AAPP Practice Toolkit: Clinical Research in Psychiatric Pharmacy

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This toolkit is intended to highlight both the evidence-base, available literature as well as strategies of clinical decision making used by expert clinicians. The content reflects the views and practice of the authors as substantiated with evidence-based facts as well as opinion and experience. The opinions and recommendations in this document reflect those of the authors and do not necessarily reflect those of their employers or AAPP.

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American Association of Psychiatric Pharmacists (AAPP)

AAPP is a professional association representing psychiatric pharmacists nationwide. Our members integrate into teams of health care professionals, making a difference in overall costs, treatment efficiencies, patient recovery and quality of life. Learn more at aapp.org/psychpharm.

Integrating Research into Your Career

Research activities may encompass someone's entire role, represent only a small percentage, or be completed on discretionary efforts. Entry into research has no one path. While it may be formal for some (e.g., fellowship, PhD training) it may develop spontaneously from patient specific questions that arise in clinical practice. In academic settings, research may also be pedagogic in nature. While research as a career (or an element of a career) may not be suitable for all pharmacists, it is likely that many pharmacists have identified a problem, implemented a possible solution, and reassessed it for improvement. In this spirit, quality improvement (QI) projects may represent activities that are in many ways like formal research while recognizing that their methods, structure, and application have some key differences.

Outside of pharmacists with formal research training, how do pharmacists get involved with research? One answer involves clinical residency training of a psychiatric pharmacist. Almost 80% of pharmacy residents have reported to have interest in scholarly activity beyond their residency project. Publication of their residency research increases the likelihood of publishing another manuscript within the subsequent 5 years.1 A worrisome trend for the profession of psychiatric pharmacy comes from a recent publication that suggests psychiatric pharmacy residents specifically have low and decreasing publication rates.2 It is not unsurprising that the types of manuscripts reported published were predominantly retrospective and observational. A majority (63.3%) were published by residents associated with a university, which might indicate a greater allocation of resources (statistical support, access to (larger) data, mentors who also engage in research, efficient exempt review processes) compared to non-university affiliated programs. However, funding was not a barrier as over 90% of published papers did not have (or require) financial support.

Beyond the responsibility mentors have in research education to residents, another approach for pharmacists new to and interested in research is to start small. An interesting case or clinical scenario may lead to a case report that is publishable. While this is not considered research, many of the skills learned as it relates to literature searches, writing experience, submission experience, and response to reviewer feedback can also apply to elements of a research study. Additionally, clinical (or pedagogical) questions without clear answers due to gaps in knowledge can become research questions and a subsequent QI study using methods such as retrospective chart review.

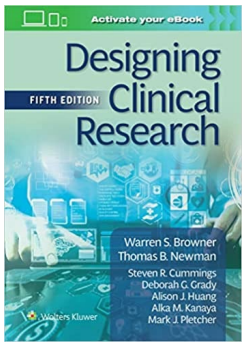
While developing research interests and skills, pharmacists should also seek out mentors in the profession. Networking, conferences, and professional organization support/resources are just some common approaches. While it may seem awkward, a "cold email" to a corresponding author or conference speaker who has similar interests is a direct and often productive approach. Individuals with established mentorship are more likely to be successful in scholarly activities. Pharmacists should seek out training resources available at their institution whether one-time seminars on “approaching research” or financial support for “research boot camps.” Several quick research guides, podcasts, and resources can also be referenced:

- Initiating and Maintaining a Relevant Research Career Across Decades - ASHP
- ACCP - Research and Scholarship
- Understanding Clinical Research: Behind the Statistics | Coursera
- The Data Scientist’s Toolbox | Coursera
- Writing a research proposal - YouTube
- Generating a research idea n - YouTube
- Overview of research designs n - YouTube
- Statistical Inference | Coursera
- Writing Abstracts and Developing Posters for National Meetings - PMC (nih.gov)

- Power and Sample Size | Free Online Calculators
- ICMJE | Recommendations | Defining the Role of Authors and Contributors

As there is progression from institutional chart reviews to large retrospective database cohort studies or even more complex institutional projects, there will be a point in which you may need funding. With progression to prospective research, funding may become more complex with more stakeholders requiring funding (lab personnel, biospecimen processing, data management, etc.). Individuals should explore both internal and external funding opportunities.

Designing Clinical Research: A Starting Point



The textbook offers a robust, comprehensive review of the entire research process. Beginning with a basic introduction to the components of the research process, including a discussion of translational research, the book takes the reader through the process in a step-by-step manner. Starting with the development of the research question and hypothesis, to research design and data collection selection, through to enrolling the study subjects and gathering and analyzing the data, this book covers the required components of quality research. Finer points within each of these areas are incorporated, allowing the reader to delve into most any area of research methodology possible. While there is no information on preparing a research manuscript after completion of the study, this information can easily be found in other sources. With an approximate price of $70 (via Amazon in May 2023), this makes this book affordable for the material it contains.

Determining Study Outcomes

Determining appropriate study outcomes is a pivotal and challenging step in research design. The specific outcomes and measures will determine whether the data is useful to the target audience and whether it is reproducible by other pharmacists. Fortunately, AAPP has developed a consensus-based set of outcomes and measures to improve research standardization by psychiatric pharmacists. The measures in this Core Outcome Set for Psychiatric Pharmacists (COS-PP) should be utilized when studying the impact of psychiatric pharmacists in caring for individuals living with psychiatric disorders through consistent, measurable, reportable, and reproducible population specific outcomes that are primarily medication-related. (Manuscript Forthcoming) While this is not an exclusive list of outcomes, it does helps address gap identified in the literature. Access the COS-PP toolkit at https://aapp.fyi/cos-pp.

Evaluating Your Research Expertise

Reflect on Your Knowledge

Rate your understanding on each of the following topics using the following scale. If the answer to any of these questions is Moderate or less, then please consider if any additional education or training is necessary before considering pursuing the leadership of a multi-site study.

What is your current level of knowledge, ability, or experience with the topic?	None	Some	Moderate	Competent	Expert	N/A
1. Research hypothesis development						
2. Basic study design						
3. Determination of study outcomes/measures						
4. Statistics						
5. Determination of research team composition						
6. Study funding (grants, etc.)						
7. Study budgeting (direct and indirect costs)						
8. IRB approval process						
9. Enrolling study subjects						
10. Collecting and analyzing data						
11. Preparing a manuscript from research results						

Reflect on Your Experience

Before attempting to coordinate a multi-site study, it is best to have as many of the following experiences as possible to maximize your success. A senior researcher is likely to answer (D) to all of these. If you answer (A) or (B) to any questions, you should consider strategies to mitigate the specific limitations through mentoring or carefully-selected co-investigators.

1. How many peer-reviewed research study manuscripts have you had successfully published in medical journals?
   A. Less than 5
   B. 5-10
   C. 11-15
   D. 16 or more
2. What is your experience in serving as the primary investigator (PI) on a clinical study (RCTs, QI study, retrospective study, etc.)?
   A. None
   B. 1-3 studies
   C. 4-6 studies
   D. 7 or more studies
3. What is your experience in serving as a co-investigator (not a PI) on a clinical study (RCTs, QI study, retrospective study, etc.)?
   A. None
   B. 1-3 studies
   C. 4-6 studies
   D. 7 or more studies
4. What is your experience in serving as a co-investigator or site coordinator (not a PI) on a *multi-site* clinical study?
   A. None
   B. 1-2 studies
   C. 3-4 studies
   D. 5 or more studies
5. How many *successful* grant applications have you had funded (please do not include internal grants from an employer or educational program)?
   A. None
   B. 1-2 studies
   C. 3-4 studies
   D. 5 or more studies

Preparing for a Multi-Site Study

Multi-site studies have the potential to strengthen outcomes and further generalize findings to a broader patient population when compared to single-site studies. Participation in a multi-site study will require additional preparation and ongoing communication among all participating sites to ensure adherence to study procedures for all participants. The following table summarizes key differences in single-site vs. multi-site research studies for psychiatric pharmacists who may consider serving as a coordinating site or secondary site investigator. Appendix A: Coordinating Site Checklist and Appendix B: Secondary Site Checklist can be utilized to prepare for or navigate the multi-site study design, execution, and reporting process.

Important Differences for Multi-Site Research

Single-Site	**Multi-Site**
Communication among investigators less structured	Regular, structured communication among all sites to ensure adherence to study design and progress toward goals is required
IRB submission process is site-specific	Requires use of a single IRB, aka IRB of record (typically the coordinating site) and a "Memorandum of Understanding" or "Reliance Agreement" from each additional participating site which will rely on the single IRB of record (typically all secondary sites)
Outcomes, methodology, and data collection are based on site specific processes	Outcomes, methodology, and data collection are feasible and standardized across study sites
Flexibility for storing data securely via various facility specific processes	Must establish process for uploading deidentified data to central database
Adherence to study design and data collection processes is site specific	Increased emphasis on quality assurance: Requires process and timeline to monitor adherence to study design and data collection processes among all sites
Statistical analysis is based on data from a single-site	Must ensure statistical plan will account for comparison of outcomes and potential bias/confounding variables among sites
Rater consistency is straightforward	Rater consistency requires investigator training to obtain inter-rater reliability
Authorship determined based upon investigator contributions to research and manuscript	Authorship can vary based upon multiple variables: study leadership and contributions, writing contributions, and other factors

Appendix A: Coordinating Site Checklist

Study development

- ☐ Develop Research Question and Specific Aims
- ☐ Literature Review
- ☐ Funding Search
- ☐ Obtain "buy-in" from key stakeholders at each site:
    - Clinicians
    - Administrators (ie, all service chiefs/supervisors of participating staff)
    - Informatics
    - Patient advocate (optional)
- ☐ Research Team
    - Identify study primary investigator (PI) and site PI's
    - Ensure each investigator is appropriately trained, especially for gold standard ratings
    - Develop "Investigator brochure"
    - Determine authorship vs acknowledgements for primary manuscript
    - Outline guidance on authorship/acknowledgements for secondary manuscripts
    - Provide template for memorandum of understanding (or "reliance agreement") to secondary site PI's
- ☐ Study Design
    - Select Outcomes that are feasible to measure for each site
    - Develop process and timeline to monitor adherence to study design among all sites (quality assurance)
    - Develop timeline for in-person or virtual site visits
- ☐ Statistics Plan
    - Identify biostatistician at coordinating or secondary site
        - Consider beginning communication when formulating your research question
        - Consider partnering with sites with biostatistician support
    - Consider commercial/independent biostatistician resources (See Appendix C)
    - Consult with statistician to ensure statistical plan will account for:
        - Comparison of outcomes between sites
        - Analysis of nesting within sites
        - Potential bias/confounding variables among sites
- ☐ Data Collection Plan
    - Must be feasible and standardized for each site (eg, data collection definitions/processes/storage/sharing)
    - Promote upload of de-identified data into central database
    - Develop process and timeline to monitor adherence to data collection procedures among all sites (quality assurance)
- ☐ Timeline
- ☐ Budgeting
    - Develop budget for coordinating center
    - Develop budget for each secondary site
    - Note that site variance in funding application may require explanation

Pre-study phase: IRB

- ☐ Institutional Review Boards research protocols (plan for collecting data), data collection materials, all plans for obtaining and forms for documenting consent and assent, and recruitment materials to ensure protection of the rights and welfare of human subjects of research" (HHS. Gov)
- ☐ "The revised Common Rule (i.e., the 2018 Requirements) requires at 45 CFR §46.114 (b) that all institutions located in the United States that are engaged in cooperative research conducted or supported by a Federal department or agency rely upon approval by a single IRB for the portion of the research that is conducted in the United States unless qualifying for exception". (HHS.gov)
- ☐ Schedule meeting with coordinating site IRB or Research and Development Committee to review process, timeline, and expectations for IRB approval of multi-site study
    - Determine Single IRB, aka IRB of Record (typically coordinating site IRB)
    - Determine Secondary site IRBs or Research and Development Committee
    - Determine process for IRB submission for multisite human subjects research studies for all sites
    - Disseminate Memorandum of Understanding template to secondary sites
    - Develop process for coordinating communication/requirements among all IRBs involved
    - If all sites unable to use Single IRB, identify procedure for requesting exception (Single IRB Exception Determinations)
- ☐ Note: Department of Veteran's Affairs recommends multi-site studies be reviewed by Central IRB (governed by VHA Office of Research and Development).
    - Primary site VA IRB may serve as the "IRB of Record" with secondary VA sites added to the central IRB application.
    - If sites are not able to use Central VA IRB or other non-VA IRBs for which the VA IRB of Record has reliance agreements, a single IRB exception can be requested to facilitate additional local IRB review for these sites
- ☐ In absence of coordinating site or secondary site IRB:
    - Association for the Accreditation of Human Research Protection Programs provides a list of accredited IRBs: http://www.aahrpp.org/learn/find-an-accredited-organization
    - Consortium of Independent Review Boards (CIRB) provides a list of commercial IRBs: http://www.consortiumofirb.org/cirb-members/

Study phase

- ☐ Project Management – Coordinating a Multi-Site Study
    - Schedule recurring, structured communication among investigators across sites throughout data collection process
    - Conduct monitoring for adherence to data collection procedure at each site (quality assurance)

Post-study phase

- ☐ Analysis/Statistics
- ☐ Conclusions
- ☐ Publication and Reporting Guidelines
- ☐ Dissemination and Supplemental Materials

Appendix B: Secondary Site Checklist

Study development

- ☐ Obtain "buy-in" from key stakeholders at study site
  - clinicians,
  - Administrators (ie, all service chiefs/supervisors of participating staff)
  - Informatics
  - patient advocate (optional)
- ☐ Research Team
  - Identify site PI's
  - Receive "Investigator brochure" from coordinating site
  - Determine authorship vs acknowledgements for primary manuscript
  - Outline guidance on authorship/acknowledgements for secondary manuscripts
  - Receive template for memorandum of understanding (or "reliance agreement) from coordinating site PI's
- ☐ Study Design
  - Review timeline and expectations for monitoring adherence to study design at study sites (quality assurance)
  - Review timeline for in-person or virtual site visits
- ☐ Data Collection Plan
  - Confirm feasibility for local study site (eg, definitions, processes, storage, sharing)
  - confirm ability to upload de-identified data into identified central database
  - Review timeline to monitor adherence to data collection procedures among all sites (quality assurance)
- ☐ Timeline
- ☐ Budgeting

Pre-study phase: IRB

- ☐ Institutional Review Boards oversee research protocols (plan for collecting data), data collection materials, all plans for obtaining and forms for documenting consent and assent, and recruitment materials to ensure protection of the rights and welfare of human subjects of research" (HHS. Gov)
- ☐ "The revised Common Rule (i.e., the 2018 Requirements) requires at 45 CFR §46.114 (b) that all institutions located in the United States that are engaged in cooperative research conducted or supported by a Federal department or agency rely upon approval by a single IRB for the portion of the research that is conducted in the United States unless qualifying for exception". (HHS.gov)
- ☐ Schedule meeting with coordinating site IRB or Research and Development Committee to review process, timeline, and expectations for IRB approval of multi-site study
  - Determine Single IRB, aka IRB of Record (typically coordinating site IRB)
  - Determine Secondary site IRBs or Research and Development Committee
  - Determine process for IRB submission for multisite human subjects research studies for all sites
  - Obtain Memorandum of Understanding template from coordinating site
  - Develop process for coordinating communication/requirements among all IRBs involved
  - If all sites unable to use Single IRB, identify procedure for requesting exception (Single IRB Exception Determinations)
- ☐ Note: Department of Veteran's Affairs recommends multi-site studies be reviewed by Central IRB (governed by VHA Office of Research and Development).

  - Primary site VA IRB may serve as the "IRB of Record" with secondary VA sites added to the central IRB application.
  - If sites are not able to use Central VA IRB or other non-VA IRBs for which the VA IRB of Record has reliance agreements, a single IRB exception can be requested to facilitate additional local IRB review for these sites
- ☐ In absence of coordinating site or secondary site IRB
  - Association for the Accreditation of Human Research Protection Programs provides a list of accredited IRBs: http://www.aahrpp.org/learn/find-an-accredited-organization
  - Consortium of Independent Review Boards (CIRB) provides a list of commercial IRBs: http://www.consortiumofirb.org/cirb-members/

Study phase

- ☐ Participate in recurring, structured communication with coordinating site and other secondary sites throughout data collection process
- ☐ Participate in monitoring for adherence to data collection procedure at each site (quality assurance)

Post-study phase

- ☐ Analysis/Statistics
- ☐ Conclusions
- ☐ Publication and Reporting Guidelines
- ☐ Dissemination and Supplemental Materials

Appendix C: Finding a Statistician

In no particular order, consider the following statistician resources

- Inquire with your local Research and Development (R&D) Committee or affiliated academic institution for available statistician resources
- Consider partnering with coordinating or secondary sites with access to a statistician
- Consider commercial IRB options. One example with positive review history: Dissertation Editor: Data Analysis (dissertation-editor.com)
- Consider academic institutions which may offer statistician services to outside organizations: Johns Hopkins Biostatistics Center (jhsph.edu)

Appendix D: IRB Memorandum of Understanding/Reliance Agreement Template

Sample text for an Institution with a Federalwide Assurance (FWA) to rely on the IRB/IEC of another institution (institutions may use this sample as a guide to develop their own agreement).

Institutional Review Board (IRB)/Independent Ethics Committee (IEC) Authorization Agreement

Name of Institution or Organization Providing IRB Review (Institution/Organization A):

_____

IRB Registration #: _____Federalwide Assurance (FWA) #, if any:_____

Name of Institution Relying on the Designated IRB (Institution B):

_____

FWA #: _____

The Officials signing below agree _____ may rely on the designated IRB for review and continuing oversight of its human subjects research described below: (*check one*)

(_X__) This agreement is limited to the following specific protocol(s):

Name of Research Project: _____

Name of Principal Investigator: _____

Sponsor or Funding Agency: _____

Award Number, if any: _____

The review performed by the designated IRB will meet the human subject protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. This document must be kept on file by both parties and provided to OHRP upon request.

Signature of Signatory Official (Institution/Organization A):

_____ Date: _____

Print Full Name: _____ Institutional Title: _____

NOTE: The IRB of Institution A must be designated on the OHRP-approved FWA for Institution B.

Signature of Signatory Official (Institution B):

_____ Date: _____

Print Full Name: _____ Institutional Title: _____

References

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