Recruitment and Retention

David Wendler
Department of Bioethics
NIH Clinical Center

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Three Aspects to 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 must collect socially valuable data.
- To collect socially valuable data, clinical trials must have sufficient completers.
- Hence, having sufficient completers is ethically important!

Problematic Trials

- Over 70% of trials are delayed due to problems with enrollment and many never get enough completers.
- These trials raise ethical concern that the risks and burdens faced by individuals who do enroll (as well as the resources devoted to the trial) are not justified.

Need to Recruit and Retain

- Active recruiting and retention is ethically critical, but overly aggressive recruiting and retention is ethically problematic.
- Need to find the right balance.

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.

Belmont Report

Choosing a Site

- Where research is conducted can have a significant impact on who enrolls.
- Low inclusion of racial minorities in some studies likely traces more to study site than widely discussed concerns regarding trust in researchers.

Standard Methods of Recruitment

- Soliciting referrals from colleagues
- Targeted recruitment
- Advertising

Learning Health Care

- Some argue that difficulties recruiting participants trace to current reliance on a "segregated" approach to clinical trials.
- Learning health care systems, which conduct research in the course of providing care, have been proposed as an alternative.

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 waived for low risk, learning health care studies (e.g. standard care vs guideline-directed care).

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.

Incentives to Enroll Participants

- Investigators are under considerable pressure to recruit participants, sometimes receiving financial incentives.

US Inspector General

- Physicians receive payments for referring their patients to trials.

Concerns about Incentives

- Do incentives to recruit and refer 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

http://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm

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 #1

- Many commentators worry that payments may undermine participant understanding.
- However: studies find individuals who are focused on payment are more likely to understand the risks of research.

Old Worry #2

- Other commentators worry higher payments may be an undue inducement in the sense of leading individuals to enroll despite the risks.
- However: studies find greater payment does not result in individuals failing to be sensitive to the risks.

New Worry

- Payments may increase inaccurate reporting of history and side effects.

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

- Include objective measures in the study?
- Don’t disclose eligibility criteria?

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.

Goldman et al. Cl Trials 2018; 15: 543-550

SUBJECT RETENTION

Subject retention involves attempts to keep participants enrolled for the duration of 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.

Lazovski J, et al. *JERHRE* 2009; 4:89-97

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.

Summary

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

Further Reading

- Glassman et al. Clinical Trials 2020;17:195-201.
- Grape et al. J Adolesc 2018;65:123-132
- 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