

# Can the referring surgeon enhance accrual of breast cancer patients to medical and radiation oncology trials? The ENHANCE study

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## ABSTRACT

**Introduction** The accrual rate to clinical trials in oncology remains low. In this exploratory pilot study, we prospectively assessed the role that engaging a referring surgeon plays in enhancing nonsurgical oncologic clinical trial accrual.

**Methods** Newly diagnosed breast cancer patients were seen by a surgeon who actively introduced specific patient- and physician-centred strategies to increase clinical trial accrual. Patient-centred strategies included providing patients, before their oncology appointment, with information about specific clinical trials for which they might be eligible, as evaluated by the surgeon. The attitudes of the patients about clinical trials and the interventions used to improve accrual were assessed at the end of the study. The primary outcome was the clinical trial accrual rate during the study period.

**Results** Overall clinical trial enrolment during the study period among the 34 participating patients was 15% (5 of 34), which is greater than the institution's historical average of 7%. All patients found the information delivered by the surgeon before the oncology appointment to be very helpful. Almost three quarters of the patients (73%) were informed about clinical trials by their oncologist. The top reasons for nonparticipation reported by the patients who did not participate in clinical trials included lack of interest (35%), failure of the oncologist to mention clinical trials (33%), and inconvenience (19%).

**Conclusions** Accrual of patients to clinical trials is a complex multistep process with multiple potential barriers. The findings of this exploratory pilot study demonstrate a potential role for the referring surgeon in enhancing nonsurgical clinical trial accrual.

**Key Words** Clinical trials, accrual strategies

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## INTRODUCTION

Clinical trials remain the “gold standard” by which new cancer treatments are assessed and through which therapeutic progress is made<sup>1–4</sup>. Although most clinicians<sup>4</sup> and patients<sup>5</sup> support clinical trial accrual, only 3%–5% of new adult cancer patients overall participate in clinical trials<sup>3,4</sup>. Low accrual rates remain a significant issue, because the duration of trials can thereby be prolonged, delaying the analysis of important results or leading to early study closure, with huge waste of invested resources.

Identified barriers to clinical trial accrual include those related to physicians, patients, protocol or eligibility, the institution, and regulations (Table 1)<sup>6–9</sup>. Surgeons often have several contacts with patients, and frequently discuss possible treatments before the patient's first visit to a medical or radiation oncologist. Because trust in a physician, particularly when the physician recommends a clinical trial, has been noted to be highly associated with trial recruitment<sup>10–15</sup>, we decided to undertake a prospective exploratory pilot study to evaluate whether specific referring surgeon-initiated interventions aimed

**TABLE 1** Common barriers to clinical trial accrual

Barrier type			
Patient-related	Protocol-related	Physician-related	Institutional and regulatory
Concerns about costs or health insurance	Trial setting	Negative effect on doctor–patient relationship	Lack of protocol availability
Transport or distance to trial site	Dislike for idea of randomization	Belief that doctor should make decisions	Inadequate organizational staffing and infrastructure
Lack of family support or increased anxiety	General unease with research process	Feeling coerced to join	Inadequate organization size
Discomfort with experimentation	Protocols too complex or stringent	Physician attitude toward trial	Lack of interdisciplinary cooperation within organization
Concern about loss of control over decision-making	Concern about assignment to placebo or no-treatment group	Stringent regulations (institutional, national, or international)	
Feelings of uncertainty	Inconvenient for everyday life	Organizational culture	
Concern that quality of life might be reduced	Potential for side effects		
Fear or mistrust of research or researchers	Trial not appropriate for serious disease		
	Trial or treatment does not offer best option		
	Trial or treatment has no benefits		
	Preference for other treatment		
	Not informed or information given was inadequate		
	Need for multiple visits		

at reducing physician and patient barriers could enhance clinical trial accrual in breast cancer patients. Accrual to clinical trials is a multidimensional problem that requires multidimensional interventions to effect improvement, and the potential influence of the referring surgeon is one dimension emphasized in the present study.

## METHODS

This 6-month prospective single-institution pilot study was called ENHANCE. All patients newly diagnosed with invasive breast cancer at our institution are seen in an initial consultation by a participating breast surgeon; they are then referred for a medical or radiation oncology opinion (or both) as required. Patients were asked to participate in ENHANCE if they had a new diagnosis of invasive breast cancer, and if they received surgery as primary therapy for their breast cancer. Once a patient consented, the surgeon actively introduced strategies aimed at increasing accrual to nonsurgical clinical trials led by local oncologists. At the time of the study, no neoadjuvant or ductal carcinoma *in situ* trials were open; only adjuvant trials in invasive breast cancer were ongoing (2 international, 3 national, and 3 institutional). Local research ethics board approval was obtained before study commencement.

### Interventions by the Surgeon Participating in ENHANCE

#### *Patient-Centred Interventions and Strategies*

All eligible patients of the participating surgeon were introduced to ENHANCE at the postoperative visit (Figure 1). Once the patient consented to ENHANCE, the surgeon first used the Ontario Institute for Cancer Research “Clinical Trials” brochure to introduce the overall concept of clinical trials (<http://www.ontariocancertrials.ca>). The patient was then

given preprinted descriptive information (lay language format) about the specific clinical trials for which the patient might be eligible based on their clinicopathologic features and the known eligibility criteria of the available trials. The participating surgeon attended weekly tumour board meetings and monthly research meetings to keep up to date on the existing clinical trials and their eligibility criteria.

#### *Physician-Centred Interventions and Strategies*

On the morning of a participating patient’s appointment with either the medical or radiation oncologist, the oncologist received an e-mail message from the surgeon giving a brief summary of the clinicopathologic features of the patient about to be seen, a list of the specific clinical trials for which the patient might be eligible and whose information had been provided to the patient, and a reminder that the patient would later be surveyed about whether they were offered clinical trial participation by the oncologist. On the day of the appointment, a brightly colored paper copy of the e-mail was also placed on the patient’s chart. Approximately 6 weeks after the initial oncology appointment, participating patients were sent a survey (developed by a survey methodologist<sup>16,17</sup>) to assess their attitudes and views toward clinical trials and strategies to improve accrual.

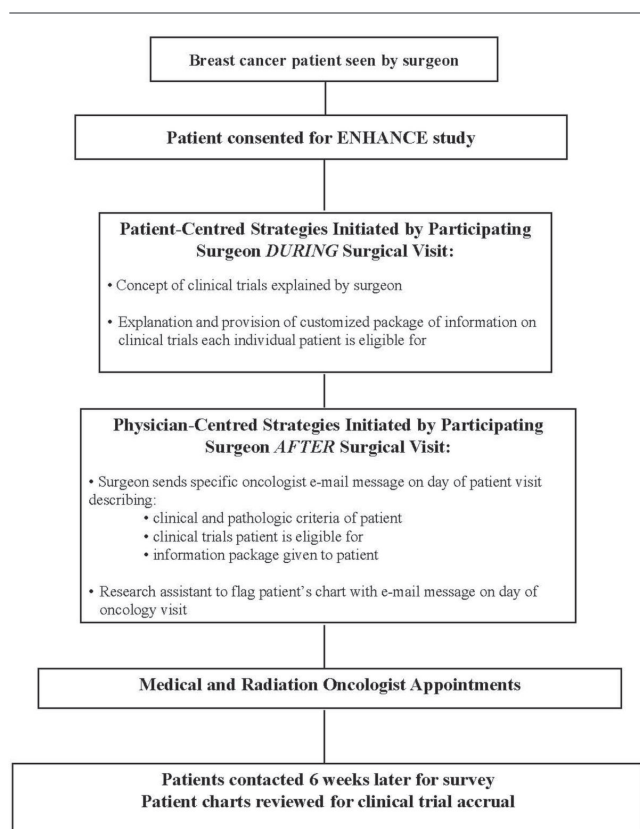
### Statistical Analysis

Descriptive statistics are used to summarize patient characteristics and trial accrual outcomes.

## RESULTS

### Patient Population

Between June 2012 and December 2012, 35 patients with invasive breast cancer were seen by the participating surgeon. Only 1 of the 35 patients withheld consent to the



**FIGURE 1** Patient flow schema for the study. To enhance clinical trial accrual, the participating surgeon used a combination of physician- and patient-centred strategies.

ENHANCE study (the patient already felt overwhelmed and was not interested in receiving more information during the surgical visit). Table II shows the clinical and pathologic characteristics of the remaining 34 patients.

### Trial Accrual

At the time of the ENHANCE study, 8 clinical trials were ongoing. Of the 34 ENHANCE patients, 27 (79%) were potentially eligible for at least 1 clinical trial. Of the 27 potentially eligible patients, 5 (19%) went on to enrol in a clinical trial, representing 15% of all patients seen (5 of 34).

### Survey Results

Overall, 26 of the 34 ENHANCE patients (77%) responded to the patient survey. All 26 were eligible for at least 1 clinical trial. All 26 patients felt that the information conveyed to them and the information package given to them by the surgeon about clinical trials was useful and that they would recommend it to others. Two patients (8%) mentioned that the information improved their view of clinical trials. Of the 26 patients, 5 (19%) researched trials using other sources of information such as the Internet, books, and conversations with other patients. Most of the patients (21 of the 26, 81%) felt that the information given during ENHANCE was appropriately given at the surgical appointment prior to their oncologist visit; the rest (19%) felt that the information should have been reserved until the oncologist appointment.

**TABLE II** Demographic, clinical, and pathologic characteristics of the ENHANCE patients

Characteristic	Value
Patients (n)	34
Mean age (years)	58.5±11.8
Ethnicity [n (%)]	
White	31 (91)
Asian	2 (6)
Black	1 (3)
Distance from cancer centre [n (%)]	
<15 km	18 (53)
≥15 km	16 (47)
Stage of breast cancer [n (%)]	
I	12 (35)
II	16 (47)
III	4 (12)
IV	2 (6)
Positive receptor status [n (%)]	
HER2	3 (9)
Estrogen	29 (85)
Progesterone	25 (74)

Nineteen patients (73%) either remembered being informed about clinical trials by their oncologist or were documented in the oncology visit notes as having been informed. Of the 21 patients who did not enrol in a clinical trial, the top reasons for not enrolling included “not interested” (7 of 21, 33%), “the oncologist did not mention trial” (7 of 21, 33%), and “too inconvenient to participate” (4 of 21, 19%).

### DISCUSSION

Currently, only about 2%–3% of newly diagnosed breast cancer patients in North America participate in clinical trials annually, and an even smaller proportion enrol onto adjuvant therapy trials<sup>1–4</sup>. Accrual to clinical trials represents a complex interaction of patients, clinicians, care delivery, and the organization. Our exploratory pilot study examined the potential role for, and impact of, a referring surgeon facilitating patient access to medical or radiation nonsurgical trials, with the intent of reducing both physician and patient barriers to accrual. The overall rate of clinical trial accrual was 15% (19% if only eligible patients are considered). That rate is more than double the historical institutional average enrolment rate of 7%<sup>18</sup> and higher than the rate of 2%–3% reported in the literature<sup>1–6,10–17</sup>. Clearly, the results have to be interpreted with caution, given that ENHANCE was only an exploratory pilot study with a small number of patients. However, it does demonstrate a potential role for the referring surgeon in enhancing nonsurgical clinical trial accrual.

It is interesting to note that, despite the appointment being held in a specialized cancer institute with a stated mission to recruit patients to trials when possible, and receipt

by the oncologist of a personal e-mail notification from the surgeon on the day of a patient's appointment, and a notification to the oncologist that the patient will be surveyed about the discussion with the oncologist, 23% of the patients who were potentially eligible for a clinical trial indicated that they were not presented with that treatment option. That rate is comparable to the rates reported in many academic centres (20%–50%)<sup>14–17</sup>; clearly, however, any strongly-held preconceptions about the merits of various treatment modalities on the part of the clinician will challenge the therapeutic equipoise necessary for a clinical trial.

Discussion with the participating surgeon revealed that the strategies used in ENHANCE were labour-intensive and increased the duration of patient visits for the participating surgeon by approximately 10–15 minutes each, raising questions about the sustainability of the strategies. Suggestions about how to improve clinic efficiency included having a nurse at the surgeon's office do the work of introducing clinical trials and perhaps targeting only the patients who are likely to be eligible for the ongoing clinical trials. The most cumbersome strategy of all was the requirement for the surgeon to personally send e-mail messages to the medical and radiation oncologists on the morning of those respective appointments. Not only was message transmission a time-sensitive issue that had to be accommodated in a busy and sometimes unpredictable surgeon's schedule, but message receipt (had the oncologists been able to read the e-mail messages before the patient's appointment?) was also not always clear. The printed e-mail message from the surgeon that was placed on the patient chart, which could be written ahead of time, would perhaps have been sufficient. Future trials should specifically evaluate the effectiveness of that strategy and others by surveying the oncologists about the degree to which each strategy affected the discussion about clinical trials.

## CONCLUSIONS

Accrual to clinical trials is a multidimensional problem that requires multidimensional interventions to effect improvement. Our study demonstrates that an intensive effort to reduce various well-recognized barriers to clinical trial accrual by engaging the referring surgeon can potentially improve accrual and should be further evaluated in a larger randomized trial.

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## 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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