

Identifying and addressing a new barrier to community-based patients accessing cancer clinical trials

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1. Introduction

Participation in clinical trials is recommended as part of the clinical care for cancer patients in most guidelines, yet patient accrual is poor [1]. Lack of awareness, understanding and accessibility of trials are commonly reported barriers [2,3]. Furthermore, participant enrollment is notoriously low in community-based hospitals compared to academic centres [4]. Community hospitals are centres that provide a range of services to a local community and are led by community-based health professionals. Traditionally, community hospitals do not tend to participate significantly in medical research. A study by Kaplan et al. reported that, in NCI-designated cancer centers, 64 % of physicians report discussing enrolment with their patients, while that lowers to 39 % in community hospitals. Moreover, 88 % of physicians in NCI-designated cancer centres refer or recruit patients into breast cancer trials vs. 70 % in community hospitals [5]. There are very few reports discussing the reasons for the discrepancy, and those that do are published from large academic centres, which have a limited perspective of the factors that affect physician and patient involvement in clinical trials from community hospitals. Understanding this discrepancy is especially

important in Ontario, Canada where community hospitals care for 65–70 % of hospitalized patients [4,6].

A major challenge in community hospitals is the lack of availability of clinical trials at their home centre. In Ontario, non-academic cancer centres run between 1 and 15 clinical trials at any one time, as compared to 100–350 trials in the larger, academic centres [2]. This adds a unique challenge to the community-based oncologist who needs to look outside of their cancer centre to increase access for clinical trials for their patients. Patients in Ontario do have access to the larger, academic centres clinical trials, however, there is no systematic process for community base patients to find these trials. With no dedicated support personnel, the treating oncologists do not have the time to search for trials, the patients and their families rarely have the skill set to understand clinical trials and the clinical trials search engines are often difficult to navigate.

In Ontario, up to 70 % of the population is treated in community hospitals and experience significant barriers to clinical trials participation [6]. Thus, one should not accept that only patients in large academic centres should be allowed meaningful access to clinical trials. This underscores the significant inequity in access to clinical trials. Other benefits of enrolling patients from community hospitals into

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clinical trials include reduced wait times for study completion which leads to faster results, improved patient outcomes and reduced costs to the entire health care system. As well, increased societal representation leads to enhanced generalizability of each study.

To address the challenges of enrolling in clinical trials, the Clinical Trials Navigator (CTN) was piloted in 2019 at Windsor Regional Hospital in Windsor-Essex, Ontario, a large community hospital. The CTN, funded by Canadian Cancer Clinical Trials Network, is designed to serve Canadian cancer patients by identifying clinical trials anywhere in North America for which they may be eligible. In its first year, more than 120 patients subscribed to this program, with 80 % residing in Windsor-Essex [2].

To better understand these challenges, our current study focused on comparing physician and patient perceptions of clinical trials knowledge, barriers and influencing factors of enrollment in a community-based hospital setting.

2. Methods

We developed two separate and anonymous online surveys – one targeted to physicians and another to cancer patients. Both surveys were hosted by Qualtrics^{XM} Platform and were distributed to physicians and patients in the Windsor-Essex, Ontario region. Therefore, the sample is a convenience, non-random sample. This study received clearance by the authors' institutional research ethics board (Windsor Regional Hospital Research Ethics Committee #20–370; The University of Windsor Research Ethics Board #20–152) and all participants expressed their informed consent prior to commencing the study.

2.1. Patient questionnaire

Patients who had used CTN services were contacted via email with a link to the survey. Patients who have previously not used CTN services were given an informational postcard by their healthcare team during a regular visit to the clinic. Recruitment posters were also displayed in the cancer centre waiting room describing the purpose of this study and inviting patients to complete an online survey. The survey consisted of 34 questions and inquired about the patients' demographics, as well as their awareness and perception of clinical trials and the CTN services. Patient demographics are found in Table 1. The survey was opened in August 2021 and closed in January 2022.

2.2. Physician questionnaire

Physicians affiliated with the Windsor Regional Hospital were emailed a link to participate in the physician survey. The survey consisted of 35 questions, including those asking for physicians' demographics, knowledge and use of CTN services, and perceptions of factors influencing patient enrolment into clinical trials. Physician demographics are found in Table 2. All hospital-based physicians in Windsor Regional Hospital were asked to participate in the survey in order to improve sample size, as there are only 15 oncologists at the host site. The survey was opened in August 2021 and closed in December 2021.

2.3. Data analysis

The survey responses were organized and analyzed using Qualtrics^{XM} and the SAS software. The CROSS checklist was used to review the paper and ensure a comprehensive and accurate manuscript [7].

Descriptive statistics are reported as total number of responses as well as percentage of responses. The perceptions of influencing factors for patient-clinical trial participation were compared between physicians and patients. This part of the analysis was carried out by using a logistic regression model in which patient and physician responses to these questions (questions 25 and 26, respectively, for patients and

Table 1
Patient demographics.

Demographic Category	Patients, n (%)
Age	
18–24	0 (0.00)
25–34	7 (9.59)
35–50	29 (39.73)
50–64	23 (31.51)
65–74	12 (16.44)
75+	2 (2.74)
Gender	
Male	14 (19.18)
Female	59 (80.82)
Other	0 (0.00)
Ethnic background	
White/Caucasian	70 (97.22)
South Asian	0 (0.00)
Black	1 (1.39)
Latin American	1 (1.39)
Arab/West Asian	0 (0.00)
Indigenous	0 (0.00)
Filipino	0 (0.00)
Prefer not to say	0 (0.00)
Other	1 (1.39)
Household Income	
<\$15,000	2(2.74)
\$15,000-\$29,999	6 (8.22)
\$30,000-\$49,999	11 (15.07)
\$50,000-\$74,999	7 (9.59)
\$75,000-\$100,000	10 (13.70)
> \$100,000	26 (35.62)
Prefer not to answer	11(15.07)
Highest level of education completed	
Did not complete high school	1 (1.37)
High school diploma	6 (8.22)
Some university or community college, trade, technical school	9 (12.33)
College Diploma or University Degree	38 (52.05)
Graduate Degree	9 (12.33)
Professional degree (Law, Medicine, Dentistry)	3 (4.11 %)
Post-graduate degree	5(6.85 %)
Other	2(2.74 %)
Current employment/main activity	
Working a full-time job	26 (35.62 %)
Working a part-time job	10 (13.70 %)
Self-employed	3 (4.11 %)
Looking for work	1(1.37 %)
On maternity/paternity leave	0 (0.00 %)
On long-term disability	10 (13.70)%
Homemaking/caregiving	0 (0.00 %)
Going to school	0 (0.00 %)
Retired	23 (31.51 %)

physicians) were categorized into Important(=1–3) and Unimportant (=4,5) and a grouping variable (Physician vs Patient) was used as an independent variable.

The logistic regression was applied to each sub-item separately and the significance of the difference between physicians and patients was tested by using the Benjamini-Hochberg multiple testing adjustment method on the resulting p-values [8]. The differences in opinion between physicians and patients are reported as odds ratios, confidence intervals and adjusted p-values. The sub-item about “No other option” was not included in this analysis, as 100 % of the physicians responded “Important” while 80 % of the patients responded as such.

Table 2
Physician demographics.

Demographic Category	Physicians, n (%)
Length of Medical Practise	
1–5 years	7 (17.50 %)
6–10 years	6 (15.00 %)
11–15 years	6 (15.00 %)
16–20 years	5 (12.50 %)
>20 years	16 (40.00 %)
Speciality	
Oncology: Medical	4 (9.30 %)
Oncology: Radiation	1 (2.33 %)
Oncology: Hematological	3 (6.98 %)
Internal Medicine	3 (6.98 %)
Critical Care Medicine	2 (4.65 %)
Diagnostic Radiology	2 (4.65 %)
Emergency Medicine	1 (2.33 %)
Family Medicine	8 (18.60 %)
Neurology	1 (2.33 %)
Obstetrics/Gynecology	1 (2.33 %)
Ophthalmology	1 (2.33 %)
Pediatrics	3 (6.98 %)
Surgery	5 (11.63 %)
Other	7 (16.28 %)
Field of oncology practised	
Breast	3 (16.67 %)
Lung	1 (5.56 %)
Prostate	3 (16.67 %)
Pancreatic	2 (11.11 %)
Gynecology	2 (11.11 %)
Hematology	5 (27.78 %)
Other	2 (11.11 %)
Field of internal medicine practised	
Rheumatology	1 (100 %)
Field of surgery practised	
General	3 (75 %)
Plastic Surgery	1 (25 %)

3. Results

3.1. Patient demographics

The survey was completed by 73 patients (Table 1), of which 38 (47.5 %) were currently being treated at the Windsor Regional Cancer Program, 31 (41.3 %) were no longer being treated, and 6 (11.3 %) were being treated at a different cancer centre.

3.2. Physician demographics

Forty physicians completed the survey and demographic information was collected (Table 2). For the physicians, 15 oncologists and 200 hospital-based physicians were asked to participate in this survey. 7/15 (47 %) oncologists and 34/200 (17 %) of the hospital-based physicians responded.

3.3. Oncologist vs non-oncologist physician response

We found that 100 % (7/7) of responding oncologists felt strongly that clinical trials participation increased patient outcomes. Of the non-oncologist-physicians this was 53 % (7/15). When asked if they would refer a patient to a clinical trial if a trial were available, 100 % (7/7) oncologists felt strongly that they would, and 53 % (7/15) non-oncologists felt strongly that they would.

3.4. Involvement of physicians and patients from a large community hospital in clinical trials

The majority, 40 %, of physicians reported referring less than 10 patients to clinical trials over the previous five years, while 20 % of physicians reported referring more than 50 patients (Fig. 1A).

Most patients (50 %) reported that they have never been invited to participate in clinical trials, 8.3 % of patients were unsure and 23.6 % of patients had been invited to participate (Fig. 1B). Despite the majority of patients not being invited to participate in clinical trials, most patients are very (40.1 %) or somewhat (40.1 %) willing to participate in a clinical trial if given the opportunity (Fig. 1C). All physicians practiced in a large community hospital.

3.5. Physicians vs. patient perceptions of influencing factors for patient clinical trial participation

Patients were asked to rank factors as important or not important influences on participating in a clinical trial. Physicians were also asked to rate how important they perceived each factor to be for their patients in deciding to participate in a clinical trial. Physicians’ perceptions of how patients would rank these factors differed significantly for 5 of the 14 listed factors, including side effects, family and online opinions, time and travel. (Table 3).

Table 3 reports odds ratios of physicians relative to patients in answering “Important” to the question about factors influencing participation in clinical trials. 95 % confidence intervals of the odds

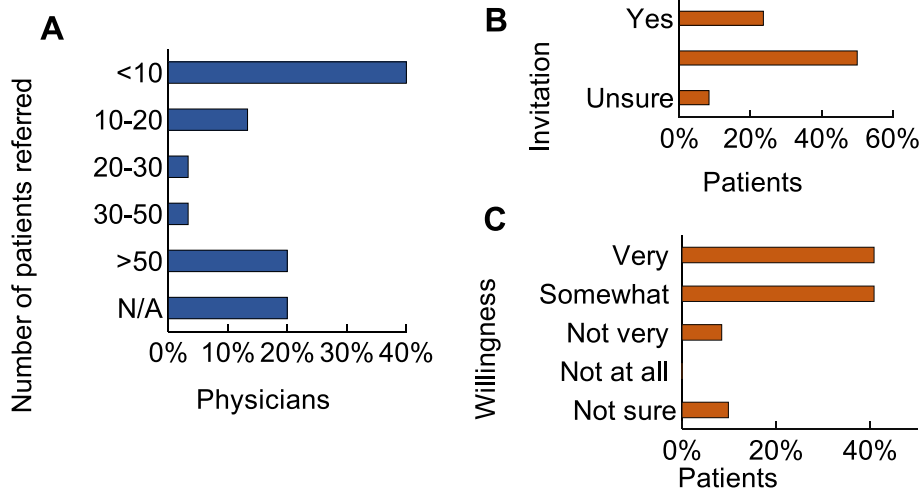


Fig. 1. Clinician and patient involvement in clinical trials. (A) Number of patients each physician referred to a clinical trial over the last 5 years (n = 30). (B) Patients that have been invited to participate in clinical trials (n = 59). (C) Patients’ willingness to participate in a clinical trial (n = 71).

Table 3

Odds ratios of physicians relative to patients in answering “Important” to the question about factors influencing participation in clinical trials.

Variable	OR	LC	UC	Unadjusted p value	Adjusted p value
Guaranteed no placebo	0.987	0.285	3.413	0.9833	0.9833
Help others in the future	1.098	0.35	3.449	0.8728	0.9399
Terminal illness	0.771	0.218	2.727	0.6868	0.8013
Chance for a cure	2.95	0.354	24.61	0.3176	0.4042
Financial compensation	2.1	0.558	7.907	0.2727	0.3818
Doctor's opinion	2.245	0.589	8.554	0.2361	0.3673
Others good experiences	4.62	0.986	21.634	0.0521	0.0912
Chronic illness	0.327	0.112	0.957	0.0414	0.0828
Free treatment	10.633	1.34	84.35	0.0253	0.0590
Side effects	7.605	1.636	35.351	0.0097	0.0272
Family/friends opinion	5.25	1.584	17.401	0.0067	0.0235
Time commitment	6.192	1.845	20.782	0.0032	0.0149
Travel time	9.811	2.606	36.938	0.0007	0.0049
Online opinions	6.875	2.285	20.687	0.0006	0.0049

Legend: OR (Odds Ratio); LC (Lower Confidence); UC (Upper confidence).

ratios and adjusted as well as unadjusted p-values are also reported in the table.

The odds of physicians perceiving as “important” were 5–10 folds more as compared to patients’ perception for the following factors: side effects, family opinion, social media opinion, time required, and how far patients had to travel. These differences were statistically significant at $\alpha = 0.05$ by judging from their 95 % confidence intervals and Benjamini-Hochberg adjusted p-values.

Also, physicians and patients differed in their opinions in a marginally significant way (at $\alpha = 0.1$) in the importance of: opinion of others, whether or not the illness was chronic and whether or not the trials was free of charge. For instance, the odds that a physician perceived “Chronic illness” as important was 67 less than that of a patient perceiving it as important.

3.6. Barriers and enabling factors for clinical trial accrual of patients at a large community hospital

When physicians were asked to rank barriers that keep them from enrolling patients in clinical trials the majority of physicians ranked factors of eligibility criteria, explaining clinical trials to patients, lack of knowledge of available clinical trials, lack of support, and unavailability of trials as important or very important barriers (Fig. 2A). Trials deviating significantly from the standard of care was ranked by physicians as not important most often (23.5 %), compared to all other factors listed (Fig. 2A).

Physicians were asked to rank the importance of factors that would enable patient accrual to clinical trials. Factors listed as important and every important include a clinical trial navigator, software development, workload credit and structural supports (Fig. 2).

3.7. Physician awareness and use of a CTN program in a large community hospital

The CTN was piloted in 2019 and designed to serve Canadian cancer patients by identifying clinical trials across North America for which they may be eligible. Any patient, caregiver or health care professional can access this program. In its first year, 118 patients subscribed to this program, with 80 % residing in Windsor-Essex. Potential clinical trials were identified for approximately one-third of these patients [2]. We assessed its use by local physicians, especially since these physicians

have ranked such services as important or very important enabling factors for patient accrual (Table 3). Of physicians who participated in the survey, 37 % were aware of the CTN services at Windsor Regional Hospital (Fig. 3A). Of those who were aware of the CTN, 60 % reported using CTN services in the past (Fig. 3B). Physicians who reported using the CTN referred up to 20 % of their patients for their services.

3.8. Patients’ awareness and likelihood to engage with a CTN service

When patients were asked if they were aware of a CTN program at Windsor Regional Hospital the majority (88 %) of patients were not aware (Fig. 4C). However, when asked how likely they would be to speak with a CTN to help find a clinical trial, most patients (61.4 %) responded likely or very likely (Fig. 4D).

4. Discussion

The purpose of this study was to survey barriers and influencing factors for both physicians and patients in a community-based hospital setting to participate in a clinical trial. We have identified a new barrier in community-based patients and their physicians regarding entering clinical trials. This unique barrier is the difference in patient and physician perception of challenges associated with clinical trial enrollment, including opinions, side effects, time and travel. Previous studies have cited extensive travel distances to clinical trials sites as a reason for patient refusal to participate in clinical trials [8]. Conversely, our study found patient assessment of the importance of time and money spent in travelling to a clinical trials site was statistically different from the physician opinion of the importance of these factors ($p < 0.05$). Patients were less likely to rank these factors as important whereas the physicians ranked these factors as more important in deciding whether or not to refer a patient to a different clinical trials site. This could be a major barrier to clinical trials accrual, as the treating oncologist is central in the process of referring their patients to the appropriate clinical trials in Canada. This process is important as the treating oncologist knows the patient best, knows the landscape of standard treatment options and is most qualified to assess the benefits of a potential clinical trial for an individual patient. If the physician feels that the investment of time and money would not be in the best interest of the patient, they are less likely to refer the patient. Our study indicates that physicians may not be aware that most patients are willing to travel for clinical trials than they perceive.

We also identified that there is a large variation in referral patterns between the clinicians that referred patients to clinical trials and those that referred very few. This phenomenon also needs to be examined as it is another barrier to clinical trials accrual for patients, although this is not likely unique to the community-based practice.

This study demonstrated that even though physicians ranked a CTN service as important or very important enabling factor for patient accrual, very few physicians used its services. Based on the findings in this study, this seems to be due to not having knowledge of the CTN at Windsor Regional Hospital or the unforeseen barrier already discussed above. Furthermore, in our pilot CTN project, we reported that 25 % of doctors who requested a list of possible clinical trials from the CTN for patients never actually referred their patient to any clinical trials [2]. However, in this study, physicians who have used the CTN services on average report about 2-fold increase in patient referrals outside their centre. To address the setback of the CTN not being used to its fullest potential, pre-screening new cancer patients for clinical trial accessibility before treatment commences has been proposed. This idea has been supported by physicians in past studies [9,10]. Optimal procedures and additional studies will be required for moving forward with this proposal.

Further research into the reasons for the discrepancy of results between the patients and physicians is needed. Perhaps the patients were overly optimistic in their ability to travel to a different cancer centre in

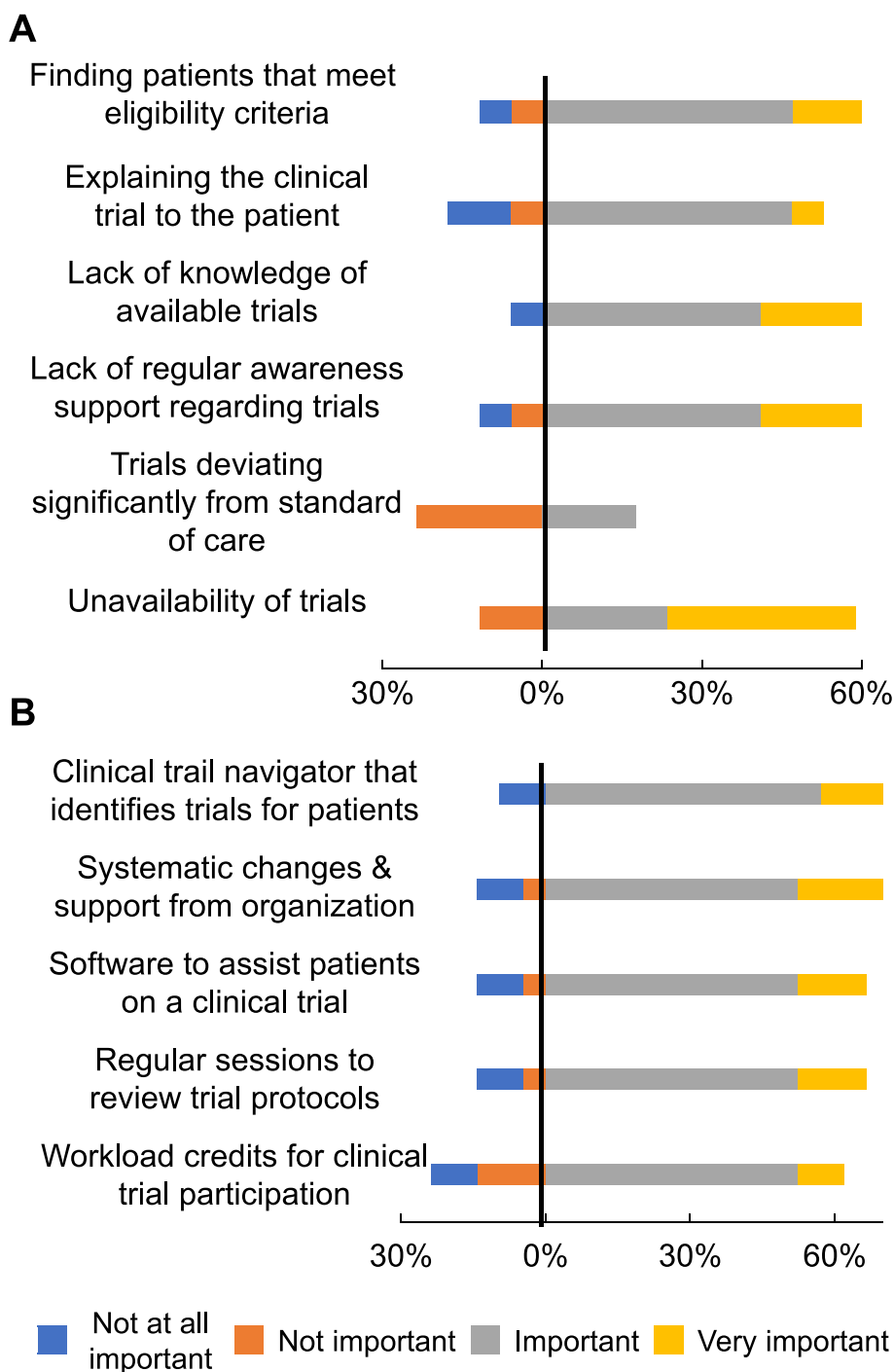


Fig. 2. Physician related barriers and enabling factors. (A) Physician’s ranking of barriers that prevent them from enrolling patients in clinical trials (n = 17). (B) Physician ranking of enabling factors that could increase patient accrual to clinical trials (n = 21).

their current physical state, and the physicians more experienced in this part of the patient journey. We also have to acknowledge that this patient population may not represent the average patient in a community cancer clinic, as over 35 % had a household income of more than \$100,000. As well we may have a younger population with 38 % of respondents between ages of 35 and 49 years. However, it is important that physicians are aware of the discrepancies between theirs and the patients’ perceptions of patient barriers to and motivations for participating in clinical trials. In addition, we are now collecting equity, diversity and inclusion information on the patients who use the CTN program.

A second limitation to this study is the small sample size of patients and clinicians. Medical oncologists made up <10 % of physician survey respondents in this study. Other studies have found that clinical trial referral ideals and behaviours tend to differ between medical oncologists and other specialties [5], so it is difficult to generalize our results to the field of medical oncologists. To address this, we plan to expand the survey to medical oncologists across Canada to validate these findings.

5. Conclusion

In this study, we have identified a new barrier to clinical trials

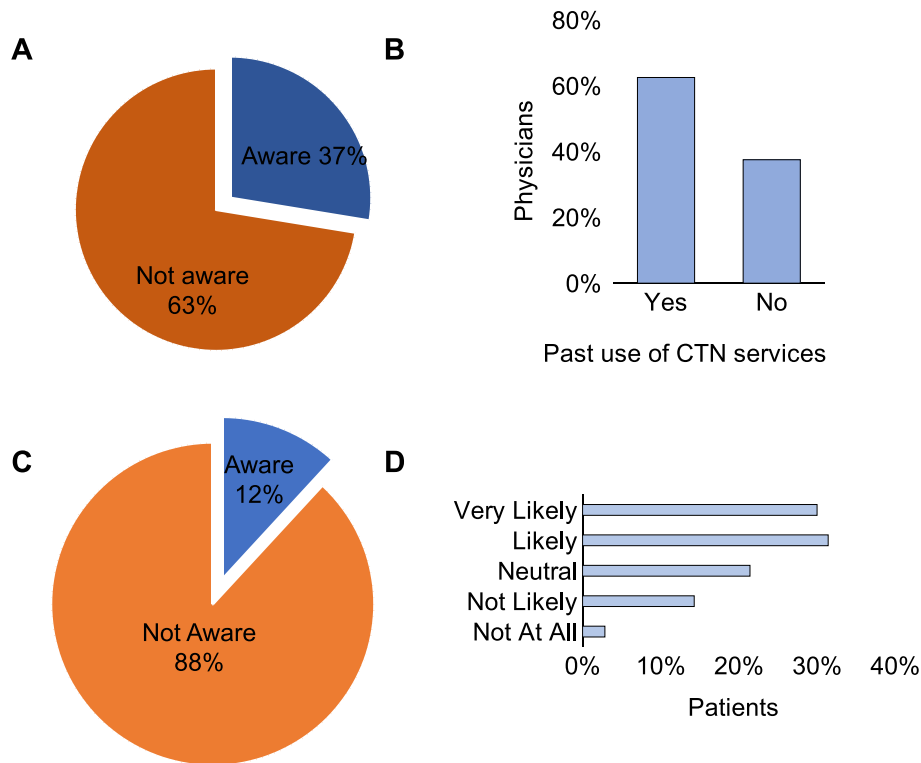


Fig. 3. Physician and patient awareness and use of Windsor Regional Hospital Clinical Trials Navigator. (A) Physicians' awareness of the Clinical Trials Navigator (CTN) at Windsor Regional Hospital (n = 29). (B) The usage by aware Physicians' of the CTN and referral of patients (n = 8). (C) Patient's awareness of a CTN program at Windsor Regional Hospital (n = 59). (D) Likelihood of patients speaking with a CTN to find a clinical trial (n = 70).

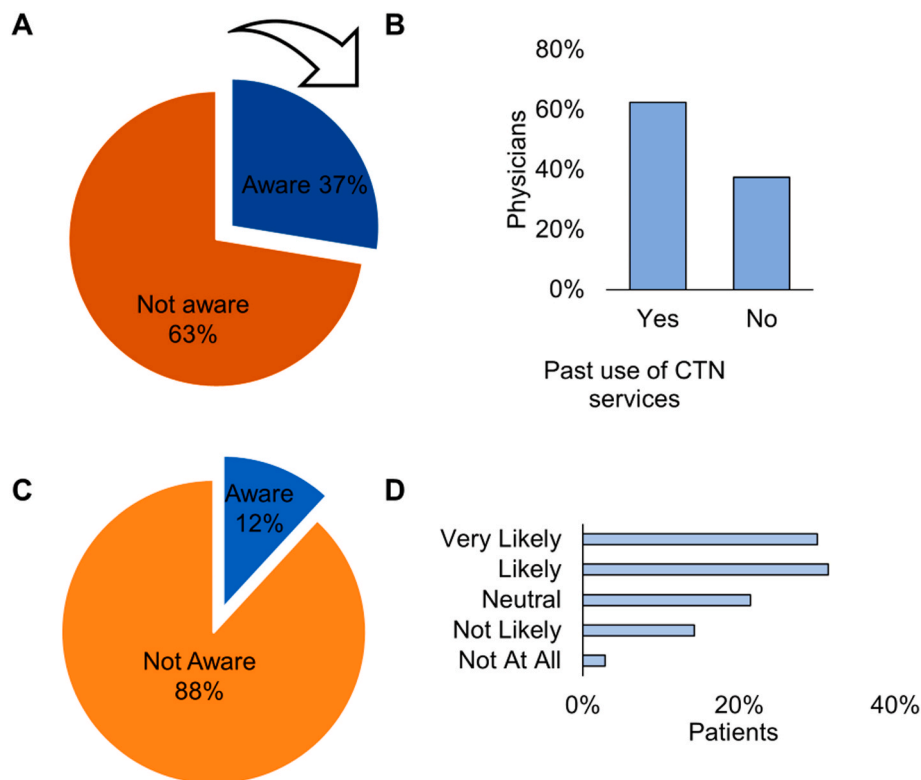


Fig. 4. Physician and patient awareness and use of Windsor Regional Hospital Clinical Trials Navigator. (A) Physicians' awareness of the Clinical Trials Navigator (CTN) at Windsor Regional Hospital (n = 29) (B) Physicians' usage of CTN and referral of patients (n = 8). (C) Patient's awareness of a CTN program at Windsor Regional Hospital (n = 59) (D) Likelihood of patients speaking with a CTN to find a clinical trial (n = 70).

accrual. This barrier is the perception by the physician that patients are less willing to spend time and money travelling to a clinical trials site, outside of their own cancer treatment site. We demonstrated in this study that patients are interested and motivated to travel for clinical trials. In Canada, this is a significant barrier, as patients cannot self-refer for clinical trials participation as this must be done by the treating physician.

Further research to better understand the rationale behind the perceptions of both physicians and patients are needed. As well, dissemination of this finding is needed to better educate physicians of this discrepancy, in order to increase awareness of a potentially unsubstantiated bias.

Credit roles

Melissa Fenech: Data curation; formal analysis; investigation; original draft writing; review and editing. **Maegan Miklas:** Data curation; formal analysis; investigation; review and editing. **Youshaa El-Abed:** Conceptualization; data curation; methodology. **Devinder Moudgil:** Conceptualization, data curation; investigation; methodology; project administration; review and editing. **Rhonda Abdel-Nabi:** **Kayla Touma:** **Mahmoud Hossami:** **Olla Hilal:** Data curation **Milica Paunic:** Data Curation **Renee Nassar:** **Farwa Zaib,** **Sanghyuk Rim,** **Roaa Hirmiz:** data curation, investigation; **Dora Cavallo-Medved:** Conceptualization; data curation; investigation; methodology; supervision. **Caroline Hamm:** Conceptualization; data curation; funding acquisition; investigation; methodology; project administration; resources; supervision; original draft writing; review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

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