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Recruitment & Retention; Eligibility and screening; IRB and human subjects

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1

DEFINING YOUR SAMPLE

2

Eligibility: Who Do You Want to Recruit?

- Who is most at risk for the disease/condition?
- What analyses do you want to conduct (e.g., effect modification based on gender?)
- To what population do you want to generalize?
- Will you need to draw a random or representative sample?
- Balance: Minimal inclusion exclusion/criteria vs. ideal individuals for the study

3

Specify Inclusion/Exclusion Criteria

- Inclusion criteria
  - Demographic characteristics (e.g., age range, gender, race/ethnicity/nationality)
  - Clinical characteristics
  - Geography (e.g., patient in a certain clinic)
  - Temporal characteristics (e.g., between 2/1/22 and 8/2/22)
- Exclusion criteria
  - An inability to consent or provide good data (e.g., language barrier, disoriented)
  - Being at high risk of adverse events
  - Who can safely participate? (health exclusion)

4

- Participants: Inclusion Criteria: Participants must be presenting at the Campbell Clinic to schedule TKR surgery that will result in the prescribing of opioid medication (e.g., oxycodone-acetaminophen 5mg-325mg). Participants must be at least 18 years old, have access to a telephone, and be able to understand consent. Exclusion Criteria: Participants will be excluded if they have a contraindication to opioid medication.

5

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Human Subjects: Grant Requirements

- **You must specify the age range**
  - Are you enrolling children (younger than 18 years of age)?
  - Do you have an upper limit on age?
- **Must specify gender composition of the target sample and justify scientifically**
- **Must specify the racial background of the targeted sample and justify scientifically**
  - Don't limit yourself to "representative of the community"– show the review committee that you will make an effort to obtain a diverse sample of the population

6

Inclusion Plans **Applicable Only for Human Subjects research and not IRB Exemption #4.**
• Sex/Gender: Distribution justified scientifically • Race/Ethnicity: Distribution justified scientifically • For NIH-Defined Phase III trials, Plans for valid design and analysis: Not applicable • Inclusion/Exclusion Based on Age: Distribution justified scientifically Comments (Required Unless Not Applicable): • Will Include adult women of childbearing age, racially diverse

7

Questions?

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8

RECRUITMENT and SCREENING

9

10

Recruitment

- Have a plan
  - Describe it briefly in the Research Plan
  - Detail previous recruitment efforts that give you estimates of how many participants can be recruited each week/month
- Have a back-up plan
  - Describe it briefly in the Research Plan
- Potentially have a plan for alternative strategies, to be described at the end of the Research Plan
- Overbudget for recruitment costs

11

5.2.a. Recruitment and Informed Consent
Participants will be community college students between the ages of 18-29 who are regular drinkers. Individuals will be recruited through in-class screening and mass email invitations, as well as through participant referrals (refer-a-friend). Our research team has a long history of successful recruitment in assessment and clinical trials; we are often asked to "over-recruit" in our center to make up for the shortfalls in others. Once a potential participant responds to our recruitment strategy and expresses interest in the study, a screen will be conducted that includes a check for all inclusion and exclusion criteria. If eligible for participation, the potential participant will be provided a detailed description of the research study and be assigned a subject number. Project staff (i.e., investigators and study staff) will answer any questions about the entire process and an informed consent will be obtained.

The consent form will be reviewed with each participant in-person. No assessment will take place prior to obtaining consent from each subject. Standard language in our consent form assures the participants of the confidential nature of the study and the ability to withdraw from the study at any time. The consent forms will contain HIPAA language. This study will be approved by the UTHSC IRB.

12

Recruitment Possibilities

- Social Media ($)
- Television ads ($$)
- Radio ($)
- Flyers, posters, brochures ($)
- Listserv postings
- Movie theater/bowling alley ads ($$)
- TV/radio/newspaper interviews
- Billboards ($$)
- Bus shelter ads ($$)
- Craigslist ads
- Postcards with a purchased mailing list ($$)
- Letters to patients (physical/ EHR portal)
- Approaching patients in clinic
- Research Match
- Community presentations
- Businesses that recruit for academic researchers

13

Make the Study Attractive

- Efficient– avoid unpleasant or unnecessary tasks/measures
- Meaningful incentives
- Reimbursing for parking/transportation
- Bilingual staff and translated consent/questionnaires
- Attractive treatment components (e.g., free medication)
- Recruitment materials that reflect the population you are attempting to recruit
- Accessibility

14

Screening: Assessment of Inclusion/Exclusion Criteria

- Demographic characteristics: Self-report
- Clinical characteristics: Self-report vs. Exam vs. Clinical report
- Make sure to use operational definitions
  - E.g., What is "problematic alcohol use"?

15

Screening and Enrollment Procedures to Choose From

- How many visits do you need to assess eligibility?
  - Website screening or self-screening for main criteria
  - Phone screening for items that may need discussion
  - Consent
  - Screening and/or baseline visit to complete questionnaires
- Participants who are non-adherent during screening are likely to be non-adherent during the study: Consider what you will accept

16

Interventions: Behavioral Run-In

- **If you have an intervention that may require significant participant commitment:**
  - Consider a behavioral run-in, where participants get a taste of the intervention to help them decide whether it is right for them
  - E.g., logging medication use for a week prior to randomization

17

RETENTION

18

Use a Proactive Retention Plan

- If there is more than 2 months between contacts, consider how you will stay in touch (e.g., newsletter, cards, small gift)
- Schedule the next visit at the current visit, even if it might change
- Maintain a personal touch– birthday, sympathy, get well soon, & holiday cards
- Establish staff schedules for flexibility with appointment times (evenings, weekends)
- Define the length of the data collection window (i.e., ideal & acceptable)

19

- **D9. Retention.** To assist with follow-up assessment retention, we plan to follow guidelines proposed in the literature,[90,91] as well as methods from our current smoking cessation RCT (N=738) which has a 12-month retention rate of 89%. First, we will employ consistency in contact at multiple time points to ensure participants remember the study name as they will be more likely to engage in follow-up visits. In addition, we will make efforts to foster trust between the researchers and study participants through respectful and sensitive communications at all stages of the study. This will include clear descriptions of study procedures and participant protections. We will also provide small participation incentives provided in between assessments with the study name and logo (e.g., we have found that t-shirts and water bottles are very well-received incentives in past studies).[72,73,81,92]

20

Participants at High-Risk for Loss to Follow-up

- Who will contact the participant and in which order?
  - Data collector
  - Interventionist
  - Study Coordinator
  - PI
- How and in which order?
  - Email
  - Phone
  - Text
  - Social media
  - Mail
- When (i.e., how many days after the previous attempt)?

21

Eligibility/Recruitment/Retention: What to Include in the Grant?

- Main inclusion/exclusion criteria
- Primary and back-up plan for recruitment
- Screening procedures
- Retention procedures
- Expected retention rate (likely & conservative)
- Do not assume that the reviewer will look at the Form F materials
  - Guide the reviewer to Form F by making references to it in the Research Plan

22

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23

Part II

24

Designing Clinical Research

Hulley, Cummings, Brower, Grady, & Newman (Eds) 2013.

Chapter 14

25

ETHICS

26

Historical Events that Formed Regulations

- **Tuskegee:**
  - A study of the "natural course" of untreated syphilis
  - Researchers lied to African American/Black patients and kept them from successful treatment
- **World War II:**
  - Nazi "research" on victims in concentration camps
- **Resulted in strong oversight of research according to 3 principles**

27

Ethical Principles

1. **Respect for Persons**
2. **Beneficence**
3. **Justice**

28

Ethical Principles

1. Respect for Persons:

- All persons have the right to make their own decision about participation
- Informed and voluntary consent required
- Can discontinue participation at any time
- Special attention to those who cannot freely consent
  - **Is the individual able to understand the consent process (5th grade reading level)?**
  - **Is the individual able to say no?**
- What does this look like in a grant?
  - **Describe the consent process – privacy, language, process, participant involvement, ability to withdraw, HIPAA compliance**

29

EXAMPLE TEXT

Protection of Human Subjects Section of Grant Application

Section 3 - Protection and Monitoring Plans

Recruitment and Informed Consent: Potential participants will be identified from the appointment schedule at the beginning of each day by qualified study staff. A study staff member is then able to approach the patient, introduce the study, and see if the patient would be interested in participating.

If eligible for participation, the potential participant (or, if under age 16, the participant and legal guardian) will be taken to a private room where they will be provided a detailed description of the research study. Project staff (i.e., investigators and study staff) will answer any questions about the entire process and an informed consent will be obtained.

Assent from participants under age 18. For individuals under age 18, consent will be obtained by the parent or legal guardian, and assent to participate will be obtained from the participant. Participants under age 18 will be provided a shortened form with a description of study procedures and asked if they have any questions about the study. Participants under age 18 will be asked to sign the assent form after their parent/guardian has signed consent and if they agree to participate.

No study assessment will take place prior to obtaining consent (or for those under age 18, assent from participant and consent from parent or legal guardian) from each subject. Standard language in our consent form assures the participants of the confidential nature of the study and the ability to withdraw from the study at any time. The consent forms will contain HIPAA language. This study will be approved by the UTHSC IRB.

30

Ethical Principles

2. Beneficence:

- Scientific knowledge to be gained must outweigh risks to participants
  - Risks must be minimized
- Risks can include
  - Physical risks from interventions
  - Psychological risks (breaches of confidentiality, stigma, discrimination, distress)
- Risks monitored via "Adverse Events" which are measured regularly, and evaluated by a study physician or psychologist
- Exclude those most likely to suffer those risks

31

EXAMPLE TEXT

Section 3 - Protection and Monitoring Plans

3.1. Protection of Human Subjects

Adequacy of Protection against Risks

Potential Risks

Potential risks will be explained to each participant when informed consent is obtained. Potential research risks to the participants with this study include those associated with completion of the study assessments and blood draws.

Participants may be inconvenienced by the completion of study assessments. We have flexibility in the scheduling of in-person assessments and will make every attempt to work around participant schedules. Participants may experience possible embarrassment or discomfort from answering personal questions.

Blood collection (approximately 10 ml) presents a minimal risk. Blood collection can cause a bruise or minor nerve damage, which would be expected to heal on its own within 3 days. Sterile blood collection techniques will be used to prevent infection. All blood will be collected in a clinical office by a nurse or other clinical staff.

32

EXAMPLE TEXT

Section 3 - Protection and Monitoring Plans

3.1. Protection of Human Subjects

Adequacy of Protection against Risks

Monitoring of adverse events

Adverse Events (AEs) could include distress associated with answering study interview questions and by needle prick during blood draw. Participants will be informed that they may choose not to answer questions that make them uncomfortable and may discontinue participating in the study at any time.

In the event that study staff are informed of maltreatment, neglect, or abuse, contact numbers of social workers will be made available for study staff to report the event.

For any Adverse Event reported during the study, the nature, onset, duration, intensity, and remedial action taken will be recorded. This can be collected at the follow-up assessments.

Although highly unlikely, in the case of any study-related AE, the study staff will contact the MPIs directly. The MPIs will be responsible for managing and reporting all AEs to the UTHSC IRB and NIH.

33

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Ethical Principles

3. Justice:

- Benefits and burdens of research must be distributed fairly
  - **Cannot take advantage of populations that are easily targeted (i.e., disadvantaged, impaired, incarcerated)**
  - **If research can be conducted with non-vulnerable, it should be**
- (flip side) Equitable access
  - **Access to new therapies must be available regardless of income, insurance, or education**
  - **Now NIH requires a response to question: Are you including women, children, and minorities in research?**
    - **Need to justify if these groups are under-represented**

34

EXAMPLE TEXT

Section 2 - Study Population Characteristics

2.4. Inclusion of Women, Minorities, and Children

In this study, we anticipate recruiting at least 50% women and over 40% minority participants. We have a long history of recruiting in clinical trials and have a targeted recruiting system that is highly effective. In an ongoing clinical trial (Derefinko Site PI), we have met or exceeded our recruitment goals every month with a final enrollment of 852 participants (62% females; 37% African Americans). In our pilot studies with the University of Tennessee Health Science Center Oral & Maxillofacial Surgery Clinic patients, about 65% of participants are women and 55% are African American.

We are recruiting children age 16 - 18 in the study due to the prevalence of this age group in 3rd molar extraction surgery and ACL surgery. We will not recruit individuals younger than age 16. Individuals younger than age 18 will be assented and will be required to have parental consent prior to engagement in any study activity.

There are no upper age limits to recruitment as there are no specific contraindications for study medication or treatment for any adult age individual.

35

1. Using an Existing Dataset or Resource: **No**
2. Enrollment Location Type: **Domestic**
3. Enrollment Country(ies): **United States**
4. Enrollment Location(s): **UTHSC**
5. Comments: **n/a**

Racial Categories	Ethnic Categories					
	Not Hispanic or Latino		Hispanic or Latino		Total	
	Female	Male	Female	Male		
American Indian/ Alaskan Native	2	2	0	0	4	*0.67%*
Asian	2	2	0	0	4	*0.7%*
Native Hawaiian or Pacific Islander	2	2	0	0	4	*0.67%*
Black or African American	119	119	0	0	238	*39.7%*
White	161	161	7	7	336	*56.00%*
More than one Race	7	7	0	0	14	*2.3%*
Total	293	293	7	7	600	
						100.00%

36

IRB AND HUMAN SUBJECTS

37

Federal Regulations

- **Apply to ALL federally funded research and to research submitted to the FDA**
  - Research = Systematic investigation designed to develop or contribute to generalizable knowledge
  - Human subjects = Living individuals about whom an investigator obtains either data through interaction with the individual or identifiable private information
  - Private information = Information that a person can reasonably expect is not being recorded, and that can reasonably be expected not to be made public

38

Institutional Review Board (IRB) Approval

- Do not conduct research without IRB approval
- Your IRB will determine if:
  - Risks to participants are minimized
  - There is equitable selection of participants
  - Informed consent will be obtained
  - Confidentiality will be maintained

39

Federal Regulations

- How to protect privacy?
  - Know what information is considered private
    - Name
    - Birthdate
    - Address
    - SSN
    - Medical record number
  - Give participants a study ID code
    - Link to their name only on a separate, encrypted form

40

Informed Consent

- Participants must be informed about procedures and voluntarily consent to be in the study
  - Purpose
  - Procedures
  - Risks
  - Benefits
  - Alternatives to participation
- Understanding must be established to meet criteria of informed consent
- Voluntary consent = Free from coercion or undue influence
  - Student?
  - Excessive payments?

41

Minimizing Risks

- Confidentiality
  - Some data could incriminate a person if released (substance use)
    - Do not attach name to assessments
    - Code data so that they are not readily understood (1 = cocaine, 2 = heroin, 3 = no substance use)
    - Certificate of confidentiality = Allocated to all federally funded projects automatically
      - Researchers will not break confidentiality even upon court order or subpoena
      - But will break confidentiality if informed of ongoing abuse or harm to self/others (mandated reporting)
- HIPAA Health Privacy Rule
  - Protects identifiable health information
  - Researchers must obtain permission from the individual to use PHI
    - This is not necessarily subsumed under informed consent

42

Conflict of Interest

- Financial
  - Do you have a stake in a drug, device, therapy, company?
- Is an investigator also the participant's physician?
  - Will the patient's care differ if they are in your study?
- How to address this issue:
  - Reduce bias through study design (random assignment, blinded assessment)
  - Separate conflicting roles (treating physician should not be involved in enrollment)
  - Ensure investigators have control over findings
  - Always disclose your conflicts of interest (failure to do so may harm your reputation and cause discontinuation of your research)

43

Other Ethical Issues: Randomized Designs

- Assignment to placebo
  - Acceptable in short duration, low risk trials
- Assignment to control
  - Control should receive the standard of care if possible
- Continuation
  - Study should be suspended or terminated if safety issues become apparent, or there is futility (failure to recruit enough participants to answer the study question)

44

Other Ethical Issues: Archival Data and Previously Collected Samples

- Often, participants will consent to future research being carried out with their data
  - This should not be considered a green light for all possible work
  - Consent forms should specify acceptable uses of data in the future
    - I consent to my data being used in future studies that are IRB-approved
    - I consent to my data being used in the future only for studies of cancer-related conditions, and only my ____ data will be used
    - I consent to have my data used only for the current study, and not in future work

45

Other Ethical Issues: Participant Payment

- Compensation is often needed to enroll and retain participants
  - How much should you pay?
  - Coercion occurs when the payment is so great that lower income participants will negate risks in favor of participation (against their better judgement)
  - Grant application should describe the amount of incentive offered

46

Questions?

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47