Efforts to Improve the Evidence Base for Treating Older Adults with Cancer

Laura Levit, JD, American Society of Clinical Oncology

Heidi D. Klepin, MD, MS, Wake Forest School of Medicine

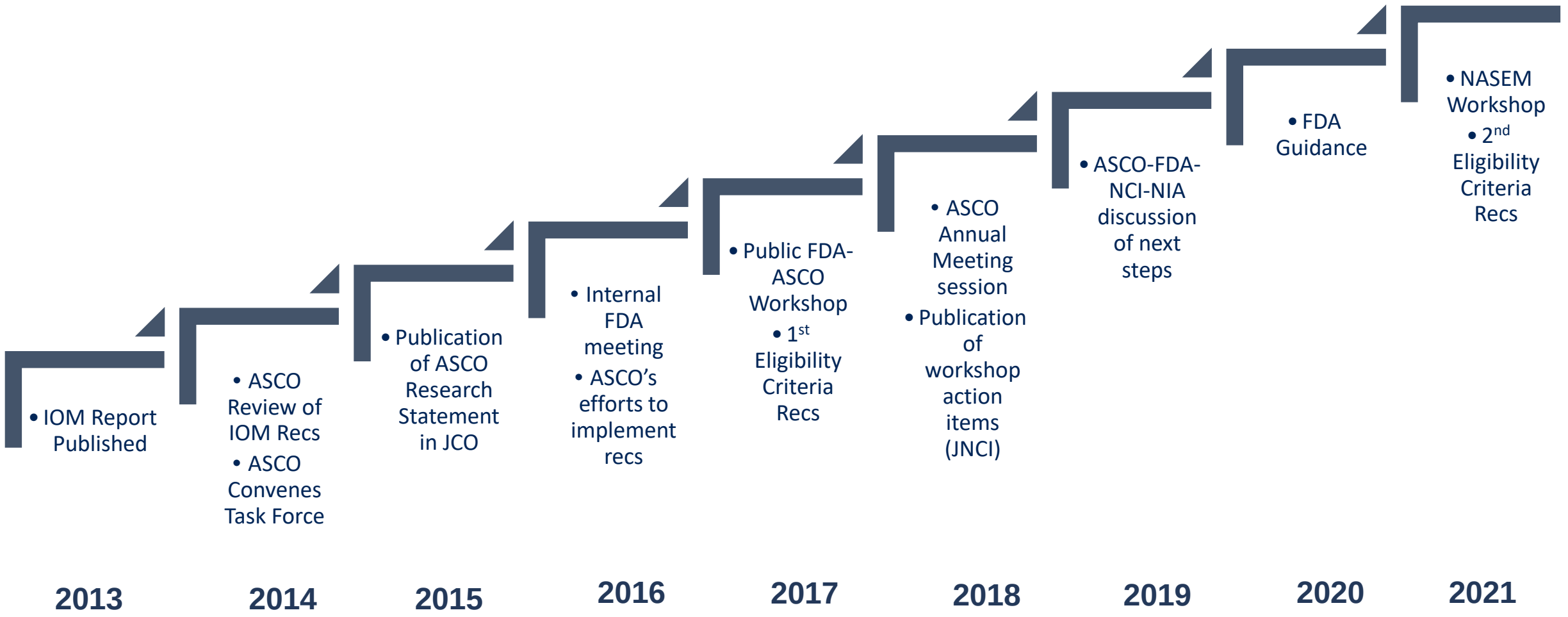
January 22, 2021

Goal

Improve the **evidence** base for treating older adults with cancer

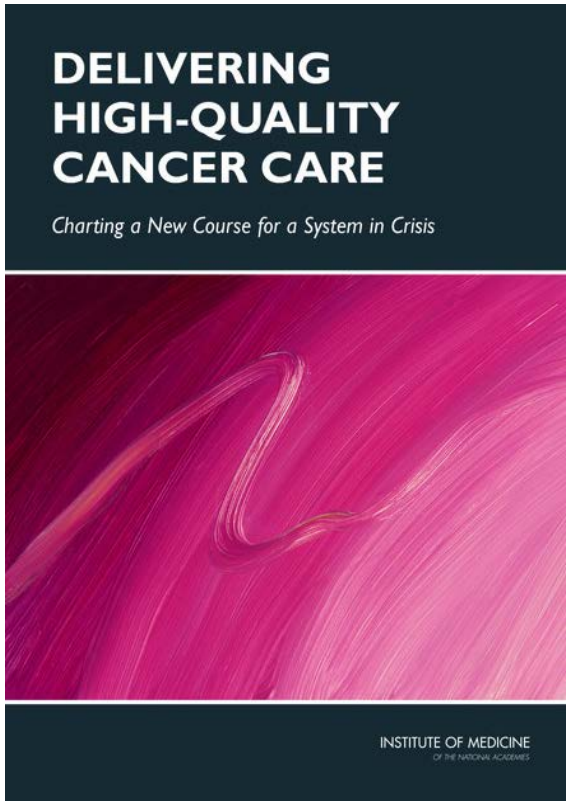
Improve the **quality of care** received by older adults with cancer

Timeline


• IOM Report Published
2013
• ASCO Review of IOM Recs
• ASCO Convenes Task Force
2014
• Publication of ASCO Research Statement in JCO
2015
• Internal FDA meeting
• ASCO's efforts to implement recs
2016
• Public FDA-ASCO Workshop
• 1st Eligibility Criteria Recs
2017
• ASCO Annual Meeting session
• Publication of workshop action items (JNCI)
2018
• ASCO-FDA-NCI-NIA discussion of next steps
2019
• FDA Guidance
2020
• NASEM Workshop
• 2nd Eligibility Criteria Recs
2021

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

- Number of cancer cases on the rise
- Majority of cancers occur in older adults
- Older adults under-represented in research
- Projected shortage of healthcare providers with geriatrics expertise
- IOM Committee makes recommendations to improve our evidence base and strengthen the national workforce that cares for older patients with cancer



Improve Evidence-Based Care of Older Adults

IOM Committee Recommendations:

Increase breadth of collected data by matching the characteristics of the study population to that of patients with the disease (i.e. enroll more elderly patients onto clinical trials)

Increase depth of collected data by capturing a more detailed characterization of the study population through evaluation tools such as a comprehensive geriatric assessment

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Improving the Evidence Base for Treating Older Adults With Cancer: American Society of Clinical Oncology Statement

Recommendation
To improve the conduct of research
Use clinical trials to improve evidence for treating older adults with cancer
Leverage research designs and infrastructure for generating evidence on older adults with cancer
To improve the research environment
Increase FDA authority to incentivize and require research involving older adults with cancer
Increase clinicians' recruitment of older adults with cancer to clinical trials
Use journal policies to improve researchers' reporting of age distribution and health risk profiles of research participants

Hurria et al, JCO, 2016, slide courtesy of Arti Hurria

Designing Clinical Trials for Older Adults

November 2017: FDA/ASCO Geriatric Oncology Symposium

Multi-stakeholder meeting to discuss the need for improved evidence generation and identify strategies to generate evidence

Session 1: Designing clinical trials for older adults with cancer
Session 2: Increasing enrollment to FDA registration trials
Session 3: Leveraging real world evidence
Session 4: Lessons from pediatrics, payers, and the EMA

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

Action Item 1: Increase enrollment of older adults in clinical trials

Goal	Action
Plan for enrollment	FDA works with sponsors to outline development plans for new drugs to enroll representative numbers of older adults.
Broaden eligibility	Sponsors should implement ASCO-FDA-Friends eligibility criteria recommendations for organ dysfunction, concurrent malignancy, and comorbidities.
Enhance opportunity	Sponsors should open more trials in community settings.
Engage experts	Sponsors should work with social and behavioral scientists, patient advocates, geriatricians, and geriatric oncologists to consider the needs of older adults when designing clinical trials.
Ensure representation	NCI should implement the NIH Inclusion Across the Lifespan Policy with the goal of increasing the representation of older adults (trial population matches population affected).

Action Item 2: Collect more information on treating older adults from clinical trials

Goal	Action
Expand trial outcomes	Sponsors and researchers should work with statisticians to design trials with coprimary or composite endpoints, including elements of geriatric assessment and PROs that are important to older adults.
Design trials for older adults	FDA and NCI should work with sponsors to design trials that collect more information on treating older/frail adults. • Older adult specific trials • Alternative trial designs • Characterization of patients enrolled (comorbidity, functional status)

Action Item 3: Expand the use of Real World Data (RWD) in research on older adults

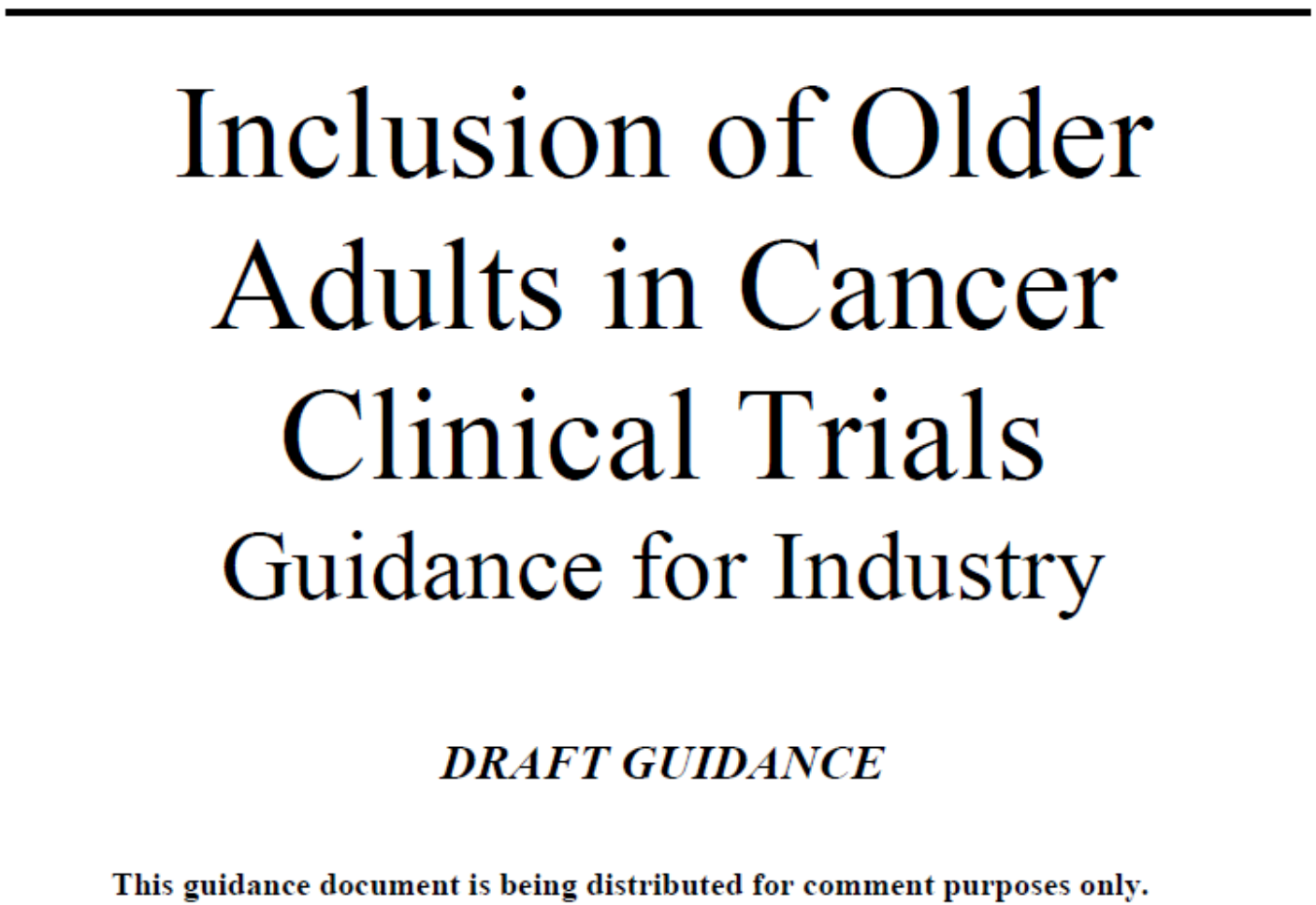
Goal	Action
Identify and facilitate unique contributions of RWD to fill evidence gaps	Geriatric oncology researchers should work with ASCO, FDA and other stakeholders to develop a framework for using RWD in clinical research • Propose demonstration projects through CancerLinQ and other data sources
Enhance quality of EHR data to support evidence generation	Clinicians should incorporate geriatric assessment (GAs) into clinical care and record this information in EHRs, payers should reimburse for this time, and quality metrics programs should assess clinicians' performance of GAs.
Improve electronic health record systems to facilitate data collection	Developers of large EHR databases should partner with EHR vendors to ensure GA elements can be entered EHRs as standard data elements.

Action Item 4: Strengthen collaboration between stakeholders to develop advocacy and policy solutions

Goal	Action
Advocacy to accelerate change	The geriatric oncology community should strengthen its advocacy efforts to be more cohesive and propose specific policy solutions.
Create policy incentives	Geriatric oncologists should discuss with developers of value frameworks how their definitions of “value” could be updated to consider the representativeness of the evidence to the population with the disease.

Additional Developments

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

Broadening Eligibility Criteria to Make Cancer Clinical Trials More Representative

Addressing Systematic Exclusion

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

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.

FDA Guidance

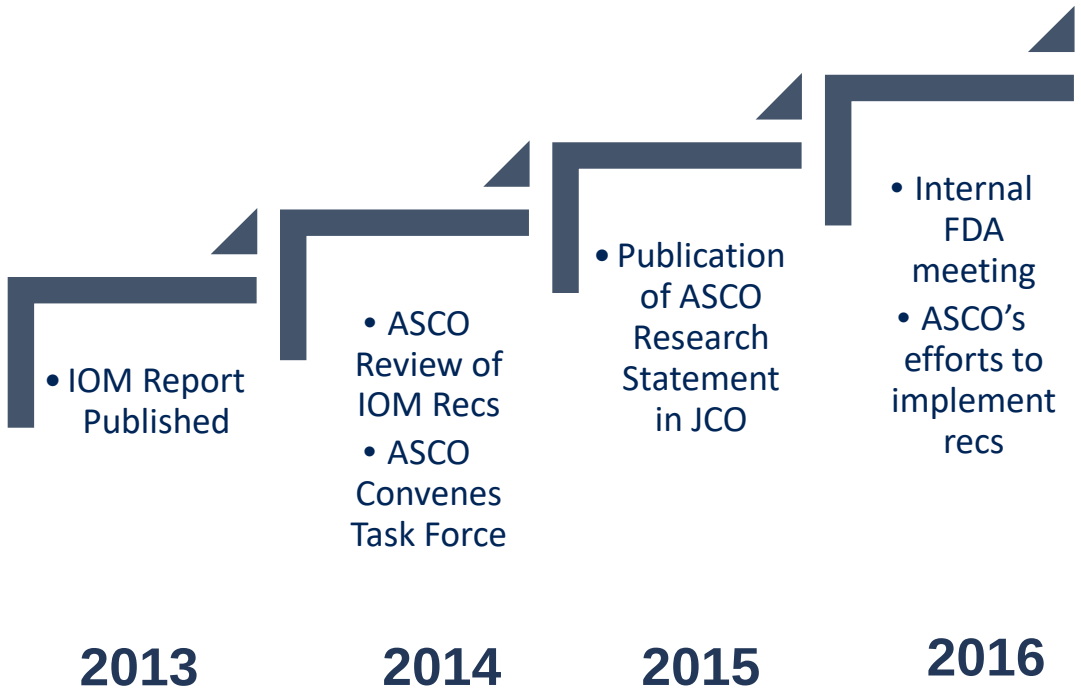
GUIDANCE DOCUMENT

Cancer Clinical Trial Eligibility Criteria: Patients with Organ Dysfunction or Prior or Concurrent Malignancies

JULY 2020

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

Creating a Sense of Urgency



Factors associated with age disparities among cancer clinical trial participants. JAMA Oncology 2019

302 Phase 3 therapeutic RCTs

- N=262,354 participants
- Lung, colon, breast, prostate cancer
- 83% industry funded

Trial participants were on average 6.5 years younger than population median age for each disease.

The gap between trial age and population age was increasing over time

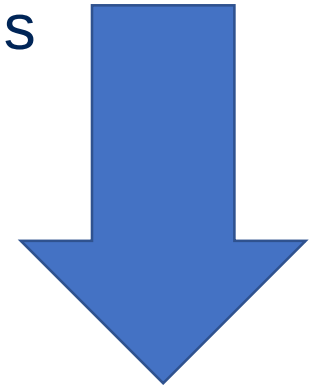
Ludmir et al. JAMA Oncology, 2019,5(12):1769-1773

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Moving Forward: Overcoming Barriers

Multi-stakeholder engagement

Systematic actions



A culture change

Evidence gap is closed rapidly

Addressing Challenges:

- Patient-centered trial design
- Access to trials
- Complexity of trials
- Designing older adult specific treatment trials-treatment, outcomes, population?
- Characterizing frailty in clinical trials
- Enrolling pre-frail/frail older adults
- Concern regarding excess toxicity
- Incentives for enrolling and post marketing commitments