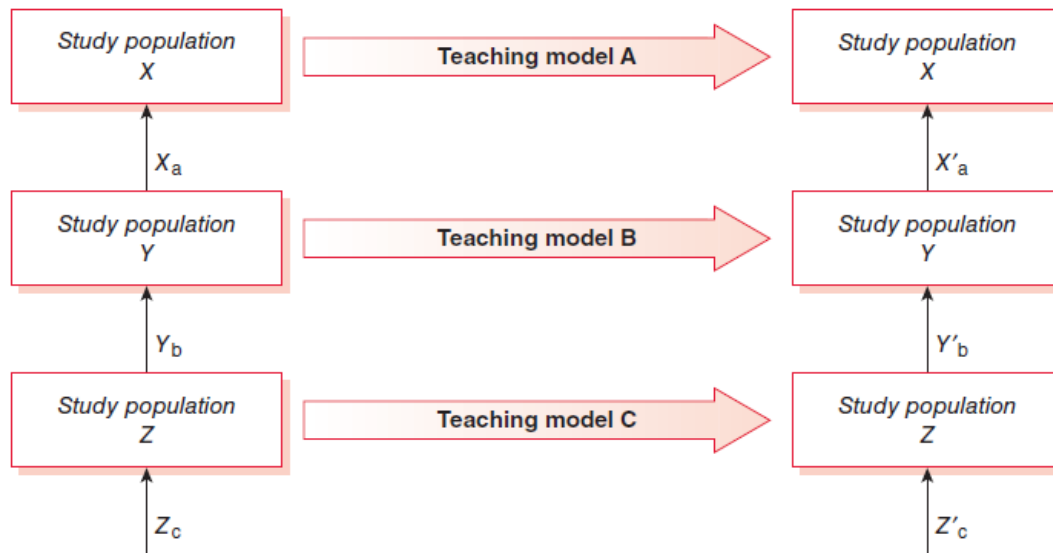
**Tufts**  
UNIVERSITY

Friedman School  
of Nutrition Science  
and Policy



# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative



Difference in outcome between all the different groups

**Eg:** Effect of resistance exercise and whey protein on insulin sensitivity among pre-diabetic

Intervention1: Resistance Exercise  
Intervention2: Whey protein Exercise  
Intervention3: Whey protein+Exercise

Figure 8.12 Comparative experimental design

How many comparisons?

Kumar, Ranjit. *Research Methodology: A Step-by-Step Guide for Beginners, 4th Edition*. Sage Publications (UK), 01/2014 [Bookshelf Online]



**USAID**  
FROM THE AMERICAN PEOPLE



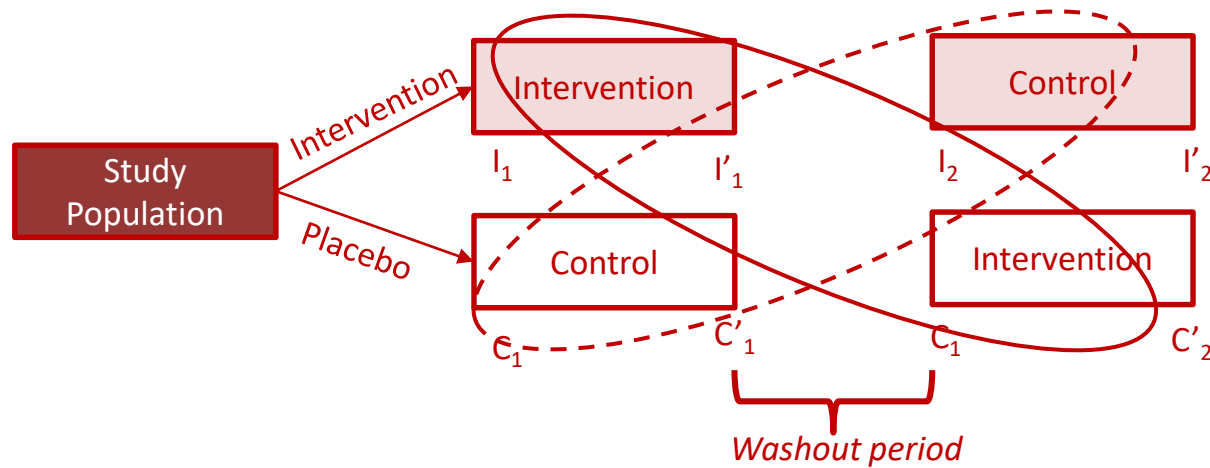
**JOHNS HOPKINS**  
BLOOMBERG SCHOOL  
of PUBLIC HEALTH

**Tufts**  
UNIVERSITY

Friedman School  
of Nutrition Science  
and Policy



## Cross-over trials



Effect would be pooled intervention effect-pooled control effect  
Eg: Trial to find effect of rice bran oil vs vegetable oil on lipid profile

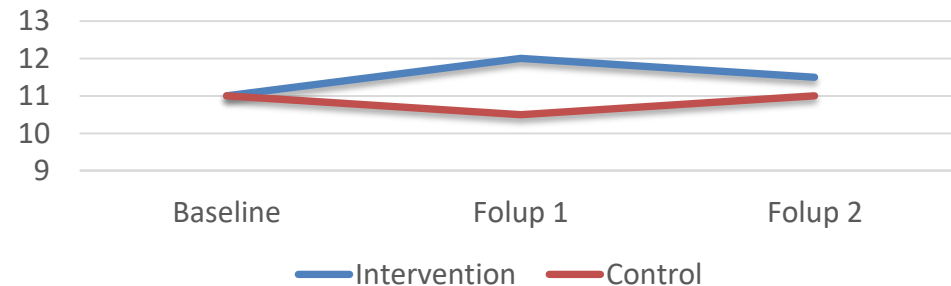


## Trials with multiple follow up visits



- Useful when the intervention is for a long period of time
- When natural changes are expected at different points of time during intervention period
- Additional data is helpful when large dropout rate is expected
- Eg: Studies in children, pregnancy

### Hb in pregnancy



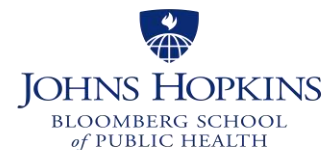


# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

## COMMUNITY INTERVENTION TRIALS

- Groups or clusters are randomly allocated to groups
- Eg: multiple RUFs trial on MAM.
- Intervention is delivered at cluster level
- Outcome is measured at individual level
- Cluster effects adjusted in sample size and data analysis



Friedman School  
of Nutrition Science  
and Policy

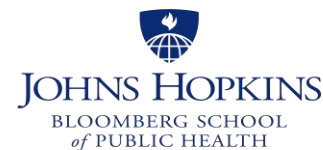


# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

## ADVANTAGES AND DISADVANTAGES OF EXPERIMENTAL STUDIES

- Can examine cause effect relationship
- Can ascertain causality
- More expensive and more difficult to implement as at least two contacts are required.
- Longer time to complete-need to wait until intervention is completed or achieved reasonable coverage before collection of the second set of data.
- Attrition in the study population



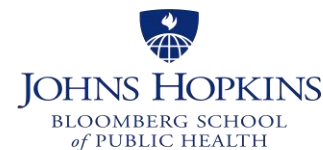


# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

## WHY RANDOMIZE?

- Participants in various groups should not differ in any systematic way..
- Proper randomization ensures no a priori knowledge of group assignment and allocation concealment
- The ideal way of balancing covariates among groups is to apply sound randomization in the design stage of a clinical trial instead of after data collection.
- Random assignment is necessary and guarantees validity for statistical tests of significance that are used to compare treatments



Friedman School  
of Nutrition Science  
and Policy



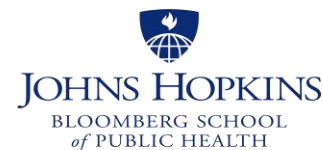
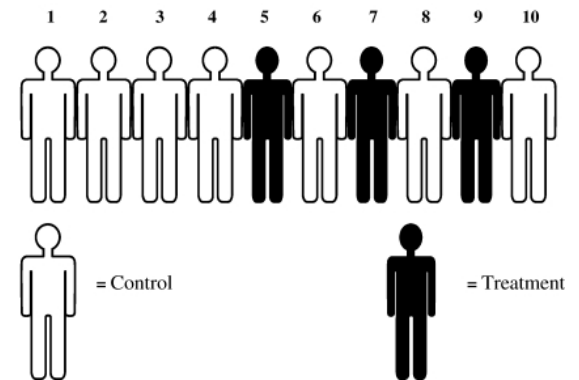


# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

- **Simple Randomization**
- Simple sequence of random assignments
- Problem of imbalance at intermediate stages of the study
- Not a big problem in large sample studies
- Eg: If there is more drop out among the last set of recruits, can result in imbalance if the initial part of list is not balanced

First 10 assignments



Friedman School  
of Nutrition Science  
and Policy

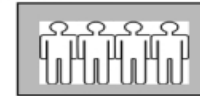


# FEED THE FUTURE

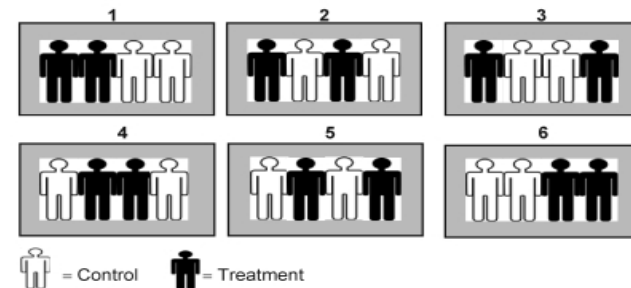
The U.S. Government's Global Hunger & Food Security Initiative

- Block Randomization-random allocation within blocks
- It is possible to vary the block length, again at random, perhaps using a mixture of blocks of size 2, 4, or 6-  
Permuted block design

A) Block size



B) Possible balanced combinations (ie, 2 to control group, 2 to treatment group)



**USAID**  
FROM THE AMERICAN PEOPLE



**JOHNS HOPKINS**  
BLOOMBERG SCHOOL  
of PUBLIC HEALTH



**Tufts**  
UNIVERSITY

Friedman School  
of Nutrition Science  
and Policy



# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

- Stratified Randomization-The stratified randomization method addresses the need to control and balance the influence of covariates
- Eg: random allocation within each strata such as normal weight male

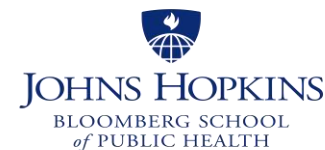
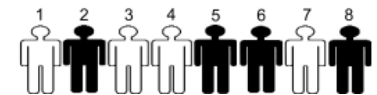
2 Covariates:

Sex (2 levels: male, female)  
Body mass index (3 levels: underweight, normal, overweight)

		Sex		Marginal total
		Male	Female	
Body mass index	Underweight	7	5	12
	Normal	8	8	16
	Overweight	7	5	12
Marginal total		22	18	40

Random assignment of "male" and "normal"; simple randomization by flipping a coin

 = Control  = Treatment



Friedman School  
of Nutrition Science  
and Policy



# FEED<sup>THE</sup>FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

## OTHER CONSIDERATIONS

- Random allocation concealment
- Random list generation-Graphpad



**USAID**  
FROM THE AMERICAN PEOPLE



**JOHNS HOPKINS**  
BLOOMBERG SCHOOL  
of PUBLIC HEALTH

**Tufts**  
UNIVERSITY

Friedman School  
of Nutrition Science  
and Policy



# FEED<sup>THE</sup>FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

[www.feedthefuture.gov](http://www.feedthefuture.gov)

