Overcoming Human Nature to Enhance Plausibility of Causal Inference through Study Design

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1

2

Human nature

"What we know from people's behavior is they will make a decision where they can minimize costs, which includes either money or their time or their effort, to maximize results. It's human nature. We treat that like it's laziness, but we all do it on a regular basis."

David Lankes, USC Library and information Science. USCTIMES, February 2017.

3

Establishing causality

- Design
- Accumulation of evidence
- Understanding the phenomena

4

Clinical Trial

- Human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. (NIH)
- Makes the causal direction clear because the investigators assign the condition rather than participants selecting the condition.
- Plausibility of inference depends on design (e.g., counterfactual, randomization)
- Have to be registered (e.g., clinicaltrials.gov) and reported according to guidelines (CONSORT)

Selection issues related to data system

Honduras study (Cohen et al.,1994)

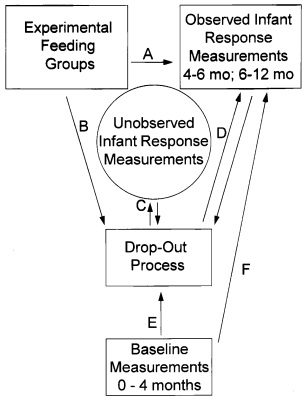
- Examined effects of introducing complementary foods at 4 versus 6 months
- Infants randomized to three groups
  - Breast-feeding ad libitum
    Received solid food starting at 4 months
    (n=47)
  - Maintained breast-feeding frequency
    Received solid food starting at 4 months
    (n=44)
  - Exclusive breast-feeding to 6 months
    Received no solid foods until 6 months
    (n=50)
- Solid food hygienically prepared and nutritionally adequate
- Multiple infant and maternal responses examined

	EBF	SF
Dropout	13	10
Completed	50	91
Total	63	101
% Dropout	21	10

P-value: 0.052

Frongillo and Habicht (1997)

	Drop-Out Process Depends On:			
Type	Missing Resp	Observ Resp	Fixed Covar	Rand Coeff
MCAR				
Cov-Dep			●	
Missing Rand		●	●	
NI Resp Based	●	●	●	
NI Rand Coeff Based			●	●



Frongillo and Rowe (1999)

Reason	EBF	SF
Moved	0	4
Went back to work, used milk substitutes	4	1
Refused permission to continue	5	4
Other reason	1	0
"Insufficient milk"	1	0
Intro. other food or fluid	1	0
Not follow procedures	0	1
Husband took baby, fed by bottle	1	0
Total	13	10

Comparison of drop-out and completed subjects in Honduran infant feeding study.

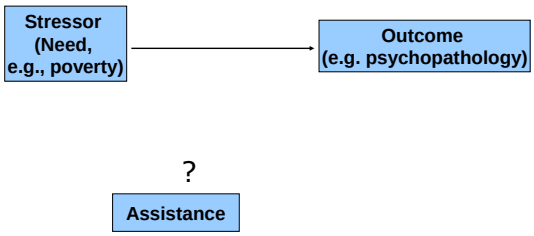
	EBF		SF	
	Drop	Comp	Drop	Comp
Sample size	13	50	10	91
Milk volume 4 mo (g/d)	748 (127)	807 (127)	763 (108)	792 (134)
Weight 4 mo (g)	6476 (682)	6547 (818)	6648 (732)	6354 (768)
Weight gain 0-4 mo (g)	3683 (502)	3691 (591)	3614 (665)	3593 (617)

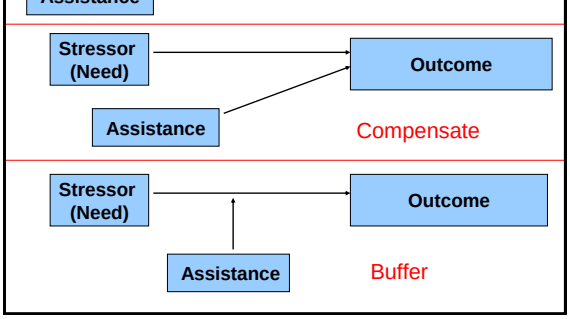
Selection issues related to participation

Concepts and terms for program up-take

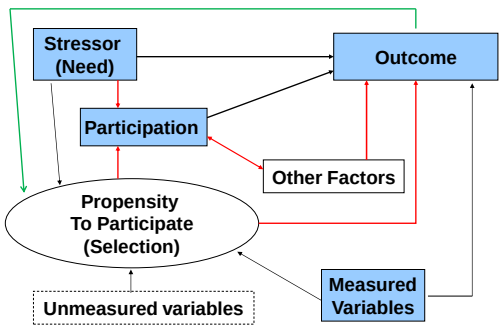
- Compliance
  - Comply: to conform, submit, or adapt
- Adherence
  - Adhere: to bind oneself to observance
- Participation
  - Participate: to take part

14





Compensation model



Definition of counterfactual

- Relating to or expressing what has not happened or is not the case

https://en.oxforddictionaries.com/definition/counterfactual

18

Counterfactual (quoted from Gertler et al., 2011, pp. 34-35)

- The causal impact (α) of a program (*P*) on an outcome (*Y*) is the difference between the outcome (*Y*) with the program (in other words, when *P* = 1) and the same outcome (*Y*) without the program (that is, when *P* = 0).
- We can think of the impact (α) of a program as the difference in outcomes (*Y*) for the same individual with and without participation in a program.
- Counterfactual is what the outcome (*Y*) would have been in the absence of a program (*P*).

19

Counterfactual (quoted from Gertler et al., 2011, p. 35)

- It is relatively easy to obtain the first term of the basic formula ($Y \mid P = 1$)—the outcome under treatment.
- We simply measure the outcome of interest for the population that participated in the program.

20

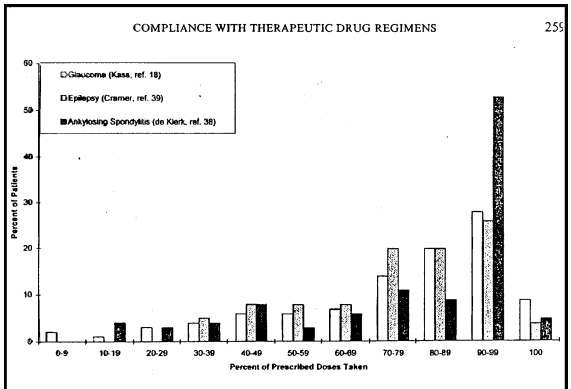
Intention-to-treat vs. per-protocol

- Comparison of intervention groups that includes:
  - all participants as originally allocated (intention-to-treat)
  - only those participants who completed the intervention as originally allocated (per-protocol or as-treated or treatment-on-the-treated)
- *Alive & Thrive* to improve young child feeding
  - Bangladesh, high participation, ITT
  - Vietnam, modest participation, PP (≥1 visits to social franchise)

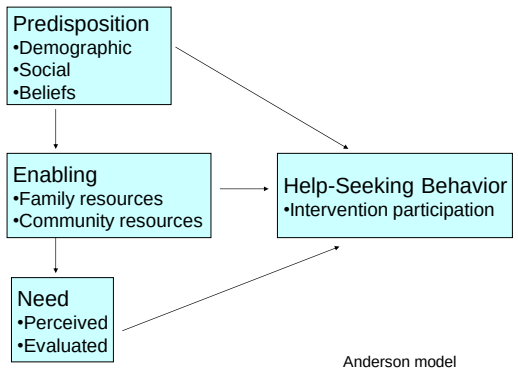
21

Forms of non-compliance

- Taking more or less than prescribed
- Not adhering to treatment schedule
- Withdrawing from treatment
- Taking food or drug or other action prohibited by protocol
- Crossing over to other treatment arm in study
- Increasing dose just prior to follow-up visit
- Taking larger dose to catch-up just prior to follow-up visit
- Relax behavior right after follow-up visit
- Redistribution of treatment dose to others
- Seeking to determine identity of blinded treatment and subsequently changing behavior once known



e.g., iron tablets for pregnant women in Thailand: 2/3 had ≥70% adherence



Anderson model

25

MINIMat Study

- Maternal Infant Nutritional Interventions Matlab
- Randomized control trial comparing something to something else (n=3300)
  - Early vs. usual invitation to food supplement
  - Low-dose iron-folate vs. usual iron-folate vs. low-dose iron-folate plus multiple micronutrients
  - Lactation counseling vs. usual health counseling
- On-going surveillance of reproductive events identified women when 8-10 wk pregnant

MINIMat study design: prenatal interventions

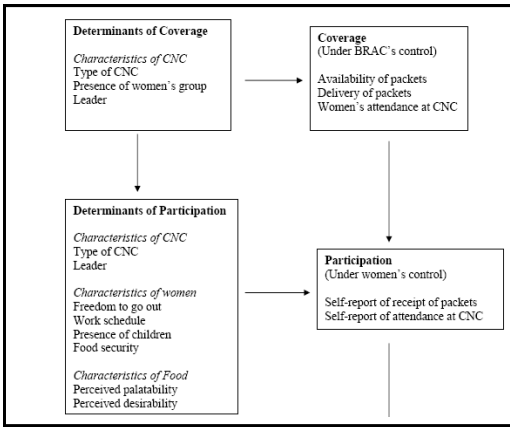
	Micronutrients		
Food supplement	30 mg iron, 400 µg folate	60 mg iron, 400 µg folate	30 mg iron, 400 µg folate, 13 other MN
Early			
Usual			

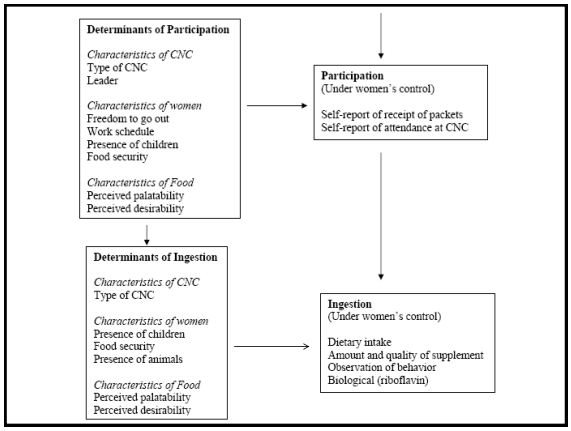
Micronutrient supplements
- Dose monitoring monthly using bottle microchips
- 12 weeks of gestation until 12 weeks postpartum

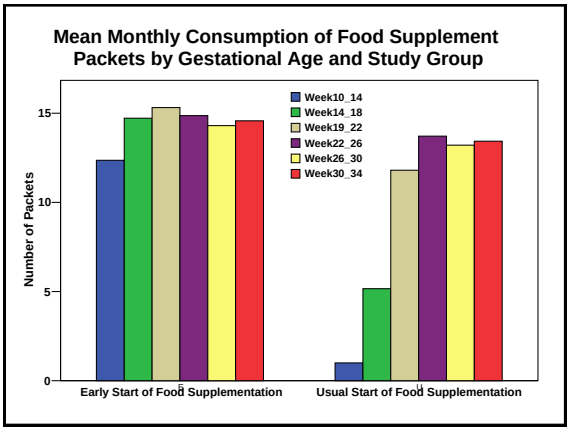
Persson et al. (2012) JAMA

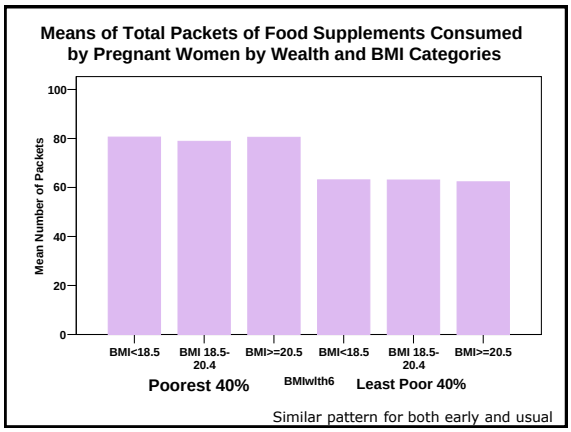
Supplementation center Matlab Bangladesh

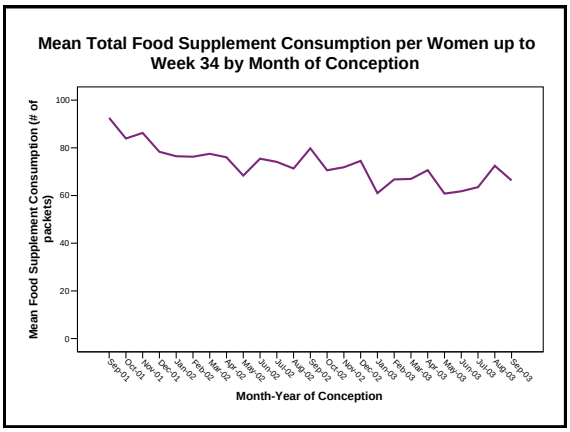
Supplement:
- fried rice powder (80 g)
- fried pulse powder (40 g)
- molasses (20 g)
- soybean oil (12 ml)

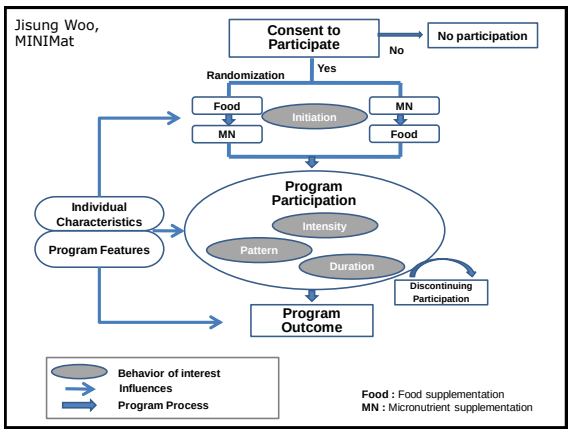












Qualitative study

- Ethnographic study to explore socio-cultural factors affecting the use of nutritional supplements
- In-depth interviews
  - Semi-structured interview guide
  - 24 women previously on program

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Enhanced participation

- Support from family
- Decreased access to food
- Advice from medical professionals
- Positive attitude toward supplementation
- Recognition of the benefits of supplements
- Strong individual intention to consume the supplements

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Inhibited participation

- Perceptions of poor appetite
- Fear of needing a Cesarean delivery caused by a large-sized baby
- Gap between anticipated and experienced benefits of supplements
- Disapproval by husbands and mothers-in-law

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Other findings

- Sharing the supplements with others and replacing home diet with the supplement
- Pregnant women afflicted with potentially two different consequences of consuming supplements: large-sized baby vs. healthy baby
- Some inhibitors with potential to become enhancers through appropriate actions for modifying women's perceptions, where role of medical professionals and family members needs emphasis

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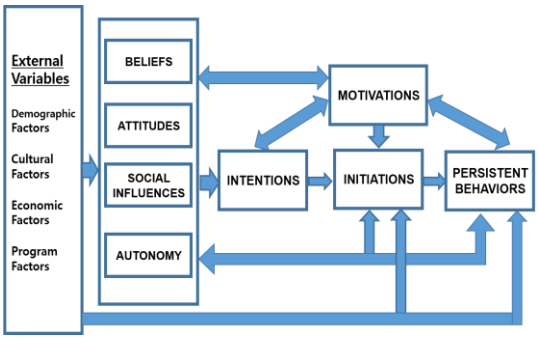
Theoretical model



Quantitative results

- Participants utilized micronutrient more than food supplementation when provided simultaneously
- Shared food supplement with others and often replaced home meals with food supplements
- Participants who started food before micronutrient supplementation showed better participation
- Only 10% of the total participants consumed both types of nutrition supplements persistently

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Quantitative results (continued)

- Women in the early food group where program provider's active recommendation on consumption of food supplements occurred showed greater participation
- Strong cultural perceptions and practices negatively associated with food supplementation
- Women's autonomy showed positive relationships

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Quantitative results (continued)

- Greater utilization of micronutrient supplementation was related to positive perceptions and attitudes toward supplementation
- Influences of husbands on pregnant women's consumption of supplements positively associated with consumption of both types of supplements

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Conclusions

- More attention needed to promote persistent participation
- Cultural concerns and perceptions need to be addressed appropriately
- Enhance autonomy and understanding about supplementation to improve effectiveness through better participation

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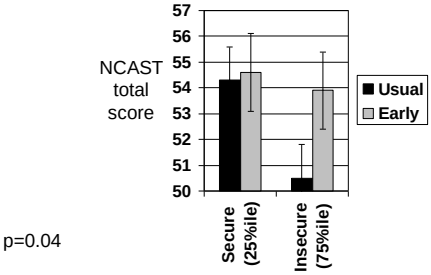
Early vs. usual supplementation and maternal-infant interaction



p=0.04

Frith et al. (2012)

Important to understanding selection biases to obtain information on the attained growth of infants who, despite being eligible, could not be included in the growth curves.

Five Groups

- **Failed to comply**: mother entered study but introduced formula feeding or started smoking two or more weeks after delivery

A. **Refusal to participate**: mother eligible, invited, but refused

B. **Refusal to comply**: mother eligible, invited, but not willing to comply with feeding recommendations

C. **Excluded for formula/smoking**: mother entered study but introduced formula feeding or started smoking within two weeks after delivery

D. **Drop-outs**: mother entered study but later refused to continue

Multicentre Growth Reference Study (WHO)

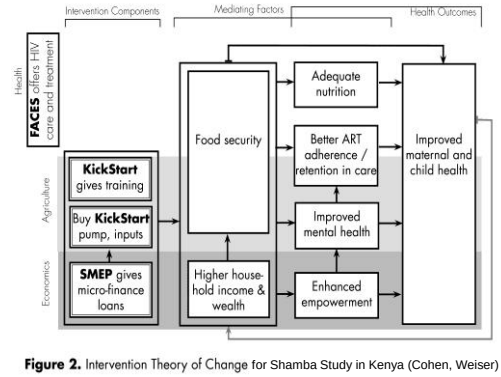


Figure 2. Intervention Theory of Change for Shamba Study in Kenya (Cohen, Weiser)

Shamba design

- Intervention vs. control group
- Cluster-randomized design
  - 8 intervention facilities
  - 8 control facilities
- Facilities matched by pairs
- 44 individuals per facility for total of 352 per group
- Baseline and follow-up every 6 months for 24 months

Inclusion criteria (clinicaltrials.gov)

- HIV-infected
- 18-49 years old
- Currently receiving HAART
- Belong to a patient support group or demonstrate willingness to join a support group
- Access to farming land and surface water
- Evidence of food insecurity, hunger, and/or malnutrition based on last year medical records
- Agree to save down payment (~$7) required for loan and to participate in training

First two intervention sites

- 9 of 88 initially enrolled in first 2 intervention facilities "agreed" to, but did not make, down-payment on loan, so cannot get loan
- Questions raised
  - What does it mean to "agree"?
  - Should these 9 be included?
  - Should these 9 be followed in data collection?
  - Potential selection bias in intervention group that is not in control group?

Lessons

- Humans make choices (i.e., selection) even if we want to make their choices for them
- Process of dropping out (or missing) data collection is different than process of participation
- Assignment to invitation to, or promotion of, participation in intervention may be more realistic than assignment to intervention

Design features to minimize selection: Data system

- Incentives and reasonable burden to keep people in study
- Follow-up of all units regardless of participation
- Collection of qualitative and quantitative data to explain and adjust for selection due to dropout and missing data

Design features to minimize selection: Participation

- Clarity about inclusion criteria that account for likely behavioral choices
- Reasonable prescriptions for, and promotion of, participation in intervention
- Counterfactual group with sufficient similarity in prescriptions to engender similar selection
- Collection of qualitative and quantitative data to explain and adjust for selection due to participation