

## Agenda

- Overdiagnosis
- Pitfalls of Screening
- Fewer Benefits + More Harms
- Heterogeneity of Cancer
- Patients Should Decide
- Communication Strategies

## Agenda

- **Overdiagnosis**
  - Definition
  - Drivers
  - Classification
  - Invisibility
  - Importance
- Pitfalls of Screening
- Fewer Benefits + More Harms
- Heterogeneity of Cancer
- Patients Should Decide
- Communication Strategies

## Over-Diagnosis

- **Overdiagnosis** is the diagnosis of "disease" that will never cause Sx or death during a patient's lifetime. Overdiagnosis is a side effect of testing for early forms of disease, which may turn people into patients unnecessarily and may lead to treatments that do no good and perhaps do harm.
- Overdiagnosis occurs when a disease is diagnosed correctly, but the Dx is irrelevant. A correct Dx may be irrelevant because treatment for the disease is not available, not needed, or not wanted.
- Because most people who are diagnosed are also treated, it is difficult to assess whether overdiagnosis has occurred in an individual. Overdiagnosis *in an individual* cannot be determined during life. Overdiagnosis is only certain when an individual remains untreated, never develops Sx of the disease, and dies of something else.

Wikipedia 2015

## Overdiagnosis

- The Dx of disease that will never cause symptoms or death in a person's lifetime.
  - 1/2 Prostate, 1/3 Breast, 1/5 Lung Cancers
- Correct Dx, but irrelevant because Tx is not available, not needed, or not wanted.
- Harms:
  - Physical
  - Psychological
  - Economic

## Overdiagnosis occurs when ...

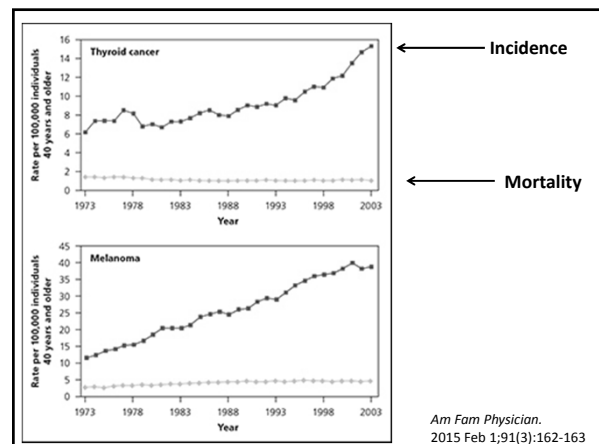
- There is a silent reservoir of a disease or condition

AND

- People do things (especially screening tests) that result in detection of the condition

Diagnostic Imaging

Overdiagnosis occurs *more often* when *either* of these are increased



## How could we increase the reservoir of a condition or disease?

... by altering the definition. Consider:

- Hypoactive Sexual Desire Disorder
- ADHD, RLS, CKD, GDM, Low-T
- DCIS vs. CIN
- Evolving definitions of HTN, DM2:
  - Sweet-tasting urine
  - 1979: FPG  $\geq 140$
  - 1997: FPG  $\geq 126$
  - 2009: A1c  $\geq 6.5\%$

Each step expanded the population with DM

	<u>False Positive</u>	<u>Over Diagnosis</u>
<b>Definition</b>	Initial result that suggests presence of disease; later proved not present	Detection of a disease that will never cause symptoms or death
<b>Patient Experience</b>	Told the test was wrong; don't have the disease	Told they have the disease
<b>Physician Action</b>	Reassurance	Treatment
<b>Potential Harms</b>	Phys Effects: Discomfort and complications from invasive tests Psych Effects: anxiety from "cancer scare" Economic Burden: cost of additional tests	Phys Effects: side effects, mortality risk from Tx Psych Effects: labeled as "diseased;" increased sense of vulnerability Economic Burden: Tx costs, lost wages, inability to get insurance

## Classification/Typology of Overdiagnosis

- Over-detection: Identification of harmless conditions through screening or other testing
  - Most prostate and thyroid + many breast cancers
  - Incidentalomas
- Mis-Classification: Classifying benign/non-progressive conditions as diseases
  - Lower cut-off levels: GDM, DM2/pre-diabetes, HTN, NQMI
  - Disease-mongering: trivial; part of ordinary life:
    - Baldness, low-T, menopause, female sexual dysfunction, infant GER
- Misdiagnosis: Labeling conditions in ways that imply they are (more) harmful
  - Very small PEs on CT; DCIS
  - Strep pharyngitis; bronchitis

## Why does Overdiagnosis Occur?

- Extreme case of lead-time bias
  - Exacerbated by advanced diagnostics
- Well-intentioned screening and early Dx
  - More likely to find turtles (indolent conditions that spend a long time in pre-clinical phase)
- Special Interests: advocacy groups, specialty societies, researchers
- Disease expansion (pre-diabetes, CKD-1/2, ADHD)
- Financial profits (low-T)
- Medicolegal factors ( $\rightarrow$  more testing)
- P4P
- Historical "accident" (strep pharyngitis, DCIS)

## Mammography Cuts Breast Cancer Mortality in Half!

- Norway, where a nationwide mammography screening program was gradually implemented from 1996 – 2005.
- Women ages 50 – 69 years; 77% attended.
- Cancer registry that includes 100% of diagnosed cancers.
- Compared incidence of invasive breast cancer with and without screening.

Ann Intern Med 2012;156:491-9

## For every 2500 women invited to mammography every 2 years:

	No Screening	Screening
Died from Any Cause		
Died from Breast Cancer		?
Diagnosed with Breast Cancer		

Ann Intern Med 2012;156:491-9

For every 2500 women invited to mammography every 2 years:

	No Screening	Screening
Died from Any Cause		
Died from Breast Cancer	?	1
Diagnosed with Breast Cancer		

*Ann Intern Med 2012;156:491-9*

For every 2500 women invited to mammography every 2 years:

	No Screening	Screening
Died from Any Cause		
Died from Breast Cancer	2	1
Diagnosed with Breast Cancer		

**Benefit: 50% mortality reduction**

*Ann Intern Med 2012;156:491-9*

For every 2500 women invited to mammography every 2 years:

	No Screening	Screening	
Died from Any Cause	15	15	No Net Benefit
Died from Breast Cancer	2	1	Benefit
Diagnosed with Breast Cancer	20	26 - 30	Harm

**6 – 10 women overdiagnosed**

*Ann Intern Med 2012;156:491-9*

What do people who experienced overdiagnosis say?

- Not :
  - “my mastectomy was not necessary”
  - “I’m a victim; look what the system did to me”
- Rather:
  - “Thank God”
  - “That [mammogram/PSA/etc.] saved my life”
  - “Dr. \_\_\_\_\_ saved my life”

**Overdiagnosis is invisible**

**\$4,000,000,000 per year**

By Mei-Sing Ong and Kenneth D. Mandl

### National Expenditure For False-Positive Mammograms And Breast Cancer Overdiagnoses Estimated At \$4 Billion A Year

**ABSTRACT** Populationwide mammography screening has been associated with a substantial rise in false-positive mammography findings and breast cancer overdiagnosis. However, there is a lack of current data on the associated costs in the United States. We present costs due to false-positive mammograms and breast cancer overdiagnoses among women ages 40–79, based on expenditure data from a major US health care insurance plan for 702,154 women in the years 2011–13. The average expenditures for each false-positive mammogram, invasive breast cancer, and ductal carcinoma in situ in the twelve months following diagnosis were \$852, \$91,837 and \$12,369, respectively. This translates to a national cost of \$4 billion each year. The costs associated with false-positive mammograms and breast cancer overdiagnoses appear to be much higher than previously documented. Screening has the potential to save lives. However, the economic impact of false-positive mammography results and breast cancer overdiagnoses must be considered in the debate about the appropriate populations for screening.

*Health Affairs, 34, no.4 (2015):576-583*

## Agenda

- Overdiagnosis
- Pitfalls of Screening
  - Trade-offs
  - Working “Upstream”
  - “Conventional Wisdom” re: Cancer Screening
  - Enthusiasm for Cancer Screening
  - Prevailing Messages
- Fewer Benefits + More Harms
- Heterogeneity of Cancer
- Patients Should Decide
- Communication Strategies

## Screening Always Involves **Trade-Offs**

- **Possible Benefits**
  - True negative → Reassurance
  - True positive (sometimes) → Early Detection (→) more successful treatment
- **Possible Harms**
  - False negative → may result in missed opportunity
  - False positive → cascade of tests; associated risks
  - Overdiagnosis (and treatment) of cases never destined to cause problems

## A Historical Perspective: 500 BC – 1950s

- Patients sought care for conditions that were causing symptoms: pain, dysfunction, etc.
- Without Tx: progressive decline
- Harms associated with Tx therefore acceptable
- Characteristics of Tx:
  - Efficacy: poor
  - Supporting evidence: poor
  - Rationale for Tx: strong

## A Historical Perspective: 1950s -- Today

- Scientific advances
  - Understanding of pathophysiology
  - Identification of risk factors
  - Better interventions (immunizations, antibiotics, etc.)
  - Proliferation of procedures and potent medications
- Growing confidence led to rapid dissemination and wider application of interventions
  - Even when not supported by evidence
- Optimism, enthusiasm, financial reward

## A Historical Perspective: Moving “Upstream”

- Tremendous reduction in IDs, improvements in public health and lifestyle → increased longevity → more people living with chronic disease
- Growing ability to
  - Provide rescue care
  - Prolong life
  - Identify people at risk for conditions: advent of screening
- **Interventions for people with risk factors, not diseases**

## Upstream Problems/Challenges

- The “miracles of modern medicine” have altered our perspectives; there is a presumption that more medicine is better.
- Remember: everything we do to people has the capacity to cause harm.
  - Even more so with potent drugs and invasive diagnostic testing and procedures
- When we work upstream, we are doing these things to **healthy** people.
  - **this renders harms less acceptable**

## Conventional Wisdom regarding Cancer Screening

	Lay people	Policy Makers	Clinicians
Early detection is always helpful			
More screening is better			
Newer technologies are superior			
Cancer screening is not harmful			
Screening is always cost-effective			
Most cancers would cause death			
Improved survival rates always indicate a successful screening program			

## Conventional Wisdom regarding Cancer Screening

	Lay people	Policy Makers	Clinicians
Early detection is always helpful	++	++	+
More screening is better	++	++	+
Newer technologies are superior	++	++	++
Cancer screening is not harmful	+++	+++	++
Screening is always cost effective	++	++	++
Most cancers can be cured	+++	++	+
Improved survival rates always indicate a successful screening program	+++	++	++

## Fundamental Challenges of Cancer Screening

- Cancers are heterogeneous
  - Screening tests are imperfect
- Therefore:**
- There is risk for harms
  - There are choices to be made
    - These should be made by patients informed by:
      - the best available evidence and
      - their own values and preferences

## Fundamental Challenges of Cancer Screening

- Cancers are heterogeneous
  - Screening tests are imperfect
- These facts are:**
- Not widely known
  - Not universally accepted
  - Not readily disclosed
    - Consider the procedures for which we feel obliged to obtain “informed consent”
    - Why is this standard not applied to cancer screening?

For 1000 women who get annual screening mammography for 10 years, how many will ...

... avoid death from breast cancer?	
... experience at least 1 false positive?	
... have an unnecessary biopsy?	
... be diagnosed with an indolent cancer?	

JAMA Intern Med. doi:10.1001/jamainternmed.2013.13635  
Published online December 30, 2013

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For 1000 women who get annual screening mammography for 10 years, how many will ...

... avoid death from breast cancer?	1
... experience at least 1 false positive?	400-700
... have an unnecessary biopsy?	
... be diagnosed with an indolent cancer?	

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For 1000 women who get annual screening mammography for 10 years, how many will ...

... avoid death from breast cancer?	1
... experience at least 1 false positive?	400-700
... have an unnecessary biopsy?	50-100
... be diagnosed with an indolent cancer?	

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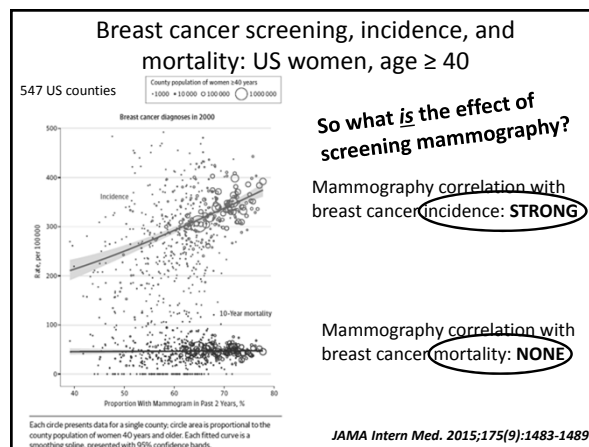
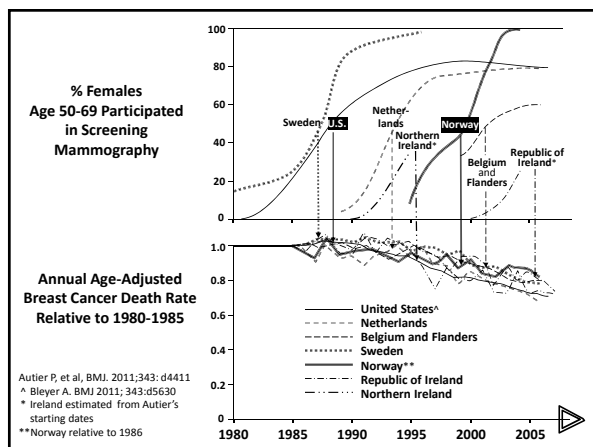
For 1000 women who get annual screening mammography for 10 years, how many will ...

... avoid death from breast cancer?	1
... experience at least 1 false positive?	400-700
... have an unnecessary biopsy?	50-100
... be diagnosed with an indolent cancer?	3-20

Do we tell our patients this?

Why not?

JAMA Intern Med. doi:10.1001/jamainternmed.2013.13635  
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## Cervical Cancer Mortality Rates: 1950 - 2000

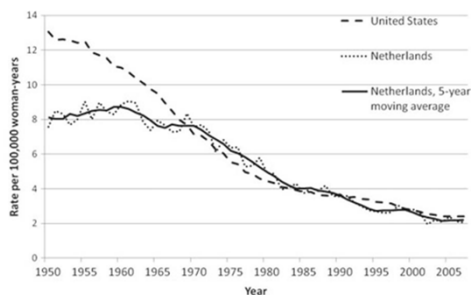


FIGURE 2. Cervical Cancer Mortality Rates in the United States and in the Netherlands, Age Standardized to the U.S. 2000 Population

## Enthusiasm for Cancer Screening

Special Interests:  
Clinical, Research

Consumer  
Advocates

Lawyers

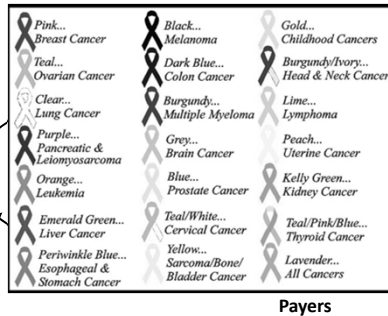
Payers

Early Dx is  
Beneficial

## Enthusiasm for Cancer Screening

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Clinical, Research

Lawyers



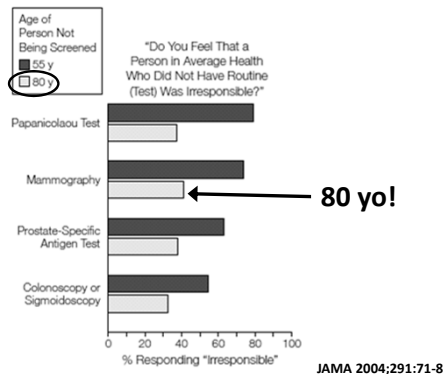
## Enthusiasm for Cancer Screening\*

500 US adults. Women  $\geq 40$ y; men  $\geq 50$ y. No Hx of cancer.

- 87% believe routine cancer screening is “almost always a good idea.”
- 74% believe that finding cancer early saves lives “most” or “all of the time.”
- 66% would want to be tested for a cancer for which nothing could be done.
- Many even view it as an obligation ...

\*JAMA 2004;291:71-8

## Cancer Screening as “Obligation”



## Concerning Cancer:

### Common Public Misconceptions

- It’s a single disease
- It always means death
- If found by screening it will be cured

### Inconvenient Facts

- There are always harms associated with cancer Dx and Tx.
- Cancers are very heterogeneous.
- For individuals, it is often impossible to tell how their cancer will behave.

## Current State: Uncritical Promotion of Cancer Screening

- Benefits are misleadingly exaggerated
- Harms are ignored:

### Physical Harms

Direct harms from screening procedures

W/u of false alarms

Unnecessary treatment of indolent cancers

### Psychological Harms

Financial Costs

Opportunity Costs

## Current State: Uncritical Promotion of Cancer Screening

Inspired by the (erroneous) concept of inevitable progression:

Every cancer will eventually cause death.

If so, then:

- Early detection usually saves lives.
- Harms associated with cancer screening are unimportant because screening saves lives.

## Current State: Uncritical Promotion of Cancer Screening

Inspired by the (erroneous) concept of inevitable progression:

~~Every cancer will eventually cause death.~~

**Definitely not true**

If so, then:

- Early detection usually saves lives.
- Harms associated with cancer screening are unimportant because screening saves lives.

## Current State: Uncritical Promotion of Cancer Screening

Inspired by the (erroneous) concept of inevitable progression:

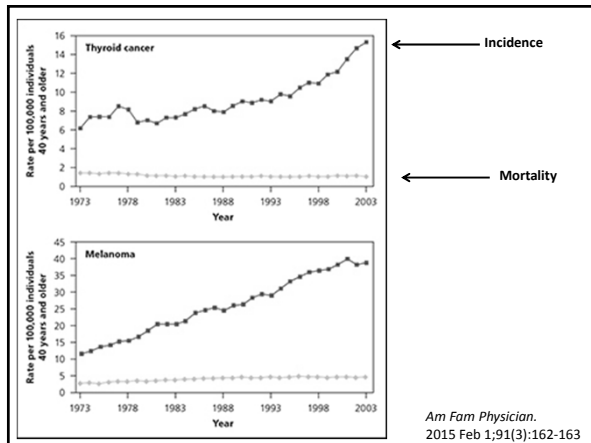
Every cancer will eventually cause death.

If so, then:

- ~~Early detection usually saves lives.~~

**No, but it does always improve survival rates**

- Harms associated with cancer screening are unimportant because screening saves lives.



## Current State: Uncritical Promotion of Cancer Screening

Inspired by the (erroneous) concept of inevitable progression:

Every cancer will eventually cause death.

If so, then:

- Early detection usually saves lives.
- ~~Harms associated with cancer screening are unimportant because screening saves lives.~~

**More people experience harms than benefits.**

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## LDCT for Lung Cancer Screening

For every 1000 people screened annually x 3 years per NLST criteria, there will be:

- **3** lung cancer deaths averted (NNS = 320)
- **4** lung cancers found that are overdiagnosed
- **375** people called back for false positives:
  - 41 will have a Bx for a benign nodule
  - 10 will have a surgical procedure for a benign nodule
  - 3 will have a complication from an invasive procedure
- For every 2500 people screened, **1** person will die of radiation-induced cancer



## Effect of PSA on death from prostate cancer:

“There were about 20% fewer deaths in the men who had PSA screening.”

-- American Society of Clinical Oncology

Misleading with RRR (relative risk reduction) ...

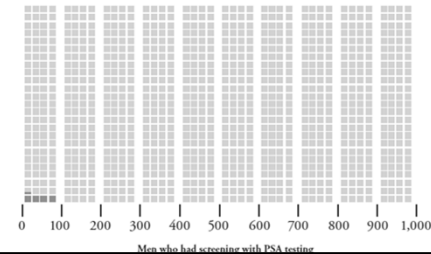
## With Screening:

The first set of pictographs, below, show the chances of dying of prostate cancer. These numbers are from the men in the study over an 11 year period.

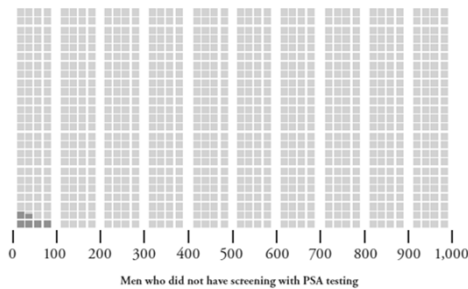
### Effect of having PSA test on death from prostate cancer

Out of 1000 men who had screening, about 4 died of prostate cancer. Out of 1000 men who did not have screening, about 5 died of prostate cancer.

There were about 20% fewer prostate cancer deaths in the men who had PSA screening.<sup>2</sup>



## Without Screening:



2. Scholder FH, Hugoson J, Roebol MJ, et al. Prostate-cancer mortality at 11 years of follow-up. *N Engl J Med*. 2012;366(11):981-90.

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American Society of  
Clinical Oncology  
Decision Aid Tool

How not to say it:

“There were about 20% fewer deaths in the men who had PSA screening.”

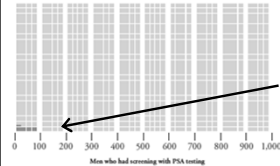
Data from *NEJM* 2012;  
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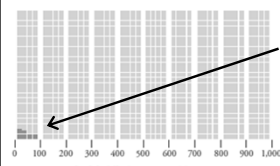
Out of 1000 men who had screening, about 4 died of prostate cancer. Out of 1000 men who did not have screening, about 5 died of prostate cancer.

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Much better:

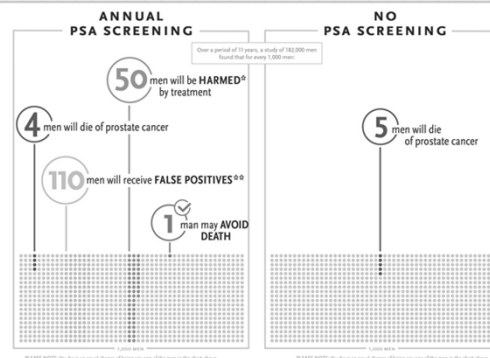
“Out of 1000 men who had screening, about 4 died of prostate cancer.”



“Out of 1000 men who did not have screening, about 5 died of prostate cancer.”

Data from *NEJM* 2012;  
366(11):981-90

## Is the PSA test right for you?



## Is the PSA test right for you?

**THE HARMS of TREATMENT**

Among 1,000 men who get screened, TREATMENT for those diagnosed with prostate cancer WILL RESULT IN:

- 29 men becoming IMPOTENT
- 18 men becoming INCONTINENT
- 2 men suffering a HEART ATTACK or STROKE
- 1 man's death

SEE PAGE XX FOR Possible Screening Test Outcomes

**WHAT is a FALSE POSITIVE?**

In this case, a false positive is a PSA result that SUGGESTS A MAN HAS PROSTATE CANCER – WHEN HE DOES NOT. This leads to additional testing: repeat PSAs and/or biopsy.

**WHO IS MORE AT RISK?**

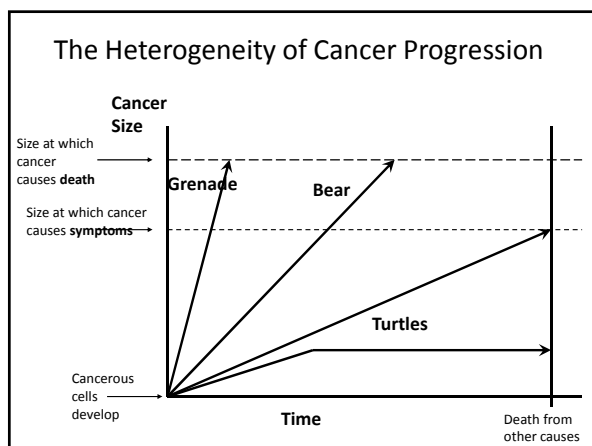
- As men get older, they are more likely to get prostate cancer.
- African-American men are more likely to get prostate cancer than other men.

Now that you know the facts, **TALK WITH YOUR DOCTOR** about which approach is best for you and your health.

- ## Agenda
- Overdiagnosis
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  - Fewer Benefits + More Harms
  - **Heterogeneity of Cancer**
  - Patients Should Decide
  - Communication Strategies

- ## Common Public Misconceptions about Cancer
- It's a single disease
  - It always means death
  - If found by screening it will be cured

- ## The Heterogeneity of Cancers
- Cancers are very heterogeneous:
    - Consider pancreatic vs. prostate
- AND**
- The cancers of a given organ can be very heterogeneous:
    - Lethal
    - Potentially treatable
    - Indolent



- ## Cancer Screening: Consider Biological Variation
- Some cancers are
- very aggressive and nearly always lethal:
  - potentially lethal, but often treatable, especially when found early:
  - indolent; even if left alone, they would never cause symptoms or harm:

### Who benefits from cancer screening?

*As an individual*, you only benefit if:

- You test negative **AND** you don't have cancer:
  - Benefit = Reassurance
  - Small benefit; large number of people

**OR**

- You have cancer, **AND** you test positive, **AND** it's a treatable cancer, **AND** you receive successful Tx:
  - Large benefit, but very small number of people

**All other situations produce no benefit.**

### All other situations produce no benefit, and ...

#### **Many cause harms:**

- False positive
- Anxiety
- False reassurance
- Over-Diagnosis
- Over-Treatment
- Loss of insurability/employability

### The "Costs" of Cancer Screening

**For individuals**, cancer screening is **harmful** when any of the following occur:

- There is pain, discomfort, or anxiety associated with screening.
- There is injury caused by screening.
- Indolent cancers are identified and treated, causing:
  - Anxiety, adverse effects, increased costs, lost wages, loss of future insurability

**The Achilles' Heel of cancer screening programs is their propensity to find turtles.**

### A Rock and a Hard Place?

- |   |            |                                  |
|---|------------|----------------------------------|
| • Patients have been "taught" to expect cancer screening. | <b>Vs.</b> | • Harms are surprisingly high.   |
| • Payers want to see higher rates of cancer screening.    |            | • Benefits are surprisingly low. |

### What's a PCP to do?

### Agenda

- Overdiagnosis
- Pitfalls of Screening
- Fewer Benefits + More Harms
- Heterogeneity of Cancer
- **Patients Should Decide**
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### Shared Decision-Making (SDM) Defined:

Decisions shared by clinicians and patients, informed by the best evidence available **and** the specific characteristics, preferences, and values of the patient.

## IOM: *Crossing the Quality Chasm* (2001) 10 Rules for Redesign

1. Care is based on continuous healing relationships.
  2. **Care is customized according to patients' needs and values.**
  3. **The patient is the source of control.**
  4. **Knowledge is shared, and information flows freely.**
  5. **Decision-making is evidence-based.**
- SDM**
6. Safety is a system property.
  7. Transparency is necessary.
  8. Needs are anticipated.
  9. Waste is continuously decreased.
  10. Cooperation among clinicians is a priority.

**"Patient values should guide all clinical decisions."**

## Locus of Control

- The clinician is responsible for creating the opportunity for a healthy, appropriate decision-making process.
- The patient is ultimately responsible for the decision.

Therefore, cancer screening rates are **not** an appropriate measure of the quality of care provided by a PCP.

## Barriers to SDM

- Clinicians
  - Challenge to autonomy; feel threatened by sharing power
  - "Over-certain:" fail to recognize preference-sensitive situations
  - Knowledge/Evidence Deficits
    - Difficult to keep current, interpret, and communicate
- Patients
  - Variations in role preference
    - Among patients and within individuals for different decisions
  - Literacy/Numeracy Challenges
- Practice
  - Lack of time/compensation
  - Logistical challenges:
    - Availability of appropriate decision aids

**Time**

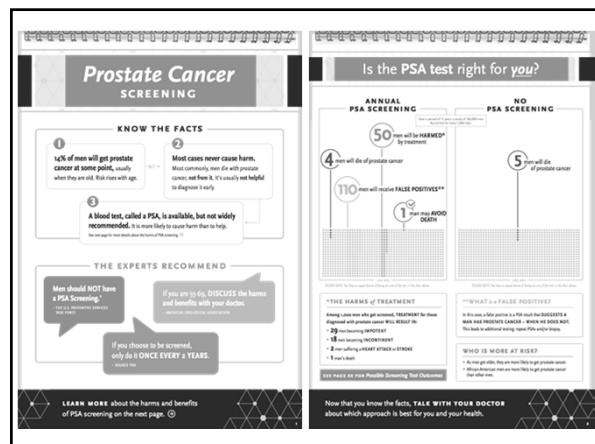
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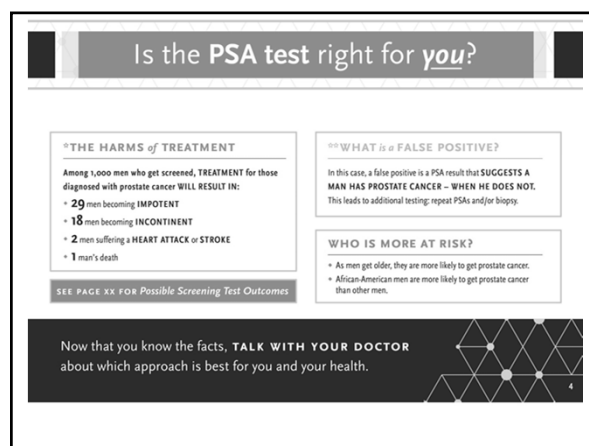
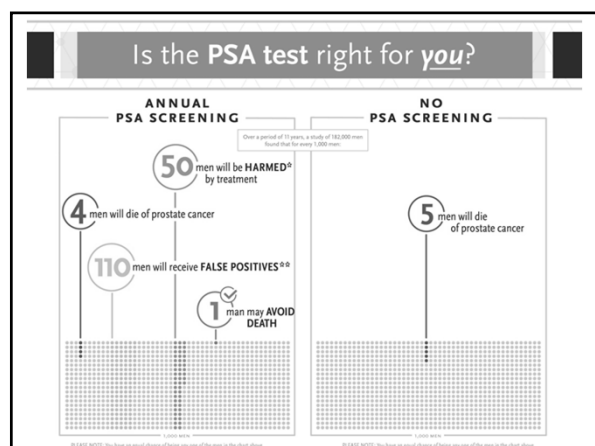
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- **Communication Strategies**
  - Decision Aids

## Decision Aids

- Decision aids do a better job than usual care in:
  - improving patients' knowledge about options
  - reducing their decisional conflict
  - stimulating patients to take a more active role in decision making without increasing their anxiety
- "Compared with simpler versions, more detailed aids improve patients' comfort with decision making and marginally improve knowledge."

O'Connor et al., 1999 from BMJ





## Resources

- Ottawa Hospital Research Institute
  - <http://decisionaid.ohri.ca>
- Foundation for Informed Medical Decision Making
  - <http://www.informedmedicaldecisions.org/index.html>
- Mayo Clinic
  - <http://shareddecisions.mayoclinic.org>
- AHRQ: Questions are the Answer
  - <http://www.ahrq.gov/questions/>
- Australian Screening Mammography Decision Aid
  - <http://www.mammogram.med.usyd.edu.au/>
- Decision Boxes
  - [www.decisionbox.ulaval.ca](http://www.decisionbox.ulaval.ca)
- Should I be screened with mammography?
  - <http://www.canadiantaskforce.ca>

## Suggestions to Mitigate Overdiagnosis Associated with Cancer Screening

- Campaign for better information
- Promote shared decision-making
- Refine screening strategies
  - Restrict to higher-risk sub-populations
  - Increase screening intervals
  - Raise thresholds for interventions (Bx or recall)
- Re-name some turtles (cf. CIN vs. DCIS)
- Don't use cancer screening rates as a P4P "quality" measure

## Conclusions

### Regarding Cancer Screening:

- The benefits are less than most believe.
- The harms are greater than most believe.
- It is our professional responsibility to:
  - Understand the projected harms/benefits.
  - Communicate the projected harms/benefits.
  - Facilitate shared decision-making.
- We need a new generation of cancer screening educational "campaigns."

To do these, we must appreciate and address the heterogeneity of cancers

## Conclusions

### Regarding Overdiagnosis:

- Prevalence is rising
  - More screening
  - More sensitive tests
  - Evolving disease definitions
- An inevitable consequence of screening
- Often remains unrecognized
- Clinicians and patients should be more aware of overdiagnosis
- Decision aids can facilitate understanding