Conducting Prospective Research as a Trainee

Experiences with the DRIVE-SAFE Study

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ABSTRACT

Conducting clinical research during a 2-year critical care fellowship is a challenging endeavor. Fellows are often met with multiple barriers when considering clinical research projects during fellowship, including time, mentorship, resources, and clinical support. This paper presents the perspective and experiences of a group of critical care fellows who conducted the DRIVE-SAFE (Driving Pressure in Assisted Ventilation as a Predictor for Successful Liberation from Invasive Mechanical Ventilation) feasibility study, which aimed to determine measurable physiological variables that could be associated with lung injury and affect duration of mechanical ventilation. This paper provides a guide for trainees on how to conduct prospective clinical research at the bedside. We describe three key steps, including formulating a research question, developing appropriate methodology, and establishing outcomes. We also present the challenges that trainees may encounter when conducting prospective studies and how to overcome these challenges with proper mentorship, training, and collaboration with key stakeholders. These perspectives may provide useful guidance for current and future trainees interested in conducting prospective clinical research at the bedside.

Keywords:
mechanical ventilation; diagnostic tools; trainee research

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Research scholarship is a mandatory component of many critical care medicine (CCM) fellowship programs. For most trainees, given the competing time commitments, this involves choosing a research project that can be completed quickly, as a pragmatic way to "check the box." CCM trainees describe many barriers to research involvement, including time commitment, lack of opportunities, and inadequate mentorship (1). For a group of CCM fellows at McMaster University in Hamilton, Ontario, Canada, bedside clinical research was aspirational and, despite the anticipated challenges, a pursuit we were willing to commit substantial time and energy toward. It was with this enthusiasm that the DRIVE-SAFE (Driving Pressure in Assisted Ventilation as a Predictor for Successful Liberation from Invasive Mechanical Ventilation) study was developed and, with proper mentorship, successfully conducted.

DESIGNING A PROSPECTIVE STUDY

In this paper, we provide a guide to trainees hoping to conduct prospective clinical research at the bedside. We use our experience in carrying out the DRIVE-SAFE feasibility study to illustrate each of these broad steps.

Formulate a Research Question and Review the Literature

The formation of a research question often goes together with a thorough literature review. After brainstorming potential topics of interest, it is useful to format questions in the form of population, intervention, comparator, and outcome (PICO) for any research question. This approach can guide the development of useful questions and efficient searches on the topic. Our group was broadly interested in patients who were weaning off the ventilator and aimed to determine measurable physiological variables that could be associated with lung injury and affect the duration of mechanical ventilation.

The avoidance of ventilator-associated lung injury (VALI) is an important focus in critical care, and optimizing the management of patients requiring invasive mechanical ventilation is a major passion of many CCM fellows (2). Lung-protective ventilation is an established strategy for patients with acute respiratory distress syndrome (ARDS), performed to mitigate VALI. Beyond traditional VALI, patient self-inflicted lung injury may play an important role, contributing to injurious effects of excessive intrathoracic pressure swings in patients with high respiratory drive and effort (3). Driving pressure, measured by taking a plateau pressure during an end-inspiratory hold, has been identified as a key prognostic marker in patients with ARDS who are on a controlled mode of ventilation (4–7); however, markers of VALI, and specifically patient self-inflicted lung injury, have not been well established in patients using assisted ventilation or spontaneously breathing on the ventilator (8). The research question of the DRIVE-SAFE study was to prospectively measure true driving pressure in all patients on pressure support ventilation and assess the association between driving pressure and duration of invasive mechanical ventilation and weaning or extubation success.

Develop Appropriate Methodology

Once a research question and objectives are delineated, the next step is to decide on the type of research methodology. For DRIVE-SAFE, this fostered multiple points of discussion. Our initial intention of organizing a prospective, multicenter, observational study was ambitious.

We planned to systematically perform inspiratory holds on patients on pressure support ventilation, to obtain their true driving pressure. Specifically, given that it was a novel research question using an as-yet unstudied technique as a marker of ventilatory parameters, questions arose regarding if systematically and effectively measuring driving pressure in spontaneously breathing patients would be valid and reproducible. This facilitated a pivot to a single-center feasibility study to start. It is based on this experience that we write this paper. It is crucial that the methodology selected for a study makes sense for a study question and considers the resources available to a group.

In the context of our study, inclusion and exclusion criteria were developed, and a plan for screening and consenting eligible patients was made. Most importantly, a protocol to measure driving pressure for patients breathing spontaneously on the ventilator (on pressure support mode of ventilation) was developed. This protocol was reviewed by experts in the field and disseminated to ensure consistency and accuracy of measurements. Study variables were carefully selected based on prior research studies and feedback after study protocol review. These variables were then delineated and included in case report forms. In the context of trainees conducting research, it is typical that the same trainees would be the ones responsible for data collection. Such was the case for our group, in which a group of interested CCM fellows coordinated research blocks dedicated to data collection.

Establishing Outcomes

Conducting any research study requires one to critically think about what the most important outcomes to measure will be. A major shift in the development of DRIVE-SAFE was the conversion to a feasibility study. Initially, our primary outcomes were all clinical, such as ventilator-free days, reintubation rate, length of stay in the hospital and intensive care unit (ICU), and mortality. Once it was determined that a feasibility study was what was required, outcomes such as protocol adherence rate, recruitment rate, consent rate, and interrater reliability of plateau pressure measurements became most relevant.

CHALLENGES TO CONDUCTING PROSPECTIVE STUDIES

To the group of McMaster CCM fellows, initiating a prospective observational study in April of 2020 examining a novel study question seemed like a straightforward task. In retrospect, we were naive to the demands that doing prospective research as a fellow entails, exacerbated by a global pandemic. Leading this project as trainees and early career researchers was an eye-opening experience. Notably, in leading this study, we were responsible for all aspects, including protocol development, funding application, case report form development, ethics submission, screening, research consent encounters, drive pressure measurements, data collection, analysis, and writeup. Thankfully, we benefited from mentorship and guidance from a group of committed ICU researchers and clinicians based at McMaster University. Herein, we describe the main challenges we faced, how these barriers were overcome, and lessons learned.

Ultimately, much of the work required was unrelated to the specifics of our research question but had more to do with learning to successfully implement changes to the usual institutional processes at our center. Frequently, we would refer to aspects of Kotter's model of change

management for guidance and approaches to overcoming barriers (9). Figure 1 is Kotter's model for change management, reproduced from his original paper on leading change (10). We believe many of the approaches taken and lessons learned are ubiquitous to doing prospective research during training and that guidance will be generalizable to other fellows considering similar research endeavors. Below, we describe the challenges, solutions, and lessons we learned conducting prospective bedside clinical research (Table 1).

1. Bedside staff orientation
   - Challenge: We underestimated how difficult it would be to orient staff to our research. Our initial approach involved a mass e-mail, and this quickly proved to be insufficient. We received early feedback from registered respiratory therapists (RRTs), registered nurses (RNs), and research coordinators at our center, who did not feel adequately informed about the project at its inception. Even though these staff members were not required to help with the study, they needed to be aware of what the fellows were doing and what was being done to their patients.
   - Facilitator: Our solution was first to conduct in-person meetings with allied health educators (RRT, RN, and research coordinator). We then sent targeted e-mails to each stakeholder group (RRTs, RNs, physicians) at more regular intervals, disseminated through key study champions. As the project expanded, these were distributed to all study sites. Regular updates, including progress reports to the core steering committee, became of paramount importance to maintain group enthusiasm and keep the team well informed. Finally, providing simple, easy-to-digest, "one-pagers" helped facilitate rapid communication for busy teams.
   - Lesson learned: To facilitate any effective change, two vital principles are: *1*) build a guiding coalition or team of study champions; and *2*) effectively communicate the vision or strategy for change (9). Including representative interdisciplinary champions on our team was essential. The importance of properly orienting staff with targeted, specific, and concise information in a unit where research is to be undertaken cannot be overstated. We advise future trainees hoping to embark on prospective research that no amount of education and priming of the relevant stakeholders is too much.
2. Collaboration with the healthcare team
   - Challenge: Despite our attempts at study orientation, we still experienced confusion at the bedside, especially from RRTs, if they were unsure who was "playing with the ventilator" and why. Similarly, we encountered bedside nurses who had suggestions about appropriate patients on whom to perform measurements and optimal timing to take measurements. For example, it was embarrassing to attempt to measure variables on a ventilator, only to learn a patient was progressing toward comfort measures.
   - Facilitator: We discovered the importance of engaging with the bedside team before enrolling a patient and before each measurement. The clinical team was most informed about the dynamics of a certain family, especially with respect to what their thoughts were about research, thereby maximizing the chances for success with including them in research. This included close collaboration with the most responsible physician, the patient's assigned nurse or RRT, or another ICU-based research coordinator who had already achieved rapport with the patient or family. Our approach was to identify ourselves as Critical Care fellows and explain that we were recruiting and conducting measurements for the DRIVE-SAFE study. We ensured assent from the most responsible physicians, RRTs, and RNs before proceeding with enrollment and study measurements. This became ingrained

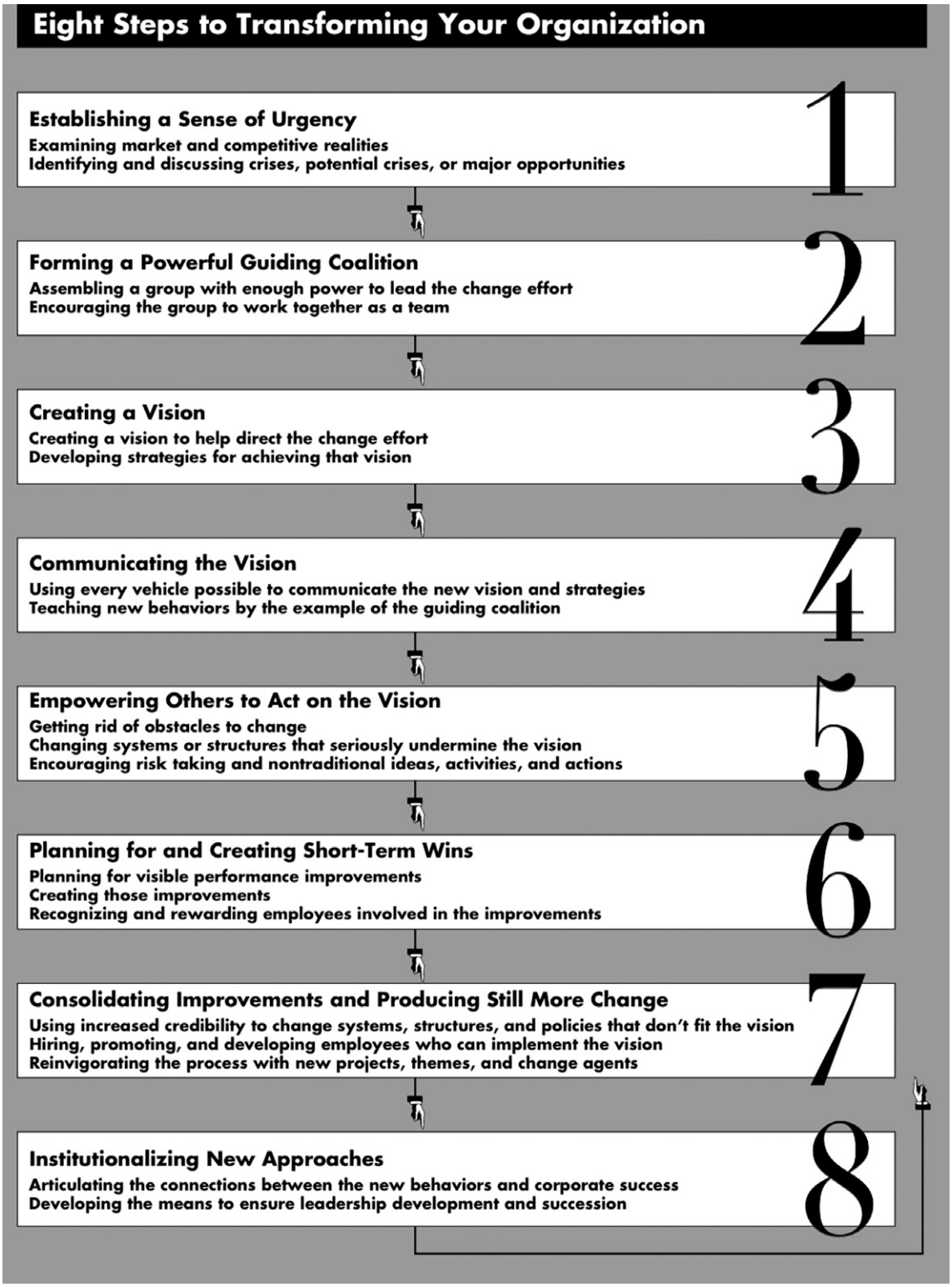

Figure 1. Kotter's model for change management. Reprinted by permission from Reference 10.

Table 1. Challenges with prospective studies and mitigating solutions

Challenges Faced	Techniques to Resolve Challenges
Orientation of bedside staff	• Assign study champions (physicians and allied health professionals) • Disseminate brief targeted e-mails and updates for orientation and ongoing enthusiasm
Collaboration with healthcare team	• Engage staff when at bedside • Standardize processes and measurements • Create transparency and avenues for feedback and contribution
Patient recruitment	• Incorporate formal research consent training in the academic curriculum • Appreciate differences between obtaining consent for clinical purposes compared with research consent

into a preenrollment checklist, which proved invaluable.

- Lesson learned: Another fundamental concept of Kotter's change management model is enabling the healthcare team to work toward a shared vision for a project. This is facilitated by removing obstacles and barriers to a process as much as possible (9). Personal, on-the-ground, at-the-bedside interactions between trainee researchers and healthcare providers help facilitate study conduct. We advise all trainee researchers to use the resources available to them. When it comes to bedside clinical research, it is vital to communicate and collaborate with members of the healthcare team, especially if they are directly involved in a patient's care. The standardization of as many elements of the process as possible also helps to eliminate variability and create transparency in the work, thus empowering other members of the healthcare team to contribute.

3. Formalized research consent training and process
   - Challenge: Our initial expectation was that we had experience with acquiring clinical consent for treatment-related decisions and that this would generalize easily to acquiring research consent. This proved to be an important oversight. This observational study involved performing an end-inspiratory hold on the ventilator. Although this allowed for measurement of a true driving pressure, it is a maneuver that is not routinely performed on a patient receiving pressure support ventilation. The explanation of the study to patients and families required skill and practice. Not only that, but there are unique features of research consent that we had not considered. It became clear that a signed consent form alone did not necessarily imply that effective informed consent had been achieved and that we required formal training in obtaining research consent if this study was to be successful.
   - Facilitator: We spent some time observing consent encounters done by experienced ICU research coordinators, which proved highly beneficial. A senior clinician-investigator and trialist based at McMaster University provided an academic half-day to discuss how research consent encounters are unique and some strategies for acquiring them, especially when dealing with challenging situations. Finally, we used a standardized research consent note in the chart for every patient who was approached and enrolled, to explicitly inform all caregivers about the involvement of the patient in the study.
   - Lesson learned: To be able to sustain "any change in a system, there must be

a change in culture (9). This applied to creating not only an acceptance of our group's assessments of the ventilator in the ICU but also a broader culture shift to an acceptance of trainees performing bedside clinical research. One of the most basic principles of research ethics is respect for persons, which requires that patients or their substitute decision-makers be given the opportunity to make an informed decision regarding participation in a research study. We advise all trainees embarking on clinical research at the bedside to undergo formal research consent training, as experience in acquiring clinical consent is not sufficient. Formal training improves the confidence of all members of the healthcare team and improves confidence in those obtaining the consent that it is an effective and informed process. Developing formal training and infrastructure tailored to preparing learners to embark on clinical research is vital to the success of trainees performing research.

FEASIBILITY

Although we encountered a number of hurdles, this feasibility study led to useful insights and learnings for the trainees participating in the DRIVE-SAFE observational study. We enrolled a total of 29 patients in the feasibility stage of the study, which included 89 measurements of drive pressure. Most importantly, we showed that a prospective study measuring true driving pressure in patients receiving a spontaneous ventilatory support mode was feasible, reliable, and safe. Figure 2 shows an example of an end-inspiratory hold on pressure support and how the true driving pressure may be different from the expected driving pressure set on

Figure 2. True driving pressure on pressure support ventilation. On the Hamilton-G5 ventilator, patient is on pressure support of 5 cm H_2O on positive end-expiratory pressure of 5 cm H_2O. When an end-inspiratory hold maneuver is performed, plateau pressure is found to be at 18 cm H_2O (top right of image). This translates to the patient exerting an additional 8 cm H_2O of negative pressure (Pmus = 8) to the expected 5 cm H_2O of pressure support, to generate their tidal volume of 363 ml. The true driving pressure is 13 cm H_2O. PEEP = positive end-expiratory pressure; Pmus = difference between plateau pressure and peak pressure; Psupport = Pressure support.

the ventilator. Based on this feasibility study, we made several protocol updates and embarked on a larger multicenter observational study, still led by McMaster CCM fellows. This larger study is also examining new research questions, such as the utility of P0.1 (pressure generated during the first 100 ms of a breath) and Pmus (difference between plateau pressure and peak pressure) to titrate pressure support and to predict spontaneous breathing trial and extubation success.

CONCLUSIONS

It is possible for CCM fellows to conduct prospective clinical research at the bedside. In this perspective, we share our experience with the DRIVE-SAFE feasibility study as a guide to learners conducting prospective clinical research. Key components to success include comprehensive bedside staff education, engaging key stakeholders and leadership, a consistent and organized approach to bedside data collection, and formalized research consent encounter training. Periodic holistic program assessments of the aptitude of a training program to empower and guide its trainees in the conduct of prospective research is advised.

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