

# Addressing the Evidence Gap for Older Adults with Cancer



*Supriya Mohile, MD, MS*

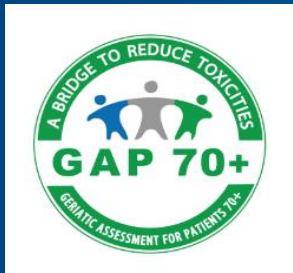
*Philip and Marilyn Wehrheim Professor*

*Co-Director, Cancer Control Program, WCI*

*Director, Geriatric Oncology Research Program*

*Editor-in-Chief, Journal of Geriatric Oncology*

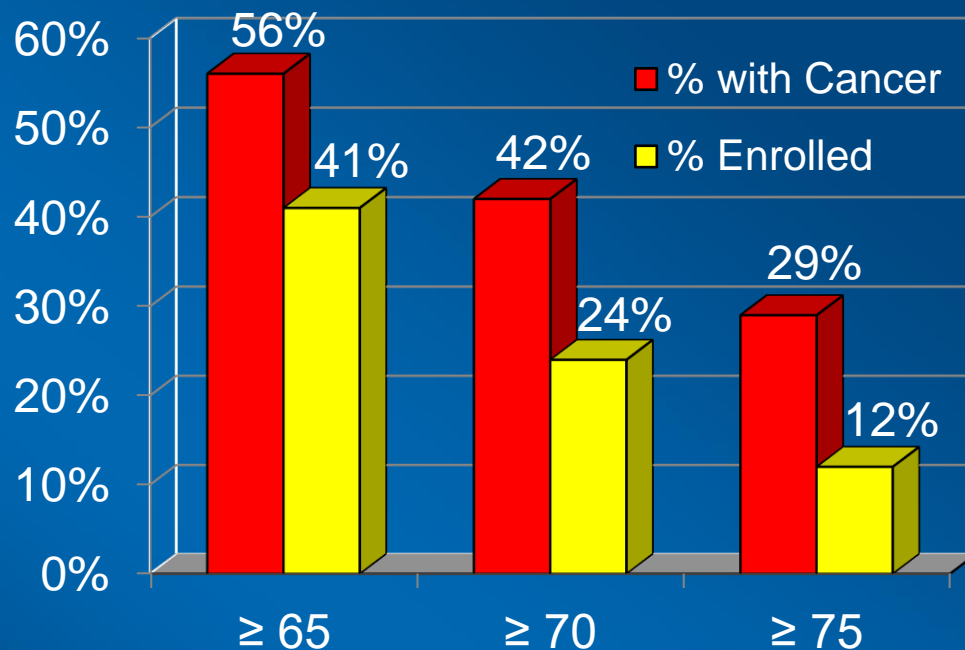
*Co-Lead, Cancer and Aging Research Group*



# Under-representation of Older Adults on FDA Registration Trials (ASCO 2017)

- 10-yr perspective
  - 2005-2015
- 105 FDA registration trials
- 224,766 patients

Disparity is Greatest for Patients Age  $\geq 75$



Singh et al, ASCO Annual Meeting, 2017

Arti Hurria, MD

MEDICINE of  
THE HIGHEST ORDER



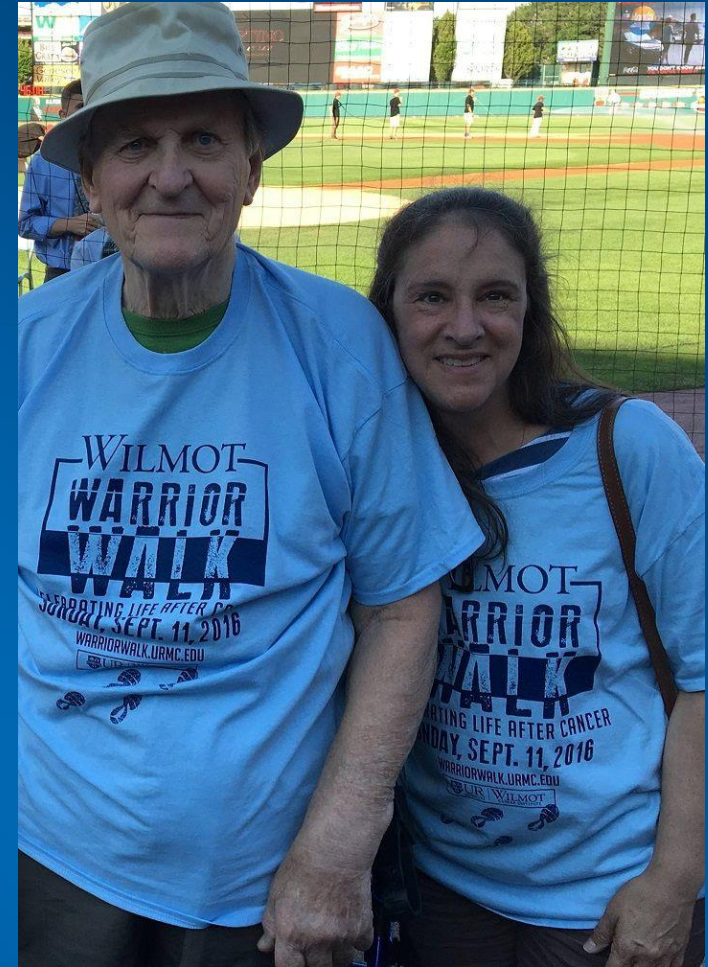
UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

# Common Concerns for Older Patients

- Needs assistance with daily activities
- Multiple comorbid medical conditions
- Mild cognitive impairment
- Limited social support
- Lives alone
- Transportation issues
- Polypharmacy
- Frailty

Likely Did Not Participate in  
Registration & Cooperative Group Studies



# 2013 Institute of Medicine Report *Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis*

## Recommendations:

- There is a critical need for research in older adults with

## Potential

- Increase research
- Consider the following:
  - Research design & infrastructure
  - Recruitment of older adults
  - Reporting of results

VIEWPOINT

Improving the Quality of Cancer Care  
in an Aging Population  
Recommendations From an IOM Report

*Hurria et al. JAMA 2013*

DELIVERING  
HIGH-QUALITY  
CANCER CARE

INSTITUTE OF MEDICINE  
OF THE NATIONAL ACADEMIES

IOM, 2013

MEDICINE of  
THE HIGHEST ORDER



WILMOT  
CANCER INSTITUTE

# Barriers to enrolling vulnerable older adults to clinical trials

- Research question
  - Lack of data on tolerability
  - Inappropriate comparators
- Study design
  - Inattention to what is known about aging
- Infrastructure
  - Procedures are not patient-centered
- ?Ageism

# Geriatric Assessment

- Geriatric assessment (GA) is an approach to the evaluation of the older patient, leading to the early identification and treatment of areas of vulnerability.
- The GA evaluates the following domains:
  - Functional and physical status
  - Objective physical performance
  - Comorbid medical conditions
  - Cognition
  - Nutritional status
  - Psychological status
  - Social support
- Each domain is an independent predictor of morbidity and mortality in older patients with cancer



Mohile, Dale, Hurria and Panel. ASCO Guidelines in Geriatric Oncology. JCO; 2018.

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

# Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy: ASCO Guideline for Geriatric Oncology

*Supriya G. Mohile, William Dale, Mark R. Somerfield, Mara A. Schonberg, Cynthia M. Boyd, Peggy S. Burhenn, Beverly Canin, Harvey Jay Cohen, Holly M. Holmes, Judith O. Hopkins, Michelle C. Janelsins, Alok A. Khorana, Heidi D. Klepin, Stuart M. Lichtman, Karen M. Mustian, William P. Tew, and Arti Hurria*

MEDICINE *of*  
THE HIGHEST ORDER



UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

# Goals of our PCORI-funded NCORP Study

- To improve communication about age-related concerns of older patients with advanced cancer and their caregivers
  - Direct communication about age-related concerns in clinical encounters
  - Patient satisfaction with communication about age-related concerns
- Providing a summary of geriatric assessment results with recommendations for GA-guided interventions
  - Has potential to improve communication about age-related concerns of older patients with cancer and their caregivers



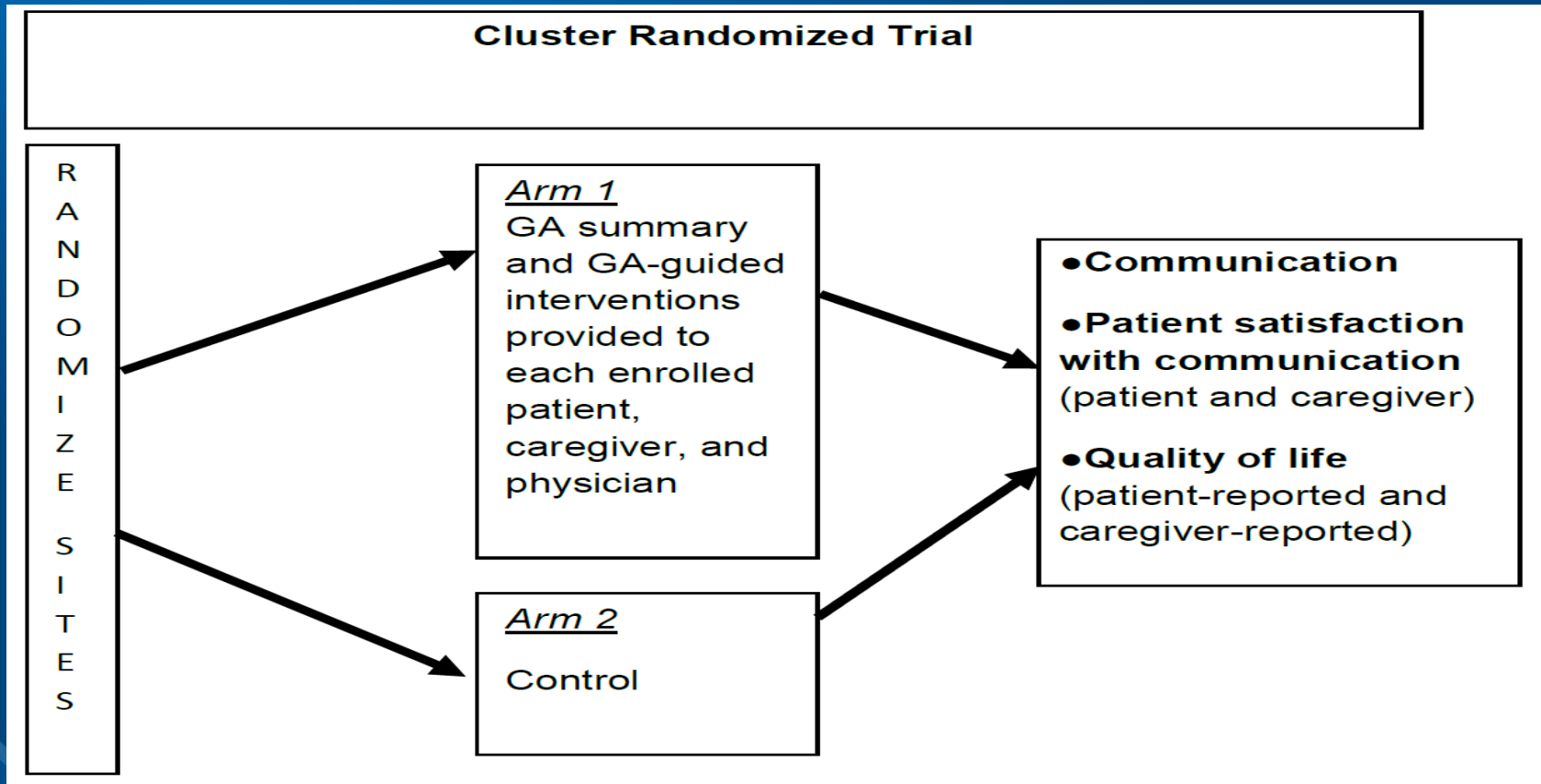
MEDICINE *of*  
THE HIGHEST ORDER



UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

# Study Design and Eligibility



Audio recorded clinic visit for each patient after GA



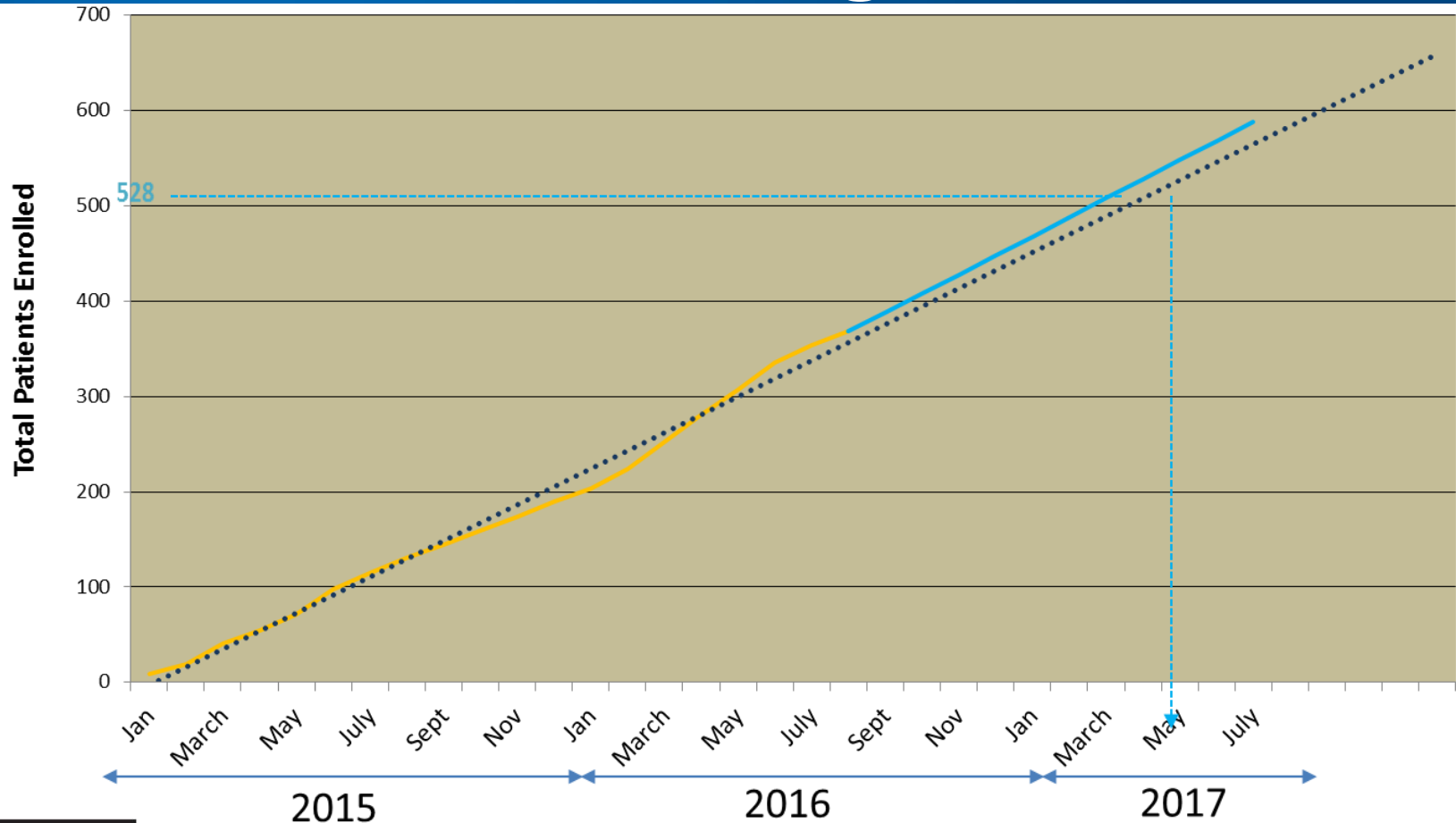
MEDICINE of  
THE HIGHEST ORDER



UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

# Accrual: 305 oncologists, 541 patients, 414 caregivers



MEDICINE of  
THE HIGHEST ORDER

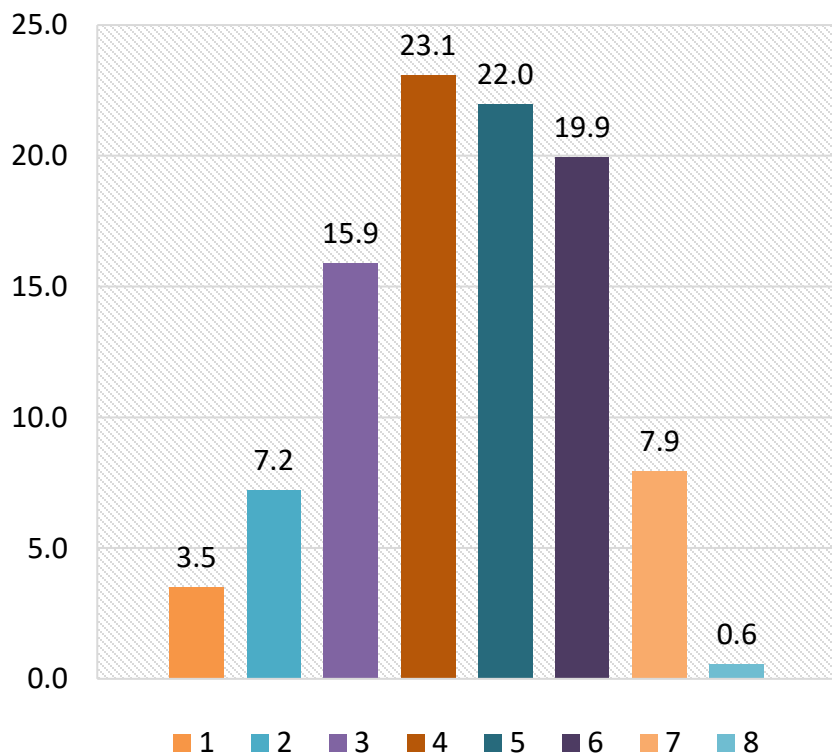


UR  
MEDICINE

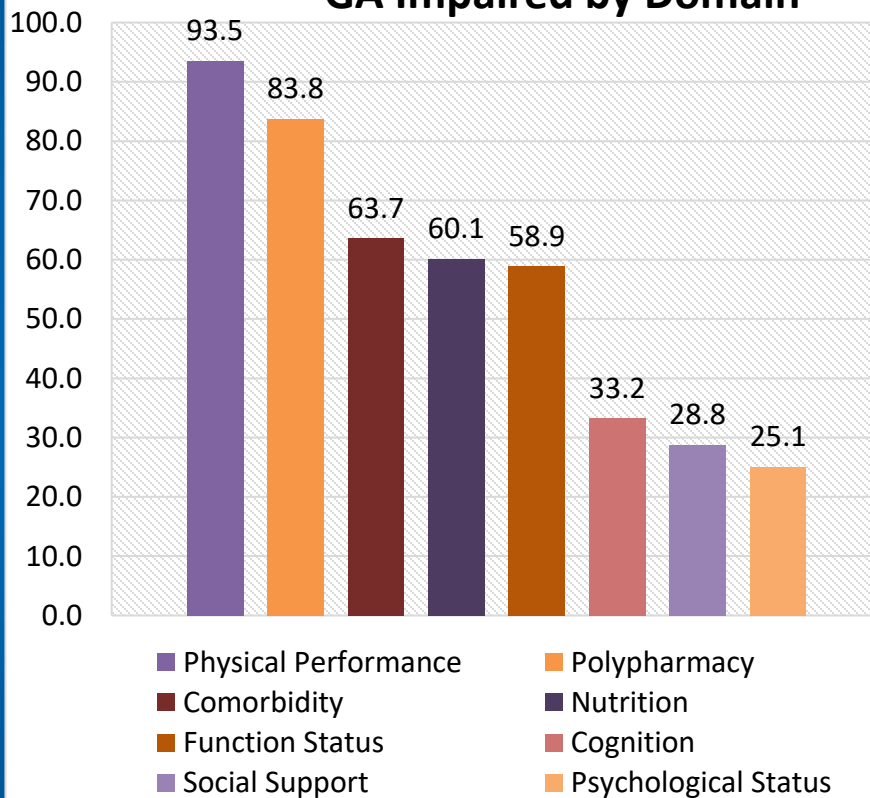
WILMOT  
CANCER INSTITUTE

# GA domains for all patients (N=541)

## Percentage of Number of GA Domains Impaired



## Percentage of GA Impaired by Domain

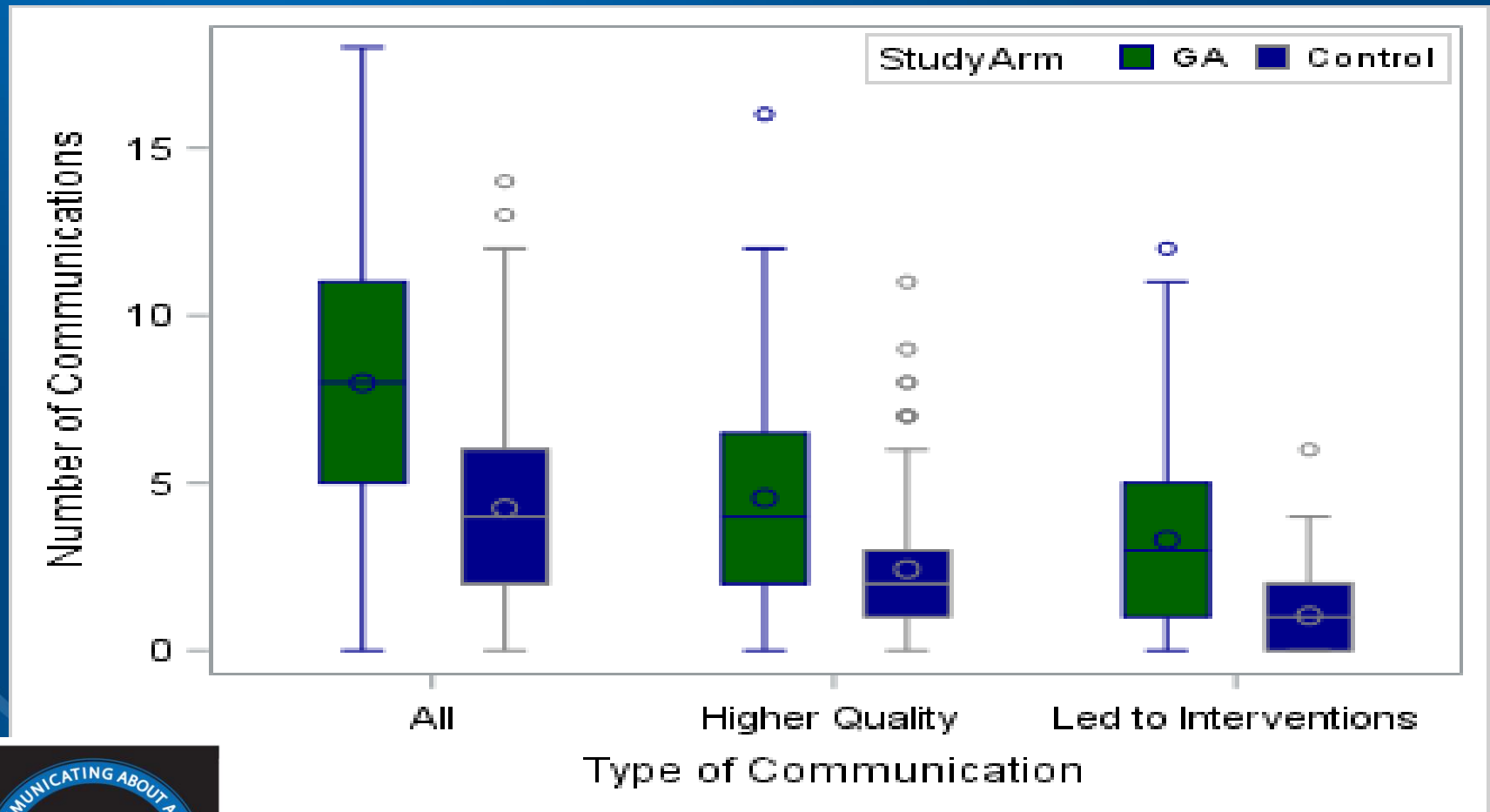


MEDICINE of  
THE HIGHEST ORDER



Mohile et al, ASCO 2018

# GA Improves Communication about Age-Related Concerns



MEDICINE of  
THE HIGHEST ORDER



UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

Mohile et al, ASCO 2018

# Goal of our R01-funded NCORP Study

- **Primary Aim:**
  - To evaluate if providing a GA summary with recommendations for management to oncologists reduces grade 3-5 toxicity (CTCAE v4) in patients aged 70+ starting a new regimen with chemotherapy and/or other agents which cause toxicity for advanced cancer
- **Secondary Aims:**
  - Survival at 6 months
  - Treatment decisions
  - Functional and Physical Performance



MEDICINE *of*  
THE HIGHEST ORDER

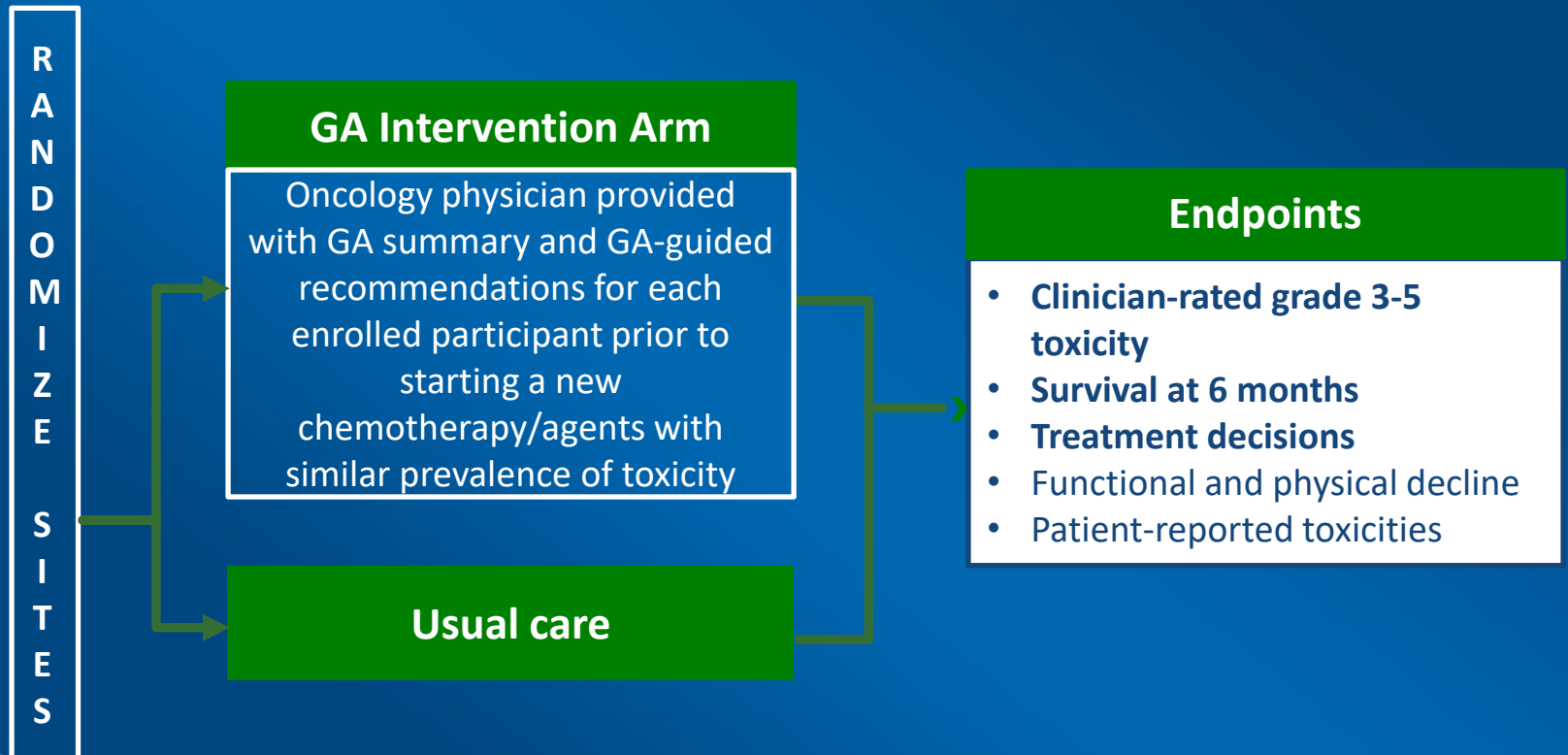


UR  
MEDICINE

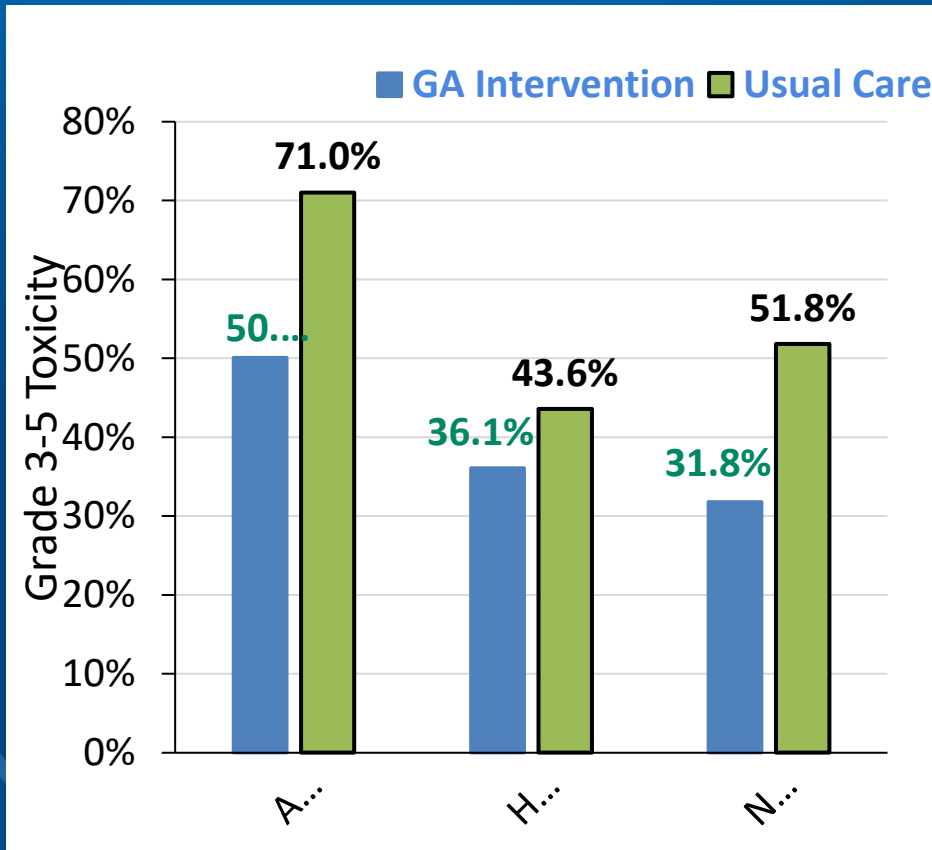
WILMOT  
CANCER INSTITUTE

# Study Schema

## Geriatric Assessment for Patients 70+



# Any Grade 3-5 CTCAE Toxicity in 3 Months (n=718)



- **Any Grade 3-5 Toxicity**  
Adjusted Risk Ratio: 0.74  
95% CI: (0.63-0.87), P < 0.01  
Clustering effect: P = 0.15
- **Any Grade 3-5 Hematologic Toxicity**  
Adjusted Risk Ratio: 0.85  
95%CI: (0.69-1.05), P = 0.13  
Clustering effect: P = 0.30
- **Any Grade 3-5 Non-hematologic Toxicity**  
Adjusted Risk Ratio: 0.73  
95% CI: (0.53-0.996), P = 0.047  
Clustering effect: P < 0.01



MEDICINE of  
THE HIGHEST ORDER



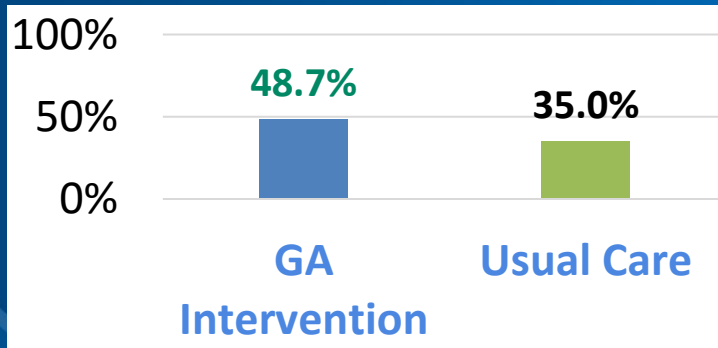
UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

# Treatment Intensity

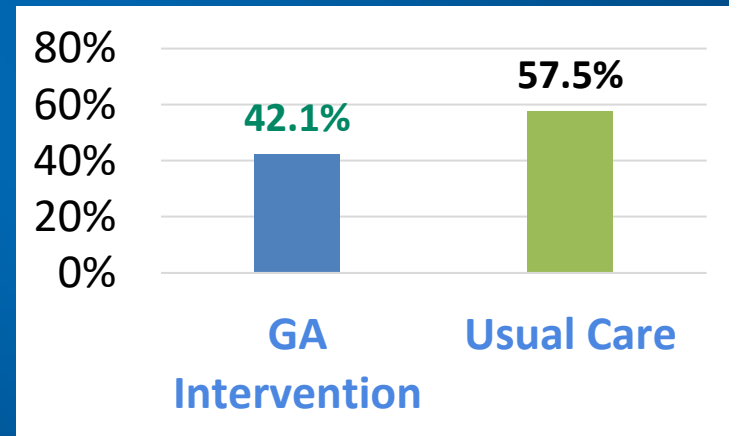
- Adjusted Risk Ratio=1.37  
95% CI: (1.06-1.76), P=0.016  
Clustering effect: P=0.03

Reduced Dose Intensity at Cycle 1

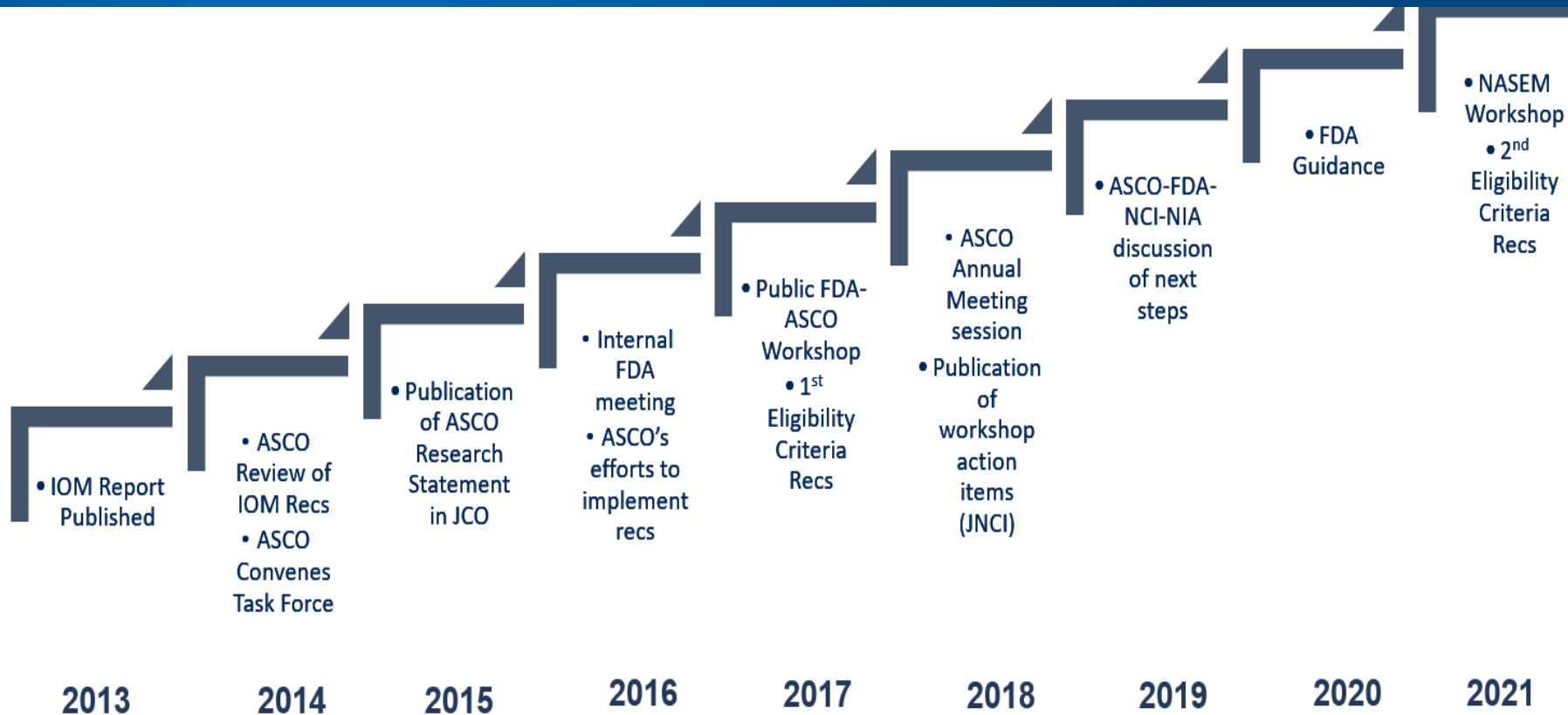


- Adjusted Risk Ratio=0.85  
95% CI: (0.67-1.08), P=0.190  
Clustering effect: P<0.01

Dose modification at 3 months Related to Toxicity



# Improving Evidence-base of Older Patients with Cancer



MEDICINE of  
THE HIGHEST ORDER



UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

NASEM 2021 presented by Dr. Heidi Klepin

OXFORD

JNCI J Natl Cancer Inst (2018) 110(11): djy169

doi: 10.1093/jnci/djy169

First published online October 17, 2018

Commentary

COMMENTARY

## Expanding the Evidence Base in Geriatric Oncology: Action Items From an FDA-ASCO Workshop

Laura A. Levit, Harpreet Singh, Heidi D. Klepin, Arti Hurria

### Action Items:

1. Increase enrollment of older adults on trials
2. Collect more information on older adults from treatment trials
3. Expand the use of real-world data in research on older adults
4. Strengthen the collaboration between stakeholders to develop advocacy and policy solutions

MEDICINE *of*  
THE HIGHEST ORDER



UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

# Addressing Systematic Exclusion

## Broadening Eligibility Criteria to Make Cancer Clinical Trials More Representative

### Series

**First round** (October 2017): ASCO-Friends Joint Research Statement and four work group manuscripts published as a *Journal of Clinical Oncology Special*

**Second round** (January 2021): ASCO-Friends Joint Research Statement, four work group manuscripts, and an impact analysis paper are in press with *Clinical Cancer Research*

## Organ dysfunction, Prior or Concurrent Malignancies, Comorbidities Working Group

### Recommendations to address:

- Creatinine clearance
- Cardiac disease
- Hepatic dysfunction
- Hematologic function
- Prior or concurrent malignancy

## Performance Status Working Group

### Recommendations to address:

- Inclusion of ECOG performance status 2
- Alternative trial design for inclusion of patients with lower-functioning PS
- Use of validated physical function measures

Kim ES, Bruinooge SS, Roberts S, et al: Broadening Eligibility Criteria to Make Clinical Trials More Representative: American Society of Clinical Oncology and Friends of Cancer Research Joint Research Statement. *Journal of Clinical Oncology* 35:3737-3744, 2017

Lichtman SM, et al. Modernizing Clinical Trial Eligibility Criteria: Recommendations of the American Society of Clinical Oncology-Friends of Cancer Research Organ Dysfunction, Prior or Concurrent Malignancy, and Comorbidities Working Group. *JCO* 2017 Nov 20; 35(33): 3753-3759.

MEDICINE of  
THE HIGHEST ORDER



WILMOT  
CANCER INSTITUTE

FRIENDS  
of CANCER  
RESEARCH

## FDA Guidance

---

# Inclusion of Older Adults in Cancer Clinical Trials Guidance for Industry

*DRAFT GUIDANCE*

This guidance document is being distributed for comment purposes only.

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/inclusion-older-adults-cancer-clinical-trials>

MEDICINE *of*  
THE HIGHEST ORDER



UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

# Cancer and Aging Research Group

NIA R33; MPIs: Drs. William Dale, Supriya Mohile, Heidi Klepin

## Build the support network:

- Bring together mentors
- Bring together peers
- Present, discuss, and develop research ideas
- Collaborate



## Goals:

- Mentor junior geriatric oncology investigators and promote academic productivity
- Design intervention studies
- Improve accrual of older adults to clinical trials

Slide c/o Arti Hurria and team Hurria, JCO; 2008



MEDICINE *of*  
THE HIGHEST ORDER



UR  
MEDICINE

WILMOT  
CANCER INSTITUTE

# Engaging Older Adults in Cancer Clinical Trials Conducted in the NCI Clinical Trials Network: Challenges and Opportunities

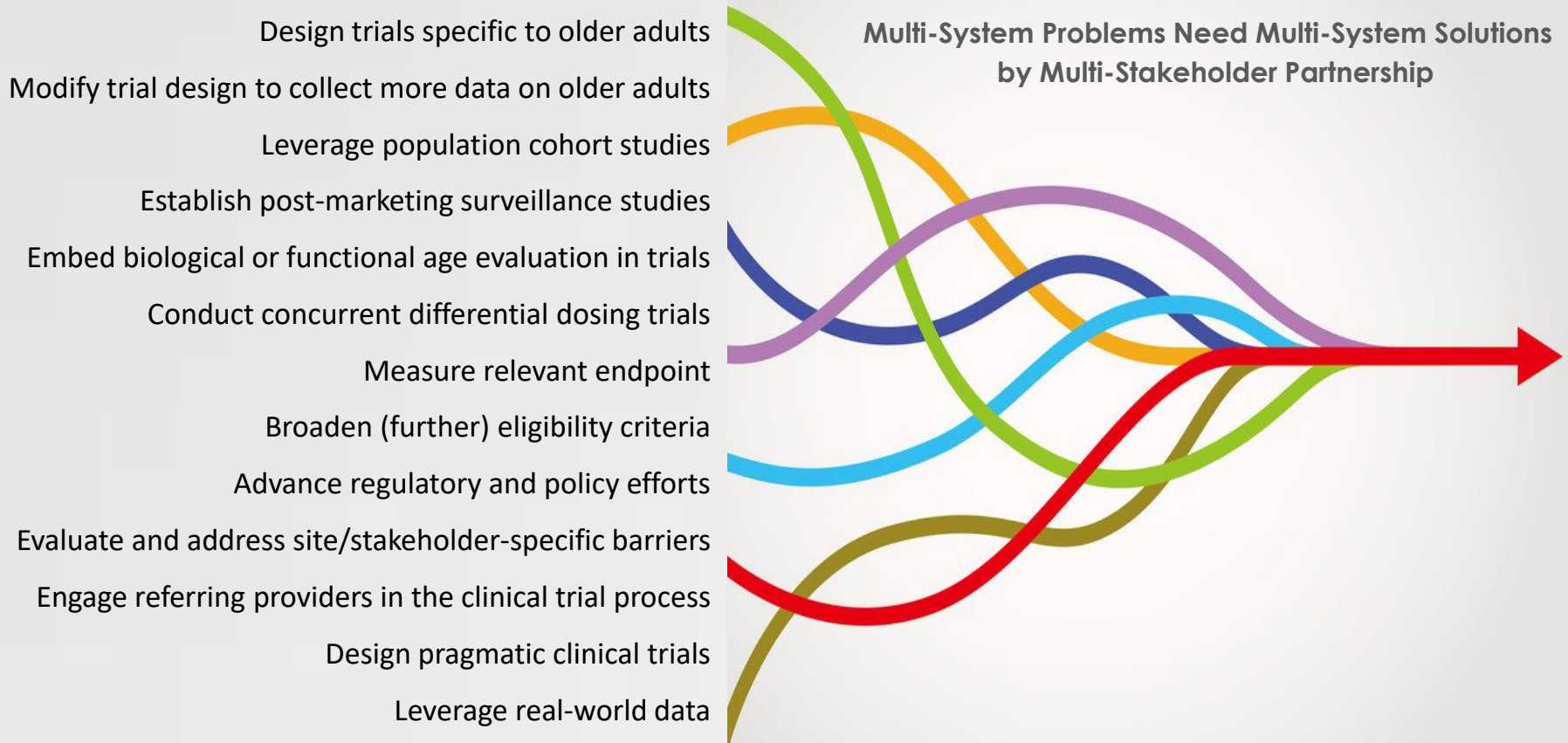
## A Cancer Moonshot<sup>SM</sup> Workshop

---

*Diane St. Germain*  
*Supriya Mohile*

September 14, 2020

# Restructuring cancer clinical trials so that the translational power of personalized oncologic medicine is inclusive of older and frail adults with cancer



# Solutions

- Stakeholder engagement
  - Patients; Caregivers and families
  - Community Oncology teams
- Multidisciplinary Input
  - Experts in aging and cancer should work together
- Standardization of:
  - Measures and criteria for vulnerability
  - Processes for developing and reviewing trials
  - Tolerability metrics: include patient-reported outcomes and function
- Novel study designs and infrastructure
  - Integration of geriatric assessment-guided interventions
  - Telemedicine for procedures



Development of a telehealth geriatric assessment model in response to the COVID-19 pandemic



Grace DiGiovanni <sup>a</sup>, Kathryn Mousaw <sup>b</sup>, Terri Lloyd <sup>a</sup>, Nancy Dukelow <sup>c</sup>, Bryan Fitzgerald <sup>d</sup>, Heidi D'Aurizio <sup>b</sup>, Kah Poh Loh <sup>a</sup>, Supriya Mohile <sup>a</sup>, Erika Ramsdale <sup>a</sup>, Ronald Maggiore <sup>a</sup>, Jason Zittel <sup>a</sup>, Sindhuja Kadambi <sup>a</sup>, Allison Magnuson <sup>a,\*</sup>

<sup>a</sup> Division of Hematology/Oncology, University of Rochester Medical Center, Rochester, NY, USA

<sup>b</sup> Wilmot Cancer Institute Nursing, University of Rochester Medical Center, Rochester, NY, USA

<sup>c</sup> Occupational Therapy, University of Rochester Medical Center, Rochester, NY, USA

<sup>d</sup> University of Rochester Specialty Pharmacy, University of Rochester Medical Center, Rochester, NY, USA



WILMOT  
CANCER INSTITUTE

Gilmore et al; Cancer, 2019

Magnuson et al; JGO, 2020