Investigator-initiated Studies at Ochsner: Chart Reviews Through External Grant Applications

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IRB GCP Lecture Series
Main Objectives

Determine
Determine when I am doing Human Subjects Research

Identify
Identify the main regulatory and compliance requirements for investigator-initiated protocols

Identify
Identify administrative requirements for investigator-initiated protocols
Am I Doing Human Subjects Research?

• Human Subjects Research Defined
  • Human Subject: a LIVING individual about whom an investigator is conducting research
  • Human Subjects Research:
    • Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies or analyzes the information or biospecimens
    OR
    • Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens
Examples of Human Subjects Research may include:

- Collecting blood
- Conducting a survey
- Changing participants’ environments
- Administering medicine
- Interviewing
- Administering a psychological test
- Collecting data
- Conducting a focus group
- Testing a new educational technique
- Implanting a device
Am I Doing Human Subjects Research?

Clinical Question
• I think my ALS patients should be assessed with the ALS Functional Rating Scale – will this help me determine the right support services for my patients?

Research Question
• Were ALS Clinic patients, who were assessed with the ALS Functional Scale, matched to support services in less time than those who were not assessed?

A Clinical Question helps me do my work better and directly impacts my individual patients.

A Research Question may offer no promise of benefit to my patients or my practice but may help others.
Am I Doing Human Subjects Research?

Quality Improvement
If I train my fellow residents to use a behavioral plan with people who want to quit smoking, will we reduce the number of active smokers in the primary care clinic in 12 months?
- **Target**=process used in clinic to help people quit smoking
- **Intervention**=resident education
- **Outcome**=# of active smokers in clinic after the program (group level data)

Research
If I use this behavioral intervention with people who want to quit smoking, how many people who use my program will become nonsmokers compared to those who do not use my program over 12 months?
- **Target**=individual patients
- **Intervention**=behavioral plan vs standard of care
- **Outcome**=% nonsmokers after 12 months in the group that used program (patient level data – Who chose this plan? Who was successful?)
Am I Doing Human Subjects Research?

- Clinical Questions
  - Affect patients
  - Affect medical practice

- QI Projects
  - Affect processes
  - Affect systems

- Research Questions
  - Inform others through generalizable knowledge
  - May have no effect on patients
  - May have no effect on processes
<table>
<thead>
<tr>
<th>Clinical Question vs Research Question</th>
<th>Quality Improvement vs Research Question</th>
<th>Pre-research Activity vs Research Activity</th>
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<tbody>
<tr>
<td><strong>Clinical</strong>: I think my ALS patients should be assessed with the ALS Functional Rating Scale – will this help me determine the right support services for my patients?</td>
<td><strong>QI</strong>: If I train my fellow residents to use this behavioral intervention with people who want to quit smoking, will we reduce the number of active smokers in our clinic over the next 12 months?</td>
<td><strong>Pre-research</strong>: I am interested in studying a behavioral intervention to help people quit smoking. Let me use SlicerDicer to see if I have enough smokers in my clinic to meet the target sample size.</td>
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<td><strong>Research</strong>: Were ALS Clinic patients, who were assessed with the ALS Functional Scale, matched to support services in less time than those who were not assessed?</td>
<td><strong>Research</strong>: If I use this behavioral intervention with people who want to quit smoking, how many people who use my program will become nonsmokers compared to those who do not use my program over 12 months?</td>
<td><strong>Research</strong>: How many people in my clinic using this behavioral intervention have been a nonsmoker for 12 months or longer versus those using nicotine gum?</td>
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I’m Still Not Sure if I am Doing Human Subjects Research

- Ask the IRB for a determination
  - Not human subjects research
  - It is Quality Improvement/Process Improvement
  - It is pre-research activity

- If you submit a full application, they may also determine:
  - It is human subjects research, and it falls into the exempt category (most retro chart reviews)
  - It is human subjects research that requires continued oversight
I Want to Perform Human Subjects Research

01 Complete required training (e.g., CITI)
02 Develop a Hypothesis
03 Do a Literature Search
How Do I Complete CITI Training?

• Go to the HRPP website and click on IRB Education & Training

• Click on Collaborative Institutional Training Initiative (CITI)

• Create a login

• Affiliate with Ochsner Clinic Foundation and the required modules will load
I want to ask a Research Question: How do I formulate a testable hypothesis?

**PICO Strategy**

P (Patient or Population)

I (Intervention)

C (Comparison)

O (Outcome)
How do I formulate a testable hypothesis?

**Migraine Example**

For adults with migraine, does eptinezumab versus standard oral treatment affect migraine frequency?

- **P (Patient or Population)** = people ≥ 18 yr. with migraine
- **I (Intervention)** = 2 infusions of eptinezumab over 6 mo.
- **C (Comparison)** = standard oral preventative treatment
- **O (Outcome)** = average number of migraines per mo. for 6 mo.
For adults with hypertension, does participation in the Digital Hypertension Program lower blood pressure?

**P** (Patient or Population) = people ≥ 18 yr. with blood pressure ≥ 130/80

**I** (Intervention) = active participation in Digital Hypertension (weekly BP entries)

**C** (Comparison) = prescription and follow up visits every 3 months

**O** (Outcome) = blood pressure 6 months after enrollment in Digital Hypertension or initial hypertension prescription
Research Question: Start with a Literature Search

Has my question been answered in the literature?

• If I cannot find the answer, will others learn from my results? **Novel & Relevant**

• What if only one publication offers an answer to your question – is a second study important? **Generally speaking, yes – it is important to try to replicate research findings.**

• If your question has been reliably answered, can you extend your question to contribute to the scientific literature? **What hasn’t been examined? Will my patient population add something unique to the reported findings?**
Can I use the same (PICO) strategy to do a literature search?

For patients with Hyperkinetic movement disorders, does botulinum toxin injection (as opposed to no Tx) improve functional outcomes?

**P** (Patient or Population) = Patients with Hyperkinetic movement disorders

**I** (Intervention) = botulinum toxin injection

**C** (Comparison) = no injection

**O** (Outcome) = functional testing
For patients with Hyperkinetic movement disorders, does botulinum toxin injection (as opposed to no Tx) improve functional outcomes?

**Patients**
1) Myoclonus or Tremors or Dystonia

**Intervention**
2) Botulinum Toxins

**Search Terms**
3) Combine 1 and 2
   
   ("Myoclonus or Tremors or Dystonia" and "Botulinum Toxins")
Limit Retrieval to Target Relevant Literature

- Age Group
- Human
- Animal
- Language
- Publication Type
  - Letter, article, etc.
- Methodology of Study
  - Article Type

Limit by text availability e.g., if you only want full text or free full text

Limit by type – like “Clinical Trials”

What are additional filters?
This is what pops up when you click “Additional Filters”

There are a number of clinical article types that will narrow your search, as well as other choices mentioned: age, sex, language, etc.
I Want to Perform Human Subjects Research

01 Complete required training (e.g., CITI)
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I Want to Perform Human Subjects Research

If you are a trainee, have you selected a research mentor?

Choose a Study Design

Develop a Protocol
Ready to Develop My Protocol

• Accessing Protocol Builder
• Go to the HRPP website and click on eIRB
• Click on Protocol Builder
• Use your SSO to access
• Click Start Document to begin a new protocol
• All your projects are saved
I Just Need to Complete a Chart Review

Try the Residency Research Protocol Form

2-page outline of the required components of a protocol for most chart reviews

Includes a data dictionary to help you identify exactly which data elements you need for your project

Reach out to your Directors; they can share a Word version of this form and provide feedback on your protocol before you submit it to the IRB

Residency Project Proposal

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<th>Title</th>
<th>Resident: Project Advisor: Project Committee:</th>
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Background

Briefly summarize scientific background and any related studies (provide citations) conducted previously. Identify gap(s) in the literature that your research project aims to address.

Purpose/Objectives

Most sentences start with “To characterize”, “To evaluate”, etc.

1.
2.

Research Question/Hypothesis

Final research question (from PICO/FINER worksheet): Null Hypothesis ($H_0$): Alternate Hypothesis ($H_a$):

Methods

1. Retrospective Cohort
2. Prospective Cohort
3. Case-Control
4. Other (please specify):

Setting

Single center vs multicenter? Inpatient vs outpatient?

Participants

Inclusion Criteria:

1.
2.

Exclusion Criteria:

1.

Intervention/Exposure

What intervention/exposure will define your intervention/exposure cohort (for case-control studies, what outcome will define your outcome cohort)

Comparator

If applicable

Study Period and Follow-Up

When will the study period begin and end? What criteria must be met for termination of follow-up? (Typically, follow-up should be terminated upon occurrence of the primary outcome, death, etc)

Patient Identification

How will patients be identified? (SlicerDicer vs other software, ICD-10 codes, medication exposures, etc)

Anticipated Study Size

How many patients will be targeted/anticipated?
Create Data Collection Tools

• Questionnaires
• Excel spreadsheets
• REDCap data forms
  • Place a request through The Hub to receive access to REDCap (an ‘existing application’)

• Anything that a participant engages with must be included in your protocol and reviewed by the IRB, such as surveys, scales and questionnaires
• Other data collection tools should be described in your protocol, including your data security plan and data sharing plan (if applicable)
Other Considerations for Human Subjects Research

- Do I need a consent form?
  - Prospective studies may require a consent form

- Should I register my study with clinicaltrials.gov?
  - Generally, yes if using drug/device and/or an interventional trial

- Can I bill insurance for research activities?
  - Work with Research Finance

- Can I share data with collaborators?
  - If outside Ochsner, may need a data use agreement

- Should I consult with Biostats?
  - Design phase is the perfect time to ask for help
I Have a Protocol – What’s Next?

Go to the Office of Epidemiology & Biostatistics and submit a request for help.

Submit the protocol through eIRB.

Register for an account if you are a first-time user.

- Trainees and collaborators may register using their professional email address (does not have to be an Ochsner email).
You can access the Biostats site externally through the research.Ochsner.org site or through their Sharepoint site.

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Center for Outcomes and Health Services Research

Office of Epidemiology and Biostatistics

How to Request a Consultation

Step 1: Submit a Request form
Step 2: A biostatistician will contact you for an initial consult
Step 3: Send your assigned biostatistician your summary sheet [consult template]

Things to know:
- During the initial consultation we will review your study design, research question(s) and hypothesis, variables and how these are measured, so please have these items finalized.
- Requests take at least 4 weeks from initial consultation and/or receipt of final data.
- Results will include statistical methods, statistical results, and basic interpretation.
- If you need further explanation of your results or additional analysis, you may contact your biostatistician directly.
- The magnitude of services provided by your biostatistician may merit co-authorship. Discuss this with your biostatistician prior to any abstract or manuscript submission.
Submitting Your Protocol through eIRB

Go to the HRPP site and click the link for eIRB on the right.

On the next page, click Login at the top right and use your Ochsner SSO to login.

Go to the IRB tab and choose “Create New Study” on the left.
If your study meets the definition of Human Subjects research, you will need a **study binder** for keeping records of your study activities, including deviations from your protocol, adverse events, training and communication with your research team, enrollment, etc.

If you need a **data pull**, go to the “Research Information Analytics” link on the Outcomes Research page on the research.Ochsner.org site.

- Download a data request template and submit it via the REDCap survey form.
Go back to the Biostatistics site and submit a form for help with analysis and interpretation.

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I’m Ready to Share My Results

• Prepare to share your results using de-identified data
• Poster presentations often begin with creating and submitting an abstract
  • Introduction/Background
  • Purpose/Hypothesis
  • Design/Methods
  • Results/Conclusion
• Manuscript preparation follows the same general format
• Be sure to ask your mentor, colleagues, and/or clinical research directors to review your work and provide feedback
Choosing the right journal

• Use your references to help determine the right readership
• Is your target journal a fit for your topic
• Does the journal publish findings based on your methods (e.g., not all Journals publish case studies)
• Identify society journals based on your subspecialty (e.g., AHA has several, including Stroke, Circulation, and Hypertension)

• Try a journal finder
  • Elsevier journals: https://journalfinder.elsevier.com/
  • Wiley journals: https://journalfinder.wiley.com/search?type=match
  • Springer journals: https://journalsuggester.springer.com/
Applying for a Grant to Fund Your Project

• Work with the Ochsner Grants Office and your Director of Clinical Research to:
  • Identify appropriate funding opportunities
  • Complete a budget that includes all labor and supply needs
  • Submit an application with all the required legal and executive signatures

• Step 1 is to Complete the Application Initiation Form (AIF) on the Grants website
Application Initiation Form (AIF)

- The Grants website can be found on the research.Ochsner.org site (https://research.ochsner.org/opportunities/grants)

The AIF can be accessed on several pages, including the home page. It requests basic information about the project, as well as contact info for team members.

Your Director of Clinical Research will receive a notification when you submit a form. This provides an opportunity for engagement and assistance as you prepare your grant budget and application.

It is best to begin working with the Office of Grants Development at least 3-4 weeks prior to the application due date.
Grant Applications

- Grant applications include more than just a protocol
  - Biosketch
  - Budget
  - Budget Justification
  - Letters of Support

- May need to provide organization information and may have sections regarding how the project is innovative, meets the funding priority, and addresses minority recruitment
Concepts Reviewed

- Performing Human Subjects Research
- Developing a Research Hypothesis
- Completing a Literature Search
- Building a Protocol
- Submitting to the IRB
- Sharing My Results
- Submitting a Grant Application
Resources to be Shared

**Emailed to invitation list**
- Presentation
- Quick Start Guide with Links to Research Resources

**Available today to research leaders in shared onboarding folder**