

Recruitment to Cancer Clinical Trials: Challenges and Strategies

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Disclosure for Participants

Criteria for Successful Completion:

- ✓ Attendance at 80% of the session and submission of an evaluation form
- No one with the ability to control content of this activity has a relevant financial relationship to disclose with an ineligible company
- National Cancer Institute is approved as a provider of nursing continuing professional development by the Ohio Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation. (OBN-001-091). The approved provider unit activity number is 2022005

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Introduction

- Validity of clinical research studies are dependent on:
 - Recruitment of adequate numbers of a required participant population
 - Retaining participants
 - Ensuring the protocol is followed
- Inefficient recruitment may have scientific, economic, and ethical consequences

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Impact of Poor Accrual

- Hinders the progress of research
- Demonstrates poor stewardship of our most valuable resource, study participants
- Leads to early closure which exposes participants to risk for potentially no benefit
- Lack of dissemination
- Financial impact of maintaining open trials that are not enrolling

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The Issue

- 86% of all clinical trials fail to finish on time
 - 60% of clinical trials are delayed or terminated due to lack of enrollment
 - 19% of clinical trials terminate early
 - 20% delayed 6 months or longer
- Hard to reach populations
- Traditional methods of recruitment are costly with low participation rates

Huang et al, 2018

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Recruitment in Cancer Clinical Trials (CTTs)

- Estimated 20% of adult cancer patients are eligible for a clinical trial
- 15-25% of eligible patients participate in a clinical trial
- Only 2-8% of cancer patients in U.S. participate in a cancer clinical trial
- 25% of CCTs fail to enroll enough patients
- 18% closed with less than 50% of the targeted sample size
- 40% of CCTs sponsored by NCI never reach completion and publication
- Participation decreases with age
- Ethnic and minority groups are underrepresented

Morain & Largent, 2019; Cartmell et al, 2020; Unger et al, 2021

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Barriers to Participation

- Clinician
- System
- Patient



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Clinician Centered Barriers

- Impact on doctor-patient relationship
 - Losing trust
- Concern for patients
- Patients will be unable to comply
- Lack of interest in the specific research question
- Fear of not being kept informed about patient's care

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System Barriers

- Institutional
 - NIH IRP – research only
- Protocol Issues
 - Eligibility
 - Procedures
- Expense
- Competition
- Sponsor-centered
 - Adequate funding
 - Site selection
 - Investigator selection

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General Population Barriers

- Lack of Awareness
- Mistrust
- Misperceptions
- Portrayal as guinea pig
- Comfort level with physician
- Demands of the study
- Preference for a particular treatment
- Health literacy
- Concerns about side effects
- Loss of privacy
- Geographical limitations
- Financial

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Barriers to Recruiting Underserved/Underrepresented...

- Lack of awareness of clinical trials
- Lack of awareness of benefits to participation
- Distrust of doctors
- Different values or beliefs
- Lack of cultural sensitivity
- Language or literacy barriers

Underserved/underrepresented: older adults, racial/ethnic minorities, sexual/gender minorities, adolescents and young adults, patients with well-managed comorbidities

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... Barriers to Recruiting Underserved/Underrepresented

- Employment obligations
- Comorbid conditions
- Presentation at late stage of disease
- Limited transportation
- Sense that participants don't get anything from participation
- Lack of minority Principal Investigators

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Black Americans & CCTs

- Constitute 12-13% of the general population
- Under-represented in cancer clinical trials
- FDA cancer drug approval between 2014-2018 average enrollment was 7%

Clinical Trials	Patients	Health System
Trial Design	Access to care	Racism
Eligibility criteria	System or provider distrust	Lack of incentives to participating hospitals
Participating centers	Availability awareness	Lack of laws to enforce equal representation
Lengthy enrollment and follow-up requirements	Lack of clinical trials education	

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Awidi & Al Hadidi, 2021 13

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Older Adults (≥ age 70) & CCTs

- 42% of overall cancer population
- FDA registered trials average enrollment is 24%

Provider	Patient	System	Caregiver
Concern for toxicity	Knowledge	Eligibility criteria	Preferences
Concern for patient age	Transportation	Consent form language	Burden
Time/burden	Time/burden	Trial availability	
Preference for another treatment	Concerns about efficacy and toxicity		
	Finances		

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Sedrak et al, 2020 14

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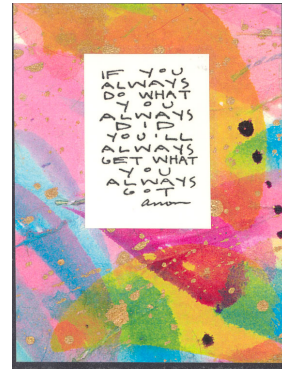
Good News!

- 94-96% participants said that they would participate in a clinical trial again

<https://www.cisr.org/wp-content/uploads/2020/01/The-majority-of-volunteers-would-participate-in-a-clinical-trial-study-again.png>

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STRATEGIES

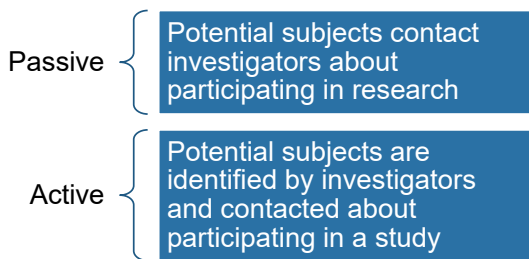


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Recruitment Strategies



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Stating the Obvious

- Identify and remove barriers
 - Assess barriers to clinical trial participation
 - Identify actions to remove barriers
 - Prioritize actions
- Introduce clinical research/clinical trials earlier within the patient experience

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Recruitment Plan...

- Outlined in the protocol and approved by the IRB
- Occurs during protocol development process and throughout active accrual
- How will potential participants be initially identified for this study? Who will identify them?
- How and when will potential participants be approached/contacted about study participation?
- Who will conduct these activities and where will they occur?
 - Activities that can be done w/o consent

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...Recruitment Plan...

- If recruitment plan involves contacting an individual multiple times to secure their initial enrollment in the study, describe how frequently and in what manner individuals will be contacted.
- Identify all recruitment methods that will be used.
 - If recruitment plan involves using any email, address and/or telephone lists, how will those lists be obtained?
- Describe any provisions to protect the privacy and/or confidentiality of potential participants.

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...Recruitment Plan

- Will screening procedures be used? If so, who will conduct the screening procedures?
- Will there be collection of any information/data from potential participants during the recruitment and/or screening process?
 - How will it be collected (i.e., what procedures will be used)?
 - Identify all data points that will be collected prior to their enrollment in the study.

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Recruitment Strategies

- Describe how participants will be identified, note efforts to include under-represented minorities.
- [Include for all trials posted on clinicaltrials.gov] This study will be posted on NIH websites [add for treatment trials] and on NIH social media forums.
- Add any other ways you will advertise the study as well as how potential subjects might be selected to be contacted or referred to you. These can include referrals from physicians, drawing from populations in NIH Clinics, etc. Recruitment advertisements and letters must be submitted to the IRB

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Patient Recruitment Services

The NIH Clinical Center Office of Patient Recruitment Services

<http://intranet.cc.nih.gov/recruit/index.html>

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ResearchMatch

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How ResearchMatch works



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Leveraging Technology

- Use of EMR/EHR to trigger an alert if a patient is likely eligible for an ongoing clinical trial
- Clinical trial management software

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Protocol

- What makes this protocol exciting/important?
- What type of competition is out there?
- Why would a patient enroll in this study?
- Why would a patient not want to enroll in this study?
- Why would a physician be reluctant to refer a patient to this study?

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Study Population

- Know your catchment area
 - Demographics
 - Cancer risk factors
 - Cancer rates
- Study population should be appropriate for the research question being asked
- Involve members of the study population in planning efforts when possible

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Broadening Eligibility Criteria...

- 2016: American Society of Clinical Oncology (ASCO) and Friends of Cancer Research began a joint project to evaluate current eligibility criteria and determine how to broaden the criteria
- FDA published guidances:
 - Brain Metastases
 - HIV/AIDS
 - Organ Dysfunction and Prior and Concurrent Malignancies
 - Minimum Age for Enrollment

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... Broadening Eligibility Criteria

- February 2021 additional recommendations published to broaden criteria related to:
 - Washout periods and concomitant meds
 - Performance status
 - Laboratory test intervals and reference ranges
 - Prior therapies

UPCOMING JOURNAL CLUB
 March 16th 1PM -2PM
*Continuing to Broaden Eligibility Criteria to Make Clinical Trials
 More Representative and Inclusive: ASCO-Friends of Cancer
 Research Joint Research Statement*

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Underserved/Underrepresented...

- Enhance credibility of study by using a community spokesperson/lay outreach workers
 - Getting the word out (e.g., Community events; Health Fairs; Workshops)
- Invest in community education and outreach programs
 - Speak the language of the community
 - Provide culture and language-appropriate informational materials

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...Underserved/Underrepresented

- Reach out to key decision makers in targeted groups
- Leverage satellite sites to conduct clinical trials
- Involve minority researchers/physicians
- Staff/researcher education
 - Recruitment and retention of minority populations
 - Cultural awareness/sensitivity
 - Bias

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Navigator...

- Member of the healthcare team who helps patients “navigate” the healthcare systems
 - Help patients understand the healthcare system
 - Connect patients with resources
 - Enhance patient-clinician communication
- Identify barriers and facilitate strategies to eliminate the barriers on an individual basis
- Increase patient clinical trial access, awareness, and knowledge as well as appropriately match trials for patients

Nipp et al, 2019; Cartmell et al, 2020

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...Navigator

- Provide input on study design and recruitment for underserved/underrepresented populations
- Include a culturally competent navigator as a member of the clinical trial team to promote patient participation
- Patient navigators
 - Nurse navigators
 - Lay navigators

Nipp et al, 2019 ; Cartmell et al, 2020

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Promising Research With Social Media as a Recruitment Tool

- HIV vaccine clinical trials (2009 – YouTube, Wikipedia, Facebook, Craigslist)
- Occipital nerve studies (2013)
- Pediatric cancer (2015 - Facebook)
- Depression prevention (2013)
- Smoking cessation (2013 – Google AdWords, WebMD.com, Facebook, Twitter; 2014 - Facebook)
- Hard to reach populations:
 - Young cancer survivors (2014 – online newspapers, Craigslist, university website, email to advocacy groups, Facebook, Twitter)
 - Gay Latino males (2014 – Facebook, Craigslist, smartphone apps [Grindr, SCRUFF, Jack'd])
 - Deaf community(2013 – project website)

Gelinas, 2018

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Social Media

- | Advantages | Disadvantages |
|-------------------------------|--|
| ▪ Wider audience | ▪ Information chaos! |
| ▪ Low cost (?) | ▪ Misinformation abounds |
| ▪ Instantaneous communication | ▪ Communication “too easy”–just a click |
| ▪ Easy updating | ▪ Lack of patient/physician boundaries |
| ▪ Interactive | ▪ “Private” information becomes “public” |
| ▪ Self-education | ▪ Self-selection bias |

Topolovec-Vranic et al, 2016

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But.....

- Lack of regulatory guidance
 - Informed consent process begins with recruitment
 - IRB review of recruitment materials
 - PI should be able to recruit the required number of participants in a specified timeframe
- Few resources

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Ethical Principles Applied to Participant Recruitment

- | | |
|----------------------------|---|
| Respect for Persons | <ul style="list-style-type: none"> • Accurate information to assure the potential participant can make an informed, and voluntary decision to enroll and withdraw, without coercion or inappropriate inducement • Accurate and full disclosure of anticipated benefits (if any) and a disclosure of the possible risks of the study |
| Beneficence | <ul style="list-style-type: none"> • Recruitment process should ultimately describe all the steps to maximize the study's benefit (if any) and minimize or avoid undue risk(s). |
| Justice | <ul style="list-style-type: none"> • Study should be seen by the participant as <u>fair</u> in that it's open to all those in the cohort who could possibly benefit from the study. • The risks and benefits are interpreted by the participant as equitably distributed. |

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Things to Consider When Using Social Media...

- Online recruitment materials should follow the same guidelines applicable to traditional recruitment methods
- Recruitment materials must be reviewed and approved by the IRB
 - Investigator contact information, information about the purpose of the study, any eligibility criteria, benefits to the subject, and time commitment required for participation in the study
 - No promise free medical treatment, imply unanticipated benefits, or emphasize payment

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...Things to Consider When Using Social Media...

- Potential participants interested in the study should be directed to contact the study team via non-public means
- Research teams need to:
 - be familiar with the terms and conditions of any sites used for recruitment to ensure potential participants are not asked to violate a service agreement
 - consider informing participants that they should be aware of the terms and conditions of the website to understand what, if any, data may be used/maintained by the website itself
 - consider how the target population uses social media

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...Things to Consider When Using Social Media

- Inform participants of third-party risk of interception when transmitting data and data back-up processes
 - *"Your confidentiality will be kept to the degree permitted by the technology being used. No guarantees can be made regarding the interception of data sent via the Internet by any third parties."*
 - *"Data may exist on backups or server logs beyond the time frame of this research project."*

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Social Media Resource

- Harvard Catalyst Regulatory Foundations, Ethics, & Law Program. *The Use of Social Media in Recruitment to Research: A Guide for Investigators and IRBs.*
 - Investigator checklist
 - IRB checklist
 - https://catalyst.harvard.edu/pdf/regulatory/Social_Media_Guidance.pdf

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Precautions with SM and CTs at NIH

- NIH IRP [Guidance Regarding Social Media Tools](#)
- Lists questions to be considered by investigators

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Apps

- Examples:
 - University specific (e.g., Univ of Kansas CC)
 - Pharma (e.g., Roche's Clinical Trial Match)
 - Clinical Trials App
 - Journal Club: Medicine
 - CUREiTT
 - FDA's MyStudies (open source)
- Risk of therapeutic misbranding
- Needs IRB approval
- Similar considerations as with social media
- "Pay to play"

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Retention Strategies

- Ongoing informed consent
 - Effective communication with the research participant
 - Thank you cards
 - Share study results
 - Discuss the need for ongoing contact information to ensure accurate phone numbers, address and emergency contacts.
- Engaging the participant's family/significant other and established/referring providers
- Lost to follow up

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Summary

- Advances in cancer treatment require efficient clinical trial processes especially focused on recruitment
- Recruitment can impact the ability to answer research questions
- Assess local/regional barriers to recruitment and identify strategies to overcome these barriers
- Plan up front for recruitment!!

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QUESTIONS



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