This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike License. Your use of this material constitutes acceptance of that license and the conditions of use of materials on this site.

Copyright 2009, The Johns Hopkins University and Holly Taylor. All rights reserved. Use of these materials permitted only in accordance with license rights granted. Materials provided “AS IS”; no representations or warranties provided. User assumes all responsibility for use, and all liability related thereto, and must independently review all materials for accuracy and efficacy. May contain materials owned by others. User is responsible for obtaining permissions for use from third parties as needed.

JOHNS HOPKINS
BLOOMBERG
SCHOOL of PUBLIC HEALTH

Optional Section D: Design Choices

Steven N. Goodman, MD, PhD

Summary of Design Choices with Ethical Implications

- Whether or not to do study
- Need for randomization
- Recruitment and eligibility
- Choice of comparison group
  - Placebo?
  - Blinded?
- Endpoints
  - Surrogate?
  - Definitive?

Summary of Design Choices with Ethical Implications

- Methods for determining endpoints
  - Medical records? discharge summaries? etc.
- Length of follow-up
- Sample size
- Handling of drop-out, cross-over, and loss to follow-up

Tale of Two Trials: The Introduction

- Projected perinatal HIV transmission rates under three treatment regimens:

Placebo	40%
Short course	30%
Medium course	20%

Tale of Two Trials: The "Tough Love" Trial

- Group 1
  - Medium course therapy
    - 20% transmission
- Group 2
  - Placebo
    - 40% transmission
- Sample size
  - 50 per group

Tale of Two Trials: The “Compassionate” Trial

- Group 1
  - Medium course therapy
    - 20% transmission
- Group 2
  - Short course therapy
    - 30% transmission
- Sample size
  - 200 per group

“Tough Love” Trial Outcomes

- What happens to the first 400 children?

- “Tough love” trial, N = 50 per group
  - Group 1 (medium course therapy)
    - 20% x 50 = 10 infected children
  - Group 2 (placebo)
    - 40% x 50 = 20 infected children
  - Total = 30 infected children

“Tough Love” Trial Outcomes: The Next 300 Children

- Next 300 given “winning” (medium course) therapy
  - 20% x 300 = 60 infected children

- **Grand total = 90 infected children**

“Compassionate” Trial Outcomes

- What happens to the first 100 children?

- “Compassionate” trial, N = 200 per group
  - Group 1 (short course therapy)
    - 30% x 50 = 15 infected children
  - Group 2: (medium course therapy)
    - 20% x 50 = 10 infected children
  - Total = 25 infected children

“Compassionate” Trial Outcomes: The Next 300 Children

- Next 300, still on the trial
  - Group 1
    - 30% x 150 = 45 infected children
  - Group 2
    - 20% x 150 = 30 infected children
  - Total = 75 infected children

- **Grand total = 100 infected children**

AIDS Multidisciplinary Working Group Suggestion: 1

1. Asking harder questions about whether the medical questions justify an RCT, and whether an RCT is the only way (as opposed to the fastest way) to answer it

AIDS Multidisciplinary Working Group Suggestions: 2, 3

2. Community consultation should be sought in the early stages of trial planning for the purposes of planning, not just approval; IRBs should also include community representatives; get "community consent"

3. All RCTs should have data monitoring boards, pledged to secrecy, with "stopping rules"

Source: Levine et al. (1991). *IRB*, 13, 1–17.

AIDS Multidisciplinary Working Group Suggestion: 4

4. Goals of both investigators and participants should be to provide the best personal care consistent with protocol requirements, and assist participants who wish to alter their participation; consider involving a personal physician independent of the RCT and offering disadvantaged populations the same alternatives available to some others—e.g., an explicit range of options, referral to a private facility or caretaker, medical and social support services equal to or greater than might be expected from a personal physician

Source: Levine et al. (1991). *IRB*, 13, 1–17.

AIDS Multidisciplinary Working Group Suggestion: 5

5. Informed consent is an ongoing process; participants should be made aware of all relevant clinical trial results in a timely and effective fashion, avoiding premature release of unsubstantiated data, or obtain consent for incomplete disclosure

Source: Levine et al. (1991). *IRB*, 13, 1–17.

Conclusion

"I do not believe that heightened resistance here must cripple research, which cannot be permitted; but it may indeed slow it down by the smaller numbers fed into experimentation in consequence. This price—a possibly slower rate of progress—may have to be paid for the preservation of the most precious capital of higher communal life … whose loss, possibly caused by too ruthless a pursuit of scientific progress, would make its dazzling triumphs not worth having. … With all our striving to wrest from mortality what we can, we should bear its burden with patience and dignity."

— H. Jonas, 1969

New Yorker Cartoon

JHSPH OpenCourseWare was not able to secure permission to use this image.