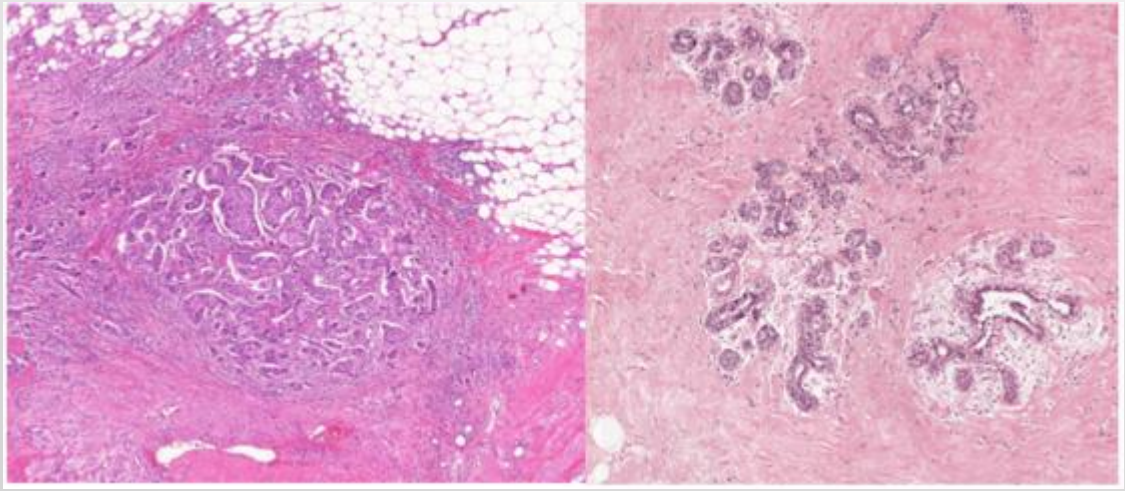
Cancer: a serious worldwide health problem

Cancer is a group of diseases in which abnormal **cells divide without control** and can **invade nearby tissues**. Cancer cells can also spread to other parts of the body through the blood and lymph systems.
Most types of cancer cells eventually form a **lump or mass called a tumor**, and are named after the part of the body where the tumor originates.

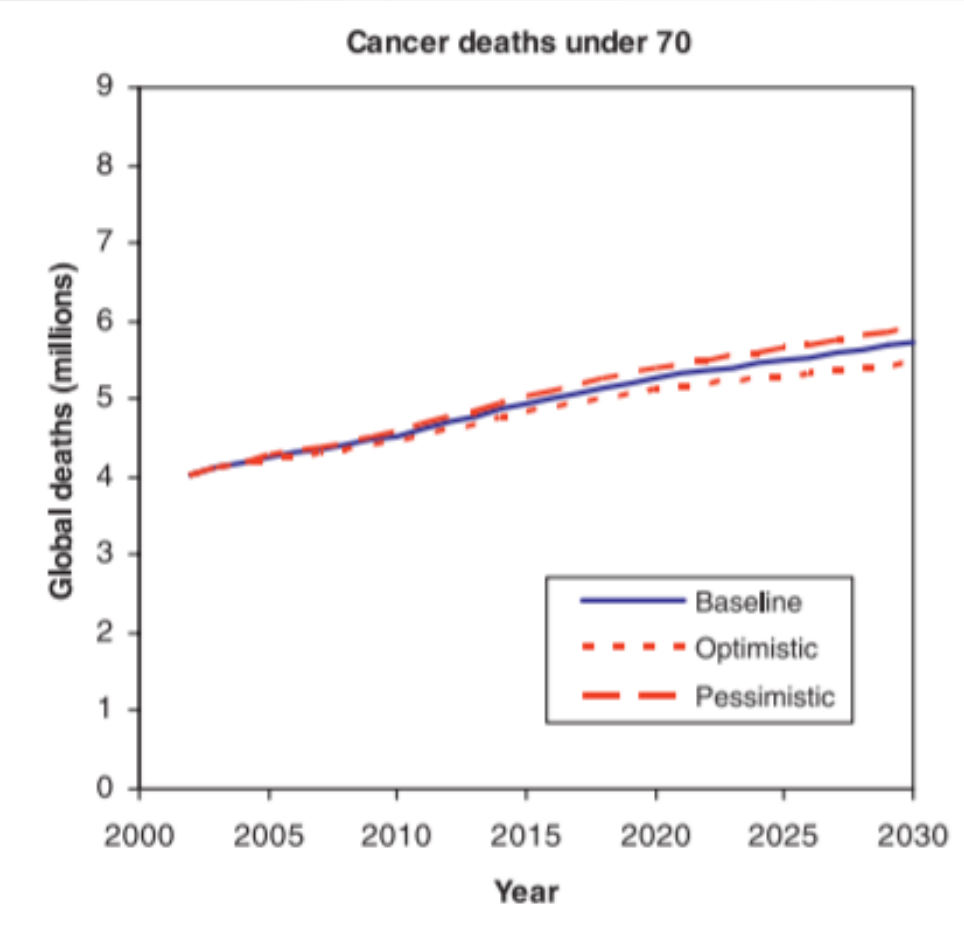
Examples:
-carcinoma = cancer that begins in the skin or in tissues that line or cover internal organs such as the lung or breast.
-leukemia = cancer that starts in blood-forming tissue such as the bone marrow



Invasive ductal carcinoma Normal breast tissue

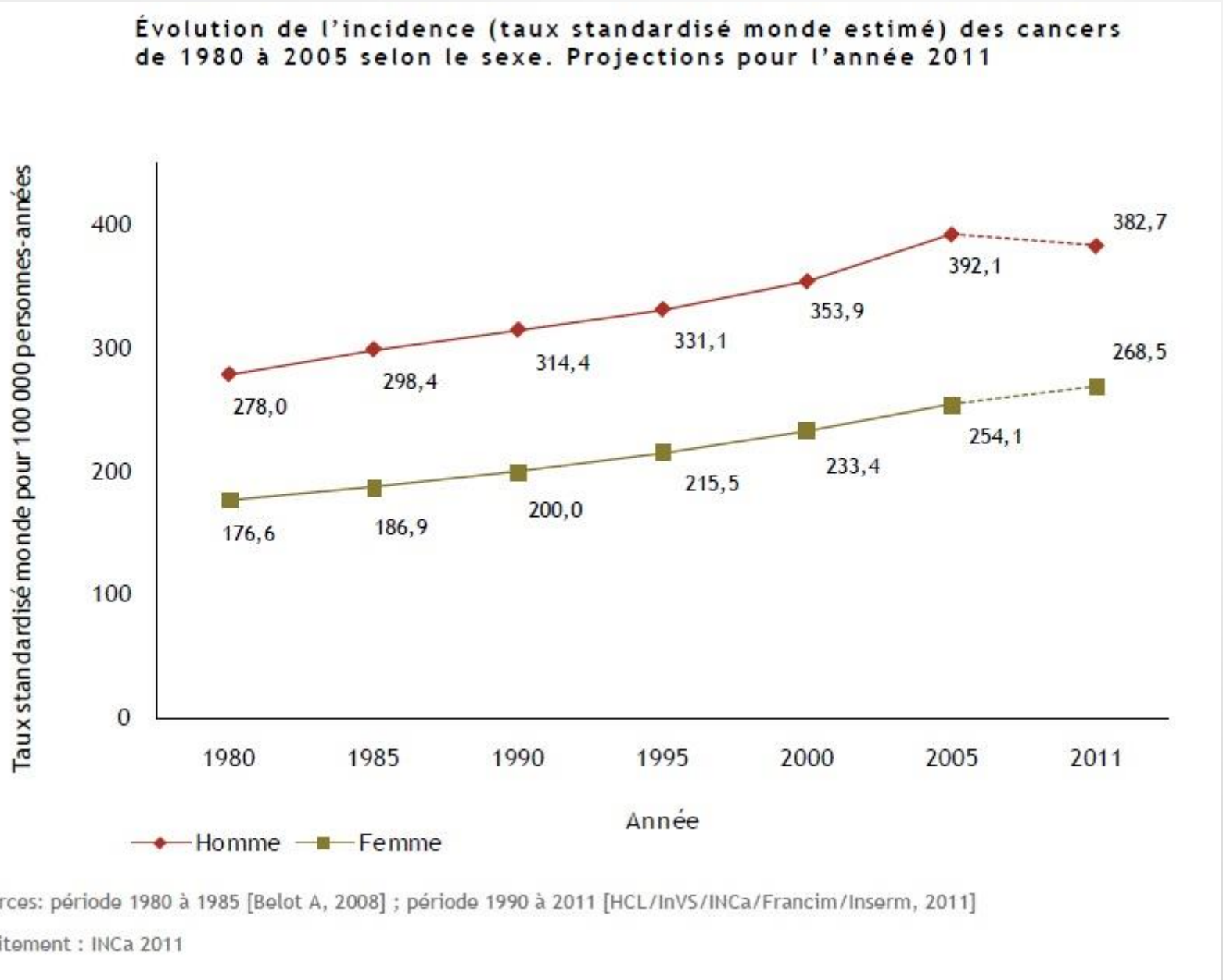
Cancer: a serious worldwide health problem

Cancer is the **second leading cause of death worldwide** over the past 30 years



Mathers & Loncar .doi:10.1371/journal.pmed.0030442

Incidence of cancer in France



Sources: période 1980 à 1985 [Belot A, 2008] ; période 1990 à 2011 [HCL/InVS/INCa/Francim/Inserm, 2011]

Traitement : INCa 2011

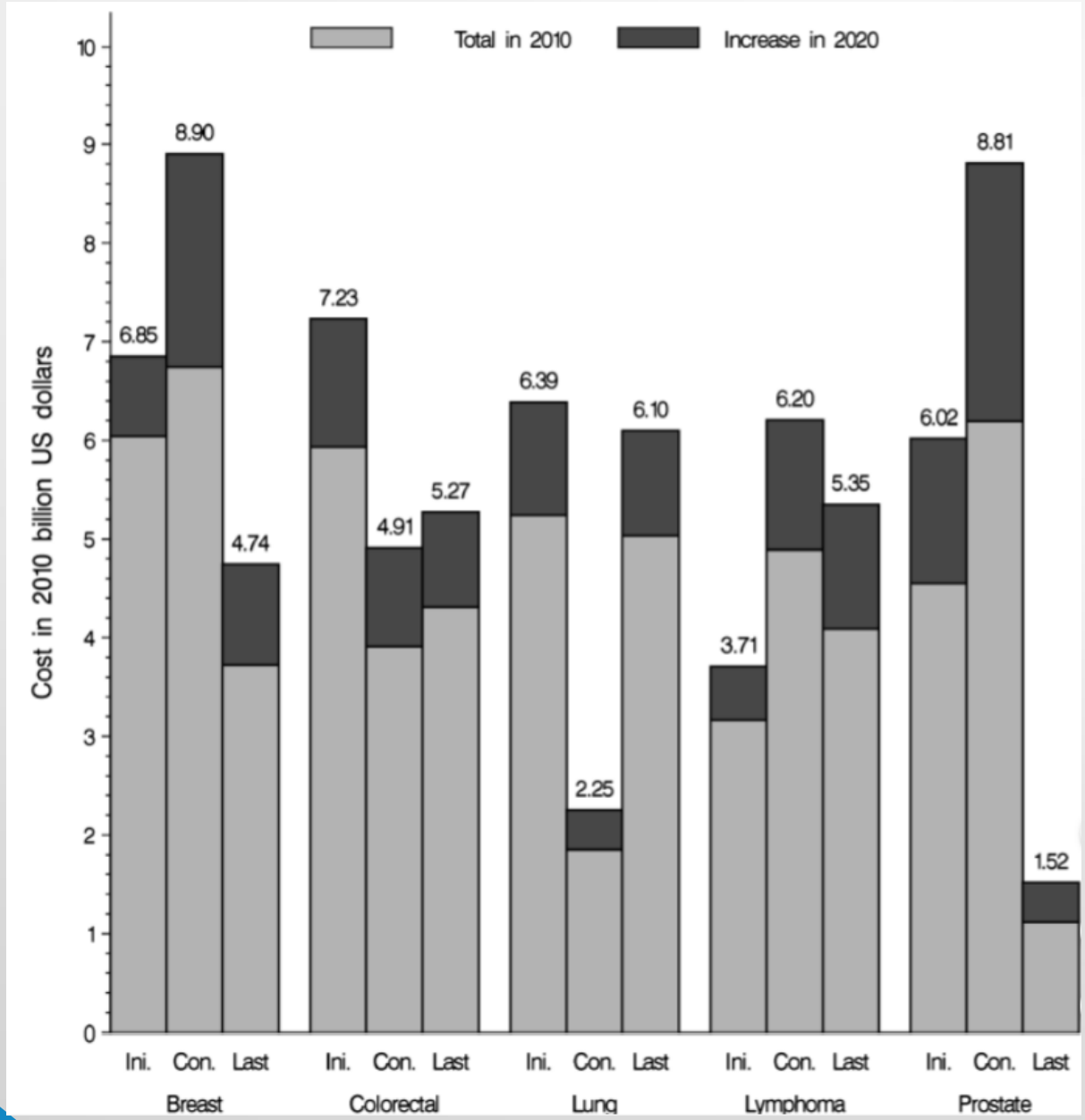
Cancers with the highest mortality in France

Femmes				
Localisations	Incidence		Mortalité	
	Effectif(*)	Part(%)	Effectif(*)	Part(%)
Sein	53 000	33,4	11 500	18,3
Côlon-rectum	19 000	12	8 300	13,2
Poumon	12 000	7,6	8 100	12,9
Corps de l'utérus	6 800	4,3	2 080	3,3
Lymphome malin non hodgkinien	5 300	3,3	1 680	2,7
Mélanome de la peau	5 100	3,2	720	1,1
Thyroïde	4 970	3,1	230	0,4
Ovaire	4 620	2,9	3 150	5
Pancréas	4 560	2,9	nd	-
Rein	3 680	2,3	1 290	2
Lèvre, cavité orale, pharynx	3 100	2	720	1,1
Col de l'utérus	2 810	1,8	1 000	1,6
Myélome multiple et maladie immunoprolifération	2 720	1,7	1 460	2,3
Estomac	2 200	1,4	1 620	2,6
Système nerveux	2 090	1,3	1 300	2,1
Vessie	1 880	1,2	1 170	1,9
Foie	1 830	1,2	nd	-
Leucémie aiguë	1 810	1,1	1 480	2,3
Leucémie lymphoïde chronique	1 650	1	450	0,7
Oesophage	1 140	0,7	760	1,2
Maladie de Hodgkin	920	0,6	120	0,2
Larynx	510	0,3	130	0,2
Tous cancers	158 500	100	63 000	100

Hommes				
Localisations	Incidence		Mortalité	
	Effectif(*)	Part(%)	Effectif(*)	Part(%)
Prostate	71 000	34,3	8 700	10,3
Poumon	27 500	13,3	21 000	24,9
Côlon-rectum	21 500	10,4	9 200	10,9
Vessie	9 100	4,4	3 500	4,1
Lèvre, cavité orale, pharynx	7 600	3,7	2 550	3
Rein	7 400	3,6	2550	3
Lymphome malin non hodgkinien	6 400	3,1	1 990	2,4
Foie	6 400	3,1	nd	-
Pancréas	4 480	2,2	nd	-
Estomac	4 220	2	2 810	3,3
Mélanome de la peau	4 680	2,3	900	1,1
Myélome multiple et maladie immunoprolifération	3 210	1,6	1 590	1,9
Oesophage	3 140	1,5	2 680	3,2
Larynx	2 720	1,3	830	1
Système nerveux	2 680	1,3	1 700	2
Testicule	2 320	1,1	90	0,1
Leucémie lymphoïde chronique	2 140	1	610	0,7
Leucémie aiguë	1 970	1	1 740	2,1
Thyroïde	1 630	0,8	140	0,2
Maladie de Hodgkin	920	0,4	170	0,2
Tous cancers	207 000	100	84 500	100

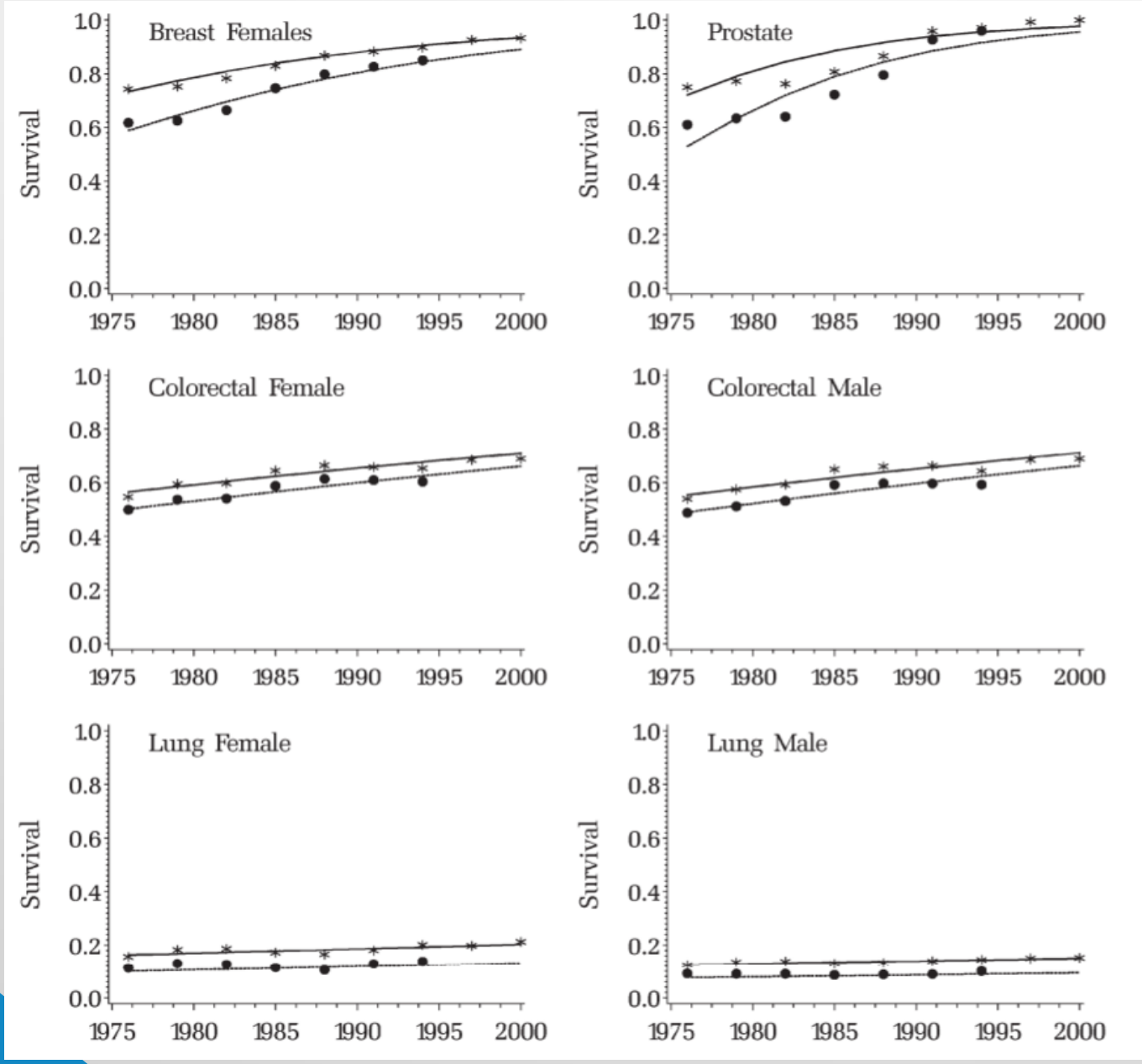
(*) : Effectif total arrondi Source : Projection de l'incidence et de la mortalité par cancer en France en 2011 (Hospices civils de Lyon, InVs, INCa, Francim, Inserm). Traitement : INCa 2011

Cancer: a very expensive pathology too



Mariotto *et al*. doi:10.1093/jnci/djq495

Improvement of overall survival of oncological patients



● 10-year

✱ 5-year

65< ages <74

Mariotto *et al*. doi:10.1093/jnci/djq495

Breast cancer survivors: patients at risk for CVD

The **prevalence** of end-stage **heart failure** (HF) induced by chemotherapeutic agents has **increased to 2.5%**
CVD are the leading cause of long-term morbidity and mortality among **cancer survivors**.

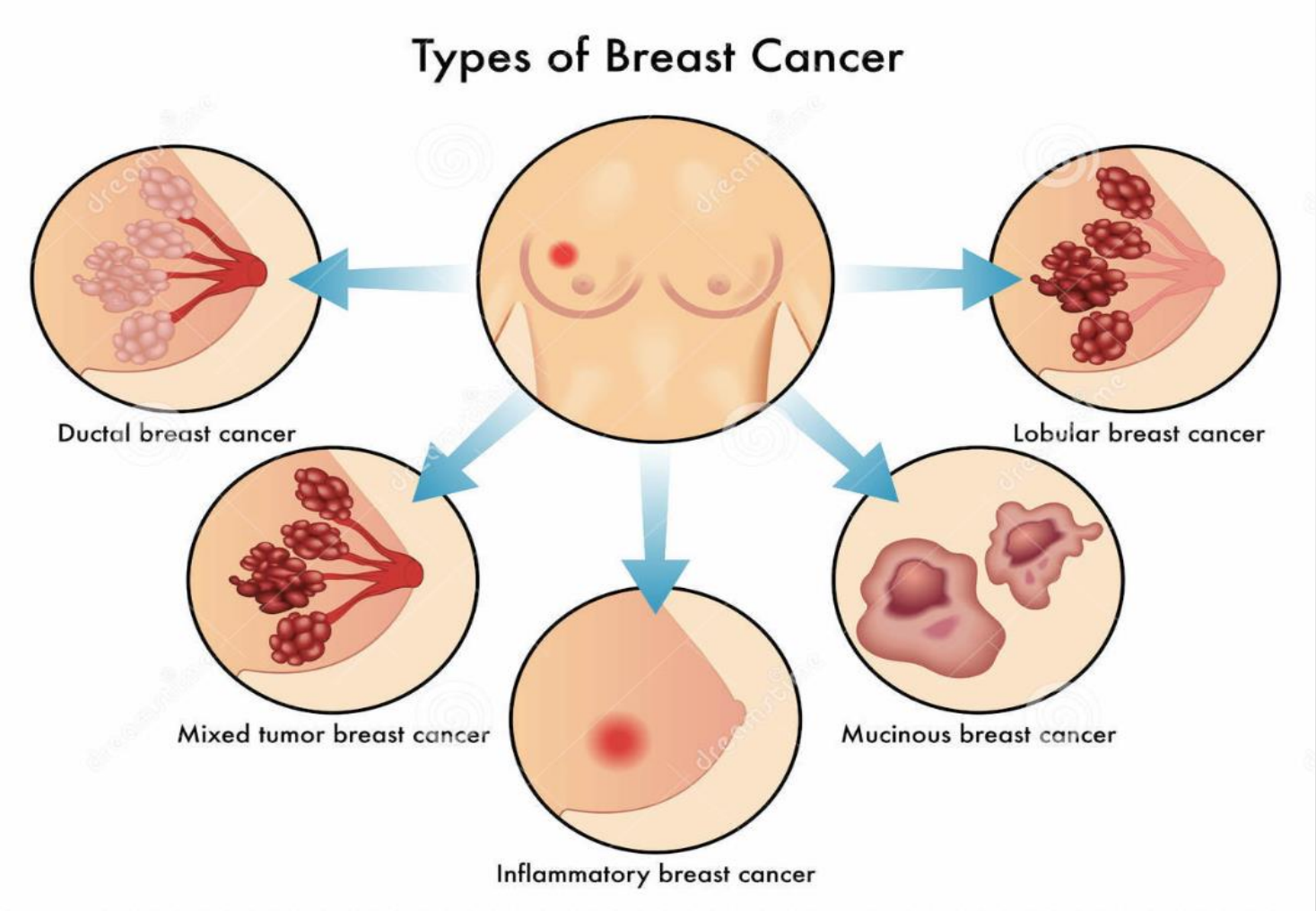
As the population ages, there will likely be **more women with breast cancer, CVD, or both.** Current cancer treatments might increase the risk of both short- and longterm cardiotoxicity

Chemotherapy-induced cardiomyopathy (CIC) = a new problem for breast cancer survivors

Mehta *et al*. doi:10.1161/cir.0000000000000556; Oliveira *et al*. doi:10.1016/j.healun.2012.03.018

Breast cancer survivor: patients at risk for CVD

1) What is breast cancer ?



Breast cancer survivor: patients at risk for CVD

1) What is breast cancer ?

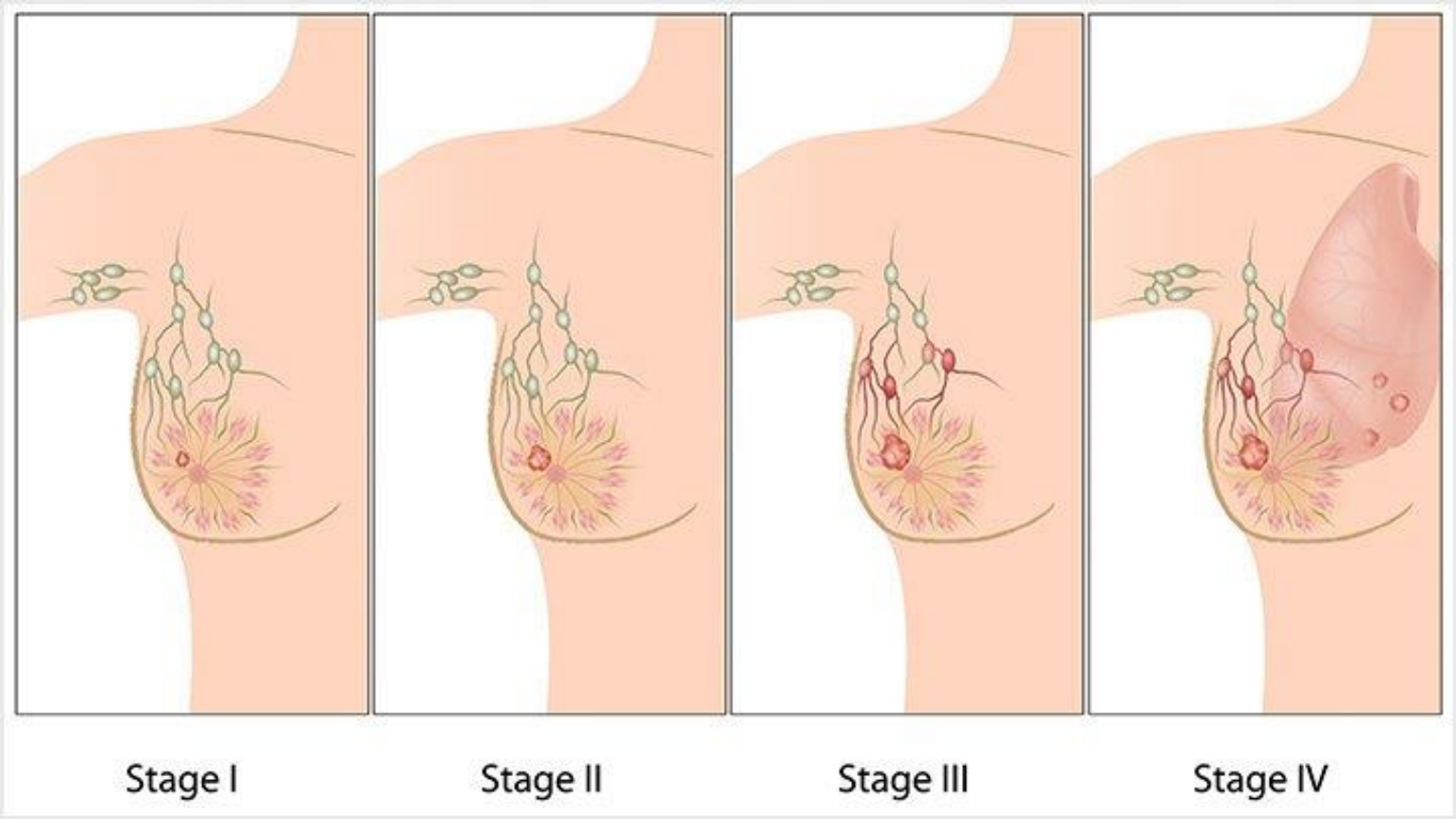
-One type of breast cancer is called *in situ*

-One type of breast cancer is called *invasive* (80% of cases)

Cancer cells have broken through the walls of the glands or ducts where they originated and grown into surrounding breast tissue.

Breast cancer survivor: patients at risk for CVD

2) The 4 severity stages of breast cancer



Breast cancer survivor: patients at risk for CVD

3) Treatments of breast cancer

a) Diagnostic:

-screening examination (mammography, MRI, ultrasounds)

-notification of a lump in a breast by the patient

-microscopic analysis to determine the extent of spread (stage)

-microscopic analysis to characterize the type of the disease
(*in situ* or invasive, presence of hormone receptors (estrogen and progesterone), presence of the human epidermal growth factor receptor 2 (HER2) and high expression of *HER2* gene)

Breast cancer survivor: patients at risk for CVD

3) Treatments of breast cancer

b) Main treatments:

- **Stages I and II**

Surgery + radiation therapy (RT)

- **Stage III**

Mastectomy + RT + chemotherapy

- **Stage IV**

RT and/or chemotherapy

Breast cancer survivor: patients at risk for CVD

1) Impact of anthracyclines on cardiac function

-cumulative dose of 400–450 mg/m^2 doxorubicin = **5% rate of HF**
-in patients aged over 65 years = **10%**
-rate of mortality is >60% at 2 years

-**cardiomyocyte damage** occurs too and patients **become vulnerable to both natural and iatrogenic sequential stresses** that may then precipitate the presentation of previously unrecognized overt cardiac damage.

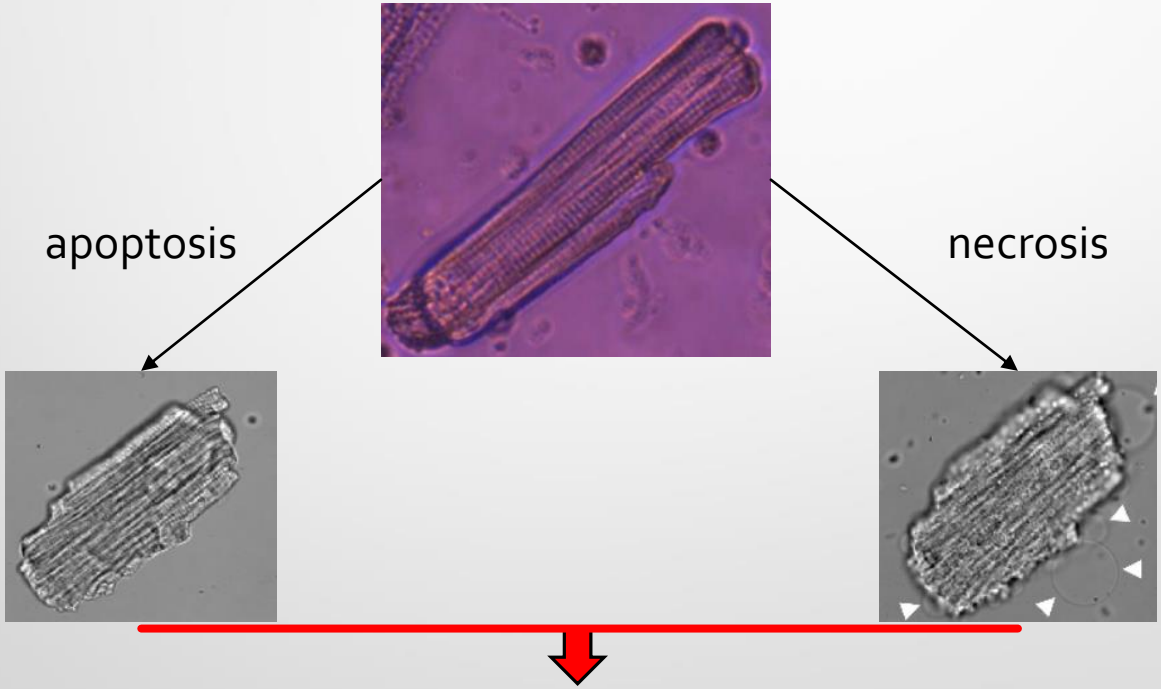
For review: Eschenhagen *et al*. doi:10.1093/eurjhf/hfq213

Breast cancer survivor: patients at risk for CVD

1) Impact of anthracyclines on cardiac function

Anthracyclines (*e.g.* doxorubicin)

Oxidative stress (Nox2)



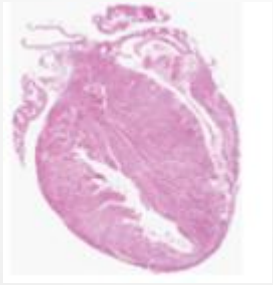
LV dysfunction, arrhythmias, ventricular repolarization abnormalities, myocarditis, HF

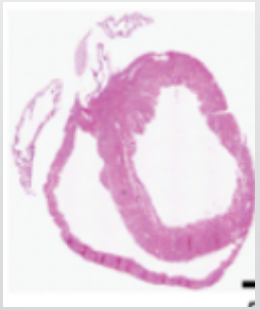
For review: Adao *et al*. doi:10.1016/j.repce.2012.11.019; Eschenhagen *et al*. doi:10.1093/eurjhf/hfq213

Breast cancer survivor: patients at risk for CVD

2) Impact of anti-HER2 gene on cardiac function

Gene deletion of HER2 in mouse (*e.g.* trastuzumab)





Trastuzumab in combination with anthracycline-based treatment = 28% rate of HF and 16% incidence of NYHA class III/IV in patients with breast cancer

Jawa et al. doi:10.1097/md.0000000000005195 ; De Keulenaer *et al.* doi:10.1161/circresaha

Breast cancer survivor: patients at risk for CVD

3) Impact of angiogenesis inhibitors on cardiac function

Angiogenesis inhibitors (*e.g. lapatinib*)

Hypertension

(rate of 15-20% in cancer patients)

Venous thrombosis

LV dysfunction, drop of LVEF

(and cardiomycoytes apoptosis)

For review: Adao *et al*. doi:10.1016/j.repce.2012.11.019; Eschenhagen *et al*. doi:10.1093/eurjhf/hfq213

Breast cancer survivor: patients at risk for CVD

4) Impact of immunosuppressive agent on cardiac function

Alkylating agents (*e.g.* cyclophophamide)

ROS production

LV dysfunction, myocarditis, pericarditis, arterial thrombosis, bradycardia, atrial fibrillation, myocardial ischemia, HF

For review: Adao *et al*. doi:10.1016/j.repce.2012.11.019; Eschenhagen *et al*. doi:10.1093/eurjhf/hfq213

Breast cancer survivor: patients at risk for CVD

5) Impact of hormonal agent on cardiac function

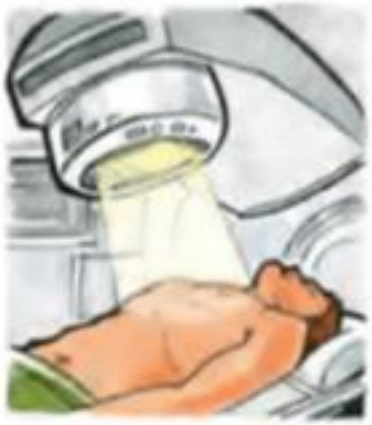
Tamoxifen (anti-estrogen agent)

Deep vein thrombosis, pulmonary embolism, peripheral atherosclerosis, valvular dysfunction, HF

For review: Adao *et al*. doi:10.1016/j.repce.2012.11.019; Eschenhagen *et al*. doi:10.1093/eurjhf/hfq213

Breast cancer survivor: patients at risk for CVD

6) Impact of radiotherapy on cardiac function



Valve disease

Atherosclerosis
(Symptomatic or asymptomatic)

Pericardial disease
(Acute pericarditis; chronic pericarditis; pericardial effusion; constrictive pericarditis)

Myocardial and endocardial disease
(Pancarditis, cardiomyopathy)

Conduction disturbances
(Right bundle branch block, atrioventricular block)

For review: Adao *et al*. doi:10.1016/j.repce.2012.11.019

Breast cancer survivor: patients at risk for CVD

7) The main molecular mechanisms of CIC

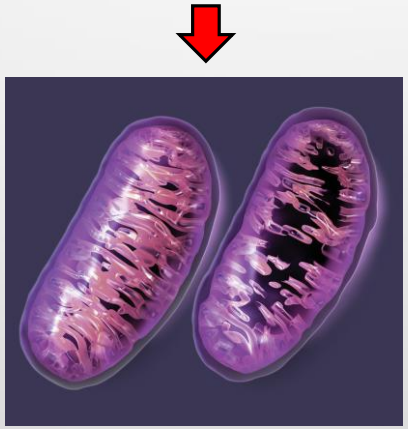
(mainly reported after doxorubicin treatment and still not completely understood…)

-increased production of ROS into the myocardium (Nox2, eNOS)

-alterations in cardiac energy metabolism (CK and AMPK)

-ultrastructural changes of cardiomyocytes (titin, Frank-Starling)

-suppression of myofilament protein synthesis (depletion of cardiac progenitor cells pool)



Octavia *et al.* doi:10.1016/j.yjmcc.2012.03.006

Tokarska-Schlattner *et al.* doi:10.1152/ajpheart.01057.2004

Lim *et al.* doi:10.1074/jbc.m308033200

De Angelis *et al.* doi:10.1161/circulationaha.109.895771

Breast cancer survivor: patients at risk for CVD

To date there is no specific treatment for CVD induced by chemotherapy

The "classical" treatment of HF is recommended for patients suffering from CIC

Pharmacological treatments indicated in patients with symptomatic (NYHA Class II-IV) heart failure with reduced ejection fraction

Recommendations	Class [a]	Level [b]	Ref [c]
An ACE-I[d] is recommended, in addition to a beta-blocker, for symptomatic patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A	2, 163–165
A beta-blocker is recommended, in addition an ACE-I[d], for patients with stable, symptomatic HFrEF to reduce the risk of HF hospitalization and death.	I	A	167–173
An MRA is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACE-I[d] and a beta-blocker, to reduce the risk of HF hospitalization and death.	I	A	174, 175

ACEI = angiotensin-converting enzyme inhibitor; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.
[d]Or ARB if ACEI is not tolerated/contraindicated

Recommendations for treatment of patients with heart failure with preserved ejection fraction and heart failure with mid-range ejection fraction

Recommendations	Class [a]	Level [b]	Ref [c]
it is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.	I	C	
Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.	I	B	178, 179

HFmrEF = heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Ponikowski *et al.* doi:10.1093/eurheartj/ehw128

Breast cancer survivor: patients at risk for skeletal muscle disorders

Importance of lean body mass (LBM) to reduce breast cancer outcomes

-low LBM has been associated with increased treatment toxicity
-low LBM = decreased time to tumor progression
-low LBM = increased overall mortality in breast cancer

Age- and treatment-related factors play a role in the pathogenesis of sarcopenia and dynapenia in breast cancer patients

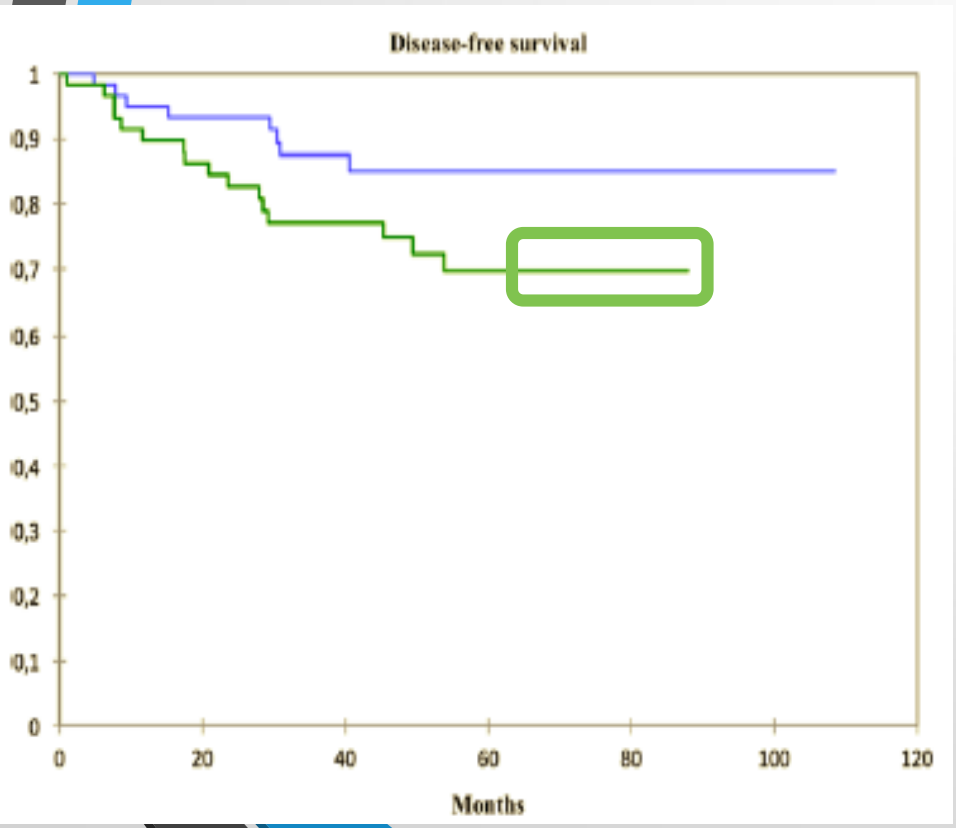
The 10-year breast-cancer-specific survival rates =
86.5 % in sarcopenic women
90.5 % in nonsarcopenic women

Adams *et al*. doi:10.1007/s10549-016-3900-2

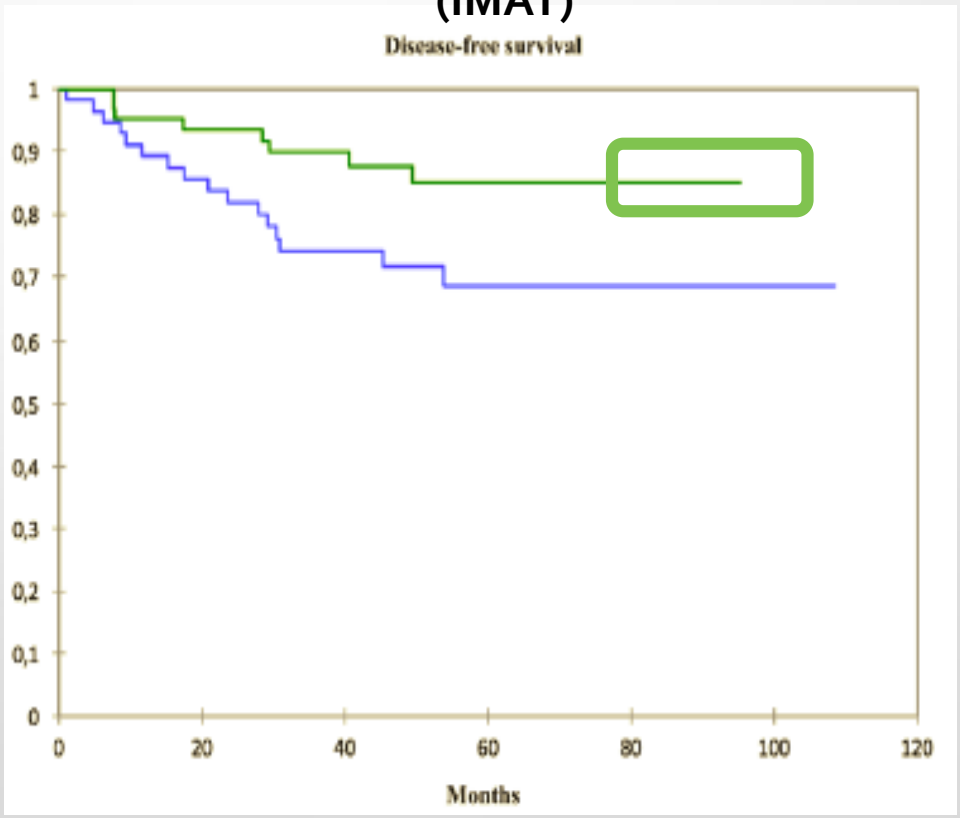
Breast cancer survivor: patients at risk for skeletal muscle disorders

Patients with **early breast cancer** with **sarcopenia** and a **high IMAT index** (> 3.5 cm^2/m^2) had a poor prognosis

Sarcopenia



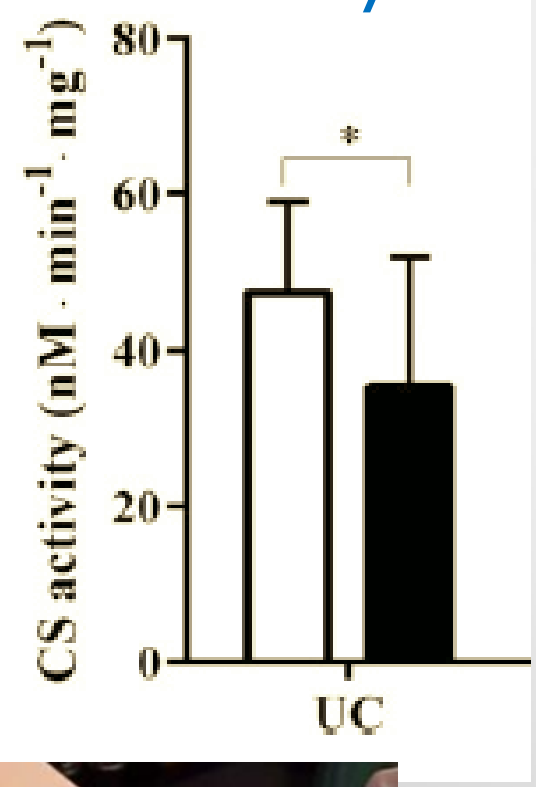
High inter-muscular adipose tissue areas (IMAT)



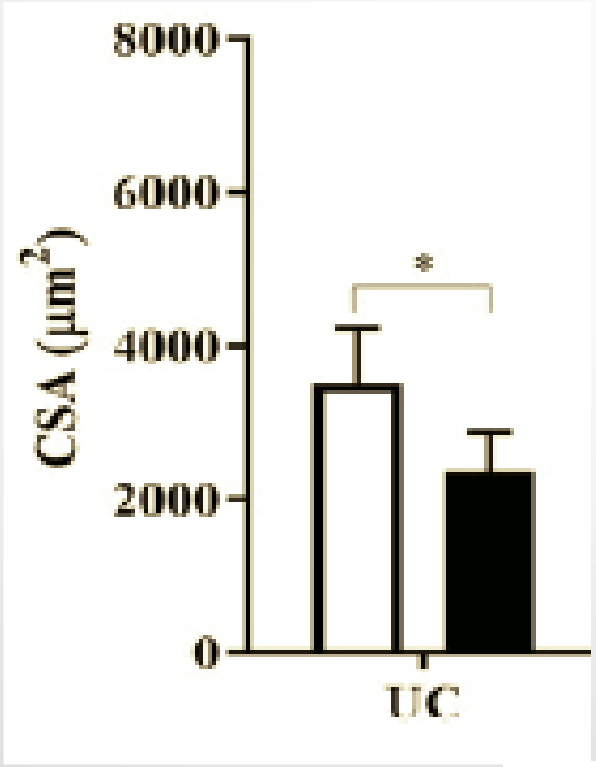
Deluche *et al.* doi:10.1007/s00520-017-3902-6

Breast cancer survivor: patients at risk for skeletal muscle disorders

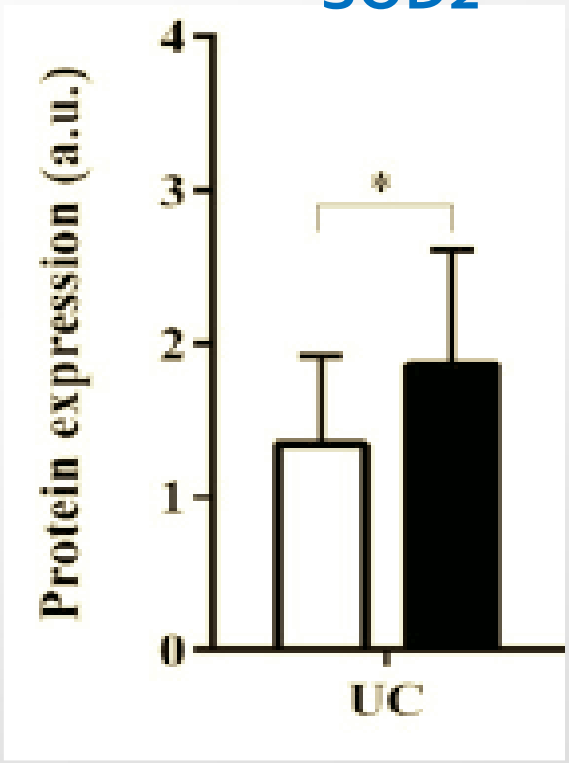
Citrate synthase

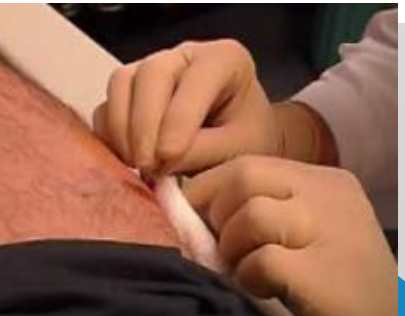


All fibers



SOD2





16-week treatment period

Beneficial effects of exercise on cardiac function in breast cancer patients

"A crucial goal is that the cured cancer patient of today does not want to become the heart failure patient of tomorrow" (Eschenhagen et al., 2011)

Beneficial effects of exercise on cardiac function in breast cancer patients

Table 1. Participant characteristics

Age (y)	53 ± 7
Height (cm)	164 ± 9
Weight (kg)	78 ± 21
Primary tumor size	
T_1, ≤ 2 cm	8
T_2, 2-5 cm	9
Nodal status	
N_0	8
N_1	3
N_2	5
N_3	1
Type of surgery	
Breast-conserving surgery	8
Mastectomy	9
Heart rate (bpm)	77 ±11
Systolic blood pressure (mmHg)	121 ± 12
Hemoglobin (g/L)	124 ± 13
Smoking status	
Current	3
Ex-smoker	4
Never	10
Diabetic	1
Medications	
Antihypertensive	3
Cholesterol lowering	1
Peak VO_2 (mL/kg/min)	20 ± 4
% Age-predicted	79 ± 18
Peak exercise heart rate (bpm)	168 ± 13
% Age-predicted	98 ± 8

NOTE: Data are mean ± SD; n = 17.p.
Abbreviations: bpm, beats per minute; VO_2, oxygen consumption.

Haykowsky *et al*. doi: 10.1158/1078-0432.CCR-09-0628

Beneficial effects of exercise on cardiac function in breast cancer patients

- **16-week aerobic training intervention (thrice-weekly):**

AT = 5-min warm-up period and **30-60 min of cycling** at a heart rate achieved at **60-90% of VO2peak** and 5-min cool-down period.

Haykowsky *et al*. doi: 10.1158/1078-0432.CCR-09-0628

Beneficial effects of exercise on cardiac function in breast cancer patients

- **Main results:**

-Despite 4-month exercise training, trastuzumab was associated with **LV dilatation and reduced LVEF**

-One limit is that exercise training **intensity might have been insufficient**, because participants attended only 59% of prescribed sessions

Haykowsky *et al*. doi: 10.1158/1078-0432.CCR-09-0628

Beneficial effects of exercise on cardiac function in breast cancer patients

In 20 patients with stage IIB-IIIC breast cancer 12-week aerobic exercise routine consisting on 3 sessions / week of cycling during 15-30 min at 60-70% of peak workload

- **Main results:**

When conducted with one-on-one supervision, 12-week AT is a safe adjunct therapy associated with **improvements** in **cardiopulmonary function** and in patient-reported outcomes during chemotherapy

Hornsby *et al*. doi: doi:10.3109/0284186x.2013.781673

Beneficial effects of exercise on cardiac function in breast cancer patients

Table 1. Demographic and Treatment Characteristics of the Participants

Characteristic	Overall	MET-h/wk ≤ 2	2.1-10.3	10.4-24.5	> 24.6	*P*
No. of participants (%)	2,973 (100)	741 (24.9)	747 (25.1)	741 (24.9)	744 (25.0)	
Age at diagnosis, mean (SD), years	58.0 (10.5)	58.7 (10.4)	56.6 (10.5)	57.2 (10.3)	55.4 (10.5)	< .001
Time from diagnosis to enrollment, mean (SD), months						
LACE (n = 1,332, 44.8%)	21.8 (6.5)	22.7 (6.7)	21.2 (6.3)	21.6 (6.3)	21.9 (6.9)	.19
Pathways (n = 1,641, 55.2%)	1.9 (0.7)	1.9 (0.6)	1.8 (0.7)	2.0 (0.8)	1.9 (0.6)	.21
Race, %						.001
Non-Hispanic white	72.3	68.8	69.5	74.5	76.5	
Other group	27.7	31.2	30.5	25.5	23.5	
BMI, mean (SD), kg/m^2	27.5 (6.2)	29.6 (7.3)	27.8 (6.1)	26.8 (5.5)	25.9 (5.1)	< .001
Smoking, %						< .001
Never	52.7	49.8	54.3	52.0	54.6	
Former	40.8	39.3	39.1	43.1	41.9	
Current	6.5	10.9	6.6	4.9	3.5	
Menopausal status, %						< .001
Postmenopausal	63.5	69.4	63.7	63.3	57.7	
Premenopausal	30.0	24.3	29.1	30.2	36.4	
Undetermined	6.5	6.3	7.2	6.5	5.9	
AJCC stage, %						.70
I	49.8	48.9	50.2	47.8	52.3	
II	42.9	43.6	42.6	44.1	41.1	
III	7.4	7.6	7.2	8.1	6.6	

Jones *et al*. doi:10.1200/jco.2015.65.6603

Beneficial effects of exercise on cardiac function in breast cancer patients

	Total (N = 2,973)
Median MET-h/wk	10.3
Cardiovascular events*	
No. of events	862
Age-adjusted HR (95% CI)	
Multivariable-adjusted HR (95% CI)†	
Coronary artery disease	
No. of events	203
Age-adjusted HR (95% CI)	
Multivariable-adjusted HR (95% CI)†	
Heart failure	
No. of events	307
Age-adjusted HR (95% CI)	
Multivariable-adjusted HR (95% CI)†	

Jones *et al*. doi:10.1200/jco.2015.65.6603

Beneficial effects of exercise on cardiac function in breast cancer patients

- **Arizona Activity Frequency Questionnaire**

-Patients reported the **frequency** and **duration** of **physical activities** performed at least **once a month** in the past 6 or 12 months

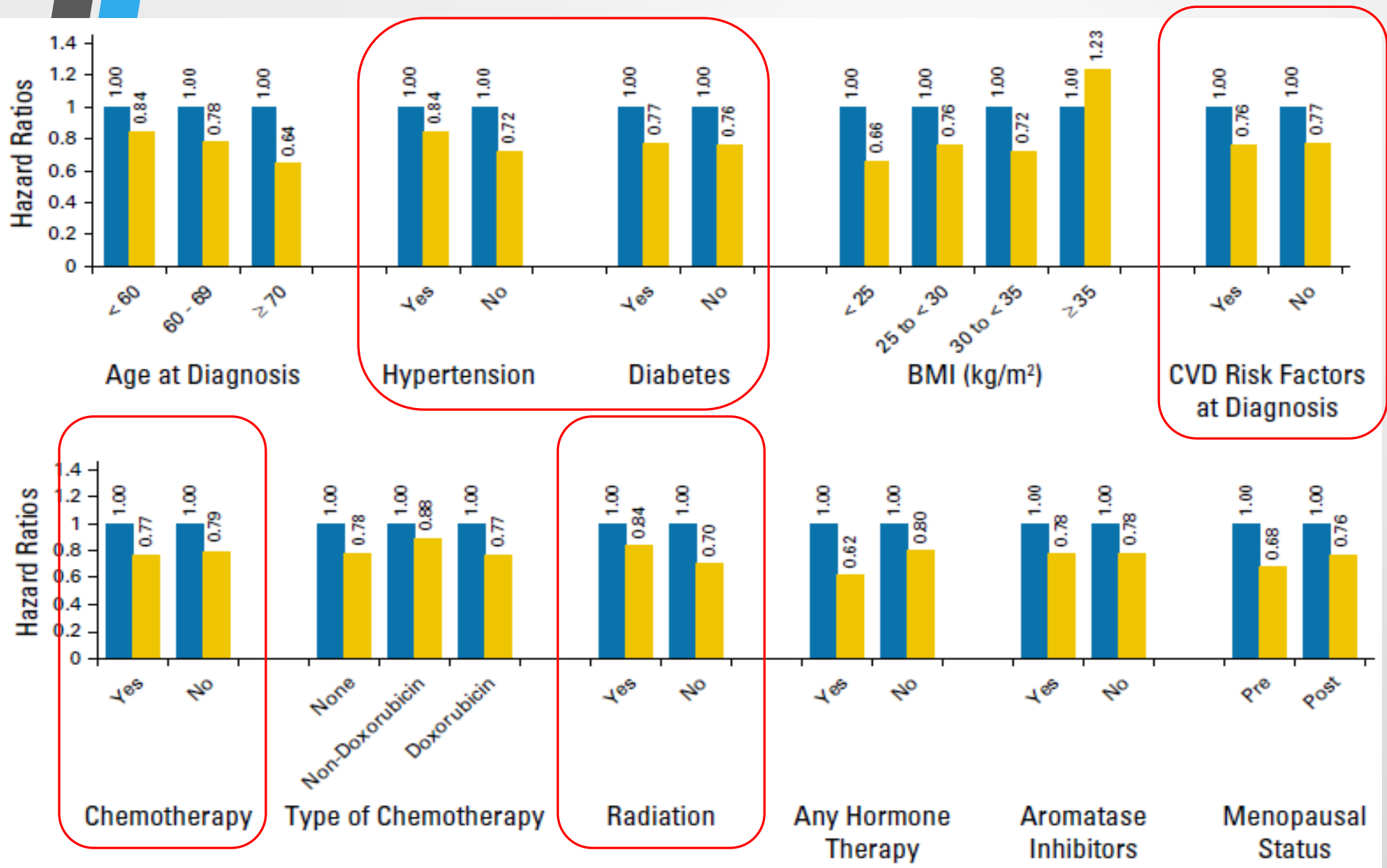
-The metabolic equivalent task (**MET**) values were assigned to each activity = **frequency of activity sessions week X average session duration**

-Individual activities were summed to derive a total MET-hours per week (MET-h/wk)

-9 MET-h/wk = 3-5 sessions of moderate- or vigorous-intensity of 20 min / week

Jones *et al*. doi:10.1200/jco.2015.65.6603

Beneficial effects of exercise on cardiac function in breast cancer patients



Jones *et al*. doi:10.1200/jco.2015.65.6603

Beneficial effects of exercise on cardiac function in breast cancer patients

- **Main results:**

Women who **exercised ≥ 9 MET-h/week** had a **23% reduction** in **CV events** compared to those who exercised < 9 MET-h/week

Jones *et al*. doi:10.1200/jco.2015.65.6603

Beneficial effects of exercise on skeletal muscle function in breast cancer patients

Table 1 Medical and demographic characteristics of START participants by sarcopenia and dynapenia status

Variable	Overall ($n = 200$)	Nonsarcopenic ($n = 149$)	Sarcopenic ($n = 51$)	p	Nondynapenic ($n = 91$)	Dynapenic ($n = 109$)	p
Age, years, mean (range)	48.8 (25–78)	48.9 (25–78)	48.8 (26–65)	0.94	47.4 (25–78)	50.1 (26–76)	0.040
Weight, kg, mean (SD)	71.2 (14.9)	74.2 (15.2)	62.3 (9.4)	<0.001	68.4 (13.2)	73.5 (15.8)	0.014
BMI, kg/m^2, mean (SD)	26.7 (5.7)	28.0 (5.9)	23.0 (3.2)	<0.001	25.3 (4.9)	27.8 (6.1)	0.002
Sarcopenia, number (%)	51 (25.5)	–	–	–	23 (25.3)	28 (25.7)	0.95
Dynapenia, number (%)	109 (54.5)	81 (54.4)	28 (54.9)	0.95	–	–	–
Overweight/obese, number (%)	149 (74.5)	108 (72.5)	41 (80.4)	0.26	58 (63.7)	91 (83.5)	0.001
Obese, number (%)	107 (53.5)	81 (54.4)	26 (51.0)	0.68	38 (41.8)	69 (63.3)	0.001
Low BMC, number (%)	23 (11.5)	17 (11.4)	6 (11.8)	0.95	10 (11.0)	13 (11.9)	0.84
Postmenopausal, number (%)	70 (35.0)	53 (35.6)	17 (33.3)	0.62	25 (27.5)	45 (41.3)	<0.05
ER positive, number (%)	144 (72.0)	105 (70.5)	39 (76.5)	0.41	68 (74.7)	76 (69.7)	0.43
PR positive, number (%)	106 (53.0)	77 (51.7)	29 (56.9)	0.62	49 (53.8)	57 (52.3)	0.93
Disease stage				0.93			0.12
I, number (%)	49 (24.5)	38 (25.5)	11 (21.6)		26 (28.6)	23 (21.1)	
IIa, number (%)	81 (40.5)	59 (39.6)	22 (43.1)		39 (42.9)	42 (38.5)	
IIb, number (%)	37 (18.5)	28 (18.8)	9 (17.6)		17 (18.7)	20 (18.3)	
IIIa, number (%)	33 (16.5)	24 (16.1)	9 (17.6)		9 (9.9)	24 (22.0)	

Adams *et al.* doi:10.1007/s10549-016-3900-2

Beneficial effects of exercise on skeletal muscle function in breast cancer patients

-Sarcopenia status = ratio of LBM (kg) / height $(m)^2$

-Dynapenia status of upper and lower extremities = ratio of weight lifted (kg) / body mass (kg)

- **17-week exercise training intervention (thrice-weekly):**

-Aerobic exercice training (AET) =
60 min (15 min at 60 % VO2peak + 45 min at 80 % VO2peak) of either treadmill, cycle ergometer, or elliptical-based exercise.

-Resistance exercise training (RET) =
2 sets of 8–12 rep of 9 exercises at 60-70 % of 1 RM

Adams *et al.* doi:10.1007/s10549-016-3900-2

Beneficial effects of exercise on skeletal muscle function in breast cancer patients

- **Main results:**

-RET better than usual care to **decrease the sarcopenia status**
-RET better than usual care to decrease upper and lower extremities muscle dysfunctions
-RET better than usual care and AET to **reverse sarcopenia and dynapenia**

-The **reversal of sarcopenia was associated with improvements in quality of life** indicators (*i.e.* lower fatigue, higher physical function)

Adams *et al*. doi:10.1007/s10549-016-3900-2

Beneficial effects of exercise on skeletal muscle function in breast cancer patients

TABLE 1. *Participant characteristics at baseline*

Participant characteristic	UC (n = 10)	AT-HIIT (n = 6)	RT-HIIT (n = 7)	P
Characteristic (mean ± SD)				
Age (yr)	51.0 ± 13.1	51.5 ± 7.0	54.3 ± 11.0	0.33
Body mass (kg)	68.4 ± 5.9	66.3 ± 13.7	70.1 ± 11.8	0.66
Height (cm)	165.3 ± 8.5	162.2 ± 7.9	167.0 ± 5.0	0.68
Activity level [n (%)]				
Inactive/low	5 (50.0)	3 (50.0)	5 (71.4)	
Moderate/high	5 (50.0)	3 (50.0)	2 (28.6)	
Tumor profile [n (%)]				0.31
Triple negative	3 (30.0)	0 (0.0)	1 (14.3)	
$HER2^+$, ER^+, PR^+	1 (10.0)	0 (0.0)	1 (14.3)	
$HER2^-$, ER^+, PR^+	2 (20.0)	5 (83.3)	3 (42.7)	
$HER2^-$, ER^+, PR^-	3 (30.0)	0 (0.0)	1 (14.3)	
$HER2^+$, ER^+, PR^-	1 (10.0)	1 (16.7)	0 (0.0)	
$HER2^-$, ER^-, PR^+	0 (0.0)	0 (0.0)	1 (14.3)	
Chemotherapy regimen [n (%)]				0.27
Anthracycline therapy	2 (20.0)	3 (50.0)	4 (57.2)	
Anthracycline + taxane therapy	8 (80.0)	2 (33.3)	3 (42.8)	
Taxane therapy	0 (0.0)	1 (16.7)	0 (0.0)	

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor.

Beneficial effects of exercise on skeletal muscle function in breast cancer patients

- **16-week exercise training intervention (twice-weekly):**

-RT-HIIT = **9 resistance exercises** of 2-3 sets of 8–12 rep at 70-80 % of 1 RM

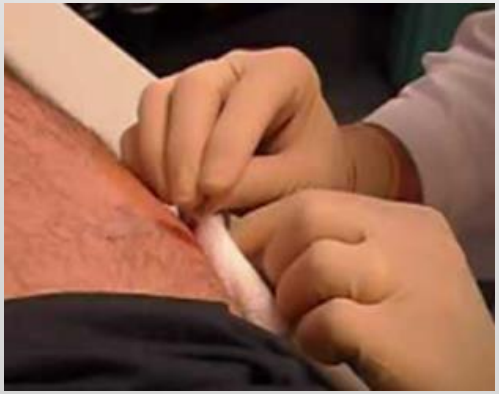
+ 3x3-min bouts of HIIT at 16-18 on the Borg 6–20 scale interspersed with 1min low-intensity active recovery

-AT-HIIT = **20 min of moderate intensity and continuous aerobic exercise** at 13–15 on the Borg 6–20 scale

+ 3x3-min bouts of HIIT at 16-18 on the Borg 6–20 scale interspersed with 1min low-intensity active recovery

Beneficial effects of exercise on skeletal muscle function in breast cancer patients

Rating of Perceived Exertion Borg RPE Scale		
6 7 8	Very, very light	How you feel when lying in bed or sitting in a chair relaxed. Little or no effort.
9 10 11	Very light Fairly light	
12 13 14	Somewhat hard	Target range: How you should feel with exercise or activity.
15 16	Hard	
17 18	Very hard	How you felt with the hardest work you have ever done.
19 20	Very, very hard Maximum exertion	Don't work this hard!

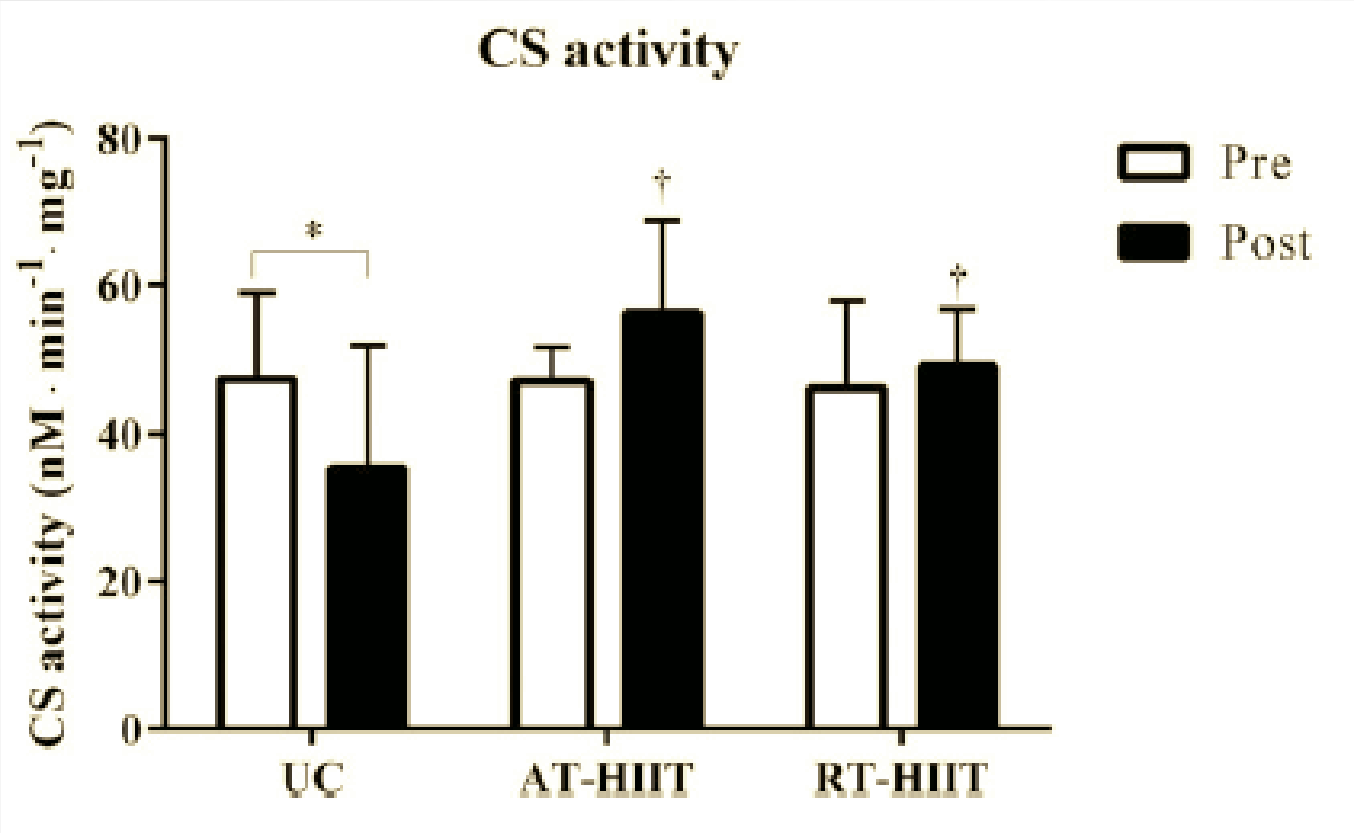


Pre

Post 16-week treatment period

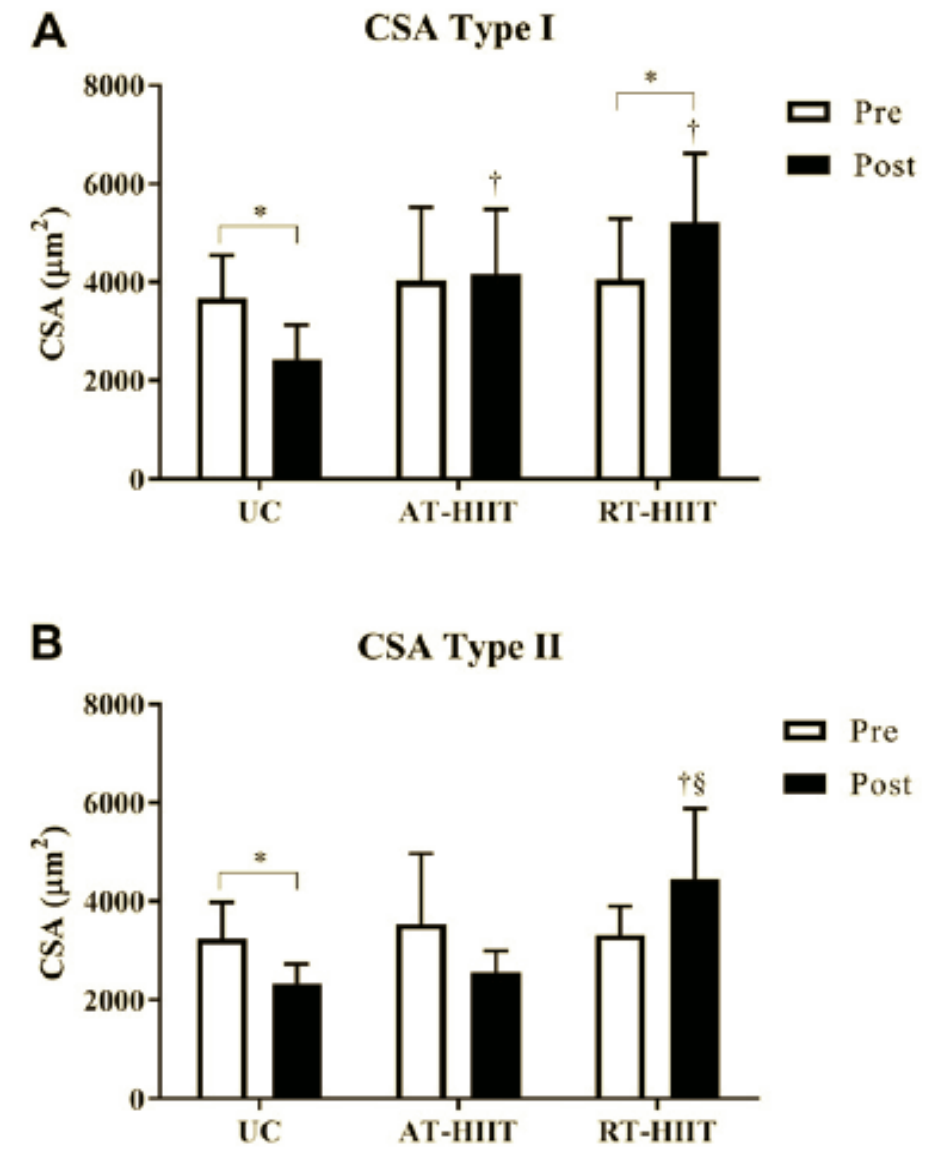
Mijwel *et al*. doi:10.1096/fj.201700968R

Beneficial effects of exercise on skeletal muscle function in breast cancer patients



*P , 0.05 at post vs. premeasurement, †P , 0.05 compared with UC

Beneficial effects of exercise on skeletal muscle function in breast cancer patients

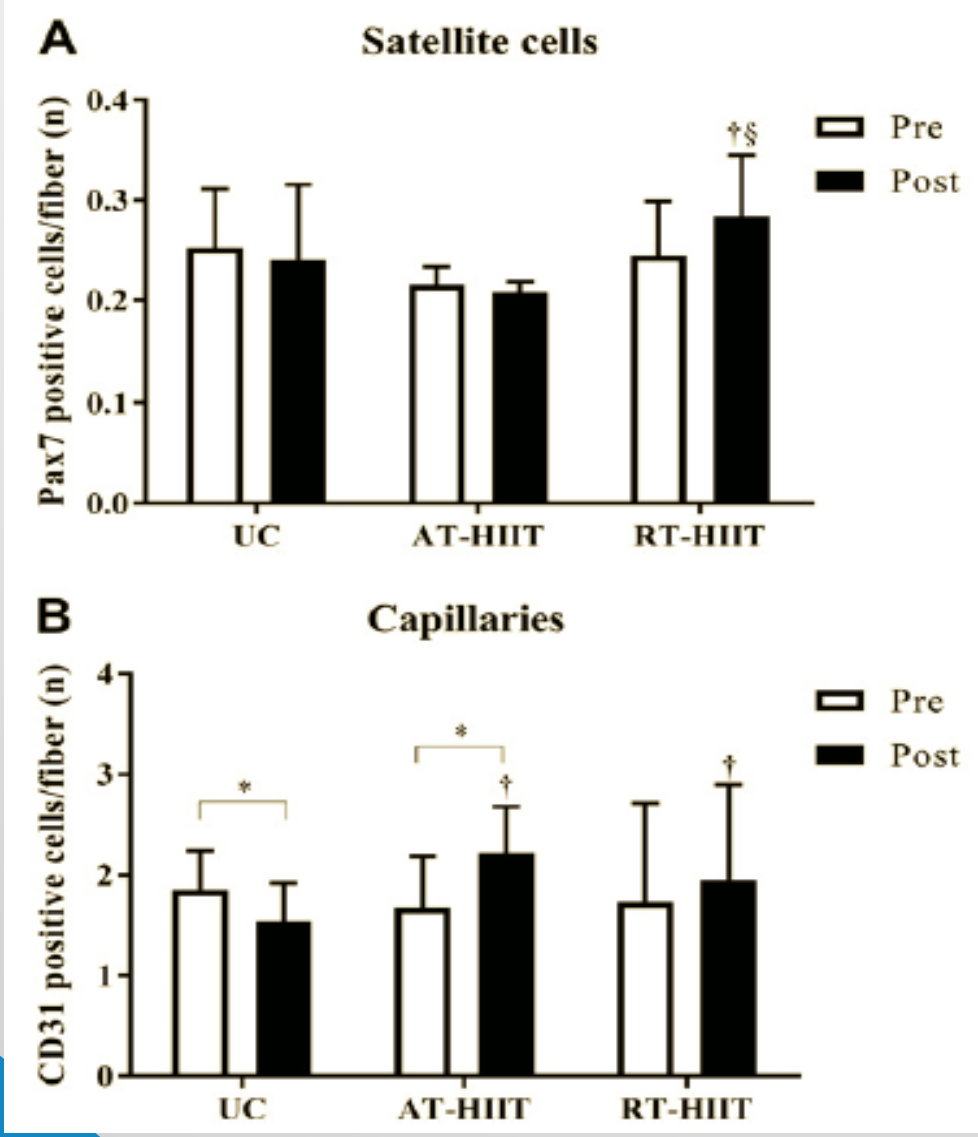


*P , 0.05 at post vs. premeasurement,
†P , 0.05 compared with UC

§P , 0.05 between RT-HIIT and AT-HIIT

Mijwel *et al*. doi:10.1096/fj.201700968R

Beneficial effects of exercise on skeletal muscle function in breast cancer patients



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§P , 0.05 between RT-HIIT and AT-HIIT

Mijwel *et al*. doi:10.1096/fj.201700968R

Beneficial effects of exercise on skeletal muscle function in breast cancer patients

- **Main results:**

-RT-HIIT and AT-HIIT counteracted CS, CSA of fibers and MHCI reductions *vs.* usual care (UC)

-AT-HIIT promoted **up-regulation of the electron transport chain protein** levels *vs.* UC

-RT-HIIT favored **satellite cell count** *vs.* UC and AT-HIIT

-AT-HIIT and RT-HIIT maintained or improved markers of skeletal muscle function compared with the declines found in the UC group during chemotherapy.

Considerations for beneficial effects of exercise on quality of life of breast cancer patients

-Lower the risk of breast cancer in **physically active** women (10%-20%) independent of BMI

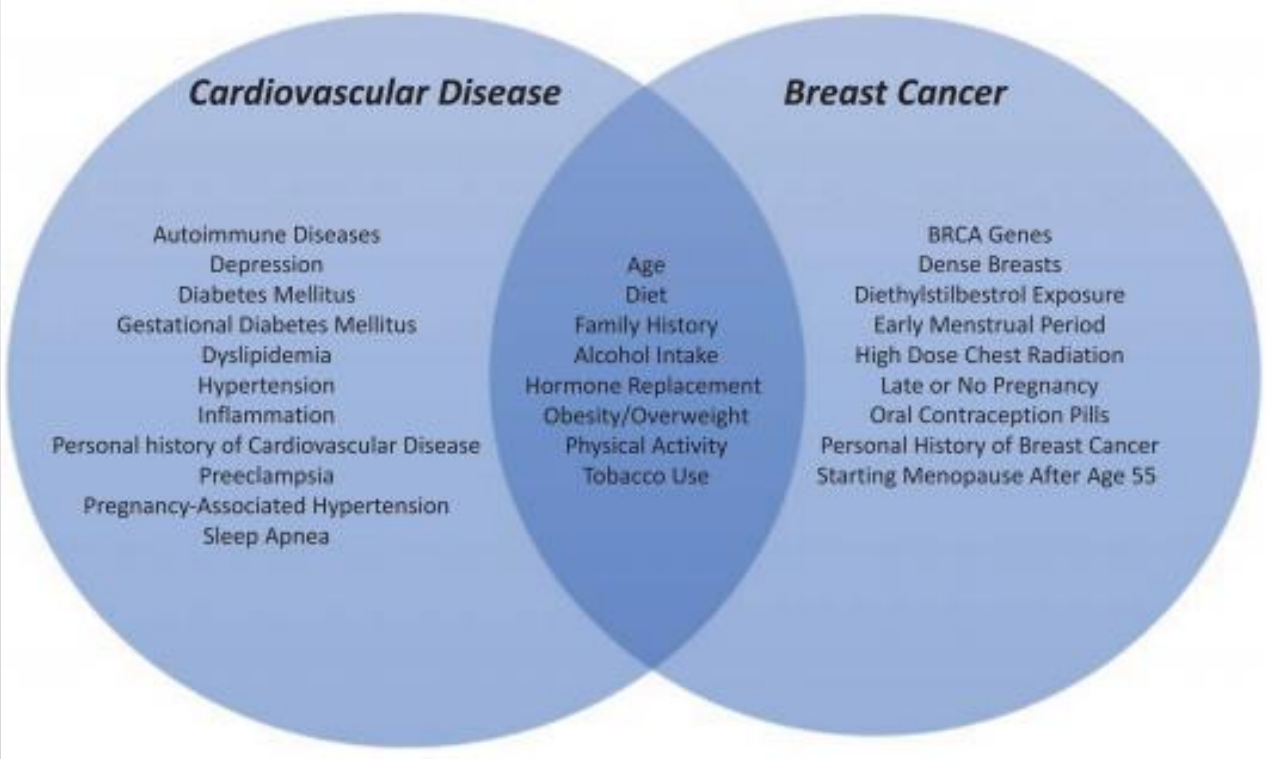
-A greater reduction in risk is associated with increasing amounts of exercise and **more vigorous activity**

-The benefit may be due to the effects of physical activity on **systemic inflammation, hormones, and energy balance**

Hildebrand *et al*. doi: 10.1158/1055-9965 ; Pizot *et al*. doi: 10.1016/j.ejca.2015.10.063

Research perspectives

Main risk factors of CVD and breast cancer



Mehta *et al*. doi:10.1161/cir.0000000000000556

Research perspectives

- To determine whether exercise during cancer therapy is a feasible and effective method for the reduction of CV morbidity and mortality in breast cancer survivors

- Cardio-oncology research programs have to be supported and applied in the future

- **These programs should focus on prevention before development of cardiotoxicity**

- **To investigate the cardiotoxicity of other chemotherapeutic agents, particularly when administered concomitantly**

- **To better define an adequate exercise prescription and the proper frequency, intensity and timing of physical exercise for the prevention of CIC**

Cavarretta et *al.* doi:10.1007/978-981-10-4304-8_8; Mehta *et al.* doi:10.1161/cir.0000000000000556

Research perspectives

- **Prospective studies integrating CT imaging and functional tests to validate the prognostic role of the two parameters in early breast cancer in a larger population of patients**

- To investigate the myotoxicity of other chemotherapeutic agents, particularly when administered concomitantly

- To better define an adequate exercise prescription and the proper frequency, intensity and timing of physical exercise for the prevention of skeletal muscle disorders

Research perspectives

A LOT OF WORK IN PERSPECTIVE !!!

Cavarretta et *al.* doi:10.1007/978-981-10-4304-8_8