Class 20:

Screening for Disease II

HLSC 2003 Introduction to Epidemiology

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Original article

Public Health Policy

Does screening for disease save lives in asymptomatic adults? Systematic review of meta-analyses and randomized trials

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Abstract

Background: Several popular screening tests, such as mammography and prostate-specific antigen, have met with wide controversy and/or have lost their endorsement recently. We systematically evaluated evidence from randomized controlled trials (RCTs) as to whether screening decreases mortality from diseases where death is a common outcome.

Methods: We searched three sources: United States Preventive Services Task Force (USPSTF), Cochrane Database of Systematic Reviews, and PubMed. We extracted recommendation status, category of evidence and RCT availability on mortality for screening tests for diseases on asymptomatic adults (excluding pregnant women and children) from USPSTF. We identified meta-analyses and individual RCTs on screening and mortality from Cochrane and PubMed.

Results: We selected 19 diseases (39 tests) out of 50 diseases/disorders for which USPSTF provides screening evaluation. Screening is recommended for 6 diseases (12 tests) out of the 19. We assessed 9 non-overlapping meta-analyses and 48 individual trials for these 19 diseases. Among the results of the meta-analyses, reductions where the 95% confidence intervals (CIs) excluded the null occurred for four disease-specific mortality estimates (ultrasound for abdominal aortic aneurysm in men; mammography for breast cancer; fecal occult blood test and flexible sigmoidoscopy for colorectal cancer) and for none of the all-cause mortality estimates. Among individual RCTs, reductions in disease-specific and all-cause mortality where the 95% CIs excluded the null occurred in 30% and 11% of the estimates, respectively.

Conclusions: Among currently available screening tests for diseases where death is a common outcome, reductions in disease-specific mortality are uncommon and reductions in all-cause mortality are very rare or non-existent.

lately in this regard. For example, for breast cancer, the United States Preventive Services Task Force (USPSTF) currently recommends against routine mammographic screening for women aged 40–49 years after retracting its previous recommendation in favour of mammography, as the data failed to show that benefit outweighed harm.[1] The decision against screening drew sharp criticism from various interest groups including patients who overestimate the benefit of screening.[2] Similarly, USPSTF now recom-

There are many potential underlying reasons for the overall poor performance of screening in reducing mortality: the screening test may lack sufficient sensitivity and specificity to capture the disease early in its process; there are no markedly effective treatment options for the disease; treatments are available but the risk-benefit ratio of the whole screening and treatment process is unfavourable; or competing causes of death do not allow us to see a net benefit. Often, these reasons may coexist. Whether screening saves lives can only be reliably proven with RCTs.[108]

seen many hot debates. Screening may still be highly effective (and thus justifiable) for a variety of other clinical outcomes, besides mortality. However, our overview suggests that expectations of major benefits in mortality from screening need to be cautiously tempered.

Epi in the News

Breast Cancer Screening: Controversies and Improvements

Women aged 40-49 years

If you decide to have screening mammograms, what are your chances of experiencing the screening outcomes (as shown in Figure 1)?

Imagine 1000 women aged 40 years starting screening and being screened once every year over 10 years. What would happen? We found that these women will typically experience the following outcomes:

- 981 women will not have breast cancer.
- 451 women will have normal results.
- 549 women will have abnormal results at some point during 10 years.
    - 533 of the abnormal results will be false alarms, which turn out to be normal after further testing.
- 16 women will have breast cancer detected by screening.
- 3 women will develop breast cancer in between screening visits

Since screening aims to reduce the risk from dying from breast cancer we can look at the estimated number of woman that needs to be screened to prevent one death.

If we screen 1,000 women **aged 40-49 years** once a year for a period of 10 years:

- 1 death from breast cancer will be prevented.
- 12 women will die from some cause other than breast cancer.
- 2 women will die of breast cancer despite breast cancer screening.

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Do 3-D mammograms improve screening

Content from Sunnybrook Hospital
Published Wednesday, Oct. 29, 2014 2:42PM EDT
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Sunnybrook researchers open the first Canadian clinical trial as part of the launch of T-MIST (Tomosynthesis Mammographic Imaging Screening Trial), the first, large randomized, multi-centre, multi-system study of digital tomosynthesis (3-D breast mammography) compared to the current standard of digital mammography, for breast cancer screening.

"Our hope is that digital tomosynthesis will take us further, to result in fewer false alarms, potentially a 30 to 40% reduction, to lessen anxiety for patients, and to find up to one-third more of the small, invasive cancers that would be missed with current mammography, and that really need to be treated," says Dr. Roberta Jong, Sunnybrook Health Sciences Centre breast-dedicated radiologist, and study co-investigator of the first Canadian clinical trial with Dr. Martin Yaffe, a senior scientist, and an expert in Breast Imaging (Physical Sciences) in the Odette Cancer Research Program at Sunnybrook Research Institute.

Digital tomosynthesis uses the strengths of digital mammography, but instead of taking two X-ray views, tomosynthesis quickly takes up to 15 low-

Class Objectives:

1. Understand the value of, and how to calculate Positive and Negative Predictive Values (PPV & NPV)

2. Learn the difference between large-scale population screening, target screening, and case finding

3. Learn about potential biases in screening studies

4. Become familiar with some common screening programs in Alberta

Story time:

A physician visited his general internist for a regular annual medical examination, which included an screening test for colon cancer (an occult blood test). One of the three stool specimens was positive. The internist told his physician-patient that the result was of no significance because he regularly encountered many false positive test results in his busy medical practice. The test was repeated and, this time, all three tests were negative.

The patient-physician continued to have lingering concerns, and so made a phone call to his good friend, a practicing gastroenterologist. The gastroenterologist said that in his experience, a positive stool finding in serious as it is almost always associated with pathologic gastrointestinal disorders. The subsequent negative tests, he advised, were non conclusive as they could not have detected a tumor that only bleeds intermittently.

- Which opinion was correct?

Predictive Values

- **Sensitivity and specificity** are specific to the screening test and **do not change relative to prevalence** of disease

1.1

Screening Test	Gold Standard Test: Positive	Gold Standard Test: Negative	
Positive	6	7	13
Negative	21	966	987
	27	973	1000

1.2

Screening Test	Gold Standard Test: Positive	Gold Standard Test: Negative	
Positive	33	8	41
Negative	117	842	959
	150	850	1000

Predictive Values:

Screening tests CAN vary, however, in their ability to PREDICT the true disease state of an individual, **depending on prevalence**. **Predictive values** allow us to predict how ***well the test performs in a specific population*** (which could have varying prevalence).

*Positive Predictive Value = TP / (TP+FP)

*Negative Predictive Value = TN / (FN+TN)

Example:

		Gold Standard Test: Positive	Gold Standard Test: Negative	
Screening Test	Positive	6	7	13
	Negative	21	966	987
		27	973	1000

		Gold Standard Test: Positive	Gold Standard Test: Negative	
Screening Test	Positive	33	8	41
	Negative	117	842	959
		150	850	1000

Interpreting Predictive Values:

- PPV: interpreted to mean that a person who is screened and tests positive, has a ___ % chance of really having the disease.

- NPV: Interpreted to mean that a person who is screened and test negative, has a ___% chance of really being free of disease (i.e. NOT having the disease).

WHY IS THIS USEFUL? For clinicians? For epidemiologists?

- The same test can have very different predictive value when administered to a high-risk (high prevalence) or a low-risk (low prevalence) population

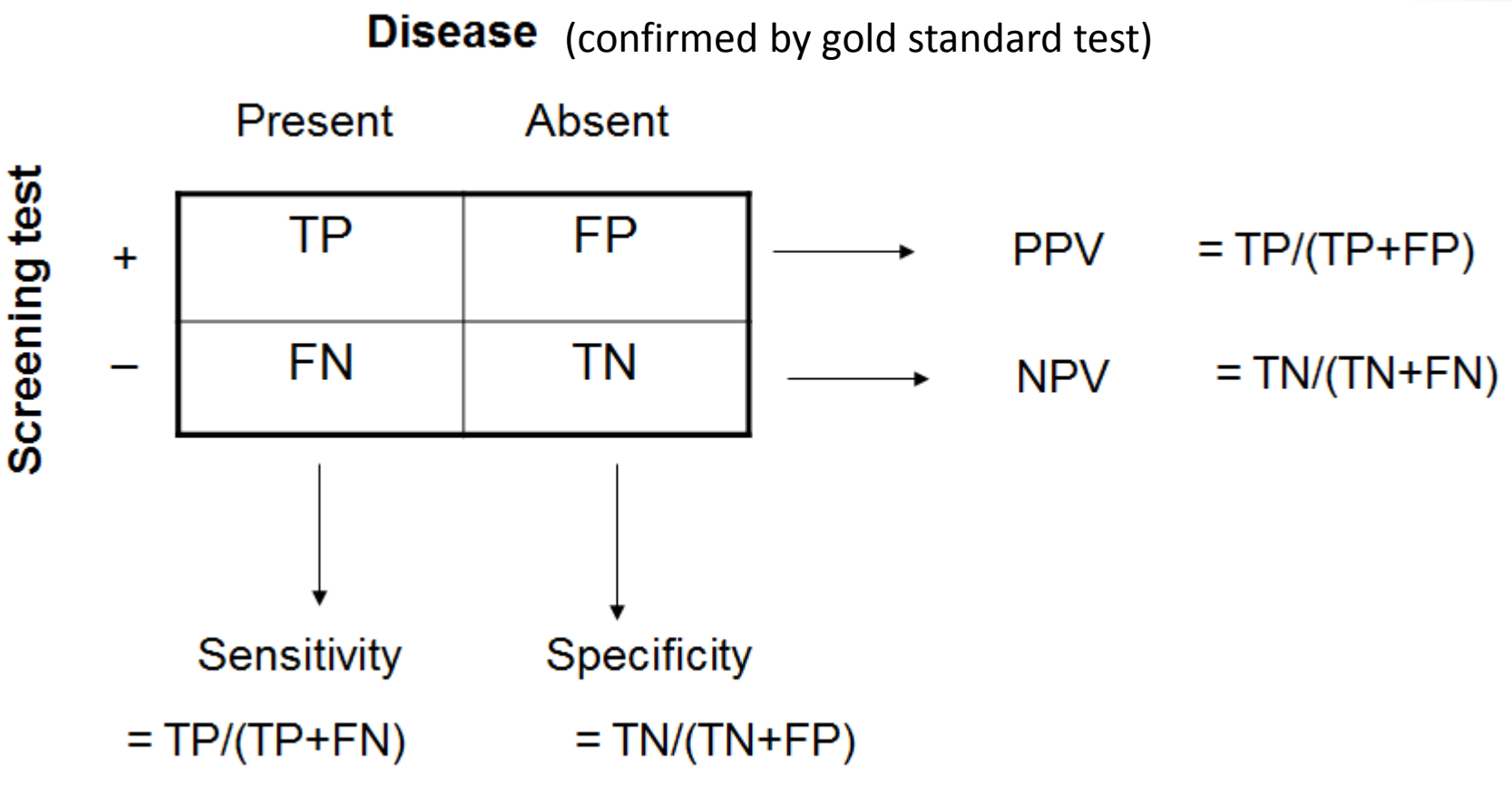
Sensitivity and Specificity

- Measure accuracy of the screening test
- Used to measure the screening test itself
- Does not change based on the population

Predictive values

- Allows us to predict how well a particular screening program will perform in a particular population
- Is related to prevalence in a population

*Summary of Screening Formulas:



Screening Approaches

- Targeted screening programs – aimed at groups with increased risk of disease – based on characteristics or exposure status

(e.g. Immigrates screened for TB and HIV; Hypertensive people screened for cholesterol and blood glucose; women who test positive for BRCA1, BRCA2, or have sister, mother, daughter with Breast Ca)

- Mass screening programs – population based, regardless of risk level

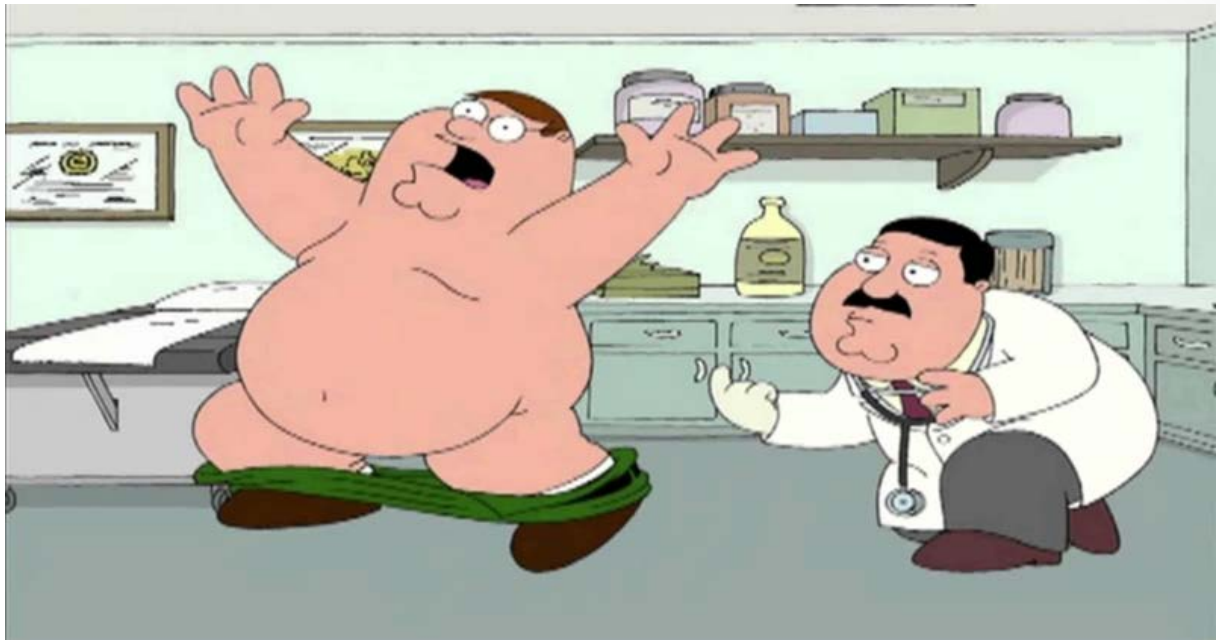
(e.g. cancer screening – cervical, breast, colon; Neonatal metabolic screening; prenatal Syphilis/HIV screening)

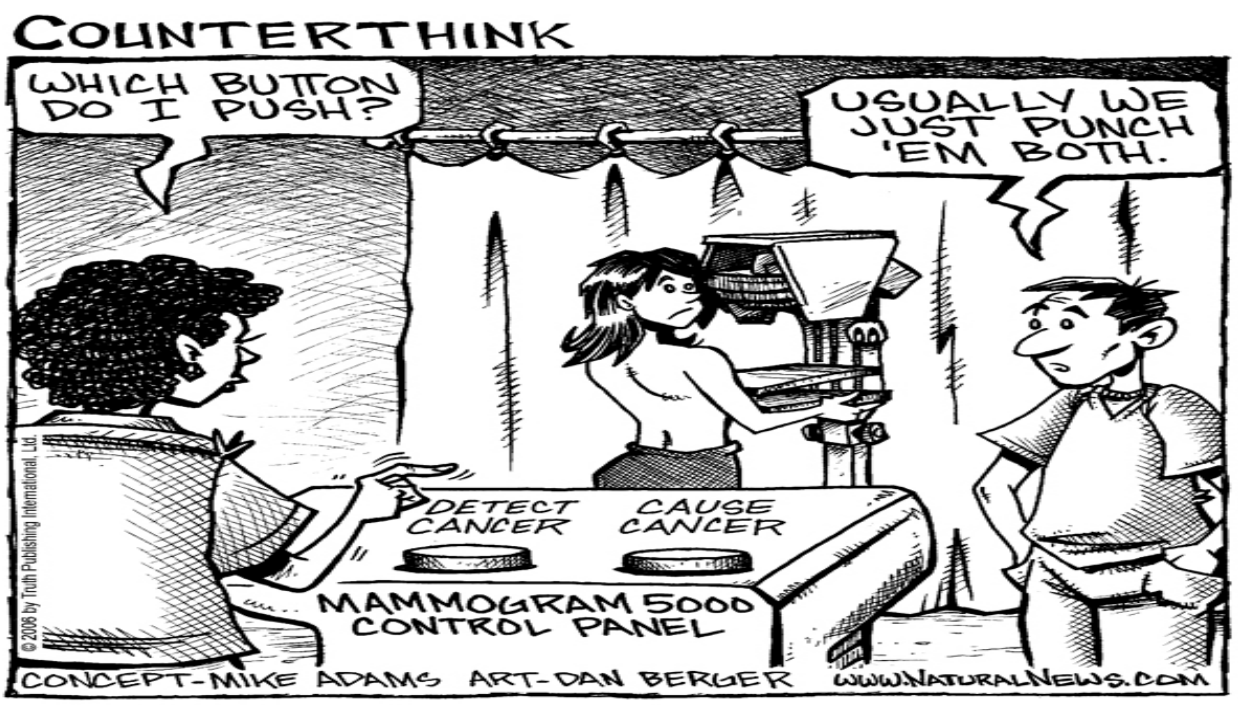
- Case finding – opportunistic attempts at early detection

(e.g. patient comes to a clinicians office for flu-like symptoms and gets screened for syphilis)

Sources of Bias when evaluating Screening Programs:

1. Volunteer Bias
2. Lead-time Bias
3. Length Bias




COUNTERTHINK
WHICH BUTTON DO I PUSH?
USUALLY WE JUST PUNCH 'EM BOTH.
DETECT CANCER
CAUSE CANCER
MAMMOGRAM 5000 CONTROL PANEL
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Volunteer Bias

In the general population, who do you think are the most likely to attend screening programs?

- Wealthy
- Healthy
- Wise (willing to comply w/ treatment)
- Those with strong family history of disease (the "worried well")

Caution: Is a better prognosis determined by the test and treatment, or is it the result of other favourable health determinants?

This would be considered what type of Bias?

A. Measurement
B. Selection

Survival Rate: the percentage of patients who are alive 5-years after diagnosis (or beginning of treatment)

$$\frac{\text{\# of cases that are alive in a given period following diagnosis}}{\text{\# of cases diagnosed at the beginning of that period}} \times 100$$

*Used to express mortality/prognosis of long-term chronic diseases (i.e. cancer, diabetes)

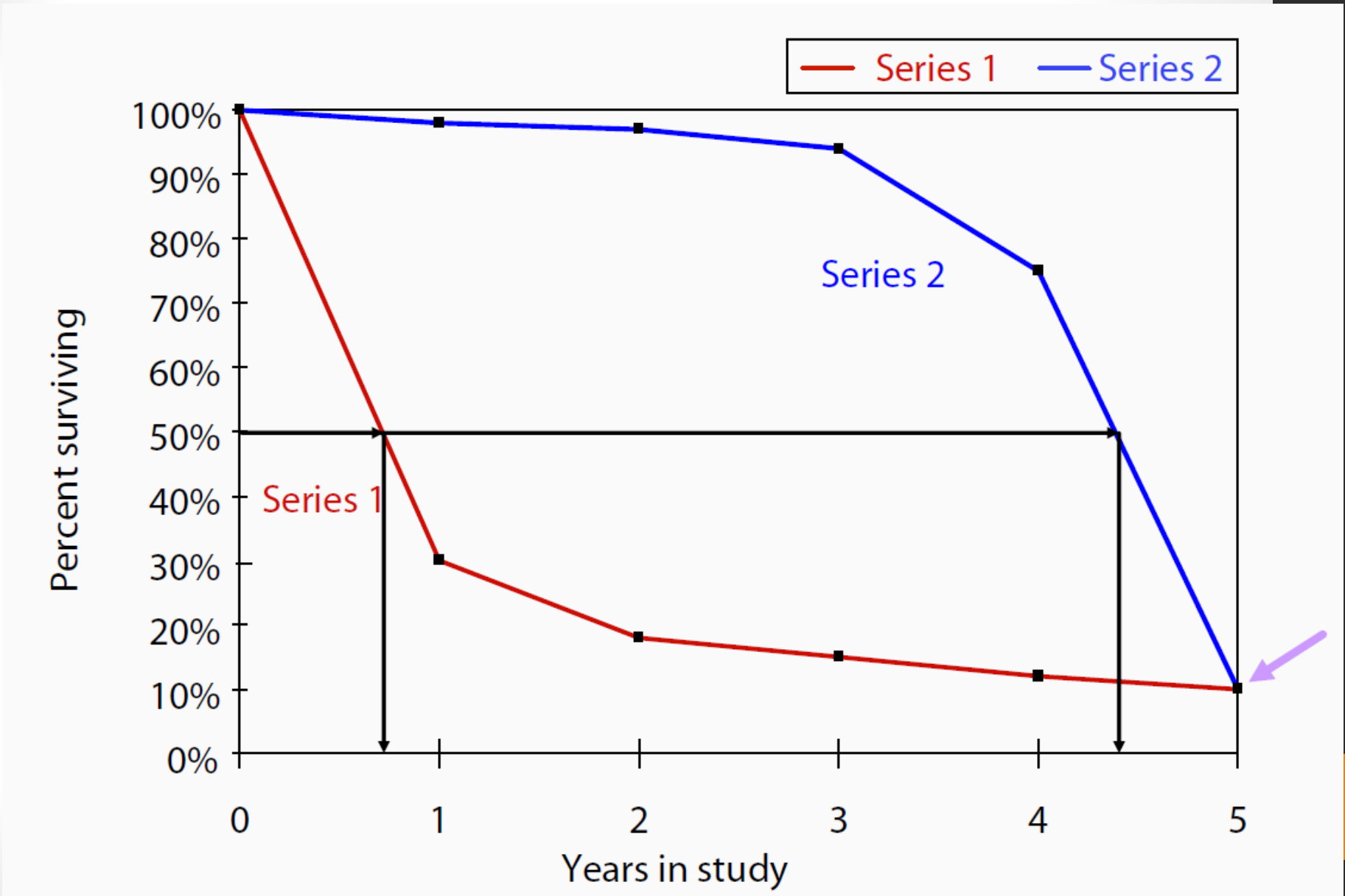
*often a 5-year time period is used

*not a rate, a proportion

The Problem with Survival Rates:

- Affected by screening programs (i.e. lead time bias)
- Often use a 5-year criteria (which excludes those diagnosed more recently)
- Inverse survival curves (can have the same survival rate, with completely different natural history of disease; next slide)
- Determined by availability of treatment or change of diagnosis (not reflected in the survival rate)

The survival Experience:

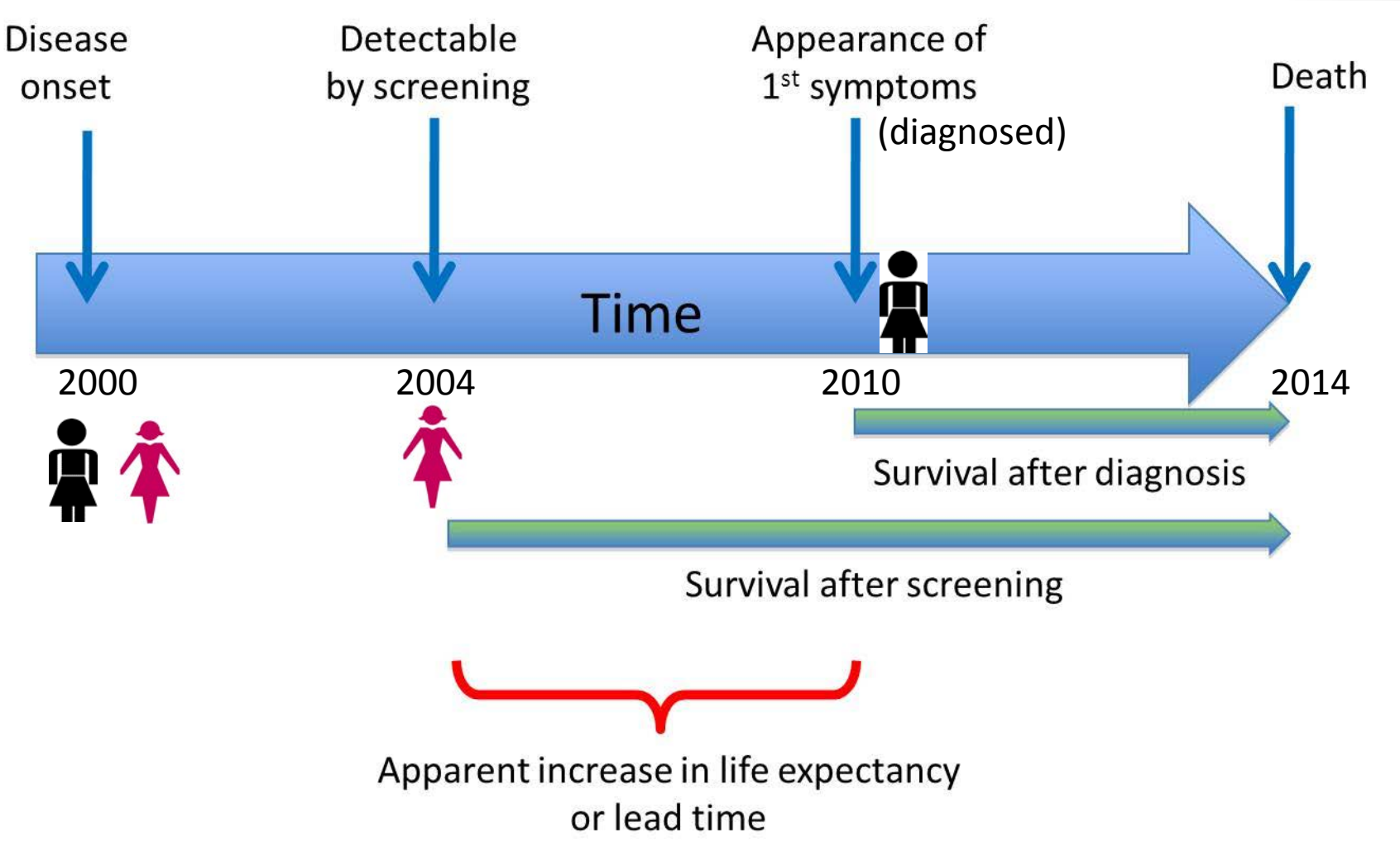


Kanchanarakas, S. (2008). ocw.jhsph.edu/courses/fundepi/PDFs/Lecture9.pdf

Lead-time Bias:

- Delay between when the disease in detectable by screening and when it is likely to produce symptoms that would lead to diagnosis
- This is a problem with evaluating a program based on disease outcome, particularly survival rates (which is typically counted from time of diagnosis)
- Gives the illusion of better outcome because of earlier detection when there may not truly have been any benefit from screening and early detection

Lead-time bias



Lead-time Bias:

- If ignored, a lead time bias would give a **false impression of survival rates** when comparing screened and unscreened groups by altering the numerator in the calculation of survival rate to look more favourable.

Length time bias summary:

Fact

- The natural history of disease is not the same in every individual

Fact

- Screening is more likely to detect cases wherein disease progression is slow.

Fact

- Diseases that progress slowly typically have more favourable outcomes

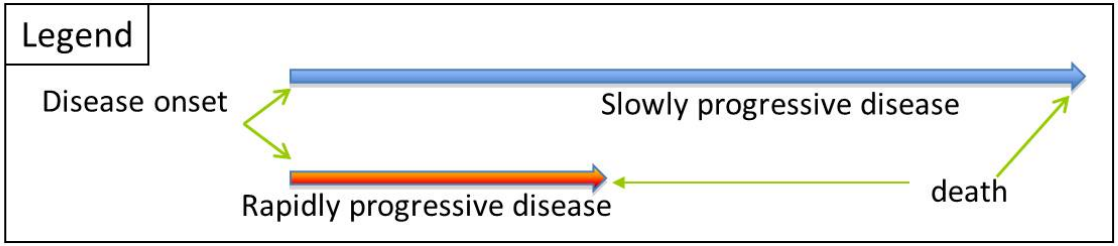
Impression

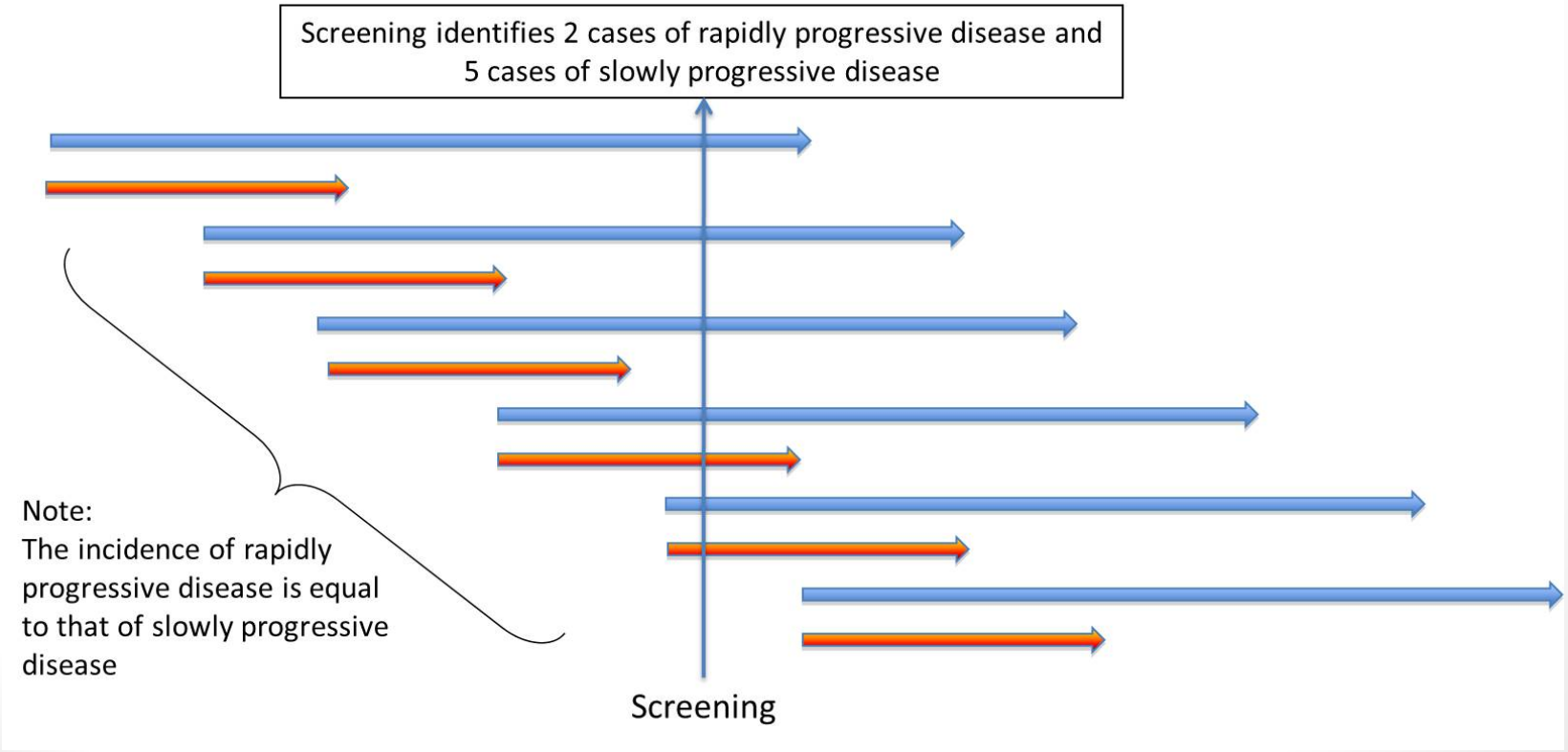
- Screening may appear to be more effective than it actually is because screening detects cases with a better prognosis.

Reality

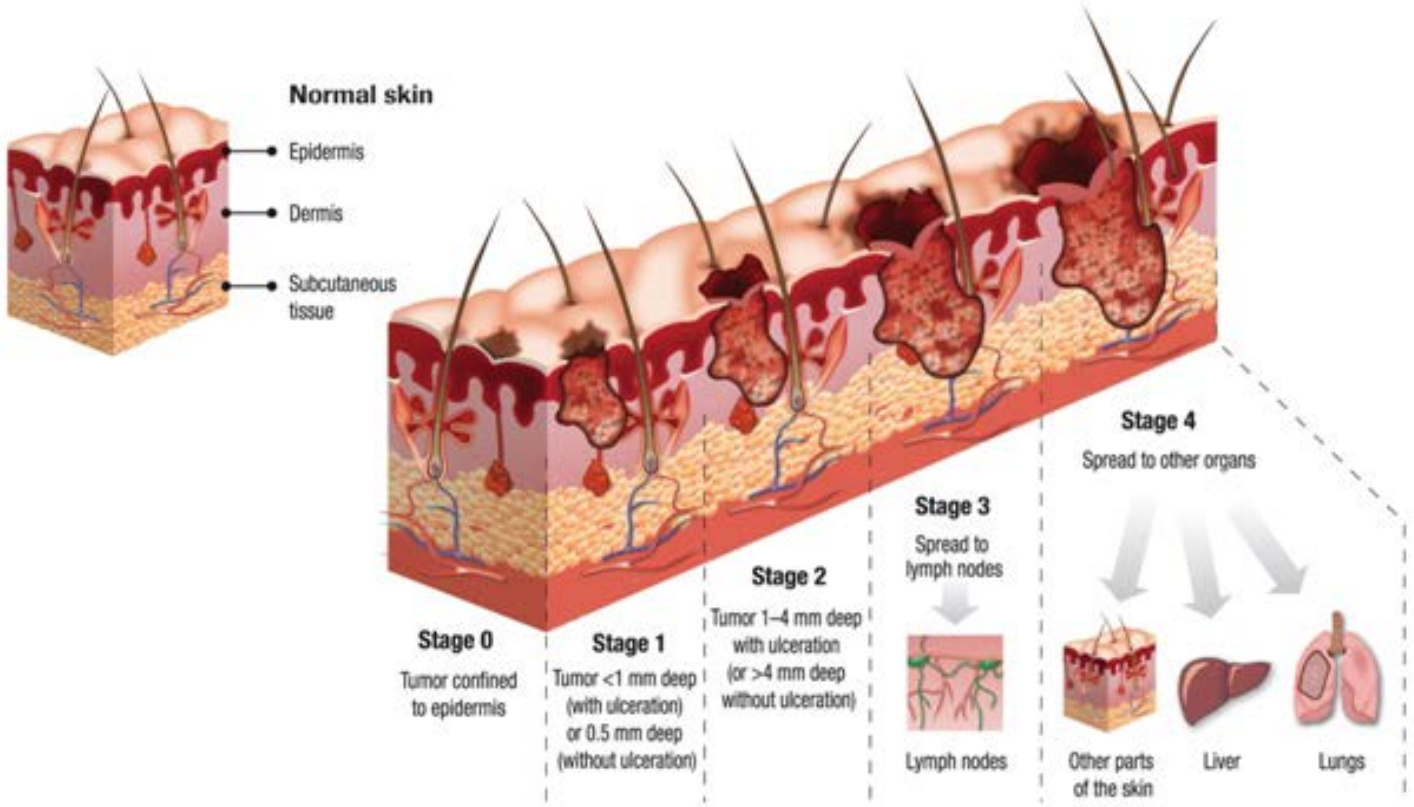
- Less dangerous diseases (with a more favourable outcome) are more likely to be detected by screening

Length time bias

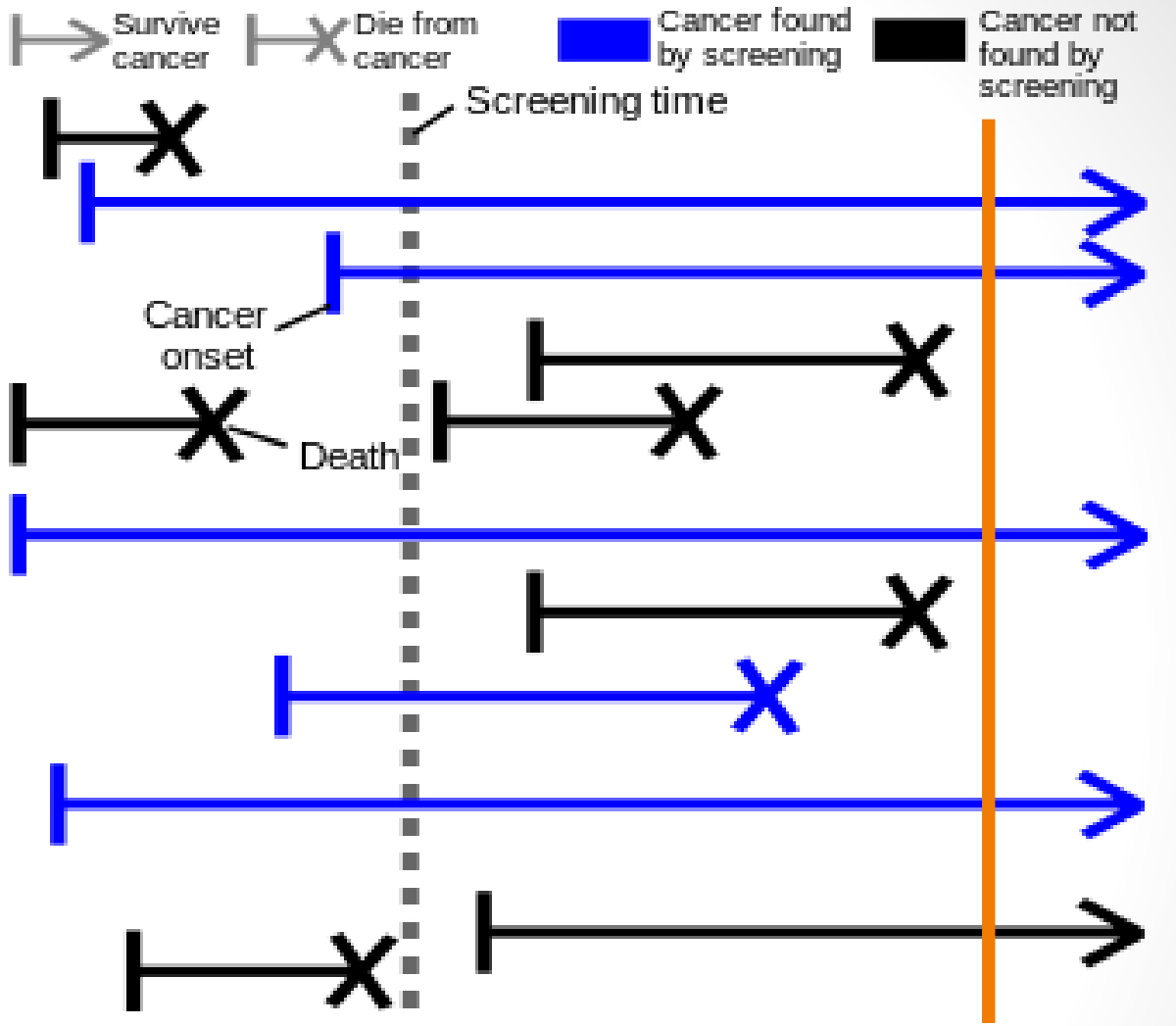




Example:
Skin Cancer



Length-time Bias



	Death from cancer	Survive cancer	% surviving cancer
Cancer discovered through screening	1	4	80%
Truly had cancer	7	5	41.7%

Disease Screening in Alberta:

Cancer Screening

- http://www.screeningforlife.ca/risk-assessment-tool

Newborn Metabolic Screening

- http://www.albertahealthservices.ca/services.asp?pid=service&rid=1056756

Prenatal Screening

- http://www.google.ca/url?sa=t&rct=j&q=&esrc=s&source=web&cd=2&ved=0CDUQFjAB&url=http%3A%2F%2Fwww.health.alberta.ca%2Fdocuments%2FPrenatal-Screening-Program-July-2007.pdf&ei=YIs8U8nNFeSMyAGUqYG4Ag&usg=AFQjCNFXdsyODcyj7oOGhk2r40RoXSVpaA&sig2=IcCh-T02hIx6ikKN2IP_YQ&bvm=bv.63934634,d.aWc

In class assignment - Screening

40 minutes

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