Translational Products for Systematic Reviews: A Stakeholder Workshop

Welcome and Purpose of the Workshop

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The Need for Evidence in Decision Making

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Chief Engagement and Dissemination Officer and
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PCORI's Research Agenda is Driven by Stakeholders' Needs

"The purpose of the Institute is to **assist patients, clinicians, purchasers, and policy-makers in making informed health decisions** by advancing the quality and relevance of evidence concerning the manner in which diseases, disorders, and other health conditions can effectively and appropriately be prevented, diagnosed, treated, monitored, and managed **through research and evidence synthesis...**

The Institute shall **identify national priorities** for research, taking into account factors of disease incidence, prevalence, and burden in the United States (with emphasis on chronic conditions), **gaps in evidence in terms of clinical outcomes, practice variations and health disparities in terms of delivery and outcomes of care**, the potential for new evidence to improve patient health, well-being, and the quality of care…

--from PCORI's authorizing legislation

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What Does the Game of Baseball Have to do With the Use of Evidence in Decision Making?

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Some Examples of What Decision Makers Want to Know

- *Can* it work?
- *Will* it work?
  - For me or my family?
  - For this patient?
  - In this setting?
- Is it *worth* it?
  - Do benefits outweigh harms?
  - How big are the benefits?
  - Does it offer important advantages over existing alternatives?

adapted from ***Brian Haynes, ACP Journal Club***

Why is Translation of Findings Needed?

"Evidence may be necessary, but it is certainly not sufficient. The findings of research need to be translated into information that is useful for each health care decision maker."

Eisenberg, JM. JAMA 1999; 282:1865-9.

Consequences of Not Having Access to Best Available Evidence

- Decisions are made without knowing what is most likely to be beneficial or harmful
  - Choices may be made on factors that are not related to improved health outcomes or preferences
  - Health outcomes are less likely to be consistent and care may be less safe
  - Patients and their clinicians are not able to adequately assess their treatment options inline with their values and preferences

Thank You for Sharing Your Insights!

9:10 AM **Evidence and Its Translation for Decision Making**

The Need for Evidence in Decision Making

Jean Slutsky, PA, MSPH

Systematic Review: What Is Its Role?

Jennifer Croswell, MD, MPH, Senior Program Officer, Office of the Chief Science Officer

The Elements of Information Products

Bill Lawrence, MD, MS, Senior Program Officer, Communication and Dissemination Research

Systematic Evidence Review: Its Role In Decision Making

Jennifer Croswell, MD, MPH

Senior Program Officer, Office of the Chief Science Officer

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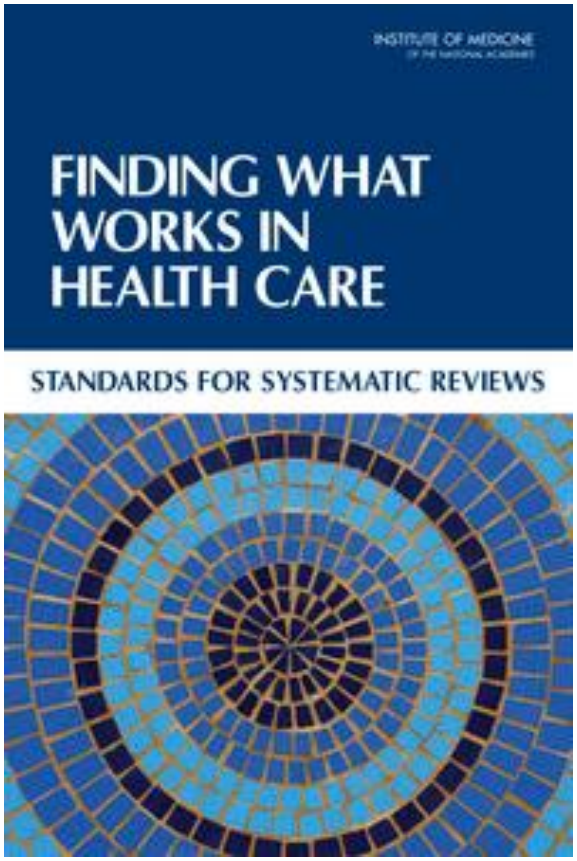
Systematic Evidence Review: What Is It?

"A scientific investigation that focuses on a specific clinical question and uses explicit, planned scientific methods to systematically identify, select, assess, and summarize the findings of similar but separate studies, in order to make clear what is known and not known."

--Institute of Medicine
Standards for Systematic Reviews
2011



Systematic Evidence Review: What Is It?

- An **objective**, **transparent** way to locate, critically appraise, and summarize all evidence relevant to a particular question
- **Comprehensive**, **rigorous**, and **reproducible**
- Stands in **contrast** to the traditional *narrative review*, which is a selective citation of findings supporting an expert's opinion about the state of science for a topic

Systematic Evidence Review: Why Do It?

- Gain **power** and **precision** from combining the results of multiple studies addressing the same active treatments and comparisons
  - One study rarely produces landmark results or is definitive
  - Knowledge develops through a series of experiments and their cumulative impact on understanding

- Obtain a summary of "**what we know**" (consistent conclusions and magnitude of effect) and "**how surely we know it**" (our certainty that conclusions are unlikely to change with future research)

- Explain **differences** (**heterogeneity**) **in findings** across similarly designed active treatment-comparison studies

Systematic Evidence Review: Why Do It?

- The **most reliable way to identify benefits and harms** associated with various treatment options

- Can be essential for:
  - **Clinicians** striving to integrate research findings into their practices
  - **Patients** trying to make well-informed choices about their care
  - **Professional medical societies** and other organizations developing clinical practice guidelines
  - **Payers** making medical coverage decisions

Systematic Evidence Review: Why Do It?

- Can also be used to set **research agendas** by highlighting gaps in evidence

- PCORI **requires** the use of systematic reviews to identify gaps to support proposed research concepts

Systematic Evidence Review: PCORI Standards

- **PCORI has adopted the IOM Standards for Systematic Reviews into its own Methodology Standards**:
  1. Formulate the topic, develop and peer-review the protocol, and publish the final protocol with timely amendments as warranted
  2. Conduct and document a comprehensive, systematic search for evidence, with attention to addressing potential sources of bias in research results reporting
  3. For individual studies:
     1) Assess and document assessment of individual studies for inclusion/exclusion according to protocol
     2) Conduct and document critical appraisal of individual studies for bias, relevance, and fidelity of interventions using pre-specified criteria

Systematic Evidence Review: PCORI Standards

- **PCORI has adopted the IOM Standards for Systematic Reviews into its own Methodology Standards**:
  4. Use standard and rigorous data collection and management approaches
  5. Synthesize the body of evidence qualitatively and, if warranted, quantitatively, using pre-specified methods
  6. Evaluate the body of evidence on characteristics related to overall quality and confidence in the estimates of effect on pre-specified outcomes
  7. Report the results using a structured format, peer review the draft report (including public comment period), and publish the final report to allow free public access

The Elements of Information Products

Bill Lawrence, MD, MS

Senior Program Officer, Communication and Dissemination Research

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Overview

- Introduction: Informing decision making
- A brief summary: The **format** of information products (the "how")
- Focus: **The content** of information products (the "what")
- Your experiences

PCORI Mission Statement

PCORI helps people make informed healthcare decisions, and improves healthcare delivery and outcomes, by producing and promoting high-integrity, evidence-based information that comes from research guided by patients, caregivers, and the broader healthcare community.

Introduction: Informing Decision Making

Producing information is not enough.

- Information itself is of little use unless:
  - It reaches those who need it
  - It is clear and comprehensible
- PCORI is interested in helping people use research evidence to make better informed decisions
- Today, we'll discuss how PCORI can best assemble this information to include the evidence content that stakeholders need in a usable format

Our Approach

Our process for determining the content and format elements of information presentation:

- Literature review: systematic reviews on the barriers and facilitators to uptake of evidence synthesis products
- Environmental scan of existing evidence synthesis products
- Literature review + environmental scan = framework on the following slides

Format: Facilitators to Uptake

- How to best present information?
  - Make it short!
  - Be comprehensive
  - Graphics and tables
  - Plain language
  - Address nuance necessary to make decisions
  - "Bottom line" explicit

- Often a tension between these facilitators

Content: Element Types

Our framework:

- Background
- Research findings on benefits and harms
- Current recommendations
- Strength of evidence
- Research gaps (or remaining uncertainty)
- Risk/Probability
- Personal preference
- Other patient considerations
- Testimonials and narratives
- Action steps

Background

Key Facts

- There has been a substantial amount of research on supplements of omega-3s, particularly the types of omega-3s found in seafood and fish oil, and heart disease. The findings of individual studies have been inconsistent. In 2012, two combined analyses of the results of these studies did not find convincing evidence that these omega-3s protect against heart disease.
- There is some evidence that omega-3s of the types found in seafood and fish oil may be modestly helpful in relieving symptoms in rheumatoid arthritis. For most other conditions for which omega-3s have been studied, definitive conclusions cannot yet be reached, or studies have not shown omega-3s to be beneficial.
- Omega-3 supplements may interact with drugs that affect blood clotting.
- It is uncertain whether people with fish or shellfish allergies can safely consume fish oil supplements.
- Fish liver oils (which are not the same as fish oils) contain vitamins A and D as well as omega-3 fatty acids; these vitamins can be toxic in high doses.
- Tell all your health care providers about any complementary or integrative health approaches you use. Give them a full picture of what you do to manage your health. This will help ensure coordinated and safe care.

National Institutes of Health, 2015

Background

What is human papillomavirus (HPV)?

Human papillomavirus (HPV) is a ***virus***. Like all viruses, HPV causes infection by entering ***cells***. Once inside a cell, HPV takes control of the cell's internal machinery and uses it to make copies of itself. These copies then infect other nearby cells.

How many types of HPV are there?

There are more than 100 types of HPV. About 40 types infect the genital area of men and women and are spread by skin-to-skin contact during vaginal, anal, or oral sex. Genital HPV infection can occur even if you do not have ***sexual intercourse***.

How common is HPV infection?

HPV infection is the most common ***sexually transmitted infection (STI)*** in the United States. Almost everyone who is sexually active will get an HPV infection at some point during their life.

What are the signs and symptoms of HPV infection?

Like many other STIs, genital HPV infection often has no signs or symptoms. The infected person usually is not aware that he or she has been infected and can unknowingly pass the infection to others.

What diseases are caused by HPV?

HPV can cause the following diseases:

- Genital warts—About a dozen types of HPV cause genital warts. These types are called "low-risk types." Most cases of genital warts are caused by just two low-risk types of HPV: 1) type 6 and 2) type 11. Genital warts are growths that can appear on the outside or inside of the ***vagina*** or on the ***penis*** and can spread to nearby skin. Genital warts also can grow around the ***anus***, on the ***vulva***, or on the ***cervix***. Genital warts are not cancer and do not turn into cancer. Warts can be

American College of Obstetricians and Gynecologists, 2015

Research Findings

Findings:

- Core-needle biopsies and surgical biopsies both work well for finding breast cancer. Out of every 100 women who have breast cancer:
  - Surgical biopsies will find 98 to 99 of those cancers;
  - Ultrasound or stereotactic-guided core-needle biopsies will find 97 to 99 of those cancers; and
  - Freehand core-needle biopsies will find 86 of those cancers.

- Side effects, such as bleeding, severe bruising and infection are rare with core-needle biopsy, affecting fewer than 1 out of 100 women.

- Side effects are more common with surgical biopsy:
  - Up to 10 out of 100 women get severe bruising;
  - About 5 out of 100 women get an infection; and
  - Women who have a surgical biopsy are more likely to need prescription pain medication after the procedure.

- There is not enough evidence to determine the accuracy of MRI-guided core-needle biopsies.

- Core-needle breast biopsies may miss areas of invasive cancer in specimens in which the lesion is predominantly noninvasive. Research studies support the widespread clinical practice of performing open surgical biopsy on all women whose core-needle biopsy is read as ductal carcinoma in situ (DCIS) or atypical ductal hyperplasia (ADH).

Agency for Healthcare Research and Quality, 2016

Research Findings

What are the possible benefits and harms of lung cancer screening with LDCT?*

BENEFIT: Greater chance of not dying from lung cancer

- If 1,000 people are not screened with LDCT for lung cancer, **21 will die from lung cancer**.
- If 1,000 people are screened with LDCT once a year for 3 years, **18 will die from lung cancer**.
- This means that with LDCT screening, **3 fewer people will die from lung cancer**.

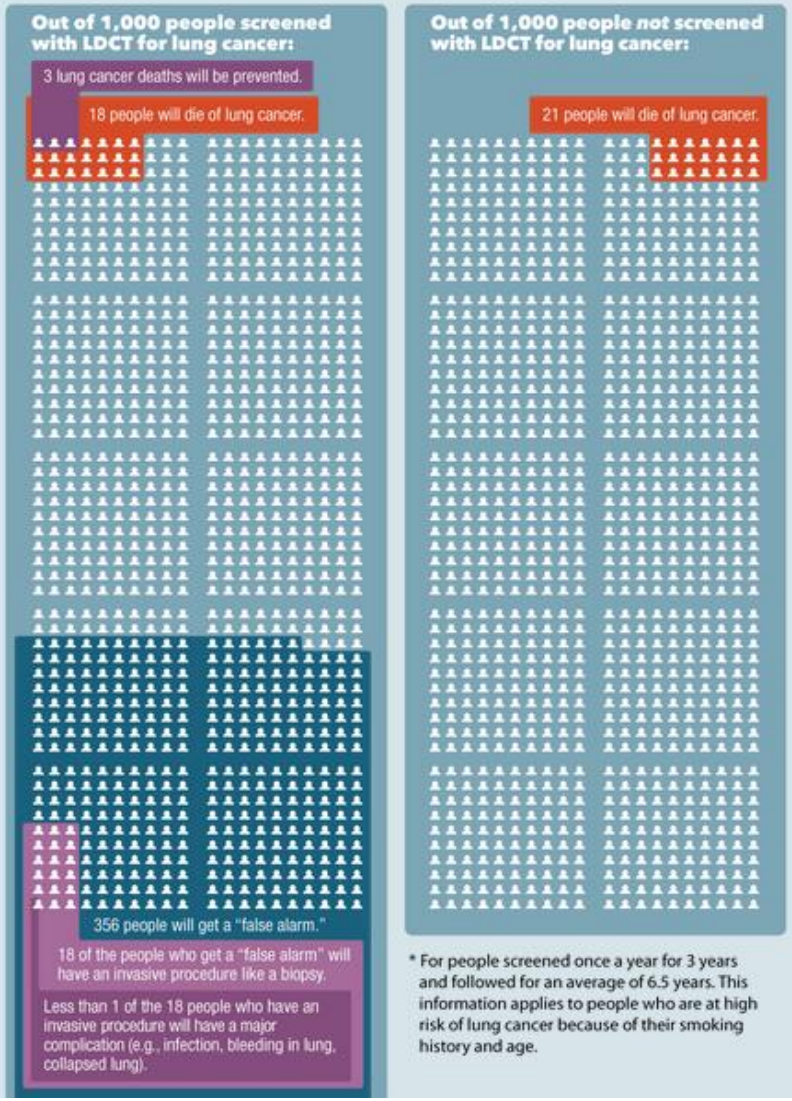
BENEFIT: Greater chance of not dying from any cause (not just lung cancer)

- If 1,000 people are not screened with LDCT for lung cancer, **75 will die from any cause**.
- If 1,000 people are screened with LDCT once a year for 3 years, **70 will die from any cause**.
- This means that with LDCT screening, **5 fewer people will die from all causes**.

HARM: False alarms and unneeded additional testing

A false alarm happens when a person has a positive screening test but does not actually have lung cancer.

- If 1,000 people are screened every year for 3 years, about **356 will have a false alarm**.
- Of these 356 people with a false alarm, **18 will have an invasive procedure** such as a biopsy (a tiny piece of lung tissue is removed to test for cancer).



Agency for Healthcare Research and Quality, 2016

Current Recommendations

Current Recommendations

Hormone therapy can help relieve some of the symptoms that affect women at menopause. However, it is important to weigh the benefits and the risks for your individual situation. Before making a decision about hormone therapy, talk to your health care provider about what may work best for you based on your symptoms and your personal and family medical history.

In general, hormone therapy use should be limited to the treatment of menopausal symptoms at the lowest effective dose for the shortest amount of time possible. Continued use should be reevaluated on a yearly basis. Some women may require longer therapy because of persistent symptoms.

American College of Obstetricians and Gynecologists, 2015

Current Recommendations

1. The Task Force recommends initiating low-dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer (CRC) in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years. **Grade B**

2. The decision to initiate low-dose aspirin for the primary prevention of CVD and CRC in adults aged 60 to 69 years who have a greater than 10% 10-year CVD risk should be an individual one. Persons who are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years are more likely to benefit. Persons who place a higher value on the potential benefits than the potential harms may choose to initiate low-dose aspirin. **Grade C**

3. The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults younger than age 50 years. **I Statement**

4. The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults age 70 years and older. **I Statement**

U.S. Preventive Services Task Force, 2015

Strength of Evidence

Clinical Bottom Line

Summary of Key Findings and Strength of Evidence for the Benefits and Adverse Effects of Radiotherapy for Head and Neck Cancer

Outcome	3DCRT vs. IMRT	3DCRT or IMRT vs. SBRT	3DCRT or IMRT vs. PBT
Tumor control and survival	○○○	○○○	○○○
Grade ≥2 late xerostomia*	Significantly reduced incidence with IMRT (●●●)	○○○	○○○
Quality of life related to late xerostomia	Improved with IMRT (●●○)	○○○	○○○
Other RT-associated grade >2 toxicities (e.g., acute or late dysphagia, salivary gland dysfunction, swallowing dysfunction)	○○○	○○○	○○○
Effects of specific patient and tumor characteristics on the relative effectiveness of RT modalities	○○○	○○○	○○○
Effects of user experience, treatment planning, and treatment delivery on the relative effectiveness of RT modalities	○○○	○○○	○○○

Strength of Evidence Scale

- High: ●●● High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
- Moderate: ●●○ Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
- Low: ●○○ Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.
- Insufficient: ○○○ Evidence either is unavailable or does not permit a conclusion.

Agency for Healthcare Research and Quality, 2015

Research Gaps

Gaps in Knowledge and Limitations of the Evidence Base

The following gaps in research and/or other issues were identified by the updated review:

- Because of insufficient evidence, high-quality studies are needed to determine the comparative effectiveness of IMRT, 3DCRT, SBRT, and PBT:
  - In achieving tumor control and improving patient survival
  - In reducing adverse events (e.g., dysphagia) and improving quality of life
  - In understanding how outcomes are affected by the characteristics of the tumor, the patient, and the physician/RT team (e.g., experience), or by radiation treatment planning (e.g., target volume delineation, dosimetric parameters), or by systemic therapy (e.g., chemotherapy)

An important area of investigation is the potential impact of human papillomavirus-positive tumors on oncologic outcomes. Studies are needed to identify reduced-intensity RT regimens that still yield satisfactory oncologic outcomes in this patient population.

Well-designed, multicenter, prospective observational studies—where randomized trials are not practical or advisable—would improve the usefulness and generalizability of the evidence.

The body of evidence would be improved by studies:

- Employing standardized patient selection to assure comparability of patients and to minimize bias
- Using standardized intervention protocols
- Employing prespecified follow-up criteria and methods

Agency for Healthcare Research and Quality, 2015

Risk

Surgery for plantar fasciitis has risks.

In this surgery the plantar fascia is cut at the heel. Often, this does not relieve symptoms. Risks include:

- Nerve damage.
- Permanent changes in foot shape.
- Flat feet. (You may need to wear arch supports for the rest of your life.)
- More pain than before the surgery. (You may need more surgery to relieve the pain, and you may have permanent numbness in the heel.)

If you want to be athletic or active, think carefully about whether surgery is right for you.

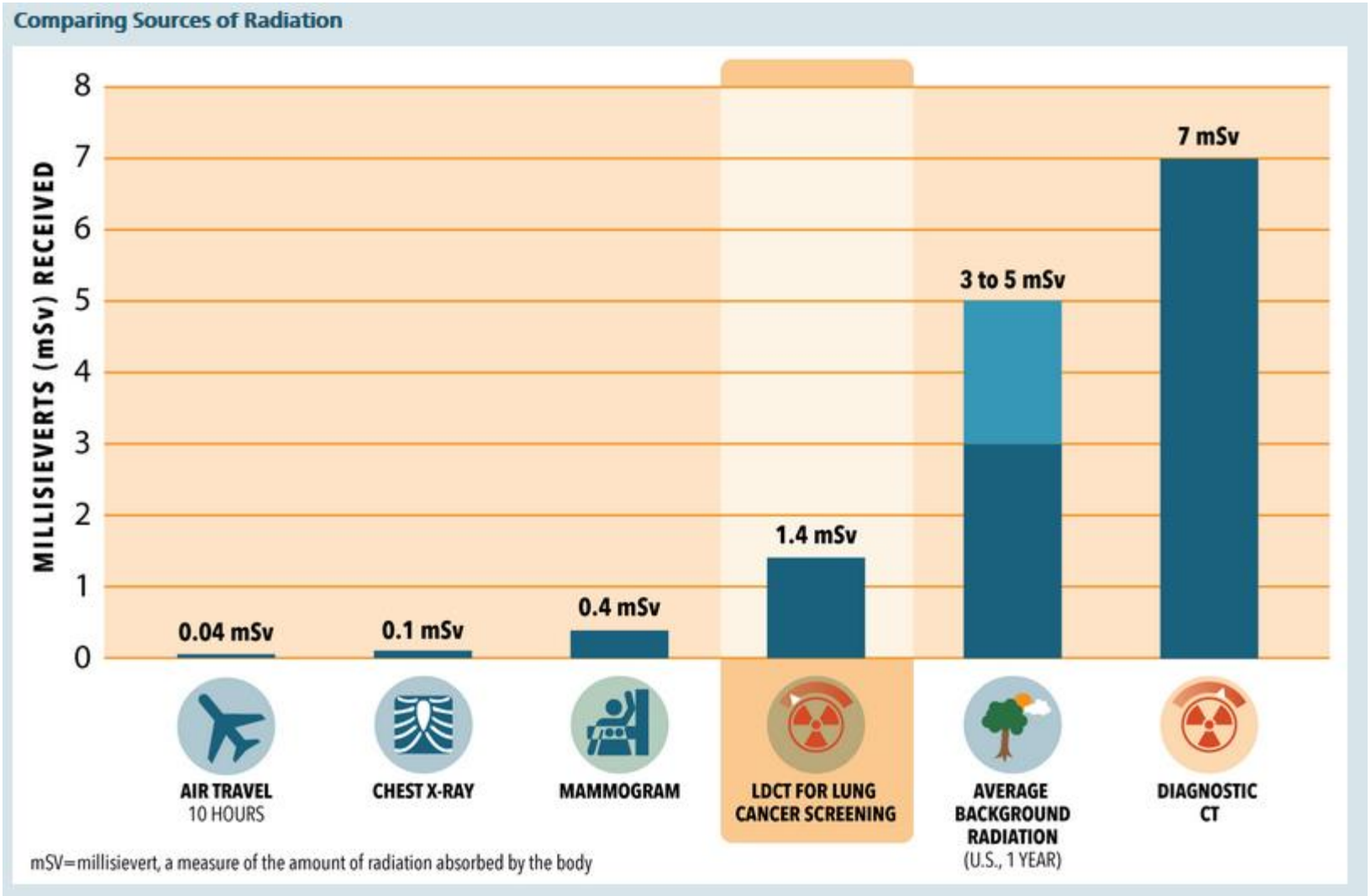
Choosing Wisely, 2015

Risk

	Benefits		Side Effects
Exercises	Stopped leaking	Had less leaking	
Pelvic floor muscle training (PFMT) or Kegel exercises	3 in 10	4 in 10	Not known
PFMT with biofeedba		10	Not known
Medical Devices			
Vaginal weights and inserts	Not known	Not known	Not known
Electrical stimulation	2 in 10	2 in 10	Not known
Magnetic stimulation	Not known	3 in 10	Not known
Medicines			
Topical estrogen	Not known	Not known	Not known
Duloxetine (Cymbalta®)	Not known	Less than 1 in 10	Less than 1 to 2 in 10

Agency for Healthcare Research and Quality, 2016

Risk



Agency for Healthcare Research and Quality, 2016

Personal Preference

What is important to you when deciding about screening for lung cancer?

There are many things to think about when deciding whether lung cancer screening is right for you. Below is a list of questions that may help you decide.

	Favors Screening				Favors No Screening
How important is:	**Very Important**				**Not Important**
Finding lung cancer early when it may be more easily treated?	○	○	○	○	○
How concerned are you about:	**Not Concerned**				**Very Concerned**
Having a false alarm?	○	○	○	○	○
Having other tests if you have a positive screening test?	○	○	○	○	○
Being exposed to radiation from lung cancer screening?	○	○	○	○	○
Being treated for lung cancer that never would have harmed you?	○	○	○	○	○
Being harmed by the treatments you receive for lung cancer?	○	○	○	○	○

Agency for Healthcare Research and Quality, 2016

Other Patient Considerations

Click on the icons (🔭, 🛟, 📖) in the table below to see information that is more detailed.

Immediate treatment	What to expect during treatment	Risks and harms of treatment	What does research tell us?
Surgery (radical prostatectomy, or RP)			
Open surgery (radical retropubic or perineal prostatectomy)	🔭	🛟	📖
Laparoscopic RP (LP)	🔭	🛟	📖
Robot-assisted RP (RARP)			
Radiation			
3D conformal radiation therapy (3DRT)			
Intensity-modulated radiation therapy (IMRT)			
Proton radiation therapy			
Brachytherapy			
Other			
Cryoablation (aka cryosurgery)	🔭	🛟	📖

What to expect during treatment: Open surgery ✖

Most patients stay in the hospital for 2 to 3 days after surgery.
Most patients need a catheter for about 2 weeks after surgery. (A catheter is a small tube that is placed through the penis and into the bladder after surgery to carry urine and to allow the area to heal.)
Patients can usually return to work 2 to 6 weeks after surgery.

Agency for Healthcare Research and Quality, 2011

Other Patient Considerations

What about insurance coverage for lung cancer screening?

Private insurance plans cover lung cancer screening for people age 55 through 80, with no out-of-pocket costs.

Medicare pays for lung cancer screening with no out-of-pocket costs for people up to age 77 if you meet the following criteria:

- You must have a written order from your health care professional (your doctor, nurse practitioner, or physician assistant).
- Your visit with your health care professional must be a "shared decisionmaking visit." In this visit your health care professional must use one or more decision aids and must discuss benefits and harms. Your health care professional must also talk about followup diagnostic testing, overdiagnosis, false alarms, and total radiation exposure from screening.
- You must go to a screening facility that participates in the lung cancer screening registry set up for Medicare patients.

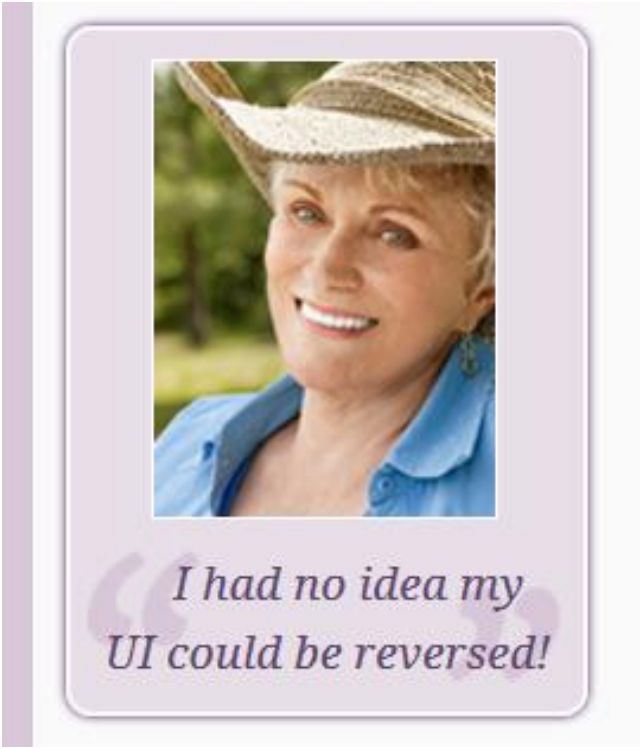
Ask your health care professional about the criteria if you have Medicare coverage.

There may be additional costs for followup tests and/or treatments after the initial screening exam. Contact your insurance company to see if the procedures are covered and what the cost to you would be.

Agency for Healthcare Research and Quality, 2016

Testimonials and Narratives

Centers for Disease Control and Prevention, 2016



Agency for Healthcare Research and Quality, 2016

Action Steps

Share Your Concerns

It is okay to be concerned about the decisions you have to make because of your UI. Here are some examples of concerns you might have:

- ☐ I am worried that I will not be able to do Kegel exercises correctly.
- ☐ I am worried that I do not have time to do Kegel exercises.
- ☐ I am worried about the potential side effects of treatment.
- ☐ I am worried about possibly having to be treated for the rest of my life.

Share Your Preferences

Here are some examples of things you might want to tell your doctor:

- ☐ I am willing to take a pill every day.
- ☐ I am willing to come to my doctor's office for clinic visits.
- ☐ I prefer having my treatment prescribed rather than having to do exercises on my own.

Agency for Healthcare Research and Quality, 2016

Summary

- Research can help inform various stakeholders to make better decisions
- We've offered some examples of different elements of information, both for format of the presentation, and for content
- Keeping these in mind, we want to know what is important to you

Our “Ask" for Today

- Goal for today: To better understand what people consider essential in the presentation of health care information
  - Understand different perspectives about format and content
  - We're not designing products today, but this conversation will help inform how we make future products to disseminate evidence to audiences with potentially very different information needs

Our “Ask" for Today

Based on your experience (or what you would want to experience) in using products that summarize health care evidence to inform decisions:

- Thinking about the CONTENT of the information:
  - What has been done well? What not so well?
  - What elements of content do you find most valuable?
  - Are there elements you find consistently missing?
- Thinking about the FORMAT of the information:
  - What has been done well? What not so well?
  - What presentation formats do you find most valuable?
  - When presentation formats work well for you, what is it about them that makes them work?
- Where do you go to get information? What makes these sources useful?

Thank You!

Q&A

Breakout Sessions Dialing Instructions

For all breakouts dial **866.640.4044** then enter the passcode below the session of interest.

All breakouts are via *teleconference only*. There is no webinar access for breakouts.

- Patients/Consumers A
  - **134531#**
- Patients/Consumers B
  - **783315#**
- Clinicians
  - **109712#**
- Purchasers (Employers)
  - **628131#**
- Payers (Insurers)
  - **465469#**
- Industry
  - **134255#**