Getting Started in Research: Research & Institutional Resources

Nicole Villemarette-Pittman, PhD

Director, Clinical Research, Ochsner Clinic Foundation

Associate Professor, Xavier Ochsner College of Medicine

Associate Professor (Hon), University of Queensland Medical School

Objectives

1. Determine when I am doing human subjects research
2. Be able to formulate a research question
3. Be able to conduct a literature search
4. Understand basic research designs using EMR

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?

A Clinical Question helps me do my work better and directly impacts my individual 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 Research Question may offer no promise of benefit to my patients or my practice but may help others.

Am I Doing Human Subjects Research?
How is Research Different from Quality Improvement?

Quality Improvement/Process Improvement/Quality Control/Quality Assurance

Safety: Avoid harming patients

Time: Reduce delays for patients and providers

Efficacy: Provide evidence-based care

Efficiency: Avoid waste (equipment, ideas, energy, etc.)

Equity: Provide care that does not vary in quality based on personal characteristics

Patient-Centered: Provide care that respects patient preferences, needs, and values

FOCUS: Process or System or Practice or Methods regardless of the individual characteristics of the members (patients, trainees, providers, etc.)

Am I Doing Human Subjects Research?
How is Research Different from Quality Improvement?

Quality Improvement

If I give prophylactic antibiotics 5 days prior to non-traumatic knee replacement surgery, will that have a positive impact on my post-surgical infection rate?

- Target=**process** used to prevent infection in **ALL** patients having non-traumatic knee replacement surgery
- Intervention=prophylactic antibiotics
- Outcome=% of post-surgical infections during the 12 months prior to this process change versus the 12 months after this process change (group level data)

Research

Do my patients who had prophylactic antibiotics 5 days prior to non-traumatic knee replacement surgery have different rates of post-surgical infection compared to those who did not have prophylactic antibiotics?

- Target=**individual** patients
- Intervention= prophylactic antibiotics
- Outcome =% of post-surgical infections in prophylactically treated vs untreated in non-traumatic knee replacement surgical patients (patient level data – what is different about the patient groups? If outcomes differ, could it be attributed to antibiotic use prior to surgery?)

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 compared to the # of active smokers in clinic prior to 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 compared to those who did not (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

Am I Doing Human Subjects Research?

Clinical Question vs Research Question	Quality Improvement vs Research Question	Pre-research Activity vs Research Activity
• **Clinical**: 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**: 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?	• **QI**: If I train my fellow residents to use a 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? • **Research**: If I use a 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?	• **Pre-research**: 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. • **Research**: How many people in my clinic using this behavioral intervention have been a nonsmoker for 12 months or longer versus those using nicotine gum?

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 are doing human subjects research, they may also determine:
  - It is human subjects research, and it falls into the exempt category (most retro chart reviews)
    - Exempt is a research category that does not require continued oversight as long as the reviewed protocol does not change
  - It is human subjects research that requires continued oversight

I Want to Perform Human Subjects Research

01

Complete required training

(e.g., CITI)

02

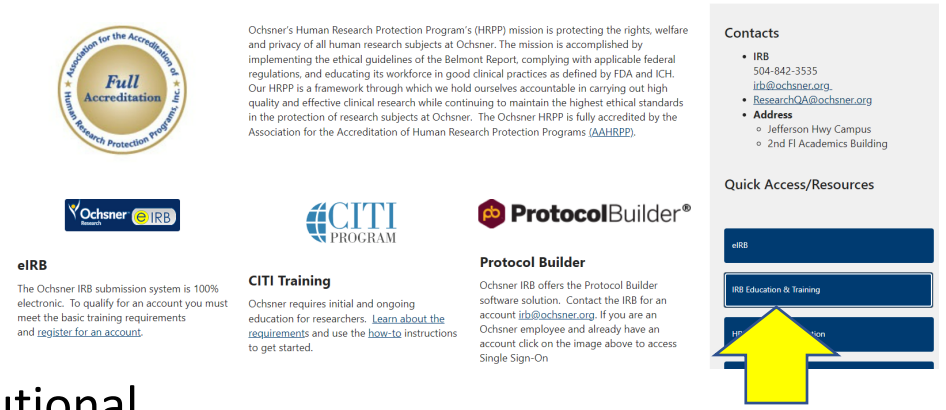
Develop a Hypothesis

03

Do a Literature Search

How Do I Complete CITI Training?

- Go to the HRPP website and click on IRB Education &Training https://ochsnerhealth.sharepoint.com/sites/OchsnerAcademics/SitePages/Human-Research-Protection-Program-(HRPP)---Institutional-Review-Board-(IRB).aspx



- Click on Collaborative Institutional Training Initiative (CITI)

- Create a login
- **Affiliate with Ochsner Clinic Foundation** and the required modules will load

I want to do ask a Research Question: How do I formulate a testable hypothesis?

PICO Strategy

P (**P**atient or **P**opulation)

I (**I**ntervention)

C (**C**omparison)

O (**O**utcome)

How do I formulate a testable hypothesis? Migraine Example

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

P (**P**atient or **P**opulation) = patients with migraine

I (**I**ntervention) = 2 infusions of eptinezumab over 6 mo

C (**C**omparison) = standard oral preventative treatment

O (**O**utcome) = average number of migraines per month

How do I formulate a testable hypothesis? Hypertension Example

For adults with hypertension, does participation in the Ochsner Digital Hypertension Program lower blood pressure?

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

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

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

O (**O**utcome) = blood pressure 6 months after enrollment in Digital Hypertension or initial hypertension prescription

How do I formulate a testable hypothesis? Post-op Pain Example

For adult females receiving a pelvic procedure, do non-narcotic medications versus narcotic medications result in different post-op pain scores?

P (**P**atient or **P**opulation) = females ≥ 18 yr. receiving a pelvic procedure for either benign or malignant reasons

I (**I**ntervention) = any post-op dose, formulation, route or duration of non-narcotic pain medication

C (**C**omparison) = any post-op dose, formulation, route or duration of narcotic pain medication

O (**O**utcome) = avg day 7 subjective pain rating score entered 3x/day for 7 days post-op

How do I formulate a testable hypothesis? GYN Surgical Technique Example

For adult females undergoing gynecological surgery, is there a difference in adverse events between robotic surgery versus other surgical approaches?

P (**P**atient or **P**opulation) = females ≥ 18 yr. receiving gynecological surgery for either benign or malignant reasons

I (**I**ntervention) = robotic surgery

C (**C**omparison) = laparoscopic, abdominal, or vaginal gynecological surgery

O (**O**utcome) =# of Adverse Events (infection, mesh erosion, hemorrhage, GI/GU injury, VTEs)

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? **Make your idea novel & relevant**
- What if only one publication offers an answer to my question – is a second study important? **Generally speaking, yes – it is important to try to replicate research findings (and publish negative findings).**
- If my question has been reliably answered, can I 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 (**P**atient or **P**opulation) = Patients with Hyperkinetic movement disorders

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

C (**C**omparison) = no injection

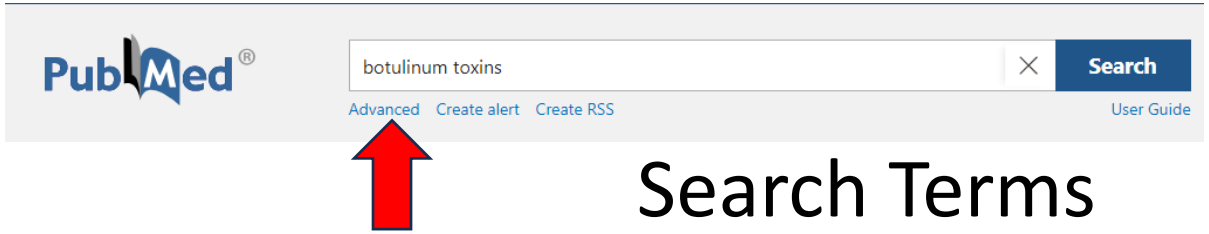
O (**O**utcome) = functional testing

Combine PICO Terms to Build Search

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

Patients

Intervention



Search Terms

History and Search Details

Search	Actions	Details	Query
#2	•••	›	Search: **botulinum toxins**
#1	•••	›	Search: **Myoclonus or Tremors or Dystonia**

1) Myoclonus or Tremors or Dystonia

2) Botulinum Toxins

3) Combine 1 and 2

("Myoclonus or Tremors or Dystonia" and "Botulinum Toxins“)

Limit Retrieval to Target Relevant Literature

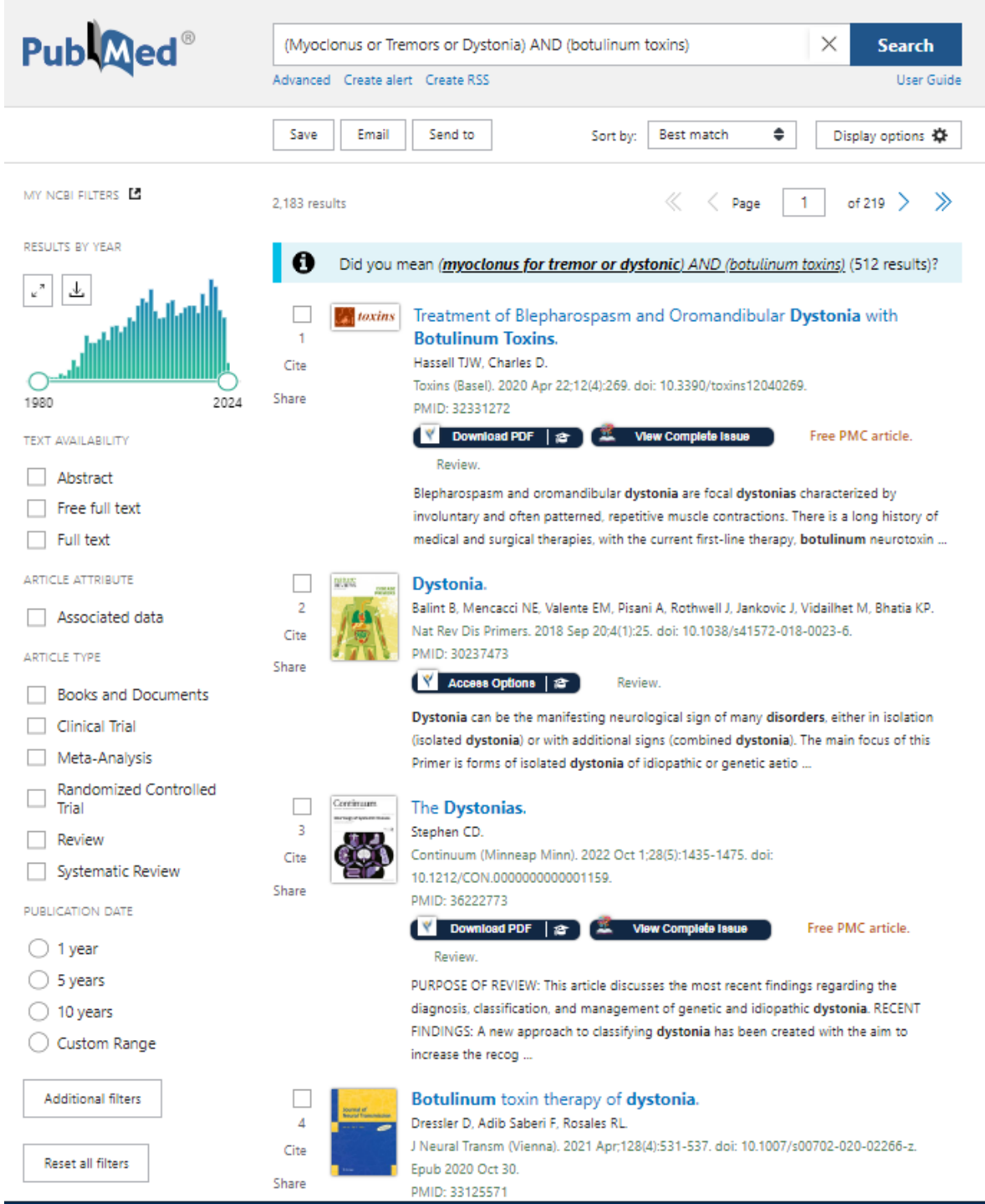
- Age Group
- Human
- Animal
- Language
- Publication Type
  - Letter, article, etc.
- Methodology of Study
  - Article Type

2,183 results

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

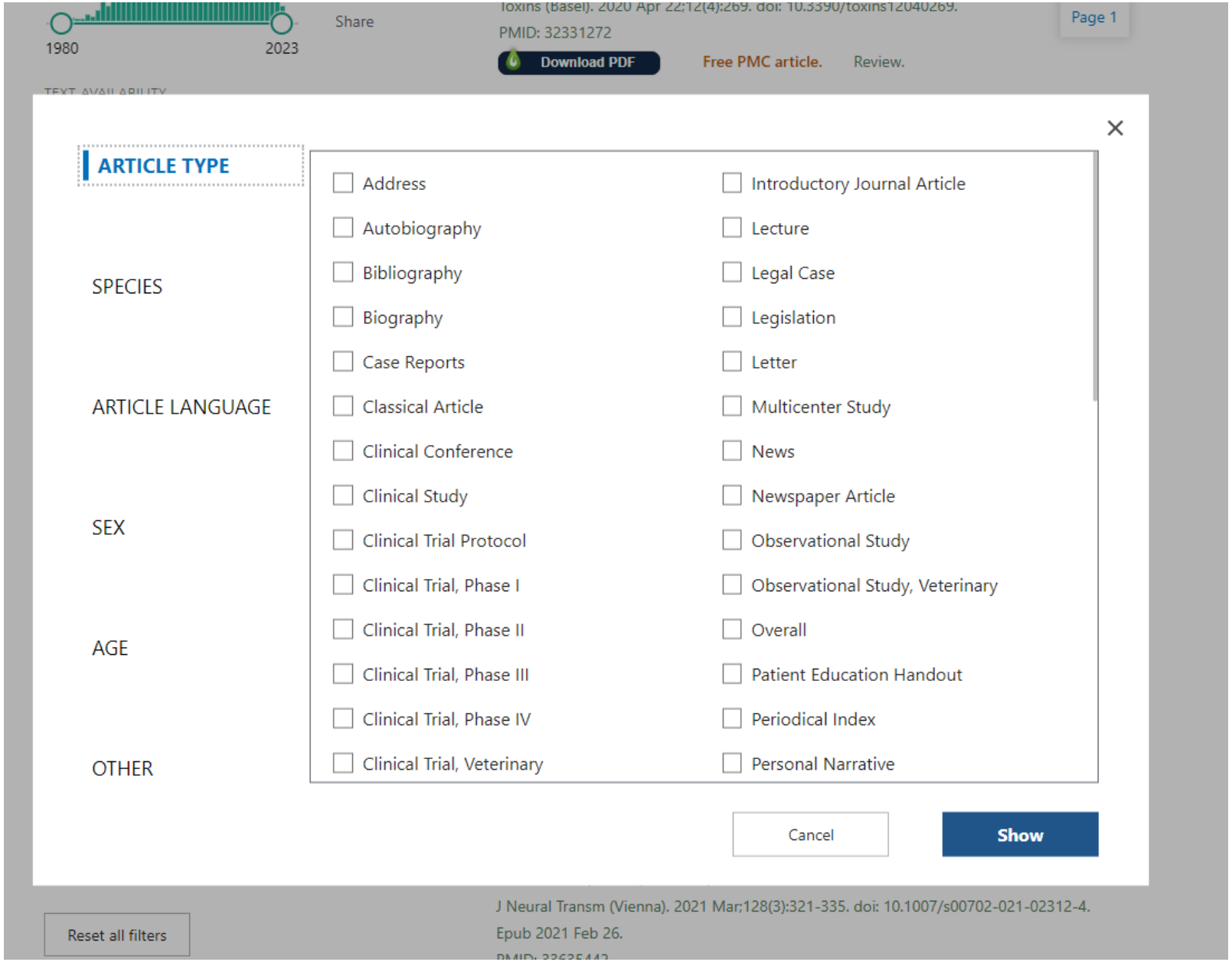
Limit by type – like “Clinical Trials”

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)

02

Develop a Hypothesis

03

Do a Literature Search

I Want to Perform Human Subjects Research

If you are a trainee, have you completed your eligibility determination request and selected a research mentor?

Choose a Study Design

Develop a Protocol

Hierarchy of Evidence for Questions About Interventions

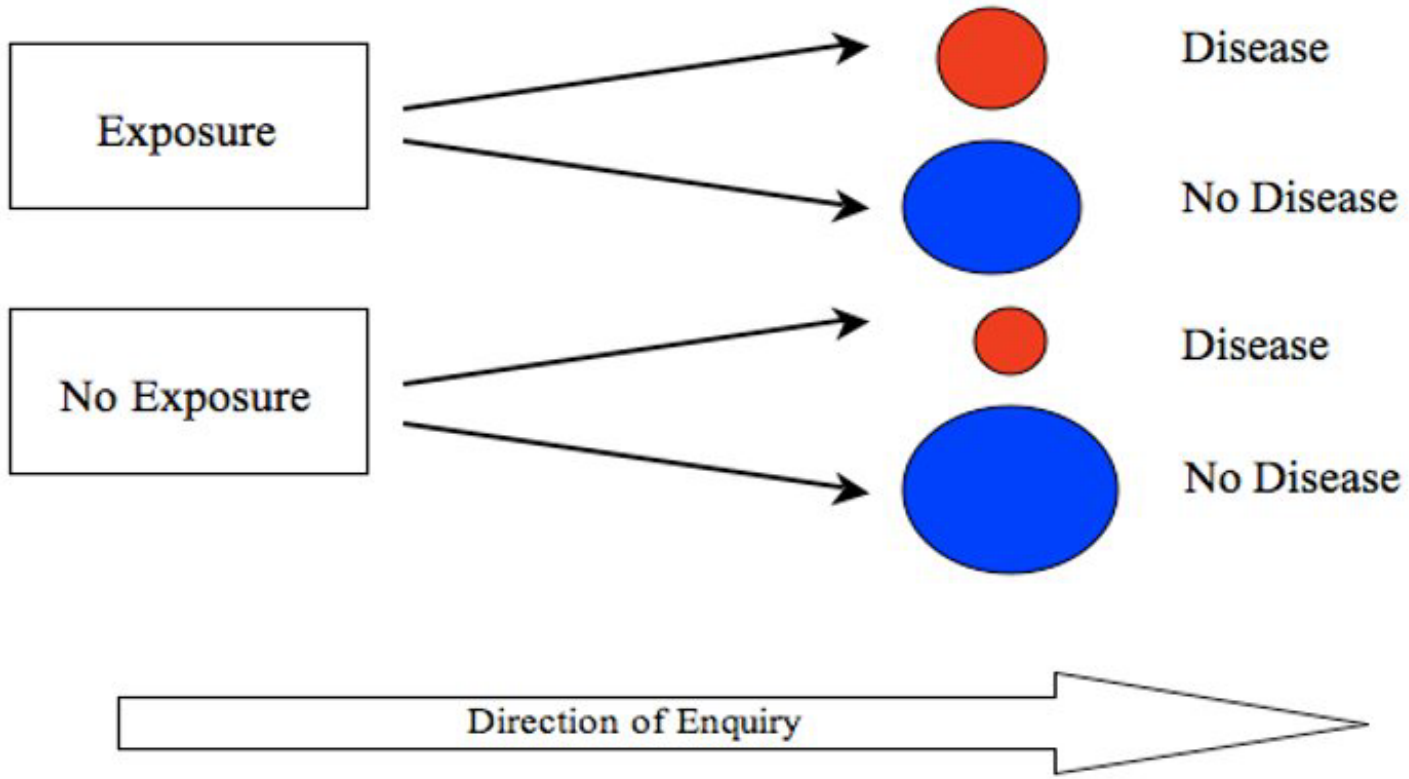
Observational Studies

- **Observational studies: exposure (e.g., treatment) not assigned by investigator**
  - **<u>Descriptive</u>: do not test a hypothesis; collect information on the distribution of disease patterns across demographics or clinical characteristics (i.e., nothing is manipulated)**
  - **<u>Analytic</u>: do test a causal hypothesis of the relationship between exposure and disease**

Analytical Observational Studies

- **TEST a causal hypothesis of the relationship between exposure and disease**
  - **Cohort studies**
    - **retrospective**
    - **prospective**
  - **Case-Control Studies**

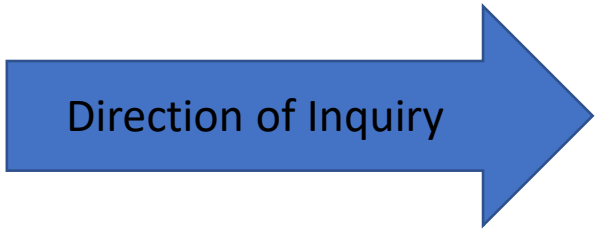
Cohort Study Design



Note the direction of inquiry:
starting with exposure and asking about the outcome
Can be retrospective or prospective

Cohort=group of people with something in common (like an exposure)

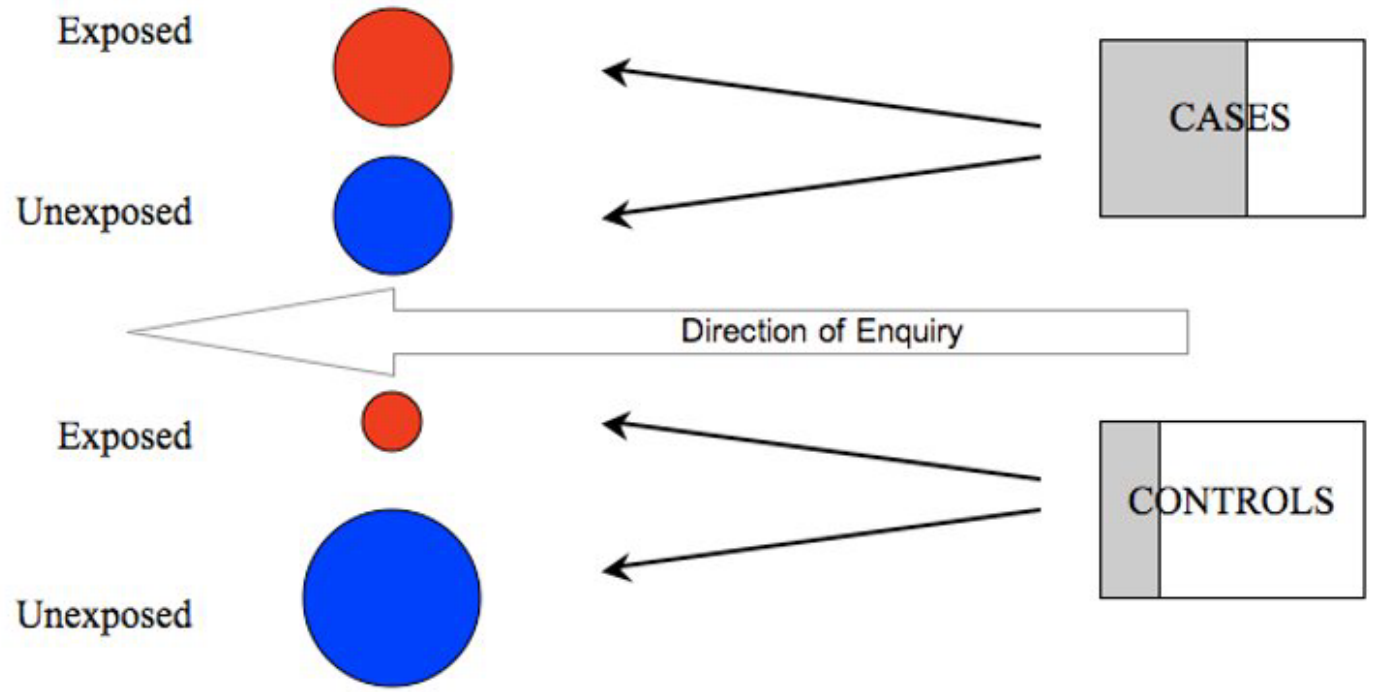
Cohort Study Example



- Retrospective
  - In people with exposure to known environmental toxins, was there an increased risk for developing ALS?
    - Take a known historical exposure and look forward in time to see who developed ALS and if there was a difference in risk based on exposure history.

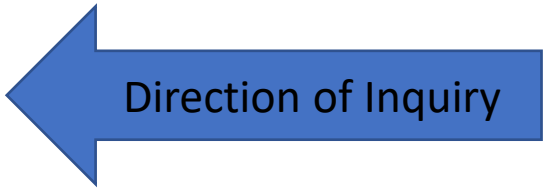
- Prospective
  - In people who use e-cigarettes, will there be an increased risk in developing lung cancer compared to those who abstain from traditional cigarettes and e-cigarettes?
    - Take a current known exposure and follow people into the future to document whether they develop lung cancer.

Case-Control Study Design



Note the direction of inquiry:
<u>starting with outcome</u> and asking about the frequency of exposure and non-exposure
<u>Retrospective</u> studies by nature.

Case Control Study Example



If someone has valvular heart disease, what are the odds that they were treated with a dopamine agonist?

Sample answer provided by Schade R, Andersohn F, Suissa S, Haverkamp W, Garbe E. Dopamine agonists and the risk of cardiac-valve regurgitation. N Engl J Med. 2007 Jan 4;356(1):29-38. doi: 10.1056/NEJMoa062222. PMID: 17202453.

8.78 times greater chance you were treated with a dopamine agonist if you have valvular heart disease than if you do not have valvular heart disease

I Want to Perform Human Subjects Research

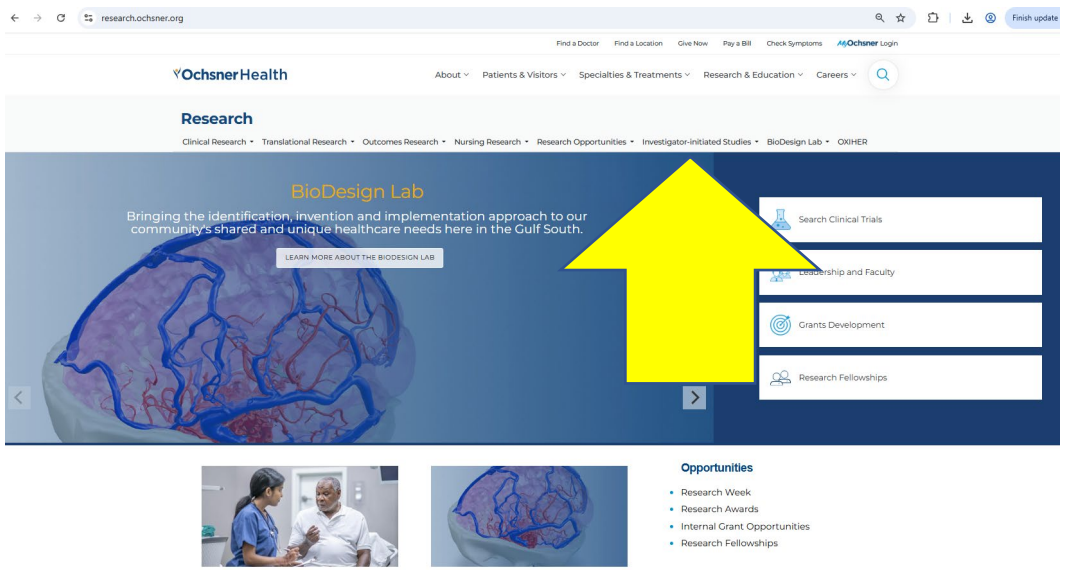
If you are a trainee, have you completed your eligibility determination request and selected a research mentor?

Choose a Study Design

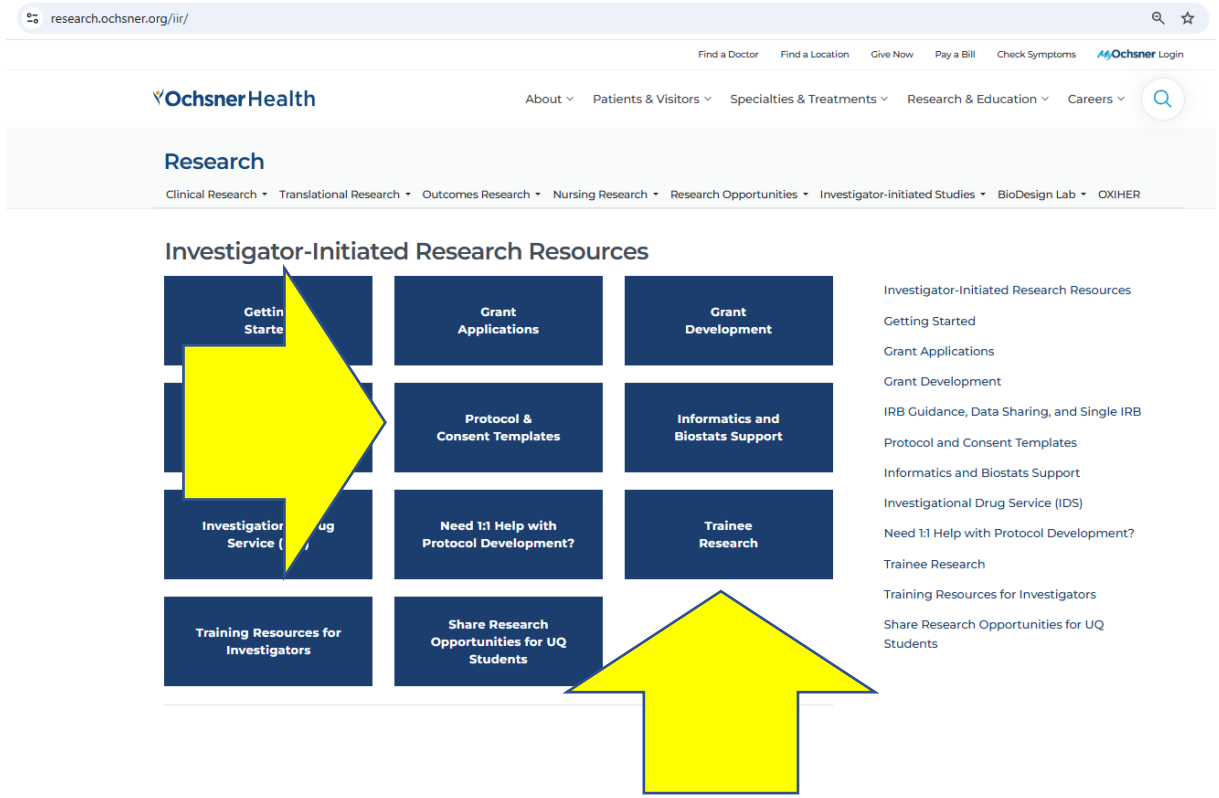
Develop a Protocol

Ready to Develop My Protocol

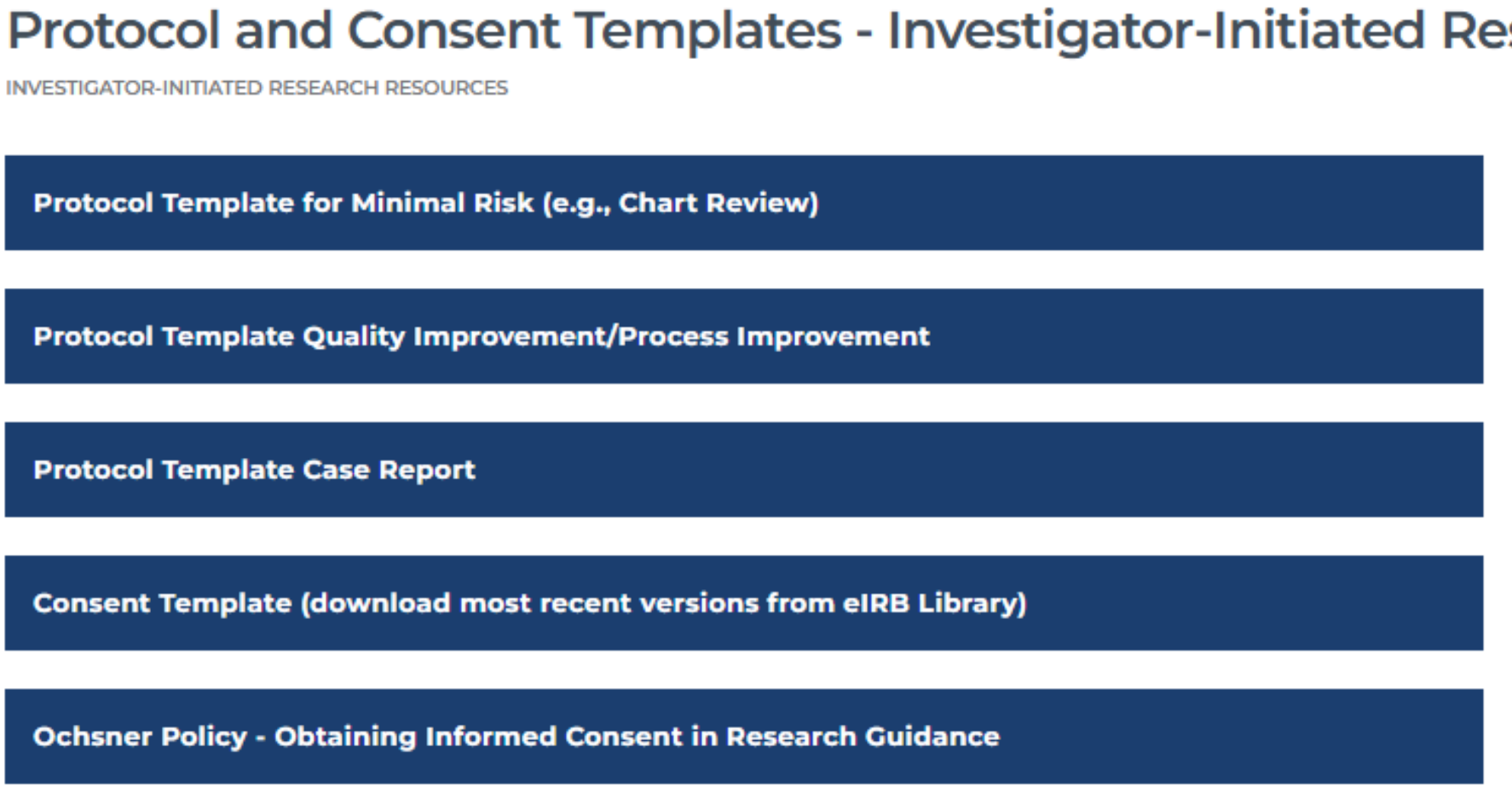
Google “Ochsner Research” or go to Research.Ochsner.org and click on “Investigator-initiated Studies” at the top



Click on “Protocol & Consent Templates” or “Trainee Research” to find resources (Trainee Resource tab has more instructions for ‘how to’)



Ready to Develop My Protocol



"Protocol & Consent Templates" provides quick access to 3 protocol templates:
Minimal Risk (e.g., chart reviews)
Quality Improvement
Case Reports

I Just Need to Complete a Chart Review

OCHSNER CLINIC FOUNDATION

Minimal Risk

Instructions

Utilize this template if you are submitting a Minimal Risk study. Do not remove any sections; if a section is not applicable, enter "N/A" on the line beneath the heading.

Minimal Risk to subjects means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical and psychological examinations or tests and that confidentiality is adequately protected. This category includes protocols that pose "no greater than minimal risk" according to federal regulations.

Examples of Minimal Risk are:

- Study poses no more risk than expected in daily life (e.g., blood draw, physical exam, routine psychological testing)
- Non-interventional studies (e.g., observational studies of behavior or nutrition)
- Survey/Questionnaire studies of a non-sensitive nature
- Electrophysiological studies in healthy subjects or clinical populations (surface recordings such as EEG, ERP, MEG)
- Genomic studies
- Non-invasive imaging (e.g., MRI and fMRI) in healthy subjects or clinical populations to investigate basic mechanisms of brain function
- Research involving the collection or meta-analysis of existing data, documents, records, pathological specimens, or diagnostic specimens to understand basic biobehavioral processes

Minimal Risk Template

Outline of the required components of a protocol

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

Reach out to your Directors; they can provide feedback on your protocol before you submit it to the IRB

Access Resources https://research.ochsner.org/iir/templates/

Create Data Collection Tools

- For Prospective Studies you may need questionnaires or surveys
- For Prospective and Retrospective Studies you need a tool to collect the data
  - Excel spreadsheets shared via OneDrive
  - REDCap data forms
    - Place a request through the Self-Service Portal from OCHWEB page to receive access to REDCap (an ‘existing application’)
- Anything that a participant engages with must be included with your IRB application and reviewed by the IRB, such as surveys, scales, questionnaires, and recruitment messages
- Other data collection tools should be described in your protocol, including your data security plan and data sharing plan (if applicable)
- **Data should never leave the Ochsner-maintained environment** (i.e., do not download data to a personal device)

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?

Only in special circumstances: Work with Research Finance

Can I share data with collaborators?

If outside Ochsner, will need a data use agreement (DUA)

Should I consult with Biostats?

Design phase is the perfect time to ask for help

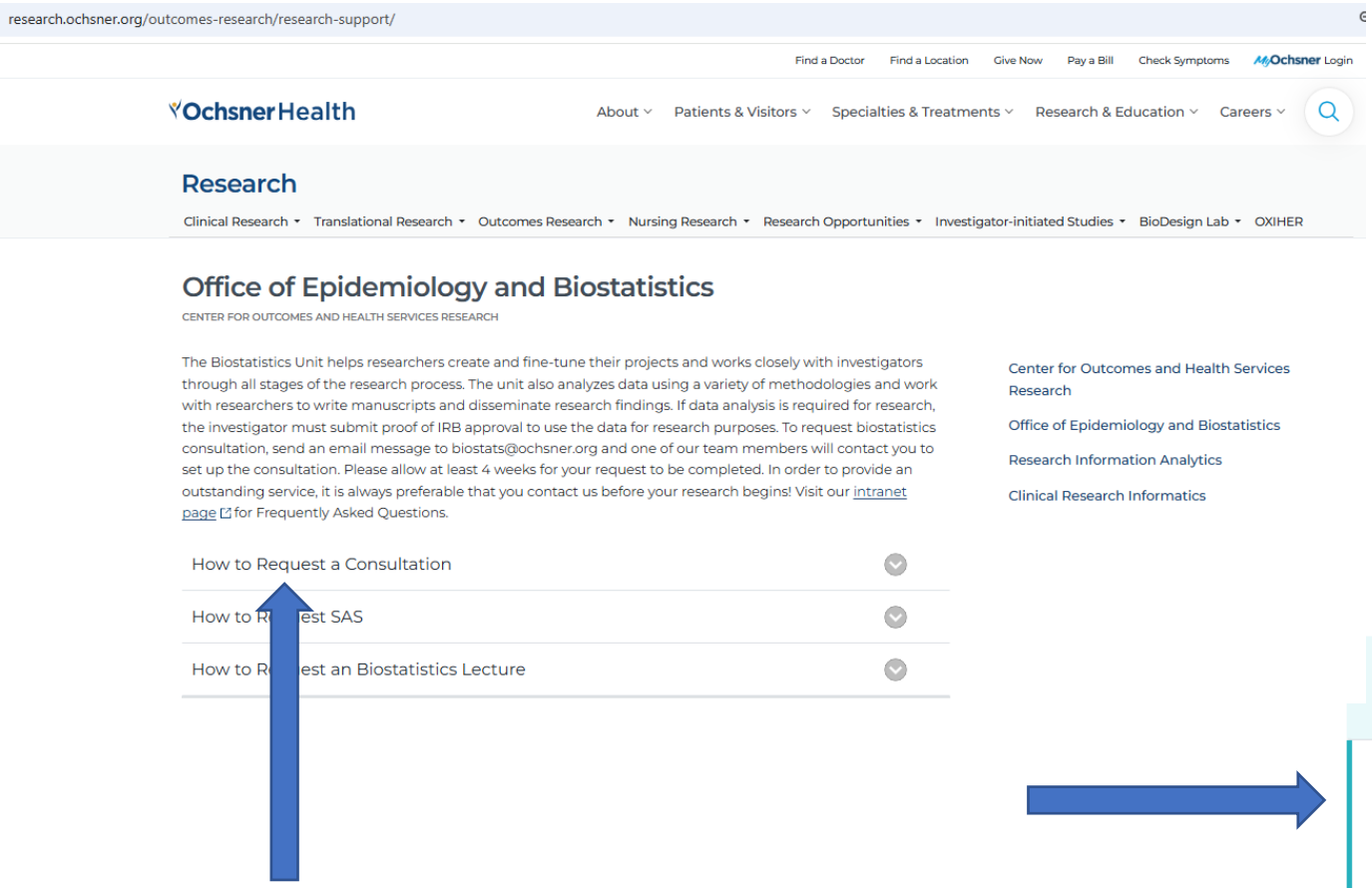
I Have a Protocol – What's Next?
Sample size analysis? Study design check?

Go to the Office of Epidemiology & Biostatistics and submit a request for help
https://research.ochsner.org/outcomes-research/research-support

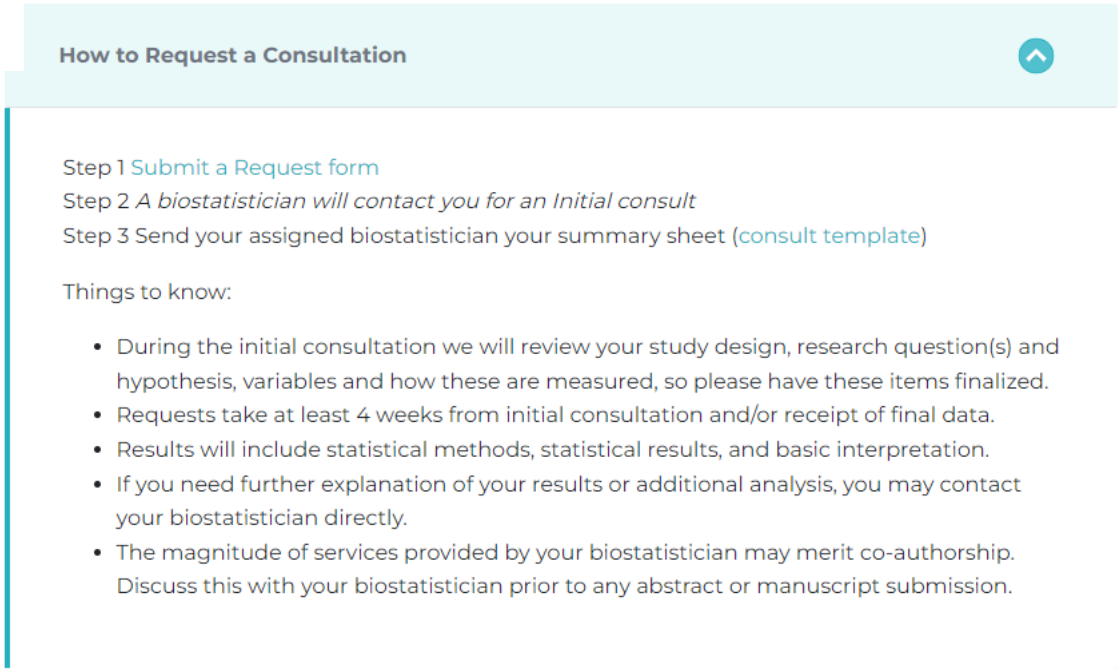
Submit the protocol through eIRB

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)

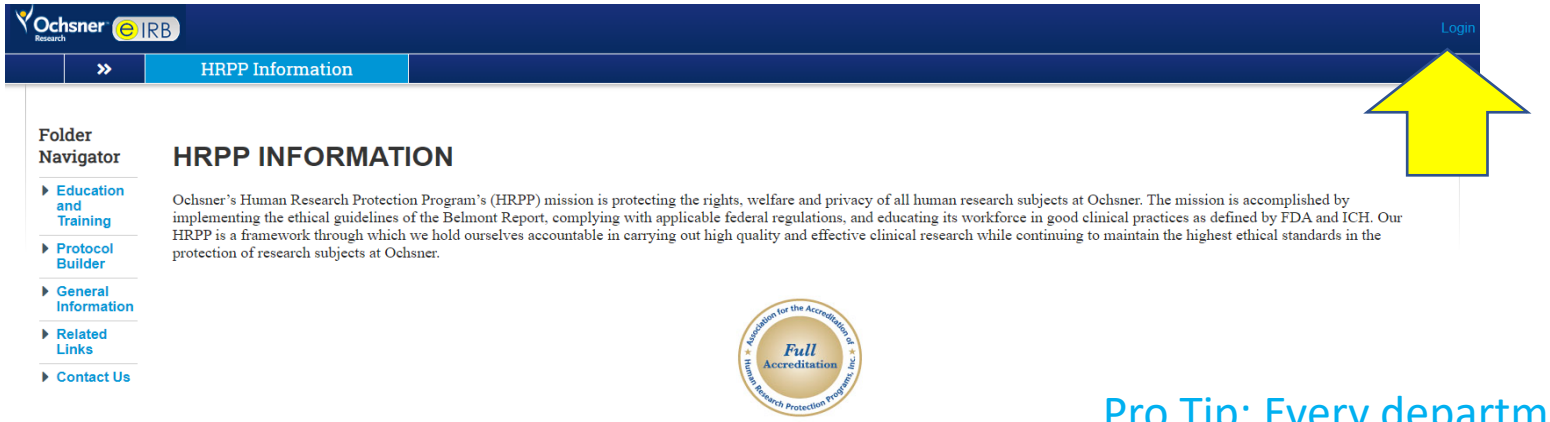


You can access the Biostats site externally through the research.Ochsner.org site or through their Sharepoint site



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

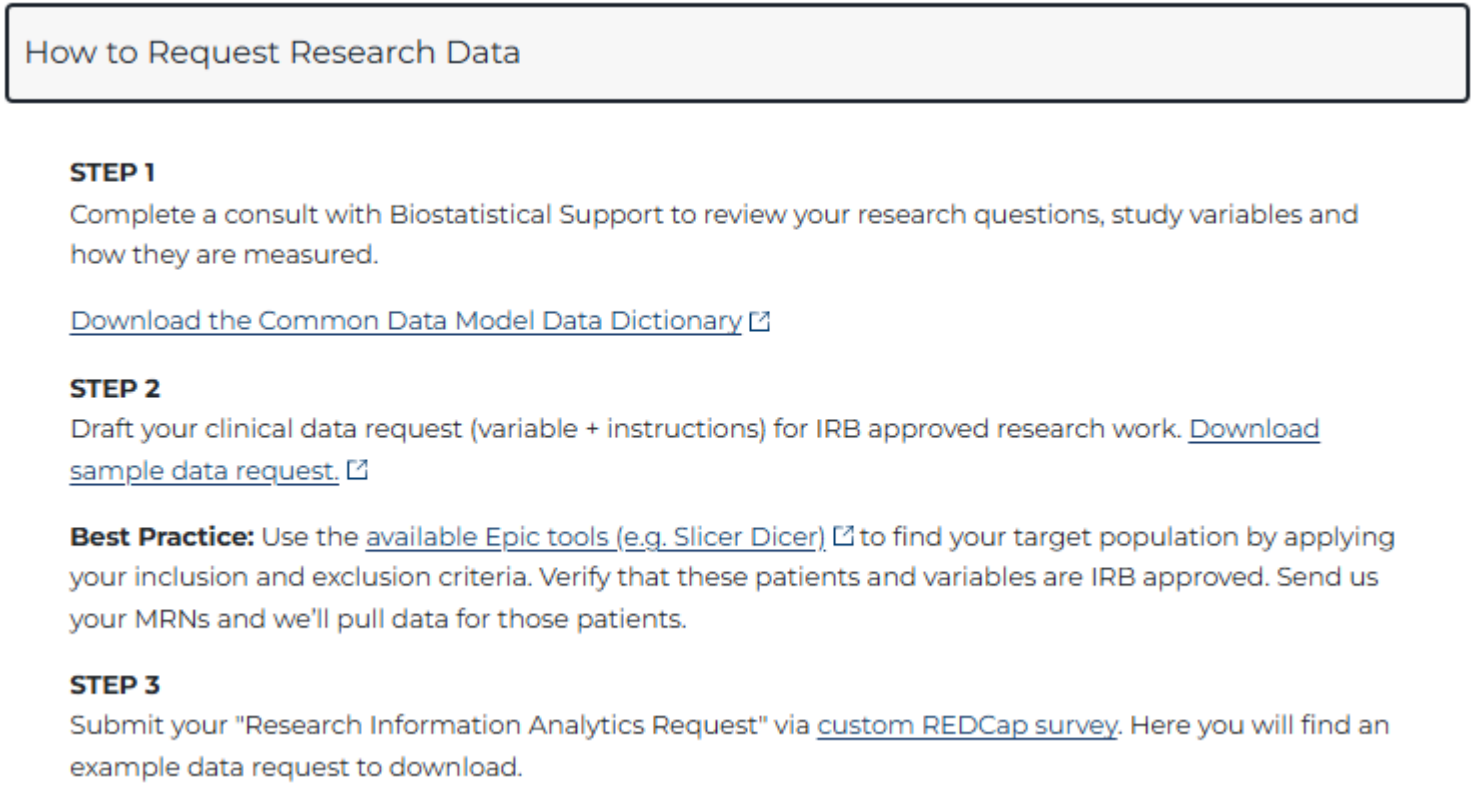
Go to the IRB tab and choose "Create New Study" on the left

Pro Tip: Every department has a Research Director and Regulatory Team Member assigned – ASK FOR HELP

IRB Review is Complete & I'm Ready to Begin

- 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.



Data Collection is Complete: I Need Help with My Analysis

Go back to the Biostatistics site and submit a form for help with analysis and interpretation

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.

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/

Resources to be Shared

Go to the Trainee Research public-facing site https://research.ochsner.org/iir/trainee

Click on the Quick Start Guide with links to research resources
Download the Resident Research Protocol Template

Choose the Sharepoint Site link and login for more trainee resources

Go to https://medical-school.uq.edu.au/ochsner-student-research-hub for Medical Student guidance and access to this PowerPoint.