



Physical activity and cancer prevention

Dr. Thierry Bouillet



Physical activity and cancer prevention

Physical activity and cancer risk
Primary prevention

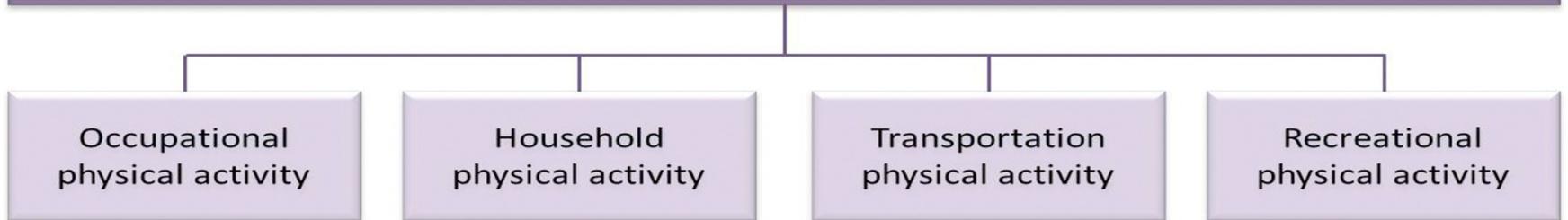
Physical activity and cancer mortality in
survivors
Tertiary prevention

Common mechanisms of action

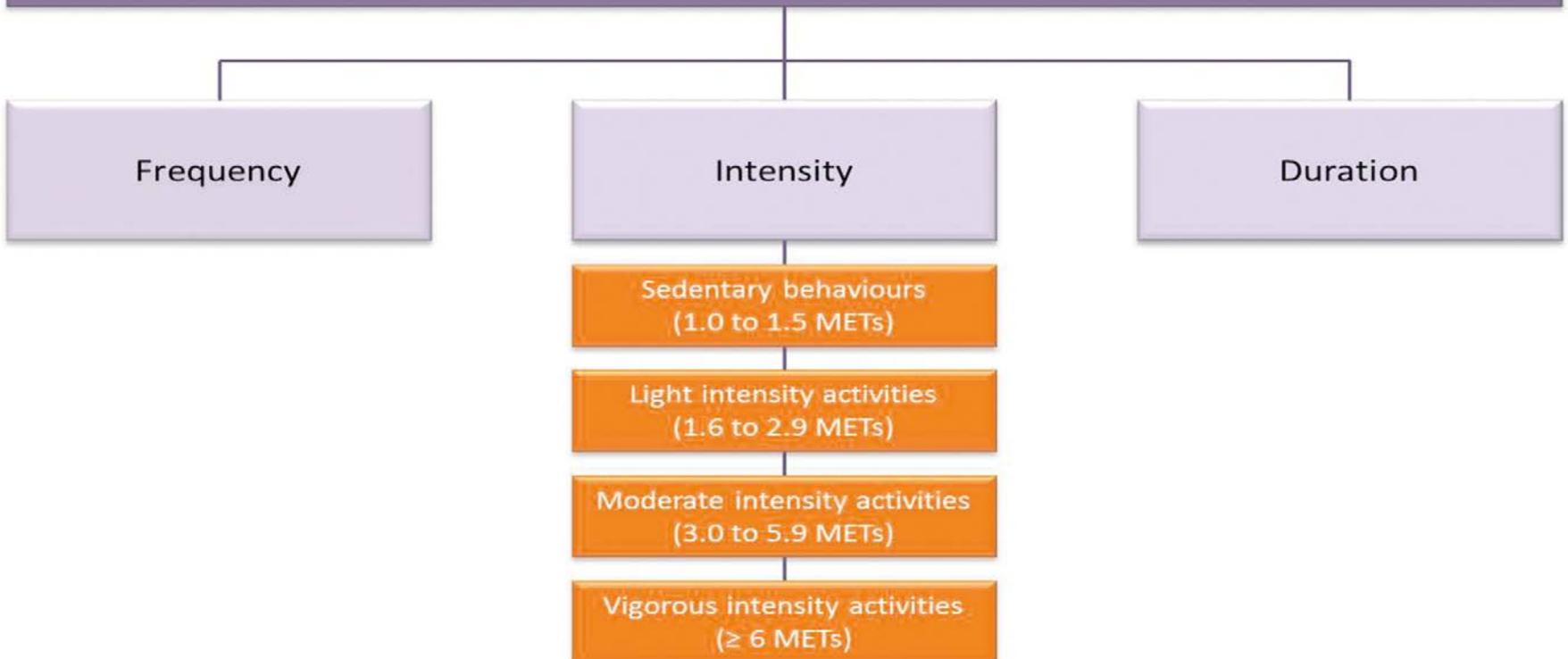
What is physical activity (PA) ?

- PA : Movement of the body in relation with skeletal muscles that increases energy expenditure / basal level
- Physical exercise (PE) : planned, structured, repetitive to improve fitness
- PE : Isometric or static (no movement of the limb)
Isotonic or dynamic (movement of the limb)
- PE : aerobic O₂ for muscle Heart rate and energy used
Anaerobic no O₂ muscle size and strength
- Intensity rate of energy expenditure
MET : 3.25 ml O₂/Kg/min

Types of physical activity



Components of physical activity



Primary prevention PA

Estimated associations between high versus low physical activity levels and incidence of specific cancers.

Cancer Type	Number of studies	Relative risk
Colon	21	0.74 (0.68-0.80)
Endometrial	20	0.82 (0.75-0.90)
Breast	31	0.88 (0.85-0.91)
prostate	24	0.94 (0.91-0.98)
stomach	18	0.90 (0.76-1.06)
ovary	9	0.89 (0.79-1.01)
kidney	19	0.89 (0.80-0.99)
lung	14	0.77 (0.73-0.81)
pancreas	5	0.72 (0.52-0.99)

PA and primary prevention of breast cancer

- **PA at different ages reduction in BC risk**

(Lynch BM and al 2011 PA and cancer spring verlag)

PA Adolescence	16 %
PA early adulthood	8 %
PA middle adulthood	15 %
PA > 50	17 %

- **PA adolescences**

Relative Risk (RR) of Premenopausal Breast Cancer by Patterns of Total Physical Activity During Youth (12–22 years) and Adulthood (≥ 23 years)
(Nurses' Health Study II)

Activity by Age group	Person/year	Number of BC	Multivariable RR
Low Youth / Low adulthood	59947	118	1.00
Low youth / high adulthood	13945	22	0.83 (0.53-1.32)
High youth / low adulthood	11874	13	0.63 (0.35-1.11)
High youth / high adulthood	69462	89	0.70 (0.53-0.93)

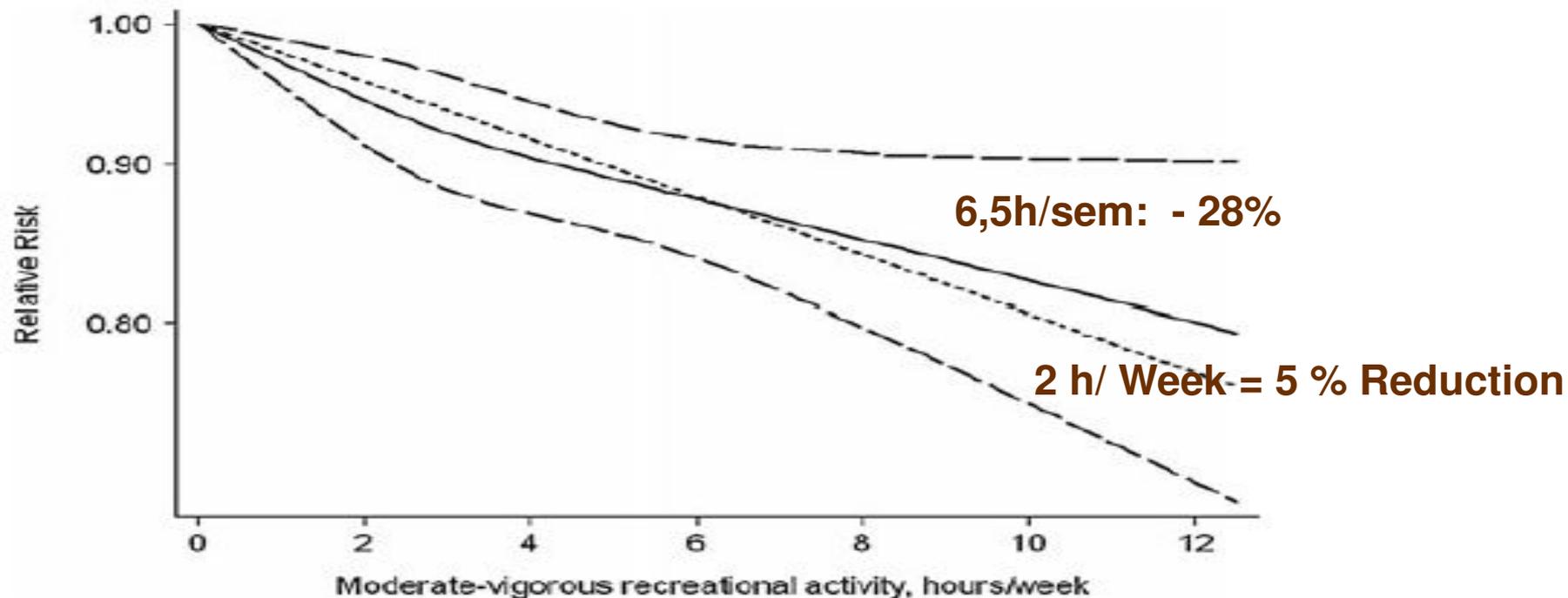
PA and primary prevention for breast cancer

Reduction of 20 %

Benefit of PA both for pre and postmenopausal BC

Benefit at different ages: Whole life PA

Dependency on exercise intensity and duration



Wu et al. Breast Cancer Res Treat 137: 869-82, 2013

31 prospective studies
63786 cases

RR 2-3h/sem : -7% → RR 6,5h/sem: -28%

Monninkhof *et al.* Epidemiology 18: 137-57, 2007

PA and primary prevention of gastric and colon cancer

- **Gastric cancer**

16 studies 11 111 cases

RR Most / least PA RR = 0.79 (0.71-0.87)

(Singh S et al Cancer Prev Res 2013)

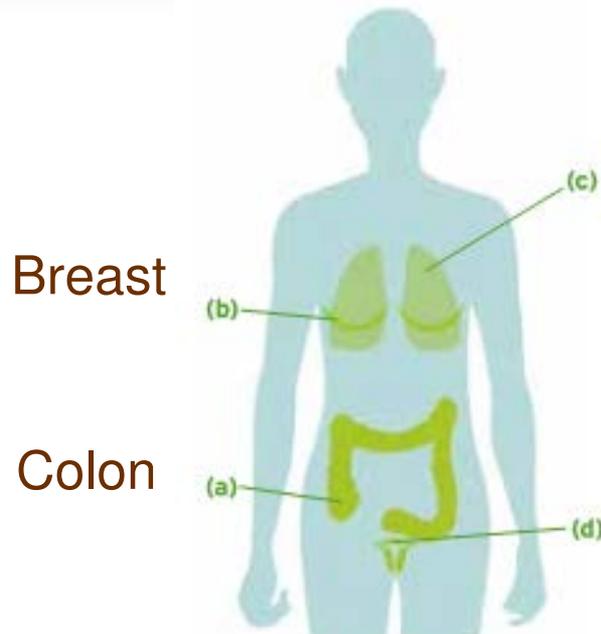
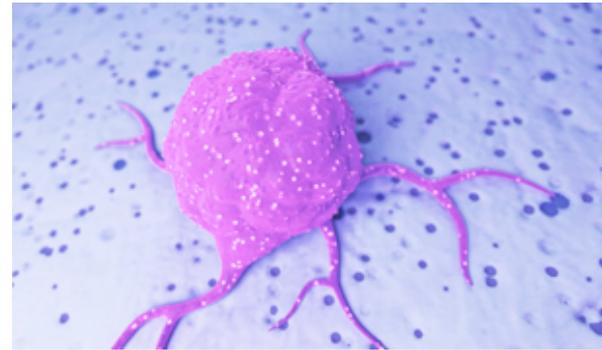
- **Colon cancer**

21 studies

Proximal colon RR most /least PA RR = 0.73
(0.66 -0.81)

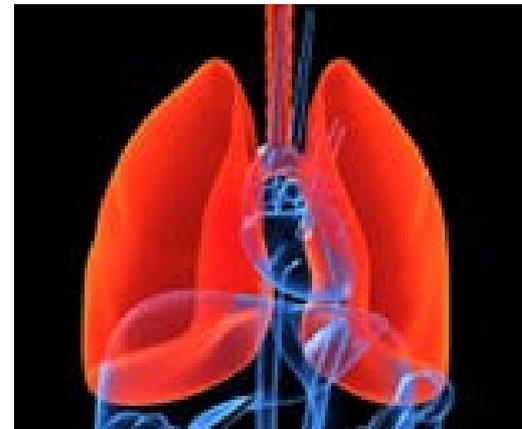
Proximal colon RR most /least PA RR = 0.74
(0.68 -0.80)

(Boyle T et al J Natl Cancer Inst 2012)



Breast

Colon



Lung cancer

-20-30%



Endometrial cancer

-20-30%

Effects of PA independent of the impact of the major respective cancer risk factors

(Sun JY et al, 2012; Keum N et al, 2014)

World
Cancer
Research Fund



American
Institute for
Cancer Research

RECOMMENDATION

PHYSICAL ACTIVITY

Be physically active as part of everyday life

PERSONAL RECOMMENDATION

Be moderately physically active, equivalent to brisk walking, for at least 30 minutes every day

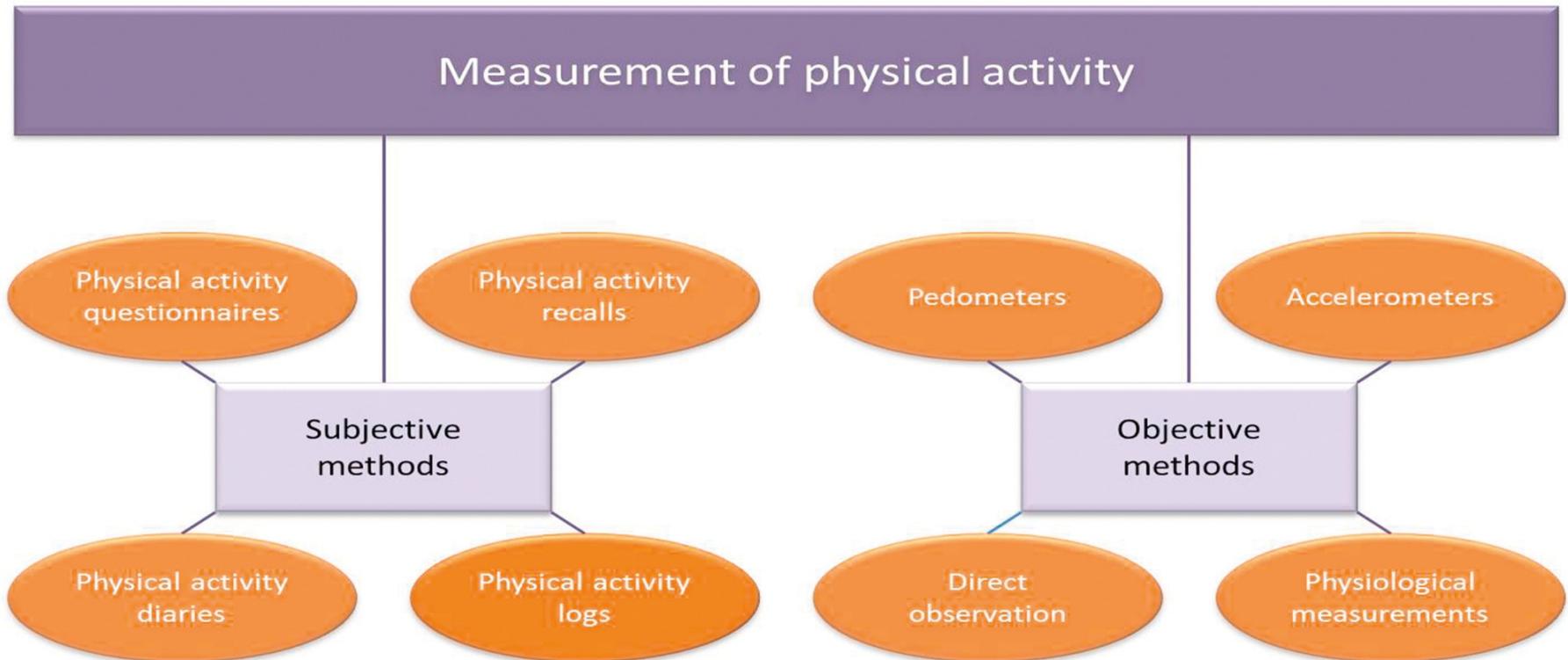
As fitness improves, aim for 60 minutes or more of moderate, or for 30 minutes or more of vigorous, physical activity every day

Limit sedentary habits such as watching television

More is better

2008 Physical activity guidelines for Americans

- 150 min / Week moderate intensity PA
- 75 min / Week vigorous intensity PA
- Single session or separate sessions of 20 to 30 min each



PA and tertiary prevention



PA after therapy and breast cancer induced mortality

8 cohorts localised BC prospectively assessed
benefits 5 and 10 years survival 4 - 6 %

Multivariate analysis

Study	Nber Ptes	MET-H	HR	IC	p
NHS	2 987	9	0,63	0,48-0,81	0,004
WHEL	1 490	9	0,56	0,31-0,98	0,04
CWLS	4 482	8	0,63	0,31-0,88	0,01
HEAL	933	9	0,33	0,15-0,73	0,046
WHI	4 643	9	0,61	0,35-0,99	0,049
LACE	1 970	> 6 h/sem	0,66	0,42-1,03	0,04
CTS	3539	> 3 h/sem	0,53	0,35-0,80	0,003
SBCSS	4 826	8,3	0,60	0,47-0,76	0,049

Meta analysis PA and BC Mortality

- Post diagnostic PA is associated with decreased all cause mortality
HR = 0,59 (0,53-0,65) $p < 0,00001$
- Post diagnostic PA is associated with decreased BC specific mortality
HR = 0,66 (0,57-0,77) $p < 0,00001$



E Ibrahim, A Al-Homaidh (2010) *Med Oncol* Apr 22

PA post therapy and breast cancer mortality

- Post-diagnostic PA levels is associated with a significant trend of decreased all-cause and breast cancer-specific mortality
- Benefit = 5 % survival 5 years
- Dose-response trend
- Threshold effect 9 MET /H / Week
- Mortality all cause and BC-specific increase among women who reduced their post diagnostic PA level.

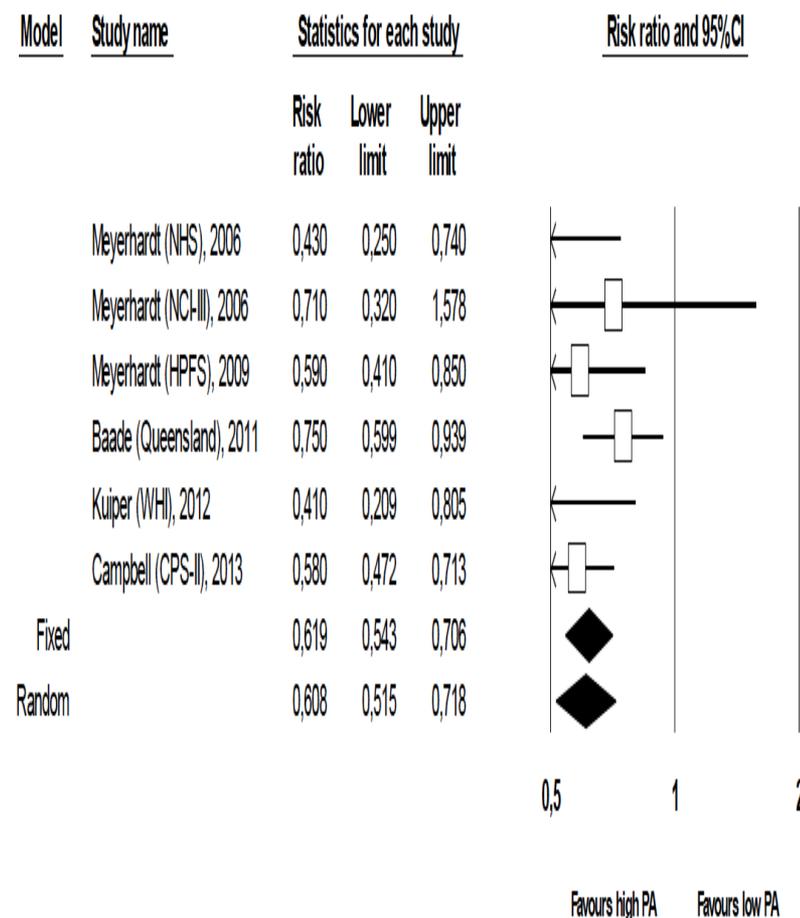
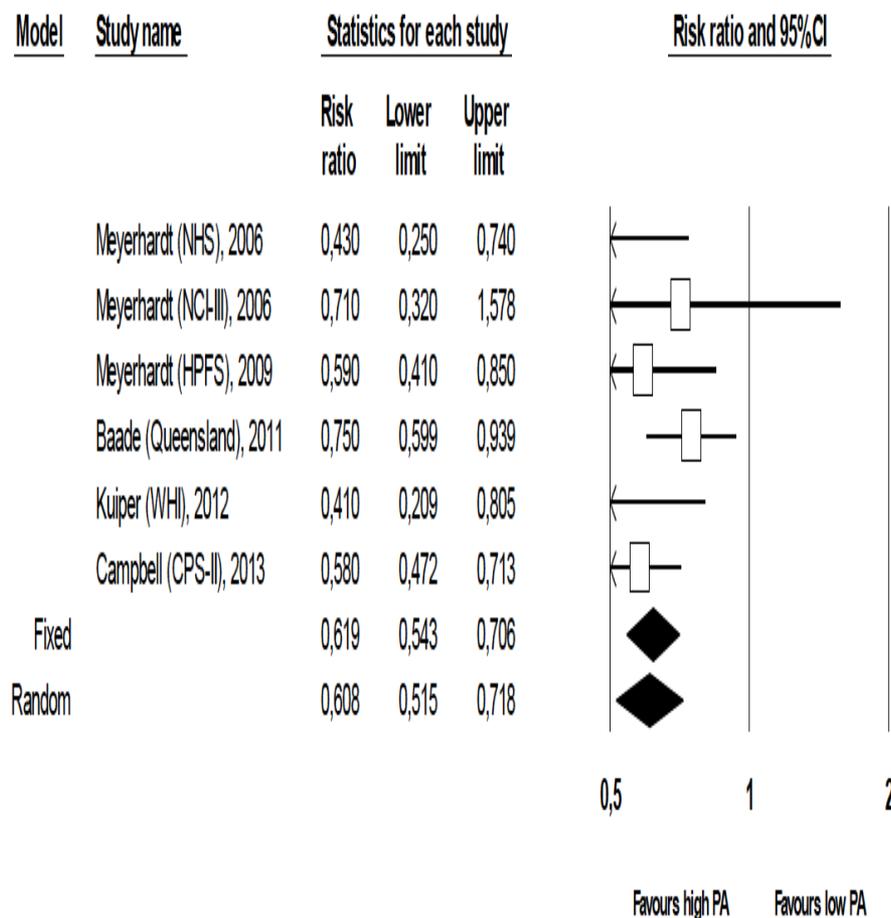
Borch et al BMC Cancer 2015 15

Influence of physical activity on recurrence and survival of colorectal cancer patients : a Meta-analysis

T. Bouillet ASCO 2013

CRC overall survival and post-diagnostic physical activity

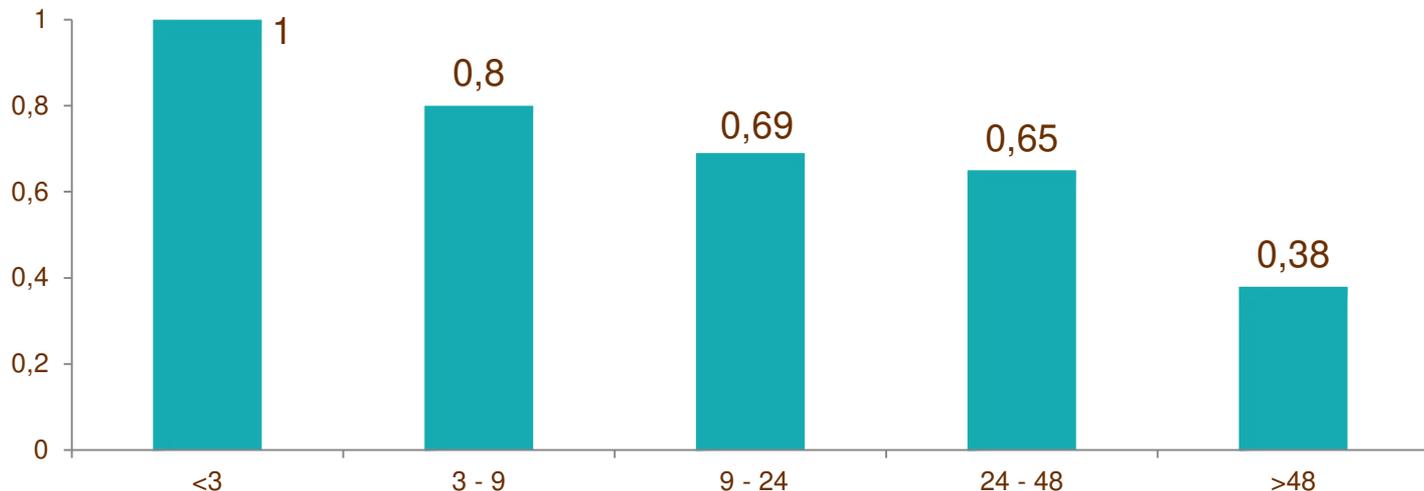
CRC overall survival and post-diagnostic physical activity



Influence of physical activity on recurrence and survival of prostate cancer patients

Studies	Num of pts	exercise	HR OS	HR CSS
NHS	2705	> 9 MET h / week	0.67 (0.56-0.82)	0.63 (0.43-1.00)
PSURE	1455	Brisk walking 3 hours/w	Relapse 0.43 (0.21-0.91)	
Friedenreich	830	> 26 vs < 4 MET H /W/Y	0.66 (0.49-0.88)	0.56 (0.35-0.90)

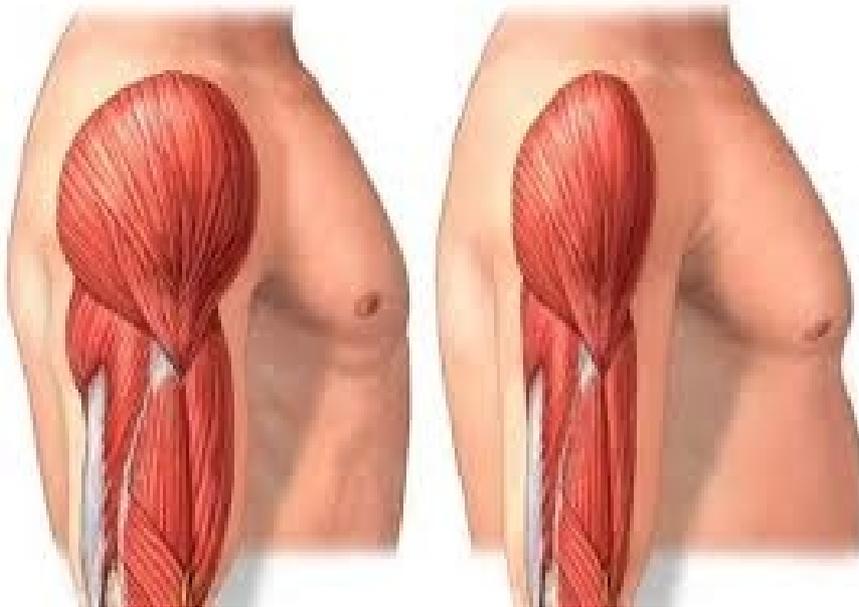
Recreational physical activity after diagnosis of prostate cancer is associated with a lower risk of Pca death with a dose response relation



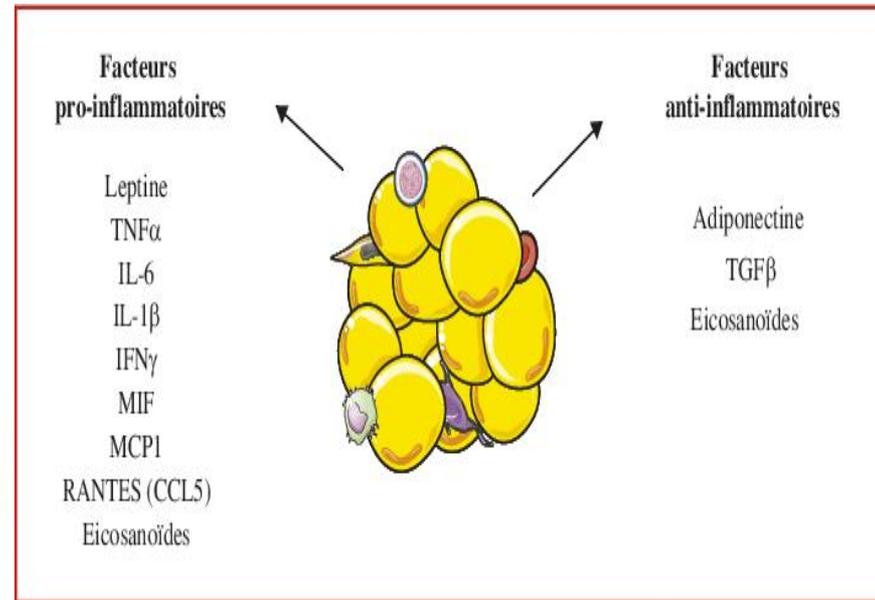
All in all

- Association between PA after diagnosis and overall and specific survival
- PA is associated with a sustained increase in both specific and overall survival (diabetes, cardiovascular diseases, degenerative neuro, osteoporosis...)
- Dose effect with a minimum threshold intensity and duration
- PA increases quality of life and physiological parameters (weight, muscle tone, bone, cardiorespiratory)
- PA reduces fatigue

PA and Cancer Prevention : Mechanisms

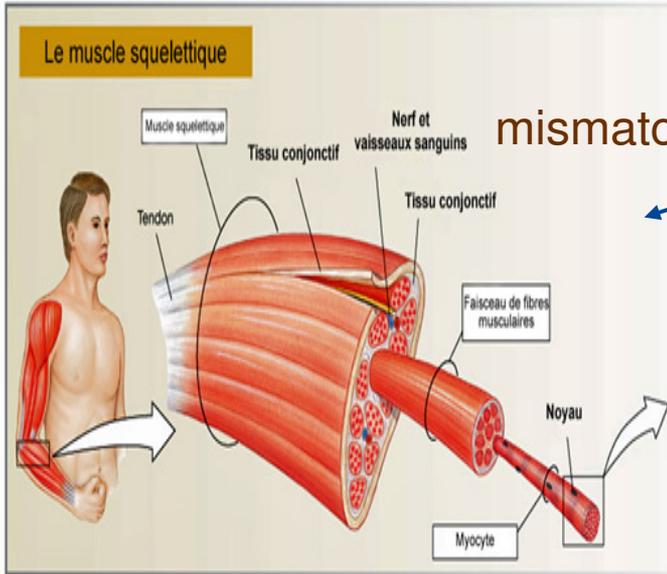


REDUCED CONSUMPTION OF
GLUCOSE

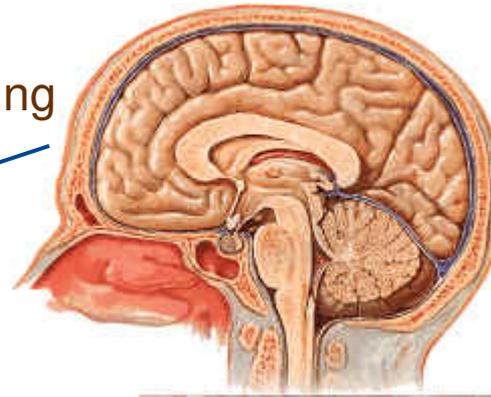


CYTOKINE PRODUCTION

Trilogy (TMF) Tumor Muscles Fat cytokines



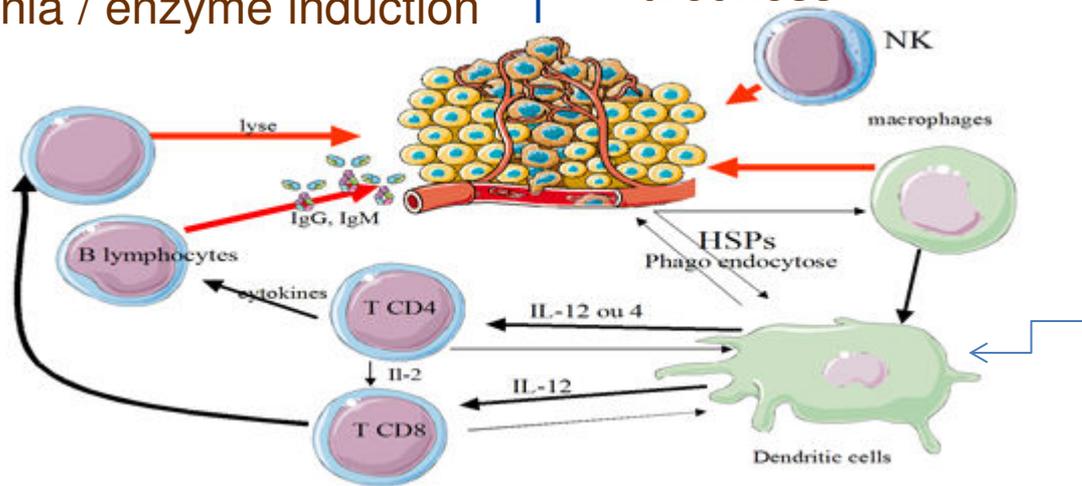
mismatching



behavior disorders
tiredness
muscle abnormalities
hormonal abnormalities

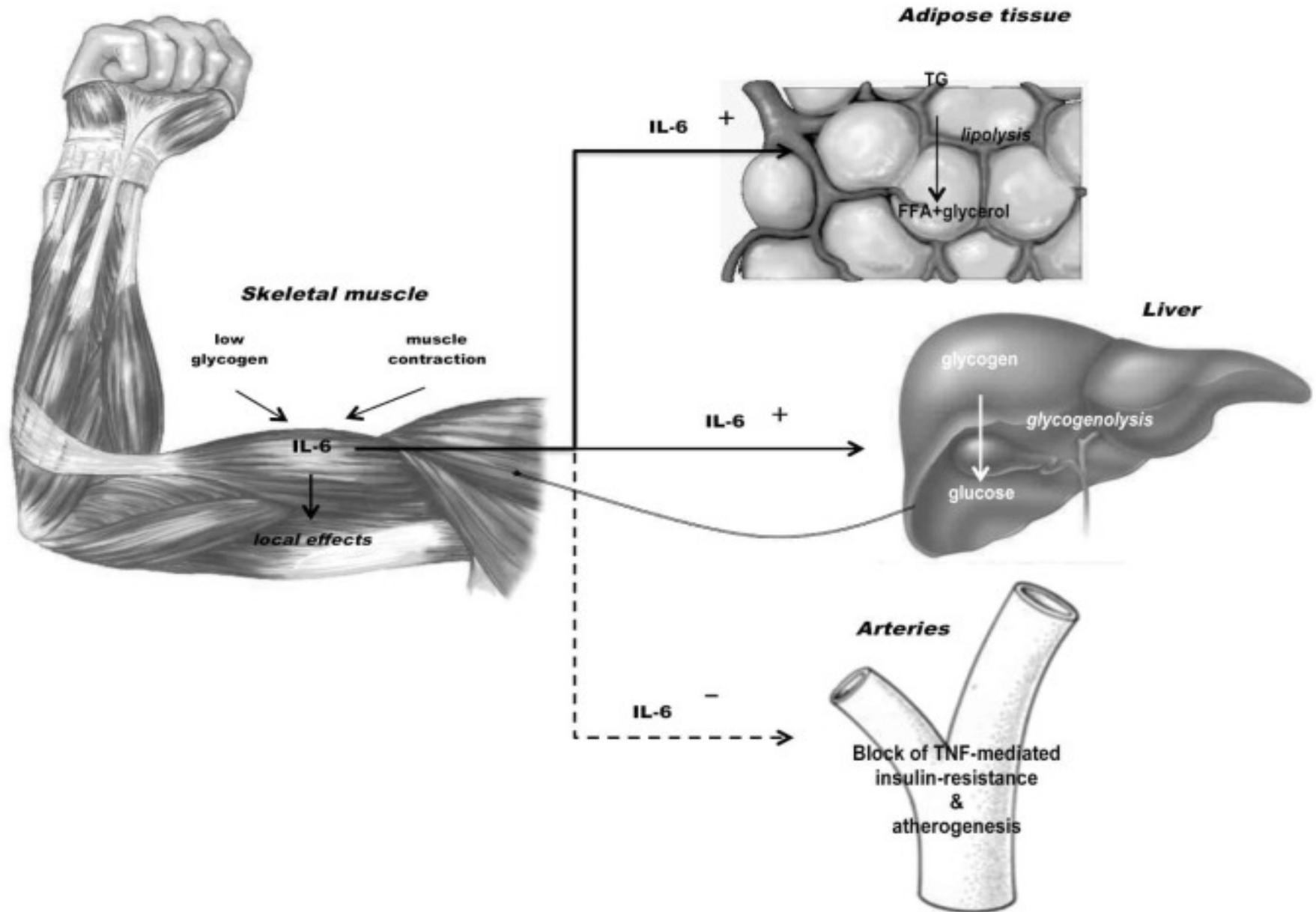
cytokines
Sarcopenia / enzyme induction

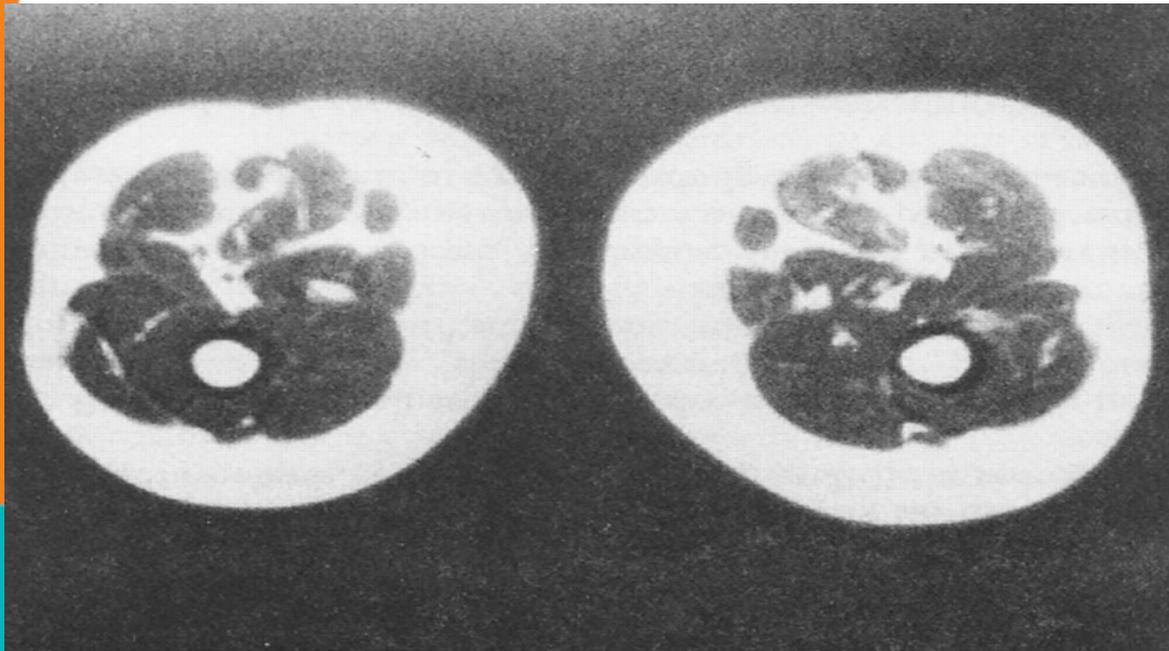
cytokines
Behavioural disorders
tiredness



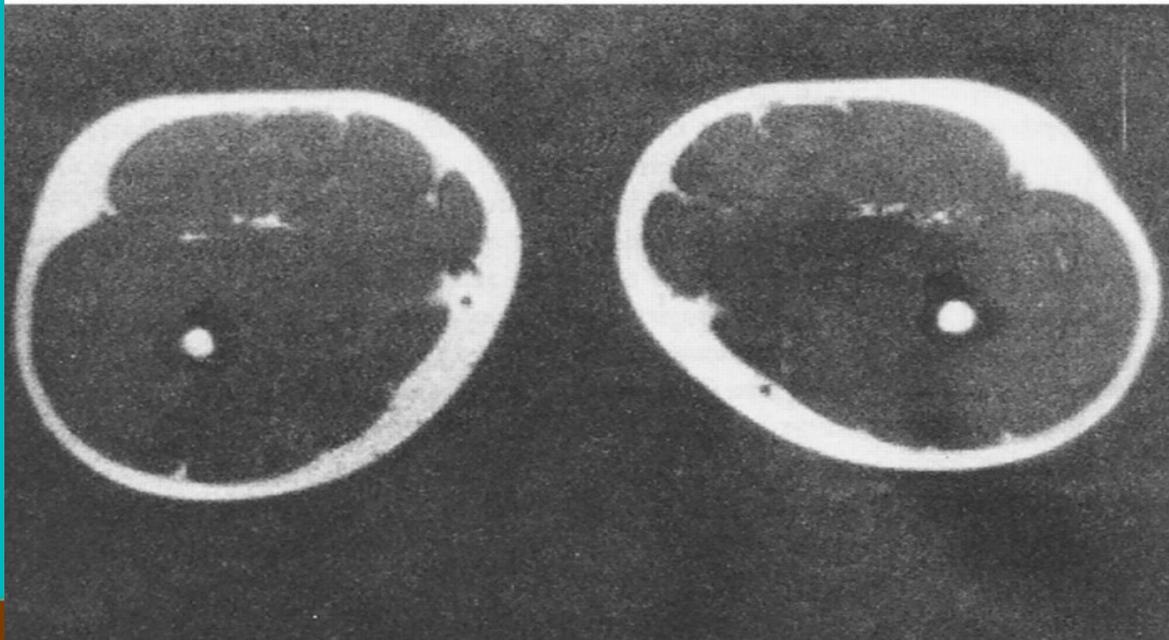
Fat Taken by:
AP decrease
cortisol
TNF α
Eating disorders

Muscles = endocrine tissues - Effects IL 6





SARCOPENIE
MESURE
TDM



Mesures graisse et muscles

Muscles : Volume et fonction

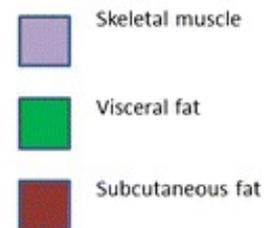
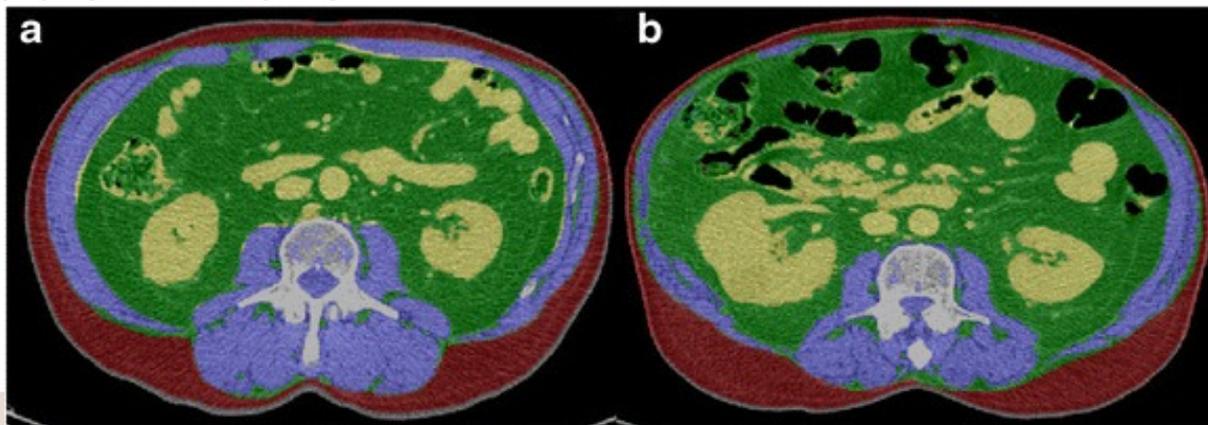
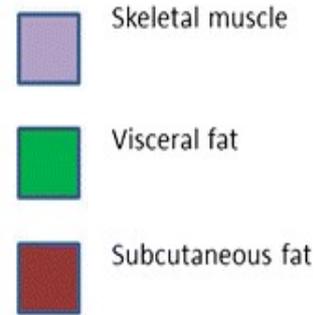
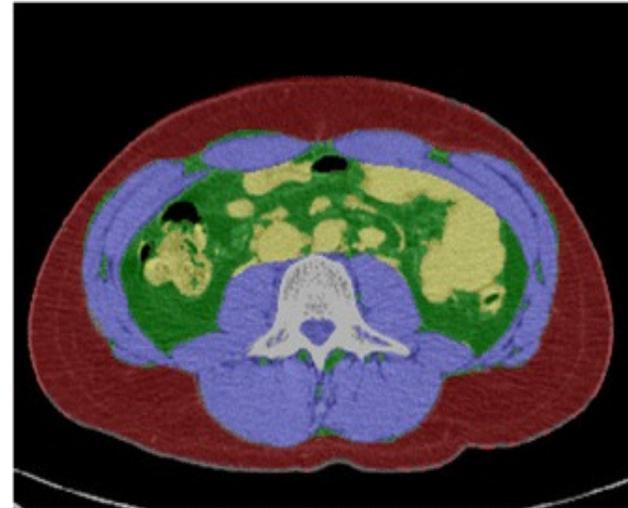
Hand grip

Graisse et muscle

Bioimpédance

TDM et IRM coupe L3 psoas vertébraux abdominaux

Graisse abdominale



Sarcopénie et complications post op

- Mesure masse musculaire en L3 en cm² sur scanner pré opératoire / normalisation SC

Sarcopénie si :

< 385 mm²/m² femme

< 545 mm²/m² homme

100 pts résection colique pour cancer

- 15 % sarcopénique
- Risque de complication grade 3 ou plus
RR 5,41 (1,45-20,15) p 0.01

Sarcopénie et complications de la chimiothérapie

89 pts chimio néo adjuvante pour T oeso gastrique

DLT = Réduction de posologie, report ou arrêt de chimio

DLT 41,6 % des cas

Multivariable sarcopénie associée DLT

RR 2,95 (1,23-7,09) p 0,015)

Tan BH et al EJSO 2015

229 pts colon stade III Fol Fox adjuvant

Sarcopénie associée accroissement toxicité grade 3-4

Univariable RR 1,69 (1,18-2,27)

Mutivariable RR 1,56 (1,05-2,38)

Jung HW et al Support Care Cancer 2015

K Sein et sarcopénie impact sur survie

HEAL study 471 ptes suivi moyen de 9.2 ans

16 % sarcopéniques dont 38 % sont aussi obèses

Impact sarcopénie sur survie en situation adjuvante

Mortalité globale HR 2.86 (1.67 – 4.89)

Mortalité spécifique HR 1.95 (0.87 - 4.35)

Villasenor A J Cancer Surv 2012

Impact identique en situation métastatique

55 ptes métastatiques 25 % sarcopénie

TTP 101 jours (59-142) vs 173 j (126 -220) p=0.05

Prado CM Clin Cancer Res 2009

Sarcopénie prédictive de survie à 5 ans post résection cancer colique

220 pts cancer colique Stade I-III

25 % sarcopénique

- Survie globale et sans récurrence à 5 ans plus faible si sarcopénie

	Muscles Nx	Sarcopénie	p
SG 5 ANS	85 %	68 %	0.015
SSR 5 ans	79 %	56 %	0.006

- Multivariable

Sarcopénie associée à une réduction survies

	RR	p	
SG 5 ans	2,27 (1,147-4.494)	0.019	
SSR 5 ans	2,176 (1,200-3,943)	0.010	

Muscle Dysfunction which consequences ?

Care and sarcopenia

Increased toxicity of chemotherapy and biotherapy
(limiting care) breast, colon, kidney

(Jung HW Support Care cancer 2014 Prado C et al Clin Cancer Res 2009)

Partial hepatectomy on colon cancer

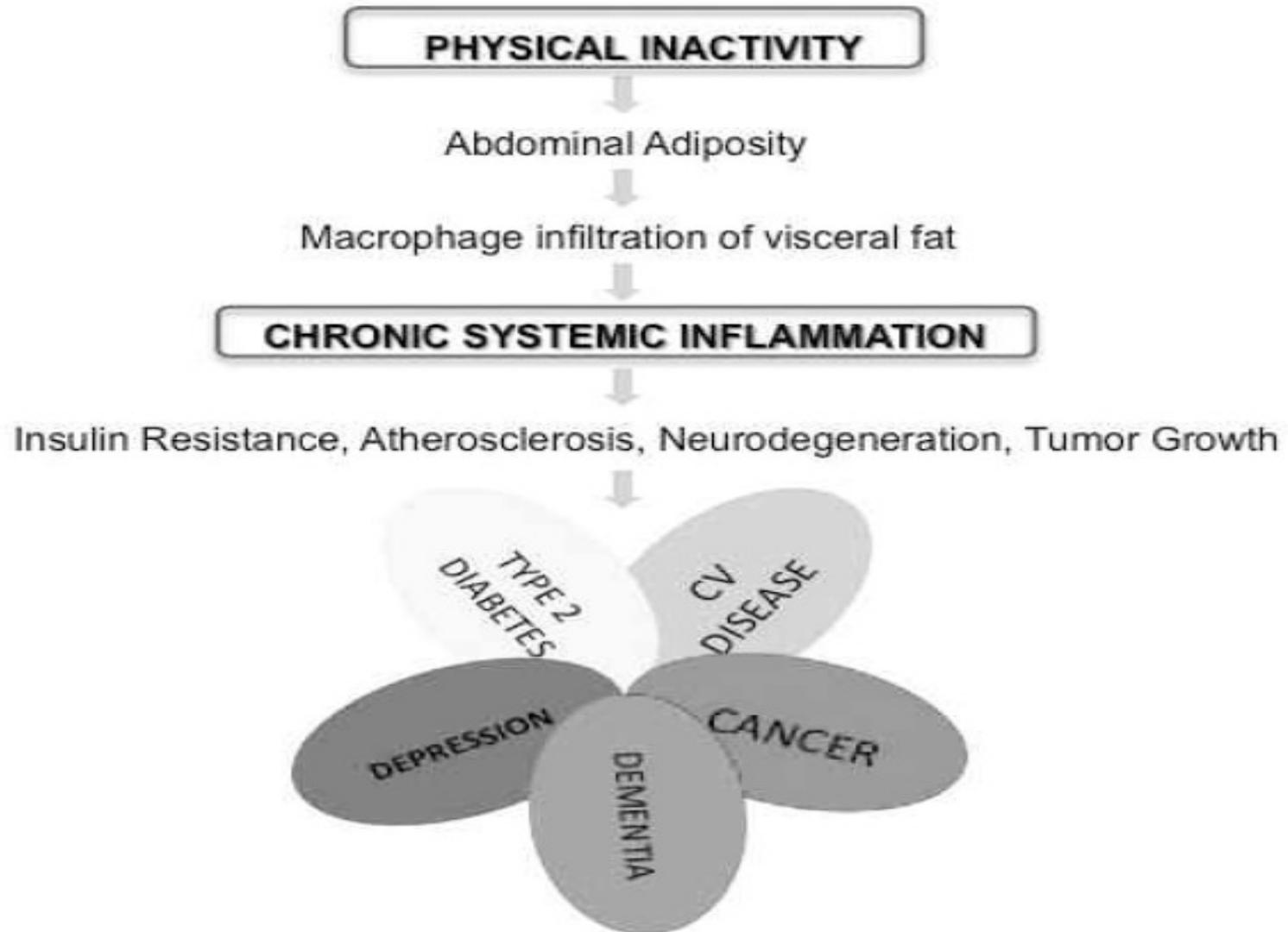
Severe complication rates OR = 3.12

Esophagectomy, increased length of stay if low
muscle strength of hands (hand grip)

Christensen JF et al Ann oncology 2014

Impact on global and specific survival

Polypathologies and physical inactivity



Sport & physical activity (S PA) and fat - muscles

- Reduces visceral fat
- Increases muscle mass (0.8 kg muscle if PA during adjuvant chemotherapy for Breast C)

(Christiensen JF Ann Oncol 2014)

Different actions depending exercises type:
Aerobic increases respiratory cardio
fitness increases muscle strength

(Courneya K J Clin Oncol 2007)



S PA effects on insulin resistance and cytokines

S PA REDUCES INSULIN RESISTANCE FROM 1st SESSION AND ON \geq 72 HOURS

The effect in subsequent sessions require a steady increase efforts

Decrease fat and increase muscle mass

S PA REDUCES CYTOKINES of INFLAMMATORY TISSUE

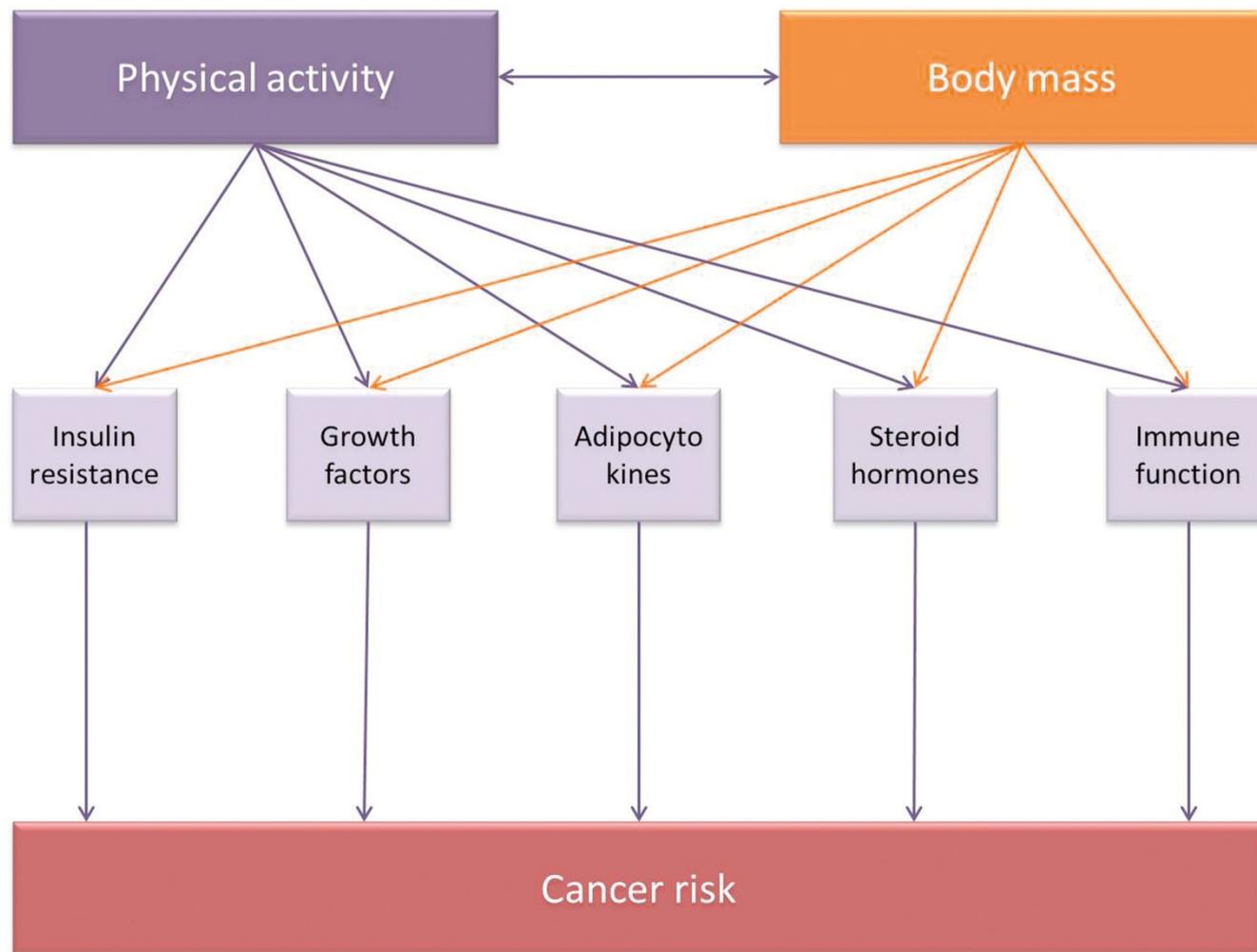
S PA INCREASES ADIPONECTIN

EFFETS = 72 HOURS EXPENDED BY SESSIONS
DURATION

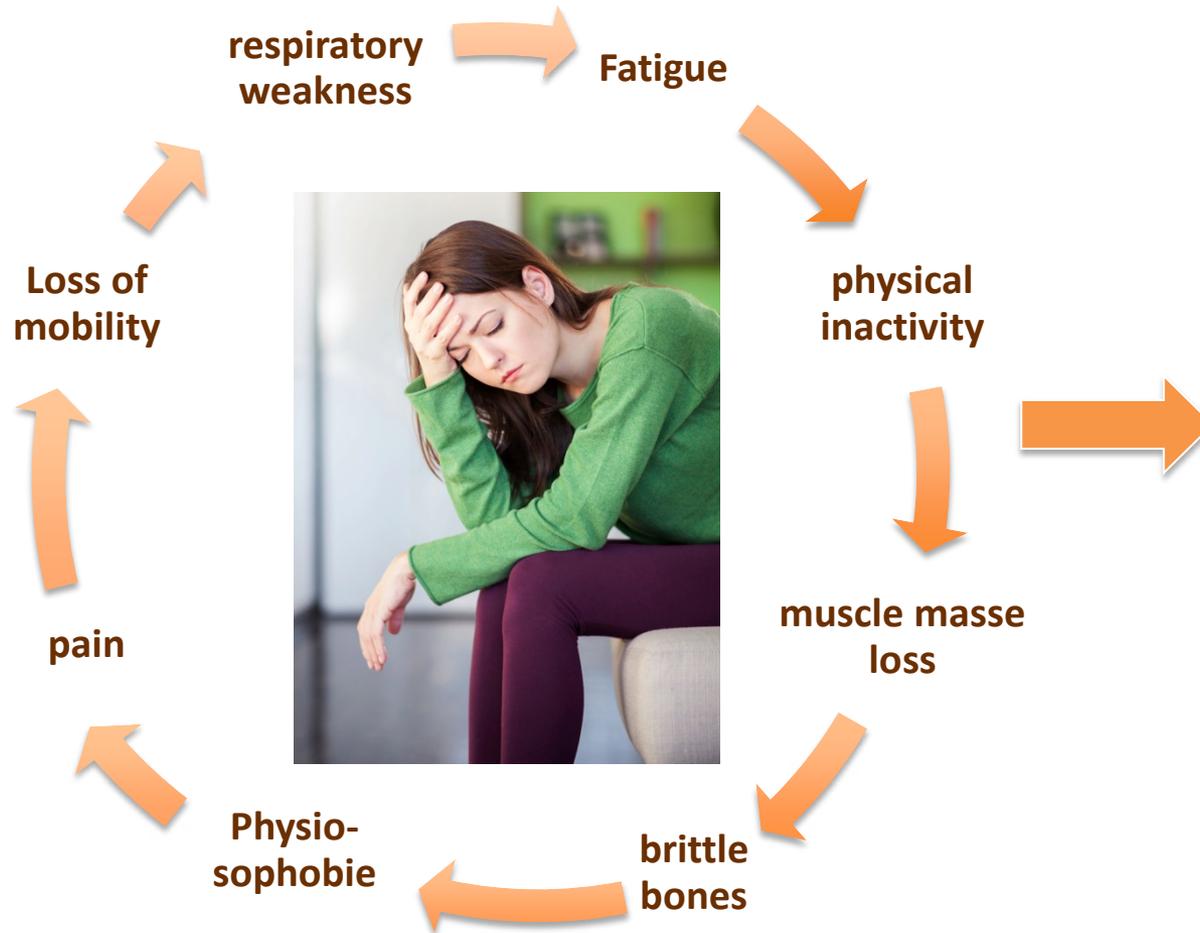
PRATICE > 6 MOIS

Golbidi S J Diab Res 2014

Nelson R et al Appl Physiol Nutr Metab 2014



Cancer treatments on the body : a vicious circle



- Increased toxicity risk
- handicap
- comorbidities
- Cancer cell proliferation
- Immune system down
- proinflammatory
- Altered sleep
- medication overuse

S PA and cancer : what advice?



- Early onset - Inflammation and sarcopenia exist from the Dg
- Sustained intensity, duration > 50 minutes, 3 times / week, duration effects Insulin
- Combined exercise endurance and aerobic
- Period > 6 months
- Structured courses (reported activities > real activities)
(Ekblom-Bak E Eur J Cardiovasc Prev Rehabil 2010)

Let's talk some sports talk ...

Sport is good for health!



Recommendations and references



CCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Cancer-Related Fatigue

Version 1.2012

NCCN.org



**AMERICAN COLLEGE
of SPORTS MEDICINE®**

The meeting of three worlds :
the patients, medical and sports worlds

for Three effects :
Fatigue, Quality of life,
Survival



Obesity, physical activity and cancer

There is a strong link between being overweight or obese & an **increased risk** of 9 cancers:

- ◆ Advanced prostate
- ◆ Ovarian
- ◆ Gallbladder
- ◆ Kidney
- ◆ Colorectal (bowel)
- ◆ Oesophageal*
- ◆ Postmenopausal breast
- ◆ Pancreatic
- ◆ Endometrial (womb)

1.6 billion adults worldwide are overweight or obese. This exceeds the population of China

Physical inactivity is the 4th leading cause of death worldwide

There is a strong link between being physically active & a **decreased risk** of 3 cancers:

- ◆ Postmenopausal breast
- ◆ Colorectal (bowel)
- ◆ Endometrial (womb)

Top 10 countries* with the highest % of overweight or obese adults

- ◆ Mexico 71.3%
- ◆ United States 68.6%
- ◆ Chile 64.5%
- ◆ New Zealand 63.8%
- ◆ Australia 63.4%
- ◆ Israel 62.2%
- ◆ United Kingdom 61.9%
- ◆ Hungary 61.6%
- ◆ Ireland 61%
- ◆ Finland 59.2%
- ◆ Luxembourg 59.2%





World
Cancer
Research
Fund International

10 CANCER PREVENTION RECOMMENDATIONS

World Cancer Day 4 February 2015



**MAINTAIN A
HEALTHY WEIGHT**

**MOVE
MORE**



**EAT MORE
VEG, FRUIT
WHOLEGRAINS
& PULSES**



**LIMIT
SUGAR
AND
FAT**



**LIMIT RED
MEAT, AVOID
PROCESSED
MEAT**



**CUT DOWN ON
ALCOHOL**



**EAT LESS
SALT**

**FOR CANCER
PREVENTION
DON'T USE
SUPPLEMENTS**



**BREASTFEED
YOUR BABY**



**AFTER TREATMENT,
CANCER SURVIVORS
SHOULD FOLLOW THE
CANCER PREVENTION
RECOMMENDATIONS**





Les spécialistes d'accord sur les bienfaits du sport pour la santé

15 minutes d'activité physique par jour prolongent la vie de 3 ans*

L'activité physique régulière réduit de 50 % le risque d'hypertension artérielle, de plus de 60 % la récurrence du cancer du sein et du côlon*

*Enquête « Découvrez le meilleur des médicaments » Santé-médecine.net et Journal des Femmes Santé 2012



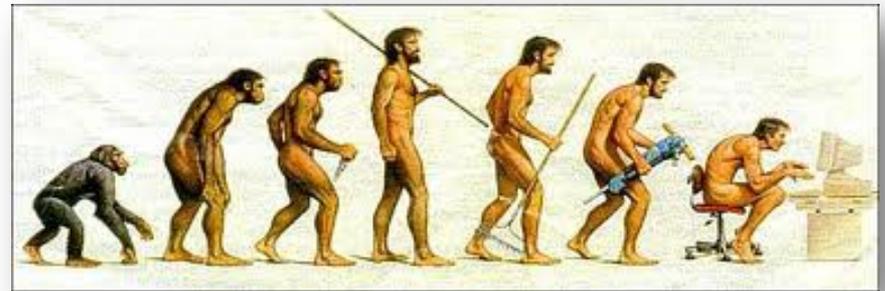
Les pouvoirs publics investissent dans des messages

Les PNNS : un programme de recherche et d'information grand public, près de 270M€ investis depuis sa création

Plan National Nutrition et Santé

PNNS 1 - 2001 à 2005	10 M€ / an
PNNS 2 - 2006 à 2010	47 M€ / 4 ans (~12 M€ / an)
PNNS 3 - 2011 à 2015	210 M€ / 4 ans (~52 M€ / an)

Partenariat avec l'INSERM, l'INRA et l'ANR
 Evaluation en 2008 par l'OFSEPS et l'INSERM
 Evaluation en 2011 par l'IGAS et l'OQALI



...que tout le monde écoute et intègre

87 % des Français accueillent favorablement les messages sanitaires insérés dans les publicités alimentaires,

71 % les ont mémorisés*

*Enquête de l'impact des messages sanitaires PNNS réalisée par l'Inpes auprès de 1063 personnes



Mais ça ne marche pas !!!

75 % des Français n'atteignent pas l'objectif santé des 10.000 pas quotidiens (80% en 2013)

Les freins à l'activité physique ou sportive sont d'ailleurs beaucoup moins souvent financiers que liés au manque de temps*

* Enquête Assureurs Prévention sur le niveau d'activité physique ou sportive et de sédentarité de la population française



Patients at the heart of the CAMI's commitment

- **1600 patients** cared for per week
- **5000 hours** of classes per year
- **120 sessions** per week in class (oncology)
- **80 individual sessions** per week (hematology / pediatric oncology)
- **12-15 patients** per session

- **No time limit** during treatment
- Median Supported: 8 months / 2 times per week

- **A deliberately minimal financial contribution**
 - Low financial contribution from patients for in town session
 - Solidarity Operation for the poor
 - Free programs within the Sport et Cancer Department



- **Cost for the CAMI of one session per patient in oncology in town : € 8**
- **cost for the CAMI of one session per patient oncology Pole: € 10**
- **Cost for the CAMI of a patient session in Hematology / Pediatric Oncology: € 30**

A unique intervention model





In treatment or in remission your doctor hands you a certificate of non-cons to the practice of adapted physical activity.



You contact your CAMI Committee to make an appointment with a medical-sports instructor.



The sports medical educator defines with you the program that best fits your needs.

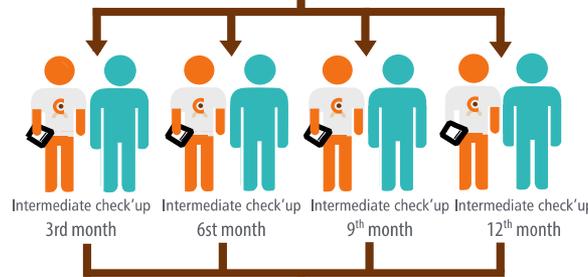
You get access to our Médiété® programs in town or in the hospital.



- Outpatient Program
- Sports after cancer program



- Sport & Cancer Pole program



Every three months, you get a new interview to assess your progress and redefine your Médiété® program in town or at the hospital.

We consider treatment changes, your general physical condition and your needs. You can leave CAMI at any time. You will be directed to other sports facilities through our exit check'out.



Foreword

APS en ONCOLOGIE UN MUST !!!



- COUPLE GRAISSE MUSCLE
- CYTOKINES CANCER INFLAMMATION GRAISSES
- INSULINO RESISTANCE
- COMPLICATIONS
- SURVIE
- URGENCES THERAPEUTIQUES
- SECURITE BONHEUR PRINCIPES FORMATIONS