Published in final edited form as:

Acad Psychiatry. 2018 August ; 42(4): 529–533. doi:10.1007/s40596-017-0848-4.

The transition to precision psychiatry and pragmatic inquiry methods in academic psychiatry: The example of Point-of-Care Clinical Trials

Jane Paik Kim¹ and Laura Weiss Roberts¹

¹Stanford University, Stanford, CA, USA

Advances in understanding the optimal approaches for caring for people living with mental illness have been slower than hoped and slower than needed. Few new treatments have been developed and robust clinical studies involving children, adolescents, adults, and elders have been inadequate to address the health needs of the public. Moreover, studies of treatments for individuals across the age spectrum with multiple diagnoses, whether physical, mental, developmental, or substance related, are rare. Compared to other fields of medicine, research on services and systems of care in psychiatry are underdeveloped.

The transition to precision psychiatry, in which the science of prevention and tailored treatment is brought to the care of individual patients who have undergone “deep phenotyping,” is an important movement in our field. This work offers hope for improved treatment for people living with diverse mental illnesses. Academic departments of psychiatry are leading the way by adopting new approaches in which such scientific advances are incorporated into academic subspecialty and training clinics, primarily through innovative clinical trials and technologies. One such innovative approach is the Point-of-Care Clinical Trial (POCCT).

POCCTs compare the effects of different decisions made in the clinical care of individual patients in usual care settings [1–2]. In POCCTs, trials are “embedded” in usual care; patients who have consented are randomized to one of several treatment decisions to which their providers are indifferent and their symptoms, side effects, and outcomes are tracked systematically and with great care. In this way, the design offers the advantage of non-obtrusive follow-up seen in an observational study setting with the benefits of randomization. By “embedding” trials into regular care, inclusion is made as broad as possible (in contrast to the strict exclusions in traditional trials), enabling the study of patients across the life span living with diverse conditions and comorbidities. In addition, study data collection is integrated in the electronic medical record. The data that are gathered prospectively are used to contribute to generalized understanding. Because the intent is to optimize care for individual patients while at the same time contributing new knowledge to the field, POCCTs and other pragmatic inquiry methods have received increasing recognition for their value to clinical science and academic medicine more

Corresponding author: Jane Paik Kim janepkim@stanford.edu.

Disclosure: On behalf of both authors, the corresponding author states that there is no conflict of interest.

broadly. In psychiatry, such pragmatic clinical trial methods may help with the design of “precise” care for individual patients in the future.

Academic departments of psychiatry are often hard pressed for resources and cannot afford the full infrastructure of traditional clinical trials, especially on a broad scale. POCCTs and other pragmatic inquiry approaches may be more readily adopted than traditional trials because they are embedded in the context of actual clinical practice. POCCTs are advantageous because they eliminate the need for study-specific personnel and infrastructure, which would ordinarily be required to carry out controlled trials. With broad inclusion criteria, non-coercive recruitment processes, and lower costs overall, researchers may conduct POCCTs in diverse patient care settings in academic centers and in affiliated community-based programs. Most POCCTs conducted to date have leveraged electronic health records (EHR) and other digital data sources to allow for designs that readily enable enrollment by offering the treatment under study at the point of care, adapt randomization with the intent of limiting patient enrollment in treatments that are ineffective, and revise clinical protocols to nimbly incorporate effective treatments. POCCTs involve longitudinal data collection and entry into the EHR, a resource that is shared across clinics, offering greater potential to enhance learning models and clinical decision-making. POCCTs, as an example of innovative inquiry methods in clinical medicine, fit within the logic of “continuous learning” in the health system, improving quality of care and health outcomes.

For all of these reasons, innovative inquiry methods are important for leaders of academic departments of psychiatry to consider for potential adoption. They are the first step in transitioning to a more modern model of precision psychiatric care in academic settings and they are a way of contributing to clinical science.

Pragmatic Inquiry Methods: the example of the Point of Care Clinical Trial

Pragmatic inquiry methods are a recent innovation in the biomedical sciences. D’Avolio et al [2] describe the first POCCT as an open-label trial comparing sliding scale versus weight-based insulin therapies for non-intensive care unit patients with diabetes. In this study, patients were randomly assigned to treatment arms using a Bayesian adaptive randomization method, which adapts over time to favor the winning intervention. When a clinical provider was ready to place an order for sliding scale or weight-based insulin regimen from the VA order screen, a third option was included to “randomize to sliding scale or weight based insulin” if there was no preference. The clinician would decide whether the patient might be approached, and if not, would proceed with usual care. If the clinician selected “yes”, i.e., that the research team had permission to approach the patient for consideration of enrollment, a study nurse would explain the study to the patient and obtain informed consent. Another POCCT [1] allocated patients with a high risk of cardiovascular disease to receive one of two statins already in widespread clinical use. In such examples, the trial was integrated in usual care decisions, therefore yielding a number of benefits besides the noticeable one of randomization. Study data collection required no additional infrastructure as it was integrated with the patients’ existing electronic medical records. Another consequence of embedding studies in care is that study participants are more diverse and span multiple conditions, aptly reflecting populations seen in actual clinical practice,

compared to study participants in traditional studies who are required to meet a specific set of inclusion and exclusion criteria.

With POCCTs, once researchers are able to compare treatments, the best alternative can be immediately implemented in the physician ordering system of the clinic. Traditional research methods are not so nimble; changes to clinical care practices and standards take much more time. Empirical findings must be analyzed, written up, reviewed by peers, and published, and then clinicians must evaluate the results and adopt and adapt into new clinical approaches. Utilizing the new clinical study design of POCCTs, once beneficial findings have been revealed, changes to clinical care are implemented almost immediately and the results from the embedded research study are tailored to specific populations [3]. The trials conducted by D'Avolio et al [2] and va Staa et al [1] are among the first concrete examples of this new approach to clinical study design, demonstrating that research can be integrated directly into clinical care.

Point-of-Care clinical trials can be compared with traditional randomized clinical trials (RCT) (see Table). Both POCCTs and RCTs involve explicit procedures for recruitment, randomization, and intervention/care delivery, as well as careful monitoring and follow up. Both POCCTs and RCTs must meet human subjects regulatory requirements, e.g., scientific equipoise and appropriate participant safeguards, including prospective IRB approval, informed consent, and confidentiality protections. POCCTs and RCTs differ, however, in that POCCTs are more easily implemented and are more rapidly revised through “continuous learning” as protocols are put into practice. The findings of RCTs are more readily interpreted, perhaps, but they are not easily translated into the realities of clinical care, especially with patient populations that were excluded from the studies. POCCTs do not require unique or separate infrastructure, and so are overall less costly than RCTs.

From an ethical point of view, POCCTs pose a number of advantages. Overall, POCCTs involve comparing treatments that are anticipated to benefit patients to some degree, so there is a greater likelihood that all participants will receive at least some help by participating in the trial. POCCTs have broader inclusion criteria and fewer exclusion criteria, allowing for greater diversity of participants and enabling greater distribution of access and potential benefits of research. For example, Winhusen et al [4] describe two prospective POCCTs in which opioid dependent pregnant mothers are enrolled and randomized into two forms of maintenance therapy, i.e., methadone or buprenorphine. By design, POCCTs, unlike RCTs, leverage usual infrastructure and data-gathering processes through the EHR and avoid imposing risks and burdens beyond what is needed for clinical care.

The roles of researcher and clinician are blurrier in POCCTs, however, and this ambiguity may be ethically problematic if participants choose to enroll without understanding how the POCCT differs from usual care with the usual clinical care team. Such ambiguities could increase the risk for therapeutic misconception as patients may not understand protocol-based constraints on decisions by the clinician investigator. Further, informed consent issues in POCCTs are especially complex. Federal guidelines indicate that for studies involving randomization and intervention, all potential risks of the intervention should be considered risks related to research and should be disclosed; however, in observational studies that

compare treatments chosen by clinicians and patients, the risks are not considered to be intrinsic risks of research and do not typically need to be disclosed beyond usual clinical practice [5].

Fearing that informed consent procedures will become burdensome in POCCTs and worrying that the unique scientific value of POCCTs will be lost, Kim and Miller [6] have advocated the use of “integrated consent” where the topic of the protocol and the randomization to treatment are embedded in the usual patient care processes. Their suggestion is as follows:

... if standard informed-consent processes for randomized clinical trials are required, no busy primary care office would be able to accommodate this practice in its existing day-to-day routine of patient care. This loss of the ability of the trial to mirror the everyday delivery of patient care would compromise the primary scientific benefit of a pragmatic trial — its generalizability to the actual, frontline practice setting.

To sort through such complex issues, our sense is that informed consent in the context of POCCTs should be studied as a feature of the scientific work and, as with other aspects of POCCTs, informed consent procedures may be adapted over time. As one of us (LWR) has written elsewhere, the process of scientific innovation often leads to such challenges, but also leads to their resolution. “Controversial or problematic designs may be discarded as they become scientifically obsolete or alternatively, special methodological approaches will arise around them to ensure that they are conducted ethically” [7].

Academic Psychiatry and Pragmatic Inquiry Methods

Academic psychiatry’s primary responsibility is to create a better future for people living with mental illness through advancing science, clinical innovation and service, educational activities, community engagement, and leadership. Psychiatric clinics should serve individuals across the age spectrum with a wide range of health conditions. Community engagement programs in partnership with academic psychiatry centers should help to foster population health and prevent illnesses in at-risk groups. Clinics and clinical settings are the training ground for early career physicians as well as psychologists and translational scientists. With POCCTs and other pragmatic inquiry methods, clinics also can increasingly serve as continuous learning environments where research is conducted in tandem with clinical care and where interventions can be observed, documented, and compared in real people and populations. As leaders of their respective academic departments and institutions, chairs play an integral role in fostering and advancing novel ways to combine research and clinical care.

Looking ahead, we believe that academic departments of psychiatry will increasingly emphasize novel methods that use existing infrastructure, such as the EHR and clinic ‘bricks and mortar’, to engage in “continuous learning” in health systems, not only for quality improvement but also to enable and define optimal care approaches. To the extent that clinic health IT systems can seamlessly integrate study decisions into work orders, clinical workflows can be minimally disturbed. The development and advancement of electronic

record systems will therefore represent another priority. Integration of research into the ecology of our clinics will allow for the creation of a more robust evidence base for our field by including a broader base of patients and potentially reaching patients with complex conditions or multiple comorbidities who traditionally have been difficult to study as a result of being excluded from highly controlled studies. This will be immensely important in light of the prevalence of disabling mental disorders. An equally important priority in academic psychiatry is the use of pragmatic inquiry methods to train early career psychiatrists for the future, a future in which clinicians will use the EHR and other data gathering and data-sharing approaches to rapidly revise and strengthen clinical practices. Pragmatic inquiry methods may make the resources of academic centers more broadly available to communities and populations. In these ways, greater attention to and wide adoption of POCCTs by academic departments of psychiatry may become a helpful tool in clinical care, research, and education to help current and future patients.

References

1. van Staa TP, Klungel O, Smeeth L. Use of electronic healthcare records in large-scale simple randomized trials of care for the documentation of value-based medicine. *J Intern Med.* 2014; 275:562–9. [PubMed: 24635449]
2. D'Avolio L, Ferguson R, Goryachev S, et al. Implementation of the Department of Veterans Affairs' first point-of-care clinical trial. *J Am Med Inform Assoc.* 2012; 19(e1):e170–6. [PubMed: 22366293]
3. Fiore LD, Brophy M, Ferguson RE, et al. A point-of-care clinical trial comparing insulin administered using a sliding scale versus a weight-based regimen. *Clin Trials.* 2011; 8:183–95. [PubMed: 21478329]
4. Winhusen T, Wilder C, Wexelblatt SL, et al. Design considerations for point-of-care clinical trials comparing methadone and buprenorphine treatment for opioid dependence in pregnancy and for neonatal abstinence syndrome. *Contemp Clin Trials.* 2014; 39:58–65.
5. Cho MK, Magnus D, Constantine M, et al. Attitudes Toward Risk and Informed Consent for Research on Medical Practices: A Cross-sectional Survey. *Ann Intern Med.* 2015; 162:690–6. [PubMed: 25868119]
6. Kim SY, Miller FG. Informed consent for pragmatic trials—the integrated consent model. *N Engl J Med.* 2014; 370:769–72. [PubMed: 24552326]
7. Roberts LW, Dyer AR. Concise Guide to Ethics in Mental Health Care Washington DC: American Psychiatric Publishing; 2004

Table 1

A comparison of design features of a traditional randomized controlled trial and point of care trial

	Design Features	Randomized Controlled Trial	Point of Care Trial	Similarity of Difference
1	Randomization	Research infrastructure required	Embedded in digital clinical care or administrative platform; leverages use of Electronic Health Record data; option for adaptive randomization	Point of care trial (PoC) easier to implement
2	Recruitment to study	Research infrastructure required; recruited after cohort identification, enrollment, and consent	Occurs at usual health encounter: if the patient has no preference and they elect the option of randomization then they are recruited	PoC easier to implement
3	Monitoring	Responsibility of data and safety monitoring board, i.e. additional research infrastructure required	Embedded in clinical practice with routine follow up visits	PoC easier to implement
4	Follow-up	Additional research infrastructure required	Mirrors an observational study; minimal need for study specific visits	PoC easier to implement
5	Interpretability/Applicability	Emphasis on generalizability to populations	Results directly relevant to local subpopulations, greater acceptance by providers	Statistical inferences remain the same; implication on generalizability is different
6	Translation to clinical practice	Contingent upon peer review of scientific findings and the speed of adoption into clinical practice	Immediate; automated implementation of the better treatment	Faster translation in PoC

Table 2

A comparison of regulatory features of a traditional randomized controlled trial and point of care trial

	Human Subjects Regulatory Features	Randomized Controlled Trial	Point of Care Trial	Similarity or Difference
1	Clinical equipoise	Tests two treatments or tests new therapies	Tests two treatments commonly used in practice; not concerned with testing new therapies or testing biological/behavioral mechanisms	Same
2	Informed consent	Research infrastructure required to explain research risks	Research infrastructure required; ability to embed the process into clinical care remains ambiguous	**PoC needs innovation; presents greater nuances in obtaining authentic informed consent
3	Prospective IRB approval	Must be obtained before study commences	Must be obtained before study commences	Same
4	Scientific review	Peer review of scientific findings as usual	Peer review of scientific findings as usual	Same
5	Confidentiality	Use and reliance of existing safeguards to protect participants' confidentiality	Use and reliance of existing safeguards to protect participants' confidentiality	Same
6	Role conflict / Conflict of interest management	Research and clinical care staff are distinguished, though therapeutic misconception happens	Research and clinical care staff overlap; roles more nuanced due to potential for therapeutic misconception	Greater alignment with therapeutic role in point of care trial