

We can prevent more than half of  
cancer now:  
An update on evidence including  
weight gain and breast cancer

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Montreal, Canada**

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Graham A. Colditz, MD DrPH, FAFPHM  
Department of Surgery  
Division of Public Health Sciences



Washington University in St. Louis

SCHOOL OF MEDICINE

# Goals of talk

Review potential for cancer prevention

Consider time frame and next steps to achieve sustained cancer prevention

Issues/Lessons:

- Improving cancer prevention,
- Implementing what we know,
- Integrating risk factors across life course, and
- Clarifying our time frame is essential to achieving our goals.

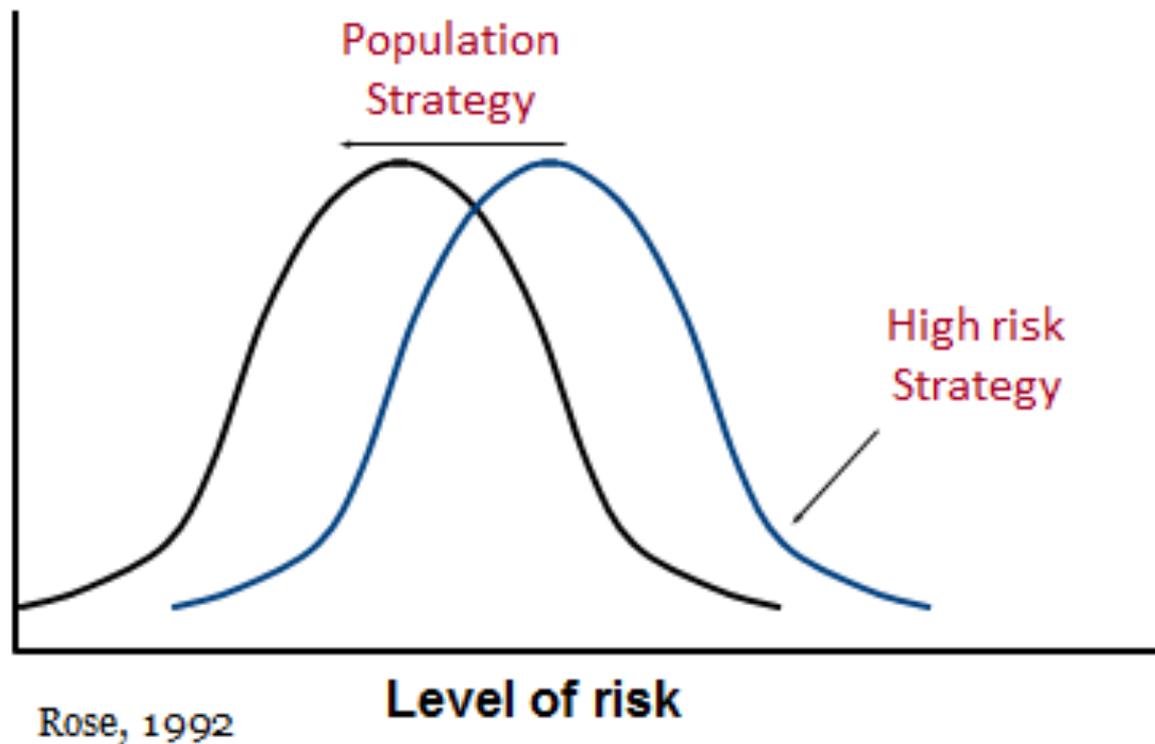
# Medical interventions proven to prevent cancer

(Colditz et al. Sci Trans Med 2012)

Intervention	Target	Magnitude of reduction	Time (yrs)
Aspirin	Colon mortality	40%	20+
SERMs	Breast incidence	40-50%	5+
Salpingo oophorectomy	Familial breast ca	50%	3+
Screening for colorectal ca	Colon ca mortality	30-40%	10
Vaccination	Cervical ca incidence	50-100%	20+
	Liver ca incidence	70-100%	20+
Mammography	Breast ca mortality	30%	10-20
Serial CT lung	Lung ca mortality	20%	6+

# Population approach versus high risk strategy

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# Behavioral, Social and Policy interventions that impact Cancer Prevention

Intervention	Target	Type of Ix	Evidence review
Reduce tobacco use	Children and Adolescents  Smokers to quit	Combined Pharmaco/ behavioral Ixs Smoke-free policies Tobacco taxes	Surgeon General, USA
Increase physical activity	Individuals and community norms	Urban design Stairs and workplace	Surgeon General, USA
Reduce Obesity	Population	School & work environment Physical activity Food & beverage	Inst. of Medicine report
Limit alcohol intake	Population	Taxes	WHO

# When we implement what we know, we prevent cancer

Tobacco –

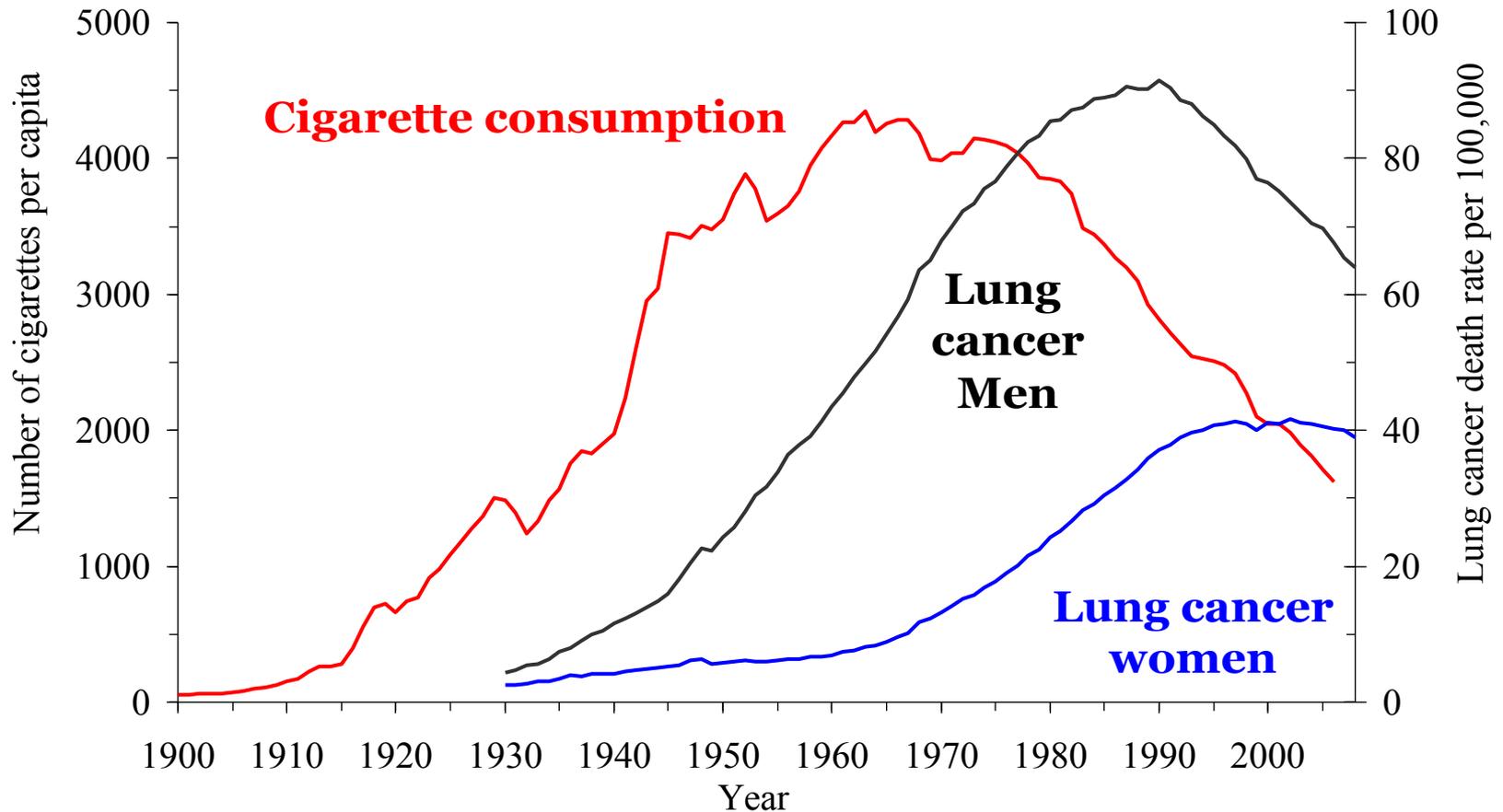
lung cancer mortality decreased by one third

- Adolescent smoking decrease 35% (1999) to 18% (2011)

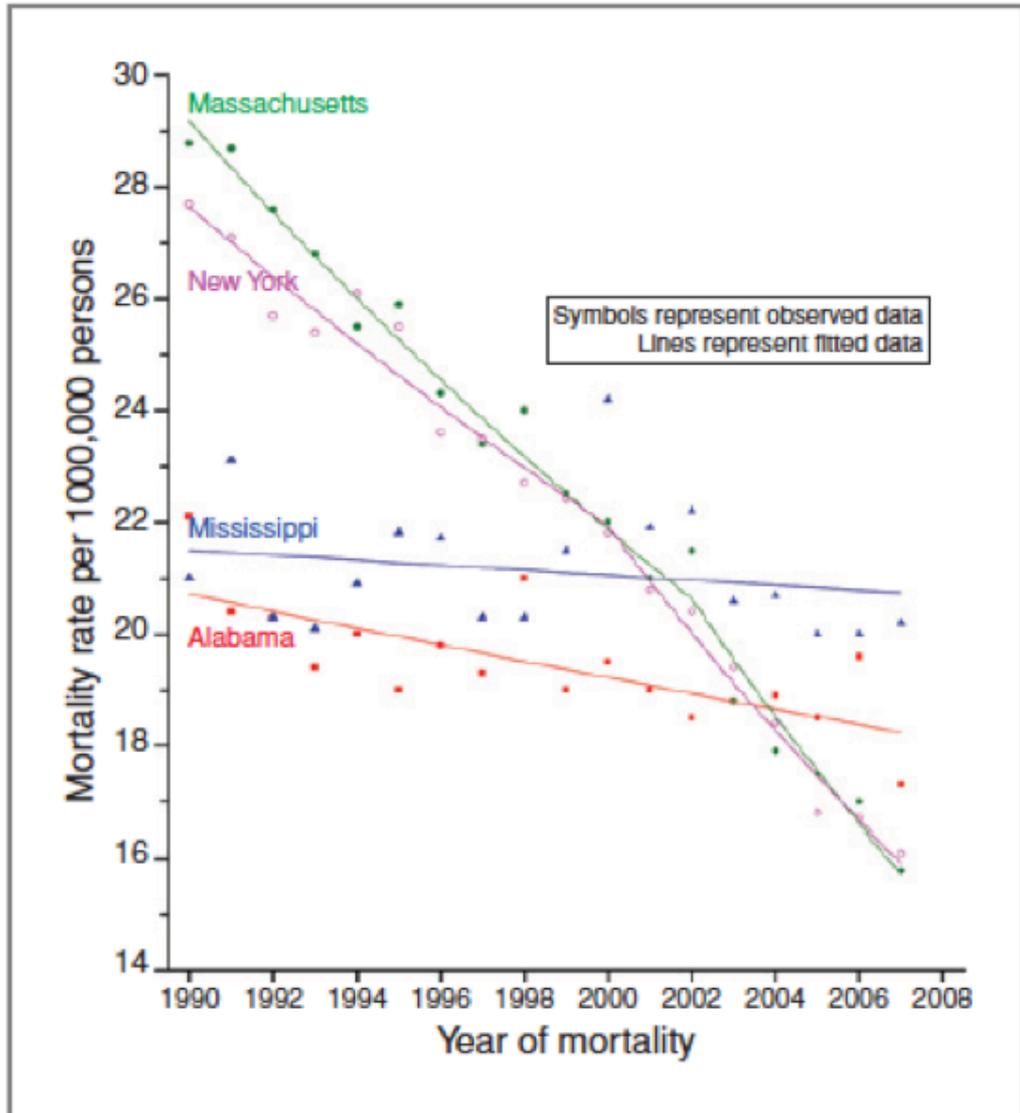
Colorectal cancer screening –

steady increase in use and reduction in CRC mortality over time

# Trends in smoking and lung cancer, USA

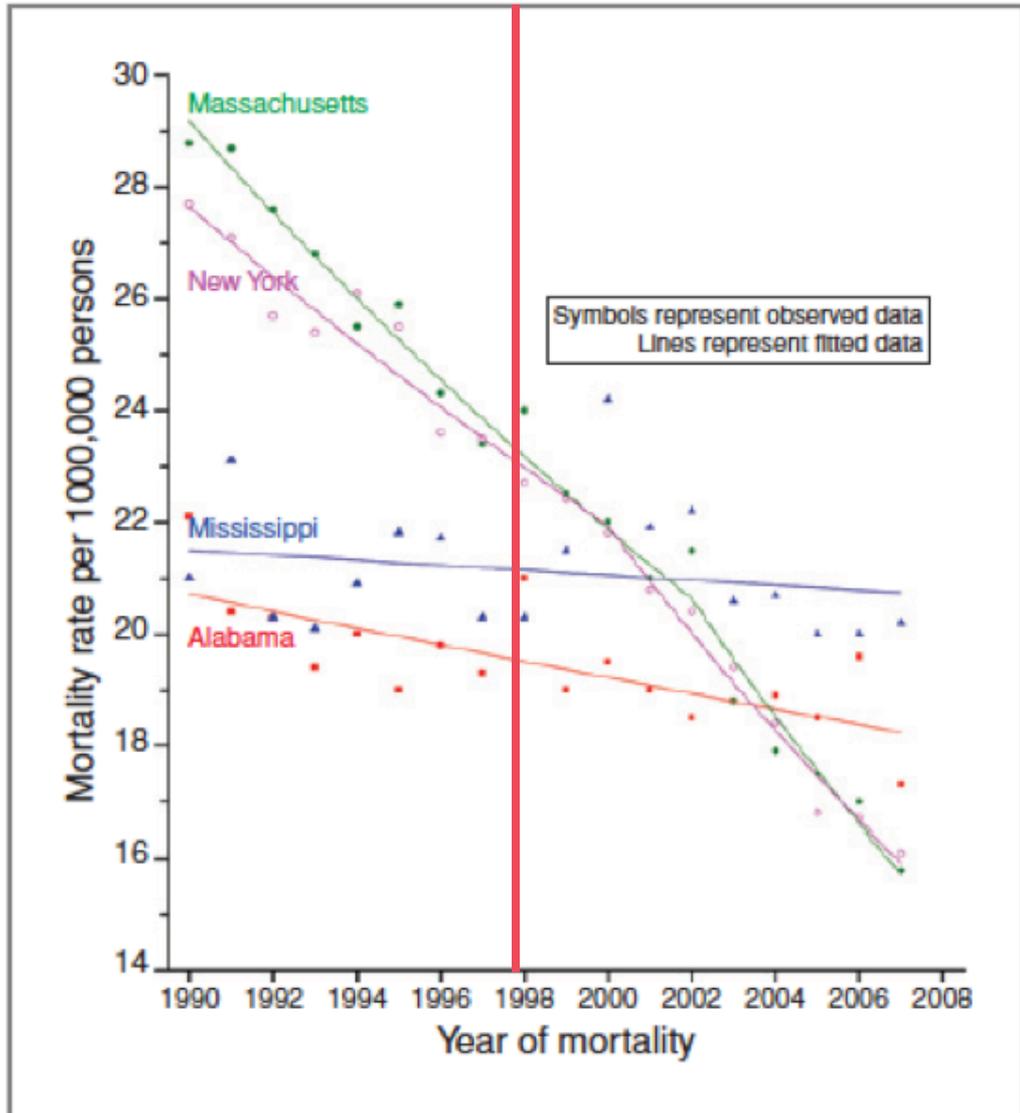


# Trends: CRC mortality



Naishadham et al  
CEBP 2011

# Trends: CRC mortality



Naishadham et al  
CEBP 2011

# Lifestyle: high income countries

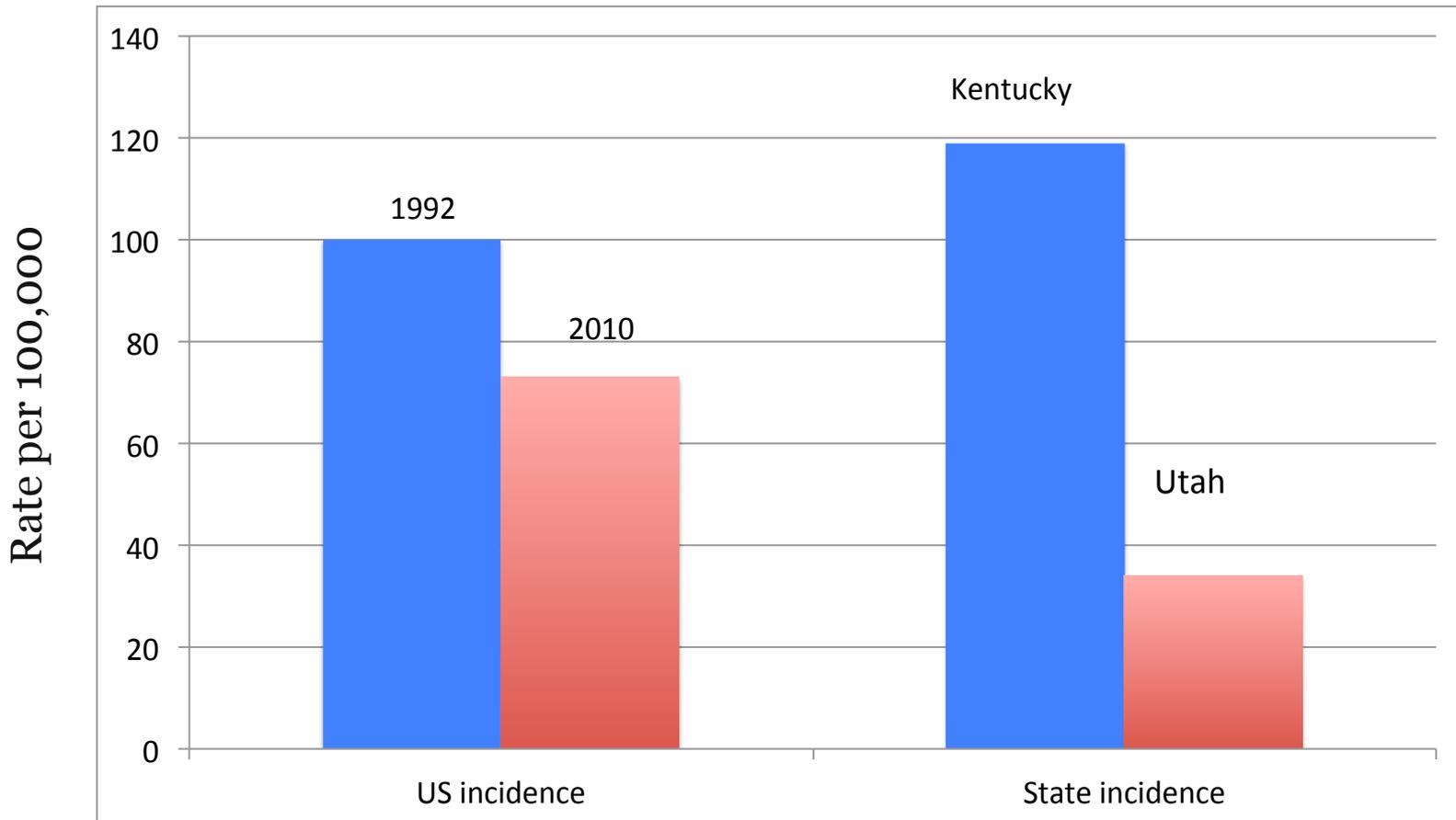
Cause	% cancer caused	Magnitude possible reduction	Time (yrs)
Smoking	33		
Overweight/obesity	20		
Diet	5		
Lack of exercise	5		
Occupation	5		
Viruses	5-7		
Family history	5		
Alcohol	3		
UV/ionizing radiation	2		
Reproductive	3		
Pollution	2		

Colditz et al. Sci Transl Med 2012: March 28

# Lifestyle: high income countries

Cause	% cancer caused	Magnitude possible reduction	Time (yrs)
Smoking	33	75%	
Overweight/obesity	20	50%	
Diet	5	50%	
Lack of exercise	5	85%	
Occupation	5	50%	
Viruses	5-7	100%	
Family history	5	50%	
Alcohol	3	50%	
UV/ionizing radiation	2	50%	
Reproductive	3	0	
Pollution	2	0	

# Burden Cigarette Smoking, USA



# Lifestyle: high income countries

Cause	% cancer caused	Magnitude possible reduction	Time (yrs)
Smoking	33	75%	10-20
Overweight/obesity	20	50%	2-20
Diet	5	50%	5-20
Lack of exercise	5	85%	5-20
Occupation	5	50%	20-40
Viruses	5-7	100%	20-40
Family history	5	50%	2-10
Alcohol	3	50%	5-20
UV/ionizing radiation	2	50%	2-10
Reproductive	3	0	N/A
Pollution	2	0	N/A

## Risk of Cancer with Increased BMI

Cancer	Sample Size	Follow-up (yrs)	RR Men	RR Women
Breast (premenopausal)	2.5 mil	11.0	-	0.92**
Breast (postmenopausal)	2.5 mil	11.0	-	1.12***
Colon	4.8 mil	11.0	1.24*	1.09*
Endometrium	3.0 mil	10.6	-	1.59*
Gallbladder	3.3 mil	12.7	1.09	1.59***
Gastric	4.7 mil	10.8	0.97	1.04
Leukemia	4.7 mil	13.7	1.08**	1.17***
Liver	3.3 mil	12.7	1.24	1.07
Lung	2.6 mil	11.9	0.76*	0.80***
Multiple myeloma	5.2 mil	14.6	1.11*	-
Non-Hodgkin lymphoma	5.0 mil	12.4	1.06*	1.07
Oesophageal adenocarcinoma	4.7 ml	10.8	1.52*	1.51*

Relative risk for a 5 point increase in BMI. For example, the relative risk linked to a BMI of 28 compared to a BMI of 23; or a BMI of 32 compared to 27.

\*p < .0001; \*\*p < .01; \*\*\*p < .05

# 1 Maintain a healthy weight

## Weight loss lowers risk

Risk of breast cancer dropped by 60% in women who lost more than 10 kg (22 pounds) after menopause

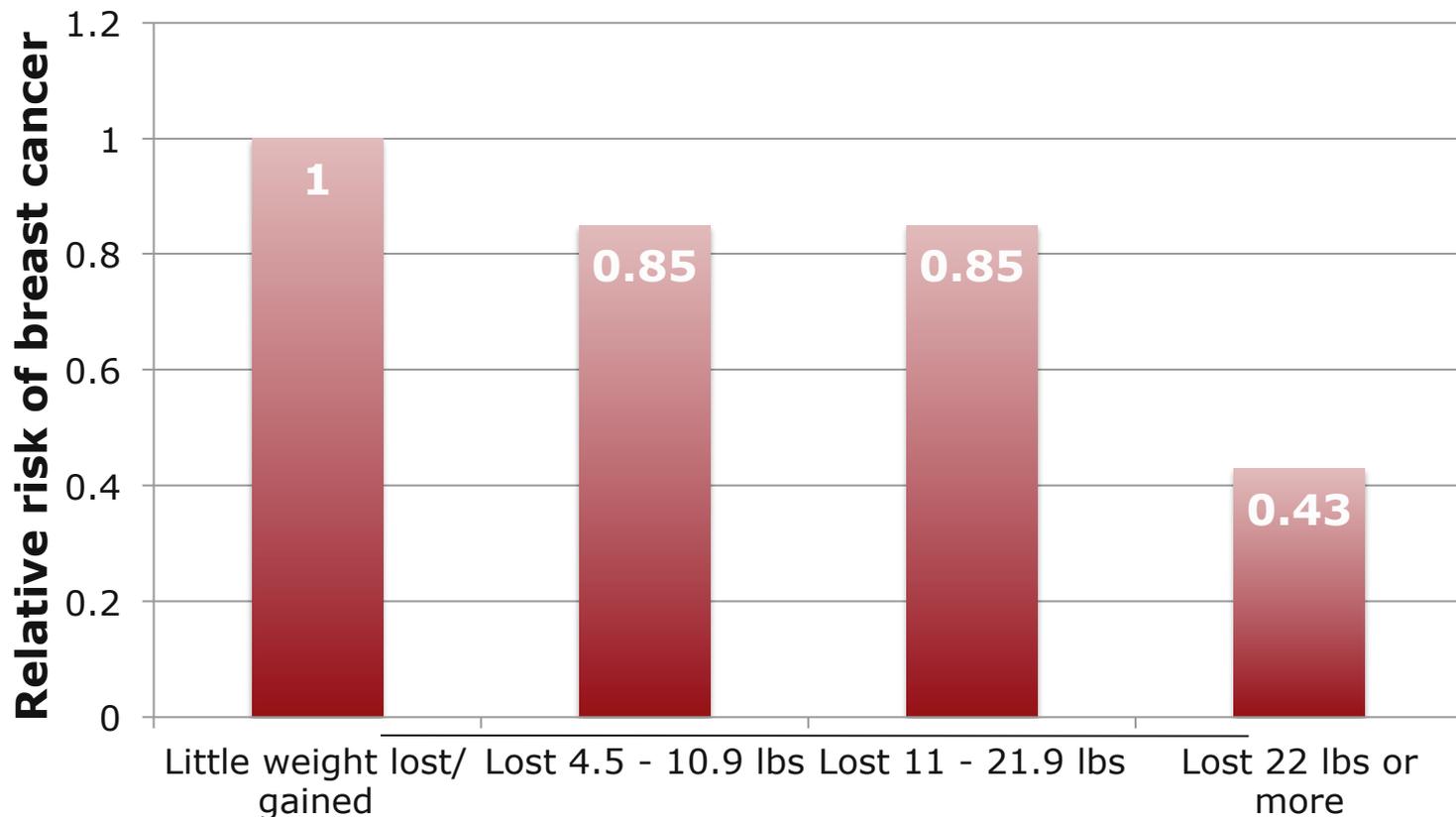
Loss of just 5 pounds lowered risk by 15%

Eliassen et al JAMA 2006



8 WAYS TO  
PREVENT CANCER

# Sustained Weight Loss and Risk of Breast Cancer in Postmenopausal Women Who Never Used Postmenopausal Hormones



**Amount of sustained weight loss since menopause**

Eliassen et al, JAMA 2006

TREC – Cross TREC project

# **DISENTANGLING WEIGHT WEIGHT GAIN AND TIMING**

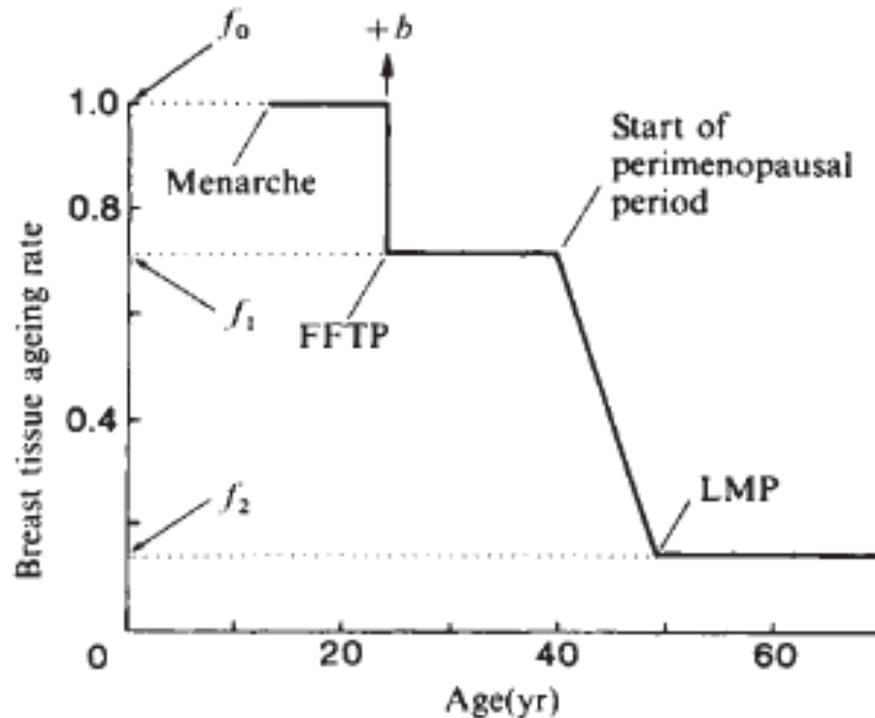
U54 CA155496

# Risk factors account for 76% discrepancy China vs. US

- Compared age-specific incidence in Shanghai prospective cohort vs. SEER.
- Then fit Rosner-Colditz model to account for risk factors:
  - Age at menarche, age at first and subsequent births, height, weight at 18 and through adult life, alcohol, menopause, type of menopause (natural, surgical), use of postmenopausal hormone therapy (E alone, E+P), benign breast disease, family history breast ca.
- 76% of the US excess incidence controlled away with the established risk factors.
- Leaves open the dynamics of growth, childhood and adolescence

Linos,...,Colditz JNCI 2008;100:1352-60

# Pike model – Nature 1983



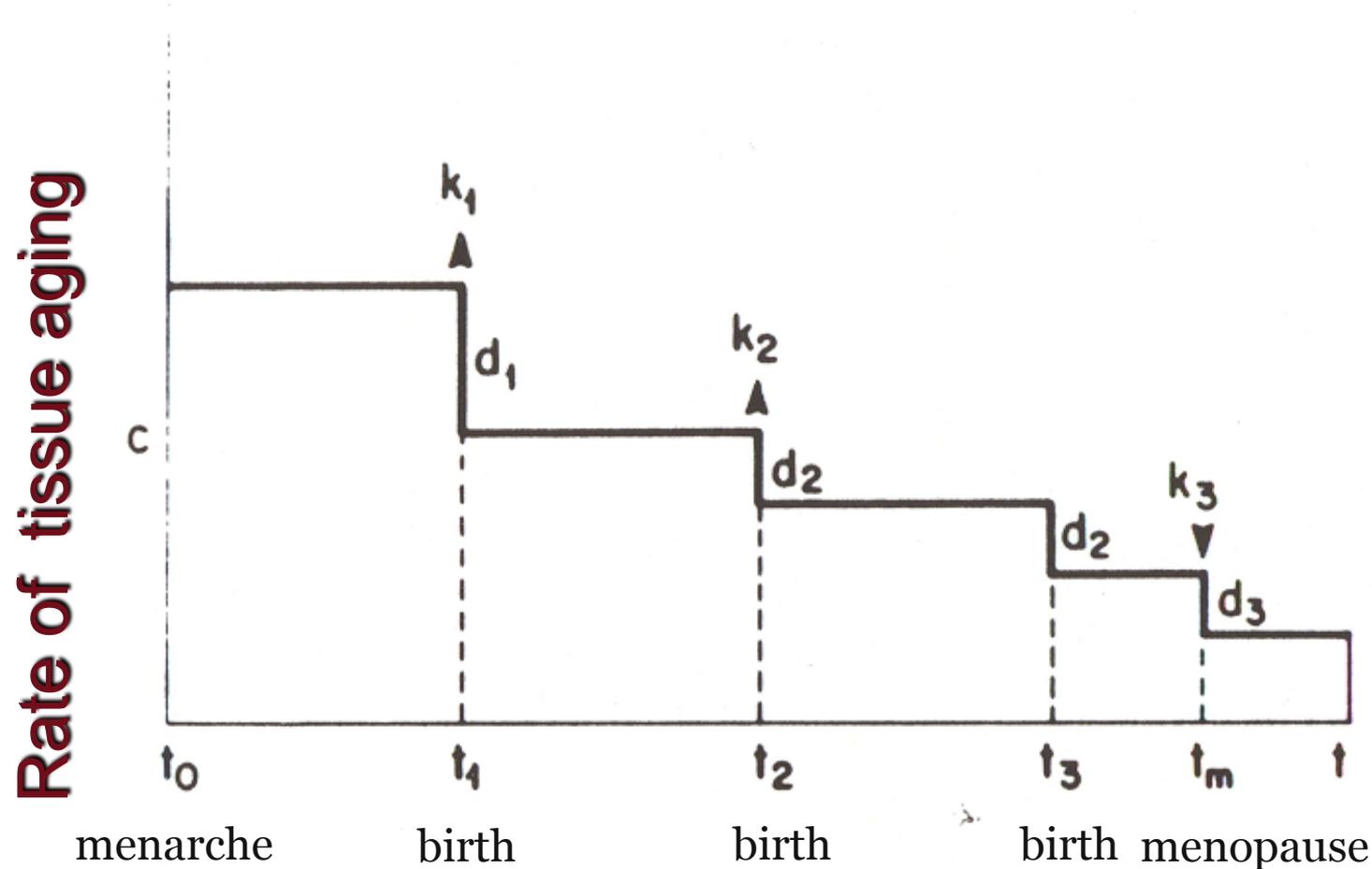
To accommodate the higher incidence with late first birth, we add a constant representing an increase in risk with FFTP

(+b) in figure

**Fig. 2** Model of rate of breast tissue ageing (see text). LMP, last menstrual period.

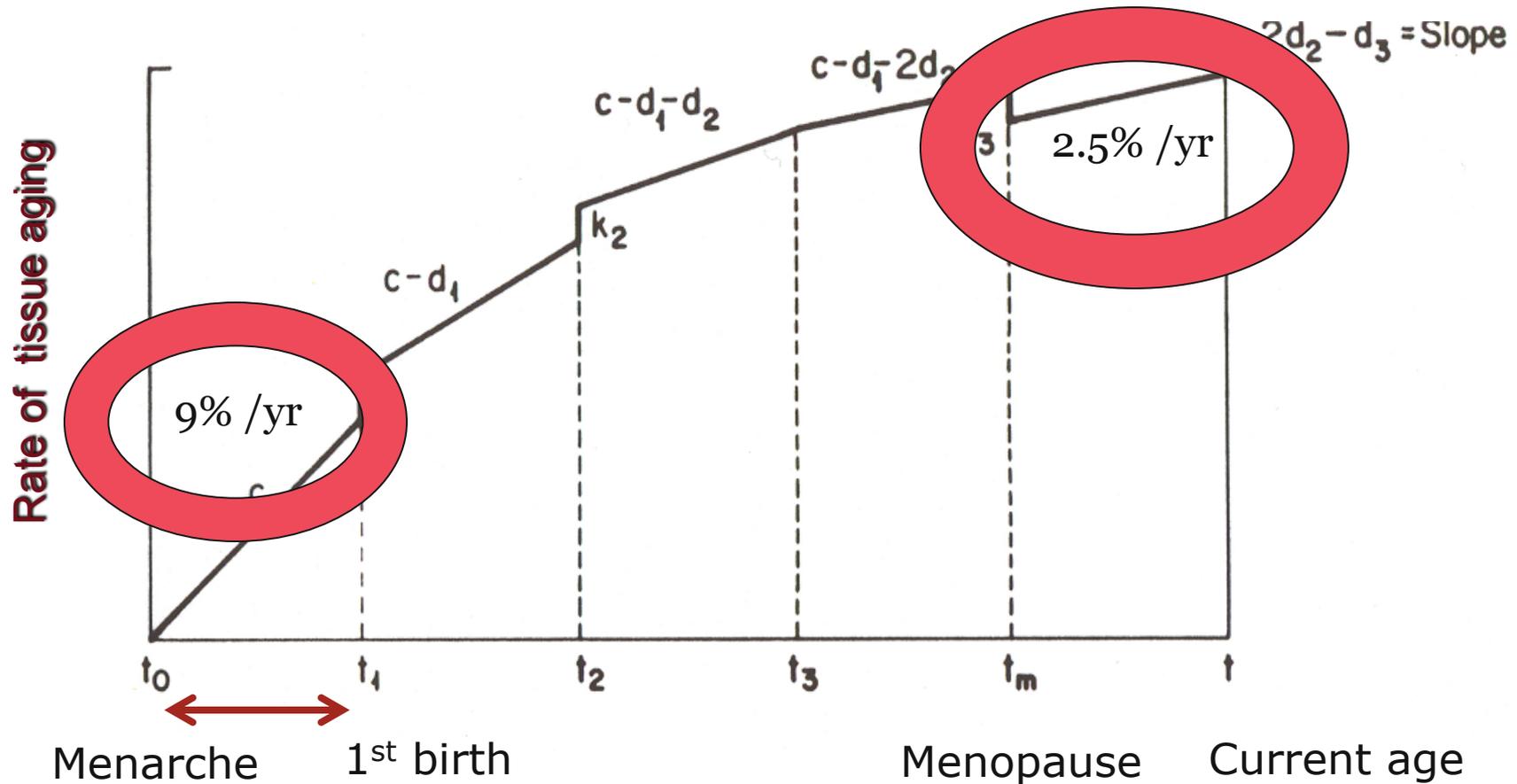
Pike, et al. Nature 1983

# Accumulating risk, multiple birth model



Rosner, Colditz, Willett, Am J Epidemiology 1994;139:826

# Accumulating risk, multiple birth model



Rosner, Colditz, Willett Am J Epidemiology 1994;139:826

# Effects of obesity on breast cancer

- Obesity is well-established as a risk factor for post-menopausal breast cancer.
- Obesity is protective for pre-menopausal breast cancer

# Short-term effects of weight gain on breast cancer incidence

- Short-term effects of weight change on breast cancer risk are largely unknown
- We investigated short-term effects of obesity on breast cancer using NHS data

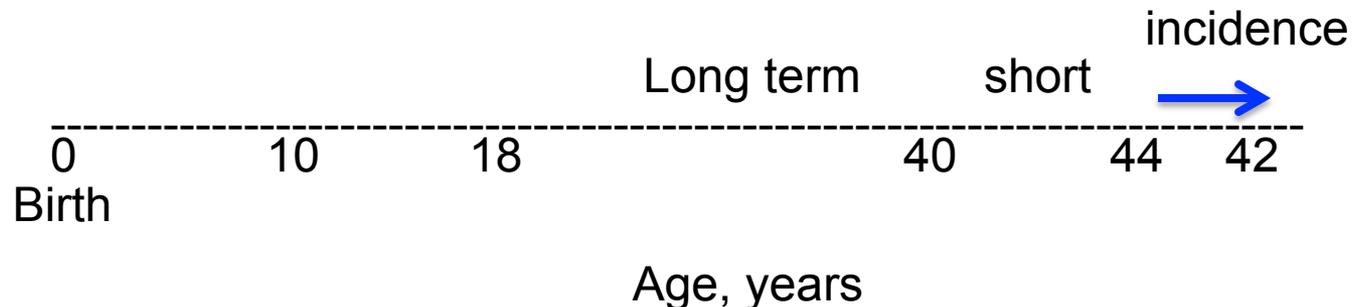
# Study Population – Nurses' Health Study

- 77, 232 women followed over 1,445,578 person-years from 1980-2008
- 4,196 incident cases of invasive breast cancer

Rosner et al Breast Cancer Res Treat 2015

# Analytical approach

- Log incidence model of breast cancer (Colditz, et al AJE 2000) used to predict incident breast cancer as a function of
  - 1) Average BMI before menopause
  - 2) Average BMI after menopause
  - 3) Other breast cancer risk factors
- Short-term weight gain  $\equiv$  weight gain over previous 2 cycles ( $\approx$  4 years) added as an additional risk factor



**Association between 4-year weight change (1990-1994)**  
**and selected breast cancer risk factors in 1994, NHS,**  
**45,009 women**

Variable		Wt loss of > 5lbs	No change	Wt gain of 5.1-9.9lbs	Wt gain of 10.0-14.9lbs	Wt gain of ≥ 15.0lbs
	N	5,610	22,202	5,207	5,732	6,258
Age	Mean	<b>61.8</b>	<b>60.8</b>	<b>59.6</b>	<b>58.8</b>	<b>57.9</b>
Pre-menopausal	(%)	<b>9</b>	<b>12</b>	<b>14</b>	<b>17</b>	<b>18</b>
Weight at age 18	Mean	<b>130.7</b>	<b>124.1</b>	<b>123.3</b>	<b>126.2</b>	<b>131.8</b>
Current weight	Mean	<b>153.2</b>	<b>147.1</b>	<b>152.4</b>	<b>164.5</b>	<b>185.4</b>
Current HT use	(%)	<b>35.9</b>	<b>43.6</b>	<b>45.5</b>	<b>44.2</b>	<b>44.1</b>
Age at 1 <sup>st</sup> birth	Mean	<b>25.5</b>	<b>25.3</b>	<b>25.1</b>	<b>25.0</b>	<b>24.9</b>
Parity	Mean	<b>3.0</b>	<b>3.0</b>	<b>2.9</b>	<b>2.9</b>	<b>2.9</b>

# 4-year weight change, breast ca. incidence

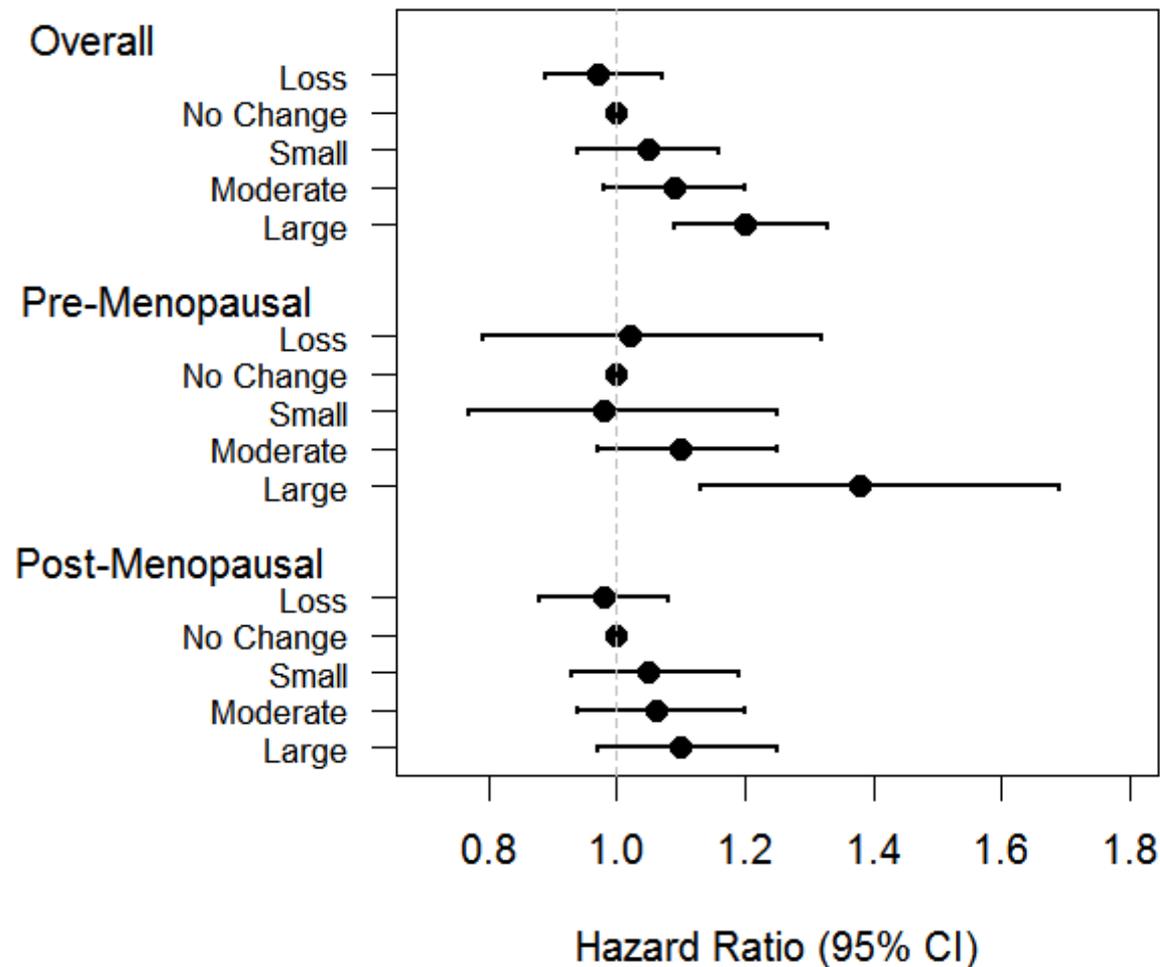
Group	Number of Cases	Loss of > 5lbs	No change (ref)++	Gain of 5.1-9.9lbs	Gain of 10.0-14.9lbs	Gain of ≥ 15.0lbs	RR**	P_trend
overall	4196	0.97* (0.89-1.07)	1.0	1.05 (0.94-1.16)	1.09 (0.98-1.20)	1.20 (1.09-1.33)	1.13 (1.06-1.21)	<0.001
Pre-menopausal +	736	1.02 (0.79-1.32)	1.0	0.98 (0.77-1.25)	1.10 (0.88-1.38)	1.38 (1.13-1.69)	1.26 (1.08-1.48)	0.004
Post-menopausal +	3443	0.98 (0.88-1.08)	1.0	1.05 (0.93-1.19)	1.06 (0.94-1.20)	1.10 (0.97-1.25)	1.08 (1.00-1.16)	0.063

\*HR (95% CI)  
 \*\* per 25 lbs.  
 + at both time points  
 ++ weight change of ≤ 5lbs.

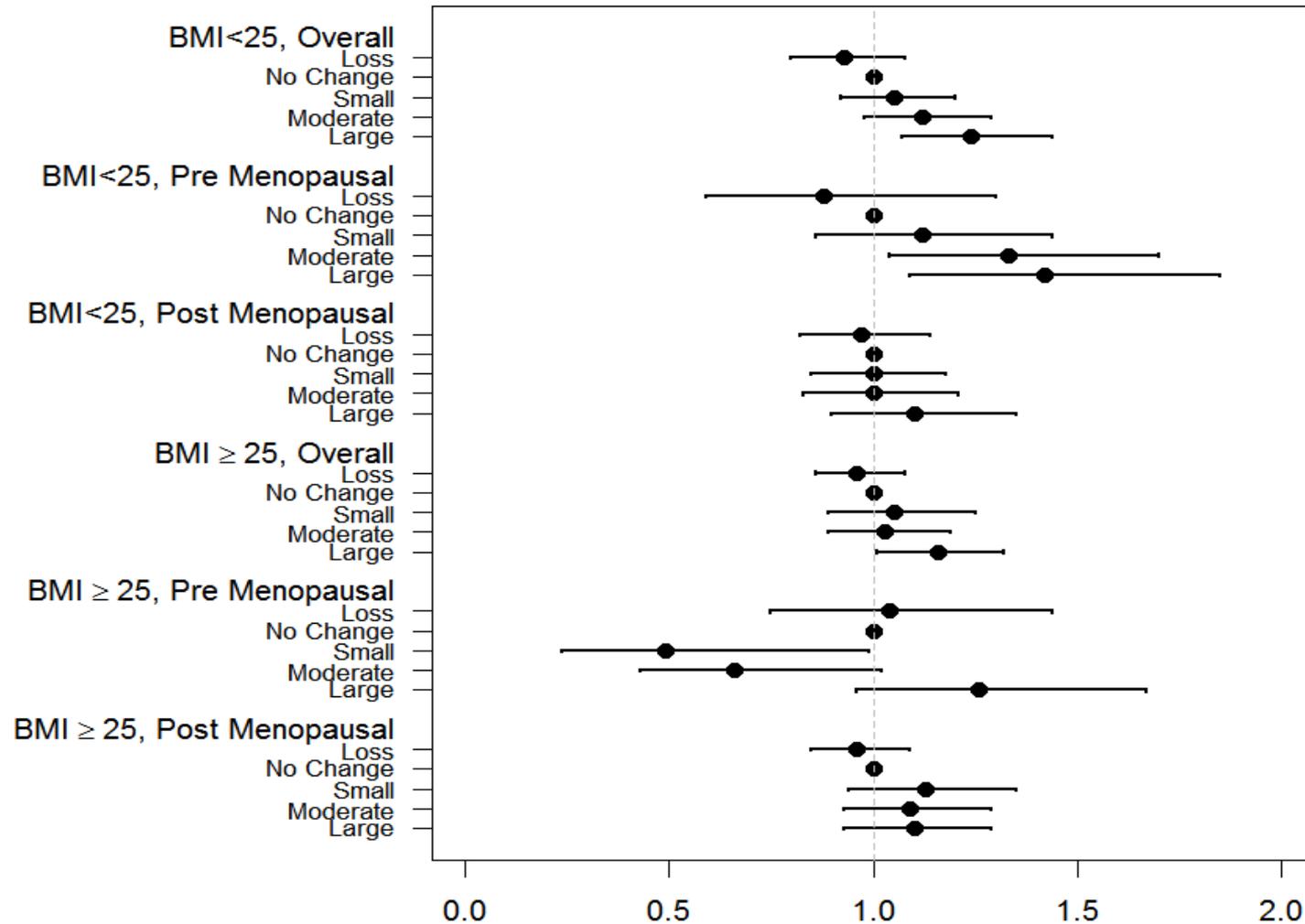
Rosner et al Breast Cancer Res Treat 2015

Overall there is a significant association of short-term weight gain with breast cancer incidence, particularly during pre-menopause.

# Short term weight change, risk of breast ca



# Weight gain and risk according to starting BMI



# Associations of short-term weight gain by tumor subtype, pre-menopausal women

Group	Number of cases	Loss of > 5lbs	No change	gain of 5.1-9.9lbs	gain of 10.0-14.9lbs	gain of ≥ 15.0lbs	RR **	P_trend	P_het <sup>†</sup>
ER+/PR+	316	0.94* (0.63-1.40)	1.0	0.92 (0.63-1.34)	1.16 (0.83-1.61)	1.2 (0.93-1.73)	1.13 (0.89-1.42)	0.32	---
ER+/PR-	42	1.34 (0.50-3.58)	1.0	1.11 (0.41-2.95)	0.60 (0.18-1.99)	1.7 (0.80-3.89)	2.19 (1.33-3.61)	0.002	0.019
ER-/PR-	100	1.07 (0.50-2.29)	1.0	1.13 (0.57-2.26)	2.10 (1.23-3.56)	2.0 (1.21-3.31)	1.61 (1.09-2.38)	0.01	0.12

\*HR (95% CI)  
 \*\*per 25lbs  
 †vs ER+/PR+

Associations of pre-menopausal weight gain are stronger for ER+/PR- and ER-/PR- breast cancer, although case counts are small

# Association of short-term weight gain by tumor subtype, post-menopausal women

Group	Number of cases	Loss of > 5lbs	No change	gain of 5.1-9.9lbs	gain of 10.0-14.9lbs	gain of ≥ 15.0lbs	RR **	P_trend	P_het <sup>†</sup>
ER+/PR+	1518	0.96* (0.84-1.10)	1.0	1.03 (0.87-1.23)	1.01 (0.84-1.21)	1.06 (0.88-1.27)	1.05 (0.94-1.16)	0.40	---
ER+/PR-	419	0.73 (0.54-0.97)	1.0	1.21 (0.90-1.64)	0.80 (0.55-1.14)	0.91 (0.63-1.30)	1.25 (1.01-1.54)	0.043	0.15
ER-/PR-	419	1.36 (1.06-1.75)	1.0	1.00 (0.70-1.41)	1.39 (1.02-1.90)	1.01 (0.70-1.46)	0.99 (0.80-1.23)	0.93	0.65

\*HR (95% CI)  
 \*\*per 25lbs  
 †vs ER+/PR+

No significant heterogeneity by tumor type for post-menopausal women

## Summary – short-term weight gain

- Overall, there is a significant positive association of short-term weight gain on breast cancer incidence
- Associations are stronger among pre-menopausal women and women with BMI < 25
- Results are consistent with EPIC /PANACEA study (Emaus, et al., Int. J. Cancer 2014: 10.1002/ijc28926)

## Summary – long-term weight change

- Overall, there is a protective effect of weight at age 10 on breast cancer incidence, which is present for all breast cancer subtypes.
- Premenopausal weight change since age 18 positively related to breast cancer incidence for ER+/PR+ tumors.

# Possible Mechanisms

- Adiposity at age 10 is related to lower peak height growth which is related to lower risk of pre and post menopausal breast cancer
- Short-term weight gain leads to increase in glucose, a likely pathway for short-term weight gain and breast cancer incidence
- Long-term weight gain and ER+ breast cancer largely attributed to higher circulating estrogen levels, particularly after menopause
- Other pathways cannot be ruled out (inflammation)

# **8 WAYS** to **Stay Healthy & Prevent Cancer**

- 1 Maintain a healthy weight**
- 2 Exercise regularly**
- 3 Don't smoke**
- 4 Eat a healthy diet**
- 5 Drink alcohol only in moderation**
- 6 Protect yourself from the sun**
- 7 Avoid sexually transmitted infections**
- 8 Get screening tests**

# Possible Mechanisms

Short-term:

- Short-term weight gain leads to increase in glucose a likely pathway for short-term weight gain and breast cancer incidence
- Evidence stronger among leaner women where change in glucose may be more marked with short term weight gain

# Possible Mechanisms

## Long-term weight gain

- Adiposity at age 10 is related to lower peak height growth velocity, which is related to lower risk of pre and post menopausal breast cancer
- Long-term weight gain and ER+ breast cancer largely attributed to higher circulating estrogen levels, particularly after menopause

**my results** **zoom** health tracker

Results can be sent to your doctor, family, friends, or even to yourself to print.

Michelle

**my risks** Tap each to learn more

high  
above average  
average  
below average  
low

- stroke & heart disease
- lung cancer
- diabetes
- breast cancer
- colon cancer

**my profile**

Female  
59 years old  
5 feet, 7 inches tall  
27 pounds

**my healthy habits**  
daily aspirin  
little TV or screen time  
regular cancer screenings  
eat a lot of nuts, fruits & vegetables and whole grains

**my challenge**  
weight: too heavy  
smoking  
diet: not enough fish and healthy fats  
diet: too much full-fat dairy

my modified risk     
my original risk

Washington University School of Medicine in St. Louis

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**What is your risk?**

<b>Cancer:</b> There's much more to it than just smoking and lung cancer.	What's your cancer risk?
<b>Diabetes:</b> Over 18 million in the U.S. suffer from it. Take steps now to lower your risk.	What's your diabetes risk?
<b>Heart disease:</b> The #1 killer in the U.S. is also one of the most preventable.	What's your heart disease risk?
<b>Osteoporosis:</b> Calcium isn't the only way (or even the best way) to protect yourself.	What's your osteoporosis risk?
<b>Stroke:</b> Most cases of this feared disease can be avoided by lifestyle changes.	What's your stroke risk?

**Cancer News in Context**  
From the Prevention Team at the Siteman Cancer Center

Home | About CNIC | Prevention Snapshot | Extras | Cancer Screening | Glossary | Zero Conflicts

THURSDAY, OCTOBER 6, 2011

6 Ways to Prevent Breast Cancer

Ask women what they think is the biggest threat to their health, and most will answer "breast cancer." And even though lung cancer and heart disease kill more women each year,



facebook

**Your Disease Risk**  
THE SOURCE ON PREVENTION  
www.yourdiseaserisk.wustl.edu

Wait | Info | Links | Discussions | Notes

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**a Risk** Your Disease Risk News "Cancer News in Context" post.  
Cancer News in Context: Adolescent & Young Adult Drinking, Better Breast Disease, and Cancer Risk  
www.cancernewsincontext.org  
New results indicate that drinking a new study has found strong links between the drinking behavior of young women and adolescent girls and their risk of developing benign breast disease, a marker...

**a Risk** Your Disease Risk News research from YOR's Dr. Graham Colditz, showing that early life can have an important impact on later cancer risk.  
Adolescent drinking adds to risk of breast disease, breast cancer | Newsroom | Washington University  
www.wustl.edu  
Girls and young women who drink alcohol increase their risk of benign (noncancerous) breast disease, since a study by researchers at Washington University School of Medicine in St. Louis and Harvard University. Being breast disease increases the risk for developing breast cancer.

**a Risk** Your Disease Risk Cancer News in Context: Despite New Results - Keep Eating Your Fruits and Vegetables  
www.cancernewsincontext.org  
The headlines this week about fruits and vegetables doing little, if anything, to lower cancer risk may entice you to reach for a candy bar rather than a carrotstick, but there's still plenty of good...

**a Risk** Your Disease Risk Cancer News in Context: Health care reform and prevention of cancer  
www.cancernewsincontext.org  
In Sunday's New York Times (Story), Robert Pear writes about the many disease prevention initiatives contained in the new health care law recently passed by congress and approved by the president. It's important to stress and consider the full implications of this...

**Your Disease Risk**  
@YourDiseaseRisk

Healthy tweets from the team at the award winning website site at Washington University School of Medicine. Know your risk. Change your future.  
St. Louis, MO · <http://yourdiseaserisk.org>

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**Your Disease Risk** @YourDiseaseRisk 25 Sep  
Wonder about your ovarian cancer risk and what you can do to lower it? Visit "Your Disease Risk": [yourdiseaserisk.wustl.edu/hccpqulz.pl?la...](http://yourdiseaserisk.wustl.edu/hccpqulz.pl?la...) (#ovariancancer) Details

**Your Disease Risk** @YourDiseaseRisk 24 Sep  
Follow up is important but cost an issue for both



Graham Colditz, MD, DrPH  
Niess-Gain Professor of Surgery  
Chief, Division of Public Health Sciences,  
Dept. of Surgery  
Campus Box 8100  
660 South Euclid  
St. Louis, MO 63110  
(314) 454-7939  
[colditzg@wustl.edu](mailto:colditzg@wustl.edu)

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