



UNIVERSITY *of* MARYLAND  
SCHOOL OF MEDICINE

# Selection of comparators and outcomes

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Clinical Research

# Disclosures

- PCORI Patient Engagement Advisory Board Member (2015-Present)
- Funding:
  - American Society of Radiation Oncology
  - PCORI
  - Keep Punching Brain Tumor Foundation

# Objectives

- Describe the importance of patient engagement in selecting study comparators and outcomes
- Describe methods for effective patient engagement in selecting comparators and outcomes
- Discuss a real-world example of patient engagement in pragmatic randomized clinical trial
- Understand the patient perspective on choosing comparators and outcomes
- Understand the industry perspective on patient engagement

# University of Maryland **10-STEP FRAMEWORK FOR CONTINUOUS PATIENT ENGAGEMENT IN RESEARCH\***

## A. PLANNING RESEARCH

1. Topic Solicitation
2. Prioritization
3. Framing the Question

## B. DOING IT

4. Selection of Comparators and Outcomes
5. Creation of Conceptual Framework
6. Analysis Plan
7. Data Collection

## C. DELIVERING SOLUTIONS

8. Reviewing & Interpreting Results
9. Translation
10. Dissemination

Most crucial part of study design?



Most crucial step for meaningful patient engagement



\*Based on: Mullins CD, Abdulhalim AM, Lavalley DC. Continuous Patient Engagement in Comparative Effectiveness Research. JAMA 2012; 307(15): 1587-8.

# Benefits of patient engagement: Step 4

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## Patient interest in study comparators

- Are we addressing real-world decisions?
- Improved enrollment

## Patient interest in outcomes

- Answering questions that patients will care about → practice changing

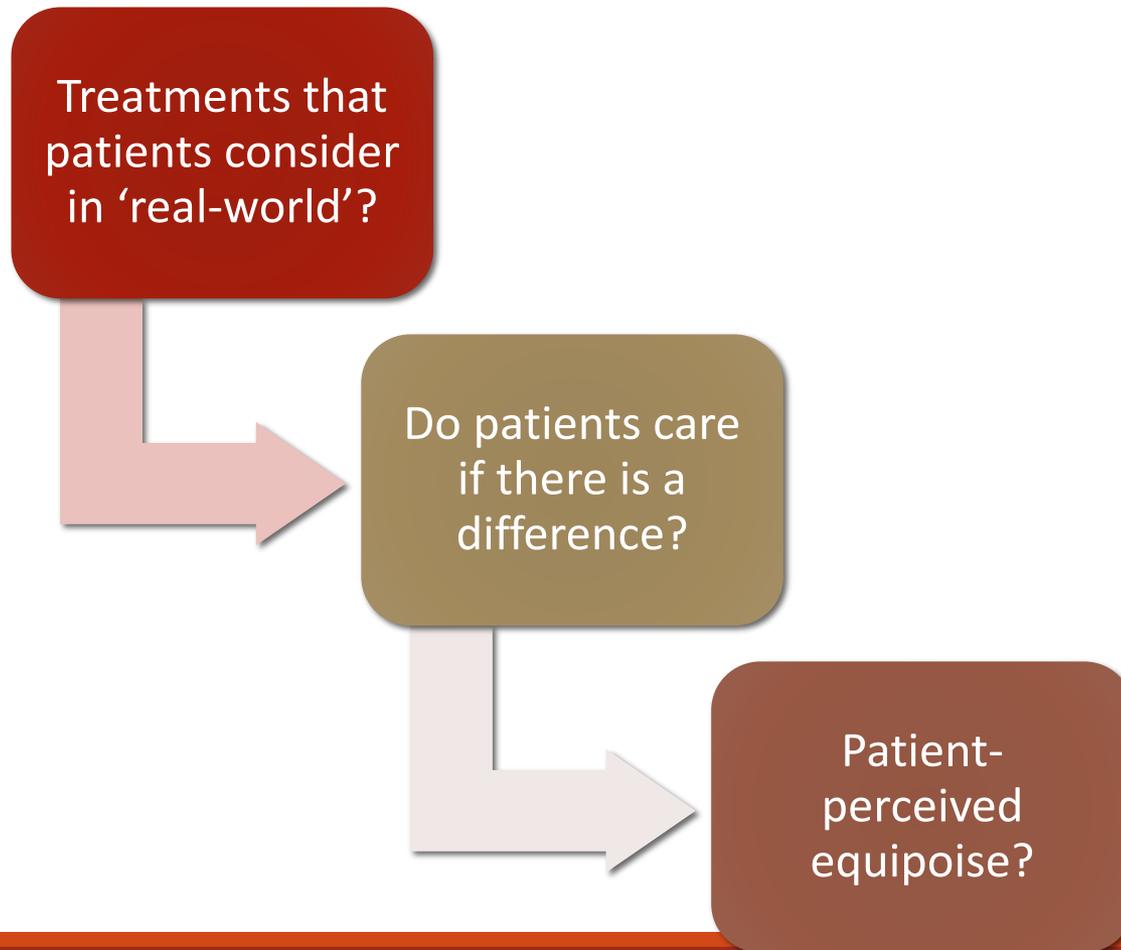
# Choosing comparators for a CER study

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# Choosing comparators for a CER study

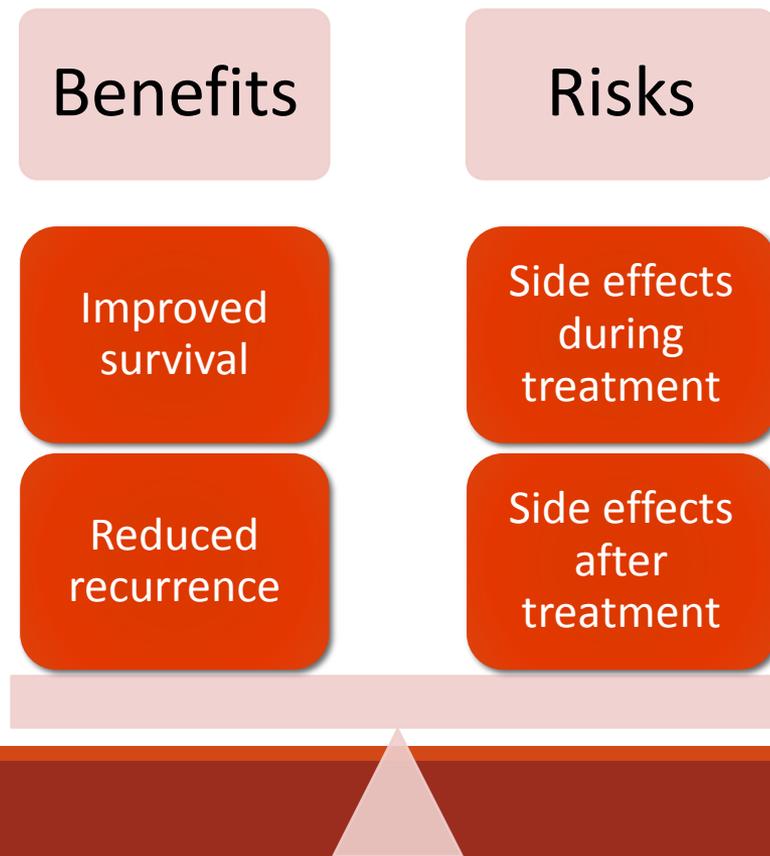
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# Example: Breast Cancer

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Radiation therapy is a standard part of treatment for patients with localized breast cancer



# Real world patient dilemma: Two treatment options

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## Patient Stories:

Twenty-nine year old patient diagnosed with locally-advanced breast cancer after palpating a mass in her left breast

- Surgery: Mastectomy and lymph node dissection
- Chemotherapy: 6 months of chemotherapy
  - Improve chances of cure but potential damage to heart
- Referred for radiation therapy to her chest wall and lymph nodes

# Real world patient dilemma: Two treatment options

**PHotons**

FDA-approved

Currently used to  
treat breast  
cancer

Long-term data;  
side effects well-  
documented

Widely available

**PRotons**

FDA-approved

Currently used to  
treatment breast  
cancer

Not as well  
studied, but  
thought to have  
less side effects

Requires travel

# Real world patient dilemma: Two treatment options

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Patient interested in proton beam therapy due to possibility of reduced side effects

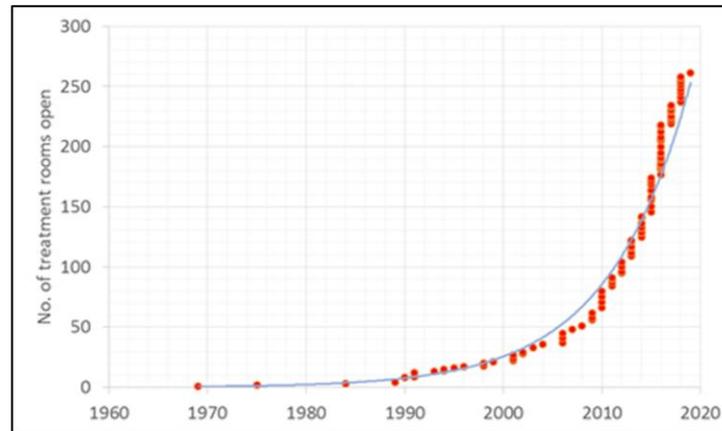
- Radiation oncologist #1: You should receive Photon therapy
- Radiation oncologist #2: You are a good candidate for protons due to young age and potential dose to heart
- Radiation oncologist #3: ME

**Which treatment is better for me and why??**

# Impact of NO patient engagement

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- Physicians did not think that a study comparing the two treatments was necessary
  - Proton therapy research funded since 1961 by NCI
  - Little comparative data



# Impact of NO patient engagement

OPINIONATOR

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By EZEKIEL J. EMANUEL and STEVEN D. PEARSON

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*Do patients agree with the comparators for this study?*

*Will any patient agree to go on a randomized study?*

*What are the questions that patients want answered?*



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# Patient engagement

- Patient advisors
  - Individual interviews with current and former breast cancer patients
- Patient focus groups
  - Cancer center support groups
- Patient Advocacy Groups
  - Susan G. Komen, NCCS, Living Beyond Breast Cancer

# Patient engagement

- Patient perspective
  - “I would motivated to participate in such a study”
    - Patient interviews, patient advocates, focus groups

Clinical Investigation: Genitourinary Cancer

## Prospective Preference Assessment of Patients' Willingness to Participate in a Randomized Controlled Trial of Intensity-Modulated Radiotherapy Versus Proton Therapy for Localized Prostate Cancer

Anand Shah, M.D., M.P.H.,\* Jason A. Efstathiou, M.D., D.Phil.,<sup>||</sup> Jonathan J. Paly, B.S.,<sup>||</sup> Scott D. Halpern, M.D., Ph.D., M.B.E.,<sup>†,‡,§,¶</sup> Deborah W. Bruner, Ph.D., R.N.,\*\*  
John P. Christodouleas, M.D., M.P.H.,\* John J. Coen, M.D.,<sup>||</sup>  
Curtiland Deville, Jr., M.D.,\* Neha Vapiwala, M.D.,\* William U. Shipley, M.D.,<sup>||</sup>  
Anthony L. Zietman, M.D.,<sup>||</sup> Stephen M. Hahn, M.D.,\* and Justin E. Bekelman, M.D.\*<sup>¶</sup>

\*Department of Radiation Oncology, <sup>†</sup>Department of Medicine, <sup>‡</sup>Center for Clinical Epidemiology and Biostatistics, <sup>§</sup>Center for Bioethics, and <sup>¶</sup>Leonard Davis Institute of Health Economics, University of Pennsylvania, Philadelphia, PA; <sup>||</sup>Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA; and \*\*Winship Cancer Institute, Emory University, Atlanta, GA

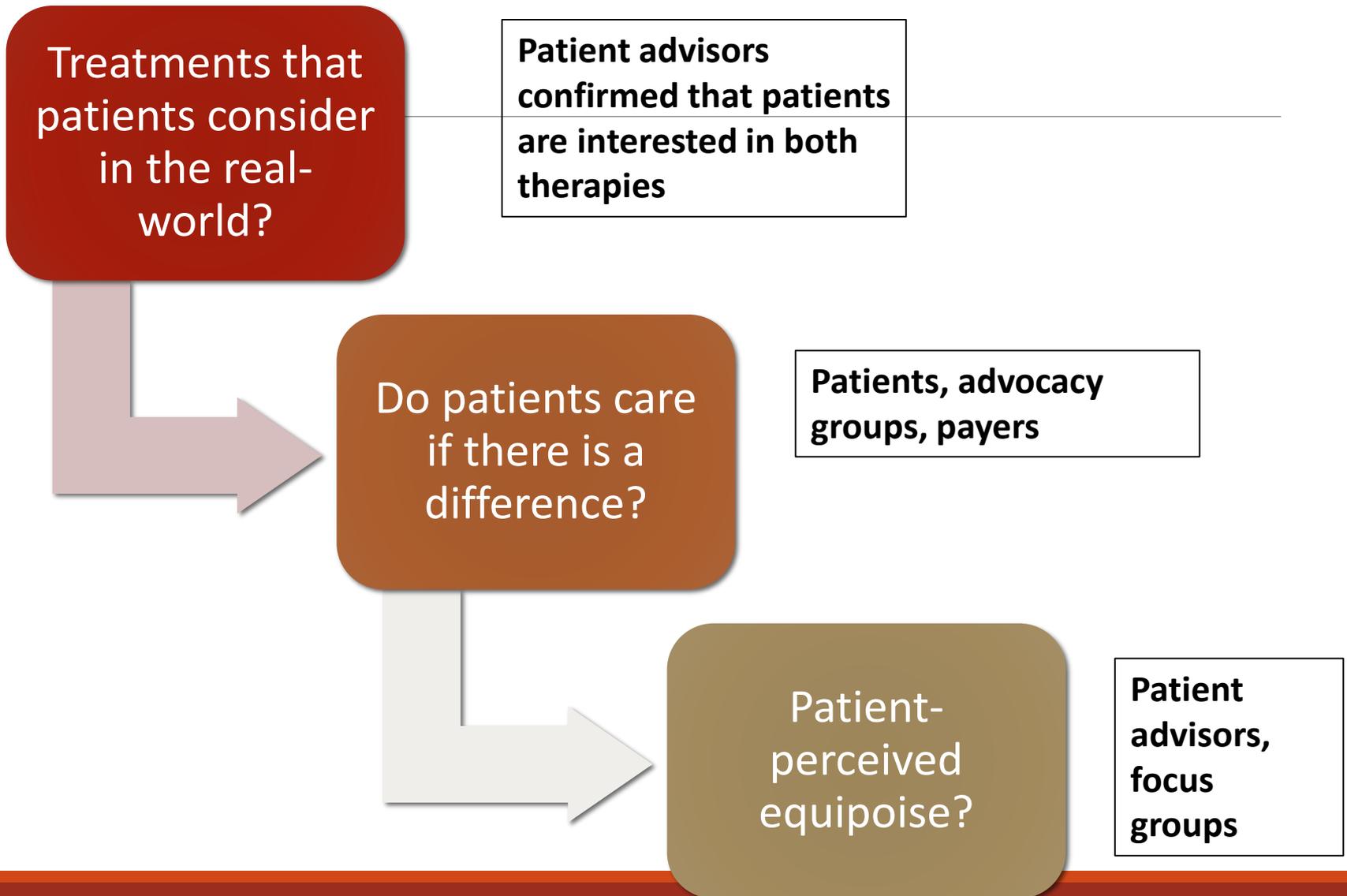
**59% of patients stated they would either “definitely” or “probably” participate in a RCT**

# Choosing comparators for a CER study

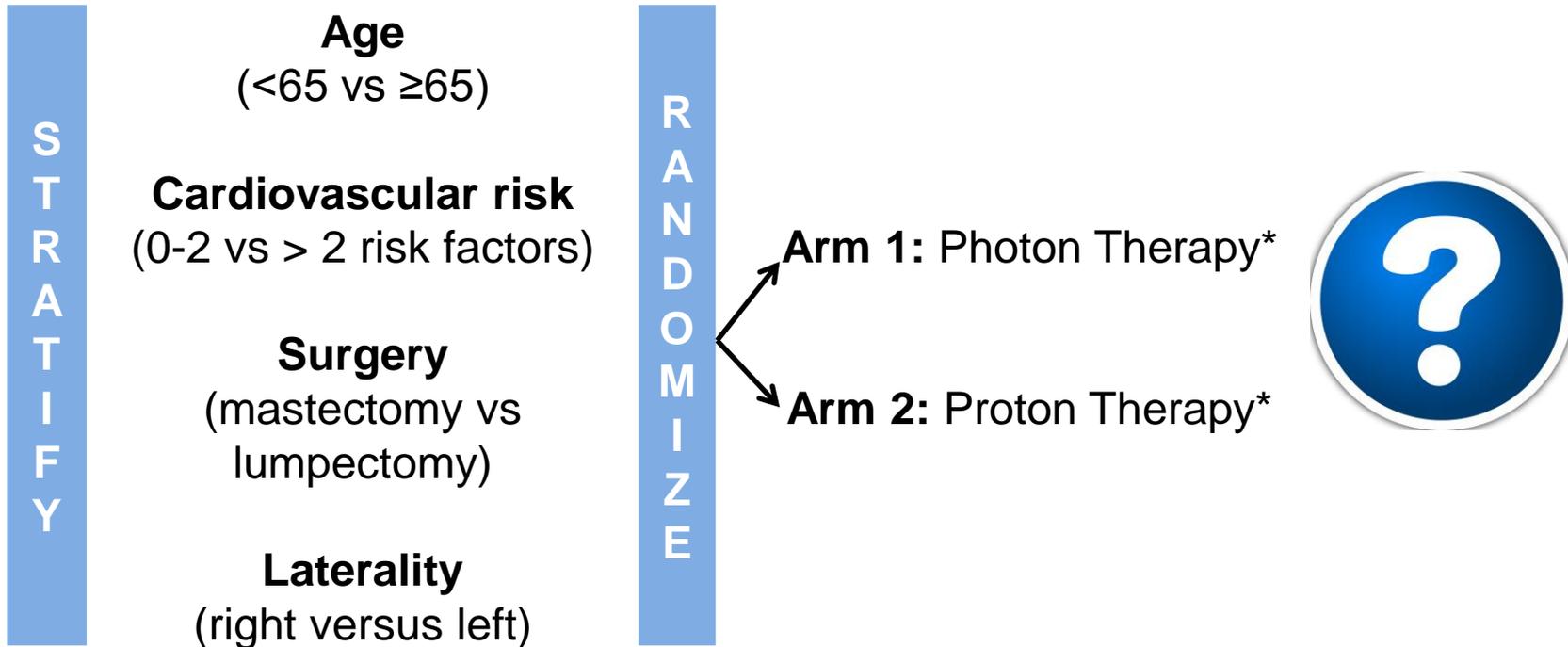
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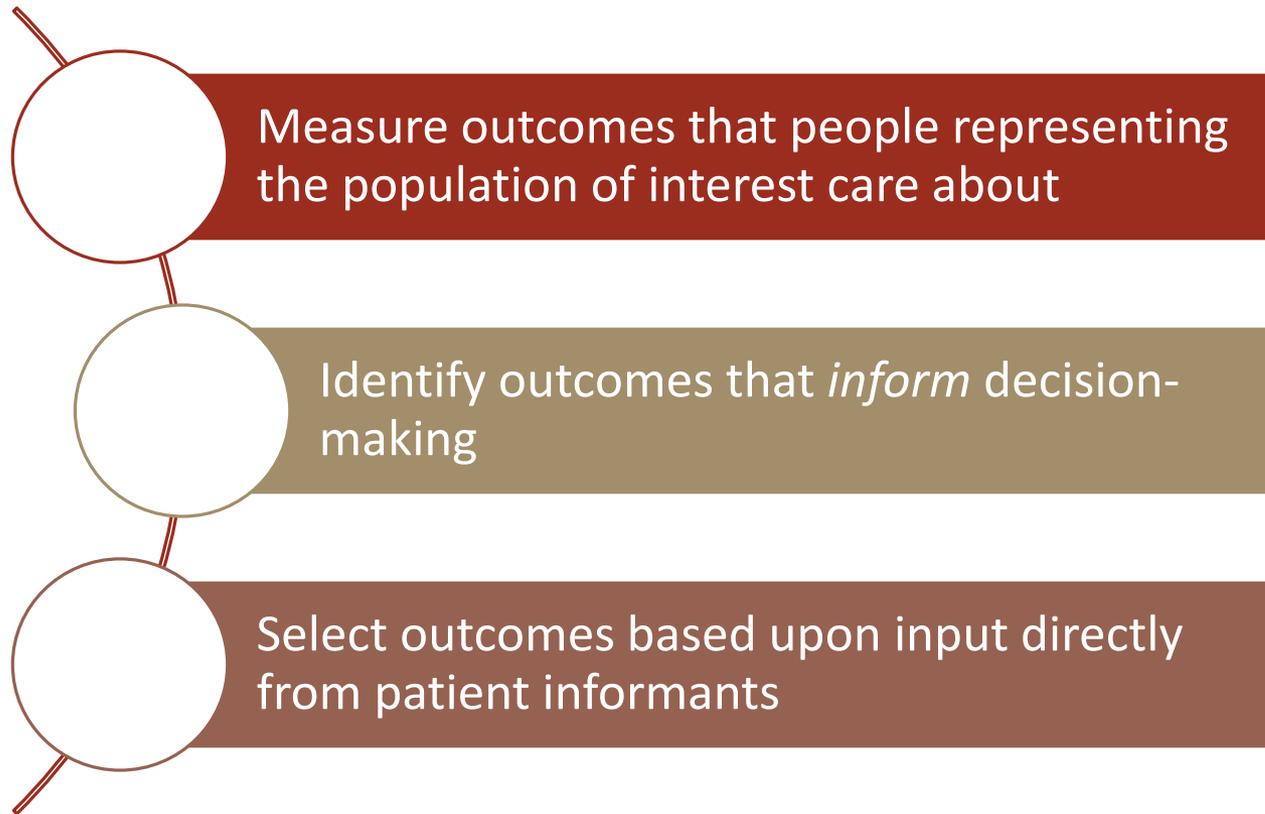


# Breast Cancer Example



# PCOR Crossing Cutting Standards: Choosing Outcomes

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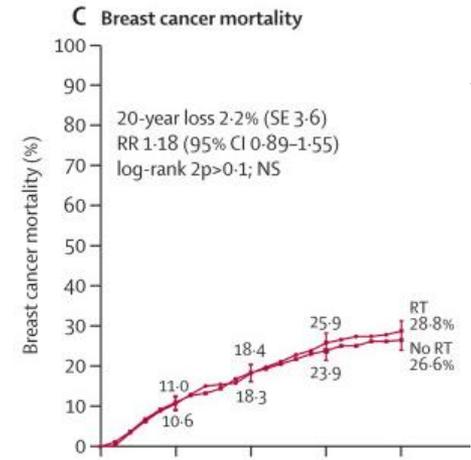
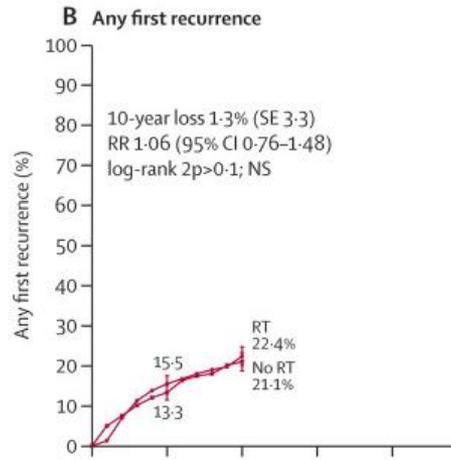
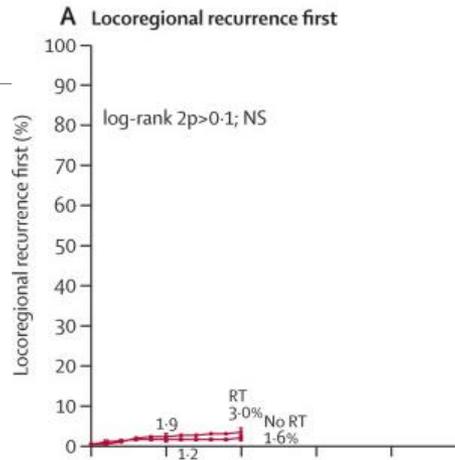


# Patient-reported outcomes

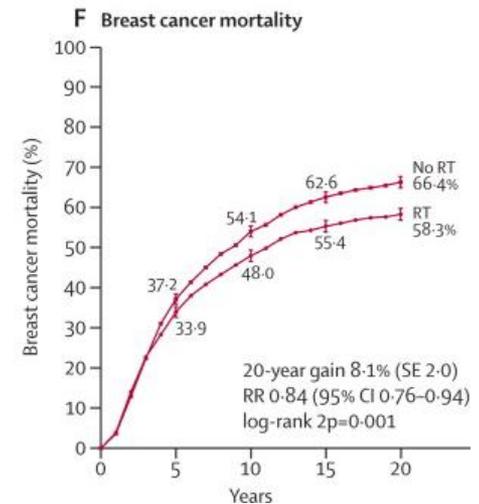
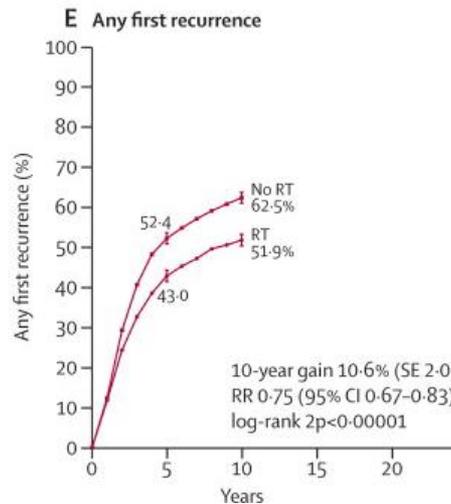
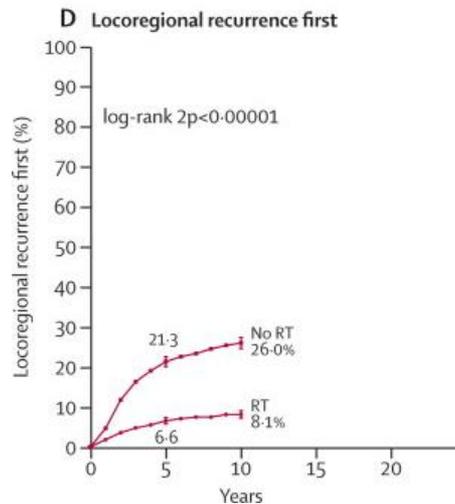
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When patients or people at risk of a condition are the best source of information regarding outcomes of interest, then the study should employ patient-reported outcome (PRO) measures

# Choice of outcome: Prior to engagement



3131 pN+ women with Mast+AD



# Patient Feedback

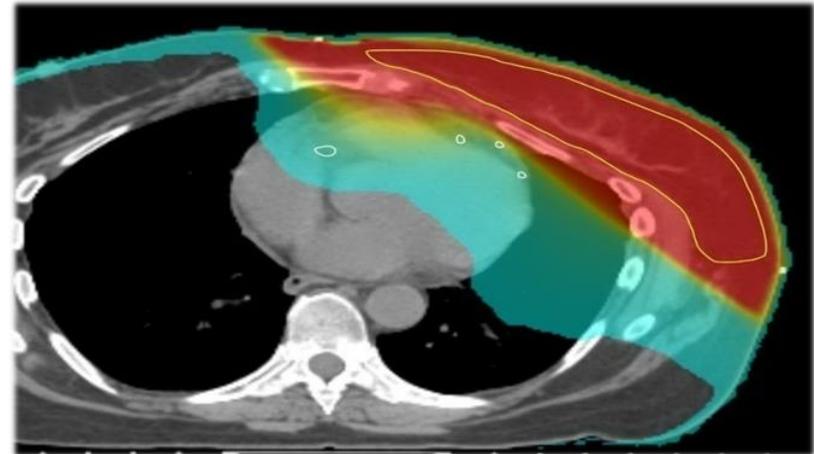
- Direct patient feedback
    - 10 conference calls with individual patient advisors
    - Focus groups with patient and patient advocates
      - Engage with patients who are outside of your patient advisory group
    - Multi-stakeholder meeting/conference call at NCI
      - Patients
      - Patient Advocates
      - Researchers
      - Payers
- } Engaging together

# Patient Viewpoints: Outcomes

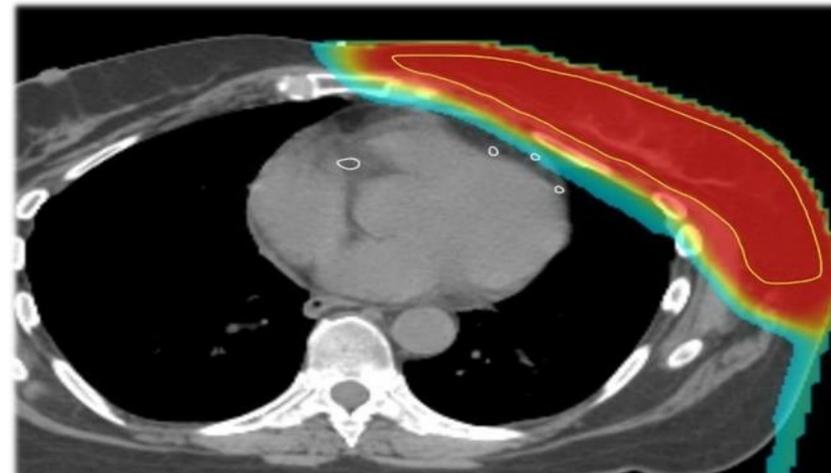
*I would be more motivated to participate in a big study if I knew we would learn whether proton therapy could avoid causing problems with my heart. That would help me weigh whether the long-term benefits of radiation outweigh the long-term side effects*

*I don't only want to know about dying from heart problems from the radiation. I want to know about the heart problems that I would have to live with and the impact on my quality of life after cancer treatment*

## Photon Radiation Therapy



## Proton Therapy



# Patient Viewpoints: Outcomes

*I would be more motivated to participate in a big study if I knew we would learn whether proton therapy could avoid causing problems with my heart. That would help me weigh whether the long-term benefits of radiation outweigh the long-term side effects*

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**Patient identified outcome of interest:**

Major cardiovascular events following Protons and Photons

# Patient Viewpoints: Outcomes

*I want to know whether a new therapy might reduce my cough or the feeling of the chest tightness after radiation*

*I would want to know if proton therapy will improve the skin burn or my tiredness*

*Would proton therapy allow me to get back to doing the things I enjoy sooner*



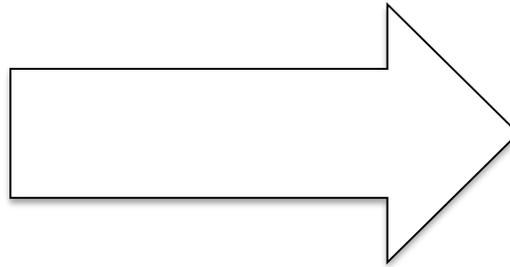
## **Patient identified outcome of interest:**

- Treatment toxicity (patient-reported outcome)
  - Lung, chest, skin, fatigue
- Quality-of-life

# Patient Viewpoints: Outcomes

*Even if I knew that a bus wasn't going to kill me if I were hit, I still want to look both ways before crossing the street*

*Learning more about the chances of heart problems allows me to make more informed decisions. I might decide to stop smoking or alter some other behavior*



## **Patient identified outcome of interest:**

To develop predictive models to examine the association of radiation dose distribution to heart and MCE and HRQOL outcomes

# Final study outcomes

## Primary

- To assess the effectiveness of proton vs. photon therapy in reducing major cardiovascular events

## Secondary

- To assess the non-inferiority of proton vs. photon therapy in reducing any recurrence
- To assess the effectiveness of proton vs. photon therapy in improving patient-reported body image and function, fatigue and other measures of HRQOL
- To develop predictive models to examine the association of radiation dose distribution to heart and MCE and HRQOL outcomes

Outcomes also discussed with payers, who agreed with study measures

# Pre-patient engagement

OPINIONATOR

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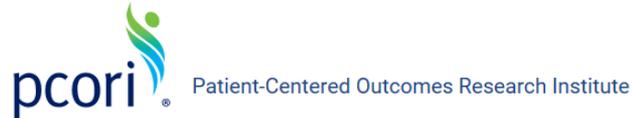
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# Post-patient Engagement



## Pragmatic Randomized Trial of Proton vs. Photon Therapy for Patients with Non-Metastatic Breast Cancer Receiving Comprehensive Nodal Radiation: A Radiotherapy Comparative Effectiveness (RADCOMP) Trial



**Principal Investigator**  
Justin Bekelman, MD

**Organization**  
University of Pennsylvania

**State**  
Pennsylvania

**Year Awarded**  
2015

**Primary Condition/Disease**  
Cancer

**Funding Announcement**  
Pragmatic Clinical Studies and Large Simple Trials to Evaluate Patient-Centered Outcomes

**Project Budget**  
\$11,830,530

**Project Period**  
60 months

**Project Status**  
Awarded; In progress-Recruiting

# Real world patient dilemma: Two treatment options

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## Patient Stories:

Twenty-nine year old patient diagnosed with locally-advanced breast cancer after palpating a mass in her left breast

- Surgery: Mastectomy and lymph node dissection
- Chemotherapy: 6 months of chemotherapy
  - Improve chances of cure but potential damage to heart
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# Real world patient dilemma: Two treatment options

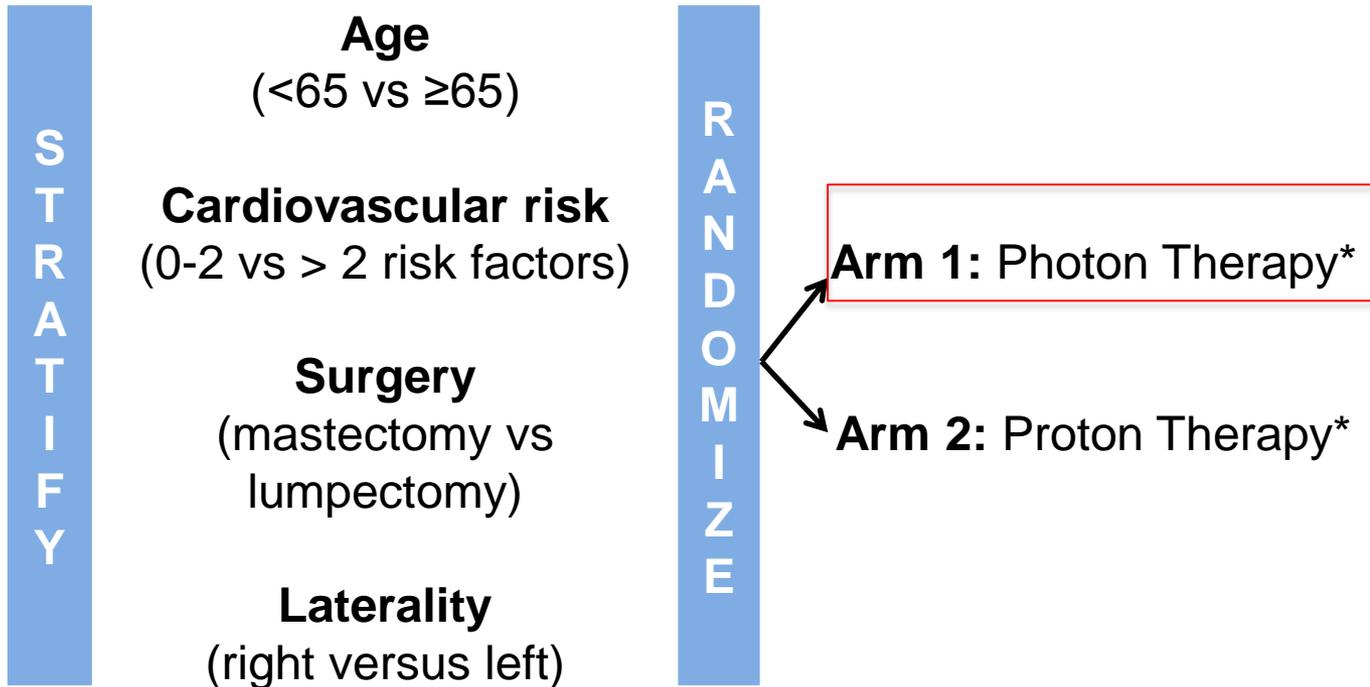
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Patient interested in proton beam therapy due to possibility of reduced side effects

- Radiation oncologist #1: No role for protons
- Radiation oncologist #2: You are a good candidate for protons due to young age and potential dose to heart
- Radiation oncologist #3: ME

**Which treatment is better for me and why??**

# Breast Cancer Example



# Patient Perspective



Cynthia Chauhan

Mayo Clinic

Patient Advisor, RADCOMP Study



Lori Abrams

Director, Diversity & Patient  
Engagement at Bristol-Myers Squibb,  
Princeton, New Jersey