

Unnecessary variation in practice: how to improve cancer care through pragmatic trials

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Oncologists are frequently faced with multiple “reasonable” treatment options, without sufficient evidence to choose one over the other. In those situations, idiosyncratic decision-making processes take precedence, with practitioners choosing what they think is best. That practice results in significant differences in standard-of-care practice, whereby the treatment a patient receives can vary from one physician to another, from one institution to another, and for the same physician at different times.

A simple example is the choice of adjuvant chemotherapy for patients with early-stage breast cancer. In Ontario, 10 established regimens, vastly different in cost and toxicity, are funded, but very little evidence is available to guide the optimal choice for an individual patient. In an era in which patients are communicating with each other more and more and are asking questions about why they are receiving a particular treatment from a particular oncologist, such variations in practice have to be addressed. In short, large comparative effectiveness trials are required to determine the best treatment options for optimized patient outcomes and a reduction in needless practice variation.

Clinical equipoise exists when the medical community has genuine uncertainty about the benefits of one treatment over another. Importantly, clinical equipoise provides the moral foundation for conducting a clinical trial.

In the studies that accompany this editorial^{1,2}, the authors note that vascular access is a topic of evolving interest, particularly as it relates to breast cancer patients, to whom a large proportion of the chemotherapy and vascular access resources in North America are dedicated. Chemotherapy for early-stage breast cancer can be administered through a peripheral vein, a peripherally inserted central venous catheter, or a tunneled subcutaneous venous port. Despite major changes in the types of chemotherapy used (fewer anthracyclines) and the duration of treatment (for example, adjuvant trastuzumab), methods of vascular access remain an area of great variation in practice between and within hospitals, and current clinical guidelines lack specificity for oncology patients³ despite the efforts of international research groups such as the Italian Study Group on Long-Term Central Venous Access and the World Congress on Vascular Access.

The complications associated with various access strategies are well recognized. Central venous access is associated with risks of infection and thrombosis and with higher cost. Peripheral access can be limited by poor reliability, extravasation, and sclerosis of the veins.

The two studies accompanying this editorial asked breast cancer patients, oncologists, and oncology nurses about vascular access strategies, perceived rates of complications, and perceived risk factors for lymphedema. The last question was based on the idea that insertion of a central line reduces the risk of lymphedema by avoiding the veins on the surgical side. The study results add to the limited data available about this topic^{3,4} and highlight a number of interesting points from the standpoint of the patient and the health care team alike. One of the most perplexing findings is the heterogeneity in practice seen for the use of peripheral access compared with central access—even for the same chemotherapy regimen. Furthermore, even though perceived complication rates remain high, many providers still recommended central access because it is perceived to be associated with improved quality of life for patients—a perception that is largely conjecture, not evidence-based, and not informed by direct patient input. Interestingly, most patients could not recall being involved in the decision-making process for venous access. Finally, it is disappointing to see that perceived risk factors for lymphedema (for example, blood pressure measurement or phlebotomy in the surgical arm, and air travel) continue to be perpetuated. Although health care professionals deny that they are the source of those myths, they might want to read the papers and see who was named by patients as sources of this misinformation!

Although these publications have limitations, they do confirm the presence of clinical equipoise in practice. But most importantly, while recognizing that all types of access have particular advantages and disadvantages, the evidence base for choosing the most appropriate vascular access remains limited. With that in mind, the Rethinking Clinical Trials (REACT) Program has developed and opened two trials to answer those questions for the HER2-negative and HER2-positive breast cancer populations (see NCT02632435 and NCT02688998 at <http://ClinicalTrials.gov>). These pragmatic comparative effectiveness trials are using novel

strategies and methodologies to overcome many of the challenges of performing traditional clinical trials⁵. The REACT program has now randomized more than 1000 patients onto a series of ten trials addressing areas of unmet comparative evidence in medical, surgical, and radiation oncology. We hope that other investigators will join in the REACT studies so that many of the simple and practical questions that will have a very real impact on the care and well-being of oncology patients can be answered.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

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