Journal of Clinical and Translational Science

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Leveraging oncology collaborative networks and biomedical informatics data resources to rapidly recruit and enroll rural residents into oncology quality of life clinical trials

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Research Methods and Technology Research Article

Cite this article: Davis HA, Hoberg AA, Jacobus LS, Nepple K, Seaman AT, Sorensen J, Weiner GJ, and Gilbertson-White S. Leveraging oncology collaborative networks and biomedical informatics data resources to rapidly recruit and enroll rural residents into oncology quality of life clinical trials. *Journal of Clinical and Translational Science* **8**: e135, 1–8. doi: 10.1017/cts.2024.576

Received: 9 March 2024
Revised: 12 June 2024
Accepted: 25 June 2024

Keywords:
Cancer; subject recruitment; rural health; informatics tools; supportive oncology

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Abstract

Purpose: This study assesses the feasibility of biomedical informatics resources for efficient recruitment of rural residents with cancer to a clinical trial of a quality-of-life (QOL) mobile app. These resources have the potential to reduce costly, time-consuming, in-person recruitment methods. *Methods:* A cohort was identified from the electronic health record data repository and cross-referenced with patients who consented to additional research contact. Rural–urban commuting area codes were computed to identify rurality. Potential participants were emailed study details, screening questions, and an e-consent link via REDCap. Consented individuals received baseline questionnaires automatically. A sample minimum of $n = 80$ [$n = 40$ care as usual (CAU) $n = 40$ mobile app intervention] was needed. *Results:* $N = 1298$ potential participants ($n = 365$ CAU; $n = 833$ intervention) were screened for eligibility. For CAU, 68 consented, 67 completed baseline questionnaires, and 54 completed follow-up questionnaires. For intervention, 100 consented, 97 completed baseline questionnaires, and 58 completed follow-up questionnaires. The CAU/intervention reached 82.5%/122.5% of the enrollment target within 2 days. Recruitment and retention rates were 15.3% and 57.5%, respectively. The mean age was 59.5 ± 13.5 years. The sample was 65% women, 20% racial/ethnic minority, and 35% resided in rural areas. *Conclusion:* These results demonstrate that biomedical informatics resources can be highly effective in recruiting for cancer QOL research. Precisely identifying individuals likely to meet inclusion criteria who previously indicated interest in research participation expedited recruitment. Participants completed the consent and baseline questionnaires with zero follow-up contacts from the research team. This low-touch, repeatable process may be highly effective for multisite clinical trials research seeking to include rural residents.

Introduction

Rural residents experience significant barriers in their cancer management including disjointed clinical care, traveling long distances for treatment, and lack of locally available supportive care resources. Compared to non-rural counterparts, these barriers contribute to care inequities and worse outcomes, including higher symptom burden and [1] increased rates of mortality and morbidity [2,3]. These barriers also impact participant recruitment for therapeutic clinical trials and other research, such as quality-of-life (QOL) studies [4]. Consequently, rural residents not only have decreased opportunity to participate in research, but their experiences are underrepresented in the literature [5].

Significant reduction in QOL during cancer treatment has been associated with symptom burden, feelings of isolation and uncertainty, change in role function, and financial toxicity [6,7]. While there is a large body of research describing efficacious QOL interventions [8], the majority of this research consists of individuals living in urban and suburban communities with relatively easy access to clinical research [9]. The specific challenges related to cancer QOL in rural residents are not well established [10]. There is a critical need to increase rural residents' participation in cancer QOL trials [6].

In-person recruitment of participants for cancer QOL studies can be challenging [11]. Cancer centers are often less than optimal settings to recruit participants, as they can have long

days, with multiple appointments, with competing priorities and stressors. Typically, the day starts early with testing, meeting with the oncologist to review test results, and assessment of therapeutic response to treatment, blood collection, and/or treatment. In addition, in-person recruitment is expensive and time consuming. Space is often at a premium, making it challenging to have private conversations about study participation prior to obtaining informed consent. People living in rural areas or at a distance from the cancer center often feel additional stress related to their travel home after appointments [2].

Participant recruitment is consistently identified as the most significant barrier to successful clinical trial research. Inadequate recruitment may result in expensive delays and/or early cessation of trials [12,13]. In fact, the most frequently used strategies (e.g., in-person recruitment, reviewing the electronic medical records for prescreening) are also the most inefficient [11]. Recruiting study participants from underrepresented groups, such as rural residents, often requires multiple sites to achieve adequate sample sizes in a timely manner. Strategies that do not rely solely on in-person recruitment processes and can be replicated at other sites are needed to increase access to and enrollment is cancer QOL trials [14].

Biomedical informatics (henceforth called informatics) resources can be leveraged to address the unique challenges of recruiting rural residents to cancer QOL trials [12]. Informatics resources can be used to create scalable screening, consenting, and data-collection protocols to recruit and enroll participants to cancer QOL trials. Such resources include (1) structured data models to create reproducible cohort definitions [15,16], (2) blanket consent processes to connect researchers to potential participants [17,18], and (3) secure applications to support data capture for research [19,20]. Investigators can then utilize collaborative networks such as Oncology Research Information Exchange Network (ORIEN)[21] and enterprise data warehouses for research (EDW4R)[22] resources to identify and recruit participants in an efficient and standardized manner across multiple sites. Utilization of these resources benefit from expertise such as that provided through Iowa Health Data Resource (IHDR), to leverage informatics and data expertise [23]. The purpose of this study is to evaluate the feasibility of using informatics resources to rapidly recruit rural residents to a pilot clinical trial of a QOL mobile app intervention [24].

Materials and methods

Biomedical informatics resources

Informatics resources and collaborative networks used in this study include: (1) The Iowa Health Data Resource (IHDR), Enterprise Data Warehouse for Research (EDW4R), and TriNetX; (2) Oncology Research Information Exchange Network (ORIEN) and Patients Enhancing Research Collaborations at Holden (PERCH); and (3) Research Electronic Data Capture (REDCap).

IHDR is an ecosystem designed to provide support to health science research at the University of Iowa. It facilitates access to health science data, promotes data literacy, implements transformative datasets for scientific advancements, and provides secure, compliant space to analyze data for the electronic health data (EHR) for research [23]. Part of the IHDR, EDW4R is a centralized repository that collects, curates, transforms, and stores large volumes of data collected from various sources. EDW4R repositories are key infrastructure at Clinical and Translational Science Award (CTSA) hubs [22]. Within this infrastructure are common data models that can be used across institutions and tools to simplify data management and sharing. informatics data analysts in the IHDR use a web-based tool called TriNetX to define research cohorts (i.e., a computable phenotype), conduct retrospective studies, and identify potential participants for clinical trials [15,16]. TriNetx allows researchers to explore de-identified patient data, using EHR standardized code ontologies (e.g., ICD and CPT), from local institutions or research networks in preparation for research.

ORIEN is a collaborative oncology network that supports rapid, multisite recruitment for clinical research [21]. ORIEN aims to accelerate cancer research by providing a platform where researchers across participating centers can share information, resources, and expertise to develop innovative therapies tailored to individual patients. Patients Enhancing Research Collaborations at Holden (PERCH) provides research infrastructure for ORIEN at the University of Iowa. One element of PERCH is a blanket consent in which patients seeking cancer care are approached for participation in observational, longitudinal research. Participation includes surveys, blood samples, and permission to use their cancer tissue and clinical information in research. Additionally, participation in PERCH includes permission to be re-contacted about participation in future studies. The PERCH consent creates an efficient resource to identify and recruit potential participants for both survey research and clinical trials.

REDCap is a secure web platform for building and managing online research databases. REDCap streamlines the process for creating and designing projects using an array of tools tailored to the data collection strategy, including e-consenting [19,20] and automated survey distribution. REDCap is used at more than 6900 institutions in 155 countries.

Procedure

Using the described informatics resources, a "touchless," repeatable process was developed to enroll people with cancer into a pilot QOL clinical trial comparing a mobile app intervention with care as usual (CAU). To minimize contamination of the intervention group, a two-phased quasi-experimental design was used. Phase one consisted of CAU participants; and phase two consisted of intervention participants. Identical procedures were used to identify and screen, invite, consent, and collect data from both groups.

Participant identification and screening

Inclusion criteria that were identifiable through the computable phenotype were: >18 years, diagnosis of cancer specified by ICD code, received cancer treatment within the past 6 months at University of Iowa Hospital and Clinics. The principal investigator worked with an informatics data analyst to operationalize these criteria into a clear, unambiguous cohort definition in TriNetX (Table 1). Additional inclusion criteria were be fluent (speak, read, and write) in English, have access to a SMART phone or tablet, and be experiencing one or more distressing cancer-related symptom. Exclusion criteria were completion of cancer treatment and temporary or permanent cognitive disability that would limit ability to complete questionnaires or other study activities.

Working as a data broker, the data analyst extracted a list of medical record numbers (MRNs) for individuals who met these criteria which was then sent to the PERCH study coordinator. The list of individuals who signed the PERCH consent was filtered to identify a subset of individuals on TriNetX-based MRN list. The resulting list of potential participants was delivered to the research team into a secure research space [23]. Rural–urban commuting

Table 1. Inclusion criteria used to define cohort in TriNetX

Cohort definition	
Age	>= 18
Group1A	
Must have one or more of the following	Must have one or more of the following: C00-C14 Malignant neoplasms of lip, oral cavity, and pharynx C15-C26 Malignant neoplasms of digestive organs C30-C39 Malignant neoplasms of respiratory and intrathoracic organs C40-C41 Malignant neoplasms of bone and articular cartilage C43-C44 Melanoma and other malignant neoplasms of skin C45-C49 Malignant neoplasms of mesothelial and soft tissue C50-C50 Malignant neoplasms of breast (C50) C51-C58 Malignant neoplasms of female genital organs C60-C63 Malignant neoplasms of male genital organs C64-C68 Malignant neoplasms of urinary tract C69-C72 Malignant neoplasms of eye, brain, and other parts of central nervous system C73-C75 Malignant neoplasms of thyroid and other endocrine glands C76-C80 Malignant neoplasms of ill-defined, other secondary and unspecified sites C7A-C7A Malignant neuroendocrine tumors (C7A)
Group 1B	
Any instance of Treatment After occurred within 6 months on or after the first instance of Group 1A	Must have one or more of the following: AN000 Antineoplastics 1001 Radiation 1003 Targeted Therapy 1002 Chemotherapy 1004 Hormone Therapy 1005 Stem Cell Transplant
Data elements returned	sex, race, ethnicity, date of birth, medical record number or patient ID, first name, middle name, last name, address, city, state, county, zip code, telephone, email

area (RUCA) codes were computed for each individual on the list. Individuals living in rural communities, defined as *large rural city/town (micropolitan)* [codes: 4.0, 4.2, 5.0, 5.2, 6.0, 6.1], *small rural town* [codes: 7.0, 7.2, 7.3, 7.4, 8.0, 8.2, 8.3, 8.4, 9.0, 9.1, 9.2], and *isolated small rural town* [codes: 10.0, 10.2, 10.3, 10.4, 10.5, 10.6] were flagged to receive study invitation emails. Individuals from the *urban* RUCA codes were randomly selected from the total list of potential participants for recruitment. This workflow is depicted in step 1 of Fig. 1.

Study invitation, consent, and data collection

The REDCap project for this study was designed so that once the list of potential participants was uploaded, an automated process commenced to invite, consent, collect baseline, and follow-up questionnaires for participants in both the CAU and interventional groups of the research study.

The workflow consisted of: 1) The final list of potential participants identified using PERCH and TriNetX was uploaded into a REDCap project. 2) Potential participants received a study invitation email that briefly described the study purpose, inclusion criteria, participation expectations, a link to the informed e-consent form, and contact information for the research team for questions. 3) Potential participants wanting to learn more about the study clicked the link to review the REDCap e-consent and self-identify that they met the inclusion criteria and consented to participate in the study. 4) Once the consent was complete, REDCap automatically advanced to the baseline questionnaire for participants to complete. 5) Participants in the intervention group were then automatically emailed instructions on how to install and set up the mobile app. Additionally, email and phone call contact occurred for participants requesting assistance with this step. 6) Six weeks after starting the study, all participants received the follow-up questionnaire via a REDCap email. 7) Study compensation was sent by the research team after completing each set of questionnaires. This workflow is depicted in step 2 of Fig. 1.

At any point during the process if potentially participants had questions or concerns they were provided information about how to contact the research team (i.e. study email account and study telephone number). Individuals could pause the process without consequence to get their questions answered. In addition, research team members readily provided technology support to individuals who were encountering challenges with completing the consent or questionnaires via REDCap as well as with the challenges downloading the app and setting up their user profile.

Steps 2–4 and 6 of this process were completely automated through REDCap. The researcher monitored the study email account as well as the REDCap dashboard to identify and respond to questions, errors, and glitches.

Results

A total of $n = 1298$ people from the PERCH database were screened for eligibility ($n = 393$ for CAU, $n = 905$ for intervention). In the CAU group, 365 were invited, 68 consented, 67 completed the baseline survey, and 54 completed the follow-up survey 6-weeks after baseline. In the intervention group, 833 were invited, 100 consented, 97 completed the baseline survey, and 58 completed the follow-up survey 6-weeks after baseline. The recruitment and retention rates were 15.3% and 57.5% for the full sample (18.6 and 55% for CAU; 12.0 and 60% for intervention) (Consort Diagram Fig. 2).

For both phases of recruitment, the target sample was reached within 4 days of sending the invitation email. The CAU group reached 82.5% of the enrollment target ($n = 40$) within two days and reached final N within 50 days. The intervention group reached 122.5% of the enrollment target ($n = 40$) within two days and reached final N within 21 days. Across both groups, participants completed the consent and baseline questionnaires with zero follow-up contact from the research team (Table 2).

The mean age of participants was 59.5 ± 13.5 years (61.5 ± 13.5 for CAU, 57.51 ± 3.5 for intervention). Self-reported gender for both groups was similar with women composing approximately 65% of the sample. Approximately, 20% of the total sample identified as a racial or ethnic minority, with a larger proportion in CAU compared to intervention. Breast, urinary, and digestive care

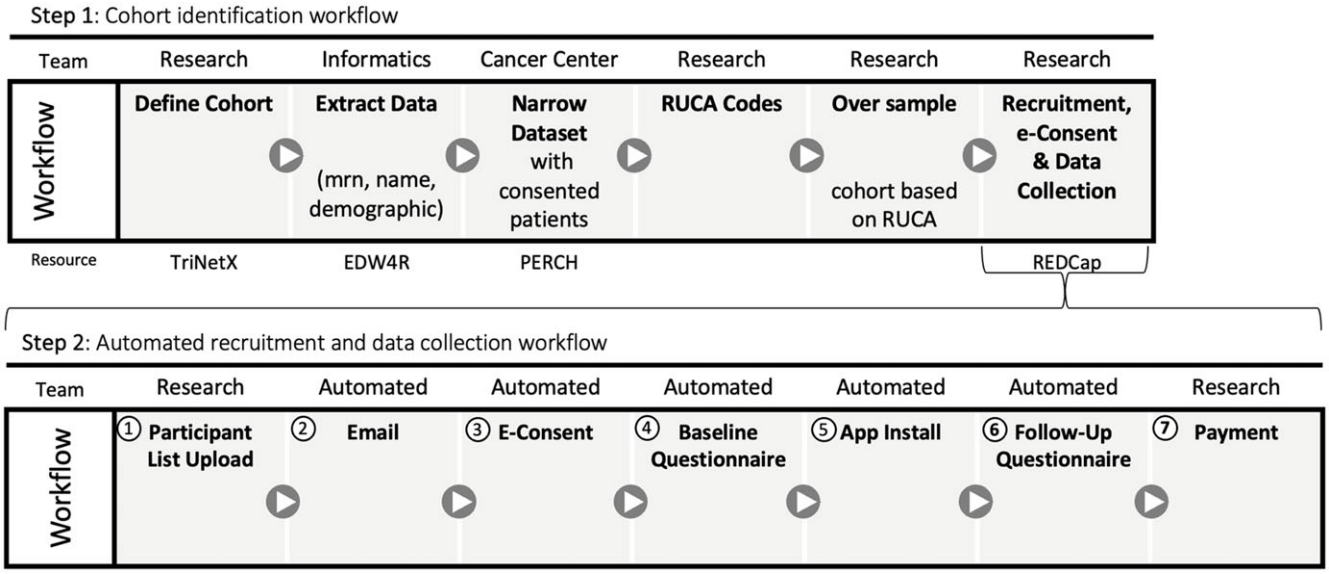

Figure 1. Step 1: The workflow used to identify potential participants for recruitment. Step 2: The workflow to contact, enroll, and collect data from potential participants. Enterprise Data Warehouse for Research (EDW4R); Patients Enhancing Research Collaborations at Holden (PERCH); Rural-Urban Commuting Area (RUCA).

were the most common primary sites in both groups. Regarding cancer stage, CAU had a higher proportion of participants with in situ and regional staging (44.3%), in comparison to intervention which has more people with distant staging (11.3%). Time since diagnosis, CAU had a higher proportion of participants (41.8%) within 12 months of their diagnosis compared to the Intervention group (35.1%). (Table 3). Approximately, 35% of the total sample lived in one of the three rural RUCA codes. A larger proportion of CAU was rural (66.9%) compared to intervention (14.0%) (Table 4).

Discussion

This study demonstrates that informatics resources can be leveraged to recruit rural residents effectively and efficiently into cancer QOL clinical trials [14,25]. The PERCH consent, TriNetX, and EDW4R facilitated our ability to identify and recruit patients who are underrepresented and difficult to access using traditional in-person or mail-based recruitment techniques. TriNetX allowed us to precisely identify individuals likely to meet inclusion criteria. The blanket consent streamlined the process such that we were only approaching people who previously indicated interest in participating in research. By leveraging EDW4R infrastructure and services, including standardized data models that provide the foundation for tools like TriNetX, this process can be replicated across institutions to recruit participants for multisite trials.

Rapid recruitment was observed in both the CAU and intervention groups. The target sample size ($n = 40$ participants per group) was reached in four days for CAU and one day for intervention. These recruitment rates are quite extraordinary given this was a completely "touchless" process. Time from trial activation to first enrollment in cancer clinical trials is associated with overall accrual rates [26]. Specifically, shorter time between activation to first enrollment is significantly associated with the overall accrual rate and successful completion of the trial. While email study invitations, e-consenting, and data collection may not work for all study participants, these results demonstrate that the access gap in reaching rural residents can be partially addressed by leveraging informatics resources. This process relies heavily on the assumption that the email addresses are current and will be received by potential participants. For the group of individuals who did not respond to the email invitation, it is not known if the email was sent to an out-of-date address, automatically sent to a spam folder, not opened, or opened but the person was not interested. For this reason, in-person recruitment may be necessary depending on the nature of the study or target population. However, these results demonstrate that this touchless approach can be used to recruit individuals who have already indicated interest and need minimal support to proceed with the self-screening procedures, the consent form, and self-report questionnaires. In alignment with recommendations in the literature [11], time consuming and expensive human resources should be intentionally used to reach individuals who need a more high-touch approach.

With regard to recruitment and retention rates, CAU and intervention were comparable. A larger total sample was enrolled in the intervention group, anticipating possible attrition associated with the expected weekly use of the mobile app. Such attrition was observed in the intervention group after completing the consent and completing the baseline questionnaire. However, that attrition occurred prior to downloading the app and starting the intervention. There were no differences in the demographic or clinical characteristics between the participants that advanced to using the app ($n = 75$) and the participants that did not ($n = 22$). Reasons for this attrition are not known. Similar retention rates were observed between the 67 participants in CAU group (55%) and 75 participants in intervention group (60%) who advanced to downloading and using the app. While this retention rate is lower than recommended for clinical trials, it is consistent with typical retentions rates of ~50% [27,28]. Notably, these results are comparable to a recently published trial of digital psychotherapy in which the authors explored the impact of various amounts of monetary incentives on retention [29]. Future research is needed to explore how touchless strategies for recruitment and data collection can be combined with other approaches (such as monetary compensation) known to retain participants in cancer clinical trials.

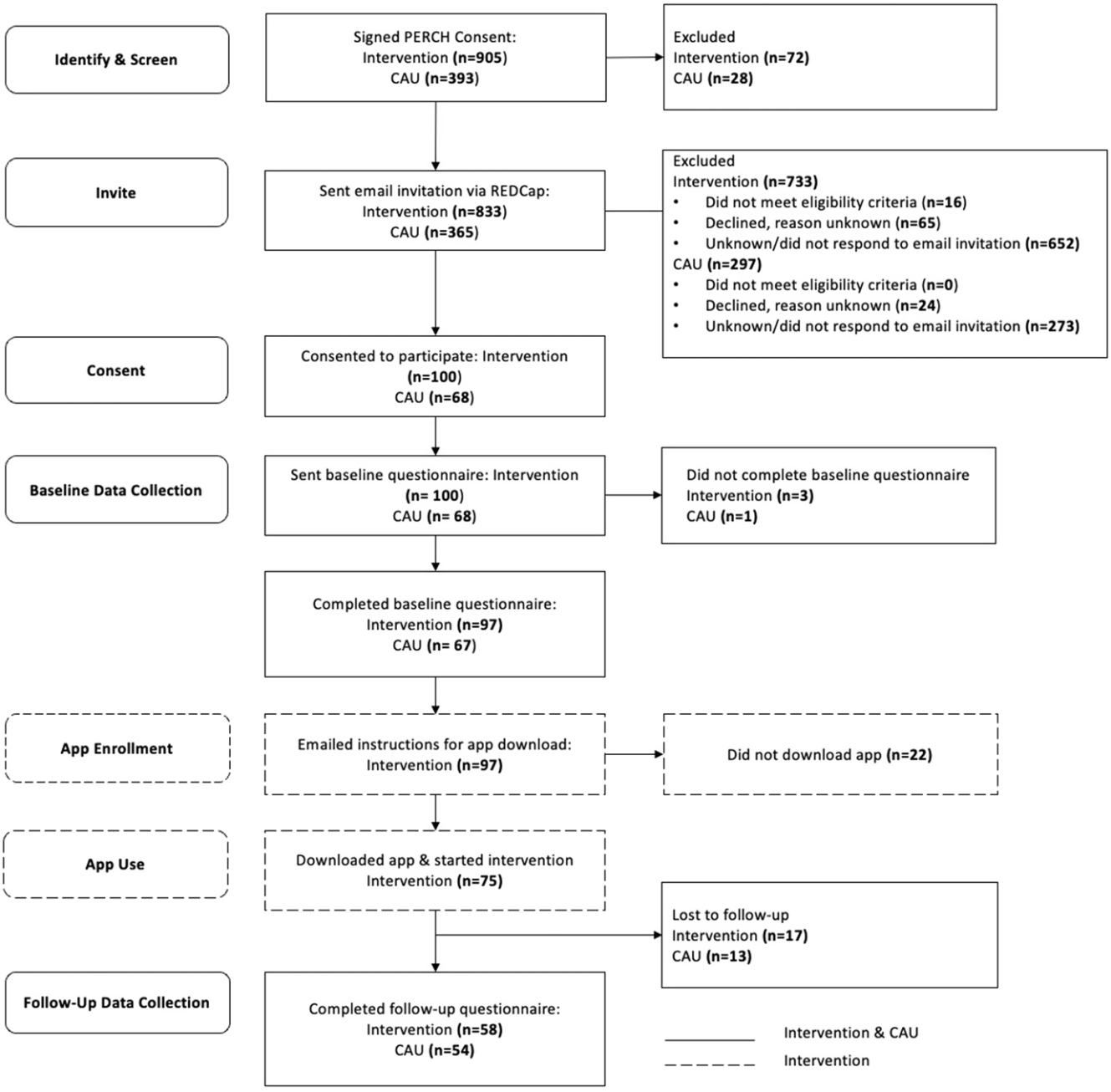

Figure 2. CONSORT Diagram for both Care As Usual (CAU) and Intervention conditions from identification and screening to completion of follow-up questionnaires.

Table 2. Number of days from invitation email to completed self-screening, signing e-consent, and completion of baseline questionnaires

Days from invitation to target sample size		
Sample size	CAU $n = 67$	Intervention $n = 97$
$n = 10$	0 days	0 days
$n = 20$	0 days	0 days
$n = 30$	1 day	1 days
$n = 40$ (target)	4 days	1 day
$n =$ final	50 days	21 days

Care As Usual (CAU).

The demographic and cancer characteristics of the sample are representative of adults in Iowa with cancer. Notably, with regard to rural residents, our participation rate from the three rural RUCA categories was 35.3% of the total sample. We observed minor differences between CAU and intervention for age, racial/ethnic minorities, RUCA codes, cancer stage, and time since diagnosis. Intervention had a higher percentage of participants with a cancer stage of distant and a more recent time since diagnosis. CAU was slightly older, with more participants with minority racial/ethnic identities, and from rural RUCA code. The differences between groups in race/ethnic and RUCA codes can be attributed to the sequential recruitment process. Screening of the PERCH database for potential participants seen within the previous 6 months and

Table 3. Participant characteristics for total sample as well as by condition, Care As Usual (CAU) and Intervention

Sample demographics and cancer characteristics						
	Total $n = 164$		CAU $n = 67$		Intervention $n = 97$	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	59.5	13.5	61.5	13.5	57.5	13.5
	Range	20-87	Range	20-87	Range	25-82
	N	%	N	%	N	%
Gender						
Men	54	32.9%	21	31.3%	33	34.0%
Women	107	65.2%	46	68.7%	61	68.9%
Non-binary	1	0.6%	–	–	1	1.0%
Unknown	2	1.2%	–	–	2	2.0%
Race & Ethnicity						
Hispanic or Latino	8	4.9%	6	9.0%	2	2.0%
American Indian/Alaska Native	1	0.6%	1	1.5%	–	–
Asian	3	1.8%	3	4.4%	–	–
Black or African American	3	1.8%	2	3.0%	1	1.0%
White	132	80.5%	60	89.6%	72	96.0%
More than 1 race	2	1.2%	1	1.5%	1	1.0%
Unknown	2	1.2%	–	–	2	2.0%
Cancer primary site						
Breast	68	41.5%	27	40.3%	41	42.3%
Urinary	17	10.4%	1	1.4%	16	16.5%
Digestive	19	11.6%	6	9.0%	13	13.4%
All others*	50	30.5%	29	43.3%	21	21.6%
More than one	10	6.1%	4	6.0%	6	6.2%
Cancer stage						
In situ	29	17.7%	14	20.9%	15	15.6%
Localized	41	25.0%	19	23.4%	22	22.7%
Regional	15	9.1%	6	9.0%	9	9.3%
Distant	11	6.7%	0	–	11	11.3%
Unstaged	8	4.9%	5	7.5%	3	3.1%
Unknown	60	36.6%	23	34.3%	37	38.1%
Time since diagnosis						
0-6 months	21	12.8%	5	7.5%	16	16.5%
6-12 months	41	25.0%	23	34.3%	18	18.6%
1-2 years	34	20.7%	13	19.4%	21	21.7%
>2 years	68	41.5%	26	38.1%	42	43.3%

**All others* for cancer primary site include: brain, bone, colorectal, female genitourinary, hematopoietic, male genitourinary, respiratory, sarcoma, skin, thyroid, and other not described. These were grouped if the total number for either group was less than 10.

subsequent email invitations for CAU happened in December 2022. All potential participants who were racial/ethnic minorities or living in rural RUCA codes were invited. Of the remaining list of ~2000 potential participants from the PERCH database, a random sample was selected to achieve the total of 393 that would be screened for the study. We repeated this process in March 20023 to recruit for intervention. We anticipated there would be a similar proportion of individuals who were racial/ethnic minorities or living in rural RUCA codes in the pool of potential participants in the PERCH database for second wave of recruiting. For unknown reasons this was not the case. The result was an imbalance between the groups. Despite this imbalance, these results demonstrate patients with cancer at various stages and at any time since diagnosis are interested and willing to participate in cancer QOL

Table 4. Percentage of participants from rural and urban areas based on Rural-Urban Commuting Area (RUCA) codes for total sample as well as by condition, Care As Usual (CAU) and Intervention. *Large rural city/town (micropolitan)* [codes: 4.0, 4.2, 5.0, 5.2, 6.0, 6.1], *small rural town* [codes: 7.0, 7.2, 7.3, 7.4, 8.0, 8.2, 8.3, 8.4, 9.0, 9.1, 9.2], *isolated small rural town* [codes: 10.0, 10.2, 10.3, 10.4, 10.5, 10.6]

Rurality of participants based on RUCA codes						
	Total $n = 164$		CAU $n = 67$		Intervention $n = 97$	
	N	%	N	%	N	%
Isolated Small Rural Town	21	12.8%	19	23.4%	2	2.1%
Small Rural Town	32	19.5%	24	35.8%	8	8.25%
Large Rural City/Town (micropolitan)	5	3.1%	1	1.5%	4	4.12%
Urban	106	64.6%	23	34.3%	83	85.6%

research. Future studies should employ random sampling procedures from the pool of participants once the oversampling for underrepresented individuals has occurred as well as randomization to study arm.

Limitations

There are three key limitations in this study. First, the recruitment strategy relied on email communication to invite potential participants to this study. EHR systems may vary in their clinical practices that ensure the email address is current. Many email clients have automatic filters that block messages deemed spam. In addition, email may not be the preferred means of communication for some potential participants. Future research is needed to adapt this strategy to sending study invitations through a vetted and endorsed system such as EHR patient portals. Second, participants were recruited in two phases, CAU followed by intervention. It is unknown if the recruitment and retention rates would be similar if potential participants were recruited to a trial that included randomization as part of the protocol. Finally, the recruitment strategy used to enroll rural residents and racial/ethnic minorities was successful overall, there was imbalance between the groups. As noted above, future research should use alternate strategies, such as randomization or stratified recruitment, to ensure balance across conditions.

This pilot served as a proof of concept of the feasibility of using informatics resources as a primary approach to identify, consent, and enroll participants in an oncology QOL mobile app trial. Additional strategies are needed with future research to mitigate the potential selection bias of only approaching individuals who have already consented to being approached about clinical trials. These strategies include 1) approaching individuals who are potentially eligible based on a computable phenotype created with tools such as TriNetX and not limiting recruitment to patient registries such as PERCH; 2) recruitment messaging to potential participants through EHR patient portals which may reduce the frequency of messages ending up going to out-of-date email accounts or being filtered into spam folders; and 3) engage stakeholders at oncology community-based clinics who serve small town and rural residents to serve as champions and liaisons who will endorse and recommend research opportunities. In addition, the extent of a technology gap between rural and nonrural residents with regard to using email, EHR patient portals, and mobile apps is rapidly changing [30]. Future research is needed to determine how rural and nonrural patients differ in their use of these technologies in the context of healthcare and research as well as how other social determinants of health may compound or exacerbate inequities (e.g. poverty).

Conclusions

Informatics resources were instrumental in identifying and inviting individuals likely to meet inclusion criteria into a cancer QOL trial. Leveraging blanket consents for future research expedited recruitment. Using secure, automated tools such as REDCap to allow self-screening, obtaining consent, and completion questionnaires rapidly advanced potential participants from identification to enrollment. This low-touch, repeatable process can be utilized in multisite clinical trials with focusing on underrepresented populations, such as rural residents [5]. While the focus of this study was on the rural underserved, urban underserved communities also experience access to cancer care challenges [31]. The approach described here can be used to identify and recruit a wide range of populations.

Author contributions. H.A.D., A.T.S., and S.G.W. conceptualized the research question and methodologic approach. G.J.W., L.S.J., and K.N. developed and oversee the PERCH consent registry. H.A.D., A.A.H., and L.S.J. developed and implemented methodology used in this study. J.S., A.A.H., and L.S.J. oversaw the recruiting, consenting, and data collection for this study. H.A.D. and S.G.W. wrote the manuscript with contributions from A.A.H., L.S.J., K.N., A.T.S., J.S., and G.J.W. All authors reviewed and proved the final manuscript.

Funding statement. Research was supported by Betty Irene Moore Fellowship for Nurse Leaders and Innovators; College of Nursing, University of Iowa, Center for Advancing Multimorbidity Science (CAMS) NINR (National Institute for Nursing Research) P20 1P20NR018081; Holden Comprehensive Cancer Center, University of Iowa, National Cancer Institute (NCI) P30 P30CA086862; Iowa Health Data Resource (IHDR), University of Iowa https://strategicplan.uiowa.edu/public-private-partnership-p3/p3-program-support-strategic-priorities/p3-proposals-funded-fy-2022; and Institute for Clinical and Translational Science, CTSA University of Iowa UL1TR002537.

Competing interests. G.J.W. is chairman of the ORIEN Steering Committee. G.J.W. and ORIEN were not involved in developing the research question, determining the research methodology, or conducting the analyses. ORIEN did not provide financial support for this study.

H.A.D., A.A.H., L.S.J., K.N., A.T.S., J.S., and S.G.W. have no competing interests.

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