

# Recruitment and Retention

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# Disclaimer

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# Three Aspects of Subject Selection

- A. Selection: determining who is eligible
- B. Recruitment: inviting eligible individuals
- C. Retention: retaining enrolled participants

I will focus on recruitment and retention



# Need to Recruit and Retain

- To be ethical, clinical trials need to collect socially valuable data.
- To collect socially valuable data, clinical trials need to enroll and retain a sufficient number of participants.
- Hence, enrolling and retaining enough participants is ethically important!

# Many Trials Fall Short

- Delays and failures to recruit enough participants undermines many trials.

Treweek et al Cochrane Database Syst Rev 2018;2:MR000013

- Almost half of NCI trials fail to enroll enough subjects for meaningful results.

Kolata. Lack of Study Volunteers Hobbles Cancer Fight. NY Times. 2009

- 44% of randomized trials in the UK fail to enroll a sufficient number of subjects.

Walters et al. BMJ Open 2017;7:e015276

# Need to be Proactive

- These trials raise concern that the risks and burdens faced by individuals who enroll (as well as the resources devoted to the trial) are not justified.
- Trials need to plan in advance how to recruit and retain enough participants.



# Finding the Right Balance

- This is a strong ethical reason to increase recruitment and retention in clinical trials.
- At the same time, individuals get to make their own decisions about research participation.
- Moreover, overly aggressive recruitment and retention are ethically problematic.

# The Wrong Response

- For example, one way to improve retention would be to forbid participants from withdrawing for any reason.
- That would be problematic.
- What are ethically better methods of recruitment and retention?



# SUBJECT RECRUITMENT

Subject recruitment involves active attempts to attract specific individuals within the pool of eligible participants.

# Recruitment for good reasons

- Do not focus recruitment on individuals who are (or appear to be) vulnerable.
- Ensure participants are recruited for reasons of science, not compromised (nor privileged) position.

# Site Impact

- Where a study is conducted can have a significant impact on who enrolls.
- Low inclusion of minority groups in some studies likely traces more to inconvenient study sites than more widely discussed concerns regarding trust in researchers.



# Choosing a Site

- When choosing study sites, researchers should consider the impact on recruitment and retention, and consider how they can go to participants.
- NIH institutes have had study sites at clinics in DC, including the Unity Health Care Upper Cardozo Health Center.

# Methods of Recruitment

Once the sites have been identified, researchers need to recruit participants:

- Solicit referrals from colleagues
- Incentives for referrals
- Incentives for researchers
- Targeted recruitment
- Advertising

# Incentives to Enroll Participants

- Physicians receive payments for referring their patients to trials.
- Investigators are under considerable pressure to recruit participants, sometimes receiving financial incentives.

US Inspector General



# Concerns about Incentives

- Do incentives to refer and recruit patients pose a conflict of interest?
  - To what extent might use of incentives encourage investigators to refer and enroll riskier/inappropriate participants?

# Role of Advertising

- Advertising plays an increasingly important role in recruiting research participants.
- However, there is significant concern about the ethics of advertising, and not much guidance.

# FDA Guidance

- Advertising is “the start of the informed consent and subject selection process.”
- IRBs should determine Ads are: not unduly coercive; do not promise a cure; use appropriate font size and visual effects; explain that test articles are investigational; do not emphasize payment or the amount



# Proposed T.V. Ad

- Thumping music, swirling tie-dye colors:  
“Attention alcohol users...you are a candidate for a new research study.
- We are enrolling men and women, 18-40, to study how alcohol affects the brain.

# Effect of Ads

- Does advertising affect which groups enroll?
- Does advertising affect understanding?
- Does advertising affect subject motivations (does it matter?)?

# Payment

- What role should payment play in recruiting research participants?
- To what extent is it acceptable to advertise payment?
- What does “do not emphasize” payment mean in practice?



# Proposed Bar Coaster

Research Participants Wanted

Earn \$50-\$1295

Call

555-555-5555

# Old Worry

- Many commentators and IRB members express ethical concern over payment.
- In particular, they worry that payments may undermine voluntariness, understanding, or altruism.

Gelinas et al. *NEJM* 2018;378:766-771

Largent, Lynch. *Yale J Health Policy, Law, Ethics* 2017;17:61-82

# Data

- Empirical studies find that: individuals who focused on payment are more likely to understand; greater payment does not lead to greater willingness to take risks; payment does not undermine altruism.

Bentley, Thacker. *J Med Ethics* 2004;30:293-298; Halpern et al. *Arch Intern Med* 2004;164:801-803; Cryder et al. *Soc Sci Med* 2010;70:455-464; Halpern et al *Ann Intern Med* 2010;152:358-365



# New Worry

- The potential to make money may result in participants not being truthful.

Devine et al. *Clin Trials* 2013;10:935-948

Dickert. *Clin Trials*. 2013;10(6):840-841

- For example, they may misreport their history to enroll, or fail to report side effects to stay enrolled.

# Possible Safeguards

- Rely on objective measures in the study.
- Use pro-rated and sequential rather than lump sum payments.
- Don't disclose inclusion/exclusion criteria.

McCaul, Wand. *Alcohol Clin Exp Res* 2018; 42:230–237

Devine et al. *Contemp Clin Trials Commun* 2017;5:67–71

# Other Challenges

- Data suggest that many problems recruiting participants trace to practical concerns: awareness of studies, transportation, parking, child care.
- Who addresses these concerns?



# Difficult to Reach Participants

- Given all the challenges, recruitment efforts may focus on those who are most easy to identify and recruit.
- Yet, more difficult to recruit individuals may differ in scientifically relevant ways.

# Learning Health Care

- Some argue that difficulties recruiting participants trace to current reliance on a “segregated” approach to clinical trials.
- Learning healthcare systems have been proposed as a way to address this concern.

Olson et al. The learning healthcare system. IOM report 2007  
<https://rethinkingclinicaltrials.org/>

# Increased Recruitment?

- Conducting research in the course of providing health care has the potential to increase enrollment.
- To further increase enrollment, some argue consent should be replaced with notification for low risk studies.

Cumyn et al. <https://doi.org/10.1002/lrh2.10206>  
Asch et al. Healthcare 2020; 8:100462



# Research Cohorts

- Alternatively, some have proposed to invite patients to consent to being entered into a pool of potential participants.
- Those who are eligible for a trial will be enrolled, possibly without notification.

# eStudies

- During COVID, use and acceptance of telehealth has increased significantly.
- More reliance on virtual participation might improve research enrollment.

Naito et al. NPJ Parkinsons Dis. 2021;7(1):34.

# Need for Data

- Many trials do not describe their recruitment methods and few studies have assessed which methods are effective.
- Trials that use new methods should evaluate them systematically.

Rosser et al. *CI Trials*. 2022;19:239-250



# Assessment of 4 Methods

Real time screening in electronic medical record: effective

Defer consent for EEG if parents not in the hospital: controversial but effective

Weekend screening: expensive

Expand sites: very effective

# SUBJECT RETENTION

Subject retention involves attempts to keep enrolled participants in the study.

# Retention of participants

- To collect valid data, recruited participants need to be retained.
- Data suggest that enrolled participants can experience problems in their personal lives as a result of their participation in clinical research.



# Obligations

- Some argue that regarding individuals as having an obligation to participate might increase enrollment and retention.

Schaefer et al JAMA 2009; 302: 67–72

- Others worry this approach may actually decrease participation.

# Subjects versus Participants

- Alternatively, to encourage retention it might help to turn research *subjects* into research *participants*?
- Do research WITH individuals, NOT on them.

# Encouragement?

- Participants make vital contributions to research.
- We need to find ways to emphasize this fact, and encourage retention, without undermining voluntariness.



# Results from NIH Participants

- Yes: they tell me that I can withdraw.
- But: they never explain why I shouldn't!

How do we ethically address this concern?

# Treatment and Treats

How people are treated affects their willingness to contribute to joint activities.

- Explain importance of contribution?
- Add perks, like good meals?
- Throw parties?

# Payment Schedules

- Some studies modify their payment schedules to encourage participants to stay in the study: pay more for later procedures; completion bonuses.
- These practices raise their own ethical concerns.



# Some Data

- Regular phone calls did not increase retention.

Glassman et al. Clinical Trials 2020;17:195-201

- Payment, in-person contact, and study flexibility increased retention.

Grape et al. J Adolesc 2018;65:123-132

# Summary

- Recruitment and retention are vital to ethical clinical research.
- The challenges they raise have not received the attention they deserve.

# Further Reading

- Ewing et al. Dev Cogn Neurosci 2018;32:130-137
- Robinson et al. Trials 2016;17(1):294
- Schoeppe et al. Int J Behav Med 2014;21(5):794-803
- Tobler, Komro, Eval Programm Plan 2011;34(2):87-96
- Zook et al. Clin Trial 2010;7(4):400-410
- Robinson et al. J Clin Epidemiol 2007;60(8):757-765
- Villarruel et al. J Spec Pediatr Nurs 2006;11(4):244-250