2021

A Multilevel Mixed Methods Examination of Treatment Nonadherence Among Rural Cancer Survivors

Bonny Morris
Virginia Commonwealth University

A Multilevel Mixed Methods Examination of Treatment Nonadherence
Among Rural Cancer Survivors

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of
Philosophy at Virginia Commonwealth University

By

Bonny B. Morris
Master of Science in Public Health, Emory University, 2009
Bachelor of Science in Nursing, George Washington University, 2012
Bachelor of Science in Public Health, University of North Carolina at Chapel Hill, 2007

Director: Bernard Fuemmeler, Ph.D.
Professor, Department of Health Behavior and Policy

Virginia Commonwealth University
Richmond, Virginia
April 2021

Acknowledgements

I would first like to think my advisor, Dr. Bernard Fuemmeler, for his countless hours of mentorship and without whom this work would not have been possible. I am incredibly grateful for his support in my research and in navigating very difficult times in my life. Special thanks also go to my committee members, Dr. Roy Sabo, Dr. Vanessa Sheppard, and Dr. Kathryn Weaver, for their guidance and expertise throughout my doctoral program.

I would not be the person I am today without my mom, my grandparents, and my children. I am so thankful to have had my mom as my steadfast cheerleader, fully supporting my middle school dream of curing cancer. I know my grandparents are smiling down from Heaven and would have been so proud of this accomplishment. My Sweet Caroline and my Sweet Baby James – thank you for giving me the ultimate reason to be the best version of myself and set the kind of example that you two deserve. I love you.

Finally, this dissertation is dedicated to the patients and research participants who shared their time, energy, and experiences in the development of this research and scientific knowledge. I will always strive to live up to the confidence you placed in me and to make a difference in the lives of all those touched by cancer.

Dissertation Abstract

While mortality rates have been decreasing over the last 40 years, cancer remains a leading cause of death in the United States. Over 1.7 million people were diagnosed with cancer in 2019, and there were more than 600,000 cancer deaths. Of the 15 million cancer survivors in the US, nearly 3 million reside in rural areas and experience 3% higher cancer incidence and 10% higher cancer mortality compared to their nonrural counterparts. During 2006-2015, the annual age-adjusted mortality rates for all cancer sites combined decreased at a slower pace in rural areas versus nonrural areas (-1.0% vs -1.6% per year, respectively), widening the disparity in mortality rates. Although the reasons for these disparities are not fully known, rural cancer survivors tend to be older, have additional comorbidities and poorer general health, and have a higher prevalence of lifestyle risk factors, such as smoking and lack of physical activity, that complicate survival and may contribute to the higher mortality rate. Nonadherence to cancer treatment is associated with poorer cancer outcomes, including higher rates of cancer recurrence or treatment failure and decreased survival. Reports of mortality have been up to four times as likely in nonadherent compared with adherent survivors. A growing set of studies have begun to document that cancer treatment adherence is poorer among rural populations, which may also partially explain the higher mortality rate observed in rural areas. This dissertation is comprised of three studies: 1) a systematic review of the role of digital health in rural oncology; 2) a data analysis of hospital and billing claims data examining geographic differences in sociodemographic and clinical factors associated with radiation treatment nonadherence; and 3) a multilevel, theory-driven examination of rural cancer treatment nonadherence utilizing survey and individual interview data.

Table of Contents

CHAPTER 1: Introduction

BACKGROUND

While mortality rates have been decreasing over the last 40 years, cancer remains a leading cause of death in the United States.[1] Over 1.7 million people were diagnosed with cancer in 2019, and there were more than 600,000 cancer deaths. Rural residents represent approximately 14% of the 328M people living in the U.S., with the majority being white (76%) or people of color (13%). Compared with national averages, rural residents earn a lower income, have lower levels of educational attainment, experience a higher poverty rate, and have a higher unemployment rate.[2]

Of the 15 million cancer survivors in the US, nearly 3 million reside in rural areas and experience 3% higher cancer incidence and 10% higher cancer mortality compared to their nonrural counterparts.[3] During 2006-2015, the annual age-adjusted mortality rates for all cancer sites combined decreased at a slower pace in rural areas versus nonrural areas (-1.0% vs -1.6% per year, respectively), widening the disparity in mortality rates.[4] Although the reasons for these disparities are not fully known, rural cancer survivors tend to be older, have additional comorbidities and poorer general health, and have a higher prevalence of lifestyle risk factors, such as smoking and lack of physical activity, that complicate survival and may contribute to the higher mortality rate.[5–8] A growing set of studies have begun to document that cancer treatment adherence is poorer among rural populations, which may also partially explain the higher mortality rate observed in rural areas.[9–16,37–44]

Nonadherence to cancer treatment is associated with poorer cancer outcomes, including higher rates of cancer recurrence or treatment failure and decreased survival.[9–16] Reports of mortality have been up to four times as likely in nonadherent compared with adherent survivors. Treatment adherence can be defined as the degree to which a patient's behavior corresponds to the agreed upon treatment plan. There are many ways treatment nonadherence has been operationalized in the literature, including: two or more missed treatment appointments;[17] actual treatment cycle length exceeding planned treatment cycle length;[18,19] ratio between received and planned radiation therapy doses;[20] unwarranted treatment interruption greater than one week;[21] and medication possession ratio.[9,12] To enhance our understanding of treatment adherence, it is important to distinguish between treatment adherence versus medication adherence, and adherence versus compliance or concordance. While medication adherence is more concerned with patient-administered doses and can be measured by medication possession ratio or pill counts, treatment adherence considers healthcare provider-administered treatments and may involve a unique set of barriers. The term 'treatment compliance' has evolved over the past decade to be more patient-centered and acknowledge the importance of shared decision-making with the term 'treatment adherence'. Despite this evolution, it is difficult for researchers to document that the patient was involved in the selection of the treatment course, especially in secondary analysis of hospital data, often resulting in these terms being used interchangeably. Treatment concordance is clearer cut however, with a direct comparison between a set of discipline-recognized treatment guidelines and the treatment received by the patient. While treatment concordance is focused on the type and sequence of treatments received, treatment

adherence focuses on the amount of treatment received during a specific treatment type and course.

Potential Factors Related to Cancer Treatment Nonadherence among Rural Population

There has been little attention to factors that might help explain why adherence is poorer among rural cancer survivors. To understand reasons for cancer treatment nonadherence, it is imperative to understand the complex interplay between sociodemographic, cultural, and systems factors experienced by individuals living in rural settings. Below, the literature on each of these are highlighted.

Sociodemographic. Rural residents are more likely to have lower educational attainment, higher poverty rates and are more likely to report treatment-related financial hardship compared with their nonrural counterparts, all of which may affect treatment adherence.[6,22] A number of studies have shown that lower health literacy is related to poor medication adherence.[23] With regard to financial distress, prior studies have shown that the degree to which treatment has created a financial burden is associated with medication nonadherence.[22,24,25] Specifically, investigators found that nearly half of participants reported experiencing some form of financial distress and did not adhere to recommended prescription medication because of cost. Rural populations also have a higher proportion of elderly residents, who are more likely to be diagnosed with cancer and are at greater risk for polypharmacy issues and medication treatment nonadherence.[6,7,26]

Culture. Culture is defined as the customary beliefs, social norms, material traits and characteristic features of everyday existence shared by people in a place or time.[27] Culture may contribute to health beliefs, health behaviors and care-seeking behaviors, with these behaviors and beliefs being reinforced through close family and social networks.[28] Rural culture is grossly understudied as it relates to cancer treatment adherence, yet culture provides the context to rural health challenges and a lens to better understand rural health disparities. The few available US studies come from examinations of rural culture in Appalachia, which may differ from rural culture in the South, Deep South, and Midwest. Key characteristics reported are family cohesion, strong Christian beliefs, medical mistrust, self-reliance, and a commitment and dedication to work.[29] The lack of literature on rural culture indicates a need for community-engaged mixed methodology to ensure an accurate representation of rural culture in the design of culturally-sensitive interventions that capitalize on the strengths of rural culture.

Access to Care. Healthcare access barriers also contribute to the observed geographic disparity cancer mortality rates. Rural areas have a lower county-level physician supply, and importantly, a lower density of specialists and radiation oncologists than nonrural areas.[30] Only 3% of medical oncologists practice in rural areas.[31] Rural residents have longer median travel times to treatment centers, oncology specialists, and academic centers; higher volume centers are associated with improved patient outcomes.[30,32] Median travel times range from 51 minutes to 97 minutes.[33] Poverty creates substantial transportation barriers, making it a challenge for rural residents to afford gas or even a car. It has been estimated that over 1.6M rural households do not have cars, mostly concentrated in the South, Appalachia, and the Southwest.[34] Rural residents have limited access to patient support services. Notably, only 2% of health social workers practice in rural areas, with specialized oncology social workers being virtually nonexistent.[35] Moreover, rural residents are less likely to have access to palliative care and hospice services.[30]

The substantial access barriers faced by rural populations in turn influence treatment adherence and cancer outcomes.

Access to Technology. Digital health technologies can support patient, provider, and system-level needs, which may serve to mitigate rural health disparities, including those related to access; however, a digital divide is also apparent. 26% of rural residents live in areas that lack the infrastructure for broadband coverage.[36] Of the remaining 74% who live in areas with the infrastructure, only 63% subscribe to it. This could be due to cost, lack of interest, or internet speed, given that 30% of those who subscribe lack high speed service.[37] Additionally, rural patients are less likely to contact their provider by email or online messaging. [38] However, 91% of rural residents own a cell phone of some type, so digital communication could still represent a viable communication strategy.

Study Design for Understanding Cancer Treatment Nonadherence in Rural Populations

Reducing nonadherence represents a tangible solution to improve cancer outcomes. While prior studies have shown that cancer treatment adherence is poorer among rural populations, there are methodological limitations to consider. In reviewing the literature, 16 manuscripts considered cancer treatment adherence in rural populations with minimal variation in study design.[9–16,39–46] Most studies (11/16) were conducted among breast cancer survivors. Only 3 studies involved qualitative methods (2 interview-based studies and 1 focus group-based study);[39,42,43] the remaining 13 articles relied on quantitative data sources. Only 1 study involved a prospective survey, which was limited by sample size (N=31).[47] The other 12 studies utilized secondary data sources largely consisting of healthcare claims data. There were no studies identified that employed mixed methodology, which would provide rich insight into factors contributing to nonadherence. Evidence of theory-driven approaches was even more limited, with only one manuscript describing a theoretical model or framework guiding the study development.[9] Theories that can inform our understanding of the factors contributing to poor adherence as well as guide intervention development are needed.

THEORETICAL FOUNDATION

The Theory Derivation process, the structured set of procedures in which a parent theory or model is used to guide the development of a new model or theory in conjunction with a comprehensive review of the current literature, was employed to understand how potential factors related to treatment nonadherence may fit together and influence outcomes in rural populations.[48] Two parent theories were considered: the Information-Motivation-Behavioral Skills Theory (IMB) and the Chronic Care Model (CCM).[49,50]

IMB Model. IMB posits that individuals will likely initiate and maintain patterns of a target behavior if they are well-informed about the behavior, motivated to act on that behavior, and possess the behavioral skills required to act effectively in support of that behavior.[51] Key model components include: 1) information that is directly relevant to the performance of the health behavior and can be easily enacted; 2) personal motivation (i.e., attitudes toward personal performance of the health behavior) and social motivation (i.e., social support for enactment of the health behaviors); and 3) behavioral skills, or an individual's objective abilities and sense of self-efficacy concerning performance of the health behavior.[49] IMB theory assumes that health-

related information, motivation, and behavioral skills are fundamental determinants of performance of a health behavior, and that information and motivation are independent contributors to the performance of the health behavior. That is, well-informed individuals are not necessarily motivated to engage in a particular health behavior, and that highly motivated individuals are not necessarily well-informed about the target behavior.[49] Additionally, the effects of information and motivation are seen primarily as a result of the application of behavioral skills to the initiation and maintenance of health promotion behavior.[49] While the IMB model was originally established to guide interventions focused on reducing HIV risk behaviors (e.g., condom use), it is viewed as a generalizable approach to understanding and promoting health behavior more broadly.[49] For example, it has been successfully applied to smoking cessation interventions,[52] interventions to increase physical activity,[53] breast self-examination interventions,[54] and interventions to improve medication adherence.[55] Although an individual level model and thus limited in application to individual behaviors, an important benefit is that IMB takes into account behavioral skills, a component missing from previous theoretical models aside from Bandura's Social Cognitive Theory.[56]

Chronic Care Model. Given that multilevel factors contribute to cancer treatment nonadherence, with unique aspects likely associated with the observed disparities between rural and nonrural populations, a multilevel theoretical basis is required in the design and implementation of research in this area. The Chronic Care Model (CCM) is a well-established and validated framework that positions chronic care in the context of community.[50] The CCM was designed to help improve the quality of chronic care delivery and health outcomes. The model highlights the interdependent importance of self-management support, delivery system design, decision support, and clinical information systems to support patients and their care providers in having productive interactions and improved patient outcomes. A 2009 review summarized the literature relevant to the CCM as observation, intervention, and evaluation studies focused on organizational characteristics, quality improvement, and cost effectiveness to benefit patients with congestive heart failure, asthma, and diabetes.[57] A benefit to this model is its flexibility acts more as a framework than a packaged intervention, allowing researchers to tailor CCM elements to individual organizations, yet it lacks patient-level factors that influence care delivery.

Critique and Synthesis of the IMB and CCM Model. While both the IMB and the CCM have demonstrated utility in health promotion and quality improvement, neither fully capture the multilevel factors relevant to adherence in rural cancer survivors. Bringing the IMB and the CCM together as the Information-Motivation-Behavioral Skills theory - Chronic Care Model (IMB-CCM; Fig. 1) provides a novel framework from which to study and address treatment nonadherence in rural cancer survivors. The IMB-CCM identifies that receipt of information during the cancer journey is necessary but not sufficient to achieve positive behavioral and health outcomes like treatment adherence and survival. In addition, behavioral skills to promote self-management through patient engagement, along with personal and social motivation shaped by rural culture, information access and information utilization, are critical determinants. Individual, community and health system-level factors interact to influence outcomes, with unique aspects likely associated with the observed disparities between rural and nonrural populations. The combined IMB-CCM provided the theoretical foundation for the design of the dissertation studies and interpretation of results. Specifically, the IMB-CCM was used to inform survey and interview development, allowing me to systematically generate data that more fully explain factors contributing to treatment nonadherence in rural oncology. Furthermore, survey data

allowed for assessing additional constructs hypothesized to be related to rural culture, encompassing each aspect of the IMB-CCM, which were then utilized to further explore potential factors related to treatment nonadherence through in-depth interviews with rural cancer survivors.
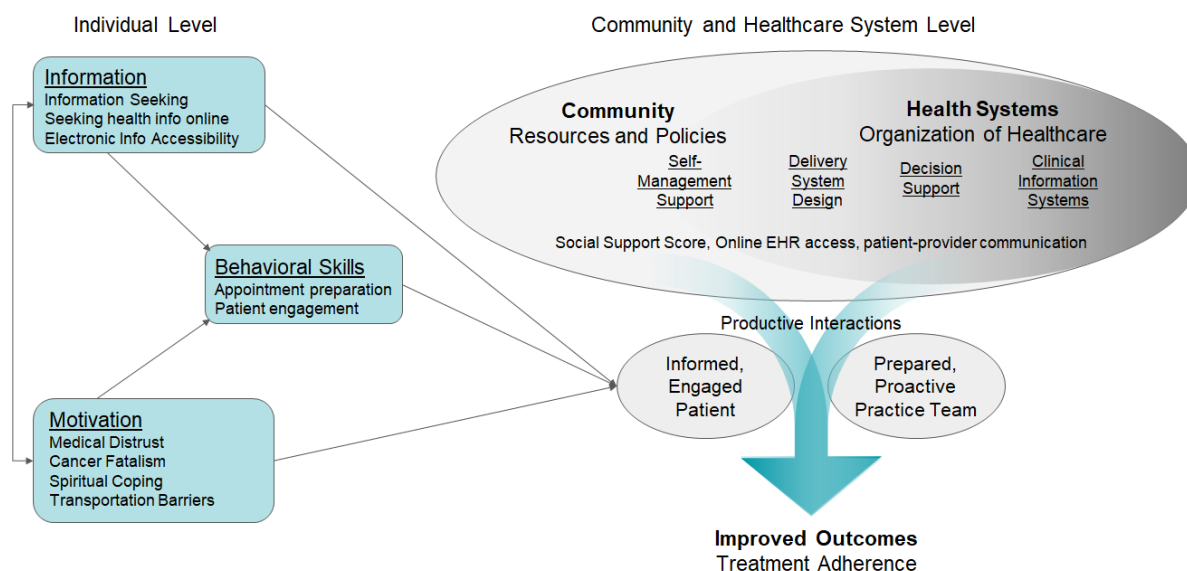
Figure 1. Information-Motivation-Behavioral Skills Theory applied to the Chronic Care Model in rural cancer care

RESEARCH AIMS

The premise of the dissertation research is that multilevel factors contribute to the observed geographic differences in cancer treatment adherence and outcomes, including sociodemographic inequities, differences in information and motivational factors, and diminished access to healthcare, psychosocial services, and technological advances. Rural cultural factors serve as barriers and facilitators to treatment adherence and may be positively impacted by digitally mediated interventions. However, extant studies aimed at determining factors contributing to nonadherence among rural cancer survivors have not fully investigated the social, behavioral, and systems-level factors that might be contributing to nonadherence. The purpose of the dissertation research was to elucidate factors associated with rural cancer treatment nonadherence that are amenable to targeted, tailored approaches to improve rural oncology outcomes. These goals were accomplished by a rigorous mixed methods approach utilizing a systematic review of available literature, cancer registry and hospital billing claims data, population-based surveys, and semi-structured interviews.

Aim 1. Systematically and critically examine existing literature to understand how digital technologies have been used to support rural oncology care.

Hypothesis: Digital health strategies have been less extensively utilized in rural cancer populations compared with the general cancer population and other chronic diseases.

Rationale: Digital technology has the potential to support treatment adherence, yet it is unclear the extent that it has been utilized in rural cancer populations.

Aim 2. Determine sociodemographic and clinical factors associated with nonadherence among rural and nonrural cancer patients using healthcare claims data. We utilized cancer registry and hospital billing claims data to distinguish sociodemographic and clinical factors associated with first-line cancer treatment nonadherence based on federally defined geography classifications (USDA 2013 Rural-Urban Continuum Codes).

Hypothesis: Geography plays a significant role in radiation treatment nonadherence, with higher nonadherence rates being observed among rural cancer patients.

Rationale: Rural cancer patients experience a 10% higher mortality rate compared with their nonrural counterparts, with geographic differences in adherence as a possible contributor to this increased mortality rate. Radiation treatment is both time and resource intense, making adherence especially challenging.

Aim 3. Delineate social and behavioral determinants of treatment nonadherence among rural cancer patients using a mixed method approach. We administered a quantitative survey with constructs guided by Information-Motivation-Behavioral Skills theory. We then conducted an in-depth examination of factors salient to rural culture in oncology patients within an asset-based framework, informed by survey results, and considering the potential acceptability for digitally mediated interventions (e.g., text messaging, mobile apps, Voice Assistant technology).

Hypothesis: Factors relevant to the IMB-CCM are associated with treatment nonadherence.

Rationale: Multilevel factors contribute to cancer treatment nonadherence yet have not been fully investigated.

CHAPTER 2: Paper One

The Role of Digital Health in Rural Oncology: A Systematic Review

ABSTRACT

Background

Rurality is associated with higher cancer incidence rates, mortality rates, and treatment nonadherence. Rural residents face significant challenges, including higher poverty rates, lower educational attainment, diminished access to health and psychosocial services, and are more likely to be elderly. Health technologies may serve to address some of these disparities, yet a digital divide is also apparent in rural residents.

Purpose

To systematically and critically examine existing literature to understand how digital technologies have been used to support rural oncology care. We hypothesized that digital health strategies have been less extensively utilized in rural cancer populations compared with the general cancer population and other chronic diseases.

Methods

PubMed, CINAHL Complete, PsycINFO and Embase were searched using a combination of Medical Subject Headings terms and keywords. Studies were eligible for inclusion if they presented empirical data aimed at investigating the use of technology in rural oncology survivors and published in English in a peer-reviewed journal within the last decade. The Mixed Methods Appraisal Tool was used to assess methodological quality.

Results

Of the 515 unique articles identified, 69 articles were eligible for full-text screening, and 53 articles met study inclusion criteria. Studies were classified into 4 categories Telemedicine (n= 31), telephone (n= 11), internet (n= 9), and mobile phone (n= 3). Of the 53 articles, 12 were RCTs, 17 were quasi-experimental, 3 were descriptive, 11 were mixed methods and 10 were qualitative. Most of the studies involved patients only (n=30), did not provide a definition of 'rural' (n=37), and were not specific to a cancer type (n=41). An in-depth examination of each study and its quality are presented and discussed.

Conclusions

While there are literature gaps regarding other technologies, further implementation and expansion of telemedicine and phone-based strategies in rural cancer care delivery is warranted. Overall, there is considerable room for growth in digital health for rural oncology. Social and behavioral determinants of health and access to technology must be considered. Future studies can be expanded across the cancer care delivery model to include family-, provider-, and system-level interventions.

BACKGROUND

Cancer remains a leading cause of death in the United States, despite decreasing mortality rates, accounting for more than 600,000 deaths in 2019.[1] Of the 15 million cancer survivors in the US, nearly 3 million reside in rural areas and experience 10% higher cancer mortality compared to their nonrural counterparts.[3] During 2006-2015, the annual age-adjusted death rates for all cancer sites combined decreased at a slower pace in rural areas versus nonrural areas, widening the disparity in mortality rates.[4] Rural cancer survivors tend to be older, have additional comorbidities and poorer general health, and as a group have a higher prevalence of lifestyle risk factors that complicate survival, such smoking, lack of physical activity and obesity.[5–8]

Access to care is a major factor driving geographic disparities. Rural areas have a lower county-level physician supply, and importantly, a lower density of specialists like radiation oncologists.[30] Less than 3% of medical oncologists practice in rural areas.[31] Rural residency has been associated with higher unmet care needs and reduced access to supportive care services among cancer survivors, including social work, palliative care, and hospice services.[30,34,58] Access to care issues are further exacerbated by the increased rate of rural hospital closures in recent years.[59] Limited local health services means patients must travel further for care, with median travel times ranging from 51 minutes to 97 minutes.[33] Additionally, poverty creates substantial transportation barriers, making it a challenge for rural residents who are also poor to afford gas or even a car. Since over 1.6M rural households do not have cars, transportation to treatment appointments presents a very real challenge.[34] Web-based needs assessments have facilitated exploration of unmet rural cancer survivor needs, captured enduring survivorship issues and recommended the use of technology to better inform and support patients and connect providers.[60,61] Digital health can support patient, provider, and system-level needs for distance-based care strategies, which may serve to ultimately mitigate rural disparities in cancer outcomes that arise due to lack of access to care.

Digital health

Digital health can be defined as "using digital information, data, and communication technologies to collect, share, and analyze health information for purposes of improving patient health and health care delivery."[62] Telemedicine, which employs technology to administer distance-based healthcare, is one of the more widely used subcategories of digital health, while mobile applications (apps) are increasingly used for real-time or regular symptom assessments, health-related reminders, and tailored health feedback with studies reporting significantly improved health outcomes.[63,64] While digital health technologies have potential to optimize health care delivery, key barriers impede broad implementation and the rate of healthcare digitalization and consumer demand has exceeded the healthcare systems' ability to modernize its infrastructures and adapt to new workflows.[65] Across all disease types and patient populations, there is a need to address these barriers to catch up with the technological curve and implement tools and strategies that are evidence-based.

Digital health in chronic disease management

Previous articles have reviewed the use of digital health technology in the management of a variety of chronic diseases, including hypertension, diabetes mellitus, rheumatology, chronic

obstructive pulmonary disease, inflammatory bowel disease, and mental illness.[66–71] A 2015 scoping review of information and communication technology (ICT) chronic disease interventions identified 350 studies targeting diabetes mellitus (n=103), cardiovascular disease (n=89), chronic respiratory disease (n=73), cancer (n=67), and stroke (n=18).[72] With respect to cancer, this scoping review found that use of ICT interventions were most broadly applied in cancer care compared with other chronic diseases, with a wider variety of activities involving self-management and engagement in their healthcare. Studies were more likely to include ICT interventions for one-way delivery of educational materials versus a patient-centered exchange of information and shared decision-making. Additional articles have reviewed availability and features of mobile applications related to cancer across the care continuum.[73,74] Specific to the cancer treatment phase, Davis categorized apps by the following use cases: supporting patient-provider communication, patient information management, and managing treatment side effects.[74] Digital health strategies have also been examined within subpopulations, including adolescent, young adult and geriatric cancer survivors, but have yet to be examined within the rural context.[75,76]

Digital health in rural healthcare delivery

A 2019 study found that those living in rural areas had reduced odds of having internet access compared with those residing in nonrural areas (OR 0.75; 95% CI 0.67-0.84).[77] In this paper we will refer to the rural digital divide as the inability of rural populations to access services and information through technology. A key contributor to the rural digital divide and critical to the deployment of digital health strategies is access to the mobile, internet or broadband infrastructure that supports these tools. Access could occur through a fixed connection at home or work, or through cellular service on a mobile phone. The Federal Communications Commission's 2019 Broadband Deployment Report found that over 26% of Americans in rural areas lack coverage from fixed terrestrial 25 Mbps/3 Mbps broadband that would allow for home internet access, as compared to only 1.7% of Americans in nonrural areas.[36] Deployment of mobile Long-term Evolution, more commonly known as LTE and the pathway to achieve high speed cellular internet service, still lags in rural areas. Specifically, only 70% of the rural population has service with a median speed of 10 Mbps/3 Mbps versus 93% of the nonrural population. An important step in addressing these disparities is to develop more granular broadband availability maps, a step taken by Congress in March 2020 in passing the Broadband Deployment Accuracy and Technological Availability Act.[37]

Social drivers relevant to technology access and use include higher poverty rates, lower educational attainment, and a higher proportion of elderly residents in rural communities.[6,9,12,40,78] The Pew Research Center reported that 63% of rural residents say they have a broadband internet connection at home, compared with 75% of nonrural residents.[79] Similarly, 71% of rural residents reported having a smartphone, versus 83% of nonrural residents. Additionally, 15% of rural adults say they never go online, compared with 9% of those who live in nonrural communities. Specific to use as a health resource, rural residents are less likely to manage personal health information online or email a healthcare provider.[38] Technology tools such as mobile apps are being used in the general cancer survivor population,[73] yet the extent to which they are being employed in rural cancer populations is unknown.

Purpose

Digital health strategies may be used to mitigate rural cancer disparities. Despite progress made in understanding how digital health can enhance cancer care, previous reviews have not focused on their use in rural populations. The aim of this study was to systematically and critically examine existing literature to understand how digital technologies have been used to support rural oncology care. We hypothesized that digital health strategies have been less extensively utilized in rural cancer populations compared with the general cancer population and other chronic diseases.

METHODS

We conducted a systematic literature review of technology use in rural oncology research studies. Studies were eligible for inclusion if they presented empirical data from a human subjects study aimed at investigating the use of technology in rural cancer care delivery and published within the last decade (January 2009 – December 2019). Articles were excluded if they did not involve cancer survivors (defined from diagnosis forward), did not include rural participants, or were not available in English in a peer-reviewed journal. Searches were performed in PubMed, CINAHL Complete, PsycINFO and Embase to identify relevant articles using a combination of Medical Subject Headings terms and keywords determined based on the literature (Paper 1 Appendix 1).

Data collection

We first reviewed titles and abstracts of search results. Full text of likely eligible articles was retrieved, screened by one research team member, and then verified by a second. Disagreements between authors were resolved by discussion or consultation with a third author. Reasons for the exclusion of full text articles were recorded. Data was extracted onto a standardized data abstraction sheet by the first and second authors independently. Discrepancies were discussed and resolved by the study team. The following information was extracted: publication year, first author, country, study design, study population, rural definition (if provided), rural sample size, total sample size, cancer site(s), type of technology considered and study outcome(s). Technology type was categorized as telemedicine (video phone visits and telemonitoring systems), telephone, mobile phone (text messages and phone-based apps), and internet (websites and web-based applications). These categories were selected to compare use of digital health in the rural cancer context with general cancer and other chronic disease populations presented by Wildevuur et al.[72]

Quality appraisal

Each study that met inclusion criteria were assessed for study quality using the Mixed Methods Appraisal Tool (MMAT), which allows for the critical appraisal of quantitative, qualitative, and mixed methods studies.[80,81] The MMAT was developed to address the challenges of critical appraisal in systematic reviews involving more than one study design. Each study type is assessed by five quality indicators, items that were developed from the literature as well as consultations and workshops with experts.[81,82] Its efficiency and reliability have been previously demonstrated.[81,83]

RESULTS

The initial search yielded 595 articles. An additional 5 articles were identified through review of reference lists. After removing duplicates, there were 515 unique articles remaining. Review of titles and abstracts resulted in 69 articles eligible for full-text screening, and 53 of these articles met study inclusion criteria (Figure 1).

Study Quality

Of the 53 articles that met inclusion criteria, only 22 provided sufficient information to assess study quality using a standardized tool (Figure 2). Information was most complete for qualitative studies. Eight out of 10 qualitative studies provided complete MMAT assessment information, while 5 out of 12 randomized controlled trials, 3 out of 17 quasi-experimental studies, 2 out of 3 descriptive studies, and 4 out of 11 mixed methods studies provided complete MMAT assessment information. Five qualitative studies and 1 mixed methods study performed the best in quality reporting per the MMAT, meaning that reporting was sufficient to assess all five of the MMAT quality criteria for the respective study type (Figure 3). Quantitative non-randomized studies were the lowest performing.

Methodological Characteristics

Of the 53 articles, 12 were randomized controlled trials (RCTs), 17 were quasi-experimental, 3 were descriptive, 11 were mixed methods and 10 were qualitative. Most of the studies involved patients only (n=30), did not provide an explicit definition of 'rural' (n=37), and were not specific to a cancer type (n=41) (Table 1). Of the 12 RCTs, the median sample size was 142 (mean=181.91 [45-451]). Technology utilized in the 53 articles were categorized as Telemedicine (n= 31), telephone (n= 11), internet (n= 9), and mobile phone (n= 2). Table 2 quantitatively compares the categorical findings of this study with the digital technology review by Wildevuur and colleagues across five chronic diseases.[72] Telemedicine makes up a much larger percentage of studies for rural cancer survivors versus the general cancer population, while internet and mobile strategies were less commonly used.

Types of Technology

Telemedicine. Telemedicine articles focused on care delivery (n=22), training (n=4), multidisciplinary cancer teleconferences (i.e., tumor boards, n = 2), telemonitoring (n=2), and cancer support (n=1). The most thoroughly described rural teleoncology model is the Townsville Cancer Centre (TCC) teleoncology program established in 2007 for rural cancer care delivery, totaling 974 participants.[84] Medical oncologists at TCC provide their services via videoconference with rural-based doctors, chemotherapy-competent nurses, allied health workers and patients in consultation. Initially patients were required to attend at least one face-to-face appointment at TCC, which became optional in 2009. The program was expanded to radiation oncology in 2011.[85] The studies conducted were able to establish that teleoncology was feasible, acceptable to patients and healthcare workers, and cost-effective.[86–90] High patient satisfaction was reported with the quality of the video consultation and in establishing rapport with the specialist over video conference. Patients overall preferred video conference to face-to-face consultations and were very satisfied with care received via the teleoncology program.[85,87,91]

Healthcare professionals similarly reported high satisfaction in the program, including patient convenience, interprofessional communication, expanded scope of practice, and continuity of care and maintenance of patient safety.[90] Thaker determined that the TCC model resulted in a net savings of $320,118 over 56 months and that costs would have to increase by 72% to negate the savings.[88] Two additional telemedicine studies examined use of mobile chemotherapy units in rural areas of the United Kingdom.[92,93] Specialty care delivery examined via the use of telemedicine in rural areas included speech pathology services for head and neck cancer patients, pharmacy services, mental healthcare, pain management, genetic counseling, and palliative care.[94–103] These studies were in agreement that telehealth is less expensive, equal quality, more efficient, and had high satisfaction for delivering rural oncology care.

Telemedicine as a training platform was examined in the rural cancer setting in four studies and was a feasible and satisfactory means of delivering real-time, interactive training to providers who might not otherwise have access to such programs. Training included continuing medical education, training on a cancer support intervention, and surgical oncology telementoring.[99,104–106] Connecting community oncologists with multidisciplinary cancer conferences (tumor boards) via teleconference was considered in two articles.[107,108] These articles demonstrated initial feasibility of providing oncologists in rural areas and at smaller institutions access to tumor boards to improve the quality and continuity of care.

Feasibility of telemonitoring for rural cancer patients was considered in two articles, with the first determining that the potential exists for melanoma follow-up telemonitoring if the technology is tailored by age, skill level, area of residence and time since diagnosis.[109] Petitte and colleagues remotely collected physiologic data in lung cancer patients who were post-hospital discharge.[110] Despite low sample size, telemonitored data transmission was feasible in rural areas with high satisfaction. Lastly, one study considered the acceptability of telehealth support group services for rural American Indian and Alaskan Native communities and found that participants valued the opportunity to connect with other similar survivors living in remote areas.[111]

Telephone. Telephone studies (n= 11) were composed of group or individual phone calls. Studies focused on weight loss (n=4), palliative care (n=2), caregiver support (n=3), and decision support (n=2). A quasi-experimental study by Befort utilized weekly group phone sessions in addition to a specified reduced calorie diet and physical activity plan.[112] The intervention resulted in significantly improved clinical outcomes and quality of life. This study demonstrated feasibility and favorable outcomes in a group of rural breast cancer survivors, though the benefits could not be directly attributed to the technology portion of the intervention. The second phase of the study involved a 12-month intervention in which participants were randomized to either continued biweekly phone-based group counseling or mailed newsletters.[113] The study concluded that the technology intervention improved the magnitude of weight loss maintained over 18 months as well as increased the proportion of participants who maintained clinically significant weight loss. Additionally, Fazzino reported that this intervention was successful in improving physical activity outcomes over 18 months, as measured by accelerometer.[114] A follow-up qualitative study revealed technology-related themes of the group phone counseling sessions providing benefits of accountability and connectedness, as well as the inconvenience of scheduling and duration of the sessions (1 hour).[115]

Rural residents are less likely to have access to palliative care and hospice services.[30] The ENABLE II randomized controlled trial, based on its predecessor, Project ENABLE, was designed to facilitate early integration of palliative care.[116] Rural patients with advanced cancer were randomly assigned to a phone-based, nurse-led educational and care coordination palliative care intervention or to receive usual care. Patients receiving the technology intervention were found to have significantly higher self-reported quality of life and mood, while comparisons of symptom intensity and days in the hospital, ICU and emergency department visits were not significantly different.[116] When the intervention was applied using a waitlist control, patients receiving the technology intervention upon enrollment versus 3 months later had higher 1-year survival rates.[117] The ENABLE intervention was extended to caregivers in the ENABLE III randomized controlled trial, which was found to lower depression scores among caregivers.[118] The ENABLE research team conducted a qualitative study to support further scalability of the intervention in rural settings and found that caregivers perceived intervention delivery via telephone to be acceptable, while there was concern that internet-based technologies may have limited use due to lower skill and access.[119]

Providing treatment decision support within the constraints of a fast-paced clinic environment has led to remote delivery of consultation planning. One method involves coaching patients to develop a list of personalized questions to bring to their next clinic appointment to promote patient involvement in their care and treatment decisions. Two studies included in this review examined treatment decision support. These studies found that remote consultation planning was equally effective, with comparable quality, cost and value as in-person consultation planning, while increasing accessibility of decision support services in rural communities.[120,121]

Internet. Studies utilizing websites (n=9) included in this review examined educational, symptom management, and lifestyle support programs delivered in an online format to address access issues in the rural setting. In one such example, the Oncology Associated Symptoms and Individualized Strategies (OASIS) program was developed to provide tailored cancer symptom self-management support delivered through an online format to address access to care issues in rural cancer populations.[122] The team used a three-phase mixed methods design engaging rural stakeholders to develop the program and assess usability. One of the qualitative themes that emerged regarded technology access and highlighted that while not all patients used technology, they often had family members and caregivers who did. This OASIS research program is still in progress, with results on feasibility and acceptability of the intervention incorporating nurse-coach contact forthcoming.

Syrjala described a personalized, Internet-based survivorship care program targeting emotional distress, depression, and fatigue for hematopoietic cell transplant survivors.[123] Survivors more likely to engage with the online site were female, had active graft-vs-host disease as a side effect to their cancer treatment, and had moderately elevated levels of cancer distress. Importantly, engagement was strong in subgroups with less access to care, including rural survivors, although eligibility criteria excluded those without computer or email access.

Fennell presented a website with community involvement to address psychosocial information needs that are relevant, accessible and acceptable to increase rates of support service use among rural cancer survivors.[124] Importantly, website design not only incorporated information targeted to rural populations but also sought to address attitudinal barriers to service use (e.g. medical

mistrust, belief that help is unnecessary or shows weakness, finding help is too hard) and tailored information by stage of change and level of distress. Survey results documented that participants were significantly more willing to access professional and peer support after using the website, and that 67% of respondents were more motivated and confident in accessing resources. 73% of respondents also felt less isolated after utilizing the website.

One qualitative study used semi-structured interviews to examine the use of an online lifestyle intervention and found that the program motivated participants to increase their walking and improved self-reported physical and quality of life outcomes.[125] Key benefits of the program discussed by participants included individualized step goals, the website's ease of use, and the program contributing to the participant's self-awareness and engagement in their health. Participants would have preferred the program to be more interactive, with the ability to make comments on their activity and engage online with study staff. Methodological limitations of this study were the low sample size (N=9) and eligibility excluding those without access to the internet.

Support groups have been shown to improve psychosocial symptoms associated with cancer and improve quality of life, yet access is an issue for rural residents.[126,127] CancerChatCanada offered professional-led live-chat support groups for cancer patients and caregivers that were held weekly for 90 minutes over the course of 10-12 weeks. The program led 55 of these online support groups, enrolling 351 participants with more than half from rural areas. Of the 55 groups, 19 were for breast cancer survivors and 19 were for caregivers. Weekly attendance in the group sessions averaged 75% with a 26% dropout rate. Participants reported high satisfaction and psychosocial benefit, with any initial discomfort in communicating online in a live chat group being outweighed by access to support at home. Typing versus talking was viewed as a benefit by giving added time for reflection, organizing thoughts and not impending emotional expression (e.g. able to cry while typing but not while talking).

Koczwara described an online education program incorporating palliative and supportive care, as well as strategies to support multidisciplinary care in the rural setting.[128] Content was developed by utilizing stakeholder surveys and focus groups. Use of the online format allowed for a broader reach than in-person instruction, and program evaluation indicated high satisfaction.

Mobile phone. Only 2 studies focused on using a mobile app among rural cancer survivors. The first study used a mixed methods approach and developed a health services locator app for both providers and cancer survivors; however, additional studies are needed to evaluate the feasibility, acceptability and effectiveness of implementing this app on a broader scale.[129] Secondly, Baseman and colleagues developed a breast cancer survivorship care app called SmartSurvivor.[130] Components of the app included a medical profile, a journal section with a tracking tool for self-monitoring, calendar links for reminders and appointments, tailored survivor tips and tools, and the ability to audiorecord for documenting notes and appointment questions. Qualitative results highlighted key features and utility of the app, while also discussing the need for it to be tailored for rural users. Overall, the app was found to be both feasible and acceptable as a breast cancer survivorship tool and could serve as a foundation for developing a tool to support rural breast cancer survivors.

DISCUSSION

While there have been other reviews focused on digital technology use in cancer care delivery, this is the first within the rural cancer setting.[73–76,131] The overall aim of this study was to systematically and critically examine existing literature to understand how digital technologies have been used to support rural oncology care. Rurality is associated with higher cancer incidence and mortality rates, and rural residents face significant challenges influencing access to healthcare. Health technologies may serve to address some of these disparities, yet we correctly hypothesized that digital health strategies have been less extensively utilized in rural cancer populations compared with the general cancer population and other chronic diseases.

We identified 53 studies that addressed the use of technology in rural cancer care delivery, a comparatively small number, representing a significant gap in the literature. The limited number of studies is surprising since digital health strategies could improve access to care issues faced by rural cancer survivors; however, mobile and broadband availability remains an issue in rural areas.[36,79] Across all studies was the consensus that rural cancer survivors value digital technology approaches to their care, with results varying by type of technology.

A notable finding from the present review was that most studies used telemedicine approaches. While the designs and approaches differed across these studies, it was generally concluded that telemedicine is a feasible and acceptable approach to improving care delivery. Telemedicine studies were able to demonstrate both improved patient outcomes and improved access to care. Specifically, a randomized controlled trial examining telecare management on pain and depression outcomes among rural and nonrural cancer patients found a significant increase of 60 depression free days, as well as an increase in quality-adjusted life years compared to the usual care group.[98] A palliative care telemedicine study found significantly improved anxiety and appetite at the first follow-up visit among rural cancer patients.[102] Implementing a comprehensive program of telemedicine and patient navigation, genetic counseling increased for ovarian cancer patients increased from 37% to 96% and for triple negative breast cancer patients from 69% to 91%. Genetic testing doubled for ovarian cancer patients and increased from 59% to 86% in triple negative breast cancer patients.[101] These studies speak to the potential utility of telemedicine approaches to address cancer survivorship in rural settings.

Due to limited access to oncology specialists, including palliative care, rural cancer patients rely on their local medical providers to manage their illness, yet there is a need to support cancer management education for these providers.[128,132,133] While only four studies that examined telemedicine as a training platform and telementoring met study inclusion criteria, widespread success of telementoring models exist in other areas of medicine.[8] For instance, Project ECHO (University of New Mexico [UNM] Health Sciences Center, Albuquerque, NM) is a telementoring platform for implementing best practices at scale by employing interdisciplinary teams of experts to mentor multiple rural providers participating remotely from their practices using videoconferencing technology.[134] The Cancer ECHO Initiative has 75 cancer ECHO hubs worldwide (39 in the United States) offering 135 programs in 14 countries. Project ECHO was originally initiated to improve hepatitis C care delivery in 2003 and has since been expanded to 393 hubs with 850 programs in 39 countries that cover training for community providers on more than 70 conditions, including cancer. The findings herein support continued expansion of telemedicine and telementoring approaches to address rural cancer care delivery.

While telemedicine represented the largest category of studies in the present review, phone-based studies had the most RCTs for both quantity and percentage (7/11, 64%). Phone-based interventions supported weight loss in cancer survivors and improved patient outcomes in palliative care. Phone-based strategies increased survivors' feelings of connectedness and facilitated access to care, and, as noted by the ENABLE team, was preferred over internet-based technologies that may have limited use due to lower skill and access.[119] Future studies should focus on implementation strategies to optimize these programs for long-term sustainability.

Internet-based digital health approaches involving patients may emerge as being useful but may also pose a potential challenge for implementation in rural populations. Rural residents are less likely to have regular access to the internet, manage personal health information online or email a healthcare provider.[38] Participants have reported concern with using internet-based interventions for palliative care due to lower comfort with technology and access to the internet.[119] Patients may be more likely to attend in-person counseling, attributed to a significant association found between decreased computer comfort and attendance rate in telegenetics.[100] Other telemedicine studies did not support this finding, but the discord may be attributed to the skills and technology needed to virtually attend a genetic counseling appointment from home versus teleconference with a oncology specialist from a cancer clinic or primary care facility closer to home.

Ease of use and technological requirements are important considerations in rural populations. For instance, applications or 'apps' can be desktop, mobile, and/or internet-based. Desktop apps usually have all the features of a program, whereas the mobile equivalent is a simpler and easier-to-use version. Internet or web apps can have extensive features too, but they must leverage the capabilities of the internet connection and the web browser program. Only 2 studies involved a mobile app, yet the more streamlined format may be preferred over web-based versions in rural populations. To this point, a prior secondary analysis of the National Cancer Institute's Health Information National Trends Survey found that rurality was associated with the use of mHealth applications for making treatment, indicating mobile phone apps as a means to increase access to health information.[135] There is a need to further expand this area of research.

The majority of studies (37/53) did not provide a definition of 'rural'. There are a number of ways that geography can be classified for the purposes of rural research and policy. Each classification has its own unique attributes and implications, further complicating comparison across studies even when the classification is reported (see Paper 1 Appendix 2). In the US, the main classifications are provided by the US Census Bureau, the US Office of Management and Budget (OMB), and the US Department of Agriculture (USDA). The USDA utilizes two classifications, the Rural-Urban Commuting Area (RUCA) codes and the Rural-Urban Continuum Codes (RUCC).[136,137] Australia, from which a number of the telemedicine studies presented in this review were published, uses the Accessibility/Remoteness Index of Australia (ARIA). Similarities do exist between the 4 US-based classifications; namely, the same definition of urban area (UA) and urban cluster (UC), incorporating UAs as a key attribute, and basing population sizes on 2010 Census data. The US Census Bureau defines its categories as "Urban Area", "Urban Cluster", and "Rural Area" by population size and density in census areas.[138] A limitation of this method is apparent for single census tracts that are composed of both urban and non-urban census block groups or census blocks. OMB defines its categories by population size in counties, first defining Metropolitan and Non-Metropolitan, then further

subdividing Non-Metropolitan into Micropolitan and Non-core).[139] This classification system has the similar limitation of the Census Bureau definition, with larger counties having the potential to include both urban and rural areas and being more likely to underestimate the rural population. USDA RUCA codes range from 1 to 10 based on population density, proximity to an UA, and daily commuting patterns. While it has the benefit of including the functional relationship of commuting rates, it fails to account for distance to services and sparse populations in large census tracts. RUCC is also provided by the USDA, but is based on population size, proximity to an UA, and adjacency to a metro area. In this respect it is more similar to OMB but minimizes the effects of county size variations by defining geographic units of finer granularity. Aside from the broad implication of complicating comparisons across studies, the definition chosen can result in different areas being classified or not classified as rural, such that estimates of the rural US population range from 15 - 19.3% and estimates of rural land ranging from 72 - 95%.

As evident by the present review and assessed by the MMAT, there are limitations to the state of the science. Despite the availability of standardized reporting guidelines by study design like CONSORT and STROBE, there is room for improvement in practice in terms of both study design and reporting results. Overall, there were few randomized trials and samples sizes low. Most studies restricted participants to those with internet access without reporting on how many potential participants were excluded due to access. Few studies measured access to care variables. No studies examined the use of interactive voice response, electronic health records, patient portals, or social media in the context of rural cancer survivors. Despite the benefits of text messaging as an intervention strategy, including reach, engagement, low cost, and documented effectiveness in directly supporting behavior change, no studies using text messaging were identified for inclusion in this study.[140] Given the study limitations and knowledge gaps identified in this review, we recommend the following: Investigators should take advantage of available guidelines like CONSORT at both the study design and reporting phase to improve the quality of literature in this research area. Furthermore, studies should continue to build upon and expand telemedicine and phone-based interventions as digital health strategies at a more widespread scale, yet also consider innovative or underutilized strategies like interactive voice response and text messaging.

This review is not without some limitations. We could not measure quality in every study and were restricted to evaluating the information reported. Broad variation in study design prevented us from performing meta-analyses. Varying definitions of rurality presented by the US Census Bureau (urban vs not urban), the US Office of Management and Budget (metropolitan vs non-metropolitan), the US Department of Agriculture (Rural-Urban Commuting Area Codes and Rural-Urban Continuum Codes), Australia (Accessibility/Remoteness Index of Australia), and research teams (patient travel distance), and thus adopted inconsistently in the literature led to difficulty in generating comparisons across studies. As is the case with other systematic reviews, there may be publication bias present, with studies finding null results being less likely to be published and therefore included in this review. Despite the limitations, our study synthesizes lessons learned thus far on designing and implementing digital health studies among rural cancer survivors and highlights the gap in knowledge on technology use in this population.

To conclude, unique challenges faced by rural cancer survivors require targeted approaches. More research is needed involving studies of high scientific and methodological rigor and employing cutting-edge technology to support this underserved population. Critical to reducing

the rural digital divide and the deployment of digital health strategies is increasing mobile, internet or broadband service in rural areas. While steps are being taken to address this geographic disparity, the fact remains that nearly 30% of Americans live in areas that lack the coverage needed for home internet. The findings of this review suggest further implementation and expansion of telemedicine and phone-based strategies in rural cancer care delivery. Ease of use and technological requirements are important considerations in rural populations. Future rural cancer control studies would benefit from the use of mixed methodology and a theoretical framework to guide study development. There are significant gaps in the literature regarding patient portals, mobile apps, interactive voice response, social media, and text messaging that should be investigated. Opportunities exist for innovative digital health technologies to address rural cancer control.

Table 1. List of studies included in systematic review

Study	Year	First Author	Country	Design	Rural definition	Population	n Rural	n Non-Rural	N total	Cancer Type	Outcomes
Telemedicine											
A comprehensive program enabling effective delivery of regional genetic counseling	2018	Brown, J	US	Quasi	Distance from clinic	Patients	--	--	118	Multiple	Utilization of genetic counseling (in-person and telemedicine)
A pilot trial of a speech pathology telehealth service for head and neck cancer patients	2012	Burns, CL	Australia	Quasi	Not defined	Multiple	20	0	20	Head and neck	Program evaluation
A tele-oncology model replacing face-to-face specialist cancer care: perspectives of patients in North Queensland	2014	Sabesan, S	Australia	Qual	Not defined	Patients	35	0	35	Multiple	Exploratory, thematic analysis of interviews
Acceptability and feasibility of an e-mental health intervention for parents of childhood cancer survivors: "Cascade"	2016	Wakefield, CE	Australia	RCT	ARIA	Caregivers	9	36	45	Multiple	Feasibility, acceptability
Assessing the feasibility of a virtual tumor board program: a case study	2014	Shea, CM	US	Mixed	Not defined	Healthcare providers	12	16	28	Multiple	Acceptability, barriers, value
Can we use technology to encourage self-monitoring by people treated for melanoma? A qualitative exploration of the perceptions of potential recipients	2014	Hall, S	Scotland	Qual	Not defined	Patients	14	5	19	Melanoma	Thematic analysis of interviews
Cost effectiveness of telecare management for pain and depression in patients with cancer: results from a randomized trial	2014	Choi Yoo, SJ	US	RCT	Not defined	Patients	--	--	405	Multiple	Intervention costs, depression-free days, QALYs
Cost savings from a telemedicine model of care in northern Queensland, Australia	2013	Thaker, DA	Australia	Quasi	Not defined	Patients	147	0	147	Multiple	Cost-savings
Development of a virtual multidisciplinary lung cancer tumor board in a community setting	2013	Stevenson, MM	US	Quasi	Not defined	Healthcare providers	10	0	10	Lung	Acceptability, barriers, value
Do teleoncology models of care enable safe delivery of chemotherapy in rural towns?	2015	Chan, BA	Australia	Quasi	Not defined	Patients	89	117	206	Multiple	Dose intensity, toxicity rates
Enhancing access to cancer education for rural healthcare providers via telehealth	2011	Doorenbos, AZ	US	Quasi	Not defined	Healthcare providers	71	0	71	Multiple	Program evaluation
Enhancing Chemotherapy Capabilities in Rural Hospitals: Implementation of a Telechemotherapy Model (QReCS) in North Queensland, Australia	2018	Sabesan, S	Australia	Quasi	Not defined	Patients	62	0	62	Multiple	Enablers, barriers, provision, Rates of treatment delays, adverse events, and hospital admissions
Feasibility study: home telemonitoring for patients with lung cancer in a mountainous rural area	2014	Petitte, TM	US	Quasi	Not defined	Patients	10	0	10	Lung	Enrollment and retention characteristics, symptoms, program satisfaction
Identifying the readiness of patients in implementing telemedicine in northern Louisiana for an oncology practice	2017	Gurupur, V	US	Descr	Not defined	Patients	78	69	147	Multiple	Feasibility

Study	Year	First Author	Country	Design	Rural definition	Population	n Rural	n Non-Rural	N total	Cancer Type	Outcomes
Improving access to specialist multidisciplinary palliative care consultation for rural cancer patients by videoconferencing: report of a pilot project	2013	Watanabe, SW	Canada	Quasi	Not defined	Patients	44	0	44	Multiple	Utilization, symptom management, cost-savings, satisfaction
Medical oncology clinics through videoconferencing: an acceptable telehealth model for rural patients and health workers	2012	Sabesan, S	Australia	Mixed	Not defined	Multiple	68	0	68	Multiple	Satisfaction
Patient perceptions of a mobile cancer support unit in South Wales	2011	Iredale, R	UK	Mixed	Not defined	Patients	97	0	97	Multiple	Quantitative and qualitative patient satisfaction
Patients' experiences of receiving chemotherapy in outpatient clinic and/or onboard a unique nurse-led mobile chemotherapy unit: a qualitative study	2013	Mitchell, T	UK	Qual	Not defined	Patients	20	0	20	Multiple	Thematic analysis of interviews
Randomized controlled trial of a multisite speech pathology telepractice service providing swallowing and communication intervention to patients with head and neck cancer: Evaluation of service outcomes	2017	Burns, CL	Australia	RCT	Not defined	Multiple	--	--	82	Head and neck	Service efficiency, satisfaction
Randomized trial of telegenetics vs. In-person cancer genetic counseling: cost, patient satisfaction and attendance	2015	Buchanan, 2015	US	RCT	Not defined	Patients	162	0	162	Multiple	Cost, satisfaction, utilization
Remote chemotherapy supervision model for rural cancer care: perspectives of health professionals	2016	Jhaveri, D	Australia	Qualitative	Not defined	Healthcare providers	19	0	19	Multiple	Thematic analysis of interviews
Role of telehealth/videoconferencing in managing cancer pain in rural American Indian communities	2012	Haozous, E	US	Quasi	Not defined	Healthcare providers	52	0	52	Multiple	Satisfaction and self-perceived competence
Safe introduction of laparoscopic colorectal surgery even in remote areas of the world: The value of a comprehensive telementoring training program	2015	Forgione, A	Russia and Italy	Quasi	Not defined	Healthcare providers	1	0	1	Colorectal	Program evaluation
Satisfaction with telehealth for cancer support groups in rural American Indian and Alaska Native communities	2010	Doorenbos, AZ	US	Quasi	Not defined	Patients	32	0	32	Multiple	Satisfaction, distance, time
Telehealth in radiation oncology at the Townesville Cancer Centre: Service evaluation and patient satisfaction	2018	Hamilton, E	Australia	Quasi	Distance from clinic	Patients	311	0	311	Multiple	Service evaluation, satisfaction
Telemedicine for rural cancer care in North Queensland: bringing cancer care home	2012	Sabesan, S	Australia	Quasi	Not defined	Patients	158	0	158	Multiple	Service provision
Teleoncology for indigenous patients: the responses of patients and health workers	2012	Mooi, JK	Australia	Qual	Not defined	Multiple	15	0	15	Multiple	Satisfaction
Telepharmacy in a rural alberta community cancer network	2012	Gordon, HL	Canada	Mixed	Not defined	Healthcare providers	47	0	47	Multiple	Utilization, satisfaction
Timely access to specialist medical oncology services closer to home for rural patients: experience from the Townsville Teleoncology Model	2014	Sabesan, S	Australia	Quasi	Not defined	Patients	70	0	70	Multiple	Time to specialist review, hospital transfers
Using telehealth to train providers of a cancer support intervention	2015	Brandon, AR	US	Mixed	Not defined	Healthcare providers	3	5	8	Multiple	Knowledge, satisfaction, self-confidence

Study	Year	First Author	Country	Design	Rural definition	Population	n Rural	n Non-Rural	N total	Cancer Type	Outcomes
Using videotelephony to support pediatric oncology-related palliative care in the home: from abandoned RCT to acceptability study	2009	Bensink, ME	Australia	Quasi	ARIA	Multiple	10	7	17	Multiple	Acceptability, QOL, depression, social support, satisfaction, cost-effectiveness
Internet											
The quality of cancer patient experience: perspectives of patients, family members, providers and experts	2010	Wagner, EH	US	Qual	not defined	Multiple	--	--	54	Multiple	Barriers, facilitators
The experiences of participants in an innovative online resource designed to increase regular walking among rural cancer survivors: a qualitative pilot feasibility study	2014	Frensham, LJ	Australia	Qual	not defined	Patients	8	0	8	Multiple	Feasibility, acceptability
The consumer-driven development and acceptability testing of a website designed to connect rural cancer patients and their families, carers and health professionals with appropriate information and psychosocial support	2017	Fennel, KM	Australia	Mixed	ARIA	Multiple	111	0	111	Multiple	Acceptability, perceived impact, utilization
Reaching further with online education? The development of an effective online program in palliative oncology	2010	Koczwara, B	Australia	Mixed	Not defined	Healthcare providers	90	0	90	Multiple	Utilization and satisfaction
Evaluation of cancerchatcanada: A program of online support for Canadians affected by cancer	2013	Stephen, J	Canada	Mixed	Population size	Multiple	77	274	351	Multiple	Program evaluation
Evaluating Adaptation of a Cancer Clinical Trial Decision Aid for Rural Cancer Patients: A Mixed-Methods Approach	2018	Pathak, S	US	Mixed	RUCA	Patients	46	0	46	Multiple	Decisional conflict, decision self-efficacy, knowledge, communication self-efficacy, attitudes
Engaging Stakeholders in the Development of an eHealth Intervention for Cancer Symptom Management for Rural Residents	2018	Gilbertson-White, S	US	Mixed	Population size	Multiple	26	0	26	Multiple	Useability
Engagement with INSPIRE, an Online Program for Hematopoietic Cell Transplantation Survivors	2018	Syrjala, KL	US	RCT	ZIP codes using cms.gov categories	Patients	95	356	451	Multiple	Engagement, utilization
Assessing cancer survivors' needs using web-based technology: a pilot study	2012	Lavoie Smith, EM	US	Descr	Not defined	Patients	318	229	547	Multiple	Symptoms, needs assessment
Phone											
A qualitative evaluation of a group phone-based weight loss intervention for rural breast cancer survivors: Themes and mechanisms of success	2016	Fazzino, TL	US	Qual	Not defined	Patients	186	0	186	Breast	Thematic analysis of interviews
Change in Physical Activity During a Weight Management Intervention for Breast Cancer Survivors: Association with Weight Outcomes	2017	Fazzino, TL	US	Quasi	Population density	Patients	142	0	142	Breast	Physical activity
Outcomes of a weight loss intervention among rural breast cancer survivors	2012	Befort, CA	US	Quasi	RUCA	Patients	35	0	35	Breast	Weight, diet, physical activity, serum biomarkers, QOL

Study	Year	First Author	Country	Design	Rural definition	Population	n Rural	n Non-Rural	N total	Cancer Type	Outcomes
Weight loss maintenance strategies among rural breast cancer survivors: The rural women connecting for better health trial	2016	Befort, CA	US	RCT	RUCA	Patients	172	0	172	Breast	Weight loss maintenance, cost-effectiveness
Cost-benefit analysis of decision support methods for patients with breast cancer in a rural community	2013	Wilson, L	US	RCT	Not defined	Patients	68	0	68	Breast	Program delivery costs and willingness-to-pay
Decision support by telephone: Randomized controlled trial in a rural community setting	2012	Belkora, J	US	RCT	population density	Patients	67	0	67	Breast	Decisional self-efficacy, anxiety, satisfaction, preparation for decision-making
Benefits of Early Versus Delayed Palliative Care to Informal Family Caregivers of Patients With Advanced Cancer: Outcomes From the ENABLE III Randomized Controlled Trial	2015	Dionne-Odom	US	RCT	RUCA	Multiple	--	--	122	Multiple	QOL, depression and burden
Adapting an Early Palliative Care Intervention to Family Caregivers of Persons With Advanced Cancer in the Rural Deep South: A Qualitative Formative Evaluation	2018	Dionne-Odom, JN	US	Qual	RUCA	Multiple	64	0	64	Multiple	Thematic analysis of interviews
Family Caregiver Depressive Symptom and Grief Outcomes From the ENABLE III Randomized Controlled Trial	2016	Dionne-Odom	US	RCT	Not defined	Multiple	--	-	123	Multiple	Depressive symptoms and complicated grief
The project ENABLE II randomized controlled trial to improve palliative care for rural patients with advanced cancer: baseline findings, methodological challenges, and solutions	2009	Bakitas, MA	US	RCT	RUCA	Patients	147	132	279	Multiple	Symptoms, QOL, mood, and functional status
Early Versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial	2015	Bakitas, MA	US	RCT	RUCA	Multiple	--	--	207	Multiple	QOL, symptom impact, mood, 1-year survival, and resource use
Mobile											
Developing NaviCanPlan: A Mobile Web Resource Locator for Cancer Providers and Survivors	2015	Dahlke, DV	US	Mixed	Not defined	Multiple	--	--	150	Multiple	Needs assessment
A Mobile Breast Cancer Survivorship Care App: Pilot Study	2017	Baseman, J	US	Qual	Not defined	Multiple	4	7	11	Breast	Thematic analysis of interviews

Table 2. Comparison of digital health strategies across populations[72]

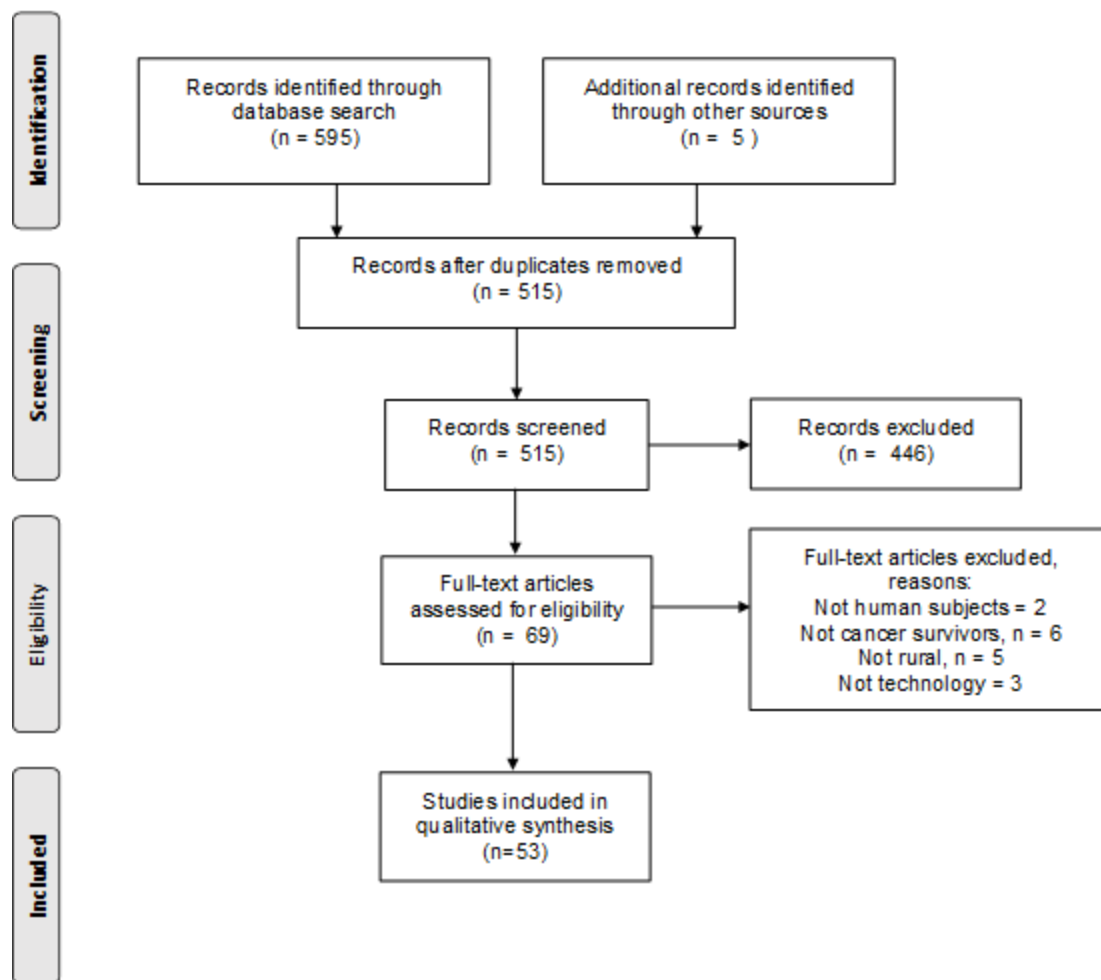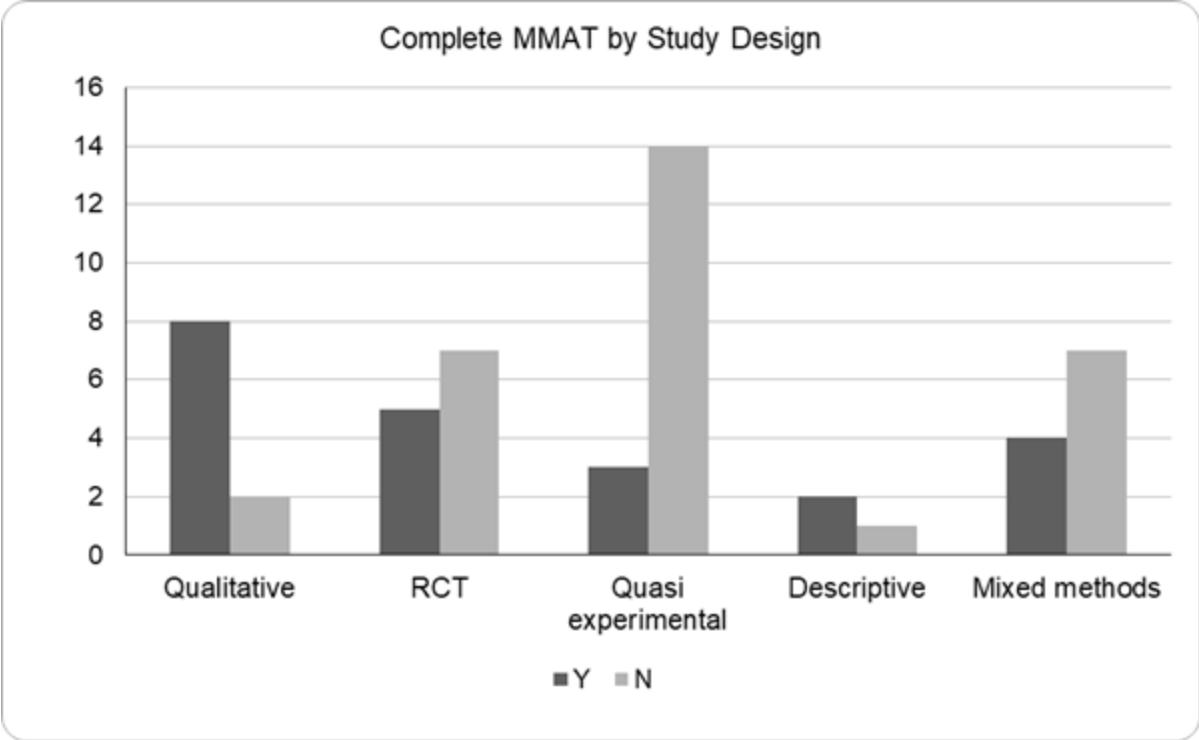|	Rural Cancer (present study)	Cancer	Diabetes	Chronic Respiratory	Chronic Cardiovascular
Telephone	n=11, 21%	n=16, 24%	n=17, 16.5%	n=15, 21%	n=21, 24%
Mobile apps	n=2, 4%	n=8, 12%	n=25, 24%	n=11, 15%	n=7, 8%
Internet	n=9, 17%	n=30, 45%	n=29, 28%	n=38, 52%	n=13, 15%
Telemedicine	n=31, 58%	n=20, 30%	n=42, 41%	n=21, 29%	n=63, 71%

Figure 1. PRISMA Flowchart

Figure 2. Studies with sufficient information to assess by MMAT
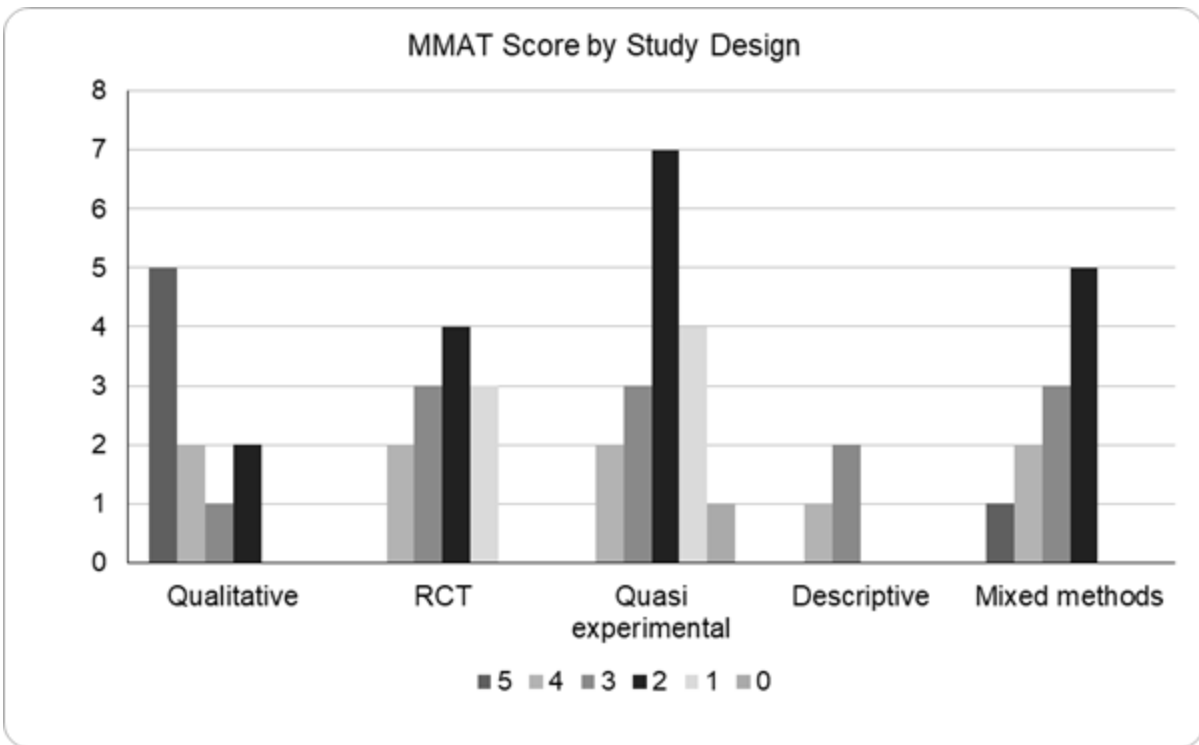
Figure 3. MMAT score by study design

CHAPTER 3: Paper Two

Geographic Differences in Sociodemographic and Clinical Factors Associated with Radiation Treatment Nonadherence

ABSTRACT

Purpose. Nonadherence to cancer treatment is associated with higher rates of cancer recurrence or treatment failure and decreased survival. Rural cancer patients experience a 10% higher mortality rate compared with their nonrural counterparts; geographic differences in adherence may contribute to this increased mortality rate. Radiation treatment is both time and resource intense, making adherence especially challenging. The goal of this study was to determine sociodemographic and clinical factors associated with radiation treatment nonadherence among rural and nonrural cancer patients.

Methods and materials. We utilized cancer registry and hospital billing claims data to measure radiation treatment nonadherence, defined as at least 2 missed appointments, among cancer patients at least 18 years of age who received their first line radiation treatment course at our academic medical center. Geography was based on USDA 2013 Rural-Urban Continuum Codes, and patient age, race, sex, cancer type, cancer clinical stage, radiation treatment modality, and insurance type were included as covariates. We used multivariable logistic regression to estimate odds ratios, 95% Wald confidence intervals, and Wald p-values.

Results. We identified 2161 cancer patients who met the study eligibility criteria, with 15% living in a rural area. Patients had an average of 20 treatment appointments and 25% of patients missed at least 2 appointments. Rural patients were more likely to have stage 4 disease than their nonrural counterparts. Rural cancer patients who lacked health insurance and who had more appointments were more likely than nonrural patients to be nonadherent, with the odds of nonadherence increasing by 14% with each additional appointment (OR 1.14, 95% CI 1.09-1.20). Patients with clinical stage 4 cancer also had an increased odds of being nonadherent.

Conclusions. This analysis revealed actionable clinical implications, identifying geographic disparities and specific patient population subsets in need of additional treatment adherence support. Major factors that contribute to missed radiation therapy appointments included total number of scheduled appointments, advanced cancer stage and insurance status. Based on these results, large catch-net hospitals may want to consider offering more hypofractionated treatment options to these patient populations.

BACKGROUND

Despite improvements in prevention and treatment, cancer remains a leading cause of death in the United States.[1] Over 1.7 million people were diagnosed with cancer in 2019, with more than 600,000 cancer deaths. Nonadherence to cancer treatment is associated with higher rates of cancer recurrence or treatment failure and decreased survival.[9–16] Reports of mortality have been up to four times as likely in nonadherent compared with adherent patients. Treatment adherence represents a modifiable risk factor that can be targeted to directly improve cancer outcomes.

Radiation therapy is a mainstay of cancer treatment for many cancer types, yet treatment adherence is especially challenging in this context since most treatment plans with curative intent involve daily radiation for up to 8 weeks. Interruptions to the schedule, such as missed appointments, are thought to reduce treatment efficacy by allowing additional time for the tumor cells to repopulate.[141,142] With conventional fractionation, even one missed appointment could reduce the local control rate by about 1.4%, regardless of the fractionation schedule and primary tumor site.[143]

Treatment nonadherence has been measured in a variety of ways in the literature, yet results have consistently documented it as a significant predictor of poorer clinical outcomes. Studies examining specific tumor subsets have included head and neck, cervical, prostate, lung and breast cancer.[19,21,143–145] Defining nonadherence as a >14 day treatment interruption, patients with advanced head and neck cancer had a nonadherence rate of 35%, and nonadherence was significantly associated with persistent regional disease.[144] Defining nonadherence as interruptions in the treatment schedule resulting in increased overall treatment time yielded similar results in tumor control and survival for patients with invasive carcinoma of the uterine cervix.[18,19] Recent studies of patients with high-risk prostate cancer found similar evidence, with nonadherence - defined as missing 3+ days in the planned treatment course - predicting poorer overall survival.[145] In lung cancer patients, treatment interruption 5+ days has shown significantly worse local control and survival outcomes.[143] Even in patients treated adjuvantly, such as in post-operative radiation for breast cancer, treatment interruptions >5 days impacted local control and interruptions >8 days reduced both local control and overall survival.[21]

Recognizing the importance of radiation treatment adherence on tumor control and survival in a variety of cancers, Ohri et al. sought to identify significant predictors of nonadherence within a nonrural patient population.[142] The team examined 7 of the most commonly treated malignancies and considered nonadherence to be missing two or more scheduled radiation therapy appointments. 20% of patients were classified as nonadherent. Significant predictors of nonadherence were diagnoses of head and neck, cervical, or uterine cancer, treatment during the winter months, low socioeconomic status, and longer treatment course. Within the same nonrural patient population, the team identified that this strict definition of nonadherence (2+ missed appointments) was associated with poorer outcomes (recurrence, recurrence-free survival, and overall survival.[17]

Geographic differences in adherence between rural and nonrural cancer patients have been cited as a possible reason for disparities in cancer outcomes.[10,20,41,146–148] A growing set of studies have begun to document that cancer treatment adherence is poorer among rural populations.[13,20,39–]

[46,146–151] Rural residents are more likely to have lower educational attainment, higher poverty rates and are more likely to report treatment-related financial hardship than their nonrural counterparts, all of which may affect treatment adherence.[22,24] A number of studies have shown that lower health literacy is related to poor medication adherence.[23,25] With regard to financial distress, prior studies have shown that the degree to which treatment has created a financial burden is associated with medication nonadherence.[24,25] Specifically, investigators found that nearly half of participants reported experiencing some form of financial distress and did not adhere to recommended prescription medication because of cost. Rural populations also have a higher proportion of elderly residents, who are more likely to be diagnosed with cancer and are at greater risk for polypharmacy issues and medication treatment nonadherence.[22,30,152]

An increasing number of studies are considering cancer treatment nonadherence in rural populations, with a particular focus on treatment guideline concordance;[13,39–45,149] however, none to-date have considered geographic disparities in radiation treatment nonadherence. The goal of this study was to determine sociodemographic and clinical factors associated with radiation treatment nonadherence among rural and nonrural cancer patients using cancer registry and healthcare claims data. We hypothesized that geography would play a significant role in radiation treatment nonadherence and that rural cancer patients would be less adherent than nonrural patients.

METHODS

Study population
This study utilized the institution's hospital cancer registry and billing claims data. Eligibility for selection included patients of any cancer diagnosis at least 18 years of age who completed their full course of first line radiation therapy at the medical center between 1/1/2013 and 12/31/2017. Exclusion criteria were incarcerated patients and any patient whose treatment had not yet ended (to calculate treatment adherence).

Measures
The outcome of interest was radiation treatment nonadherence. Radiation treatment visits included all unique treatment appointments. Missed appointments were scheduled appointments to which the patient did not cancel and did not attend. Canceled appointments were classified as those that were canceled by the patient prior to the appointment but not rescheduled. The 'canceled' category did not include appointments canceled by the medical team. We treated nonadherence as a binary variable, classifying patients as either missing or canceling 0/1 appointments or 2+ appointments.[17,142]

The exposure of interest was rurality based on USDA 2013 Rural-Urban Continuum Codes [RUCC].[153] Within the RUCC classification, metropolitan or 'metro' areas are defined as broad labor-market areas that include central counties with one or more urbanized areas that are densely populated with 50,000 or more people [RUCCs 1-3]. Nonmetro areas are outside the boundaries of metro areas [RUCCs 4-9].[154] RUCCs were obtained by matching patient ZIP codes at time of diagnosis to their corresponding FIPS codes. FIPS codes were then matched to the 2013 USDA RUCCs. In the present analysis, RUCCs 1-3 were categorized as 'nonrural' and

RUCCs 4-9 as 'rural'. Two patients were missing ZIP codes, precluding RUCC assignment, so these patients were excluded from the analysis.

Additional covariates extracted from the hospital cancer registry included patient age, race, sex, cancer type, cancer clinical stage at diagnosis, radiation treatment modality, and insurance type. Cancer types were categorized as breast, gastrointestinal, genitourinary, head and neck, and respiratory based on the codes assigned by the cancer registry.

Analyses
Descriptive analyses were first performed using means, standard deviations and two-sample t-tests for continuous variables and counts, proportions, and Chi-square tests for categorical variables. A multivariable logistic regression model including all covariates and interaction terms was generated. Backwards elimination was used to sequentially remove factors not related to the outcome to create the most parsimonious model with the exit criteria set equal to the significance level (0.05). Odds ratios, 95% Wald confidence intervals, and Wald p-values were estimated, controlling for cancer type. All data analysis was conducted using SAS version 9.4.

RESULTS

Table 1 summarizes the sample characteristics of the patient population contributing to the present analysis. Weidentified 2161 cancer patients who met the study eligibility criteria, with 15% living in a rural area. While 26% of nonrural patients were classified as nonadherent versus 19% of rural patients (p=0.02), rural patients had significantly fewer total appointments than nonrural patients (mean 18 vs 20, p=0.002). Patients missed an average of 2.6 appointments and 12% of their treatment, with no significant geographic differences.

Rural patients were older (mean=64 vs 62, p=0.02) and more likely to be male (49% vs 43%, p=0.03) than their nonrural counterparts. There were significant geographic differences by insurance type, with rural patients more often having Medicare and nonrural patients more often having commercial insurance (p<0.0001). Rural patients were more likely to have stage 4 disease than nonrural patients (32% vs 26%, p=0.02). A higher proportion of breast cancer patients resided in nonrural areas (33% vs 20%, p<.0001). There were no significant geographic differences by average or proportion of missed/cancelled appointments, race, and radiation treatment type in univariate analyses.

Table 2 presents the final multivariable model of radiation treatment nonadherence while Figure 1 depicts corresponding odds ratios and 95% confidence intervals. Geography, total number of treatment appointments, clinical stage, and insurance type were significant predictors of treatment nonadherence, controlling for cancer type. The model suggested a significant interaction between geography and the total number of appointments (p=0.001). While an increasing number of total treatments increased the odds of nonadherence across all geographic categories, rural uninsured patients had the highest increased odds. Specifically, the odds of nonadherence increased by 14% with each additional appointment for rural uninsured patients. Patients with clinical stage 4 cancer had a 90% increased odds of being nonadherent compared with stage 1 disease.

DISCUSSION

The goal of this study was to determine sociodemographic and clinical factors associated with radiation treatment nonadherence among rural and nonrural cancer patients using cancer registry and healthcare claims data. We hypothesized that geography would play a significant role in radiation treatment nonadherence, which indeed our data supported. Specifically, we found that geography, total number of treatment appointments, insurance type and clinical stage were significant positive predictors of treatment nonadherence. We also hypothesized that rural cancer patients would be less adherent to their radiation treatment than nonrural patients. This result turned out to be more nuanced and directly influenced by the number of treatments, with a geographic disparity resulting from an increasing number of treatment appointments and insurance type.

Rural patients, especially those who lacked health insurance, who had more total treatments were more likely to be nonadherent, translating to the odds of nonadherence increasing significantly with each additional appointment. This finding may be indicative of an access to care issue, including financial toxicity, which may be encountered as the number of treatment appointments increase. Rural residents are more likely to have higher poverty rates and are more likely to report treatment-related financial hardship, which may affect treatment adherence.[22,24,25,30] Prior studies have shown that the degree to which treatment has created a financial burden is associated with medication nonadherence.[23–25] While we were not able to include a robust measure of financial toxicity in this secondary analysis, we did find that insurance type, which can contribute to financial toxicity,[155] exerted a significant effect on treatment nonadherence. While there is a paucity of literature examining financial toxicity among patients treated with radiation therapy, this treatment type has been identified as a predictor of financial toxicity among cancer survivors.[25] Additionally, patients diagnosed with stage 4 cancer were more likely to be nonadherent compared with patients presenting with stage 1 disease. Fatalistic views of cancer or cancer fatalism, 'the belief that death is inevitable when cancer is present', can result in lower cancer screening and delayed care seeking behaviors and increase the risk of a late stage cancer diagnosis.[156,157] While we did not find a significant interaction effect between geography and stage, this finding still has implications for rural patients given they are more likely to be diagnosed with Stage 4 cancer. [158]

Our study population had similar sample characteristics to those previously reported, with approximately 15% living in a rural area and rural patients being older. Distribution of cancer diagnoses and clinical stage are also similar to those in the literature, with a higher proportion of breast cancer patients residing in nonrural areas and a higher proportion of gastrointestinal and genitourinary cancer patients residing in rural areas.[158] Also similar to previous reports, a higher proportion of patients in rural areas were initially diagnosed with Stage 4 cancer than in nonrural areas.[158] In a geographically diverse sample population of cancer survivors, we found a nonadherence rate of 2 or more missed/cancelled appointments to be 25%. That is similar to the 20% nonadherence rate previously reported in a nonrural population with the same definition of nonadherence.[142]

It is important to recognize this study's strengths and limitations. While our analysis was derived from a secondary data source, we were able to utilize both cancer registry data and hospital

billing claims, resulting in a large database with a mix of cancer diagnoses and increasing our confidence in the accuracy of the appointment dates and completeness used to define nonadherence over self-reported information. There may be bias inherent in this data, since patients with the means necessary to attend at least a portion of their radiation treatment appointments in a nonrural academic setting comprised our dataset. We do not have data on patients who chose not to receive radiation treatment at our cancer facility or chose a different treatment modality, perhaps due to access limitations or treatment frequency requirements. While we utilized a literature-supported definition of nonadherence, we did not differentiate between appointments missed during treatment and early treatment discontinuation, which could have disparate implications for patient outcomes. Lastly, while we were able to consider health insurance in our analysis, as a secondary data analysis of hospital data we did not have access to other more nuanced measures that could influence nonadherence such as more complete measures of financial toxicity.

This analysis revealed actionable clinical implications. Uninsured rural patients with more total treatment appointments were more likely to be nonadherent, as well as those with stage 4 disease. In recognition of this finding, the healthcare team can focus on risk stratification based on insurance type and clinical stage; identifying key access barriers for each patient, or adopting additional assessments of barriers to care for this patient population; offering additional support resources; and scheduling a check in halfway through the treatment plan to support treatment adherence. The evidence-based practice of shorter radiation treatment regimens should continue to be considered.[159] While we were able to identify key contributors to radiation treatment nonadherence, we were limited to cancer registry and hospital billing claims data. Future studies could benefit by including social and behavioral measures that may influence adherence, like perceived barriers to care, financial toxicity, and cancer fatalism.

Table 1. Summary of patient sample population characteristics

	Overall		Rural (RUCC 4-9)		Nonrural (RUCC 1-3)		p-value
	n or mean	% or SD	n or mean	% or SD	n or mean	% or SD	
Total	2161		329	15.2	1832	84.8	<0.0001*
Total treatments	19.7	14.3	17.5	14.4	20.1	14.2	0.002*
Missed or cancelled treatments	2.6	2.7	2.2	2.1	2.7	2.8	0.1
Proportion missed or cancelled treatments	0.1	0.1	0.1	0.2	0.1	0.1	0.2
Age	62.2	11.9	63.6	11.8	61.9	11.9	0.02*
Nonadherence							0.02*
0/1 appts	1630	75.4	265	80.6	1365	74.5	
2+ appts	531	24.6	64	19.4	467	25.5	
Sex							0.03
Female	1213	56.1	167	50.8	1046	57.1	
Male	948	43.9	162	49.2	786	42.9	
Race							0.66
White	1383	64.0	207	62.9	1176	64.2	

Black	778	36.0	122	37.1	656	35.8	
Insurance							<.0001*
Medicare	973	45.0	179	54.4	794	43.3	
Commercial	734	34.0	67	20.4	667	36.4	
Medicaid	155	7.2	28	8.5	127	6.9	
Uninsured	244	13.3	55	16.7	244	13.3	
Clinical stage							0.02
1	572	26.5	67	20.4	505	27.6	
2	566	26.2	87	26.4	479	26.2	
3	447	20.7	69	21.0	378	20.6	
4	576	26.7	106	32.2	470	25.7	
Cancer Site							<.0001*
Breast	676	31.3	67	20.4	609	33.2	
Gastrointestinal	279	12.9	48	14.6	231	12.6	
Genitourinary	174	8.1	38	11.6	50	2.7	
Gynecologic	67	3.1	17	5.2	50	2.7	
Head and Neck	355	16.4	55	16.7	300	16.4	
Hematology	61	2.8	9	14.8	52	2.8	
Respiratory	549	25.4	95	28.9	454	24.8	

Treatment Type							0.3
Conformal Therapy	294	13.6	51	15.5	243	13.3	
External Beam	1191	55.1	169	51.4	1022	55.8	
IMRT	531	24.6	82	24.9	449	24.5	
SRS	145	6.7	27	8.2	118	6.4	

IMRT: Intensity modulated radiation therapy; SRS: Stereotactic radiosurgery

Table 2. Multivariable model of treatment nonadherence, controlling for cancer type

|	Estimate	SE	Chi-Square	P-value
Intercept	-4.21	0.24	307.0	<.0001
Total appts	0.12	0.007	292.7	<.0001
Geography (ref = Nonrural [RUCC 1-3])				
Rural [RUCC 4-9]	-0.22	0.10	4.73	0.03
Insurance (ref = Medicare)				
Commercial	-0.37	0.16	5.47	0.02
Medicaid	0.05	0.21	0.06	0.8
Uninsured	0.35	0.16	4.87	0.03
Total appt x Insurance x Geography interaction				
Total appts - Rural, Commercial	-0.09	0.01	0.75	0.39
Total appts - Rural, Medicaid	-0.01	0.01	1.71	0.19
Total appts - Rural, Uninsured	0.01	0.01	4.80	0.03*
Clinical stage (ref = 1)				
2	0.09	0.11	0.68	0.41
3	-0.09	0.12	9.89	0.002*
4	0.55	0.13	18.90	<.0001
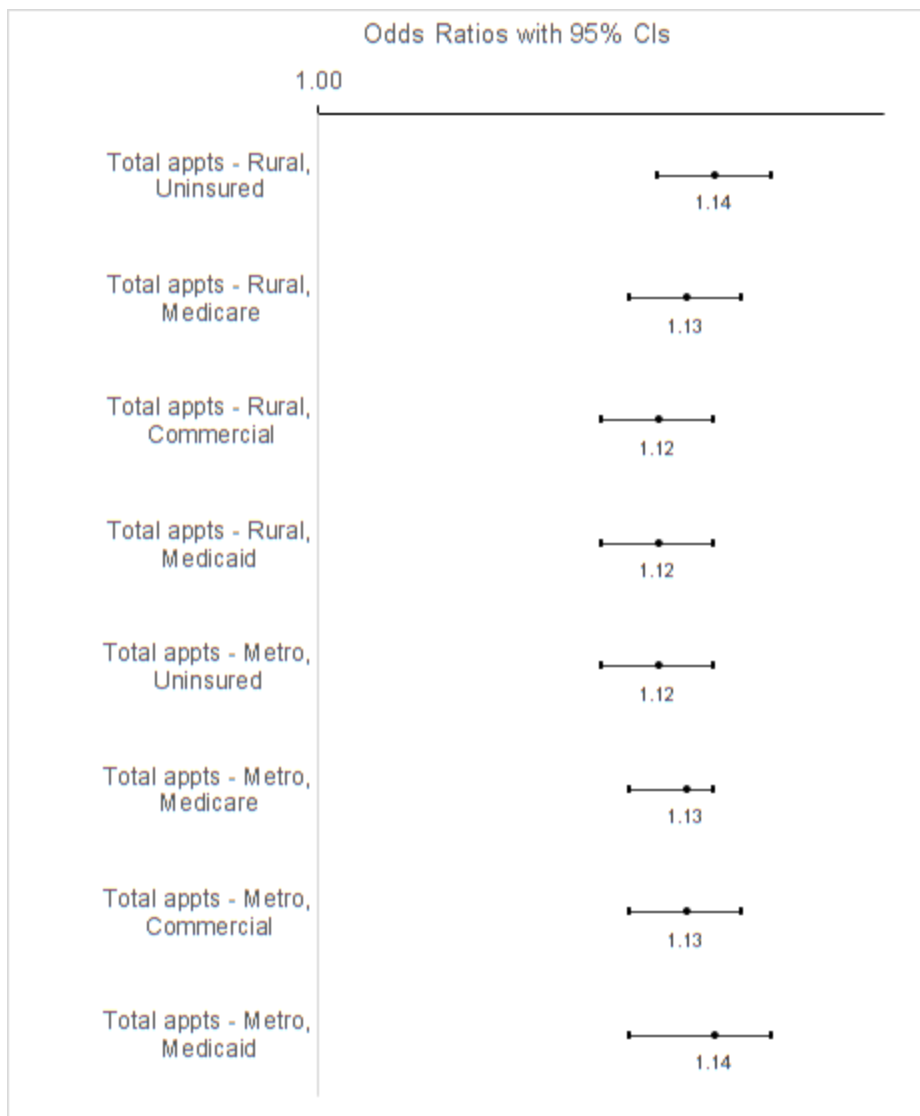
Figure 1. Odds ratios and 95% confidence intervals for interaction term in final multivariable model

CHAPTER 4: Paper Three

A Multilevel, Theory-Driven Examination Of Rural Cancer Treatment Nonadherence

ABSTRACT

Background

Nonadherence to cancer treatment is associated with higher rates of cancer recurrence or treatment failure and decreased survival. A growing set of studies have begun to document that cancer treatment adherence is poorer among rural populations. Information-Motivation-Behavioral Skills theory assumes that health-related information, motivation, and behavioral skills are fundamental determinants of performance of health behaviors, while the Chronic Care Model highlights the interdependent importance of self-management support, delivery system design, decision support, and clinical information systems to support patients and their care providers in having productive interactions and improved patient outcomes. Despite their utility, evidence of theory-driven approaches is limited in cancer treatment nonadherence literature to-date.

Purpose

Treatment adherence represents a modifiable risk factor that can be targeted to directly improve cancer outcomes. Multilevel factors contribute to cancer treatment nonadherence yet have not been fully investigated. The purpose of this study was to delineate social and behavioral determinants of rural cancer treatment nonadherence using a mixed method approach. The combined Information-Motivation-Behavioral Skills-Chronic Care Model provided the theoretical foundation for the design of the present study and interpretation of results.

Methods

We conducted a sequential explanatory mixed methods study among rural cancer survivors, classified by RUCC 4-9, and nonrural survivors who completed first-line cancer treatment in the past five years. Potential participants were randomly selected from the Cancer Center survivor database. Rural participants who agreed in the survey to be recontacted and provided either a phone number or email were recruited for the rural cancer-focused interviews. We utilized cancer registry and hospital billing claims data to define treatment nonadherence (2+ missed appointments), geography based on USDA 2013 Rural-Urban Continuum Codes, and the additional covariates based on survey measures of the Information-Motivation-Behavioral Skills Chronic Care Model and sociodemographics. We used multivariable logistic regression to estimate odds ratios, 95% Wald confidence intervals, and Wald p-values. Interpretative phenomenological analysis was used to gain insight into how cancer survivors experience the cancer journey when living in a rural area and to more comprehensively extend quantitative study results.

Results

Survey efforts resulted in 430 participants (188 rural and 242 nonrural cancer survivors). Rural cancer survivors reported lower levels of educational attainment and income (p=0.005 and 0.003, respectively). Rural cancer survivors reported higher levels of spiritual coping and expressed a more fatalistic view of cancer than nonrural survivors (p=0.04 and p=0.01, respectively), which was also expressed in individual interviews. Nearly half (47%) of rural cancer survivors said it was somewhat or very hard to pay for transportation to treatment appointments, compared with only 19% of nonrural participants (p<0.0001). Additionally, 37% of rural cancer survivors reported that accessing transportation for treatment appointments was somewhat or very hard, compared with only 17% of nonrural participants (p<0.0019). Interview participants described the importance of care coordination with local clinics or access to academic medical center satellite clinics for reducing transportation burden. Rural cancer survivors were significantly less likely to seek health information online, to access their online medical record, and reported accessing electronic health information to be significantly more challenging (p=0.001, p=0.01, and p=0.0008, respectively). Reasons for this were described by interview participants as related to lack of internet access or slow data transfer speeds, or reliance on family members to perform online functions. In multivariable logistic regression, increasing barriers to transportation were significantly associated with treatment nonadherence (p=0.02; OR: 1.56, CI: 1.09-2.24). The interaction between geography and the behavior skill of bringing a list of questions to a clinic appointment was significant, with rural cancer survivors who do not bring a list of questions to appointments having over 3 times greater odds of being nonadherent (p=0.05; OR: 3.37, CI: 1.02-11.14). Interview participants highlighted challenges in question generation, a behavioral skill that could be supported by the healthcare system.

Conclusions
The factors identified in this study provide theory-based opportunities for interventions designed to improve treatment adherence among rural populations. Rural cancer survivors face significant barriers to transportation for treatment appointments and lack important skills for patient engagement. Addressing transportation barriers and supporting appointment preparation could reduce cancer treatment nonadherence.

INTRODUCTION

Despite improvements in prevention and treatment, cancer remains a leading cause of death in the United States.[1] The nearly 3 million US cancer survivors residing in rural areas experience 10% higher cancer mortality compared to their nonrural counterparts.[3] Nonadherence to cancer treatment is associated with higher rates of cancer recurrence or treatment failure and decreased survival.[9–16] The interaction of individual, community and health system-level factors, with unique aspects likely associated with the observed disparities between rural and nonrural populations, contributes to cancer treatment nonadherence. To-date there has been little attention to factors that might help explain treatment nonadherence among rural cancer patients, and prior research has lacked a unifying theoretical approach to framing how factors at multiple levels contribute to nonadherence among rural populations. A better explanation of these factors and how they interact can guide novel, theory-based strategies to improve treatment adherence among rural populations.

A growing set of studies have begun to document that cancer treatment adherence is poorer among rural populations.[9–16,39–46] Most of these studies (11/16) were conducted among breast cancer patients. Only 3 studies involved qualitative methods (2 interview-based studies and 1 focus group-based study);[39,42,43] the remaining 13 articles relied on quantitative data sources. Only 1 study involved a prospective survey, which was limited by sample size (N=31).[47] The other 12 studies utilized secondary data sources largely consisting of healthcare claims data. There were no studies identified that employed mixed methodology, which would provide rich insight into factors contributing to nonadherence. Evidence of theory-driven approaches was even more limited, with only one manuscript describing a theoretical model or framework guiding the study development.[9] Treatment nonadherence represents a modifiable risk factor that can be targeted to directly improve cancer outcomes, yet successful interventions may require a theoretically-driven, multilevel approach.

The Theory Derivation process, the structured set of procedures in which a parent theory or model is used to guide the development of a new model or theory in conjunction with a comprehensive review of the current literature, was employed to understand how potential factors related to treatment nonadherence may fit together and influence outcomes in rural populations.[48] We considered two parent theories: the Information-Motivation-Behavioral Skills Theory (IMB) and the Chronic Care Model (CCM).

IMB posits that individuals who are well-informed about a behavior, motivated to act on that behavior, and possess the behavioral skills required to act effectively in support of that behavior, will likely initiate and maintain patterns of the target behavior.[51] The IMB model specifies that the effects of health promotion information and motivation are seen primarily as a result of the application of health promotion behavioral skills to the initiation and maintenance of health promotion behavior.[49] While the IMB model was originally established in HIV risk behavior interventions, it is viewed as a generalizable approach to understanding and promoting health behavior more broadly.[49] For example, it has been successfully applied to smoking cessation interventions,[52] interventions to increase physical activity,[53] breast self-examination interventions,[54] and interventions to improve medication adherence.[55]

While IMB theoretically accounts for the individual level, multilevel factors contribute to cancer treatment nonadherence. The Chronic Care Model is a well-established and validated framework that positions chronic care in the context of community, with observation, intervention, and evaluation studies focused on organizational characteristics, quality improvement, and cost effectiveness to benefit patients with congestive heart failure, asthma, and diabetes.[50,57] The model highlights the interdependent importance of self-management support, delivery system design, decision support, and clinical information systems to support patients and their care providers in having productive interactions and improved patient outcomes. A benefit to this model is its flexibility acts more as a framework than a packaged intervention, allowing researchers to tailor CCM elements to individual organizations, yet it lacks patient-level factors that influence care delivery.

While both the IMB and the CCM have demonstrated utility in health promotion and quality improvement, neither fully capture the multilevel factors relevant to adherence in rural cancer survivors. Bringing the IMB and the CCM together as the Information-Motivation-Behavioral Skills theory - Chronic Care Model (IMB-CCM; Fig. 1) provides a more complete framework from which to study and address treatment nonadherence in rural cancer survivors. IMB-CCM identifies that receipt of information during the cancer journey is necessary but not sufficient to achieve positive behavioral and health outcomes like treatment adherence and survival. In addition, behavioral skills to promote self-management through patient engagement, along with personal and social motivation shaped by rural culture, information access and information utilization, are critical determinants. Individual, community and health system-level factors interact to influence outcomes, with unique aspects likely associated with the observed disparities between rural and nonrural populations. The combined IMB-CCM provided the theoretical foundation for the design of the present study and interpretation of results. The purpose of this study is to delineate social and behavioral determinants of rural cancer treatment nonadherence. A theory-driven mixed methods study design was employed to directly assess constructs hypothesized to be related to treatment nonadherence and then results explored through in-depth interviews with rural oncology survivors and caregivers.

METHODS

Study Design. We conducted a sequential explanatory mixed methods study[160] in which first conducted a survey of rural and nonrural cancer survivors, with survey results informing the qualitative interview guide, and the interview perspectives providing an enhanced understanding of the survey results. The IMB-CCM was used to inform survey and interview development to systematically generate data that would more fully explain factors contributing to treatment nonadherence in rural oncology.

Population. Rural cancer survivors, classified by USDA 2013 Rural-Urban Continuum Codes (RUCC)[153] 4-9, and nonrural survivors who completed first-line cancer treatment in the past five years at our academic medical center were eligible for the study. 1050 rural and 1050 nonrural potential participants were randomly selected from the hospital's cancer registry out of the 1091 rural and 6012 nonrural eligible cancer survivors. After individuals from the same household and bad addresses were removed, 961 surveys were mailed to rural survivors and 1037 surveys were mailed to nonrural survivors in December 2019 (Paper 3 Appendix 1). Survey participants who also consented to study team access to their medical records were included in the present

analysis to allow for calculating treatment adherence. Rural participants who agreed in the survey to be recontacted and provided either a phone number or email were recruited for the rural cancer-focused interviews.

Survey design and administration. Valid and established measures in the field were included to assess study constructs. Per the Tailored Design Method, surveys are written in large font with clear instructions for answering each survey item and more interesting questions at the front of the survey to promote engagement. Surveys were mailed according to the Dillman method to increase response rate. These standard survey methods were used to reduce bias in response.

Survey measures and constructs assessed were selected based on IMB-CCM and included: Seeking health information, seeking health information online as the first source of information, and electronic information accessibility (Information); medical distrust, cancer fatalism, spiritual coping, and transportation barriers (Motivation); appointment preparation, and engagement in during and outside an appointment (Behavioral skills); social support (Community); and accessing their online medical record, using an app to communicate with a healthcare provider, and patient-provider communication (Health systems). The sociodemographic variables of age, race, sex, education, income, cancer clinical stage, insurance type were also included.

IMB Constructs

Information: Seeking health information was assessed by, "Have you ever looked for information about health or medical topics from any source?" (Yes/No) The measure of seeking health information online as the first source of health information was derived from the follow-up question, "The most recent time you looked for information about health or medical topics, where did you go first?" with "internet" as one of the choices.[161]

The Electronic Info Accessibility Score was constructed as a summary scale of four Likert-type questions with responses ranging from strongly agree to strongly disagree (Cronbach's alpha = 0.83). The questions were: Based on your most recent search for information about health, how much do you agree or disagree with each of the following statements? 1) It took a lot of effort to get the information you needed; 2) You felt frustrated during your search for information; 3) You were concerned about the quality of information; 4) The information you found was hard to understand.[79] Responses were summarized such that higher scores indicate easier perceived accessibility of online information.

Motivation: Medical distrust was measured as a single item, How much do you trust information about cancer from a doctor? ranging from not at all to a lot.[161] Cancer fatalism was measured as a single item, There's not much you can do to lower your chances of getting cancer, ranging from strongly agree to strongly disagree.[161] Medical distrust was dichotomized as Not at all/A little and Some/A lot. Cancer fatalism was dichotomized as Strongly agree/Somewhat agree and Somewhat disagree/Strongly disagree.

The Spiritual Coping Score consisted of three Likert-type questions with responses ranging from, I haven't been doing this at all to I've been doing this a lot (Cronbach's

alpha = 0.85). The questions were: I've been trying to find comfort in my religion or spiritual beliefs; I've been praying or meditating; and I've been going to church or church activities.[162] Responses were summarized such that higher scores indicate more spiritual coping practices.

The Transportation Barriers Score developed by the study investigators consisted of 3 Likert-type questions with responses ranging from Very Easy to Very Hard (Cronbach's alpha = 0.73). Leading with "Imagine you are receiving treatment for a disease at your preferred hospital. If you needed to go to the hospital for this treatment 5 days a week for 6 weeks, with each appointment lasting about 30 minutes, how easy or hard would it be for you to:" and then following with "Have a way to get to the hospital? Examples may be you driving, someone else driving you, taking a bus, taking a train, biking, walking?", "Pay for transportation to the hospital? Examples may be paying for gas, a train ticket, a bus pass, parking", "Take time off or afford time off from work for these appointments?" Responses were summarized such that higher scores indicate more perceived barriers to transportation for treatment appointments.

Behavioral skills: Survey items related to behavioral skills consisted of appointment preparation and patient engagement. Responses options ranged from Never to Always; however, we chose to dichotomize the responses as Never/Sometimes and Usually/Always. Questions led with "In general, how often do you…" asked: 1) take with you to your doctor visits a list of questions; 2) take a list of all your prescribed medicines to your doctors visits; 3) ask your doctor to explain a test, treatment or procedure to you in detail; 4) read information about a new prescription, such as side effects and precautions; 5) do your own research on a health or medical topic after seeing your doctor; 6) take with you to your doctor visit any kind of information you found.[161]

CCM Constructs

Community: The Social Support Score included 6 Likert-type questions with responses ranging from Never to Always: 1) Is there anyone you can count on to provide you with emotional support when you need it, such as talking over problems or helping you make difficult decisions? 2) Do you have friends or family members that you talk to about your health? 3) Do you have someone to prepare your meals if you are unable to do it yourself? 4) Do you have someone to take you to the doctor if you need it? 5) Do you have someone to help you with daily chores if you are sick? 6) Do you have someone to run errands if you need it?[161] Responses were summarized such that higher scores indicate better perceived social support (Cronbach's alpha = 0.90).

Health Systems:

Accessing their online medical record was measured by the survey question, "Have you ever looked at your medical records online?" (Yes/No)

The measure of Using an app to communicate with a healthcare provider was derived from the question, "Have you ever used any 'health-related app' that tracks your behavior (such as exercise, diet, or sleep); reminds you to take medication or drink water; helps

you stay calm or meditate; or gives health information or advice? Mark all that apply." in which the response "Communicating with my doctor or other provider" was selected.

Patient-provider communication was measured by a 7-item Likert scale with responses ranging from Always to Never (Cronbach's alpha = 0.91). The scale led with, "The following questions are about your communication with all doctors, nurses or other health professionals you saw during the past 12 months. How often did they…1) Give you a chance to ask all the health-related questions you had? 2) Give the attention you needed to your feelings and emotions? 3) Involve you in decisions about your health care as much as you wanted? 4) Make sure you understood things you needed to do to take care of your health? 5) Explain things in a way you could understand? 6) Spend enough time with you? 7) Help you deal with feelings of uncertainty about your health or health care?[161] Responses were reverse coded then summarized such that higher scores indicate better perceived patient-provider communication.

Interview design and administration. Interviews were conducted in-person or by phone, with the location and time selected at the convenience of the participant. All interviews began with describing the study as an effort to "better understand the challenges you may have faced and the resources you have had during your cancer journey as a rural resident". The interviewer then went on to thank the participant for his or her time, reminded them that participation in the interview was voluntary, and that the interviews would be audiorecorded.

The opening set of questions asked for the participant to describe their community and their perceptions of rurality. Topics within the semi-structured interview guide considered experiences with the overall cancer journey, social support, healthcare access, finances, treatment adherence and engagement, medical distrust, shared decision-making, support services, clinical trials, and information access. Interview guide questions are listed in Paper 3 Appendix 2. Interviews were audio-recorded, with recording times ranging from 40 to 84 minutes. Participants received $20 upon completion of the interview.

Analysis. Response and refusal rates were calculated based on Response Rate 1 and Refusal Rate 1 of the American Association for Public Opinion Research Standard Definitions. Summary scales were assessed for internal consistency with Cronbach's alpha. We described our study population using means, standard deviations and two-sample t-tests for continuous variables and counts, proportions, and Chi-square tests for categorical variables. The outcome variable was treatment nonadherence, defined as 2 or more missed or cancelled treatment appointments. A multivariable logistic regression model including all covariates and interaction terms was generated. Backwards elimination was used to sequentially remove factors not related to the outcome to create the most parsimonious model with the exit criteria set equal to the significance level (0.05). Odds ratios, 95% Wald confidence intervals, and Wald p-values were estimated. All quantitative data analysis was conducted using SAS version 9.4.

Interpretative phenomenological analysis (IPA) was used to analyze the interviews. This methodology was selected because of its emphasis on describing a "common meaning for several individuals of their lived experiences of a concept or phenomenon".[163] IPA most frequently draws on accounts of an average of 6 interview participants, although 3 to 15 participants is acceptable.[164] Significant statements were selected that "provide an understanding of how

participants experienced the phenomenon," in this case, the cancer journey as a rural resident, through a process called horizontalization.[163]

RESULTS

Survey efforts concluded at the end of January 2020 and generated a 22% response rate (20% in rural, 23% in nonrural)(Paper 3 Appendix 1). Completing the survey by mail was the preferred method in this population, though 21% opted to complete the survey online. Refusal rates were 3% for both rural and nonrural residents. There were 188 rural participants and 242 nonrural participants, for a total of 430 participants. Participants who provided HIPAA consent for accessing medical records were more likely to be White, more educated and with higher incomes than participants who did not provide HIPAA consent (Table 1). Participants who did and did not provide HIPAA consent did not significantly differ by age, geography, gender, or insurance type (all p-values > .05).

Table 2 presents the study sample's key characteristics by geographic residency. Rural participants were on average 85 minutes from their usual source of cancer care versus 32 minutes for nonrural participants (p<0.0001). Rural cancer survivors reported lower levels of educational attainment and income (p=0.005 and 0.003, respectively). Insurance type differed by geography, with a higher percentage of nonrural participants reporting commercial insurance and rural participants reporting Medicaid (p=0.03).

Table 3 describes rural-nonrural differences in the IMB-CCM constructs. Rural cancer survivors were significantly less likely to seek health information online as their first information source and to access their online medical record (p=0.001 and 0.001, respectively. When talking about seeking health information online, Participant 2 said, "I'm not one to do that but my wife is," reflecting the support system involvement with obtaining health and cancer-related information.

Accessing electronic health information was deemed significantly more challenging for rural cancer survivors than nonrural survivors (p=0.0008). Interview participants emphasized how expensive and slow the internet is in their areas:

> "Slow! Well, of course the more you pay the faster your internet, and our bill had gone up so high I thought to myself something's gotta go…so I went to the cheaper plan, but it is slow." (Participant 1)

Survey participants in rural areas expressed a more fatalistic view of cancer than nonrural survivors (p=0.01). Cancer fatalism was also highlighted in the rural cancer interviews. One caregiver, when speaking of her husband's reaction to his stage 2 cancer diagnosis, said,

> "In his mind, they had just signed his death [sentence]. He had only maybe months to live. Cuz on the way home from VCU, I was driving, and um, just out of the clear blue, he says, well I reckon I might as well go ahead and sell my boat now. And to me, that was, he's already given up." (Participant 1)

Rural cancer survivors reported higher levels of spiritual coping than nonrural cancer survivors (p=0.04). All interview participants remarked how important their church support system was during their cancer journey, with their pastor coming to pray with them at the hospital and church members taking turns helping with transportation to appointments.

Nearly half (47%) of rural cancer survivors said it was somewhat or very hard to pay for transportation to treatment appointments, compared with only 19% of nonrural participants (p<0.0001). Additionally, 37% of rural cancer survivors reported that accessing transportation for treatment appointments was somewhat or very hard, compared with only 17% of nonrural participants (p<0.0019). Interview participants brought up the benefit of oncologists' coordinating some of the treatments (e.g. chemotherapy) with community medical centers, as well as academic medical center satellite clinics with extending access to care to more rural areas and reducing the transportation burden. Participant 2 described being able to see his oncologist at a satellite clinic, "He comes up here from VCU a couple times a week so I go to him and think he's a fantastic doctor, you know I trust him" as well as the reduction in travel time from an hour one-way to 10 minutes.

While only 50% of rural cancer survivors regularly brought a list of questions to their treatment appointments, 70% brought a list of their medications. Rural cancer survivors reported more often bringing a list of medicines and requesting an explanation of a test or treatment than nonrural survivors (77% vs 65%, p=0.02; 83% vs 71%, p=0.01). Other behavioral skills measured did not significantly differ by geographic residence.

Significant rural-nonrural differences were not detected for seeking health information, medical distrust, social support, and patient-provider communication.

In multivariable logistic regression, three variables significantly predicted treatment nonadherence. First, the summary score variable of Transportation Barriers that indicates increasing barriers to transportation were significantly associated with treatment nonadherence (p=0.02; OR: 1.56, CI: 1.09-2.24). The interaction between geography and the behavior skill of bringing a list of questions to a clinic appointment was significant, with rural cancer survivors who do not bring a list of questions to appointments having over 3 times greater odds of being nonadherent (p=0.05; OR: 3.37, CI: 1.02-11.14). Patient interviews highlighted that the issue mainly stemmed from not knowing what to ask: "I didn't have any trouble asking questions, I probably had trouble knowing what to ask. (Participant 3)"

DISCUSSION

The purpose of this study was to delineate social and behavioral determinants of rural cancer treatment nonadherence. We found that rural cancer survivors reported significant barriers to transportation access for cancer treatment appointments, and that transportation barriers were associated with treatment nonadherence. Half of rural participants reported sometimes or never bringing a list of questions to their treatment appointments. For these participants, nonadherence was 3 times the odds of nonadherence in nonrural participants. Mitigating transportation barriers and supporting appointment preparation could reduce cancer treatment nonadherence. The healthcare system is in a unique position to address these issues that could improve treatment adherence and cancer patient outcomes.

Results from this study support what is found in the literature regarding rural disparities with regard to educational attainment, income, spiritual coping, and cancer fatalism.[6,22,30] Rural cancer survivors were less likely to utilize online resources, including the internet as an information

source and accessing their online medical record. Greenberg and colleagues also found that rural residents are less likely to manage personal health information online or email a healthcare provider.[38] In the present study, interview participants cited challenges with internet access, speed, and cost. A key contributor to this rural digital divide and critical to the deployment of digital health strategies is access to the mobile, internet or broadband infrastructure that supports these tools.

A 2019 study found that residents of rural areas had reduced odds of having internet access compared with residents of nonrural areas (OR 0.75; 95% CI 0.67-0.84).[77] Similarly, the Pew Research Center reported that 63% of rural residents say they have a broadband internet connection at home, compared with 75% of nonrural residents.[79] The Federal Communications Commission's 2019 Broadband Deployment Report found that over 26% of Americans in rural areas lack coverage from fixed terrestrial 25 Mbps/3 Mbps broadband that would allow for home internet access, as compared to only 1.7% of Americans in nonrural areas.[36] Deployment of mobile Long-term Evolution, more commonly known as LTE and the pathway to achieve high speed cellular internet service, still lags in rural areas. Specifically, only 70% of the rural population has service with a median speed of 10 Mbps/3 Mbps versus 93% of the nonrural population. An important step in addressing these disparities is to develop more granular broadband availability maps, a step taken by Congress in March 2020 in passing the Broadband Deployment Accuracy and Technological Availability Act.[37]

Rural cancer survivors reported significant barriers to transportation for treatment appointments, specifically related to cost and access. Our study also demonstrated that transportation barriers are significantly associated with treatment nonadherence. Rural residents face longer median travel times to treatment centers, oncology specialists, and academic centers, yet higher volume centers are associated with improved patient outcomes.[30,32] Median travel times reported in the literature range from 51 minutes to 97 minutes.[33] Our study results are similar, with an average travel time of 85 minutes from rural participants' usual source of cancer care. Poverty creates substantial transportation barriers, making it a challenge for some rural residents to afford gas or a car. It has been estimated that over 1.6M rural households do not have cars, mostly concentrated in the South, Appalachia, and the Southwest.[34] When specifically asked about transportation challenges for treatment appointments, nearly half of rural participants reported difficulty with paying for transportation, and 37% had difficulty. Our study documents that the substantial access barriers faced by rural populations do indeed influence treatment adherence.

Our study identified that bringing a list of questions to clinic appointments was especially important in improving treatment adherence for rural cancer survivors. Various strategies to support appointment preparation have been implemented in the literature, including appointment preparation and Question Prompt Lists (QPLs). Roter pioneered in-person appointment preparation in the 1970s, and found that when patients were coached with a prompt sheet reviewing "possible questions in the areas of etiology, duration, severity, and prevention of illness," they asked more questions and kept more appointments.[165] While this area of research focuses on the interactive preparation prior to an appointment, a subset of studies highlight the use of QPLs. QPLs consist of a structured list of questions that patients can use as examples to gather information during clinic appointments, with the aim of information provision that is more personally relevant and sufficient to improve psychological and cognitive outcomes like anxiety and information recall.[166] QPLs have been found to enhance question asking, decrease patient

anxiety at follow-up, improve information recall.[166] Future rural cancer delivery research could utilize appointment preparation to support question development and treatment adherence.

Regarding the theoretical model this study was based, two of the three IMB constructs significantly predicted nonadherence, Motivation and Behavioral Skills. When applied to medication adherence, the authors of the IMB model suggested that adherence information and motivation will be primarily expressed through adherence behavioral skills.[49] The role of the IMB information construct has been inconsistent in the prediction of preventative behavior, and in the degree of independence between the information and motivation constructs.[13] Additionally, the relatively more modest correlation between information and the intended health behavior (compared to motivation and behavioral skills) is expected based on the IMB model's assertion that information needs to be easily operationalized for it to result in behavior change, which is not always the case.[9] While our measures of the CCM did not significantly predict adherence, aspects of the CCM can support behavioral skills and motivation, to ultimately improve adherence.

Study strengths include the mixed methods approach utilized that combined survey data from validated scales with in-depth reflection from individual interviews. While the response rate from our study is modest compared with clinic based recruitment of cancer survivors, it is comparable to the response rate of mailed surveys. Follow-up with those who did not return a survey or opt-out was limited by pandemic restrictions. The response rate could have been higher had we been able to recruit participants in the clinic or follow-up with nonrespondents.

Whereas the total participant sample was 26% Black, Black participants made up 24% of the study sample that consented to medical records access (p=0.04). Additionally, those who consented to medical records access skewed to higher levels of educational attainment and income (p<0.0001 and p=0.0004, respectively). Our results may not be fully representative of our target population because of this selection bias. However, the survey was able to recruit a high percentage of rural participants and approximately equal numbers of rural and nonrural respondents. The majority (78%) consented to medical records release, which did not differ by geographic location. The majority (77%) of rural survivors also consent to future contact, allowing us to contact them for recruitment into the interview portion of this study. We were able to allow the option of completing the survey online if the respondent preferred, which was selected by about 21% of participants.

The factors identified in this study provide theory-based opportunities for interventions designed to improve treatment adherence among rural populations. Rural cancer survivors face significant barriers to transportation for treatment appointments and lack important skills for patient engagement. Mitigating transportation barriers and supporting appointment preparation could reduce cancer treatment nonadherence. The healthcare system is poised to address these issues that could improve treatment adherence and cancer patient outcomes.

Table 1. Sample population characteristics by medical records consent release

	Total (N = 430)		HIPAA Consent (N = 334)		No HIPAA Consent (N = 96)		
	Mean or N	SD or %	Mean or n	SD or %	Mean or n	SD or %	t-test p-value
Age	63.6	12.6	63.3	13.0	64.7	11.1	0.32
Geography							0.99
Rural	188	43.7	146	43.7	42	43.8	
Nonrural	242	56.3	188	56.3	54	56.3	
Gender							0.16
Male	159	37.9	130	39.6	29	31.5	
Female	261	62.1	198	60.4	63	68.5	
Race/Ethnicity							0.04*
White	287	74.2	234	76.5	53	65.4	
Black	100	25.8	72	23.5	28	34.6	
Education							<0.0001*
Less than HS degree	48	11.5	27	8.3	21	23.3	
HS degree	74	17.8	51	15.6	23	25.6	
Some college/tech school	114	27.3	92	28.1	22	24.4	
College degree	97	23.3	85	26.0	12	13.3	
Post college educ	84	20.1	72	22.0	12	13.3	
Income							0.0004*
<$20,000	70	16.8	52	15.9	18	20.2	
$20,000 - <$50,000	76	18.2	61	18.6	15	16.9	
$50,000 - <$75,000	62	14.9	51	15.6	11	12.4	
$75,000 - <$100,000	53	12.7	47	14.3	6	6.7	

>$100,000	70	16.8	63	19.2	7	7.9	
Unknown/Prefer not to say	86	20.6	54	16.5	32	36.0	
Health Insurance							0.75
Commercial	99	27.5	79	27.6	20	27.0	
Medicare	185	51.5	149	52.1	36	48.7	
Medicaid	45	12.5	33	11.5	12	16.2	
Other	31	8.6	25	8.7	6	8.1	

Table 2. Study population characteristics by geographic residence

	Total (N = 334)		Rural (N = 146)		Nonrural (N = 188)		p-value
	Mean or N	SD or %	Mean or n	SD or %	Mean or n	SD or %	
Age	63.3	13.0	63.3	12.1	63.3	13.7	0.99
Distance to care	54.7	51.7	85.3	61.6	31.5	24.0	<0.0001
Nonadherence to chemo or radiation							0.47
0/1 appts	271	81.1	121	82.9	150	79.8	
2+ appts	63	18.9	25	17.1	38	20.2	
Gender							0.40
Male	130	39.6	53	37.0	77	41.6	
Female	198	60.4	90	62.9	108	58.4	
Race/Ethnicity							0.68
White	234	76.5	104	75.4	130	77.4	
Black	72	23.5	34	24.6	38	22.6	
Education							0.005*
Less than HS degree	27	8.3	14	9.9	13	7.0	
HS degree	51	15.6	27	19.0	24	13.0	
Some college/tech school	92	28.1	47	33.1	45	24.3	

College degree	85	26.0	36	25.4	49	26.5	
Post college educ	72	22.0	18	12.7	54	29.2	
Income							0.0027*
<$20,000	52	15.9	31	21.8	21	11.3	
$20,000 - <$50,000	61	18.6	30	21.1	31	16.7	
$50,000 - <$75,000	51	15.6	22	15.5	29	15.6	
$75,000 - <$100,000	47	14.3	17	12.0	30	16.1	
>$100,000	63	19.2	15	10.6	48	25.8	
Unknown/Prefer not to say	54	16.5	27	19.0	27	14.5	
Insurance							0.028*
Commercial	79	27.6	22	18.8	57	33.7	
Medicare	149	52.1	65	55.6	84	49.7	
Medicaid	33	11.5	18	15.4	15	8.9	
Other	25	8.7	12	10.3	13	7.7	
Clinical stage							0.87
1	35	32.1	15	36.6	20	29.4	
2	36	33.0	12	29.3	24	35.3	
3	17	15.6	6	14.6	11	16.2	
4	21	19.3	8	19.5	13	19.1	

Access to transportation for treatment appointments[i]							<0.0001*
Very/somewhat easy	245	74.5	90	63.4	155	82.9	
Somewhat/Very hard	84	25.5	52	36.6	32	17.1	
Able to or could afford time off work for treatment appointments[i]							0.0019*
Very/Somewhat easy	230	76.4	82	67.2	148	82.7	
Somewhat/Very hard	71	23.6	40	32.8	31	17.3	
Able to pay for transportation to treatment appointments[i]							<0.0001*
Very/Somewhat easy	217	69.3	70	53.4	147	80.8	
Somewhat/Very hard	96	30.7	61	46.6	35	19.2	

[i]The three transportation access questions comprise the Transportation Barriers scale included in Table 3 and the multivariable model

Table 3. IMB-CCM constructs

	Total (N = 334)		Rural (N = 146)		Nonrural (N = 188)		p-value
	Mean or N	**SD or %**	**Mean or n**	**SD or %**	**Mean or n**	**SD or %**	
Information							
Seek health info							0.60
No	53	16.3	25	17.2	28	14.9	
Yes	278	83.7	118	80.8	160	85.1	
Seek health info online							0.001*
No	179	53.6	93	63.7	86	45.7	
Yes	155	46.4	53	36.3	102	54.3	
Electronic Info Accessibility Score	2.8	0.77	2.6	0.79	3.0	0.74	0.0008*
Motivation							
Medical Distrust							0.21
Not at all/A little	3	0.9	2	1.4	1	0.5	
Some/A lot	321	99.1	139	98.6	182	99.5	
Belief that cancer prevention isn't possible							0.01*
Strongly/somewhat agree	89	27.4	49	34.3	40	22.0	
Somewhat/Strongly disagree	236	72.6	94	65.7	142	78.0	

Spiritual Coping Score	2.7	1.1	2.8	1.1	2.6	1.1	0.04*
Transportation Barriers Score	1.8	0.84	2.1	0.88	1.6	0.76	<0.0001*
Behavioral Skills							
Bring a list of questions to medical appointments							0.1
Always/usually	182	55.0	72	50.0	110	58.8	
Sometimes/never	149	45.0	72	50.0	77	41.2	
Bring a list of medicines to medical appointments							0.02*
Always/usually	233	70.2	112	76.7	121	65.1	
Sometimes/never	99	29.8	34	23.3	65	35.0	
Bring health information to a medical appointment							0.85
Always/usually	70	21.0	30	20.6	40	21.4	
Sometimes/never	263	79.0	116	79.5	147	78.6	
Request an explanation of a test or treatment							0.01*
Always/usually	255	76.4	121	82.9	134	71.3	
Sometimes/never	79	23.7	25	17.1	54	28.7	
Read information about a new prescription							0.31
Always/usually	246	74.3	111	77.1	135	72.2	
Sometimes/never	85	25.7	33	22.9	52	27.8	

Do your own research on a health or medical topic							0.58
Always/usually	169	51.1	76	52.8	93	49.7	
Sometimes/never	162	48.9	68	47.2	94	50.3	
Community							
Social Support Score	4.3	0.9	4.3	0.9	4.3	0.9	0.59
Health Systems							
Access online medical record							0.01*
No	105	31.6	57	39.0	48	25.8	
Yes	227	68.4	89	61.0	138	74.2	
Use app to communicate with a healthcare provider							0.17
Yes	79	28.4	29	24.2	50	31.7	
No	199	71.6	91	75.8	108	68.4	
Patient-Provider Communication	2.61	0.53	2.57	0.58	2.65	0.48	0.20

Table 4. Multivariable model of treatment nonadherence

	Estimate	SE	Chi Square	P-value	OR	95% CI
Intercept	-2.56	0.42	36.80	<.0001	--	
Transportation Barriers score	0.44	0.18	5.83	0.02	1.56*	1.09-2.24
Geography (ref = Nonrural)	-0.37	0.19	3.95	0.05	--	
Bring a list of questions to doctor's appt (Ref = Always/Usually)	0.26	0.18	2.07	0.15	--	
Geography*List of Questions	0.35	0.18	3.69	0.05	Nonrural: 0.84 Rural: 3.37*	0.39-1.80 1.02-11.14

CHAPTER 5: Discussion

Nonadherence to cancer treatment is associated with poorer patient outcomes, yet represents a modifiable target for health behavior interventions.[9–16] The purpose of the dissertation research was to elucidate social and behavioral factors related to oncology treatment nonadherence to inform the development of targeted, tailored approaches to improve rural oncology outcomes. These goals were accomplished by a rigorous mixed methods approach utilizing a systematic review of available literature, cancer registry and hospital billing claims data, population-based surveys, and semi-structured interviews.

Digital health strategies have the potential to mitigate rural cancer disparities. Despite progress made in understanding how digital health can enhance cancer care, previous reviews have not focused on their use in rural populations. Paper 1 systematically and critically examined existing literature to understand how digital technologies have been used to support rural oncology care. We identified 53 studies that addressed the use of technology in rural cancer care delivery, a comparatively small number, representing a significant gap in the literature. Across all studies was the consensus that rural cancer survivors value digital technology approaches to their care, with results varying by type of technology. Ease of use and technological requirements are important considerations in rural populations.

Critical to reducing the rural digital divide and the deployment of digital health strategies is increasing mobile, internet or broadband service in rural areas. While steps are being taken to address this geographic disparity, the fact remains that nearly 30% of Americans live in areas that lack the coverage needed for home internet. The findings of this review suggest further implementation and expansion of telemedicine and phone-based strategies in rural cancer care delivery. There are significant gaps in the literature regarding patient portals, mobile apps, interactive voice response, social media, and text messaging that should be investigated. Opportunities exist for innovative digital health technologies to address rural cancer control.

The goal of Paper 2 was to determine sociodemographic and clinical factors associated with radiation treatment nonadherence among rural and nonrural cancer patients. We utilized cancer registry and hospital billing claims data to define radiation treatment nonadherence and potential covariates and confounders. We found that uninsured rural cancer patients with more appointments were more likely to be nonadherent, with the odds of nonadherence increasing by 14% with each additional appointment date (OR 1.14, 95% CI 1.09-1.20). Patients with clinical stage 4 cancer also had an increased odds of being nonadherent. This analysis revealed actionable clinical implications. Rural patients with more total treatment appointments and those with more advanced disease were more likely to be nonadherent. In recognition of this finding, the healthcare team can focus on risk stratification; identifying key access barriers for each patient or adopting additional assessments of barriers to care for this patient population; offering additional support resources; and scheduling a check in halfway through the treatment plan to support treatment adherence. The evidence-based practice of shorter radiation treatment regimens should continue to be considered. While we were able to identify key contributors to radiation treatment nonadherence, we were limited to cancer registry and hospital billing claims data. Paper 3 built upon these results.

Paper 3 found that rural cancer survivors reported significant barriers to transportation access for cancer treatment appointments, and that transportation barriers were associated with treatment nonadherence. Half of rural participants reported sometimes or never bringing a list of questions to their treatment appointments. For these participants, nonadherence was 3 times the odds of nonadherence in nonrural participants. Mitigating transportation barriers and supporting appointment preparation could reduce cancer treatment nonadherence. The healthcare system is in a unique position to address these issues that could improve treatment adherence and cancer patient outcomes. Survey results from Paper 3 also found that 94% of participants reported having a cell phone. Most participants also reported having a smartphone, though 21% of rural survivors did not (vs 9% nonrural, p=0.002). A higher percentage of rural participants reported having an android versus and iPhone, which has implications for app development.

Dissertation Conclusions

Treatment nonadherence rates in the dissertation studies ranged from 19 to 25%. While the overall nonadherence rate was not significantly different by geographic location, rural adherence rates were higher with increasing length of treatment regimen. We identified several key social and behavioral factors that served as barriers and facilitators to treatment adherence among rural cancer survivors.

Transportation access was a significant issue faced by rural cancer survivors, both in terms of cost and physical access. While the healthcare system can serve to mitigate transportation barriers, religious communities are also a significant source of support. Patients readily reported relying on members of their church to meet transportation needs, defining faith as a cohesive factor that connected people across families, social circles, and sociodemographics. Across all studies was the consensus that rural cancer survivors value digital technology approaches to their care, yet technology type can create a barrier. Ease of use and technological requirements are important considerations in rural populations. Rural cancer survivors were also very amenable to research, including those involving digital health interventions and treatment clinical trials. Half of rural participants reported sometimes or never bringing a list of questions to their treatment appointments, yet those who did had improved treatment adherence. Conversely, rural cancer survivors were engaged in their appointments and readily requested explanations of tests or treatments. These findings support future research emphasis on question generating and supporting question recall versus coaching to reduce cultural barriers to question asking.

I also identified several ways that health systems can play a key role in reducing treatment nonadherence. First, shorter radiation treatment regimens have been established as evidence-based practice, and hypofractionated treatment options should continue to be offered and encouraged. Secondly, the healthcare team can focus on identifying key access barriers for each patient or adopting additional assessments of barriers to care for this patient population; offering additional support resources; and scheduling a check in halfway through the treatment plan to support treatment adherence. Risk stratification can be utilized when implementing interventions to improve treatment adherence.

Critical to reducing the rural digital divide and the deployment of digital health strategies is increasing mobile, internet or broadband service in rural areas. While steps are being taken to

address this geographic disparity, the fact remains that nearly 30% of Americans live in areas that lack the coverage needed for home internet. Findings from this dissertation research suggest further implementation and expansion of telemedicine and phone-based strategies in rural cancer care delivery. There are significant gaps in the literature regarding patient portals, mobile apps, interactive voice response, and text messaging that should be investigated, with text messaging being the most pragmatic in the rural patient population. Of note, 94% of the survey participants reported having a cell phone, while significantly fewer rural survivors had a smartphone, 79% vs 91%. Opportunities exist for innovative digital health technologies that healthcare systems are well-positioned to implement and address rural cancer control.

Finally, we identified gaps in the literature and study design recommendations. Overall, the literature includes very few randomized trials and samples sizes are low. Most studies examining the use of digital health technology that involve rural populations restrict participants to those with internet access yet do not report the number of potential participants that were excluded due to access. Few studies measured access to care variables. While this phase of research did not include a randomized trial, we did attempt to address literature gaps by having large study samples, not restricted by internet access, and including access measures in the survey. Despite the availability of standardized reporting guidelines by study design like CONSORT and STROBE, there is room for improvement in practice in terms of both study design and reporting results. Investigators should take advantage of available guidelines to improve the quality of literature in this research area.

In summary, multilevel factors contribute to the observed geographic differences in cancer treatment adherence and outcomes, including sociodemographic inequities, reduced self-management skills, and diminished access to healthcare, psychosocial services, and technology. Self-management skills, including appointment preparation, that engage patients as active and effective managers of their health result in more positive patient outcomes, including treatment adherence; yet these skills are not routinely performed by patients or incorporated as part of oncology care. Digital health strategies can support patient self-management, which may serve to mitigate rural health disparities, and these dissertation studies supported the acceptability of technology-based research in rural cancer populations. Barriers to technology access among rural residents remain, however, and need to be considered in study design. Innovative strategies to integrate self-management support within oncology care may be a promising way to reduce rural cancer disparities and improve outcomes.

REFERENCES

1. US Department of Health and Human Services, Centers for Disease Control and Prevention, Division of Cancer Prevention and Control. An Update on Cancer Deaths in the United States. Published July 2, 2020. https://www.cdc.gov/cancer/dcpc/research/update-on-cancer-deaths/index.htm

2. Selected rural statistics for the United States. Accessed March 4, 2021. https://www.ruralhealthinfo.org/states/united-states

3. Blake KD, Moss JL, Gaysynsky A, Srinivasan S, Croyle RT. Making the Case for Investment in Rural Cancer Control: An Analysis of Rural Cancer Incidence, Mortality, and Funding Trends. *Cancer Epidemiol Biomarkers Prev*. 2017;26(7):992-997.

4. Henley SJ, Anderson RN, Thomas CC, Massetti GM, Peaker B, Richardson LC. Invasive Cancer Incidence, 2004-2013, and Deaths, 2006-2015, in Nonmetropolitan and Metropolitan Counties - United States. *MMWR Surveill Summ*. 2017;66(14):1-13.

5. Weaver KE, Palmer N, Lu L, Case LD, Geiger AM. Rural-urban differences in health behaviors and implications for health status among US cancer survivors. *Cancer Causes Control*. 2013;24(8):1481-1490.

6. Bolin JN, Bellamy GR, Ferdinand AO, et al. Rural Healthy People 2020: New Decade, Same Challenges. *J Rural Health*. 2015;31(3):326-333.

7. Jones CA, Kandel W, Parker T. Population dynamics are changing the profile of rural areas. *Journal of Rural Mental Health*. 2007;31(3):46-53.

8. Levit LA, Byatt L, Lyss AP, et al. Closing the Rural Cancer Care Gap: Three Institutional Approaches. *JCO Oncol Pract*. 2020;16(7):422-430.

9. Tan X, Camacho F, Marshall VD, Donohoe J, Anderson RT, Balkrishnan R. Geographic disparities in adherence to adjuvant endocrine therapy in Appalachian women with breast cancer. *Res Social Adm Pharm*. 2017;13(4):796-810.

10. Xuan Q, Gao K, Song Y, et al. Adherence to Needed Adjuvant Therapy Could Decrease Recurrence Rates for Rural Patients With Early Breast Cancer. *Clin Breast Cancer*. 2016;16(6):e165-e173.

11. Chow CJ, Al-Refaie WB, Abraham A, et al. Does patient rurality predict quality colon cancer care?: A population-based study. *Dis Colon Rectum*. 2015;58(4):415-422.

12. Camacho FT, Tan X, Alcalá HE, Shah S, Anderson RT, Balkrishnan R. Impact of patient race and geographical factors on initiation and adherence to adjuvant endocrine therapy in medicare breast cancer survivors. *Medicine* . 2017;96(24):e7147.

13. Monson JRT, Probst CP, Wexner SD, et al. Failure of evidence-based cancer care in the United States: the association between rectal cancer treatment, cancer center volume, and geography. *Ann Surg*. 2014;260(4):625-631; discussion 631-632.

14. Craft PS, Buckingham JM, Dahlstrom JE, et al. Variation in the management of early breast cancer in rural and metropolitan centres: implications for the organisation of rural cancer services. *Breast*. 2010;19(5):396-401.

15. Chu QD, Zhou M, Medeiros KL, Peddi P, Wu XC. Impact of CALGB 9343 trial and sociodemographic variation on patterns of adjuvant radiation therapy practice for elderly women (≥ 70 Years) with Stage I, estrogen receptor-positive breast cancer: analysis of the national cancer data base. *Anticancer Res*. 2017;37(10):5585-5594.

16. Dragun AE, Huang B, Gupta S, Crew JB, Tucker TC. One Decade Later: Trends and Disparities in the Application of Post-Mastectomy Radiotherapy Since the Release of the American Society of Clinical Oncology Clinical Practice Guidelines. *International Journal of Radiation Oncology*Biology*Physics*. 2012;83(5):e591-e596.

17. Ohri N, Rapkin BD, Guha C, Kalnicki S, Garg M. Radiation Therapy Noncompliance and Clinical Outcomes in an Urban Academic Cancer Center. *Int J Radiat Oncol Biol Phys*. 2016;95(2):563-570.

18. Perez CA, Grigsby PW, Castro-Vita H, Lockett MA. Carcinoma of the uterine cervix. I. Impact of prolongation of overall treatment time and timing of brachytherapy on outcome of radiation therapy. *Int J Radiat Oncol Biol Phys*. 1995;32(5):1275-1288.

19. Goel V, Singh. JK, Pandey MK. Impact of prolongation of overall treatment time and timing of brachytherapy on outcome of radiation therapy in carcinoma of uterine cervix. *Journal of Clinical Oncology*. 2006;24(18_suppl):15032-15032. doi:10.1200/jco.2006.24.18_suppl.15032

20. Borel C, Lamy S, Compaci G, et al. A longitudinal study of non-medical determinants of adherence to R-CHOP therapy for diffuse large B-cell lymphoma: implication for survival. *BMC Cancer*. 2015;15:288.

21. Bese NS, Sut PA, Ober A. The effect of treatment interruptions in the postoperative irradiation of breast cancer. *Oncology*. 2005;69(3):214-223.

22. McDougall JA, Banegas MP, Wiggins CL, Chiu VK, Rajput A, Kinney AY. Rural Disparities in Treatment-Related Financial Hardship and Adherence to Surveillance Colonoscopy in Diverse Colorectal Cancer Survivors. *Cancer Epidemiol Biomarkers Prev*. 2018;27(11):1275-1282.

23. Zhang NJ, Terry A, McHorney CA. Impact of health literacy on medication adherence: a systematic review and meta-analysis. *Ann Pharmacother*. 2014;48(6):741-751.

24. Bestvina CM, Zullig LL, Rushing C, et al. Patient-oncologist cost communication, financial distress, and medication adherence. *Journal of Clinical Oncology*. 2013;31(31_suppl):2-2. doi:10.1200/jco.2013.31.31_suppl.2

25. Kent EE, Forsythe LP, Robin Yabroff K, et al. Are survivors who report cancer-related financial problems more likely to forgo or delay medical care? *Cancer*. 2013;119(20):3710-3717. doi:10.1002/cncr.28262

26. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf*. 2014;13(1):57-65.

27. Webster M. Definition of culture. *Retrieved from http://www merriam-webster com/medical/culture*. Published online 2010.

28. Bernadette Mazurek Melnyk, PhD, APRN-CNP, FAANP, FNAP, FAAN, Dianne Morrison-Beedy, PhD, RN, WHNP, FNAP, FAANP, FAAN. *Intervention Research and Evidence-Based Quality Improvement, Second Edition: Designing, Conducting, Analyzing, and Funding*. Springer Publishing

Company; 2018.

29. Coyne CA, Demian-Popescu C, Friend D. Social and cultural factors influencing health in southern West Virginia: a qualitative study. *Prev Chronic Dis*. 2006;3(4):A124.

30. Singh R, Goebel LJ. Rural Disparities in Cancer Care: A Review of Its Implications and Possible Interventions. *W V Med J*. 2016;112(3):76-82.

31. Kirkwood MK, Kelsey Kirkwood M, Bruinooge SS, Goldstein MA, Bajorin DF, Kosty MP. Enhancing the American Society of Clinical Oncology Workforce Information System With Geographic Distribution of Oncologists and Comparison of Data Sources for the Number of Practicing Oncologists. *Journal of Oncology Practice*. 2014;10(1):32-38. doi:10.1200/jop.2013.001311

32. Lin CC, Bruinooge SS, Kirkwood MK, et al. Association Between Geographic Access to Cancer Care, Insurance, and Receipt of Chemotherapy: Geographic Distribution of Oncologists and Travel Distance. *J Clin Oncol*. 2015;33(28):3177-3185.

33. Onega T, Duell EJ, Shi X, Wang D, Demidenko E, Goodman D. Geographic access to cancer care in the U.S. *Cancer*. 2008;112(4):909-918. doi:10.1002/cncr.23229

34. *Rural Transportation at a Glance*. U.S. Department of Agriculture, Economic Research Service; 2005.

35. National Association of Social Workers, Center for Workforce Studies. *Assuring the Sufficiency of a Frontline Workforce: A National Study of Licensed Social Workers ; Executive Summary*.; 2006.

36. 2018 Broadband Deployment Report. Published February 5, 2018. Accessed August 8, 2020. https://www.fcc.gov/reports-research/reports/broadband-progress-reports/2018-broadband-deployment-report

37. Wicker RF. *Broadband Deployment Accuracy and Technological Availability Act or the Broadband DATA Act*.; 2020.

38. Greenberg AJ, Haney D, Blake KD, Moser RP, Hesse BW. Differences in Access to and Use of Electronic Personal Health Information Between Rural and Urban Residents in the United States. *J Rural Health*. 2018;34 Suppl 1:s30-s38.

39. Heiney SP, Hilfinger Messias DK, Felder TM, Phelps KW, Quinn JC. African American Women's Recollected Experiences of Adherence to Breast Cancer Treatment. *Oncol Nurs Forum*. 2017;44(2):217-224.

40. Guy GP, Lipscomb J, Gillespie TW, Goodman M, Richardson LC, Ward KC. Variations in Guideline-Concordant Breast Cancer Adjuvant Therapy in Rural Georgia. *Health Services Research*. 2015;50(4):1088-1108. doi:10.1111/1475-6773.12269

41. Heitz F, Bender A, Barinoff J, et al. Outcome of early breast cancer treated in an urban and a rural breast cancer unit in Germany. *Onkologie*. 2013;36(9):477-482.

42. Torres E, Dixon C, Richman AR. Understanding the Breast Cancer Experience of Survivors: a Qualitative Study of African American Women in Rural Eastern North Carolina. *J Cancer Educ*. 2016;31(1):198-206.

43. Lavoie JG, Kaufert J, Browne AJ, O'Neil JD. Managing Matajoosh: determinants of first Nations' cancer care decisions. *BMC Health Serv Res*. 2016;16(1):402.

44. Lipscomb J, Gillespie TW, Goodman M, et al. Black-white differences in receipt and completion of adjuvant chemotherapy among breast cancer patients in a rural region of the US. *Breast Cancer Res Treat*. 2012;133(1):285-296.

45. Gilbar P, Lee A, Pokharel K. Why adjuvant chemotherapy for stage III colon cancer was not given: Reasons for non-recommendation by clinicians or patient refusal. *Journal of Oncology Pharmacy Practice*. 2017;23(2):128-134. doi:10.1177/1078155215623086

46. Le D, Holt CL, Pisu M, et al. The role of social support in posttreatment surveillance among African American survivors of colorectal cancer. *J Psychosoc Oncol*. 2014;32(3):245-263.

47. Lea CS, Bohra S, Moore T, Passwater C, Liles D. Exploring behaviors, treatment beliefs, and barriers to oral chemotherapy adherence among adult leukemia patients in a rural outpatient setting. *BMC Res Notes*. 2018;11(1):843.

48. Walker LO. StrategieS for theory Con Stru Ction in nur Sing. Accessed March 11, 2021. http://catalogue.pearsoned.ca/assets/hip/ca/hip_ca_pearsonhighered/preface/0134754077.pdf

49. Fisher WA, Fisher JD, Harman J. The Information-Motivation-Behavioral Skills Model: A General Social Psychological Approach to Understanding and Promoting Health Behavior. *Social Psychological Foundations of Health and Illness*.:82-106. doi:10.1002/9780470753552.ch4

50. Wagner EH, Austin BT, Davis C, Hindmarsh M, Schaefer J, Bonomi A. Improving chronic illness care: translating evidence into action. *Health Aff* . 2001;20(6):64-78.

51. Fisher JD, Fisher WA. Changing AIDS-risk behavior. *Psychol Bull*. 1992;111(3):455-474.

52. Cooperman NA, Lu S-E, Richter KP, Bernstein SL, Williams JM. Pilot Study of a Tailored Smoking Cessation Intervention for Individuals in Treatment for Opioid Dependence. *Nicotine Tob Res*. 2018;20(9):1152-1156.

53. Bang KS, Lee IS, Kim SJ, Song MK, Park SE. [The Effects of Urban Forest-walking Program on Health Promotion Behavior, Physical Health, Depression, and Quality of Life: A Randomized Controlled Trial of Office-workers]. *J Korean Acad Nurs*. 2016;46(1):140-148.

54. Misovich SJ, Martinez T, Fisher JD, Bryan AD, Catapano N. Breast self-examination: A test of the information, motivation, and behavioral skills model. *J Appl Soc Psychol*. Published online 2001.

55. Fisher JD, Fisher WA, Amico KR, Harman JJ. An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychol*. 2006;25(4):462-473.

56. Locke EA. Social Foundations of Thought and Action: A Social-Cognitive ViewSocial Foundations of Thought and Action: A Social-Cognitive View, by Bandura Albert. Englewood Cliffs, NJ: Prentice-Hall, 1986, 617 pp., cloth. *Academy of Management Review*. 1987;12(1):169-171. doi:10.5465/amr.1987.4306538

57. Coleman K, Austin BT, Brach C, Wagner EH. Evidence on the Chronic Care Model in the new millennium. *Health Aff* . 2009;28(1):75-85.

58. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care

needs of people with cancer? A systematic review. *Support Care Cancer*. 2009;17(8):1117-1128.

59. Kaufman BG, Thomas SR, Randolph RK, et al. The Rising Rate of Rural Hospital Closures. *J Rural Health*. 2016;32(1):35-43.

60. Wagner EH, Aiello Bowles EJ, Greene SM, et al. The quality of cancer patient experience: perspectives of patients, family members, providers and experts. *Qual Saf Health Care*. 2010;19(6):484-489.

61. Smith EML, Skalla K, Li Z, et al. Assessing cancer survivors' needs using web-based technology: a pilot study. *Comput Inform Nurs*. 2012;30(2):71-81.

62. Sharma A, Harrington RA, McClellan MB, et al. Using Digital Health Technology to Better Generate Evidence and Deliver Evidence-Based Care. *J Am Coll Cardiol*. 2018;71(23):2680-2690.

63. Lee J-A, Choi M, Lee SA, Jiang N. Effective behavioral intervention strategies using mobile health applications for chronic disease management: a systematic review. *BMC Med Inform Decis Mak*. 2018;18(1):12.

64. Rathbone AL, Prescott J. The Use of Mobile Apps and SMS Messaging as Physical and Mental Health Interventions: Systematic Review. *FOCUS*. 2018;16(4):456-465. doi:10.1176/appi.focus.16406

65. Meskó B, Drobni Z, Bényei É, Gergely B, Győrffy Z. Digital health is a cultural transformation of traditional healthcare. *Mhealth*. 2017;3:38.

66. Parati G, Pellegrini D, Torlasco C. How Digital Health Can Be Applied for Preventing and Managing Hypertension. *Curr Hypertens Rep*. 2019;21(5):40.

67. Cahn A, Akirov A, Raz I. Digital health technology and diabetes management. *Journal of Diabetes*. 2018;10(1):10-17. doi:10.1111/1753-0407.12606

68. Kataria S, Ravindran V. Digital health: a new dimension in rheumatology patient care. *Rheumatol Int*. 2018;38(11):1949-1957.

69. Ding H, Fatehi F, Maiorana A, Bashi N, Hu W, Edwards I. Digital health for COPD care: the current state of play. *J Thorac Dis*. 2019;11(Suppl 17):S2210-S2220.

70. Yin AL, Hachuel D, Pollak JP, Scherl EJ, Estrin D. Digital Health Apps in the Clinical Care of Inflammatory Bowel Disease: Scoping Review. *J Med Internet Res*. 2019;21(8):e14630.

71. Batra S, Baker RA, Wang T, Forma F, DiBiasi F, Peters-Strickland T. Digital health technology for use in patients with serious mental illness: a systematic review of the literature. *Med Devices* . 2017;10:237-251.

72. Wildevuur SE, Simonse LWL. Information and communication technology-enabled person-centered care for the "big five" chronic conditions: scoping review. *J Med Internet Res*. 2015;17(3):e77.

73. Geng Y, Myneni S. Patient Engagement in Cancer Survivorship Care through mHealth: A Consumer-centered Review of Existing Mobile Applications. *AMIA Annu Symp Proc*. 2015;2015:580-588.

74. Davis SW, Oakley-Girvan I. mHealth Education Applications Along the Cancer Continuum. *J

Cancer Educ. 2015;30(2):388-394.

75. Fallahzadeh R, Rokni SA, Ghasemzadeh H, Soto-Perez-de-Celis E, Shahrokni A. Digital Health for Geriatric Oncology. *JCO Clin Cancer Inform*. 2018;2:1-12.

76. Devine KA, Viola AS, Coups EJ, Wu YP. Digital Health Interventions for Adolescent and Young Adult Cancer Survivors. *JCO Clinical Cancer Informatics*. 2018;(2):1-15. doi:10.1200/cci.17.00138

77. Greenberg-Worisek AJ, Kurani S, Rutten LJF, Blake KD, Moser RP, Hesse BW. Tracking Healthy People 2020 internet, broadband, and mobile device access goals: an update using data from the Health Information National Trends Survey. *J Med Internet Res*. 2019;21(6):e13300.

78. Patrick JL, Hasse ME, Feinglass J, Khan SA. Trends in adherence to NCCN guidelines for breast conserving therapy in women with Stage I and II breast cancer: Analysis of the 1998–2008 National Cancer Data Base. *Surg Oncol*. 2017;26(4):359-367.

79. Perrin A. Digital gap between rural and nonrural America persists. *Pew Research Center*. 2017;19. https://www.pewresearch.org/fact-tank/2019/05/31/digital-gap-between-rural-and-nonrural-america-persists/

80. Hong QN, Gonzalez-Reyes A, Pluye P. Improving the usefulness of a tool for appraising the quality of qualitative, quantitative and mixed methods studies, the Mixed Methods Appraisal Tool (MMAT). *J Eval Clin Pract*. 2018;24(3):459-467.

81. Pace R, Pluye P, Bartlett G, et al. Testing the reliability and efficiency of the pilot Mixed Methods Appraisal Tool (MMAT) for systematic mixed studies review. *Int J Nurs Stud*. 2012;49(1):47-53.

82. Pluye P, Gagnon M-P, Griffiths F, Johnson-Lafleur J. A scoring system for appraising mixed methods research, and concomitantly appraising qualitative, quantitative and mixed methods primary studies in Mixed Studies Reviews. *Int J Nurs Stud*. 2009;46(4):529-546.

83. Souto RQ, Khanassov V, Hong QN, Bush PL, Vedel I, Pluye P. Systematic mixed studies reviews: updating results on the reliability and efficiency of the Mixed Methods Appraisal Tool. *Int J Nurs Stud*. 2015;52(1):500-501.

84. Sabesan S, Brennan S. TeleOncology for cancer care in rural Australia. *Telemedicine techniques and applications*. Published online 2011:289-306.

85. Hamilton E, Van Veldhuizen E, Brown A, Brennan S, Sabesan S. Telehealth in radiation oncology at the Townsville Cancer Centre: Service evaluation and patient satisfaction. *Clin Transl Radiat Oncol*. 2019;15:20-25.

86. Sabesan S, Larkins S, Evans R, et al. Telemedicine for rural cancer care in North Queensland: bringing cancer care home. *Aust J Rural Health*. 2012;20(5):259-264.

87. Mooi JK, Whop LJ, Valery PC, Sabesan SS. Teleoncology for indigenous patients: the responses of patients and health workers. *Aust J Rural Health*. 2012;20(5):265-269.

88. Thaker DA, Monypenny R, Olver I, Sabesan S. Cost savings from a telemedicine model of care in northern Queensland, Australia. *Med J Aust*. 2013;199(6):414-417.

89. Sabesan S, Senko C, Schmidt A, et al. Enhancing Chemotherapy Capabilities in Rural Hospitals: Implementation of a Telechemotherapy Model (QReCS) in North Queensland, Australia. *J Oncol*

Pract. 2018;14(7):e429-e437.

90. Jhaveri D, Larkins S, Kelly J, Sabesan S. Remote chemotherapy supervision model for rural cancer care: perspectives of health professionals. *Eur J Cancer Care* . 2016;25(1):93-98.

91. Sabesan S, Kelly J, Evans R, Larkins S. A tele-oncology model replacing face-to-face specialist cancer care: perspectives of patients in North Queensland. *J Telemed Telecare*. 2014;20(4):207-211.

92. Iredale R, Hilgart J, Hayward J. Patient perceptions of a mobile cancer support unit in South Wales. *Eur J Cancer Care* . 2011;20(4):555-560.

93. Mitchell T. Patients' experiences of receiving chemotherapy in outpatient clinic and/or onboard a unique nurse-led mobile chemotherapy unit: a qualitative study. *Eur J Cancer Care* . 2013;22(4):430-439.

94. Burns CL, Ward EC, Hill AJ, et al. A pilot trial of a speech pathology telehealth service for head and neck cancer patients. *J Telemed Telecare*. 2012;18(8):443-446.

95. Burns CL, Ward EC, Hill AJ, Kularatna S, Byrnes J, Kenny LM. Randomized controlled trial of a multisite speech pathology telepractice service providing swallowing and communication intervention to patients with head and neck cancer: Evaluation of service outcomes. *Head Neck*. 2017;39(5):932-939.

96. Gordon HL, Hoeber M, Schneider A. Telepharmacy in a rural Alberta Community Cancer Network. *J Oncol Pharm Pract*. 2012;18(3):366-376.

97. Wakefield CE, Sansom-Daly UM, McGill BC, et al. Acceptability and feasibility of an e-mental health intervention for parents of childhood cancer survivors: "Cascade." *Supportive Care in Cancer*. 2016;24(6):2685-2694. doi:10.1007/s00520-016-3077-6

98. Choi Yoo SJ, Nyman JA, Cheville AL, Kroenke K. Cost effectiveness of telecare management for pain and depression in patients with cancer: results from a randomized trial. *Gen Hosp Psychiatry*. 2014;36(6):599-606.

99. Haozous E, Doorenbos AZ, Demiris G, et al. Role of telehealth/videoconferencing in managing cancer pain in rural American Indian communities. *Psychooncology*. 2012;21(2):219-223.

100. Buchanan AH, Datta SK, Skinner CS, et al. Randomized Trial of Telegenetics vs. In-Person Cancer Genetic Counseling: Cost, Patient Satisfaction and Attendance. *J Genet Couns*. 2015;24(6):961-970.

101. Brown J, Athens A, Tait DL, et al. A Comprehensive Program Enabling Effective Delivery of Regional Genetic Counseling. *Int J Gynecol Cancer*. 2018;28(5):996-1002.

102. Watanabe SM, Fairchild A, Pituskin E, Borgersen P, Hanson J, Fassbender K. Improving access to specialist multidisciplinary palliative care consultation for rural cancer patients by videoconferencing: report of a pilot project. *Support Care Cancer*. 2013;21(4):1201-1207.

103. Bensink ME, Armfield NR, Pinkerton R, et al. Using videotelephony to support paediatric oncology-related palliative care in the home: from abandoned RCT to acceptability study. *Palliat Med*. 2009;23(3):228-237.

104. Doorenbos AZ, Kundu A, Eaton LH, et al. Enhancing access to cancer education for rural

healthcare providers via telehealth. *J Cancer Educ*. 2011;26(4):682-686.

105.   Brandon AR, Song L, Deal AM, et al. Using Telehealth to Train Providers of a Cancer Support Intervention. *Telemed J E Health*. 2015;21(10):793-800.

106.   Forgione A, Kislov V, Guraya SY, Kasakevich E, Pugliese R. Safe introduction of laparoscopic colorectal surgery even in remote areas of the world: the value of a comprehensive telementoring training program. *J Laparoendosc Adv Surg Tech A*. 2015;25(1):37-42.

107.   Stevenson MM, Irwin T, Lowry T, et al. Development of a virtual multidisciplinary lung cancer tumor board in a community setting. *J Oncol Pract*. 2013;9(3):e77-e80.

108.   Shea CM, Haynes-Maslow L, McIntyre M, et al. Assessing the Feasibility of a Virtual Tumor Board Program: A Case Study. *Journal of Healthcare Management*. 2014;59(3):177-193. doi:10.1097/00115514-201405000-00005

109.   Hall S, Murchie P. Can we use technology to encourage self-monitoring by people treated for melanoma? A qualitative exploration of the perceptions of potential recipients. *Support Care Cancer*. 2014;22(6):1663-1671.

110.   Petitte TM, Narsavage GL, Chen Y-J, Coole C, Forth T, Frick KD. Feasibility study: home telemonitoring for patients with lung cancer in a mountainous rural area. *Oncol Nurs Forum*. 2014;41(2):153-161.

111.   Doorenbos AZ, Eaton LH, Haozous E, Towle C, Revels L, Buchwald D. Satisfaction with telehealth for cancer support groups in rural American Indian and Alaska Native communities. *Clin J Oncol Nurs*. 2010;14(6):765-770.

112.   Befort CA, Klemp JR, Austin HL, et al. Outcomes of a weight loss intervention among rural breast cancer survivors. *Breast Cancer Res Treat*. 2012;132(2):631-639.

113.   Befort CA, Klemp JR, Sullivan DK, et al. Weight loss maintenance strategies among rural breast cancer survivors: The rural women connecting for better health trial. *Obesity* . 2016;24(10):2070-2077.

114.   Fazzino TL, Fabian C, Befort CA. Change in Physical Activity During a Weight Management Intervention for Breast Cancer Survivors: Association with Weight Outcomes. *Obesity* . 2017;25 Suppl 2:S109-S115.

115.   Fazzino TL, Sporn NJ, Befort CA. A qualitative evaluation of a group phone-based weight loss intervention for rural breast cancer survivors: Themes and mechanisms of success. *Support Care Cancer*. 2016;24(7):3165-3173.

116.   Bakitas M, Lyons KD, Hegel MT, et al. The project ENABLE II randomized controlled trial to improve palliative care for rural patients with advanced cancer: baseline findings, methodological challenges, and solutions. *Palliat Support Care*. 2009;7(1):75.

117.   Bakitas MA, Tosteson TD, Li Z, et al. Early versus delayed initiation of concurrent palliative oncology care: patient outcomes in the ENABLE III randomized controlled trial. *J Clin Oncol*. 2015;33(13):1438.

118.   Dionne-Odom JN, Azuero A, Lyons KD, et al. Benefits of Early Versus Delayed Palliative Care to Informal Family Caregivers of Patients With Advanced Cancer: Outcomes From the ENABLE III

Randomized Controlled Trial. *J Clin Oncol*. 2015;33(13):1446-1452.

119.   Dionne-Odom JN, Taylor R, Rocque G, et al. Adapting an Early Palliative Care Intervention to Family Caregivers of Persons With Advanced Cancer in the Rural Deep South: A Qualitative Formative Evaluation. *J Pain Symptom Manage*. 2018;55(6):1519-1530.

120.   Belkora J, Stupar L, O'Donnell S, et al. Decision support by telephone: randomized controlled trial in a rural community setting. *Patient Educ Couns*. 2012;89(1):134-142.

121.   O'Donnell S, Moore D. Cost-benefit analysis of decision support methods for patients with breast cancer in a rural community. *EXPANDYOUR OPTIONS*.:47.

122.   Gilbertson-White S, Yeung CW, Saeidzadeh S, Tykol H, Vikas P, Cannon A. Engaging Stakeholders in the Development of an eHealth Intervention for Cancer Symptom Management for Rural Residents. *J Rural Health*. 2019;35(2):189-198.

123.   Syrjala KL, Crouch M-L, Leisenring WM, et al. Engagement with INSPIRE, an Online Program for Hematopoietic Cell Transplantation Survivors. *Biol Blood Marrow Transplant*. 2018;24(8):1692-1698.

124.   Fennell KM, Turnbull DA, Bidargaddi N. The consumer-driven development and acceptability testing of a website designed to connect rural cancer patients and their families, carers and health professionals …. *J Cancer*. Published online 2017. https://onlinelibrary.wiley.com/doi/abs/10.1111/ecc.12533

125.   Frensham LJ, Zarnowiecki DM, Parfitt G, King S, Dollman J. The experiences of participants in an innovative online resource designed to increase regular walking among rural cancer survivors: a qualitative pilot feasibility study. *Support Care Cancer*. 2014;22(7):1923-1929.

126.   Rehse B, Pukrop R. Effects of psychosocial interventions on quality of life in adult cancer patients: meta analysis of 37 published controlled outcome studies. *Patient Educ Couns*. 2003;50(2):179-186.

127.   Gottlieb BH, Wachala ED. Cancer support groups: a critical review of empirical studies. *Psychooncology*. 2007;16(5):379-400.

128.   Koczwara B, Francis K, Marine F, Goldstein D, Underhill C, Olver I. Reaching further with online education? The development of an effective online program in palliative oncology. *J Cancer Educ*. 2010;25(3):317-323.

129.   Vollmer Dahlke D, Kellstedt D, Weinberg AD. Developing NaviCanPlan: A Mobile Web Resource Locator for Cancer Providers and Survivors. *J Cancer Educ*. 2015;30(4):670-676.

130.   Baseman J, Revere D, Baldwin L-M. A Mobile Breast Cancer Survivorship Care App: Pilot Study. *JMIR Cancer*. 2017;3(2):e14.

131.   Rao R, Shukla BM, Saint-Cyr M, Rao M, Teotia SS. Take two and text me in the morning: optimizing clinical time with a short messaging system. *Plast Reconstr Surg*. 2012;130(1):44-49.

132.   Ben-Ami S, Shaham J, Rabin S, Melzer A, Ribak J. The influence of nurses' knowledge, attitudes, and health beliefs on their safe behavior with cytotoxic drugs in Israel. *Cancer Nurs*. 2001;24(3):192-200.

133.   McCarthy A, Hegney D, Brown L, Gilbar P, Brodribb TR, Swales J. Characteristics of chemotherapy practice in rural and remote area health facilities in Queensland. *Aust J Rural Health*. 2003;11(3):138-144.

134.   Arora S, Byers EL. Leveraging Local Expertise to Improve Rural Cancer Care Outcomes Using Project ECHO: A Response to Levit et al. *JCO Oncol Pract*. 2020;16(7):399-403.

135.   Jiang Y, West BT, Barton DL, Harris MR. Acceptance and Use of eHealth/mHealth Applications for Self-Management Among Cancer Survivors. *Stud Health Technol Inform*. 2017;245:131-135.

136.   Rural-Urban Continuum Codes. Accessed April 13, 2021. https://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx

137.   Rural-urban commuting area codes. Accessed April 13, 2021. https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes/

138.   US Census Bureau. Urban and Rural. Accessed April 13, 2021. https://www.census.gov/programs-surveys/geography/guidance/geo-areas/urban-rural.html

139.   Defining Rural Population. Published April 28, 2017. Accessed April 13, 2021. https://www.hrsa.gov/rural-health/about-us/definition/index.html

140.   Willcox JC, Dobson R, Whittaker R. Old-Fashioned Technology in the Era of "Bling": Is There a Future for Text Messaging in Health Care? *J Med Internet Res*. 2019;21(12):e16630.

141.   Gapany M. Hyperfractionated or accelerated radiotherapy in head and neck cancer: a meta-analysis. *Yearbook of Otolaryngology-Head and Neck Surgery*. 2007;2007:290-291. doi:10.1016/s1041-892x(07)70240-8

142.   Ohri N, Rapkin BD, Guha D, et al. Predictors of Radiation Therapy Noncompliance in an Urban Academic Cancer Center. *International Journal of Radiation Oncology*Biology*Physics*. 2015;91(1):232-238. doi:10.1016/j.ijrobp.2014.09.030

143.   Bese NS, Hendry J, Jeremic B. Effects of prolongation of overall treatment time due to unplanned interruptions during radiotherapy of different tumor sites and practical methods for compensation. *Int J Radiat Oncol Biol Phys*. 2007;68(3):654-661.

144.   Patel UA, Patadia MO, Holloway N, Rosen F. Poor radiotherapy compliance predicts persistent regional disease in advanced head/neck cancer. *Laryngoscope*. 2009;119(3):528-533.

145.   Hasan S, Gorovets D, Lehrer E, et al. Optimal timing of radiotherapy in high risk prostate cancer: Do missed days matter? *Clin Transl Radiat Oncol*. 2021;26:47-54.

146.   Hershman DL, Shao T, Kushi LH, et al. Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. *Breast Cancer Res Treat*. 2011;126(2):529-537.

147.   Ganesan P, Sagar TG, Dubashi B, et al. Nonadherence to imatinib adversely affects event free survival in chronic phase chronic myeloid leukemia. *Am J Hematol*. 2011;86(6):471-474.

148.   Ibrahim AR, Eliasson L, Apperley JF, et al. Poor adherence is the main reason for loss of CCyR and imatinib failure for chronic myeloid leukemia patients on long-term therapy. *Blood*. 2011;117(14):3733-3736.

149.   Allemani C, Storm H, Voogd AC, et al. Variation in "standard care" for breast cancer across Europe: A EUROCARE-3 high resolution study. *European Journal of Cancer*. 2010;46(9):1528-1536. doi:10.1016/j.ejca.2010.02.016

150.   Smith GL. Completion of Adjuvant Radiation Therapy Among Women With Breast Cancer. *Breast Diseases: A Year Book Quarterly*. 2009;20(3):307-308. doi:10.1016/s1043-321x(09)79347-6

151.   Srokowski TP, Fang S, Duan Z, et al. Completion of adjuvant radiation therapy among women with breast cancer. *Cancer*. 2008;113(1):22-29. doi:10.1002/cncr.23513

152.   Coyne CA, Demian-Popescu C, Friend D. Peer reviewed: social and cultural factors influencing health in southern west Virginia: a qualitative study. *Prev Chronic Dis*. 2006;3(4). https://www.ncbi.nlm.nih.gov/pmc/articles/pmc1779288/

153.   Rural-Urban Continuum Code - SEER Datasets. Accessed February 7, 2021. https://seer.cancer.gov/seerstat/variables/countyattribs/ruralurban.html

154.   Parker K, Horowitz J, Brown A, Fry R, Cohn D, Igielnik R. What unites and divides urban, suburban and rural communities. *Pew Research Center*. Published online May 22, 2018. Accessed April 13, 2021. https://apo.org.au/node/173886

155.   Lentz R, Benson AB 3rd, Kircher S. Financial toxicity in cancer care: Prevalence, causes, consequences, and reduction strategies. *J Surg Oncol*. 2019;120(1):85-92.

156.   Lyratzopoulos G, Liu MP-H, Abel GA, Wardle J, Keating NL. The Association between Fatalistic Beliefs and Late Stage at Diagnosis of Lung and Colorectal Cancer. *Cancer Epidemiol Biomarkers Prev*. 2015;24(4):720-726.

157.   Powe BD, Finnie R. Cancer fatalism: the state of the science. *Cancer Nurs*. 2003;26(6):454-465; quiz 466-467.

158.   Zahnd WE, Fogleman AJ, Jenkins WD. Rural–Urban Disparities in Stage of Diagnosis Among Cancers With Preventive Opportunities. *Am J Prev Med*. 2018;54(5):688-698.

159.   Gillespie EF, Tringale KR, Bach PB, Bekelman JE. Evaluation of Use of Shorter Radiation Regimens for Breast and Prostate Cancer in the US, 2015-2017. *JAMA Netw Open*. 2020;3(7):e2010519.

160.   Creswell JW, Plano Clark VL. *Designing and Conducting Mixed Methods Research*. SAGE Publications; 2017.

161.   Nelson DE, Kreps GL, Hesse BW, et al. The Health Information National Trends Survey (HINTS): development, design, and dissemination. *J Health Commun*. 2004;9(5):443-460; discussion 81-84.

162.   Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. *Int J Behav Med*. 1997;4(1):92-100.

163.   Creswell JW. *Qualitative Inquiry and Research Design: Choosing Among Five Approaches*. SAGE Publications; 2013.

164.   Reid K, Flowers P, Larkin M. Exploring lived experience. *Psychologist*. 18(1):20-23.

165.   Roter DL. Patient participation in the patient-provider interaction: the effects of patient question asking on the quality of interaction, satisfaction and compliance. *Health Educ Monogr*. 1977;5(4):281-315.

166.   Brandes K, Linn AJ, Butow PN, van Weert JCM. The characteristics and effectiveness of Question Prompt List interventions in oncology: a systematic review of the literature. *Psychooncology*. 2015;24(3):245-252.

APPENDICES

Paper 1 Appendix 1. Systematic Literature Review Search

Pubmed search

Search set #1: ("Rural Population"[Mesh] OR "Rural Health Services"[Mesh] OR "Rural Health"[Mesh] OR "Hospitals, Rural"[Mesh] OR "rural" [TIAB])

Search set #2: ("Mobile Health Units"[Mesh] OR "Mobile Applications"[Mesh] OR "Telemedicine"[Mesh] OR "Text Messaging"[Mesh] OR "Internet"[Mesh] OR "Patient Portals"[Mesh] OR "Technology/diagnosis"[Mesh:NoExp] OR "Technology/diagnostic imaging"[Mesh:NoExp] OR "Technology/instrumentation"[Mesh:NoExp] OR "Technology/therapeutic use"[Mesh:NoExp] OR "Medical Informatics"[Mesh] OR "health information technology"[TIAB] OR "health IT"[TIAB] OR "patient portal*"[TIAB] OR "patient internet portal*"[TIAB] OR "decision support*"[TIAB] OR "clinical reminder*"[TIAB] OR "electronic reminder*"[TIAB] OR "reminder system*"[TIAB] OR "computer assisted decision making"[TIAB] OR "computer assisted detection"[TIAB] OR "computer assisted diagnosis"[TIAB] OR "computer assisted treatment"[TIAB] OR "computer assisted therapy"[TIAB] OR "decision support"[TIAB] OR "decision aid"[TIAB]) OR "app"[TIAB] or "text message"[TIAB] or "mobile"[TIAB] or "digital"[TIAB] or "mhealth"[TIAB] or "ehealth"[TIAB] or "phone"[TIAB] or "social media"[TIAB]

Search set #3: ("cancer"[TIAB] OR "neoplasms"[MeSH] OR "tumor"[TIAB] OR "tumour"[TIAB] OR "oncolog*"[TIAB])

Limitations: Last 10 years and articles in English

Pubmed Total: 341

 CINAHL Complete search

Search set #1: (MH "Rural Health Centers") OR (MH "Rural Health Personnel") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Health Nursing") OR (MH "Rural Areas") OR (MH "Rural Health") OR "rural"

Search set #2: (MH "Mobile Health Units") OR (MH "Telehealth") OR "mobile health unit" OR (MH "Mobile Applications") OR "mobile applications" OR (MH "World Wide Web Applications") OR (MH "Telemedicine") OR "telemedicine" OR (MH "Telerehabilitation") OR (MH "Telepsychiatry") OR (MH "Text Messaging") OR "text messaging" OR (MH "Internet") OR "internet" OR "patient portal" OR (MH "Technology/ES/ED/EV") OR "technology" OR (MH "Medical Informatics") OR "medical informatics" OR (MH "Information Technology") OR "health information technology" OR (MH "Decision Support Systems, Clinical") OR "decision support" OR "clinical reminder" OR (MH "Reminder Systems") OR (MH "Decision Making, Computer Assisted") OR (MH "Diagnosis, Computer Assisted")

Search set #3: (MH "Neoplasms+") OR "cancer" OR (MH "Cancer Patients") OR (MH "Cancer Screening") OR (MH "Cancer Survivors") OR (MH "Early Detection of Cancer") OR (MH "Oncology") OR "oncology" OR "tumor"

Limitations: Last 10 years, articles in English, exclude MEDLINE articles

CINAHL Complete: 54

PsychINFO search

Index Terms: {Rural Environments} *AND* Index Terms: {Neoplasms} *AND* Index Terms: {Telemedicine} OR {Internet} OR {Computer Mediated Communication} OR {Computer Assisted Therapy} OR {Computer Assisted Diagnosis} OR {Mobile Devices} OR {Computers} OR {Electronic Communication} OR {Technology} OR {Text Messaging} OR {Cellular Phones} OR {Text Messaging} OR {Mobile Devices} OR {Internet} OR {Telemedicine} OR {Social Media} OR {Online Therapy} OR {Online Experiments} OR {Websites} OR {Information Technology} OR {Decision Support Systems} OR {Artificial Intelligence} OR {Computer Applications} *AND* Peer-Reviewed Journals only *AND* Year: 2008 *To* 9999

PyschINFO: 4 (all duplicates)

 Embase search

Search set #1: rural health/ or rural area/ or rural health nursing/ or rural.mp. or rural health care/ or rural population/

Search set #2: mobile application/ or technology/ or telemedicine/ or mobile phone/ or mobile health.mp. Or telemedicine.mp. or telemedicine/ or telecommunication/ or text messaging.mp. or text messaging/ or decision support system/ or computer assisted diagnosis/ or internet.mp. or Internet/ or patient portal.mp. or information technology/ or information technology device/ or health information technology.mp. or medical informatics/ or computer assisted diagnosis/ or computer assisted.mp. or reminder system/ or reminder.mp.

Search set #3: cancer.mp. or malignant neoplasm/ or tumor.mp. or neoplasm/ or surgical oncology/ or oncology/ or oncology.mp. or oncology nursing/ or radiation oncology/

Limitations: Last 10 years and Embase journal articles in English

Embase: 204

Articles from Pubmed, CINAHL Complete, PsychINFO and Embase = 595

Articles from reference lists = 5

Total duplicates removed = 85

Paper 1 Appendix 2. Comparison of Main Geographic Classification Systems

	US Census Bureau	Office of Management and Budget	USDA RUCA	USDA RUCC	ARIA
Categories	Urban Area (UA), Urban Cluster, Rural	Metro and Non-Metro (Micro and Non-core)	1-10	1-9	0 - 15
Defining attributes	Population size and density in census areas	Population size in counties	Population density, proximity to an UA, daily commuting patterns	Population size, proximity to a UA, adjacency to a metro area	Distance via road access to urban ("service") centers by population size
Category definitions	**Urban Area**: Census areas with at least 50,000 people, a population density of at least 1,000 individuals/sq mile and may include surrounding census blocks with an overall density of at least 500 individuals/sq mile; **Urban Cluster**: at least 2,500 but <50,000 people; **Rural Area**: <2,500 people	**Metro**: at least one central county with an UA (population at least 50,000); **Non-Metro**: Counties that are outside the boundaries of a Metro area, with <u>Micro</u> being urban clusters of 10,000 - <50,000 people and <u>Non-core</u> being all remaining counties	**1**: Metro area core; **2**: Metro high commuting; **3**: Metro low commuting; **4**: Micro area core, **5**: Micro high commuting; **6**: Micro low commuting, **7**: Small town core, **8**: Small town high commuting, **9**: Small town low commuting, **10**: Rural	**1**: Counties in metro area with 1M+ population; **2**: Counties in metro area 250,000 - <1M; **3**: Counties in metro area <250,000; **4**: Urban population 20,000+ adjacent to metro area; **5**: Urban population 20,000+ not adjacent to metro area; **6**: Urban population 2,500 - <20,000 adjacent to metro area; **7**: Urban population 2,500 - <20,000 not adjacent to metro area; **8**: Completely rural or <2,500 urban population adjacent to metro area; **9**: Completely rural or	**0 - 0.2**: service to Category A (250,000+ population service area); **>0.2 - 2.4**: service to Category B (48,000 - <250,000 pop service area); **>2.4 - 5.92**: service to Category C (18,000 - <48,000 pop service area); **>5.92 - 10.53**: service to Category D (5,000 - <18,000 pop service area); **> 10.53**: Service to Category E

	and population density <500 people/sq mile			<2,500 urban population not adjacent to metro area	(1,000 - <5,000 population service area)

Paper 3 Appendix 1. Summary of participant recruitment

	Rural	%	Nonrural	%	Total
Surveys	1050		1050		2027
Same household or bad address	89		13		102
Total mailed	961	48%	1037	52%	1998
Total participants	188	44%	242	56%	430
Completed by mail	153	81%	186	77%	242
Completed online	35	19%	56	23%	188
Consent to Registry	154	82%	204	85%	358
Consent to Future Contact	144	77%	194	80%	338
Consent to Medical Records	146	78%	188	78%	334
Eligible, Non-response (reason: refusal)	30	51%	29	49%	59
Unknown eligibility, No Returned Questionnaire	744	49%	768	50%	1512
Response Rate[i]		20%		23%	
Refusal Rate[i]		3%		3%	

[i] Calculated based on Response Rate 1 and Refusal Rate 1 of the American Association for Public Opinion Research Standard Definitions

Paper 3 Appendix 2. Semistructured Interview Guide

Thank you so much for your time and willingness to participate. As a brief introduction, the goal of this conversation is to better understand the challenges you may have faced and the resources you have had during your cancer journey as a rural resident. The documents that we just went over explain the purpose of the study, the steps we are taking to protect your privacy, and give us permission to audiorecord the conversation for research purposes. We audiorecord so that we can make sure we capture everything that is discussed, since learning about your experiences is important to us and I can't take notes as fast as I would like! The conversation will take about 1 hour, and you will receive $20 as a thank you for your time. Do you have any questions before we begin?

I.   **Rurality**

Thank you again for your time. Since this study is interested in learning about rural residents' experiences with cancer, I'd like to first start out with learning a little about the area in which you live. Could you please describe your community?

> Prompts: town name, how long they've lived there, main areas/businesses, what the town is known for

When you hear people talking about rural areas, what do you think defines rural? What does 'rural' mean to you?

II.   **Cancer experience**

We know that no two cancer survivors' situations and experiences are the same. Your experience and reactions may be quite different from another survivor at the same stage or with a similar diagnosis. As a rural resident, it could also be quite different from someone living in a city. Please tell us a little bit about your cancer journey.

> Prompts: When were you diagnosed, what treatment did you receive, what is the status of your cancer now

Social Support

Can you tell me about who has been most involved in your cancer care?

> Prompts: who are your sources of support? Family, friends, church, support groups, online forums? How important is faith or religion to you? Can you tell me about how it has influenced your cancer journey?

Healthcare access

Can you tell me about where you received cancer care for your first type of treatment?

> Prompts: How long does it take to get there? How do you normally get there? Challenges?

Finances

How did cancer treatment affect your finances?

How did cancer treatment impact your work?

Treatment adherence and engagement

Can you please tell me about what you had to do for treatment?

> Prompts: How often did you have to go to the doctor for cancer treatment?

Can you please tell me what you had to do for each appointment?

> Prompts: How many appointments do you think would be ok to miss? Did you ever miss an appointment? What might help you to not miss an appointment? What made it harder to attend an appointment? How would you feel if you missed an appointment? Would you do anything to prepare for it? What would you normally bring with you? Would you ever prepare a list of questions beforehand? Take notes during?

Healthcare team: medical distrust, shared decision-making, support services

Can you tell me about your cancer care team?

> Prompts: Who is part of your cancer care team? Who did you talk with the most? Have you ever worked with a social worker or a nurse navigator? Someone with palliative care?

Tell me about how you interact with your cancer care team.

> Prompts: How comfortable are you with the medical team? Do they seem trustworthy? How do you feel about the way the medical team talks with you? How they explain your treatment? When you have needed to make decisions about your cancer care, who normally makes them?

Non-standard of care

How important do you feel medical care is in treating cancer?

> Prompts: Have you heard of clinical trials? How do you feel about them? How do you feel about alternative therapies?

Information

Where do you usually go for information about your cancer and treatment?

> Prompts: e.g. Doctors, more experienced survivors, online? What sources of information do you find most useful? Why?

Can you tell me about how your cancer care team described your cancer and treatment plan?

> Prompts: How well do you think your cancer care team described your cancer and cancer care plan? How do you feel about asking your cancer care team questions?

How do you usually access the internet? How often do you use it?

> Prompts: Do you have a smartphone? How would you feel about getting text messages related to your cancer care? How do you feel about using an online portal to message your cancer care team? To look at your medical information?

III. Closing

We know that it's not always easy for people to share their experiences as cancer survivors, and we're very grateful to you for talking with us. We've come to the end of our questions. Do you have any questions for me?

Thank you for your time.