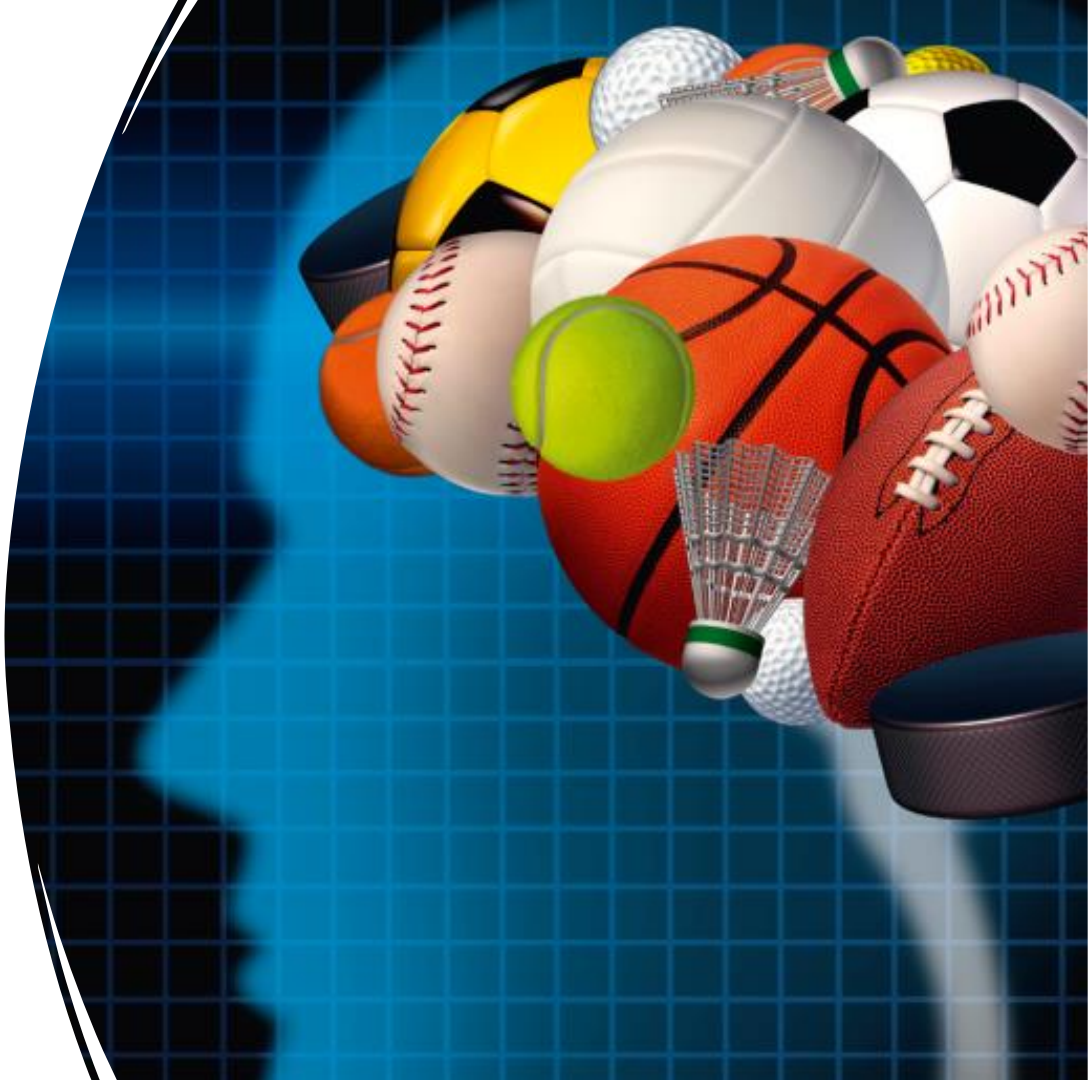
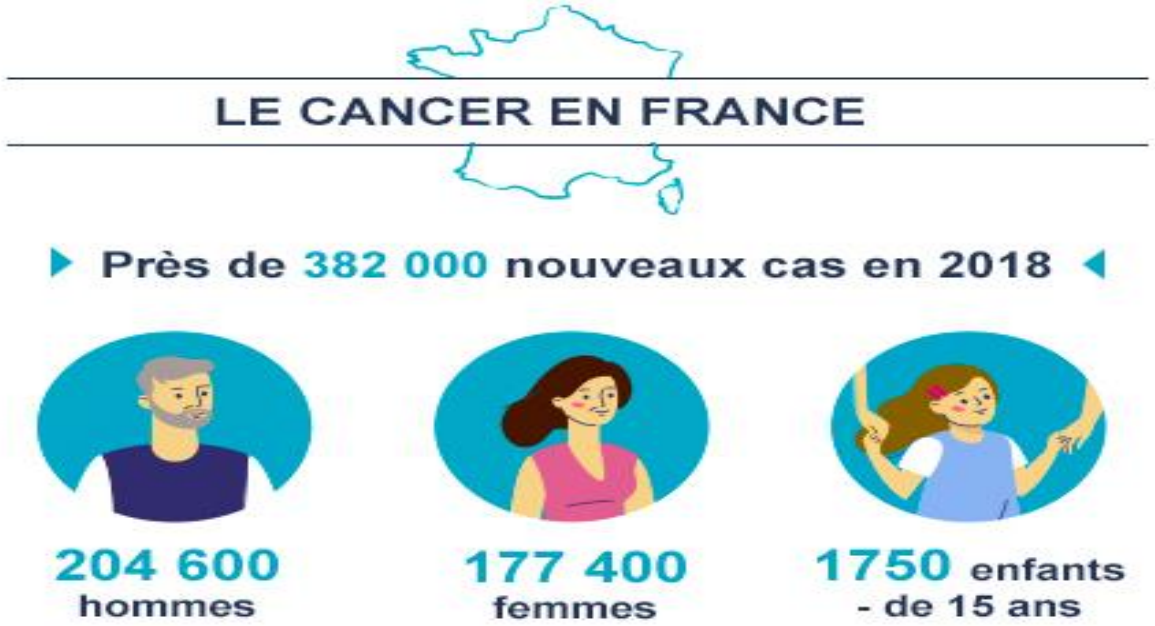
Quels sont les bénéfices cardiovasculaires de l'activité physique chez le cancéreux?

Dr Laura SERRANO
Clinique SMR Cardio-vasculaire
Cardiocéan
La Rochelle

Aucun conflit d’intérêt



Épidémiologie



Épidémiologie

LES CANCERS LES PLUS FRÉQUENTS

Chez l'homme

1. Cancer de la prostate
2. Cancer du poumon
3. Cancer colorectal

Chez la femme

1. Cancer du sein
2. Cancer colorectal
3. Cancer du poumon

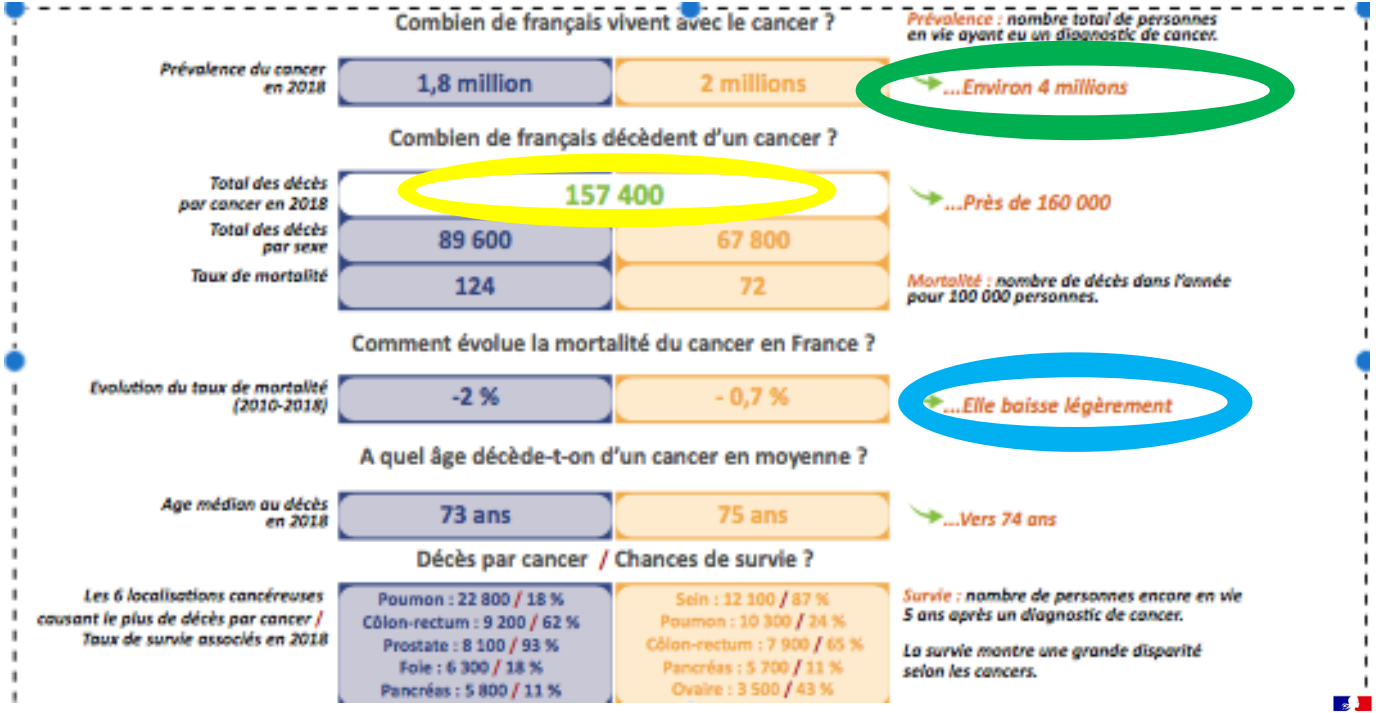
Chez l'enfant

1. Leucémies
2. Tumeurs du système nerveux central
3. Lymphomes

AGIR AU PLUS VITE, CHAQUE JOUR COMPTE

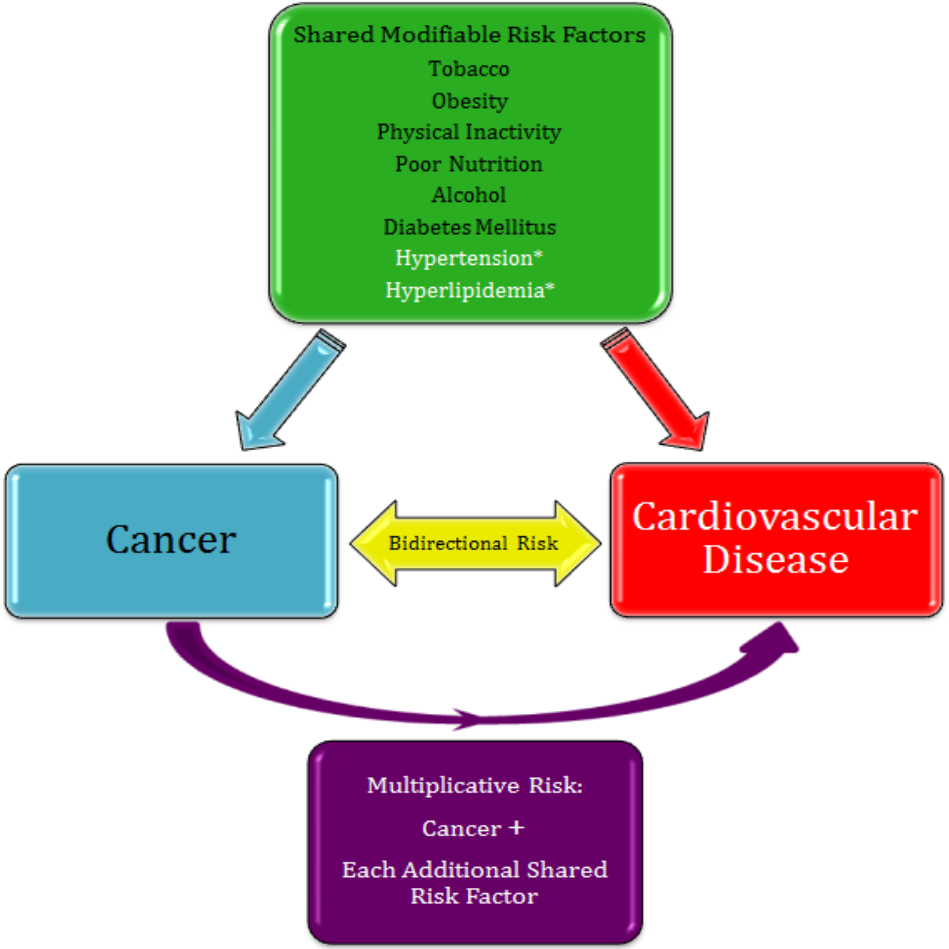
157 400
décès en 2018

Épidémiologie



RÉPUBLIQUE FRANÇAISE
Liberté
Égalité
Fraternité

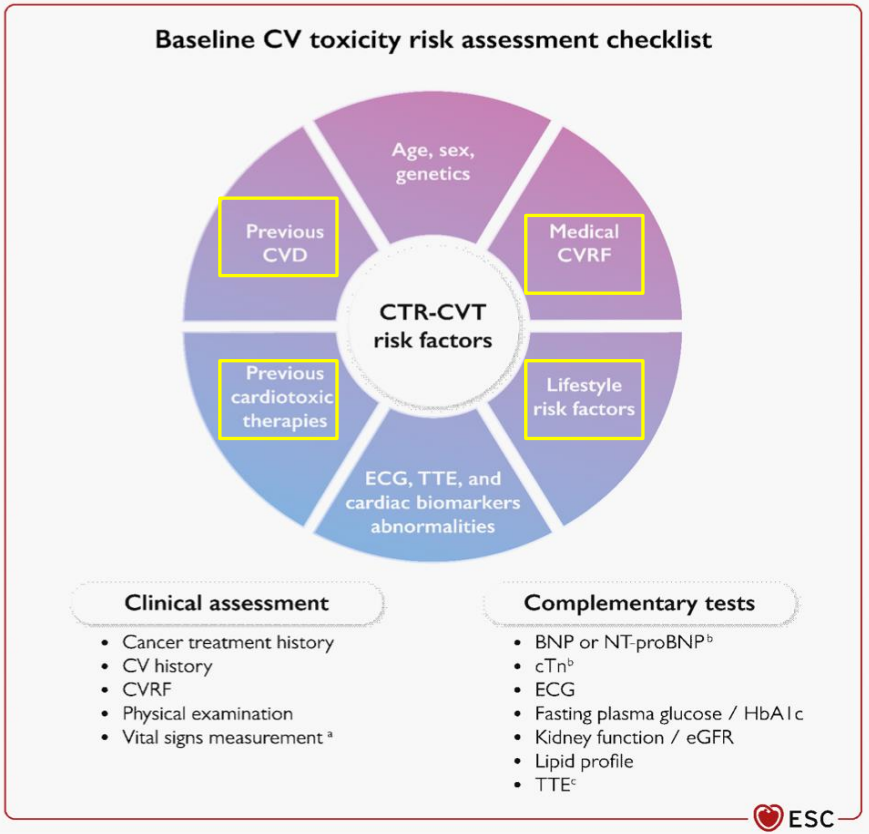
INSTITUT NATIONAL DU CANCER



Shared Modifiable Risk Factors Between Cancer and CVD, Apr. 2017

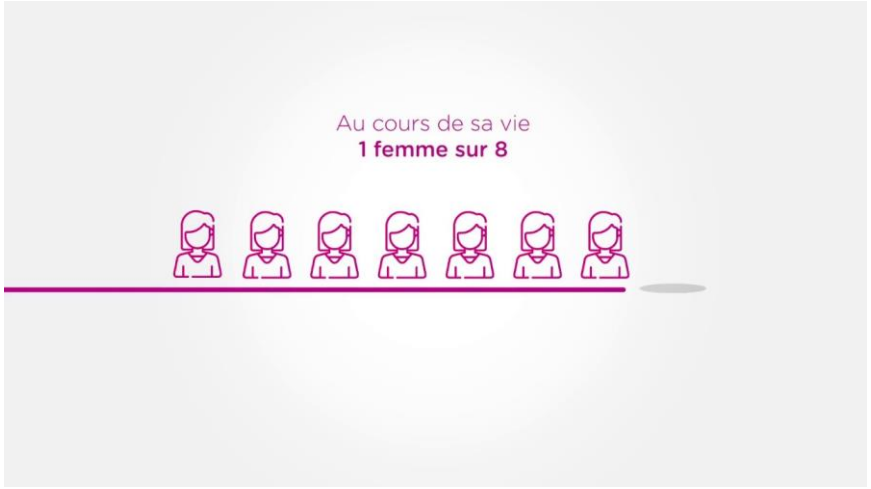
Figure 3

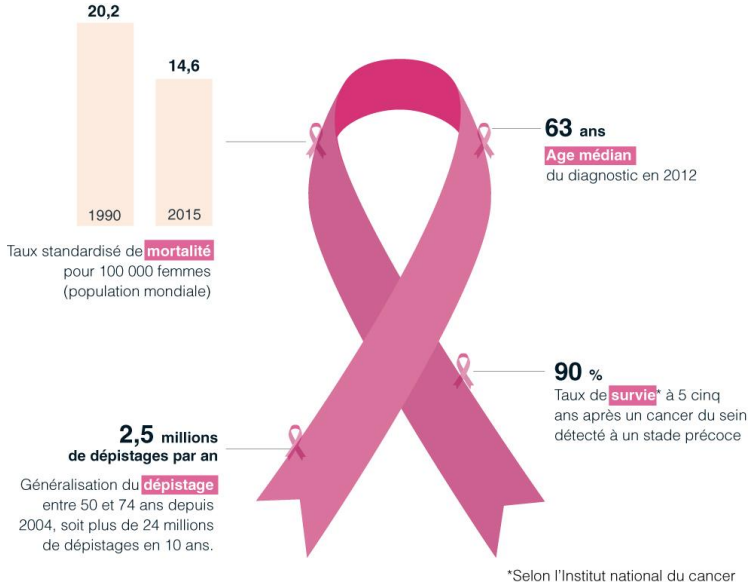
Baseline cardiovascular toxicity risk assessment checklist



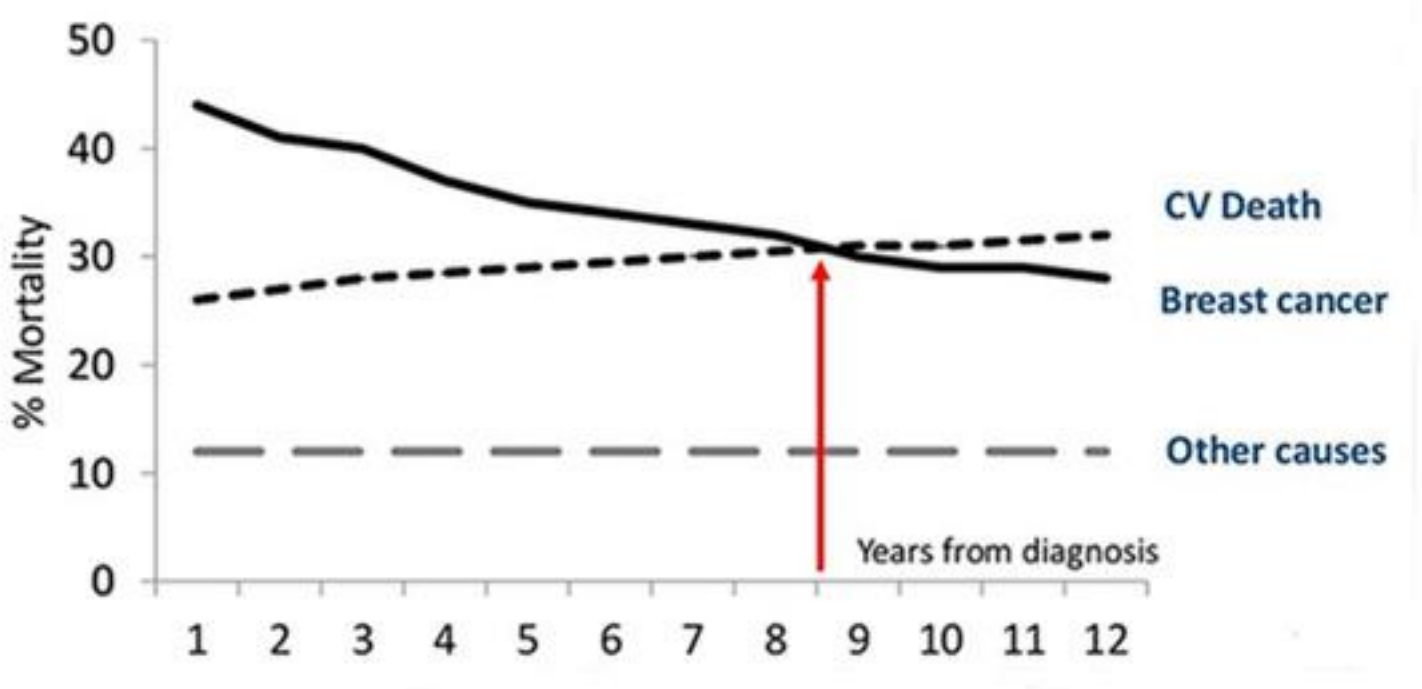
2022 ESC Guidelines on cardio-oncology
(*European Heart Journal*; 2022 – doi: 10.1093/eurheartj/ehac244)

Épidémiologie cancer du sein



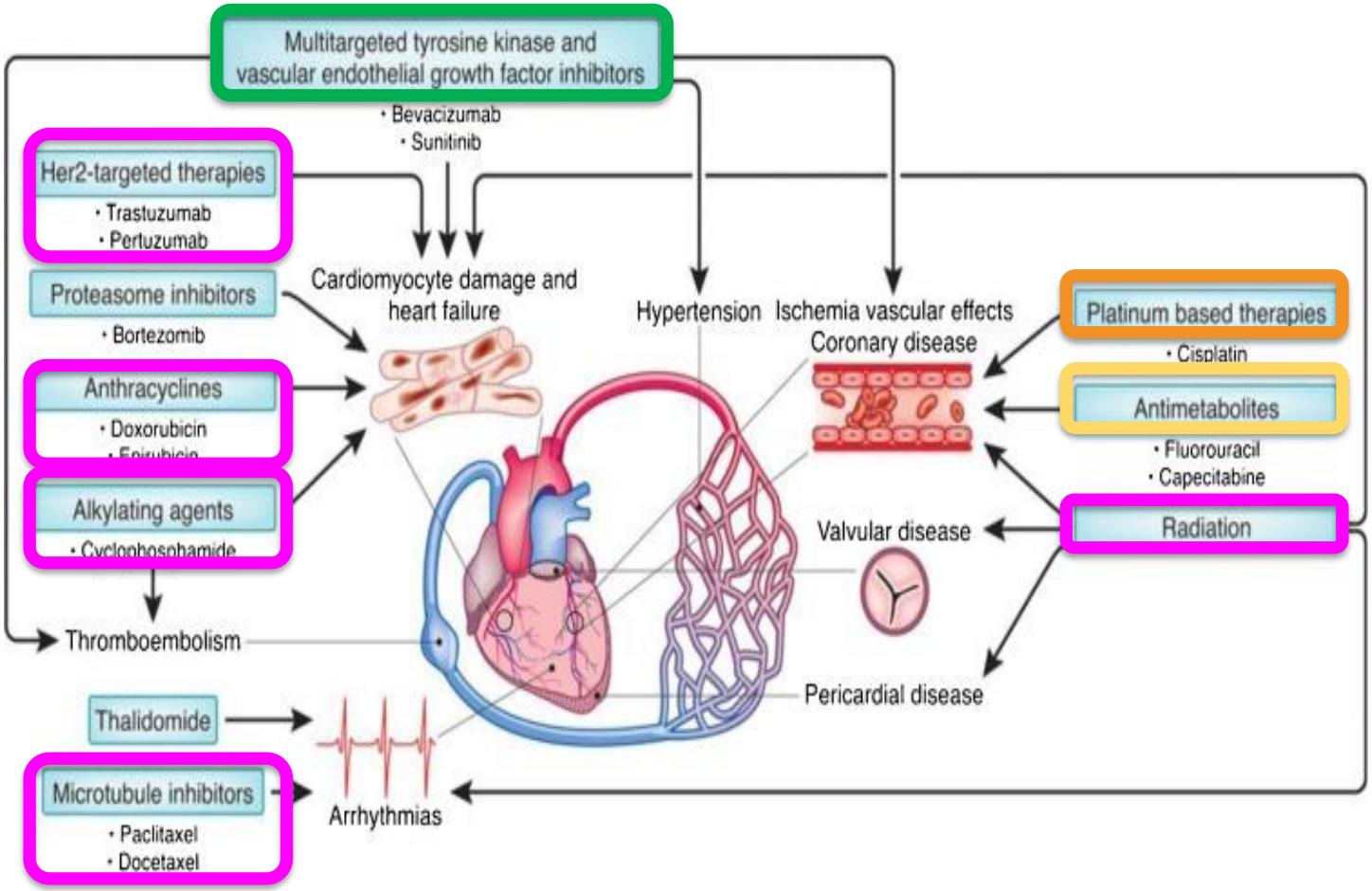


Augmentation incidence chez les jeunes 30/50 ans depuis 2012



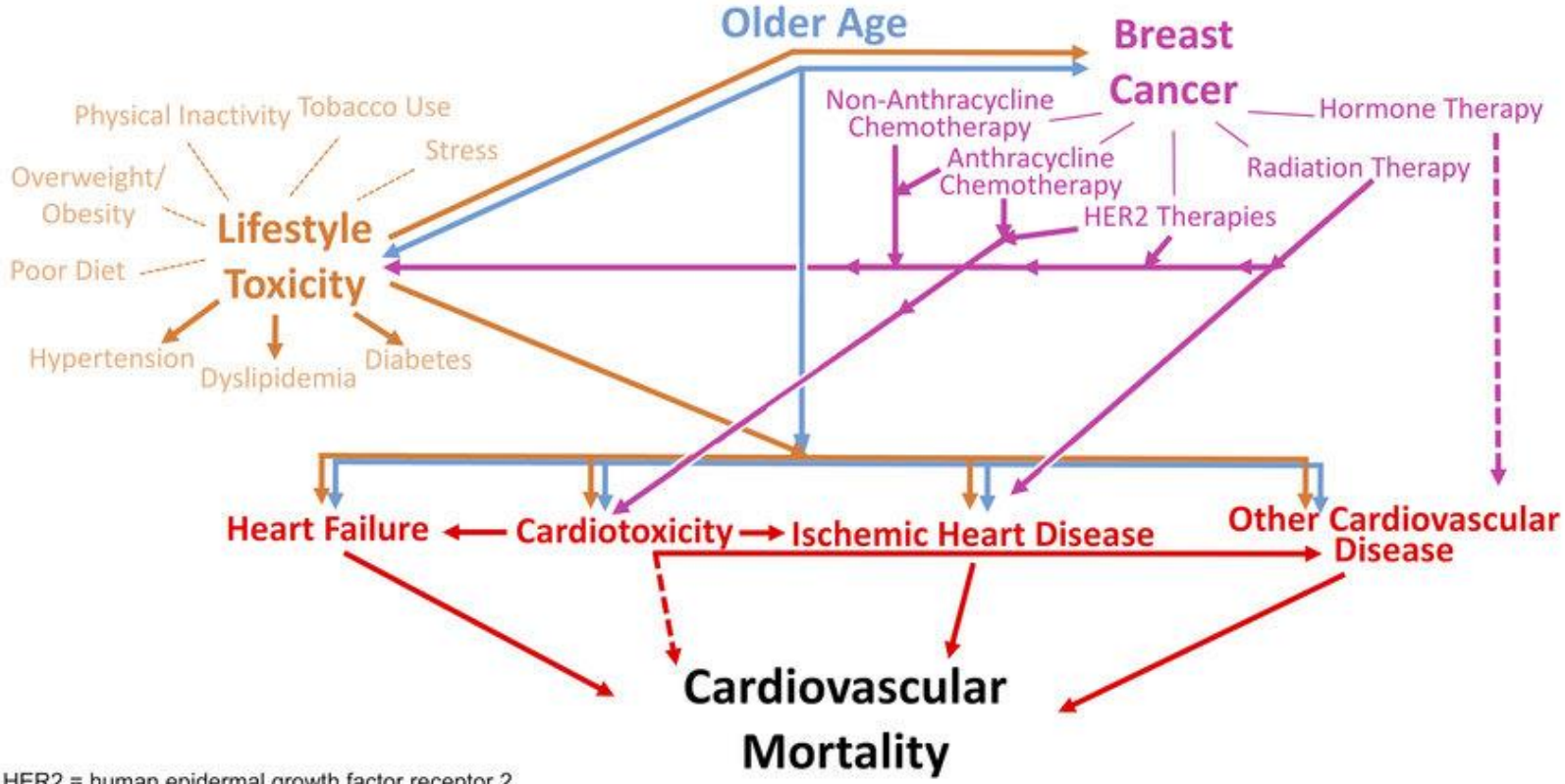
Proportional distribution of the main causes of death by time since the diagnosis of breast cancer.

Cardiovascular disease competes with breast cancer as the leading cause of death for older females diagnosed with breast cancer: a retrospective cohort study. Patnaik JL. And al. Breast Cancer Research 2011, 13:R64



Cardiotoxic effects of chemotherapy: A review of both cytotoxic and molecular targeted oncology therapies and their effect on the cardiovascular system.Crit. Reviews in oncology and hematology. Babiker et al. 2018, Pages 186-200

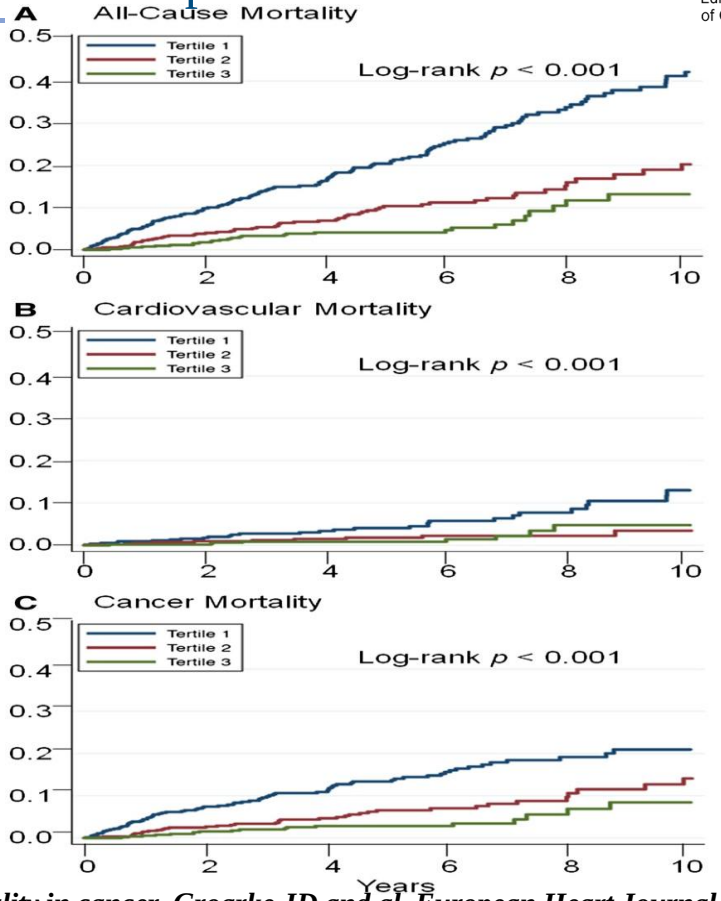
Figure 1: Interaction of risk factors for elevated cardiovascular mortality in women diagnosed with breast cancer



HER2 = human epidermal growth factor receptor 2

Curing breast Cancer and killing the heart: A novel model to explain elevated cardiovascular disease and mortality risk among women with early stage breast Cancer., Kairkham A. et al. Research gate, Feb. 2019

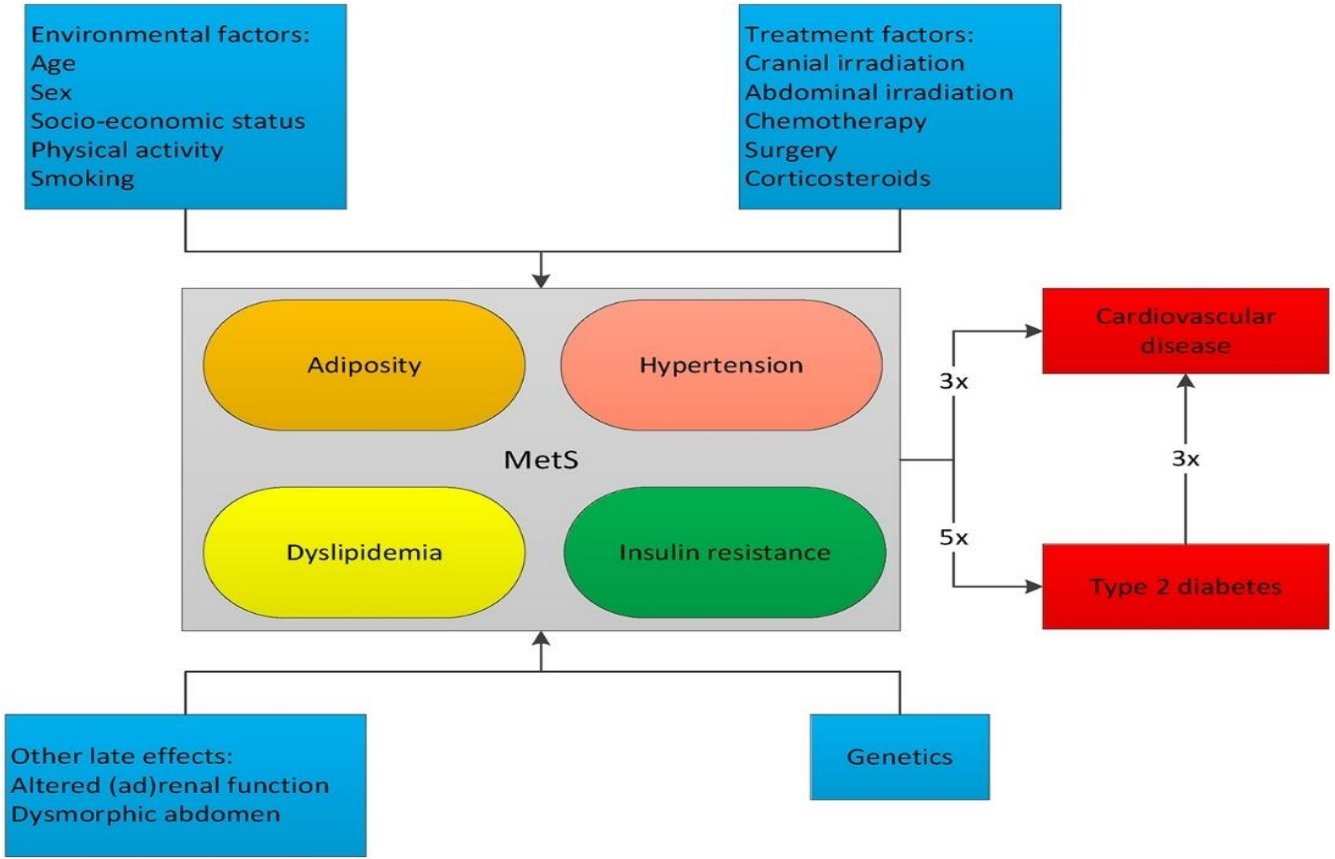
Mortalité cardio-vasculaire / fonction capacité cardio-respiratoire



Probability of all-cause mortality (*A*), cardiovascular mortality (*B*), and cancer mortality (*C*) in cancer patients according to cardiorespiratory fitness tertiles achieved during exercise treadmill testing:
low cardiorespiratory fitness (blue line),
intermediate cardiorespiratory fitness (red line),
and high cardiorespiratory fitness (green line).

Association of post-diagnosis cardiorespiratory fitness with cause-specific mortality in cancer. Groarke JD and al. European Heart Journal - Quality of Care and Clinical Outcomes, Volume 6, Issue 4, October 2020, Pages 315–322

Risque MCV et hémopathie maligne



Metabolic syndrome as cardiovascular risk factor in childhood cancer survivors. Pluimakers VG and al. Critical Reviews in Oncology/Hematology Vol. 133 Jan. 2019, Pages 129-141

Risque MCV post-greffe de moelle osseuse

Table 1
Incidence of CVD risk factors and overt CVD following HCT.

Outcome	Incidence
CVD Risk Factors	
Hypertension	28%–74%[7,10,137,61,27,138]
Dyslipidemia	33%–58%[7,10,26,137,23]
Diabetes	10%–41%[7,10,26,137,23]
Obesity	20–44%[26,61,23]
Low exercise tolerance	100%[125]
Decreased LVEF	5%–43%,[139,140]
Overt CVD	
Arrhythmia	2%–13%[7,10,137]
Stroke	0.2%–4.8%[7,10,26,137,61]
Transient ischemic attack	0.3%[4]
Myocardial ischemia	1%–6%[7,10,77,137]
Heart failure	1% to 9%[3–5,61]

Cardiovascular disease following hematopoietic stem cell transplantation: Pathogenesis, detection, and the cardioprotective role of aerobic training. Scott JM and al. Critical Reviews in Oncology/Hematology Vol 98., Feb. 2016, 222-234.

Pourquoi pratiquer une AP durant la p.e.c de son cancer ?

Effets entraînement in vivo rats traités par DOX

40 Rats mâles adultes, entrainés 60/90 minutes par jour

Table 6. Effects of endurance running training and DOX on heart antioxidant enzyme activity:

Groups	tSOD	MnSOD	Cu/ZnSOD	GPx	GR
NT + P	94.88±2.64	46.07±1.27	49.80±1.96	1.14±0.23	$1.13\times10^{-4}\pm2.84$
NT + DOX	87.17±5.03	43.25±4.69	43.91±3.55	1.85±0.42	$1.17\times10^{-4}\pm4.54\times10^{-5}$
T + P	139.95±7.58*	74.05±5.46*	65.90±4.36*	2.10±0.47	$2.26\times10^{-4}\pm7.27\times10^{-5}$
T + DOX	129.23±2.96*	70.13±2.99*	59.09±2.62*	1.58±0.51	$1.30\times10^{-4}\pm4.97\times10^{-5}$

Enzymes anti oxydantes mitochondriales cardiaques

Moderate endurance trainning prevents doxorubicine-induced in vivo mitochondriopathy and reduces the development of cardiac apoptosis Ascansao A. and al, Am J Physiol Heart Circ Physiol 289: H722-H731, 2005.

Effets entraînement in vivo rats traités par DOX

Mitochondries plus sensibles à apoptose sous DOX

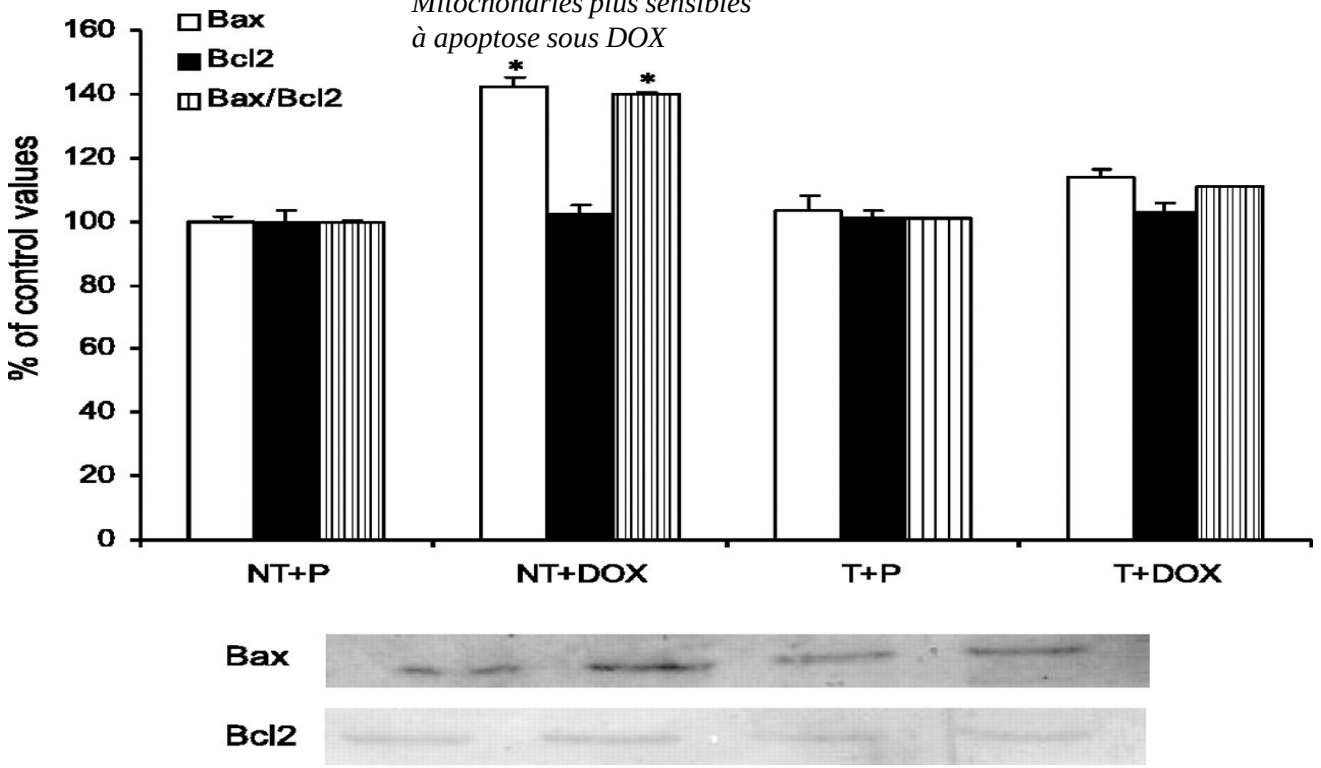
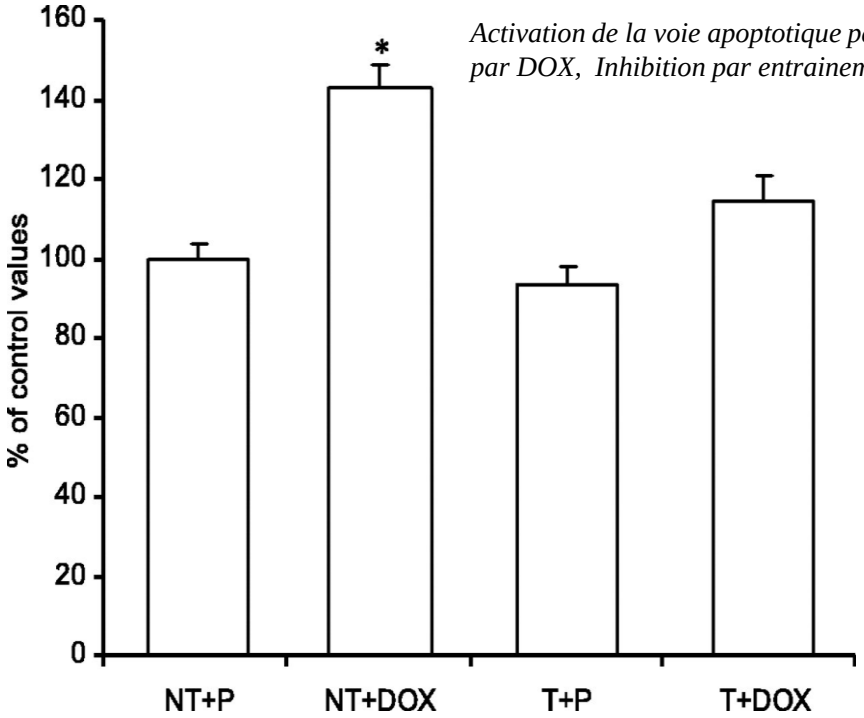


Fig. 5. Effect of training and DOX treatment on Bax and Bcl-2 protein expression and Bax-to-Bcl-2 ratio in rat heart mitochondria. Representative Western blots of Bax (21 kDa) and Bcl-2 (25 kDa) are shown for each group. Values are means ± SE of results obtained from 10 independent experiments. *$P < 0.05$ vs. all other groups.

Moderate endurance trainning prevents doxorubicine-induced in vivo mitochondriopathy and reduces the development of cardiac apoptosis Ascansao A. and al, Am J Physiol Heart Circ Physiol 289: H722-H731, 2005.

Effets entraînement in vivo rats traités par DOX



Activation de la voie apoptotique par les caspases 3 sous traitement par DOX, Inhibition par entrainement en endurance

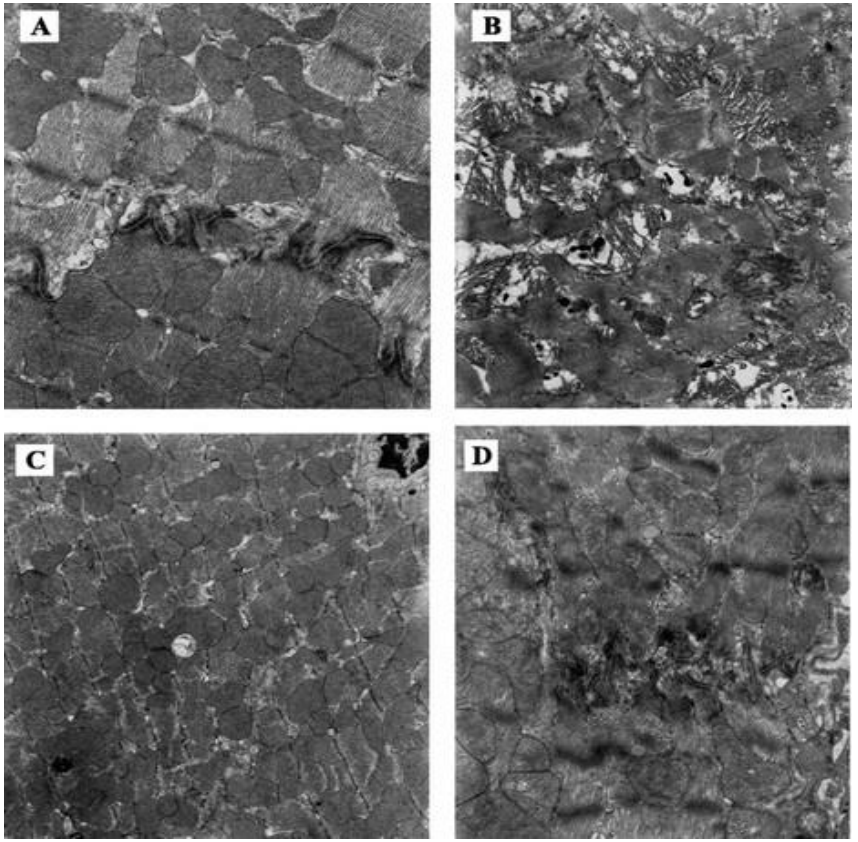
Fig. 6. Effect of training and DOX treatment on cardiac muscle homogenate caspase-3 activity. Values are means ± SE of results obtained from 10 independent experiments. *P < 0.05 vs. all other groups.

Moderate endurance trainning prevents doxorubicine-induced in vivo mitochondriopathy and reduces the development of cardiac apoptosis Ascansao A. and al, Am J Physiol Heart Circ Physiol 289: H722-H731, 2005.

Effets entraînement in vivo rats traités par DOX

Fig. 7.Representative electron micrographs of cardiac tissue from NT + P (A), NT + DOX (B), T + P (C), and T + DOX (D) groups.

NT + DOX group (B)
T + DOX group (D).



- ***Vacuoles cytoplasmiques***
- ***Désorganisation myofibrillaire***
- ***Sévères Dommages mitochondriaux***
- ***Dégénérescence extensive***

Moderate endurance trainning prevents doxorubicine-induced in vivo mitochondriopathy and reduces the development of cardiac apoptosis Ascansao A. and al, Am J Physiol Heart Circ Physiol 289: H722-H731, 2005.

Effets entraînement in vivo rats traités par DOX

AP endurance sous DOX :

- Protection mitochondriale cardiaque
- Réduction du stress oxydatif mitochondrial médié par DOX
- Réduction de la voie de l'apoptose médiée par DOX

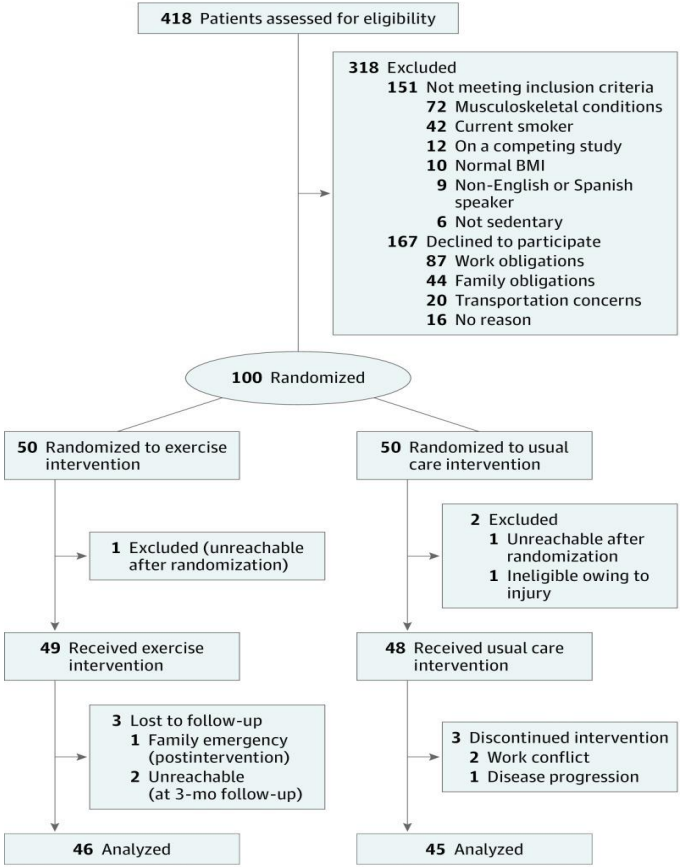
Moderate endurance trainning prevents doxorubicine-induced in vivo mitochondriopathy and reduces the development of cardiac apoptosis Ascansao A. and al, Am J Physiol Heart Circ Physiol 289: H722-H731, 2005.

Etude randomisée
Monocentrique
100 Patientes
Cancer du sein Stade I à III
Sédentaires
Surpoids ou obèses IMC > ou égal à 25
TTT complet dans les 6 mois
Avant inclusion

1er Aout 2012 / 2 octobre 2018

Usal care Vs Exercise Group

Gp ExG: Exercice aérobie + exercice en résistance supervisé, 3 fois par semaine durant 16 semaines



Effect of Aerobic and Resistance Exercise Intervention on cardiovascular Disease Risk in Women With Early-Stage Breast Cancer. A Randomized Clinical Trial. Kyuwan L. and al. JAMA Oncol. 2019 May; 5(5):710-714

Table. Comparison of FRS Variables Between Exercise and Usual Care Groups[a]

Variable	Baseline, Mean (SD)	Postintervention		Postintervention Between-Group Difference	
		Mean (SD)	*P* Value[b]	Mean (95% CI)	*P* Value[c]
SBP, mm Hg					
Exercise	132.9 (13.0)	120.7 (9.5)	.001	−13.7 (−16.5 to −8.7)	.001
Usual care	133.7 (9.7)	135.9 (9.8)	.22		
FRS preset point for SBP[d]					
Exercise	0.0 (2.0)	−3.0 (2.0)	<.001	−3.0 (−5.0 to −1.0)	.002
Usual care	0.0 (2.0)	0.0 (2.0)	>.99		
HDL-C, mg/dL					
Exercise	43.1 (6.6)	64.7 (7.8)	.001	24.4 (27.9 to 17.9)	.001
Usual care	41.0 (4.3)	39.9 (4.0)	.45		
FRS preset point for HDL-C[d]					
Exercise	2.0 (1.0)	−2.0 (1.5)	<.001	4.0 (0.5 to 6.0)	<.001
Usual care	2.0 (1.0)	2.0 (2.0)	.97		
LDL-C, mg/dL					
Exercise	167.9 (19.7)	119.3 (12.1)	<.001	−48.6 (−61.2 to −27.6)	.001
Usual care	172.4 (20.3)	178.3 (21.7)	.59		
FRS preset point for LDL-C[d]					
Exercise	2.0 (1.0)	0 (1.0)	.002	−2.0 (−4.5 to −0.5)	.001
Usual care	2.0 (1.0)	2 (1.0)	.98		
Diagnosis of diabetes, No. (%)					
Exercise	20 (40)	10 (20)	<.001	−10.0 (−18.2 to −6.4)	<.001
Usual care	22 (44)	24 (53)	.45		
FRS preset point for diabetes[d]					
Exercise	2.0 (1.5)	1.0 (0.5)	.001	−1.0 (−2.5 to −0.5)	.003
Usual care	2.0 (1.0)	3.0 (1.0)	.21		
Total FRS					
Exercise	12.0 (2.0)	2.0 (1.5)	<.001	−9.5 (−13.0 to −6.0)	<.001
Usual care	12.0 (2.0)	13.0 (3.0)	.67		
FRS-predicted 10-y risk, %					
Exercise	13.0 (3.0)	2.0 (0.5)	<.001	−11.0 (−15.0 to −5.0)	<.001
Usual care	13.0 (3.0)	13.0 (3.0)	.97		

Abbreviations: FRS, Framingham Risk Score; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

[a] Two of the 6 groups (age and smoking status) did not apply in this comparison.

[b] *P* value for repeated-measures analysis of variance comparing changes in the exercise group and in the usual care group from baseline to postintervention.

[c] *P* value for mixed-model analysis comparing changes between the exercise and usual care group from baseline to postintervention.

[d] Assigned preset point for the respective variable based on calculating the FRS to assess FRS-predicted 10-year cardiovascular disease risk.

50 femmes UC /50 femmes AP
55% origine hispanique
Moyenne âge 53,5 ans =/-10,4

J1 et 3:résistance et aérobie
80 minutes
J2: 50 min aérobie (65% à 80% FC max)

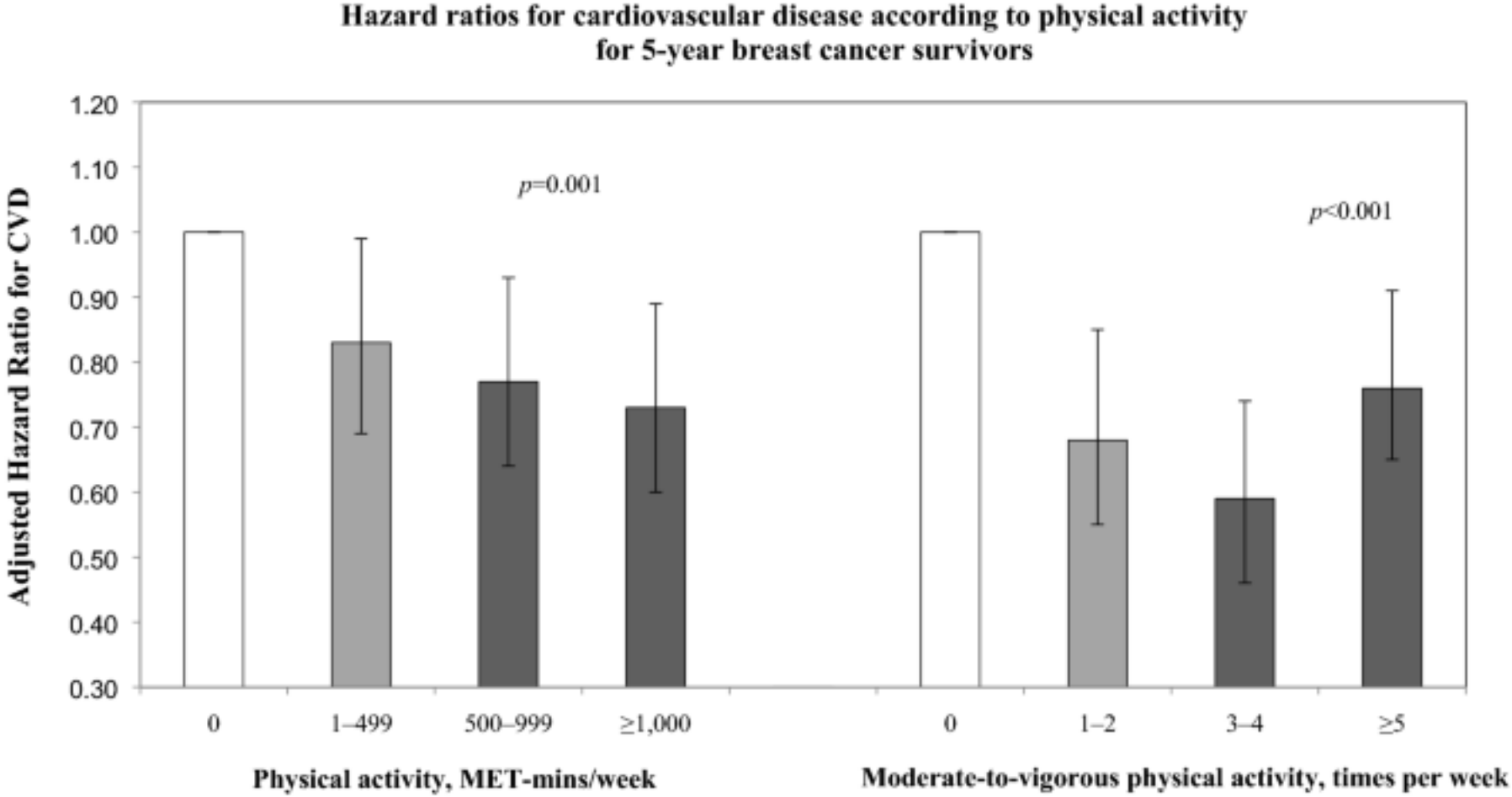
AP: Aérobie: Marche, rameur, bicyclette ergométrique
Résistance: presses mb inf, Extension, flexion mb inf, presse mb sup,
Seated row, RM: biceps, triceps
60%/80% FMMax.

Am coll of sports medicine/am Cancer society exercise guidelines for cancer survivors
> ou = 150 min ap aérobie
2/3 fois par semaine

ON

Etude rétrospective
39775 patientes diagnostiquées entre 2006 et 2011
Cancer du sein précoce
Korean National Health Insurance Service database.
Suivi à partir de 5 ans après le diagnostic de cancer du sein
Suivi: durant 5 ans ou s'arrête après évènement cv ou le décès
Activité minime, modérée, intense

Association between physical activity and subsequent cardiovascular disease among 5-year breast cancer survivors. Kim KH. and al. Breast Cancer Res Treat. 2021 Jul;188(1):203-214.



Association between physical activity and subsequent cardiovascular disease among 5-year breast cancer survivors. Kim KH. and al. Breast Cancer Res Treat. 2021 Jul;188(1):203-214.

Table 4 Sensitivity analysis on the association of physical activity with cardiovascular disease risk among 5-year breast cancer survivors with healthy lifestyle behaviors or no cardiotoxic cancer treatment

Variables	Adjusted hazard ratio (95% CI) according to Physical activity, MET-mins/week[a]				P_{trend}
	0	1–499	500–999	≥ 1,000	
Total participants					
	1.00 (reference)	0.83 (0.69–0.99)	0.77 (0.64–0.93)	0.73 (0.60–0.89)	0.001
Lifestyle behaviors					
Never smokers	1.00 (reference)	0.82 (0.69–0.99)	0.78 (0.65–0.94)	0.70 (0.57–0.85)	< 0.001
Non-drinkers	1.00 (reference)	0.82 (0.68–0.98)	0.77 (0.63–0.93)	0.78 (0.64–0.96)	0.011
Cancer treatment					
No cardiotoxic chemotherapy	1.00 (reference)	0.78 (0.63–0.97)	0.81 (0.65–1.00)	0.71 (0.56–0.91)	0.009
No tamoxifen	1.00 (reference)	0.82 (0.68–0.98)	0.77 (0.63–0.92)	0.74 (0.61–0.91)	0.002
No aromatase inhibitor	1.00 (reference)	0.82 (0.68–0.99)	0.76 (0.63–0.92)	0.75 (0.61–0.92)	0.003
No radiotherapy	1.00 (reference)	0.79 (0.63–1.00)	0.82 (0.64–1.03)	0.73 (0.56–0.95)	0.025

[a]The 500 MET-mins/week correspond to 152, 125, and 62.5 min per week of light-, moderate-, and vigorous-intensity physical activity, respectively

Adjusted hazard ratios calculated by Cox proportional hazards regression after adjustments for age, household income, smoking, alcohol intake, body mass index, systolic blood pressure, fasting serum glucose, total cholesterol, cardiotoxic chemotherapy, tamoxifen, aromatase inhibitor, radiotherapy, Charlson comorbidity index, and diagnosis year

MET metabolic equivalent of task

Association between physical activity and subsequent cardiovascular disease among 5-year breast cancer survivors. Kim KH. and al. Breast Cancer Res Treat. 2021 Jul;188(1):203-214.

Table 3 Adjusted hazard ratios for cardiovascular disease according to physical activity and body mass index for 5-year breast cancer survivors

Variables	BMI ≥ 23.0 kg/m^2		BMI < 23.0 kg/m^2		BMI ≥ 23.0 kg/m^2		BMI < 23.0 kg/m^2	
	PA < 500 MET-mins/week[a]	PA ≥ 500 MET-mins/week[a]	PA < 500 MET-mins/week[a]	PA ≥ 500 MET-mins/week[a]	MVPA ≤ 2 times/week	MVPA ≥ 3 times/week	MVPA ≤ 2 times/week	MVPA ≥ 3 times/week
Number of participants	10,352	10,850	8,212	10,361	13,054	8,148	10,404	8,169
Cardiovascular disease								
aHR (95% CI)[b]	1.00 (reference)	0.90 (0.77–1.06)	0.87 (0.72–1.05)	0.62 (0.50–0.76)	1.00 (reference)	0.80 (0.67–0.95)	0.83 (0.70–0.99)	0.54 (0.43–0.69)
aHR (95% CI)[c]		1.00 (reference)	–	0.69 (0.56–0.86)		1.00 (reference)	–	0.69 (0.53–0.89)
aHR (95% CI)[d]			1.00 (reference)	0.72 (0.57–0.91)			1.00 (reference)	0.67 (0.52–0.86)
Coronary heart disease								
aHR (95% CI)[b]	1.00 (reference)	0.90 (0.71–1.16)	0.77 (0.57–1.05)	0.47 (0.33–0.67)	1.00 (reference)	0.79 (0.61–1.04)	0.70 (0.53–0.93)	0.44 (0.30–0.66)
aHR (95% CI)[c]		1.00 (reference)	–	0.53 (0.36–0.76)		1.00 (reference)	–	0.59 (0.38–0.92)
aHR (95% CI)[d]			1.00 (reference)	0.62 (0.41–0.93)			1.00 (reference)	0.65 (0.42–1.01)
Stroke								
aHR (95% CI)[b]	1.00 (reference)	0.90 (0.73–1.11)	0.94 (0.73–1.20)	0.71 (0.55–0.93)	1.00 (reference)	0.80 (0.64–1.01)	0.93 (0.75–1.15)	0.61 (0.46–0.82)
aHR (95% CI)[c]		1.00 (reference)	–	0.80 (0.61–1.05)		1.00 (reference)	–	0.74 (0.53–1.03)
aHR (95% CI)[d]			1.00 (reference)	0.79 (0.59–1.05)			1.00 (reference)	0.67 (0.50–0.92)

Adjusted hazard ratios calculated by Cox proportional hazards regression after adjustments for age, household income, smoking, alcohol intake, systolic blood pressure, fasting serum glucose, total cholesterol, cardiotoxic chemotherapy, tamoxifen, aromatase inhibitor, radiotherapy, Charlson comorbidity index, and diagnosis year

[a]The 500 MET-mins/week correspond to 152, 125, and 62.5 min per week of light-, moderate-, and vigorous-intensity physical activity, respectively

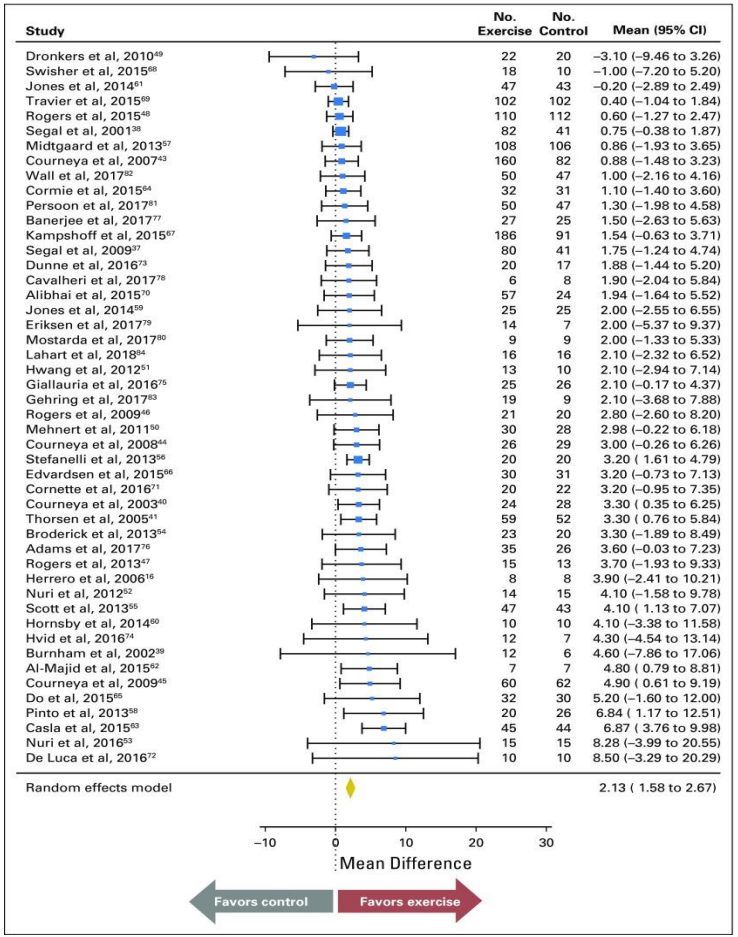
[b]Risk calculated with the overweight/obese and physically inactive group as the reference group

[c]Risk calculated with the overweight/obese and physically active group as the reference group

[d]Risk calculated with the normal weight and physically inactive group as the reference group

BMI body mass index, *PA* physical activity, *MET* metabolic equivalent of task, *aHR* adjusted hazard ratio, *CI* confidence interval

Association between physical activity and subsequent cardiovascular disease among 5-year breast cancer survivors. Kim KH. and al. Breast Cancer Res Treat. 2021 Jul;188(1):203-214.

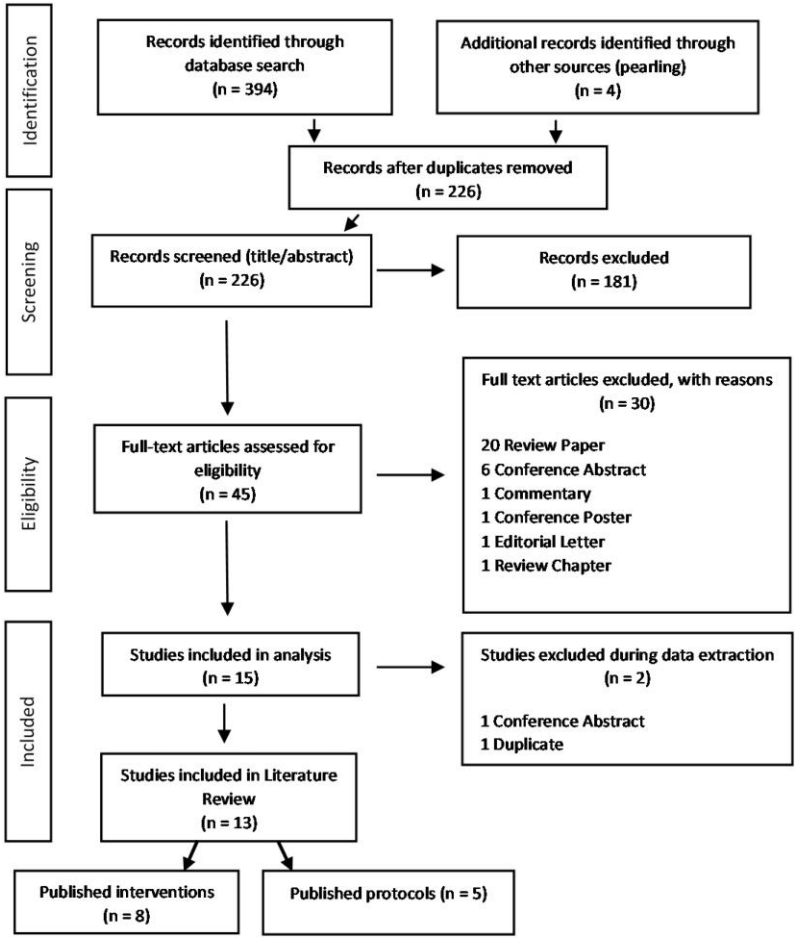


Efficacy of Exercise Therapy on Cardiorespiratory Fitness in Patients With Cancer: A Systematic Review and Meta-Analysis. Scott M. and al. J Clin Oncol. 2018 Aug 1;36(22):2297-2305.

<u>Métanalyse</u>:
Femmes
Cancer du sein précoce
Canada

***AP Pendant** la chimiothérapie*

SLG et / ou FEVG avant et après ttt



The role of exercise in the prevention of cancer therapy-related cardiac dysfunction in breast cancer patients undergoing chemotherapy: systematic review
Murray J. and al. European Journal of Preventive Cardiology (2022) 29, 463–472.

- Toutes publiées entre 2009 et 2019

- **Anthracyclines** 87,5% des études
- **Anthracyclines + trastuzumab** 12,5% des études

- **Groupe AP: Moyenne 12.7 ± 6.9 (9–31) Femmes 48.6 ± 3.7 ans**
- **Groupe contrôle: Moyenne 10.8 ± 8.5 (8–33) Femmes 50.1 ± 4.7 ans**

- En moyenne **10.1 ± 4.4 (1–16) semaines AP**
- **28.4 ± 16.5 (1–48) sessions**
- **43.4 ± 13.7 (15–60) min / session**
- Intensité déterminée par recherche pic VO_2, FCM, FC reserve

- **50% des études**: exercice aérobie, continu
- **37.5% des études**: exercice aérobie continu, IT, travail en résistance
- 12,5% des études: IT

The role of exercise in the prevention of cancer therapy-related cardiac dysfunction in breast cancer patients undergoing chemotherapy: systematic review
Murray J. and al. European Journal of Preventive Cardiology (2022) 29, 463–472

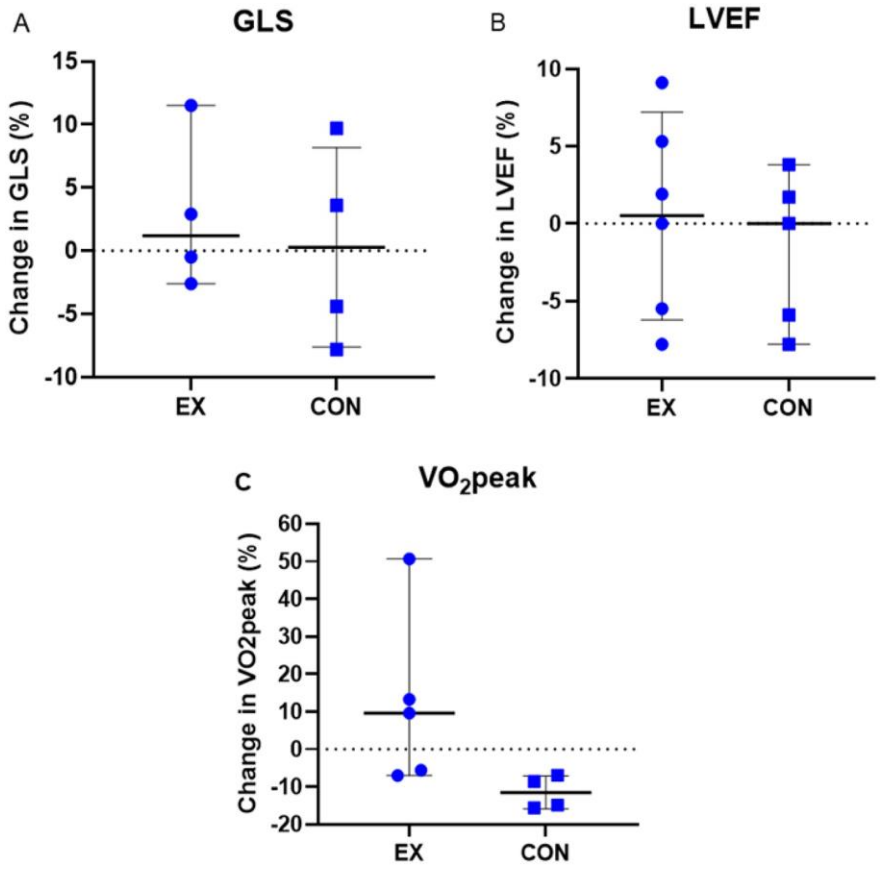


Figure 2 Relative change (from baseline) in GLS (A), LVEF (B) and VO2 peak (C) in studies reporting pre- and post-outcomes for either EX or CON groups.

The role of exercise in the prevention of cancer therapy-related cardiac dysfunction in breast cancer patients undergoing chemotherapy: systematic review
Murray J. and al. European Journal of Preventive Cardiology (2022) 29, 463–472 .

Etude rétrospective
Pays-Bas
559 patientes ayant présenté un cancer du sein entre 5 et 12 ans
Questionnaire d'AP sur les douze derniers mois
Inactive, AP minime, modérée, intense.

	Time Spent in Sports and Cycling (h/wk)			
	None	**≤3.5**	**>3.5 to ≤7.0**	**>7.0**
Sedentary	Inactive	Moderately inactive	Moderately active	Active
Standing	Moderately inactive	Moderately active	Active	Active
Manual	Moderately inactive	Active	Active	Active
Heavy manual	Active	Active	Active	Active
Unknown/missing	Inactive	Moderately inactive	Moderately active	Active

Table 1: Calculation of the Cambridge Physical Activity Index: A Cross-Tabulation of Occupational Activities With Recreational Activities

Physical Activity and Cardiac Function in Long-Term Breast Cancer Survivors: A Cross-Sectional Study. Naaktgeboren WR.and al. JACC CardioOnc.2022 Jun, 4 (2) 183–191

	Inactive (n = 28)	Moderately Inactive (n = 127)	Moderately Active (n = 154)	Active (n = 250)	Total (N = 559)
Age at diagnosis, y	46.8 (44.5-48.7)	46.4 (43.7-49.5)	46.3 (43.3-49.6)	47.1 (44.0-49.4)	46.9 (43.8-49.5)
Age at inclusion, y	55.2 (51.9-57.0)	56.0 (53.4-59.2)	55.1 (52.2-57.6)	55.4 (53.0-58.6)	55.5 (52.7-58.5)
Follow-up time, y	7.4 (6.9-11.1)	10.4 (6.8-11.6)	10.4 (6.9-11.6)	10.1 (6.7-11.6)	10.2 (6.8-11.6)
5-7 y	19 (67.9)	58 (45.7)	76 (49.4)	121 (48.4)	274 (49.0)
10-12 y	9 (32.1)	69 (54.3)	78 (50.6)	129 (51.6)	285 (51.0)
Cardiovascular risk factors[a]					
Hypertension	15 (53.6)	45 (35.4)	57 (37.5)	93 (37.2)	210 (37.7)
Hypercholesterolemia	9 (32.1)	43 (33.9)	45 (29.2)	79 (31.6)	176 (31.5)
Diabetes mellitus	4 (14.3)	8 (6.3)	9 (5.8)	17 (6.8)	38 (6.8)
Smoking					
Never	12 (42.9)	47 (37.0)	65 (42.2)	99 (39.6)	223 (39.9)
Former	10 (35.7)	55 (43.3)	65 (42.2)	123 (49.2)	253 (45.3)
Current	6 (21.4)	24 (18.9)	23 (14.9)	28 (11.2)	81 (14.5)
Unknown	0	1 (0.8)	1 (0.6)	0	2 (0.4)
Body mass index, kg/m^2	29.3 ± 6.0	26.2 ± 4.8	25.3 ± 4.1	25.7± 4	25.9± 4.4
Anthracyclines	15 (53.6)	66 (52.0)	88 (57.1)	137 (54.8)	306 (54.7)
Cumulative doxorubicin equivalent dose,[b] mg/m^2	202.5 (191-243)	240.0 (203-242)	240.0 (203-300)	240.0 (203-300)	240.0 (203-293)
Radiotherapy field					
Left sided	15 (53.6)	52 (40.9)	57 (37.0)	114 (45.6)	238 (42.6)
Right sided	9 (32.1)	61 (48.0)	79 (51.3)	107 (42.8)	256 (45.8)
IMNs	3 (10.7)	9 (7.1)	7 (4.5)	18 (7.2)	37 (6.6)
None	1 (3.6)	5 (3.9)	11 (7.1)	11 (4.4)	28 (5.0)
Trastuzumab	2 (7.1)	12 (9.4)	16 (10.4)	19 (7.6)	49 (8.8)

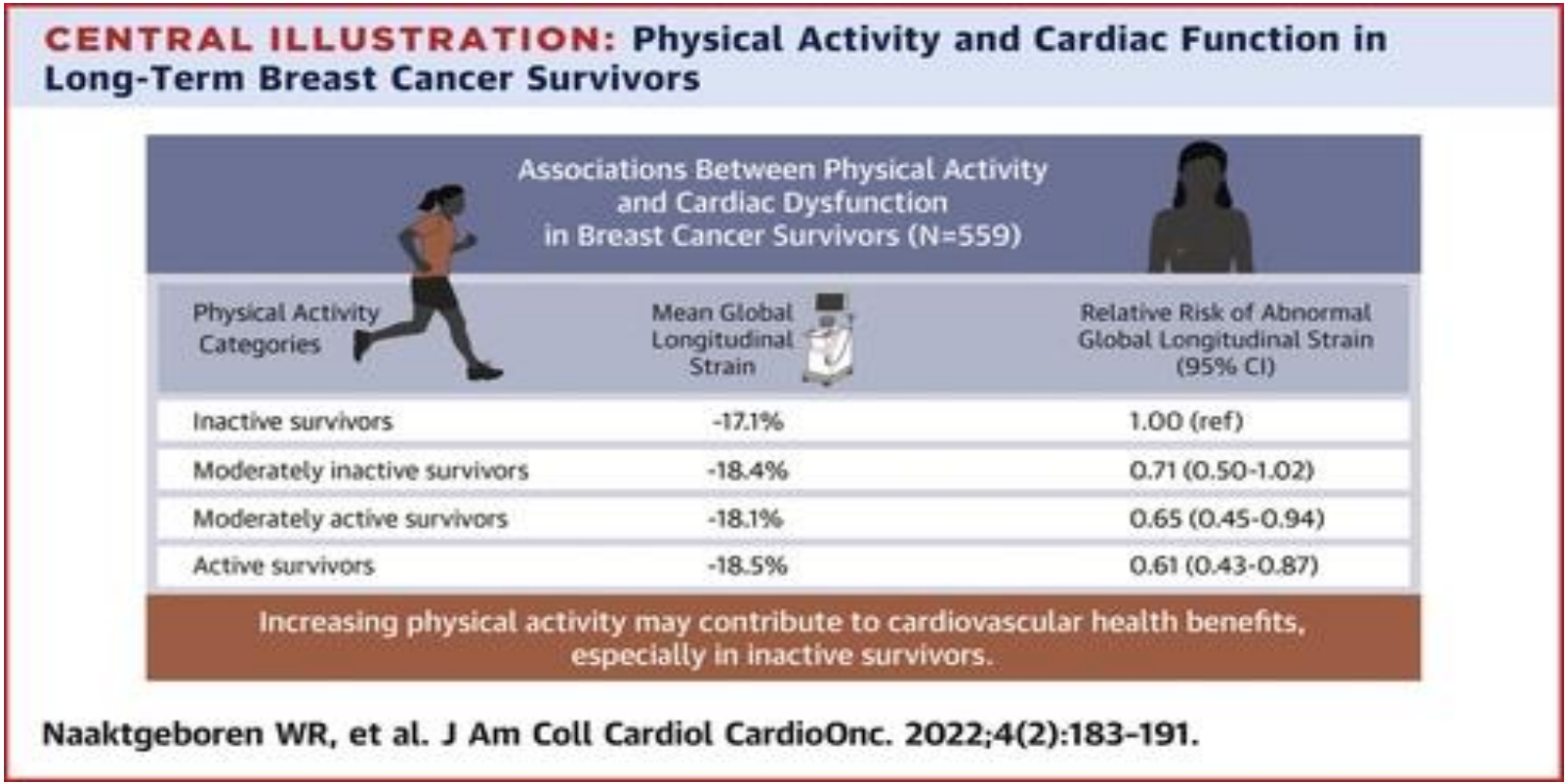
Table 2Characteristics of Participants According to Cambridge Physical Activity Index Category
Values are median (Q1-Q3), n (%), or mean ± SD.

Physical Activity and Cardiac Function in Long-Term Breast Cancer Survivors: A Cross-Sectional Study. Naaktgeboren WR.and al. JACC CardioOnc.2022 Jun, 4 (2) 183–191

	Inactive (n = 28)	Moderately Inactive (n = 127)	Moderately Active (n = 154)	Active (n = 250)
GLS (%)[a]				
Mean GLS (%)	17.1 ± 2.31	18.4 ± 3.40	18.2 ± 2.55	18.5 ± 3.14
Unadjusted Î(95% CI)	Ref	â˜’1.31 (2.59 to 0.02)[b]	1.12 (2.39 to 0.15)	1.47 (2.70 to 0.24)[b]
Partially adjusted (95% CI)[c]	Ref	1.14 (2.43 to 0.15)	0.87 (2.16 to 0.42)	â˜’1.29 (2.54 to 0.05)[b]
Fully adjusted (95% CI)[d]	Ref	1.12 (2.41 to 0.17)	â˜’0.92 (â˜’2.21 to 0.38)	1.31 (2.55 to 0.06)[b]
Abnormal GLS (>-18%)[a]				
At risk	17/26 (65.4)	54/115 (47.0)	57/130 (43.8)	87/214 (40.7)
Unadjusted RR (95% CI)	Ref	0.72 (0.51-1.01)	0.67 (0.48-0.94)[b]	0.62 (0.45-0.86)[b]
Partially adjusted RR (95% CI)[c]	Ref	0.72 (0.50-1.03)	0.68 (0.47-0.98)[b]	0.61 (0.43-0.88)[b]
Fully adjusted RR (95% CI)[d]	Ref	0.71 (0.50-1.02)	0.65 (0.45-0.94)[b]	0.61 (0.43-0.87)[b]
LVEF (%)				
Mean LVEF (%)	58.7 Â± 4.61	59.2 Â± 3.97	58.9 Â± 4.48	59.1 Â± 5.00
Unadjusted Î² (95% CI)	Ref	0.49 (1.40 to 2.38)	0.25 (1.61 to 2.11)	0.40 (1.40 to 2.21)
Partially adjusted Î² (95% CI)[c]	Ref	0.37 (1.55 to 2.28)	0.28 (1.62 to 2.18)	0.39 (1.44 to 2.23)
Fully adjusted Î² (95% CI)[d]	Ref	0.27 (1.64 to 2.18)	0.20 (1.70 to 2.09)	0.35 (1.48 to 2.18)
LVEF (<53%)				
At risk	1/27 (3.6)	5/127 (3.9)	10/163 (6.5)	18/249 (7.2)

Physical Activity and Cardiac Function in Long-Term Breast Cancer Survivors: A Cross-Sectional Study. Naaktgeboren WR.and al.

JACC CardioOnc.2022 Jun, 4 (2) 183–191



Chez les survivantes du cancer du sein à long terme des niveaux d'activité physique plus élevés ont été associés à une amélioration GLS mais pas FEVG.

Physical Activity and Cardiac Function in Long-Term Breast Cancer Survivors: A Cross-Sectional Study. Naaktgeboren WR.and al. JACC CardioOnc.2022 Jun, 4 (2) 183–191

Cancer du sein, ATC, Anti HER2 +: EMBRACE MRI 1

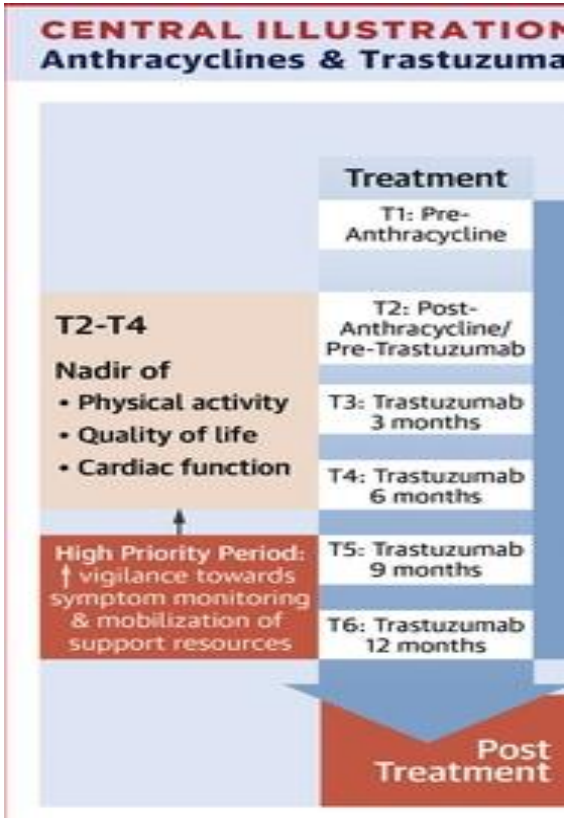
Evaluation of Myocardial Changes During Breast Adenocarcinoma Therapy to Detect Cardiotoxicity Earlier With MRI

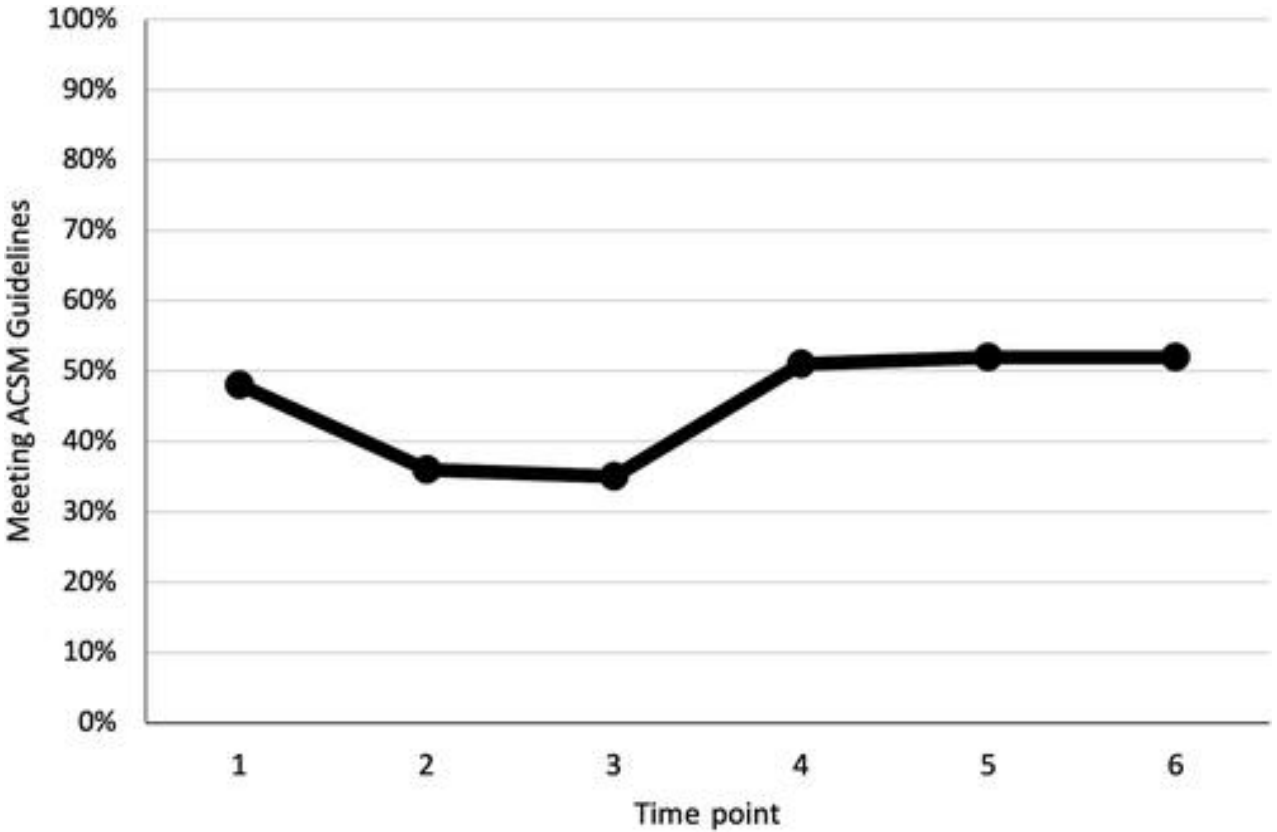
.Objectif: **Evaluer les associations d'activité physique auto-déclarée d'intensité modérée à intense (MVPA) avec des mesures simultanées, pendant le traitement du cancer patientes atteintes d'un cancer du sein HER2 +:**

- ***qualité de vie (MLHFQ** Minnesota Living With Heart Failure Questionnaire scores**, EQ5D),***
- ***fonction cardiaque (SLG, FEVG),***
- ***aptitude cardiorespiratoire post-traitement .***

- 90 min AP / semaine= Active patient
- ***88 patientes***
- ***51,4 ans +/-8,9ans moyenne âge***

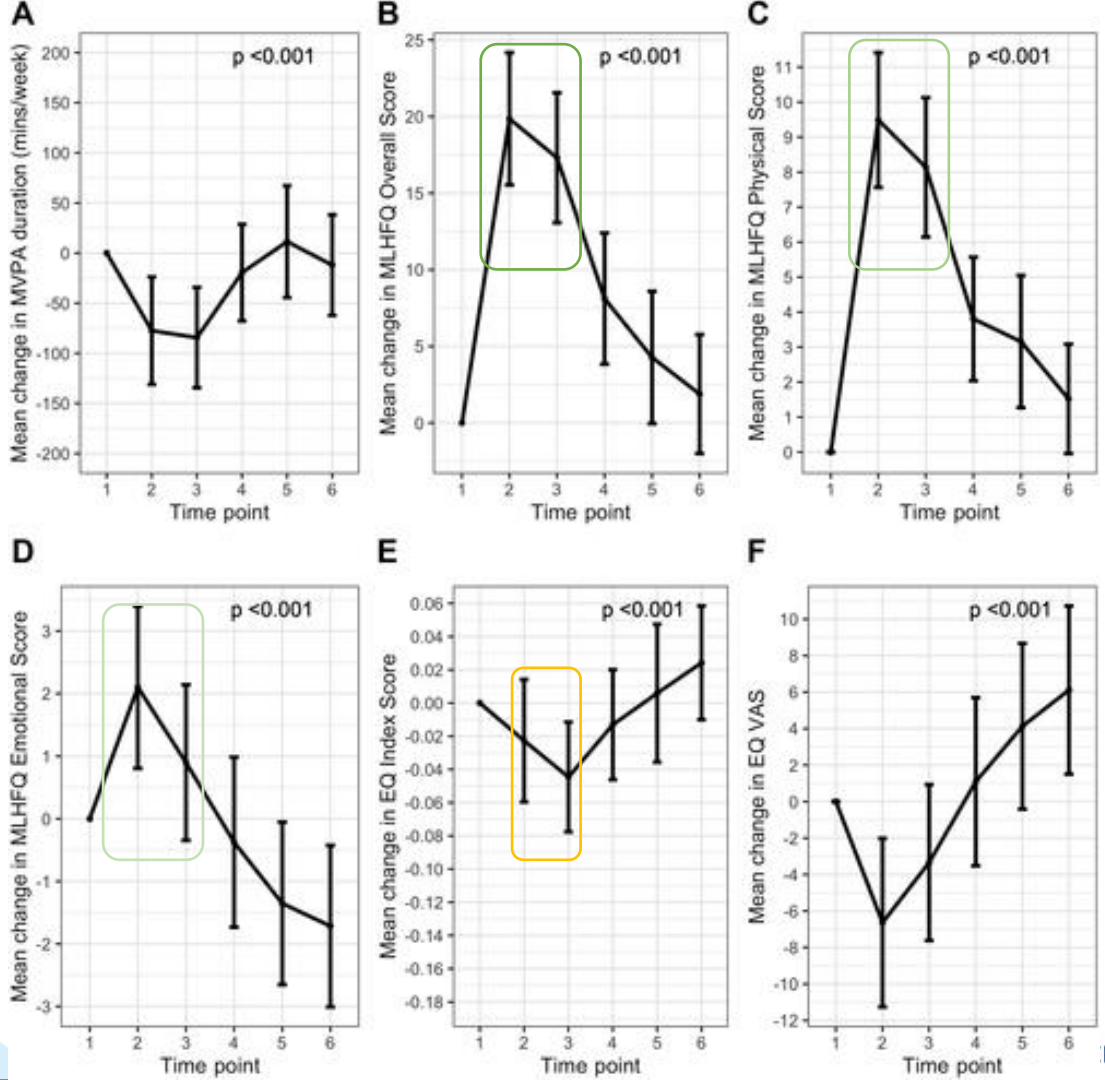
Self-Reported Physical Activity, QoL, Cardiac Function, and Cardiorespiratory Fitness in Women With HER2+ Breast Cancer. Peck S. and al. JACC CardioOncol. 2022 Sept; 4(3): 387–400.





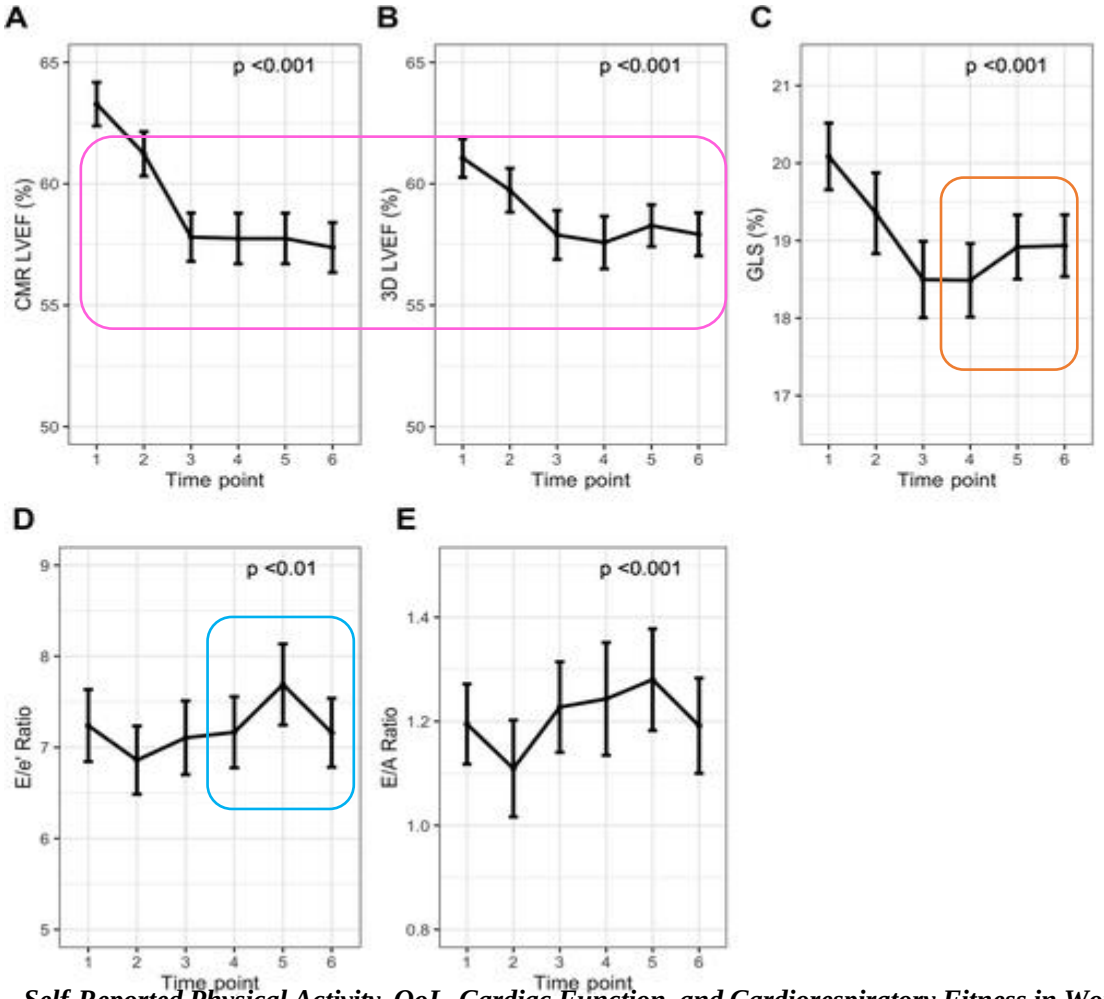
Proportion of Active Participants at Each Time Point During Treatment: Active participants engaged in ≥90 minutes of moderate to vigorous physical activity.
The proportion meeting this target was the lowest at time points 2 and 3. ACSM = American College of Sports Medicine.

Peck S. and al. JACC CardioOncol. 2022 Sept; 4(3): 387–400.



Mean Changes From Baseline for MVPA and QoL

Largest changes in **(A)** MVPA and **(B to F)** QoL measures occurred at time points 2 and 3.



CMR LVEF and Echocardiographic Measures During Treatment.

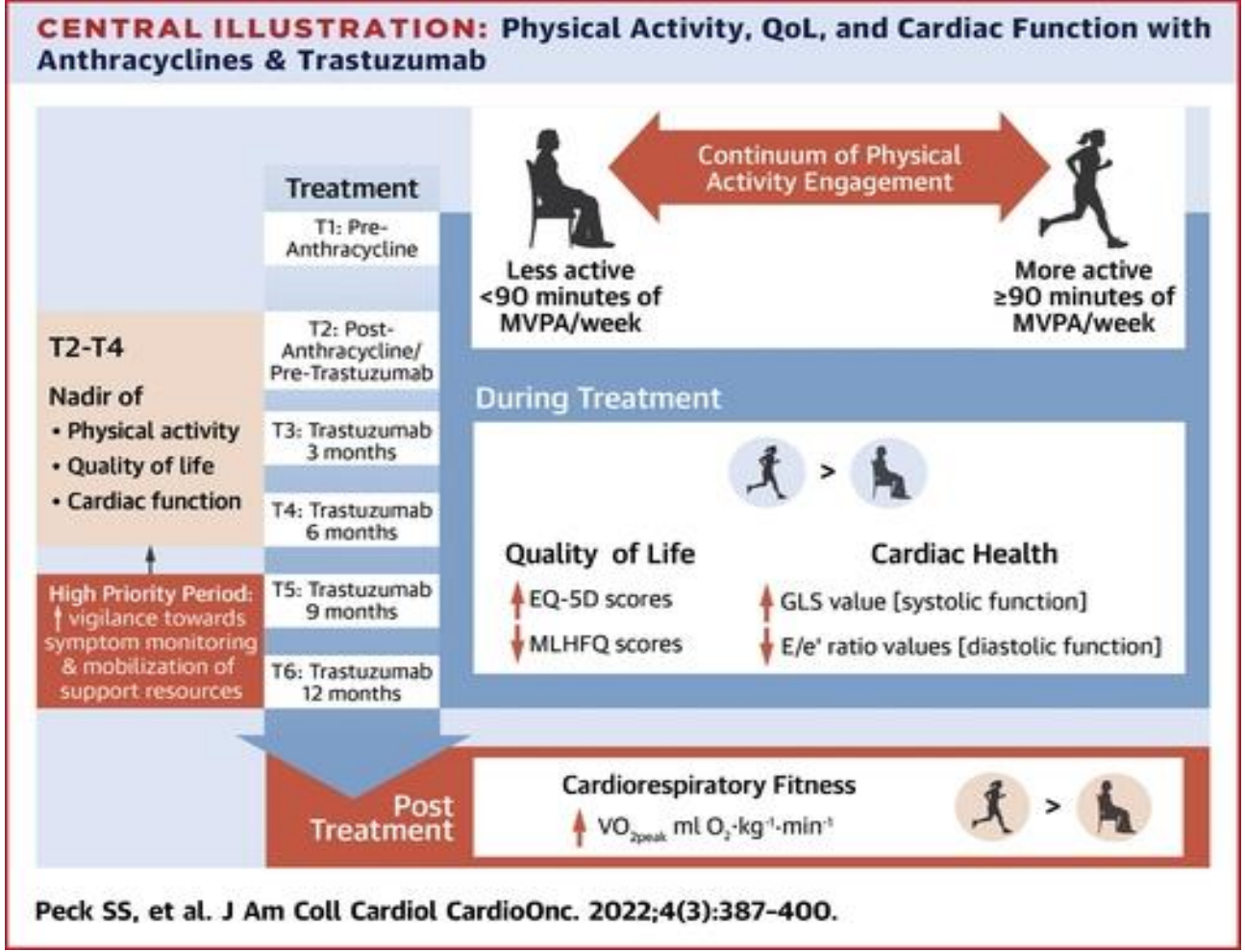
Augmentation du SLG de 0,04% (30 min MVPA) a la fin ttt

Self-Reported Physical Activity, QoL, Cardiac Function, and Cardiorespiratory Fitness in Women With HER2+ Breast Cancer. Peck S. and al. JACC CardioOncol. 2022 Sept; 4(3): 387–400.

Association Between Overall Physical Activity Status During Cancer Treatment and Post-Treatment Cardiorespiratory Fitness

Overall PA Status	n	Active at Baseline[a]	Active ≥1 Visit Between Time Points 2 and 4[b]	Mean Vo_{2peak} (mLO_2/kg/min)	Univariable Association, Coefficient (95% CI)	*P* Value	Multivariable Association, Coefficient [95% CI][c]	*P* Value
Inactive	27	6 (22%)	3 (11%)	16.2	—	—	—	—
Somewhat active	35	22 (63%)	31 (89%)	19.1	2.82 (0.72 to 4.92)	0.009	2.66 (0.69 to 4.63)	0.009
Highly active	26	26 (100%)	26 (100%)	23.6	7.39 (5.14 to 9.64)	<0.001	5.74 (3.51 to 7.96)	<0.001

Self-Reported Physical Activity, QoL, Cardiac Function, and Cardiorespiratory Fitness in Women With HER2+ Breast Cancer. Peck S. and al. JACC CardioOncol. 2022 Sept; 4(3): 387–400.



Self-Reported Physical Activity, QoL, Cardiac Function, and Cardiorespiratory Fitness in Women With HER2+ Breast Cancer. Peck S. and al. JACC CardioOncol. 2022 Sept; 4(3): 387–400.

Quand pratiquer une activité physique pour un patient atteint de cancer en cours de traitement pour améliorer sa cap. Cardio-respiratoire ?

Pendant? Ou après ? Ou Pendant et après ?

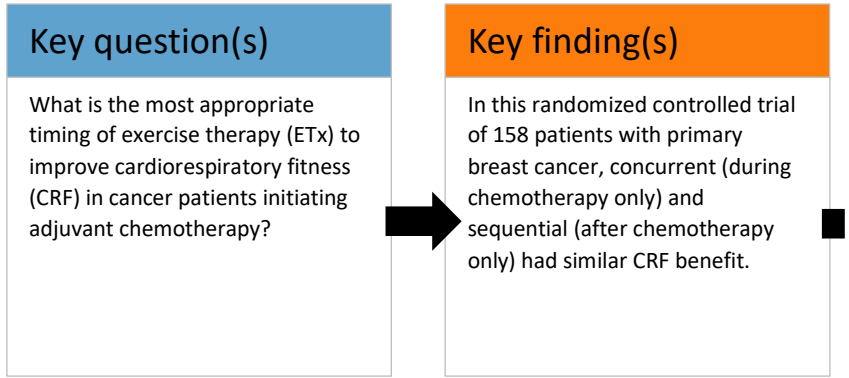
Etude randomisée

158 patientes inactives

Cancer du sein

Chimiothérapie adjuvante ou néo-adjuvante

- *Usual care*
- *Concurrent (pendant la chimiothérapie uniquement)*
- *Sequential (après chimiotherapie)*
- *Concurrent and sequential ? (continu, pendant et après la chimiothérapie)*



Timing of Exercise Therapy in Patients Initiating Adjuvant Chemotherapy for Breast Cancer. Scott Jkines and al. On published.

Activité physique :

- *Tapis roulant 3 fois par semaine*
- *20/50 minutes à 55/100% du pic VO2*
- ***16 semaines pendant ou après la chimiothérapie (sequential and concurrent)***
- ***32 semaines pendant et après traitement (continuous)***

- *Objectif primaire:*
- *évaluation du pic de VO2*
- *pré traitement (T0)*
- *Immédiatement après chimiothérapie (T1)*
- *16 semaines après chimiothérapie T2 puis 32 semaines*

Timing of Exercise Therapy in Patients Initiating Adjuvant Chemotherapy for Breast Cancer. Scott Jkines and al. On published.

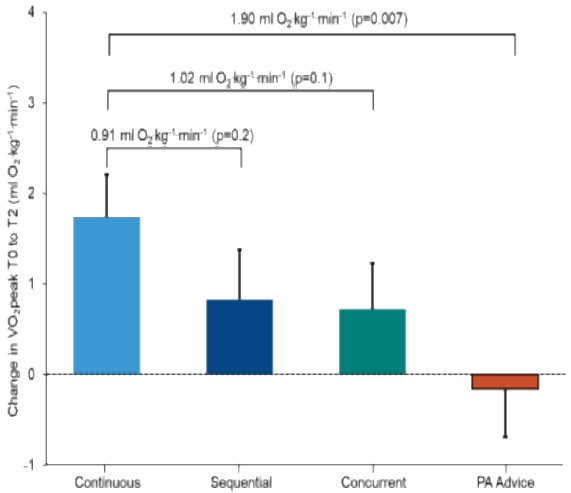
Usual Care vs. During, After, and Continuous Exercise in Newly Diagnosed Breast Cancer Patients

- n=158 breast cancer patients receiving chemotherapy

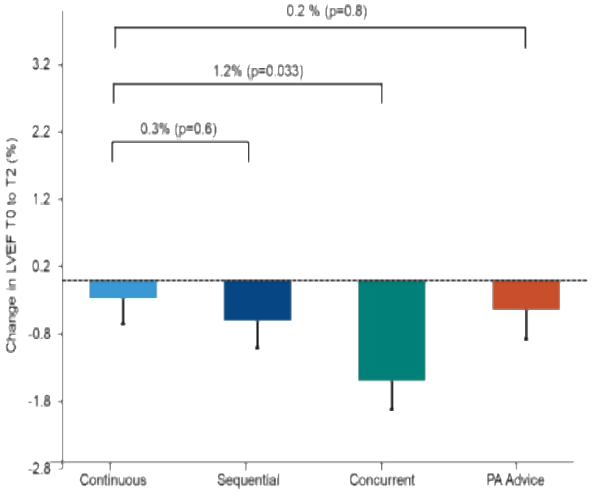
Randomized to ~32 weeks of:

- PHYSICAL ACTIVITY ADVICE
- CONCURRENT EXERCISE
- SEQUENTIAL EXERCISE
- CONTINUOUS EXERCISE

Primary Endpoint: VO_2peak

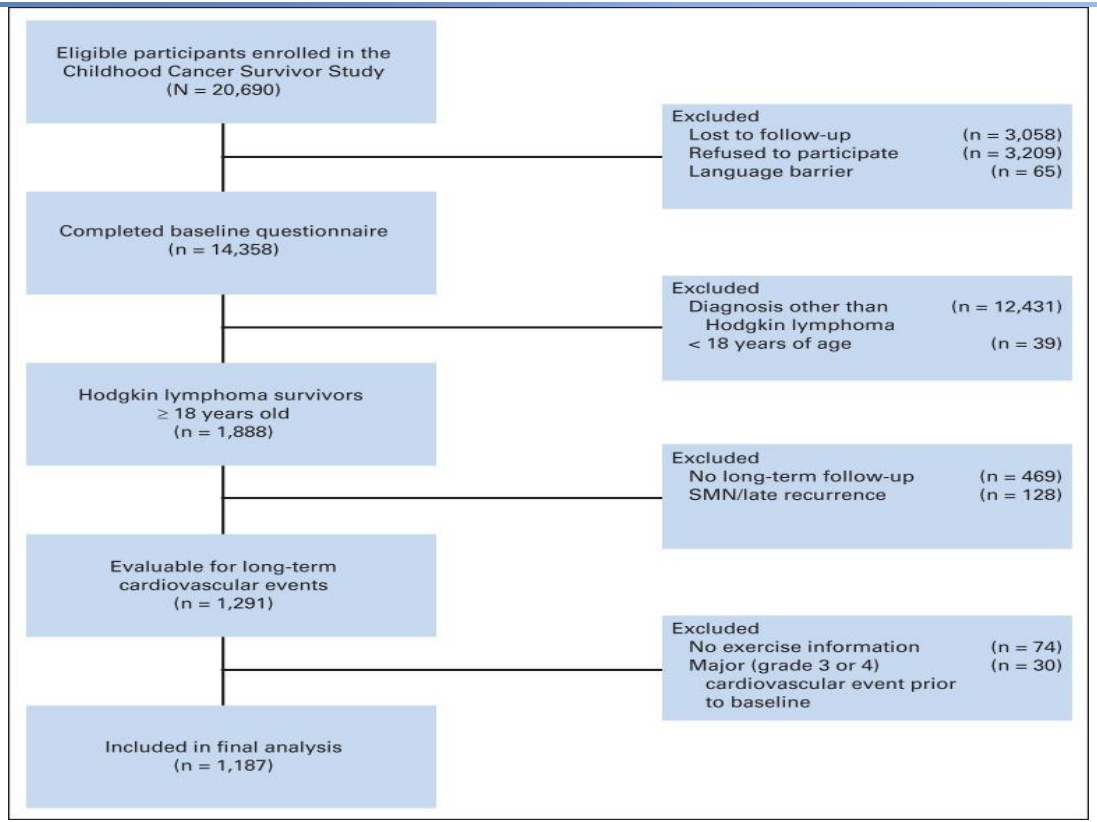


Secondary Endpoint: LVEF



Timing of Exercise Therapy in Patients Initiating Adjuvant Chemotherapy for Breast Cancer. Scott Jkines and al. On published.

Activité physique et hématologie



Exercise and Risk of Major Cardiovascular Events in Adult Survivors of Childhood Hodgkin Lymphoma: A Report From the Childhood Cancer Survivor Study. Jones L. and al. J Clin Oncol. 2014 Nov 10;32(32):3643-50.

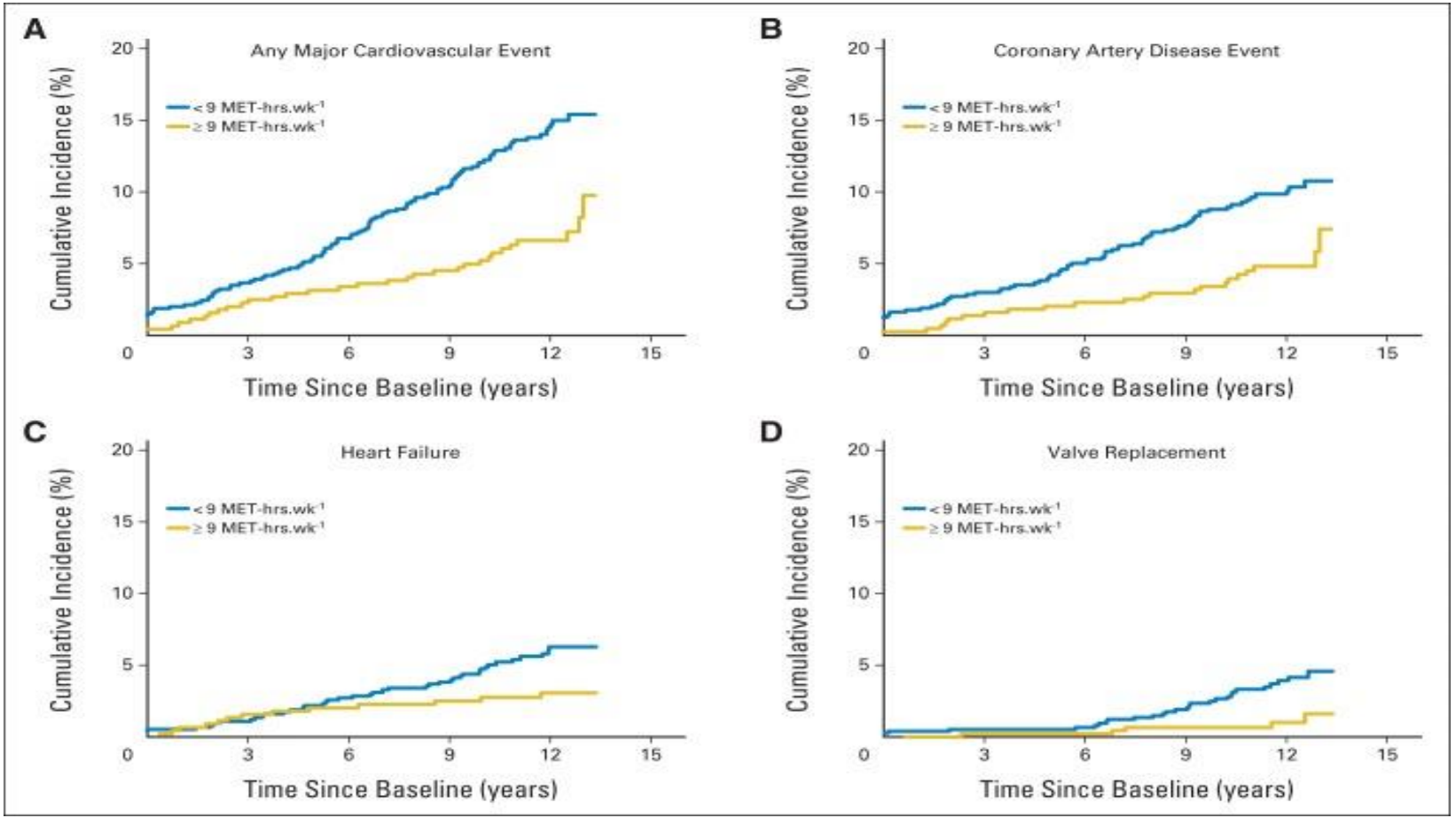
- *Suivi médian:*
- *11,9 ans (1,7 à 14,3ans)*

Table 1. Demographic and Treatment Characteristics of the Participants

Characteristic	All Patients		MET · hours/week^{-1} 0		3 to 6		9 to 12		15 to 21		P
	No.	%	No.	%	No.	%	No.	%	No.	%	
Participants	1,187	100	426	35.9	317	26.7	269	22.7	175	14.7	
Age at interview, years											
Mean	41.9		42.7		41.6		41.5		41.0		.008
Range	21.9-57.9		23.5 - 57.7		24.7 - 57.9		21.9 - 55.5		24.9 - 56.5		
Age at diagnosis, years											
Mean	14.4		14.7		14.3		14.1		13.8		.06
Range	2.4-21.0		2.5 - 21.0		2.7 - 21.0		2.4 - 20.9		3.7 - 20.9		
Interval between diagnosis and study entry, years											
Mean	16.7		17.6		16.8		16.5		16.5		.014
Range	8.2-28.7		8.2 - 27.8		8.2 - 28.5		8.3 - 28.7		8.2 - 28.6		
Male	632	53.2	209	49.1	162	51.1	142	52.8	119	68.0	< .001
Race											.47
Non-Hispanic white	1,080	91.0	387	90.8	288	90.9	250	92.9	155	88.6	
Other group	107	9.0	39	9.2	29	9.1	19	7.1	20	11.4	
BMI, kg/m^2											
Mean	26.1		26.3		26.3		26.0		25.7		.61
Range	12.8 - 65.8		14.6 - 47.9		12.8 - 63.2		15.6 - 65.8		15.4 - 46.1		
Smoking											.046
Current	179	15.1	79	18.5	50	15.8	27	10.0	23	13.1	
Former	325	27.4	113	26.5	76	24.0	82	30.5	54	30.9	
Never	683	57.5	234	54.9	191	60.3	160	59.5	98	52.0	
Cancer treatment											
Chemotherapy											
Any chemotherapy	674	63.0	241	63.6	174	60.0	163	64.4	96	64.9	.73
Alkylating agent	637	59.8	229	60.7	162	55.9	156	61.9	90	61.2	.46
Anthracycline	213	20.0	75	19.9	52	17.9	55	21.8	31	21.1	.70
Anthracycline dose, mg/m^2											.95
None	302	81.2	238	82.6	197	79.1	116	81.1	853	81.1	
< 250 mg/m^2	41	11.0	27	9.4	28	11.2	16	11.2	112	10.6	
≥ 250 mg/m^2	29	7.8	23	8.0	24	9.6	11	7.7	87	8.3	
Radiation therapy											
Any radiation therapy	1,026	91.4	361	89.8	280	92.1	237	91.2	148	94.3	.37
Chest	908	85.7	324	85.3	254	88.5	198	80.8	132	89.2	.044
Chest RT dose											
None	152	14.4	56	14.7	33	11.5	47	19.3	16	10.9	.054
< 20 Gy	22	2.1	11	2.9	4	1.4	5	2.0	2	1.4	
20-< 30 Gy	188	17.8	57	15.0	51	17.8	44	18.0	36	24.5	
30-< 40 Gy	350	33.1	137	36.1	98	34.1	62	25.4	53	36.1	
40-< 50 Gy	320	30.2	110	28.9	93	32.4	78	32.0	39	26.5	
≥ 50 Gy	26	2.5	9	2.4	8	2.8	8	3.3	1	0.7	
Abdominal or pelvic	620	58.5	214	56.5	169	58.9	148	60.4	89	60.1	.75
CV risk factors											
Diabetes mellitus	52	4.4	20	4.7	20	6.3	8	3.0	4	2.3	.11
Hypertension	294	24.8	120	28.2	87	27.4	57	21.2	30	17.1	.011
Dyslipidemia	224	18.9	96	22.5	62	19.6	48	17.8	18	10.3	.006
Obesity	231	19.6	85	20.1	69	21.8	46	17.4	31	17.7	.52
Any of the above 4 factors	517	43.6	195	45.8	151	47.6	111	41.3	60	34.3	.021

Abbreviations: BMI, body mass index; CV, cardiovascular; MET, metabolic equivalent.

Exercise and Risk of Major Cardiovascular Events in Adult Survivors of Childhood Hodgkin Lymphoma: A Report From the Childhood Cancer Survivor Study. Jones L. and al. J Clin Oncol. 2014 Nov 10;32(32):3643-50.



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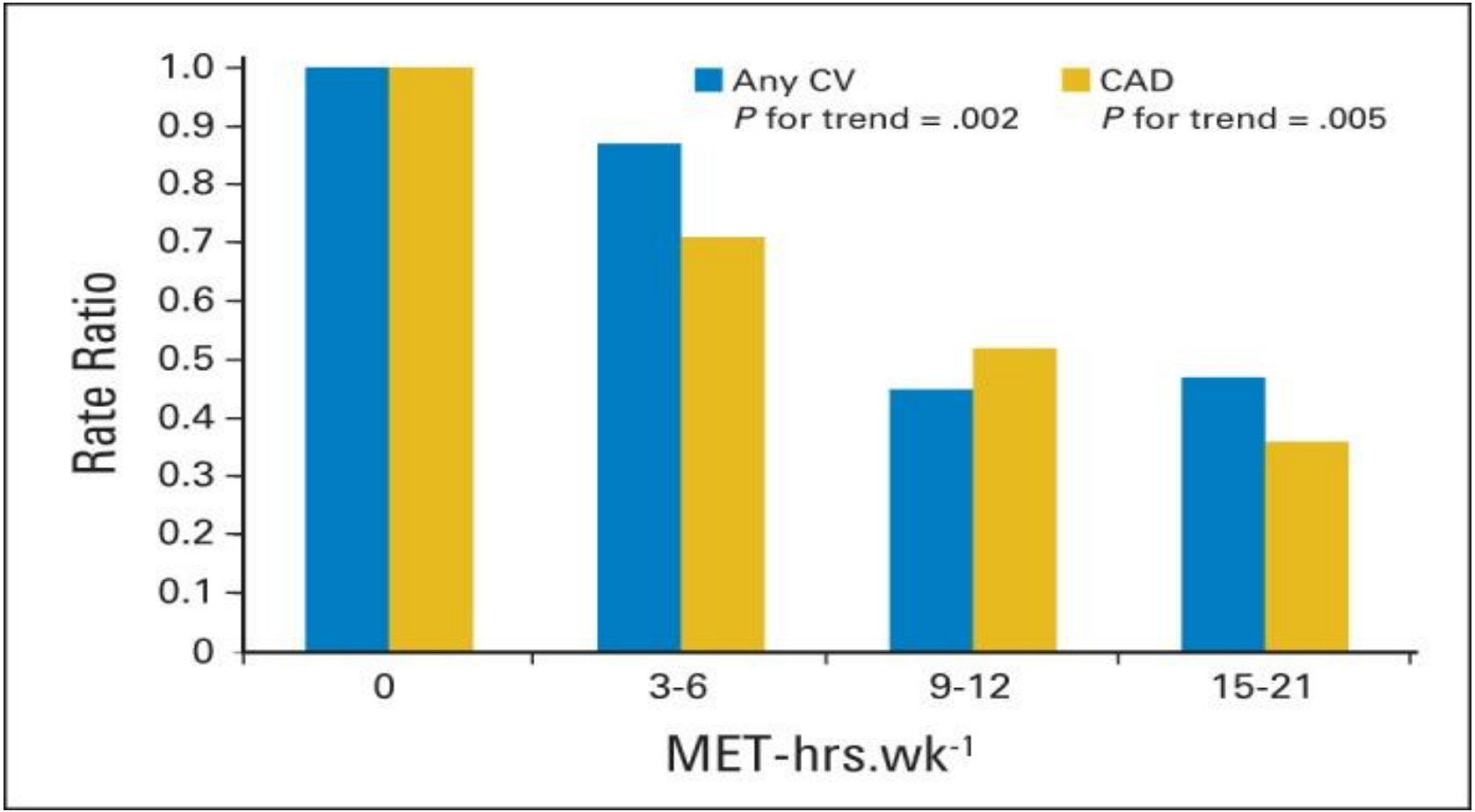

Exercise and Risk of Major Cardiovascular Events in Adult Survivors of Childhood Hodgkin Lymphoma: A Report From the Childhood Cancer Survivor Study. Jones L. and al. J Clin Oncol. 2014 Nov 10;32(32):3643-50.

Table 3. RRs of Major (grade 3 to 5) CV Events According to Meeting National Guidelines for Vigorous-Intensity Exercise (ie, < 9 *v* ≥ 9 MET hours/week^{-1})*

	MET hours/week^{-1}						
	< 9 (n = 743)			≥ 9 (n = 444)			
CV Event	No.	RR	95% CI	No.	RR	95% CI	*P*
Any major CV event	104	ref	ref	31	0.49	0.31 to 0.76	.002
Coronary artery disease	73	ref	ref	23	0.53	0.32 to 0.89	.01
Heart failure	41	ref	ref	12	0.63	0.33 to 1.23	.18
Valve replacement	28	ref	ref	5	0.36	0.14 to 0.95	.04
Serious arrhythmias†	13	ref	ref	4	—	—	—

Abbreviations: CV, cardiovascular; MET, metabolic equivalent; ref, referent; RR, rate ratio.

*Adjusted for attained age, age at diagnosis, sex, race, smoking status, education, and CV disease risk factor profile as time-dependent variables, anthracycline exposure, chest radiation exposure, and baseline (grade 3 or 4) chronic (non-CV) conditions.

†Result from multivariable analysis was not available as a result of the small No. of events.

AP « vigoureuse » associée risque plus faible de pathologie CV indépendamment du profil risque CV et du traitement

Exercise and Risk of Major Cardiovascular Events in Adult Survivors of Childhood Hodgkin Lymphoma: A Report From the Childhood Cancer Survivor Study. Jones L. and al. J Clin Oncol. 2014 Nov 10;32(32):3643-50.

Author	N	Cohort/Design/Setting	Exercise	Outcomes
Battaglini et al. (2009)[156]	10	Acute leukemia/intervention during treatment	30min/d; 3d/wk; 40–50% estimated HRR; 3–5 weeks	Total minutes on bicycle ergometer at 60% HRR: ↑ 88% Body weight: ↓ 4%
Coleman et al. (2003)[157]	14	Multiple myeloma/RCT during treatment	60min/d; 3d/wk; 12–15 Borg scale; 22 wks	6-Minute Walk Test: ↓ 2% in AT; ↓ 2% in control
Coleman et al. (2008)[135]	60	Multiple myeloma/RCT during treatment	20min/d; 3d/wk; 11–13 Borg scale; 15 wks	Hemoglobin: ↓ 7% in AT; ↓ 10% in control
Coleman et al. (2012)[158]	95	Multiple myeloma/RCT during treatment	30min/d; 5d/wk; 11–13 Borg scale; 15 wks	Hemoglobin: ↓ 6% in AT; ↓ 5% in control
Courneya et al. (2009)[159]	60	Lymphoma/RCT during treatment	15–45min/d; 3d/wk; 60–75% peak power output; 12 wks	Body weight: ↓ 0.4% in AT; ↓ 0.6% in control
Courneya et al. (2009)[134]	60	Lymphoma/RCT during treatment	15–45min/d; 3d/wk; 60–75% peak power output; 12 wks	Measured VO_{2peak}: ↑ 19% in AT; ↓ 1% in control
Groeneveldt et al. (2013)[160]	28	Multiple myeloma/Intervention post treatment	15–30min/d; 3d/wk; 50–60% HRR; 24 wks	Measured VO_{2peak}: ↑ 1%
Jarden et al. (2009)[161]	21	Allogeneic HCT/ RCT during treatment	15–30min/d; 5d/wk; 45–75% estimated max HR; 4–6 wks	Estimated VO_{2peak}: ↑ 0.01% in AT; ↓ 28% in control
Oechsle et al. (2014)[162]	24	Myeloablative chemotherapy/ RCT during treatment	10–40min/d; 5d/wk; intensity NR; 4 wks	Estimated VO_{2peak}: ↑ 11% in AT; ↓ 26% in control
Shelton et al. (2009)[163]	30	Allogeneic HCT/ RCT post treatment	20–30min/d; 3d/wk; 60–75% estimated max HR; 4 wks	6-Minute Walk Test: ↑ 12% in AT; ↑ 10% in control
Streckmann et al. (2014)[164]	28	Lymphoma/RCT during treatment	60min/d; 2d/wk; 60–80% estimated max HR; 36 wks	Incremental step test: ↑ in AT; ↓ in control (values NR)

Table 3: Summary of Exercise Interventions Aimed at Attenuating HCT-Induced CVD. Abbreviations: HCT, hematopoietic cell transplantation; HRR, heart rate reserve; RCT, randomized controlled trial; AT; aerobic training; HR; heart rate; NR, not reported.

Cardiovascular disease following hematopoietic stem cell transplantation: Pathogenesis, detection, and the cardioprotective role of aerobic training. Scott JM and al. Critical Reviews in Oncology/Hematology Vol 98., Feb. 2016, 222-234.

Take home message

- **Cancer** en cardiologie = **l'affaire de tous** !
- Prise en charge globale dès la consultation pré-thérapeutique
- Facteurs de risque « dits » cardio-vasculaires: sans culpabiliser mais en éduquant !
- Préconiser **Activité physique**
  - **dès l'annonce diagnostique jusqu'en post-thérapeutique**
  - *Aérobie + Résistance*
- Bénéfices CV**:**
  - **Amélioration du pic de VO2, diminue le déconditionnement, la toxicité cardiaque des traitements, les MCV, et la mortalité CV.**
  - A démontrer sur la FEVG et le SLG.
  - Penser EE + VO2
- Bénéfices Qol : fatigue cancéro-induite, anxio-dépression, mortalité toute cause, mortalité par cancer, risque de récidive.

Merci de votre attention

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Discussion: quelle prise pour les patients atteints de cancer avec ou sans cardiopathie?

Dr Laura SERRANO
Clinique SMR Cardio-vasculaire
Cardiocéan
La Rochelle

Circulation

AHA SCIENTIFIC STATEMENT

Cardio-Oncology Rehabilitation to Manage Cardiovascular Outcomes in Cancer Patients and Survivors

A Scientic Statement From the American Heart Association

Endorsed by the American Cancer Society

Circulation. 2019;139:e997–e1012. DOI: 10.1161/ May 21, 2019

Multiple-hit

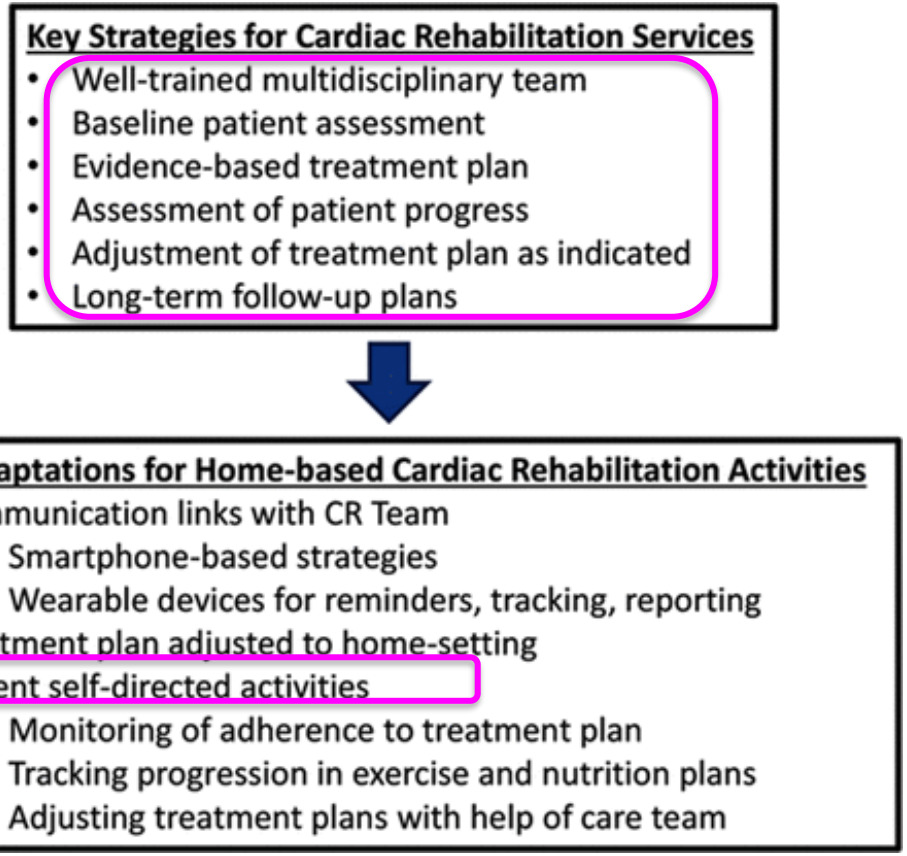
Baseline risk factors
Obesity, hypertension, age

'Direct' injury
Anticancer therapy

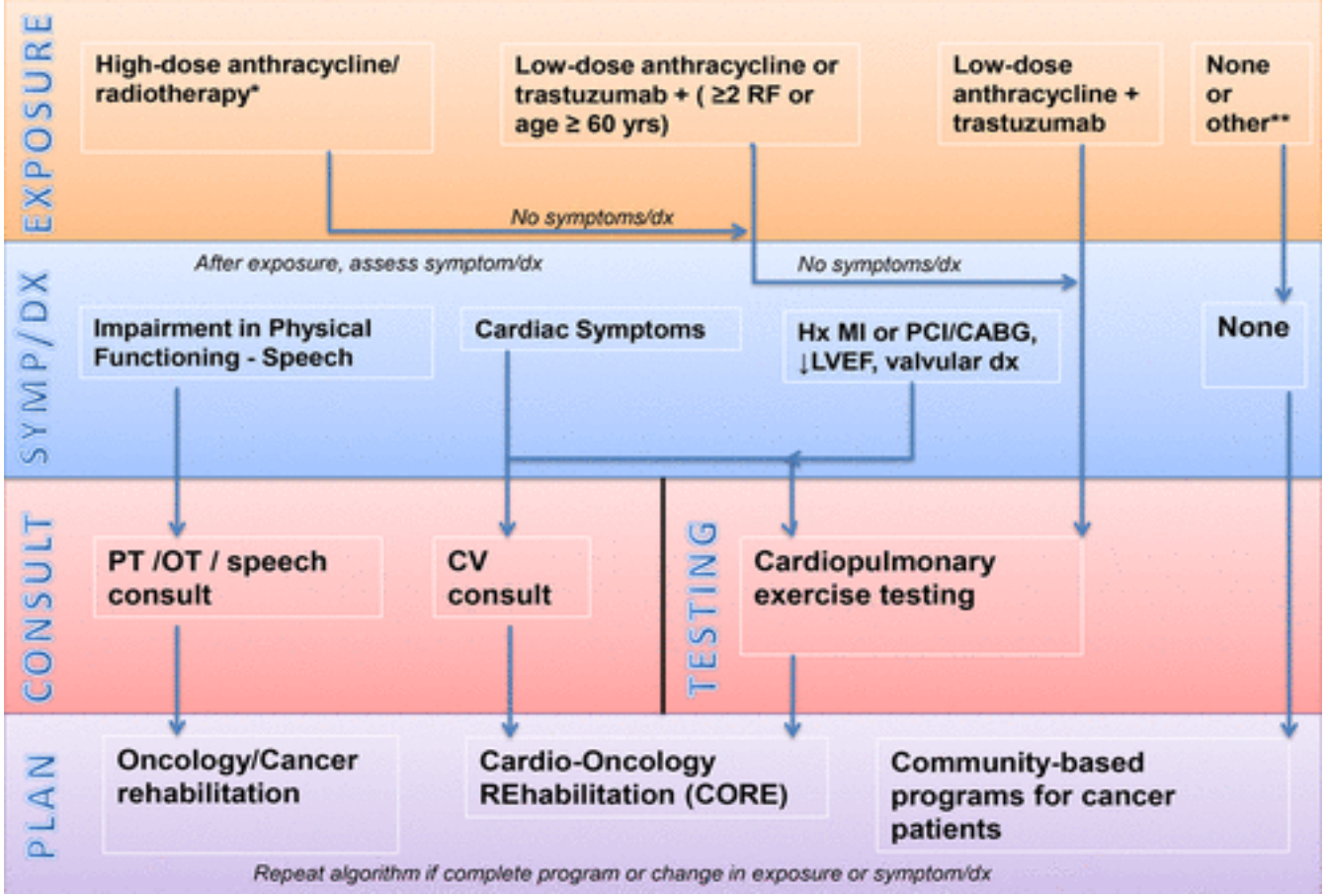
'Indirect' injury
Secondary to therapy
(deconditioning, weight gain)

Exercise to prevent / treat multiple-hit

- Cardiorespiratory fitness ↑
- QOL ↑
- Fatigue ↓
- CV risk factors ↓



Susan C. Gilchrist. Circulation. Cardio-Oncology Rehabilitation to Manage Cardiovascular Outcomes in Cancer Patients and Survivors: A Scientific Statement From the American Heart Association, Volume: 139, Issue: 21, Pages: e997-e1012,

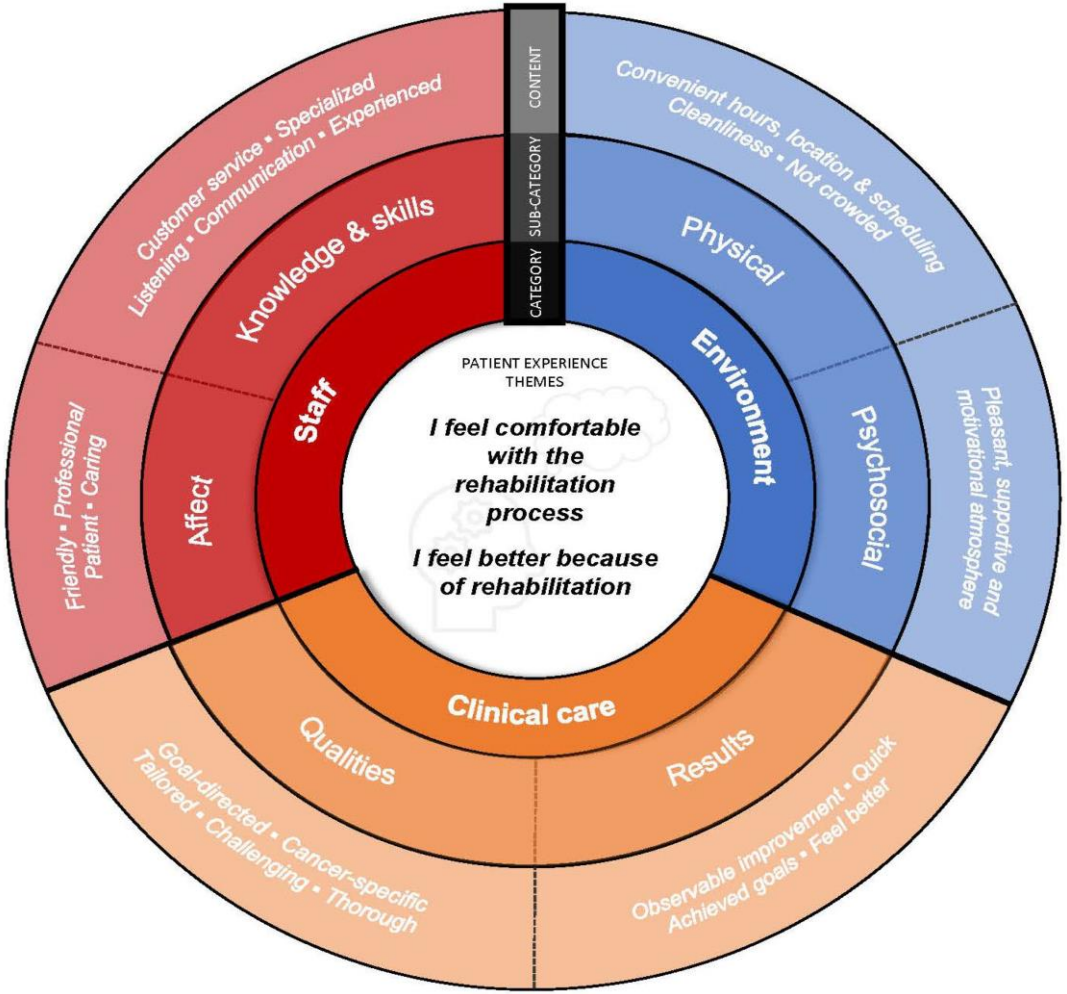


Susan C. Gilchrist. Circulation. Cardio-Oncology Rehabilitation to Manage Cardiovascular Outcomes in Cancer Patients and Survivors: A Scientific Statement From the American Heart Association, Volume: 139, Issue: 21, Pages: e997-e1012,

Cardiac Rehabilitation	Cardio-Oncology Rehabilitation
Exercise training	Same
Physical activity counseling	Same
Nutrition counseling	Same
Psychosocial management	Same
Weight management	Same
Coronary Risk Factor management: hypertension and dyslipidemia Diabetes Smoking cessation	Useful before mandatory after oncology therapy
Some of these issue also in advanced Heart Failure	Effects after oncology therapy: fatigue, surgical and radiation related impairment, pain syndromes, deconditioning/weakness/balance issues

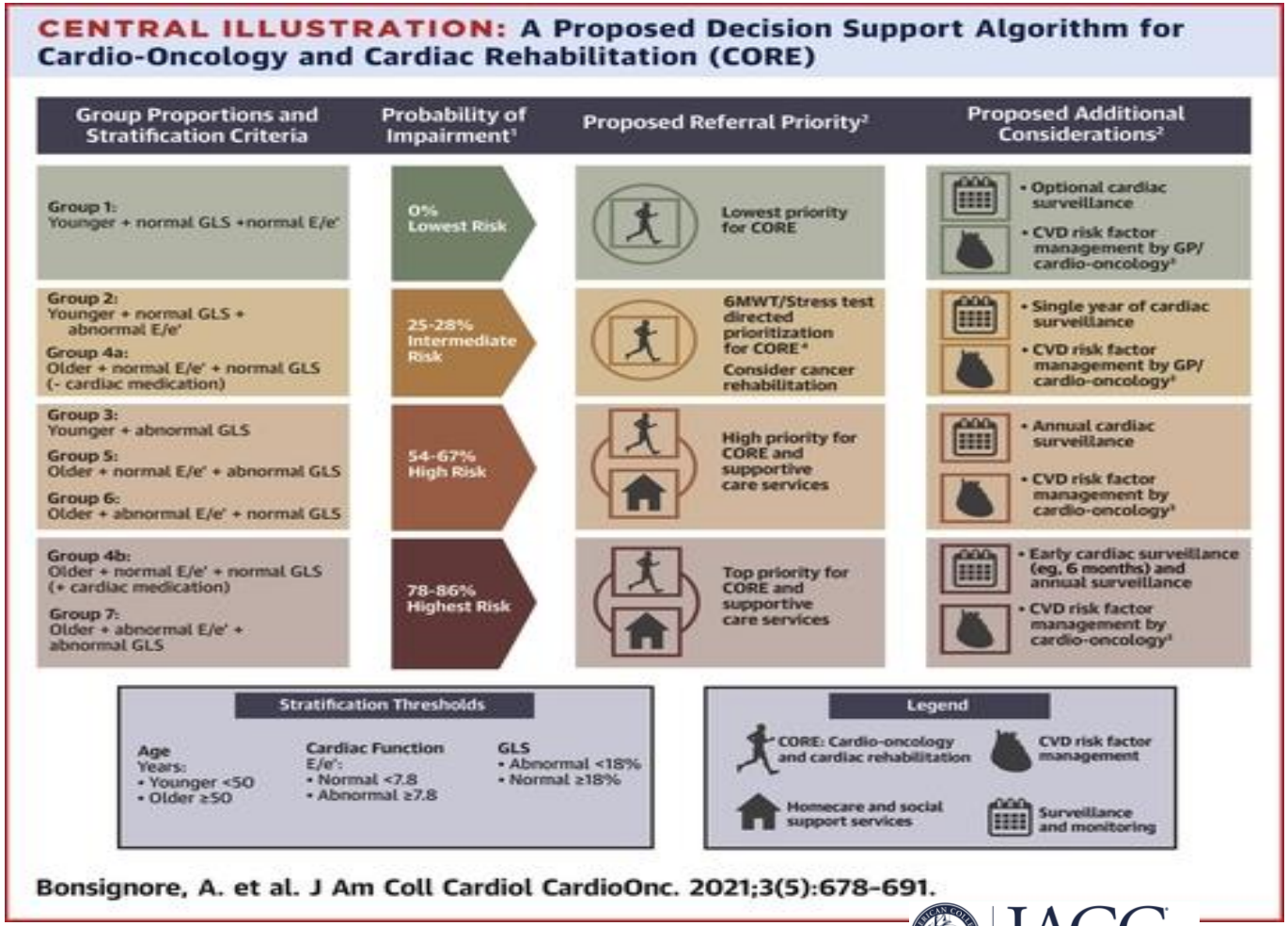
Une relation sous-estimée!

Oncology and Cardiac Rehabilitation: An Underrated Relationship. Venturini E. and Al. J. Clin. Med. 2020, 9(6), 1810.

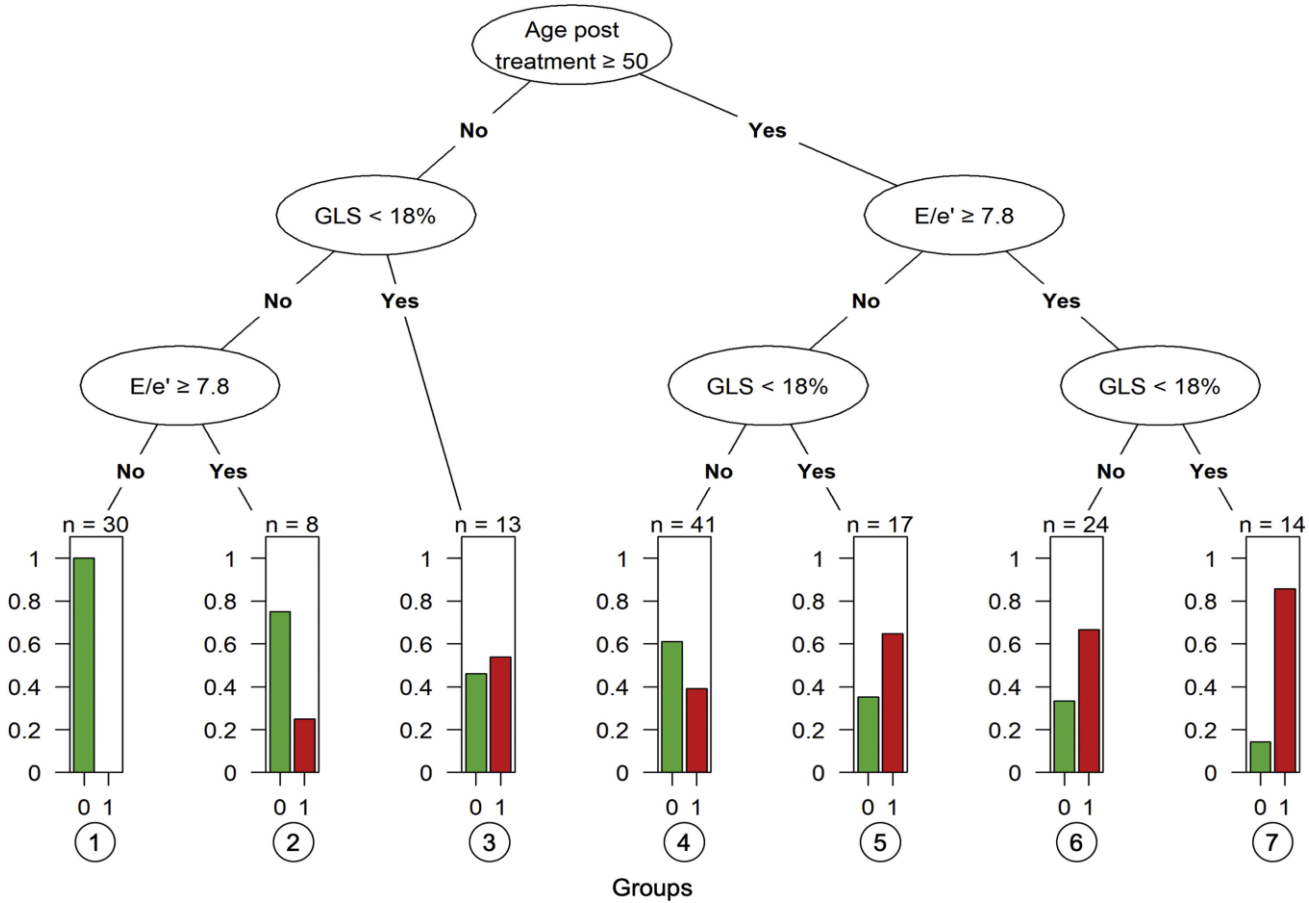


Understanding Patient Experience with Outpatient Cancer Rehabilitation Care. Wood KC. Healthcare 2023, 11(3), 348.

147 patientes rando consécutivement
AC + tzt



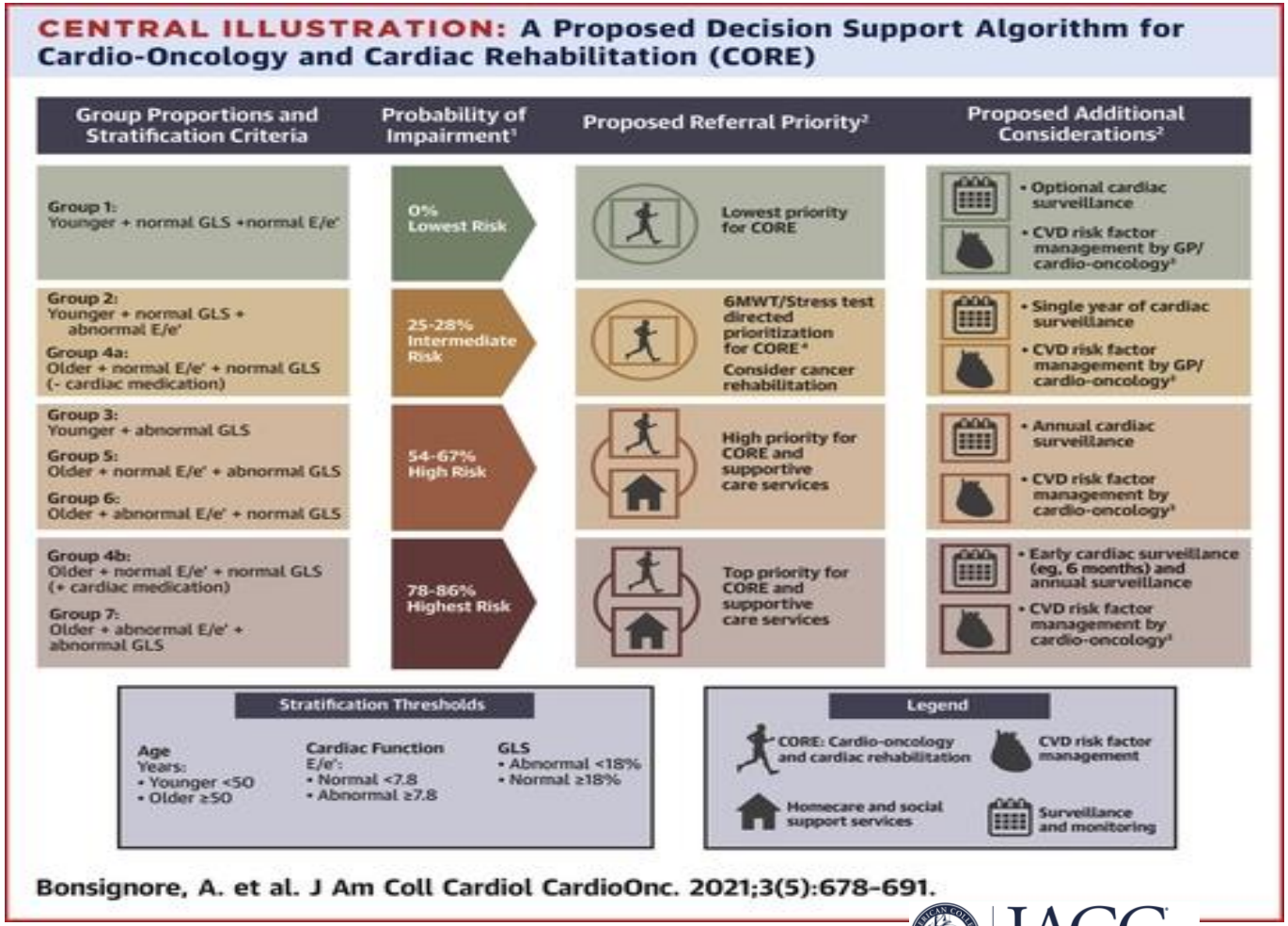
Alis Bonsignore et al. J Am Coll Cardiol CardioOnc 2021; 3:678-691.



Tree Diagram for Detection of Compromised Functional Independence

Alis Bonsignore et al. J Am Coll Cardiol CardioOnc 2021; 3:678-691.

147 patientes rando consécutivement
AC + tzt



Alis Bonsignore et al. J Am Coll Cardiol CardioOnc 2021; 3:678-691.

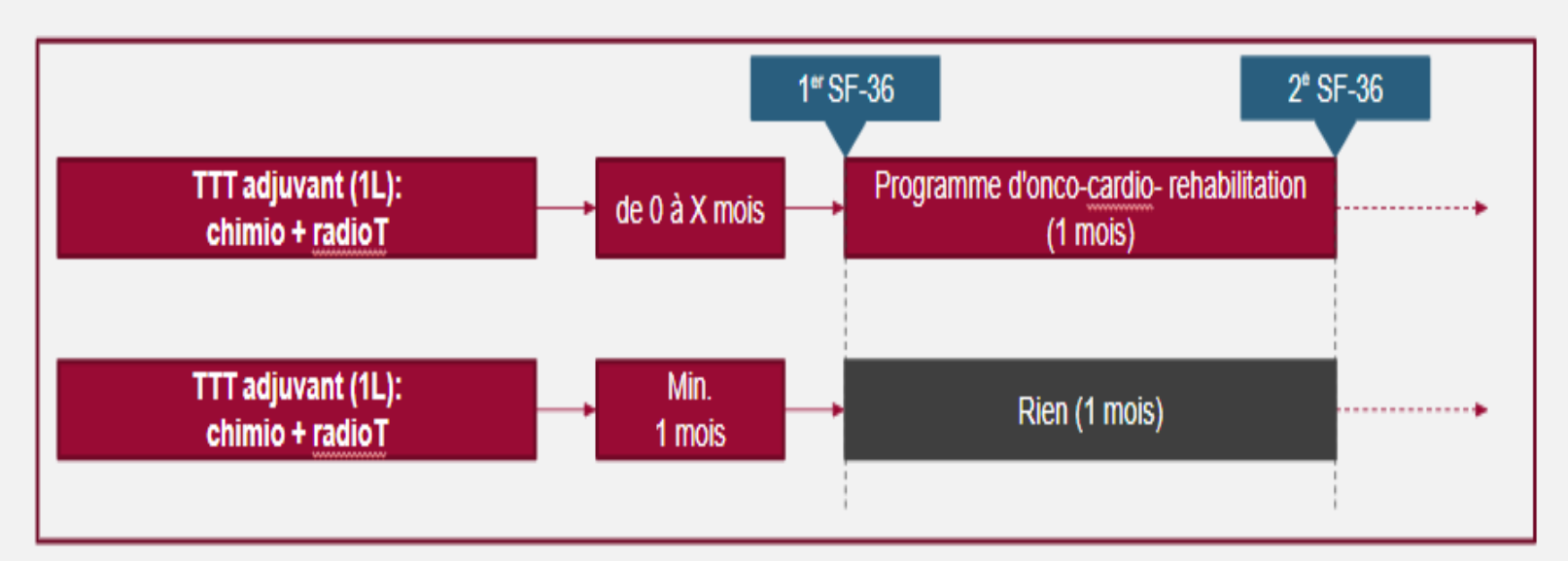
Impact of a COmprehensive cardiac REhabilitation framework among high cardiovascular risk cancer survivors: Protocol for the CORE trial
Author links open overlay panel.

Viamonte SG. International Journal of cardiology. Vol. 371.15 January 2023, Pages 384-390

En cours

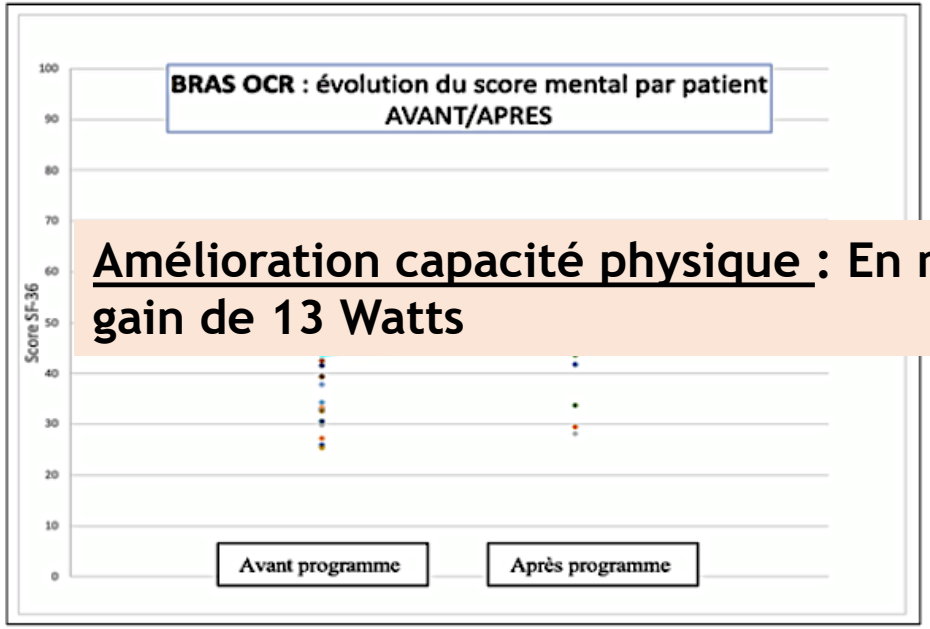
OCR des patients atteints de cancer du sein non métastatique: état des lieux et étude médico-économique de l'expérience rochelaise

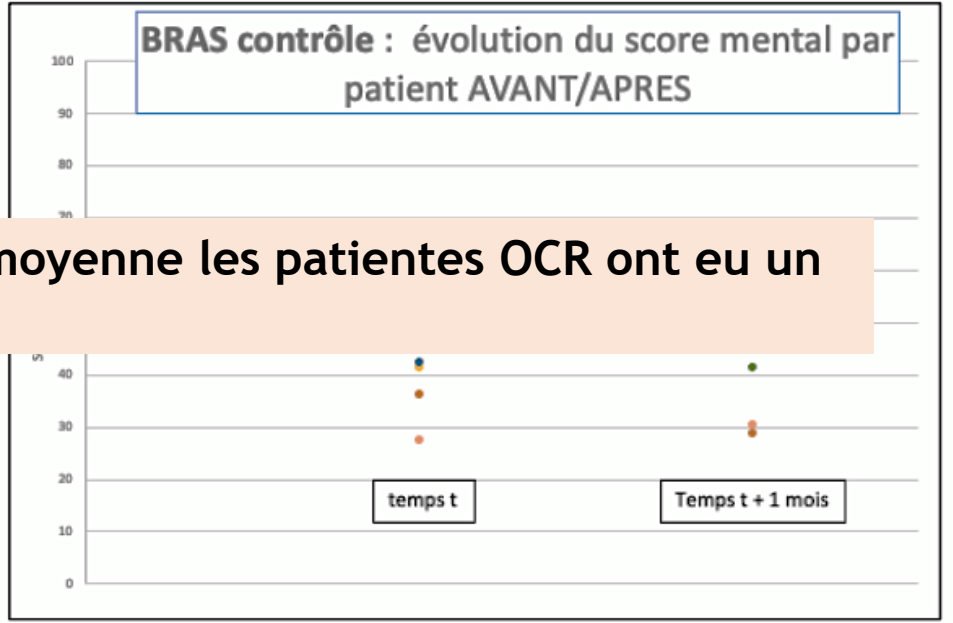
Données ont été collectées entre septembre 2018 et août 2021.
Les deux groupes étudiés suivent le même parcours de soins. La participation au programme d'OCR ou non est un choix effectué par le patient après proposition du médecin oncologue.
Critère d'utilité principal est le score au SF-36



Au total, 108 questionnaires SF-36 ont été enregistrés, soit plus de 3800 questions.

Résultats : Qualité de vie des patients OCR améliorée





<u>Amélioration capacité physique</u> : En moyenne les patientes OCR ont eu un gain de 13 Watts

$p < 0,05$

$p > 0,05$

Projection sur 5 ans sur les coûts globaux de prise en charge (méthode de Markov)

OCR		Contrôle		Différence
4 743 €	-	1979 €	=	2 764 €
4,48 QALY	-	4,43 QALY	=	0,05 QALY

ICER OU RDCR = 55 280 € / QALY

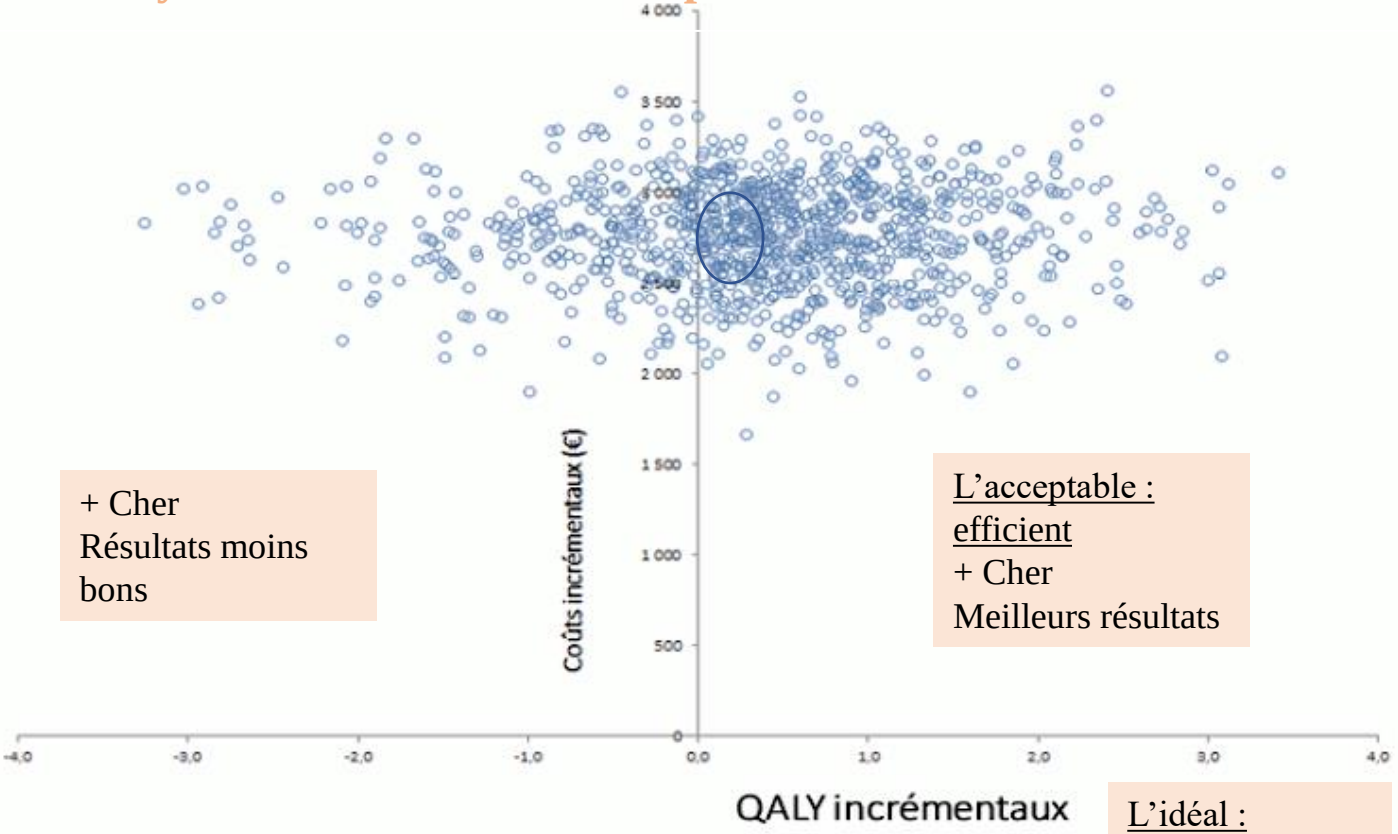
ICER = Incremental Cost-Effective Ratio (Ratio différentiel côut résultat)

QALY = Quality Adjusted Life Year (Qualité de vie ajustée par an)

indicateur économique visant à estimer la valeur de la vie

Une année en bonne santé correspond à un QALY de 1

Résultat : Analyse de sensibilité Bootstrap



+ Cher
Résultats moins bons

<u>L'acceptable : efficient</u>
+ Cher
Meilleurs résultats

<u>L'idéal :</u>
Moins Cher
Meilleurs résultats

Discussion Modèle de Markov

ICER obtenu élevé

Modélisation effectuée et analyses de sensibilité à valider par un expert :

- ❖Hypothèses
- ❖Données utilisées issues de littérature pour incrémenter les paramètres du modèle
- ❖Horizon temporel choisi

Données de vie réelle à perfectionner :

- ❖Suivre les patients sur 5 ans et non 1 mois
  (reprise du travail / consultations médicales)
- ❖Augmenter le nombre de patients inclus
- ❖Intégrer un temps d'attaché de recherche clinique
- ❖Utiliser EQ-5D pour s'affranchir de l'algorithme de conversion

Améliorer robustesse

Phase 1

- Loi sport santé
- APA / clubs de sport (professionnels, amateurs), villes, CPTS
- Dès l'annonce diagnostique

Phase 2

Décret Janvier 2022 : Mention onco-réhabilitation, revue du PRS 2022/2023
Onco-cardio réhabilitation – SMR cardiologique / MPR…
Recommandations : Grp Onco-cardio, SFOnco/AFSOS/GERSP?
EE VO2 / ETT /SLG
4/8 semaines, 3/5 fois par semaine
APA, instituts privés… ?

Phase 3

- Parcours post-cancer (loi 26 décembre 2020)
  - Cs psy, apa, diét. bilan 180 euros par patient
- APA / clubs de sport (professionnels, amateurs) / associations (ligue contre le cancer, instituts privés…)

*Take home message