University of California
San Francisco
advancing health worldwide™

Research in disenfranchised and vulnerable populations:
What are the special challenges?

Brie Williams, MD, MS

Professor of Medicine, UCSF Division of Geriatrics

Director, The Criminal Justice & Health Program at UCSF

Director, The Criminal Justice Aging Project, Tideswell at UCSF

2019 NPCRC Webinar

Explore challenges in conducting research with vulnerable populations

…Thru the lens of a participant in the Healthy Aging SF Study

- **The Healthy Aging SF Study is an epidemiologic longitudinal study designed to:**
  - Describe symptoms in older adults in jail
  - Assess the relationship between symptoms, functional decline and community ED use over time
- **Basic study design:**
  - Participants are enrolled soon after they arrive in jail
  - Participants check-in one week after release from jail
  - 6 Monthly follow ups (in jail or in the community)

Meet Mr. Q – a research participant in the Healthy Aging SF Study

62 years old, homeless man

- **Income** – recycles cans
- **PMHx:** DM2, COPD, CHF
- **Geriatric syndromes:**
  - Falls: 3 in 3 months - doesn't know how or why
  - New onset urinary incontinence
- **Substance use:**
  - Tobacco (scavenged butts), ETOH, crack but "I just don't get the same pop from it anymore"
- **Arrested for public urination and drug possession**
  - When trying to explain health problems to arresting officer was charged with resisting arrest
  - Sentenced to 60 days in jail

UCSF University of California San Francisco

Division of Geriatrics

Goals

1. **Define the term “vulnerability”**
2. **Discuss early critical steps in research with vulnerable populations**
   - IRB / CHR approval
   - How to build and train a research team
3. **Identify special considerations in study design**
   - Approach and intake
   - Informed consent
   - Use of incentives
   - Other retention strategies
   - Handling unanticipated events
4. **Remind ourselves that research with vulnerable populations is worth the effort**

UCSF University of California San Francisco

Division of Geriatrics

Goals

1. **Define the term "vulnerability"**
2. **Discuss early critical steps in research with vulnerable populations**
   - IRB / CHR approval
   - How to build and train a research team
3. **Identify special considerations in study design**
   - Approach and intake
   - Informed consent
   - Use of incentives
   - Other retention strategies
   - Handling unanticipated events
4. **Remind ourselves that research with vulnerable populations is worth the effort**

What are "vulnerable populations?"

Many definitions

- **The U.S. Centers for Disease Control:**
  - Racial and ethnic minorities, and others defined by SES, geography, gender, age, disability, risk status related to sex and gender, and others who are at-risk for health disparities

- **Can you be a vulnerable research participant even if you are not among a vulnerable population?**

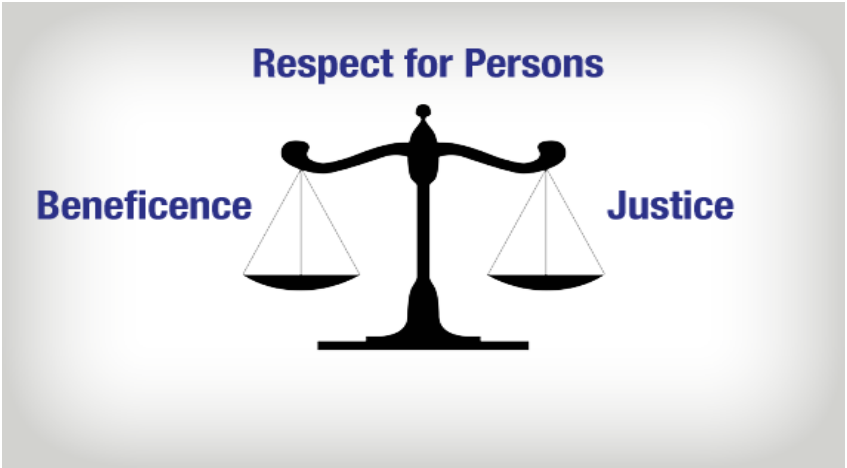
Nuremberg Code introduces concept of "vulnerable research participants"…

- **Nuremburg Code (1949)**
  - Marks first introduction of the concept of *vulnerable populations* in research
  - But "Vulnerability" is not defined
    - Simply a recognition that some people are not able to give true consent

Over time the need for mandatory research guidelines evolves…

Tuskegee Syphilis Study (1932-72)

- **Prompt release of Belmont Report (1979)**
- **Outlines mandatory guidelines for research involving human subjects**
  - 3 core principles:
    - **Respect for persons** (autonomy)
    - **Justice** (reasonable, non-exploitative)
    - **Beneficence** ("do no harm")



Over time the definition of "vulnerable research participants" evolves

- **Belmont Report (1979)**

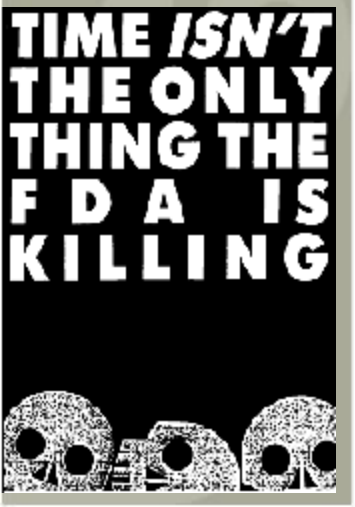
  *"Certain groups, such as racial minorities, the economically disadvantaged, **the very sick**, and the institutionalized may be sought as research subjects, owing to their ready availability in settings where research is conducted.*

  Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research …

Decade following Belmont Report (1980s) AIDS epidemic spreads in the U.S.

- **AIDS – the "gay plague" stigma and discrimination in a vulnerable population**
- **Medical professionals reluctant to study AIDS**
  "I remember calling an ID physician to describe what was occurring. He said 'I don't know what you're making such a big deal of it for. If it kills a few of them off, it will make society a better place.'"

- **ACT UP is formed (1986) demanding:**
  - Access to experimental AIDS treatments
  - Shorter drug approval processes
  - More patients with HIV in more clinical trials…



UCSF
University of California
San Francisco

Division of Geriatrics

Activated "vulnerable" research subjects push for expanded access to research for vulnerable populations

Legacies:

1. **Push for liberalized access** to potentially life-saving but experimental (high-risk) drugs
2. **Demand to reverse protective stance towards research participants** as cause of serious inequities in availability of medical treatments (e.g., no children in research = no pediatric drugs)

UCSF University of California San Francisco

Division of Geriatrics

Who are vulnerable research participants?

Where we are today

- **Research with vulnerable populations is now an established priority of the NIH**
  - ***NIH has called for more research in health disparities***

How do we operationalize the NIH definition of vulnerability?

1. **At its core, definition is about willingness to volunteer and protecting those who are:**
   - Unduly influenced by expectation of benefits
   - Unduly influenced by expectation of retaliation

2. **According to NIH, 1 factor alone rarely defines vulnerability except for:**
   - Pregnant women, human fetuses and neonates
   - Prisoners
   - Children

3. **Some IRBs identify "special" research populations:**

   Students; investigator's staff; **dementia; terminally ill**

UCSF
University of California
San Francisco
Division of Geriatrics

Instead of adding more pre-determined

“vulnerable populations,”

researchers are encouraged to consider

all potentially relevant factors

intrinsic (participant)

and extrinsic (environmental)

to make their own determination of vulnerability

Examples of *potentially relevant* intrinsic and extrinsic factors in determining vulnerability

Vulnerability

Willingness to volunteer unduly influenced by:

- Expectation of benefits
- Expectation of retaliation

Examples of *potentially relevant* intrinsic and extrinsic factors in determining vulnerability

Vulnerability

Willingness to volunteer unduly influenced by:

- Expectation of benefits
- Expectation of retaliation

Intrinsic:

- Race/ethnicity, gender identity, sexual orientation, Income, educational attainment, SES
- Low literacy / low health literacy
- Health status / serious illness
- Vocation, housing, legal status

Examples of *potentially relevant* intrinsic and extrinsic factors in determining vulnerability

Vulnerability

Willingness to volunteer unduly influenced by:

- Expectation of benefits
- Expectation of retaliation

Intrinsic:

- Race/ethnicity, gender identity, sexual orientation, Income, educational attainment, SES
- Low literacy / low health literacy
- Health status / serious illness
- Vocation, housing, legal status

Extrinsic:

- What does the study require?
- Where does the study take place?
- Who is conducting the study?
- Could participation put an individual at risk of retaliation?
- How does the research relate to the standard of care?

UCSF University of California San Francisco

Division of Geriatrics

Goals

1. Define the term “vulnerability”
2. **Discuss early critical steps in research with vulnerable populations**
   - IRB / CHR approval
   - How to build and train a research team
3. Identify special considerations in study design
   - Approach and intake
   - Informed consent
   - Use of incentives
   - Other retention strategies
   - Handling unanticipated events
4. Remind ourselves that research with vulnerable populations is worth the effort

More and more frequently, special IRB panels requested for vulnerable population research

Prisoner example:

1. **A majority of the IRB shall have no association with the prison(s) involved.**
2. **At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity**
3. **Additional OHRP review for NIH-funded prison health studies** - Certification to make sure that regulatory provisions are met

IRB may ask for a Certificate of Confidentiality

- **Document issued by the NIH**
- **Allow investigator to refuse to disclose information on research participants in any:**
  - Civil
  - Criminal
  - Administrative
  - Legislative, or other proceeding, whether at the federal, state, or local level
- **Not ironclad protection, but does offer measure of protection for participants disclosing information about illicit activities**
- **Goal is to promote participation in studies by helping assure confidentiality and privacy to participants**

Applying for Certificate of Confidentiality "C of C"

- **You do not need to have NIH funding to apply**
- **Applications are automatically approved if NIH funding**
  - https://grants.nih.gov/policy/humansubjects/coc/how-to-apply.htm
- **Apply to a specific agency at NIH**
- **Initiate IRB process**
  - In consent forms, note that you are applying for C of C
- **Apply to NIH for C of C with conditional IRB approval**
- **Once your receive C of C, revise consent forms to state you have received approval**

Applying for Certificate of Confidentiality "C of C"

- **You do not need to have NIH funding to apply**
- **Apply to a specific agency**
- **Initiate IRB process**
  - In consent forms, note that you are applying for C of C
- **Apply to NIH for C of C with conditional IRB approval**
- **Once your receive C of C, revise consent forms to state you have received approval**

- **Note: language of C of C (like HIPAA forms) is written at a high grade level and cannot be modified**

The bottom line: IRBs and vulnerable populations

- Many IRBs consider persons with serious or terminal illness to be a “vulnerable” or at least a “special” research population
- As we develop studies for IRB approval, we need to be constantly thinking through how to mitigate vulnerability in study design

First critical steps - Building a Community Advisory Board

Community Advisory Boards

- **Should be formed prior to research plan development**
- **Comprised on interested stakeholders**
  - "Consumers" or individuals from population being studied
  - Representatives from community based organizations, safety net health systems, social services agencies
- **Consumers may need extra training/support to participate**
  - Assign a partner to meet with them prior to meeting and be with them throughout meeting and debrief after to make sure their voice is heard

Tasks of a Community Advisory Board

1. Help with research plan development
2. Staff recruitment (use their network)
3. Interpretation of results
4. Implementation/Dissemination

- Involve Board from the outset
- Meet regularly
- Take steps to insure researchers don't dominate discussion

- NIH funds can be used for stipends and their travel

First critical steps - Building a research team and training a research team

Objectives in building a team:

1. Rapport building and relate-ability with participants
2. Team that can remain faithful to protocol in stressful situations
3. Good at setting / keeping boundaries
4. Cultural sensitivity
5. Comfort discussing difficult topics
6. Active listening skills
7. Knowledge of community

Preventing staff burnout and secondary trauma

Staff is at risk for secondary trauma from hearing participant reports

- **Provide regular space to debrief**
- **Support around difficult issues**
- **Support around staff emotions related to participant trauma, illness, death**

First critical steps - Building a research team and training a research team

Objectives in training a team:

- **Practice:**
  - Develop great familiarity with material - staff more free to be responsive to participants and situations
- **Role playing:**
  - *Emphasis on procedural fairness* - fidelity to study protocols by role play challenging / “unexpected” events
- **Real world, practical experience prior to study:**
  - Senior Ex-Offenders Program staff conducted faux interviews with our research staff
  - Feedback to staff on what they need to change/unexpected landmines
- **Training is never-ending**
  - Regular team meetings provide to discuss challenges…

UCSF University of California San Francisco

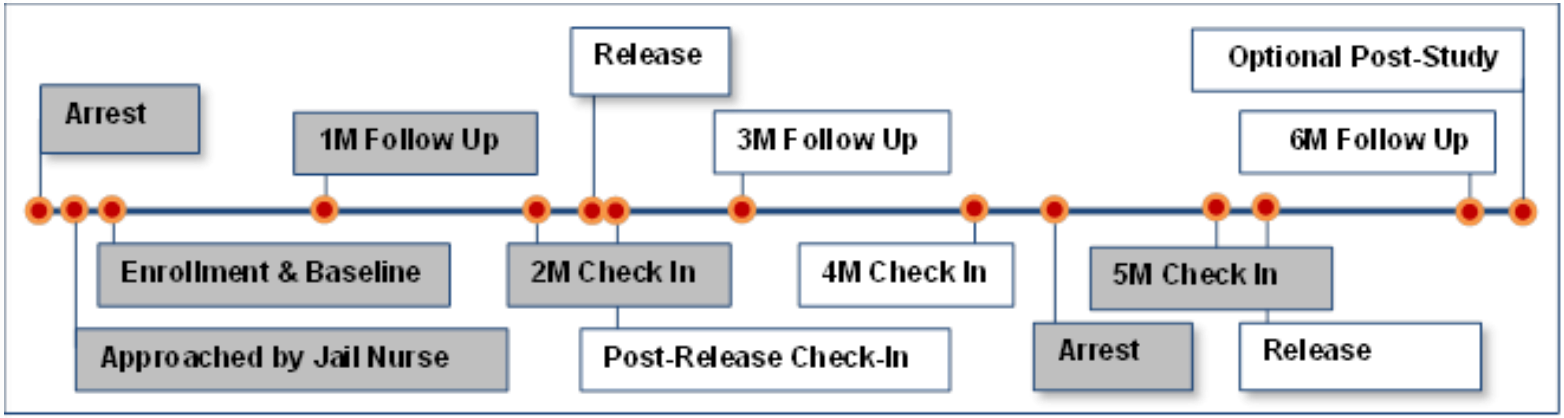
Division of Geriatrics

Goals

1. Define the term “vulnerability”
2. Discuss early critical steps in research with vulnerable populations
   - IRB / CHR approval
   - How to build and train a research team
3. **Identify special considerations in study design**
   - Approach and intake
   - Informed consent
   - Use of incentives
   - Other retention strategies
   - Handling unanticipated events
4. Remind ourselves that research with vulnerable populations is often worth the effort

Designing a study for vulnerable subjects

Mr. Q's 6 months in the Healthy Aging SF Study



Study design: approach and intake

- **Timing of approaching participant about study**
  - *"Timing is everything"*

Study design: approach and intake

- **Timing of approaching participant about study**
  - A jail nurse called our study offices, “We have someone who said he wasn’t interested then, after a day in jail, he said he was interested ONLY if it didn’t mess with his court case.”
  - We found the vast majority get through court within 48 hours
  - Designed our study so that intake starts at 48 hours after admission to jail

Study design: approach and intake

- **Location of interview**
  - *"Location, location, location"*
  - Can mean the difference between an in-depth response to questions or simple yes/no answers and shrugs

Study design: approach and intake

- **Location of interview**
  - The nurse says Mr. Q wants to hear more about the study
  - Mr. Q only wants to be interviewed if other inmates cannot see him speaking to a study staff member
  - Clear that we needed both a confidential, private room and also a closed-door interview room out of view of any other inmates

Study design: Informed consent

- **Confirmation of *informed* consent is critical with vulnerable populations**

Teach-to-Goal Modified Informed Consent is used to address poor comprehension

- **Iterative, educational process**
  - To assess and improve consent comprehension in vulnerable populations with limited literacy
- **The basic steps:**
  1. Participants are read consent form (usu 6th grade level)
  2. Asked to describe procedures or answer questions about study
  3. Misperceptions are corrected before consent
- **Promoted by National Quality Forum and Agency for Healthcare Quality and Research**

McCrady, Bux, 1999; Zetola, et. al, 2008; Coyne, et. al, 2003; Sudore, et. al, 2008.

Study design: Informed consent

Consent form – written at less than 6th grade level

- Interviewer reads form to Mr. Q
- Then interviewer asks Mr. Q 10 true / false questions... "To make sure I explained everything I need to explain. If you get one wrong, it's because I didn't go over it well enough and we'll go over it again."

UCSF
University of California
San Francisco

Division of Geriatrics

CONSENT VERIFICATION

[READ] I need to make sure that I explained this study to you clearly so I am going to ask you a few true or false questions about the study. Feel free to look over the consent form. If something isn't clear, we can look over the information together. If you don't know the answer, please just say that you don't know. It's not good to guess. If you think the statement is true, answer "True." If you think the answer is false, answer "False." If don't know or if you're not sure, answer "I don't know." Again, if you are not sure it is better to say "I don't know" instead of to guess. It is OK if you don't know the answer or if you answer incorrectly. It just means that I didn't do my job in explaining the study well enough.

Ask all the questions and record the participant's "1st try" responses (T, F, or IDK). When you have finished asking all of the questions once, return to questions that were answered incorrectly. Review the relevant sections of the consent forms and then repeat the question(s). Repeat for 2nd and 3rd tries.

If a participant is unable to answer one or more of the questions correctly on their 3rd try (i.e. after reviewing the correct answer twice), say: "**I am sorry but only patients who can correctly tell us what this study is about can be in it. But thank you for taking the time to hear about the study.**"

Before each statement, be sure to say the phrase: "True, False, or I Don't Know."

1. **True, False, or I Don't Know: The reason for this study is to know what kind of healthcare services older people need when they're leaving jail and reentering the community.**

   Answer: *TRUE*

1st Try	2nd Try	3rd Try	Could Not Complete

   Relevant section from the Consent Form: *Why is this study being done? (Page 1).*

2. **True, False, or I Don't Know: Anybody can participate in this study.**

   Answer: *FALSE*

1st Try	2nd Try	3rd Try	Could Not Complete

   Relevant Section from the Consent Form: *Introduction (Page 1), You are being asked to take part in this study because....*

Mr. Q's teach-to-goal consent process

Mr. Q gives wrong answer to: *"Are their risks to participating in this study?"*

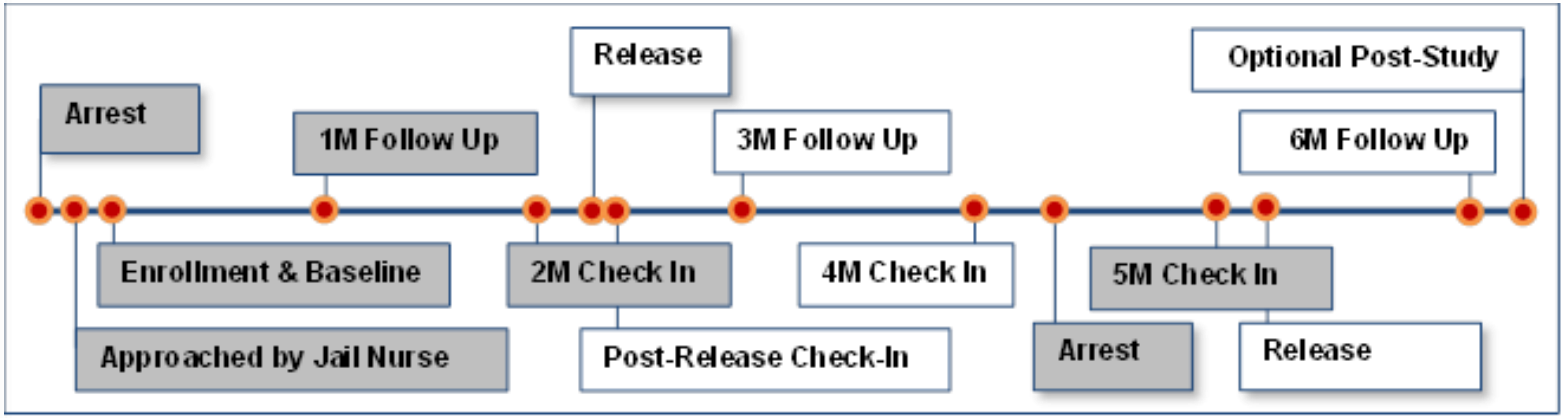
- **Mr. Q:** "Those aren't real risks to me"
- **Interviewer:** "OK, but I have to make sure that I've reviewed all the important information with you. Let's look back at the Consent Form where they talk about risks."
- **Interviewer:** "Here," (she points to the text). "We're saying that information about you and your health could get out if you participate in this study. If that happened, it's possible that information about you that you want to be private becomes public and people know things about you that you might not want them to know. Even if you're not worried about it for you, we think this is real risk. Do you want to talk about this or do you have any questions about this?"
- **Mr. Q** says no. Interviewer asks question again, Mr. Q says "there are risks even if I'm not bothered by them" and he selects "True"

UCSF
University of California
San Francisco
Division of Geriatrics

A note on proxy consent

- Dementia, seriously ill or close to death
- Proxys often benefit from teach to goal as well

Study design and retention: Incentives



- **Incentives to participate**
  - Considerable debate about the ethics of this issue

Ethical considerations when offering incentives to vulnerable populations

Incentives:

- A benefit to motivate to action (employee bonus for productivity)
- A compensation which makes up for a loss (per diem for jury duty service)
- Considered alternative to other forms of power –
  - Persuasion (undue influence)
  - Coercion (threat of harm)
- **Incentives *themselves* are not considered an ethical problem per se but they can become problematic…**

How should we think about incentives?
An ethical framework for considering incentives

Altruism is the ideal

- A free gift of time to unknown others
- Rare – the supply of these types of volunteers do not meet demands of medical research

Think about incentives using 3 established principles that guide research (Belmont Report):

- Respect for persons (autonomy)
- Beneficence (Do no harm)
- Justice (reasonable non-exploitative)

QUESTION TO ASK YOURSELF:

Does using incentive alter ethical judgments in any of these areas?

Grant RW, Sugarman J. Ethics in Human Subjects Research: Do Incentives Matter? Journal of Medicine and Philosophy, 29(6): 717–738, 2004

A framework for considering incentives – Respect for persons

Respect for persons: Autonomy, focus - decisions are made that are free of undue/coercive influence

- Generally framed in the example of offering monetary incentives to homeless participants
  - **Coercion**: Even a small amount of money could operate like coercion (make a judgment against his/her will). Therefore, be wary of offering incentives to vulnerable populations
  - **Free choice**: Coercion side of the debate is paternalistic. The scenario is about inequality not coercion. The desire to have the money more than anything else is free choice. To deny the destitute an opportunity offered to wealthy denies their liberty (and their autonomy)
- Most hotly debated / unresolvable ethical debate
  - **Little motion in recent years – choose your side!**

A framework for considering incentives – Beneficence

Beneficence: "Do no harm." Focus - level of risk (harm) of study is reasonable in relation to the prospect of benefit

- Have concern when: participants will only consent to a study if the incentive is relatively large because their aversion to the study is strong
  - NO GOOD: Aversion to the study and/or risk is so great that you are calibrating the incentive to overcome it…

A framework for considering incentives - Justice

Justice:

1. **Protection from exploitation**
2. **Fair access to participate in research**

- **Protect from exploitation:** Wrong if want to spend least amount so you preferentially recruit poor participants
- **Fair access:** It is important to consider importance of including participants who might benefit from research even if they are hard to recruit and retain historically

Bottom line on incentives

Always consider the points of concern:

- Where the subject is in a dependency relationship with the researcher (student, patient)
- Where the risks are particularly high
- Where the research is degrading
- Where the participant will only consent if the incentive is relatively large because the participant's aversion to the study is strong

When conditions are present, use of incentives highly questionable

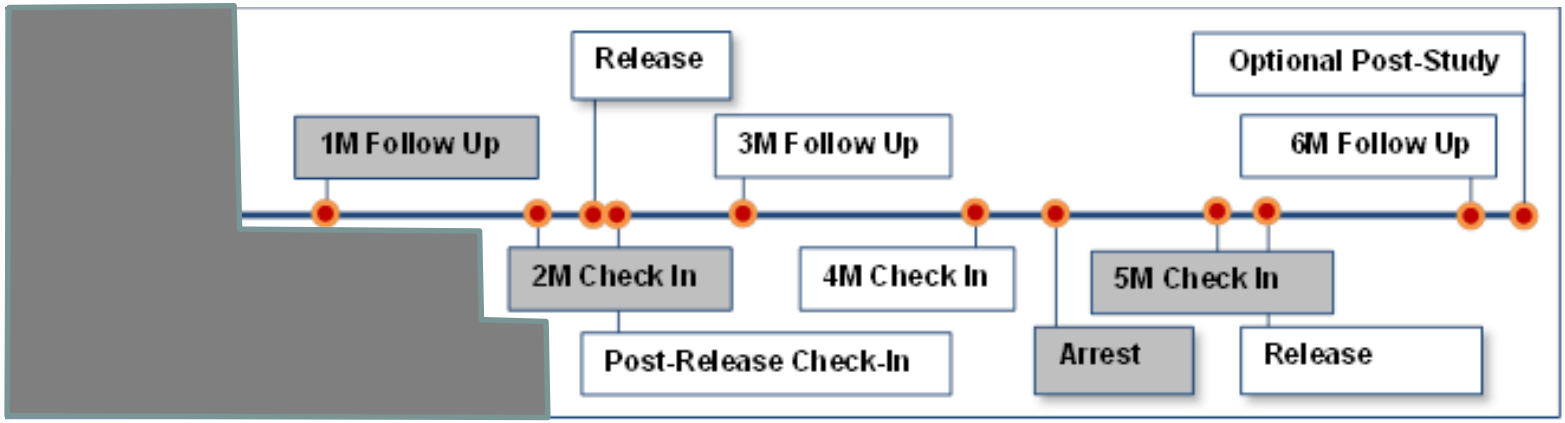
UCSF University of California San Francisco

Division of Geriatrics

Incentives—practical issues

- **NIH may be more comfortable with gift cards**
- **If use gift cards, get input from Community Advisory Board on what would be most useful/acceptable to participants**

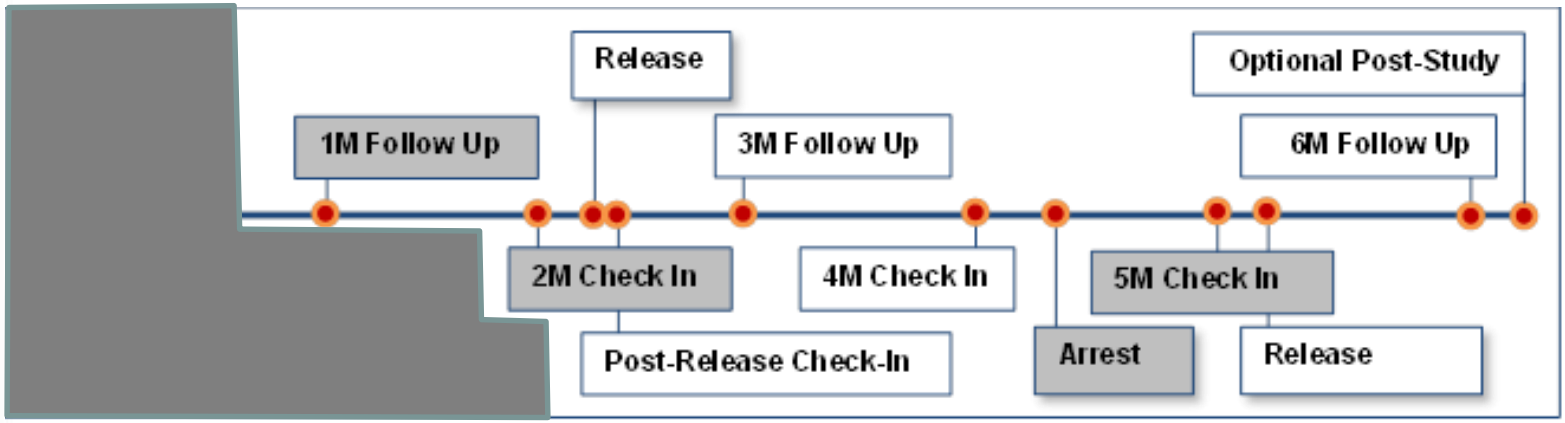
Study design: Other Retention Strategies



Retention: begins at first study visit

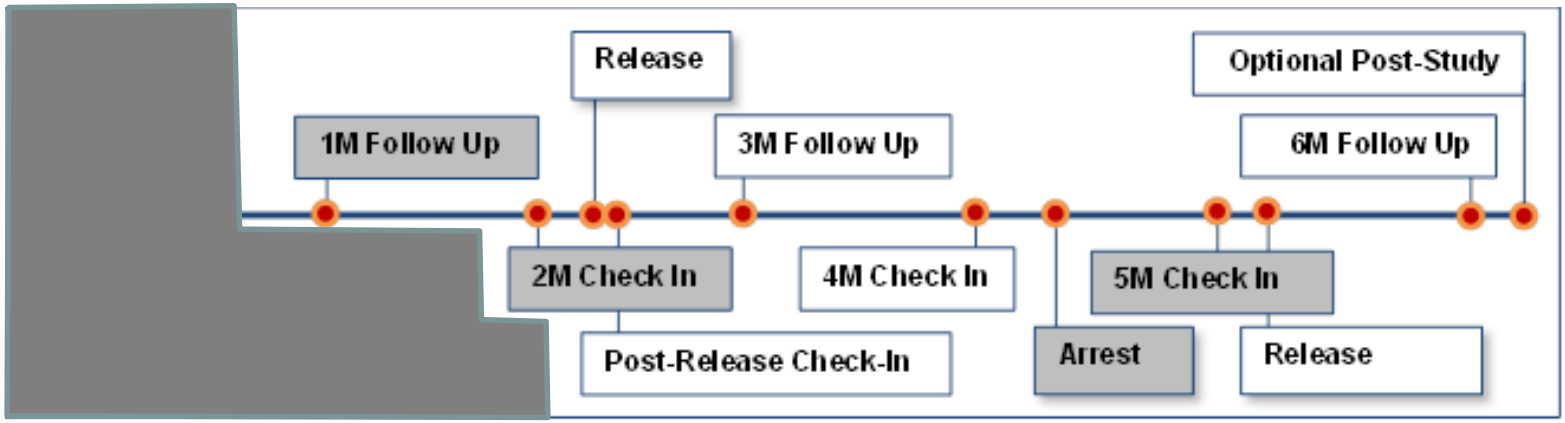
- **Collect contact information**
  - Anyone who might know where you are with full contact information (address, phone, email)
  - Relatives, friends, case managers, acquaintances
  - Ask for permission to leave messages
- **Collect location information**
  - Addresses, businesses, churches, parks…
  - Ask for permission to go there and ask after participant, leave messages
- **Take picture (if participant allows)**
  - Ask for permission to show picture
- **Written permission to get Social Security information on last known address**

Retention Strategies: Healthy Aging Study



- **Retention Strategies**
  - Tenderloin-based office - safe place with a big lobby participants can stop by anytime for water, restroom, phone calls
  - Each interview starts with a snack and catch-up; Time is budgeted to let “talkers” talk and be heard
  - Celebrate positive news (e.g. reach out on birthdays, share sobriety news with team for next appointment)
  - A ‘proactive follow up list’ - those who have missed a meeting receive reminders ahead of future appointments

Handling unanticipated events



- **Importance of training and retraining staff in vulnerable populations research**
  - Mr. Q remains in jail for 60 days
  - While in jail another study participant threatened a deputy during his 1 month follow up visit
  - Staff retrained on threatening behavior and new IRB reporting requirements developed based on new event
  - Events → need to develop new protocols and document that staff retraining occurred

UCSF University of California San Francisco

Division of Geriatrics

Goals

1. **Define the term "vulnerability"**
2. **Discuss early critical steps in research with vulnerable populations**
   - IRB / CHR approval
   - How to build and train a research team
3. **Identify special considerations in study design**
   - Approach and intake
   - Informed consent
   - Use of incentives
   - Other retention strategies
   - Handling unanticipated events
4. **Remind ourselves that research with vulnerable populations is often worth the effort**

UCSF University of California San Francisco

Division of Geriatrics

Why research with vulnerable populations is worthwhile

- **Academically – being in a smaller group → more opportunities at earlier stage in career**

UCSF
University of California
San Francisco
Division of Geriatrics
UCSF

Why research with vulnerable populations is worthwhile

- **NIH health disparities strategic plan**

Why research with vulnerable populations is worthwhile

Give voice to the voiceless

- *"I'll be honest with you. In the beginning, it wasa little bit more about the money. Sitting in [jail], knowing how hard it is coming out. I was like, damn. Yeah. That money could help. But since I've started your project? It's not about the money anymore. I like coming here. Talking with you guys. Giving something back. I'm gonna miss it."*

- *"I'll tell you why I don't like some of these other places. Everybody always has these preconceived ideas about me. Cause of things I've done and all that – things in my past. But I like coming here. Here we can just talk and it's cool."*

Resources for working with vulnerable research subjects

- **The US Department of Health and Human Services has a section on Vulnerable Populations under Policy and Guidance: http://www.hhs.gov/ohrp/policy/populations/index.html**

UCSF

University of California
San Francisco

advancing health worldwide™

Some more questions for you

- What are the challenges that you have experienced (or are concerned about experiencing) in conducting research with vulnerable populations?
- Have you overcome them? If so, how? What would you do differently next time?
- Have you opted not to conduct research with vulnerable populations because the challenges are too great? When?
- If you have conducted research with vulnerable populations, what were the benefits?