

Examining Enrollment Barriers to Adult Cancer Clinical Trials

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Abstract

Advancing knowledge in cancer treatment can only be achieved with the conduct of clinical trials. Barriers to adult cancer clinical trial participation have been extensively examined, yet nearly 20% of trials fail due to low patient enrollment. This dissertation considers the gaps in knowledge related to health policy, healthcare industry changes, and variation in oncology service provider behavior in the conduct of cancer clinical trials.

In the first study, we used data collected from an internet-based survey of cancer clinical trial sites across the nation and found that sites continued to receive insurance coverage denials for patients seeking treatment through participation in a cancer clinical trial after the 2010 Affordable Care Act's mandate requiring most private health insurers to cover routine patient care costs for trial participation. Organizational characteristics of being National Cancer Institute designated and having previous state legislation related to coverage for clinical trial participation were not associated with receiving denials, while being an academic medical center and using a precertification process were significantly associated with receiving insurance denials. These results suggest that insurance denials and delays continue to be formidable barriers to the research community in achieving adequate and timely trial enrollment, thus negatively affecting the pace of cancer discovery.

The second study used previously collected qualitative data and a validated theoretical framework to understand the substantial decrease in clinical trial enrollment related to changes in community cancer site personnel behavior after being acquired by a large, tertiary health system. These staff perceived many barriers to enrollment being present after the acquisition, particularly related to the opportunity and their capability to conduct clinical trials. The lack of support to conduct clinical trials by having adequate staff and available trials within which to enroll were

perceived to be the primary barriers. Use of a theoretical model to understand changes in behavior adds to the empirically-based clinical trial enrollment barrier literature, and may be more helpful in matching future interventions to behavior determinants to address remaining barriers.

There is demonstrated variation in providers following treatment guidelines. The final study was a retrospective analysis of data from a large health system's electronic health record and clinical trial management systems to assess radiation oncologist variation in the completion of a field for recording patient assessment for trial participation. Completion of this field may serve as a proxy for radiation oncologist awareness of available clinical trials. We found radiation oncologist characteristics are not significantly correlated with recording patient assessment for clinical trial participation. This field was completed just over 40% of the time, identifying the need for additional evaluation of the factors motivating radiation oncologists to complete this field.

Overall, there are organization and provider factors that negatively affect cancer research centers efforts to identify and enroll adult cancer patients into clinical trials.

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“If it wasn’t hard, everyone would do it.”

-Tom Hanks, *A League of Their Own*

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“That which does not kill us, makes us stronger.”

-Friedrich Nietzsche

Life is funny in that it continues, even though you think it won’t. Mom, I miss you every day and know you would be front and center cheering through this graduation ceremony, as you always were. I promise I have not become a professional student.

“Prior Planning Prevents Piss Poor Performance.”

-Wise Mentor

My family and friends have been (mostly) understanding as I’ve been on this crazy and winding road. Shawn, you know I love you dearly but I must ask, “What’s next?”

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List of Abbreviations

AIC	Akaike information criterion
AACI-CRI	American Association of Cancer Institutes- Clinical Research Initiative
ACA/PPACA	Affordable Care Act/Patient Protection and Affordable Care Act
ASCO	American Society of Clinical Oncology
CMS	Centers for Medicare & Medicaid Services
COM-B	Capability, Opportunity, Motivation behavior framework
CONSORT	Consolidated Standards of Reporting Trials
CTMS	Clinical Trial Management System
e.g.	Latin <i>exempli gratia</i> , meaning for example
EHR	Electronic Health Record
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
i.e.	Latin expression <i>id est</i> , which translates to “that is”
MA	Medicare Advantage
NCD	National Coverage Determination
NCI	National Cancer Institute
PIS	Patient Information Sheet
TDF	Theoretical Domains Framework
TWM	Temporary Work Modification
US	United States

Chapter I: Introduction

Although it is estimated that over 1.7 million new cancer cases will be diagnosed and there will be nearly 610,000 deaths in the United States (US) throughout 2018, the overall cancer death rate has fallen by 25% over the last 25 years.¹ Decreases in the overall death rate from cancer in the US have been attributed to a number of factors including more effective treatments, which are only available after rigorous evaluation through the conduct of clinical trials. Clinical trials are required for identifying new, more effective therapies for disease prevention, treatment, and rehabilitation for many diseases.² Lack of timely and adequate clinical trial enrollment limits generalizability of results, can result in trial cancellation, and increases the timeline for regulatory approval of new therapies,³⁻⁵ consequently delaying information needed to develop improvements in patient care. Low trial accrual also jeopardizes institutional accreditation from key credentialing bodies such as the American College of Surgeons⁶ and National Cancer Institute (NCI),⁷ potentially reducing patient access to the most innovative and specialized care from a team of cancer experts.

The NCI is the world's largest funder of cancer research with a 2019 fiscal year budget just over \$5.6 billion,⁸ and throughout the past decade, had an average yearly enrollment to cancer clinical trials of over 20,000 patients.⁹ The Institute of Medicine's 2010 assessment of the NCI's clinical trial network found that nearly 40% of trials never completed¹⁰ and subsequent analysis of NCI funded trials reported similar findings. Cheng et al. analyzed trials conducted from 2000-2004 and reported nearly forty percent (37.9%) of trials failed to achieve enrollment goals.¹¹ Considering phase III trials from 2000-2007, Korn et al. estimated nearly a third (28%) of the trials were discontinued due to meeting less than 90% of the recruitment goal.¹²

The largest cost in the research and development of new treatments for biopharmaceutical companies is the conduct of clinical trials; billions of dollars are spent every year in this stage of development.¹³ A seven year evaluation of enrollment to adult cancer clinical trials reported to clinicaltrials.gov (the largest clinical trials database run by the National Institutes of Health), found a similar rate of the number of trials that failed to meet enrollment (39%), and industry sponsored trials were more likely than federally funded trials to not be completed.¹⁴ The cost of low enrolling trials to clinical trial sites is also significant. One institution estimated the cost of uncompensated patient care for low enrolling trials to be \$1 million a year, not including investigator time and effort, and a greater number of low-enrolling trials were government funded over industry-sponsored.¹⁵

The significant investments wasted when trials fail to achieve enrollment goals are not solely related to the financing of conducting trials. There are lost opportunity costs for those funds. The funds are unable to be spent supporting more successful programs. There are ethical challenges when patients willingly participate in clinical trials, yet their contribution is never realized. Finally, the wait to get new treatments to those most in need is prolonged. Gaining a better understanding of the barriers that contribute to low enrollment into adult cancer clinical trials is the first step in eliminating these barriers, with the goal to achieve greater trial completion.

Researchers have long sought to explain low trial enrollment, but despite the barriers to enrollment having been extensively examined and reported in the literature,^{4,16-22} timely and adequate enrollment to clinical trials remains a challenge. Researchers have identified barriers to clinical trial enrollment as specifically related to the organization, physician, and patient.^{21,23-25} Patient-related factors are based upon an individual's decision to participate in a trial and take

into account family, faith, and trust in the health care system,²⁶ factors generally beyond the control of health care administrators. Non-patient barriers, specifically those related to research organizations (clinical trial sites) and physicians, have the potential to be more actionable by cancer center leadership in mitigating enrollment barriers due to the likelihood of these barriers affecting all potential trial patients. Organizations successful in achieving trial enrollment goals have infrastructure including adequate staff and research support,²⁰ physician-level accrual expectations established by organizational leadership,²⁴ and mechanisms in place to address the financial costs of conducting and participating clinical trials.²⁷

Conceptual Framework

The process of enrolling a patient into a clinical trial is complex and is shaped by the engagement of the stakeholders at multiple levels, including interaction between the patient, physician and the broader environment in which care is being provided (the organization). Previous research evaluating adult cancer clinical trial enrollment identified the barriers to enrollment specifically related to the organization, physician and patient.^{21,23-25}

The framework by Ford et al. describes influences on recruitment and retention of patients by detailing three key factors: *Awareness, Opportunity and Acceptance* (Appendix A). These researchers posit that in order for a patient to accept or refuse trial participation, they must first be aware of the trial, then have the opportunity to participate.²⁸ The patient deciding to participate in and being eligible for a trial is the ideal outcome, however there are elements that must be in place to get to the point of the patient making this decision.

Barriers to trial participation were grouped into structural, clinical and attitudinal categories by Unger et al. (Appendix B). In this simplified flow diagram of the trial enrollment process, these researchers also recognized that there are sequential steps to be taken before a

patient could even consider participating in a trial.²¹ Many of these steps are related to organization and physician characteristics. Additionally, this work identified the need to increase efforts to reduce these non-patient related barriers to facilitate increased clinical trial enrollment.²¹

Each model effectively identifies the broad pillars describing barriers to enrollment, yet synergistically may offer a stronger framework for evaluating the complexity of trial enrollment within a larger context. Therefore, adapting and combining the works of Ford²⁸ and Unger,²¹ I developed a framework conceptualizing the trial enrollment process depicting these dynamic relationships, with a focus on organizations and providers, to identify key factors influencing trial enrollment (Figure 1).

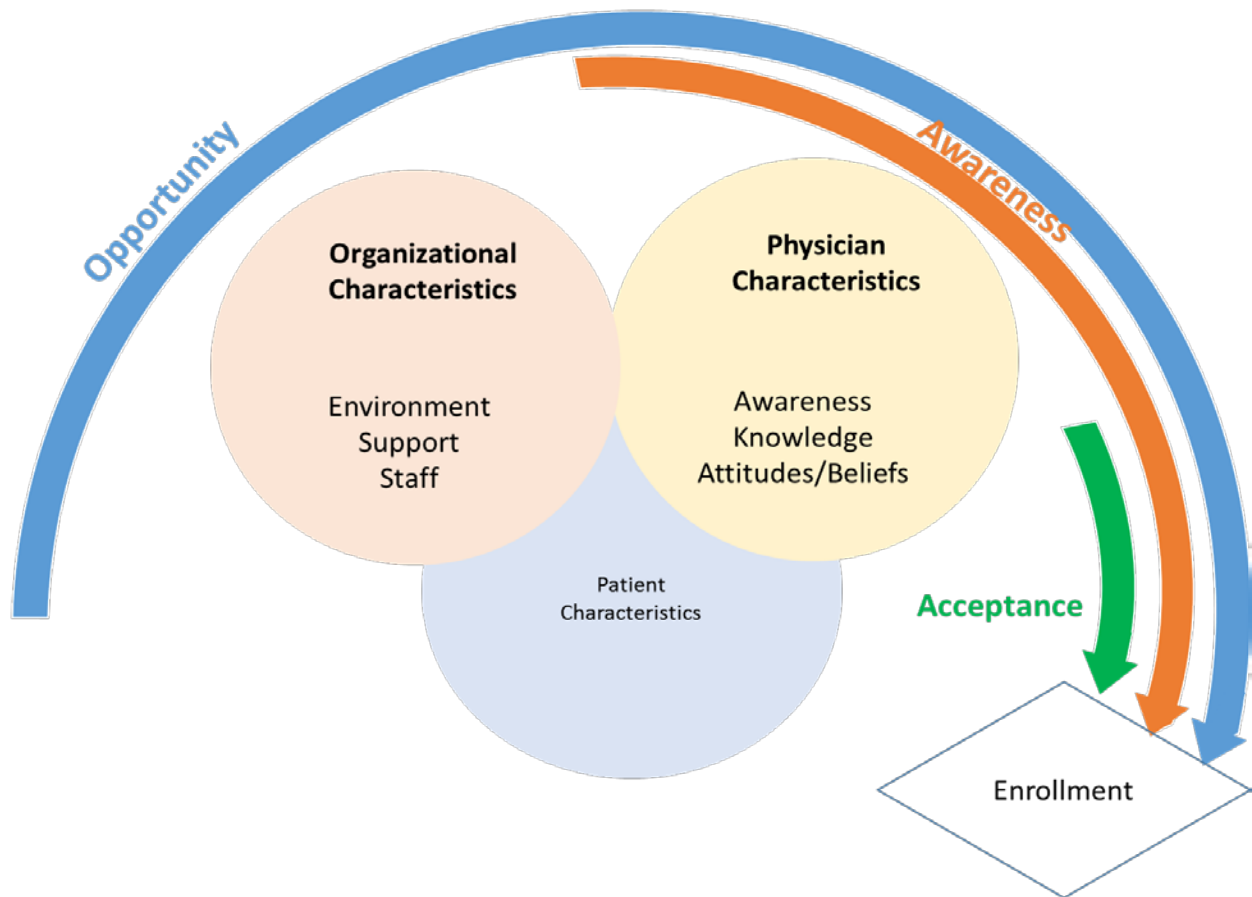


Figure 1 Conceptual Framework

Organizational characteristics include the location of the facility, the culture and personnel hierarchy (*environment*). The level of support for enrolling patients into clinical trials from the organization's leadership such as establishing accrual expectations, offering trainings and giving incentives to enroll patients, has been shown to lead to increased enrollment.²⁴ Successful trial sites have adequate infrastructure (*support*) to conduct clinical trials, including dedicated research personnel such as coordinators and nurses (*staff*),²⁰ an efficient research approval process,²⁹ and mechanisms in place to address the financial costs of conducting and participating in clinical trials.²⁷ With the necessary organizational support in place, the next crucial factor in successful trial enrollment is the physician.

Physicians have the most significant impact on trial enrollment, and it is often an oncologist's failure to offer a trial that substantially contributes to low accrual.³⁰⁻³² A physician's lack of *awareness* of available trials has been cited as one of the main reasons for low enrollment.^{4,33-35} A physician's *knowledge* of the clinical trial process, and more specifically a trial's design (i.e., inclusion/exclusion criteria and treatment groups) also affect patient clinical trial enrollment.^{36,37} Further, a physician's *attitudes and beliefs* about the scientific value, appropriate treatment course for the patient, and a patient's ability to complete the trial protocol requirements, all directly affect whether participation in a trial is even discussed.^{38,39} There are tools and interventions that can be used by physicians as decision aids when choosing a treatment path with their patients, but it is unknown to what degree tools are used and what physician characteristics are associated with their use.

Failing to offer a trial may be a result of a lack of physician awareness of available trials, a misunderstanding of the purpose of clinical trials, or limits on sufficient resources to thoroughly discuss trial participation with the patient (*structural barriers*).⁴⁰ Most of the

frameworks used for evaluating barriers to cancer clinical trial enrollment have come from empirical findings and may be incomplete. These frameworks have been used for assessing policy, organizations, providers, and patients. Using a comprehensive theoretical framework to investigate factors affecting enrollment has been suggested as a method for further exploring enrollment barriers⁴¹ and may be more helpful in matching future interventions to determinants.

The Theoretical Domains Framework (TDF), is an integrative framework that synthesizes 128 theoretical constructs drawn from 33 theories into 14 domains relevant to implementation behavior.⁴² The TDF was specifically developed to identify determinants of healthcare professional behavior,⁴² allowing for targeted change intervention. In 2012, the framework was further refined and validated, and includes the COM-B⁴³ (Appendix C). The developers of the COM-B framework suggest that an individual's behavior (B) is shaped by three essential conditions: Capability (C), Opportunity (O), and Motivation (M), collectively referred to as COM-B.⁴⁴ Capability refers to individual's psychological and physical capacity to engage in intended activities. Opportunity is defined as factors external to the individual that prompt or make behavior possible. Motivation is defined as internal psychological processes that energize and direct behavior. This framework allows for structured exploration of potential facilitators and barriers to trial enrollment.

Structure

This dissertation follows a three-essay format and explores the gaps in knowledge related to organization and oncologist characteristics influencing the conduct of cancer clinical trials. Particularly, I examine the characteristics of cancer research sites experiencing denials for health insurance coverage of adult cancer patients seeking treatment through participation in a clinical trial following the passing of national policy aimed at eliminating clinical trial insurance denials.

Next, the role of organizational transition in mediating the conduct of clinical trials is evaluated using a validated theoretical framework to understand a substantial decrease in clinical trial enrollment at sites previously recognized as high enrollers. Finally, I evaluate the variation in oncologist's use of an embedded field within an electronic health record for recording patient assessment for participation in a clinical trial.

The first essay in this dissertation assesses organizational characteristics associated with receiving insurance denials for cancer patients seeking treatment through participation in a clinical trial after the Affordable Care Act (ACA) clinical trials mandate using nationally survey data collected from research sites conducting cancer clinical trials. The ACA significantly increased the number of Americans with health insurance, and was the first national mandate to require most private health plans and insurers to provide coverage of routine patient care costs for items and services furnished in connection with participation in a clinical trial.⁴⁵ Many assumed that national policies would alleviate this enrollment barrier, since insurance denial of routine care costs for trial participation and the length of time to receive a response from the insurer about coverage, have both been identified as formidable barriers to adult cancer clinical trial enrollment.^{3-5,27,46-50} It was unknown whether comprehensive legislation would eliminate this barrier, and subsequently increase enrollment, especially since prior research on the effectiveness of state and federal policies enacted prior to the ACA and aimed at eliminating the insurance denial barrier yielded variable results regarding the impact of these policies on cancer clinical trial participation.^{3,5,18,51-54} Through this work, we sought to investigate the impact of the ACA clinical trial mandate on cancer centers, and to identify organizational characteristics that may be associated with receiving insurer denials-

Another strategy cancer centers use to increase clinical trial accrual is structural. Cancer centers can merge with or acquire high performing sites, to expand their clinical trial offerings. However, the degree to which these strategies are effective is unknown and unintended consequences of these approaches have not been assessed. Therefore, the second essay examines the experiences of community-based oncology clinic personnel to explain the significant drop in accrual to adult cancer clinical trials after acquisition by a large, tertiary academic medical center. Data from this original research included observations of each practice, conducting focus groups, and performing semi-structured interviews. These data are analyzed using the TDF to identify key organizational and provider barriers and facilitators that influence trial enrollment. This assessment follows the model to examine the overlap of *organization* and *physician* characteristics. The results provide evidence that the change in organizational structure significantly impacted the community sites' opportunity to enroll patients, providing insights into the 70% decline in clinical trial enrollment that occurred around the time of the acquisition.

Using an Electronic Health Record (EHR) has been shown to increase clinical trial participation.⁵⁵ As a strategy to address limited memory and attention related to following guidelines, the use of a prompt within the EHR for documenting assessment of patients being evaluated for palliative care substantially increased adherence to guidelines.⁵⁶ The utility of a similarly embedded field within an EHR for recording patient assessment for possible trial participation has not been assessed. My final essay uses secondary data analysis to evaluate the completion of this field by all radiation oncologists across one major health system. Radiation oncologists were studied because they see all types of cancer patients, were located across this health system's many clinics, and play an important role in trial recruitment and conduct.^{38,39}

Specific physician characteristics such as gender, time in practice, practice type, and patient volume have been found to be associated with treatment decisions and trial enrollment,^{57,58} and are used to understand the variation in provider completion of this embedded field. From February 2017 to January 2018, data extracted from both the EHR and clinical trial management system (which captures data from patients considering or enrolled into a clinical trial), are used to evaluate radiation oncologist characteristics to predict completion of the embedded field for recording patient clinical trial assessment. Then, assessment of the congruency between the recorded response and the patient's actual trial status are compared. The aims of this study are to identify key characteristics of radiation oncologists related to completion of the patient assessment for trial participation field in the electronic health record, and to estimate the level of congruency between the recorded assessment and the patient's actual trial status.

Statement of Purpose

The purpose of this multi-method study is to gain a better understanding of organizational and provider characteristics that influence enrollment to adult cancer clinical trials within the umbrella of opportunity and awareness. The dissertation contributes to the literature in three key ways. This work provides new evidence regarding cancer research center characteristics and experiences with receiving insurance denials for patients considering trial participation following enactment of the ACA's mandate for most insurers to cover cancer clinical trial participation. Next, this work is the first to analyze the motivation of the apparent behavior changes of personnel resulting in a decline in trial enrollment after acquisition by a larger entity using a validated behavior change framework. Finally, the use of an embedded field within an electronic health record by providers, specifically radiation oncologists, for recording patient assessment

for trial participation has a strong potential for large-scale, low-cost implementation across institutions that use electronic health records. This last essay contributes early evidence of physician characteristics related to field completion and awareness of patient trial status.

Chapter II: Insurance Denials for Cancer Clinical Trial Participation After the Affordable Care Act Mandate

Sections of this chapter are reprinted with permission from Mackay, C.B., Antonelli, K.R., Bruinooge, S.S., Saint Onge, J., Ellis, S.D. (2017) Insurance Denials for Cancer Clinical Trial Participation After the Affordable Care Act Mandate. *Cancer* 123, 2893-2900. The sections contributed by C.B. Mackay are presented in this chapter in full alongside new, never-before published results.

Introduction

The Affordable Care Act (ACA) has not only significantly increased the number of Americans with health insurance, but was also the first national mandate to require most private health plans and insurers to provide coverage of routine patient care costs for items and services furnished in connection with participation in a clinical trial.⁴⁵ This component of the legislation is important because insurance denial of routine care costs for trial participation and the length of time to receive a response from the insurer about coverage, have both been identified as formidable barriers to adult cancer clinical trial enrollment.^{3-5,27,46-50} An examination of this self-implementing⁶⁰ statute has yet to be reported. Research on the effectiveness of state and federal policies enacted prior to the ACA and aimed at eliminating the insurance denial barrier, yielded variable results regarding the impact on cancer clinical trial participation.^{3,5,18,51-54}

Prior to the ACA, federal regulations required trial coverage for Medicare beneficiaries. State statutes were in place to cover patients under other plans, but varied in the types of trials, beneficiaries, and payors affected, creating inconsistency in coverage. For example, Medicaid coverage rules are set by each state and not every state requires trial coverage for Medicaid plans.⁶¹ Under the ACA, some plans (i.e., grandfathered plans) are exempt from the trial coverage mandate.

Grandfathered plans are insurance plans that existed on or before the date of ACA implementation (March 23, 2010) that have not made significant coverage changes since that date. These plans are not required to meet the ACA's clinical trial provision as long as they maintain their pre-ACA set of benefits.⁶² Health insurance plans federally regulated under the Employee Retirement Income Security Act of 1974 (ERISA) can qualify as grandfathered health plans, and be exempt from the coverage requirement.⁶³ The degree to which these exempt plans affect trial participation is unknown.⁶⁴ The current national initiative to accelerate cancer research to "end cancer as we know it" by doubling the pace of cancer research over the next five years,⁶⁵ will likely involve conducting more clinical trials and enrolling more patients in trials. The success of this "Cancer Moonshot"¹ may be impacted if insurance denials and delays for trial participation continue.

The goal of this study was to assess early implementation of the ACA clinical trials mandate for cancer patients. Specifically, we aimed to understand if insurance denials persist, and if so, to evaluate the reasons insurers used to justify denying coverage, as well as to identify specific research site characteristics associated with denials.

Method

Study Sample

We surveyed diverse organizations conducting cancer clinical trials in 2015 regarding their experience with insurance coverage denials throughout the 2014 calendar year; the first year of the ACA trial mandate. The sampling frame consisted of academic- and community-based research sites conducting cancer clinical trials and affiliated with the American

¹ In 2016, the National Cancer Moonshot Initiative was launched to increase efforts aimed at the prevention, diagnosis, and treatment of cancer by achieving a decade's worth of progress in five years.

Association of Cancer Institutes-Clinical Research Initiative (AACI-CRI), American Society of Clinical Oncology- Research Community Forum, Midwest Cancer Alliance, and the Oncology Nursing Society-Clinical Trials Nurses Special Interest Group. Approximately 550 non-duplicate, distinct research sites were represented by these four organizational membership lists in the initial survey, with a subset of these sites represented in the focused survey. Survey participants were incentivized with opportunities to receive a tablet computer and gift cards. The institutional review board at the University of Kansas-Lawrence exempted this study from human subjects review.

Survey Design

The survey questions were drafted using an iterative design process, with review by content experts. The survey asked participants to report on interventional treatment trials to narrow the scope of the project to include only cancer treatment (versus prevention or detection) trials. Pre-testing of the survey questions was performed with four representatives from the sampling frame. Based upon feedback and a review of the data, the survey was divided into two instruments using multiple choice and open-ended responses to improve clarity. Survey administration followed the recommendations of Dillman et al.⁶⁶ for internet-based surveys and both surveys were administered through SurveyMonkey[®].⁶⁷

Data Collection

Initial survey

To rapidly ascertain if insurance denials continued after ACA's directive, effective January 1, 2014, the initial survey (Appendix D) was launched on April 6, 2015, capturing responses over a five-week period. Emails with the survey link were sent by the respective organizations to 1,412 individuals associated with at least one of the participating organizations.

The initial five-question survey asked respondents to report experience with receiving denials from insurance companies for patients seeking trial participation along with basic site characteristics. Respondents were also asked to identify an organizational representative who could provide more thorough information about their oncology clinical trials program, including the process for determining insurance coverage for potential trial participants. This brief questionnaire provided a timely, broad assessment of the status of clinical trial insurance denials.

Focused survey

The follow-up focused survey (Appendix E) was conducted May-July 2015 and was sent to key informants identified from the initial survey, as well as interested individuals identified during the July 2015 AACI-CRI meeting. This survey included 31 items pertaining to additional detailed experiences with insurers related to coverage for trial participation as well as a more comprehensive set of organizational characteristics.

Measures

The main outcome variable was responses from insurers to cover routine care costs for trial participation (no/yes). Having confirmed that sites were experiencing denials, we sought to identify research site characteristics associated with denials and to evaluate the reasons sites recorded as the insurers' explanations for denying coverage. We collected the reasons sites were given from the insurers for denying coverage (non-mutually exclusive categories). Delays in the initiation of treatment for cancer are known to significantly affect morbidity and mortality,^{68,69} thus we evaluated the number of days to receive the insurer's response regarding trial coverage.

Site characteristics included type of organization (academic or community), any National Cancer Institute (NCI) designation, annual clinical trial enrollment, and use of a precertification process, all coded as (no/yes). Precertification refers to obtaining approval from a patient's

insurer or health plan before ordering certain tests or administering treatments, to confirm insurance payment and to inform the patient of any healthcare costs for which the patient may be responsible. Nearly forty states and the District of Columbia enacted laws or cooperative agreements requiring insurers to cover routine care costs of cancer clinical trials prior to the ACA, thus a variable to control for previously existing state laws was included.

To minimize bias, duplicate entries from the same institution were deleted after being evaluated by two of the researchers, using an algorithm to identify identical responses by institutional name, city, and zip code. If the institution's name was identical but the city was different, both entries were retained to reflect multiple locations. If the name and city were identical, the entry reporting the highest enrollment was kept, with the expectation that with higher enrollment, sites would have greater experience interacting with insurers. Surveys returned with missing responses for the variables under evaluation were excluded from analysis.

Statistical Analysis

We summarized the reported experiences with insurance denials by number and percent response. Univariate statistical analysis was used to assess whether receiving an insurance denial occurred with use of a precertification process and separately with the presence of previous trial coverage legislation. Multivariable logistic regression was used to measure the relationship between experiencing denials and performing precertification, controlling for the number of enrollments and presence of previous state law. We used additional univariate analysis to evaluate potential associations between the variables in the focused survey. Relationships between variables were considered statistically significant at the $p \leq 0.05$ level. Analyses were conducted using Stata statistical software version 14.0.⁷⁰

Results

Denial Experience

The initial survey sample included 1,412 individuals, which yielded 309 responses (22% response rate). Following the *a priori* algorithm, we excluded 57 responses (46 duplicates and 11 incomplete), analyzing 252 unique site responses. Respondents represented 48 states and the District of Columbia. Most respondents (n=158; 62.7%), reported experiencing at least one insurance denial at their site during calendar year 2014. Sites with coverage legislation prior to the ACA experienced similar rates of denials as states without (82.3% vs. 85.1%, $\chi^2=50.7$, $p\leq 0.001$). Sites performing precertification were more likely than those not performing precertification to report experiencing denials (69.3% vs. 41.7%, $\chi^2=14.9$, $p\leq 0.001$). After controlling for institution type, presence of state laws, and enrollment volume, sites using a precertification process were still significantly more likely to experience denials than sites without a precertification process (OR 3.04, 95% CI 1.55-5.99).

Research Site Characteristics

Among the 204 academic and community-based sites identified for the detailed assessment, 97 responses were received, representing 33 states with a response rate of 48%. After removing incomplete entries, 77 responses from unique sites were analyzed. Characteristics of research sites by insurance denial experience during the 2014 calendar year are listed in Table 1. In this smaller subset analysis, although academic medical centers reported experiencing a denial more often than community sites (71.4% vs. 46.4%) and sites using a precertification process were more likely to report denials than sites without a process (58.7% vs. 41.3%), neither relationship showed statistical significance. None of the site characteristics evaluated showed statistical significance.

Table 1 Research-Site Characteristics by Insurance-Denial Experience

Research Site Characteristics (N=77)		Sites not reporting insurance denials n (%)	Sites reporting insurance denials n (%)	<i>p-value</i>
Practice Type	Academic/Academic Medical Center	6 (28.6)	15 (71.4)	0.073
	Community	30 (53.6)	26 (46.4)	
Practice Ownership	Physician	10 (59)	7 (41)	0.051
	Hospital	20 (52.6)	18 (47.3)	
	University	2 (14.3)	12 (85.7)	
	Unsure	4 (50)	4 (50)	
National Cancer Institute Designation	None/Unsure	11 (57.9)	8 (42.1)	0.299
	Yes	25 (43.1)	33 (56.9)	
Precertification Process	No	10 (71.4)	4 (28.6)	0.073
	Yes	26 (41.3)	37 (58.7)	
Prior State Law or Agreement for Trial Coverage	No	6 (66.7)	3 (33.3)	0.291
	Yes	30 (44.1)	38 (55.9)	

Note: *p*-values calculated with Fisher's exact test.

Reported Insurer responses

The survey allowed sites to report multiple reasons for insurance denials as shown in Figure 2. Of the sites experiencing denials (n=41), most (n=33; 80.5%) reported being informed that the patient's plan did not cover trial participation. Over one-third of the sites reported that the plan was grandfathered under the ACA and therefore not required to cover clinical trials (n=16; 39.0%). A similar number of sites (n=14; 34.2%) reported having a Medicare Advantage plan as a denial reason. Statistically significant reasons (Figure 2, striped bar) for denials at academic compared to community sites included mention of the trial phase not being covered ($p=0.038$), without the specific phase identified, and the research site being excluded from the plan's provider network ($p=0.009$). Other reported reasons for denials included having a Medicaid plan; tests and medications not considered standard of care by the insurer; and having

international health insurance. Only 20.8% (n=16) of the sites, reported receiving a decision from the insurer within 3 days of the initial request (Figure 3).

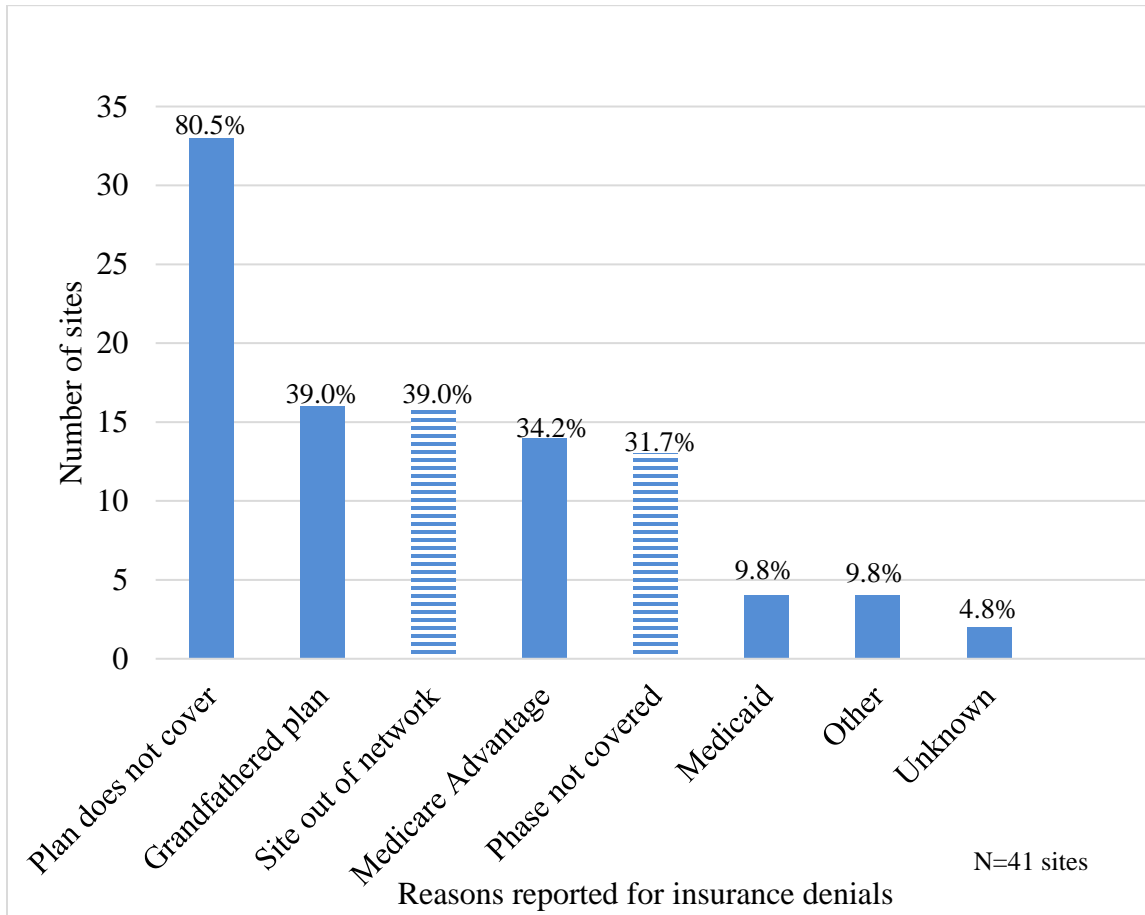


Figure 2 Reasons Reported for Insurance Denials

Note: Striped bars indicate statistical significance by Fisher’s exact test for academic versus community sites. Respondents could choose more than one reason for denial, therefore totals may not equal 100%.

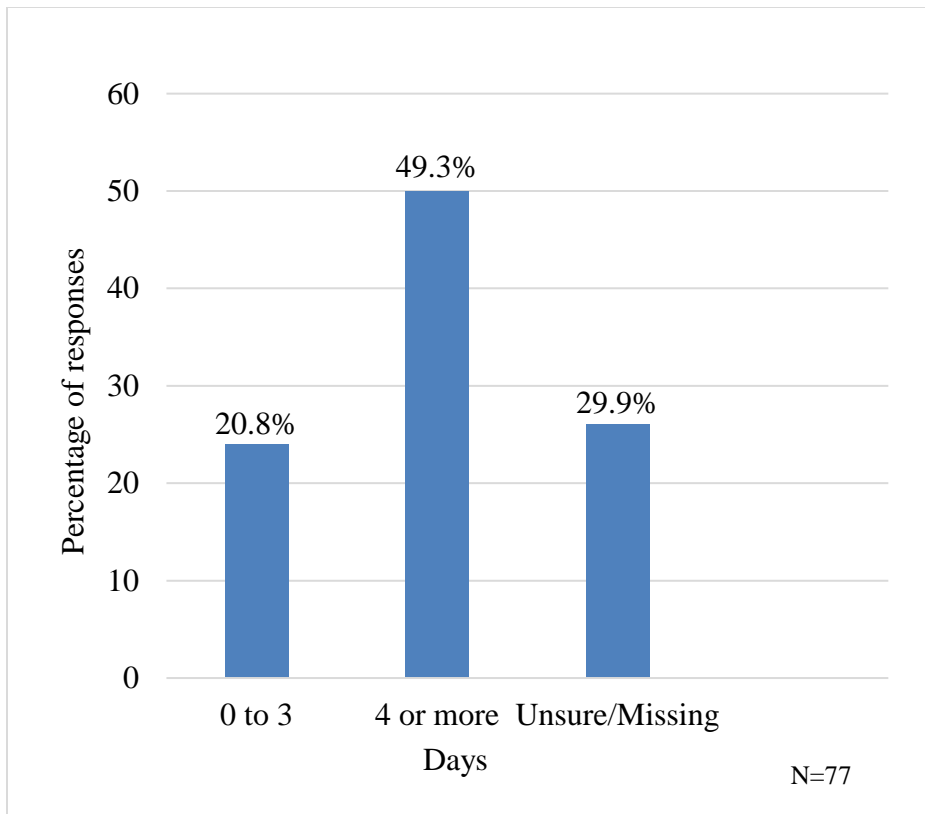


Figure 3 Time From Initial Insurer Ask for Trial Coverage to Insurer Decision

Discussion

Participation in clinical trials as part of cancer treatment is recommended by many medical and scientific professional organizations,⁷¹⁻⁷³ and insurance denial for participation has been identified as an enrollment barrier.^{2-4,23,47,49,52,53} This study was conducted in 2015 to identify persistent challenges of the ACA trial mandate within its first year. The results of this national survey drawing from a wide pool of academic and community-based research programs presents evidence that denials continued after the enactment of the ACA.

Sites reported several reasons insurers provided to justify coverage denial (Figure 2). The most frequent denial reason sites reported receiving was that the insurer claimed the plan did not cover trial participation (n=33). The site being out of the insurers' provider network (n=16) and grandfathered plans (n=16) were the second most frequently reported reasons for denials. This

finding is consistent with the case study reported by Jain et al. of grandfathered plans remaining a barrier to enrollment.⁴⁹ A 2015 Kaiser Family Foundation survey reported an average of 25% of covered workers are enrolled in grandfathered plans, with the percentage as high as 42% for individuals employed in firms with 25-49 employees.⁷⁴ This suggests that a significant segment of the population may be without trial coverage.

Plans are expected to lose grandfathered status over time. Currently, there is no publicly available list of grandfathered plans. Therefore, to assess whether a plan is truly exempt from this mandate, research centers must take additional steps to confirm an insurer's grandfathered status. While this step may cause added burden, it may ultimately result in affirming trial coverage.

The fourth reason reported for denials was due to patient's participation in a Medicare Advantage (MA) plan (n=14). These patients are protected under the clinical trials policy national coverage determination (NCD) issued by the Centers for Medicare & Medicaid Services (CMS) in 2000^{75,76} through traditional Medicare. The MA plan is only required to compensate the enrollee for the difference in out-of-pocket costs between traditional Medicare and their MA plan.⁷⁷ As such, MA plans routinely issue coverage denials because they are not required to cover clinical trials, but often do not clarify that the MA enrollee still has coverage under traditional Medicare. If MA enrollees and providers do not understand that they have protections under traditional Medicare and the MA plan does not provide information, MA participants may be left out of trial participation entirely.

A few sites reported that potential participants were excluded from trials due to Medicaid denials (n=4), which may be an appropriate exclusion. The ACA clinical trial mandate does not apply to Medicaid plans, and federal Medicaid requirements do not include clinical trial

coverage. Therefore, it is left to the individual states to determine Medicaid clinical trial coverage benefits.⁷⁸ Although ten states and the District of Columbia have rules that ensure coverage to Medicaid beneficiaries,⁶¹ the majority of states do not have language that clearly requires coverage, so Medicaid beneficiaries may not be able to participate due to the lack of coverage. Generalizability of clinical trial results is often scrutinized due to the underrepresentation of certain subgroups of the overall cancer population, including racial and ethnic minorities and the elderly. Removing the insurance barrier to Medicaid beneficiaries may help make trial participants more representative of all cancer patients.

Academic sites were more likely to indicate a denial due to phase of the trial and the site being excluded from the plan's network. Historically, early phase (especially phase I) clinical trials have been conducted by academic sites more often than community sites. This is due to the ability of academic sites to provide infrastructure to support the increased demands of early phase trial conduct, including increased personnel, specialized equipment and adequate treatment space.⁷⁹ In addition, changes in the healthcare environment have resulted in increasingly narrow networks, where many insurance plans limit the providers and sites available to enrollees, with the narrowest networks typically excluding academic centers.⁸⁰

There may be two possible explanations for the association between conducting precertification and experiencing denials. First, because claims forms may not indicate services were performed within the context of a trial, insurers may not be aware that a patient is enrolled in a clinical trial if a site does not conduct precertification. Although the Medicare program has had a clinical trials policy in place since 2000, mandatory reporting of the clinical trial number and specification of routine care and research-related procedures was not mandatory until January 2014.⁸¹

Alternatively, the precertification process itself may be engendering higher levels of scrutiny from the insurers than what might otherwise be provided. When alerted to a clinical trial, insurers may employ greater scrutiny of individual coverage elements, in addition to determining whether the specific policy provides coverage. There was not a statistically significant association in the use of a precertification by type of research site, and in fact, more of the community sites (89.8%) than academic (76.5%) centers reported using a precertification process.

Since this survey was conducted, the Departments of Labor, Health and Human Services and the Treasury issued a document dated April 20, 2016, to provide some clarification to the ACA clinical trial policy.⁸² While beneficial, the document does not fully address the amount or type of documentation that insurers can require to approve trial participation, nor does it limit the duration of time to render a determination of coverage. Consequently, implementation ambiguity may remain, leaving patients and their providers seeking alternate treatment options due to treatment initiation delays.

The lack of insurer's timely response regarding trial coverage may have profound effects on the patient. Aside from the anxiety of a cancer diagnosis or disease progression, the patient may be required to remain in the geographic area of where the planned treatment is to take place, which could mean a lengthier hospital or hotel stay. In some cases, such as acute leukemias, the need for treatment is immediate, so the possibility of being treated on trial must be abandoned and an alternate therapy considered. A shortened, standard review time for approval, if required at all, could be beneficial.

Implications

Delays and denials from insurance companies related to clinical trials coverage prolong and further complicate the process of enrolling patients into clinical trials. Described as a structural barrier to trial participation within the framework recently presented by Unger et al.,²¹ lack of insurance coverage, either real or perceived, can deter both patients and providers from considering a trial. Although just one step in the complex enrollment process, it is conceivable that by simply removing the uncertainty of trial coverage for everyone, patients, providers, and the drug development community at large, could focus on addressing the more complicated barriers affecting trial enrollment. With fewer obstacles to overcome, the number of trials that fail to complete or are suspended due to slow or inadequate enrollment will decrease, and knowledge of safe and effective therapies will grow. Ultimately, patients will benefit, and providers and payers will have evidence to recommend and cover new therapies.

Cancer centers must have effective and timely communication with the insurers to confirm patients have trial participation coverage and establish a process that allows immediate escalation when coverage is declined. However, they must also engage insurers in addressing this problem, as it cannot be solved by cancer centers alone. Our study asked cancer centers to describe the reasons insurers reported for denying trial coverage, but did not query insurers directly. It is presumed that insurers issue coverage denials due to perceived increased costs, despite evidence indicating the incremental cost of treatment on trial versus off trial is negligible⁸³⁻⁸⁵ and the potential short-term savings from not paying for trial patients' investigational therapies. However, little research has been conducted on insurers' motivations.

The degree to which denials are intentional or the result of outmoded operations inconsistent with policy are not known. Intervention strategies with insurers may be more

effectively broached if potential miscommunications identified here were the focus of initial efforts: working with Medicare Advantage providers to clarify trial coverage policies, and publicly reporting plans' grandfathered status. Long-term strategies might enable insurers to consider the return on their investment in clinical trials as opportunities to replace therapies of inferior value with more effective therapies that may reduce treatment intensity with fewer adverse effects. These efforts could be balanced by continued education to increase awareness among plan purchasers and their beneficiaries of the value of supporting the Cancer Moonshot through trial coverage.

Limitations

Several factors should be considered when reviewing these results. First, survey respondents may not reflect the experiences of all research organizations. Birken et al. emphasized “the need for a comprehensive list of programs that provide cancer treatment as a resource for researchers who study cancer programs.”⁸⁶ Without an exhaustive sampling frame that includes all organizations/providers conducting cancer clinical trials, it is difficult to know how reflective respondents are of all research sites. We addressed this by partnering with a variety of professional organizations active in cancer clinical research at diverse research sites. Second, there may be other research site characteristics that are associated with clinical trial participation that we were unable to measure, such as patient characteristics, provider attitudes towards clinical trials, and trial complexities.^{24,50,87,88}

Conclusion

This is the first empirical evaluation of the ACA clinical trial mandate. Our results showed persistence of insurance denials for routine costs associated with clinical trial despite this statutory requirement. In our sample, there was a statistically significant difference between

reported denials from academic centers versus community sites, with numerous denial reasons reported. Taken collectively, we consider the results of this study to demonstrate that insurance denials and delays continue to be formidable barriers to both the research and clinical communities in achieving adequate and timely trial enrollment, thus negatively affecting the pace of cancer research. There remains the need for further promotion of insurance coverage and evaluation of the challenges to implementation of this ACA requirement to inform future action to eliminate this enrollment barrier.

Chapter III: Declines in Adult Cancer Clinical Trial Enrollment at Community Sites Surrounding Acquisition by a Tertiary Healthcare System: A Qualitative Study Applying the Integrated Theoretical Domains and Capability-Opportunity-Motivation Behavior Frameworks

Introduction

Advances in the treatment of cancer have been achieved through successful completion of clinical trials.² National treatment guidelines for cancer recommend consideration of clinical trials as part of the standard of care treatment.⁷¹ Despite strong endorsement and proven contributions of clinical trials, only 8% of cancer patients participate in trials, delaying information needed to develop improvements in patient care.⁸⁹

Physicians have the most significant impact on trial enrollment,^{38,39} and it is often an oncologist's failure to offer a trial contributing to low accrual.³⁰⁻³² Physicians failing to offer a trial may be a result of being unaware of available trials, misunderstanding the purpose of clinical trials, or not having sufficient resources (e.g., limited staffing or limited patient contact time) to thoroughly discuss trial participation with the patient.⁴⁰ The reasons for not offering participation in a clinical trial to patients as a treatment option vary and are significantly influenced by the support the oncologist receives from the organization's leadership. Factors such as establishing accrual expectations, offering training, and giving incentives to enroll patients encourage oncologists to offer clinical trials.²⁴ Much of the previous research utilized empirical data to identify clinical trial enrollment barriers, so less is known about the factors associated with research site personnel behavior related to declining trial enrollment. Using a comprehensive theoretical framework to investigate factors affecting enrollment has been suggested as a method for further exploring enrollment barriers.⁴¹

In 2011, one group of community oncology practice sites associated with a nationwide cancer research network were acquired by a large tertiary healthcare system. Community cancer centers provide the majority of treatment to cancer patients, both as standard of care treatments and experimental treatments through participation in clinical trials.⁹⁰ The announcement of the merger was in March 2011,⁹¹ with the completion of the acquisition announced in June 2011.⁹² Public awareness of discussions regarding this particular acquisition is mostly lacking. However collaborations between these organizations began in 2007 with the combination of the blood and marrow transplant programs.⁹²

According to investment literature, acquisitions of healthcare companies can be completed as quickly as three months, but have also taken years.^{93,94} These deals, which encompass mergers, consolidations, and acquisitions are occurring more frequently. Since the last quarter of 2014, over 200 healthcare deals per quarter have been announced each quarter.⁹⁵ Reasons for these business deals are not always apparent. Typically with an acquisition, the acquired site(s) receive increased access to capital and other resources, while the acquiring site gains a greater market share.⁹⁶ According to traditional investment literature, if organizations were providing similar services prior to a merger and the goal was to continue providing those services, there should be increased opportunity for patients to receive services after the merger. However, in the case of this acquisition, the opposite occurred.

The objective of this study was to explore the reasons for this decline, and understand the ‘why’ and ‘how’ behind the enrollment decline experienced by the community cancer site personnel after acquisition. We undertook a qualitative case study approach to achieve this goal.⁹⁷ In the years prior to the acquisition by the aforementioned health system, the community-based cancer center sites that were acquired consistently ranked amongst the top ten in clinical

trial patient enrollment across the national network with which they were affiliated. Clinical trial enrollment data from these sites prior to, and after the acquisition demonstrated a 70% drop in enrollment.

Integrating qualitative and quantitative data after analysis can maximize the strengths of each technique while minimizing weaknesses. However this task can be difficult and should follow a framework.⁹⁸ Therefore, the theoretical framework underpinning this analysis was the Theoretical Domains Framework (TDF)⁹⁹ integrated with the Capability, Opportunity, and Motivation behavior (COM-B) framework.⁴⁴ Using this theoretical framework fills an identified gap in theory-based analysis of cancer clinical trial enrollment barriers.

Theoretical Framework

The TDF, is an integrative framework that synthesizes 128 theoretical constructs drawn from 33 theories into 14 domains relevant to implementation behavior.⁴² The TDF was specifically developed to identify determinants of healthcare professional behavior,⁴² allowing for targeted change intervention. In 2012, Cane et al. further refined and validated the TDF, and included the COM-B⁴³ (Appendix C). The developers of the COM-B framework suggest that an individual's behavior is shaped by three essential conditions: Capability (C), Opportunity (O), and Motivation (M), collectively referred to as COM-B.⁴⁴ Capability refers to individual's psychological and physical capacity to engage in intended activities. Opportunity is defined as factors external to the individual that prompt or make behavior possible. Motivation is defined as internal psychological processes that energize and direct behavior. This framework allows for structured exploration of potential facilitators and barriers to trial enrollment present after the acquisition.

My purpose in using the TDF with COM-B was to bring a theoretical perspective for understanding cancer clinical trial enrollment barriers, since previous work in this area has been based solely in empirical work. I theorized the decrease in clinical trial enrollment at the community-based cancer sites was related to organization level changes resulting in site personnel behaviors and could best be explained according to the TDF domains of *Environmental Context and Resources*, *Social Influences* and *Social/Professional Role and Identity*. These three domains fall under the “Opportunity and Motivation” sources of behavior, assuming behaviors within “Capability” did not change due to the acquisition. Using a theoretical perspective may be more helpful in matching future interventions to behavior determinants to further address remaining barriers to trial enrollment.

Method

Organizations

As part of the quest to become NCI-designated, a large tertiary medical center acquired a network of community-based cancer clinics. The large medical center included a hospital, university campus, and an oncology care clinic. Through these different locations, this institution offered routine patient care services, and conducted clinical trials.

The community based-cancer clinics were privately-owned cancer clinics located across the same metropolitan area as the medical center. There were thirteen locations offering patient care services, however only five of the clinics conducted cancer clinical trials. These five clinics were part of a national clinical trial network.

Participants

At the time these community cancer sites were acquired by a large tertiary medical center, the five community cancer centers were conducting 73 clinical trials.⁹² These community

clinic site personnel numbered approximately 150, including front desk clerks, treatment and triage nurses, patient schedulers, managers, research staff, physicians, nurse practitioners, schedulers, laboratory, and pharmacy personnel. There were 15 individuals working at the smallest clinic (this clinic did not offer all treatment services, but did conduct clinical trials), while the larger clinics employed from 34 to 65 employees.

We sampled from the population of personnel working at each of these five community clinics from September 2014 through March 2015, approximately four years after the acquisition. We used purposive sampling¹⁰⁰ to recruit physicians, nurse practitioners, research staff and other key individuals from these community sites for this study. These staff remained at the community sites after the acquisition and were likely individuals with knowledge and experience related to prior patient recruitment practices and clinical trial conduct.

Human Subjects

Participation was voluntary and each participant was given a copy of the Patient Information Sheet (PIS), in lieu of a consent (Appendix F). The goal of a PIS is to provide sufficient information for possible participants to make a decision or decline study participation.¹⁰¹ The University of Kansas Medical Center Human Subjects Committee approved this study.

Focus groups and interviews

Focus group participants were identified from non-participant critical observation of the paths patients follow through the clinic to identify which staff had significant patient interaction, allowing for targeted participant recruitment. These initial observations informed the development of the focus group and manager moderator guide (Appendix G). Participants were first asked to describe their experiences and feelings about clinical trials to understand the

various perspectives and trial involvement. Next, participants were specifically asked about how clinical trials were conducted prior to the acquisition, prompting discussion about the differences before, then after the merger.

Focus group participants were approached approximately one week prior to the scheduled focus group at their location and were given a PIS. Five focus groups consisting of 2 to 6 individuals, representing personnel from the front desk and radiation clinics, nurses, medical technologists and patient schedulers were conducted. These focus groups were held at each of the five community locations in a private meeting room during business hours. These focus groups did not include any managers, providers, or research staff, allowing these participants to freely share their experiences. A separate focus group with the research staff was held in a centralized location to mitigate any influence of being at any one specific clinic. Each of these six sessions lasted about an hour, was audio recorded, then transcribed verbatim.

Managers were solicited for semi-structured interview participation and were given a PIS to review. These three semi-structured interviews were held at each manager's own clinic, in a meeting room, which allowed for privacy and confidentiality. The three managers were asked the same questions as the focus groups participants. Interviews lasted about 30 minutes, were audio recorded, then transcribed verbatim.

Data from the focus groups and manager interviews informed the development of the provider interview guide (Appendix H). Providers at each of these community cancer centers included physicians and nurse practitioners. Providers were asked about their experiences with clinical trials, if they used any clinical trial reminder tools, and if so, which ones and how they were used. Providers were further probed about when participation in a clinical trial was presented in the treatment discussion with patients, and how they identified possible trial

patients. Finally, providers were encouraged to describe their thoughts and experiences specifically related to patient enrollment, both prior to and after the acquisition.

Providers were approached to participate in semi-structured interviews, using a brief questionnaire with a mix of open and closed-questions to minimize participant burden. The 27 interviews were scheduled individually at the providers' convenience to ensure privacy and anonymity. Each interview lasted approximately 30 minutes. The provider data were qualitative and quantitative in nature, and collected during the interview.

Both interview guides included questions about the processes for identifying possible trial patients before and after the acquisition. All participants were asked about their knowledge of clinical trials, including any decision support tools that were used. Providers were asked about expected yearly recruitment expectations as well as any concerns with referring patients to other health system locations for clinical trial participation. All data collected were evaluated collectively to better understand behavior changes related to *opportunity* and *awareness* that affected trial enrollment.

Analysis

Data analysis was grounded in the TDF and COM-B frameworks to provide a theoretical perspective on the barriers and facilitators that influence behavior associated with clinical trial enrollment. Transcripts from the focus groups, interviews, and responses from the provider interviews, were imported into qualitative analysis software (NVivo¹⁰²) after anonymization. Analysis was conducted using template analysis,¹⁰³ which uses a codebook to search for pre-defined themes while allowing flexibility to examine emergent themes. The codebook (Appendix I) was derived from the TDF and COM-B with definitions to identify barriers and facilitators¹⁰⁴ to clinical trial enrollment. Special attention was paid to data that did not fit into

the existing codes, which mostly represented perceived patient experiences. References to patients were not included since this study focused on organization and physician factors. The process for coding each transcript was iterative. The data were first read, then re-read and coded to a draft codebook. The data were once again reviewed, coding changes made, and the codebook revised. The documents were coded a second time using the final revised codebook. As a measure of interrater coding reliability,¹⁰⁵ the kappa statistic was run using NVivo. There was at least 90% agreement across each coding comparison. Subthemes were identified. For ease of reading, edited verbatim participant quotes are listed in the data tables describing experiences after the acquisition. Data from the closed ended questions were analyzed using descriptive statistics.

Synthesized member-checking, an in-depth method of member-checking developed by Birt and colleagues,¹⁰⁶ was used to confirm the results (Appendix J). A targeted subsample of five participants from the original data collection project, directly involved with clinical trial conduct before and after the acquisition, were included in this check: 2 physicians, 2 research staff, and 1 manager. For this additional analysis, members were contacted about their willingness to participate in an additional interview about the results section of this paper. Participants were given at least two days to review the results before scheduling the interview. Only one physician agreed to participate. Final interviews were recorded, then transcribed verbatim. Responses from the four member-checking participants are noted in the results and discussion section.

Results

Figure 4 shows the enrollment trend of participating community sites in the eleven-year span pre- and post-acquisition. The sites consistently ranked high with patient enrollment across

the network with which they were affiliated; enrolling as many as 158 patients in one year to both network and pharmaceutical company sponsored trials. Enrollment drastically dropped (70%) surrounding the acquisition (Figure 4).

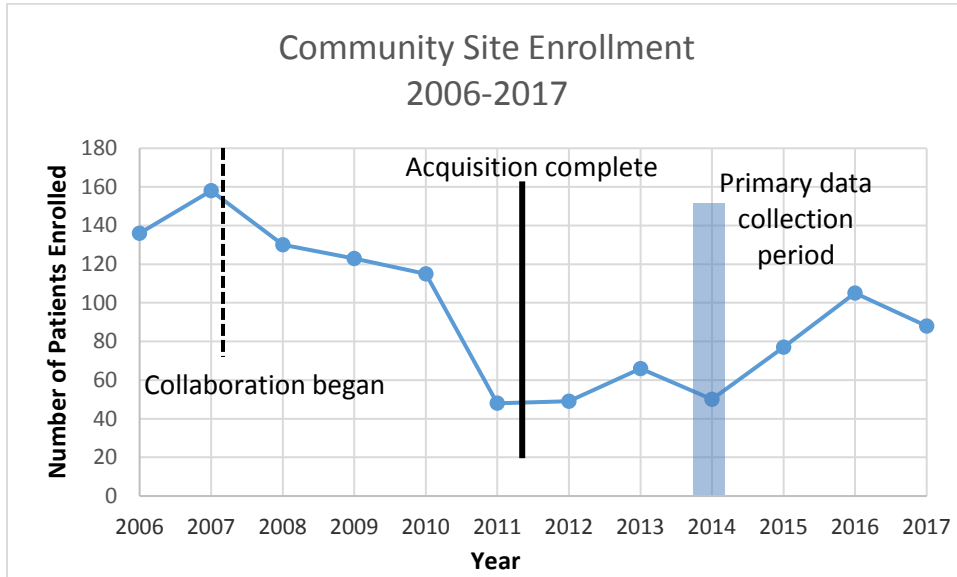


Figure 4 Community Site Enrollment 2006-2017

Focus groups and interviews

A total of 26 individuals participated in one of six focus groups, representing various support roles needed for successful trial enrollment. Half (50%) of the managers solicited for semi-structured interviews participated (Table 2). As shown in Table 2, of the 35 providers approached to participate in additional semi-structured interviews, 27 agreed (77% participation rate).

Table 2 Focus Group and Manager Interview Participants

Role	Participants		
	Six Focus Groups (6)	Thirty Interviews (30)	Four Member-checking Interviews (4)
Role	Number of Participants		
Front Desk	3		
Infusion Nurse	3		
Medical Technologist	3		
Patient Scheduler/ Intake Coordinator	6		
Radiation Oncology Personnel	3		
Research Staff	5		2
Triage Nurse	3		
Manager		3	1
Nurse Practitioner		6	
Physician		21	1
Total Participants (56)	26	30	4

Providers

Most provider participants were medical oncologists (n=18, 66.7%), followed by nurse practitioners (n=6, 22.2%), then radiation oncologists (n=3, 11.1%). There were slightly more male than female participants, their ages spanning from the 30s through the 60s, and were evenly distributed among years of clinical trial experience (Table 3).

Table 3 Demographic Characteristics of Providers Interviewed

Characteristics	Number (%) 27 (100)
Gender	
Female	12 (44)
Male	15 (56)
Age in Years	
≤45	8 (30)
46-55	11 (41)
≥56	8 (30)
Role	
Nurse Practitioner	6 (22)
Medical Oncologist	18 (66)
Radiation Oncologist	3 (11)
Years Conducting Clinical Trials	
<20	14 (52)
≥20	13 (48)

*Totals may not total 100% due to rounding.

In total, 56 community cancer clinic staff participated in this project (the 4 member-checking individuals had previously participated). We believed data saturation was achieved, meaning similar statements were made repeatedly across and within each group of participants,¹⁰⁷ and is the criterion for sample size adequacy in qualitative research.¹⁰⁸ The demonstrative quotes from all types of participants are included in the tables below.

Potential Determinants Associated with Declines in Enrollment into Clinical Trials

The community cancer clinic personnel were among the top enrollers to clinical trials prior to the acquisition. In their various roles supporting the conduct of the trials during that time, their ability to follow the rigorous trial process was proven successful. These staff had the knowledge and skills required to conduct clinical trials. Contributing to that success was having the opportunity to participate in trials and having appropriate support staff to do so. These staff were motivated to conduct clinical trials, as evidenced by several of the member-checking participants recalling the competitive fun they experienced each year when the sites challenged each other for the most patients enrolled. All member-checking participants were aware of the financial incentives that were awarded if physicians met their yearly enrollment goals, but none of them felt this bonus had much influence on enrollment. These participants described various aspects of capability, opportunity, and motivation influencing their ability to enroll patients into clinical trials after the acquisition. Most often, it was opportunity determinants identified from across all TDF domains that had the most influence.

Opportunity

The two domains linked to Opportunity are *Environmental Context and Resources* and *Social Influences*. Both domains were perceived as important in influencing community site personnel behavior related to clinical trial enrollment (Table 4). Specifically, within the domain of *Environmental Context and Resources*, participants expressed frustration related to the dearth of clinical trials available to them after having a rich and constant pipeline of studies from the former network affiliation. This scarcity of trials was suggested as one of the biggest barriers by nearly all the participants, not only the providers. Many participants, but especially the physicians, mentioned not having staff in the clinic as a significant barrier to enrollment. One of

the managers was exasperated when describing the downsizing of the research staff, which was perceived to be a result of not meeting their role expectations, but these expectations could not be accomplished without having trials on which to work.

Shortly following the acquisition, the community sites were added to the institution's electronic health record system. This affected not only the community sites, but the entire network, as everyone was learning how to use the new technology. For the community sites, moving from using hardcopy patient charts and their former network's database was reported to be especially challenging. Participants also shared concerns about specific actions and inactions they felt directly hindered trial enrollment efforts. For example, not having trials available (inaction), nor the support to conduct (action) the trials led to decreased enrollment.

Regarding *Social Influences*, the perceived distinction between the main center versus the community sites was another point of frustration, and was a *negative* social influence. The community staff were told they were part of the overall organization, yet this messaging was not consistent in the material presented to the public. The community staff mentioned the inconsistent referral patterns between the various locations. They felt they were expected to send their patients to the main campus for trials, yet the number of patients being referred to them was minimal. When patients called into the main organization's number, the community staff perceived these patients were only being scheduled with oncologists at the main site and not at the community sites. This concerned them, not only for the lack of new patients being scheduled at their sites, but also for the existing patients with whom they had built relationships.

Table 4 Community Staff Experiences Related to Trial Enrollment After the Acquisition with Sample Quotes-Opportunity

TDF Domains	Relevant Themes	Illustrative Quotes
Environmental Context and Resources	Trial availability	<ul style="list-style-type: none"> • “When we merged, it was kind of like a dead halt. We've had to jump through a lot of hoops to get started [again with clinical trials], it seems like.” -cs • "It's kind of hard to put somebody on a study when you don't have one available." -cs • "All the trials we've had out here in the past, we aren't getting out here." -cs
	Research staff	<ul style="list-style-type: none"> • "One of the more immediate challenges right now, we don't have a research nurse here." -cs • "You can't grow a research department by cutting staff. What message does it send to the organization as far as the importance of research? I think it sends very mixed messages and it makes you wonder whether the organization truly backs the research effort." -m
	Electronic health record	<ul style="list-style-type: none"> • "When we went live with Epic, we found out our clinical trial research staff was not trained at all on Epic. They were doing everything on paper which then created a, a different workflow, one that we were trying to get away from..." -m • “A hardship for this year for accruals has been the roll-out of the electronic medical record. That’s been challenging for everyone...with the rollout of the electronic medical record, we took a nosedive on accruals. ” -m
Social Influences	Distinctions between the main and community-based sites (Negative influence)	<ul style="list-style-type: none"> • "If a patient listens to the media ads, it seems like [the main center] is the only location. The ads need to be more inclusive." -p • "In the [patient] booklets, [the main center] has a large star. The community sites have smaller icons. What does this say to the patient? Academic vs. Community-- if the goal is full integration, continuing this distinction will make it difficult." -p
	Referrals	<ul style="list-style-type: none"> • “Patients are adamant about seeing specific doctors because the referring physicians told them who to see.” -cs • “You all treated my mother and this was her doctor and I want to see him too.” -cs • “...had one patient refuse to go to [the main cancer center] for a trial.” -p

*Quotes from personnel identified from cs=clinic staff, rs=research staff, m=manager, p=provider

Motivation

Within motivation, the domain *Social/Professional Role and Identity* was most prevalent (Table 5). Consistent with focus group and manager responses, nearly all providers (96%, n=26) stated that the physician was the primary individual responsible for identifying trial patients. Physicians saw trial enrollment as one of their professional responsibilities, yet to be successful, the physicians often mentioned the need to have staff, especially research staff, nearby to assist with enrollment activities. Physicians relied on the research staff to assist in study specific procedures and requirements. The research staff were also seen as resources for other clinical personnel and patients for obtaining information about clinical trials. Clinic staff, such as nurses, were mentioned by the physicians as needing to take on a more active role in identifying patients for study participation, “like the main cancer center nurses”. This is opposite of what nurse practitioners felt their role in trial conduct should encompass.

Beliefs about Consequences as another domain within Motivation, was identified in responses related to beliefs about the value of clinical trials. One hundred percent of the providers (n=27) agreed that clinical trials were good for the practice and good for patients. Many of the focus group participants also discussed perceiving clinical trials being beneficial to the practice and patient.

Table 5 Community Staff Experiences Related to Trial Enrollment After the Acquisition with Sample Quotes-Motivation

TDF Domains	Relevant Themes	Illustrative Quotes
Social/Professional Role & Identity	Physician's responsibility to identify trial patients	<ul style="list-style-type: none"> • "It's really physician driven that has really been the greatest success for identifying and moving forward with patients." -cs • "The most successful approach for getting patients on trials comes from the physician due to the hope and trust the patient has." -p • "There's nothing NPs can do to get patients on trial." -p
	Physicians want staff to be active in trial recruitment	<ul style="list-style-type: none"> • "I would like a full-time research person with me to assist with study conduct." -p • "People at [the main academic cancer center] have shadows [clinical nurse coordinators]. This would be the ideal person to identify the patient whose treatments are changing or have relapsed because they look at the scans. Research Study Coordinators won't have this information." -p • "Current road block is that doc doesn't have time to go through the patient records, so if [the research study coordinator] could determine eligibility before the patient visit, that would be helpful." -p
	Research staff	<ul style="list-style-type: none"> • "The research nurse is really the key point...a person who would be very helpful on many levels. Not only for the patient but as a resource for [staff] and physicians." -cs • "Our physicians are real good about [presenting the trial to the patient] what the doctor actually knows or feels comfortable with explaining and then they hand it over to the coordinator to finish." -cs
Beliefs about Consequences	Value of trials	<ul style="list-style-type: none"> • "I think that they (trials) are very beneficial." -cs

*Quotes from personnel identified from cs=clinic staff, rs=research staff, m=manager, p=provider

Capability

The community clinic staff discussed having difficulty enrolling patients related to *Knowledge; Memory, Attention and Decision Processes; and Behavioral Regulation*. There were few comments about *Skills*, likely because the skills needed for patient identification and enrollment did not change because of this event, so this domain was not included in this review.

Knowledge emerged as a prevalent domain, with the identification of themes directly related lack of awareness of trials and knowledge of patients' trial status after the acquisition (Table 6). Twenty-five providers (93%) reported being aware of the available trials by using various clinical trial reminder tools. Non-physician personnel felt like the physicians were more aware of available studies prior to the acquisition and suggested the lack of awareness was due to not having research staff in clinic as they did before. Support staff discussed not knowing about the trial details, while the nurses were bothered by not knowing which patients were on trial, related to the patient's safety with an investigational medication.

Themes related to *Memory, Attention and Decision Processes* emerged, particularly related to using clinical trial tools and differences in workflows. Most providers and many staff discussed frequently using the clinical trial tools to know what studies were available after the merger. Others mentioned the difficulties of using the new tools due to their complexity and length. Comments from the radiation oncologists specifically requested to have the tools available on the desktops, including for the nurses with whom they worked. Although patients were prescreened for trial participation prior to and after the acquisition, the value of prescreening was not universally accepted by physicians and research staff. This remained true with the comments from the member-checking, although one physician suggested that as a

group, physicians are not aware of the work and effort required for prescreening patients, nor the steps for initiating a study.

Behavioral Regulation

Prior to the merger, patients on clinical trials were easily identified by orange sleeves covering the medical charts. Many support staff, including clinic nurses, expressed concern about not knowing which patients were participating in trials. Several schedulers also conveyed being anxious about trial patients no longer being clearly identified as they knew patients on trial had to follow strict visit dates and procedure timelines.

Table 6 Community Staff Experiences Related to Trial Enrollment After the Acquisition with Sample Quotes-Capability

TDF Domains	Relevant Themes	Illustrative Quotes
Knowledge	Trial awareness	<ul style="list-style-type: none"> • "I think with USO, we and the doctors knew more about what was out there where I don't see as much of that here now. I don't know if it's because we don't have a research nurse or we are not getting a list anymore or what is going on." -cs • "I am aware we have clinical trials, but I don't know which ones." -m • "I don't even know what they [research staff] do." -cs
	Trial information	<ul style="list-style-type: none"> • "...I always have to call research and ask them all of this information [about the trial] that I should already have available." -cs • "We don't know the patients, we don't know what drugs they're on, we don't know the details. We don't know the ins and outs of the trial." -cs • "I had no idea it was there." [referring to clinical trial booklet] -cs
	Patient trial status	<ul style="list-style-type: none"> • "For me, it would be helpful to know, first of all, that the patient is on trial." -cs
Memory, Attention and Decision Processes	Clinical trial tools supporting decision making (post acquisition)	<ul style="list-style-type: none"> • "The most valuable thing for me personally is the physicians always get copy of the clinical trial reference guide, they always get a copy of the flowsheets, they are always on their desks." -cs • "If I were trying to help identify patients, condensing the list...I'm not going to go through the list as easily if it's 50 pages long." -cs
	Workflow processes-opposing views	<ul style="list-style-type: none"> • "All offices should have a screener to review patient records to identify for trial participation"-p • "Prescreening patients is the best way to identify for study participation."-p • "I don't think it was successful [screening new patient charts]...you have to funnel through 86 pages looking for one little thing...patients have not been fully diagnosed...so you don't even have a clear path on what clinical trial the patient could potentially fit into."-rs
Behavioral Regulation		<ul style="list-style-type: none"> • "[In the past] the charts [of patients on trial] were orange..now there is no way of knowing which patients are on trial..." -cs • "It would be great for something to either pop up or something of identifier when you're going to schedule the patient...because if they are cancelling or rescheduling you've got to be able to talk with that coordinator...so [the patient is not] kicked off study for being non-compliant. Cause for like right now, we are not taking that into account. When I'm getting calls, we are just treating them like any other patient." -cs

*Quotes from personnel identified from cs=clinic staff, rs=research staff, m=manager, p=provider

Discussion

Using the acquisition of a network of community-based cancer clinics by a large tertiary healthcare system as a case study, we sought to understand the reasons for the decline in clinical trial enrollment using a validated theoretical framework. Through focus groups and interviews, we explored the capability, opportunity, and motivation of the community-based clinic staff for identifying and enrolling patients into clinical trials. These staff perceived the shortage of clinical trial opportunities and the lack of support to conduct clinical trials as the primary barriers affecting clinical trial enrollment after the acquisition. Our working theory was that the change in organizational resources, group identity, and organizational commitment were particularly salient. This work supports some but not all the determinants associated with the TDF domains of *Environmental Context and Resources*, *Social Influences* and *Social/Professional Role and Identity*. Consistent with our *a priori* belief, the community staff perceived their opportunity and motivation for conducting trials decreased primarily due to the lack of clinical trials available at their sites, the absence of research staff from the clinic, and the introduction of an electronic health record system. Each of these factors contributed to the decrease in clinical trial enrollment after the acquisition.

The process for participating in clinical trials substantially changed for the community sites after the acquisition. The network with which they were previously affiliated operated similarly to a for-profit site management organization by providing start-up and ongoing support services. They had a centralized start-up process, staff to support the start-up efforts, and a standardized method for opening new trials. Essentially, when these sites received a new clinical trial protocol, all required start-up items had been completed, so they could begin recruiting patients for enrollment right away. These community cancer sites also contracted directly with

pharmaceutical companies to conduct clinical trials. Without the centralized support, the research staff were responsible for completing all start-up activities. It was reported that even with this extra workload, most trials were opened within 3 months and oftentimes within 6 weeks.

NCI-designated cancer centers require specific protocol reviews which must take place before any trials are launched. The academic center's processes were much more involved, and the apparent lack of communication and misunderstanding regarding the start-up process caused anger and frustration. The multiple review committee requirements did not exist with the community sites prior to the acquisition; and the reviews could take 6 months to complete.

Once the number of trials decreased, the leadership decided to reorganize the community research site staff which resulted in a decrease in the number of research personnel. Without adequate numbers of appropriately trained staff, projects could not be initiated nor completed, including clinical trials. The absence of research staff in the community clinics was also frequently mentioned as an enrollment barrier.

The community site staff perceived a lack of opportunity to conducting trials (without trials and research staff) and this affected their motivation. Organizational changes affecting the community personnel's capability, opportunity and motivation stymied their ability to enroll patients into clinical trials. The changes affected the staff's behavior in how they conducted clinical trials. Learning new workflows, the increase in the number of their professional colleagues, and discovering how to be a part of a much larger organization, can all be evaluated using the TDF to better understand the determinants of their behavior, and therefore target interventions aimed at changing the behavior.

Scant literature exists related to oncologist behavior according to the TDF and the relation to offering clinical trials. Similar to our findings, one study found physician behaviors associated with offering cancer clinical trials influenced by constructs within the TDF domains of *environmental resources; social influences; knowledge; memory, attention and decision processes; social/professional role and identity; and beliefs about consequences*.¹⁰⁹ Others used the TDF to examine the barriers and facilitators to treating patients on an experimental (not standard of care) arm of an interventional cancer clinical trial and found determinants of behavior across many of the TDF domains,⁴¹ including the three key domains of this research.

Specifically, the TDF has been used in multiple studies to understand variability in healthcare provider behavior by exploring barriers and facilitators to implementing evidence-based behaviors.^{41,104,110,111} In a study of nurses' adoption of an electronic medication medicine system (EMMS), the TDF domain *Environmental Context and Resources* emerged as a major barrier for using the EMMS, due to computer availability, the computer technology and competing demands for taking the computer to each patient.¹¹² Adopting a new computer system can affect daily performance of routine duties, as identified in the EMMS study. Our study found a similar outcome with the implementation of an electronic health record. By not being able to identify patients on trial, and some staff not having access to the EHR, this created a barrier. Our results also identified this TDF domain as a significant barrier due to the lack of available trials and absence of research staff in the clinic. Without having the resources, specifically studies and research staff, behaviors needed for the successful conduct of clinical trials were affected. Interventions for addressing these environmental influences would be to ensure clinical trials were open at the community-based clinics and to ensure appropriate research staff were available to support the conduct of the trials.

Horppu et al. also used the integrated TDF and COM-B framework to understand determinants of physician behavior related to temporary work modifications (TWM), rather than clinical trials. They found physician behavior may be influenced by factors related to having the knowledge and skills about how to apply the TWMs (capability). Behavior may also be influenced by having the physical resources to conduct TWMs, and experiencing social pressure from stakeholders to appropriately utilize TWMs (opportunity). These physicians were possibly motivated by their own beliefs regarding their capability and the consequences of their actions. Having used the TDF for conducting a theory-informed assessment, they were able to suggest several interventions to target these determinants to promote appropriate use of TWMs.¹¹¹ Our findings were similar in that the participants in our study also identified barriers in their capability (not knowing the study initiation process, or which patients were on trial), and opportunity (lack of trial opportunities and lack of research staff in the clinic) for conducting clinical trials.

Studies by Ellis et al. used the TDF to first identify behavioral determinants of rural urologists' offer of, and referral to clinical trials, then developed an intervention aimed at increasing patient referrals to cancer centers conducting urological clinical trials.^{40,109} Similar to our findings, urologists offering clinical trials were influenced by the TDF domains: *environmental resources; social influences; knowledge; memory, attention and decision processes; social/professional role and identity; and beliefs about consequences*. These researchers developed multiple intervention strategies to address the barriers, implemented the strategies, then evaluated the results. Following a similar path, developing interventions to address the obstacles to clinical trial enrollment as identified in this study may include engaging personnel from across the health system to:

- State the overall organizational goal for conducting clinical trials
- Develop processes for obtaining and conducting appropriate trials
- Conduct routine evaluations of the organization's clinical trial enterprise to recognize barriers preventing and facilitators enabling goal attainment

The results support our theory that changes at the organizational level resulted in modifications in site personnel behaviors related to clinical trial conduct. This is, to our knowledge, the first study to identify barriers and facilitators of clinical trial enrollment by community cancer clinics after acquisition by a large tertiary healthcare system using a validated behavior change framework.

Given the success in enrolling patients into clinical trials prior to the acquisition, it was surprising to observe such a dramatic decline in enrollment. The staff perceived a lack of available clinical trials for which to enroll patients as the most important obstacle. The lack of available trials has been regularly mentioned in the literature as a barrier to trial enrollment,^{4,21,90,113,114} with one study finding the primary factor limiting accrual was the small number of available trials.¹¹⁵

Once available, the timing of trials also become relevant. The staff were frequently frustrated by the length of time it took to open trials, once there were trials available for opening at the community sites. One participant described the start-up process when working with the former network and explained that once a clinical trial protocol was available on the portal, the study was often open in less than two months, and each trial was made available to all sites. Sharing the required start up process with the community staff would likely have eased some of the frustration they expressed in the length of time it took to open trials.

Identifying patients for clinical trial participation and subsequent patient enrollment into a trial may be related to the environment and resources (opportunity) to do so. Without having available trials at their sites, participants described not having the ability to enroll patients. However larger, environmental trends, rather than the organizational changes, may have impacted trial availability. One member-checking participant mentioned having more difficulty meeting study enrollment goals due to the move toward precision medicine. Many study protocols now include targeted therapies, meaning patients must have a specific gene mutation to participate. This decreases the number of eligible patients, whereas in the past, clinical studies included large numbers of patients with a specific disease. Another suggestion for boosting enrollment was for sites to have a trial portfolio to match the characteristics of the patients of their community.¹¹³ This may also become more difficult with the greater use of precision medicine.

Successful research sites have the infrastructure to support clinical trial conduct, which includes having research personnel and support staff.^{20,31} The absence of research staff in the clinics was frequently mentioned as negatively affecting trial enrollment efforts. Providers especially perceived the lack of research staff to support clinical trial conduct as a major barrier. Yet, this appeared to be related to trial availability. One member-checking participant reiterated that the research staff was downsized, justified by the lack of enrollment activity. In analyzing these data, the low enrollment activity appears to be related to the unavailability of trials in which to enroll. It is unknown if this factor was taken under consideration when the decision was made to reduce staff.

The healthcare system installed the electronic health record at the community sites in late 2014, not too long after the system had been installed at the main location. As one respondent

mentioned, it was not until they were in the process of enrolling a patient that they discovered the research staff had not been trained, nor given access to this new system. Prior to implementing significant workflow changes, an understanding of who and how the current workflow was followed may mitigate potential roadblocks.¹¹⁶

Institutional leadership has a profound effect on the well-being and satisfaction of its employees.¹¹⁷ Providing appropriate support from an organizational and clinical leadership standpoint supports cultural and system-wide adoption of change.^{118,119} Opening studies, hiring/maintaining staff, and managing technology are organizational responsibilities.⁸⁹ Organizational leadership tasked with supporting the conduct of clinical trials should consider which and how many trials to open to best serve their patient population. Steps should be taken to ensure trials, more specifically appropriate clinical trials, are made available across the organization, adequate staff are provided to support the conduct of these trials, and appropriate and timely training of new electronic systems is given.

The organization environment, support, and staff significantly influenced the community site staff's ability to enroll patients into clinical trials. Although the press release announcing the completion of the acquisition stated research would remain a main mission of the merged organization and that leadership would continue developing evidence-based patient care models, it is unknown if, prior to this action, all stakeholders were engaged in the strategy development initiative, which is often required for successful organizational change.¹²⁰

While the community personnel's knowledge about how to conduct clinical trials did not change, their awareness of trials and processes for running trials changed because of the acquisition. While participants mentioned using the new clinical trial tools to be aware of the

trials, they expressed frustration related to dearth of trials available at their own sites. This lack of opportunity to participate in trials affected their motivation to do so.

Understanding how behavior is motivated can be used to develop interventions, policies, and targeted behavior change techniques.¹²¹ Yet implementing interventions derived from theory must first be feasible, then be relevant to the location, and must have leadership support.¹¹²

Limitations

There were several challenges in identifying the perceived reasons for the decline in cancer clinical trial enrollment by community-based cancer center personnel after acquisition by a large tertiary health system. Participants self-selected to participate, thus introducing a source of selection bias. It is possible other themes could have emerged if everyone had participated, however there was good representation across support staff roles. Since the researchers were a part of the organization studied, social desirability bias related to the responses should be considered. To address this potential bias, participants were provided the PIS prior to participation and anonymity of responses was reiterated before each session. This study focused on the experiences of the staff from the acquired sites, no data were collected from the acquiring institution to understand the enrollment drop from the institution's perspective. Coding data using template analysis may take sections of text out of context, possibly resulting in loss of meaning, however the use of member-checking sought to minimize this source of error. The TDF is typically used to develop interview questions and then to analyze the data, but this was not the case for this case study. However, retrospective application of the TDF as a coding framework has been used by other researchers who reported gathering richer data by not using the TDF for drafting interview guides.¹¹¹ Finally, transferability beyond the health system evaluated in this

case study may only be possible in similar settings, such as in the 70 National Cancer Institute designated cancer centers, particularly those with academic and community sites.

Conclusion

When contemplating acquiring an entity which historically provided services at a high level, in this case enrollment to cancer clinical trials, an evaluation of what will be needed to optimally continue providing such services should be considered. The community-based personnel in this study perceived many barriers to enrollment being present after being acquired by a large tertiary health system. This study provided evidence of using the TDF for identifying enrollment barriers and suggests future interventions to assist in mitigating these barriers.

Chapter IV: Recording Patient Assessment for Clinical Trial Participation: A Study of Radiation Oncologists Across a Single Healthcare System

Introduction

Adult cancer clinical trial participation continues to lag behind national targets, jeopardizing the timely development of effective treatment options.³⁻⁵ Increasing discussions with patients about trial participation is crucial to boosting enrollment, given that the majority of oncology patients (75%) agree to participate in clinical trials when offered.³² Despite most oncologists reporting that patients may benefit from clinical trials,⁸⁷ studies have shown that when trials are available, providers offer a trial as a treatment option less than 20% of the time.³⁰ Oncologists' failure to offer trials to patients is one major barrier to patient enrollment.^{31,32}

Many physicians report being unaware of available trials.^{4,33-35,40} Even physicians who are very knowledgeable about clinical trials may have individual attitudes and beliefs about a patient's ability to participate (accurate or not), and consequently not even discuss a trial with the patient.¹²² As cancer care providers, radiation oncologists are an important but understudied group. Along with medical oncologists and surgical oncologists, radiation oncologists practicing at academic and community cancer centers play a critical role in trial recruitment.¹²³⁻¹²⁵ Studies focused specifically on radiation oncologist enrollment patterns suggested provider factors were significantly correlated with enrollment.^{122,123}

Professional organizations and national guidelines including the American Society for Radiation Oncology and the National Comprehensive Cancer Network, recommend the best management for any patient with cancer is a clinical trial.^{126,127} Having National Cancer Institute designation has been shown to increase adherence to cancer treatment guidelines.¹²⁸ Though critical for meeting standards in healthcare as well as providing higher levels of patient care,

implementing treatment guidelines can be difficult, and more so in the community setting.¹²⁹ There are several reasons physicians may not adhere to guidelines, including lack of awareness and knowledge about the guidelines, and the presence of external barriers (i.e., time constraints, lack of resources) preventing adherence.¹³⁰⁻¹³² Healthcare leaders have turned to automation for making it easier for physicians to follow practice guidelines by incorporating decision support tools within the electronic health record (EHR).¹³³⁻¹³⁵

Best practice, or “pop-up” alerts, have been integrated within the EHR to remind physicians to follow guidelines. As with alerts for safety and routine care, the EHR can also be used to facilitate clinical trial patient recruitment. Integrating within the EHR a treatment pathway containing clinical trial treatment regimens can alert physicians to the availability of a trial,^{136,137} and clinical trial alerts (CTAs) within the EHR can potentially improve patient recruitment to clinical trials.¹³⁸ Physicians have reported finding CTAs useful, but alert fatigue remains a concern.^{138,139}

The more alerts a physician is exposed to, the less likely action will be taken.¹⁴⁰ This desensitization to such messages is known as “alert fatigue.” Alert fatigue is a phenomenon found throughout the literature, yet has not been fully investigated using a qualitative approach. Thus the best way to overcome alert fatigue is not yet known.¹⁴¹

Informing physicians of available trials at the time a treatment is being ordered may be too late since the discussion of treatment options with the patient already took place. The physician needs to have trial information before discussing treatment options with the patient. Because physicians are often unaware of available trials¹⁴² and too busy providing routine patient care to remember to offer trial participation, a reminder about clinical trials should be introduced early in the patient-physician interaction.¹⁴³

One potential mechanism for avoiding alert fatigue and promoting discussions about clinical trials, is to embed a field for the physician to record assessment of the patient for trial participation into the EHR. The presence of a data input field serves as a reminder for providers to consider trial participation as a treatment option for each patient. Information about this approach is important since using the standard EHR workflow to prompt providers and facilitate patient recruitment was a recognized option in the United States (US) for meeting meaningful use standards.¹⁴⁴ Adding the field into a current workflow may prove more effective than a pop-up alert since the physicians are already familiar with the format. Documenting the assessment can show adherence to treatment guidelines, and awareness of the patient's current treatment status.¹³⁸ In fact, use of a prompt within the EHR for documenting assessment of patients being evaluated for palliative care substantially increased adherence to guidelines.⁵⁶ The addition of an embedded field has strong potential for large-scale implementation considering over 80% of US hospitals have implemented the use of an EHR.¹⁴⁵

Physician and organizational characteristics have been linked to differences in cancer clinical trial enrollment.⁸⁹ These links can be understood in the context of the (TDF), where physician decision are determined by factors in several domains including *Environmental context and resources*, *Knowledge and Skills*, and *Social/professional role and identity*.¹⁰⁴ Physician characteristics such as gender, time in practice, practice location, and volume of patient visits, are used in the literature and proxy some of these factors.^{57,58} Although imperfect, gender is likely to capture some differences in *Social/professional role and identity*, work experience and patient volume likely capture some elements of *Knowledge and skills*, and practice location likely captures elements of *Environmental context and resources*. These provider characteristics are easily available to health systems at low cost. Links between these factors and utilization of

an EHR field for clinical trial status provide an opportunity to target physician outreach and improve trial accrual without incurring the high costs of primary data collection. The literature provides some support for a link between these measures and physician adherence to guidelines, with time in practice and academic practice settings generally linked to higher trial enrollment,^{24,25,122,124} and mixed results for gender and guideline adherence, treatment decisions, and patient outcomes.^{57,58,146} The extent to which radiation oncologist characteristics are linked to use of an EHR field for clinical trial status is an open empirical question.

The main contribution of this analysis is to build upon the previous literature by assessing which radiation oncologist characteristics are linked to the likelihood that the patient assessment field is completed, which serves as a proxy for care consistent with treatment guidelines. To address the importance of provider characteristics, it is necessary to acknowledge the importance of patient characteristics in the analysis. Women have historically been underrepresented in clinical trials not focused specifically on women's cancers.¹⁴⁷ The elderly have also been poorly represented in trials,¹⁴⁸ and patient age has been associated with physicians following recommended guidelines.¹⁴⁹ Patients with a support system are more likely to enroll into a trial than those without.^{88,150} The type of insurance a cancer patient has affects clinical trial enrollment,^{3,5,114} as well as to what extent treatment guidelines are followed.¹⁵¹ As such, only patients with insurance are included in this evaluation. Because both provider and patient characteristics have been correlated with clinical trial enrollment and clinical guideline adherence, patient characteristics are included as controls in this analysis.

To our knowledge, no other study has evaluated radiation oncologist characteristics which may predict completion of the EHR field for recording patient clinical trial assessment. Radiation oncologists from one health system treating patients at both academic and community

cancer centers were included in this study. These oncologists were targeted due to using the same EHR, following identical treatment regimens, and treating a wide variety of cancers (*Environmental context and resources*). While the reasons physicians fail to follow treatment guidelines, including offering participation in clinical trials are generally known, few studies have focused specifically on radiation oncologists and the use of an embedded field within the EHR for documenting patient trial assessment.

Objective

The aims of this study were to identify key characteristics associated with radiation oncologists (i.e., *physician characteristics*) related to completion of the patient assessment for trial participation field in the electronic health record, and to estimate the level of congruency between the recorded assessment and the patient's actual trial status (i.e., *physician awareness*).

Methods and Materials

We conducted a retrospective analysis to examine radiation oncologist characteristics related to completion of a field within the EHR for documenting patient assessment for possible trial participation. Our study was conducted across a single health system where nearly 100 cancer center providers saw over twelve thousand patients each month. The Department of Radiation Oncology served five clinics and treated a wide variety of cancers through approximately 15 radiation oncologists. One radiation oncology clinic was located on the health system's main campus, while the others were stand-alone locations within communities surrounding the main campus. Distance from the main campus location to any of the community clinics was no more than 21 miles, while distance between each of the community clinics was approximately 30 miles. The University of Kansas Medical Center Human Subjects Committee approved this

study.

Data sources

Data for this study were extracted from automated monthly reports available from the health system. These monthly generated reports include data extracted from the EHR and the clinical trial management system (CTMS). The *Progress Note* template within this healthcare system's EHR was modified to add a field for recording evaluation of the patient for possible trial participation at the time of the patient visit. The purpose of adding this field was to remind all cancer center providers to consider clinical trials as a treatment option for every patient and to document the assessment outcome. The *Progress Note* template was identified as the optimal location for the addition of this field due to other required patient evaluations already existing in this location (i.e., assessing pain and the patient's ability to perform self-care). During this project, it was discovered that this added field was not a field that required completion (i.e., it was not a hard-stop). EHR fields with hard-stops will not allow the user to proceed without entering a response.¹⁵² The standardized patient assessment response options available to the oncologist are provided as a drop-down menu and include:

1	Patient currently enrolled in a treatment trial.
2	Patient currently in screening for a treatment clinical trial.
3	Patient not eligible for a treatment trial (including not needing treatment, needs palliative care, in remission).
4	No treatment clinical trial available for this patient.
5	Discussed clinical trial evaluation with patient and patient declines.

The responses from this field, the patient characteristics (i.e., gender, marital status, type of insurance, cancer type, and age), and radiation oncologist practice location, were collected from the EHR. Radiation oncologist personal characteristics, such as gender and time in practice were obtained from the organization's website featuring staff from the radiation oncology

department.¹⁵³ A few of the website biographies did not include the date of medical school graduation, so the internet was used to search the respective university websites for these dates.

The CTMS database includes patients who have consented to participate in a clinical trial and patients who have been enrolled into a clinical trial. The CTMS data included in the monthly reports reflects patient trial status, such as whether a patient is screening for participation or enrolled in a clinical trial. Examining data from February 2017 through January 2018 allowed for refinements of the monthly report from its inception in 2014, including the addition of patient demographic information included as of February 2017.

Cohort Definition

Visits to radiation oncology clinics providing continuous service from February 2017 through January 2018 were included in this evaluation. A total of 78,982 patient visits were made to radiation oncology clinics throughout this timeframe². The goal of this study was focused on radiation oncologists treating insured adult cancer patients, therefore patients who did not have a cancer diagnosis according to ICD-10-CM classification (Appendix K), were seen by a healthcare professional other than a radiation oncologist, who were younger than 21 years old, and without insurance were excluded. The frequency for receiving radiation can vary per patient³.¹⁵⁴ As such, there were multiple visits by the same patient during this timeframe, so the first documented visit with a radiation oncologist (index visit) for each patient was evaluated. Subsequent patient visits were excluded. One radiation oncologist never entered a response into this field, so these data were excluded. There were 3,729 unique patients included in the final analysis.

² Radiation treatment is given for reasons other than cancer treatment.

³ Radiation treatment regimens require treatment for 3 to 5 days for as many as 9 weeks.

Variables

The dependent variable was the completion of the patient assessment field (no/yes). The variables of interest were selected based upon the literature on organization, physician, and patient characteristics significantly related to guideline adherence and successful clinical trial enrollment. Characteristics from the EHR include clinic location (academic or community), patient visit dates (identification of index visit and allowing for calculation of clinic volume), and patient characteristics (gender, marital status, type of insurance, cancer diagnosis, and age). Patient trial assessment field completion also came from the EHR. Gender was evaluated as a binary variable. Marital status was analyzed as a dichotomous variable-married (married, life partner) and not married (divorced, separated, single, unknown, widowed) since having a support system has been associated with trial participation.⁸⁸ Insurance coverage type was analyzed as a dichotomous variable-government (Medicare, Medicare Replacement, Tricare, VA) and commercial (BCBS, commercial), since type of insurance coverage has been associated with clinical trial participation and treatment guideline adherence by physicians.^{59,146} Patient cancer diagnoses were evaluated as breast or non-breast due to breast cancer being the most common cancer in the US¹⁵⁵ and the most common malignancy treated with radiation therapy in the US.¹⁵⁶ Patient age was evaluated as a continuous variable. Radiation oncologist characteristics of gender (male or female), and clinic location were dichotomous variables. Time in practice (experience) was the time since medical school graduation and was evaluated as a continuous variable.

Analysis

First, we determined how often the patient assessment field was completed among all patient visits. Second, multivariable logistic regression was used to identify radiation oncologist

characteristics associated with any completion of the patient assessment field. We estimated multivariate models building from parsimonious specifications with heteroskedastic errors to models with more rigorous controls and error assumptions to understand the practical implications of methodological choices. The first multivariable logistic regression included only radiation oncologist characteristics, followed by a model which combined radiation oncologist and patient characteristics. The purpose of this approach was to assess changes in odds ratio estimates between the first two models, which would indicate correlations between omitted variables and increase concerns of biased estimates of provider characteristics due to omitted patient-level variables.

Next, we included controls for each of the twelve consecutive months of patient visits to account for seasonality and allow for time trends. The fourth model excludes time controls, and adds standard error clustering at the provider level. In the final model, we included controls for visit month and clustered standard error at the treatment (provider) level to understand the combined effects of these specific changes. Results are presented as odds ratios and p -values were calculated using Wald Chi-square. P -values of <0.05 were considered statistically significant. The Akaike information criterion (AIC) is reported for all models to assess differences in model fit.

To correct for heteroskedasticity, robust standard errors (Huber-White) were used in all models. Because the EHR does not identify the patient's first visit to the radiation oncology clinic, robustness checks were run by first excluding the first two months of this evaluation period (8.4 weeks during February and March 2017). The first three months were also excluded (February through April 2017) to fully account for the additional fraction of a week that could comprise the maximum oncology treatment timeframe (9 weeks) (Appendix L). This was to

ensure that only the first radiation oncologist visits were captured as any treatment begun before February 2017 would likely have been completed by April 2017.

The assessment of congruency between the radiation oncologist's recorded response and patient actual trial status was determined using Pearson Chi-square analysis. *P*-values of <0.05 were considered to indicate a statistically significant difference. Analyses were carried out using Stata version 14.⁷⁰

Results

One community clinic discontinued offering radiation services in December 2017. Thus, our analysis included the four remaining community clinics.

Sample characteristics

There were 78,982 patient visits made to these radiation oncology clinics from February 2017 through January 2018. The CONSORT diagram (Figure 5) describes the sample and the cohort examined in this study.

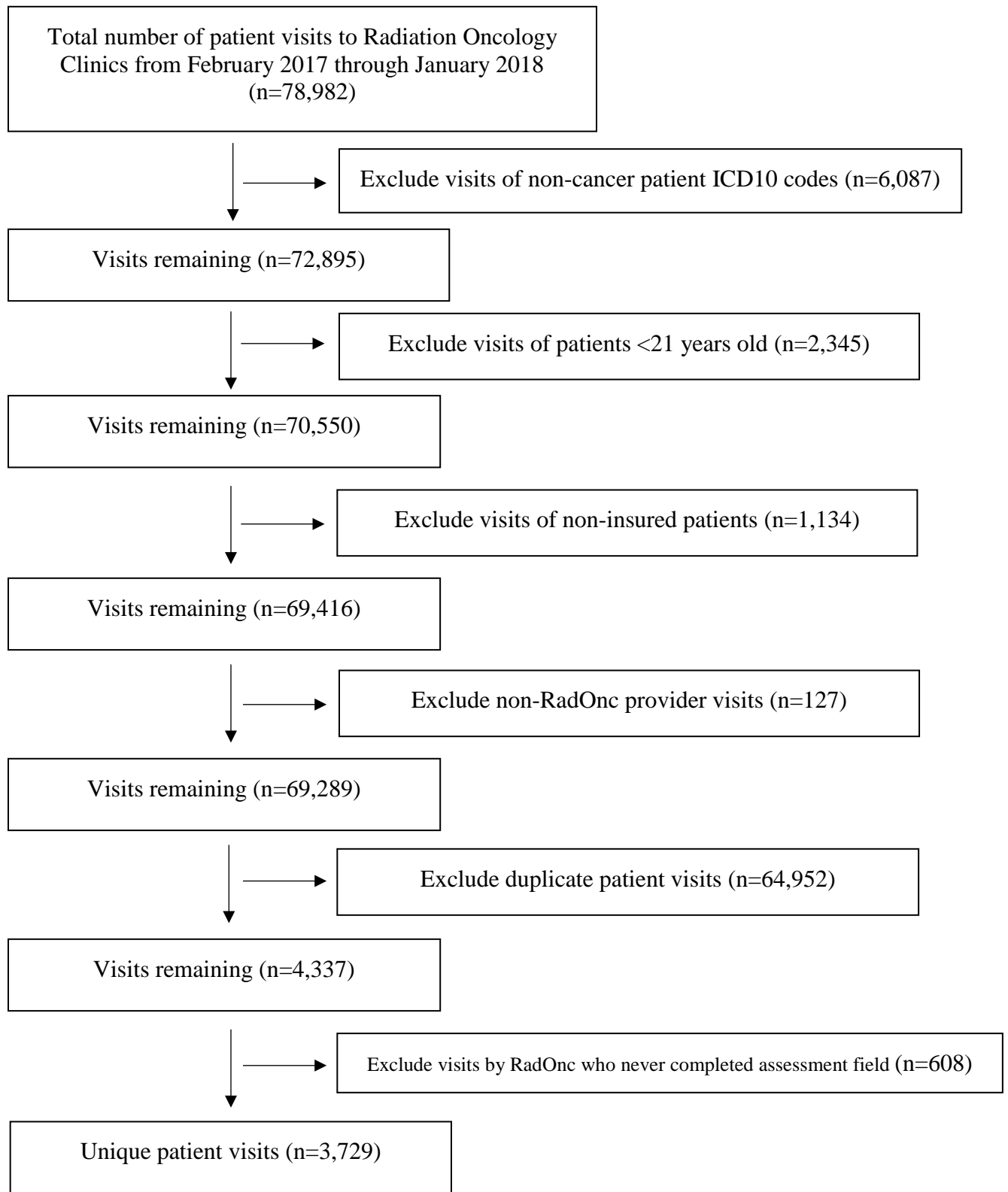


Figure 5 Radiation Oncology (RadOnc) Clinic Visits February 2017-January 2018

Table 7 displays the patient characteristics. Of the 3,729 insured patients included in this analysis, average age was 63.5 (SD=13.1) years and there were slightly more women (52.2%, n=1,946) than men (47.818%, n=1,783). Most patients were married (65.6%, n=2,409). The majority (56.8%, n=2,119) had government insurance and a diagnosis other than breast cancer (73.2%, n=2,803).

Table 7 Patient Characteristics

Patient Characteristics N=3729	No.	%
Gender		
Male	1783	47.8
Female	1946	52.2
Age, mean (SD), y	63.5	(13.1)
Marital Status		
Not Married	1320	35.4
Married	2409	64.6
Insurance Type		
Government	2119	56.8
Commercial	1610	43.2
Cancer Type		
Non-breast	2803	75.2
Breast	926	24.8

Radiation oncologist characteristics

Table 8 displays the characteristics of the included radiation oncologists. Female radiologists are approximately one-third of the staff (27.3%, n=3). The time in practice of these oncologists averaged 16.1 years (SD=9.1), with an overall average monthly patient volume of 33 unique patients.

Table 8 Radiation Oncologist Characteristics

Radiation Oncologist Characteristic N=11	No.	%
Gender		
Female	3	27.3
Male	8	72.7
Location		
Community	5	45.5
Academic	6	54.5
Time in Practice, mean (SD), y	16.1	(9.1)
Volume ⁴ , mean (SD), m	33	(12)

Field completion

The overall (unadjusted) rate of the field completion for recording assessment of the patient for trial participation was 42.5% (n=1,585). Table 9 provides field completion adjusted for radiation oncologist and patient characteristics. Column 1 includes estimates using only radiation oncologist characteristics and indicates no statistically significant correlations. This model poorly predicts variation in field completion (0.1%).

By combining both radiation oncologist and patient characteristics (column 2), radiation oncologists who were female, who worked in an academic setting, or had more experience, were more likely to enter a response into the patient assessment field. While these characteristics were statistically significant, the AIC essentially remained the same, indicating that combining radiation oncologist and patient characteristics made little difference.

⁴ Patient volume represents the average number of unique patients per month over the 12-month period for all providers.

Column 3 accounts for the time variation (using month fixed effects), revealing similar results with a slightly better model fit than column 2. Column 4 accounts for multiple observations by the same radiation oncologist by clustering standard errors. Notably, this reduced the precision of estimates and previously significant radiation oncologist characteristics are no longer statistically significant.

The final column shows data using stronger controls by combining time effects, and provider-clustered standard errors. These modifications improved the fit of the model as noted by a large reduction in the AIC, and showed that none of the radiation oncologist characteristics were statistically significantly associated with field completion.

Table 9 Logistic Regression Analysis of Radiation Oncologist and Patient Characteristics Associated with Trial Assessment Field Completion February 2017-January 2018 N=3729

Characteristics (Chars)	RO Chars OR (<i>p</i> -value)	Combined Pt and RO Chars	Combined Chars with Time Variation	Combined Chars with RO Clustering	Comb. Chars w/ Time Var. & RO Clustering
Radiation Oncologist (RO)					
Male	Ref ¹	Ref	Ref	Ref	Ref
Female	0.97 (0.69)	1.08 (0.37)	0.96 (0.68)	1.09 (0.63)	0.96 (0.86)
Community	Ref	Ref	Ref	Ref	Ref
Academic	0.97 (0.82)	0.92 (0.52)	0.96 (0.76)	0.92 (0.52)	0.96 (0.80)
Time in Practice	1.01 (0.40)	1.00 (0.73)	1.01 (0.34)	1.00 (0.80)	1.01 (0.54)
Patient					
Male		Ref	Ref	Ref	Ref
Female		1.28** (0.002)	1.40*** (<0.001)	1.28 (0.05)	1.40 (0.06)
Not Married		Ref	Ref	Ref	Ref
Married		1.00 (0.97)	1.01 (0.87)	1.00 (0.97)	1.01 (0.89)
Government Insurance		Ref	Ref	Ref	Ref
Commercial		1.13 (0.15)	1.14 (0.16)	1.13** (0.01)	1.14*** (0.001)
Non-breast Cancer		Ref	Ref	Ref	Ref
Breast Cancer		0.66*** (<0.001)	0.59*** (<0.001)	0.66 (0.15)	0.59 (0.12)
Age at Index Visit		1.00 (0.79)	1.00 (0.34)	1.00 (0.72)	1.00 (0.09)
Constant	0.70* (0.04)	0.71 (0.26)	0.11*** (<0.001)	0.71 (0.15)	0.11*** (<0.001)
<i>R</i> ²	0.001	0.005	0.115	0.005	0.115
<i>AIC</i>	5090.16	5079.63	4539.75	5079.63	4519.75

¹Reference category; *p*-values calculated using Wald Chi-square **p* < 0.05, ***p* < 0.01, ****p* < 0.001; Robust standard errors used in each model.

Robustness checks for identifying the first visit with the radiation oncologist was correctly captured showed similar results to the above model. These two different time models can be found in Appendix L.

Congruency

Radiation oncologists entered a response in the reminder field 42.5% (n=1585) of the time. When answered, radiation oncologists accurately (94.1%) recorded the patient as not being

on trial when the patient was not on trial. However, radiation oncologists identified patients already on trial or in the screening process for entering a trial only 42.7% of the time.

Additionally, when patients were on trial, radiation oncologists incorrectly recorded patients not being eligible 5.9% of the time. Further, radiation oncologists reported patients being screened or enrolled in a trial 57.3%, when they were not (Table 10).

Table 10 Congruency Between Radiation Oncologist Response and Patient Trial Status at Index Visit

Patient status	Radiation Oncologist Response		
	Screening or Enrolled on trial	Not eligible, No trial available, Patient declined	Total
Not on trial	67 57.3%	1381 94.1%	1448 91.4%
On trial	50 42.7%	87 5.9%	137 8.7%
Total	117 100.0%	1468 100.0%	1585 100.0%

Frequency and percentage represent column totals.
p-value was 0.00 by Pearson Chi-square analysis.

Discussion

Many cancer treatment guidelines include participation in a clinical trial as a treatment option.^{127,157} Patients have long reported not participating in clinical trials due to not being asked.^{4,124,158,159} Like medical oncologists, radiation oncologists play an important role in patient recruitment and enrollment,^{124,125} but are often unaware or too busy providing routine care to remember to offer a trial as a treatment option.^{4,33-35,40,142} As a reminder for oncologists to assess each patient for possible trial participation, a large Midwestern health system added a field to the page in the EHR for documenting patient assessment for possible trial participation. This field was strategically added to this page since other routine care assessments were recorded here and

oncologists were already familiar with the page as part of their documentation workflow. This is the first study assessing radiation oncologists use of a field within the EHR for recording patient assessment for possible trial participation.

Radiation oncologists entered a response into the patient assessment for clinical trial participation for just over one-third of their patients (36.6%). Patients with commercial insurance were most likely to have had this assessment field completed. These findings are consistent with other studies which identified patient characteristics, including insurance, are significant factors in patient enrollment^{24,25,122,124} and guideline adherence.^{149,151} The effect of having breast cancer (controlling for patient gender) was significant in the early models, but was not significant in the final model that more rigorously accounted for provider effects.

While the included radiation oncologist characteristics were expected to capture provider-specific differences related to field completion, none of these characteristics were statistically significant predictors of field completion, and these effects explain only 11% of the variance in completion of the patient assessment field. We still do not fully understand the underlying mechanisms influencing prompt completion. In fact, there was one radiation oncologist who never completed the field. Reasons for this oncologist never entering a response into this field are unknown. It is possible that a work-around within the EHR was developed to not show this field at all, therefore the field would display as blank in the reports. This could occur if the field was hidden or removed into one note, and providers are able to copy and paste their notes from one page to another, it is possible this field would not show up at all.

When the field was completed, most were aware of patients not being on trial (94.1%), but were less aware of patients who were already enrolled or were in the process of enrolling (5.9%). This may indicate radiation oncologists' preference for checking the default of no trial

available, without fully understanding the patient's current trial status. Consideration should be given to further collaborating with radiation oncologists to better understand the reasons for not completing this field at each patient visit. As an example, interviewing the non-responding radiation oncologist about the understanding of using the prompt and the reasons related to never recording a response.

Radiation treatment frequency can vary per patient, so evaluating the first documented (index) visit with a radiation oncologist for each patient within this evaluation period was meant to minimize bias by standardizing the evaluation time point across all patients. It was recognized that some patients within this cohort may have already been well into their treatment regimen and therefore a change in treatment would not be applicable. To minimize this potential bias, additional analyses were run excluding several months at the beginning of this evaluation period to better capture index visits. The results were similar across the three models; therefore, the entire study evaluation period is presented. Irrespective of a patient's index visit, this field could have been completed by the oncologist noting that the patient was already on trial, patient was not eligible for a trial, or that a trial was not available, rather than leaving the field empty.

While these oncologists were acutely aware of a patient not being on trial, they rarely recorded a response for patients who were already on trial or were in the screening process for entering a trial. This may represent a lack of awareness of the available clinical trials, or may indicate the oncologist not fully knowing a patient was already participating in a trial. It may also be that they knew the patient status but chose not to record a response. Administrators could encourage increased field completion overall by providing training, further education, and communication about the field's importance. Perhaps more importantly, understanding the

circumstances surrounding the reasons the one radiation oncologist never entered a response could underpin more meaningful interventions.

Future studies could further examine completion of this field, perhaps through the conduct of focus groups or semi-structured interviews with radiation oncologists across this health system. Using qualitative methods to understand radiation oncologist use of this field may provide other areas for targeting efforts for increased field completion, particularly if the evaluation is theoretically based.⁴³ The current study design could be expanded for evaluating other oncologists across this health system, allowing comparison across different specialists, but the reasons for low and inaccurate field completion rates should first be ascertained.

Limitations

This study is not without limitations. As part of the *Progress Note* in the EHR, the patient assessment field is completed at the time of the patient's visit, whereas patient trial status from the CTMS is extracted at the end of each month. It is possible the calculated congruency values could be different if patient trial status were matched at the time of the visit. It should also be noted that documenting the patient assessment for possible study participation in the EHR is not a required field, therefore it is possible that while every patient is being evaluated, it is not being documented, or may be documented in the note as text rather than in the designated field. Alternately, it is possible that patients may not have been assessed at all. Follow up with the one oncologist who never entered a response may reveal additional information about how and when this field is completed. It is unclear what training was given about the correct way to complete this field, which may have led to misunderstanding of the response categories, and for which studies patients should be assessed and responses documented.

Conclusions

Despite being added to the EHR workflow where guideline driven patient assessments were already being recorded, radiation oncologists completed the field for documenting evaluation of patients for possible trial participation less than half the time. Increasing the number of patients who participate in trials is unlikely to occur if physicians do not discuss this option with their patients. Increasing the completion rate of this field may help in recognizing the need for the patient assessment to be performed, which in turn may increase radiation oncologist awareness of available clinical trials and patient trial status. These findings did not demonstrate significant correlation between radiation oncologist characteristics and the completion of the patient assessment field. However, to optimize the completion of this field, further study is warranted to identify additional factors motivating radiation oncologists to complete this field.

Chapter V: Conclusion

The quest to identify more effective and less toxic cancer treatments can only be achieved through the conduct of clinical trials. The clinical trial process is complex and is influenced by organization and oncologist characteristics, as well as external factors such as health policy. Billions of dollars are spent each year by the government and private companies conducting cancer clinical research, yet some trials are never completed due to low and slow enrollment of patients. By using three distinct research methods, this dissertation contributes to the literature by evaluating organization and oncologist characteristics related to the conduct of cancer clinical trials.

Through survey responses from cancer research centers across the US (n=252), we discovered that despite the ACA's clinical trial mandate, insurers continued denying health insurance coverage for patients seeking treatment through participation in clinical trials. The primary reason payers reported to sites for denying patient coverage was that the plan did not cover trial participation (n=33; 80.5%). It was not known if denials were intentional or due to lack of knowledge of this mandate, but the process of appealing a denial can be lengthy and many patients need to begin treatment sooner rather than later.

Although academic sites are known for their research efforts and many are NCI-designated, these sites reported more denials than community-based clinics. Sites in states with previous laws and agreements covering trial participation experienced similar numbers of denials. Furthermore, sites using a precertification process for confirming patient coverage for trial participation were significantly more likely to report experiencing denials (69.3% vs. 41.7%, $\chi^2=14.9$, $p\leq 0.001$). These organizational characteristics, and the environment in which and through they are operating, are limiting the *opportunity* for these centers to even offer trial

participation to their patients. When an insurer is unable to respond promptly to the request to confirming patient trial coverage, physicians may develop attitudes or beliefs about a patient's ability to become a trial patient. Without the ability to conduct trials or enroll patients into trials, research sites' efforts will continue to be stymied. Research centers should consider reviewing any processes related to confirming patient insurance coverage to see if steps can be taken to facilitate receiving more timely approvals. Healthcare policy leaders should work to assess the ACA's effectiveness at the patient level to inform future efforts aimed at mitigating this barrier.

Mergers and acquisitions occur frequently in the healthcare industry. The motivation behind these events are numerous, but one likely reason for most organizations to undertake such an effort is to expand their service offerings. When the acquired or merged organization is not performing as planned, steps need to be taken to identify the cause. We applied a theoretical framework to fill the identified gap in theory-based analysis of cancer clinical trial enrollment barriers. By specifically using the Theoretical Domains Framework and COM-B behavior wheel, we evaluated the reasons for a drastic drop in enrollment from previously high enrolling sites after being acquired.

We found that the change in organizational structure was negatively associated with their *opportunity* to enroll patients into trials, and the staff perceived this to be due to a lack of available trials (50%, n=24), and lack of staff (40%, n=24) to conduct the trials. Although the physician has the most significant impact on trial enrollment, other staff are needed to perform trial procedures, such as taking vital signs, drawing blood, administering medication and documenting patient outcomes. In fact, successful research sites have adequate support staff and infrastructure to conduct clinical trials,^{20,24,160} which these sites apparently had prior to the

merger as evidenced by their prior enrollment experience (*Environmental context and resources*).

These organizational changes also affected the physicians directly responsible for patient enrollment, not in their knowledge of how to conduct trials, but in their knowledge in how to navigate the “new” process for conducting trials. These physicians frequently mentioned their previous knowledge about which trials were available and how there was a decrease in *awareness* about trials following the merger. Having identified the determinants of the staff’s behavior, targeted interventions, such as education to address the knowledge deficits, and plans to maintain human and material resources, can be developed.

Use of alerts and prompts within the EHR to assist providers in making guideline-based decisions is common. Clinical trial enrollment is required by several accrediting agencies. Inserting a field in the EHR for recording patient assessment for trial participation where other guideline required assessments are recorded was thought to increase discussions with patients about clinical trials, and ultimately increase trial enrollment.

We assessed which radiation oncologist characteristics were linked to the completion of this field and found that neither radiation oncologist characteristics, nor patient characteristics included in this study had statistically significantly relationships with this field’s completion. Further exploration of additional individual and structural factors could help to explain why less than half of the oncologists completed this field.

The dissertation contributes to the literature in three key ways. This work was the first empirical assessment of the Affordable Care Act’s clinical trial mandate. Next, this work is the first to analyze the motivation of the apparent behavior changes of personnel resulting in a decline in trial enrollment after acquisition by a larger entity using a validated behavior change

framework. This last essay contributes early evidence that physician and patient characteristics overall do not appear to have statistically significant relationships to field completion for recording patient assessment for trial participation. Future studies will continue to assess how policy affects cancer care delivery, will use theory-based assessment for targeted behavior change interventions, and will evaluate adherence to guidelines, as efforts to remove remaining enrollment barriers to adult cancer clinical trials.

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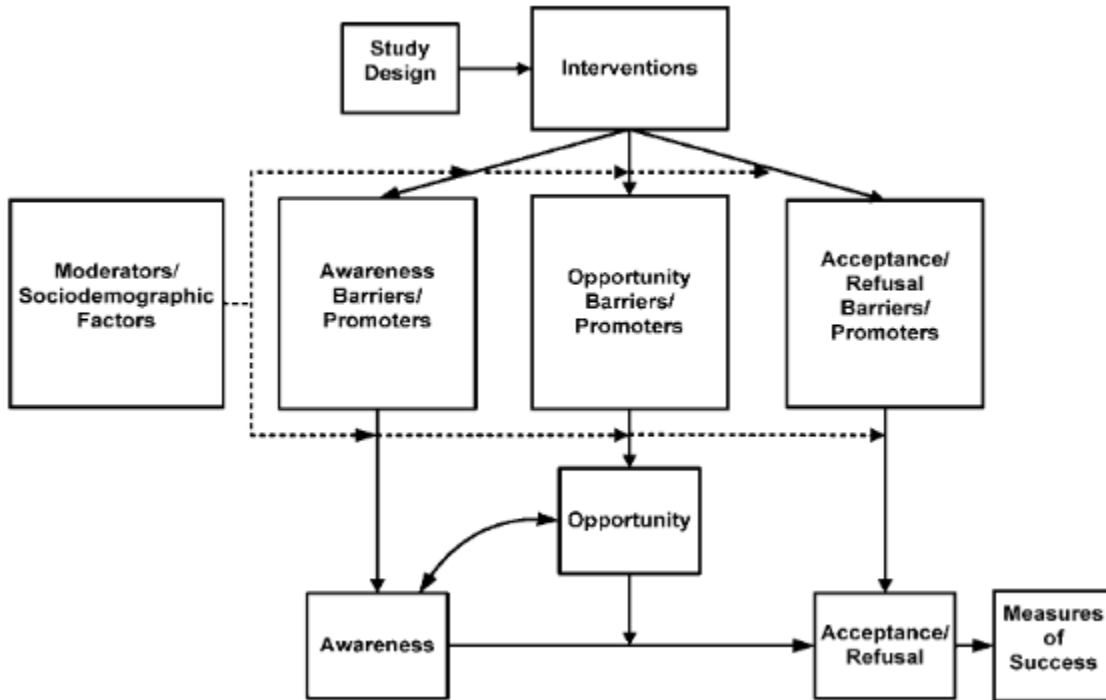
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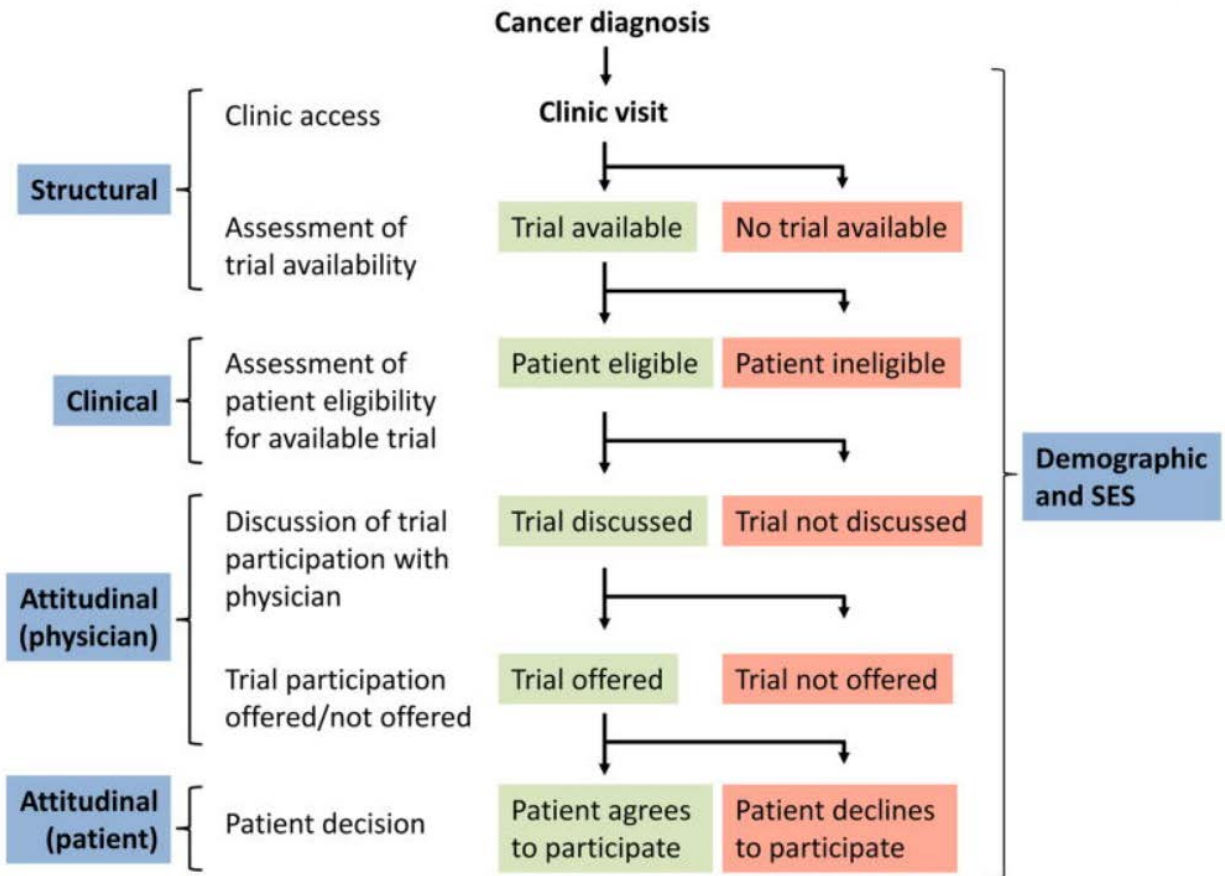
Appendices

Appendix A: Relationships Between Factors That Lead to Enrollment in a Clinical Trial



Ford et al., 2008

Appendix B: Model Pathway of Trial Enrollment Process



Unger et al., 2016

Appendix C: Theoretical Domains Framework and COM-B

COM-B component	TDF Domain	Constructs
Capability	<p>Knowledge (An awareness of the existence of something)</p>	<p>Knowledge (including knowledge of condition /scientific rationale) Procedural knowledge Knowledge of task environment</p>
	<p>Skills (An ability or proficiency acquired through practice)</p>	<p>Skills Skills development Competence Ability Interpersonal skills Practice Skill assessment</p>
	<p>Memory, Attention and Decision Processes (The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives.)</p>	<p>Memory Attention Attention control Decision making Cognitive overload/tiredness</p>
	<p>Behavioral Regulation (Anything aimed at managing or changing objectively observed or measured actions.)</p>	<p>Self-monitoring Breaking habit Action planning</p>
Opportunity	<p>Social Influences (Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviors.)</p>	<p>Social pressure Social norms Group conformity Social comparisons Group norms Social support Power Intergroup conflict Alienation Group identity Modelling</p>

	<p>Environmental Context and Resources (Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior.)</p>	<p>Environmental stressors Resources/material resources Organizational culture/climate Salient events/ critical incidents Person x environment interaction Barriers and facilitators</p>
Motivation	<p>Social/Professional Role & Identity (A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting.)</p>	<p>Professional identity Professional role Social identity Professional boundaries Professional confidence Group identity Leadership Organizational commitment</p>
	<p>Beliefs about Capabilities (Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use.)</p>	<p>Self-confidence Perceived competence Self-efficacy Perceived behavioral control Beliefs Self-esteem Empowerment Professional confidence</p>
	<p>Optimism (The confidence that things will happen for the best or that desired goals will be attained.)</p>	<p>Optimism Pessimism Unrealistic optimism Identity</p>
	<p>Beliefs about Consequences (Acceptance of the truth, reality, or validity about outcomes of a behavior in a given situation.)</p>	<p>Beliefs Outcome expectancies Characteristics of outcome expectancies Anticipated regret Consequents</p>
	<p>Intentions (A conscious decision to perform a behavior or resolve to act in a certain way.)</p>	<p>Stability of intentions Stages of change model Transtheoretical model of stages of change</p>

	<p>Goals (Mental representations of outcomes or end states that an individual wants to achieve.)</p>	<p>Goals (distal/proximal) Goal priority Goal/target setting Goals (autonomous/controlled) Action planning Implementation intention</p>
	<p>Reinforcement (Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus.)</p>	<p>Rewards (proximal/distal, valued/not valued, probable/improbable) Incentives Punishment Consequents Reinforcement Contingencies Sanctions</p>
	<p>Emotion (A complex reaction pattern, involving experiential, behavioral, and physiological elements, by which the individual attempts to deal with a personally significant matter or event.)</p>	<p>Fear Anxiety Affect Stress Depression Positive/ negative affect Burn-out</p>

Cane et al., 2012

Appendix D: Initial survey

* 1. Please complete the following basic information:

Your Name:	<input type="text"/>
Institution/Practice/Program Name:	<input type="text"/>
City/Town:	<input type="text"/>
State:	<input type="text"/>
ZIP:	<input type="text"/>
Your Email Address:	<input type="text"/>

* 2. During the 2014 calendar year (January 1-December 31, 2014), how many patients did your institution/practice/program enroll on actively accruing oncology interventional* trials (regardless of sponsor)?

***INTERVENTIONAL STUDY (or Clinical Trial)** *A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions. [Glossary of Terms, ClinicalTrials.gov]*

- 0
- 1-50
- 51-100
- 101-300
- 301-500
- More than 501

* 3. Did your cancer program/institution/practice experience insurance denials for patients participating in clinical trials in 2014?

- Yes
- No

* 4. Do you have a process to check whether a patient's insurance company provides coverage for his/her participation on a clinical trial prior to clinical trial treatment (i.e., precertification)?

- Yes
- No

*** 5. Who can we contact at your research program, network, or site to provide more detailed information about precertification, insurance coverage determinations, and demographic details on your clinical trials program? Please provide the name and contact information of the person we should contact.**

Please note, completion of this questionnaire may require collection of information from different offices within your program (i.e., clinical trials, billing or precertification offices). It is most helpful to have a single contact willing to assemble the data, but if there are multiple people you suggest we contact, please provide information for each of them below.

Name:	<input type="text"/>
Email:	<input type="text"/>
Phone:	<input type="text"/>

Appendix E: Detailed survey

Site Information

* Please complete the following basic information on the program for which you are providing data on:

Name of Institution/Center:

City/Town:

State:

ZIP:

Respondent information:

Name of Respondent:

Job Title:

Please indicate your primary role in your program.

- Research nurse/coordinator
- Billing office representative
- Clinical trials office representative
- Cancer center representative
- Investigator
- Other (please specify)

Please indicate your cancer program/institution/practice type:

- Academic
- Academic Medical Center
- Veterans' Affairs
- Community (hospital or physician practice)
- Other (please specify)

Please indicate ownership of your cancer program:

- Physician-owned
- Hospital-owned
- University-owned
- Unsure

Does your program have any of the following designations? (Select all that apply.)

- NCI Designated Cancer Center
- NCI Designated Comprehensive Cancer Center
- NCI Community Oncology Research Program (NCORP)
- NCI Cooperative Group (National Clinical Trials Network) participant
- None of the above
- Unsure

General Clinical Trials Information

For the entirety of this questionnaire, please consider your experience with clinical trials during the 2014 calendar year (January 1-December 31). We encourage you to provide as much information as is available.

During the 2014 calendar year (January 1-December 31), approximately how many patients did your institution/practice/program enroll on actively accruing oncology interventional* trials (regardless of sponsor)?

***INTERVENTIONAL STUDY (or Clinical Trial)** *A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions. [Glossary of Terms, ClinicalTrials.gov]*

If unknown, please write "unknown."

Which types of trials are you providing data on? (Select all that apply.)

- Adult trials
- Pediatric trials

* Did your cancer program/institution/practice experience insurance denials for routine costs for patients participating in clinical trials in 2014?

- Yes
- No

Coverage Denials

Please approximate the number of denials from January 1, 2014 to December 31, 2014.

If unknown, please write "unknown."

Please indicate reasons cited by insurance companies or health plans for coverage denials. (Select all that apply.)

- Plan does not cover clinical trials
- Grandfathered or self-insured plan
- Phase of trial not covered
- Medicare Advantage plan
- Site is outside of patient's network
- Don't know/not provided with reason
- Other (if possible, please specify)

Are there plans or insurers you do not contact due to previous denials?

- Yes
- No

Please list insurers or plans (optional):

Approximately how many patients elected to participate on a trial, despite being denied insurance coverage?

If unknown, please write "unknown."

How are denials tracked by your program/institution/practice? (Select as many as apply.)

- Clinical Trials Management System (CTMS)
- Electronic Medical Record (EMR)
- Practice Management Software
- Billing software
- We do not track denials
- Other (please specify)

What, if any, follow up actions are generally taken if the initial health plan response is denial?

Insurance Checking Process

* Do you have a process to check whether a patient's insurance company provides coverage for his/her participation on a clinical trial prior to clinical trial treatment (i.e., precertification)?

- Yes
- No

Precertification Questions

Who performs this coverage checking process? (Select all that apply.)

- Clinical trials office/staff
- Clinical trials billing office/staff
- Patient billing office/staff
- Study coordinator or research staff
- Precertification department/staff
- Patient
- Other (please specify)

When is this coverage checking process performed?

- Before talking with the patient about a trial
- Before informed consent is signed
- After informed consent is signed
- After treatment is initiated
- Other (please specify)

How is this coverage checking process initially performed/requested?

- Phone call to insurer
- In writing (i.e., email, fax, electronic submission)
- Review of insurance plan or policy
- Other (please specify)

Do you have standard language/script to use when talking with insurers during this coverage checking process?

- Yes
- No

Comments:

Do you use a form to contact the insurer, such as the ASCO Clinical Trial Participation Attestation Form?

- Yes, we use our own form
- Yes, we use the ASCO form
- No, we do not use a form

Comments:

How is the health plan/insurer response documented? (Select all that apply.)

- Clinical Trials Management System (CTMS)
- Electronic Medical Record (EMR)
- Practice Management Software
- Billing software
- Other (please specify)

Insurance Information

Please indicate the type of information collected regarding the insurance company/health plan. (Select all that apply.)

- Insurance company name
- Insurance type (i.e., self-funded employer plan, insurance product, Medicare, etc.)
- Employer name (for self-funded plans)
- Other (please specify)

Please estimate the number of cases where an insurer granted approval for participation on a clinical trial from January 1, 2014 to December 31, 2014.

If unknown, please write "unknown."

Approval granted on initial request:

Approval granted after appeal:

What is the typical amount of time which passes from initial request to the final decision by the payer? Please consider business working days, Monday-Friday.

- 0-3 days
- 4-9 days
- 10-14 days
- More than 14 days
- Unsure

What number of cases from January 1, 2014 to December 31, 2014 exceeded the typical amount of time you designated in the previous question?

If unknown, please write "unknown."

Please estimate the number of patients who were unable to receive treatment through participation in a clinical trial due to the approval timeline being too long.

If unknown, please write "unknown."

In what percentage of cases is participation on a trial at your institution/practice considered out-of-network for the patient?

- 0-25%
- 26-50%
- 51-75%
- 76-100%
- Unsure

Approximately how many patients, in 2014, elected not to participate on a trial because your institution/practice/program is not included in the patient's health plan network?

If unknown, please write "unknown."

If you are interested in participating in a working group to address these issues, please provide your email address below.

Would you like your name to be entered into the drawing for an Amazon gift card? (Winners will be notified via email.)

- Yes
- No

Please feel welcome to include any additional feedback or comments below, or by contacting researchpolicy@asco.org.

Thank You

Thank you again for your time and participation in this questionnaire to help our organizations learn more about your program's experience with insurance coverage of clinical trials. Please select "Submit" below to save your responses.

Appendix F: Participant Information Sheet

SCRIPT FOR INTRODUCING STUDY TO PARTICIPANTS

Thank you for your interest in this study, Evaluation of How Clinical Trial Participants Are Identified in the Community Setting. This research study seeks to learn how cancer patients being treated at The University of Kansas Cancer Center Community Cancer Practice (CCP) sites are identified for clinical trial participation. Participation in this research is optional and your participation will in no way impact your performance evaluation or employment at UKCC – CCP. Employees at each of the five CCP sites are participating in this research study. Individuals in roles that interact with the patients will be asked to participate.

If you decide to participate, you may be a part of an interview with the research staff, in a focus group with other CCP staff or both. Both interactions will focus on gathering information, but are organized and conducted differently. Your participation for the study may take up to an hour for each session. In either setting, you will be asked about your interactions with the patients and your familiarity with clinical trials.

There are no known or anticipated risks associated to participation in this study. All information you provide is considered completely confidential; your name will not be included or in any other way associated with the data collected in the study. Furthermore, because the interest of this study is in the average responses of the entire group of participants, you will not be identified individually in any way in any written reports of this research. While we do not expect you to personally benefit from this study today, we hope to learn how to improve the process for identifying possible participants for oncology clinical trials.

You may decline to answer any questions presented during the study if you so wish. Further, you may decide to withdraw from this study at any time by advising the researcher, and may do so without any penalty.

If you have any questions about the research, you can contact the study Principal Investigator, Christine Daley, PhD, at 913-588-2477. Or, if you have any questions about your rights as a research participant, you can contact:

The University of Kansas Human Subjects Committee
3901 Rainbow Boulevard, Mailstop #1032
Kansas City, KS 66160
913-588-1240

Appendix G: Focus Group and Manager Interview Guide

1. Clinical Trial Awareness
 - a. What do you think of clinical trials?
 - i. Helpful/harmful to the patients?
 - ii. Helpful/harmful to the practice?
 1. More patients to the clinic
 2. Known for cutting edge treatments
 - b. How do you know which trials are available?
 - i. Monthly Reference Guide
 - ii. Trial Flow Sheets
 - iii. Staff meetings
 - c. How are you made aware of new trials?
 - i. From research staff
 - ii. Email announcements
 - iii. Staff meetings
 - d. What would be helpful to you to remember the trials?
 - i. Desktop shortcut to Monthly Reference Guide
 - ii. Posters/pamphlets
2. Patient Identification
 - a. How were patients identified when you were part of the US Oncology network?
 - i. Newly diagnosed
 - ii. Relapsed/Recurred
 - b. How are patients identified today?
 - i. Newly diagnosed
 - ii. Relapsed/Recurred
 - c. How could we identify these patients?
 - i. Newly diagnosed
 - ii. Relapsed/Recurred
 - d. What is different in the process now than it was with USO?
 - e. Once a patient is enrolled to a trial, what type of communication do you feel is important to have available to all providers, including schedulers?
3. Patient Awareness
 - a. Of the patients you have discussed clinical trials with, what is your perception of the patient's knowledge and opinion about clinical trials?
 - b. Based upon patient feedback, what are the barriers to agreeing to participation in a clinical trial?
4. Other
 - a. Do you have any other thoughts or ideas on how to increase trial enrollment?
 - b. What can the cancer center do to help you?

Appendix H: Provider Interview Guide

1. Clinical Trial Awareness
 - a. Clinical trials are good for the practice. T/F
 - b. Clinical trials are good for the patient. T/F
 - c. I am aware of the clinical trials we offer. T/F
 - i. I use the clinical trials flow sheet
 1. On the desktop T/F
 2. As a hard copy T/F
 3. I don't use the flow sheet
 - ii. I use the clinical trials monthly booklet
 1. On the desktop T/F
 2. As a hard copy T/F
 3. I don't use the booklet
 - iii. I would find it helpful to have a hard copy flow sheet outside of each exam room T/F
 - iv. How many trials are available at your site today? _____
 - d. Patients are informed clinical trials are conducted here. T/F
 - i. Patients are informed by:
 1. New patient booklet
 2. Brochures
 3. Posters
 4. Staff (name) discuss clinical trials with patients
 5. Other: _____
 2. Patient Identification
 - a. At what point in the patient interaction do you mention clinical trial as a treatment option?
 - i. At the first visit
 - ii. At a follow up visit
 - iii. When the patient relapses or progresses
 - iv. Whenever I think about it
 - v. Other: _____
 - b. How do you communicate to the staff when you identify a possible trial participant?
 - i. Tell the study coordinator
 - ii. Tell the MA
 - iii. Tell the Triage Nurse
 - iv. Tell the Scheduler
 - v. I don't
 - vi. Other: _____
 - c. Who is the driver for identifying possible trial participants?
 - i. Physician
 - ii. NP
 - iii. Study Coordinator
 - iv. The patient

- v. The patient's family
- vi. Other: _____
- d. When reviewing a patient's records, how do you prefer to identify a patient for trial?
 - i. Review the flow sheet
 - ii. Review the clinical reference guide
 - iii. Review the flow sheet and discuss with research coordinator
 - iv. Have the research coordinator contact me if they think a patient qualifies
 - e. I primarily see patients in the following DWG:
 - i. Brain
 - ii. Breast
 - iii. GI
 - iv. GU
 - v. GYN
 - vi. Head and Neck
 - vii. Lung
 - viii. Melanoma/Sarcoma
 - ix. BMT
 - x. Leukemia
 - xi. Lymphoma/Myeloma
 - xii. Other Heme, specify: _____ -
- 3. Study Conduct
 - a. Have you experienced any difficult in enrolling patients to clinical trials over the past 3 years? Y/N
 - i. What has made it difficult to enroll:
 - 1. No eligible patients
 - 2. Patients unwilling to participate
 - 3. Lack of clinical research staff
 - 4. Lack of interest in participating in clinical trials
 - 5. Lack of available clinical trials for study population
 - 6. Other: _____
 - b. What would make it easier for you to enroll patients into clinical trials? _____
 - c. What is the expected number of patients to be enrolled by you personally this year? _____
 - d. How many patients have you enrolled? _____
 - e. What do you consider to be barriers to your recruitment efforts? _____
 - f. Have you referred any patients to other locations for clinical trial participation? Y/N
 - i. Within KU (specify where: _____)
 - ii. Outside of KU (specify where: _____)
 - g. Do you have any reservations in referring patients to WW or the CRC for trial participation? Y/N
 - i. List: _____
 - h. I want to participate in clinical research Y/N
 - i. I feel my presence in the organization is valued Y/N

4. Demog
 - a. Gender M/F
 - b. Age: _____
 - c. Years in practice: _____
 - d. Years conducting clinical research: _____
5. If there is one thing you could change today to increase your trial enrollment, what would it be and how would you accomplish it? _____
6. Is there anything I can do for you?

Appendix I: Theoretical Domains Framework and COM-B Codebook

Notes:

1. Conceptual framework is the Theoretical Domains and COM-B Framework (Cane et al., 2012)
2. Keep in mind the focus is on changes in personnel behavior surrounding the acquisition that led to the decline in clinical trial enrollment.
3. Coding can be domains, using constructs to justify the domain coding.
4. Make sure to code question as well as response when response does not reflect content of question.
5. Code both affirmative and negative responses.
6. Code both straightforward identification of issues (e.g., I don't know what trials are available) and discussion of the implications (e.g., We can't help the patient if we don't know anything).

COM-B	TDF Domain (definition) <i>constructs</i>	Decision Rules	Examples
Capability	<p>Knowledge (An awareness of the existence of something.)</p> <p><i>Knowledge (including knowledge of condition/scientific rationale)</i> <i>Procedural knowledge</i> <i>Knowledge of task environment</i></p>	Participant talks about knowledge, or what he/she does or does not know.	<p><u>Before</u> "I think with USO, we and the doctors knew more about what was out there where I don't see as much of that here now. I don't know if it's because we don't have a research nurse or we are not getting a list anymore or what is going on."</p> <p><u>After</u> "I am aware we have clinical trials, but I don't know which ones." "For me, it would be helpful to know, first of all, that the patient is on trial." "I don't even know what they [research staff] do." "I don't know where else to go to find out what studies we're participating in, so I can't direct them [patients] if I can't find them [trials]."</p>
	<p>Skills (An ability acquired through practice.)</p> <p><i>Skills</i> <i>Skills development</i> <i>Competence</i> <i>Ability</i> <i>Interpersonal skills</i> <i>Practice</i> <i>Skill assessment</i></p>	Expressing personal need Describing a skill/action	<p>"[I need to] become more familiar with the trials."</p> <p>"You can emphasize that, it's [participating in a clinical trial] going to be a commitment, and you're going to have a little bit of extra stuff to do, but here are the benefits and here are the possible benefits. You know, you can present it so it's not terrifying."</p> <p>"I refer patients to clinicaltrials.gov quite frequently because it's just a good source and it assists them and their family members to better understand their particular trial."</p>

COM-B	TDF Domain (definition) <i>constructs</i>	Decision Rules	Examples
	<p>Memory, attention, and decision processes (The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives.)</p> <p><i>Memory</i> <i>Attention</i> <i>Attention control</i> <i>Decision making</i> <i>Cognitive overload/tiredness</i></p>	<p>How clinical trial tools are being used.</p> <p>"We need to be made aware..."</p> <p>Trial reminders</p> <p>Workflow is decision process, including steps to get patient on trial</p>	<p><u>Before</u> "I don't think it was successful [screening new patient charts]... you have to funnel through 86 pages looking for one little thing...patients have not been fully diagnosed...so you don't even have a clear path on what clinical trial the patient could potentially fit into.."</p> <p><u>After</u> "If I were trying to help identify patients, condensing the list...I'm not going to go through the list as easily if it's 50 pages long."</p> <p>"The most valuable thing for me personally is the physicians always get copy of the clinical trial reference guide, they always get a copy of the flow sheets, they are always on their desks."</p>
	<p>Behavioral regulation (Anything aimed at managing or changing objectively observed or measured actions.)</p> <p><i>Self-monitoring</i> <i>Breaking habit</i> <i>Action planning</i></p>	<p>Providers regulation of their own behavior</p> <p>Goal/target setting</p>	<p><u>Before</u> "I've always heard the physicians say that 90% of the time, they already have an idea in their mind of how they're going to treat that patient before they open the door to talk to them."</p> <p>"What has worked historically [to identify patients for trial was] printing out a new list of patients coming in...whether it be on a daily basis or weekly basis..."</p> <p>"We used to have charts that instantly told us [it was a trial patient]. We have no idea now."</p> <p><u>After</u> "I don't know that there is any indication [in the EMR that the patient is on trial]"</p> <p>"Not to my knowledge [is a schedule being printed], it's not printed weekly, but I mean they could go in the system and look..."</p>

COM-B	TDF Domain (definition) <i>constructs</i>	Decision Rules	Examples
Opportunity	<p>Social influences (Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviors.) <i>Social pressure</i> <i>Social norms</i> <i>Group conformity</i> <i>Social comparisons</i> <i>Group norms</i> <i>Social support</i> <i>Power</i> <i>Intergroup conflict</i> <i>Alienation</i> <i>Group identity</i> <i>Modelling</i></p>	<p>ACP vs CCP</p> <p>Mention about anyone influencing decision making, inc social media</p>	<p>“Patients are adamant about seeing specific doctors because the referring physicians told them who to see.”</p> <p>“You all treated my mother and this was her doctor and I want to see him too.”</p> <p><u>After</u> "In the [patient] booklets, Westwood has a large star. The Community sites have smaller icons. What does this say to the patient? Academic vs. Community--if the goal is full integration, continuing this distinction will make it difficult."</p> <p>"If a patient listens to the media ads, it seems like [Westwood] is the only location. The ads need to be more inclusive."</p> <p>"Better integration across CCP and ACP. More of the clinical trials could be done in the community and not just at WW and this distinction continues to separate groups."</p>
	<p>Environmental context and resources (Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior.) <i>Environmental stressors</i> <i>Resources/material resources</i> <i>Organizational culture/climate</i> <i>Salient events/critical incidents</i> <i>Person x environment interaction</i> <i>Barriers and facilitators</i></p>	<p>References to staffing Trial materials Too busy to do trials Meetings</p>	<p><u>After</u> "When we merged, it was kind of like a dead halt. We've had to jump through a lot of hoops to get started, it seems like." "All the trials we've had out here in the past, we aren't getting out here." "It's kind of hard to put somebody on a study when you don't have one available." "The challenge, I think, in the community is that there's no information the majority of the time in O2...there are no records in O2 for us to do a pre-screening with because they've not been scanned in yet." "A hardship for this year for accruals has been the roll-out of the electronic medical record. That's been challenging for everyone...with the rollout of the electronic medical record, we took a nosedive on accruals. We really did." "When we went live with Epic, we found out our clinical trial research staff was not trained at all on Epic. They were doing everything on paper which then created a, a different workflow that we were trying to get away from..." "You can't grow a research department by cutting staff. What message does it send to the organization as far as the importance of research? I think it sends very mixed messages and it makes you wonder whether the organization truly backs the research effort." "One of the more immediate challenges right now, we don't have a research nurse here."</p>

COM-B	TDF Domain (definition) <i>constructs</i>	Decision Rules	Examples
Motivation	<p>Social/ professional role and identity (A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting.)</p> <p><i>Professional identity</i> <i>Professional role</i> <i>Social identity</i> <i>Professional boundaries</i> <i>Professional confidence</i> <i>Group identity</i> <i>Leadership</i> <i>Organizational commitment</i></p>	<p>Roles at site Research person did/does Specific staff for tasks Referral patterns</p>	<p>"The other piece as far as identifying patients, which is a very difficult one and again goes back to keeping research in the forefront of the physician's mind, then having available trials and knowing what's available when a patient relapses or progresses." "It's really physician driven that has really been the greatest success for identifying and moving forward with patients." "They're [research staff] speaking with the physicians trying to make sure the physicians know which clinical trials are out there." "The most successful approach for getting patients on trials comes from the physician due to the hope and trust the patient has." "There's nothing NPs can do to get patients on trial." "Current road block is that doc doesn't have time to go through the patient records, so if SC could determine eligibility before the patient visit, that would be helpful." "The research nurse is really the key point...a person who would be very helpful on many levels. Not only for the patient but as a resource for [staff] and physicians." "Our physicians are real good about [presenting the trial to the patient] what the doctor actually knows or feels comfortable with explaining and then they hand it over to the coordinator to finish." "Improve relationships with WW physicians for collaboration."</p>
	<p>Beliefs about capabilities (Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use.)</p> <p><i>Self-confidence</i> <i>Perceived competence</i> <i>Self-efficacy</i> <i>Perceived behavioral control</i> <i>Beliefs</i> <i>Self-esteem</i> <i>Empowerment</i> <i>Professional confidence</i></p>	<p>Knowledge/skill deficits With training, more staff could help with patient ID</p>	<p>"I would like to see more information concerning what trials are available for what particular cancer so I would be able to relay that information to them, so they know at least what to attempt to talk to the physician about when they have their visits...whether it be on the intranet or just put somewhere...compiled to say these are the studies to better educate us. Cause we can't help the patient if we don't know anything." "You'd have to dedicate definitely some staff time, a lot of time to track every single new person that came in and follow their next two to three visits. And what percentage of success would we have...statistically not much...which is why I think depending on the physicians is probably the most efficient way." "More of the trials could be done in the community and not just at WW..."</p>

COM-B	TDF Domain (definition) <i>constructs</i>	Decision Rules	Examples
	<p>Optimism (The confidence that things will happen for the best or that desired goals will be attained.) <i>Optimism</i> <i>Pessimism</i> <i>Unrealistic optimism</i> <i>Identity</i></p>		<p>"I still think if everyone had to offer the same trials at all the locations, you'd see a big jump [in enrollment]."</p>
	<p>Beliefs about consequences (Acceptance of the truth, reality, or validity about outcomes of a behavior in a given situation.) <i>Beliefs</i> <i>Outcome expectancies</i> <i>Characteristics of outcome expectancies</i> <i>Anticipated regret</i> <i>Consequents</i></p>	<p>Lose pt if pt referred for trial Acknowledge CT are important Outcomes of action/inaction</p>	<p>"I think that they (trials) are very beneficial."</p> <p><u>Before</u> "...when we were KCCC, we had a lot more opportunity with USO, CCOP, a lot more variety of clinical trials..."</p> <p><u>After</u> "...meeting with [you] has made me more acutely aware of the fact that we need to be getting back involved with research studies because we've really let it go. We've really let it go..."</p> <p>"Until the University could adequately provide training and oversight to the community group, our pipeline was cut. The new studies being brought on it took a while and I don't think really anyone realized how long it was going to take to build the department back up after that pipeline was cut. Looking at it and saying, you know that's going to take years to get them back to where they were because we went almost a year without a new trial."</p> <p>"[I need] more trials in my DWG (disease group) in the community." "[I need] more trials available in the community."</p>
	<p>Intentions (A conscious decision to perform a behavior or resolve to act in a certain way.) <i>Stability of intentions</i> <i>Stages of change model</i> <i>Transtheoretical model of stages of change</i></p>	<p>Motivational factor</p>	<p>"I've had almost no luck in finding any information on patients that are on the schedule for that week that are new. I'd like to be able to start the conversation of hey, this patient has this diagnosis or this information, can you consider this [as a possible trial participant] At least I would feel like they're benefitting, the physicians, benefitting from me being there."</p> <p>"No problem with trials if I think appropriate and reasonable."</p>

COM-B	TDF Domain (definition) <i>constructs</i>	Decision Rules	Examples
	<p>Goals (Mental representations of outcomes or end states that an individual wants to achieve.)</p> <p><i>Goals (distal/proximal)</i> <i>Goal priority</i> <i>Goal/target setting</i> <i>Goals (autonomous/controlled)</i> <i>Action planning</i> <i>Implementation intention</i></p>	<p>Goal is used</p>	<p>"...having leadership be a part of our management meetings....to let us know what the plans are and letting us know what our goal is and what we need to do to advocate (in order to increase trial participation)."</p>
	<p>Reinforcement (Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus.)</p> <p><i>Rewards (proximal/distal, valued/not valued, probable/improbable)</i> <i>Incentives</i> <i>Punishment</i> <i>Consequents</i> <i>Reinforcement</i> <i>Contingencies</i> <i>Sanctions</i></p>	<p>Methods used to ID trial pts Methods to educate people about CTs Contingency or if-then</p>	<p>"...depends on someone coming every so often, just to like check on things, how things are going exactly, making sure everything's going right..."</p> <p>"...if that message was put out more, this is something here [you can do], then KU would be put up there with Mayo and MD Anderson...it's like a huge surprise to people to hear about KU...you guys do that? I'm saying, if people knew what we had there, I think things would be different."</p> <p>"Tell Dr. X to stop yelling at the other docs. It's not motivating and is demeaning."</p>

COM-B	TDF Domain (definition) <i>constructs</i>	Decision Rules	Examples
	<p>Emotion (A complex reaction pattern, involving experimental, behavioral, and physiological elements, by which the individual attempts to deal with a personally significant matter or event.)</p> <p><i>Fear</i> <i>Anxiety</i> <i>Affect</i> <i>Stress</i> <i>Depression</i> <i>Positive/ negative affect</i> <i>Burn-out</i></p>	<p>Participant reporting about themselves.</p> <p>Feeling</p>	<p>"We have good people here--I hope the higher ups realize this. They need to be more supportive because we are being blamed for not working together and we feel like we have no support."</p> <p>"None of the docs ever thought research would be shut down in the community."</p> <p>"It's infuriating that it takes so long to open studies."</p>

Appendix J: Synthesized Member-Checking Questions

1. Did you find these comments resonating with the comments you shared during your interview/focus group participation?
2. Do you feel like anything is missing?
3. Did anything surprise you?
4. I found it interesting that providers found prescreening helpful but the staff did not. What are your thoughts?
5. Since I conducted these interviews, other stakeholders have mentioned financial bonuses being given at the end of the year if enrollment targets were met. How do you think this contributed to the low enrollment?
6. Any other comments?

Appendix K: Non-benign Neoplasm ICD-10-CM Codes

Neoplasms C00-D49

Note:

- Functional activity
- All neoplasms are classified in this chapter, whether they are functionally active or not. An additional code from Chapter 4 may be used, to identify functional activity associated with any neoplasm.
- Morphology (Histology)
- Chapter 2 classifies neoplasms primarily by site (topography) with broad groupings for behavior, malignant, in situ, benign, etc. The Table of Neoplasms should be used to identify the correct topography code. In a few cases such as for malignant melanoma and certain neuroendocrine tumors, the morphology (histologic type) is included in the category and codes.
- Primary malignant neoplasms overlapping site boundaries
- A primary malignant neoplasm that overlaps two or more contiguous (next to each other) sites should be classified to the subcategory/code .8 ('overlapping lesion'), unless the combination is specifically indexed elsewhere. For multiple neoplasms of the same site that are not contiguous, such as tumors in different quadrants of the same breast, codes for each site should be assigned.
- Malignant neoplasm of ectopic tissue
- Malignant neoplasms of ectopic tissue are to be coded to the site mentioned, e.g., ectopic pancreatic malignant neoplasms are coded to pancreas, unspecified (C25.9).

Codes

C00-C14 Malignant neoplasms of lip, oral cavity and pharynx
C15-C26 Malignant neoplasms of digestive organs
C30-C39 Malignant neoplasms of respiratory and intrathoracic organs
C40-C41 Malignant neoplasms of bone and articular cartilage
C43-C44 Melanoma and other malignant neoplasms of skin
C45-C49 Malignant neoplasms of mesothelial and soft tissue
C50-C50 Malignant neoplasms of breast
C51-C58 Malignant neoplasms of female genital organs
C60-C63 Malignant neoplasms of male genital organs
C64-C68 Malignant neoplasms of urinary tract
C69-C72 Malignant neoplasms of eye, brain, and other parts of central nervous system
C73-C75 Malignant neoplasms of thyroid and other endocrine glands
C76-C80 Malignant neoplasms of ill-defined, other secondary and unspecified sites
C7A-C7A Malignant neuroendocrine tumors
C7B-C7B Secondary neuroendocrine tumors
C81-C96 Malignant neoplasms of lymphoid, hematopoietic and related issues
D37-D48 Neoplasms of uncertain behavior, polycythemia and myelodysplastic syndromes
D49-D49 Neoplasms of unspecified behavior

Appendix L: Additional Logistic Regression Results

Logistic Regression Analysis- April 2017 through January 2018 (N=2786)

Characteristics (Chars)	RO Chars OR (<i>p</i> -value)	Combined Pt and RO Chars	Comb. Chars w/ Time Variation	Combined Chars with RO Clustering	Comb. Chars w/ Time Var. & RO Clustering
Radiation Oncologist (RO)					
Male	Ref ¹	Ref	Ref	Ref	Ref
Female	0.88 (0.12)	0.98 (0.81)	0.93 (0.53)	0.98 (0.92)	0.93 (0.81)
Community	Ref	Ref	Ref	Ref	Ref
Academic	0.95 (0.70)	0.90 (0.46)	0.94 (0.65)	0.90 (0.56)	0.94 (0.73)
Time in Practice	1.01 (0.30)	1.00 (0.55)	1.01 (0.45)	1.01 (0.70)	1.01 (0.64)
Patient					
Male		Ref	Ref	Ref	Ref
Female		1.48*** (<0.001)	1.54*** (<0.001)	1.48* (0.03)	1.54* (0.04)
Not Married		Ref	Ref	Ref	Ref
Married		1.04 (0.64)	1.03 (0.70)	1.04 (0.70)	1.03 (0.76)
Government Insurance		Ref	Ref	Ref	Ref
Commercial		1.16 (0.12)	1.17 (0.11)	1.16** (0.01)	1.17** (0.004)
Non-breast Cancer		Ref	Ref	Ref	Ref
Breast Cancer		0.58*** (<0.001)	0.56*** (<0.001)	0.58 (0.13)	0.56 (0.12)
Age at Index Visit		1.00 (0.26)	1.00 (0.27)	1.00 (0.14)	1.00 (0.09)
Constant	0.99 (0.96)	1.16 (0.66)	0.45** (0.03)	1.16 (0.66)	0.45** (0.04)
<i>R</i> ²	0.002	0.011	0.052	0.011	0.052
<i>AIC</i>	3862.021	3838.558	3696.542	3838.558	3680.542

¹Reference category; *p*-values calculated using Wald Chi-square **p* < 0.05, ***p* < 0.01, ****p* < 0.001; Robust standard errors used in each model.

Logistic Regression Analysis -May 2017 through January 2018 (n=2381)

Characteristics (Chars)	RO Chars OR (p-value)	Combined Pt and RO Chars	Combined Chars with Time Variation	Combined Chars with RO Clustering	Combined Chars with Time Variation and RO Clustering
Radiation Oncologist (RO)					
Male	Ref ¹	Ref	Ref	Ref	Ref
Female	0.80 (0.16)	0.86 (0.19)	0.85 (0.15)	0.86 (0.61)	0.85 (0.58)
Community	Ref	Ref	Ref	Ref	Ref
Academic	0.98 (0.88)	0.92 (0.61)	0.94 (0.71)	0.92 (0.68)	0.94 (0.77)
Time in Practice	1.01 (0.28)	1.01 (0.55)	1.01 (0.48)	1.01 (0.71)	1.01 (0.67)
Patient					
Male		Ref	Ref	Ref	Ref
Female		1.53*** (<0.001)	1.57*** (<0.001)	1.53** (0.04)	1.57* (0.04)
Not Married		Ref	Ref	Ref	Ref
Married		1.02 (0.81)	1.03 (0.77)	1.02 (0.86)	1.03 (0.83)
Government Insurance		Ref	Ref	Ref	Ref
Commercial		1.09 (0.45)	1.10 (0.36)	1.09 (0.14)	1.10 (0.05)
Non-breast Cancer		Ref	Ref	Ref	Ref
Breast Cancer		0.61*** (<0.001)	0.58*** (<0.001)	0.61 (0.16)	0.58 (0.13)
Age at Index Visit		0.99 (0.16)	1.00 (0.21)	0.99 (0.06)	1.00 (0.07)
Constant	1.13 (0.56)	1.54 (0.25)	0.82 (0.61)	1.54 (0.34)	0.82 (0.70)
R ²	0.003	0.011	0.034	0.011	0.034
AIC	3280.038	3262.674	3205.535	3262.674	3191.355

¹Reference category; p-values calculated using Wald Chi-square * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; Robust standard errors used in each mode