Research Involving “Edge” Populations: Ethical and Regulatory Considerations

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Welcome!

Alexandra Shlimovich
Online learning and certification coordinator

Cynthia Gómez, PhD
Founding Director
Health Equity Initiatives
San Francisco State University

Julia Gorey, JD
Public health analyst
Division of Policy and Assurances
Office for Human Research Protections (OHRP)
Department of Health and Human Services (DHHS)
Regulatory Considerations: Populations on the Edge

Julia Gorey, JD
Division of Policy and Assurances, OHRP

Population characteristics

(1) Reduced capacity to make autonomous decisions
(2) Susceptibility to coercion or undue influence
(3) Susceptibility to potential harms

- Homeless
- Substance Abusers
- HIV/AIDS
- Prisoners
- Co-occurring disorders/ overlapping populations

Regulatory basis §46.111(b)

“When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.”
Areas of regulatory concern

- Selection and recruitment of “edge” populations
- Informed consent, and waiver
- Engagement
- Confidentiality and privacy
- Application of subpart C

Selection of subjects

§46.111(a)(3) Selection of subjects is equitable.

“In making this assessment the IRB should take into account the purposes of the research and the setting in which it will be conducted and should be particularly cognizant of the special problems….”

How is the study population related to the purposes of the research?

Subject selection

- Subject population must be justified; beware of “populations of convenience”
- IRBs should not overprotect edge populations so that they are excluded from participating in research which could benefit them
- Principle of justice requires equitable selection of subjects!
Recruitment

“Edge” research may involve non-traditional recruitment settings. Keep in mind:

- IRBs must review recruitment procedures, including any advertising!
  - Recruitment should not be coercive or unduly enticing
  - Research purpose should be up-front, should not make exaggerated or unfounded claims
  - Compensation should ‘fit’ with your catchment area/special populations
- Recruitment material/ads must be consistent with protocol

Informed Consent Process: §46.116(a) & (b)

Key features:
1. Discloses information needed to make decision
2. Facilitates understanding
3. Promotes voluntariness of the decision

OHRP Informed Consent FAQS
http://answers.hhs.gov/ohrp/categories/1566

Informed consent general requirements: §46.116

- Subject or legally authorized representative
- Understandable language
- Opportunity to consider participation
- Minimize coercion and undue influence
- Avoid exculpatory language
Coercion and undue influence

- **Coercion** - an overt or implicit threat of harm
  - EXAMPLE: investigator tells prospective subject that she will lose access to needed health services if she does not participate in the research

- **Undue influence** - an offer of an excessive or inappropriate reward or other overture in order to obtain compliance
  - EXAMPLE: investigator promises a recovering addict time away from a rehab facility if they participate in the research and it is the only way the subject can earn time away.

Waiver of informed consent

45 CFR §46.116(d)

- No more than minimal risk
- Rights and welfare not adversely affected
- Research could not be practicably conducted without the waiver
- Subjects provided with pertinent information after participation

SACHRP recommendations:
http://www.hhs.gov/ohrp/sachrp/sachrpletter013108.html

Waiver of Documentation of IC

§46.117(c)(1) & (2)

The IRB may waive the requirement for a signed consent form if:

- the principal risks would be potential harm resulting from breach of confidentiality and
- the consent document is the only record linking the subject with the research; OR
- no more than minimal risk, no procedures for written consent is required outside research

IRB may require a written statement be given to subjects
Confidentiality and privacy

- §46.111(a)(7) When appropriate, there are adequate provisions to protect the privacy of subjects and the confidentiality of the data
- §46.116(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained

Protecting confidentiality

- Educating research staff
- Limiting access to identifiable data, e.g.,
  - storing research records in locked cabinets
  - password protections
  - encryption
- Substituting codes for identifiers
- Proper disposal of identifiable data/*de-identify" data in timely manner, as appropriate

Confidentiality

- Certificates of Confidentiality issued by NIH, CDC, IHS, HRSA, DOJ, FDA and SAMHSA.
- NIH has website, complete with FAQs: http://grants.nih.gov/grants/policy/coc/
- Mandated reporting
  - HIV testing
  - Suicidal ideation
  - Child abuse
Engagement: §46.103

- Whose staff is getting the informed consent?
- Whose staff is analyzing data? Is it identifiable?
- Is there an FWA?
- Whose IRB is responsible for what?

“In general, an institution is considered engaged in non-exempt human subjects research when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.”

OHRP FAQs:
http://answers.hhs.gov/ohrp/categories/1563

OHRP Guidance:
http://www.hhs.gov/ohrp/policy/engage08.html

Polling slide

As women are admitted to a battered women’s shelter, they’re informed of an HIV research study and given a brochure. Flyers advertising the study are posted within the shelter. At house meetings, shelter staff provide detailed information about the study and hand-out a confidential call-line for women who want to be screened. A shelter staff member is responsible for answering the calls, determining eligibility, and reporting names to research staff who will then do the informed consent.

Is the shelter engaged?

1. Yes
2. No
3. Not sure
Polling slide
As women are admitted to a battered women’s shelter, they’re informed of a research study and given a brochure. Flyers advertising the study are posted throughout the shelter. At house meetings, shelter staff provide detailed information about the study. A shelter staff member with access to intake documentation reviews those records for eligibility criteria, then forwards a list of eligible names to research staff who will do the informed consent.

Is the shelter engaged?
1. Yes
2. No
3. Not sure

What do these studies have in common?
- Hospital visit as opportunity for prevention and engagement for HIV-infected drug users
- Brief intervention for drug-using rural women at high risk for HIV/HCV
- Ending chronic homelessness through permanent housing, integrated treatment, case management, and peer support
- Treatment of PTSD in residents in battered women’s shelters
- Rapid HIV testing and counseling in women in shelters

45 CFR 46, subpart C
Prisoner research FAQs
http://answers.hhs.gov/ohrp/categories/1568
Prisoner research guidance
http://www.hhs.gov/ohrp/policy/prisoner.html
What’s different about “C”?

- The exemptions don’t apply
- Must have a prisoner representative
- Study must fit into §46.306 category
- Must send subpart C certification to OHRP and wait for response before starting research
  - Prisoner research certification
    http://www.hhs.gov/ohrp/policy/populations/prisoncertlet.html
- Triggered regardless of when a subject becomes a prisoner
- Emergency waiver of IC not permitted

Prisoner definition: §46.303(c)

"Prisoner" means any individual involuntarily confined or detained in a penal institution.

- Sentenced under a criminal or civil statute…
- Individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

If a subject becomes a subpart C “prisoner” after enrollment...

The study must be:
1) reviewed by IRB under C
2) certified to OHRP
3) determined to fall into one of the categories

IRB chair can grant temporary approval for the subject to remain on study
Who is not a “prisoner”?

- Voluntarily entered treatment
- Released from prison to halfway houses
- Persons court-adjudicated to attend non-residential treatment programs as alternative to incarceration while living in the community
- Civilly committed due to danger to self or others

Must fit a §46.306(a)(2) category

Category (i)
- study of possible causes, effects, and processes of incarceration and of criminal behavior

Category (ii)
- study of prisons as institutional structures or of prisoners as incarcerated persons

Category (i) and (ii) must be no more than minimal risk.
§46.306(a)(2) categories

Category (iii)
Research on conditions particularly affecting prisoners as a class
Note: Secretarial consultation required

Category (iv)
Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject...
Note: Secretarial consultation required for category (iv) HHS funded research where subjects assigned to control groups may not benefit.

Example of control group issue
Marijuana-Abusing Attention Deficit Hyperactivity Disorder (ADHD) Teens: Atomoxetine Treatment
- Objective to determine whether administering atomoxetine in a therapeutic setting improves ADHD symptoms, retention and progress in substance abuse treatment; involves a SOC comparison arm
- Cat (iv) problem: control group
- Cat (i) problem: greater than minimal risk

§46.305(a)(1)-(5)
1. Permissible category of research (Risk)
2. Possible advantages associated with research participation...are not of such a magnitude that his/her ability to weigh the risks...is impaired (Coercion)
3. The risks are commensurate with risks that would be accepted by non prisoners. (Risk)
4. Selection of subjects within the prison is fair and immune from arbitrary intervention by prison authorities or prisoners. (Recruitment)
5. The information is presented in language which is understandable to the subject population. (IC)
§46.305(a)(6)-(7)

6. Assurance exists that parole boards will not consider research participation in parole decisions; prisoners are informed in advance that participation in the research will not affect parole. (IC)

7. Adequate provision has been made for follow-up care. (Risk)

§46.305(c) Certification requirement

The institution shall certify to the Secretary...that the Board under this section have been fulfilled.

Prisoner research certification to OHRP

1. IRB reviews, makes subpart C findings

2. Institution/IRB sends prisoner research certification letter and research proposal to OHRP*

3. OHRP makes determination regarding categories

4. OHRP sends authorization letter to institution/IRB

On the OHRP website:

Julia Gorey, JD
240.453.8141
julia.gorey@hhs.gov

Prisoner FAQs
http://www.dhhs.gov/ohrp/

May 23, 2003, OHRP prisoner research guidance document
http://ohrp.osophs.dhhs.gov/humansubjects/guidance/prisoner.htm
Collaborating with HIV+ Injection Drug Users

Cynthia A. Gómez, PhD
Director, Health Equity Institute
San Francisco State University

Polling slide
In what role/capacity are you here today?
1. IRB chair
2. IRB director
3. IRB member
4. IRB administrator/coordinator
5. Compliance office/manager/director
6. Investigator
7. Other

Research in context

Rare Cancer Seen in 41 Homosexuals

Doctors in New York and California have diagnosed among homosexual men 41 cases of a rare and often rapidly fatal form of cancer. Eight of the victims died less than 24 months after the diagnosis was made.
Early assumptions

- Gay men
- Commercial sex workers
- Injection drug users

Misinformation

- Ribs

\[ \text{"Agnes, the AIDS business makes me think we should stop sharing needles."} \]

History

- Formative Study 1997-1999
- RCT - Intervention 1999-2005
National partners – INSPIRE
Intervention for Seropositive Injectors: Research & Evaluation

- Centers for Disease Control & Prevention (CDC)
- Health Resources & Services Administration (HRSA)
- New York Academy of Medicine
- University of Miami
- Johns Hopkins School of Public Health
- University of California, San Francisco

Goals of the study

- To reduce sexual and drug use practices that could transmit HIV
- To increase access to and use of HIV primary health care
- To increase access and adherence to HIV treatments

Stigma
Study design

- Each site attempted to recruit 300 HIV+ IDUs with opposite sex partners and a history of IDU in the past year from street and agency venues.
- Eligible participants completed a baseline survey on ACASI and provided blood.
- Participants who came to initial intervention visit were randomly assigned to one of two conditions.
- Participants attended 10 intervention visits.

Study design

- Participants returned for follow-up ACASI survey at 3 months post-intervention.
- Participants returned for follow-up ACASI survey and provided blood at 6 months post-intervention.
- Participants returned for follow-up ACASI survey and provided blood at 12 months post-intervention.
- Some participants returned for qualitative debrief.

Phases of vulnerability

- Prior to study entry
  - Study design
  - Recruitment coercion
  - Consent capacity
  - Retention coercion

- After study entry
  - Assessment content & confidentiality
  - Population/sample bias
  - Recruitment coercion
  - Intervention effects
Population

- Targeted sample of 375 HIV+ IDUs from around the Bay Area
- Recruitment efforts were tailored to ensure diversity in ethnicity, gender and length of positive diagnosis
- Eligibility criteria:
  - Injected within the last 12 months
  - Had sex with an opposite sex partner within the previous 3 months

Recruitment

- Extensive training and safety protocols
- Accessible: passive and referrals; 800-line
- Active: in order to reduce potential embarrassment or inadvertent disclosure of HIV status, the script included the comment, “If this doesn’t apply to you, please give it to someone you know.”

Consent process

- Screening
- Baseline Appointment:
  - HIV documentation and testing
  - Blood draw
  - Tracking
  - ACASI
  - Random Assignment
**Intervention**

- Incentives
- Ground rules
  - Drug use management
  - Timeliness
- Staff ethical guidelines and supervision
  - Boundaries

**Confidentiality**

- Staff sign pledge
- Study ID
- ACASI
- Certificate of confidentiality

**Total number of participants**

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<tr>
<th>Location</th>
<th>Count</th>
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<tr>
<td>Baltimore</td>
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<td>271</td>
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<td>279</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>1161</strong></td>
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Bay Area
Participant characteristics (N = 279)

- Gender:
  - Male 58%
  - Female 34%
  - Transgender 9%

- Race/Ethnicity:
  - African American 65%
  - API/AN 7%
  - Latino 18%
  - White 10%

- Education:
  - Less than H.S. 32%
  - H.S. diploma 35%
  - Some college+ 33%

- Ever incarcerated:
  - 71%
  - In last 6 months: 73%

- Age:
  - 42 years old (average)
  - (Range: 24-58)

Conclusion

- It is important to reach the most disenfranchised
- Early input from community advisors improves sensitivity to population needs
- Detailed protocols are needed for all phases of a study – better to have it and not need it
- In-depth training for all staff is essential throughout life of a study
- Research with edge populations can be done effectively with respect, proper ethical considerations and strong protections

Questions and comments

To submit a question, simply click on the Q & A menu at the top of the screen.

webinars@primr.org
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Please complete the evaluation.

Alexandra Shlimovich
Online learning and certification coordinator

Thank you!