Structural, Clinical, and Physician/Patient Barriers to Clinical Trial Participation

Joseph Unger, Ph.D., M.S.

Health Services Research and Biostatistics
Assistant Member, Fred Hutchinson Cancer Research Center
Affiliate Assistant Professor, University of Washington

Role of Clinical Trials in Cancer Research

- Patient participation in clinical trials forms the backbone of cancer clinical research
- Clinical trials are the key step in advancing new treatments and improving outcomes
- It is commonly assumed that only 2%–3% of adult cancer patients participate in clinical trials
- Most Americans view clinical trial participation favorably

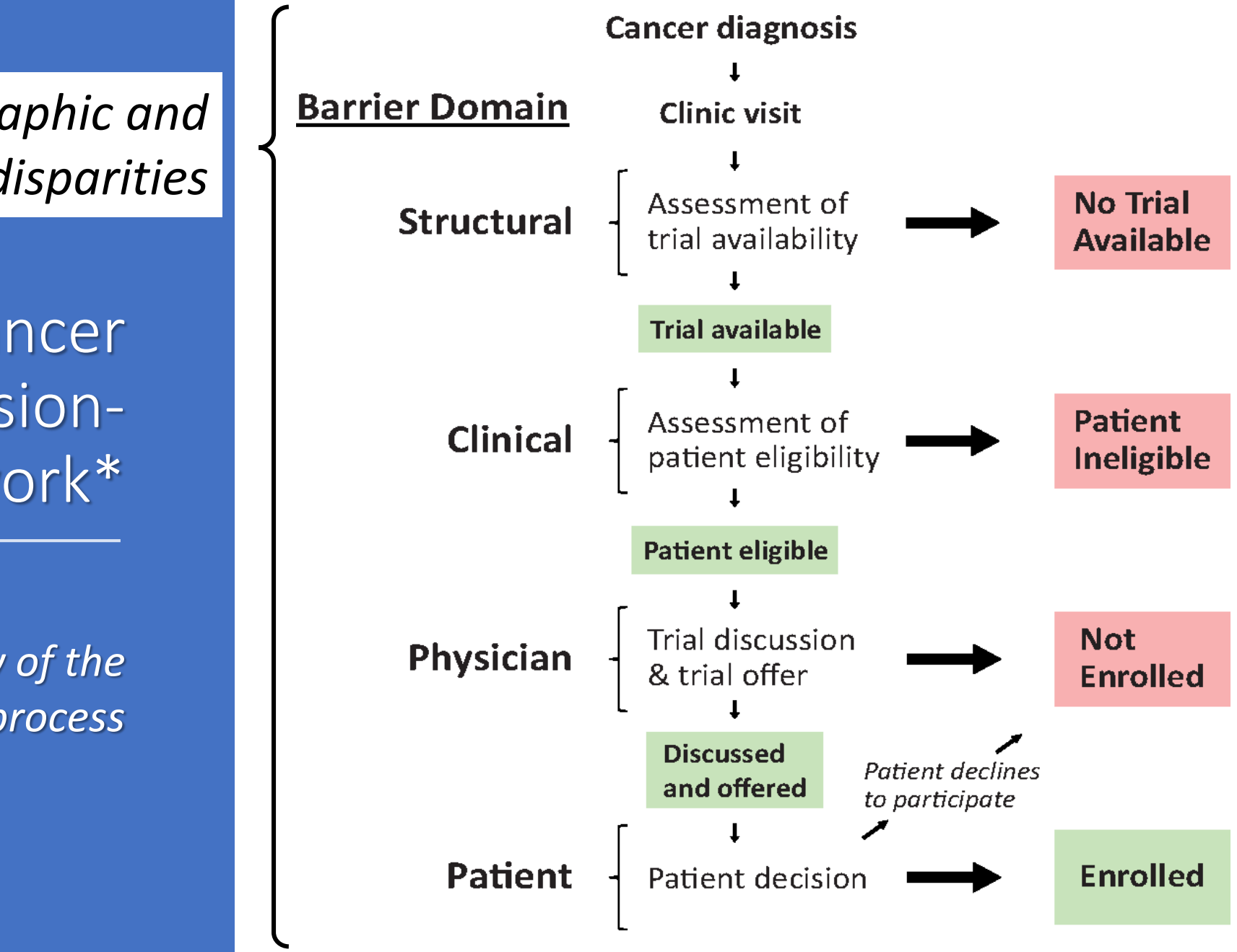
Patient Participation in Clinical Trials

- Clear gap between the willingness of patients to participate in trials and their actual participation rates
- Suggests there are numerous barriers to trial participation which may be modifiable
- Barriers to trial participation have been the subject of much research, with a major emphasis on patient-related barriers
- This emphasis often interpreted to indicate that patients are the primary limiting factor to improving trial enrollment

Demographic and socioeconomic disparities

Figure 1: Cancer clinical trial decision-making framework*

Spanning the entirety of the trial decision-making process



* Unger et al., JNCI, 2019

Structural Barriers

Access to a clinic:

- Influenced by:
  - Availability of transportation
  - Travel costs
  - Insurance status
  - Child care
- Uninsured or underinsured patients present with later stage of disease
  - Relationship to comorbidities

Absence of an available trial:

- Study is available but not at patient's site
  - Requires travel to participate, a major burden for many patients
- Rare cancer
  - Investment in new treatment not a priority given finite resources

** Unger et al., Am Soc Clin Oncol Educ Book, 2016*

Clinical Barriers

- Even if a trial is available, patients may not be eligible
- Trial eligibility attempt to satisfy opposing factors:
  - Sufficiently narrow so that treatment effect is ~constant
  - Sufficiently broad so trial results apply to a meaningful population of patients
- Trials often criticized for having narrow eligibility criteria, sacrificing generalizability and reducing access for patients
- Presence of comorbid conditions
  - Dominant reason for ineligibility exclusions (60% of trial eligibility criteria)
- ASCO, Friends of Cancer Research, and the FDA recently published recommendations to modernize eligibility criteria

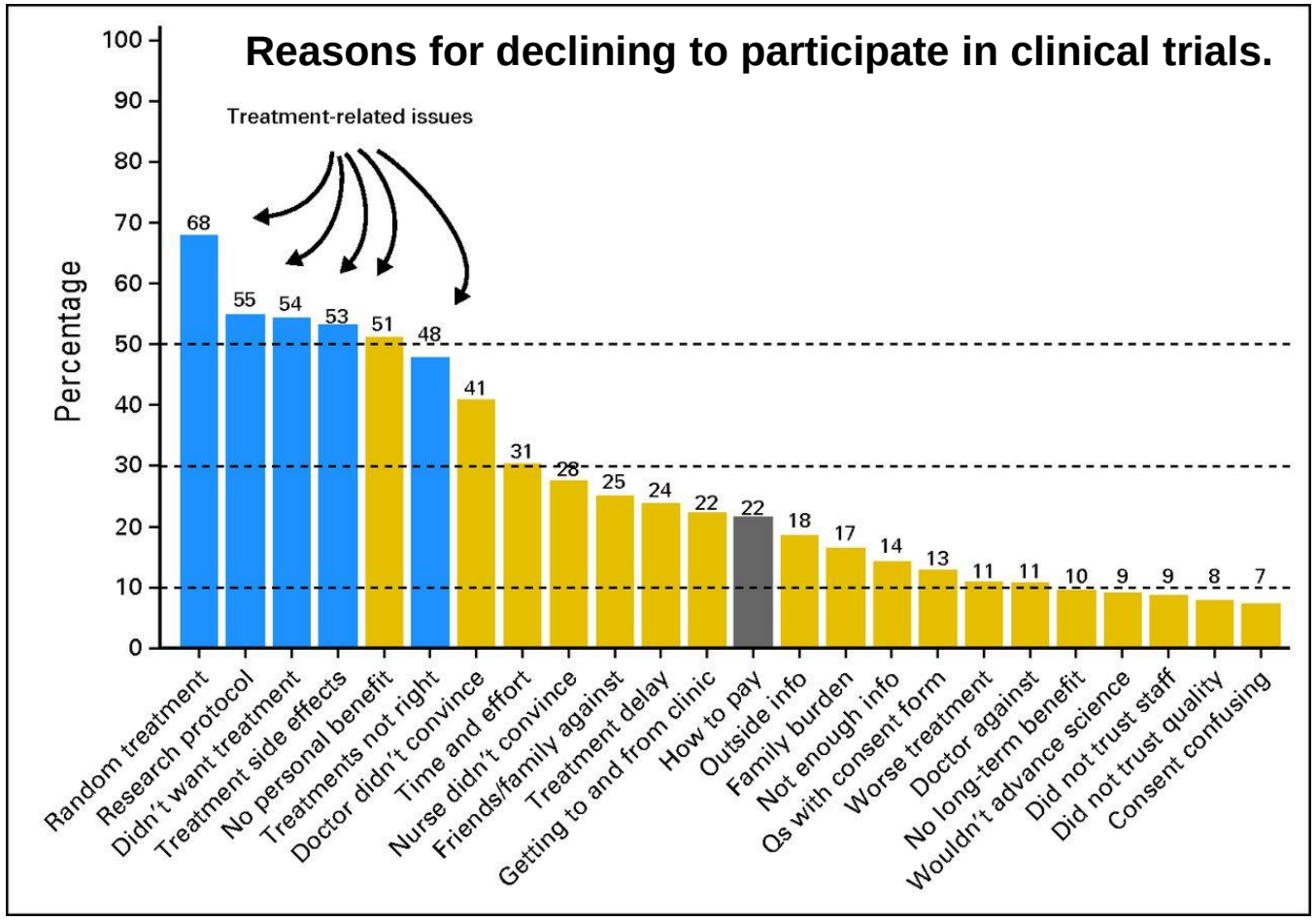
Physician's Role

- In their vital role guiding patient care, physicians may prefer a specific treatment
- Trial participation can interfere with physician-patient relationship
- Practical considerations:
  - Time and effort can be burdensome
  - Reimbursement
- This removes a key opportunity for ***eligible*** patients to participate in a trial

Patient Attitudes & Decision-Making

- Ultimate decision rests with the patient
- Motivated by both altruism and finding best treatment for their cancer
- Patients uneasy or fearful about trial participation
- Residual mistrust of medical science due to past abuses
  - e.g. Tuskegee Syphilis Study, human experimentation with radiation after WWII
- Modern attention to patient protections and informed consent has reduced fears for many
  - Belmont report (1979): Respect for Persons, Beneficence, and Justice

Patient Attitudes & Decision-Making (cont'd)



- Fear of experimentation expressed through a dislike of randomization
- Specific treatment related concerns, including:
  - Random treatment
  - Participation in a research protocol
  - Didn't want the protocol treatment
  - Treatment side effects
  - Treatment not right for them
- Other notable barriers:
  - Friends and family opposed
  - Burden to family
  - How to pay for treatment
  - Lack of trust of staff or quality

** Unger et al., JCO, 2013*

Rationale and Objective

- Key Concern: The rate of trial participation has not changed substantially over time
  - Over emphasis on patient-related barriers?
- Few studies have characterized the entire trial decision-making process with respect to trial barrier domains
- Understanding the magnitude of trial barrier domains is important to guide policy regarding research/resources to improve trial participation
- We examined the magnitude of domains of trial barriers by synthesizing prior research under a uniform framework for barrier domains

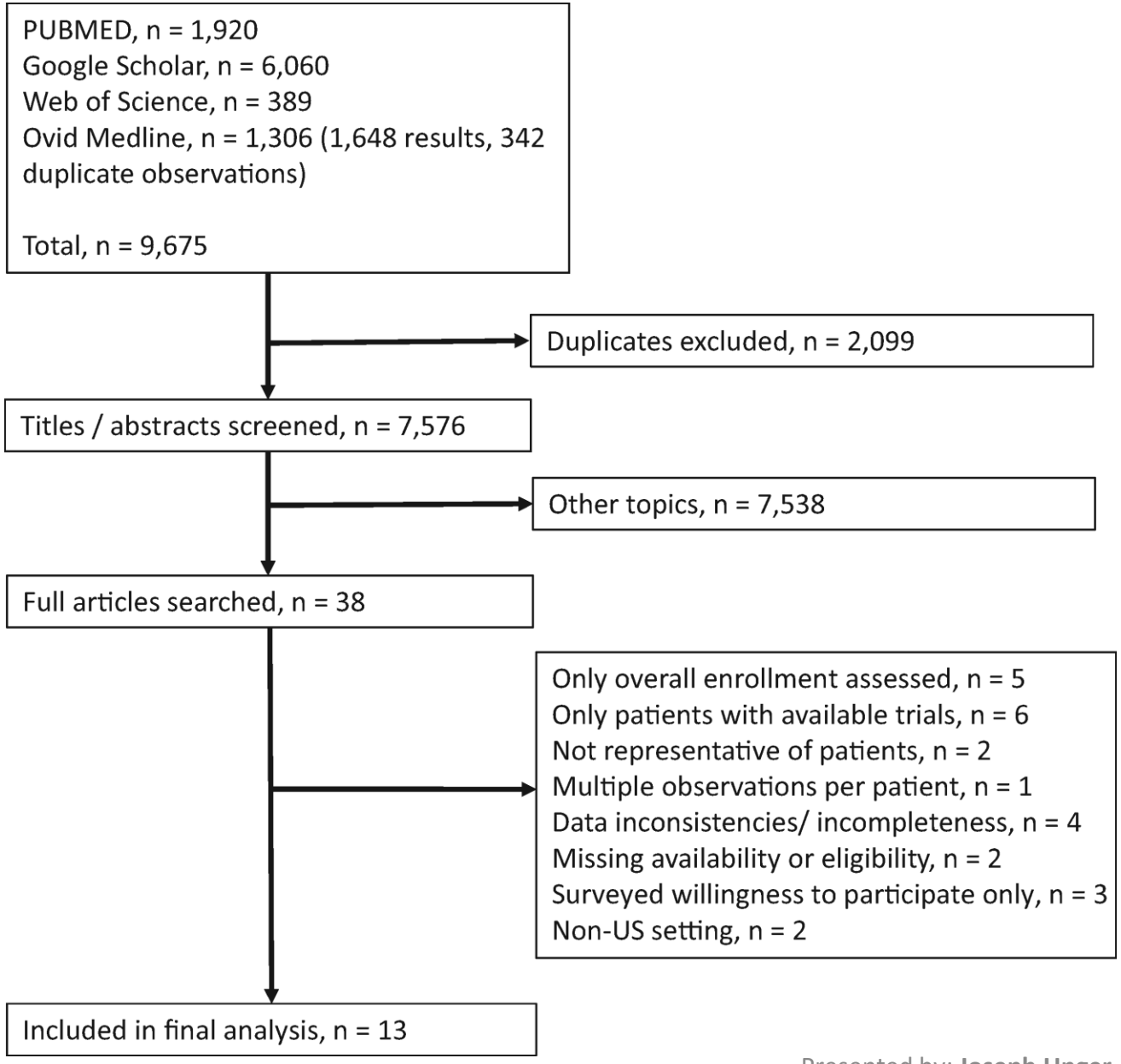
Methods

- Systematic review and meta-analysis (PRISMA)
  - PubMed, Google Scholar, Web of Science, and Ovid Medline (1999-2017)
- Inclusion criteria:
  - Domestic U.S. studies only
  - Fully documented trial decision-making process
  - Studies representative of the general cancer population
- Weighted estimates according to the proportion of patients expected to received cancer care in the academic (15%) vs. community (85%) settings

Figure 2. Selection of studies included in the analysis*

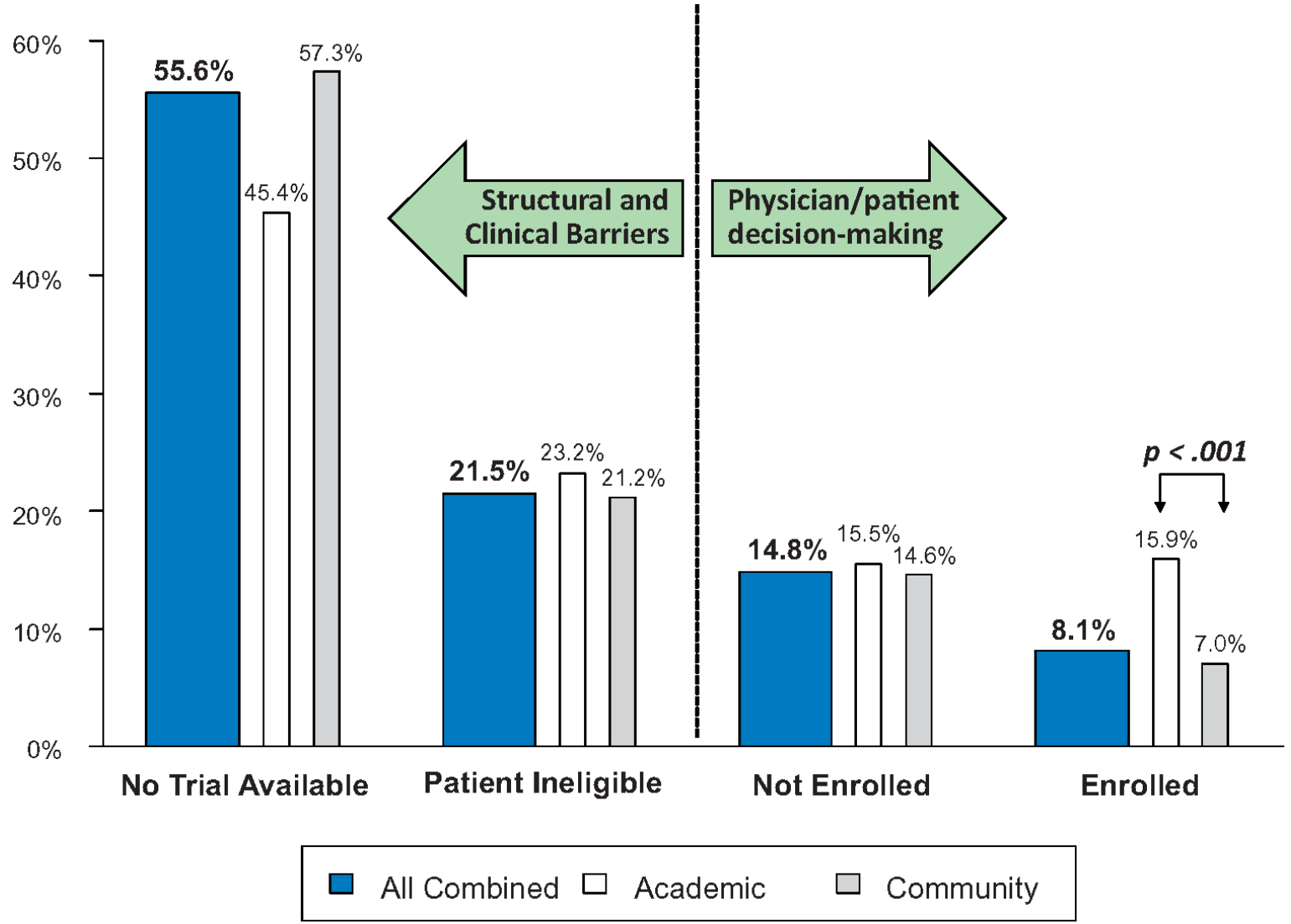
- *13 studies with n=8,883 patients*
- *9 studies focused on academic care settings*
- *4 studies focused on community care settings*

** Unger et al., JNCI, 2019*



Systematic Review and Meta-Analysis: Results

Figure 3. Magnitude of barriers for each domain for academic sites, community sites, and all sites combined*



** Unger et al., JNCI, 2019*

Discussion

- This was the first effort to systematically both define and quantify domains of clinical trial barriers
- Results reveal that more than half (55.6%) of all cancer patients did not participate in trials because no trial was available
- When a trial was available, an additional 21.5% were ineligible.
- **These structural and clinical factors are the reasons more than three of four patients (77.1%) did not participate.**
- In contrast, patient-related factors and patient choice comprised only a small portion of barriers to trial participation overall
  - When eligible patients are offered a trial, they agree to participate half the time

Discussion

- The overall trial participation rate was 8.1%, much higher than the 2%–3% rates typically assumed
  - Likely due to the contributions of industry-sponsored trials (2:1)
- But the rate remains low with numerous adverse consequences:
  - Trials often fail to complete due to poor accrual
  - Trials take a very long time to complete, generating less timely and less influential results

Conclusions

- Enormous need to address structural and clinical barriers to trial participation
- Focus should be to improve access to available trials:
  - Improved outreach to community oncologists and their patients
  - Improved use of portals to identify recruiting trials (i.e. cancer.gov)
  - Providing patients of all income levels the resources to travel to participate in available trials
- Only by addressing structural and clinical barriers will the participation rate in cancer treatment trials be increased in a substantial way