

Comparative Effectiveness Research and Its Application to Nursing Education

Claire Su-Yeon Park

Center for Econometric Optimization in the Nursing Workforce, Republic of Korea

lachael@daum.net

Eunok Park

Jeju National University, Republic of Korea

eopark@jejunu.ac.kr

Mehmet Akif Ocak

Gazi University, Turkey

maocak@gazi.edu.tr

ABSTRACT

This in-depth integrative literature review aimed to investigate comparative effectiveness research (CER) methodologies applicable to nursing research and to propose a CER design relevant to nursing education. Integration and synthesis were conducted from August 20 to December 15, 2013 and from October 20 to December 05, 2015 using electronic databases and refereed published books. The key words were “comparative effectiveness research,” “education,” “patient outcomes,” “effectiveness,” “cost-effectiveness,” and “efficiency.” All selected literatures were initially scrutinized by the principal investigator in terms of scientific rigor and then synthesized on an ongoing basis. CER methodologies in nursing research were presented to be significant in terms of enabling the distinctiveness of the nursing profession to stand out. Three CER methodologies applicable to nursing research—a Pragmatic Clinical Trial, Observational Comparative Effectiveness Research and Cost Effectiveness Research—revealed each of their distinguishable strengths and weaknesses compared to the Randomized Controlled Trial. For ethical considerations, the importance of ensuring “ equipoise ” was identified. Lastly, in a head to head comparison of two nursing education programs, a single blind, randomized crossover study design was proposed as a type of Pragmatic Clinical Trial utilizing cost-utility analysis. A mixed method Analysis of Covariance and a Doubly Multivariate Repeated Analysis of Covariance were suggested as relevant statistical analyses. Considering that CER is still inchoate in nursing research and nurse scientists’ endeavors to address the gap are urgent, this study is compelling in that it proposed a rigorous CER design not only directly applicable to nursing education, but also to other disciplines in education.

Keywords: *comparative effectiveness research, equipoise, nursing education, cost-utility analysis, propensity score analysis*

INTRODUCTION

Significance of Comparative Effectiveness Research in Nursing Science

Why is comparative effectiveness research invaluable in the present scientific literary world, particularly in nursing education? Why is there rarely a study on cost effectiveness analysis in spite of its value and importance to nursing intervention

(i.e., care or education)? By extension, how many nurse scientists are capable and prepared to conduct comparative effectiveness research and economic evaluation?

Since 2011, the Patient-Centered Outcomes Research Institute (PCORI) in the United States has kindled comparative effectiveness research and communicated its results (Neumann, 2013) to help patients make more informed decisions for a better quality of care. The scientific basis for the

Correspondence to: Eunok Park, PhD, RN, Full professor, Jeju National University, College of Nursing, Jeju-si, Jeju Special Self-Governing Province 63243, Republic of Korea, Tel. +81 064.754.3882, Fax. +81 064.702.2686, Email: eopark@jejunu.ac.kr

establishment of PCORI is that comparative effectiveness research produces strong realistic evidence for setting up strategies that can reduce unnecessary medical spending while guaranteeing a reasonable quality of care. Typical examples include improving the coordination of patient care, facilitating shared patient decision-making and practicing evidence-based medicine. Comparative effectiveness research is ipso facto more crucial, considering that providing a higher quality of care while controlling corresponding healthcare costs is a timely issue in most countries (National Evidence-based Healthcare Collaborating Agency [NECA], 2013a). Evidence-based healthcare policy decision-making is the cornerstone for achieving a healthier nation. It accordingly suggests the necessity of efficiency- or effectiveness-focused (rather than efficacy-focused) outcomes using comparative effectiveness research for improving quality of care.

Nursing values are invisible, making it difficult to reveal their particular significance. Nobody cannot deny that they are essential for advancing nursing science because they lead us to synthesize all aspects of the patients' well-being (Risjord, 2009). They also provide a "less distorted view" of nursing phenomena (Risjord, 2009, p.72). However, researchers have focused mainly on determining the efficacy of the nursing intervention of interest (by primarily using Randomized Controlled Trials [RCTs]), not on the effectiveness (which would require comparative effectiveness research). In addition, attendant costs have not been adequately considered in the nursing research. This oversight has consequently led to a failure to address all aspects of patient care, as well as a lack of sufficient rationales for patients' decision-making in choosing a better qualitative nursing care relative to costs. This proves why comparative effectiveness research is invaluable in nursing science, especially at present. It also explains why nurse scientists are relatively unfamiliar with conducting comparative effectiveness research and also why published nursing studies related to it are relatively rare.

Comparative Effectiveness Research Design-based Nursing Education Project

To address this research gap, this paper aimed to propose an implementable nursing education research program utilizing comparative effectiveness research methodology. In-depth literature reviews on comparative effectiveness research applicable to nursing research were considered while being mindful of ethical considerations. The nursing education research program was developed to compare the effectiveness of the two nursing education programs in terms of patient-centered nursing process competence and their economic efficiency, addressing the following research topic: "Quality and Safety Education in Nursing (QSEN) versus Patient-Centered Outcomes Research (PCOR) in the nursing curriculum: which is better for improving clinical nurses' patient-centered nursing process competence?" The proposed intervention is a PCOR-focused nursing curriculum, and the alternative is a QSEN-focused curriculum.

Regardless of educational discipline, comparative effectiveness research methodology has hardly been utilized in the literature. We hereby tried to contribute feasible, practical and applicable information on the comparative effectiveness research structure for the scientific progress of the field of pedagogy. Readers will accordingly be able to learn essential knowledge about comparative effectiveness research methodology and successfully apply it to their own discipline.

METHOD

Electronic search engines such as PubMed, CINAHL, Web of Science and EBSCOhost Web, and published books written in either Korean or English, were utilized to locate primary studies from August 20 to December 15, 2013 and October 20 to December 05, 2015. The key words included "comparative effectiveness research (and/or design)," "education," "patient outcomes," "effectiveness," "cost-effectiveness" and "efficiency." All selected primary refereed publications were initially scrutinized by the principal investigator in terms of scientific rigor and then synthesized for integrative in-depth literature reviews. Hand-searching reference lists presented in the primary studies was also

conducted. The synthesis processes and searching were performed simultaneously throughout the study.

RESULTS

Limitations of RCTs and Essentials of Comparative Effectiveness Research

RCTs have been considered to have the best ability to generalize research findings across disciplines because all possible confounding variables can be controlled (Portney & Watkins, 2008). Exogenous variables are also considered to be homogeneous (Portney & Watkins, 2008). The Agency for Healthcare Research and Quality (AHRQ, 2007), however, reported that RCTs had significant limitations in meeting the purpose of comparative effectiveness research because: a) the *efficacy* not *effectiveness* is pursued, b) short research duration and too small sample size, which are regarded to be impossible in reality, are applied, c) process outcomes are not adequately addressed compared to final outcomes, d) the low rate of reporting side effects and selective reports in accordance with the tendency are indicated, and e) it is mostly only the *significant* results that are published, causing a bias toward further research results (e.g., meta-analysis) (NECA, 2013a).

Comparative effectiveness research purposes to provide scientific rationales in assisting patients, clinicians and even policy makers' decision-making, rather than simply evaluating the *efficacy* for a treatment/intervention of interest compared to the placebo or the control group, as is the case with RCTs. It is thus essential to set up more than two *real* comparisons to distinguish their *effectiveness*, which will require a better or newer treatment/intervention in the research design.

However, nothing is more important than establishing *equipoise* in comparative effectiveness research. *Equipoise* means to appreciate that there is *uncertainty* about the efficacy/effectiveness of the new treatment/intervention that researchers are proposing (Egan & Mainous, 2012). That is, all researchers should hesitate to assume that new treatment/intervention is better simply because it is new and appears to be supported by scientific rigor (Egan & Mainous, 2012).

Three Comparative Effectiveness Research Methodologies Applicable to Nursing Research

Pragmatic Clinical Trial (PCT). PCT refers to the prospective randomized methodology enabling researchers to compare benefits, risks and costs of *real* interventions being served in real clinical settings (NECA, 2013a; Saag et al., 2012). Unlike RCTs, PCTs 1) have wider inclusion criteria and accordingly better generalizability as well as more statistical power, and 2) utilize easily measurable clinical endpoints as outcome variables (Saag et al., 2012).

However, PCTs also have several limitations. First, it is difficult to discern which attributes of the innovation(s) made a difference on the outcomes in the PCT, because the target of the evaluation is intervention *per se*. That is, the *overall effectiveness* of each arm (i.e., innovation(s) and the reference group) is measured and compared/contrasted to each other in the PCT (NECA, 2013a). *Ipsa facto*, a well-established protocol, becomes particularly important in PCTs, which is a necessary way to control bias as well as potential confounding variables (and is used in RCTs as well). Random assignment is also the key to establishing *equipoise* and removing potential systemic bias due to inter-subject variability (Portney & Watkins, 2008).

Nonblinding application is another way to ensure internal validity in PCTs. However, it is difficult for the blinding procedure to be tenable in realistic research such as PCTs. It is often impossible in reality—in particular, complementary treatment (NECA, 2013a)—and above all, it could be dangerous because it could prevent clinicians from responding promptly to a patient's side effects and applying a treatment fitting for the patient's biological health status.

The most significant disadvantage of PCTs is the significant expense caused by more participants and longer research duration compared to RCTs (NECA, 2013a). That point could make its application to nursing research difficult.

However, in PCTs, 1) the primary outcomes include *real-life indicators* such as quality of life—a representative psychometric measure in nursing research—or activities of daily living in addition to objective physiological/clinical endpoints (NECA, 2013a), which are considered to be major nursing

outcomes, and 2) overall effectiveness of the treatment/intervention is compared (NECA, 2013a), which can encompass the effects of significant yet invisible and intricate nursing values. These suggest that PCTs can be greatly utilized in nursing research if the research plan is well-built and efficient.

Observational Comparative Effectiveness Research (OCER). OCER refers to “analyzing the comparisons of associations” between influencing factor(s) of interest to the incidence rate of a certain disease based on whether the factor(s) have been exposed to the population with potential risks (NECA, 2013a). A case-control study is the most commonly utilized method. However, it is important to note that a case-time-control study is thought to have the most scientific rigor in OCER because the time variable as well as all possible confounding variables can be controlled (NECA, 2013a). That is to say, the odds ratio of an incident rate by case-crossover procedure in the exposed group is divided by the odds ratio of an incident rate by case-crossover procedure in the reference group.

Compared to RCTs, OCER is the best tool for researchers who need to examine multiple comparisons with low costs, because secondary data analysis—statistical analyses using previously existing data—is the key. OCER is also useful in cases where RCTs or PCTs are inappropriate. For example, a treatment/intervention could possibly go against ethical considerations for patients. In addition, OCER has a much larger effect size (i.e., statistical power) than RCTs or PCTs. A large database is its main resource; thus, the sample size is much larger than that of RCTs or PCTs. However, OCER cannot deny having a weaker internal validity while providing more generalizability than RCTs or PCTs (NECA, 2013a).

To compensate for any weaknesses, it is crucial to rigorously establish compliance to the research protocol. Specifically, the equal possibility of having a certain disease should be ensured in all groups to eliminate bias (AHRQ, 2012), which is particularly important in OCER. Exposure variable(s), outcome variable(s), and all potential confounding variables should be clearly defined (NECA, 2013a). Sox and Goodman (2012) reported that the severity of disease and patients’

age were the typical variables distorting the truth in OCER, indicating that those two variables should definitely be controlled. Inclusion and exclusion criteria should also be clearly defined and managed (NECA, 2013a).

Among the various methods used to control confounding variables, *propensity score analysis* is highly recommended. It is effective and very easily eliminates bias in OCER (NECA, 2013b). The propensity score (or “balancing score”) refers to “the distribution of measured baseline covariates” (Austin, 2011, p. 402). For example, if the propensity score between groups is the same, “the distribution of measured baseline covariates” (Austin, 2011, p. 402) is the same between groups, so the differences between comparisons are regarded to be non-significant. A *causal* explanation between exposure variable(s) and outcome variable(s) is accordingly realizable (NECA, 2013b). There are five methods used to adjust the propensity score between groups: 1) restriction, 2) matching, 3) stratification, 4) adjustment of covariates, and 5) weight; thus, it is possible to mathematically balance the propensity score between groups. After the adjustment, sensitivity analysis should be followed to ensure the stability of the original result: i.e., the differences in the results should be non-significant.

The result of the propensity score analysis per se is for another article, and considerable preparations to conduct this analysis are required. Nevertheless, it is a shame that most nursing schools do not address the *propensity score analysis* in their curricula at present. Considering that comparative effectiveness research is the calling of our time, there is a need to prepare future nurse scientists to be competent in *propensity score analysis*.

Cost Effectiveness Research (CER). CER is a research methodology that provides a criterion on which treatment/intervention is most *affordable* in terms of economic effectiveness (Muennig, 2002). CER in comparative effectiveness research is compelling because it simultaneously deals with *efficacy* and *attendant costs* among comparisons (NECA, 2013a).

Most healthcare studies, have, so far, been focused on *efficacy* (NECA, 2013a), which is an indicator of how much the treatment/intervention reduced

the duration or severity of disease or how accurately it could detect the disease of interest (Muennig, 2002). However, technological advances in medical devices and a soaring elderly population have caused rapid increases in healthcare costs relative to available healthcare resources (NECA, 2013a). More attention should therefore be given to efficiency, or efficient resource allocation (NECA, 2013a).

Effectiveness is ipso facto a more sensible indicator for future research. It is a practical and relevant measure to elucidate the overall effect (considering the risks/costs) of treatment/intervention provided in the real world (Muennig, 2002), which can enable comparisons. CER is particularly significant in nursing research because it can illuminate invisible values of nursing so that they become comparable, visible, and economic indicators. A value of money, Quality Adjusted Life Years (QALY) or Healthy Years Equivalents (HYE), is mainly used as an indicator. At present, various types of nursing intervention (e.g., care or education) are proven to have a significant *efficacy* in reality. Now is the time to determine which nursing intervention is more beneficial in terms of *affordability* from a patient-centered perspective.

Ethical Considerations

Comparative effectiveness research requires more ethical considerations than RCTs, because it could create multiple risks (Feudtner et al., 2013). The underlying reason is that we do not know if the proposed treatment/intervention is riskier than the alternative. Unknown differential/relative risks of the proposed treatment/intervention as compared to the other make *equipoise* indiscernible, because it is difficult for the risk difference between two treatments to be regarded as *zero* (Feudtner et al., 2013). This ethical concern attenuates the advantage of randomization. Even though patients would receive standard care to ensure a satisfactory or compensatory health benefit, the standard care could be relatively riskier or less cost-effective than the proposed treatment/intervention (Feudtner et al., 2013). Since no default or control group exists in comparative effectiveness research, all comparisons are presumed to be effective. However, in the end, the treatment/intervention with fewer benefits consequently leads the participants assigned to the group to potentially be harmed (Feudtner et al., 2013).

All participants have the right to be informed of all possible foreseeable risks as well as benefits caused by participation in the research (Feudtner et al., 2013), which is one of the most important guidelines of the Institutional Review Board. This guideline is particularly important in comparative effective research because *uncertainty* needs to be well-addressed.

To ensure *uncertainty*, Visit and colleagues' (2008) report could be utilized, where equivalent outcomes were presented between enrolling in the clinical trials and receiving the same treatment outside the trials. Second, participants must be informed that they could obtain unexpected undesired outcomes ranging from fewer health benefits to severe negative results (Feudtner et al., 2013). Finally, researchers' efforts to minimize those risks are necessarily required. A good example is a well-established research protocol including how to handle participants with unexpected side effects promptly without greatly altering the research process. Such a protocol is necessary to ensure the internal validity of the research findings as well as protect participants' safety and rights.

A Comparative Effectiveness Research Design for Nursing Education

Egan and Mainous (2012) proposed a cross-over design and pragmatic cluster-randomized trial design in medical educational research, which can ensure *equipoise* as well as guarantee the medical students' *educational equivalency*. The study design can also satisfy ethical considerations by avoiding the risk "of being assigned to the study group that receives less benefit" (Egan & Mainous, 2012, p. 893). The risk could be caused by the main attribute of comparative effectiveness research, namely the unknown differential/relative risk of the proposed intervention as compared to the corresponding one.

This paper proposed a head to head comparison of a nursing curriculum focused on Patient-Centered Outcomes Research (PCOR) versus Quality and Safety Education in Nursing (QSEN) in a Bachelor of Science in Nursing (BSN) program, using a single-blind, randomized cross-over study as one type of PCT (see Figure 1). The research topic is: "A QSEN versus a PCOR-focused nursing curriculum: which is better for improving nursing students' patient-centered nursing process

competence?” This research design aims to compare the *effectiveness* of the two nursing education programs from the standpoint of patient-centered nursing process competence and economic efficiency. The proposed intervention is a PCOR-focused nursing curriculum, and the alternative is a QSEN-focused one.

QSEN was initiated in 2005 to close the gap between academia and clinical practice in nursing education. QSEN defined six competencies and integrated them into undergraduate nursing programs so that future nurses would be equipped with the necessary knowledge, skills and attitudes for the improvement of quality and safety in the healthcare delivery system: 1) patient-centered care, 2) teamwork and collaboration, 3) evidence-based practice, 4) quality improvement and informatics, 5) safety, and 6) Informatics (Cronenwett et al., 2007). QSEN has been reported to have a significant effect on improving these six competencies for nursing students since 2007 (QSEN Institute, 2015).

With regard to a PCOR-focused nursing curriculum, AHRQ (2013) performed a series of forums entitled “Shape the Future of Training for Patient-Centered Outcomes Research in Primary Care” at universities across the United States. The primary aim was to gather inter-professional opinions for how to integrate PCOR findings into the curriculum of all health profession disciplines. The success of these forums strongly suggests that nursing education focused on PCOR would be delivered in the near future. Future nursing students would accordingly need to be well-prepared to have a patient-centered way of thinking (i.e., patient engagement) and comparative effectiveness research competence. The current QSEN-focused nursing education curriculum, by contrast, is insufficient in meeting these goals.

The core of nursing practice is the process by which *patient-centered nursing care* is delivered from a holistic standpoint, i.e., Nursing Assessment, Nursing Diagnosis, Nursing Planning, Nursing Implementation and Nursing Evaluation (ANA, 2015). Pre-licensure nursing programs primarily aim to prepare future nurses to be competent in professional nursing practice. Therefore, all undergraduate nursing curricula need to be evaluated in terms of nursing students’

preparedness—i.e., their patient-centered nursing process competence.

This paper proposes a comparative effectiveness research design applicable to nursing education outcomes research. Hence, we disclose here our basic assumptions:

1. QSEN and PCOR-focused nursing curricula have been developed and proven to have satisfactory reliability and validity in the previous literature.
2. The instrument for measuring patient-centered nursing process competence has also been developed and verified to have satisfactory internal consistency and face/content/construct validity. Additionally, its constructs are composed of knowledge, skill and attitude.
3. Based on the previous literature, the next boost to education needs to occur 6 months after the initial education is done.

With regard to cost-effectiveness, cost-utility analysis was proposed in this study. It enables the researchers to estimate a quality-adjusted educational effect, unlike cost effective analysis, which only measures the quantitative changes of the educational effect. Nursing education helps prospective nursing students to become competent in improving patients’ outcomes. Therefore, it is important that patients’ evaluation on the effectiveness of nursing education is reflected. Cost-utility analysis can estimate the patients’ opinion on the effectiveness of the education through a survey of clinical nurses, which is more beneficial in terms of controlling patients’ bias, particularly the risk of favoring a higher level of education effect (Yang, 2012).

Strengths and Weaknesses of the Study Design

This study design is compelling enough to control most of the threats to internal validity, i.e., history, maturation, instrumentation and regression. Above all, this study controls students’ potential bias through a single-blind study design, leading to better internal validity of the research.

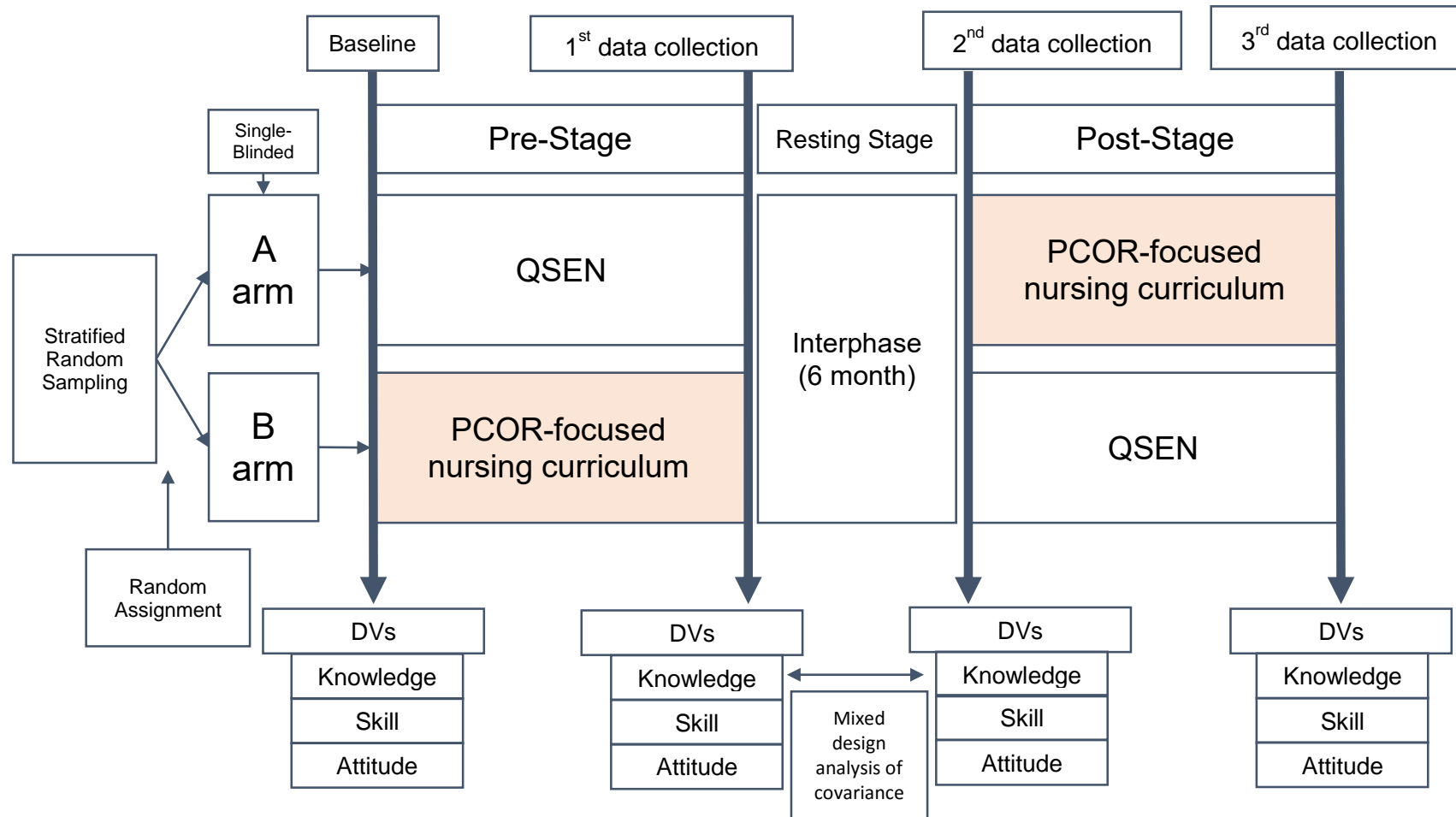


Figure 1. Research Design

The interaction between treatment and selection can also be strongly controlled by stratified random sampling and random assignment in this study, which is another strength increasing the generalizability of the study's findings. Stratified random sampling removes sampling errors and creates a more representative subset in the homogenous, non-overlapping and stratified variable (Portney & Watkins, 2008). Random assignment eliminates inter-subject variability between comparisons before the study embarks: the equal distribution of subjects to each arm guarantees no systemic bias (Portney & Watkins, 2008). Moreover, since the effective sample size for this study is relatively small, it is considered to be more cost-effective compared to those in other studies.

As with any study of this kind, it is important to consider the loss of participants and the testing effect. Loss of subjects and dropout influence the representatives of each arm/group, and the testing effect can also distort the truth due to familiarity with the measurement procedure (Portney & Watkins, 2008).

Statistical Analyses

Independent variable (IV). IV needs to be coded as follows: Yes: "1" refers to PCOR-focused nursing curriculum, and No: "0" refers to QSEN-focused.

Dependent variables (DVs). DVs are the three constructs (knowledge, skill and attitude) composing patient-centered nursing process competence and will be measured before and after each intervention. Data collection will be performed a total of four times. Each of the DVs needs to be evaluated by more than a 5-point Likert scale, which could be regarded to be a continuous variable in practice. It allows multivariate analysis with no violations of univariate analysis as well as multivariate normality. If the distribution of data is skewed, the transformation of all values to a z-score should be done first before data analysis.

Cost-Utility Analysis. All expenses associated with each type of education need to be collected to estimate the *costs*. Using the time trade-off method (Torrance, 1986), a survey of clinical nurses needs to be conducted to estimate the value of patient-

centered nursing process competence for education, i.e., *utility*. A 5% reduction needs to be applied to balance costs and health benefits, a drop believed to happen to current values in the future (NECA, 2013a; Yang, 2012). This is an acceptable rate although there is not clear agreement at present (NECA, 2013a).

Data Analyses. The mixed method Analysis of Covariance (ANCOVA) should first be performed in order to determine the significance of the potential carry-out effect between two arms. If the carry-out effect is not significant, the Multivariate Analysis of Variance (MANOVA) with one between—and one within—subjects (i.e., Doubly Multivariate Repeated Analysis of Variance [RMANOVA]) will be conducted. If the carry-out effect is significant, Doubly Multivariate Repeated Analysis of Covariance (RMANCOVA) needs to be conducted. The variable of time-order (i.e., first or second) and the initial values should be controlled as covariates. With regard to cost-utility analysis, utility divided by costs will be compared to determine which education is more cost-effective.

DISCUSSION

Innovation has enabled nursing education to meet the nation's need for improving patient outcomes. Nursing education so far has focused on closing the gap between clinical nursing and academe by improving nurses' individual competencies using QSEN. Various educational strategies fitted to specific populations have also been developed and tested with a focus on *efficacy*. Most of the study findings have been reported to be significant; however, more research is needed on *effectiveness* from a patient-centered perspective.

Patients are not just recipients of healthcare services. *They are active decision-makers in their own quality of life*; they have the right to be involved with their healthcare team and request healthcare professionals to better address their healthcare needs. However, evidence to assist their decision-making has not been developed and disclosed, revealing an urgent need for comparative effectiveness research to produce evidence-based

scientific rationales. Future nurse scientists should be equipped with a patient-centered *mind-set* and *nursing practice*. The end goal: empowering real patients with the information they need to make choices that most benefit their specific needs.

To meet this goal, it is necessary to re-evaluate the effectiveness of the current nursing education program from the standpoint of patient-centered nursing process competency. Comparative effectiveness research is still inchoate in nursing research. This study is worthwhile in that it 1) illuminates the significance of comparative effectiveness research in the context of nursing science, 2) addresses useful comparative effectiveness research methodologies for nursing research, and 3) proposes a relevant research design directly applicable to both nursing education and other educational disciplines. Compared to medicine or pharmacy, a new statistical innovation for comparative effectiveness research such as the *Instrumental Variable Analysis-based Person-centered Treatment Effects (PeT) Method* (Basu, 2014) has scarcely been applied to nursing research at present, much less covered in the nursing curriculum. The need for nurse scientists to fully address comparative effectiveness research is urgent. Consequently, innovation in nursing education will not only be realizable, but also efficient.

Acknowledgments

I, the first author, would like to thank Dr. Arch G. Mainous III, a professor in the Department of Health Service Research, Management and Policy & Department of Community Health and Family Medicine at the University of Florida College of Public Health and Health Profession for his thoughtful guidance in developing this paper.

REFERENCES

- Agency for Healthcare Research and Quality (AHRQ) (2007). *Methods reference guide for effectiveness and comparative effectiveness reviews* (Version 1.0). Rockville, MD, U.S.A.: AHRQ.
- AHRQ (2012). *Developing a protocol for observational comparative effectiveness research (OCER): A user's guide*. Rockville, MD, U.S.A.: AHRQ.
- AHRQ (2013). *Shape the Future of Training for Patient-Centered Outcomes Research in Primary Care*. A material for a forum at the University of Florida College of Health Professions, Nursing & Pharmacy (HPNP). Rockville, MD, U.S.A.: AHRQ.
- American Nurses Association (ANA) (2015). The Nursing Process. Retrieved November 26, 2015, from <http://www.nursingworld.org/EspeciallyForYou/What-is-Nursing/Tools-You-Need/TheNursingProcess.html>
- Austin, P. C. (2011). An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behavioral Research*, 46(3), 399–424. doi:10.1080/00273171.2011.568786
- Basu, A. (2014). Estimating Person-Centered Treatment (PeT) Effects using Instrumental Variables: An application to evaluating prostate cancer treatments. *Journal of Applied Economics (Chichester, England)*, 29(4), 671-691. doi:10.1002/jae.2343
- Cronenwett, L., Sherwood, G., Barnsteiner, J., Disch, J., Johnson, J., & Mitchell, P., ... , Warren, J. (2007). Quality and Safety Education for Nurses. *Nursing Outlook*, 55(3), 122-31. doi: <http://dx.doi.org/10.1016/j.outlook.2007.02.006>
- Egan, M. & Mainous, A. G. (2012). The tension between educational equivalency and equipoise in medical education research [Editorial]. *Family Medicine*, 44(1), 5-6.
- Feudtner, C., Schreiner, M., & Lantos, J. D. (2013). Risks (and benefits) in comparative effectiveness research trials. *New England Journal of Medicine*, 369, 892-894. doi: 10.1056/NEJMp1309322
- Muennig, P. (2002). *Designing and conducting cost-effectiveness analyses in medicine and health care*. San Francisco, CA, U.S.A.: Jossey-Bass.
- National Evidence-based Healthcare Collaborating Agency (NECA) (2013a). *A summary of methods for comparative effectiveness research* (Version 1.0). Seoul, Republic of Korea: NECA.
- National Evidence-based Healthcare Collaborating Agency (NECA) (2013b). *Methods for the control of measured confounders in outcomes research* (Version 1.0). Seoul, Republic of Korea: NECA.
- Neumann, P. J. (2013). Communicating and promoting comparative-effectiveness research findings. *New England Journal of Medicine*, 369(3), 209-11. doi: 10.1056/NEJMp1300312
- Portney, L. G., & Watkins, M. P. (2008). *Foundations of clinical research: Applications to practice* (3rd ed.). Upper Saddle River, NJ, U.S.A.: Prentice-Hill.

- Risjord, M. (2009). *Nursing knowledge: Science, practice, and philosophy* (p. 72). Wiley-Blackwell.
- Saag, K. G., Mohr, P. E., Esmail, L., Mudano, A. S., Wright, N., Beukelman, T., & Tunis, S. R. (2012). Improving the efficiency and effectiveness of pragmatic clinical trials in older adults in the United States. *Contemporary Clinical Trials*, 33 (6), 1211-6. doi: 10.1016/j.cct.2012.07.002. Epub 2012 Jul 5.
- Sox, H. C., & Goodman, S. N. (2012). The methods of comparative effectiveness research. *Annual Review of Public Health*, 33, 425-445. doi: 10.1146/annurev-publhealth-031811-124610
- Torrance, G.W. (1986). Measurement of health state utilities for economic appraisal. *Journal of Health Economics*, 5, 1-30.
- Yang, B. M. (2012). *Public Health Economics*. Paju, Republic of Korea: Nanam.
- Visit, G. E., Bryant, D., Somerville, L., Birmingham, T., & Oxman, A. D. (2008). Outcomes of patients who participate in randomized controlled trials compared to similar patients receiving similar interventions who do not participate. *Cochran Database Syst Rev*, 3, MR000009.
- QSEN Institute (2015). The evolution of the Quality and Safety Education for Nurses (QSEN) Initiative. Retrieved November 26, 2015, from <http://qsen.org/about-qsen/project-overview/>