Resident Research:
Get it Started Right

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Objectives

1. Describe the ASHP residency goal and objectives related to residency projects
2. Discuss the role of the Institutional Review Board (IRB)
3. Describe types of research requiring IRB oversight
4. Describe the importance of a well-devised research question
5. List criteria for devising a good research question
6. Identify metrics and outcomes suitable for pharmacy resident research
7. Outline strategies for the successful assembly and management of a research committee

PART 1: ASHP OBJECTIVES AND IRB BASICS

ASHP Goals

- Goal 2.2: Demonstrate ability to evaluate and investigate practice, review data, and assimilate scientific evidence to improve patient care and/or the medication-use system.

OR

- Goal E1.1: Conduct and analyze results of pharmacy research

ASHP Objectives

- R2.2.1: Identify changes needed to improve patient care and/or the medication-use system.
- R2.2.2: Develop a plan to improve patient care and/or the medication-use system.
- R2.2.3: Implement changes to improve patient care and/or the medication-use system.
- R2.2.4: Assess changes made to improve patient care or the medication-use system.
- R2.2.5: Effectively develop and present, orally and in writing, a final project report.

What is Research?

- “A systematic investigation* designed to develop or contribute to generalizable knowledge. This includes the development of research repositories and databases for research.”

*including developing, testing, and evaluation

Quality Improvement (QI) vs. Research

- Performance improvement or QI is a boundary activity between practice and research. Need to ask:
  - How are the data collected (identifiers, procedures longer or not usually part of care)
  - What is purpose of data collection (who benefits?)
  - How will (might) the data be used?
- Resident projects are research even if also QI

Institutional Review Board (IRB)

- Oversees all research involving humans
- Responsible for protection of the rights and welfare of human research subjects
- Each “institution” conducting research is under the oversight of one or more IRB
  - Single institution IRB
  - Health system or community-wide IRB
  - Commercial IR (Western IRB, Chesapeake Research Review, Inc.)

IRB Oversight is Required

- If the research….
  - Investigational agent of device in FDA regulated trials (FDA regulations)
  - Non-exempt human subject research conducted or supported by Dept of Health and Human Services (HHS regulations)
  - Non-exempt human subject research conducted by an institution with applicable “Assurance of Compliance”
  - Will be published (or presented)

IRB Membership

- At least 5 members of varying backgrounds
- Suitable expertise in areas of research being reviewed (variety of credentials)
- Diversity of race and gender
- At least 1 nonscientific member
- At least 1 member not affiliated with the institution
- Represent the “community” sensibilities

Research Reviewed by IRB

- Investigator initiated projects
- Industry sponsored (e.g. pharmaceutical)
- Government funded protocols
  - National Institutes of Health (NIH)
  - Human Services Research and Development
- Cooperative group trials (funding varies)
- Foundation and other privately funded
- Emergency use of investigational agents
- Expanded Access (Treatment IND)

Types of Research Reviews

- Initial review
  - Full Board
  - Expedited (not necessarily faster)
- Continuous review (ongoing oversight)
  - Adverse event reports (SAE, AE, IND)
  - Amendments (administrative, substantive)
  - Continuation report @intervals $\leq$ 1 year
- Final report

IRB Must Approve

- Protocol and Research Application
- Consent form(s) or waiver of consent
- Ads used to recruit subjects (including internet advertising)
- Education materials
- Questionnaires, surveys
- Payments to subjects
- Qualifications of investigators

Initial Review – Full Board

- Risk to subjects is minimized
- Risks are reasonable (benefits exceed risks)
- Selection of subjects is equitable
- Informed consent contains all required elements, properly obtained and documented
- Privacy protections (confidentiality maintained)
- Monitoring to ensure safety
- Additional safeguards for vulnerable subjects

Vulnerable Subjects

- Children
- Prisoners
- Pregnant women, fetuses, in-vitro fertilization
- Cognitively impaired (mental illness or disability)

- Non-English speaking subjects
- Educationally or socially disadvantaged
- Students (when research is being done by their teachers)
- Employees (when research is done by their supervisor(s))

IRB Committee Actions

- Approve protocol submission
- Require modification (approve with stipulations or “deferred approval”)
- Disapprove or defer
  - Final authority
- Place restrictions on study
- Suspend
- Cancel
- Terminate

Expedited Review

- IRB Chair or designee may approve without a full board review
  - Research involving no more than minimal risk
  - Minor changes to a previously approved protocol (amendment)
  - Retrospective studies
  - No invasive procedures

Ongoing (Continuous) Review

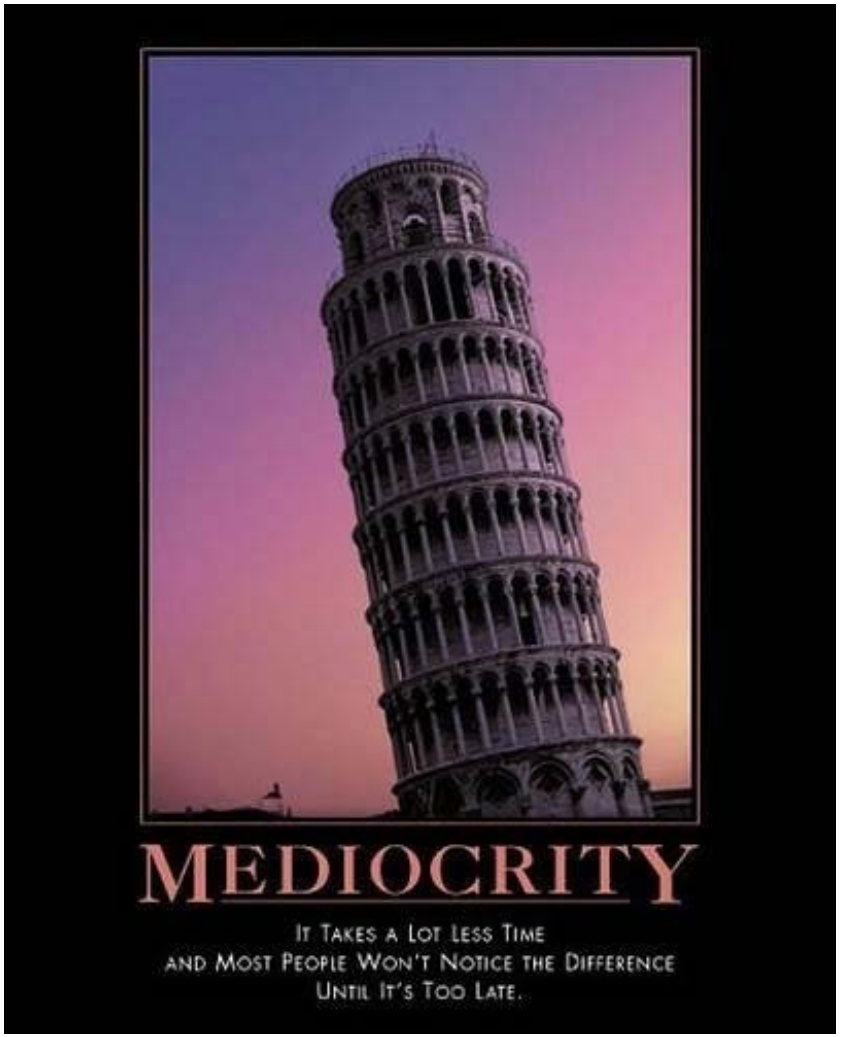
- Full board or expedited review
- At least annually (IRB sets for each study)
- Submit summary of protocol progress during the study period
  - Number of subjects enrolled, withdrawals
  - Amendments, changes to informed consent
  - Adverse Events (AE)/Serious Adverse Events (SAE)
  - Findings to date (any abstracts, publications)

Final Report

- Submit when study is closed/completed
- Include summary of results/findings

Why are these elements of research important?

Start off on the right path with the best people



PART 2: STEPS TO SUCCESS

Take time to plan your project carefully

What is a research question?

A research question is the fundamental core of a research project, study, or review of literature. It focuses the study, determines the methodology, and guides all stages of inquiry, analysis, and reporting.

Reference: https://researchrundowns.com/intro/writing-research-questions/

Criteria for a good research question

Think FINER

- **F**easible
- **I**nteresting
- **N**ovel
- **E**thical
- **R**elevant

Hulley S, Cummings S, Browner W, et al. *Designing clinical research*. 3rd ed. Philadelphia (PA): Lippincott Williams and Wilkins; 2007.

Feasible

- Adequate number of subjects?
  - Consider targeting 50-100 subjects depending on complexity of data collection
- Ability to measure/collect desired data?
  - Is your health system already collecting what you want to measure/analyze
- Adequate time and resources?
  - Does your research require staff training, EMR changes, workflow modifications, etc.
- Manageable scope?
  - Don’t bite off more than you can chew – remember, you already have a full time job ☺

Interesting

- You have to enjoy and have a sincere interest in your research – you're going to spend a lot of time with it

Novel

Does the research question

- Confirm or refute previous findings
- Extend previous findings
- Provide new findings

Ethical

May we join your research committee?
We'll get the job done, no problem.

Relevant

- To scientific knowledge
- To clinical and health policy
- To future research directions

So how do I identify a research question?

- Work backwards!
  - What is your end goal (new service, demonstrate cost savings, evaluate new clinical tool) – can you design a question related to that?
- Narrow the question
  - Make sure you're scope is manageable
- Test it out
  - Review a patient chart, department workflow, and see if you can efficiently collect the information you want to answer your question

Research Question Sample

- **Observation**: ED providers are commonly ordering 1gm of valproic acid (VPA) and fosphenytoin (FOS) for patients with status epilepticus (SE)
  - Guidelines state patient should receive 20-40 mg/kg VPA or 15-20 mg PE/kg of FOS if they are refractory to benzodiazepines
- **Goal**: "Pharmacy to dose" service in the ED for IV VPA and FOS

Can you identify a research question?

Research Question Options

Which research question is most suitable for a resident research project?

- Does weight-based dosing of FOS and VPA reduce the rate of seizure recurrence?
- Does weight-based dosing of FOS and VPA increase the number of post-load therapeutic drug levels?
- Does a “pharmacy to dose” service for FOS and VPA improve dosing compliance with national treatment guidelines for SE?
- Will patients be more satisfied with dosages of FOS and VPA selected by a pharmacist compared to a physician?

Appropriate Loading Dose Definition

A total dose of 10–20 mg/kg for fosphenytoin should be given OR 10-40mg/kg for valproate (based on indication).

Partial loading doses should only be given if the patient had a serum phenytoin concentration or valproate level below the target level.

If a second loading dose is required for the above reasons, it must be administered within four hours of the first loading dose.

The loading dose based on pharmacokinetic equations does not vary by more than 20% of the calculated dose.

Doses of <10 mg/kg should not be used

- Past medical history
- Subtherapeutic level

Research Outcomes

- Once you have a research question identified you will need to choose a primary, and possibly secondary, outcome(s).
  - A statement or status that will serve as an answer to the research question
  - Metrics will be used to support or refute the outcome
  - You MUST define outcome(s) that are not direct
    - Everything in research needs to be defined unless it is obvious
    - Watch out for words like, better, improved, appropriate, satisfied

Research Metrics

- To determine if an outcome has been achieved you will need to select, and possibly define, metrics.
  - What will you measure?
    - Direct measurement or surrogate?
  - How will you collect it?
    - Report, chart review, survey
  - How will you analyze it?
    - Statistics, power calculation?

TIP: Review examples of research in the same area and see what those researchers used for outcomes and metrics!

Research Design Summary

Research question

- What question or problem are you trying to answer?

Outcomes

- How will you determine that answer to that question?

Metrics

- What measurements support this outcome?

Research Design Example

Research question

- Does a “pharmacy to dose” service for FOS and VPA improve dosing compliance with national treatment guidelines for SE in the ED?

Outcomes

- Primary: Percentage of patients with an appropriate loading or partial loading dose of FOS and VPA for SE in the ED
- Secondary: ADE and seizure recurrence within 24 hours

Metrics

- Pt demographics, dose of medication, pt weight, drug level prior to loading dose, hypotension, recurrence of seizure

Research Committee

- A group of professionals who help design, review, implement, analyze and report your research
- May be arranged by your program or up to you to assemble
- Include key stake holders – especially from other disciplines

Research Committee Benefits

- Subject matter experts
  - Familiarity with medical literature, pathophysiology, pharmacotherapy, previous facility research findings
- Workflow refinement
  - Ensure quick integration and targeted staff education
  - Especially important for new services
- Buy in
  - Ensure engagement and participation of staff
  - Especially important if research involves disciplines outside the pharmacy department

Research Committee Etiquette

- Identify expectations
  - Explain what you will need from each member and when you'll need it, however, you are the principle investigator
- Communicate concisely and regularly
  - No long-winded emails without clear requests for action
- Ask for help!
  - Work to resolve problems on your own, but don't forget to ask for help if you encounter a barrier
- Provide ample review time
  - Your committee members are busy and will need time to thoughtfully review your protocol, poster, presentation and manuscript

In Summary

- Identify a **FINER** research question
- Design your project with outcomes and metrics that are achievable
- Assemble a group to help you design, implement, evaluate, and report your research

Have Fun!