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Pragmatic clinical trials: Increasing the rate of translating nursing research into practice†

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Abstract

Aim: Nursing research worldwide is committed to rigorous scientific inquiry that provides a significant body of knowledge to advance nursing practice. One way to advance nursing practice is to increase the rate at which nursing research findings are translated into clinical practice, and one way to do that is to use pragmatic clinical trial research designs. This article aims to describe and advocate for the increased use of pragmatic clinical trials in nursing research and to provide a summary of one nursing pragmatic clinical trial.

Methods: A review and discussion of the features of pragmatic clinical trials.

Results: This article describes the principles and benefits of pragmatic clinical trials. Nurse researchers who use these principles will generate results that are more actionable, patient-centered, and relevant in clinical practice. Focusing on research that provides practical evidence that can be translated into evidence-based practice is an important way to improve the environment for nursing research that leads more rapidly to improved nursing practice.

Conclusions: Embracing and increasing our use of pragmatic clinical trial design concepts in nursing research can enhance the significance of our findings and facilitate the translation of our research into practice.

KEYWORDS

nursing practice, nursing research, pragmatic clinical trials

1 | INTRODUCTION

Nursing academics in higher education ascribe to the tripartite role of nursing practice, education, and research. These three roles are deeply related and jointly required to make the beautiful house that is nursing. When starting to build a house, you must first have a strong foundation. Our foundation is nursing research. We then have the pillars, which are the education of our profession. The foundation and pillars support the roof of evidence-based practice (see Figure 1). Ensuring that people and knowledge transition effectively across and between each of these aspects of the professional nursing community is essential. This article advocates for taking advantage of a new research design that will facilitate more effective communication, or translation, of nursing research findings into nurses' everyday, evidence-based practice.

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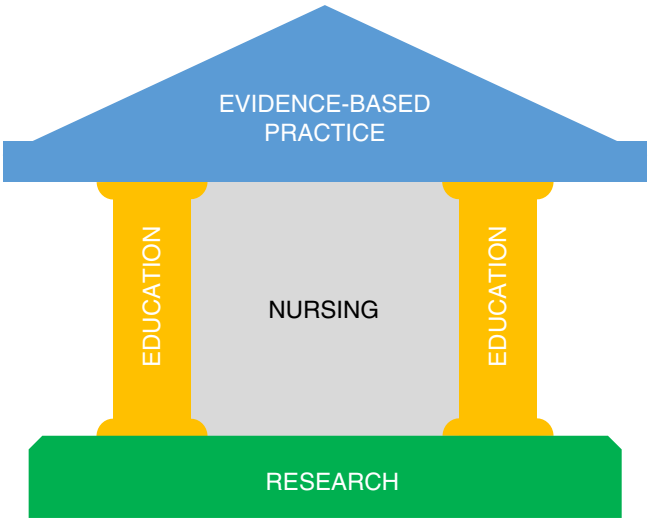

FIGURE 1 Tripartite role of nursing

1.1 | Nursing research and the limitations of traditional research design

The traditional approach in nursing science is to drive the promulgation of accepted best practices for clinical nursing based on research outcomes from classically structured randomized controlled trials (RCTs). While RCT research design is scientifically robust, readily accepted, and historically verified, if we limit ourselves strictly to this approach, we will see significant limitations to our collective progress. The classical RCT-based approach to identifying optimal interventions or practices is better at some tasks than others. It is not always capable of incorporating and addressing the complexities of patient individuality, adaptive and reactionary interventions, or the pragmatic influences of operational and policy influences in health care.

RCTs compare limited predetermined options to a null control in order to identify which option achieves the greatest influence on a specific outcome measure or measures for the average participant. RCT design is the dominant paradigm of focused, topical research studies, and this reinforces the existing clinical practice of concentrating on a single "most urgent" underlying medical problem. However, such single focus—in both research and clinical care—leaves people with multiple causal conditions, extensive comorbidities, and other complex conditions underserved or even potentially mis-served. Health issues with higher complexity, whether in underlying causes, expressed symptoms, or individual response variability, are difficult to model into quality RCTs that can generate usable conclusions.

In addition, in order for traditional RCTs to have sufficient statistical power and control to overcome the statistical noise of complex conditions, varying comorbidities, and individually unique responses, they may be over-restricted and thus risk too much artificialism. Strict participant exclusion criteria can limit the generalizability of results to people who do not meet the original restrictions. An RCT that can identify which of several treatment options will have the greatest impact on the average response of the population may be unable to identify options that have far superior effects on small subsets of the population, or subsets of people for whom the identified "best option" has little or no positive impact. Finally, RCTs routinely exert careful control over delivery dosing, timing, fidelity, and quality, which can lead to results that make an intervention appear far more beneficial than it could ever realistically be when implemented in a clinical setting (Thorpe et al., 2009).

1.2 | Research design and the translation of research into practice

The work of translating nursing research findings into practice frequently falls short of goals due to organizational, operational, and structural barriers. Interventions proven effective in an RCT will fail in practice if the necessary fidelity cannot be maintained across shift changes, if the necessary frequency of interaction or observation does not align with required staff movements between rooms, if hidden costs of implementation cannot be justified in health-care budgets, or if any aspect of the intervention conflicts with standing policies. In other words, the traditional serial approach to translating research into practice—in which we first demonstrate intervention effect, then attempt to convince practicing nurses to implement new practices to deliver that intervention—frequently falls short due to both real and perceived gaps between research conditions and real-world care settings.

One way to ensure that research results can be translated into effective practice guidelines that will be accepted and implemented in routine clinical care is to conduct the research itself within the confines of a realistic practice setting. One approach that is emerging as a way to better address many of these concerns—from complexity and adaptability to generalizability, fidelity, ability to implementation, and translation of research into practice—is the pragmatic clinical trial (PCT). The purpose of this article is to describe and advocate for the increased use of PCTs in nursing research and provide one example of a PCT study.

2 | PCT HISTORY AND DESIGN

2.1 | History of PCT design

PCT design is considered to trace back to Schwartz and Lellouch (1967). In 1998, Roland and Torgerson (1998)

published a paper titled "Understanding Controlled Trials: What Are Pragmatic Trials?" However, more recently there has been increasing interest in this concept. For example, in 2017, Brown University School of Public Health and Hebrew Senior Life's Marcus Institute for Aging Research hosted a workshop on the "State of the Science for Pragmatic Trials of Non-Pharmacological Interventions to Improve Outcomes Among Persons with Dementia and Their Caregivers" (Institute for Aging Research, 2017).

There is still only limited information available in Japanese on the subject of PCTs, which means that PCT design is new to Japanese academia, including nursing science. Among the earliest indications of a new focus on the subject in Japan were two symposia—"An Invitation to Pragmatic Clinical Trial" and "Statistical Innovations and Challenges in Small Clinical Trials"—held at the eighth annual academic conference of Japan Society of Clinical Trials and Research. In 2018, a task force within the Assessment Committee of Pharmaceutical Products of Japan Pharmaceutical Manufacturers Association issued a document titled "An Invitation to Pragmatic Trials" (Data Science Working Group, 2018). Although interest in PCTs has clearly been increasing in Japan in other fields of research, it is our responsibility and privilege to establish and promulgate PCT design in the field of nursing science (NIH Health Care Systems Research Collaboratory, 2017).

2.2 | Advantages of PCT design

PCTs are conducted within the health-care delivery setting and are primarily designed to determine the effects of an intervention under the usual conditions in which it will be applied (Loudon et al., 2015). A PCT is more practical because it is designed to identify interventions that can achieve success in realistic, typical, functioning health-care settings without artificial nursing workloads or availability. Specifically, PCT research design: (a) has broad inclusion and few exclusion criteria, enhancing the generalizability of findings; (b) engages health-care providers integral to the setting but who may have little research experience, such as nurses, in delivering the interventions; (c) delivers interventions in a way similar to usual care and incorporates them into a typical health-care workflow; and (d) collects data in the context of routine clinical care, usually from the electronic health-care records.

A properly configured PCT is inclusive both by using the broadest possible criteria for participation and by engaging with all stakeholders, such as health-care administrators and providers to incorporate their input into the study design, data collection, interpretation of the results, and implementation of the conclusions (Califf & Sugarman, 2015). Finally, PCTs are highly relevant because they are specifically structured to identify outcomes and recommendations that will translate readily and reliably into practice and inform realistic and implementable policy.

2.3 | Design considerations for PCTs

2.3.1 | Randomization

PCT studies are frequently distinguished from traditional RCT studies by their randomization practices. In a PCT, randomization is structured around normal health-care operational structures. This frequently means that randomization is likely to be performed at a site level (e.g., by clinic or provider) rather than at an individual level (Hemming, Haines, Chilton, Girling, & Lilford, 2015). While this practice can increase the statistical effort required, it simplifies management of intervention fidelity and minimizes the artificial disruption of existing operations within the participating health-care setting. Maintaining consistency of care by site also helps integrate the study realistically into existing health-care practices and clearly demonstrates, during the study period itself, the feasibility of translating the intervention into practice.

2.3.2 | Electronic health records

Another frequent element of PCT studies that helps to achieve the expected benefits is a focus on utilizing existing electronic health records (EHR). This supports high levels of efficiency in collecting reliable data, both on initiation and throughout the duration of a study. Integrating research outcomes data into existing EHRs also makes study-related progress visible to health-care providers. Finally, EHR utilization helps keep study practices around data logging and data-based care consistent with clinical standards of practice. This simplifies the narrative around translating study protocols into everyday practice by demonstrating the intervention within a typical care setting and tracking it in familiar recording tools and standard notations.

2.3.3 | Choice of interventions

A central consideration when planning a PCT is the need to use interventions that have already been shown to have an effect, often through an initial RCT or pilot study. Unlike an RCT, a PCT focuses more on implementation or on effectiveness of the interventions in

real-world health-care settings. Another important planning consideration is that there is no ability in a PCT to double-blind the study interventions: participants will know which treatment they are receiving. However, a positive effect of studying unblinded interventions is increased ability to keep participants engaged. A final consideration in planning a PCT is how to manage missing data. PCT designs often collect data in the context of routine clinical care, usually from the EHR, and there is thus a greater chance of greater quantities of missing data. In this context, using a complete-case approach, which removes an individual from the analysis if that individual missed a single data point, may significantly reduce the number of cases available for analysis. Therefore, it is recommended that multiple imputation be used before starting any analysis of data derived from PCT studies (Lang & Little, 2018).

3 | AN EXAMPLE OF A PCT IN NURSING

The Sequential Multiple Assignment Randomized Trial (SMART) design is a valuable PCT design that is currently receiving greater attention in nursing (Doorenbos, Haozous, Jang, & Langford, 2019). SMART designs can be used to provide relevant clinical evidence by comparative evaluation of two or more alternative interventions, by incorporating a second stage of randomization. The SMART design sequences the interventions based on a person's response (Almirall, Compton, Gunlicks-Stoessel, Duan, & Murphy, 2012), which in fact mirrors what nurses do in clinical practice.

Here we provide an example of an ongoing PCT that uses a SMART design to determine the optimal management of chronic pain (Flynn et al., 2018). The trial evaluates two different bundled interventions for chronic pain management: (a) standard rehabilitative care (SRC), which includes physical therapy and occupational therapy; and (b) complementary and integrative health (CIH) therapies, which in this study include acupuncture, mind–body therapies (e.g., yoga, mindfulness-based therapies, and biofeedback), and manual therapies (e.g., chiropractic and massage). There is no usual care or control condition arm of the study (see Figure 2).

In SMART designs, after appropriate time has passed for an individual to demonstrate response (or non-response) to a first intervention, selected participants will be re-randomized into updated interventions. This re-randomization is typically applied to those participants not showing sufficient response to the intervention they are receiving. Depending on the details of the study and the interventions in question, non-responders may be switched to an alternate intervention, may have an alternate intervention added to a continuation of their initial intervention, or may be given a "dose" increase of the initial intervention (Lei, Nahum-Shani, Lynch, Oslin, & Murphy, 2012).

In our example study, re-randomization happens after 3 weeks (Stage 1). If a participant's pain is improving with the intervention they were first assigned, they continue with the same intervention for the next 3 weeks (Stage 2). That is, responders receive the intervention pattern (a) SRC-SRC or (b) CIH-CIH. If a participant's pain is not improving after the initial 3 weeks (Stage 1), that participant is randomized to either switch to the other therapy—intervention pattern (c) SRC-CIH or (d) CIH-SRC—or to receive an augmented intervention by both continuing with their originally assigned intervention and adding the other intervention: (e) SRC-SRC + CIH or (f) CIH-CIH + SRC.

This change in interventions caused by scheduled re-randomization creates an adaptive study with multiple benefits. Participants have an increased opportunity for

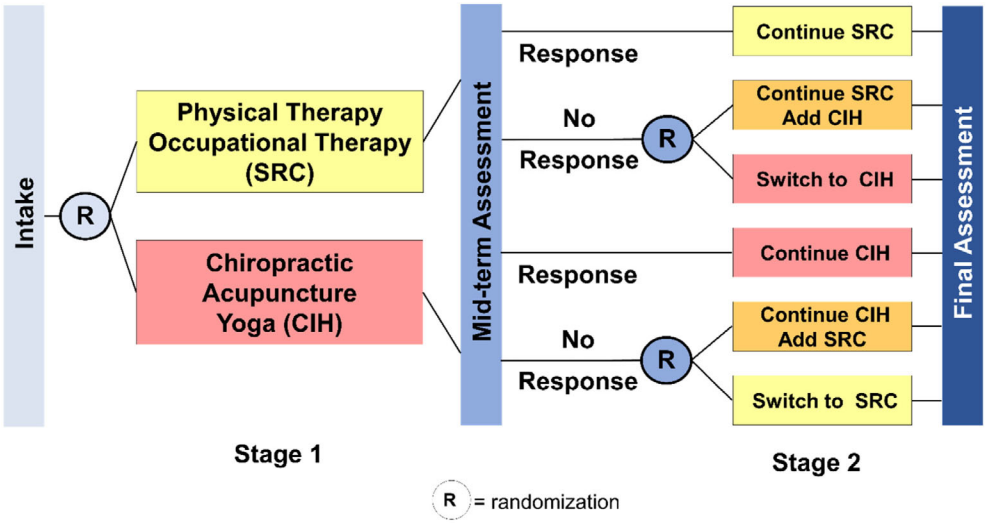

FIGURE 2 Pragmatic clinical trial design example. CIH, complementary and integrative therapies; SRC, standard rehabilitative care

successful intervention, as the secondary adaptation may prove more effective for them than their initial assignment. The study is demonstrably consistent with typical practice, in which an individual's non-response to a treatment generally leads to attempting different treatments. Finally, as this example demonstrates, the PCT gains greater insight by testing more interventions, combinations of interventions, and sequences of interventions.

4 | DISCUSSION

To summarize what distinguishes a PCT from an RCT, an RCT is designed to optimally test a specific hypothesis under ideal conditions, while a PCT is designed to compare multiple treatment options in real-world clinical conditions. This summary can be further broken down by how each type of trial addresses goals, study design, participants, data collection, and results.

- Goals—An RCT seeks to identify the effectiveness and requirements of a specific treatment, while a PCT seeks to directly improve practice and inform policy around specific treatment options.
- Design—An RCT compares differences in specified outcomes between an intervention and a placebo under rigidly controlled conditions, while a PCT compares two or more interventions under flexible protocols that allow for normal everyday clinical flexibility.
- Participants—RCT participants are selected to increase fidelity. PCT participant guidelines are less strict and thus increase representation.
- Data collection—RCT data are collected specifically for the study, while PCT data collection is built around standard clinical charting or other easy-to-implement data collection process.
- Results—RCT outcomes require greater effort to adapt for translation into clinical application than do PCT outcomes, which are generated within the context of clinical care and thus translate more easily.

The list above represents the idealized versions of PCT and RCT design. In actual implementation, nursing research studies rarely meet all of these idealized descriptions. Typical RCT designs use a combination of existing clinical EHR data and dedicated study data collection. PCT studies already underway cannot be completely adaptable to all intervention change options that arise or to all possible clinical practices, nor can they abandon scientific rigor or reliance on statistical validity. Truly, most research falls on a continuum between the theoretical constructs of basic science and the unstructured pragmatic trials of dynamic treatment (Loudon et al., 2015).

5 | CONCLUSION

While RCT design is scientifically robust, readily accepted, and historically verified, limiting ourselves too strictly to this approach will result in significant limitations to our collective progress. Using PCT principles to design nursing research studies generates results that are more actionable, patient-centered, and relevant. PCT research output is actionable because it is designed around pragmatic and realistic clinical settings and is focused on implementation. A PCT's alignment of goals and measures around individuals' goals of care and their pragmatic adaptation to non-response to interventions ensures *a patient-centered* process and results. The PCT data and results, along with adherence to practical settings and goals, produces results that are understandable, relatable, and relevant to healthcaredecision-makers and policy proponents.

The science of nursing is foundational to and predicated on the support of nursing practice (Figure 1). Given that, it is important that we nurses advance those techniques that most closely connect our scientific thinking with our clinical activity. Embracing and increasing our use of PCT design concepts in nursing research can support this connection. By doing this, we enhance the significance of our findings, the ease of translating our research into practice, and our ability to continually improve outcomes for all.

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DISCLOSURE

The authors declare they have no conflicts of interest.

AUTHORS' CONTRIBUTIONS

Both authors made substantial contributions to the conception and design of this article, were involved in drafting the manuscript, and provided final approval of the version submitted.

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