

# L'importanza dello Stile di Vita

**Alessandra Fabi**  
*Oncologia Medica 1*



**2018**  
**CARCINOMA MAMMARIO**  
I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

ROMA 26 - 27 OTTOBRE  
NH COLLECTION ROMA CENTRO



**IRE**  **ISG**  
ISTITUTO NAZIONALE TUMORI    ISTITUTO DERMATOLOGICO  
**REGINA ELENA**    **SAN GALLICANO**  
ISTITUTI DI RICOVERO E CURA A CARATTERE SCIENTIFICO

**DO ADULTS CHANGE  
THEIR LIFESTYLE  
BEHAVIOURS AFTER  
A CANCER DIAGNOSIS?**

# Individual behaviour change

- People are **more inclined to change** their lifestyle behaviour **following a cancer diagnosis**
- People are **more inclined to change** if the issue is raised by a trusted professional
- And if they are provided with a quality behaviour change intervention



Diet & Weight gain



Phisycal Activity



Alcohol & Smoke



Lifestyle and side effects beyond diagnosis and treatment

# Potential Impact of Lifestyle Factors on Survivorship

## **Diet and Weight**

- Weight and weight gain may be associated with higher rates of breast cancer recurrence and mortality, especially in<sup>1</sup>
  - Those who have never smoked
  - Premenopausal women
  - Women who were normal weight at diagnosis
  - Women with early stage cancers
- Some studies have shown that a diet high in fat may be associated with an increased risk of recurrence<sup>2</sup>

Kroenke CH et al. *J Clin Oncol*. 2005;23:1370-1378

Chlebowski RT et al. *J Natl Cancer Inst*. 2006;98:1767-1775

Holmes MD et al. *JAMA*. 2009;293:2479-2486.

National Comprehensive Cancer Network. Breast Cancer Risk Reduction-v.2.2009

# Weight gain (after BC diagnosis)

Analysis 3993 pts



Weight gain after diagnosis has been associated with a higher rate of breast cancer recurrences and with worse OS

-Analysis in stage I to III BC, each 5-kg gain was associated with a 12% increase in all-cause mortality, a 13% increase in breast cancer specific mortality, and a 19% increase in cardiovascular disease mortality (1).

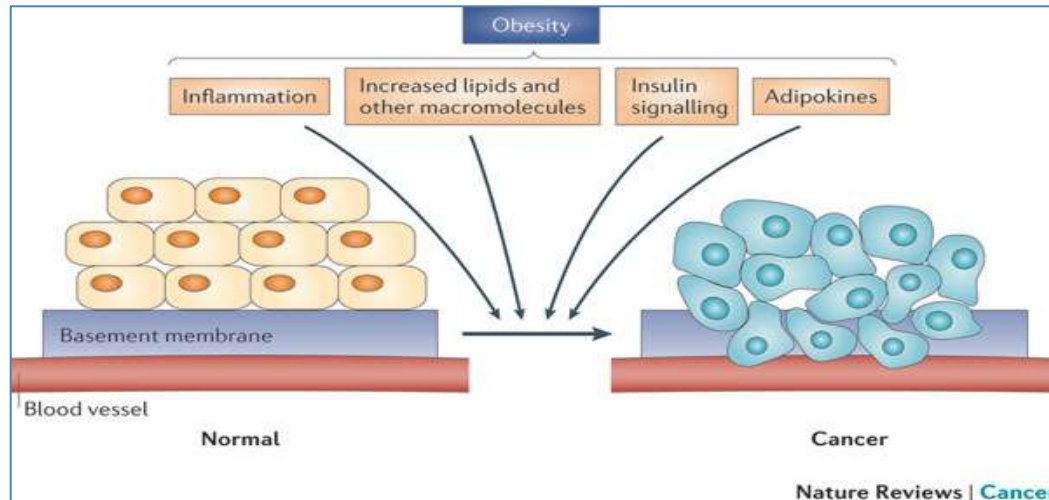
- Weight gain of greater than 10% was associated with breast cancer-specific mortality ( $p=.05$ ); but no amount of weight gain was associated with an increase in breast cancer recurrences. (2)

1. Nichols HB, Cancer Epidemiol Biomarkers Prev. 2009;

2. laydon MC, J Natl Cancer Inst 2015

# Quali sono le cause?

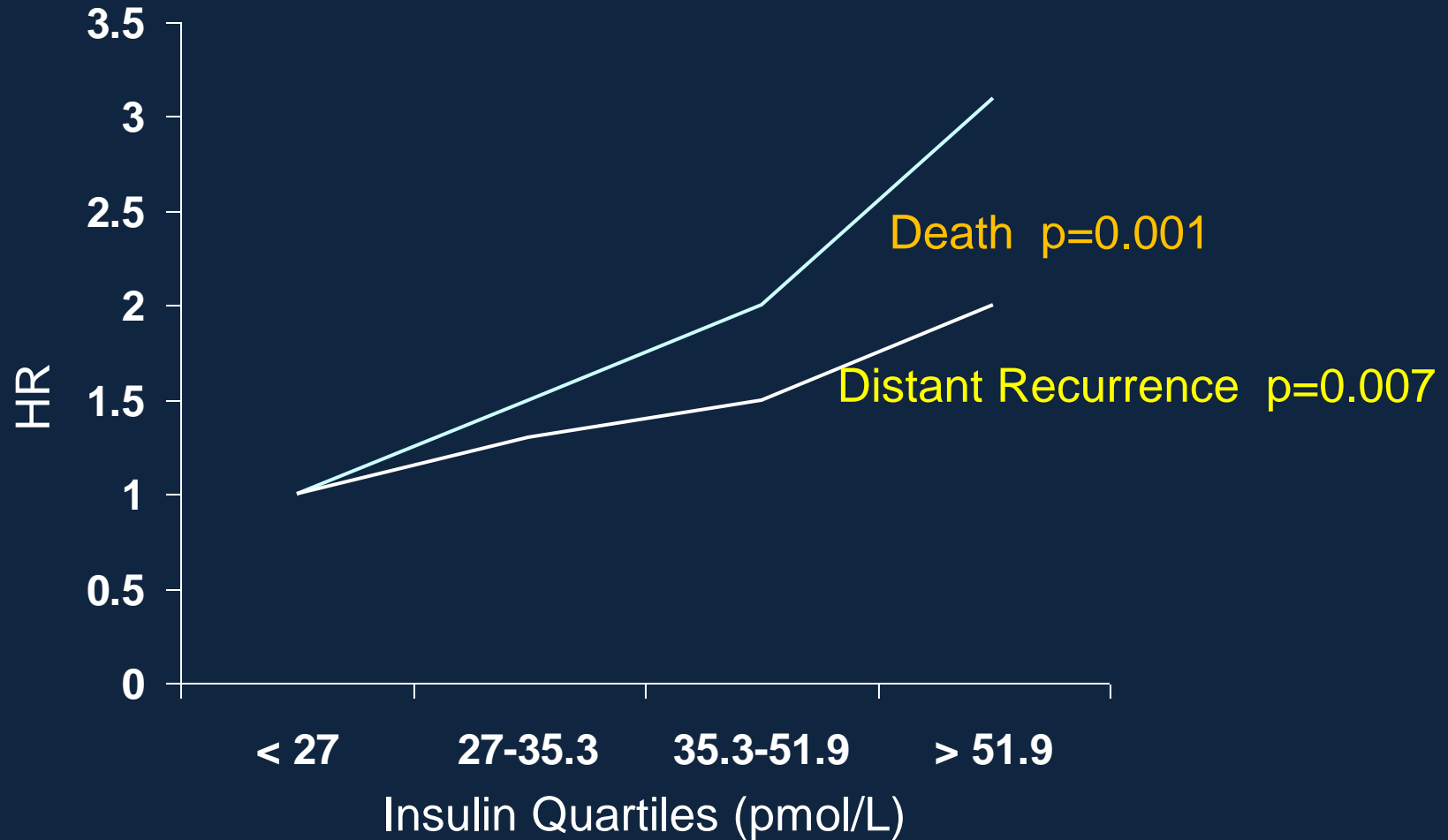
- ▶ Le basi fisiopatologiche sono da ricercarsi nella disregolazione metabolica ed endocrinologica tipica dell'obesità.



- ▶ Insulino resistenza (Insulina e IGF-1)
- ▶ Stato proinfiammatorio (IL-6, TNF $\alpha$ , PCR)
- ▶ Neoangiogenesi (PAI-1, VEGF)
- ▶ Incremento di Leptina ed Adiponectina

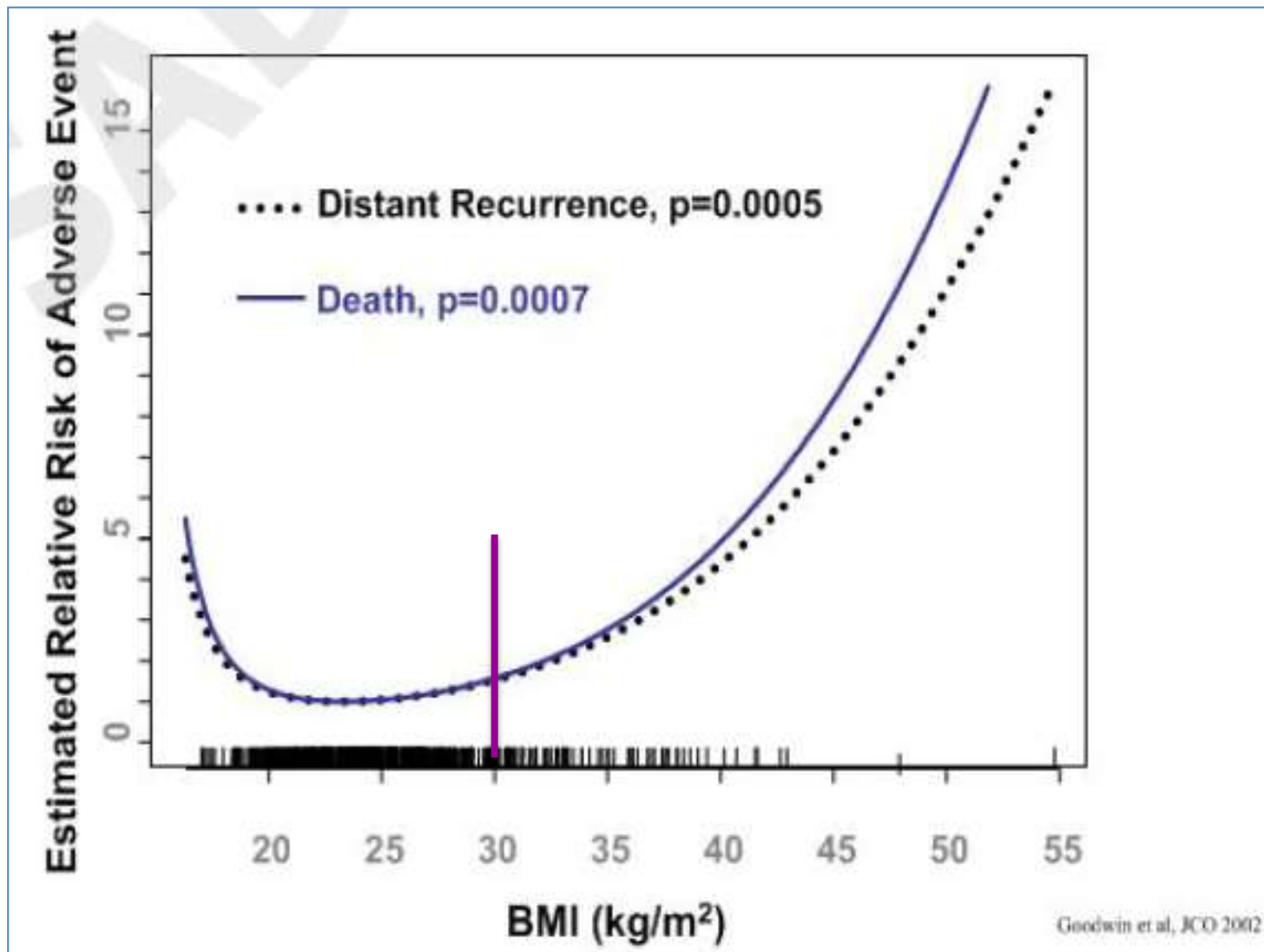
Proliferazione  
Sopravvivenza  
Invasività  
Metastatizzazione

# Insulin and Breast Cancer Prognosis

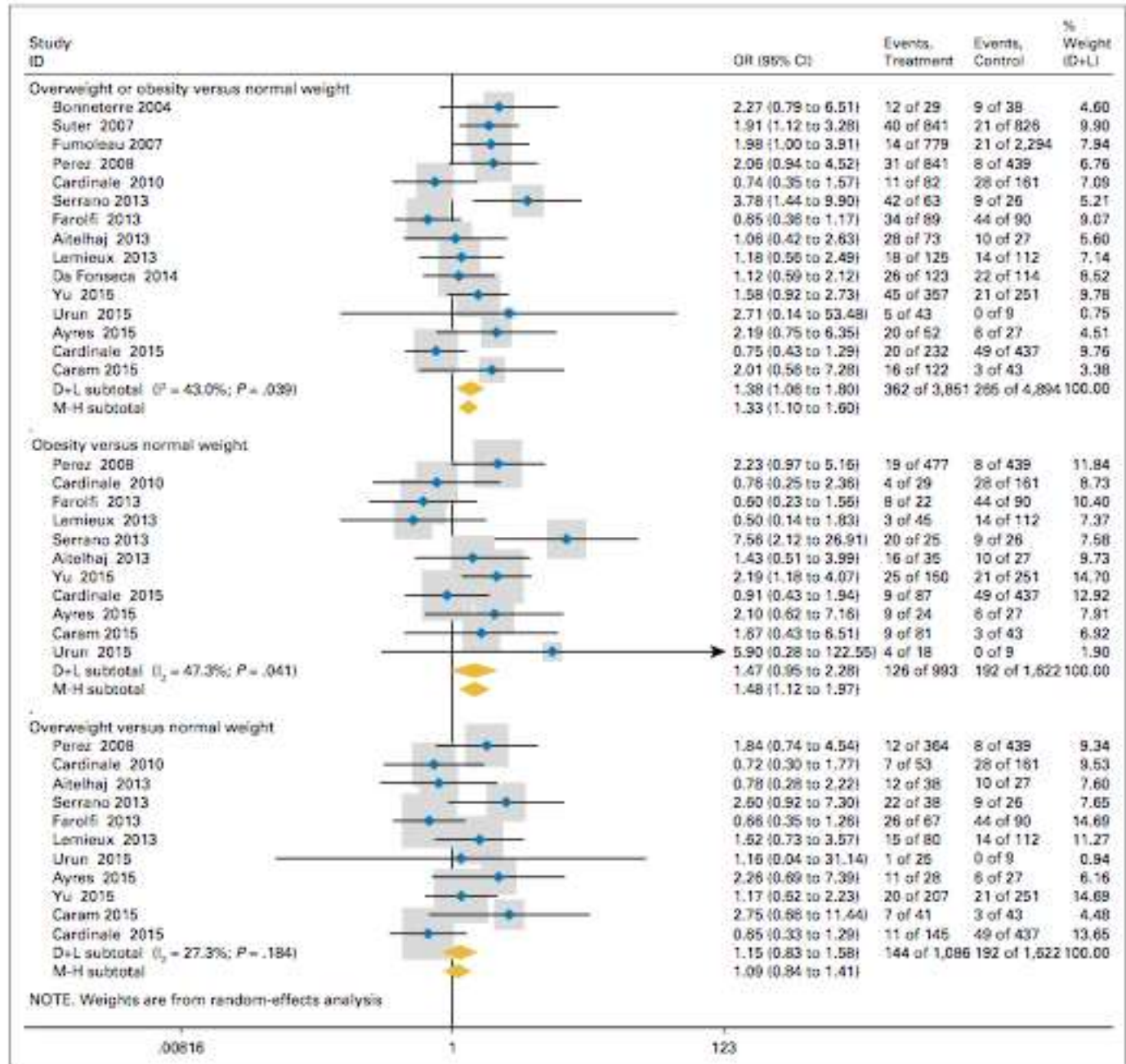




# BMI and Breast Cancer

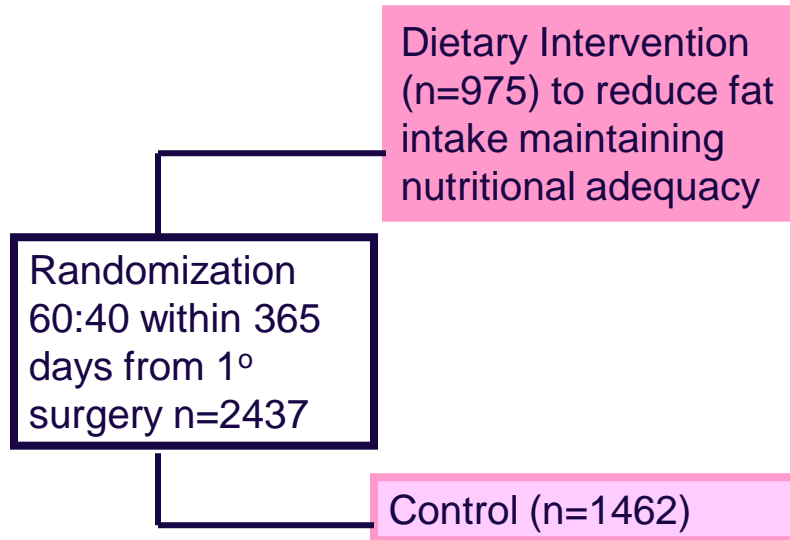


# Obesity As a Risk Factor for Anthracyclines and Trastuzumab Cardiotoxicity in Breast Cancer: Systematic Review and Meta-Analysis



## Dietary Fat Intake and Breast Cancer Recurrence Women's Intervention Nutrition Study (WINS)

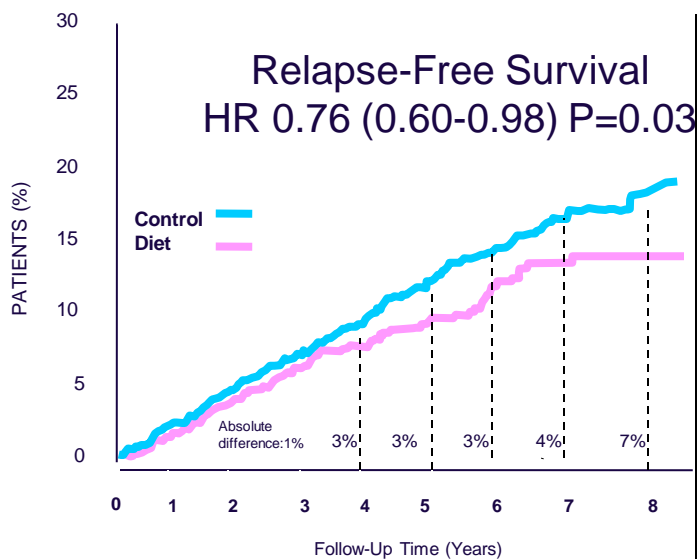
- Women 48-79 yrs
- Early breast cancer
- Surgery +/- RTx
- Systemic therapy\*
- Dietary fat intake  $\geq 20\%$  of calories



**Median follow-up 60 months**

\* Tamoxifen required, chemoRx optional for ER+; chemoRx required for ER-.

# Women's Intervention Nutrition Study (WINS): Clinical Outcomes



Overall Survival Subgroups (108 months follow-up)		
Group	N	HR, 95% CI
All	2437	0.82 (0.64-1.07)**
ER+, PR+	1549	0.90 (0.64-1.28)
ER+, PR-	320	0.93 (0.47-1.84)
ER-, PR+	82	1.19 (0.32-4.49)
ER-, PR-	362	0.36 (0.18-0.74)*** [P=0.003]

**Dietary Intervention Increased Relapse-Free Survival**

# Low-Fat Dietary Pattern and Breast Cancer Mortality in the Women's Health Initiative Randomized Controlled Trial

*Rowan T. Chlebowski, Aaron K. Aragaki, Garnet L. Anderson, Cynthia A. Thomson, Joann E. Manson, Michael S. Simon, Barbara V. Howard, Thomas E. Rohan, Linda Snetselar, Dorothy Lane, Wendy Barrington, Mara Z. Vitolins, Catherine Womack, Lihong Qi, Lifang Hou, Fridtjof Thomas, and Ross L. Prentice*

Author affiliations and support information

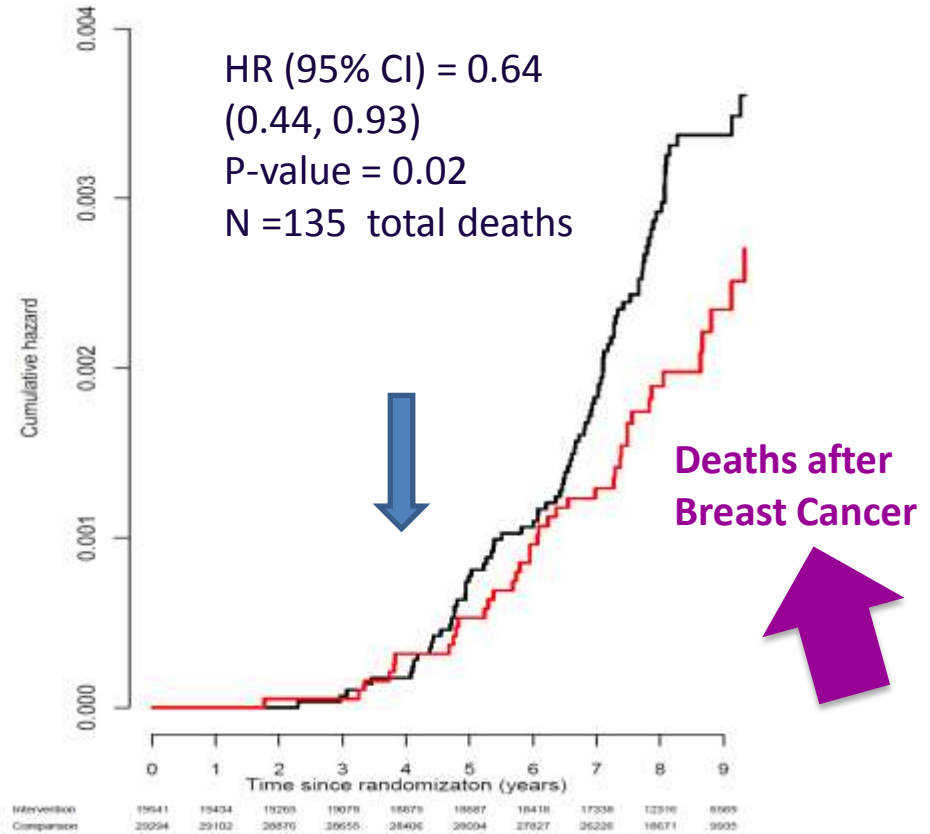
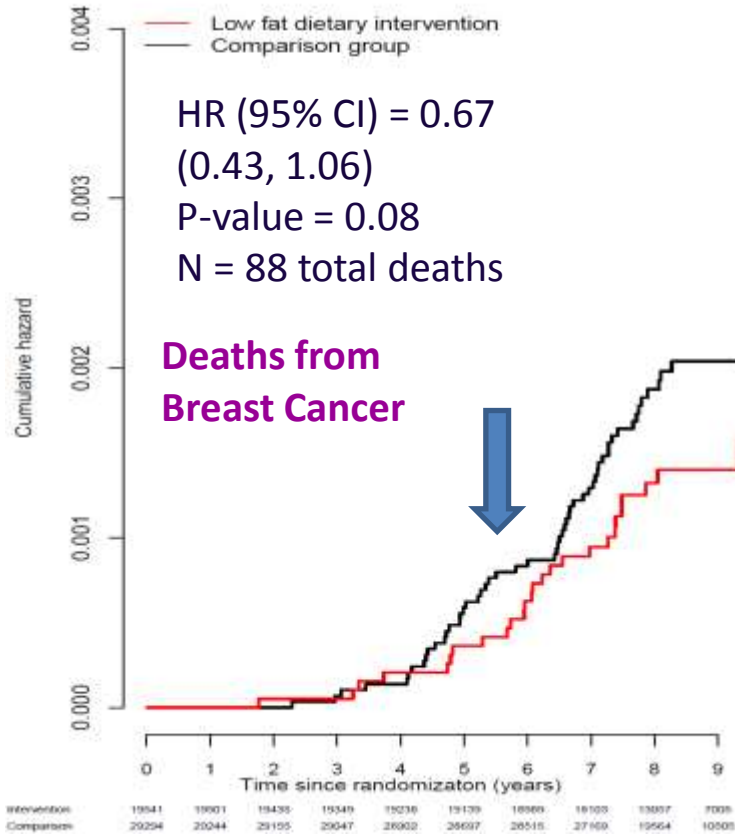
## A B S T R A C T

### WHI DM Study

#### **Purpose**

Earlier Women's Health Initiative Dietary Modification trial findings suggested that a low-fat eating pattern may reduce breast cancers with greater mortality. Therefore, as a primary outcome-related analysis from a randomized prevention trial, we examined the long-term influence of this intervention on deaths as a result of and after breast cancer during 8.5 years (median) of dietary intervention and cumulatively for all breast cancers diagnosed during 16.1 years (median) of follow-up.

# Low-Fat Dietary Pattern and Deaths from and after 1767 Breast Cancers During the 8.5 year (median) Dietary Intervention Period

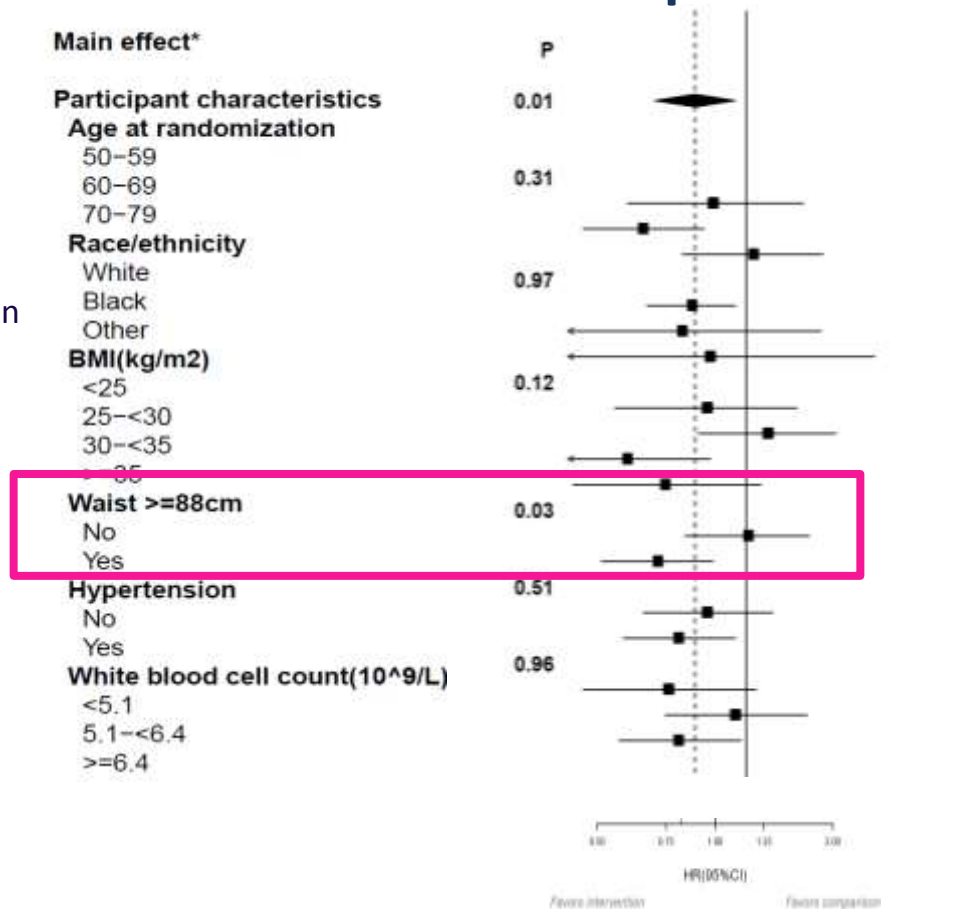


# Waist measurement and risk to health

	Increased Risk	High Risk
Men	94-101cm (37-39inches)	102cm and above (40 inches and above)
Women	80-87cm (32-34 inches)	88cm and above (35 inches and above)
South East Asian men	90cm (35 inches)	

# Subgroup Analysis/Deaths After Breast Cancer: Cumulative Follow-up

Greater dietary effect in women with waist circumference  $\geq 88$  cm





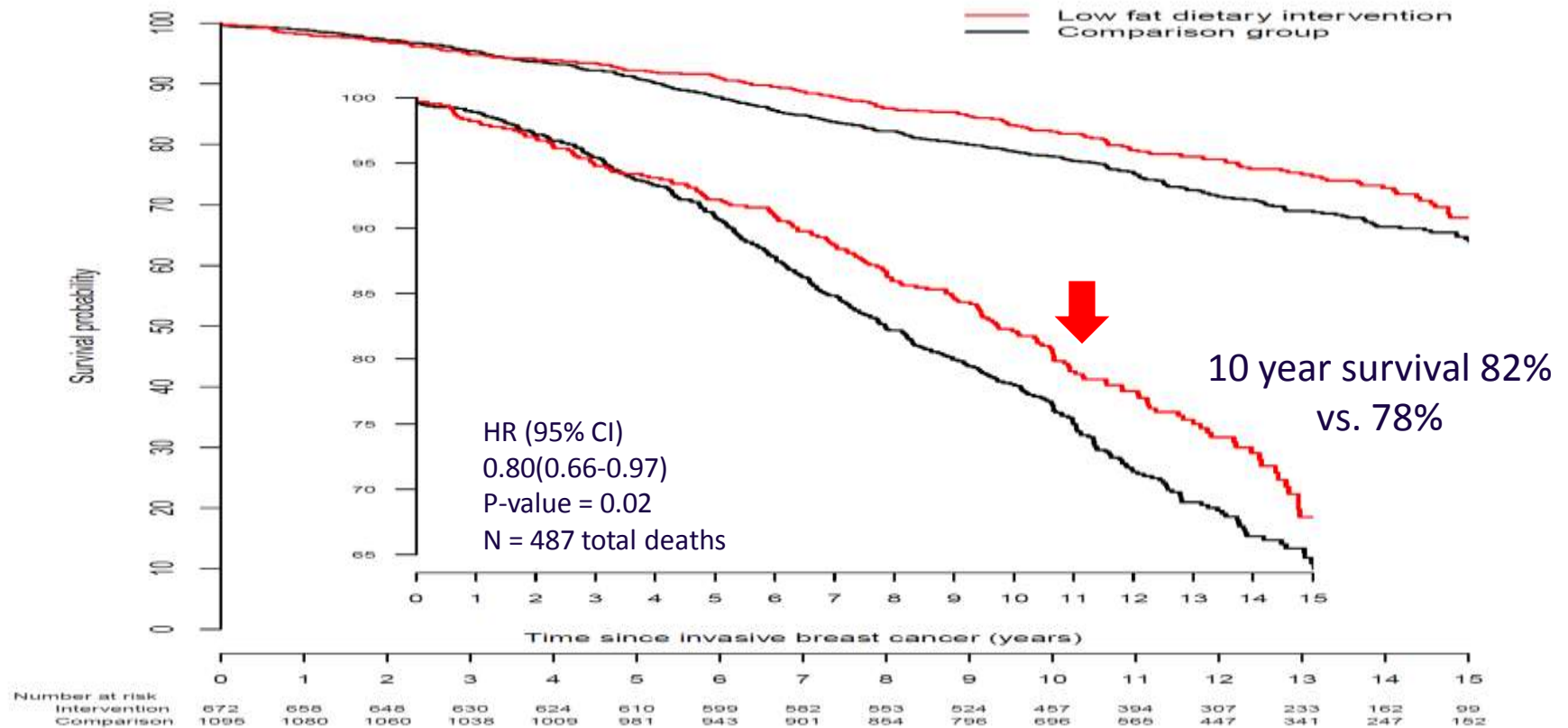
## Implications of WHI DM Findings

An intervention effect was more likely if a woman had either a lifestyle ( $\geq 36.8\%$  energy from fat) or a consequence of lifestyle ( $\geq 88$  waist circumference) associated with adverse breast cancer outcome.

A notional threshold for effect may be  $> 28\%$  calories from fat.

A modest reduction in fat intake with minimal weight loss represents an easily achievable goal by many.

# Breast Cancer Overall Survival for 1767 Women Diagnosed During the Dietary Intervention Period



# ECHO Study

- **Fondazione TERA**
- **Fondazione AIOM**
- **Programma FBO (Food Bank in Oncology)**

**Studio osservazionale prospettico sui cambiamenti delle abitudini alimentari dopo la diagnosi di carcinoma mammario (ECHO STUDY).**

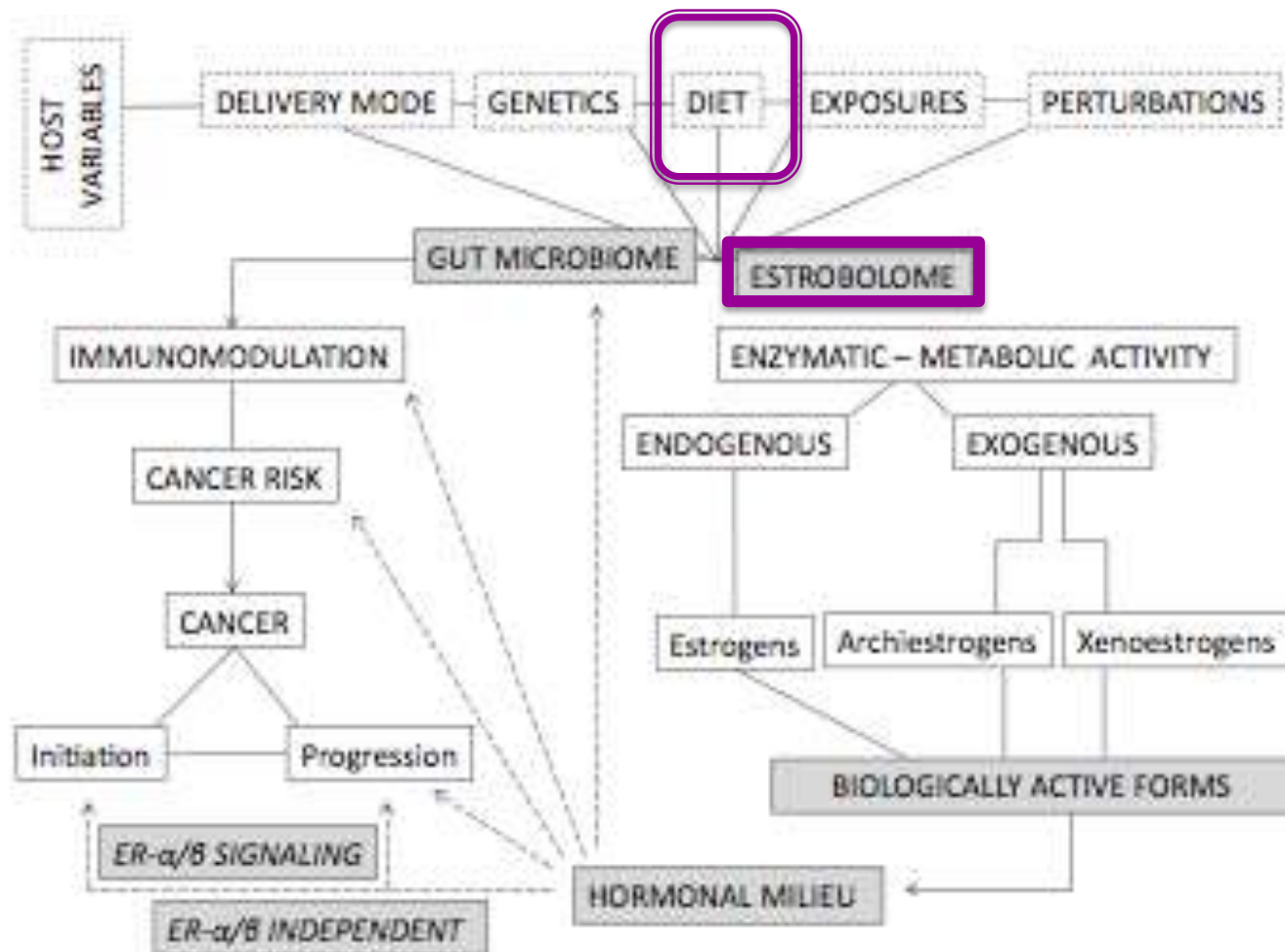
## **OBIETTIVO/ENDPOINT PRIMARIO**

Indagare le abitudini alimentari e l'eventuale utilizzo di prodotti/integratori associati alla cura del cancro, in pazienti con carcinoma mammario invasivo (stadio I-II-III).

## **OBIETTIVO/ENDPOINT SECONDARIO**

Individuare le più comuni fonti d'informazioni alla base dei cambiamenti alimentari e verificare l'eventuale comunicazione al medico oncologo.

# The Intestinal Microbiome and ER+ BC



**‘estrobolome,’** the aggregate of enteric bacterial genes” capable of metabolizing estrogens, might affect women’s risk of developing postmenopausal estrogen receptor–positive breast cancer.

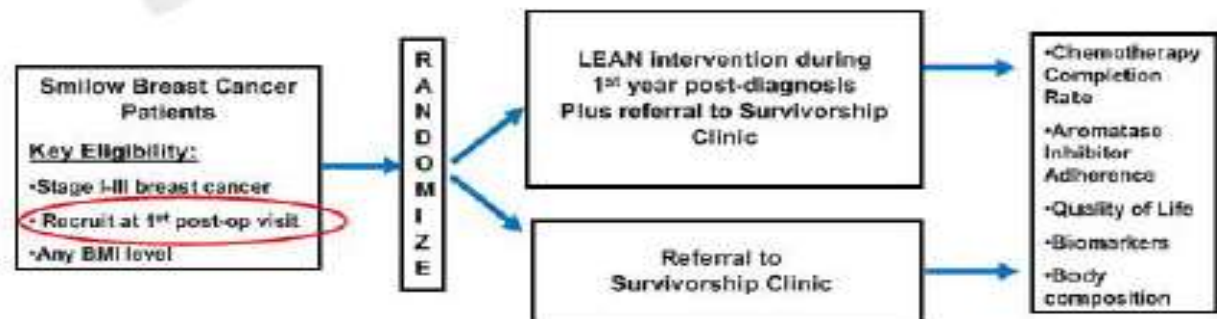
# Alliance Therapeutic Trial of Weight Loss and DFS: The BWEL Study

Jennifer Ligibel, DFCI, PI



Primary Objective: To test the impact of weight loss intervention on invasive disease free survival in women diagnosed Stage II-III breast cancer

## Lifestyle, Exercise and Nutrition (LEAN) *Early* trial at Breast Cancer Diagnosis



NCI R01CA207753

# Physical activity after cancer an evidence review



**Reduces the  
consequences  
of treatment**



**Reduces  
co-morbidities**



**Reduces  
Disease  
Progression**



**Decreases  
mortality**



**Decreases  
recurrence**

# Attività fisica...quale e come quantizzarla?

## 1. Che tipo di attività fisica?

Non esistono studi di confronto aerobica vs anaerobica



## 2. Come misurare l'attività fisica?

Equivalente Metabolico –o MET- cioè ml di  $O_2$  consumato per kg di massa corporea per minuto

# Physical activity guide for adults

## Be active

To keep your heart and mind healthy

## Build strength

To strengthen muscles, bones and joints

## Improve balance

To help reduce your chance of falling

How often?

**150**

minutes  
of moderate  
activity a week

or

**75**

minutes  
of vigorous  
activity a week

**2**

days a week

**2**

days a week

Walk



Run



Gym



Dance



Gardening



Sport



Aerobics



Tai chi



Swim



Stairs



Carry bags



Bowling



## Sit less

TV



Sofa



Computer



Break up long periods of sitting down to help keep your muscles, bones and joints strong.



Risk<sup>a</sup> of Breast Cancer Recurrence, Breast Cancer Mortality, and All-cause Mortality by Meeting (versus not meeting) Physical Activity Guidelines by BMI category, Menopausal Status, and Hormone Receptor Status, After Breast Cancer Pooling Project

	Recurrence	p <sup>b</sup>	Breast Cancer Mortality*	p <sup>b</sup>	All-Cause Mortality, HR	p <sup>b</sup>
<b>Body Mass Index, kg/m<sup>2</sup></b>		0.82		0.75		0.21
<25	0.93 (0.81–1.07)		0.72 (0.61–0.86)		0.72 (0.62–0.83)	
25.0–29.9	0.98 (0.85–1.14)		0.78 (0.65–0.94)		0.69 (0.59–0.81)	
≥ 30	0.96 (0.77–1.19)		0.72 (0.61–0.86)		0.86 (0.70–1.06)	
<b>Menopausal Status</b>		0.61		0.28		0.16
Pre-menopausal	0.92 (0.77–1.10)		0.82 (0.66–1.02)		0.84 (0.68–1.03)	
Post-menopausal	0.98 (0.85–1.11)		0.71 (0.60–0.83)		0.70 (0.62–0.79)	
<b>ER/PR Status</b>		0.49		0.44		0.88
ER+/PR+	0.94 (0.82–1.07)		0.75 (0.63–0.89)		0.72 (0.63–0.83)	
ER-/PR+	0.72 (0.45–1.14)		0.74 (0.44–1.24)		0.72 (0.44–1.18)	
ER+/PR-	1.05 (0.80–1.37)		0.91 (0.44–1.24)		0.81 (0.62–1.06)	
ER-/PR-	1.03 (0.81–1.31)		0.64 (0.49–0.84)		0.72 (0.57–0.91)	

adhesion to the PA Guidelines may be an important intervention target for reducing mortality among breast cancer survivors

older/post-menopausal women; those engaging in at least 10 MET-hours of physical activity per week had a **27 % reduction** in all-cause mortality) and a **25 % reduction in breast cancer-specific mortality** (compared with women performing <10 MET-hours/week

Risk<sup>a</sup> of breast cancer recurrence, breast cancer mortality, and all-cause mortality by meeting physical activity (PA) guidelines and quintiles of PA, After Breast Cancer Pooling Project

PA Quintile, HR (95% CI)	Recurrence, n=10,685 (1,421 events)	Breast Cancer Mortality, n=11,282 <sup>b</sup> (971 events)	All-Cause Mortality, n=11,315 (1,468 events)
Meets PA Guidelines, HR (95% CI)	0.96 (0.86–1.06)	0.75 (0.65–0.85)	0.73 (0.66–0.82)
PA Quintile, HR (95% CI)			
Q2 vs. Q1	1.00 (0.84–1.18)	1.00 (0.83–1.21)	0.90 (0.77–1.04)
Q3 vs. Q1	1.07 (0.90–1.26)	0.87 (0.71–1.06)	0.77 (0.66–0.90)
Q4 vs. Q1	1.00 (0.84–1.18)	0.74 (0.60–0.91)	0.71 (0.60–0.84)
Q5 vs. Q1	0.95 (0.80–1.14)	0.73 (0.59–0.91)	0.60 (0.51–0.72)
Test for Trend	0.60	0.0001	<0.0001

# The potential biochemical pathways

Class of effector molecule	Effector molecule	Effects of physical activity on the effector molecule
Cell growth regulators	IGF1 IGFBP3	Decreased levels Increased levels
Proteins involved in DNA damage and repair	BRCA1 BRCA2	Increased expression Increased expression
Regulator of apoptosis and cell cycle arrests	p53	Enhanced activity
Hormones	Oestrogen Vasoactive intestinal protein Leptin	Decreased levels Decreased levels Decreased levels (indirect)
Immune system components	NK cells Monoocyte function Circulating granulocytes	Enhanced activity Enhanced activity Increased proportion

# Alcohol and BC

**Lace Cohort**  
**1867 pts early BC**

**Alcohol increased risk of breast cancer and death as a result of BC**

The increased risk of recurrence was most pronounced in postmenopausal and overweight/obese women

**Wheil Trial**  
**3088 pts early BC**

Light alcohol intake did not increase the risk of BC recurrence or all-cause mortality in middle-aged women previously diagnosed with BC

Alcohol intake was associated with other favorable prognostic indicators that may explain its apparent protective effect in non-obese women

**After BCPooling Project**  
**9329 pts**

The association between alcohol intake and recurrence may depend on menopausal status at BC diagnosis

Alcohol intake was not associated with overall mortality, possibly because of a cardioprotective effect and a reduction in noncancer deaths

Sternfeld, 2009

Kwan, 2013

Flatt, 2010

Smoking status	No.	Breast cancer recurrence			Breast cancer mortality			All-cause mortality		
		Event	HR (95% CI)	Pt	Event	HR (95% CI)	Pt	Event	HR (95% CI)	Pt
Never smokers	4812	824	Referent		499	Referent		780	Referent	
Former smokers										
<20 pack-years	2744	453	0.98 (0.87 to 1.11)	.78	259	0.99 (0.85 to 1.15)	.88	410	0.97 (0.86 to 1.09)	.58
20-34.9 pack-years	808	156	1.22 (1.01 to 1.48)	.04	93	1.14 (0.91 to 1.43)	.26	177	1.26 (1.07 to 1.48)	.01
≥35 pack-years	785	155	1.37 (1.13 to 1.66)	.001	111	1.54 (1.24 to 1.91)	<.001	227	1.68 (1.44 to 1.96)	<.001
Current smokers†	710	139	1.41 (1.16 to 1.71)	<.001	97	1.61 (1.28 to 2.03)	<.001	209	2.17 (1.85 to 2.54)	<.001
<i>P</i> <sub>trend</sub>			<.001			<.001			<.001	

Smokers

pack-year

20 -> 34.9

35 -> more

current

Recurrence

22%

37%

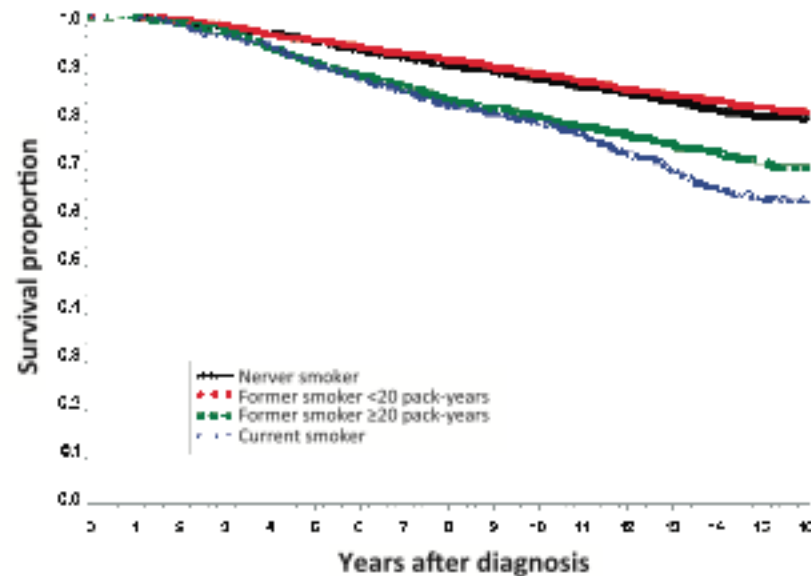
41%

All cause-mortality

26%

54%

60%





Lymphedema incidence in group A was 4.0% (2 of 50), whereas in group B it was 26.0% (13 of 50) (Table 1). By assessing the difference between the before- and after-exercise measures (Tables 8 and 9), we noted a marked improvement in the degree of lymphedema in group A women (Table 9); a better quality of life ( $P < .0001$ ); a reduction in symptoms such as fatigue ( $P = .02$ ), insomnia ( $P = .001$ ), and dyspnea ( $P = .03$ );

and a significant reduction in physical-related disorders ( $P < .0001$ ), emotional ( $P = .001$ ), cognitive ( $P = .01$ ), and relational/role ( $P = .005$ ) (Table 10). When considering BMI, we also observed that in group A lymphedema was not documented in the group with a BMI greater than  $25 \text{ kg/m}^2$ , whereas it had a 5% incidence rate in the group with a BMI of less than  $25 \text{ kg/m}^2$ . These rates in the control group were 30% and 20%, respectively, suggesting no interactions among factors.





GRAZIE