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A large, high-resolution image of the Earth as seen from space, showing the curvature of the planet and the blue oceans. The image is centered in the background of the slide.

# Challenges in clinical trials participation

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# The problem

Estimated number of new cases from 2022 to 2045, Females, age [65-85+]



Breast  
World

2022



**790k**

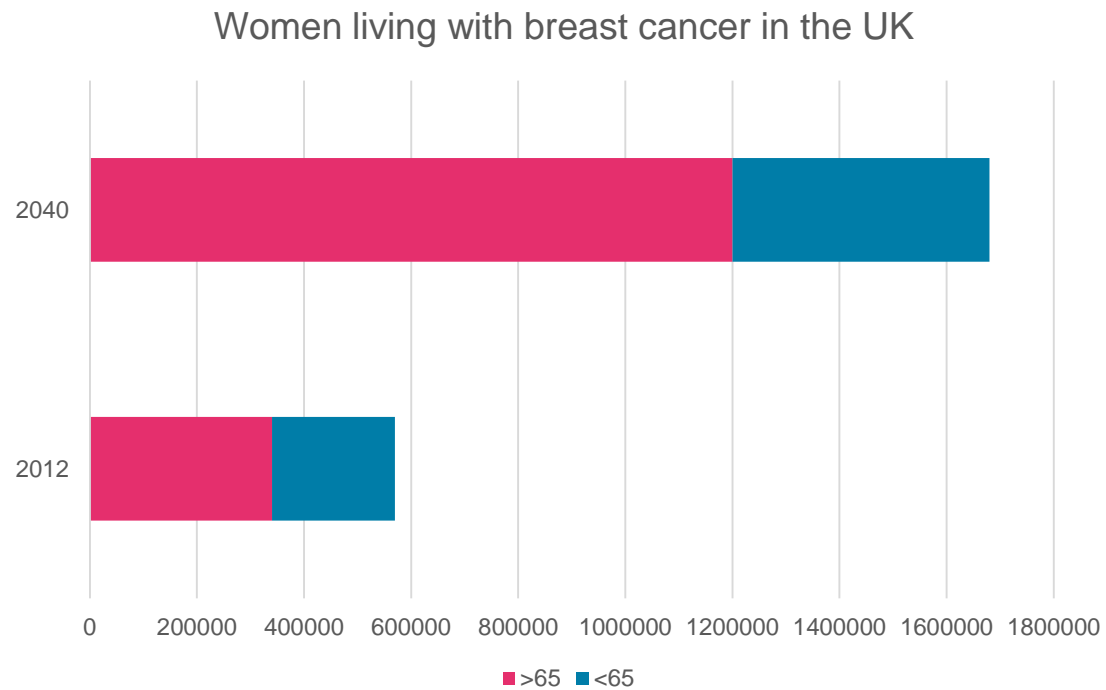
2045



**1.46M**



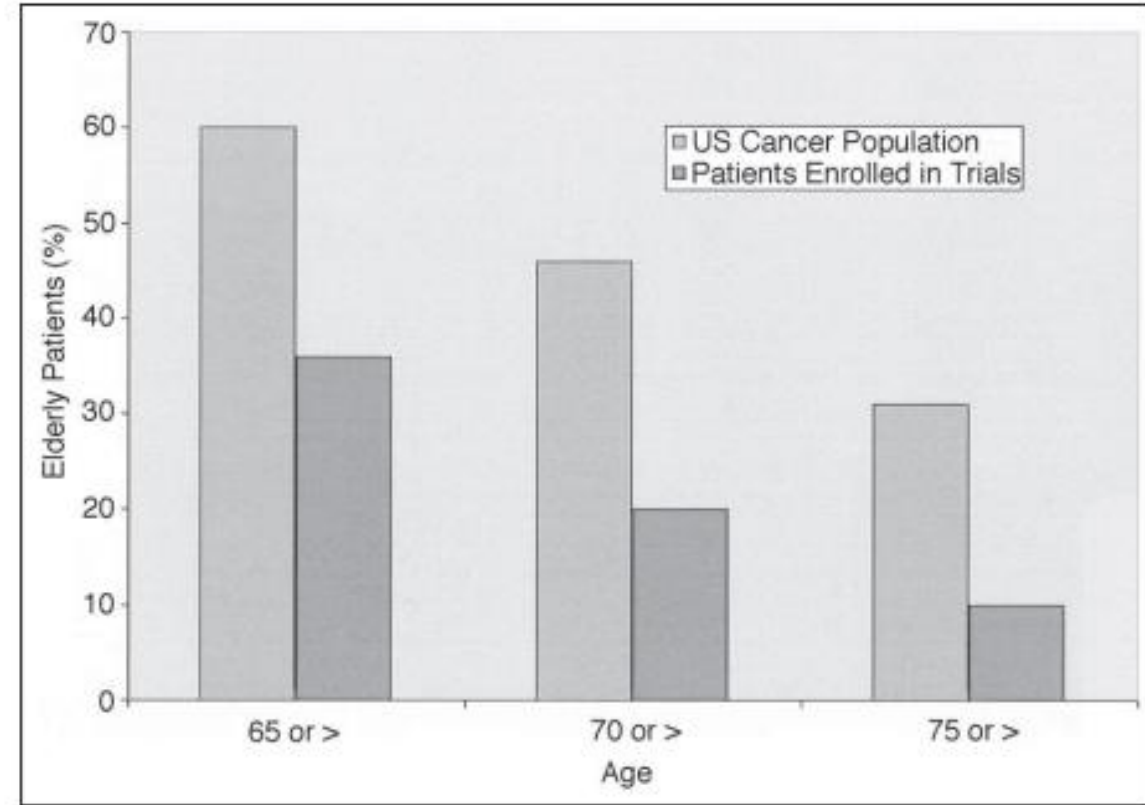
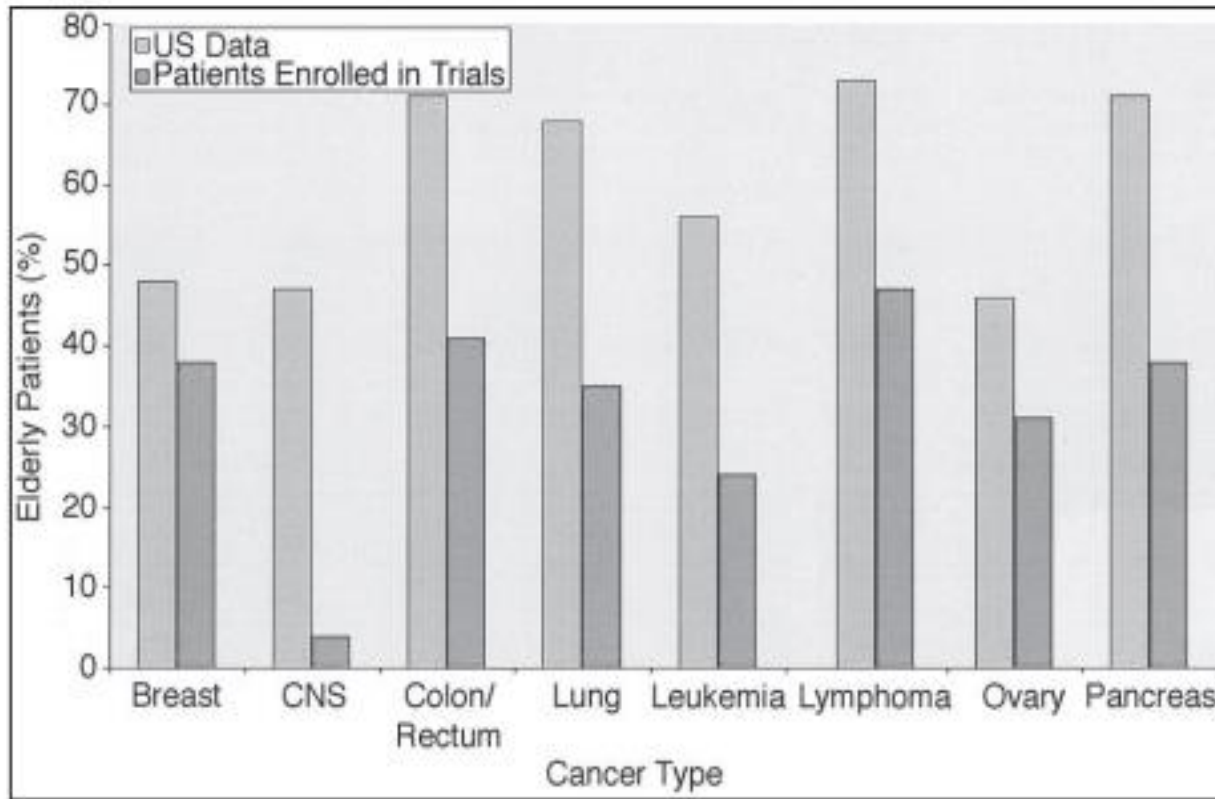
# The problem



*Maddams J, Utley M, Møller H. Projections of cancer prevalence in the United Kingdom, 2010-2040. Br J Cancer 2012; 107: 1195-1202.*



# The problem



*Talarico L, Chen G, Pazdur R. Enrollment of elderly patients in clinical trials for cancer drug registrations: a 7-year experience by the US Food and Drug Administration, 2004, J Clin Oncol, 22 (22): 4626 – 31.*



# The problem

## CA: A Cancer Journal for Clinicians

The flagship journal of the American Cancer Society

Review Article | Free Access

### Older adult participation in cancer clinical trials: A systematic review of barriers and interventions

Mina S. Sedrak MD, MS , Rachel A. Freedman MD, MPH, Harvey J. Cohen MD, Hyman B. Muss MD, Aminah Jatoi MD, Heidi D. Klepin MD, Tanya M. Wildes MD ... [See all authors](#)

First published: 01 October 2020 | <https://doi.org/10.3322/caac.21638> | Citations: 204



Journal of Geriatric Oncology

Volume 13, Issue 1, January 2022, Pages 20-26



### Disparities in older adult accrual to cancer trials: Analysis from the alliance for clinical trials in oncology (A151736)

Noam A. VanderWalde <sup>a</sup> , Travis Dockter <sup>b</sup>, Daniel V. Wakefield <sup>a</sup>, Daniel Satele <sup>b</sup>, Jeff Sloan <sup>b</sup>, Reshma Jaggi <sup>c</sup>, Stuart M. Lichtman <sup>d</sup>, Rachel A. Freedman <sup>e</sup>, Jacqueline M. Lafky <sup>b</sup>, Hyman Muss <sup>f</sup>, Harvey Jay Cohen <sup>g</sup>, Jennifer Le-Rademacher <sup>b</sup>, Aminah Jatoi <sup>h</sup>

Oncol Ther (2021) 9:55–67  
<https://doi.org/10.1007/s40487-021-00140-w>

REVIEW

### Current Challenges Faced by Cancer Clinical Trials in Addressing the Problem of Under-Representation of Older Adults: A Narrative Review

Ruth M. Parks · Holly M. Holmes · Kwok-Leung Cheung



# Challenges

- Older adults do want to be involved in clinical trials
- Do not actively seek out trials
- Lack of evidence as to why

*Van der Cammen and Crome, Eur Geriatr Med, 2018, 9 (4): 413 – 414.*

*Yuval R, Uziel K, Gordon N, Merdler A, Khader N, Karkabi B, et al. Eur J Heart Fail. 2001;3(2): 217–23*



# Challenges

1) Protocol factors



2) Patient factors



3) Sponsor factors







# 1) Protocol factors - challenges

- Recruitment
- Study design





# 1) Protocol factors - challenges

- Recruitment
  - Time
  - Support
  - Pre-existing bias / preferences
  
- Study design
  - Design
  - Modified endpoints



# 1) Protocol factors - solutions

- Recruitment
  - Resource allocation
  - PPI involvement
  
- Study design
  - Trials that are specially designed to enroll older adults
  - Trials that include a cohort of older patients
  - Pragmatic design elements to facilitate enrollment
  - Modification of end points

## Trial Design Considerations to Increase Older Adult Accrual to National Cancer Institute Clinical Trials

FREE

Jennifer Le-Rademacher, PhD ✉, Supriya Mohile, MD, Joseph Unger, PhD, Matthew F Hudson, PhD, MPH, Jared Foster, PhD, Stuart Lichtman, MD, Jane Perlmutter, PhD, MBA, Efrat Dotan, MD, Martine Extermann, MD, Kevin Dodd, PhD ...  
[Show more](#)

*JNCI Monographs*, Volume 2022, Issue 60, December 2022, Pages 135–141,  
<https://doi.org/10.1093/jncimonographs/lgac023>

**Published:** 15 December 2022    **Article history** ▼



Design	Description/Characteristics
Pragmatic Trial	Intervention typically performed in the context of standard care Patients recruited from a variety of practice settings, using broader, more inclusive eligibility criteria
Randomized Controlled Trial	Subjects are randomly assigned to treatment arms To generate data on the older patient population: -Accrue only older adults, -Stratify enrollment into age groups Adaptive design: modifications are made as the study proceeds based on interim data analysis
Prospective Cohort Study	Assessment of treatments already approved by the FDA Cohort defined by host, tumor, or treatment factors Observational Hypothesis-driven
Extended Trial	Addition of a cohort of older patients to the superior treatment arm
Embedded Study (Correlative or Ancillary Study)	Includes additional measures of interest in the infrastructure of a parent study
N-of-1 (Single-Subject Trial)	Determines the optimal therapy for a single individual



## 2) Patient factors - challenges

- Motivation
- Maintenance of quality of life
- Impact of comorbidity
- Positive relationship between study staff and participants
- Physical obstacles
- Cognitive impairment



## 2) Patient factors - solutions

- Develop targeted interventions
- Capture relevant endpoints
- Integration of GA as routine in cancer clinical trials
- Standard protocols for cognitive impairment
- Functional or biological age considered rather than hard cut-offs
- PPI

[J Clin Med](#). 2020 May; 9(5): 1571.

PMCID: PMC7291007

Published online 2020 May 22. doi: [10.3390/jcm9051571](https://doi.org/10.3390/jcm9051571)

PMID: [32455877](https://pubmed.ncbi.nlm.nih.gov/32455877/)

### Strategies to Improve Participation of Older Adults in Cancer Research

[Jennifer Liu](#),<sup>1,†</sup> [Eutiquio Gutierrez](#),<sup>2,†</sup> [Abhay Tiwari](#),<sup>1</sup> [Simran Padam](#),<sup>1</sup> [Daneng Li](#),<sup>1</sup> [William Dale](#),<sup>3</sup> [Sumanta K. Pal](#),<sup>1</sup> [Daphne Stewart](#),<sup>1</sup> [Shanmugga Subbiah](#),<sup>1</sup> [Linda D. Bosserman](#),<sup>1</sup> [Cary Presant](#),<sup>1</sup> [Tanyanika Phillips](#),<sup>1</sup> [Kelly Yap](#),<sup>1</sup> [Addie Hill](#),<sup>1</sup> [Geetika Bhatt](#),<sup>1</sup> [Christina Yeon](#),<sup>1</sup> [Mary Cianfrocca](#),<sup>1</sup> [Yuan Yuan](#),<sup>1</sup> [Joanne Mortimer](#),<sup>1</sup> and [Mina S. Sedrak](#)<sup>1,\*</sup>



## 2) Patient factors - solutions

- Patients with cognitive impairment do want to participate
- They remain excluded
- Vital role of the care giver

Original Article

### Eligibility criteria in NIH-funded clinical trials: Can adults with intellectual disability get in?

[Katherine E. McDonald PhD](#)<sup>a1</sup>  , [Ariel E. Schwartz PhD](#)<sup>b1</sup> ,  
[Maya Sabatello PhD](#)<sup>c</sup> 

[Res Gerontol Nurs. 2022 Mar-Apr; 15\(2\): 76–84.](#)

Published online 2022 Feb 11. doi: [10.3928/19404921-20220131-01](#)

PMID: [351](#)

### Next on diversity: inclusion of participants with cognitive impairment in clinical trials

Clinical Trials Arena dives into a frequently forgotten aspect of clinical trial diversity: participation of people with cognitive disabilities.

Urtē Fultinavičiūtė | December 8, 2022

### Willingness to Participate in Clinical Research among Individuals with Cognitive Impairment

[Mengchi Li](#),<sup>1</sup> [Hyejin Kim](#),<sup>2</sup> [Susan M. Sereika](#),<sup>3</sup> [Trevor J. Nissley](#),<sup>4</sup> and [Jennifer Hagerty Lingler](#)<sup>3</sup>



### 3) Sponsor factors - challenges

- Under rep of older adults in trials by regulatory bodies
- Inappropriate age limits and exclusion of frail patients
- No penalty if older adults not included
- Variation by physical site
- Healthcare professional bias / concerns





## 3) Sponsor factors – challenges

> [J Clin Oncol. 2003 Jun 15;21\(12\):2268-75. doi: 10.1200/JCO.2003.09.124.](#)

### **Barriers to clinical trial participation by older women with breast cancer**

M Margaret Kemeny <sup>1</sup>, Bercedis L Peterson, Alice B Kornblith, Hyman B Muss, Judith Wheeler, Ellis Levine, Nancy Bartlett, Gini Fleming, Harvey J Cohen

> [J Geriatr Oncol. 2020 Mar;11\(2\):327-334. doi: 10.1016/j.jgo.2019.07.017. Epub 2019 Jul 31.](#)

### **Barriers to clinical trial enrollment of older adults with cancer: A qualitative study of the perceptions of community and academic oncologists**

Mina S Sedrak <sup>1</sup>, Supriya G Mohile <sup>2</sup>, Virginia Sun <sup>3</sup>, Can-Lan Sun <sup>4</sup>, Bihong T Chen <sup>5</sup>, Daneng Li <sup>6</sup>, Andrew R Wong <sup>6</sup>, Kevin George <sup>6</sup>, Simran Padam <sup>6</sup>, Jennifer Liu <sup>6</sup>, Vani Katheria <sup>6</sup>, William Dale <sup>4</sup>

Affiliations + expand

PMID: 31375399 PMCID: PMC6989372 DOI: 10.1016/j.jgo.2019.07.017



### 3) Sponsor factors - solutions

- Ban on upper age limit
- Penalty for not providing info on number of older adults recruited
- Pressure on sponsors to raise awareness of these issues
- Training for HCPs



# 3) Sponsor factors - solutions

SCIENCEINSIDER | HEALTH

## FDA pushes cancer trials to include more elderly people

New guidance aims to improve understanding of drug safety, effectiveness in older adults

3 MAR 2022 • 1:10 PM ET • BY [JENNIFER COUZIN-FRANKEL](#)



*J Natl Cancer Inst Monogr* (2022) 2022(60): lgac025

<https://doi.org/10.1093/jncimonographs/lgac025>  
Monograph

GUIDANCE DOCUMENT

## Inclusion of Older Adults in Clinical Trials

*Guidance for Industry*

MARCH 2022

[Download the Final Guidance Document](#)

[Read the Federal Register Notice](#)

MONOGRAPH

## Infrastructure to Support Accrual of Older Adults to National Cancer Institute Clinical Trials

Gretchen Kimmick, MD, MS <sup>1,\*</sup> Mina S. Sedrak, MD, MS <sup>2</sup>



# 3) Sponsor factors - solutions

## CANCER IN OLDER ADULT COMMITTEE CHECKLIST FOR STUDY CONCEPT REVIEW

Reviewed by \_\_\_\_\_

Date: \_\_\_\_\_

1. Is this concept applicable to older patients with cancer ( $\geq 65$  years of age)?

- Yes, proceed to next question.
- No, your review is complete and the rest of the form does not need to be completed.

Additional comments for consideration:  
\_\_\_\_\_  
\_\_\_\_\_

2. Is there an upper age limit on this concept (and/or is Inclusion Across the Lifespan addressed in this concept)?

- No.
- Yes, the upper age limit is appropriate for this concept and rationale for the age cut-off is provided.
- Yes, the upper age limit is appropriate for this concept; however, a rationale for the age cut-off is not provided and needs to be included.
- Yes, the upper age limit is NOT appropriate for this concept. Please explain your concerns and provide recommendations: \_\_\_\_\_

Note: If possible/relevant, please provide a reference(s) to support your recommendation:  
\_\_\_\_\_  
\_\_\_\_\_

3. Are inclusion criteria appropriate and as broad as possible with respect to enrolling older patients?

- Yes, no changes recommended.
- No, explain your concerns and provide recommendation: \_\_\_\_\_

4. Are endpoints relevant to older adults with cancer (such as the impact of treatment on quality of life)?

- Yes, skip the next question.
- No, but this is not relevant to this concept.
- No, please consider the following endpoints relevant to older adults with cancer (cite references): \_\_\_\_\_

Comments and recommendations:  
\_\_\_\_\_  
\_\_\_\_\_

5. Are there measures to ensure that sufficient numbers of older patients are enrolled to reflect the proportions in the population?<sup>a</sup>

- Yes, not applicable, this study is dedicated to older patients with cancer.
- Yes, the study design specifies the number of older patients with cancer that will be enrolled.
- Yes, other, explain.
- No, not applicable to this study.
- No, I would recommend adequate numbers of older patients be enrolled to this study.

6. Is the geriatric assessment included?

- Yes.
- No, I do not recommend that the geriatric assessment be included.
- No, I recommend that the geriatric assessment be included. Please provide details for this recommendation (eg, rationale for including, correlative endpoint, time points recommended): \_\_\_\_\_

7. Independent of the geriatric assessment, are there other core measures included for this study regarding comorbidity, or baseline blood work that should be collected?

- Yes, what are they? \_\_\_\_\_
- No, I recommend that the following core measures be considered: \_\_\_\_\_

8. Has the study team already engaged someone from the Cancer in the Older Adult Committee in designing this study?

- Yes (Name \_\_\_\_\_)
- No
- N/A I don't think this is necessary.<sup>b</sup>

9. If this concept is approved for protocol development (and it is appropriate to add a committee member to the study team), would you be willing to serve as the Cancer in the Older Adult co-chair for this study?

- Yes.
- No, please provide a recommendation for a Cancer in the Older Adult Co-Chair: \_\_\_\_\_
- No, Older Adult Committee member not necessary.

Additional comments for study team consideration:  
\_\_\_\_\_  
\_\_\_\_\_



# Real-world data

- Interviews with 39 patients about their experience with phase 1 trials >65 with advanced cancer
- Trial participation was an interactive process that unfolded over time
- Guidance to navigate process
- Age not a limitation
- QOL most important



Journal of Geriatric Oncology  
Volume 13, Issue 5, June 2022, Pages 594-599



Decision-making about clinical trial options among older patients with metastatic cancer who have exhausted standard therapies

[Mazie Tsang](#)<sup>a</sup>  , [Rebecca J. DeBoer](#)<sup>a</sup> , [Sarah B. Garrett](#)<sup>b</sup> , [Daniel Dohan](#)<sup>b</sup> 



- Feeling overwhelmed by current health status
- Mistrust of research
- Hesitancy to participate in a deprescribing study

Clinical Trial > [Trials](#). 2023 Jul 18;24(1):456. doi: 10.1186/s13063-023-07506-7.

## Why do older adults decline participation in research? Results from two deprescribing clinical trials

Thomas E Strayer<sup>1 2</sup>, Emily K Hollingsworth<sup>3 4</sup>, Avantika S Shah<sup>3 5</sup>, Eduard E Vasilevskis<sup>3 6 7</sup>, Sandra F Simmons<sup>3 4 6</sup>, Amanda S Mixon<sup>3 6 7</sup>



- RCT to test geriatric education intervention to improve accrual to trials
- Randomised to received standard information or education intervention
- This did not improve accrual to trial

Clinical Trial > [J Clin Oncol. 2005 Apr 1;23\(10\):2201-7. doi: 10.1200/JCO.2005.01.222.](#)

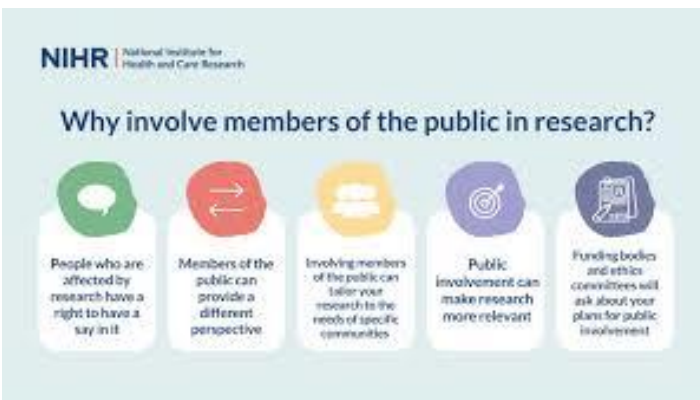
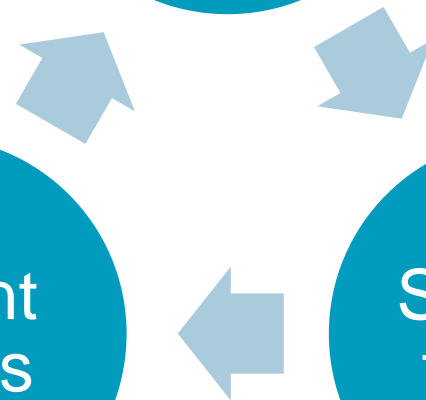
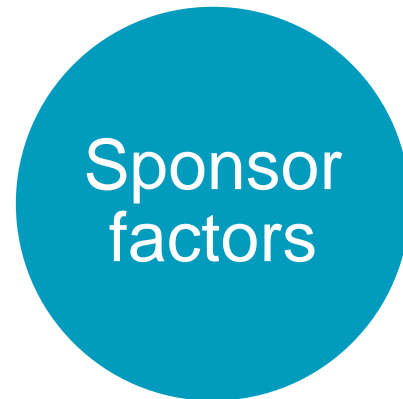
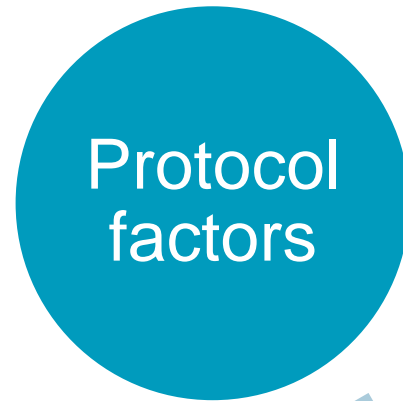
## **Improving accrual of older persons to cancer treatment trials: a randomized trial comparing an educational intervention with standard information: CALGB 360001**

Gretchen G Kimmick <sup>1</sup>, Bercedis L Peterson, Alice B Kornblith, Jeanne Mandelblatt, Jeffrey L Johnson, Judith Wheeler, Robin Heinze, Harvey J Cohen, Hyman B Muss





# Future directions





# Summary

- Older adults are willing to participate in research
- Alternative study designs should be considered
- Specific funding
- Specific PPI
- Patients with cognitive impairment should not be automatically excluded
- Trials sponsors have a duty to raise awareness



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**Thank you**

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