Cancer Overdiagnosis Explained: A Simple Graphical Model

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Disclosure

• Images to be shared today are from my book/decision aid, *Cancer Screening Decisions: A Patient-Centered Approach*, which will be published in November.
The Challenges

• Overdiagnosis in cancer screening remains poorly understood by patients, policy-makers, and clinicians.

• “Early detection saves lives” is widely accepted as fact.

• People are often surprised to learn that there can be harms associated with cancer screening. These include:
  • The harms and burdens associated with screening
  • False positive results and the downstream effects
  • Detection of indolent cancers (= overdiagnosis)

• Cancer screening is uncritically promoted, and PCPs are incentivized to do it.

• Overdiagnosis is “invisible.”

• Overdiagnosis is difficult to understand and explain.
Cancer Overdiagnosis Defined

• Diagnosis of a cancer which was not destined to ever cause symptoms, harm, or death in the person’s lifetime.

• Harms result from:
  • The diagnosis itself (psychological, financial)
  • Treatment, and the attendant harms and costs

• There is no opportunity to benefit from diagnosing an indolent cancer.
• Yet there are always harms associated with it.
Understanding Overdiagnosis in Cancer Screening Requires:

• Understanding the heterogeneity of cancer progression

• Understanding that screening is particularly good at detecting indolent cancers

• Adopting a population-level view

• At least a basic understanding of probabilities
This diagram, a conventional model of inevitable cancer progression, illustrates how we would expect a bear-type cancer to behave over time.

With this in mind, we can see the value of cancer screening, which is based on the idea that early detection saves lives.

**“TURTLES”**

Cancers that are surprisingly common — they move slowly and are non-threatening. They never cause death and don’t even cause symptoms.

Finding it early (or at all) is NEVER HELPFUL.

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**“BEARS”**

Cancers that are potentially lethal, but often treatable, especially when found early.

Finding it early MAY BE HELPFUL.

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**“GRENADES”**

Cancers that are very aggressive — they grow fast and are almost always deadly, even when found early.

Finding it early is RARELY HELPFUL.

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Heterogeneity of Cancer Progression

Cancer Stage

- **Point at which cancer causes death**
- **Point at which cancer causes symptoms**
- **Cancer Cells Develop**
- **Screening Test Conducted**
- **Death from Other Causes**

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**Grenades**
Usually diagnosed from symptoms

**Bears**
May be diagnosed by screening, incidental finding or from symptoms.

*Early detection by screening may help, but as cancer treatments have improved, many patients experience equal, good outcomes even in the absence of early detection.*

**Turtles**
Only diagnosed by screening or incidental findings.

*Detection produces only harms, never benefits.*

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From Adler R: *Cancer Screening Decisions: A Patient-Centered Approach*
Philadelphia: Wolters Kluwer, 2018
This chart shows how screening can be harmful, when it leads to overdiagnosis.

There are also many turtle-type cancers that would never cause any symptoms or harm.

Finding a turtle type cancer cannot possibly help. It can only cause harm.

This is overdiagnosis.

From Adler R: Cancer Screening Decisions: A Patient-Centered Approach
Philadelphia: Wolters Kluwer, 2018
Cancer screening is **helpful** when:

1. A person without cancer has a negative (normal) screening test result. This is a small benefit that many people get to experience.

2. A person with cancer has a positive (abnormal) test result, and:
   - the cancer they have is treatable, and
   - they receive successful treatment, and
   - the treatment is more successful than it would have been if the cancer was diagnosed later because of symptoms.
   This is a huge benefit that a relatively small number of people get to experience.
   This can only occur for Bear-type cancers.

Cancer screening is **harmful** when:

1. A person experiences *burdens of testing*, such as inconvenience, discomfort, or large expenses.

2. A person without cancer receives a *false positive* test result, in which her/his cancer screening test is abnormal, raising worries about cancer, resulting in:
   - *additional tests*, which may cause more inconvenience, discomfort, and expense
   - *problems from more invasive tests*, such as biopsies (minor surgery to remove a piece of the body for more precise testing)
   - *cancer anxiety*, which can last for years after the false positive test result.

3. A person experiences *overdiagnosis and overtreatment*: the diagnosis and treatment of a cancer that — if not for the screening test — would have never caused the patient any problem in their lifetime.

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IMAGINE COMPARING 2 GROUPS OF 1000 PEOPLE ELIGIBLE FOR LUNG CANCER SCREENING.
1 group chooses screening (annual LDCT scan for 3 years), while the other group chooses not to be screened.
All people are followed for 6.5 years. What happens?

**ANNUAL LDCT SCREENING**

- 960 people will NOT have lung cancer
  - 595 will test NEGATIVE and feel reassured
  - 365 will receive a FALSE POSITIVE
    - 25 will have an unnecessary BIOPSY
    - 3 will have a MAJOR MEDICAL COMPLICATION from the biopsy
- 36 will be DIAGNOSED with lung cancer from screening or experiencing symptoms
  - 18 will SURVIVE
  - 18 will DIE of Lung Cancer
- 4 will be OVERDIAGNOSED – they will be diagnosed and treated for lung cancer that would never cause them harm. Overdiagnosis can only cause harm.

**NO LDCT SCREENING**

- 960 people will NOT have lung cancer
  - NO TESTING!
  - NO FALSE POSITIVES!
- 36 will be DIAGNOSED with lung cancer from experiencing symptoms
  - 15 will SURVIVE
  - 21 will DIE of Lung Cancer
- 4 will AVOID OVERDIAGNOSIS – No symptoms. No testing. No diagnosis. No treatment. No worry.

You have an equal chance of being any one of the 1000 people in the chart above.

From Adler R: Cancer Screening Decisions: A Patient-Centered Approach
Philadelphia: Wolters Kluwer, 2018
**Prostate Cancer**

**Imagine Comparing 2 Groups of 1000 Men.**
1 group chooses regular PSA screening (every 1-4 years), while the other group chooses no screening. All men are followed for 11 years. What happens?

### REGULAR PSA SCREENING
- **890 men will NOT have prostate cancer**
  - **780 people will test NEGATIVE and feel reassured**
  - **110 men will receive a FALSE POSITIVE**
  - **100 men will have an unnecessary BIOPSY**
  - **32 people will have a MAJOR or MODERATE PROBLEM from the biopsy**
- **66 men will be DIAGNOSED with prostate cancer from screening or symptoms**
  - **62 men will SURVIVE**
  - **4 men will DIE of prostate cancer**

### NO PSA SCREENING
- **890 men will NOT have prostate cancer**
  - **NO TESTING!**
  - **NO FALSE POSITIVES!**
- **66 men will be DIAGNOSED with prostate cancer from symptoms**
  - **61 men will SURVIVE**
  - **5 men will DIE of prostate cancer**

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*From Adler R: Cancer Screening Decisions: A Patient-Centered Approach*  
Philadelphia: Wolters Kluwer, 2018
IMAGINE COMPARING 2 GROUPS OF 10,000 WOMEN IN THEIR 50s.
1 group chooses to have annual mammograms, and the other group does not.

What happens?

**ANNUAL SCREENING**

- 46 women will eventually **DIE** of breast cancer
- 8 women will **AVOID DYING** of breast cancer

**NO SCREENING**

- 54 women will eventually **DIE** of breast cancer

You have an equal chance of being any one of the 10,000 women in the chart above.
Imagine comparing 2 groups of 2500 women in their 50s. 1 group chooses annual mammograms for 10 years, and the other group does not. What happens?

**ANNUAL SCREENING**

- 2442 women will NOT have breast cancer
  - 909 women will test **NEGATIVE** and feel reassured
  - 1533 women will receive a **FALSE POSITIVE**
    - 235 women will have an unnecessary **BIOPSY**
  - 43 women will be **DIAGNOSED** with breast cancer from screening or symptoms
    - 31 women will **SURVIVE**
    - 12 women will **DIE** of breast cancer

**NO SCREENING**

- 2442 women will NOT have breast cancer
  - **NO TESTING!**
  - **NO FALSE POSITIVES!**

43 women will be **DIAGNOSED** with breast cancer from symptoms
  - 29 women will **SURVIVE**
  - 14 women will **DIE** of breast cancer

15 women will be **OVERDIAGNOSED** – they will be diagnosed and treated for breast cancer that would never have caused harm. Overdiagnosis can only cause harm, though they will believe that testing and treatment “saved” them.

You have an equal chance of being any one of the 2500 women in the chart above.

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Breast Cancer (50s)

Imagine comparing 3 groups of 2500 women in their 50s. 1 group chooses to have a mammogram every year, while 1 group chooses to have a mammogram every other year, and the other group chooses not to be screened. What happens?

**Regular Screening**

Women who have mammograms **EVERY YEAR**
- 1,533 women will receive **FALSE POSITIVES**
- 235 women will have an **UNNECESSARY BIOPSY**
- 15 women will be **OVERDIAGNOSED**
- 12 women will **DIE** of breast cancer

Women who have mammograms **EVERY OTHER YEAR**
- 1,050 women will receive **FALSE POSITIVES**
- 160 women will have an **UNNECESSARY BIOPSY**
- 15 women will be **OVERDIAGNOSED**
- 12 women will **DIE** of breast cancer

*Having mammograms every other year preserves most of the benefits, while reducing some of the harms.

**No Screening**

Women who **DO NOT HAVE** mammograms
- 0 women will receive **FALSE POSITIVES**
- 0 women will have an **UNNECESSARY BIOPSY**
- 0 women will be **OVERDIAGNOSED**
- 14 women will **DIE** of breast cancer

2500 women followed for 10 years

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Conclusions

• One cannot adequately weigh the benefits and harms of cancer screening without considering the risk of overdiagnosis.

• Most people will require some pictorial representation to understand:
  • The heterogeneity of cancer progression
  • The concept of overdiagnosis
  • The likelihood of overdiagnosis for a given proposed cancer screen
Questions/Discussion

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