Paradoxe de l'obésité sur la mortalité…

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intérêts: Santinov, Ethicon, Covidien, Lilly, Novo, Roche, Sanofi

Pas de CI

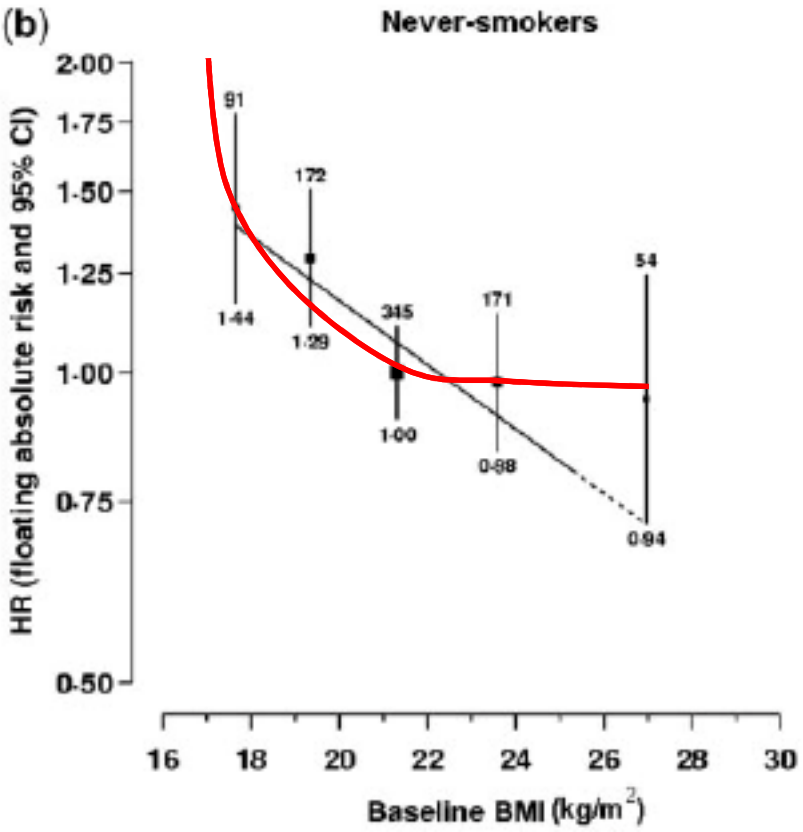
Introduction

- Le paradoxe de l'obésité est:
  - Une mortalité moindre chez les patients de poids élevé (surpoids ou obèse)
  - Que dans une population contrôle (IMC 18,5-25)
  - Malgré un rôle démontré de l'obésité sur des facteurs de risque de décès
- Lien épidémiologique entre IMC et évènements
- Etudes de cohortes avec leurs puissances et leurs défauts
- Explosion des publications, sur des sujets aussi variés que maladie coronarienne, jusqu'à la maladie de Chagas…

Plan

- Une situation connue: BPCO
- Une situation beaucoup plus complexe: maladie coronarienne
- Facteurs confondants
- Quid de la perte de poids?
- Conclusion

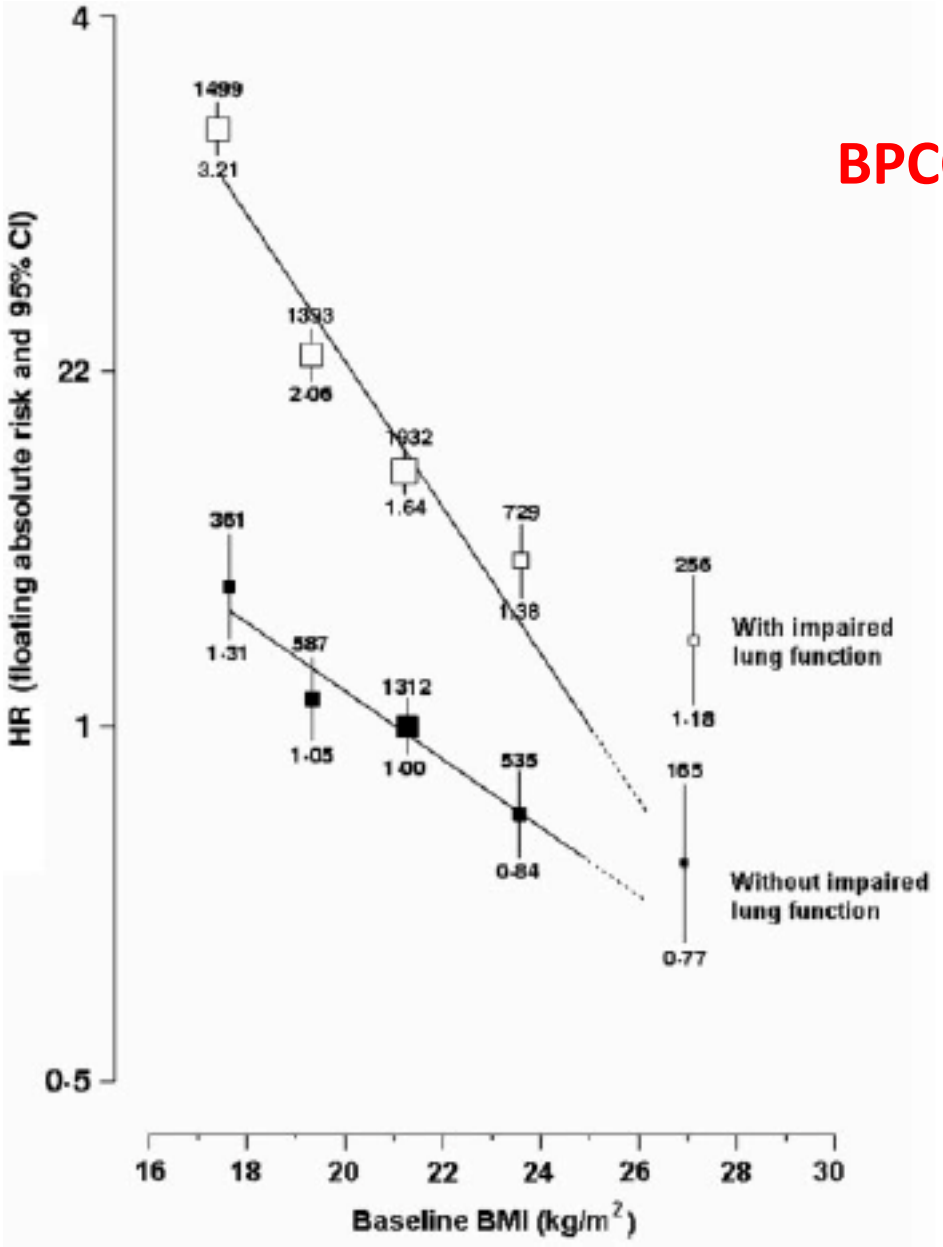
BPCO Cohorte chinoise



Peu de patients au delà de 25
Moins exposé aux fdr

Ling Y et al. Int J Epidemiol 2010;39:1027–36

BPCO Cohorte chinoise



Ling Y et al. Int J Epidemiol 2010;39:1027–36

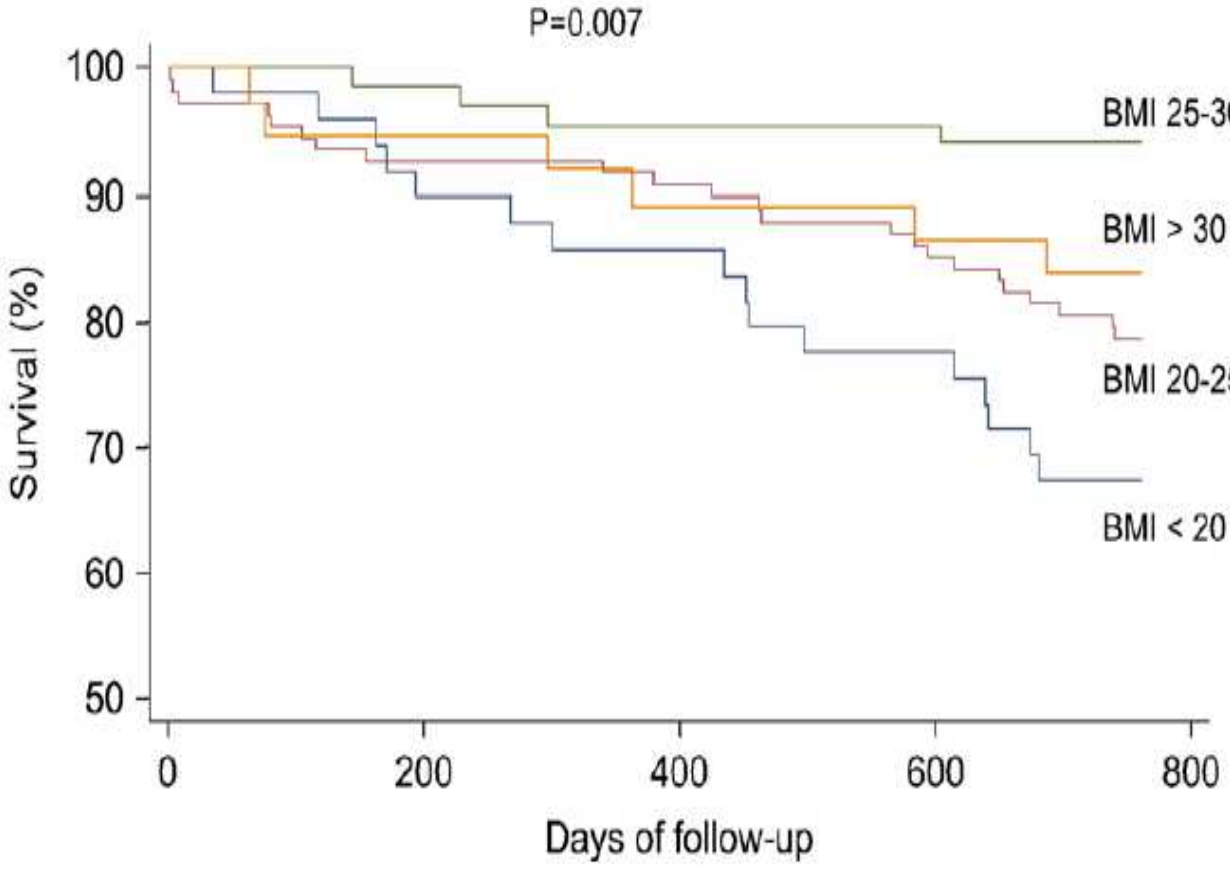


Figure 1 Survival in relation to body mass index.

	HR death
BMI 25-30 kg/m2	**1**
BMI > 30 kg/m2	**7.7**
BMI 20-25 kg/m2	**6,5**
BMI < 20 kg/m2	**13**

Les fumeurs
Hommes
FEV1 altéré
Diabétiques
Mauvaise santé perçue
Meurent plus

Hallin L et al. Respir Med 2007;101:1954-60

ALL-CAUSE MORTALITY AND MORTALITY FROM CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN RELATION TO BODY MASS INDEX IN 2,132 SUBJECTS WITH COPD IN THE COPENHAGEN CITY HEART STUDY

	Men (*n = 1,218*)			Women (*n = 914*)		
	Deaths	RR	95% CI	Deaths	RR	95% CI
All-cause mortality						
BMI, kg/m^2						
< 20	48	1.64	1.20–2.23	72	1.42	1.07–1.89
20–24.9	301	1.0	Reference	172	1.0	Reference
25–29.9	295	1.01	0.86–1.19	83	0.85	0.64–1.11
⩾ 30	87	1.06	0.83–1.35	36	1.10	0.75–1.60
Test for linear trend		NS			NS	
FEV_1%pred (per 10% decrease)		1.19	1.13–1.24		1.21	1.14–1.30

Landbo C et al. Am J Respir Care Med 1999;160:1856-61

MORTALITY IN RELATION TO BODY MASS INDEX* IN 2,132 SUBJECTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE COPENHAGEN CITY HEART STUDY BY SEVERITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

	FEV_1%pred					
	(< 50)		(50–69)		(⩾ 70)	
	RR	95% CI	RR	95% CI	RR	95% CI
All-cause mortality	275 deaths		478 deaths		341 deaths	
BMI kg/m^2						
< 20	1.63	1.15–2.31	1.24	0.89–1.72	1.50	0.99–2.28
20–24.9	1.0	Reference	1.0	Reference	1.0	Reference
25–29.9	0.66	0.49–0.87	0.96	0.77–1.19	1.24	0.98–1.56
⩾ 30	0.62	0.41–0.94	1.22	0.92–1.61	1.34	0.88–2.06
Test for linear trend	$p < 0.001$		NS		NS	

Landbo C et al. Am J Respir Care Med 1999;160:1856-61

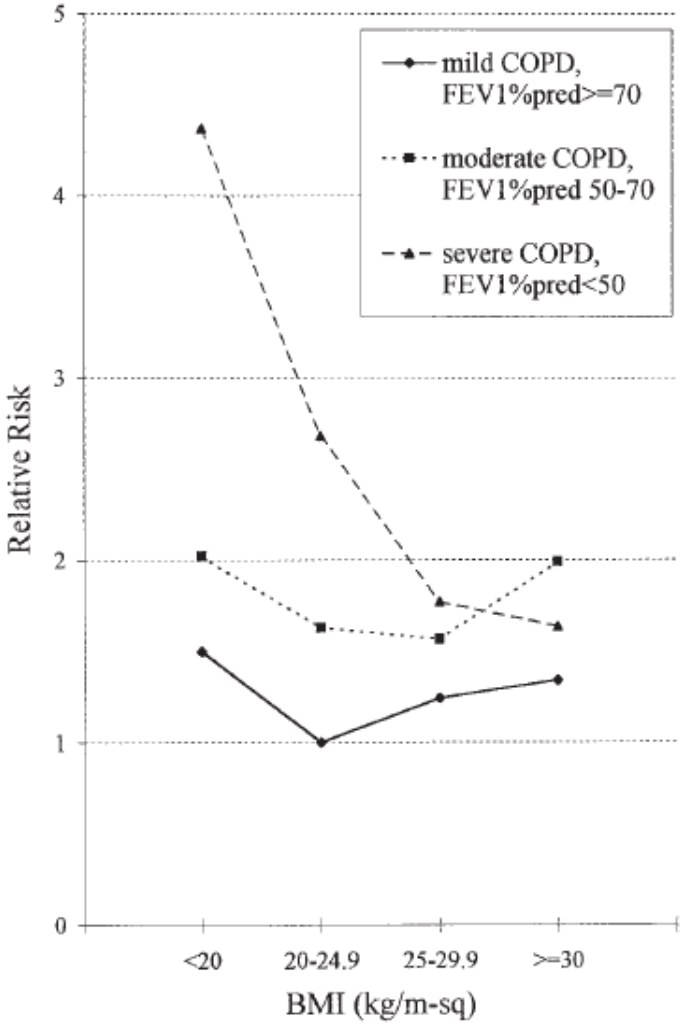


Figure 1. All-cause mortality by BMI in subjects with mild, moderate, and severe COPD. Normal-weight subjects (BMI 20 to 24.9 kg/m^2) with mild COPD were used for reference.

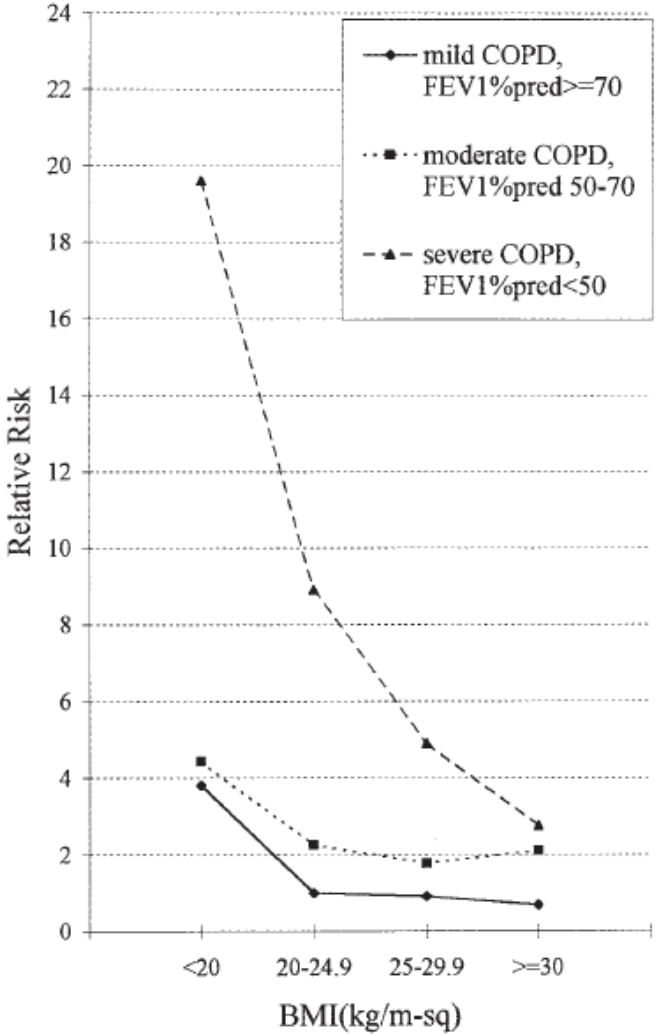


Figure 2. COPD-related mortality by BMI in subjects with mild, moderate and severe COPD. Normal-weight subjects (BMI 20 to 24.9 kg/m^2) with mild COPD were used for reference.

Landbo C et al. Am J Respir Care Med 1999;160:1856-61

Mortalité et IMC: méta-analyse

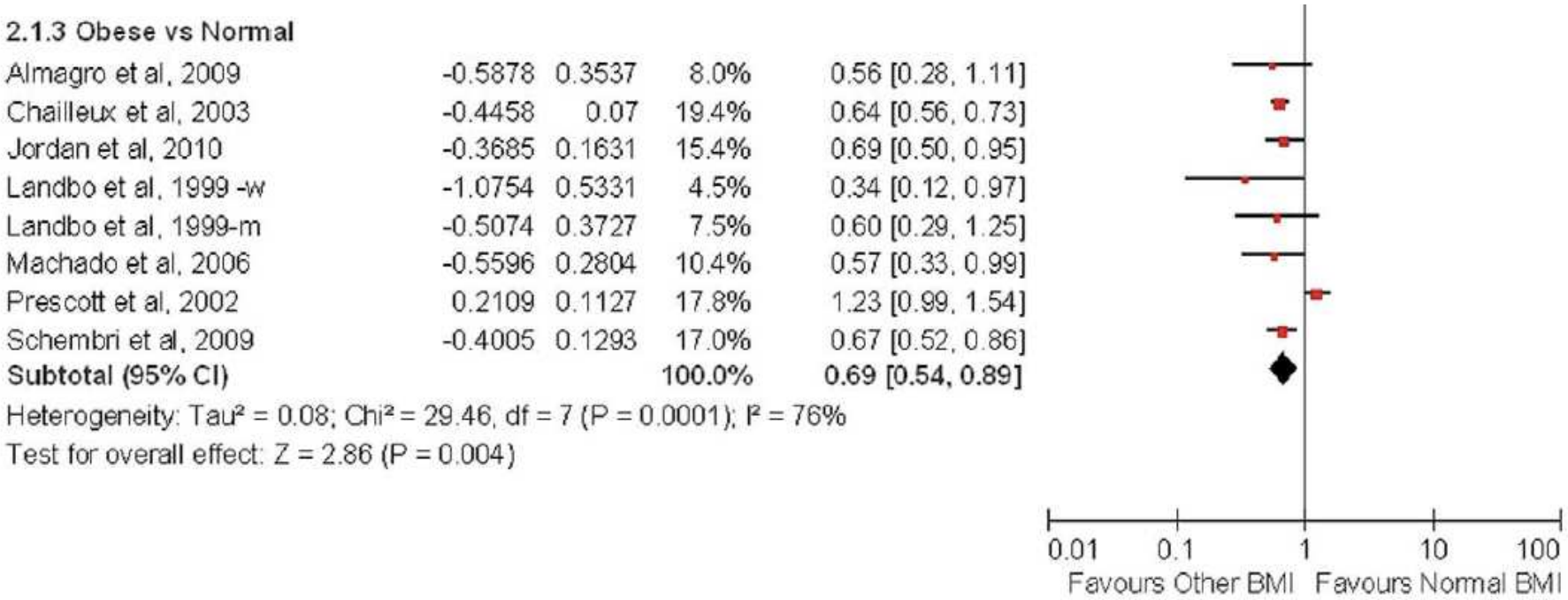


Figure 3. Hazard ratios of Mortality with Body Mass Index among Patients with Chronic Obstruct Pulmonary Disease (HR was adjusted for age, gender, FEV_1%pred, smoking and so on. The HR of Chailleux et al. was extracted by reading off survival curves).

Cao C et al. Plos One 2012;7:e43892

* Ajustement pour âge, genre, tabagisme

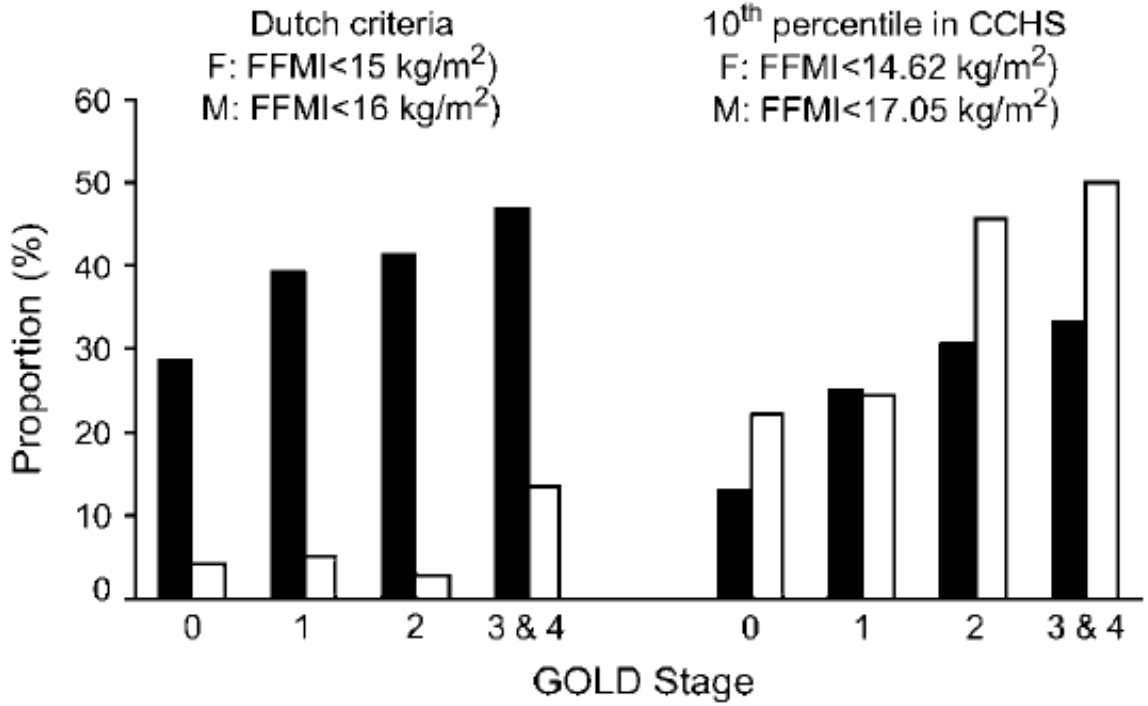


Figure 3. Proportion of patients with a low FFMI in GOLD stages for men and women with normal BMI. GOLD stages 3 and 4 have been combined because of small numbers. *White bars,* men; *black bars,* women.

Vestbo J et al. Am J Respir Care Med 2006;173:79-83

Mortalité et IMC: méta-analyse

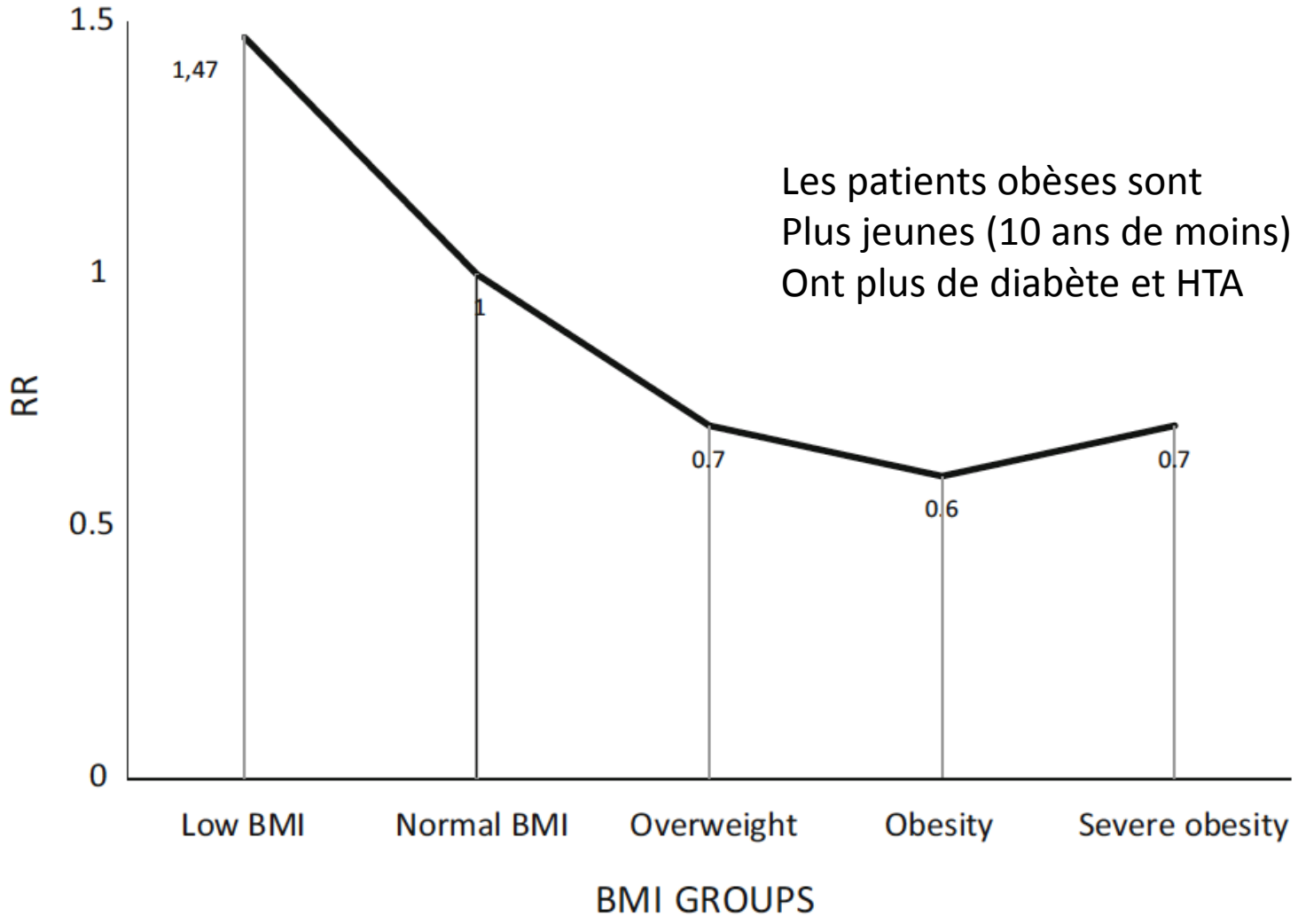
	Non ajusté		Ajusté*	
IMC	RR	95% CI	HR	95% CI
<18,5	1,34	1,01-1,78	1,48	1,26-1,75
18,5-25	Ref = 1		Ref = 1	
25-30	0,47	0,33-0,68	0,78	0,65-0,94
>30	0,59	0,38-0,91	0,69	0,54-0,89

Cao C et al. Plos One 2012;7:e43892

* Ajustement pour âge, genre, tabagisme

Mortalité par maladies coronariennes

Méta-analyse > 200 000 personnes, mortalité après IdM



Les patients obèses sont
Plus jeunes (10 ans de moins)
Ont plus de diabète et HTA

Niedzicla J et al. Eur J Epidemiol 2014; 29: 801-12

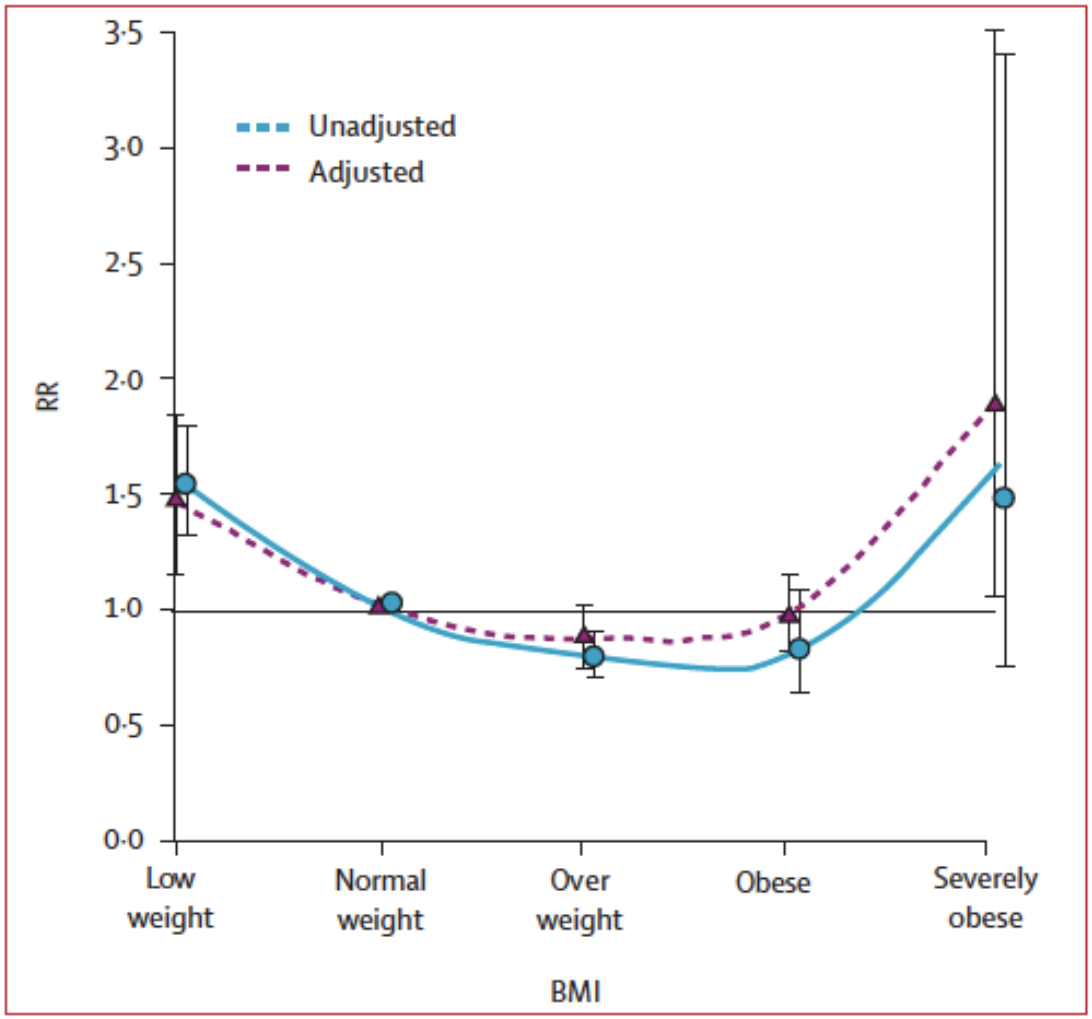
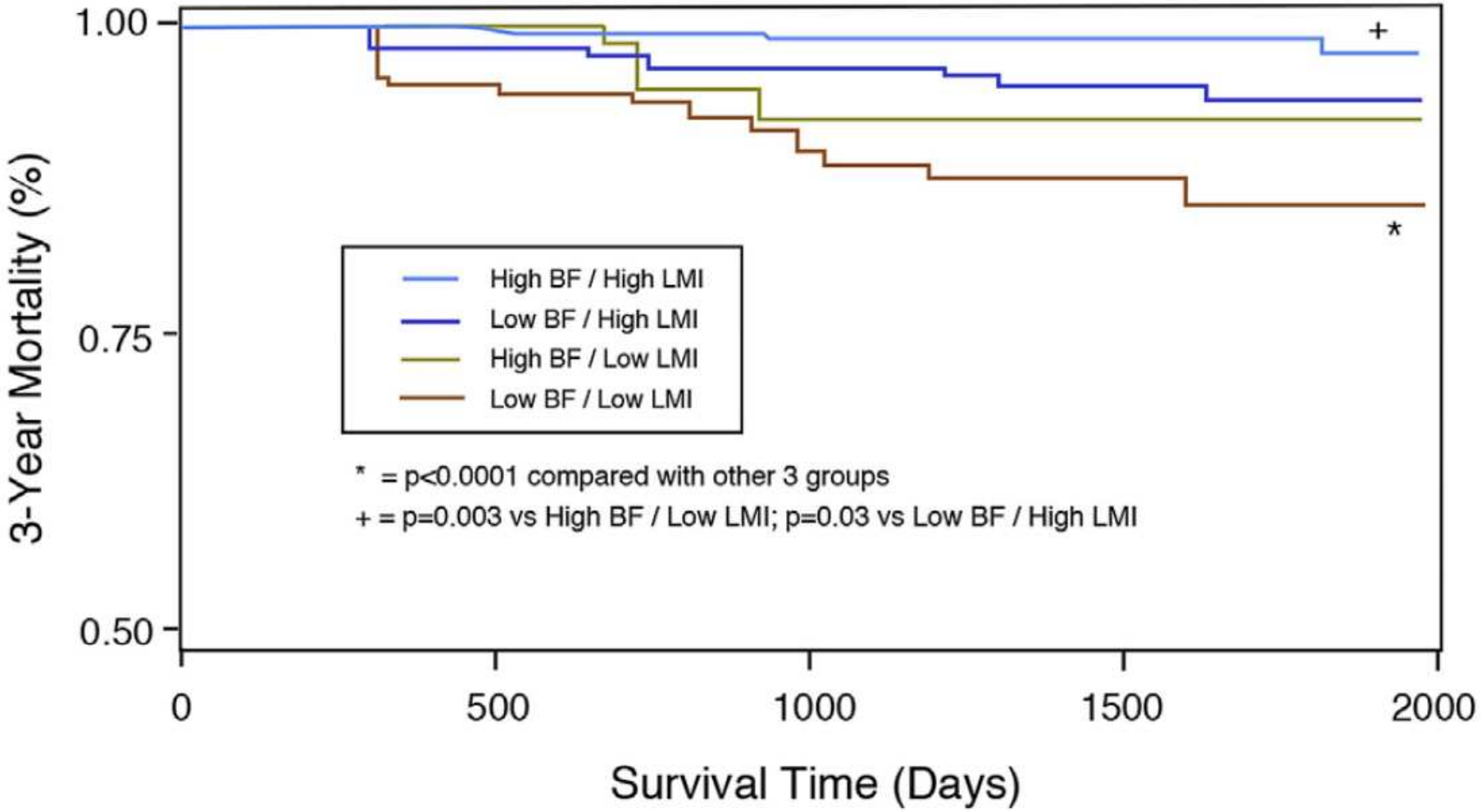


Figure 7: Unadjusted and adjusted RR for cardiovascular mortality in patients with CAD by BMI groups

es obèses sont:
Plus jeunes
Moins fumeurs
Plus diabétiques
Plus HTA
Moins de cancer

Romero-Corral A et al. Lancet 2006; 368: 666–78

Survie après IDM en fonction de la masse grasse et de la masse maigre



Lavie CJ et al J Am Coll Cardiol 2014; 63:1345-54

Qu'en est-il de la perte de poids intentionnelle?

- Peu de preuve de la réduction de mortalité par une perte de poids,
  - Par exemple Look-Ahead
  - sauf pour la chirurgie bariatrique (30-40% évènements CV et Cancers)
- Pas de preuve que la perte de poids augmente la mortalité
- Il y a des preuves que la perte de poids améliore
  - La fonction
  - Les facteurs de risque (DT2, HTA) qui au final évolueront pour leur propre compte

Table 3. – All-cause mortality in relation to weight change in 1,612 subjects with chronic obstructive pulmonary disease (COPD) and 8,812 subjects without COPD at baseline in the Copenhagen City Heart Study. Estimated rate ratios (RR) derived from proportional hazards models of Cox are stratified by sex. In addition to covariates shown, models included an interaction term sex*tobacco consumption (2*5 categories) and inhalation

	COPD FEV1/FVC<0.7	No COPD FEV1/FVC≥0.7
Subjects n	1612	8812
Deaths	1022	3287
Weight change in BMI units#		
>-3 kg·m^{-2}	1.71 (1.32–2.23)	1.63 (1.38–1.92)
-1–3 kg·m^{-2}	1.18 (1.00–1.39)	1.20 (1.08–1.32)
-1–+1 kg·m^{-2}	ref	ref
+1–3 kg·m^{-2}	1.07 (0.91–1.26)	0.99 (0.90–1.08)
>+3 kg·m^{-2}	1.26 (0.93–1.72)	1.39 (1.19–1.61)

Data are presented as RR (95% confidence interval). #: One unit body mass index (BMI) is equivalent of height in metres squared, *i.e.*, in a subject 170 cm high one unit change in BMI is equal to 3.89 kg. FEV1: forced expiratory volume in one second; FVC: forced vital capacity; ref: reference group.

Prescott E et al. Eur Respir J 2002; 20: 539–544

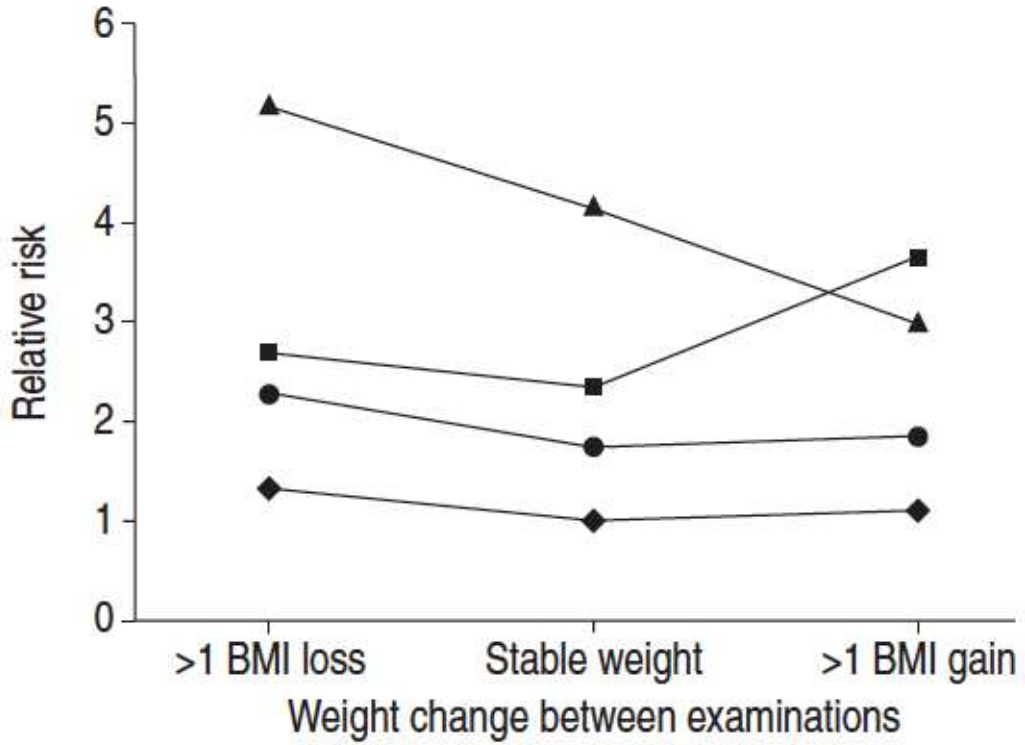


Fig. 1.–All-cause mortality by weight change in subjects with no/mild chronic obstructive pulmonary disease (COPD), moderate COPD and severe COPD. Subjects with no/mild COPD with stable weight were used for reference. ▲: severe COPD body mass index (BMI) <25; ■: severe COPD BMI >25; ●: moderate COPD; ◆: no/mild COPD.

Prescott E et al. Eur Respir J 2002; 20: 539–544

Facteurs confondants

- Gravité de la pathologie initiale (par exemple stade de BPCO)
  - Et il y a moins de « graves » dans les catégories supérieures d'IMC
- Composition corporelle
  - Sarcopénie
  - Masse grasse

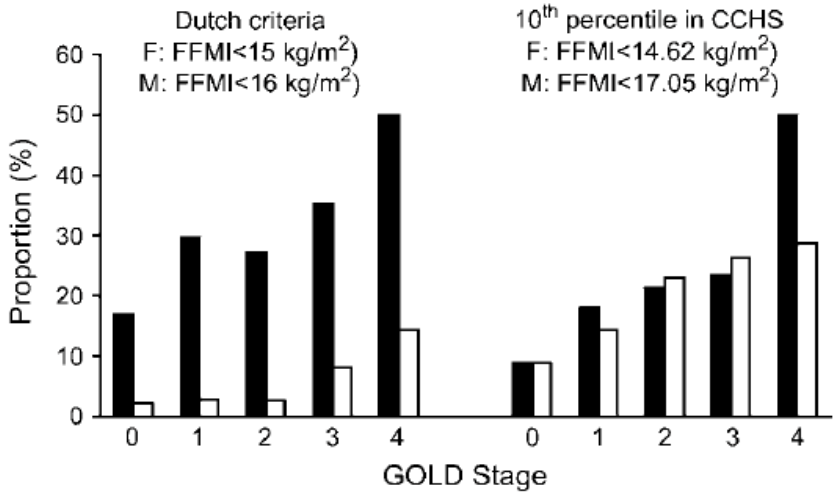


Figure 2. Proportion of patients with a low fat-free mass index (FFMI) according to GOLD stage for men (*white bars*) and women (*black bars*). CCHS = Copenhagen City Heart Study.

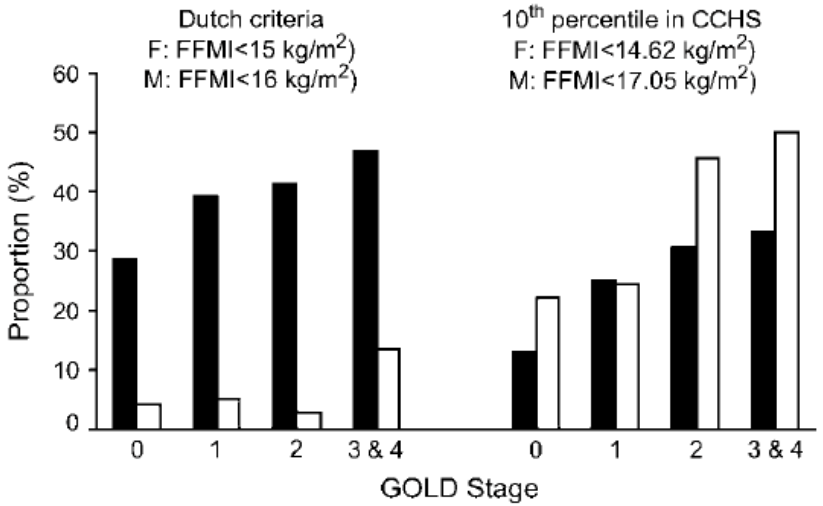


Figure 3. Proportion of patients with a low FFMI in GOLD stages for men and women with normal BMI. GOLD stages 3 and 4 have been combined because of small numbers. *White bars*, men; *black bars*, women.

Vestbo J et al. Am J Respir Care Med 2006;173:79-83

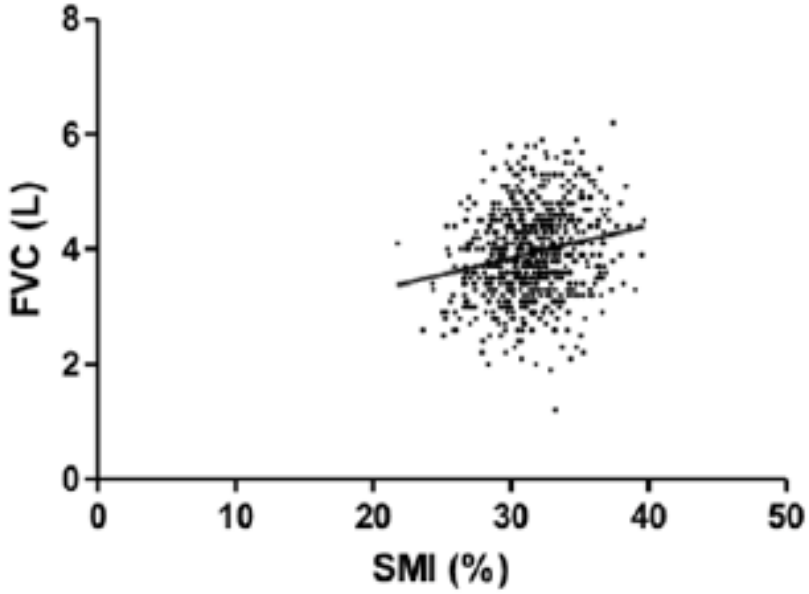
TABLE 2. MORTALITY RISK ASSOCIATED WITH LOW FAT-FREE MASS INDEX AND LOW BODY MASS INDEX

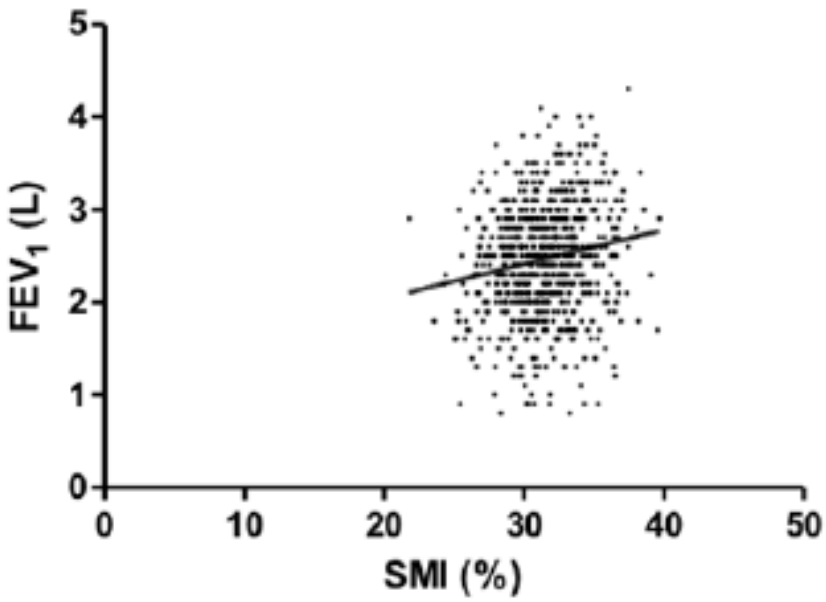
	Low FFMI†	Low BMI‡
All subjects with COPD		
Overall mortality	1.5 (1.2–1.8)	1.8 (1.3–2.7)
COPD mortality	2.4 (1.4–4.1)	3.2 (1.5–7.0)
Subjects with normal BMI*		
Overall mortality	1.3 (1.1–1.7)	—
COPD mortality	2.0 (0.9–4.5)	—

Definition of abbreviations: BMI = body mass index; COPD = chronic obstructive pulmonary disease; FFMI = fat-free mass index.

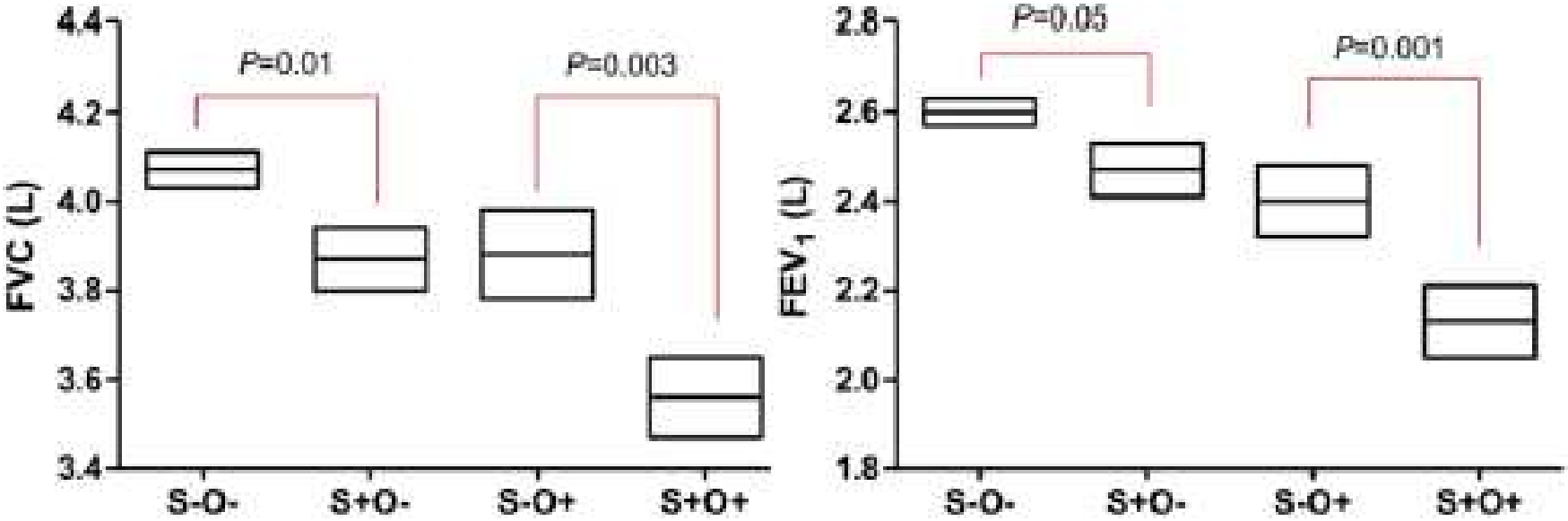
Values are expressed as hazard ratios, with 95% confidence intervals in parentheses. Hazard ratios are from a Cox regression model, with age, sex, smoking, chronic mucus hypersecretion, and FEV_1 % predicted as covariates.

Vestbo J et al. Am J Respir Care Med 2006;173:79-83





Hyeon-Kyoung K et al Plos One 2014 oct;9;e110448



Hyeon-Kyoung K et al Plos One 2014 oct;9;e110448

Table 2. Factors associated with advanced COPD (% FEV_1<80).

	Adjusted OR (95% CI)	7)	*P*
	Model 1	**Model 2**	
Age, mean±SD	1.03 (1.00–1.06)*	1.18 (1.11–1.26)*	0.204
Height (cm)	0.95 (0.90–1.01)	0.73 (0.65–0.81)*	0.909
Weight (kg)	1.09 (1.03–1.14)*	1.07 (1.01–1.13)*	0.275
Obesity	2.56 (1.19–5.50)*	2.48 (1.01–6.13)*	0.436
Sarcopenia	2.54 (1.57–4.09)*	1.61 (0.81–3.19)	0.005
Curr smk (%)	1.03 (0.67–1.58)	2.07 (1.08–3.98)*	0.417
Smk amt (PY)	_	_	0.946

*indicates significance.
Model 1: variables include age, height, weight, obesity, sarcopenia, and smoking status.
Model 2: variables include FVC (L) in addition to variables included in Model 1.
FEV_1 (% predicted) was not included in the multivariable analysis due to the risk of co-linearity.

Hyeon-Kyoung K et al Plos One 2014 oct;9;e110448

Table 3. Multivariate analysis for factors contributing to subjective exercise limitation.

	Adjusted OR	*P*
N	_	
Age, year, mean	1.05 (1.00–1.09)	0.05
Height. Cm	0.88 (0.78–0.98)	0.03
Weight, kg	_	
WC. Cm	_	
BMI. kg/m^2	_	
Obese, N (%)	**0.40 (0.17–0.95)**	**0.04**
SMI, %	_	
Sarcopenia, N (%)	**2.10 (1.01–4.37)**	**0.04**
Current smoker, N (%)	_	
Smoking amount, PY	_	
Hb, g/dL	0.90 (0.69–1.17)	0.43

Hyeon-Kyoung K et al Plos One 2014 oct;9;e110448

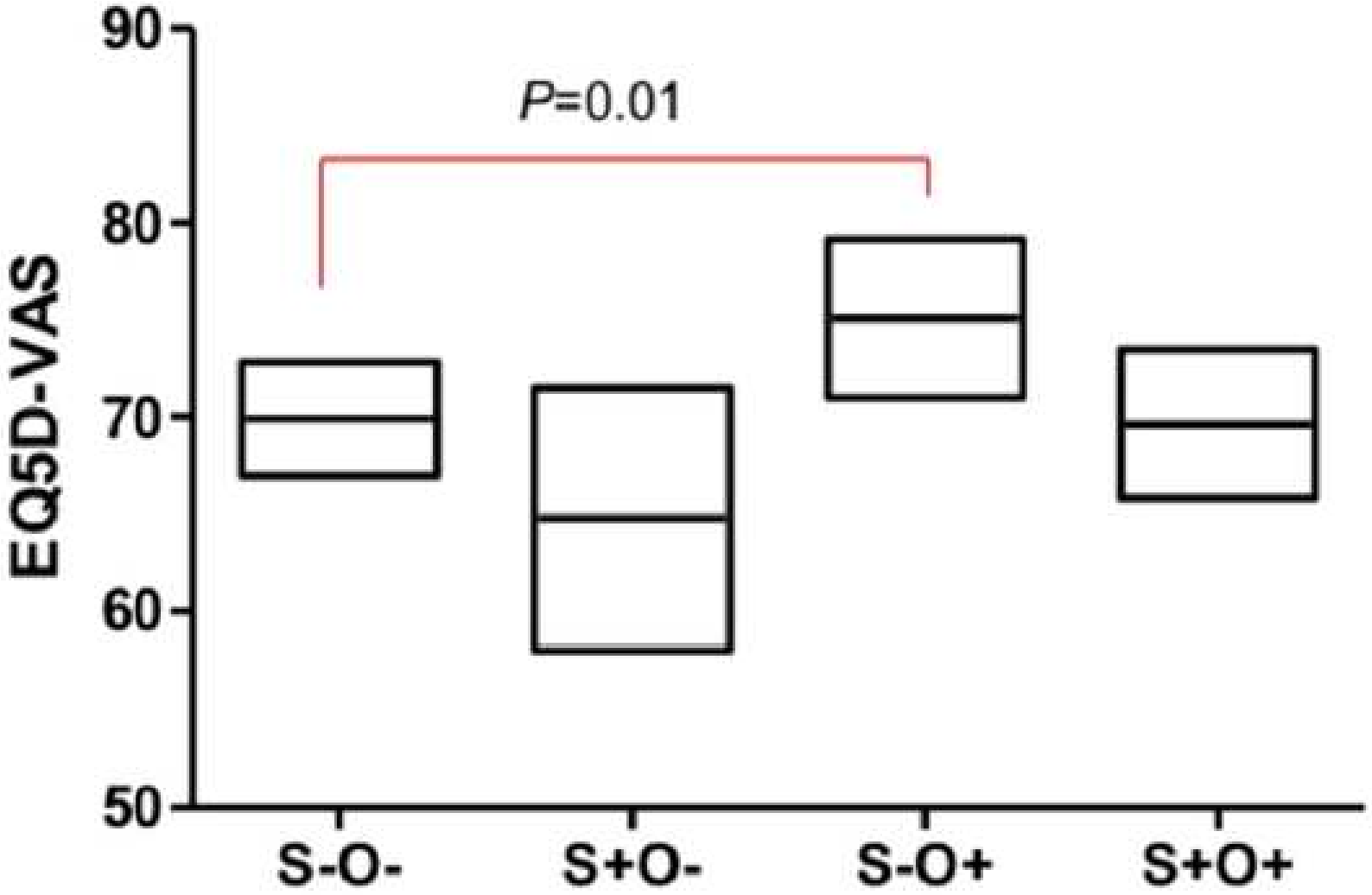


Figure 3. Comparison of quality of life according to the presence of sarcopenia and obesity (mean, 95% CI). Legend:

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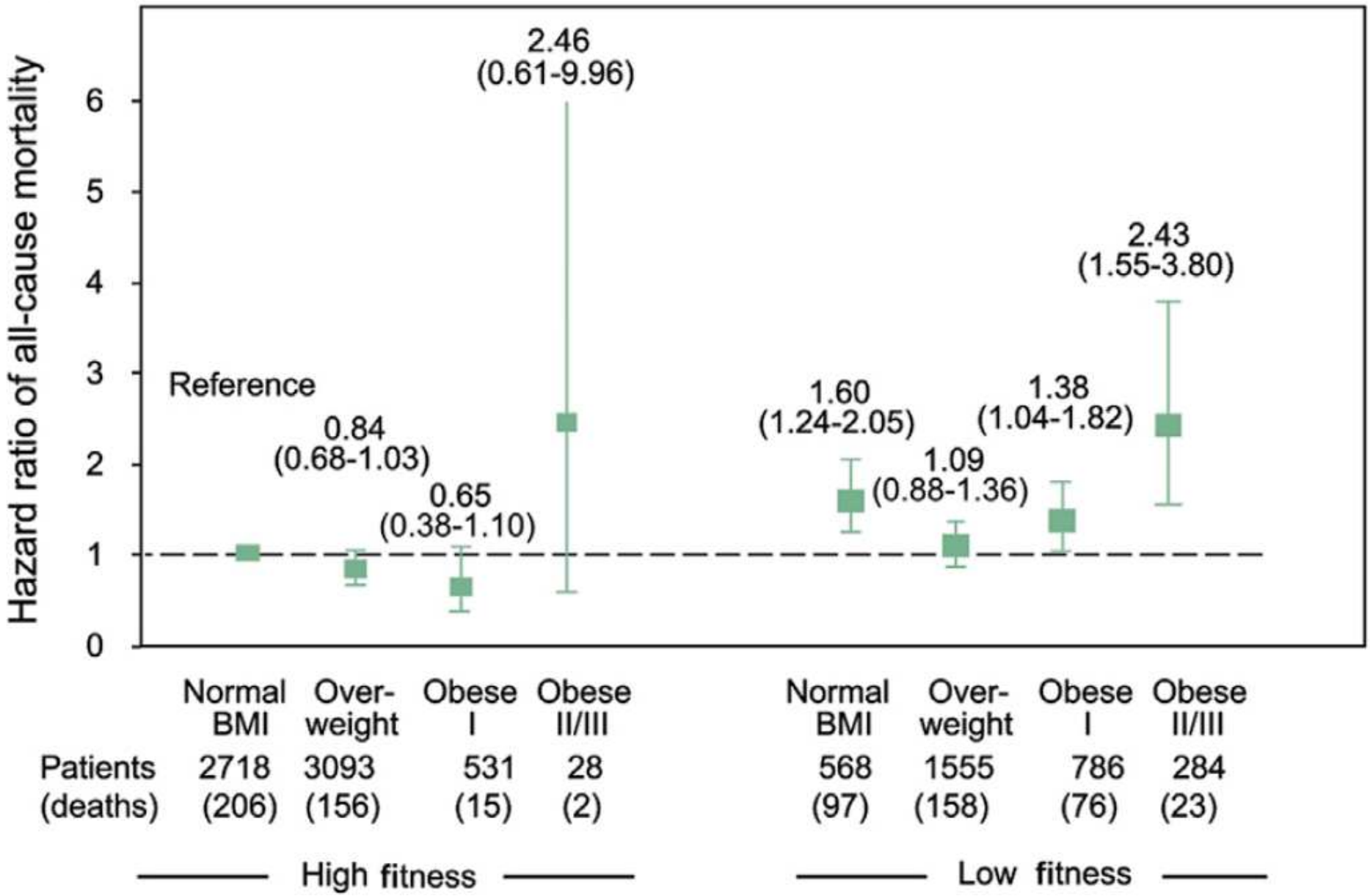
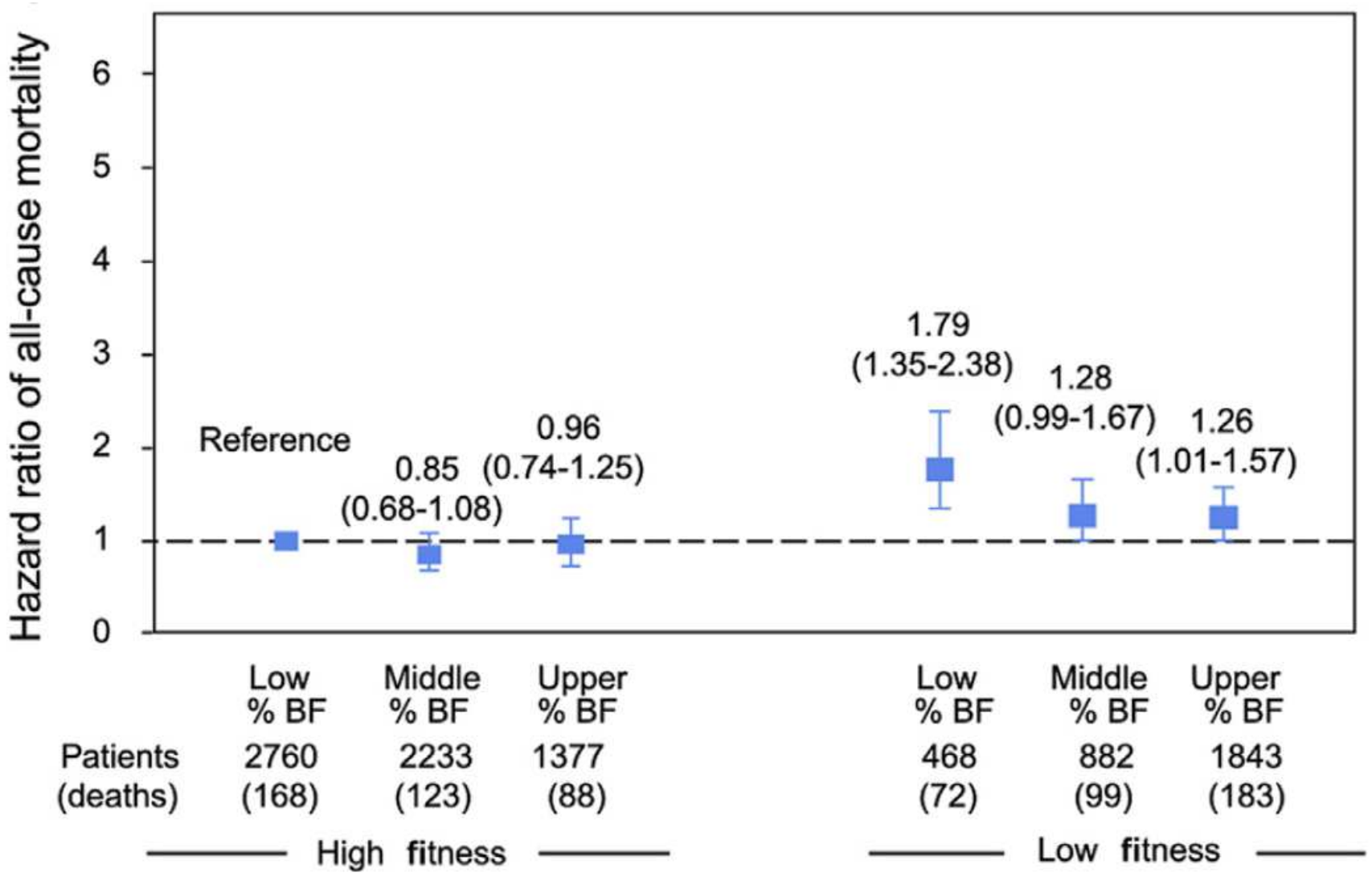


Lavie CJ et al J Am Coll Cardiol 2014; 63:1345-54



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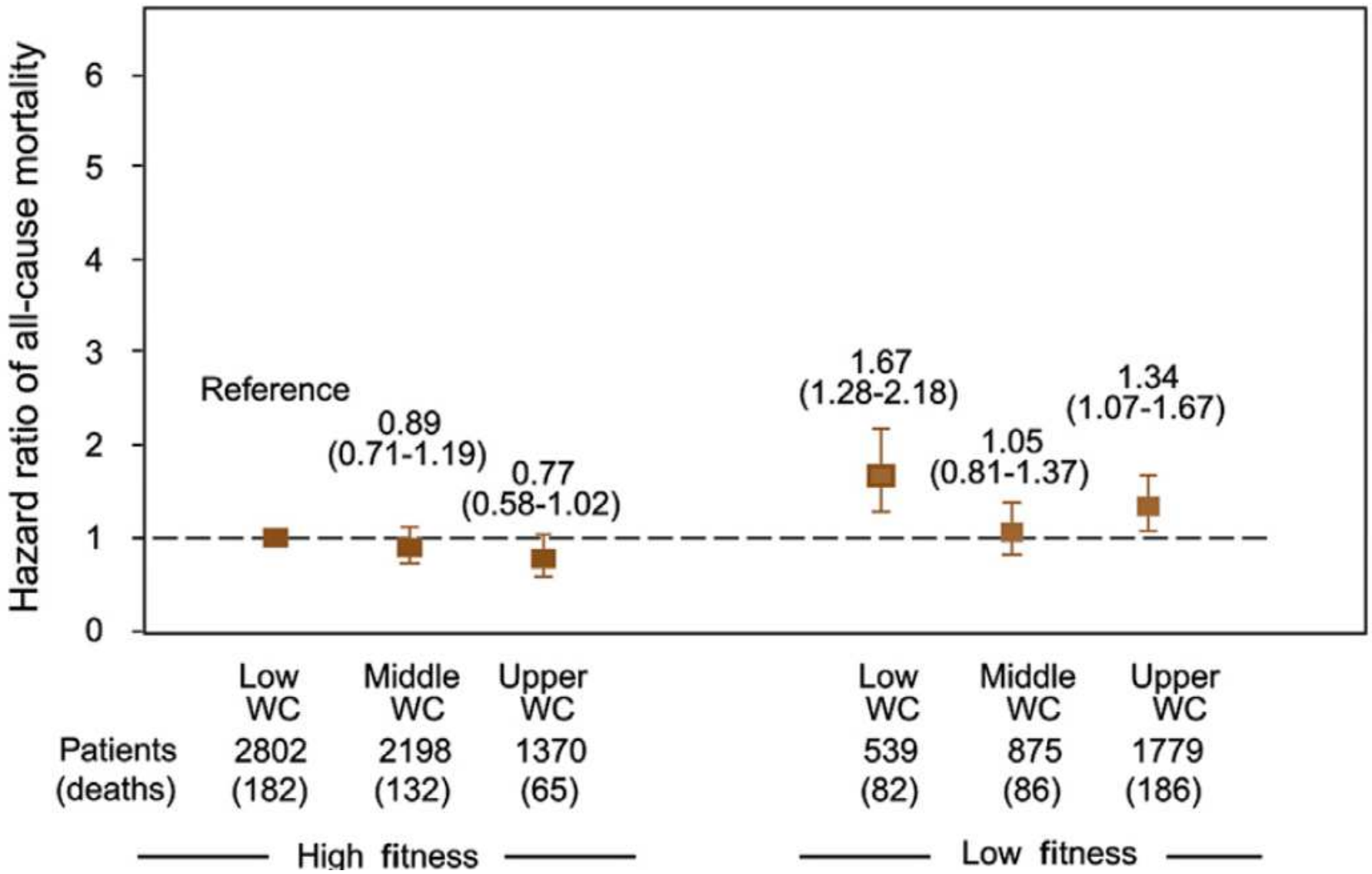

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Facteurs confondants

- Gravité de la pathologie initiale (par exemple stade de BPCO)
  - Et il y a moins de « graves » dans les catégories supérieures d'IMC
- Composition corporelle
  - Sarcopénie
  - Masse grasse
- « Fitness »

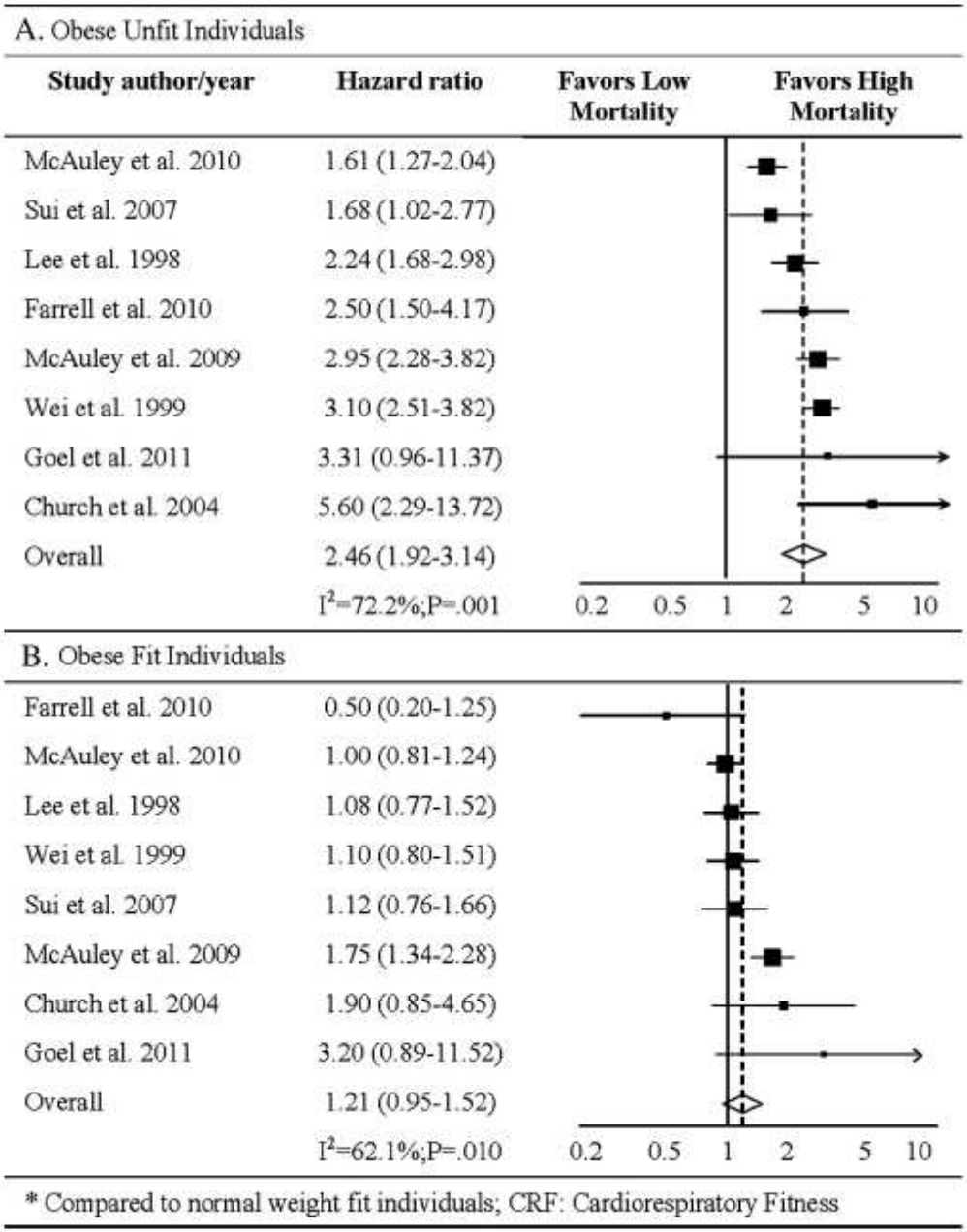

Fig. 4 – Meta-analysis of all-cause mortality on obese individuals.

Méta-analyse 10 études fitness ou BMI sur mortalité

Age est un facteur confondant+++

RR

si maladie chronique	1,81 (1,41-2,32)
Sans mal chronique	1,03 (0,9-1,19)

Barry vWJ et al. Prog Cardiovasc Dis 2014; 56: 382-90

Facteurs confondants

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- Composition corporelle
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  - Fitness
  - Masse grasse
- « Fitness »
- Facteurs « invisibles » ou « non vus »

Table 2. Association between peripheral artery disease and clinical parameters

	Patients with PAD	Patients without PAD	*P* value
No. of patients	27	60	
Age (yrs)	68.1 ± 11.6	73.6 ± 11.5	0.001
ABI	0.8 ± 0.1	1.1 ± 0.1	0.01
BMI (kg/m²)	25.5 ± 6.2	31.1 ± 7.3	0.001
AC (cm)	97.7 ± 18.3	111.7 ± 17.5	0.001
FEV1%	34 ± 8	45 ± 16	0.01

Blum A et al IMAJ 2011;13:672-5

Facteurs confondants

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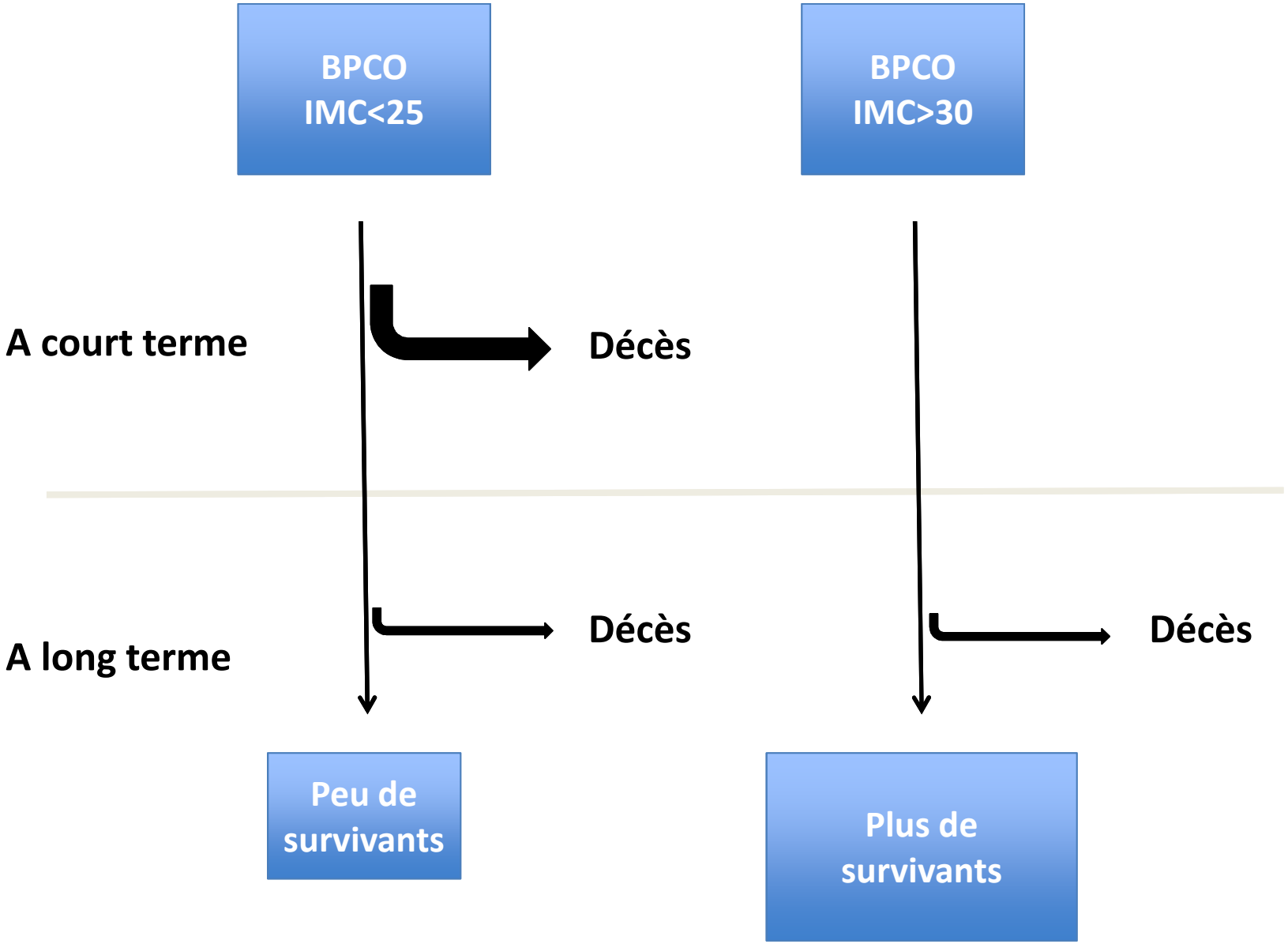
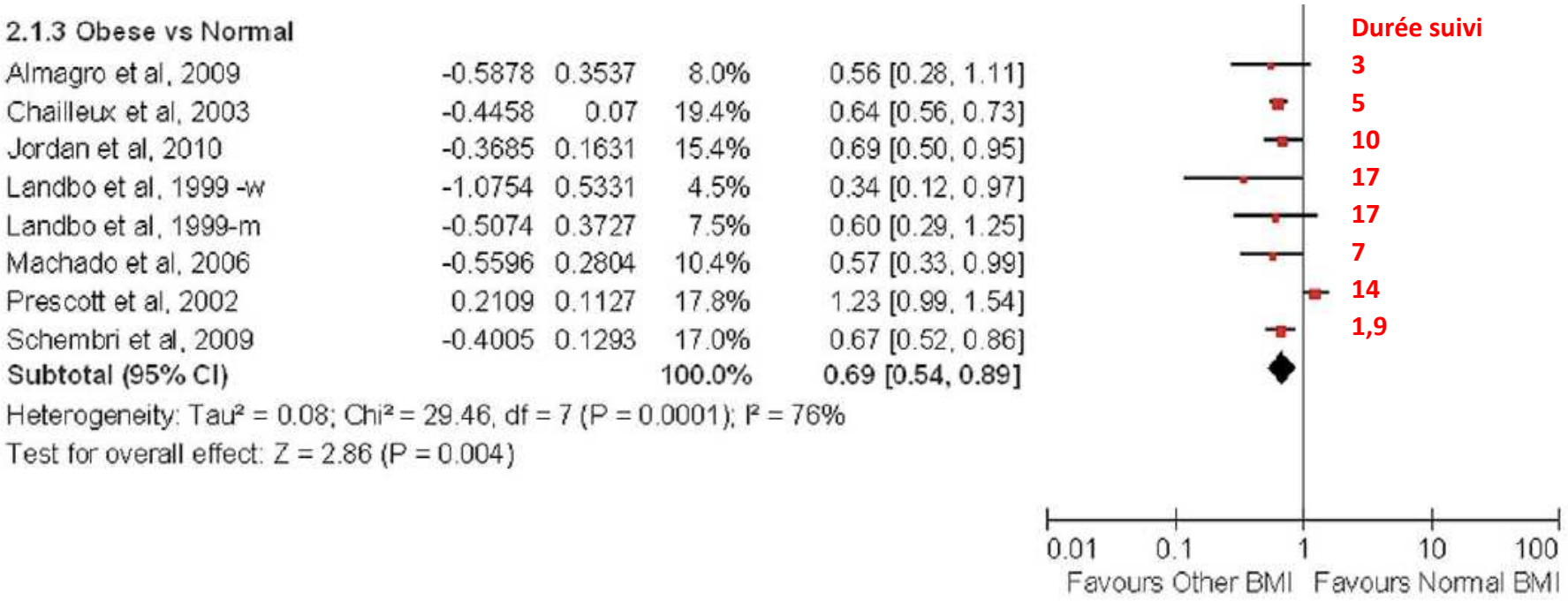
- Composition corporelle
  - Sarcopénie
  - Fitness
  - Masse grasse
- « Fitness »
- Facteurs « invisibles » ou « non vus »
- Biais de « survie »


BPCO
IMC<25
BPCO
IMC>30
A court terme
Décès
A long terme
Décès
Décès
Peu de
survivants
Plus de
survivants

Mortalité et IMC: méta-analyse



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Cao C et al. Plos One 2012;7:e43892

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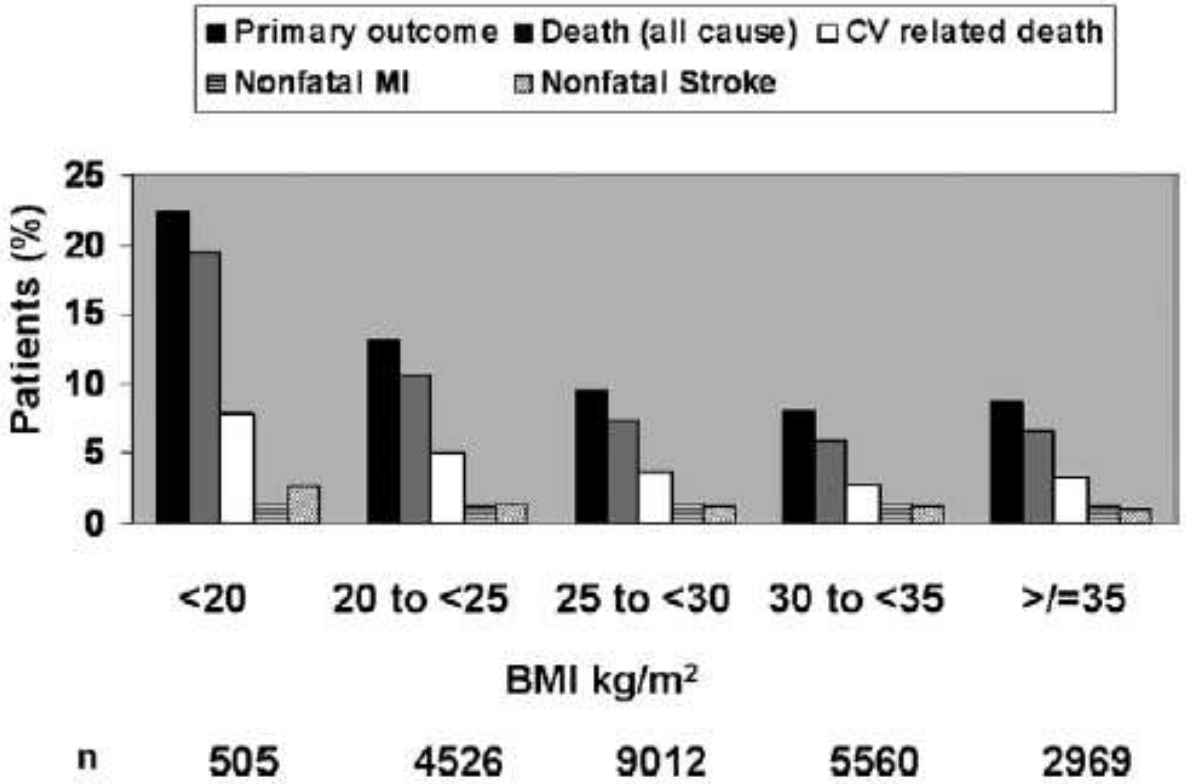


Figure 2 Percentage of patients to reach primary outcome, all-cause mortality, nonfatal stroke, and nonfatal myocardial infarction according to BMI category. BMI = body mass index; MI = myocardial infarction.

Les obèses sont:

-plus jeunes

-moins bien contrôlés TA

-moins fumeurs

-moins atcd cancer

-moins atcd évènement CV

-+diabète

Ce ne sont pas les « mêmes évènements » et l'ajustement pose problème

Uretsky S et al. The American Journal of Medicine 2007 120, 863-70

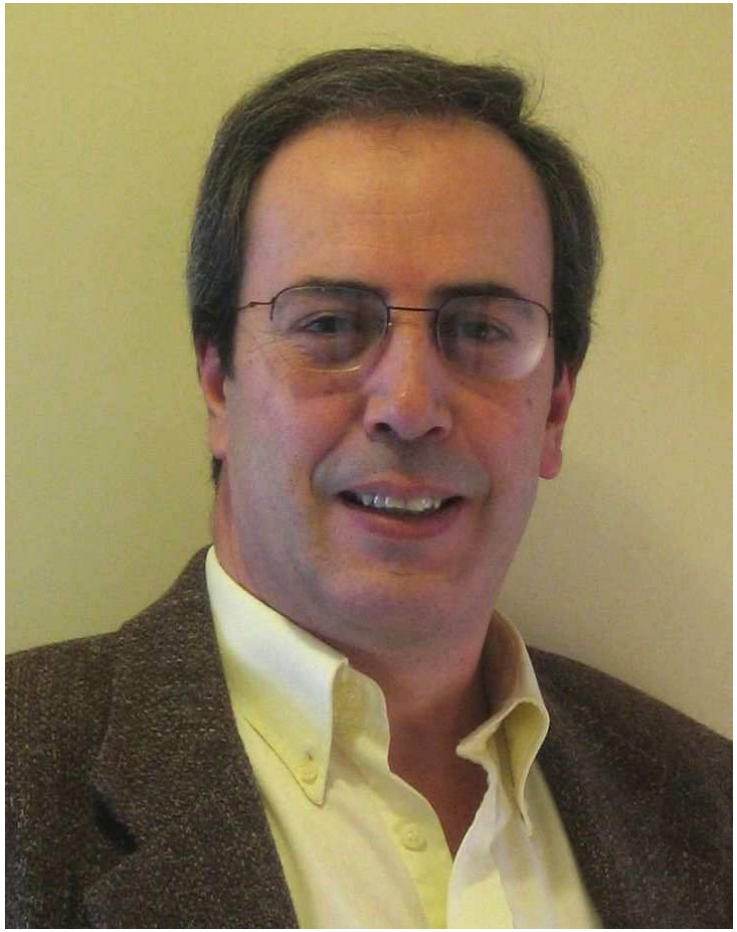
Phénotypage ou médecine personnalisée

Table 2	Potential Reasons for the Obesity Paradox in Cardiovascular Diseases
1.	Nonpurposeful weight loss
2.	Younger age at presentation
3.	Lower prevalence of smoking
4.	Greater metabolic reserves
5.	Less cachexia
6.	Lower atrial natriuretic peptides
7.	Attenuated response to renin-angiotensin-aldosterone system
8.	High blood pressure, allowing for more cardiac medications
9.	Differing etiology, associated with a better prognosis
10.	Increased muscle mass and muscular strength
11.	Implications regarding cardiorespiratory fitness
12.	Unmeasured confounding factors

Lavie CJ et al J Am Coll Cardiol 2014; 63:1345-54

The article also discusses the suggestion that greater emphasis should be placed on improving fitness rather than weight loss *per se* in the primary and secondary prevention of cardiovascular diseases, at least in patients with overweight and class I obesity (BMI 30–35 kg/m^2).

Lavie, C. J. *et al. Nat. Rev. Endocrinol.* advance online publication 30 September 2014; doi:10.1038/nrendo.2014.165



Danger

Se faire imposer ce avec quoi nous ne sommes pas d'accord
Très peu d'étude d'envergure
Faut-il en faire?

Croyances

« Retournez au texte, vous gagnerez du temps » (*Logos,* JP Vernant)

Chemin

« ce n'est pas le chemin qui est difficile, difficile est le chemin » (Antonio Machado)

Professeur Alain DECCACHE
Professeur émérite, UC Louvain

- Très peu d’études avec perte de poids volontaires
- Intérêt de lancer ces études en Europe pour la reconnaissance des compétences professionnelles (hors chirurgie)

Search	Add to builder	Query	Items found	Time
#27	Add	Search **(((((intentional weight loss[Title/Abstract]) OR weight los*[Title/Abstract])) AND obes*[Title/Abstract]) AND chronic obstructive pulmonary disease[Title]) AND ((mortality[Title/Abstract]) OR death[Title/Abstract])**	4	02:12:50