Barriers to Patient Enrolment in Oncology Clinical Trials at a Canadian Regional Cancer Centre: A Mixed Methods Study

by

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Examining Committee:

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The above committee determined that the thesis is acceptable in form and content and that a satisfactory knowledge of the field covered by the thesis was demonstrated by the candidate during an oral examination. A signed copy of the Certificate of Approval is available from the School of Graduate and Postdoctoral Studies.

ABSTRACT

Background:

Randomized controlled trials are required to assess the safety and efficacy of new cancer medications in humans for marketing approval. Thereby, efforts to inform strategies to improve low enrolment rates are imperative to prevent slower rates and increased cost of development. The aim of this study was to identify and examine the impact of barriers to clinical trials enrolment at the R. S. McLaughlin Durham Regional Cancer Centre (DRCC).

Methods and Results:

A mixed-methods approach was used for this study and the following methods were used:

(1) Retrospective exploratory analysis,

(2) Patient surveys,

(3) Key informants semi-structured interviews.

Results were analyzed using Ford's (2008) framework to categorize barriers as they pertain to awareness, opportunity, and decision to take part in oncology clinical trials. The results of this study support previous literature and was the first study to use both qualitative and quantitative to explore enrolment at the DRCC.

Keywords: barriers; enrolment; accrual; oncology; Canadian

AUTHOR'S DECLARATION

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Angelina Singson

STATEMENT OF CONTRIBUTIONS

The work described in this thesis was performed at the Durham Regional Cancer Centre (DRCC) at Lakeridge Health Hospital in Oshawa, Ontario. I was responsible for the design of the research project, recruitment, data collection and analysis. In addition, part of the work described in this thesis will be submitted for publication.

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LIST OF ABBREVIATIONS AND SYMBOLS

CTMS	Clinical trial management system
PI	Principal Investigator
RCT	Randomized Controlled Trial
TCPS	Tri-Council Policy Statement

1 INTRODUCTION

1.1 BACKGROUND

1.1.1 What are clinical trials?

Randomized controlled trials (alternatively referred to in this study as “clinical trials”), their participants, and their advocates have made considerable contributions to advances in medical treatments (Goldberg et al., 2017; Jenkins et al., 2013). Randomized controlled trials are types of clinical research designed to evaluate medical, surgical, or behavioral treatments in human participants (National Institute on Aging, 2020). Since the first modern randomized controlled trial of streptomycin for pulmonary tuberculosis in 1948, the clinical trials landscape has continuously evolved. Nowadays, trials can be large and complex projects. They can often involve various treatment protocols, are multi-institutional, international and may require longer time commitments as trials can span across several years (Moorcraft et al., 2016).

Consequently, clinical trials face issues such as larger price tags and complex operational demands. Moreover, the challenge of recruiting participants endures even with several decades of research to overcome such issues (Eichler & Sweeney, 2018; Jenkins et al., 2013). Ideally, where recruitment targets are met and trials are completed, whether they produce positive or negative results, the findings make an invaluable contribution to scientific innovation.

1.1.2 What is the importance of clinical trials?

Well-designed clinical trials, whether they produce positive or negative results, play an important role in advancing medicine. Before new medical treatments or vaccines are approved for clinical use and marketing, they must show success under four phases of clinical trials: phase

I trials to determine the dose at which drugs are safe for the human body, phase II trials to determine the efficacy of a new treatment, phase III trials to compare standards of care with new investigational medical products, and phase IV studies to determine long term safety and efficacy after receiving marketing approval (Goldberg et al., 2017; Unger et al., 2016b).

The success and completion of clinical trials depend on factors such as the level of efficacy of a novel treatment and sufficient enrolment within targeted timelines. Although many trials may fail to show efficacy, generally, whether they produce positive or negative results, trials that are well planned and completed can potentially provide opportunities for improvement in oncology (Fogel, 2018). Among cancer trials, along with small to moderate improvement in survival, Unger et al. (2016b) found a relative reduction in cancer mortality by 5% due to innovations in treatments and in 2% of cases, the death rate was cut by more than 50%.

1.1.3 What are characteristics of contemporary clinical trials?

Whereas clinical trials were historically isolated projects conducted in specific regions around the world, modern trials are now often global, involving multiple institutions, treatment arms, and novel endpoints. Many modern-day clinical trials are sponsored by the pharmaceutical and biomedical industries to support licensing approval to use, offer and market new treatments worldwide. Accordingly, there has been an increased need to conduct global trials in recent years. In their study of 127 pivotal trials (trials that seek to demonstrate the safety and efficacy of a treatment), Qiao and colleagues (2019) found that among the 91,415 patients from 13,264 sites, 60.3% of the patients and 57.3% of the institutions responsible for recruiting patients were outside of North America. However, studies have found that despite the globalization of clinical trials, North America still maintains a large share of patients and sites among world regions (George et al., 2013; Qiao et al., 2019).

In addition to globalization, trials are becoming increasingly complex. Over the recent decades, study designs have required more procedures and volunteer visits from their participants. An analysis based on 9,737 clinical trial protocols approved by research ethics boards (REBs) between 2001 and 2015, revealed that protocol design elements have grown rapidly within the decade (Getz & Campo, 2017). Phase 3 trials showed the highest relative growth in total procedures carried out, increasing by 70% between 2001 and 2015. Meanwhile, the mean number of planned study volunteer visits per protocol increased by 25% (Getz & Campo, 2017). Furthermore, multi-arm trials with 3 or more groups to compare multiple treatments concurrently are also relatively common (Juszczak et al., 2019).

At large, technology has played a significant role in shaping what trials are now today. For example, mobile technologies can now generate novel trial endpoints and data can be continuously collected through wearable technologies. Such devices can provide insights including an individual's mental well-being and indicate the stability of an individual's daily routine (Forum on Neuroscience and Nervous System Disorders, 2016; Moore et al., 2018).

Recent technological advances create opportunities to use real-world data (RWD) as a method of collecting data (Khozin et al., 2017). Khozin and colleagues (2017) define real-world data (RWD) as "a general term that can be described as data generated or obtained outside of conventional clinical trials" (Khozin et al., 2017, para. 1). This information can be captured from electronic health records and patient registries and can be used in either place of or in combination with results from clinical trials. With innovations in technology to facilitate it, the growth and evolution of clinical trials are only likely to continue. However, given the transient nature of the clinical trials landscape, there is a need to regularly re-evaluate the impact of such

changes to the conduct of clinical trials and most importantly, there is a need to examine how these changes impact the patients who participate in them.

1.1.4 What are major challenges of contemporary clinical trials?

1.1.4.1 Increased cost and operational complexity.

The major challenges of global and multi-institutional clinical trial designs include increasing cost and operational complexities. One study found that on average, clinical trials may cost anywhere between $12.2 million to $33.1 million (Moore et al., 2018). Other recent estimates have ranged from a median of $648 million for novel oncology treatments to $2.8 billion for pharmaceutical company development costs for general medications. Increased costs were attributed to factors such as larger sample size requirements (Moore et al., 2018).

Moreover, patient recruitment can be a costly endeavor. Advertisements alone could cost upwards of thousands of dollars for clinical trial sponsors. For their study on assessing the efficacy of nicotine gum and counseling to aid low-income African American smokers to quit, Okuyemi and colleagues (2007) reported spending $156 per participant enrolled through direct marketing, and roughly $5,000 for each participant enrolled through gas-pump advertising

After a patient is recruited and enrolled in a study, costs to cover additional study procedures, treatment and reimbursements are also taken into consideration. A study of bacterial pneumonia reported that the cost of a 200-recruitment site, and 1,000 patient Phase 3 study was roughly $89,600 per patient. Despite the costs for enrolled patients, however, the researchers noted that screening failures were the largest contributor to this hefty price tag (Fogel, 2018).

Eichler and Sweeney (2018) cited that increases in the financial burden of clinical trials are also in part due to the logistic demands of globalizing and expanding clinical trials.

Globalizing and increasing the complexity of clinical trials elicit a growing "superstructure" which includes complex monitoring, reporting requirements, and governance. Although there has been much improvement in terms of harmonizing the conduct of clinical trials between nations, disagreements between regulations and ethical considerations governing the approval and conduct of clinical trials continue to increase the operational complexity of global clinical trials (Eichler & Sweeney, 2018).

With the large financial demands of clinical trials, many studies are often underfunded and may not yield clinically beneficial outcomes. Thus, improving clinical trials and preventing them from failing would not just be important to funding agencies and institutions involved in the conduct of clinical trials, but also for the clinical trial participants who have already invested their time and resources to participate in these studies.

1.1.4.2 Patient enrolment.

Generally, the aim of clinical trials is to advance current knowledge in a particular therapeutic area and patients are hopeful that their participation in a trial will lead to such a contribution. Due to issues such as under-enrolment, however, clinical trials may fail to produce clinical significance and thereby, fail to meet requirements for marketing approval. Desai (2020) reports that more than 80% of trials worldwide do not meet enrolment targets in time.

Clinical trials often have recruitment targets to meet to appropriately evaluate the safety and efficacy of the study intervention. If these targets are left unmet, researchers may make efforts to evaluate new investigational products based on limited generalizability and reduced statistical power at the expense of reducing the trial's validity (Van Epps et al., 2016).

In other cases, trials are consequently terminated early (Mahmud et al., 2018; Moorcraft et al., 2016; Williams et al., 2015). A cross-sectional study of prematurely terminated clinical trials published in 2015, determined that 905 of 7,646 trials were closed for scientific data-related reasons. Of those, 39% (n=350) were closed early because they had not accrued enough patients (Williams et al., 2015). Similarly, a study on registered urology trials published in 2020 found that the leading reason for failure is poor accrual, which accounts for 41% of failed trials (Bandari et al., 2020).

1.1.5 What are characteristics of contemporary clinical trials in oncology?

In oncology, medical treatments can include surgery, radiation therapy, chemotherapy, immunotherapy, hormone therapy or a combination of several types of therapies. Through clinical trials, we develop novel and improved oncology treatments; thus, we can expect higher rates of patients cured of locally advanced cancers and a portion of patients cured of metastatic cancers (Goldberg et al., 2017).

With growing knowledge in cancer biology and biomarkers, the approach toward treating cancer moves increasingly away from a “one-size-fits-all” approach to commonly targeting a person’s germline and somatic (tumour) molecular profiles (Janiaud et al., 2019). Thereby, in response to such developments, innovative trial designs have been introduced in recent years. Novel clinical trial designs include umbrella trials, basket trials, adaptive trials, and enrichment trials (Jaffee et al., 2017; Janiaud et al., 2019;).

These innovative trials come with both advantages and disadvantages. Designs such as umbrella and basket trials are molecularly driven and are more flexible than traditional clinical trial designs and this allows expansion of access to cancer patients in new therapeutic areas

rather than the need to initiate new trials (Jaffee et al., 2017). A caveat of these trials, however, is the increased financial costs and increased time required to conduct such studies (Janiaud et al., 2018). Other trials may be more statistically complex or may be more likely to produce increased false positive results. As new clinical trial designs emerge, there is a need to re-evaluate how the advantages and disadvantages of these designs affect patients and their involvement in these studies.

1.1.6 What is the importance of successful clinical trials in oncology?

Higher clinical trial enrolment rates in oncology trials have shown a positive association with reduced cancer patient mortality and survival of cancer patients because of the advancements in medicine developed using clinical trials. This relationship can be observed between higher accrual rates in children's (ages under 15) clinical trials and the decrease in children's mortality rates due to cancer since the 1970s (Unger et al., 2016b).

In their study, Unger et al. (2016a) analyzed the scientific impact of published articles that had enrolled a total of n = 46,424 patients (Unger et al., 2016a). They found that nearly half of the clinical trials that had produced positive results met their enrolment targets and among negative trials, the studies that were terminated early due to poor accrual had the least scientific impact. Therefore, regardless of whether studies produce positive or negative results, if they are well-designed and completed, they can provide important contributions to scientific advancement**.**

1.1.7 What are the barriers to patient enrolment in oncology clinical trials?

Without doubt, patient participation is essential to the success of clinical trials (Ford et al., 2008; Goldberg et al., 2017; Jenkins et al., 2013, Unger et al., 2016b). In this study, patient

enrolment (alternatively “accrual” or “participation”) will be defined as “a participant, or their legally authorized representative’s agreement to participate in a clinical study following completion of the informed consent process.” (National Institute of Health, 2017).

Based on current literature, there are various multi-level and interconnected factors that can influence patient enrolment in an oncology clinical trial (Sedrak et al., 2019; Willison et al., 2019). As proposed by Ford and colleagues (2008), factors that influence clinical trial enrolment include barriers to awareness, opportunity, and decision to participate in clinical studies. These barriers can be patient-related (i.e., fear of side effects), physician-related (i.e., patient mistrust in physician), structurally related (i.e., trial availability or type of institution), and related to the protocol/study design (i.e., stringent eligibility criteria or complexity of a study protocol) (Ford et al., 2008; Sedrak et. al., 2019; Unger et al., 2019b). Furthermore, sociodemographic characteristics such as a person’s age, gender, culture, and location can also play an important role and impact the effectiveness of strategies aimed to mitigate barriers to awareness, opportunity, and acceptance of clinical trials (Napoles et al., 2017). For Canadian cancer patients, a study by Jones and colleagues (2007) concluded that although they reported willingness to take part in trials, Canadian patients had generally poor understanding of what trials were and how trials are conducted.

1.1.8 Ford’s et al. (2008) conceptual framework.

Ford’et al’s conceptual framework (2008) was developed through a systematic review on underrepresented populations in oncology clinical trials, and it models barriers that impact patient enrolment. Ford’s et al. framework places emphasis on the barriers that impact a patient’s decision to take part in a trial as opposed to more recently developed frameworks that focus more broadly on issues that impact patient enrolment, such as protocol design (Unger et al., 2019b).

Although more recently developed frameworks help illustrate a broader view of issues involved in reduced enrolment rates, study-design related barriers may not easily be overcome at the site-level. Clinical trial "Sites" may be healthcare centres, hospitals or clinics that work with "Sponsors" (individuals, institutions, or pharmaceutical/biotechnological companies who initiate, manage and/or fund clinical trials) to recruit and conduct clinical trials. For example, although stringent eligibility criteria are one of the most widely cited barriers to patient accrual, for many multi-centred, industry-sponsored studies, little to nothing can be done to amend study design issues (Unger et al., 2019b).

Ford and colleagues (2008) group the barriers to clinical trials enrolment into three major categories, awareness barriers (i.e., knowledge of clinical trials), opportunity barriers (i.e., eligibility criteria), and acceptance barriers (i.e., trust in a physician recommending a trial). Based on a qualitative synthesis of previous literature, this model hypothesizes that a patient's decision to enroll in a clinical trial is affected by both their awareness of clinical trials and whether they are given the opportunity to take part in trials. Strategies can be aimed to mitigate barriers; however, the researchers suggest that sociodemographic factors (i.e., age, gender) can influence how well certain strategies might work (Ford et al., 2008).

1.1.9 The importance of clinical trials in a Canadian regional cancer center.

Although Canadians generally have a positive attitude towards clinical trials, the overall participation rate of cancer patients in clinical trials has remained substantially low (Willison et al., 2019). The Canadian Partnership against Cancer (2018) estimates that around 1% to 5% of adult cancer patients take part in clinical trials in Canada. Researchers argue, however, that this estimate fails to illustrate the various barriers that may prevent patients from taking part in clinical trials (Unger et al., 2021). While a recently published systematic review and meta-

analysis shows that over half (55%) of American patients who are offered clinical trials do choose to participate, currently, there remains limited knowledge on clinical trials participation in Canada (Unger et al., 2021).

Given the several factors that influence clinical trial enrolment and the differences between Canada and the US's healthcare structure and geography, it is important to understand barriers in a Canadian context. Continuing to build upon our current understanding of barriers to patient participation within a Canadian setting could help inform present or future strategies and facilitate medical research within the country.

1.1.9.1 R. S. McLaughlin Durham Regional Cancer Centre (DRCC) as a representative Canadian Cancer centre.

The DRCC, located at Lakeridge Health Hospital in Oshawa, Ontario, Canada, provides cancer care to over 100,000 families in Durham Region. The Central East Regional Cancer Program at the DRCC is one of fourteen regional cancer programs that work with community hospitals to provide cancer care in their respective communities.

The Central East Regional Cancer Program is a network of hospitals and cancer services that serve around 1.6 million people living in Northumberland, Kawartha Lakes, Durham, and Scarborough (Lakeridge Health, n.d.). The DRCC treats various types of cancers in adults including breast cancer, gastrointestinal cancer, genitourinary cancer, gynaecological cancer, hematology, melanoma, skin, and thoracic cancer (Lakeridge Health, n.d.).

As of 2019, DRCC had been involved in over 230 clinical trials for adult oncology patients since its inauguration in 2007 (Lakeridge Health, 2020). Currently, the DRCC's oncology research program participates in over 60 active clinical trials for lung, hematology,

melanoma, skin, breast, genitourinary and gastrointestinal clinical trials (Lakeridge Health, n.d.). To date, there have been no published statistics on DRCC clinical trial enrolment.

Despite the DRCC's involvement in clinical trials, it is important to emphasize that Lakeridge Health is considered a "community hospital." Although it may be challenging to define a "community hospital", they can be generally understood as centres which primarily focus on delivering patient care to communities (Gehrke et al., 2019). Community hospitals account for around 84% of hospitals in Ontario (Gehrke et al., 2019). Whereas academic centres may be traditional settings for health research, physicians and health staff at community hospitals may not usually be involved in research (Gehrke et al., 2019). Compared to academic centres, community hospitals may face unique challenges when it comes to conducting and recruiting for trials, despite accounting for 65% of hospital beds in Canada (Gehrke et al., 2019). Addressing these issues and improving research at community hospitals may provide an opportunity to include patients who may otherwise have been excluded.

This study focuses on identifying barriers that impact patient enrolment to oncology clinical trials at the DRCC to inform strategies that may enhance research at this centre and other Canadian centres alike.

1.2 RESEARCH QUESTIONS

1. What are the characteristics of DRCC patients who have refused participation in an oncology clinical trial and the characteristics of the oncology trial in which they have refused to participate?
2. What are the perceived barriers to awareness, opportunity, and decision-making that impact patient enrolment in oncology clinical trials at the DRCC?

1.3 RESEARCH AIM AND OBJECTIVES

The aim of this study is to inform enrolment strategies at a Canadian Regional Cancer Center, the R. S. McLaughlin Durham Regional Cancer Centre (DRCC), through the identification and exploration of barriers to oncology clinical trial enrolment.

The study objectives are as follows:

1. To characterize the most and least accruing protocols by sponsor type, therapeutic area, stage, and type of therapy.
2. To compare the sociodemographic characteristics of patients who join and do not join oncology RCTs at the DRCC
3. To identify current perceived barriers to oncology RCT enrolment at the DRCC.
4. To analyze current perceived barriers as they relate to clinical trial awareness, opportunity to participate and acceptance of enrolment at the DRCC.
5. To provide recommendations to the Lakeridge Health Research Program on strategies to increase accrual rates to oncology clinical trials.

1.4 ORGANIZATION OF THESIS

This thesis is written in a traditional format and contains six chapters: Chapter 1 introduces the study, provides relevant background information on the thesis topic, its significance, aim, and research questions. Chapter 2 includes a review of the current literature on barriers to enrolment in oncology clinical trials. Chapter 3 presents the methodology used in this study. Chapter 4 discusses the study's results and Chapter 5 includes a discussion of the study results. Lastly, Chapter 6 summarizes the study, its objectives, strengths/limitations, and opportunities/directions for future research.

2 LITERATURE REVIEW

2.1 INTRODUCTION

The objective of this chapter is to critically review and examine current literature on the barriers to patient participation in oncology clinical trials and to identify current gaps and of research focus. The literature review findings are discussed as they relate to patient awareness, opportunity, decision to take part in oncology clinical trials and sociodemographic factors as outlined in Ford's and colleagues' (2008) conceptual framework in the previous chapter.

2.2 SEARCH PROCESS

2.2.1 Search Strategy and Inclusion Criteria.

A search of the electronic databases, Google Scholar, and PubMed, was conducted for articles published between January 1st, 2000 and January 1st, 2020.

The keywords used to search for articles in this study were divided into three main themes and searched for in study titles and abstracts: 1. Patient Barriers, 2. Clinical Trials, and 3. Cancer. Keywords related to patient barriers used for the search were: "Barrier*" OR "Recruit*" OR "Participant*" OR "Accrual" OR "enroll*" OR "Attitude*". Keywords related to clinical trials were: "Trial*" OR "Clinical Trials" OR "Drug Trials". Keywords used related to cancer were "Cancer*" OR "Oncolog*". Each keyword group was added using "AND".

Studies were included if they met all of the following criteria:

- Published from January 1st, 2000 to January 1st, 2020
- Included data on adult cancer patient (age≥18) participation in oncology clinical trials
- Written in English
- Used either quantitative, qualitative or a mixed-methods approach

- Primary and secondary literature
- Peer-reviewed

Studies were excluded if they met any of the following criteria:

- Not made available online
- Not conducted on adults (age <18)
- Editorials

2.2.2 Justification for Inclusion/Exclusion Criteria.

Because children and adolescents may face barriers to clinical trials that differ from adult patients (Burke et al., 2007), studies were included only if they contributed to the identification and understanding of current barriers to adult cancer patient participation in oncology clinical trials. Furthermore, although studies on clinical trials and patient enrolment have been published before the year 2000, this paper will only include articles published within the two latest decades so that recent developments in this area can be of focus. In addition, only studies written in English are included. Of the current literature, 15 studies will be discussed in this chapter (See Appendix A for literature review matrix).

2.3 LITERATURE REVIEW FINDINGS

The findings of the 15 articles will be discussed in this section and will be categorized based on Ford and colleagues' (2008) framework. The categories include barriers related to: awareness, opportunity, decision to take part in clinical trials and sociodemographic factors.

2.3.1 Awareness barriers.

Awareness is defined by Ford and colleagues (2008) as the knowledge and education that patients have on clinical trials. Ford and fellow researchers conclude that there is statistically

significant evidence that lack of knowledge and education is associated with reduced trial enrolment.

Of the published studies included in this review, four out of 15 identify awareness as a barrier to clinical trials participation (Ford et al., 2008; Jones at al., 2007; Moorcraft et al., 2016; Staniszewska et al., 2018). All four studies agree that awareness and lack of knowledge on clinical trials impact willingness to participate in trials. Most participants have heard of clinical trials; however, there are notable differences in their information sources (Jones et al., 2007; Moorcraft et al., 2016). Depending on their source of information, patients may develop misconceptions or may lack understanding of clinical trials. A study on Polish cancer patients found that the most frequent source of clinical trial knowledge was mass media, while a study on Canadian cancer patients found that almost half of patients learn about clinical trials through their family physician or specialist (Jones et al., 2007; Staniszeska et al., 2018).

A limitation to the studies that assess awareness of oncology clinical trials is the use of cross-sectional designs limit cause-and-effect conclusions. There is also a lack of qualitative data to support quantitative findings (Jones et al., 2007). Thereby, the significance of varying levels of clinical trial knowledge on a patient's decision to participate in a clinical trial has yet to be both qualitatively and quantitatively evaluated further.

2.3.2 Opportunity barriers.

Ford and colleagues' (2008) framework describes *opportunity* barriers as a lack of invitation to join a trial or lack of trial access. These barriers include aspects of the study design (e.g. exclusion and inclusion criteria), physician-related barriers (e.g. communication of trial-related information) or patient-related (e.g. costs to the patient).

Seven of the 15 studies included in this review identified opportunity barriers. Most of the studies identify protocol/study design-related barriers - mainly the stringency of inclusion/exclusion criteria - as a major barrier to trial enrolment (Ford et al., 2008; Jones et al., 2007, Moorcraft et al., 2016; Sedrak et al., 2020; Somkin et al., 2013; Unger et al., 2019a; Unger et al., 2019b). Moorcraft and colleagues' (2016) survey results show that although a high proportion of their patient sample consented to a trial, 36% of the patients did not pass screening for pre-screening trials.

These results are consistent with the findings of a recent study by Unger and colleagues published in the Journal of the National Cancer Institute in March 2019, which provides one of the first meta-analysis of barriers to clinical trial participation. Unger's et al. findings suggest that opportunity barriers such as ineligibility for the study accounted for 77.1% of the cancer patients included in their analysis (Unger et al., 2019b).

Physician-related barriers were identified in the literature such as lack of resources or time to go over trials with patients (Ford et al., 2008; Jones et al., 2007; Sedrak et al., 2020; Somkin et al., 2013). Moreover, some physicians report unawareness of currently enrolling trials and relevant trials; thereby, patients are not informed of available studies within an institution (Jones et al., 2007; Sedrak et al., 2020).

In their systematic review, Unger and colleagues (2019b) find that trial unavailability accounts for over half of non-enrolled patients. In addition to patients not being made aware of currently enrolling trials, study availability can be affected by factors such as distance from a treatment centre that offers a relevant clinical trial (Ford et al., 2008).

In terms of methodology, aspects of the studies included in this category of barriers would suggest that generalizability could be limited. Patients included in these studies may not

be representative of all cancer types (Unger et al., 2019b). This could lead to issues such as an overestimation of opportunity barriers' impact on trial enrolment. In addition, studies on opportunity barriers heavily focused on protocol design characteristics; however, in many multi-institutional studies, recruitment sites may have little to no control over protocol characteristics (Unger et al., 2019b).

2.3.3 Acceptance/refusal barriers.

Acceptance or refusal barriers are factors associated with a patient's decision not to enroll into a clinical trial. Ford and colleagues (2008) identified these barriers as trust in patients' physicians, fear of adverse effects of drugs, lack of transportation, stress, or lack of time

Of the articles included in this literature review, 13 out of 15 articles discuss acceptance or refusal barriers. The most frequently identified barriers to acceptance of clinical trials are patient-related: fear of side effects/adverse events, lack of resources (i.e., time or transportation), and additional costs associated with trial participation (Sedrak et al., 2020; Zdenkowski et al., 2019).

One of the surveys conducted in the US by Echeverri and colleagues (2018), add that patients were less willing to participate in trials if they involved new interventions or tissue donations. This is supported by the retrospective analysis by Bennette and colleagues (2016), which found that accrual rates were lower in trials that involved tissue or biopsy for screening or multiple interventions.

Notably, Nielsen and Berthelsen's (2019) qualitative meta-synthesis finds that the perception of relatives has an impact on patient decisions to participate in trials. This finding is consistent with Moorcraft and colleagues' (2016) survey findings, where they find that 88% of their sample (219 patients) discussed the trial with one or more people, usually a family member.

However, limited studies explore the importance of family, or friends on the patient's decision to take part in trials further (Moorcraft et al., 2016; Nielsen & Berthelsen, 2019). Given that many patients have reported discussing trials with other individuals such as their family and relatives, future research and strategies may aim to place focus on not only the barriers to patients, but these individuals as well. Another limitation is that most qualitative studies were based on American populations. Seven out of the 9 articles included in Nielsen and Berthelsen's (2019) meta-synthesis were conducted on American cancer patients.

Additionally, Unger and colleagues' (2019b) systematic review on US publications found that research-oriented cancer centres tend to experience higher enrolment rates. This is supported by Echeverri's et al (2018) survey results concluding that patient willingness is affected by type of institution and trust in institution.

2.3.4 Sociodemographic factors.

Ford's et al framework (2008) proposes that *sociodemographic* factors can impact the level of clinical trial awareness, opportunity, and the final decision-making process to enter a clinical trial. Sociodemographic barriers are identified as racial minority status, older age, lower socioeconomic status, and lack of or insufficient health insurance coverage and were associated with reduced patient participation in clinical trials (Ford et al., 2008).

Six of 15 of the studies included in this review examine the influence of sociodemographic factors on enrolment in clinical trials. Findings on the association between sociodemographic factors such as age and education level differ between studies. One survey conducted on Australian cancer patients concluded that education level does not have a significant association with willingness to take part in clinical trials; however, patients who lived

in rural areas and were of lower socioeconomic status were more likely to participate (Zdenkowski et al., 2019).

Moreover, although Staniszewska and colleagues' (2018) survey conclude that age is also not associated with willingness to participate in clinical trials. Greenwade and colleagues' (2017) retrospective analysis shows that older patients were less likely to be enrolled in a trial. This is supported by Sedrak and colleagues (2020), which explores the perceptions of oncologists on barriers to clinical trial accrual of older adults with cancer. Qualitative data were analyzed from the content of semi-structured interviews conducted with 44 medical oncologists at the City of Hope from March 2018 to June 2018. Stringent eligibility criteria and provider concerns for treatment toxicity were the most cited barriers for older adults (Sedrak et al., 2020).

Additionally, in agreement with Ford's et al (2008) findings, there is evidence to support that ethnicity may also be associated with willingness to take part in clinical trials (Byrne et al., 2014). Byrne and colleagues conducted a telephone survey using the Florida cancer registry for White, Black and Hispanic patients diagnosed with breast, lung, colorectal or prostate cancer. The researchers found that although White, Black, and Hispanic patients were equally willing to participate in a clinical trial, non-English speaking Hispanics were less likely to participate.

The cross-sectional methodologies used in these studies present limitations as causal relationships between certain sociodemographic characteristics and trial enrolment cannot be adequately established.

For example, Greenwade and colleagues (2017) do not provide an explanation as to why older patients did not enroll: eligibility, physician bias or patient choice. In addition, survey findings could not confirm a cause-and-effect relationship between the reduced likelihood of

participation of non-English speaking Hispanic cancer patients and factors such as language barriers (Byrne et al., 2014).

2.4 CONCLUSION

In conclusion, most of the literature included in this review do agree with Ford's and colleagues' (2008) framework and identifies barriers to awareness, opportunity and acceptance that impact adult cancer patient enrolment to oncology clinical trials. Studies identify significant associations between a lack of clinical trial knowledge and awareness and trial enrolment (Ford et al., 2008; Jones at al., 2007; Moorcraft et al., 2016; Staniszewska et al., 2018). Over half of the studies identify opportunity barriers and agree that study-related issues, such as inclusion/exclusion criteria, contribute to low enrolment rates (Ford et al., 2008; Moorcraft et al., 2016; Sedrak et al., 2020; Unger et al., 2019a).

Moreover, studies identify patient-related barriers, such as fear of side-effects, which reduce patient willingness to enroll in trials (Sedrak et al., 2020; Zdenkowski et al., 2019). Additionally, sociodemographic factors have been found to impact enrolment; however, study findings are often inconsistent as some studies do not find associations between certain sociodemographic factors (such as age or education level) and trial enrolment (Staniszewska et al., 2018; Zdenkowski et al, 2019;)

Most currently published studies primarily use survey methods to explore barriers (Jenkins et al. 2013). There is a need to strengthen and validate findings using mixed methods approaches. The incorporation of both quantitative and qualitative methodologies allows for cross-validation of findings through triangulation (Creswell & Plano Clark, 2010). Future studies will also need to explore certain aspects that are only briefly discussed in current research such

as the significance of clinical trial awareness to enrolment and the role that relatives and friends have on a patient's decision to participate in trials (Jones et al., 2007; Moorcraft et al., 2016).

Lastly, there is a lack of published literature on patient barriers to oncology clinical trials enrolment in non-primarily research oriented Canadian settings (Jones et al., 2007). There is a need to conduct studies in a Canadian context to inform the development of relevant and effective strategies for improving clinical trial enrolment in Canada (Willison et al., 2019).

3 METHODS

This chapter focuses on describing the study design, ethical considerations, and research approvals, as well as establishing trustworthiness.

3.1 RESEARCH DESIGN

To meet the outlined objectives, this study was conducted in three parts:

3.1.1 Part 1 - Retrospective exploratory analysis.

A cross-sectional exploratory retrospective analysis was conducted on the DRCC's aggregate study information captured in the DRCC's clinical trials management system (which will be referred to in this study as "CTMS"). For this quantitative component of the study, pre-screening data from studies conducted between December 1st, 2015 and December 1st, 2019 was collected (n=666). Using this method, the goal was to determine whether the DRCC has had historically lower or higher proportions of acceptance when compared to refusals and explore these proportions as they relate to protocol-related/patient-related factors.

Information on protocols conducted at the DRCC, such as the short title; project sponsor; disease site; line of therapy; study population; site open to recruitment date; site closed to recruitment date; and target number of participants were collected. Protocol titles were replaced with unique codes specific to this study and were not shared outside of Lakeridge Health. Moreover, patients' personal health information was not available on this system.

3.1.1.1 Description of Data.

The structural and protocol-barrier related explanatory variables of interest for this study are sponsor type, therapeutic area, stage, and type of therapy. The patient-barrier related

variables of interest include patient gender, off-study reason (clinical or patient) and reason for non-enrolment. The outcome variable is enrolment versus non-enrolment.

Aggregate study information available on CTMS was collected and analyzed. The DRCC uses CTMS, an online platform, to track research study metrics including screening and enrolment activities. Data from studies that opened to accrual between December 1st, 2015, and December 1st, 2019 were collected. Of the studies available on CTMS, 52 opened within this period. However, 7 studies did not pre-screen patients and were excluded from the analysis. The structural and protocol-barrier related explanatory variables of interest for this study are sponsor type, therapeutic area, type of study, and target stage. *Sponsor type* is coded as "Industry" or "Academic" sponsored studies. In terms of *therapeutic area*, studies are categorized into 7 major groups including "Gastrointestinal"; "Hematology"; "Breast"; "Lung"; "Skin / Melanoma"; "Genitourinary"; and "Other". *Type of study* describes what the study involves - for example, whether it is an "Observational Study", "Survey", "Adjuvant", "Neoadjuvant", "First Line", ">First Line" and "Other". ">First Line" meaning that the study is intended to explore an intervention for patients who have already received previous treatment. *Target Stage* is coded as "Advanced/Metastatic", "Early", and "Unspecified."

The patient-barrier related variables of interest include patient gender, off-study reason (clinical or patient) and reason for non-enrolment. *Gender* is coded as "Male", "Female", or "Not known". *Off-study decision* is defined as the off-study decision maker - coded as "Clinical", "Patient" or "Unknown". Lastly, *reason for off-study* is coded into 17 major groups. The outcome variable in this study will be enrolment - "Y" indicates that the patient was enrolled and "N" indicates not enrolled.

Protocol titles were replaced with unique code specific to this study and will not be shared outside of Lakeridge Health. Moreover, patient personal health information is not available on this system.

3.1.1.2 Statistical Methods.

This study involved a retrospective exploratory analysis using IBM Statistical Package for the Social Sciences (SPSS 27 for macOS). Frequencies were used to analyze categorical variables (See Table 1 and Table 2). Two-way tables were used to analyze enrolments versus non-enrolment groups (See Table 3). Chi-squared tests were used to detect differences among proportions of enrolments versus non-enrolments with respect to protocol and patient-related variables. Cramer's V was used to examine the correlation between variables. Lastly, bar charts were used to summarize and visualize data.

3.1.2 Part 2 - Patient survey.

This study included a pilot-tested and REB-approved patient survey to be conducted either at the DRCC, by email or online through Google Forms depending on the patient's preference. For the online survey option, the patient's decision to complete and return the survey was to be interpreted as an indication of their agreement to participate in the study. Information collected in this survey will be used to analyze distributions of sociodemographic characteristics, and knowledge of randomized controlled trials (RCTs) between adult DRCC patients who had indicated that they were willing to and/or have agreed to take part in clinical trials and those who had indicated that they were not. Data collected from the survey was also intended to quantitatively analyze the influence that the most frequently identified barriers reported in literature have on a patient's decision-making processes (Ford et al., 2008; Jones et al., 2007;

Jenkins et al., 2013; Unger et al., 2016a), Unfortunately, due to the COVID-19 pandemic and the limited timeframe, an insufficient sample size was recruited for the study; however, the findings were analyzed for this paper.

3.1.2.1 Sampling Methods.

A combination of both convenience and criterion sampling methods was used to recruit for the study. The target sample size and target population were 69 adult oncology patients in the DRCC waiting area based on the following inclusion/exclusion criteria.

3.1.2.2 Inclusion.

1. Adult patients at the DRCC (≥18) diagnosed with cancer

3.1.2.3 Exclusion.

1. Unable to speak, read, and write in English

In consideration of the recent 2019 novel coronavirus pandemic, both electronic and limited in-person methods were used. One method was to post an REB-approved digital poster advertisement on the Lakeridge Health website (See Appendix B). The website posting included contact information and a brief introduction of the study. In-person methods included the use of REB-approved study posters in clinic areas (See Appendix C). Additionally, oncologists and members of a patient's circle of care were permitted to identify and introduce the study during a pre-scheduled follow up visit or over a telephone follow-up. If a patient expressed interest in the study, the patient was either given the Principal Investigator's (PI) contact information or provided their contact information for the PI to reach out to them. Additional methods of informed consent delivery were implied consent through completion of online survey, through email or verbally over the phone.

3.1.2.4 Data Collection.

The survey used in this study was modified from Jenkin's' and colleagues' (2013) survey and incorporated elements of Jones and colleagues' (2007) survey interview. The survey consisted of 49 questions (Please see Appendix D). The first section asked about the patient specific information such as sociodemographic characteristics (i.e., age, sex, ethnicity, education, income, field of work, insurance provider, and transportation) and the patient's cancer information (i.e., cancer type and stage). The next section asked about the patient's knowledge and willingness to take part in cancer clinical trials. Lastly, patients were asked how much influence certain factors might have on their decision to take part in a clinical trial using Likert scales. The survey was intended to take approximately 15 to 20 minutes to complete.

3.1.2.5 Sample Size Calculation.

This sample size was calculated using an estimated population size of 100, 000 DRCC patients (Lakeridge Health, n.d.). An assumed population proportion of 50%, a confidence interval of 90% and a margin of error of 10% was inputted into the following formula:

$$\text{Sample size} = \frac{\frac{z^2 \times p\,(1-p)}{e^2}}{1 + \left(\frac{z^2 \times p\,(1-p)}{e^2 N}\right)}$$

A low survey sample size would be meaningful because the study does not only rely on survey results, but it also involves a retrospective exploratory analysis and a qualitative analysis.

3.1.3 Part 3 - Phenomenological approach.

The purpose of the phenomenological component of this study was to analyze the described experiences and feelings of oncology patients who have been approached to take part in a clinical trial at the DRCC and have declined as well as key informants (who are referred to in the study as "research staff", which includes oncologists and research nurses) who have approached patients who had declined.

3.1.3.1 Sampling Methods.

If a patient indicated in the survey that they have previously been approached to take part in a clinical trial and have declined, they were invited to take part in the semi-structured telephone interview (See REB-approved semi-structured interview guide in Appendix E). In addition, DRCC nurses were permitted to introduce the study to patients that have been referred to a clinical trial, approached and declined to participate in the trial. If the patient agreed to participate in the telephone interview, they were able to either volunteer to provide their contact information or be given the PI's contact information if they choose to reach out themselves. The ideal date and time were arranged either at the same visit or over the phone later.

In addition to patients, research staff who have had experience conducting the informed consent process with patients who have previously refused to participate in oncology clinical trials were also invited to semi-structured telephone interviews as "key informants". An email to research staff was sent to introduce the study and provide details on how they could participate.

An amendment to the initial protocol was made to include research staff in this study (See amendment approval in Appendix F and key informant consent form in Appendix G) and an REB-approved interview guide was used to facilitate the interviews (See Appendix H). Research

staff were asked to describe their experiences of enrolling patients in clinical trials and what barriers patients had previously reported to them (for example, “What concerns have patients expressed about taking part in a clinical trial?”).

3.1.3.2 Mixed-Methods Phenomenological Approach.

The rationale for including both quantitative and qualitative components to the study was to “mirror the complexity of the phenomenon being studied, and also to allow for confirmation and cross-validation” (Creswell & Plano Clark, 2010).

The exploratory retrospective analysis was conducted in this study to explore factors that may impact enrolment rates which are not associated with an individual’s conscious decision to accept or refuse trial enrolment. For example, if clinical trial enrolment rates are low, but the appropriate clinical trials were unavailable for patients at the site, the non-enrolment is not influenced by the patient’s conscious decision. Rather, the non-enrolment is due to the absence of an opportunity for the patient to take part in an appropriate trial. To explore the issue of clinical trial enrolment, both possibilities need to be considered.

The goal of Husserl’s descriptive phenomenology is to understand all objectivity, while also acknowledging the importance of human subjectivity (Gadamer, 2004). This appreciation of both subject and object emphasizes the potential for both inductive phenomenological frameworks and more deductive forms of inquiry to work complementary to one another (Mayoh & Onwuzegbuzie, 2015). Despite philosophical differences between quantitative and qualitative research, the adoption of *mixed methods phenomenology* can be justified by the potential for the scientific nature of the phenomenological method to work in correspondence with deductive approaches (Mayoh & Onwuzegbuzie, 2015).

In some ways, this study can be considered a *multimethods* study, which has been previously defined as a ‘‘combination of two or more methods, particularly in the health sciences’’ (Plano Clark et al., 2016, p. 59–60). However, my intent was to use a *mixed methods* research approach which Plano Clark and colleagues (2016) define as ‘‘a process of research when researchers integrate quantitative methods of data collection and analysis and qualitative methods of data collection and analysis to understand a research problem’’ (p. 59).

3.2 ETHICAL CONSIDERATIONS AND RESEARCH APPROVAL

This study was conducted as per the Tri-Council Policy Statement 2 (2018), ICH GCP guidelines, and as per applicable institutional policies.

3.2.1 Minimal Risk.

This research did not involve therapeutic intervention and involved no more than minimal risk to the safety of participants. However, if a participant were to express that they were uncomfortable at any time during the survey or interview, the participant was told that they could skip to the next question or be free to withdraw without any consequence to their care or employment for the research staff.

To minimize risk during the COVID pandemic or similar conditions, additional face-to-face patient interaction was limited. The survey was made available online or sent through email. A verbal consent option was also made available for the patient interviews.

3.2.2 Informed Consent Process.

The retrospective analysis portion of this study used information available on CTMS. As this system does not include personally identifiable information, individual informed consent was not required.

For the survey and interview, informed consent for each participant was obtained and documented using an REB approved informed consent form in accordance with TCPS 2 (2018) (See Appendix I for TCPS certification, Appendix J for written consent form and Appendix K for the verbal consent form for semi-structured interviews).

No person was to be subjected to coercion or undue pressure in determining whether to participate. It was made clear in the written consent form that the patient's care or research staff's employment at Lakeridge Health will not be affected by his or her decision to accept or refuse study participation. Patients were given time to read over the consent form and understand their rights. Research only began after the participants had provided informed consent.

3.2.2.1 Privacy and Confidentiality.

Every measure was taken to ensure that a participant's confidentiality would be maintained. After data collection, participants were de-identified and identifiable information was replaced with unique participant numbers (for surveys) and pseudonyms (for interviews). Per the protocol, audio-recordings were destroyed after each interview once transcribed verbatim. Study documents such as signed informed consent documents and patient lists containing patient information were to be maintained in a secure and locked place on-site at the DRCC during the study and up to 7 years after study closure or in accordance with institutional requirements.

3.2.2.2 Research Approval.

To conduct this research, the PI received permission from administrators at the DRCC (Clinical Trials Manager, and Clinical Team Director), Chief of Clinical Trials, the Lakeridge Health Research Ethics Board (LH REB), and permission for the deferral of research ethics review and approval from Ontario Tech University Research Ethics Board to LH REB (See initial LH REB approval in Appendix L, administrative approval in Appendix M, and OT REB deferral in Appendix N). Prior to recruiting and consenting healthcare professionals, an amendment to the protocol was submitted and approved by the REB as well. Lastly, per ethics board requirements, an annual renewal submission was made one year after initial approval (See Appendix O).

3.3 Establishing trustworthiness

Using Lincoln and Guba's evaluative criteria (1985), several techniques were used in this study to establish trustworthiness. To establish credibility, dependability, and confirmability, multiple methods of data collection were used in this study. By incorporating both qualitative and quantitative methods, a more comprehensive understanding of study enrolment at the DRCC may be established to achieve these three criteria. In addition, one transcript was reviewed and analyzed by a Supervisory committee member. Thick descriptions are used to achieve transferability.

3.3.1 Researcher positionality.

As a Durham Regional Cancer Centre (DRCC) clinical research staff member, I believe that there is importance in facilitating patient enrolment and facilitating the overall success of clinical trials at a site level. I understand the disappointment of early clinical trial termination

due to poor enrolment rates, not only for the research team who has invested time and effort to start up and conduct closely regulated oncology clinical trials at the site, but for patients who look forward to taking part in the development of new and highly innovative cancer treatments.

Although I do not directly approach patients or enrol patients in our oncology clinical trials, I work closely with research nurses who have. Throughout my three years of working with the team, I have heard of various reasons why a patient might accept or refuse to participate in clinical trials. These factors might exist within or beyond a patient's control. I believe that I fall somewhere between realist and idealist. I believe that there are areas in reality that we must learn to accept, but there are things that we can change and improve on. As a site that is only involved with the recruitment and treatment of patients, there is not much we can do if what is preventing patients from enrolling in a clinical trial is the complexity of its research design. However, if the barriers pertain to a patient's knowledge or attitudes towards clinical trials then this information could be used towards efforts such as educational strategies at the DRCC.

Regardless, both internal and external factors need to be identified and understood in order to explore the issue of patient enrolment at the DRCC, and to effectively inform current or future enrolment facilitative strategies at the site.

4 RESULTS

This chapter reports the findings of the study.

4.1 RETROSPECTIVE ANALYSIS

Data from 52 studies opened to accrual at the DRCC between December 1st, 2015, and December 1st, 2019, were collected and retrospectively analyzed to identify protocol features (i.e., therapeutic area, type of study and target stage) and patient-related/reported barriers (i.e., gender and reported reasons for non-enrolment) that may be associated with non-enrolment. In total, 52 unique protocols were included in this study. Of the studies, the majority (n=40, 76.9%) were industry sponsored. Seventeen (32.7%) were genitourinary studies, 11 (21.2%) were breast, and 7 (13.5%) were lung. Four protocols (7.7%) fell in each disease site category: Skin/Melanoma, Gastrointestinal and “Other”.

4.1.1 Summary statistics.

Tables 1 below summarizes the variables of importance to the study including enrolment, gender, sponsor type, line (type of study), disease site and target stage. A total sample size of 666 observations were analyzed. There were 59.3% (n = 395) patients who were not enrolled in a study and 40.7% (n = 271) patients enrolled (See Table 1).

Table 1

Frequency of enrolment (Y or N), protocol-related variables of interest from the DRCC's clinical trials management system.

Measure	Frequency	Percent
Enrolled		
N	395	0.593
Y	271	0.407
Sponsor Type		
Academic	205	0.308
Industry	461	0.692
Type of study		
>First Line	170	0.255
Adjuvant	106	0.159
First Line	248	0.372
Neo-Adjuvant	2	0.003
Observational	39	0.059
Other	10	0.034
Supportive Care	54	0.081
Survey	37	0.056
Disease Site		
Breast	127	0.191
Gastrointestinal	24	0.036
Genitourinary	214	0.321
Hematology	10	0.015
Lung	162	0.243
Other	72	0.108
Skin / Melanoma	57	0.086
Target Stage		
Advanced/Metastatic	411	0.6171
Early	45	0.0676
Unspecified	210	0.3153

Table 2 summarizes patient-related variables of interest such as gender, off-study decision, and off-study reason. Of this sample, 40.2% (n = 268) were female, 52% (n = 347)

were male, and 7.7% (n = 51) genders were unknown which were excluded from the analysis on gender and enrolment.

Table 2

Frequency of enrolment (Y or N), patient-related variables of interest from the DRCC's clinical trials management system.

Measure	Frequency	Percent
Enrolled		
N	395	0.593
Y	271	0.407
Gender		
Female	268	0.402
Male	347	0.521
Not known	51	0.077
Off-study decision		
Clinical	369	0.554
Patient	118	0.177
Unknown	179	0.269
Reason for off-study		
Deceased	66	0.099
Disease Progression	4	0.006
Family / Carer / Social reasons	1	0.002
Inappropriate to approach	1	0.002
Inconvenience of Study / Treatment	14	0.021
Ineligible – criteria failure / pre-screening failure	239	0.359
Ineligible – screening tests failure	44	0.066
Lost to follow up	1	0.002
No reason given	220	0.33
None of the above	35	0.053
Patient does not want / is unable to attend additional visits/travel to hospital	7	0.011
Patient does not want additional tests	1	0.002
Patient does not want to be randomized	9	0.014
Patient in too much discomfort to continue	4	0.006
Patient wants the current standard of care	8	0.012
Psychological Stress of study	4	0.006
Sponsors Decision	8	0.012

Most pre-screened males, 65.20% (n = 244), were not enrolled (See Table 3). Gender was found to have a moderate association with enrolment (See Table 3). Of 127 pre-screened breast cancer patients, 77.2% (n=98) were enrolled, while in other disease sites, such as lung and genitourinary cancer studies, less than 30% of patients pre-screened (n=38 or 23.5% of 162 total lung patients pre-screened; n=58 or 27.1% of 214 total genitourinary cancer patients pre-screened) were enrolled (See Table 3).

Table 3

Summary of enrolment and non-enrolment proportions across gender, sponsor type, type of study, disease site and target stage.

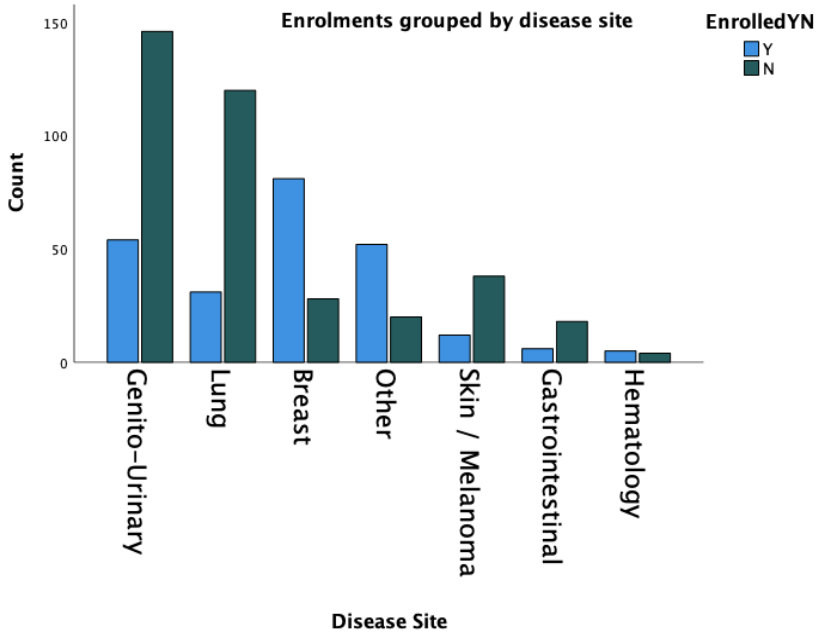
Enrolled:	N		Y					
	N	%	n	%	Chi-square value	*df*	Asymptotic Significance (2-sided)	Cramer's V
Gender (n=615)								
Female	130	34.8	138	57.3	30.18	1	<0.001	0.222
Male	244	65.2	103	42.7				
Sponsor Type (n= 666)								
Industry	300	75.9	161	59.4	20.64	1	<0.001	0.176
Academic	95	24.1	110	40.6				
Type of study (n= 666)								
>First Line	108	27.3	62	22.9	147.64	7	<0.001	0.471
Adjuvant	50	12.7	56	20.7				
Neoadjuvant	1	0.3	1	0.4				
First Line	199	50.4	49	18.1				
Observational	1	0.3	38	14				
Survey	4	1	33	12.2				
Supportive Care	30	7.6	24	8.9				
Other	2	0.5	8	3				
Disease Site (n=666)								
Breast	29	7.3	98	36.2	144.93	6	<0.001	0.466
Genitourinary	156	39.5	58	21.4				

Enrolled:	N		Y					
	N	%	n	%	Chi-square value	*df*	Asymptotic Significance (2-sided)	Cramer's V
Other	20	5.1	52	19.2				
Lung	124	31.4	38	14				
Skin / Melanoma	43	10.9	14	5.2				
Gastrointestinal	18	4.6	6	2.2				
Hematology	5	1.3	5	1.8				
Unspecified	66	16.7	144	53.1				
Target Stage (n=666)								
Advanced/Metastatic	303	76.7	108	39.9	103.06	2	<0.001	0.393
Early	26	6.6	19	7				

Across disease sites, the highest proportion of non-enrolments were from patients pre-screened in genitourinary studies (39.5%, n = 156, p-value = <0.001) and highest proportion of enrolments were pre-screened in breast studies (36.2%, n = 98, p-value = <0.001) (See Figure 1).

Figure 1

Enrolment versus non-enrolment across disease sites



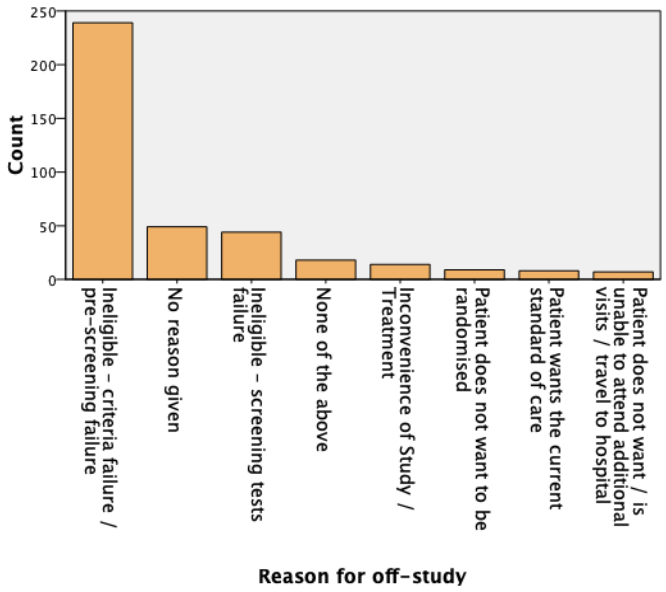
Among protocol related variables, disease site, type of study and stage were moderately to strongly associated with enrolment. As per these results the type of Sponsor (industry vs. academic) had a weak association with enrolment (See Table 3).

4.1.2 Reasons for non-enrolment.

Among total non-enrolments (n = 395), 71.6% (n = 283) were due to ineligibility (this is the sum of pre-screening and screening failures) (See Figure 2). Of the ineligible patients, 15.5% (n = 44, p-value = <0.001) were approached and consented, but failed screening tests (See Figure 2). Patient decision barriers (i.e., inconvenience of study, unable to attend extra visits, patient does not want to be randomized, and preference for standard of care) only accounted for 11.3% (n = 44) of non-enrolments (See Figure 2). Of non-enrolments, 12.4% (n = 49), did not provide a reason, and 4.6% (n = 18) of reasons did not fit into one of the 11 categories of reason for off-study.

Figure 2

Top 8 reasons for non-enrolment in clinical trials at the DRCC



Additional barriers reported were psychological stress of the study, family/social reasons, and additional tests; however, this only accounted for 1.9% of non-enrolments.

Based on information from CTMS, most non-enrolments were due to not meeting enrolment criteria. - Only a small proportion of reasons for "off-study" were due to patient-reported reasons such as inconvenience of treatment or preference for standard of care. The highest proportion of non-enrolments compared to enrolments were found in genitourinary trials. The highest proportion of enrolments were found in breast studies.

4.2 PATIENT SURVEY

Adult oncology patients (≥18) were asked to complete a survey to identify patient barriers to enrolment prospectively. Patients for this study were recruited via patient posters behind clinic doors and a Lakeridge Health website ad. Patients were also introduced to this

study by a member of their circle of care. If the patient expressed interest in participating, they were either provided with the option to contact the PI themselves or share their contact information with the PI. The survey included questions related to sociodemographic characteristics, knowledge/experience with clinical trials, and perceived barriers on decision making.

4.2.1 Sociodemographic characteristics.

Due to COVID-19 restrictions during the 2020-2021 data collection period, the target recruitment and sample size for this portion of the study was not met and only 5 patients completed the patient survey. Four out of the 5 respondents were female, and all respondents were between the ages of 50 to 77. All five respondents indicated that their ethnicity was Caucasian and indicated English as their primary language of preference. The majority (80%, n=4) of respondents indicated an annual household income of over $100,000. Sixty percent (n=3) of the respondents had a university degree (Bachelor's degree or higher). Eighty percent (n=4) of the respondents were covered under OHIP (Ontario Health Insurance Plan) and 60% (n=3) of the respondents were covered under both OHIP and private insurance. A high proportion (80%, n=4) of the participants lived greater than 50 km from the DRCC. Forty percent (n=2) of the respondents had genitourinary cancer and 80% (n=4) had either Stage 3 or 4 cancer.

4.2.2 Awareness barriers.

Of the 5 respondents, 80% (n=4) were familiar with clinical trials. Respondents had indicated that they had learned of clinical trials from school (40%, n=2), their healthcare provider (40%, n=2) or family/friends (20%, n=1). Sixty percent (n=3) were not familiar with clinical trials at the DRCC. Regarding whom the patient would trust for information on cancer, all 5

respondents (100%, n=5) indicated that they would trust their oncologist. One respondent indicated that they would trust their nurse practitioner and research team for information. Two of the 5 patients indicated that they agreed or strongly agreed with the statement "I have a good understanding of what cancer clinical trials are."

4.2.3 Opportunity barriers.

Of the 5 respondents, 60% (n=3) were previously approached to take part in a clinical trial at the DRCC. Of the three that had been approached, 2 agreed to participate, but only one patient had enrolled. The third patient who was previously approached did not indicate whether or not they agreed to participate. Sixty percent (n=3) indicated that they would participate in a trial if asked that day. One of those patients had also previously been enrolled in a trial.

4.2.4 Acceptance/refusal barriers.

Most of the respondents had either disagreed or strongly disagreed with the statement, "The idea of taking part in a clinical trial cause me stress." Four out of the 5 respondents either agreed or strongly agreed with the statement, "I believe that participating in a clinical trial will help get rid of my cancer". Of the 7 decision barriers listed at the end of the survey, five were considered "High Importance" by one or more of the respondents, "Whether or not I have access to transportation to and from the hospital" (60%, n=3), "My healthcare provider's suggestions" (40%, n=2), "The trial's benefit to society" (40%, n=2), "Side effects of the study treatment." (20%, n=1), and "My friends, family and/or community's support" (20%, n=1). Most of the respondents indicated that extra costs (60%, n=3) and extra time needed for the clinical trial (80%, n=4) had "Little Importance" to them.

In summary, most of the patients surveyed were aware of clinical trials in general; however, most of the respondents were not familiar with the clinical trials being conducted at the DRCC. Although three patients were approached to take part in clinical trials, only one had enrolled. In terms of refusal/acceptance (decision) barriers, the majority of the participants disagreed with the statement that the idea of taking part in clinical trials caused them stress. The majority believed that taking part in clinical trials would help their conditions improve. Their provider's opinions, benefit to society, and friend/familial support were important factors to consider when thinking of entering a trial and extra costs/time for trials had the least importance.

4.3 SEMI-STRUCTURED INTERVIEWS WITH RESEARCH STAFF (KEY INFORMANTS)

Seven research staff participated in the semi-structured interviews (4 research nurses and 3 oncologists). The interviews ranged from approximately 10 to 20 minutes each. Most interviewees had over a decade of clinical trials recruitment experience. Although this research focused on identifying barriers to patient enrolment, interviewees were also asked to come up with suggestions on clinical trial awareness, opportunity and acceptance promoters that may help facilitate enrolment.

4.3.1 Awareness barriers.

4.3.1.1 Lack of Education on Clinical Trials.

A recurring theme found in the interviews was that patients who do not enroll in trials were perceived by the clinical trial staff as not understanding what clinical trials are, or their importance and benefits to society. Some interviewees believed that patients often had

misconceptions about clinical trials and did not want to be considered a "guinea pig" to be experimented on:

- *"Um many people are in the camp where you mention a study and they[‘re] like I don't want to be experimented [on], which is the common misconception that people have."*
- *"I think they worry about being a guinea pig."*
- *"I think that some of [them] think that they might be a guinea pig… They might be a bit suspicious about um why you're offering them a study. Um. I don't recall having anyone ask me outright if we get paid for their participation. But I always talk to them about… Um.. I tell them that here…[there are] research ethics [boards] that independently reviewed studies to see whether or not they are in the patient's best interest… and that they are first priority - their well-being."*

The key informants' responses also suggested that perhaps media may have an influence on patients' perception of clinical trials:

- *"they've probably seen on tv. Experiments in television shows that have been sensationalized. But I don't think it's because of necessarily a bad experience with previous clinical, most I would say most, with the exception of a few, haven't been on a clinical trial before."*

4.3.2 Awareness promoters.

4.3.2.1 Accessible Clinical Trial Information.

The research staff suggested having clinical trial information readily available for patients, for example having information on clinical trials available for them as part of their take home package as a new patient at the cancer center:

- *"maybe just having more information from the Get Go. Like have something written in their bag that they go home with about sort of clinical trials and what they are and you know the fact that at some point you know that's something you could talk to your doctor about. Or giving them internet resources to look up trials."*

Another individual suggested being able to search clinical trials in a user-friendly way to improve accessibility:

- *"a more user-friendly way to search clinical trials, um that's more accessible to patients."*

4.3.3 Opportunity barriers.

4.3.3.1 Screening.

The research staff and oncologists often noted that eligibility criteria were a major limiting factor to clinical trials enrolment. They often mentioned that oncology trials conducted at the site may focus on populations with specific mutations or those are able to perform daily activities (higher performance status) which may exclude most patients:

- *"It really depends because some of these studies are very narrow. …Now they're looking at a lot of targeted therapy. So specific mutations…"*
- *"I think it depends on how many patients have a study that's eligible, but I think that the bigger picture is patients' performance status… is going to take out a huge group of patients."*

Another consideration that was brought up by one of the respondents regarding screening was the extensiveness of screening tests. They spoke about extensive screening tests (i.e., MRI

scans, biopsies, CT scans, ECG, etc.) potentially posing as an additional burden for patients who have not yet been enrolled in a study:

- *"A lot of them are like, for all the testing in [one of the potential patients] right now, like I'm putting her through the wringer, but I keep having to encourage and remind her that once you're on, [it's] not going to be this craziness like you just have to bear with me for a few more days, screening tests."*

The interviewees emphasized that eligibility criteria in itself already excludes a majority of the patients and thereby, only a few are able to decide whether or not to take part in the trials.

4.3.3.2 Provider's Communication.

A common theme also considered as a potential opportunity barrier discussed by the key informants was provider's communication. In the interviews, provider's communication was defined as the way in which health professionals present information to patients. Topics related to provider's communication included the informed consent form. Although the respondents acknowledged the importance of obtaining informed consent and all the necessary details related to clinical trial participation, the typed informed consent document may be overwhelming for a patient and may not be helpful in terms of motivating patients to join clinical trials:

- *"The consent form…I think it scared a lot of them. Nobody opens up a bottle of Tylenol and reads every single side effect that Tylenol gives you, but in a consent form, every single adverse event whether it's 1% chance of getting it or 50…it's listed."*
- *"Because it's so comprehensive and inclusive. Which is what needs to be done… we understand a consent form, but patients don't understand a consent form… clinical trial consent is 50 pages of typed stuff… if you buy a new phone, nobody hands you the 500 page instructions and says this is an awesome phone, check it out."*

In addition to the way that clinical trial information is presented in a document, the way that the provider verbally introduces the trial was also a common theme in the interviews. One of the respondents noted that having the clinical trial presented as an option rather than another commitment can be reassuring to patients:

- *"I think they just need the reassurance that it's meant as an option."*

Another respondent also emphasizes the importance of having the patient's oncologist take the time to thoroughly discuss the trial before inviting clinical trial staff who are outside of the patient's circle of care to approach the patient:

- *"...when [discussing the trial is] not done properly, or they're too vague. Or they say, "Oh we have a study" and then [not] say anything more about it… it can be a little bit more difficult because when I get called in… I don't know anything about [the patient], about their background, their history."*

4.3.4 Opportunity promoters.

4.3.4.1 Physician Attitude.

A common theme from the interviews was the physician's attitude as a positive influence on the way clinical trials are received by participants. The interviewees believed that patients were more amenable to clinical trials when physicians had a positive attitude towards a clinical trial and were able to provide a good rationale behind offering the trial to the patients:

- *"Sometimes it's basically they feel that if [physicians] endorse the study as a good option for them… The recommendation is being made with their best interest in mind, and they say, "Okay that's something I can be interested in.""*

- *"If the physician clearly presents the reason why they're offering them the trial. There's good reasoning behind it. They will more eagerly be willing to participate"*

4.3.5 Acceptance/refusal barriers.

4.3.5.1 Time, Transportation and Costs.

Most barriers identified fell under the acceptance/refusal barriers category. A common theme among the interviews was time, transportation, and cost as a barrier to trial enrolment. Time off work and trips to the hospital for extra visits were often cited as a perceived barrier for patients:

- *"Time to get time off work. Or the extra study visits cause a lot of the studies have extra visits that are above standard of care. So they're worried about that. It could be a loss of wage for some of them. Some of them have started a brand new job, so they're worried about how it's gonna impact their job."*
- *"I think the distance to the trial and the amount of extra time. Those have been like the two major barriers"*
- *"They just don't want to feel like they're wasting their time. I'm being stuck in this box being all rigid but I'm not getting the drug for sure why bother? if I can get the same standard of care treatment that they're offering with the placebo off study. Why would I put myself through that?"*

4.3.5.2 Stress.

Additional stress was also often discussed as a potential barrier to clinical trials. The research staff believed that clinical trial participation may considered an additional burden considering the extra treatments and procedures involved above standard of care:

- *"Discussion on clinical trial participation may be seen as a stressful topic or clinical trials maybe seen as additional responsibilities."*
- *"Usually we have more visits involved than the standard of care therapy. So there's that to consider. Um some patients, um, just don't want to participate in studies because they don't want the extra responsibility. They don't want to come in more than one extra blood work."*
- *"...they just got information on the chemo they're going to be taking the possible radiation they're gonna be getting, the surgery they might be getting, to throw in a clinical trial, at that time, is the wrong time to do it. The patients are feeling way too overwhelmed."*

4.3.5.3 Family and Friends.

Family and friends were reported as a common influence on a patient's decision to participate in the trial. The research staff felt as though, patients often consider the opinions of their family and friends when deciding to part in trials:

- *"Family and friends may have involvement or influence on the patient's decision."*
- *"I think that family have the biggest impact on that decision making. Um you know certainly they get a lot of time and um energy and explanation from clinical trial nurses to help with the decision making. Um but I think that ultimately that middle group that wants to take it home think an under it's really going to be swayed by family."*

Another take on how family and friends may prevent a patient from taking part in trials is how extra visits and travel distance may take time away from being spent with them:

- *"We had a lovely gentleman, he came from a two hour drive to come and see us. And that was just to get the consent and hear about the trial. Then he drove home, him and his*

wife, they were elderly and that was just to get the consent and for that study, they had to come in every two weeks for the first two cycles. And he said, "I'm older, and after we came home, my wife and I both had to sleep for a couple of hours, so I appreciate your offer, but that took away time from my grandchildren, and I will not do that."

4.3.6 Acceptance/refusal promoters.

4.3.6.1 Perceived benefits.

The discussions with key informants also suggest that a common acceptance promoter is the patients' perceived benefits of clinical trials. Several found that generally, patients express that they are interested and willing to take part in clinical trials:

- *"I think that patients are interested in clinical trials and are appreciative when we offer it to them."*

Not only do patients believe that they will be benefiting society, but they also believe that they could potentially benefit as well. For some cancer patients who have progressed on previous lines of standard of care treatments, participating in a clinical trial provides an opportunity to access advanced treatments and presents a potential option for them.

- *"Well um some of them want to do it because they feel they want to contribute to um others by finding out better treatments perhaps. Um. Some of them are feeling a little bit desperate because they might have run out of other treatment options. Um. How do they feel? I think they often times feel hopeful."*
- *"Yeah that's complicated. I mean I think that but you know, you can review the consent for me to talk about things that people have emotional responses to emotional expectations about their life. And so, I think you always say that they're investing their*

time and energy into a clinical trial and I think they're hoping that something good is going to come out of it. Maybe they are gambling a little bit. Hoping that there's going to be something positive. I don't think they're ever misled and what the purpose of the study is or the facts, but what they do with that information, how they filter it through their emotions… we don't have control over that."

Major themes identified by the key informants were related to lack of knowledge of clinical trials, eligibility criteria stringency, stress of participating in trials, lack of transportation/time, and influence of family/friends. To overcome these barriers, major themes identified as potential enrolment promoters were accessible clinical trial information, provider communication and attitude towards trials.

5 DISCUSSION

This study provided an opportunity to explore and identify potential study participation barriers that oncology patients at the DRCC face and to inform prospective solutions. Using Ford and colleagues' framework (2008) to guide the analysis, the objectives of this study involved identifying any barriers that might be related to patients' awareness of clinical trials, opportunity, and decision to participate in clinical trials. To meet these objectives, this study looks at several modes of capturing study enrolment information: an exploratory analysis on DRCC's clinical research management system, patient surveys which were analyzed superficially and semi-structured interviews with research health professionals.

5.1 SUMMARY OF RESULTS

Based on the results of all three data collection methods, eligibility criteria were identified as a major barrier at the Durham Regional Cancer Centre. The CTMS exploratory

analysis findings showed that a majority of patients that were pre-screened between December 1st, 2015, and December 1st, 2019 were not enrolled due to ineligibility. Around 71.6% (n = 283) of patients were not enrolled due to pre-screen or screening failure. This result was supported by the findings of the semi-structured interviews where inclusion/exclusion criteria was identified as a common theme.

Apart from eligibility, a factor that was commonly perceived to impact trial enrolment was a lack of awareness of clinical trials. Of the 5 respondents, 80% (n=4) were familiar with clinical trials. While most of the surveyed participants reported that they were aware of clinical trials in general, interestingly, healthcare providers on the other hand, reported a lack of awareness and credible clinical trial information as a potential barrier.

Additionally, of those who responded to the patient questionnaires, most were not familiar with the clinical trials being conducted at the DRCC. From the research staff semi-structured interviews, one way to overcome this is by providing the patients accessible clinical trial information as early as their first visit at the DRCC.

Interestingly, the survey results indicated that time/costs of participating in trials had least importance to patients when deciding to take part in a trial; whereas key informants (i.e., research nurses and oncologists) commonly noted time and costs as a major barrier to clinical trial participation. It is worth noting, however, that only 5 patients were surveyed for this study and that a larger sample size is required to generalize the survey results and effectively contrast these results with those of the semi-structured interviews.

Furthermore, all three data collection methods showed that family and friends are a significant factor in a patient's decision to enroll in a trial. Family and friends were noted as a

top 8 reason for non-enrolment and was often quoted as a common perceived barrier through the key informant interviews. One of the 5 patients surveyed as well noted that "My friends, family and/or community's support" was considered of "High Importance" to them.

Lastly, it is important to note that based on this study, patients seem to be overall willing to participate in clinical trials. The results of the CTMS exploratory analysis revealed that of the pre-screened patients at the DRCC, most had enrolled in trials. Although this percentage cannot be representative of the total number of patients enrolled versus the total oncology patient population at the DRCC, it provides a sense of patient willingness to participate. Per the semi-structured interview findings, patients, especially those who have progressed on previous standard of care therapies are willing to participate in trials.

For some patients, clinical trials are seen as a possible, if not an only option for cancer treatment. In addition, although patients may have an understanding that their participation in trials may not be directly beneficial to themselves, the belief that trials provide an opportunity to advance treatments for others, serve as a motivation to participate. What these results show is that there are patients that are willing to participate in trials despite the additional travel, time, study tests and responsibilities that participation entails.

5.2 COMPARISON WITH PREVIOUS LITERATURE AND REVISITING FORD'S et al. (2008) FRAMEWORK

Overall, the study findings provide additional evidence to support that Ford's et al framework (2008) remains true over a decade since its publication. Despite the constantly evolving landscape of clinical trials, the issue of low enrolment, particularly in oncology, still plagues the industry. These issues can include barriers related to patients' awareness,

opportunity, and their decision-making process. Ford and colleagues (2008) also suggest that sociodemographic factors (such as a person's age, ethnicity, gender, income, etc.) influence the level of impact these barriers may have on individuals. In recent decades, several publications have identified and have thoroughly discussed these barriers (Staniszeska et al., 2018; Unger et al., 2019b). However, there remains a lack of empirical evidence on how these findings apply in a Canadian context, moreover, in a community hospital setting such as the Durham Regional Cancer Centre.

In agreement with previous findings, most participants who completed this study's patient survey had heard of clinical trials (Jones et al., 2007; Moorcraft et al., 2016). Although there were a few differences in their reported sources of clinical trial information. On a similar note, the findings from the key informant interviews agree with earlier study results and support that cancer patients commonly learn of clinical trials (including misconceptions) from mass media (Staniszeska et al., 2018).

Meanwhile, in consensus with results from a survey on Canadian cancer patients published back in 2007, patients who had responded to the survey portion of this study reported obtaining their clinical trials information through their family physician or specialist (Jones et al., 2007). These results suggest the key role of healthcare providers, particularly physicians in delivering clinical trials information. Furthermore, ensuring effective communication and fostering trust between patients and their healthcare providers is important especially in the context of research participation.

Not only is fostering trust with the patients important, but this study's findings also suggest that having the support of family and friends is also essential. In this study, having the support of family and friends was commonly identified as a pertinent factor which can influence

a patient's decision to participate in clinical trials. Communicating with both patients and their friends/families about the importance of their health and safety should help improve comfortability with the clinical trial process and serve a motivator in the decision-making process (Clark et al., 2019).

Although clinical trial awareness is one issue, another hurdle as noted by Ford and colleagues (2008) is the opportunity to participate in trials. In agreement with current literature, study eligibility was noted as a common barrier to enrolment in oncology clinical trials at the DRCC (Ford et al., 2008; Moorcraft et al., 2016; Sedrak et al., 2020; Unger et al., 2019b). The semi-structured interviews support this finding where key informants identified screening as a common barrier to patient enrolment, noting that cancer studies in particular tend to have narrow eligibility criteria and look for patients with specific mutations. Other exclusionary criteria may be related to restricted concomitant medications, cancer metastasis or health status of patients. Due to the nature of certain cancers, it may even be more difficult to find patients who fall within the inclusion criteria. Per Ford and colleagues' (2008) article, this issue poses as an opportunity barrier where limitations to clinical trials enrolment is a consequence of study design. Oftentimes, protocols are written based off of previous protocols and there is potential to include unnecessary exclusionary criteria (Food and Drug Administration, 2020).

What is important to discuss, however, is that for trials that may involve multiple clinical trial 'sites' (perhaps even globally) little to nothing can be done to amend stringent eligibility criteria (Unger et al., 2019b). Strategies to address stringent eligibility must be implemented at a study design and prior to site recruitment. Guidance by the Food and Drug Administration recommends the importance of reviewing eligibility criteria and ensuring that patients are not excluded without scientific justification. Where eligible study populations may be difficult to

come across, in addition to recruiting patients who are treated at a particular site, study teams may be able to reach more participants using patient connection platforms or third-party vendors that match patients with appropriate clinical trials no matter where they might live and direct them to the study site. These online platforms are intended to make sharing, enrolment and maintaining engagement in clinical trials easier for patients.

5.3 STUDY STRENGTHS

This is the first multi-methods study to explore enrolment at the Durham Regional Cancer Centre. One of the more notable strengths of this study is that it involves several ways to gather and analyze information on enrolment at the DRCC. This study utilized a mixed-methods approach which had involved both quantitative and qualitative analysis. This study also provides a 'first look' and exploration into some of the barriers patients face at the DRCC.

Moreover, the study involves several perspectives as it involves both patients and healthcare professionals. It provides an opportunity to explore consistencies and differences between patient thoughts and healthcare professionals' thoughts.

Additionally, despite its limitations, this study provides an opportunity to inform and guide the focus of future research in oncology trial enrolment at the DRCC and similar research centres. For example, while this study only provided one barrier to enrolment per participant, previous literature has noted that patients may face multiple interconnected barriers to trial enrolment simultaneously (Ford et al., 2008). Prospective research on oncology clinical trial enrolment conducted at the DRCC may incorporate both qualitative and survey methods to identify which perceived barriers are of most importance to the patients and to potentially identify areas where the DRCC research team could employ strategies to improve.

5.4 STUDY LIMITATIONS

5.4.1 Research methodology

Issues that may have impacted the conclusions of this study may be due to the possibility that the patient sample recruited for this study may not be representative of the larger Canadian oncology patient population.

Furthermore, as previously mentioned, in terms of the patient surveys only 5 patients were surveyed, and this is not a sufficient sample size from which to derive conclusions. Moreover, it is difficult to contrast semi-structured interviews with patient surveys especially when the perspectives are from two ends of the clinical trial consent process. The initial objective of the phenomenological approach was to explore barriers to patient enrolment through the patients' perspective. However, due to restrictions implemented due to the pandemic, this study was unable to enroll patients in the qualitative portion of the study. In the future, ideally, patients would be interviewed as well, and their personal thoughts/experiences can be included in the research analysis.

5.4.2 Potential biases

For this study, only medical oncologists and nurses from the DRCC research team were recruited. Including the opinions and experiences from nurses outside of the research team and other oncologists/physicians may provide different results.

Lastly, in terms of the CTMS retrospective analysis, over 15% of the responses to "Reason for non-enrolment" was either unknown or that the patients' reason did not fall into one of the "drop-down" categories that can be chosen on CTMS. Perceived enrolment barriers such as mistrust in physicians and mistrust in the institution that have been previously identified in

literature on enrolment were not captured in this study and one of the perceived barriers that did not fall into the categories available on CTMS (Echeverri et al., 2018). Additionally, although issues such as family/social reasons and psychological stress of studies were identified in this study, this analysis did not provide enough information to assess the impact of these barriers.

5.5 RESEARCH IMPLICATIONS

Based on the findings, implications of this research may involve addressing the barriers to clinical trials identified in this study. Based on the results, the DRCC may consider strategies aimed at increasing knowledge of clinical trials in general and find effective ways to promote the visibility of trials being offered at the DRCC. This study also suggests the importance of effective communication and fostering trust with not only patients, but key members of the patients' social circle - for example, their close family and friends.

In addition, this study shows the benefits of utilizing existing technologies to both identify patterns of enrolment/non-enrolments in clinical research sites and find solutions to overcome barriers. Using online platforms such as clinical trial management systems to record clinical trial metrics at a site can not only help track workflows and metrics for internal metrics, but it can also provide valuable information on enrolment at clinical trial sites as it did in this study. Opportunities for improvement would include ensuring the accuracy of the data uploaded onto CTMS in terms of trial enrolment and including a larger selection of potential reasons for non-enrolments as identified in literature. Lastly, as previously mentioned, there are technologies available that can help sites reach more patients. Exploring how these technologies can be accepted and integrated with site workflows is a fundamental step in effectively and sustainably facilitating clinical trial recruitment at sites.

5.6 FUTURE DIRECTIONS

Future directions for this research may be to involve a survey for a larger group of cancer patients to understand their perceived barriers to clinical trial participation. This evaluation can also extend to understanding their perceived motivations. Additionally, future research may include surveys for multiple health professionals and patients across Canadian Cancer Centres to identify barriers that may be more generalizable and relevant to sites other than the DRCC.

By extension, another direction for this study is to explore not only ways to increase enrolment, but also opportunities to increase diversity in research participation. A major focus in recent years is to ensure that the clinical trial patient demographics are reflective of the diversity of the overall patient population. Future research can also focus on exploring the feasibility and efficacy of existing strategies and technologies aimed to improve enrolment at the DRCC and other similar Canadian Cancer Centres.

5.7 SUMMARY OF DISCUSSION

This study supports the applicability of Ford's et al. (2008) conceptual framework in the present research landscape. Although enrolment in clinical trials have been well discussed in previous literature, there is still plenty of room to explore how these findings can be applied in the Canadian setting. Despite the persistence of these barriers throughout decades of research, recent technology can help make overcoming these challenges more possible than ever. Future areas of focus can be to build on this current study as well as to explore feasibility, utilization and barriers to utilization of existing strategies/technologies aimed to improve enrolment in Canadian oncology research settings.

6 CONCLUSION

Throughout this project, various factors that influence enrolment were explored at the Durham Regional Cancer Centre. Ford and colleagues' (2008) conceptual framework was used to guide the analysis and categorize the identified barriers into three major categories – barriers to awareness, opportunity, and acceptance. Through several methods of data collection: exploratory data analysis DRCC recruitment metrics, patient surveys and semi-structured interviews, the aim of this project was to gain a better understanding of recruitment at the centre and to inform relevant strategies to improve it.

The findings of the study supported previous literature in that a major issue identified at the DRCC were due to stringent eligibility criteria. Patient surveys and conversations with health professionals also emphasize the importance of strategies to increase the accessibility of credible clinical trial information - both general information and information on trials being conducted at the DRCC. Ensuring that both patients and their family members/friends are informed can also be beneficial as this study has shown the importance of family and friends' support in a patients' decision to participate in trials. Lastly, what this study has ben shown through this research is that patients may generally be willing to participate in clinical trials.

Future studies building on this topic may aim to include more patients to fully capture their thoughts and experiences with trial participation. Additionally, future studies may explore the opinions of a wider range of professionals involved in research to gain a better understanding of clinical trials in Canada.

Despite its limitations, this project not only highlights areas for improvement in clinical trial enrolment at the DRCC and similar Canadian cancer centres, but it also underlines the significant

contributions that Canadian community hospitals can make for research given the proper support, and appropriate resources.

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APPENDICES

Appendix A: Literature Review Matrix

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
Unger JM, Vaidya R, Hershman DL, Minasian LM, & Fleury ME. Systematic review and meta-analysis of the magnitude of structural, clinical, and physician and patient barriers to cancer clinical trial participation. JNCI: Journal of the National Cancer Institute.	United States	2019	Systematic Review and meta-analysis		Structural barrier: Trial availability Patient barrier: Exclusion/inclusion Physician barrier: Physician decision to approach	Physician barrier: Trust in provider as a source of information Patient Barrier: Fear Perceived loss of control, adverse drug effects Patient: Transportation		Only US studies included - could limit generalizability

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
Ford JG, Howerton MW, Lai GY, Gary TL, Bolen S, Gibbons MC, Tilburt J, Baffi C, Tanpitukpongse TP, Wilson RF, & Powe NR. Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. Cancer: Interdisciplinary International Journal of the American Cancer Society.	United States	2008	Systematic review	Patient barriers: Lack of knowledge and/or education on clinical trials Patient barriers: Health literacy	Study design barriers: Protocol characteristics and eligibility criteria Physician barrier: Physician knowledge/attitude towards clinical trials Physician barrier: lack of dissemination of study information to provider or patient	Physician barrier: Trust in physician or sponsor Patient barrier: Fear of clinical trials/side effects Patient barrier: Transportation Patient barrier: Stress or time		
Jones JM, Nyhof-Young J, Moric J, Friedman A, Wells W, & Catton P. Identifying motivations and barriers to patient participation in clinical	Canada	2007	Survey interview	Patient barriers: Lack of knowledge on clinical trials	Physician barriers: Difficulty initiating (Lack of) conversations about clinical trials Physician barriers: Lack of	Patient barriers: Previous negative experience in clinical trials, poorly handled trial Patient barriers: fear of placebo		

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
trials. Journal of Cancer Education.					resources/time to explain clinical trials	Patient barriers: Unwilling to take additional tests Patient barriers: Fear of potential risks Study design: Trial not in patient's best interest		
Somkin CP, Ackerson L, Husson G, Gomez V, Kolevska T, Goldstein D, & Fehrenbacher L. Effect of medical oncologists' attitudes on accrual to clinical trials in a community setting. Journal of Oncology Practice.	United States - Southern California	2013	Survey		Physician barriers: Lack of physician awareness of open trials	Physician barriers: Physician attitudes on clinical trials		

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
Moorcraft, S. Y., Marriott, C., Peckitt, C., Cunningham, D., Chau, I., Starling, N., ... & Rao, S. Patients' willingness to participate in clinical trials and their views on aspects of cancer research: results of a prospective patient survey. Trials	United Kingdom	2016	Survey	Patient barriers: Patients misunderstand aims of trials with no direct benefit	Study barrier: Although a high proportion of patients consented to a trial, 36 % of patients did not pass screening for pre-screening trials. Screen failures may increasingly become an issue due to the growing number of biomarker selected/stratified trials. 28% of trials studied required tissue as part of screening.	Patient barrier: Time from diagnosis- those recently diagnosed with cancer are less likely to participate 75% of patients would participate in a study despite it involving multiple biopsies	No significant demographic differences between the patients who consented and those who declined	Structure of the UK health service, not dependent on patients' health insurance, may facilitate trial participation. Participants predominantly white, middle-class men and report low levels of social deprivation. Researchers did not assess the educational level or health literacy
Byrne MM, Tannenbaum SL, Glück S, Hurley J, & Antoni M.	United States - Florida-statewide study	2014	Survey	Patient barriers: lack of knowledge of clinical trials		Patient barriers: Fear of side effects	Hispanics less likely than whites to take part in cancer clinical trials	

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
Participation in cancer clinical trials: why are patients not participating? Medical Decision Making.								
Sedrak MS, Mohile SG, Sun V, Sun CL, Chen BT, Li D, Wong AR, George K, Padam S, Liu J, & Katheria V. Barriers to clinical trial enrollment of older adults with cancer: A qualitative study of the perceptions of community and academic oncologists. Journal of Geriatric Oncology.	United States	2020	Semi-structured interviews		Study design barriers: Stringent eligibility criteria Physician barriers: physicians report lack of time and support	Patient barriers: Fear of treatment toxicities		

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
Nielsen ZE, & Berthelsen CB. Cancer patients' perceptions of factors influencing their decisions on participation in clinical drug trials: A qualitative meta-synthesis. Journal of Clinical Nursing.	United States (majority of primary data)	2019	Qualitative meta-synthesis.			Patient barriers: perception of relatives Patient barriers: Doubt in therapeutic gain Physician barriers: Trust in physicians as a source of information		
Jenkins, V., Farewell, V., Farewell, D., Darmanin, J., Wagstaff, J., Langridge, C., & Fallowfield, L. Drivers and barriers to patient participation in RCTs. British Journal of Cancer	United Kingdon	2013	Survey			Physician barriers: Trust in physicians Patient barriers: Duration of participation Patient barriers: Fear of randomization		

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
Greenwade, M. M., Moore, K. N., Gillen, J. M., Ding, K., Rowland, M. R., Crim, A. K., ... & Gunderson, C. C. Factors influencing clinical trial enrollment among ovarian cancer patients. Gynecologic Oncology	United States	2017	Retrospective chart review of patients diagnosed with stage II-IV epithelial ovarian cancer (EOC) from December 2009 to April 2013. This period was when multiple trials were open to all EOC types.				Older patients were less likely to be on clinical trial (median age 68 vs 61 years) Stage, race, and performance status were similar between the groups. Distance did not affect trial enrollment-almost half of all patients in both groups lived over 50 miles from the treatment center A limitation of this study is the lack of data as to why older patients did not	

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
							enroll: eligibility, physician bias or patient choice	
Zdenkowski, N., Lynam, J., Sproule, V., Wall, L., Searston, J., & Brown, S. Results of a survey of cancer patients' willingness to travel to participate in a clinical trial. Internal Medicine Journal	Australia	2019	Survey			Patient barriers: travel time, added expenses beyond usual care,	Education level, disease stage, current treatment or previous clinical trial involvement did not impact decision Individuals from rural areas, of lower socio-economic status, and those did not have private health insurance more likely to be willing to join a trial	

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
Unger, J. M., Hershman, D. L., Fleury, M. E., & Vaidya, R. Association of patient comorbid conditions with cancer clinical trial participation. JAMA Oncology,	United States	2019	Survey		Patient barriers: comorbidities			
Staniszewska, A., Lubiejewska, A., Czerw, A., Dąbrowska-Bender, M., Duda-Zalewska, A., Olejniczak, D., ... & Bujalska-Zadrożny, M. Awareness and attitudes towards clinical trials among Polish oncological patients who had never participated in a clinical trial.	Poland	2018	Survey - statistical analysis	Patient barriers: awareness of clinical trials		Patient barriers: Fear of side effects	Factors, such as age, gender, educational level, and resident area were not significantly associated with willingness to participate in clinical trials Wanting to qualify for clinical trials did not depend on the patient's knowledge of side	

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
Advances in Clinical and Experimental Medicine							effects	
Echeverri, M., Anderson, D., Nápoles, A. M., Haas, J. M., Johnson, M. E., & Serrano, F. S. A. Cancer health literacy and willingness to participate in cancer research and donate bio-specimens. International Journal of Environmental Research and Public Health,	United States	2018	Survey			Structural barriers: patient willingness affected by type of institution and trust in institution Patient barriers: Patients less willing to participate in more-invasive studies that require them to take medications, undergo medical procedures, or donate skin/tissues.	Significant differences were observed in Cancer health literacy scores by race, gender, and education, but not by age. White individuals had a significantly higher mean CHL-score than the other groups (African American, Latino, Asian) CHL-scores higher for women than men	

				Barriers				
Author/Title/Journal	**Country where primary data was collected**	**Year Published**	**Methodology**	**Awareness**	**Opportunity**	**Acceptance/Refusal**	**Sociodemographic factors**	**Limitation**
Bennette, C. S., Ramsey, S. D., McDermott, C. L., Carlson, J. J., Basu, A., & Veenstra, D. L. Predicting low accrual in the National Cancer Institute's Cooperative Group clinical trials. JNCI: Journal of the National Cancer Institute,	United States	2016	Retrospective analysis of AACT (Aggregate Analysis of ClinicalTrials.gov) database, Researchers obtained all interventional, late-phase (II or III) adult oncology trials launched between 2000 and 2011.			Study design: Use of a tissue or biopsy sample for screening, randomized design, and greater trial complexity (number of interventions evaluated)		

Awareness barriers

Opportunity barriers

Acceptance barriers

Sociodemographic factors

Appendix B: Study Website Ad

Have you been asked to take part in a cancer clinical trial?

If you are over 18 years old, this study may be for you.

Study on barriers to cancer clinical trials participation

Better cancer treatments are made available to help save lives thanks to the participation of clinical trial volunteers. However, only around **1% to 5%** of adult cancer patients participate in cancer research.

We want to learn more about your thoughts and experiences with cancer clinical trials at the DRCC.

Are you eligible for the study?

- **18 years and over**
- **a DRCC patient diagnosed with cancer**

Participants will be asked to complete a 15-20 minute survey.

Survey Link: https://forms.gle/motE5DzpXZZ3fz8q6

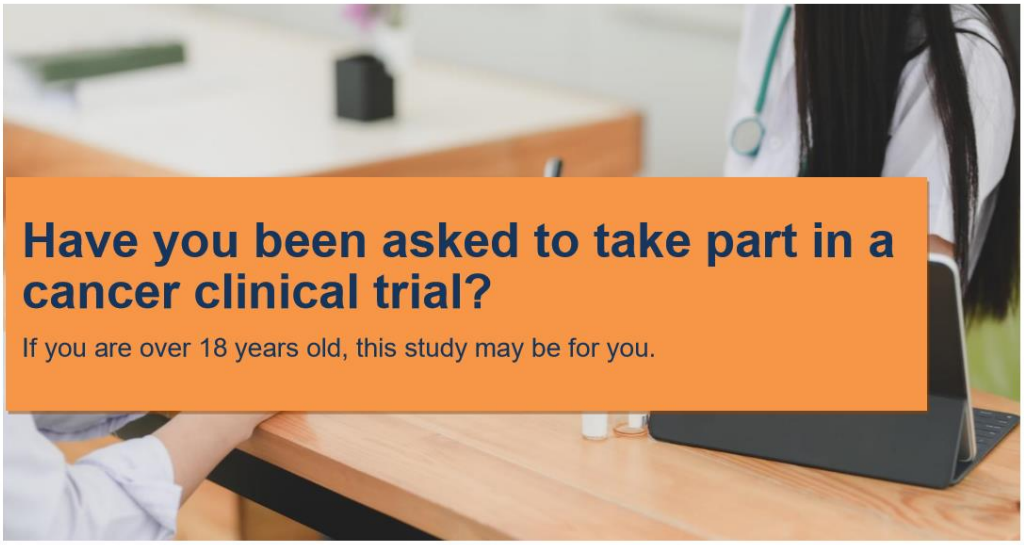
For more information, contact:
Angelina Singson at (905) 926-2707
OR email asingson@lh.ca

Version dated 20 August 2020

Lakeridge Health

OntarioTech UNIVERSITY

Appendix C: Study Poster



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Better cancer treatments are made available to help save lives thanks to the participation of clinical trial volunteers. However, only around **1% to 5%** of adult cancer patients participate in cancer research.

We want to learn more about your thoughts and experiences with cancer clinical trials at the DRCC.

Are you eligible for the study?

- **18 years and over**
- **a DRCC patient diagnosed with cancer**

Participants will be asked to complete a 15-20 minute survey.

Survey Link: https://forms.gle/motE5DzpXZZ3fz8q6
You can also use your phone camera to head to the survey directly using the QR code below:

For more information, contact:
Angelina Singson at (905) 926-2707
OR email asingson@lh.ca

Version 1 dated 20 August 2020

Lakeridge Health OntarioTech University

Appendix D: Patient Survey

Date: DD / MM / YYYY
Study ID: _____ (Please leave for the researcher to fill)

Clinical Trials Survey

Thank you for participating in this study. The results of this study will be used to inform enrolment strategies and potentially help improve clinical trials at the Durham Regional Cancer Centre (DRCC). In the following questions, I will be asking you about yourself, your knowledge and experience with cancer clinical trials, and factors that might influence whether or not you decide to take part in cancer clinical trials at the DRCC. Your participation in this study is completely voluntary and you are not required to answer any questions that you are not comfortable with answering. If you do not feel comfortable answering a question, we kindly ask that you check the "Prefer not to Answer" box. If at any point, you would like to stop, you are free to do so. Data collected from this study will be kept anonymous and confidential.

The first 13 are questions about yourself. If you prefer not to answer, please indicate, "Prefer not to answer".

1. Please indicate your age: ____ years ____ months

2. Please indicate your gender:

   ☐ Male
   ☐ Female
   ☐ Other
   ☐ Prefer not to answer

3. Please indicate your ethnicity:

   ☐ Caucasian
   ☐ Aboriginal
   ☐ African
   ☐ Caribbean

- ☐ Middle Eastern
- ☐ Latino/Hispanic
- ☐ East Asian
- ☐ South Asian
- ☐ Southeast Asian
- ☐ Other: Please Specify _____
- ☐ Prefer not to Answer

4. Please indicate your primary language of preference:
   - ☐ English
   - ☐ French
   - ☐ Other: Please specify _____
   - ☐ Prefer not to answer

5. Please indicate your annual household income:
   - ☐ Less than $50 000
   - ☐ $50 000-$100 000
   - ☐ $100 000-$150 000
   - ☐ Greater than $150 000
   - ☐ Prefer not to answer

6. Please indicate your highest level of education:
   - ☐ Elementary school
   - ☐ High school diploma
   - ☐ College diploma
   - ☐ Bachelor's degree
   - ☐ Master's degree
   - ☐ Doctoral degree
   - ☐ Prefer not to answer

7. Please indicate your employment status:
   - ☐ Full-time

☐ Part-time

☐ Temporary full-time/part-time
☐ Retired
☐ Self-employed
☐ Unemployed
☐ Other: Please specify _____
☐ Prefer Not to Answer

8. Please indicate your field of work:
   ☐ Agriculture
   ☐ Applied sciences related work
   ☐ Art/Culture/Sports
   ☐ Business/finance
   ☐ Community and social service
   ☐ Education
   ☐ Health-related work
   ☐ Hospitality and tourism
   ☐ Manufacturing
   ☐ Sales/Retail
   ☐ Trades and transport
   ☐ Other: Please specify _____
   ☐ Prefer Not to Answer

9. Please indicate your insurance provider (Check all that might apply):
   ☐ OHIP
   ☐ Private Insurance
   ☐ Unknown
   ☐ Other: Please Specify _____
   ☐ Prefer not to answer

10. Please indicate your primary mode of transportation to and from the DRCC:
    ☐ Car

☐ Public Transportation
☐ Taxi
☐ Other: Please Specify _____
☐ Prefer not to answer

11. Around how far do travel from your home to the hospital?

☐ <5 km
☐ 5 km-10 km
☐ 10 km-30 km
☐ 30 km-50 km
☐ >50 km

12. What type of cancer do you have?

☐ Colorectal
☐ Genito-urinary
☐ Breast
☐ Lung
☐ Skin
☐ Blood
☐ Other: Please Specify _____
☐ Prefer not to answer

13. What stage of cancer?

☐ 1
☐ 2
☐ 3
☐ 4
☐ I am unsure
☐ Prefer not to answer

In the next section we will be asking about your knowledge and willingness to take part in cancer clinical trials. If you prefer not to answer, please indicate, “Prefer not to answer”.

14. Are you familiar with clinical trials?

- ☐ Yes
- ☐ No *If "no", please see video below before proceeding.*
- ☐ Prefer Not to Answer

"What are clinical trials" YouTube Video

15. Where did you learn about clinical trials?

- ☐ During this survey
- ☐ Healthcare provider
- ☐ School
- ☐ Work
- ☐ Television/Film
- ☐ Social Media/Internet
- ☐ Family/Friends
- ☐ Other: Please specify _____
- ☐ Prefer Not to Answer

16. Who would you trust for information on cancer clinical trials (Check all that might apply)?

- ☐ Family Physician
- ☐ Oncologist
- ☐ Friends/Family
- ☐ Other: Please specify _____
- ☐ Prefer Not to Answer

17. Are you familiar with clinical trials at the DRCC?

- ☐ Yes
- ☐ No
- ☐ Prefer Not to Answer

18. Have you ever been approached to take part in a clinical trial at the DRCC? *If 'No' Skip to question #20.*

- ☐ Yes
- ☐ No

☐ Prefer Not to Answer

19. Have you agreed to take part in a clinical trial? *If you have agreed please skip to question #20.*
    - ☐ Yes, I agreed.
    - ☐ Yes, I agreed but I was not eligible for study treatment.
    - ☐ No, I declined.
    - ☐ Prefer Not to Answer

If you have been previously approached to take part in a trial and have declined and you have access to a telephone, would you like to take part in a 30-minute telephone interview to share this experience, and thoughts on cancer trials participation? If you agree to be contacted, you could provide your contact information below, or call Angelina Singson at (905) 926-2707 or email asingson@lh.ca.

- ☐ Yes
- ☐ No

If you would like to be contacted, please provide your name and contact phone number below.

_____

20. If someone asked you today to take part in a clinical trial for a new cancer therapy, would you consider agreeing?
    - ☐ Yes
    - ☐ No
    - ☐ Prefer Not to Answer

For the following 20 questions, we would like to ask you whether you agree or disagree with the following statements.

Scale:	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree	Prefer Not to Answer
21. I have a good understanding of what cancer	☐	☐	☐	☐	☐	☐

clinical trials are.						
22. The idea of taking part in a clinical trial causes me stress.	☐	☐	☐	☐	☐	☐
23. I believe that participating in a clinical trial may help get rid of my cancer.	☐	☐	☐	☐	☐	☐
24. I would rely on my healthcare provider as my source for clinical trials information.	☐	☐	☐	☐	☐	☐
25. I do not know a lot about clinical trials.	☐	☐	☐	☐	☐	☐
26. I think that clinical trials are too hard to understand.	☐	☐	☐	☐	☐	☐
27. I am afraid of the side effects of study treatments.	☐	☐	☐	☐	☐	☐
28. Travelling to and from the DRCC for extra appointments would be a challenge for me.	☐	☐	☐	☐	☐	☐

29. I am comfortable having my treatment decided for me.	☐	☐	☐	☐	☐	☐
30. The idea of clinical trials makes sense to me.	☐	☐	☐	☐	☐	☐
31. I have trust in my physician or main healthcare provider.	☐	☐	☐	☐	☐	☐
32. I believe that clinical trials are important to society.	☐	☐	☐	☐	☐	☐
33. I could easily get to the hospital for extra study appointments.	☐	☐	☐	☐	☐	☐
34. I have family and friends that would support my decision to take part in a cancer clinical trial.	☐	☐	☐	☐	☐	☐
35. I think that participating in cancer clinical trials would cost me to spend more money.	☐	☐	☐	☐	☐	☐

36. I don't believe that clinical trials have any benefit.	☐	☐	☐	☐	☐	☐
37. I don't have time for clinical trials.	☐	☐	☐	☐	☐	☐
38. I think that participating in a cancer clinical trial would cause stress for my friends/family.	☐	☐	☐	☐	☐	☐
39. I believe that clinical trials could worsen my cancer.	☐	☐	☐	☐	☐	☐
40. I have fear of the unknown costs to participating in trials.	☐	☐	☐	☐	☐	☐

Lastly, in your opinion, how important are each of the 9 factors listed below to your decision to take part in a clinical trial? Please rank the following statements from "No importance" to "High importance" to your decision-making.

Rank:	No Importance	Little importance	Neutral	Some importance	High importance	Prefer Not to Answer
41. Side effects of the study treatment	☐	☐	☐	☐	☐	☐
42. Complexity of the study	☐	☐	☐	☐	☐	☐
43. My healthcare provider's suggestions	☐	☐	☐	☐	☐	☐

44. The trial's benefit to society	☐	☐	☐	☐	☐	☐
45. My knowledge about clinical trials	☐	☐	☐	☐	☐	☐
46. My friends, family and/or community's support	☐	☐	☐	☐	☐	☐
47. Whether or not I have access to transportation to and from the hospital	☐	☐	☐	☐	☐	☐
48. Extra costs to me	☐	☐	☐	☐	☐	☐
49. Extra time needed for the clinical trial	☐	☐	☐	☐	☐	☐

Thank you very much for completing this survey. If you have further questions regarding this study, please do not hesitate to contact Angelina Singson at (905) 926-2707.

Additional Notes (If you would like to add to any of your answers above, please do so in the space below):

_____
_____
_____
_____
_____
_____
_____.

Appendix E: Patient Interview Guide

Clinical Trials Semi-structured Interview Guide

Date:
Time:
Participant ID:

Ensure that verbal consent is obtained before completing this interview.

Introduction:

"Thank you very much for taking the time to participate in this telephone interview. The purpose of this interview is to explore the contexts, feelings and experiences that might have led to your decision not to participate in an oncology clinical trial at the DRCC.

Your participation in this telephone interview is completely voluntary and you can choose to withdraw at any time, for any reason. If you are uncomfortable with answering any of the following questions you can choose not to answer. There are also no right or wrong answers to the interview questions as I am interested in your experiences.

With your permission, I will audio-record this interview. Once the recording is transcribed, the recording will be maintained on a secured electronic Drive at Lakeridge Health for 7 years after the study is over and afterward, it will be completely deleted. All information will be kept confidential and anonymous. Any research team member who is authorized to view the study data will be required to sign a confidentiality form. Before we proceed, do you have any questions?"

Document and answer any questions.

"If any further questions come up during the interview, please feel free to ask. May I begin the audio-recording? The following questions pertain to your experiences having been previously approached to take part in an oncology clinical trial at the Durham Regional Cancer Centre."

Questions:

How would you describe your overall experience of being invited to participate in an oncology clinical trial?
Probe: Thoughts? Did you have a negative or positive experience? What did you think of the informed consent process?

What factors are involved in your decision-making process?
Probe: Do you consider your oncologist's recommendations? Do you consider your family doctor's recommendations? Do your family members and/or friends influence your decisions?

How did you feel about taking part in a clinical trial?
Probe: Were you afraid? Were you left feeling confused?

What information do you consider when making your decision?
Probe: Where did you learn about trials? How much would you like to know about clinical trials before deciding to participate?

What were your concerns about participating in a clinical trial?
Probe: Did you think that you knew enough about clinical trials? Did you consider transportation to and from the hospital a challenge?

What suggestions might you have that would have made you feel more comfortable with participating a clinical trial?
Probe: What do you think would have helped you accept to participate in the clinical trial? Do you have any suggestions on what the DRCC could do to increase enrollment in clinical trials?

"We have now come to the end of the interview. Thank you again so much for your participation. If you have any questions you can ask them now or contact me later at asingson@lh.ca or by phone at (905) 926-2707."

Appendix F: Lakeridge Health REB Amendment Approval

Lakeridge Health

1 Hospital Court
Oshawa, ON
L1G 2B9

REB AMENDMENT APPROVAL

The Lakeridge Health Research Ethics Board (REB) operates in compliance with, and is constituted in accordance with, the requirements of the Tri -Council Policy Statement on Ethical Conduct for Research Involving Humans Version 2 (TCPS); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH/GCP); Part C, Division 5 of the Food and Drug Regulations; and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations.

RID #: 2020-015

Principal Investigator: Angelina Singson Contact Name: Angelina Singson

Study Title:	Barriers to Patient Enrolment in Oncology Clinical Trials at a Canadian Regional Cancer Centre: A Mixed Methods Study.	
REB Meeting Date(s):	28-Jun-21	[X] A Full LHREB Board Meeting or [ ] The LHREB Chair with Notification to All Board Members

Submission Date:	07-Jun-21
Approval Date:	28-Jun-21
LH REB Approval Release Date:	30-Jun-21
Study Approval Expiry Date:	28-Jun-22

Document	Version	Date
LHREB Amendment Form		
Protocol (clean and tracked copy)		19-May-21
Reseasrch Team Verbal Informed Consent Form		19-May-21
Research Team Inverview Guide		19-May-21

The Lakeridge Health Research Ethics Board has reviewed the amendment to the study and granted approval as of the date noted above.

Signed:

John Montgomery, BA, LLB
Chair, LH-REB

OR

Andy Benson, BSc, AEMCA, ACP
Vice-Chair, LH-REB

REB Amendment Approval Form, Jan2021

Page 1 of 1

Appendix G: Key Informant Consent Form for Semi Structured Interview

Study Information and Verbal Informed Consent Form
Barriers to Patient Enrolment in Oncology Clinical Trials at a Canadian Regional Cancer Centre: A Mixed Methods Study

Date:
Time called:
Participant name:

"Hi, my name is Angelina Singson.. May I please speak to <Participant Name>?" ***If participant is available, proceed. If no,*** "Thank you, I will call back another time."

"I am calling with regards to the 30-minute telephone interview that you have recently expressed interest to participate in. Is this a good time for you?" ***If yes, proceed.***

If no, "No problem, would there be an alternative best time to reach you?" ***If yes, log date and time. Proceed with introduction.***

If no, "No problem, thank you very much for your participation in the patient questionnaire. If you have any questions, please feel free to contact me at <email> and/or <phone number>. Goodbye."

Introduction

Before we begin the telephone interview. I would like to first tell you about the study and your rights as a participant. You are being invited to participate in a research study. This research is on barriers to enrolment in cancer trials at a Canadian Regional Cancer Centre. You are being invited to take part because you are a physician, nurse or research associate who has experience recruiting patients to oncology clinical trials at the Durham Regional Cancer Centre. You also have the ability to speak, write, and read in English.

This consent form is intended to provide you with the necessary information to make an informed decision on whether or not you would like to join the study. Your decision is completely voluntary. You also do not have to decide today whether or not you will participate in the research, and you can talk to anyone you feel comfortable with about the research before you make a decision. This consent form may contain words that you do not understand. If you have any questions, please let me know and I will take the time to explain.

Background

Randomized controlled trials (also called "clinical trials) are important to the development of new cancer treatments. They are types of research that assess whether or not new treatments safe for people and whether or not they work. Before new treatments are approved for use in Canada, they must show success through different phases of clinical trials. Phase I clinical trials are done to determine safe doses that cause fewest side effects, Phase II trials to see if the treatment does what it's intended to do, Phase III trials to see if the treatment is better than an

approved standard treatment, and Phase IV to see the long term effects of the treatment. Through clinical trials, we can expect better treatments and higher rates of patients being cured of cancer.

Canadians generally have a positive view on clinical trials and their importance in society. However, only around 1% to 5% of adult cancer patients participate or enrol in clinical trials. Patient participation or enrolment in clinical trials is defined as a patient being informed about study information and the patient choosing to participate in the clinical trial. Low enrolment rates might mean that the effectiveness and safety of treatments that might not apply to the general cancer populations. In other cases, low recruitment rates are also one of the reasons why many clinical trials might not continue and the development of new treatments are slowed down.

Purpose

Most of what we know about barriers adult cancer patients might face that prevent them from participating in cancer research is based on information from large research centres, from the United States or the United Kingdom. We want to learn more about what these barriers might be at a Canadian Regional Cancer Centre such as the Durham Regional Cancer Centre (DRCC). Through this study, we hope to inform strategies to help improve patient enrolment and research at the DRCC.

Type of Research Intervention

This part of the study will involve a short 30-minute telephone interview. Through this interview, we would like to learn more about why you might have chosen not to participate, your experiences, and your feelings about cancer clinical trials.

Participant selection

You are being invited to take part in this study because you are a physician, nurse or research associate who has experience recruiting patients to oncology clinical trials at the Durham Regional Cancer Centre. You also have the ability to speak, write, and read in English. Our study will involve around 69 participants in total and the interviews will involve around 5 to 6 participants.

Voluntary Participation

Your participation in this research is completely voluntary. It is your choice whether to participate or not. Your decision to participate in this study or not will have no effect on your employment at Lakeridge Health.

Procedures

The interview is roughly 30 minutes long and will be audio-recorded with your permission. The telephone interview is also completely voluntary. You can choose to freely opt in or out, even at any time during the interview. You will be asked questions that you can choose not to answer if you are uncomfortable with answering them.

The information collected and recorded in this study is confidential, your name will not be used in this research. Only a number will identify you, and no one else except authorized study team members will have access to your survey or audio-recordings. During the study, study materials will be kept on Lakeridge Health's secure Drive and paper documents will be kept in safe locked area at the DRCC. The study materials will remain with Lakeridge Health for 7 years after the study is closed and then they will be destroyed.

Right to Withdraw

You can also choose to withdraw at any time during the study (questionnaire or interview). If you are uncomfortable with asking any of the questions in the questionnaire or interview you can choose to skip to the next question.

Risks

There no currently known risks involved with your participation in this study. However, if you feel uncomfortable at all during the questionnaire or interview, please let me know and we can skip to the next question or you are free to withdraw at any time.

Benefits

This study will have no direct benefit to you; however, the information learned from this study will be used to help strategies to improve cancer research at the DRCC.

Confidentiality

Every measure will be taken to ensure that a participant's confidentiality will be maintained. Information identifying you will be replaced with unique study numbers. Audio-recordings of interviews will be transcribed and analysed by Angelina Singson and/or authorized members of the study team. Study documents and recordings will be maintained in a secure and locked place on-site at the DRCC during the study and up to 7 years after study closure or in accordance with institutional requirements.

Contacts

If you have questions about taking part in this study, contact:

Angelina Singson at (905) 926-2707

If you have questions about your rights as a participant or about ethical issues related to this study, contact:

Lakeridge Health Research Ethics Board at (905) 576-8711 ext. 32745

or

Ontario Tech University Research Ethics Board at (905) 721-8668 ext. 3693

Appendix H: Key Informant Interview Guide

Clinical Trials Semi-structured Interview Guide

Date:
Time:
Participant ID:

Ensure that verbal consent is obtained before completing this interview.

Introduction:

"Thank you very much for taking the time to participate in this telephone interview. The purpose of this interview is to explore your perspectives, thoughts, feelings and experiences with patient enrolment and enrolment barriers to oncology clinical trials at the DRCC.

Your participation in this telephone interview is completely voluntary and you can choose to withdraw at any time, for any reason. If you are uncomfortable with answering any of the following questions you can choose not to answer. There are also no right or wrong answers to the interview questions as I am interested in your experiences.

With your permission, I will audio-record this interview. Once the recording is transcribed, the recording will be maintained on a secured electronic Drive at Lakeridge Health for 7 years after the study is over and afterward, it will be completely deleted. All information will be kept confidential and anonymous. Any research team member who is authorized to view the study data will be required to sign a confidentiality form. Before we proceed, do you have any questions?"

Document and answer any questions.

"If any further questions come up during the interview, please feel free to ask. May I begin the audio-recording? The following questions pertain to your experiences having previously

approached patients to take part in oncology clinical trials at the Durham Regional Cancer Centre."

Questions:

How would you describe your overall experience of approaching and recruiting patients to participate in oncology clinical trials?
Probe: Thoughts? Did you have negative or positive experiences? What do you think of the informed consent process?

What factors do you think are involved in patients' decision-making process?
Probe: Have they previously expressed any specific factors? Do family members and/or friends influence their decisions?

In your perspective, how do you think the patients feel about taking part in a clinical trial?
Probe: Have patients expressed that they were afraid? Were patients left feeling confused?

What information do you find that patients consider when making their decision?
Probe: How much do you think patients like to know about clinical trials before deciding to participate? What sources of information do patients consider?

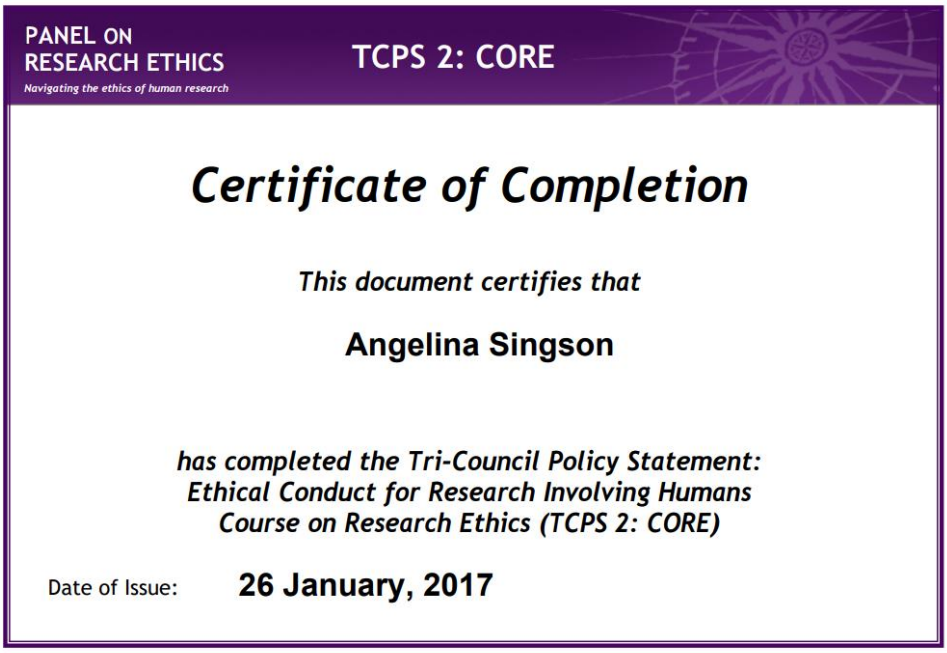
What concerns have patients expressed about participating in a clinical trial?
Probe: Did patients consider transportation to and from the hospital a challenge? Did patients find randomization an issue?

What suggestions might you have that would make patients feel more comfortable with participating a clinical trial?
Probe: What do you think would help patients accept to participate in the clinical trial? Do you have any suggestions on what the DRCC could do to increase enrollment in clinical trials?

Lakeridge Health

"We have now come to the end of the interview. Thank you again so much for your participation. If you have any questions you can ask them now or contact me later at asingson@lh.ca or by phone at (905) 926-2707."

Appendix I: TCPS - CORE



PANEL ON RESEARCH ETHICS
Navigating the ethics of human research

TCPS 2: CORE

Certificate of Completion

This document certifies that

Angelina Singson

has completed the Tri-Council Policy Statement:
Ethical Conduct for Research Involving Humans
Course on Research Ethics (TCPS 2: CORE)

Date of Issue: **26 January, 2017**

Appendix J: Patient Written Consent Form

Lakeridge Health

This script will be used with electronic survey

Study Information and Informed Consent Form

Barriers to Patient Enrolment in Oncology Clinical Trials at a Canadian Regional Cancer Centre: A Mixed Methods Study

Sponsor Investigator: Angelina Singson, HBSc. CCRP
Faculty of Health Sciences, Ontario Tech University
Research, Lakeridge Health

Introduction

You are being invited to participate in a research study. This research is on barriers to enrolment in cancer trials at a Canadian Regional Cancer Centre. You are being invited to take part because you are an adult Durham Regional Cancer Centre (DRCC) patient, diagnosed with cancer. You also have the ability to speak, write, and read in English.

This consent form is intended to provide you with the necessary information to make an informed decision on whether or not you would like to join the study. Your decision is completely voluntary. You also do not have to decide today whether or not you will participate in the research, and you can talk to anyone you feel comfortable with about the research before you make a decision. This consent form may contain words that you do not understand. If you have any questions, please let me know and I will take the time to explain.

Background

Randomized controlled trials (also called "clinical trials) are important to the development of new cancer treatments. They are types of research that assess whether or not new treatments are safe for people and whether or not they work. Before new treatments are approved for use in Canada, they must show success through different phases of clinical trials. Phase I clinical trials are done to determine safe doses that cause fewest side effects, Phase II trials to see if the treatment does what it's intended to do, Phase III trials to see if the treatment is better than an approved standard treatment, and Phase IV to see the long term effects of the treatment. Through clinical trials, we can expect better treatments and higher rates of patients being cured of cancer.

Canadians generally have a positive view on clinical trials and their importance in society. However, only around 1% to 5% of adult cancer patients participate or enrol in clinical trials. Patient participation or enrolment in clinical trials is defined as a patient being informed about study information and the patient choosing to participate in the clinical trial. Low enrolment rates might mean that the effectiveness and safety of treatments that might not apply to the general cancer populations. In other cases, low recruitment rates are also one of the reasons why many clinical trials might not continue and the development of new treatments are slowed down.

Purpose

Most of what we know about barriers adult cancer patients might face that prevent them from participating in cancer research is based on information from large research centres, or outside of Canada. We want to learn more about what these barriers might be at a Canadian Regional Cancer Centre such as the Durham Regional Cancer Centre (DRCC). Through this study, we hope to inform strategies to help improve patient enrolment and research at the DRCC.

Type of Research Intervention

This study will involve your participation in a survey which is 49-question long and may take around 15 minutes to 20 minutes to complete. Through the survey, we would like to learn more of what factors might affect your decision to participate in a trial.

If you have previously declined to take part in a clinical trial, we will also be inviting you to a second part of the study. This part will involve a short 30 minute telephone interview. Through this interview, we would like to learn more about why you might have chosen not to participate, your experiences, and your feelings about cancer clinical trials. You can choose to provide your contact information in this survey or you can reach out to me instead.

Participant selection

You are being invited to take part because you are an adult patient, diagnosed with cancer, and you are currently being treated for at the Durham Regional Cancer Centre. You

Lakeridge Health

also have the ability to speak, write, and read in English. Our study will involve around 69 participants and the interviews will involve around 5 to 6 participants.

Voluntary Participation

Your participation in this research is completely voluntary. It is your choice whether to participate or not. If you choose not to participate the care that you receive at the DRCC will continue and nothing will change.

Procedures

For this study, we would ask you to fill out a survey. If you do not wish to answer any of the questions included in the survey, you are free to skip them and move on to the next question.

Right to Withdraw

You can also choose to withdraw at any time during the survey. If you are uncomfortable with answering any of the questions in the survey you can choose to skip to the next question.

Risks

There no currently known risks involved with your participation in this study. However, if you feel uncomfortable at all during the survey, you can skip to the next question or you are free to withdraw at any time.

Benefits

This study will have no direct benefit to you; however, the information learned from this study will be used to help strategies to improve cancer research at the DRCC.

Confidentiality

Every measure will be taken to ensure that your confidentiality will be maintained. You will not be asked for information that would identify you. Study documents will be maintained in a secure and locked place on-site at the DRCC during the study and up to 7 years after study closure or in accordance with institutional requirements.

Appendix K: Patient Verbal Consent Form for Semi-Structured Interview

Lakeridge Health

This script will be used with electronic survey

Study Information and Informed Consent Form

Barriers to Patient Enrolment in Oncology Clinical Trials at a Canadian Regional Cancer Centre: A Mixed Methods Study

Sponsor Investigator: Angelina Singson, HBSc. CCRP
Faculty of Health Sciences, Ontario Tech University
Research, Lakeridge Health

Introduction

You are being invited to participate in a research study. This research is on barriers to enrolment in cancer trials at a Canadian Regional Cancer Centre. You are being invited to take part because you are an adult Durham Regional Cancer Centre (DRCC) patient, diagnosed with cancer. You also have the ability to speak, write, and read in English.

This consent form is intended to provide you with the necessary information to make an informed decision on whether or not you would like to join the study. Your decision is completely voluntary. You also do not have to decide today whether or not you will participate in the research, and you can talk to anyone you feel comfortable with about the research before you make a decision. This consent form may contain words that you do not understand. If you have any questions, please let me know and I will take the time to explain.

Background

Randomized controlled trials (also called "clinical trials) are important to the development of new cancer treatments. They are types of research that assess whether or not new treatments are safe for people and whether or not they work. Before new treatments are approved for use in Canada, they must show success through different phases of clinical trials. Phase I clinical trials are done to determine safe doses that cause fewest side effects, Phase II trials to see if the treatment does what it's intended to do, Phase III trials to see if the treatment is better than an approved standard treatment, and Phase IV to see the long term effects of the treatment. Through clinical trials, we can expect better treatments and higher rates of patients being cured of cancer.

Implied Informed consent form version dated November 20, 2020

Canadians generally have a positive view on clinical trials and their importance in society. However, only around 1% to 5% of adult cancer patients participate or enrol in clinical trials. Patient participation or enrolment in clinical trials is defined as a patient being informed about study information and the patient choosing to participate in the clinical trial. Low enrolment rates might mean that the effectiveness and safety of treatments that might not apply to the general cancer populations. In other cases, low recruitment rates are also one of the reasons why many clinical trials might not continue and the development of new treatments are slowed down.

Purpose

Most of what we know about barriers adult cancer patients might face that prevent them from participating in cancer research is based on information from large research centres, or outside of Canada. We want to learn more about what these barriers might be at a Canadian Regional Cancer Centre such as the Durham Regional Cancer Centre (DRCC). Through this study, we hope to inform strategies to help improve patient enrolment and research at the DRCC.

Type of Research Intervention

This study will involve your participation in a survey which is 49-question long and may take around 15 minutes to 20 minutes to complete. Through the survey, we would like to learn more of what factors might affect your decision to participate in a trial.

If you have previously declined to take part in a clinical trial, we will also be inviting you to a second part of the study. This part will involve a short 30 minute telephone interview. Through this interview, we would like to learn more about why you might have chosen not to participate, your experiences, and your feelings about cancer clinical trials. You can choose to provide your contact information in this survey or you can reach out to me instead.

Participant selection

You are being invited to take part because you are an adult patient, diagnosed with cancer, and you are currently being treated for at the Durham Regional Cancer Centre. You

Lakeridge Health

also have the ability to speak, write, and read in English. Our study will involve around 69 participants and the interviews will involve around 5 to 6 participants.

Voluntary Participation

Your participation in this research is completely voluntary. It is your choice whether to participate or not. If you choose not to participate the care that you receive at the DRCC will continue and nothing will change.

Procedures

For this study, we would ask you to fill out a survey. If you do not wish to answer any of the questions included in the survey, you are free to skip them and move on to the next question.

Right to Withdraw

You can also choose to withdraw at any time during the survey. If you are uncomfortable with answering any of the questions in the survey you can choose to skip to the next question.

Risks

There no currently known risks involved with your participation in this study. However, if you feel uncomfortable at all during the survey, you can skip to the next question or you are free to withdraw at any time.

Benefits

This study will have no direct benefit to you; however, the information learned from this study will be used to help strategies to improve cancer research at the DRCC.

Confidentiality

Every measure will be taken to ensure that your confidentiality will be maintained. You will not be asked for information that would identify you. Study documents will be maintained in a secure and locked place on-site at the DRCC during the study and up to 7 years after study closure or in accordance with institutional requirements.

Appendix L: Lakeridge Health REB Initial Approval

Lakeridge Health

1 Hospital Court
Oshawa, ON
L1G 2B9

INITIAL REB APPROVAL

Date:	10-December-2020
To:	Angelina Singson, Lakeridge Health
RID#:	2020-015
Study Title:	Barriers to Patient Enrolment in Oncology Clinical Trials at a Canadian Regional Cancer Centre: A Mixed Methods Study

All research studies must receive both Administrative Approval and Research Ethics Board Approval (REB) prior to commencement.

The above named study has been approved for ethical and scientific merit by the REB. This research study may commence, contingent upon the following:

(i) As a reminder, the REB and Lakeridge Health (LH) operate in compliance with applicable laws and regulations including, but not limited to, the *International Conference on Harmonization for Good Clinical Practice Consolidated Guideline (ICH/GCP)*; Part C Division 5 of the *Food and Drug Regulations* or with the definition in the *Interim Order Respecting Clinical Trials for Medical Devices and Drugs Relating to COVID-19*; the *Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans Version 2 (TCPS)* and the provisions of the *Ontario Personal Health Information Protection Act (PHIPA 2004)*. Lakeridge Health is registered with the U.S. Department of Health & Human Service under IRB registration number IRB00003507. As the Principal Investigator, you are responsible for the ethical conduct of all research team members during the course of the study, and for cooperating with monitoring activities determined by the REB. As such, you and your research team agree to undertake the study in conformity with the approved protocol, and to immediately report to the REB:

- any revisions, additions, deletions or other amendments via the *Amendment Form;*
- any local, and specifically relevant external serious adverse events via the *Internal Serious Adverse Event (SAE) Report Form;* and
- any deviation with respect to the study via the *Protocol Deviation Form*
- in the event of confidentiality concerns or privacy breach, such as inappropriate and/or unauthorized use of information, you are to immediately report these to the REB (via the *Protocol Deviation Form*) and to the LH Privacy Office (in accordance with the Ontario health privacy legislation – *Personal Health Information Protection Act, 2004*).

(ii) As the Principal Investigator, you are further expected to submit:

- an annual progress report and annual re-approval via the *Annual Renewal Form* if the study is expected to continue beyond the Expiry Date; and
- a *Study Closure Form* along with a copy of the final report when the study has been completed if available.

Lakeridge Health

1 Hospital Court
Oshawa, ON
L1G 2B9

REB Submission Date:	21-August-2020
REB Meeting Date(s):	14-September-2020
REB Review Type:	☒ A Full Board Meeting ☐ The Chair with Notification to All Board Members
REB Approval Date:	14-September-2020
REB Approval Expiry Date:	14-September-2021

Documents approved until the expiry date noted above:

Document	Version	Date
Protocol		21-Oct-20
Implied Informed Consent Form		20-Nov-20
Informed Consent Form		08-Jun-20
Verbal Informed Consent Form		08-Dec-20
Patient Survey		21-Oct-20
Script for Verbal Email Consent		19-Nov-20
Edge Participant Data Collection Form	V1	19-Aug-20
Edge Protocol Data Collection Form	V1	08-Jun-20
Interview Guide	V1	20-Aug-20
LH Website Ad		20-Aug-20

Documents Acknowledged:

Document
LH REB Application

Please feel free to contact the REB Coordinator if there are any questions.

Sincerely,

Signed: _____

John Montgomery, BA, LLB
Chair, LH-REB

Please quote your file number (RID# 2020-015) on all future correspondence.

This study CANNOT start until both the REB and Administrative approvals are in place.

Appendix M: Lakeridge Health Administrative Approval

Lakeridge Health

1 Hospital Court
Oshawa, ON
L1G 2B9

ADMINISTRATIVE APPROVAL

Date:	10-December-2020
To:	Angelina Singson, Lakeridge Health
REB#:	2020-015
Study Title:	Barriers to Patient Enrolment in Oncology Clinical Trials at a Canadian Regional Cancer Centre: A Mixed Methods Study
Funding Source:	None, PI Driven

All research studies must receive both Administrative Approval and Research Ethics Board (REB) Approval prior to commencement.

Administrative Approval requires approval of the department impact, resource utilization (including sufficient funds to cover all expenses related to the study), Research Ethics Board approval and execution of a research Contract/Agreement. The above named study has been approved for administrative and resource utilization merit by Lakeridge Health. Any changes to the agreed funding, or protocol revisions that have an impact on resources, will require re-approval.

Please feel free to contact the Research Liaison if there are any questions.

Sincerely,

George Buldo
George Buldo (Dec 10, 2020 13:57 EST)

George Buldo, MD, MHCM, FRCPC
Vice President, Medical and Academic Affairs
Lakeridge Health

Dec 10, 2020
Date

This study CANNOT start until both the REB and Administrative approvals are in place.

Appendix N: Ontario Tech University REB Review Deferral

Angelina Singson

From: Angelina Singson <angelina.singson@ontariotechu.net>
Sent: October 17, 2022 4:55 PM
To: Angelina Singson
Subject: Fwd: Ontario Tech REB Review Deferral (OT Reference File #16292)

From: researchethics@uoit.ca <researchethics@uoit.ca>
Sent: Thursday, January 28, 2021 11:07:20 AM
To: Sanchez Otto(Primary Investigator) <otto.sanchez@ontariotechu.ca>
Cc: Singson Angelina(Student Lead/Post-Doctoral Lead) <angelina.singson@ontariotechu.net>; researchethics@uoit.ca <researchethics@uoit.ca>
Subject: Ontario Tech REB Review Deferral (OT Reference File #16292)

Date:	*January 28, 2021*
To:	*Otto Sanchez*
From:	*Janice Moseley, Research Ethics Officer*
File # & Title:	*16292 - Barriers to Patient Enrolment in Oncology Clinical Trials at a Canadian Regional Cancer Centre: A Mixed Methods Study*
Status:	***REB REVIEW DEFERRED TO LAKERIDGE HEALTH***

Under Ontario Tech' REB SOP 302 (Board of Record), Ontario Tech REB has deferred the research ethics review, approval, ongoing review, monitoring and compliance oversight of the study named above to Lakeridge Health REB to ensure compliance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2 2018), applicable policies, procedures and associated regulations. Please ensure that all continuing research ethics requirements are reviewed and approved by Lakeridge Health REB.

We wish you success with your study.

Sincerely,

Janice Moseley
Research Ethics Officer
researchethics@ontariotechu.ca

NOTE: If you are a student researcher, your supervisor has been copied on this message.

Appendix O: Annual Renewal

Lakeridge Health

1 Hospital Court
Oshawa, ON
L1G 2B9

REB ANNUAL RENEWAL APPROVAL

The Lakeridge Health Research Ethics Board (REB) operates in compliance with, and is constituted in accordance with, the requirements of the Tri -Council Policy Statement on Ethical Conduct for Research Involving Humans Version 2 (TCPS); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH/GCP); Part C, Division 5 of the Food and Drug Regulations; and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations.

RID #: 2020-015

Principal Investigator: Angelina Singson Contact Name: Angelina Singson

Study Title:	Barriers to Patient Enrolment in Oncology Clinical Trials at a Canadian Regional Cancer Centre: A Mixed Methods Study.	
REB Meeting Date:	28-Jun-21	[X] A Full LHREB Board Meeting or [ ] The LHREB Chair with Notification to All Board Members

Submission Date:	15-Jun-21
Date Approval Issued:	28-Jun-21
Study Approval Expiry Date:	28-Jun-22

Document	Version	Date
LHREB Annual Renewal Form		

The Lakeridge Health Research Ethics Board has reviewed the application. This study, including all currently approved documents, has been reapproved until the expiry date noted above.

Please do not hesitate to contact us if you have any questions.

Signed:

John Montgomery, BA, LLB
Chair, LH-REB

OR

Andy Benson, BSc, AEMCA, ACP
Vice-Chair, LH-REB