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Creating Clinical Research Protocols in Advanced Practice: Part IV, Designing Research to Fit Practice

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Designing and conducting clinical research is a critical step in the development of new knowledge that improves patient care outcomes.[1,2] Advanced practice nurses (APNs) are in a key position to lead such clinical inquiry initiatives, yet integrating the skills of protocol development in clinical practice settings is challenging. In this series, we identify and address challenges that can create difficulties for APNs during the process of research protocol development.[3] These include (1) clinical practice isolation, (2) limited preparation for independent research or improvement science design, and (3) time constraints in the clinical setting. As a result of these challenges, APNs must overcome methodological and study design hurdles as well as struggle to negotiate time to conduct research as a part of their clinical practice, often alone or with limited peer support. The focus of this series has been to provide tips and tools to support APNs in the research protocol development journey.

Overview, Part I, Part II, and Part III

In part I, we began with topic selection and addressed broad issues associated with identification of clinical problems, some unique to advanced practice nursing and others applicable to clinical inquiry in general.[3] In part II of the series, we tackled the next step of protocol development, evaluating the clinical feasibility, by presenting a case example that explored practical steps for considering the implementation processes for a study, including key decision points for evaluating the feasibility of carrying out the protocol.[4] In part III of the series, we focused on the next step, selecting a method.[5] Part III built on the others by using the same example and differentiating clinical questions that are best suited for quality improvement (QI) from those that demand a research-based approach. In this fourth and final part of the APN Research Protocol Development series, we address the need for designing research to

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"fit" into clinical practice. We also provide tools to help the APN design research questions, put together methods, and develop analysis plans.

In the previous parts of the series, we used the example of implementation of an evidence-based cardiac surgery advanced life support (CALS) protocol, which is designed for managing cardiac arrest in postcardiac surgery patients by maximizing the use of early defibrillation and pacing as well as by following a protocol of organizeing key personnel for early resternotomy.[6] In part III, we offered the Project Design Tool to differentiate clinical questions that are best suited for QI from those that demand a research-based approach. Key distinguishing factors include the degree of risk to which participants are exposed, the quality of previously conducted studies, and the amount of published evidence to support the practice.

The Project Design Tool addresses the risks posed by the activity (project) to study participants in 9 specific domains: purpose, scope, evidence, staff, methods, sample, consent, benefits, and overall (summative) risk.[5] In the example of CALS, sufficient evidence to support a change in practice already existed in the published literature, so this project was appropriate for implementation and evaluation as a QI initiative. If contradictory or insufficient evidence had existed, a research-based approach would have been necessary to protect patients and monitor the risk posed by the project. In part IV, we again use the example of CALS, but in a hypothetical scenario where existing evidence does not exist and a research-based approach is required.

Determining Project Type

Risk posed to human subjects, or the probability of harm or injury from participation in research, is perhaps one of the most salient decision factors for a project. Because the risk factor also can have legal implications for the investigator, the team, and the clinical setting in which the project will take place, many institutional review boards (IRBs) have a checklist to help assess key questions about the project that ultimately determine the need for a research approach versus a QI approach (Table 1). Individual hospitals or university-based health systems may modify or add items to their checklists as needed. Make sure to check with your own IRB for additional content areas that may require assessment at the local level.

In addition to assessing the risk, IRBs also need to determine the level of evidence that already exists in the published literature about the clinical question. Many familiar tools (eg, the GRADE approach) can be used to guide evaluation of levels of evidence, both for individual studies and for systematic reviews of the body of evidence as a whole.[7,8] The decision about which of these tools to use should be based on the nature of articles identified for your topic.[9] Regardless of whether there are just a few articles about your topic or a few hundred, using a systematic approach to evaluating the literature is a critical step in coming to the right conclusion as to whether your clinical question is research or QI.

If the level of existing evidence for your clinical question is insufficient or weak, and if the primary aim is to test something new against standard care (either in a new setting or new population), or to determine whether or how well a new intervention works, then a research approach is indicated. In clinical practice settings, most research questions compare 2 or more groups. Any time we are curious about whether A is better than B or C, we are comparing and testing for a difference between the groups (eg, any intervention that you would want to compare to "standard care"). Most PICOT (population, intervention, comparison, outcome, time)[10] questions involve group comparisons. This column looks at the many ways groups can be compared and the most common statistical tests used to determine if a statistically significant difference exists between the groups.

Aligning Research Questions With Design and Analysis Plan

Once the question is determined and research is confirmed as the best approach for the project, the next step is to select the design and type of statistical test to be used. Two things determine the direction for selecting the statistical test: (1) the measurement level of the dependent variable and (2) the number of groups.

Level of Measurement

The 4 main levels of measurement for variables are (1) nominal, (2) ordinal, (3)

Table 1: Project Design Tool Checklist to Determine Research Type[a]

Key Decision Points: Questions to Ask[11]	Yes (Protocol Is Quality Improvement)	No (Protocol Is Research)
Purpose Is the activity intended to improve the process/delivery of care while decreasing inefficiencies within a specific health care setting?		
Scope Is the activity intended to evaluate current practice and/or attempt to improve it based on existing knowledge?		
Evidence Is there sufficient existing evidence to support implementing this activity to create practice change?		
Clinicians/Staff Is the activity conducted by clinicians and staff who are responsible for the practice change in the institution where the practice change will take place?		
Methods Are the methods for the activity feasible and do they include approaches to evaluate rapid and incremental changes?		
Sample/Population Will the activity involve a sample of the population (patients/participants) ordinarily seen in the institution where the activity will take place?		
Consent Will the activity only require consent that is already obtained in clinical practice, and will that activity be considered part of the usual care?		
Benefits Will future patients/participants at the institution where the planned activity will be implemented potentially benefit from the project?		
Risk Is the risk to the patients/participants no greater than what is involved in the care they are already receiving, OR can participating in the activity be considered acceptable or ordinarily expected when practice changes are implemented in a health care environment?		

[a] If all of the questions in the table can be answered as a yes, then the project qualifies as quality improvement, and review by the institutional review board is not required. If the answer to any of these questions is no, consult with the institutional review board for assistance because review by the institutional review board may be required.

interval, and (4) ratio. *Nominal variables* are categories and name the attribute being measured—for example, "yes" or "no." An important feature of nominal variables is that there is no order or rank. *Ordinal variables* are categories that can be ranked and have a natural order to them, for example, values in a Likert scale. In *interval variables*, there is distance between the attributes, and the distance is equally split and has meaning. An example of interval measures is temperature, where the interval between degrees is constant and is interpretive. *Ratio variables* are interval variables with an absolute zero that has meaning (no numbers exist below zero). Examples of ratio variables are height or weight, where the values represent a quantity with equal intervals and the value cannot go below zero. Nominal- and ordinal-level dependent variables require nonparametric statistics (Table 2), and interval and ratio level dependent variables require parametric statistics (Table 3).

Number of Groups

In addition to the level of measurement of the dependent variable, the groups need to be defined, in both number and relationship, to determine the appropriate statistical test. There can be 1, 2, or more groups. The groups

Table 2: Nonparametric Statistical Tests for Nominal and Ordinal Data

Test	Purpose of Test (By Group and Relationship)	Measurement Level	
		Independent variable	Dependent variable
Chi-square test of independence (χ^2)	To test for differences in proportions in ≥2 independent groups	Nominal	Nominal
Fisher exact test	To test for differences in proportions (2 X 2 table) when expected frequency for a cell <5	Nominal	Nominal
McNemar test	To test for differences in proportions for 2 related groups (2 X 2 design)	Nominal	Nominal
Wilcoxon rank-sum test (U)	To test for differences in the ranks of scores of 2 independent groups	Nominal	Ordinal
Wilcoxon signed-rank test (T or z)	To test for differences in the ranks of scores of 2 related groups	Nominal	Ordinal
Spearman rank order correlation (rs)	To test existence of a relationship/ correlation between 2 variables	Ordinal	Ordinal

Table 3: Parametric Statistical Tests for Interval and Ratio Data

Test	Purpose of Test (By Group and Relationship)	Measurement Level	
		Independent variable	Dependent variable
One-sample *t* test (*t*)	To test predicted value of a mean population	—	Interval, ratio
t test for independent groups (*t*)	To test for differences between the means of 2 independent groups	Nominal	Interval, ratio
t test for dependent groups (*t*)	To test the difference between the means of 2 related groups/sets scores	Nominal	Interval, ratio
Analysis of variance, or ANOVA (*F*)	To test for differences among the means of ≥3 independent groups (one-way) or groups for ≥2 (multiway)	Nominal	Interval, ratio
Repeated measures of ANOVA, or RANOVA (*F*)	To test the differences among means of ≥3 related groups/sets of scores	Nominal	Interval, ratio
Pearson product moment correlation (*r*)	To test existence of a relationship /correlation between two variables	Interval, ratio	Interval, ratio

can be related or nonrelated (ie, independent). In related groups, the same subjects are tested more than once (eg, pretest and posttest of a group of patients undergoing an intervention or survey). Another example would be a crossover study design in which the participants receive different treatments during different time periods and cross over from one treatment to another during the course of the study.

By contrast, independent groups have no overlap in the subjects receiving the treatment. In this design, the patients from one time period may be compared to patients from another time period after a change in unit practice is made. In other words, each time period uses a different group of patients. For example, in a study measuring the effect of noise reduction on sleep satisfaction, the patients' sleep satisfaction is measured preintervention in one group and postintervention in a different group after implementation of noise-reduction strategies. Other examples of various ways to define and design group comparisons are shown in Table 4.

Table 4: Many Project Opportunities From a Single Topic: The CALS Example

Test	Possible research projects from CALS Example	Hypothesis Using CALS Example
One-sample *t* test *(t)*	To evaluate the mean chest reopening time of CALS patients compared with the expected predefined value as stated in CALS protocol (< 5 minutes).[6]	Chest reopening times of patients under a CALS protocol will be shorter than the expected predefined value.
t test for independent groups *(t)*	To evaluate the mean chest reopening time of CALS patients compared with patients not on the CALS protocol.	Chest reopening times for CALS patients will be shorter than chest reopening times for patients not on the CALS protocol.
t test for dependent groups *(t)*	To evaluate the CALS knowledge scores of nurses undergoing CALS training before and after CALS training.	Nurses undergoing CALS education will have higher knowledge scores regarding the CALS protocol after CALS education than before CALS education.
Analysis of variance, or ANOVA (F)	To evaluate the mean comfort scores of nurses, fellows, and advanced practice providers after CALS training.	Comfort with CALS procedures will differ among cardiothoracic surgical fellows, CTICU APPs, and cardiac surgery nurses after CALS training.
Repeated measures of ANOVA, or RANOVA (F)	To evaluate the CALS knowledge scores of nurses undergoing CALS training before CALS training and 6 and 12 months after CALS training.	Nurses undergoing CALS education will have higher knowledge scores regarding the CALS protocol 6 and 12 months after CALS education than before CALS education.
Pearson product moment correlation *(r)*	To evaluate the effect of years of nursing experience on comfort with the CALS protocol.	Comfort with the CALS protocol will increase with the number of years of nursing experience.

Abbreviations: APP, advanced practice provider; CALS, cardiac surgery advanced life support; CTICU, cardiothoracic intensive care unit.

Selecting a Statistical Test

Once the decision has been made regarding the level of measurement of the dependent variable and you are using the appropriate *type* of statistical test (ie, nonparametric or parametric), you would then need to select a specific statistical test based on the number of groups and their relationship to one another (see column 2, Table 2 and Table 3). For example, to test the difference in the number of males versus females with heart failure, we would use the chi-square test of independence (Table 2) to determine the difference in the proportion, or percent, in 2 independent groups (ie, males vs females). In another example, to test the difference in weight loss (body mass index) in 2 groups, one with dietary counseling and one with standard educational pamphlets, we would use a parametric statistical test (Table 3).

To illustrate how to select a statistical test, we return to the example used in the previous parts of this series: implementation of a CALS protocol. In part III,[5] we used the Project Design Tool to ask questions (Table 1) to determine that implementation of the CALS protocol was a QI project. In part IV, we approach the clinical question as a hypothetical research project. If we determine that the existing evidence for the CALS protocol is insufficient to support implementing a practice change, then a research protocol would be required. In our example, the research question might be, "Is survival in cardiac surgery patients improved following cardiac arrest and also at discharge when using CALS versus when using advanced cardiac life support (ACLS)?"

Our research project compares the new CALS protocol with standard care ACLS. Our dependent variable is survival (ie, yes or no), which is a nonparametric variable. We will use 2 independent groups with patients randomized in group A or B. The correct test to use

to find differences in two independent groups is either the chi-square (χ^2) or Fisher exact test (Table 2). The decision about which test to use depends on the details of sample size: small samples benefit from the Fisher exact test, whereas samples with more than 5 participants or values expected in a given group can use a standard χ^2 (see Figure).

Logistical Considerations

Clinical Research Questions

An essential part of being able to complete a clinical research project is choosing the right project and answering the right question(s). Granger and Chulay described a practical focus group method to identify clinical research questions.[12] When considering a research question, one should use high-volume patient populations and patient needs or problems. If high-volume is not used, data collection would take too long. Avoid politically charged questions, protocols that would be difficult to implement, using large numbers of new staff to carry out the protocol, or interventions outside of nursing's domain of practice. In the CALS example, because of the infrequency of cardiac arrest following cardiac surgery, a large volume of patients would be required to show a difference between the 2 methods of resuscitation. In addition, other problems would likely be encountered with different resuscitation protocols in place for the same patient population.

Operational Feasibility

Once the project and clinical research question have been established, operational feasibility of the project should be evaluated. The Operational Project Feasibility Checklist[4] should be used prior to seeking formal leadership and IRB approval to identify and overcome common challenges. Using this operational project feasibility checklist to evaluate the CALS project example as a research protocol, we come up with the following additional resources and workflow considerations: (1) patient population, (2) method for randomization, (3) staff skills, (4) project aims, (5) stakeholder approval, and (6) implementation and communication plans.

Patient Population. The patient population for a randomized 2-group protocol necessitates evaluation of the institution's total annual surgical cases eligible for the CALS study. However, the requirement to consent may lead to loss of eligible cases, resulting in inadequate power to answer research questions. Although we have a large volume of cardiac surgery patients in our unit, the total number of annual arrests randomized to 2 groups may require a multiyear study and increase the complexity of staff resources required for the study.

Method for Randomization. The method for randomization (eg, computer-generated randomization versus randomization by geographic location in the unit) must take unit workflow into consideration. The procedure for randomization may need to be adapted or modified so as not to disrupt patient throughput, staff nurse workflow, or the ability to admit or relocate patients geographically to meet care needs. The decision on method for randomization would warrant discussion with the operational and research teams before the study. Furthermore, the ability to identify which patients are randomized to which intervention group, especially in a busy unit, is an important process and needs systematic thought and consideration before beginning. Existing resources from clinical research units and other teams should be used when available to ease many of the logistical issues of doing research in a clinical setting, and using solutions from prior studies can help smooth study preparation and planning.

Staff Skills. The staff skills include research and evidence-based practice skills, as well as the training required to participate in and conduct research. These skills may be more complex in the case of a randomized research protocol. If staff training needs are anticipated and incorporated into the study timeline with the appropriate support up front, the complexity of the staff skills is manageable and provides a potential growth opportunity for team members. In academic-affiliated health systems, the plethora of learners adds complexity, but may also add benefits to efforts to integrate a randomization scheme as a part of the study design. Staff skills related to obtaining informed consent for a research protocol may also require additional or ongoing training for new staff. Alternatively, designated staff may be identified as a cohort of "consenters" and trained to obtain consent, similar to the training commonly done for the cohort of charge nurses.

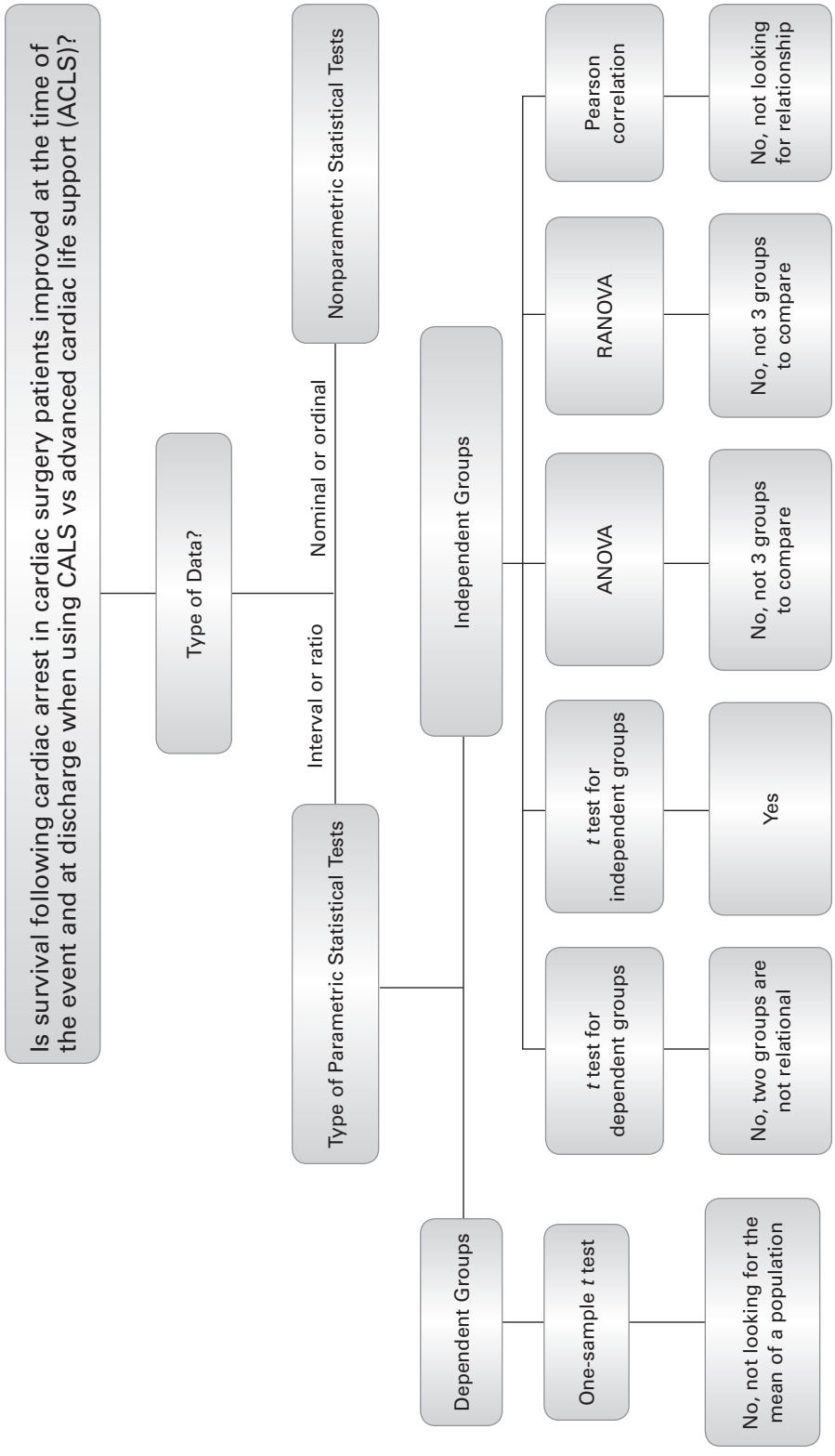

Figure: Decision tree for research designs based on question type.
Abbreviations: CALS, cardiac surgery advanced life support; ANOVA, analysis of variance; RANOVA, repeated measures analysis of variance

For the CALS example, the staff skills would also need to cross clinical settings to ensure that consent occurrs not only in the clinic setting for elective patients, but also in the inpatient setting for postoperative patients who may have been directly admitted to the unit. The evaluating of staff skills (eg, existing resources within clinical research units, other nurse researchers in the organization, partner clinicians, resources from affiliated schools of nursing) may bridge gaps in skills while serving to build relationships between the staff if thoughtfully addressed in the planning stages.

Project Aims. The project aim in the CALS example would not be markedly different for a research protocol versus a QI protocol. The timing of introduction and startup in the organization, awareness and sensitivity to competing projects, and the implications of data collection and the relative meaningfulness of the findings would remain equally important, regardless of whether the project design was QI or research. However, study duration may differ if the numbers needed to enroll are higher for a research design, for example, or if the preparation timeline needed to increase to allow time to train teams for the randomized resuscitation protocol.

Stakeholder Approval. The stakeholder approval and support for a research protocol in the CALS example would be extremely important for a protocol that was not evidence based; the risks posed to patients is more likely to be considered too high in the case of a resuscitation protocol designed to create new evidence. Support from clinical nursing and physician leadership would likely be required in addition to the added requirements for informed consent and a full board IRB review and approval.

Implementation and Communication Plans. The implementation and communication plans would not be markedly different for a CALS research versus a QI project. In each case, the dissemination audience and methods used for communicating the results would include local staff and leadership forums. Regional, national, and international audiences of clinicians would be equally interested in the results.

Conclusion

Choosing a research project that fits into clinical practice is essential for a successful project. In this fourth and final part of the APN Research Protocol Development series, we have provided APNs with the tools for determining project type, study design, and type of statistical test needed for research projects. In addition, issues surrounding operational feasibility, such as sample size, practicality, and stakeholder support have been discussed.

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