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Improving clinical trial enrollment in minority racial and ethnic patients with gynecologic malignancy

Olivia D. Lara [a], Kathryn Allen [b], Amin Yakubov [b], Bhavana Pothuri [b,*]

[a] Division of Gynecologic Oncology, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA
[b] Department of Obstetrics and Gynecology and Medicine, Division of Gynecologic Oncology, Laura and Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA

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ABSTRACT

Purpose: Racial and ethnic minorities remain underrepresented in clinical trials . Underrepresentation of racial groups leads to the selection of therapeutic interventions that may not be representative of the population expected to use the medicine. This study evaluates the effectiveness of a set of implementation strategies to increase underrepresented patients in gynecologic cancer clinical trials.

Methods: An interrupted time series analysis evaluating implementation strategies (pre-screening and fast-track referral) was conducted from January 2021 to May 2022. Descriptive analysis of gynecologic oncology patient screening and accrual was compared before and after intervention implementation.

Results: During the study period (pre- and post-intervention), 26 patients were screened, and 9 patients enrolled in therapeutic gynecologic cancer clinical trials. Prior to the intervention, 7 patients were screened and 2 patients enrolled onto a clinical trial. Following the intervention, 19 patients were screened and 7 patients enrolled in a cancer clinical trial. Black patients comprised 13 of 19 (68.4%) of patients post-intervention compared to 1 of 7 (14.3 %) of patients screened pre-intervention ($p < 0.05$). All 7 patients enrolled post intervention were racial and ethnic minorities (non-Hispanic Black [4 of 7] and Hispanic White [3 of 7]) compared to no minority patients enrolled pre-intervention ($p < 0.05$). Screening increased 2.5-fold for all patients, and 5- fold for minority patients. Clinical trial enrollment increased 3.5-fold following intervention.

Conclusions: A combination of pre-screening and fast-track referral intervention in a racial and ethnically diverse urban academic hospital was associated with a significant increase in minority screening and enrollment. Structured strategies to overcome barriers to underrepresented racial and ethnic patient accrual in academic hospitals are urgently warranted.

1. Introduction

Cancer clinical trials are critical to cancer research as they lead to new standards of care and can improve patient outcomes. Racial and ethnic minority representation in trials is imperative to establish generalizability of study results and in the development of new therapies. (Fashoyin-Aje et al., 2021; Pothuri et al., 2023) This is particularly important in gynecologic malignancies as recent trends in the United States have demonstrated increasing incidence of gynecologic cancers and survival differences from cancer by race. (Siegel et al., 2024; Lu and Broaddus, 2020; Somasegar et al., 2023; Clarke et al., 2022) Despite US Food and Drug Administration (FDA) recommendations that trials should represent the population they are intended to treat, enrollment among minority participants remains low. (Freedman et al., 1995; Duma et al., 2018) Additionally suboptimal race reporting, and lack of subgroup analysis occurs regularly in landmark oncologic trials. (Loree et al., 2019).

Low minority participation in cancer clinical trials is multifactorial. (Guerra et al., 2023) Barriers to trial enrollment include institutional inequities, patient and clinician factors. (Oyer et al., 2022) Clinician bias may limit who is screened and referred for clinical trial. Additionally, lack of time, resources, and staff may limit the recruitment of participants to trial regardless of race or ethnicity. Patients from racial and ethnic minority populations also face unique financial, language and

* Corresponding author at: Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, Perlmutter Cancer Center, NYU Langone Health, 240 East 38th Street, 20th floor, New York, NY 10016.
E-mail address: bhavana.pothuri@nyulangone.org (B. Pothuri).

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other social determinants of health related barriers often coupled with medical mistrust and lack of information to enroll in a trial. (Nipp et al., 2019) A multifaceted strategic approach must be utilized to overcome these complex issues.

NYU Langone Medical Center serves a diverse population and has a longstanding clinical partnership with NYC Health + Hospitals/Bellevue to ensure patients have equitable care and access to innovative therapies including clinical trials. Patients identified at Bellevue Hospital can be referred for participation in any clinical trial available at NYU Langone Perlmutter Cancer Center. We recognized a need to provide better access to clinical trials among our gynecologic oncology patients cared for at Bellevue gynecologic oncology clinics. Providers noted patients were often interested in clinical trial but delays in screening and follow-up created barriers to enrollment. Given these concerns, our aim was to determine how a set of pre-screening and fast-track referral strategies could increase trial participant screening and enrollment. We hypothesized that low clinical trial participation among minority patients could be partly overcome with clinician and institutional awareness and engagement.

2. Methods

2.1. Study design and patient population

We performed an interrupted time series analysis to examine the effects of pre-screening and fast-track referral interventions experienced by gynecologic cancer clinical trial participants at NYC Health + Hospitals/Bellevue Hospital a large, academic cancer center serving a diverse population. Patient accruals were documented over a 17-month period between January 1, 2021 and May 1, 2022 and were separated into 10 months of pre-intervention data (January 2021 to October 2021) and 7 months of post-intervention data (November 2021 to May 2022). Patients included from this study were seen at Gynecologic Oncology outpatient clinic. Demographic and clinical information were obtained retrospectively using the electronic medical records.

2.2. Intervention

We approached members of the Division of Gynecologic Oncology and clinical trials office at New York University Langone Hospital and NYC Health + Hospitals/Bellevue Hospital. All members of the division (7 attending Gynecologic Oncologists and 3 Gynecologic Oncology fellows) agreed to participate in the intervention. All providers attended a weekly clinical trials portfolio meeting where screening and accrual numbers were reviewed at each institution. Clinical trial study coordinators were identified at each site to coordinate screening and fast-track referral. All members of the clinical trial study team were also in attendance at weekly meetings. Interim quarterly updates were provided at this meeting to monitor screening and accrual pre- and post-study intervention. The screening intervention process included both physician-led and clinical trial coordinator pre-screening of electronic clinic schedules at the participating clinics (Fig. 1). Physicians identified patients scheduled for outpatient gynecologic oncology visits with new or recurrent gynecologic malignancy. These patients were then screened by clinical trial coordinator via their electronic medical record to assess trial protocol eligibility. The electronic medical record of these patients were reviewed at minimum 1 business day prior to their clinic appointment. Patients who met the criteria for trial eligibility were then approached at their upcoming clinic visit. Patients cared for at NYC Health + Hospitals/Bellevue Hospital who were eligible and interested

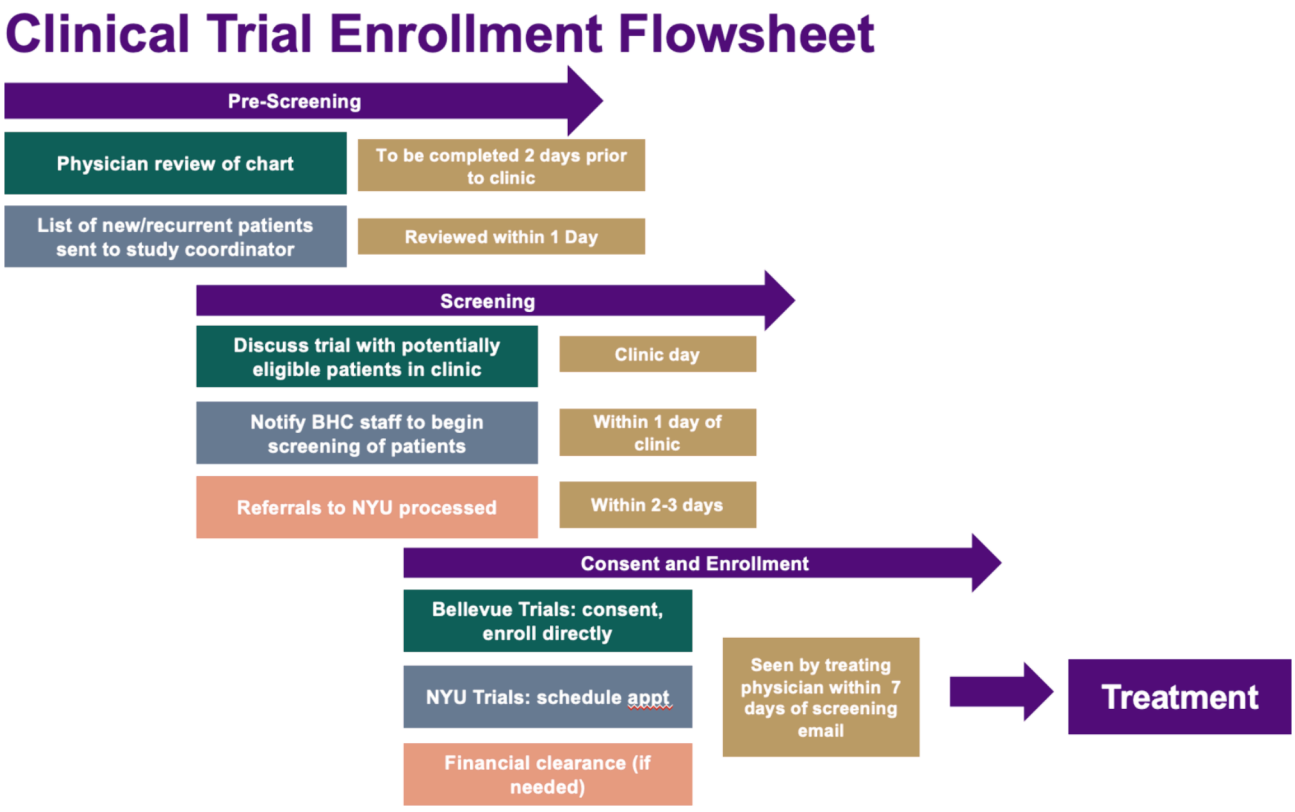

Fig. 1. Pre-screening and fast-track referral implementation strategy. Clinical trial pre-screening began with manual review of electronic medical records at Bellevue Hospital Clinic (BHC) by the Gynecologic Oncology physician team. A list of new patients and new recurrences were sent to study coordinator for pre-screening. Patients identified as potential candidates for study were approached at upcoming clinic visit. Referral and follow up appointment for patients eligible and whom voiced interest was initiated immediately by notifying fast-track team. Team consisted of New York University (NYU) study coordinator, NYU study principal investigator and financial navigator. Time from screening to follow up appointment with study team goal was within 7 days.

in clinical trial at NYU Langone Hospital were then appropriately referred. An agreement between NYU Langone Hospital and NYC Health + Hospitals/Bellevue Hospital exists that pre-dated this intervention to allow patients identified at Bellevue Hospital to access novel clinical trials at NYU Langone Perlmutter Cancer Center. Once a patient was identified for referral pre-identified personnel in financial navigation and a clinical trial coordinator at both hospital locations were notified. Referral and financial clearance were prioritized to be completed within 3 days of initiation. Clinical trial participants from NYC Health + Hospitals/Bellevue Hospital were then seen within 7 days at NYU Langone Hospital for consent and enrollment.

2.3. Statistical analysis

Monthly screening and accrual rates were collected for each of the study periods. Comparisons were made between pre- and post- intervention. Descriptive statistics including T-test and chi-squared analysis were utilized to describe the patient characteristics in the study cohort. Statistical significance was defined as $P<0.05$. All statistical analyses were performed using SPSS statistics software.

3. Results

3.1. Screening and accrual

During the entire study period (pre- and post- intervention) 26 patients with gynecologic malignancy were screened for cancer clinical trial. (Table 1). Of the entire study period (pre- and post- intervention) 9 (34.6 %) went on to enroll into clinical trial. Among the pre-intervention group, the majority of patients who were screened (n = 7) were of White race (6 of 7 [85.7 %]) and non-Hispanic ethnicity (4 of 7 [57.1%]) (Fig. 2). Notably the pre-intervention group consisted of 5 (71.4 %) non-English speaking patients. Of those screened pre-intervention only non-Hispanic White patients enrolled into trial (n = 2).

Post-intervention 19 patients were screened and 7 patients enrolled into clinical trial. Black patients comprised 13 of 19 (68.4 %) of patients post-intervention compared to 1 of 7 (14.3 %) of patients screened pre-intervention ($p < 0.05$). We saw a decrease in number of Hispanic patients screened post-intervention from 42.9 % (3 of 7) to 15.8 % (3 of 19). Overall post-intervention we saw a 2.5-fold increase in total screening and a 5-fold increase in screening of minority patients. Of those screened, 7 patients enrolled into clinical trial. All patients enrolled into trial were of minority race (4 non-Hispanic Black patients and 3 Hispanic White patients). The majority of new screenings and enrollments post-intervention were seen in patients with a new diagnosis of cervical or uterine malignancy.

Table 1
Screened Patient Characteristics.

Characteristic	All, n (%)	Pre-intervention, n(%)	Post-intervention, n (%)	P-value
Age, median, y	60	59	61	0.67
Race				0.01
White	10 (38.4)	6 (85.7)	4 (21.0)	
Black	14 (53.8)	1 (14.3)	13 (68.4)	
Asian	2 (7.7)	0 (0)	2 (10.5)	
Hispanic				0.15
Yes	6 (23.1)	3 (42.9)	3 (15.8)	
No	20 (76.9)	4 (57.1)	16 (84.2)	
Primary Language				0.02
English	15 (57.7)	1 (14.3)	14 (73.7)	
Spanish	5 (19.2)	3 (42.9)	2 (10.5)	
Other	5 (19.2)	2 (28.6)	3 (15.8)	
Cancer Type				0.04
Ovary	2 (7.7)	2 (28.6)	0 (0)	
Cervix	10 (38.5)	3 (42.9)	7 (36.8)	
Uterine	14 (53.8)	2 (28.6)	12 (63.1)	
Disease status				0.001
New	17 (65.4)	1 (14.3)	16 (84.2)	
Recurrent	9 (34.6)	6 (85.7)	3 (15.8)	
Enrolled	9 (34.6)	2 (28.6)	7 (36.8)	0.70

3.2. Clinical trial selection

Clinical trials were stratified by disease setting as upfront, advanced stage/recurrent and recurrent maintenance as well as disease type ovary, endometrial, cervical, or basket trials. Basket trials included any solid tumor histology. Only interventional therapeutic clinical trials were included in this study. Non-therapeutic trials were excluded. Overall, 18 trials were open during the study timeframe with comparable number of trials open pre- and post- implementation. 16 trials were open in the pre-implementation cohort, between January 2021 and September 2021, and 17 trials open in the post-implementation cohort, between October 2021 and May 2022 (Table 2).

4. Discussion

Our findings show that through the implementation of pre-screening and fast-track referral strategies, clinical trial screening and enrollment for minorities can be increased. Overall, after implementation, we saw an increase in racial and ethnic minority patients screened and enrolled to trial. Enrollment of racial and ethnic minorities into cancer clinical trials is crucial to ensure developing cancer therapies are representing the general population for which they intend to serve. (Fashoyin-Aje et al., 2021) We saw the most drastic increase in screening and enrollment among patients with uterine and cervical malignancies, each with striking racial disparities in incidence and mortality. (Siegel et al., 2024; Giaquinto et al., 2022) Notably we saw an over 5-fold increase in screening among patients with uterine malignancy of which the majority were patients of Black race. Given the almost two-fold increase in mortality among Black patients with uterine malignancies, these results are critical to informing strategies to improve access to innovative therapeutics for all populations.

While we found utilizing clinician and institutional awareness can increase minority clinical trial participation in cancer trials, other barriers still exist. Clinician bias regarding who is screened and referred can play a role in racial and ethnic diversity in cancer clinical trials. (Oyer et al., 2022; Barrett et al., 2023) The ASCO-ACCC guidance on increasing racial and ethnic diversity in clinical trials recommends all patients be pre-screened. (Guerra et al., 2023) To further combat clinician bias, one study investigated the feasibility and utility of an implicit bias training program followed by peer-to-peer discussions to increase racial and ethnic diversity in clinical trial selection. (Barrett et al., 2023) Not only did they find support for the ease of utility in implementing training programs but sustained knowledge on how to address implicit bias six weeks post training. Overall, participants agreed that asking patients outright about their interest in clinical trial participation can help combat implicit bias in the clinic. (Barrett et al., 2023) Institutional barriers including time, resources, and selecting which trials are open at sites can also limit racial and ethnic minority enrollment into clinical trials. (Oyer et al., 2022).

As seen with this study, ensuring staff are aware of ongoing clinical trials at an institution through the assistance of study coordinators and

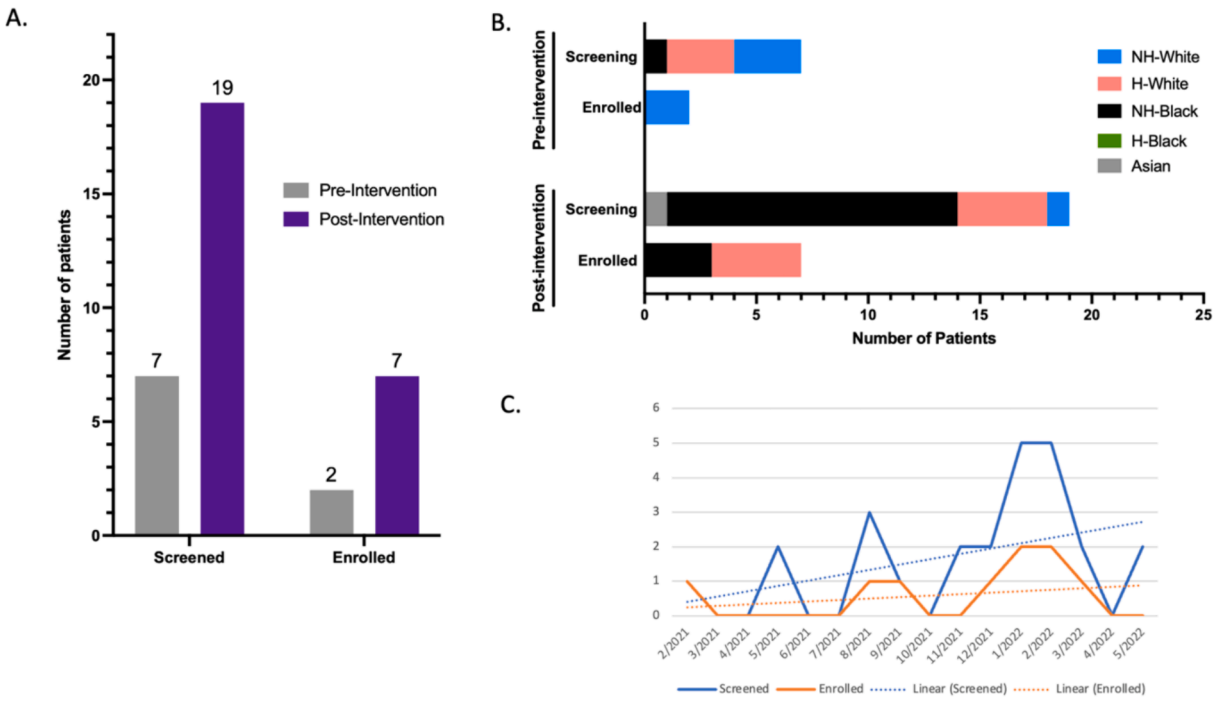

Fig. 2. A total of 26 patients were screened and 9 patients enrolled pre- and post-intervention (A). Increase in screening and enrollment largely attributed to minority populations (B). A rising increase in total enrolled and screened patients was seen over the study period (C).

Table 2
Clinical Trials Included in the Study.

Tumor Type	Upfront Treatment	Advanced Stage/ Recurrent	Recurrent Maintenance	Number Available 01/2021 to 09/2021	Number Available 10/2021 to 05/2022	Total Number available
Ovary	1	4	0	5	5	5
Endometrial	3	2	1	4	6	6
Cervical	1	2	0	3	3	3
Basket (any solid tumor)	0	4	0	4	3	4
Total	5	12	1	16	17	18

investigator involvement can help minimize this barrier. Additionally numerous studies have shown the benefit of patient navigation in clinical trial screening, enrollment and retention. (Myers et al., 2014; Wang et al., 2010; Uveges et al., 2018) However, in tandem, placing responsibility onto trial sponsors to design studies without overly limiting eligibility criteria as well as minimizing financial burden onto patients may improve study enrollment. (Kumar et al., 2022) Providing financial reimbursement through clinical trials remains a topic of discussion from the institutional level of the institutional review board (IRB) and sponsor level, to state and federal legislature. One study investigated the effect of a cancer care equity program (CCEP) on study enrollment. They found through the CCEP, which provided financial assistance for trial expenses like lodging and travel, study enrollment increased in particular with younger participants, women, and people with lower incomes. (Largent and Lynch, 2018).

Limitations to our study include a small sample size and single site selection. Broadening the pre-screening efforts across multiple sites in other urban academic settings may provide more insight as to the effects of clinician and institutional awareness on participant enrollment. Additionally, the retrospective data collection was limited in time to start in January 2021 as prior to this in 2020, COVID-19 was a confounding factor affecting in-person participant recruitment, enrollment, and study availability.

Further research is encouraged to explore the multifactorial barriers present in clinical trial enrollment for ethnic and racial minorities. While this study emphasizes the importance of pre-screening and fast-track referral strategies, other barriers to enrollment persist and require various solutions to provide patients with equal access to clinical trials and ensure the generalizability of studies to the populations they serve.

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Authors' Contributions.

O.D.L., B.P. contributed to the study design, acquired, and analyzed data, generated figures, and wrote the manuscript. K.A. and A.K. contributed to data acquisition. All authors contributed to the interpretation of data, vouched for the data analysis, contributed to the editing of the manuscript, and agreed to publication of this study.

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CRediT authorship contribution statement

Olivia D. Lara: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Kathryn Allen:** Writing – review & editing, Writing – original draft, Data curation. **Amin Yakubov:** Writing – review & editing, Data curation. **Bhavana Pothuri:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition.

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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