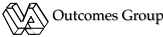


Two Misleading Statistics: *Relative Change & Survival*

Numbers in Medicine

Two Misleading Statistics:
Relative Change & Survival

H. Gilbert Welch MD, MPH



Two Misleading Statistics:
Relative Change & Survival

1. Relative change: % decrease, % increase, RR
 - *tends to exaggerate effects*
2. Survival: 5-year survival, 10-year survival
 - *not only exaggerates benefit of early detection, but also can obscure a true effect of harm*

Which is more important?

A a 30% reduction in LDL cholesterol

B a 30% reduction in diastolic blood pressure

Two Misleading Statistics: *Relative Change & Survival*

Which is more important?

- A a reduction in LDL cholesterol from 130 to 90
- B a reduction in diastolic blood pressure from 130 to 90

Which is more important?

- A a 40% reduction in death
- B a 40% reduction in hip fracture

Which is more important?

- 4 fewer deaths per 1000
- A a reduction in death from 8 to 4 per 1000 50% reduction
 - B a reduction in death from 20 to 16 per 1000 20% reduction
- 4 fewer deaths per 1000

Two Misleading Statistics: *Relative Change & Survival*

How to avoid being misled
<p>1. Relative change: % decrease, % increase, RR <i>Find the absolute change: where you start, where you end up</i></p>

The most common measure of relative change: Relative Risk			
<p>A ratio of two risks $\frac{\text{Risk in exposed}}{\text{Risk in unexposed}}$</p>			
<u>Risk in intervention</u>	<u>Risk in those taking drug</u>	<u>Risk in those exposed to toxin</u>	<u>Risk in those getting new therapy</u>
Risk in control	Risk in those taking placebo	Risk in those not exposed	Risk in those getting standard therapy

Relative risk	
<p>Absolute risk → Risk in exposed</p> <p>Absolute risk → Risk in unexposed</p>	<p>→ Relative risk</p>

Two Misleading Statistics: *Relative Change & Survival*

Interpreting a relative risk

A relative risk greater than 1 means that the exposure (intervention, toxin, new therapy) increases the chance of the outcome.

A relative risk less than 1 means that the exposure (intervention, toxin, new therapy) decreases the chance of the outcome.

A relative risk of 1 means that the exposure (intervention, toxin, new therapy) is not related to the outcome.

Interpreting RRs in words *now you try:*

*Think
"times the risk"*

RR = 0.8 for heart disease following new therapy vs. controls.

Patients taking new therapy have ____ times the risk of heart disease as controls

RR = 10 for lung cancer in smokers vs. non-smokers

Smokers have ____ times the risk of lung cancer as non-smokers

RR = 1.5 for cancer in patients taking new drug vs. those not taking it

Patients taking new drug have ____ times the risk of cancer as those not taking it

RR = 0.4 for stroke in patients taking new drug vs. placebo

Patients taking new drug have ____ times the risk of stroke as those taking placebo

Interpreting a relative risk less than 1


The percentage decrease is 1 minus the RR (then convert to %)

RR of 0.8 is a "20% decrease in risk"


The RR = 0.80
1 - 0.80 = 0.20
or a 20% decrease

Two Misleading Statistics: *Relative Change & Survival*

Relative Risks obscure Absolute Risks <i>RRs hide ARs</i>					
	RISK OF BAD EVENT			Statement of:	
	No Action	Action	RR	Relative Risk Reduction	Absolute Risk Reduction
A	500/1000	300/1000	0.6	40% decrease	200 fewer 1000
B	100/1000	60/1000	0.6	40% decrease	40 fewer 1000
C	5/1000	3/1000	0.6	40% decrease	2 fewer 1000

 Outcomes Group

Relative Risks obscure Absolute Risks <i>RRs hide ARs</i>					
	RISK OF BAD EVENT			Statement of:	
	No Action	Action	RR	Relative Risk Reduction	Absolute Risk Reduction
A	1/1000	0/1000	0.0	100% decrease	1 fewer 1000
B	5/1000	4/1000	0.8	20% decrease	1 fewer 1000
C	500/1000	499/1000	0.998	0.2% decrease	1 fewer 1000

 Outcomes Group

How to avoid being misled
<p>1. Relative change: % decrease, % increase, RR <i>Find the absolute change: where you start, where you end up</i></p>

Two Misleading Statistics: *Relative Change & Survival*

Tamoxifen for Prevention of Breast Cancer

NCI presentation

50% fewer breast cancers

Relative change

Endometrial cancers increased
from 5 to 13 per 1000 over 5 years

Absolute change

Welch presentation

Breast cancers reduced
from 43 to 22 per 1000 over 5 years

Absolute change

2.6 fold more endometrial cancers
"more than double the rate"

Relative change

Tamoxifen for Prevention of Breast Cancer JNCI 1998;90:1371-1388

Two Misleading Statistics: Relative Change & Survival

1. Relative change: % decrease, % increase, RR

- *tends to exaggerate effects*

2. Survival: 5-year survival, 10-year survival

- *not only exaggerates benefit of early detection, but also can obscure a true effect of harm*

Mammography May Be Beneficial To All Women, Regardless Of Age

In women who are 80 years or older, the 5-year survival for breast cancer patients was 82% among those who did not use mammography and 94% among those who did.

What's wrong with concluding that mammography is working?

1. Not randomized - women who choose to be screened may systematically differ from those who choose not to.

2. Biased statistic - all survival statistics are biased by early detection.

<http://www.sciencedaily.com/releases/2008/04/080421180946.htm>

Two Misleading Statistics: *Relative Change & Survival*

Survival always rises with cancer screening

- If mortality falls, survival will rise
- If mortality is unchanged, survival will rise
- If mortality rises, survival will rise

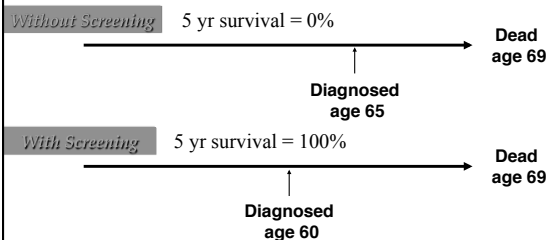
Survival always exaggerates the benefit of cancer screening

Why? Survival always rises with cancer screening

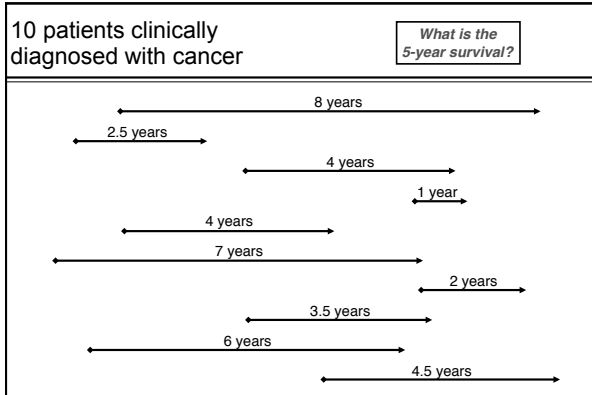
1. For a screening test to work, it must cause patients to be diagnosed earlier than they would be otherwise.

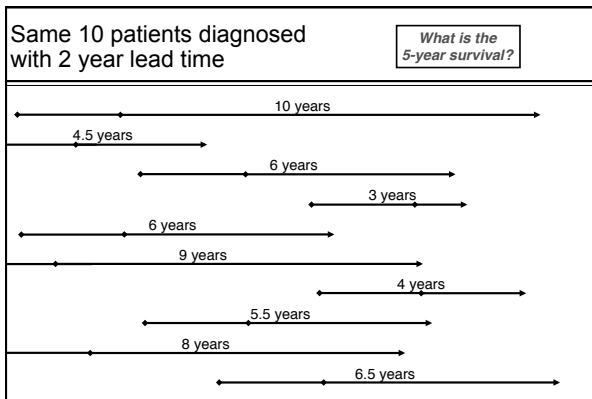
In other words, a screening test must introduce *lead time* and thus a lead time bias.

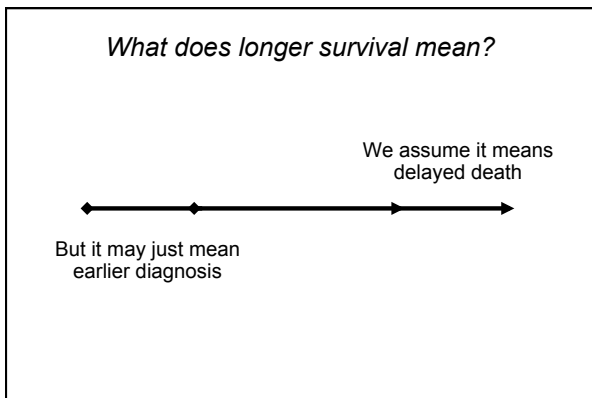
How lead time bias increases survival, even if there has been no prolongation in life



Two Misleading Statistics: *Relative Change & Survival*



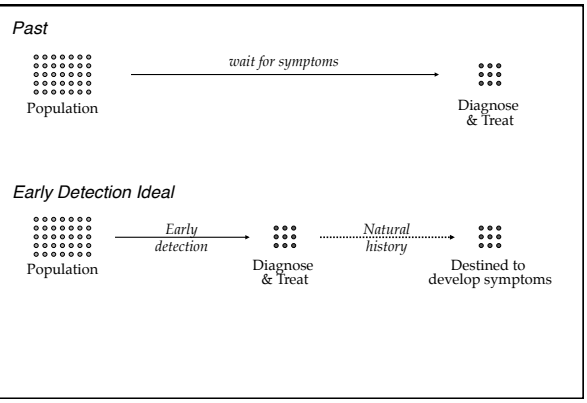


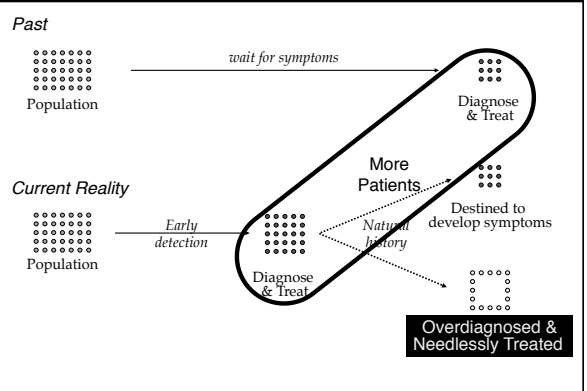


Two Misleading Statistics: *Relative Change & Survival*

Why? Survival always rises with cancer screening

1. For a screening test to work, it must cause patients to be diagnosed earlier than they would be otherwise.
 In other words, a screening test must introduce *lead time* and thus a lead time bias.
2. Because screening tests attempt to find pre-clinical disease, some degree of *overdiagnosis* is probably the rule – not the exception.
 Overdiagnosis bias results from pseudodisease inflating both the numerator and the denominator of the survival statistic.





Two Misleading Statistics: *Relative Change & Survival*

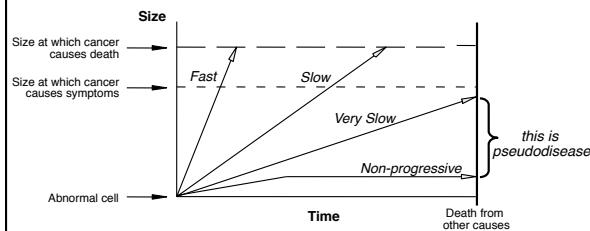
An uncomfortable reality...

The pathologic diagnosis of "cancer" encompasses a wide variety of abnormalities.

The familiar: cellular abnormalities which, if left untreated, progress to cause death.

The unfamiliar: cellular abnormalities that do not progress (and may even regress).

The heterogeneity of cancer progression



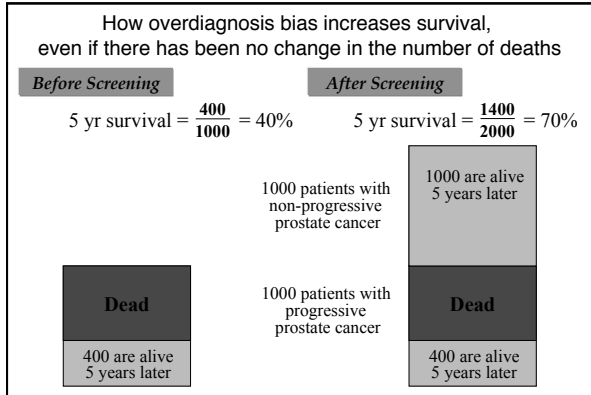
As we look harder for cancer, we always find more

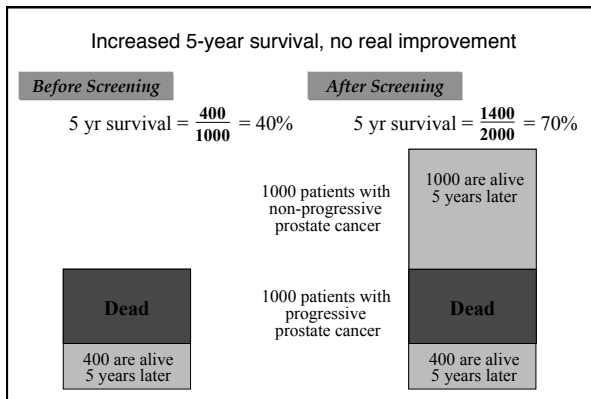
Some of the cancer we find may meet the pathologic definition of cancer,

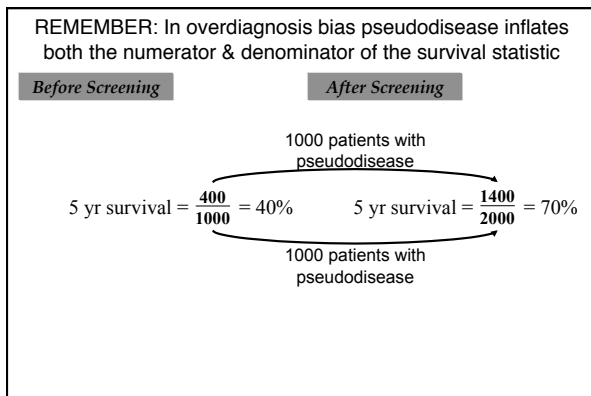
yet never progress to cause symptoms or death

Detection of pseudodisease = Overdiagnosis

Two Misleading Statistics: *Relative Change & Survival*







Two Misleading Statistics: *Relative Change & Survival*

Clinical examples of how the two biases combine
to suggest dramatic benefits following early detection
when none (or little) is present

- Lung Cancer
- Prostate Cancer
- Trends among the 20 most common cancers

Mayo Randomized Trial of Screening Chest X-rays for Lung Cancer

	Chest X-ray	Usual care
Number diagnosed with lung cancer	206	160
% Early stage	40%	26%
5-year survival	35%	19%
Lung cancer mortality (per 1000 person-years)	4.4	3.9

Marcus PM, Bergstrahl EJ, Fagerstrom RM, et al. Lung cancer mortality in the Mayo Lung Project: impact of extended follow-up. J Natl Cancer Inst. 2000 Aug 16;92:1308-16.

**This does not mean anyone has had their
"life extended" or "death delayed"**

ESTABLISHED IN 1912 OCTOBER 26, 2006 VOL. 355 NO. 17

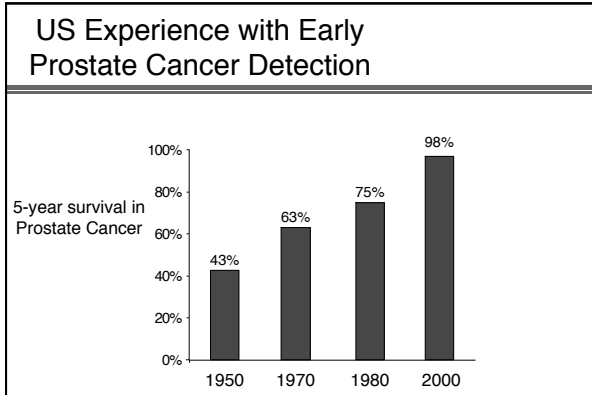
Survival of Patients with Stage I Lung Cancer Detected on CT Screening

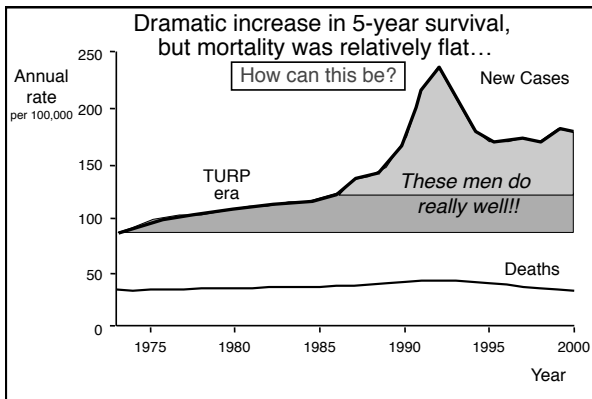
The International Early Lung Cancer Action Program Investigators*

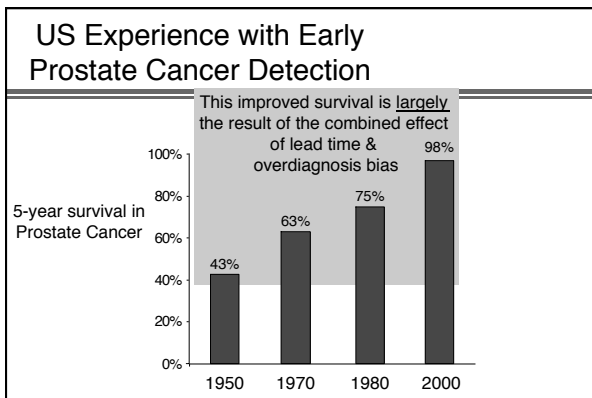
The article reports, lung cancer diagnosed by CT has a 10-year survival approaching 90% and invites the comparison to the 10-year survival of 10% for lung cancer detected through traditional means.

**These data are perfectly compatible with patients
having their life shortened by the screening process**

Two Misleading Statistics: *Relative Change & Survival*







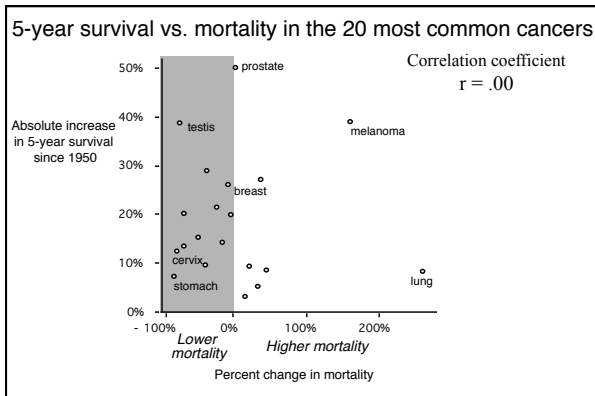
Two Misleading Statistics: *Relative Change & Survival*

In the context of cancer screening
survival is a remarkably misleading word

"increased survival" \neq "extended life"
or
"delayed death"

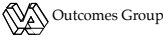
In the context of cancer screening
survival is a remarkably misleading metric

Survival rate \neq 1 - Mortality rate
Higher survival rate \neq Lower mortality rate



Two Misleading Statistics: *Relative Change & Survival*

7.6-year survival: the world's most misleading cancer statistic



Basic Measures

Numerator	Cancer patients alive 5-years after diagnosis	Cancer deaths
Denominator	Cancer patients	Entire population

↑
Early detection changes who is in the denominator (and the time they get there)

How to avoid being misled

1. Relative change: % decrease, % increase, RR
*Find the absolute change:
where you start, where you end up*
2. Survival: 5-year survival, 10-year survival
 - *Ignore the statistic when assessing the value of early detection – it is hopelessly biased*
 - *The measure you want is mortality*
