

Place de la nutrition dans la prise en charge des insuffisants respiratoire chroniques

Conférence Xavier Leverve



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Biology and Medicine



CHU Grenoble
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Alpes



JFN 2013, Bordeaux



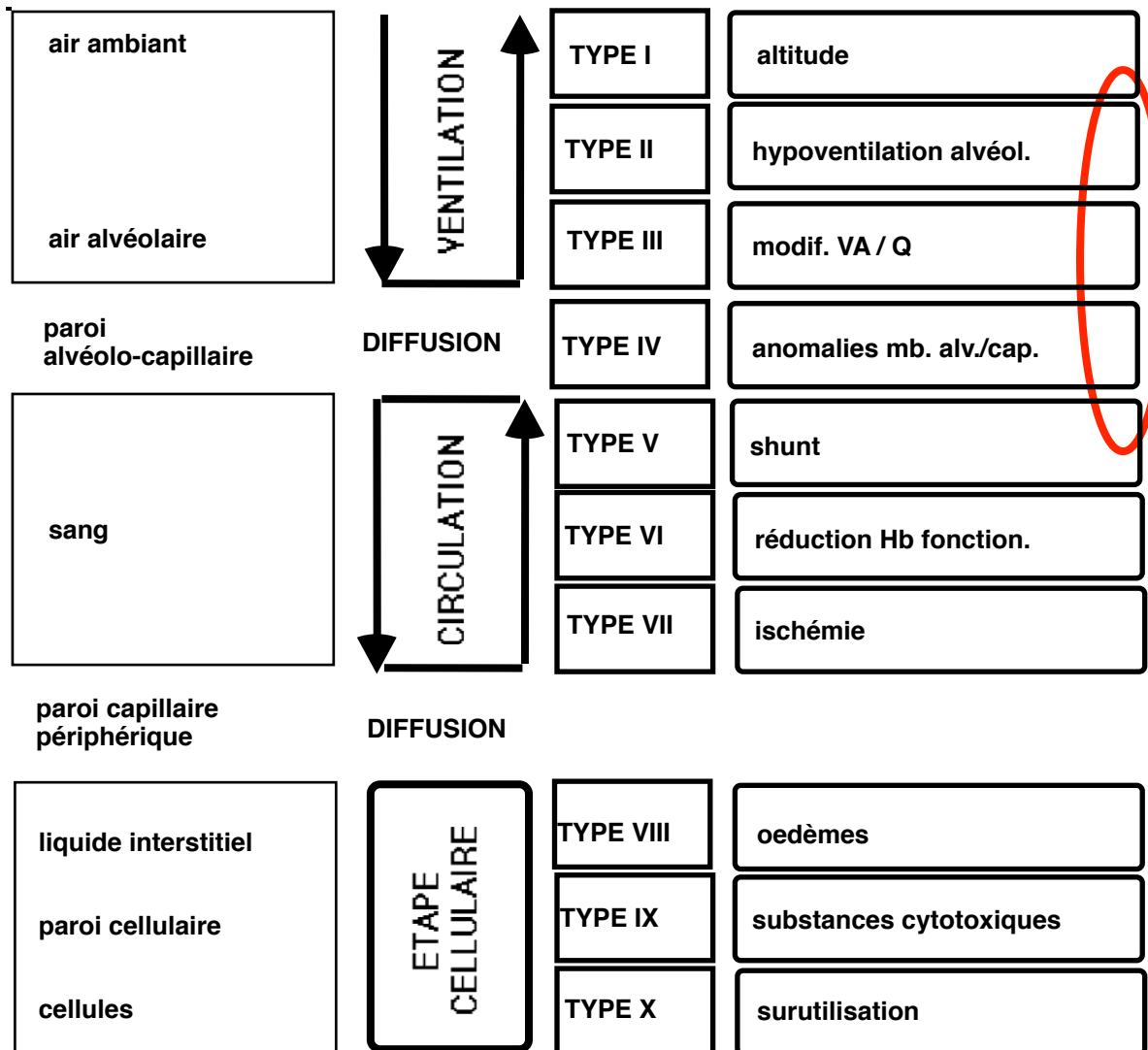
Déclaration d'intérêts en rapport avec la présentation, 5 dernières années

- **Activités de conseil, fonctions de gouvernance, rédaction de rapports**
Oui *Société : Nutricia*
- **Essais cliniques, autres travaux, communications de promotion**
Non *Société: Nutricia*
- **Intérêts financiers (actions, obligations)**
Non
- **Liens avec des personnes ayant des intérêts financiers ou impliquées dans la gouvernance**
Non
- **Réception de dons sur une association dont je suis responsable**
Oui *Sociétés : Nutricia, Astra Zeneca*
- **Détention d'un brevet, rédaction d'un ouvrage utilisé par l'industrie**
Non

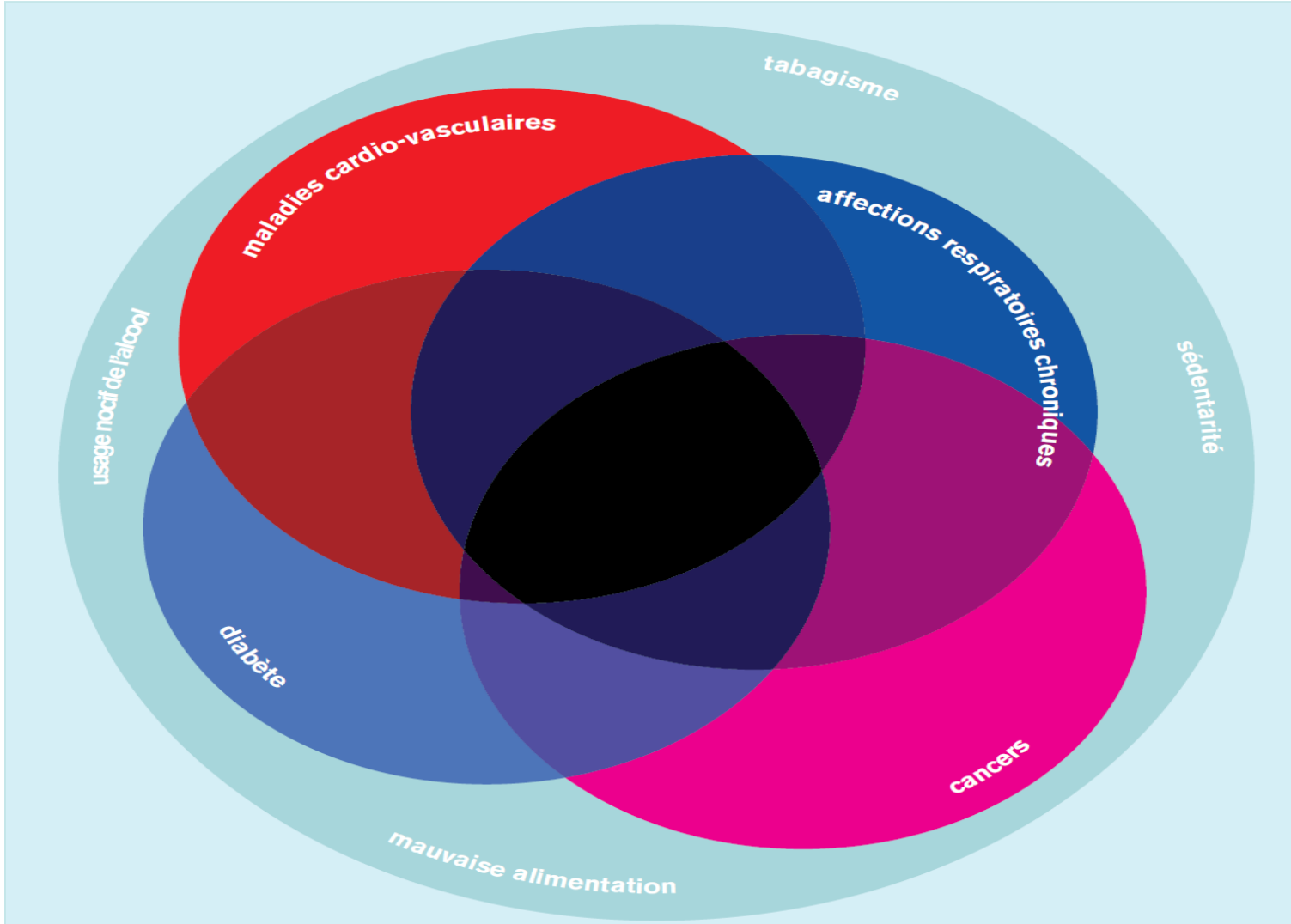


Comprendre et Agir

- **Poids de l'insuffisance respiratoire chronique**
- **Hypoxémie, Hypoxie, Oxygène conformité**
- **Evaluer**
- **Agir**
 - Intervention nutritionnelle
 - Réhabilitation nutritionnelle
- **Quelles leçons ?**



Insuffisance Respiratoire Chronique



Poids de l'insuffisance respiratoire chronique

Mannino DM, Buist AS. Lancet 2007;370:765

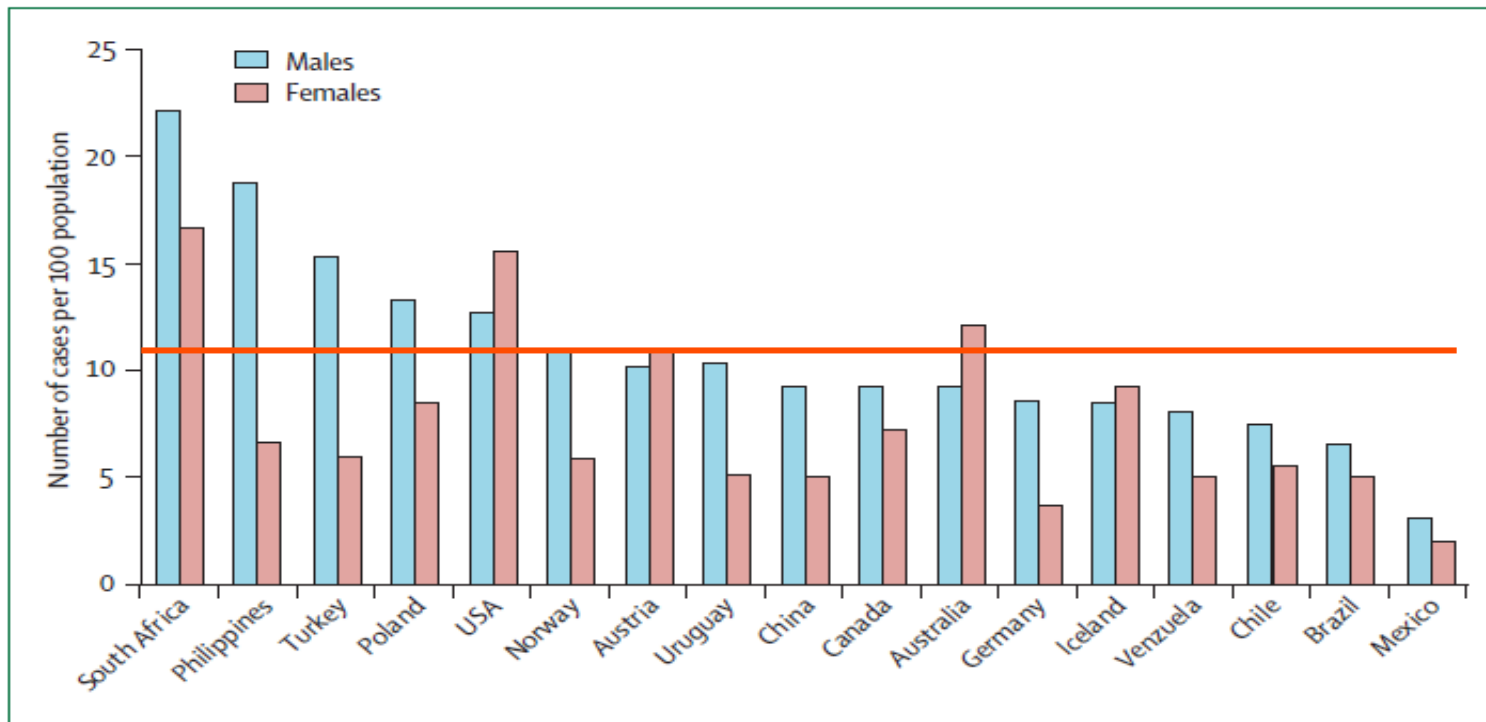


Figure 4: Estimated prevalence of GOLD stage 2 or higher COPD

Data taken from the PLATINO study⁶⁰ and the BOLD project.²⁶ Estimates are for small regions of the listed countries and do not necessarily represent national prevalence estimates.

Table 1. Top 10 Causes of Death, Years of Life Lost from Premature Death, Years Lived with Disability, and Disability-Adjusted Life-Years (DALYs) in the United States, 2010.

Cause of Death	Deaths (N = 2664)		Years of Life Lost (N = 45,145)		Years Lived with Disability (N = 36,689)		DALYs (N = 81,835)	
	Rank	No. (%)	Rank	No. (%)	Rank	No. (%)	Rank	No. (%)
		<i>in thousands</i>		<i>in thousands</i>		<i>in thousands</i>		<i>in thousands</i>
Ischemic heart disease	1	563 (21.1)	1	7165 (15.9)	16	685 (1.9)	1	7850 (9.6)
Chronic obstructive pulmonary disease	5	154 (5.8)	4	1913 (4.2)	6	1745 (4.8)	2	3659 (4.5)
Low back pain	—	—	—	—	1	3181 (8.7)	3	3181 (3.9)
Cancer of the trachea, bronchus, or lung	3	163 (6.1)	2	2988 (6.6)	73	45 (0.1)	4	3033 (3.7)
Major depressive disorder	—	—	—	—	2	3049 (8.3)	5	3049 (3.7)
Other musculoskeletal disorders	36	14 (0.5)	37	254 (0.6)	3	2603 (7.1)	6	2857 (3.5)
Stroke	2	172 (6.5)	3	1945 (4.3)	17	629 (1.7)	7	2574 (3.1)
Diabetes mellitus	6	86 (3.2)	7	1392 (3.1)	8	1165 (3.2)	8	2557 (3.1)
Road-traffic injury	12	44 (1.7)	5	1873 (4.1)	26	373 (1.0)	9	2246 (2.7)
Drug-use disorders	27	19 (0.7)	15	841 (1.9)	7	1295 (3.5)	10	2136 (2.6)

N Engl J Med 2013;369:448-57

Poids de l'insuffisance respiratoire chronique

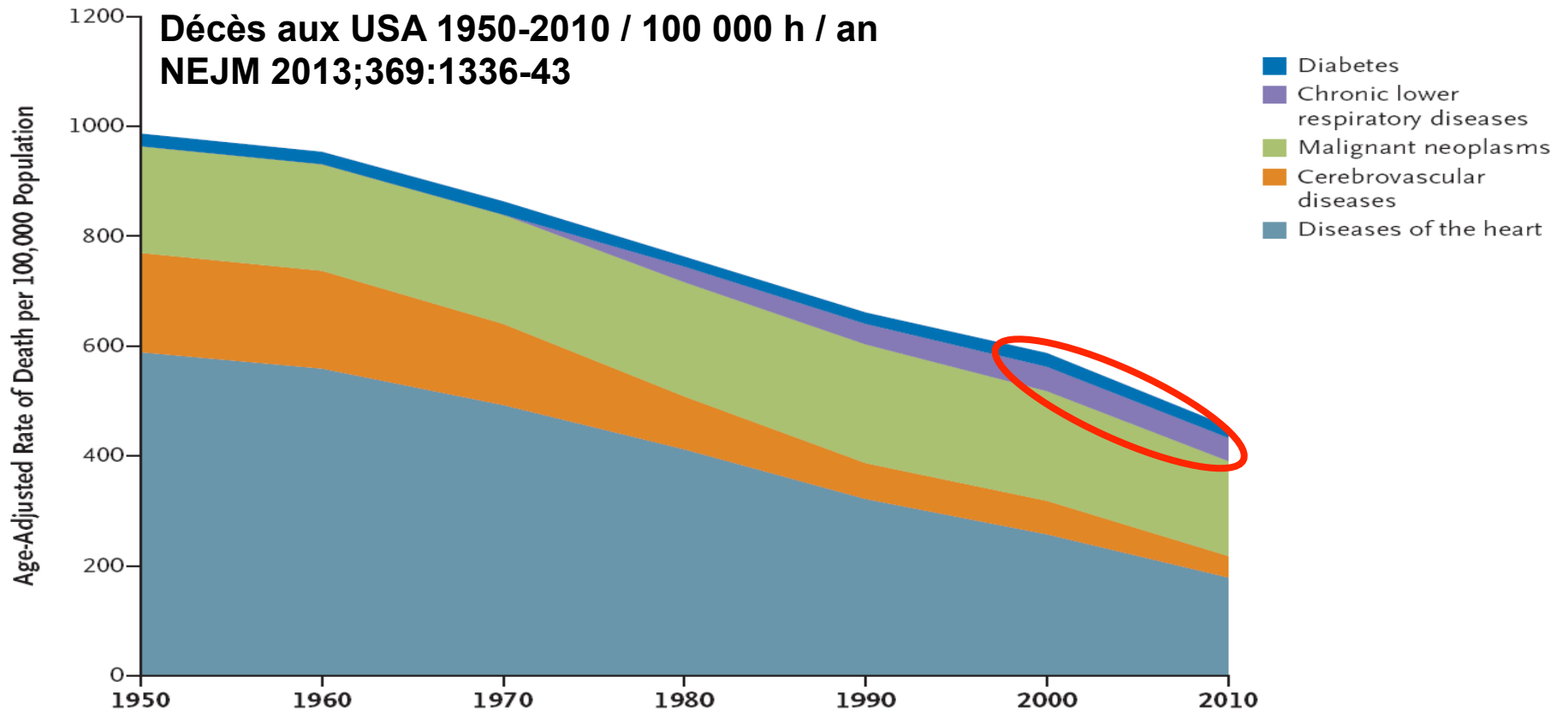
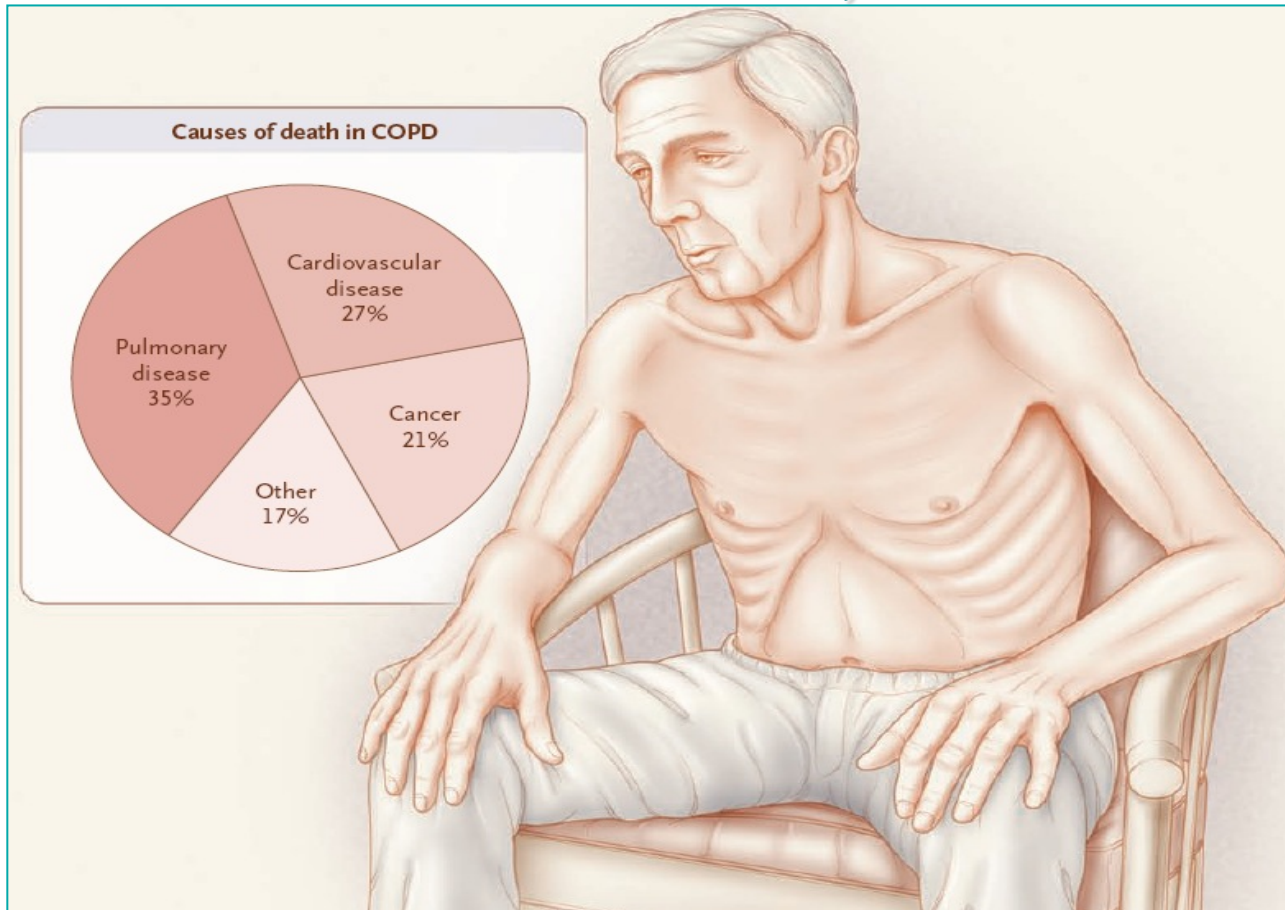


Figure 4. Declines in Rates of Death from Major Noncommunicable Diseases in the United States, 1950 to 2010.

Adapted from the National Center for Health Statistics, Centers for Disease Control and Prevention.¹⁸

Poids de l'insuffisance respiratoire chronique

étude Torch - NEJM 2007;356:775-89



Hypoxémie, Hypoxie, Oxygène conformité

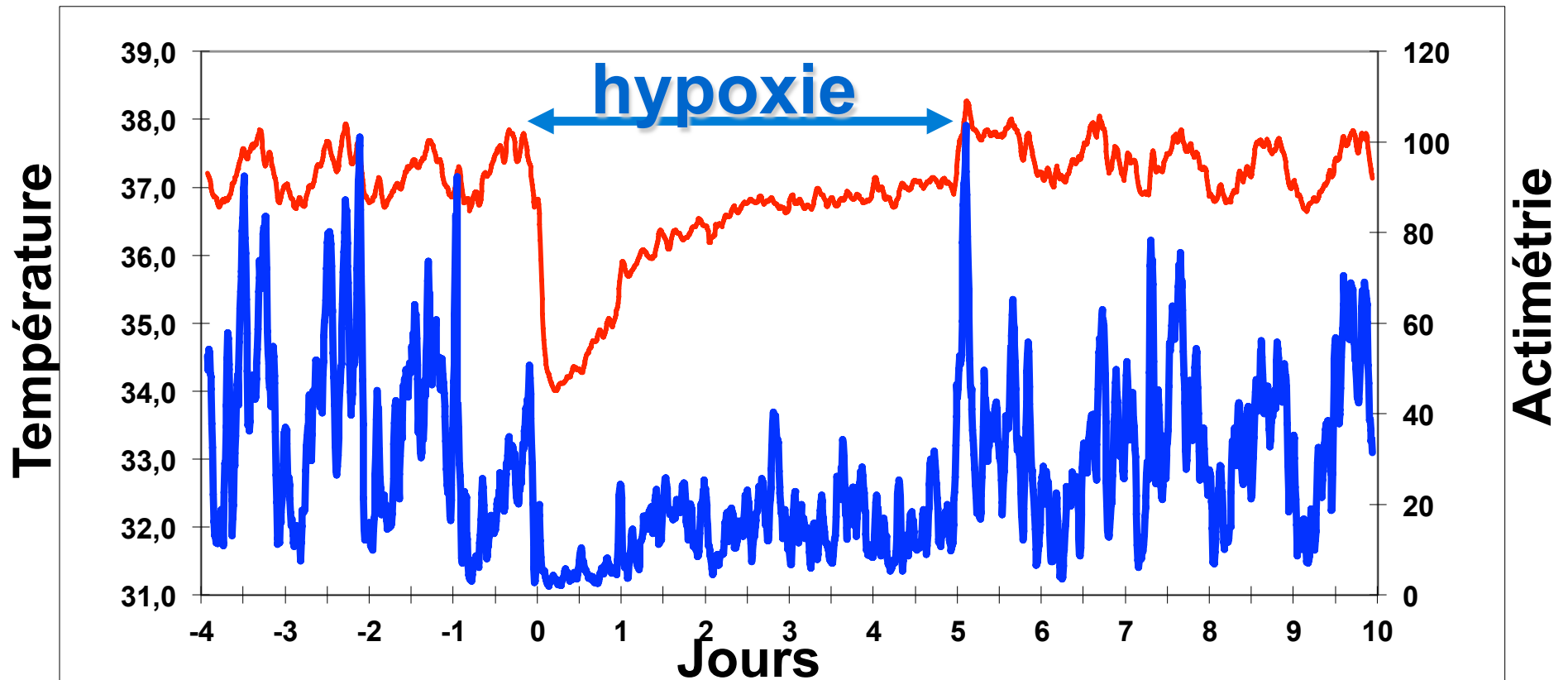
Hypoxémie Aiguë

- 26 % en Médecine en CHU avec SaO₂ < 90% à l'entrée
- RR de décès de 3,3 (1,4-8,2) dans les 4 à 7 mois
Bowton et al. Am J Med 1994; 97: 38-46

Hypoxémie Chronique

- survie à 3 ans de 35% versus 75% avec OLD 24 h/24 h
Lancet 1981; 1: 681 & Ann Intern Med 1980; 93: 391
- 26 140 patients traités OLD, suivis 10 ans, médiane 1 à 4 ans
Chailleux et al. Chest 1996; 109:741-9
- 100 000 patients sous OLD à domicile en France

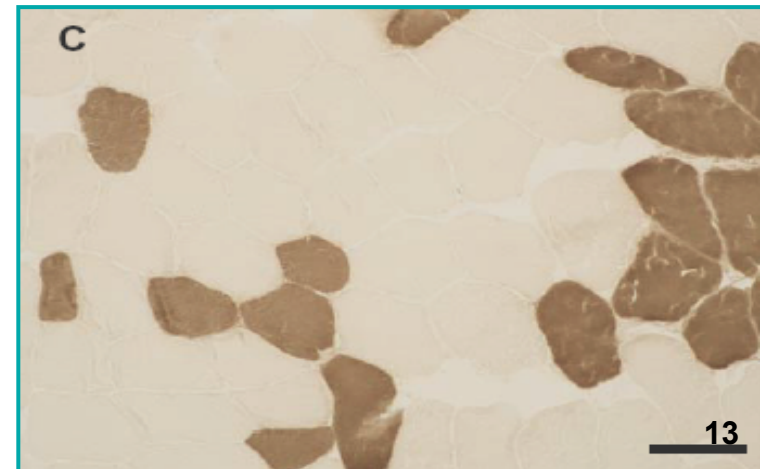
Hypoxémie, Hypoxie, Oxygène conformité



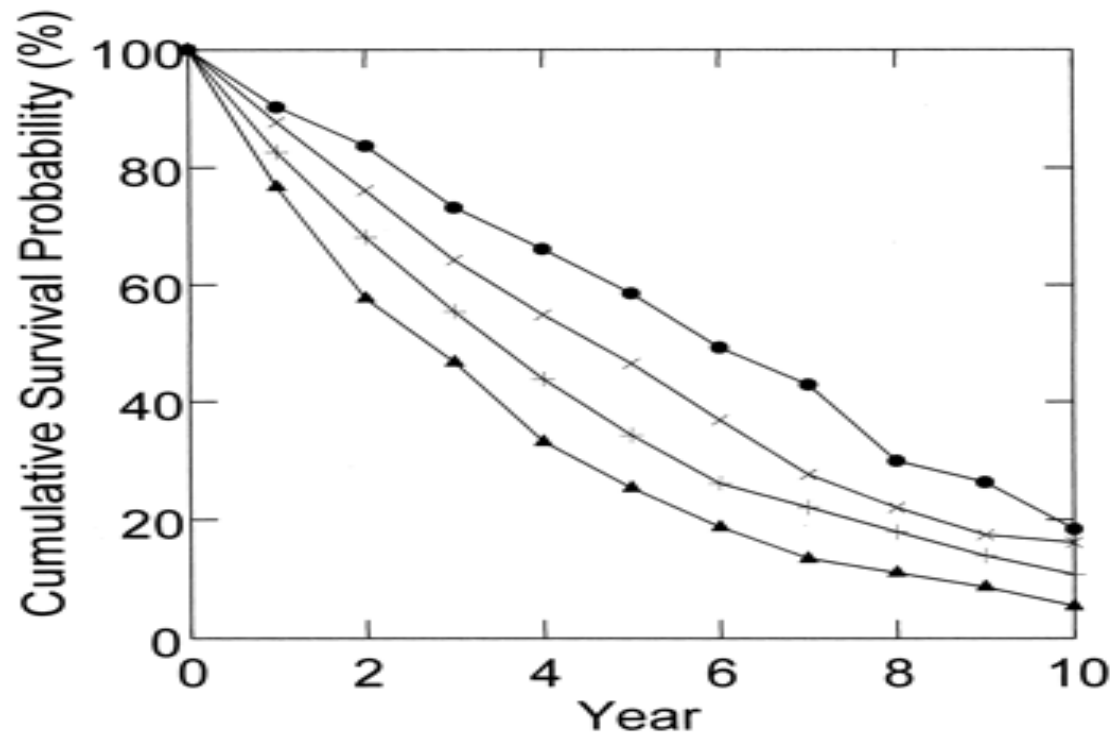
Hypoxémie, Hypoxie, Oxygène conformité

- **Capacité oxydative muscle pathologique**
Am J Respir Crit Care Med 1999; 160:57
 - 7 Tx vs 7 contrôles
 - P_{\max} , watts 88 ± 10 vs 218 ± 30
 - $VO_2\text{pic \%th}$ 56 ± 3 vs 111 ± 3
 - Fibres I % $24,9 \pm 4,4$ vs $56,1 \pm 2,4$
 - Baisse production ATP mito

- *Am J Physiol Regul 2005;289:R1144*
 - 12 Tx vs 12 contrôles
 - P_{\max} , watts 78 ± 16 vs 224 ± 56
 - $VO_2\text{pic \%th}$ 63 ± 20 vs 101 ± 16
 - Fibres I% $16 \pm 6,1$ vs 42 ± 21
 - V_{\max} mitochondrie : idem



Hypoxémie, Hypoxie, Oxygène conformité



4 088 BPCO

$\text{PaO}_2 < 8 \text{ kPa}$

$\text{VEMS} / \text{CVF} < 0,6$

OLT 1984 - 93

BMI

- 30 & +
- × 25 - 29
- + 20 - 24
- ▲ < 20

Chest 2003;123:1460

Hypoxémie, Hypoxie, Oxygène conformité

Table 2. – Anthropometric and functional characteristics according to body composition in 78 consecutive lung transplant candidates

	Nutritional group				Chi-squared or ANOVA
	I	II	III	IV	
Subjects n	22 (28)	21 (27)	13 (17)	22 (28)	NS
Sex F:M	8:14	6:15	3:10	7:15	NS
Age yrs	35.5±14.4	35.9±13.9	50.9±11.2 ^{*,+}	50.3±9.3 ^{*,+}	<0.0001
BRO/CF %	39	36	16	9	–
EMP %	23	31	4	42	–
IPF %	19	6	38	38	–
PPH %	17	17	33	33	0.01
Weight % ideal	74.2±9.9	77.7±9.8	98.8±7 ^{*,+}	105±11 ^{*,+}	<0.0001
CHI % pred	54.6±8.4	75.8±8.3 [*]	53.5±13.1 ⁺	84.6±13.7 ^{*,+,#}	<0.0001
Albumin g·L ⁻¹	32.6±7.3	36.5±6.2	30.3±5.4 ⁺	36.8±6.3 [#]	0.06
P _a O ₂ kPa	6.19±1.21	7.81±1.37 [*]	6.07±1.13 ⁺	7.44±1.72 ^{*,#}	0.003
P _a CO ₂ kPa	6.71±1.44	6.88±1.32	5.93±1.23 ⁺	5.91±1.20 ^{*,+}	0.04
6-MWD m	52±48	178±85 [*]	88±80 ⁺	140±86 ^{*,#}	<0.0001

Data are presented as mean±SD or n (%). F: female; M: male; BRO/CF: bronchiectasis/cystic fibrosis; EMP: emphysema; IPF: idiopathic pulmonary fibrosis; PPH: primary pulmonary hypertension; CHI: creatinine height index; % pred: per cent of predicted; 6-MWD: 6-min walking distance. *: corresponds to significant difference compared to Group I with the *post-hoc* test of Fisher; +: significant difference compared to Group II; #: significant difference compared to Group III. Nutritional group: I: weight <90% ideal, CHI <60% pred; II: weight <90% ideal, CHI 60% pred; III: weight ≥90% ideal, CHI <60% pred; IV: weight ≥90% ideal, CHI ≥60% pred; NS: not significant.

Schwebel C, Pin I, Barnoud D, Devouassoux G., Brichon PY, Chaffanjon Ph, Chavanon O., Sessa C, Blin D. Guignier M., Lerverve X, Pison Ch. Prevalence and consequences of nutritional depletion in lung transplant candidates.

Eur Respir J 2000 ; 16 : 1050-5

Hypoxémie, Hypoxie, Oxygène conformité

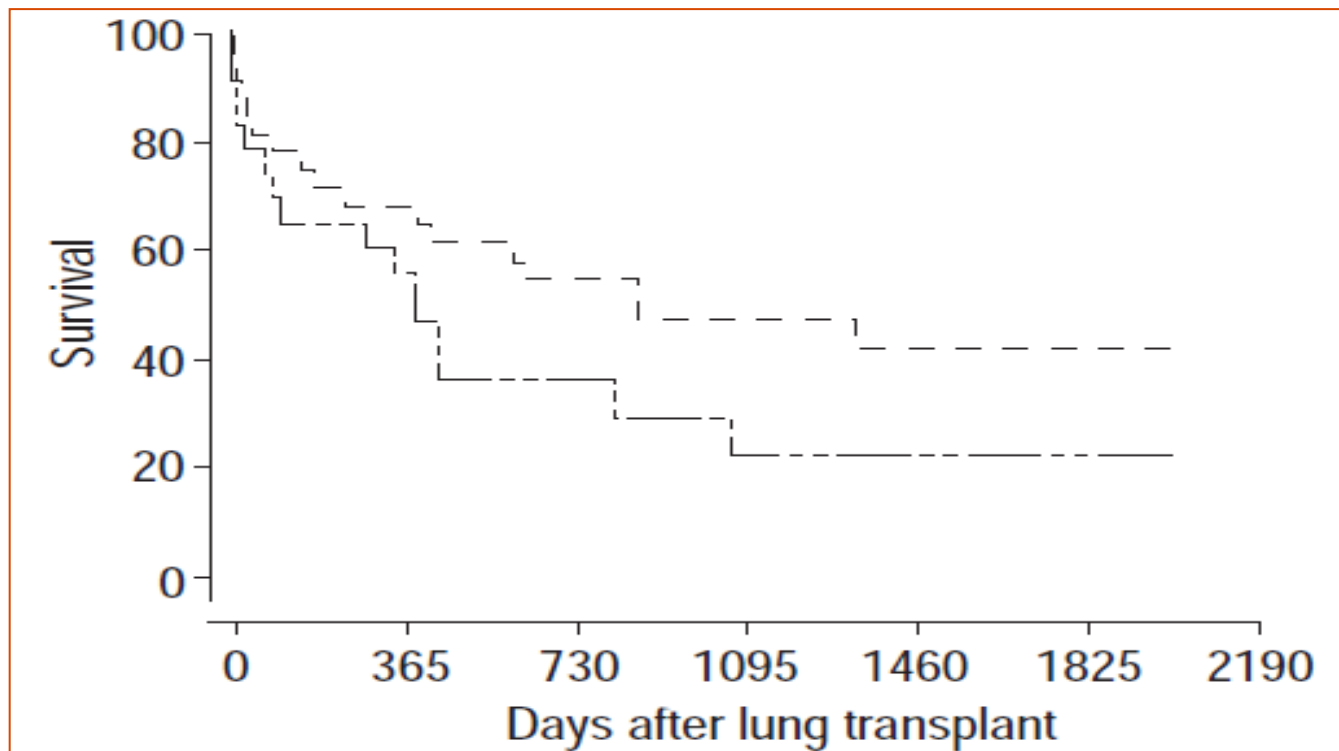
Table 3. – Consequences of body composition on the postoperative course in 48 consecutive lung transplant patients who survived >1 day

	Nutritional group				Chi-squared or ANOVA
	I	II	III	IV	
Subjects n	14 (32)	11 (25)	5 (11)	18 (32)	NS
Sex F:M	4:10	2:9	0:5	7:11	NS
Age yrs	36.2±14.9	38.5±14.6	57.6±3.3* ⁺	49.2±9.4* ⁺	0.002
BRO/CF %	41	35	12	12	
EMP %	17	28	6	50	
IPF %	30	0	20	50	
PPH %	33	0	0	67	0.18
MV days	5.5 (7–34)	1 (0.8–28)	17 (1.4–88)* ⁺	2.5 (4–29) [#]	0.05
ICU, days	17 (7–72)	17 (8–35)	53 (18–89)* ⁺	16 (12–30) [#]	0.0002

Data are presented as mean±SD, n (%) or median (range) unless otherwise stated. F: female; M: male; BRO/CF: bronchiectasis/cystic fibrosis; EMP: emphysema; IPF: idiopathic pulmonary fibrosis; PPH: primary pulmonary hypertension; MV: mechanical ventilation; ICU: in intensive care unit; *: significant difference compared to Group I with the *post-hoc* test of Fisher; ⁺: significant difference compared to Group II; [#]: significant difference compared to Group III; NS: not significant. For nutritional groups see table 2.

Schwebel C, Pin I, Barnoud D, Devouassoux G., Brichon PY, Chaffanjon Ph, Chavanon O., Sessa C, Blin D. Guignier M., Lerverve X, Pison Ch. Prevalence and consequences of nutritional depletion in lung transplant candidates. *Eur Respir J* 2000 ; 16 : 1050-5

Hypoxémie, Hypoxie, Oxygène conformité



Schwebel C, Pin I, Barnoud D, Devouassoux G., Brichon PY, Chaffanjon Ph, Chavanon O., Sessa C, Blin D. Guignier M, Lerverve X, Pison Ch. Prevalence and consequences of nutritional depletion in lung transplant candidates. *Eur Respir J* 2000 ; 16 : 1050-5

Hypoxémie, Hypoxie, Oxygène conformité

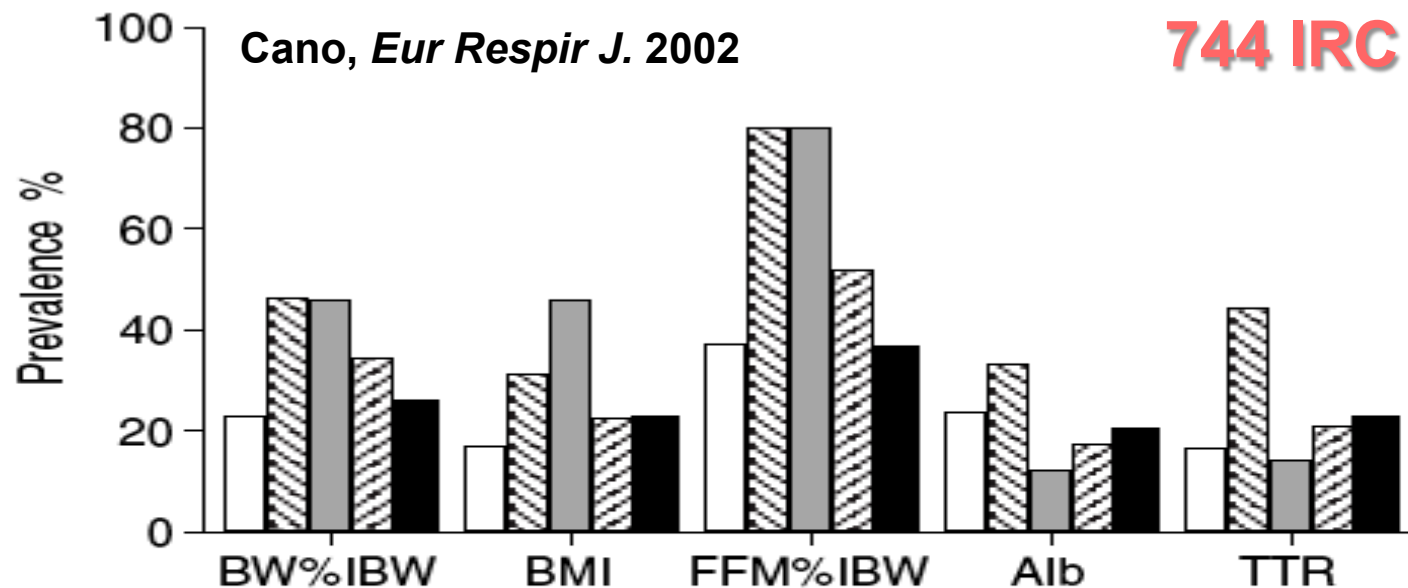


Fig. 1.—Percentage of malnourished patients as defined by per cent of ideal body weight (BW%IBW) <90%, body mass index (BMI) <20, fat-free mass expressed as a per cent of the ideal body weight (FFM%IBW) <63% in females and 67% in males, serum albumin (Alb) <35 g·L⁻¹ or serum transthyretin (TTR) <200 mg·L⁻¹, according to the disease. □: chronic obstructive pulmonary disease; ▨: bronchiectasis; ■: neuromuscular diseases; ▩: restrictive disorders; ■: mixed respiratory failure.

Hypoxémie, Hypoxie, Oxygène conformité

**446 IRC
suivis
14±6 mois**

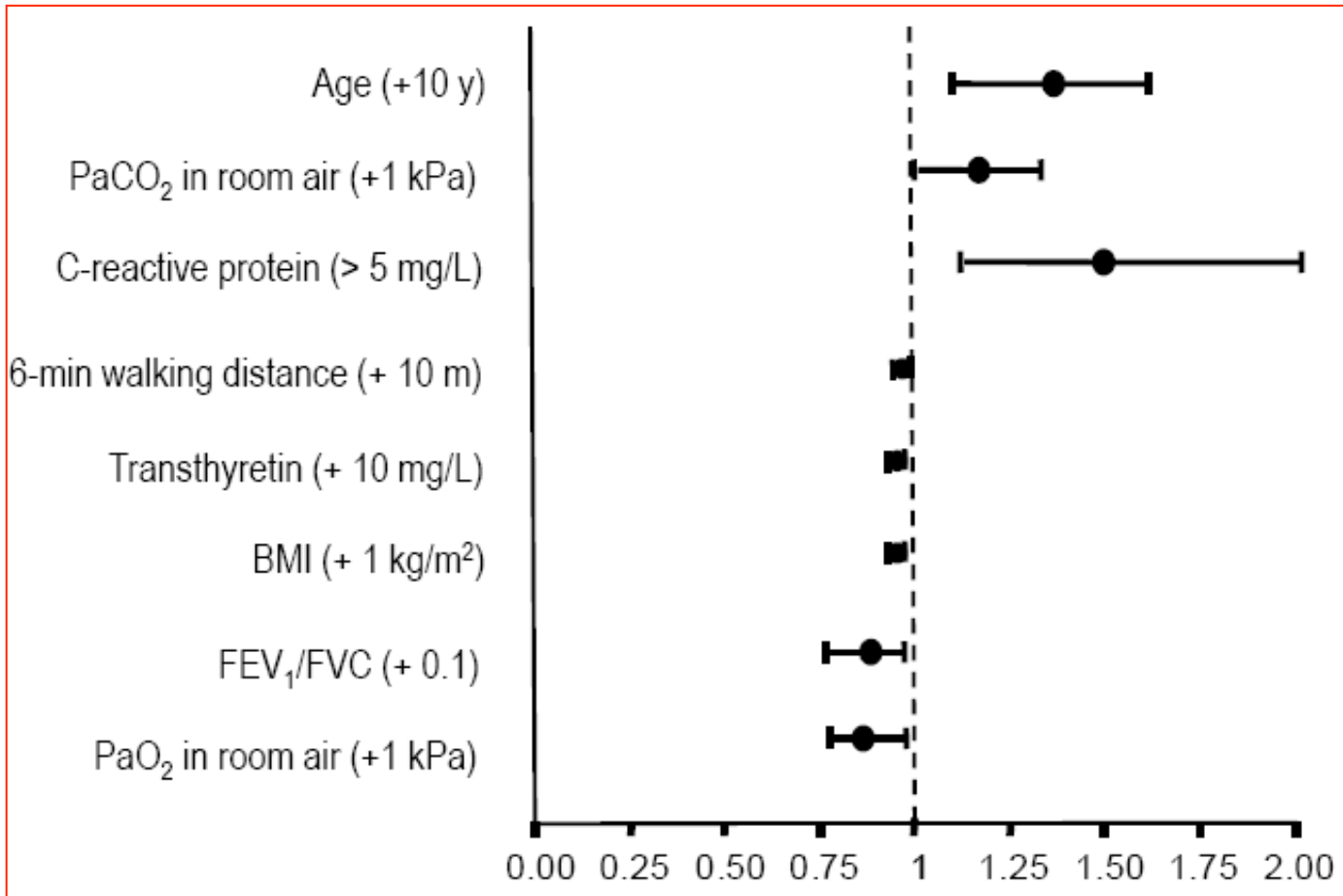
Table 3—Determinants of Survival According to Cox Univariate and Multivariate Model

Variables	p Value	χ^2
Univariate analysis		
Oral corticosteroids*	< 0.0001	
C-reactive protein	< 0.001	
PaO ₂ room air	< 0.001	
BMI	< 0.01	
Serum albumin	< 0.05	
FVC, % predicted	< 0.05	
Active smoking	< 0.05	
6-min walking test	< 0.05	
Serum transthyretin	0.05	
Multivariate analysis		
C-reactive protein	0.009	6.81
BMI	0.010	6.63
PaO ₂ room air	0.016	5.79
Oral corticosteroids*	0.018	5.60

*Corticosteroid users were defined as patients receiving oral corticosteroids for > 3 months during the previous year.

Cano NJM, Pichard C, Roth H, Court-Fortuné I, Cynober L, Gérard-Boncompain M, Cuvelier A, Jean-Pierre Laaban JP, Jean-Claude Melchior JCI, Raphaël JCI, Pison CM and the Clinical Research Group of the Société Francophone de Nutrition Entérale et Parentérale. C-reactive protein and body mass index predict outcome in end-stage respiratory failure. *Chest* 2004 ; 126 : 540-6

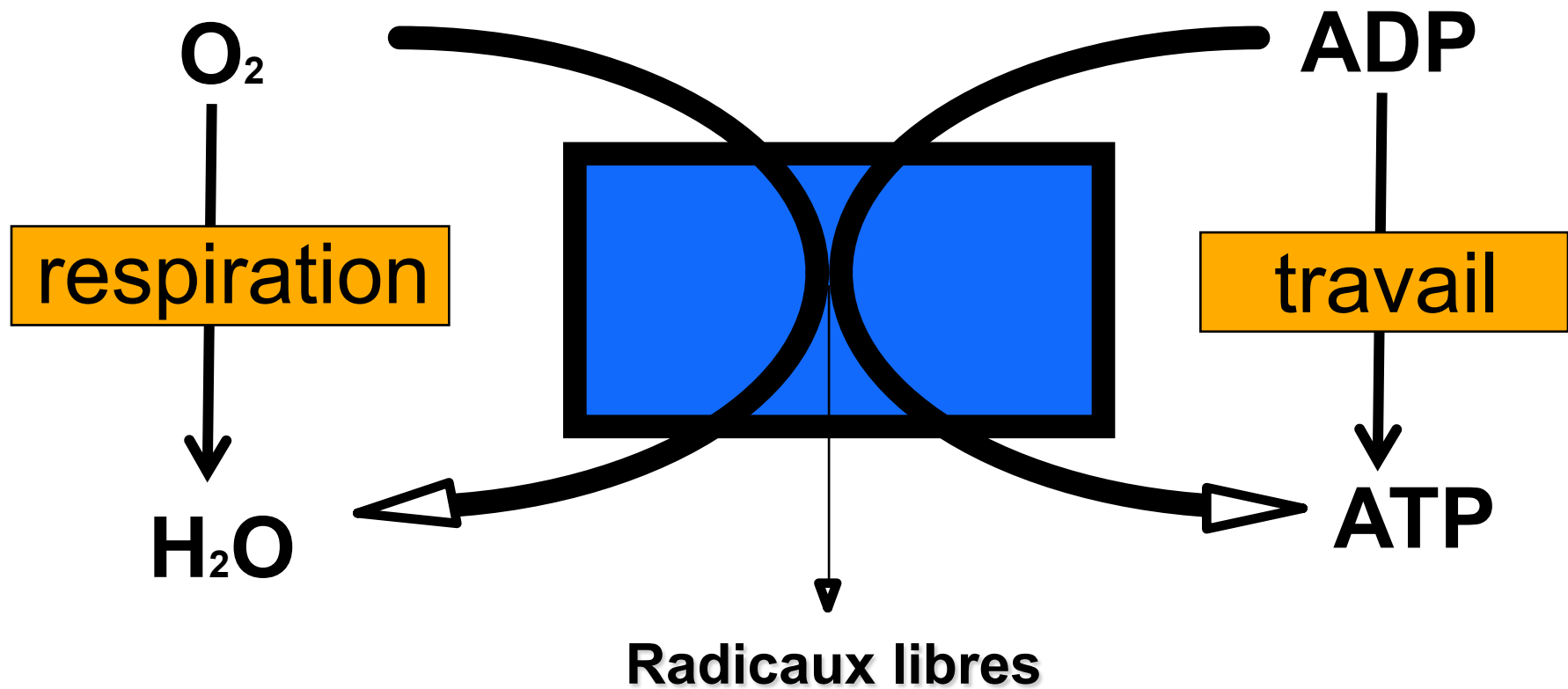
Hypoxémie, Hypoxie, Oxygène conformité



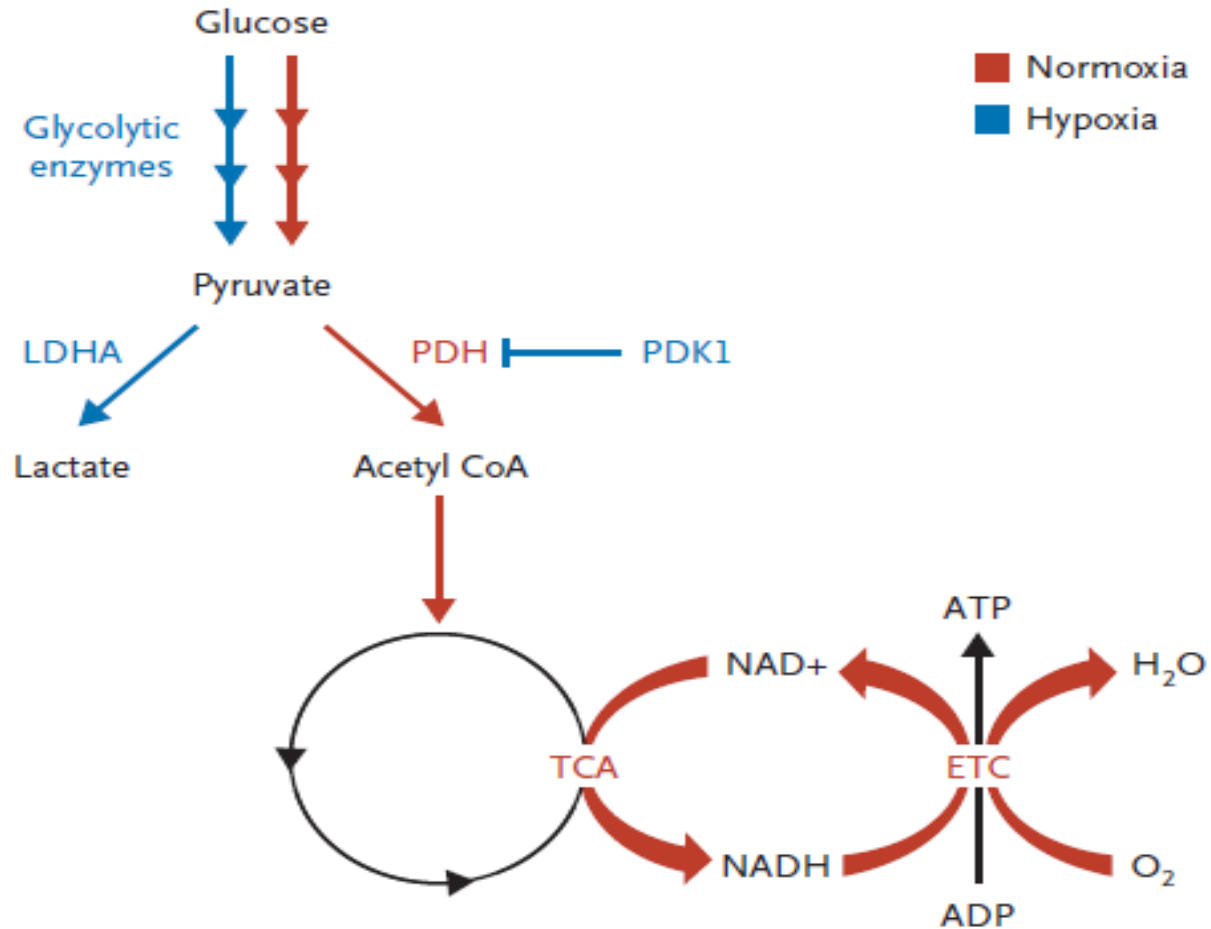
**637 IRC
suivis
53±31 mois**

Cano NJM, Pichard C, Roth H, Court-Fortuné I, Cynober L, Gérard-Boncompain M, Cuvelier A, Jean-Pierre Laaban JP, Jean-Claude Melchior JCI, Raphaël JCI, Pison CM and the Clinical Research Group of the Société Francophone de Nutrition Entérale et Parentérale. Systems approach to survival of patients with chronic respiratory failure at home. 2013, submitted

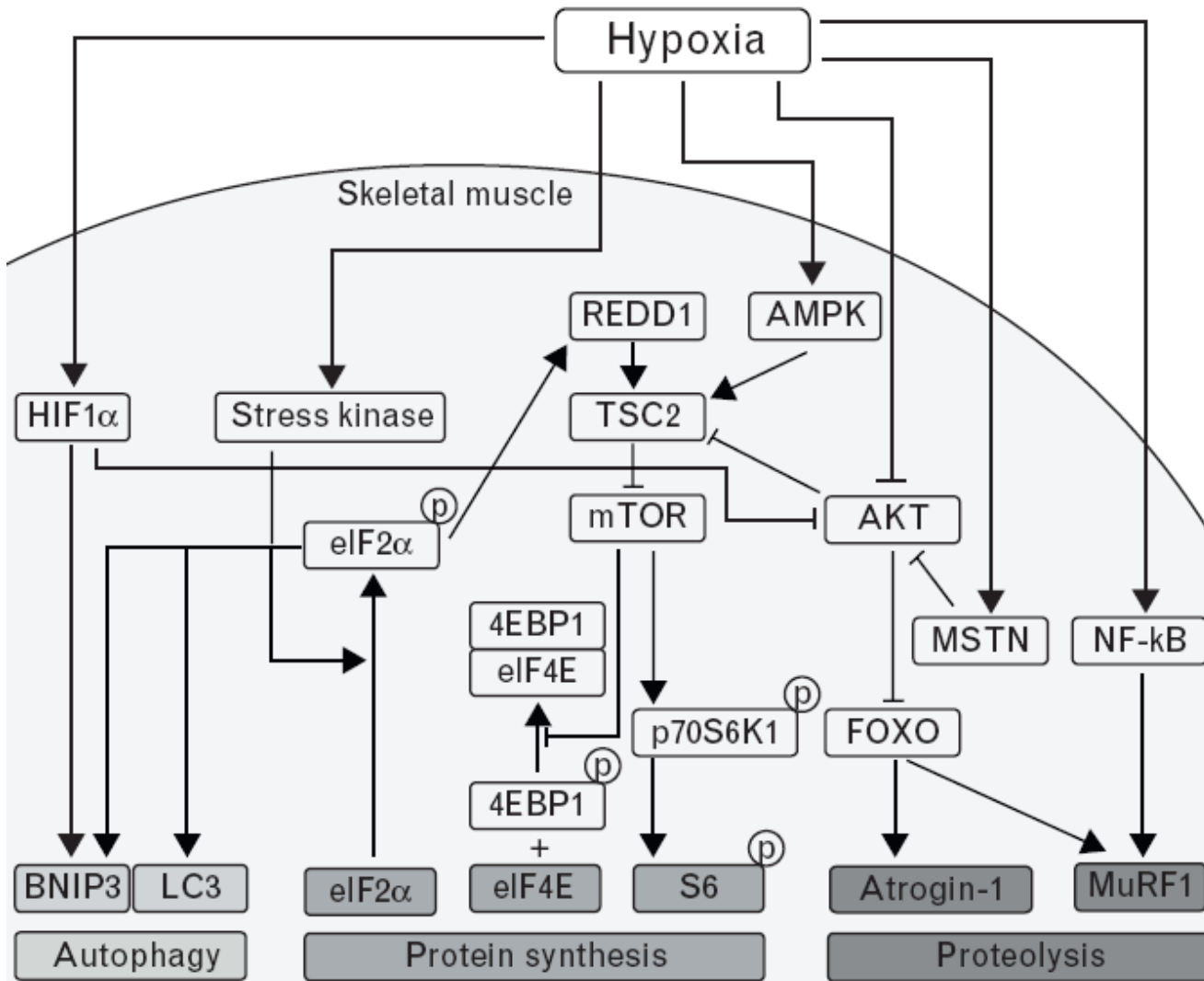
Hypoxémie, Hypoxie, Oxygène conformité, *Oxygène paradoxe*



Hypoxémie, Hypoxie, Oxygène conformité

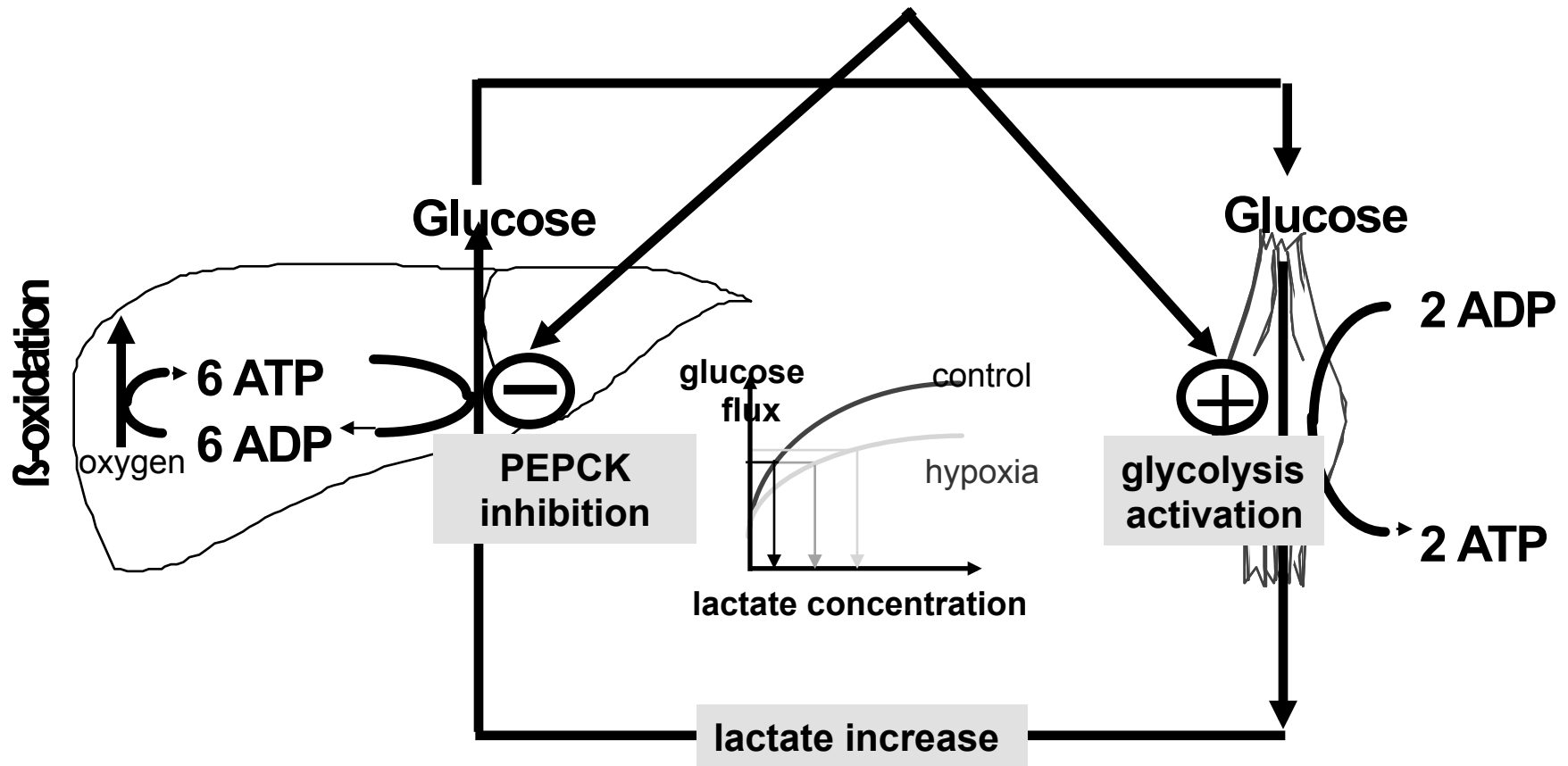


Hypoxia and muscle maintenance regulation: implications for chronic respiratory disease



Chiel de Theije,
Frédéric Costes,
Ramon C. Langen,
Christophe Pison,
and Harry R. Gosker.
Curr Opin Clin Nutr,
Metabl Care
201114:548-53

Hypoxémie, Hypoxie, Oxygène conformité



Pison C, C. Chauvin, E. Fontaine, F. Catelloni, C. Keriél, B. Paramelle, X. Leverage. Mechanism of gluconeogenesis inhibition in rat hepatocytes isolated after *in vivo* hypoxia. *Am. J. Physiol-Endocrinol Met* 1995 ; 31 : E965-73

Hypoxémie, Hypoxie, Oxygène conformité

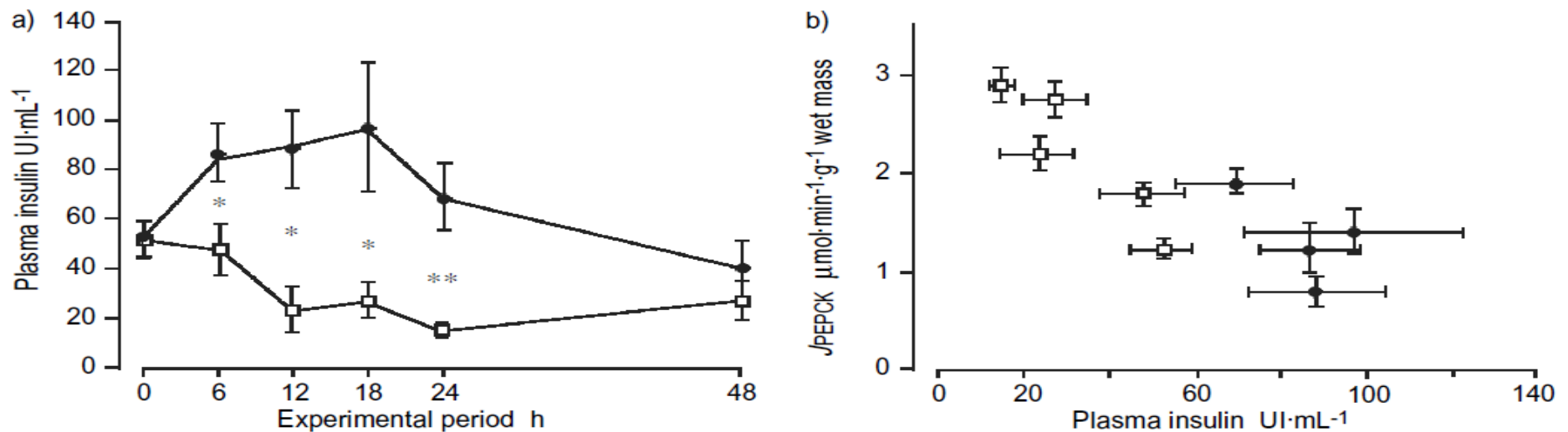
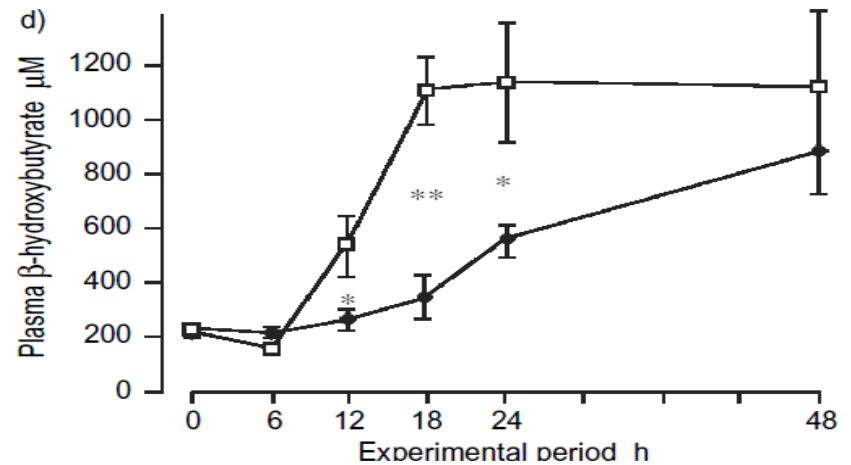
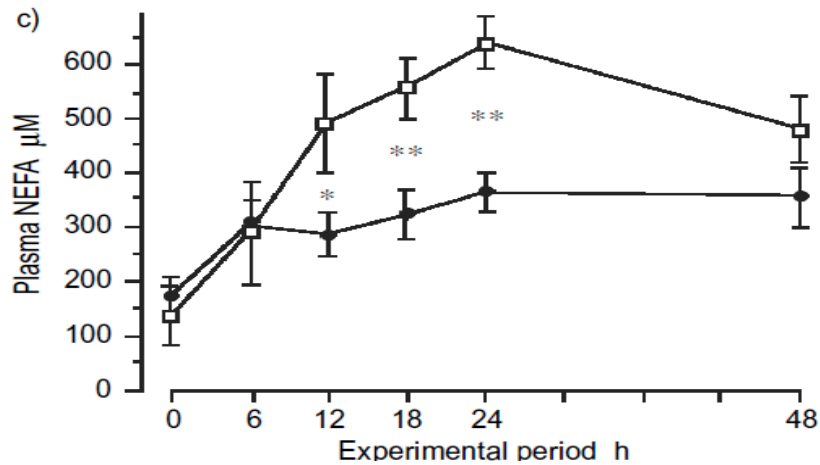
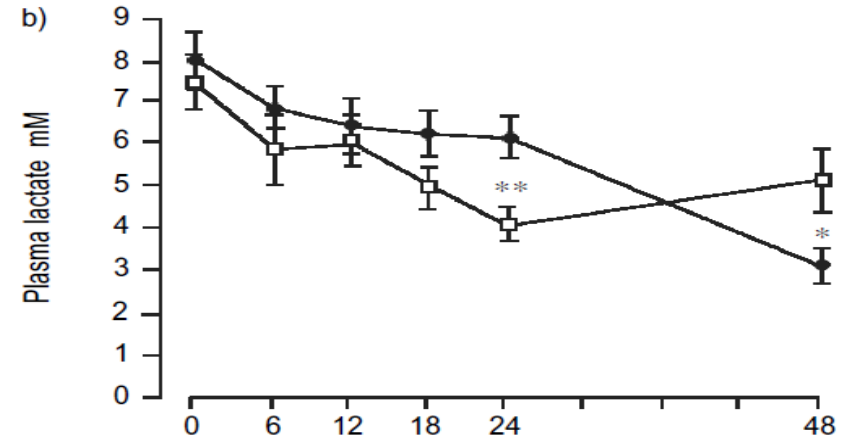
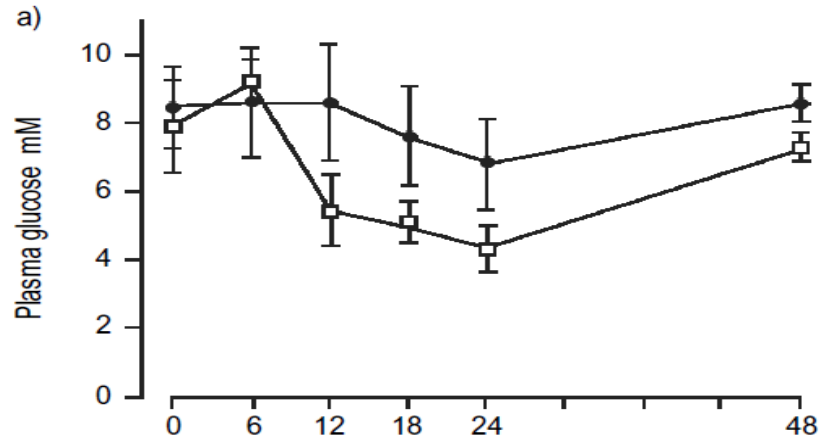


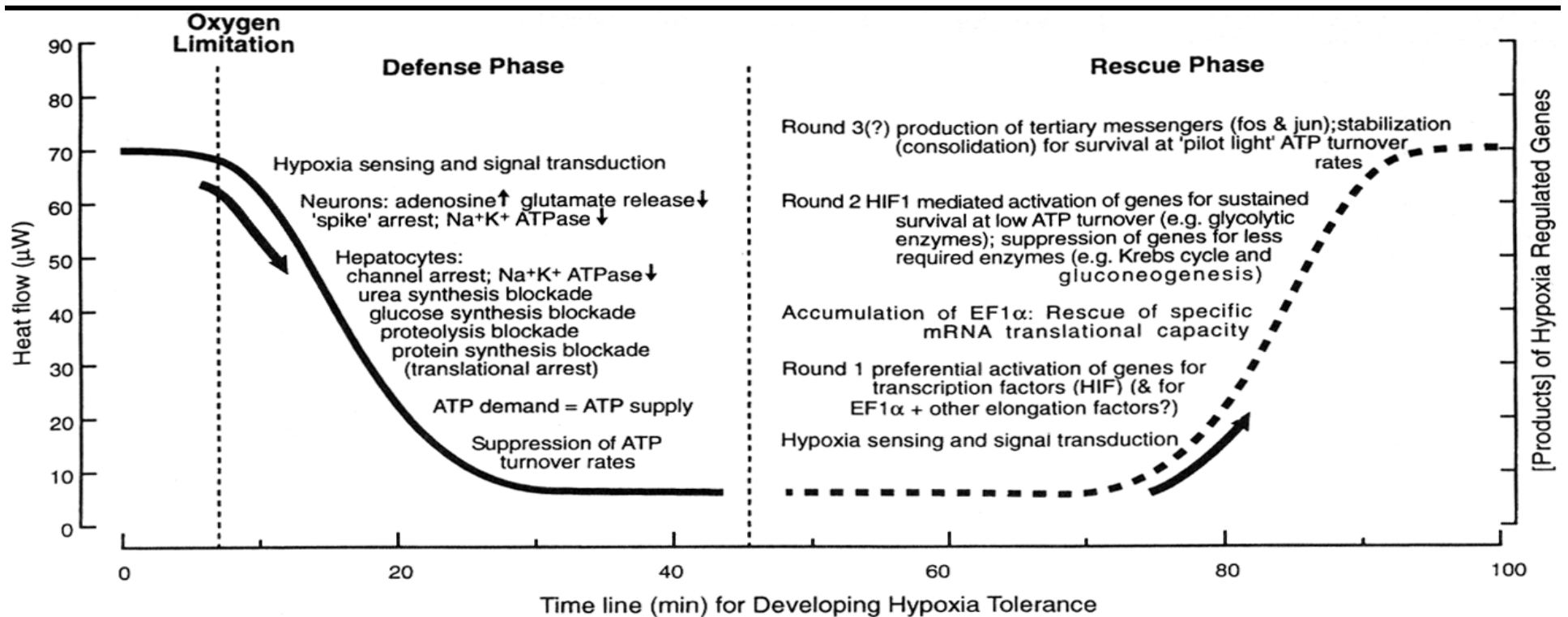
Fig. 6. - a) Kinetics of plasma insulin concentrations throughout the experimental period in fasted normoxic control rats (□) and fasted hypoxic rats (●). Two-way factorial analysis of variance for insulin concentration revealed no main effect of duration of exposure but a significant main effect of hypoxic exposure ($p < 0.0001$). At any given time throughout the experimental protocol, a significant difference between fasted normoxic controls and fasted hypoxic animals is indicated by *: $p < 0.05$; **: $p < 0.01$; $n = 6$ for each point. b) Relationship between plasma insulin concentration and liver phosphoenolpyruvate carboxykinase (PEPCK) V_{max} . A logarithmic model accounted for the relationship: $V_{max} = 5.4 - 2.2 \log(\text{plasma insulin})$; $r^2 = 0.79$, $p < 0.01$.

Pison C, Chauvin C, Perrault H., Schwebel C, Lafond JC, Boujet C, Leverve XM. In Vivo hypoxic exposure impairs metabolic adaptations to a 48 hours fast in rats. *Eur Respir J* 1998 ; 12 : 658-65

Hypoxémie, Hypoxie, Oxygène conformité

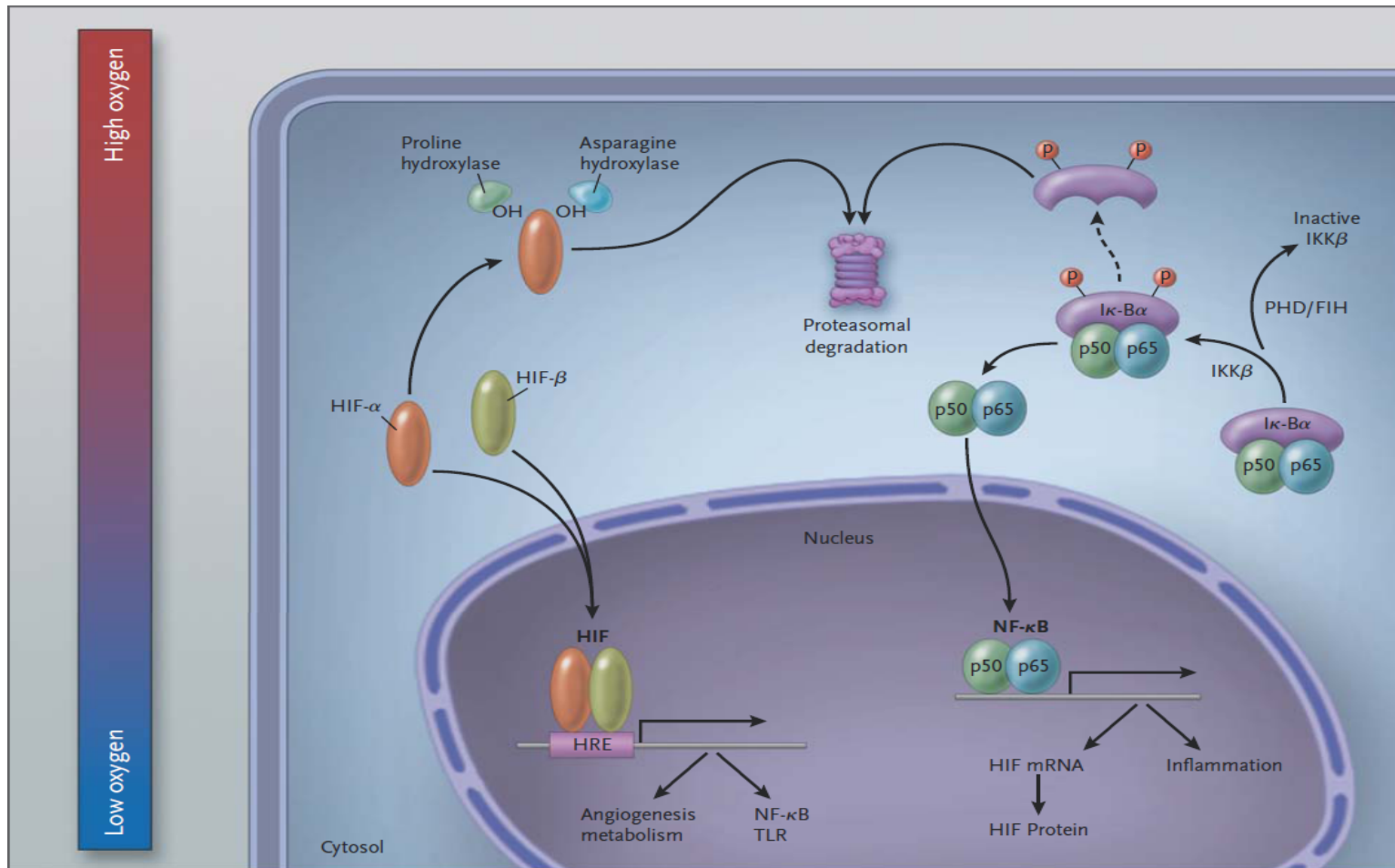


Hypoxémie, Hypoxie, Oxygène conformité



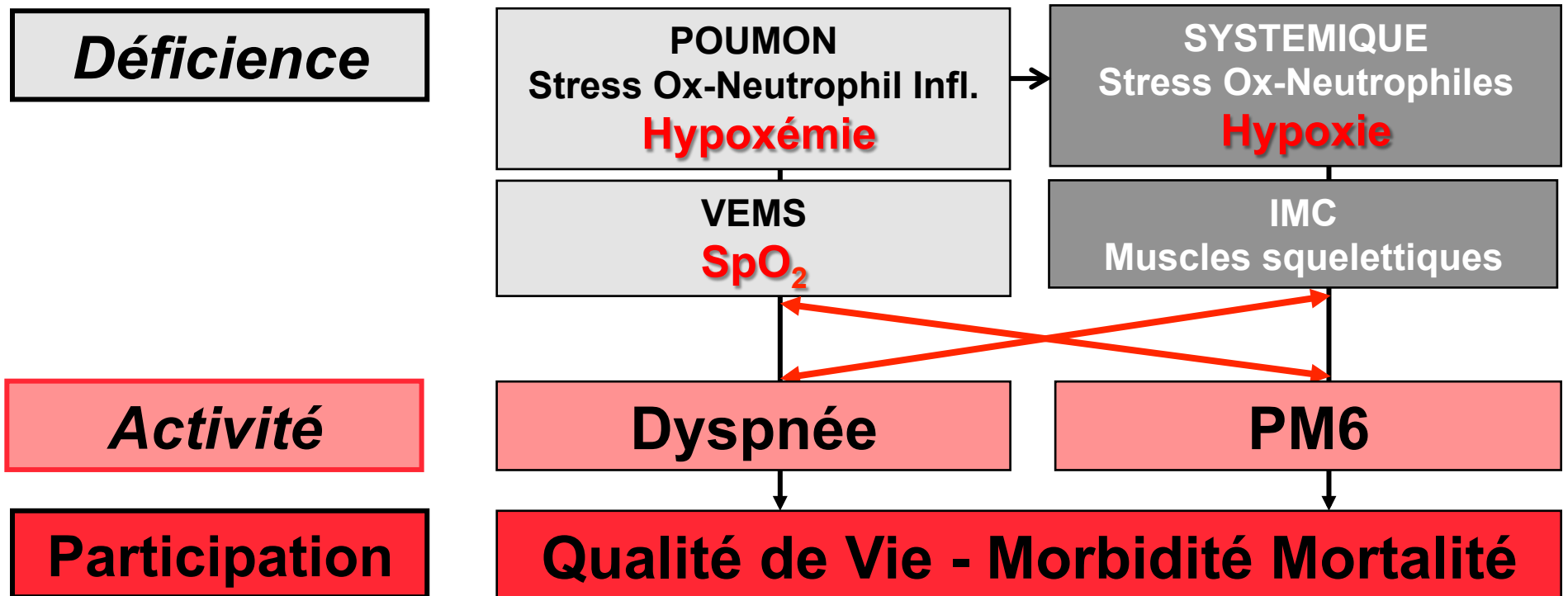
Interactions inflammation hypoxie

N Eng J Med
2011;364:
656



Evaluer

Classification Internationale du Fonctionnement-CIF, OMS, 2001



Evaluer

- Sédentarité
 - Corticothérapie systémique
 - Troubles ioniques
 - Dénutrition catabol. / anabolisme
 - Hypogonadisme
-
- **Inflam. systémique**
 - **Hypoxémie**
 - **Stress oxydatif**
 - **Anomalies réactivité vasculaire**

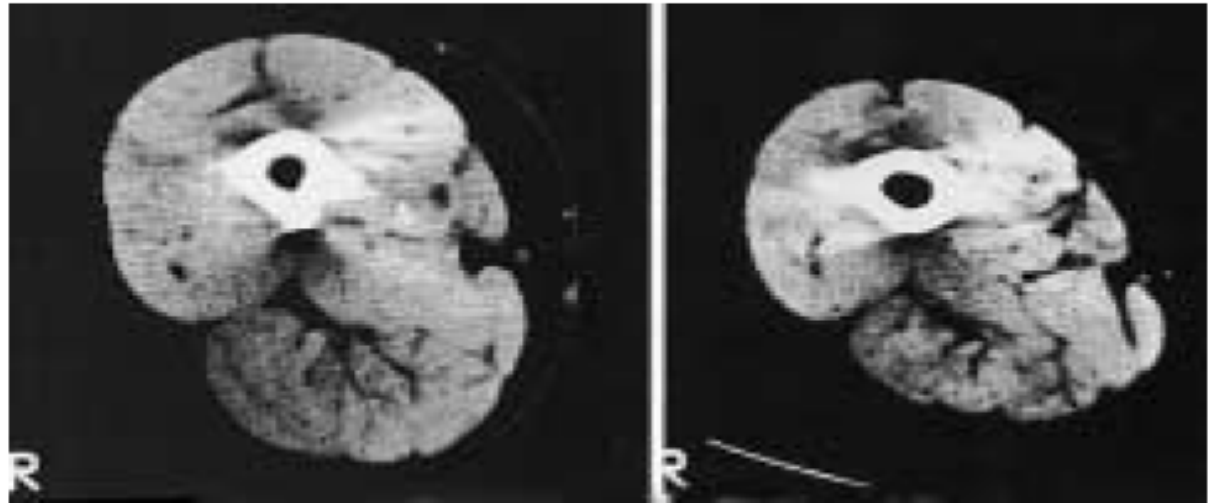


FIG. 1. — Tomographie assistée par ordinateur d'un sujet sain (à gauche) et d'un sujet atteint de BPCO (à droite) appartenant au même groupe d'âge. La surface transversale du muscle de la cuisse est considérablement réduite chez le sujet atteint de BPCO par rapport au sujet sain. Tiré de Bernard *et al.* *Am J Respir Crit Care Med* 1998;158: 629-4.

**Cluster
Measure
with**

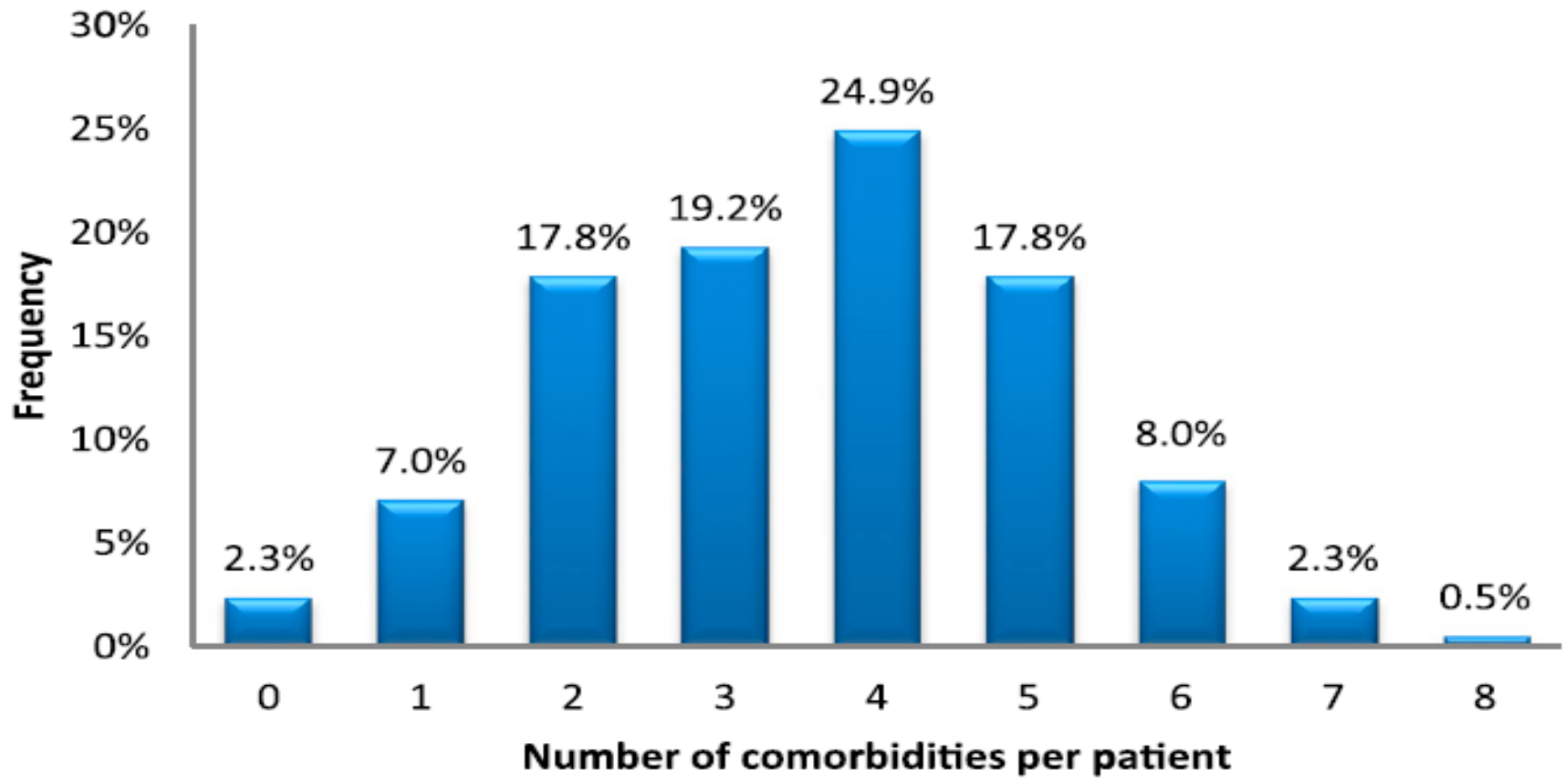
Lowie E. G.
Vanessa P.
Emiel F. M.

¹Program De
Medicine, ⁴D
Netherlands;

TABLE 1. PATIENTS' CHARACTERISTICS

	All Subjects (<i>n</i> = 213)
Age, yrs	63.6 ± 7.0
Male, %	59
BMI, kg/m ²	26.2 ± 5.1
FFMI, kg/m ²	17.0 ± 2.4
mMRC dyspnea grade	2.1 ± 1.09
Current smoker, %	28
Pack-years	46 ± 26
Long-term oxygen therapy, %	17
FEV ₁ , L	1.40 ± 0.54
FEV ₁ , % predicted	51.2 ± 16.9
FEV ₁ /FVC	0.40 ± 0.11
ITGV, % predicted	148 ± 33
TLCO, % predicted	56 ± 17
6MWD, m	470 ± 106
SGRQ, total score	51.3 ± 17.5
Updated BODE score	2.9 ± 2.5
Framingham 10-yr risk, %	9.4 ± 6.7

Evaluator



Evaluator

TABLE 2. DETAILED DESCRIPTION OF THE FIVE CLUSTERS IN TERMS OF THE NUMBER OF COMORBIDITIES AND THE PREVALENCE OF EACH COMORBIDITY

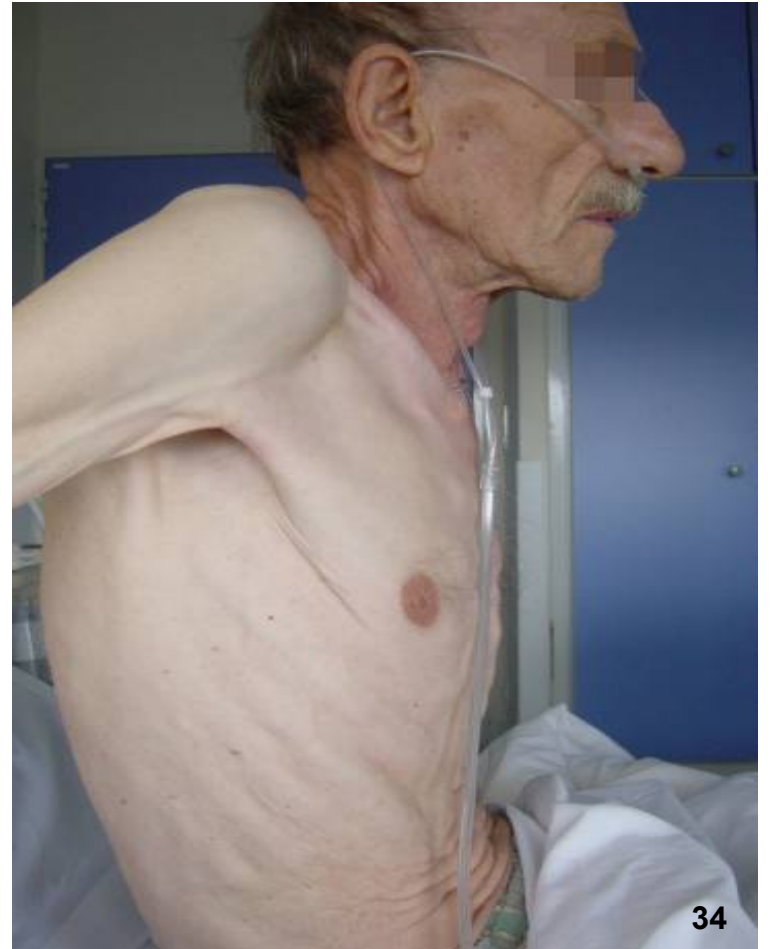
Comorbidities	Cluster 1: Less Comorbidity	Cluster 2: Cardiovascular	Cluster 3: Cachectic	Cluster 4: Metabolic	Cluster 5: Psychologic
N	67	49	44	33	20
Number of comorbidities	2.5 ± 1.4*	3.8 ± 1.7	4.2 ± 1.4 [†]	4.4 ± 1.1 [†]	4.1 ± 1.8
Renal impairment, %	16	24	45 [†]	9	5
Anemia, %	9	4	2	3	5
Hypertension, %	3*	98 [†]	43	100 [†]	5*
Obesity, %	30	14	0*	61 [†]	15
Underweight, %	0*	0*	66 [†]	3*	0
Muscle wasting, %	12*	10*	98 [†]	0*	20
Hyperglycemia, %	52	41*	43	91 [†]	60
Dyslipidemia, %	42	16*	25	67 [†]	40
Osteoporosis, %	27	37	52 [†]	0*	35
Anxiety, %	5*	28	26	0*	84 [†]
Depression, %	6*	23	7	6	68 [†]
Atherosclerosis, %	56	67 [†]	12*	81 [†]	53
Myocardial infarction, %	2*	11	7	13	32 [†]

Summary variables are presented as mean ± standard deviation for quantitative variables, and percentage for discrete variables.

* Less prevalent compared with the whole study sample (95% confidence interval).

[†] More prevalent compared with the whole study sample (95% confidence interval).

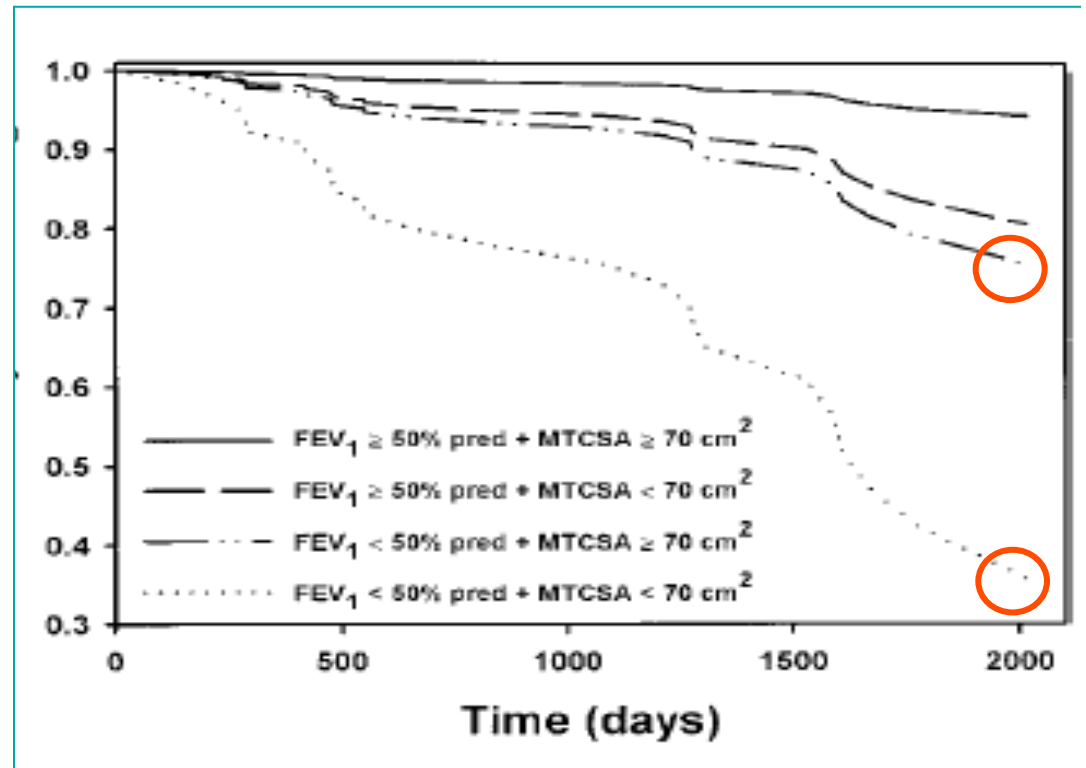
Evaluer



Evaluer

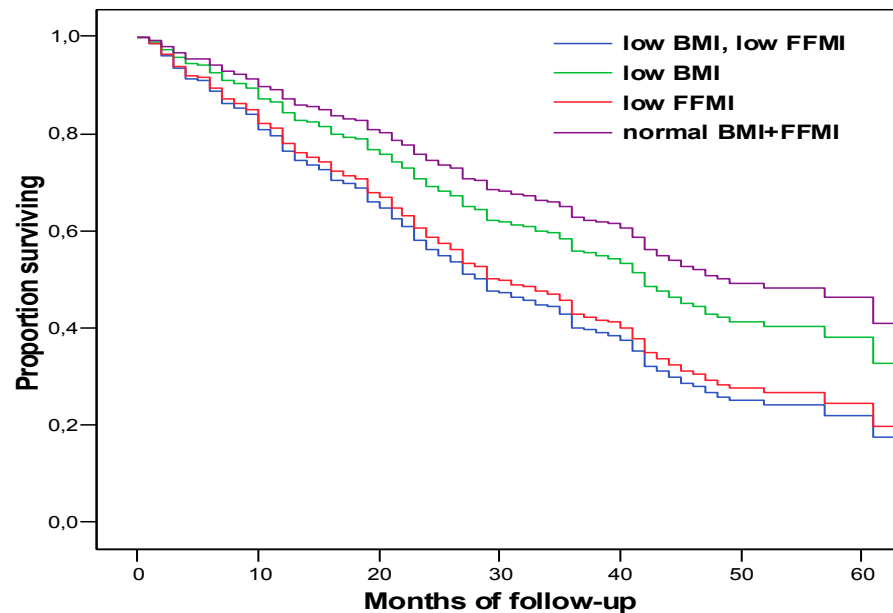
Section partie moyenne cuisse
par TDM,
142 BPCO,
65 ± 16 ans
VEMS : 42 ± 16 % th.

AJRCCM 2002;166:809



Evaluer

Survie en fonction de la composition corporelle, ajustée sur l'âge, le genre, la fonction respiratoire et le tabagisme



⇒ **Malnutrition**
⇒ **Sarcopénie**
⇒ **Cachexie**

Schols, AJCN 2005

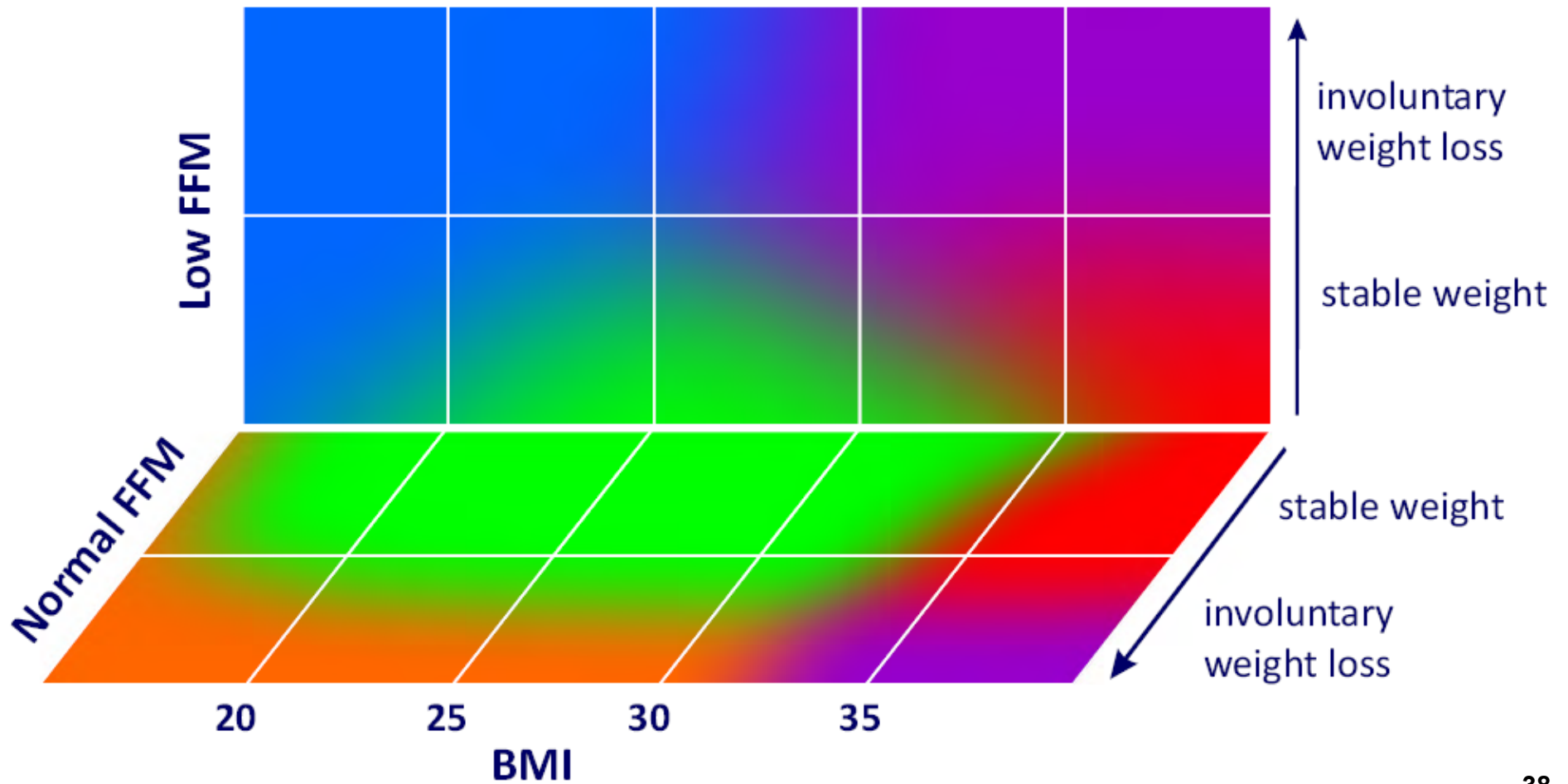
Evaluator

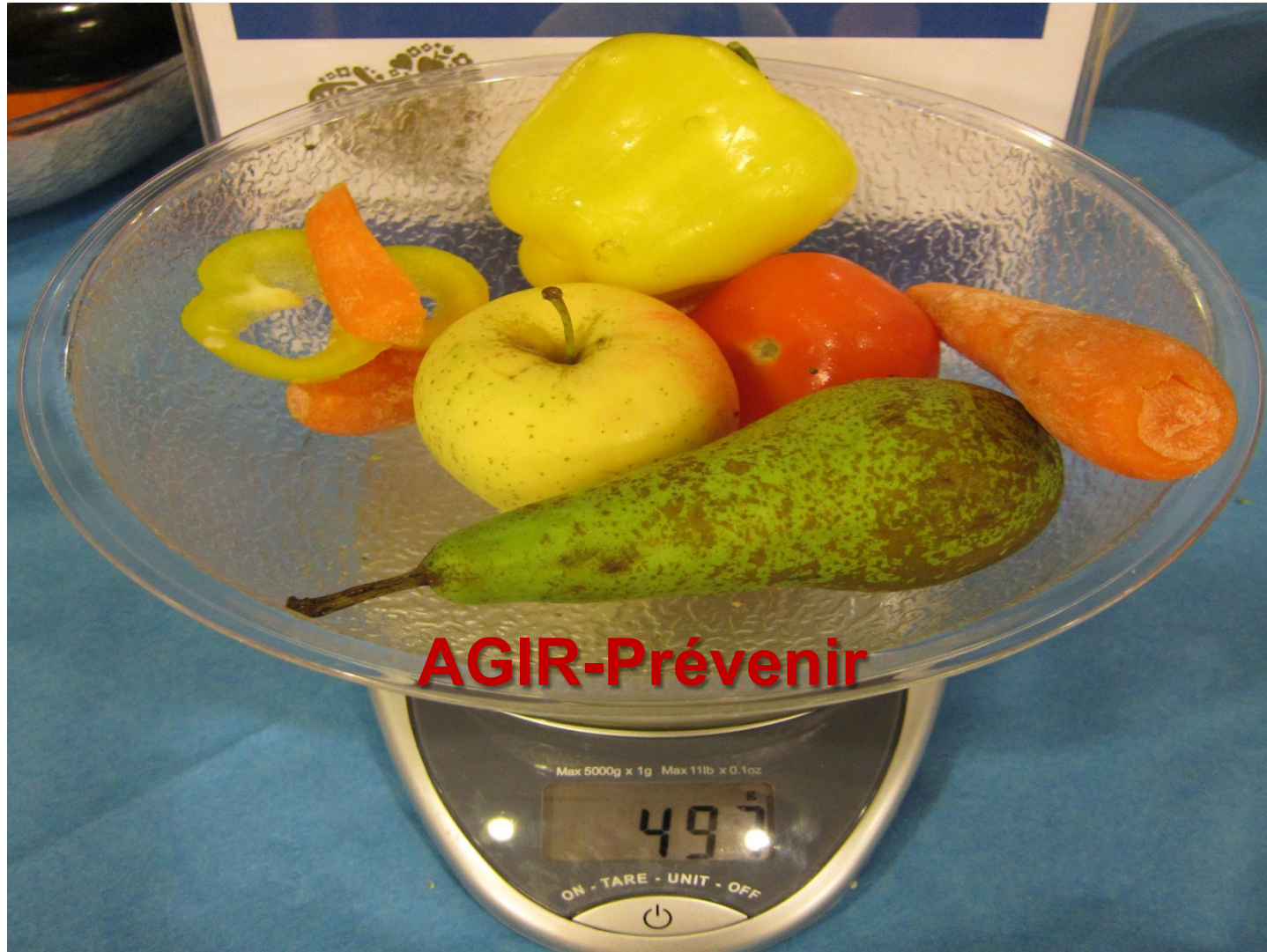
Metabolic phenotype	Definition	Clinical risk
Morbid obesity	BMI > 35	Elevated cardiovascular risk, reduced fitness
Obesity	BMI > 30	Elevated cardiovascular risk
Sarcopenic obesity	BMI > 30 Muscle loss	Elevated cardiovascular risk, reduced fitness
Pre-cachexia	Weight loss	Increased mortality risk
Sarcopenia	Muscle loss	Increased mortality risk and reduced fitness
Cachexia	Weight loss	Increased mortality risk and reduced fitness

An official European Respiratory Society statement Nutrition and COPD

Schols AM, Ferreira IM, Franssen FM, Janssen W, Langen RJ, Muscaritoli M, Pison C, Rutten van Mülken MPMH, Slinde F, Steiner M, Tzacova, Singh S, *in press*

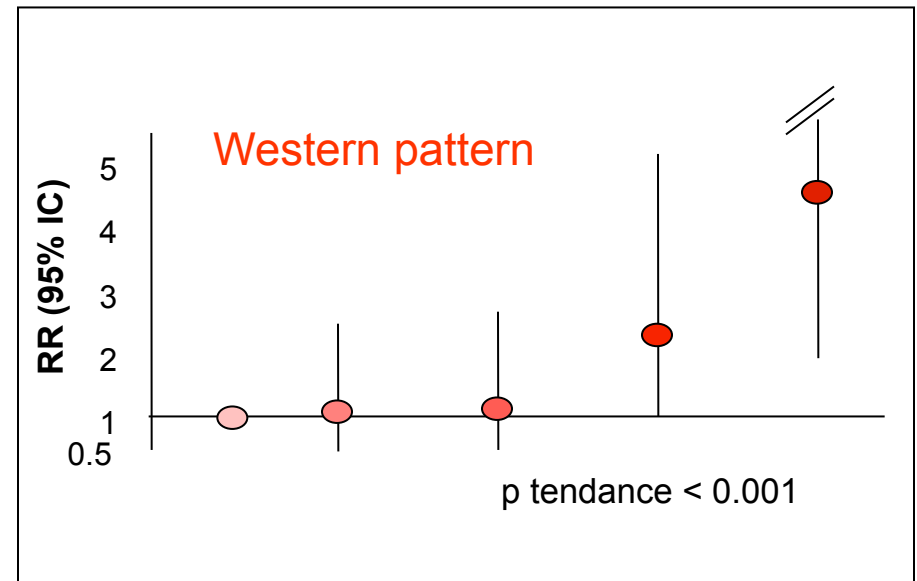
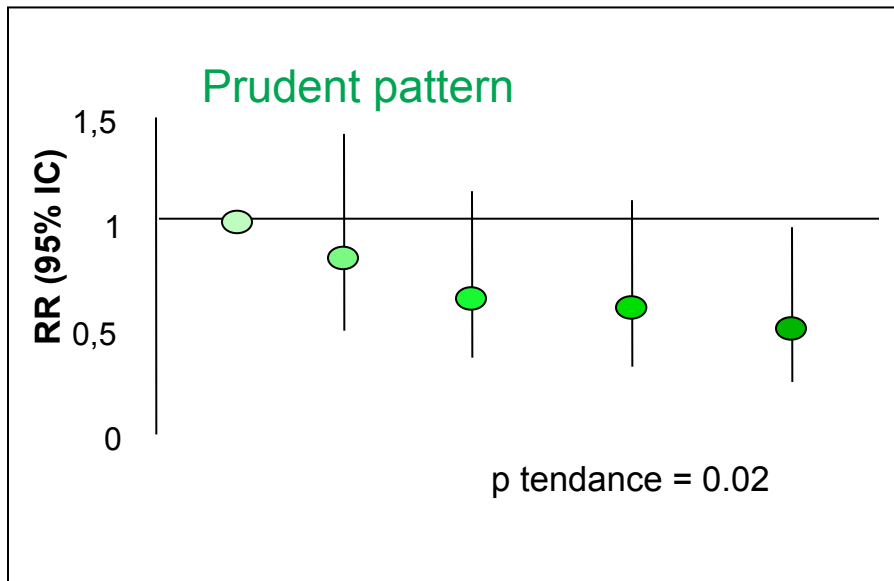
Evaluator





AGIR - Prévenir

Varraso *et al.* Thorax 2007. Dietary patterns & COPD men, longitudinal study (1986-1998), 42 915 men, 111 COPD



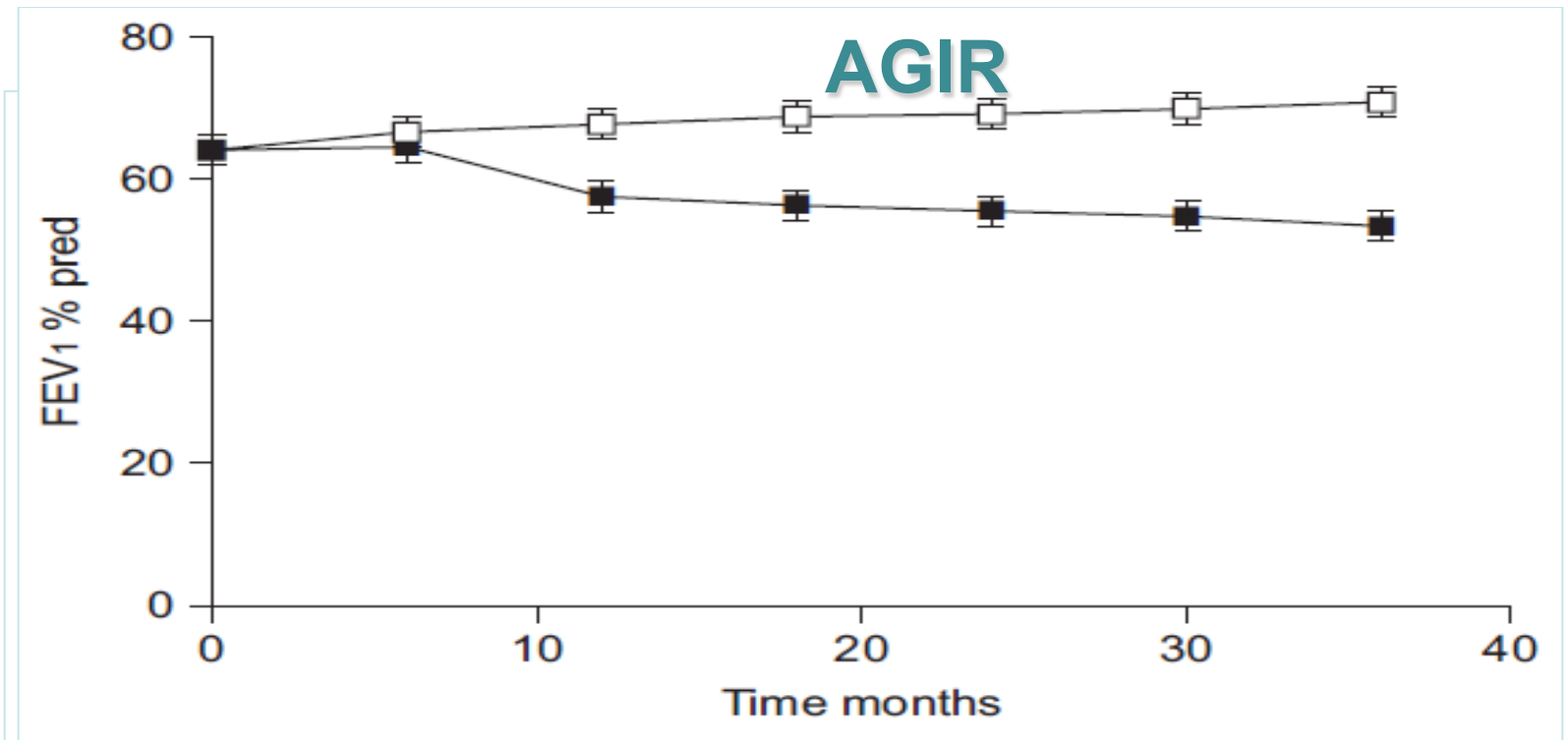


FIGURE 4. Change in forced expiratory volume in 1 s (FEV₁) over the 3-yr dietetic intervention study period in patients who followed a diet rich in fruit and vegetables (□) and in those who followed a free diet (■). Data are presented as mean ± SEM. The difference in mean annual decline in FEV₁ between the two groups obtained by a general linear model for repeated measures with Bonferroni adjustment gave a p-value of 0.03. % pred: % predicted.

AGIR



AGIR

Acute effects of ONS, fat vs. carbohydrate, 11 subjects COPD, 62 ± 8 yrs, FEV_1 $34 \pm 12\%$ pred., BMI 22.6 ± 2.3
Vermeeren et al. AJCN 2001;73:295-301

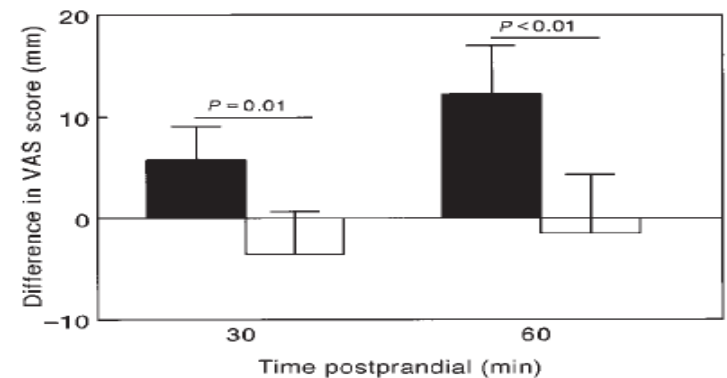
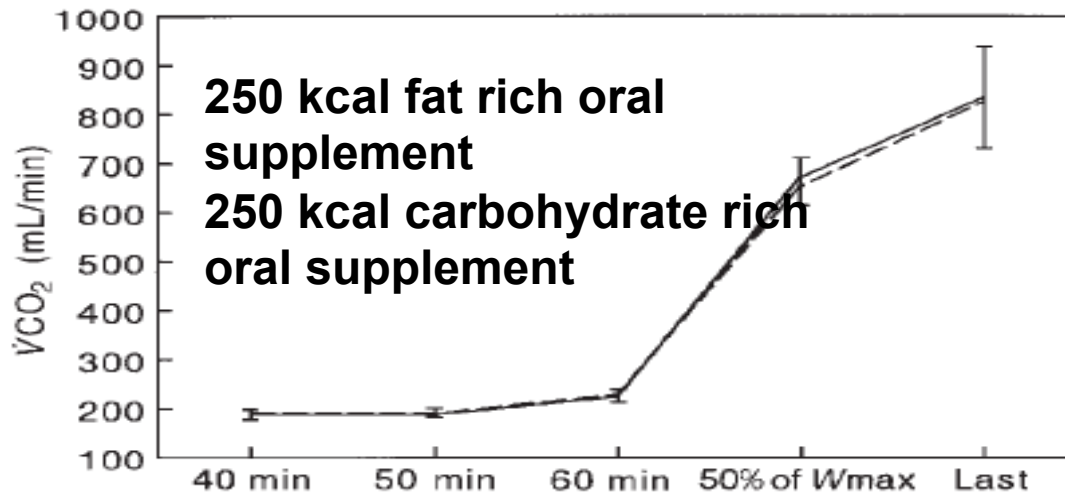


FIGURE 6. Difference between mean (\pm SEM) post- and preprandial shortness of breath score on a visual analogue scale (VAS) 30 and 60 min after consumption of a fat-rich (■) and a carbohydrate-rich (□) supplement. $n = 11$. ANOVA with postprandial value as the dependent variable, with treatment and period as fixed factors, and with patient as a random factor.

AGIR

- **IRC, métabolisme aérobie au final**
- **Lipides**
 - très grand stock et densité énergétique très élevée
 - par CO₂ produit, les lipides libèrent plus d'énergie que le glucose
 - mais, faible rendement par oxygène consommé
 - mais, couts élevés en substrats pour les cycles de Cori and Felig
- **Hydrates de carbone**
 - par O₂ consommé, le glucose libère plus d'énergie que les lipides
 - pas besoin d'hydrates de carbone pour le recyclage
 - mais, très faible stockage
 - mais, cout protéique élevé pour la synthèse

Xavier Leverve, Cuthberston lecture, Espen, Nice, 1998

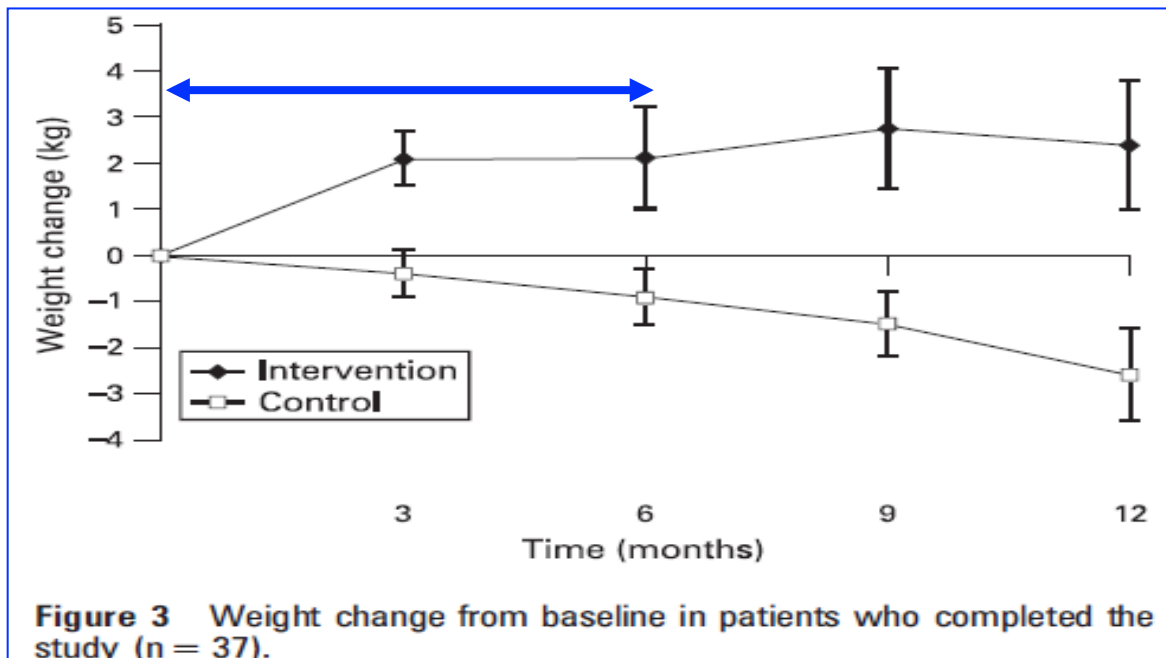
AGIR

Weekes et al. Thorax 2009;64:326-31

+ 194 kcal / j, + 11,8 g protéines / j vs. contrôles

pas de modification force des muscles et fonction respiratoire

St Georges + 10,1, MRC score + 1 , ADL score + 1,5



AGIR

- **2006-2013 ERS/ATS guidelines**
 - **BMI < 21**
 - **involuntary weight loss: >10% during last 6 months or > 5% in the past month)**
 - **depletion in FFMI, <16 males, <15 females**
- **2010 SPLF guidelines. *RMR 2010;27:522-48***
 - **No attempt to lose weight**
 - **Rehabilitation > nutritional supplementation in any cases, especially if under nutrition**
- **2014 – ERS statement on Nutrition and COPD**

Recommandations SPLF 2010

- **Une évaluation nutritionnelle est nécessaire au cours de la réhabilitation respiratoire des BPCO car elle participe à la définition du pronostic fonctionnel et vital**
- **L'évaluation nutritionnelle de la BPCO comporte une histoire du poids sur les 6 derniers mois et un calcul de l'IMC. Un IMC < 21 engage le pronostic vital. Une impédancemétrie est utile pour dépister une baisse de la masse maigre chez les patients dont l'IMC est compris entre 21 et 25**
- **Il ne faut pas chercher à faire maigrir les patients atteints de BPCO**
- **Le réentraînement par l'exercice implique de façon systématique l'augmentation des apports nutritionnels, en particulier en cas de dénutrition, c'est-à-dire en cas d'IMC < 21, de perte de poids de 10 % dans les 6 derniers mois ou d'indice de masse non grasse < 25^{ème} percentile**
- **Une supplémentation orale couplée au réentraînement à l'effort est recommandée car elle est capable d'augmenter le poids et la masse maigre chez les patients atteints de BPCO qui sont dénutris (G1+).**

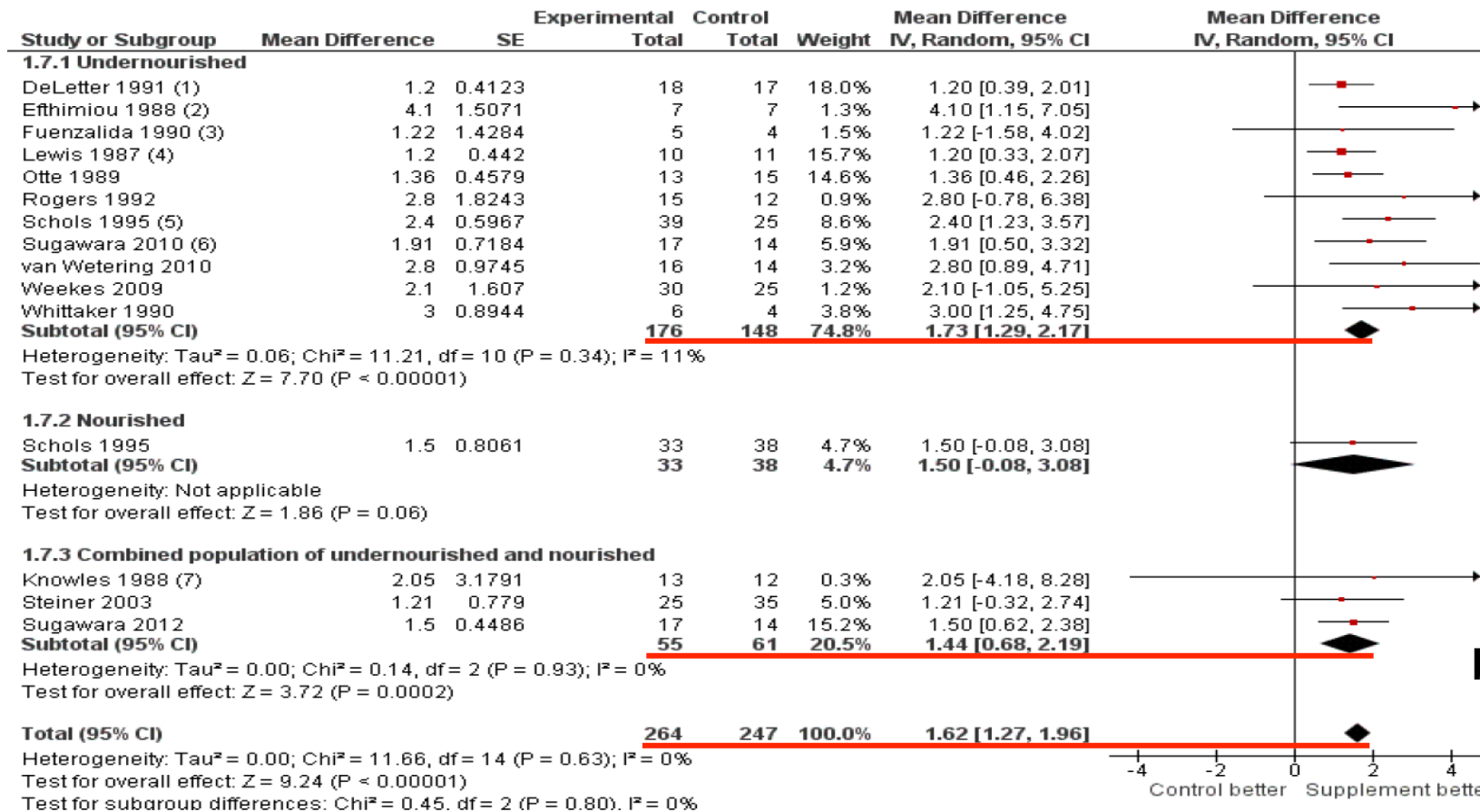
Nutritional supplementation for stable chronic obstructive pulmonary disease (Review)

Ferreira IM, Brooks D, White J, Goldstein R



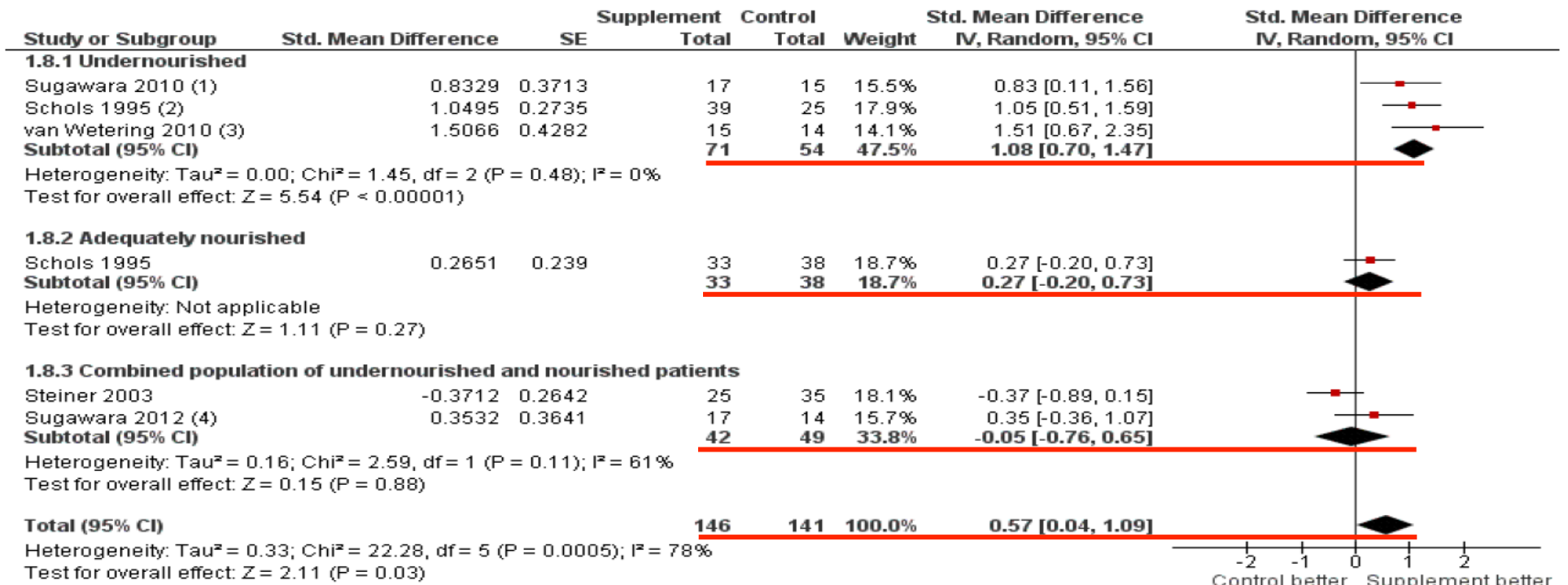
**THE COCHRANE
COLLABORATION®**

Support nutritionnel dans la BPCO, poids, kg

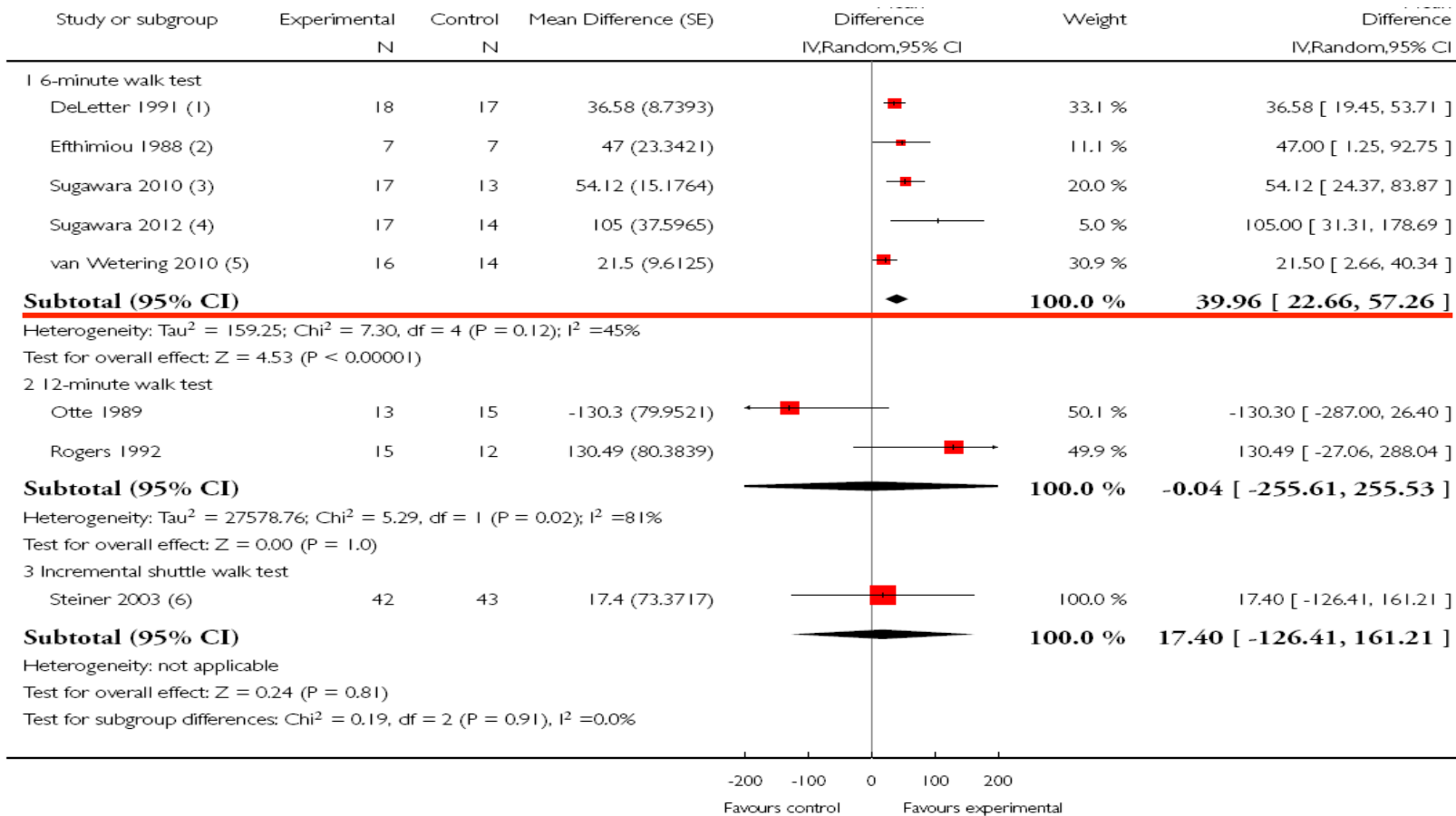


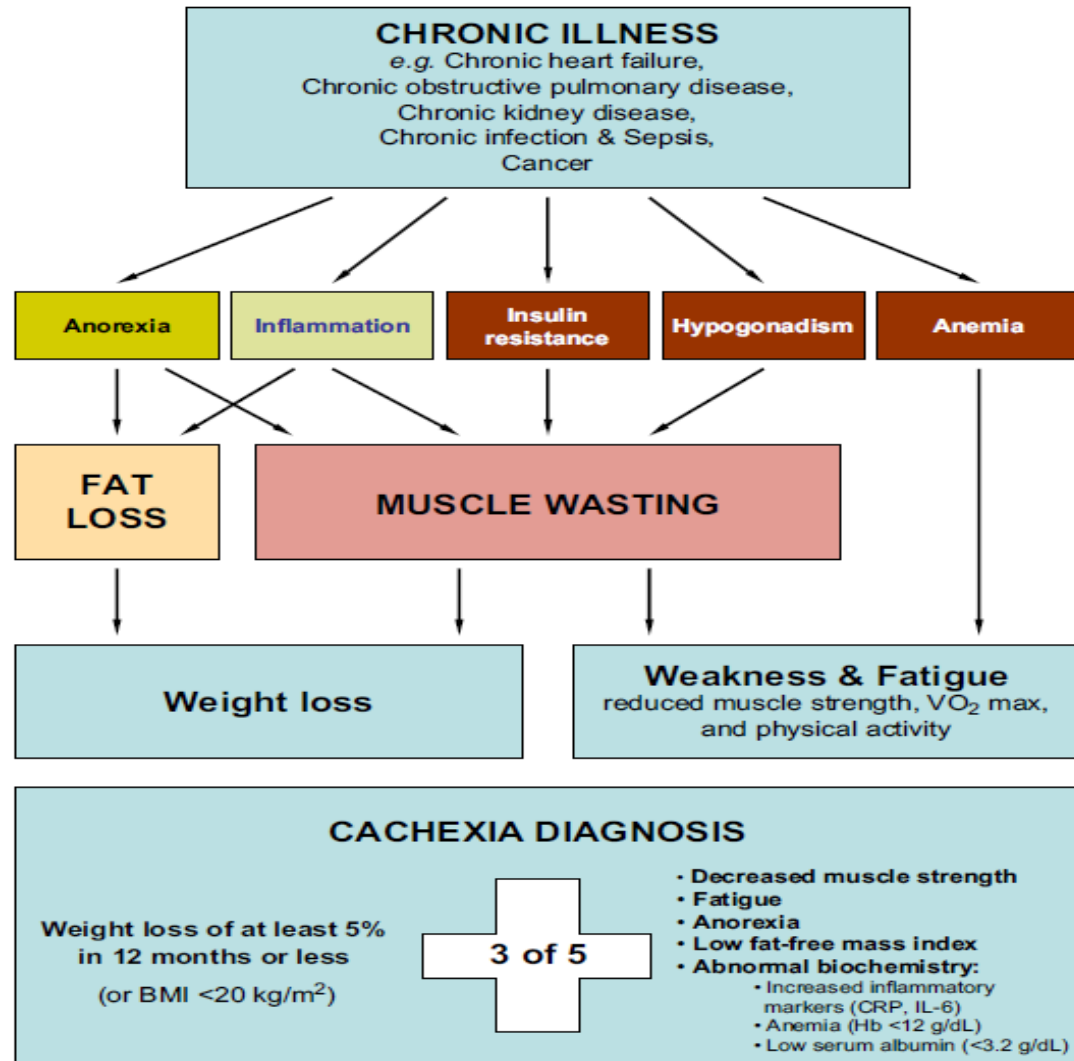
17 studies,
8 combined
with
exercise,
increased
body weight

Support nutritionnel dans la BPCO, *masse non grasse, kg*



Support nutritionnel dans la BPCO, *PM6, m*





AGIR

Schols *et al.* AJRCCM 1995;152;1268-74

- **Patients** 233, VEMS 35 ± 5 %

- **Durée** 8 semaines, réhabilitation

- **Intervention, 3 bras avec exercice en e**
 - exercice + éducation
 - exercice + éducation + SNO + placebo
 - exercice + éducation + SNO + anabolisant

- **Résultats**
 - augmentation poids avec SNO
 - augmentation masse non grasse et force maximale inspiratoire avec anabolisant

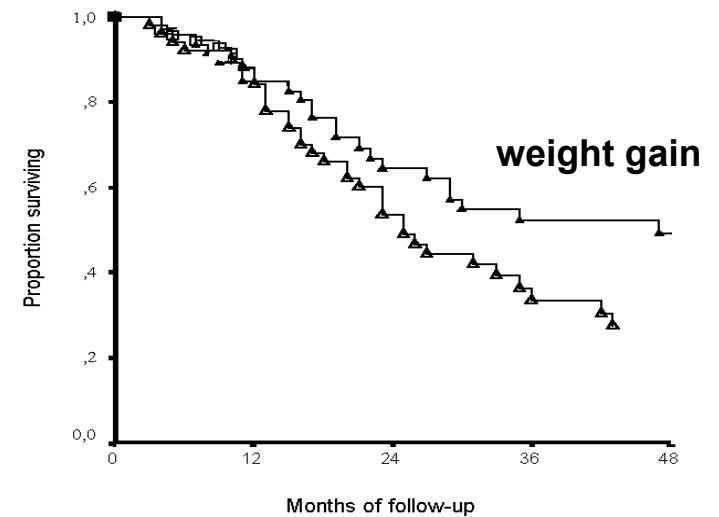
Schols *et al.* AJRCCM 1998;157;1791-7

MULTIVARIATE ANALYSIS OF PREDICTORS OF MORTALITY: PROSPECTIVE STUDY

Variables		RR	95% CI	p Value
<u>Change in weight</u>	<u>Linear*</u>	<u>0.996</u>	<u>0.992–0.999</u>	<u>0.01</u>
Change in P _I max	Linear	0.990	0.976–1.004	NS
Treatment	P versus A	0.753	0.447–1.267	NS
	N versus A	0.872	0.530–1.432	NS
<u>BMI</u>	<u>Linear</u>	<u>0.868</u>	<u>0.803–0.939</u>	<u>< 0.001</u>
FEV ₁	Linear	0.983	0.962–1.003	NS
IVC	Linear	0.995	0.982–1.008	NS
PaO ₂	Linear	0.877	0.751–1.024	NS
PaCO ₂	Linear	0.977	0.707–1.352	NS
<u>Aqe, yr</u>	<u>Linear</u>	<u>1.056</u>	<u>1.022–1.090</u>	<u>< 0.001</u>

Definition of abbreviation: P_Imax = maximal static inspiratory pressure. For other definitions, see Tables 1 and 2.

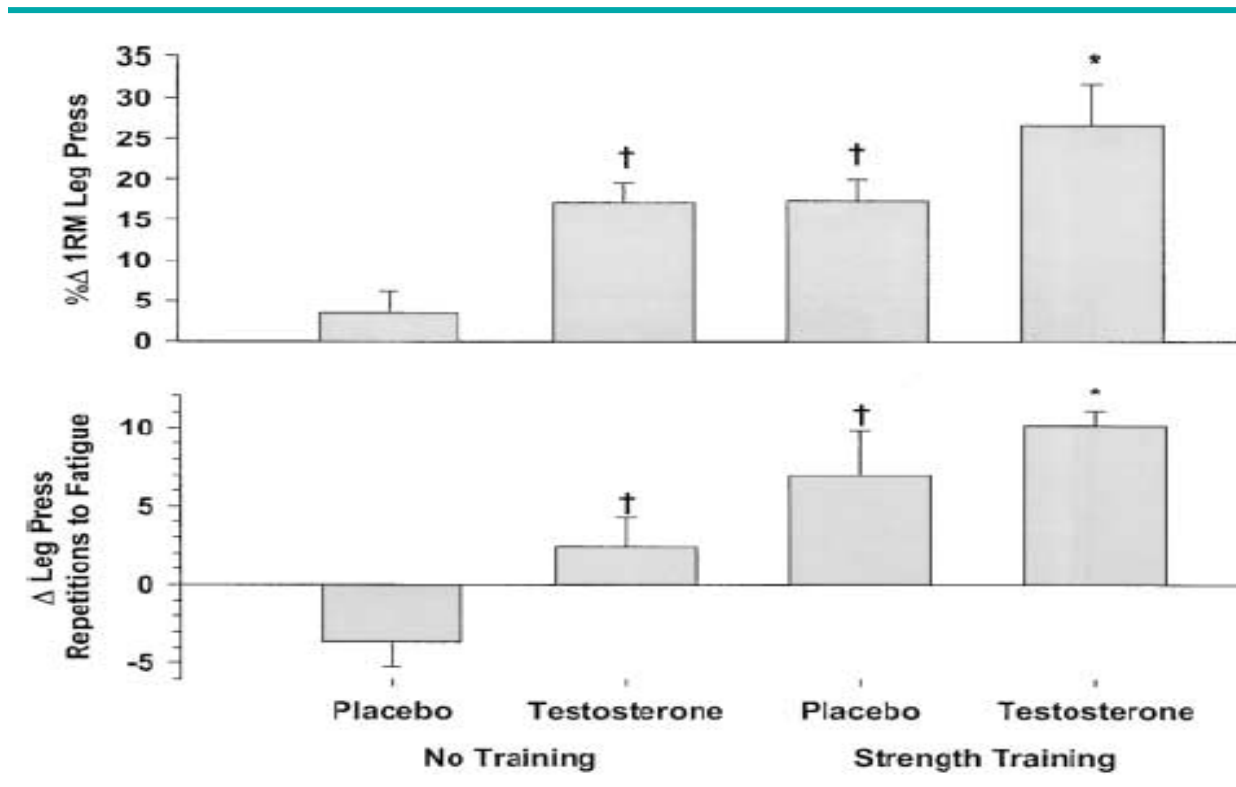
* Entered as time-dependent covariate.



AGIR

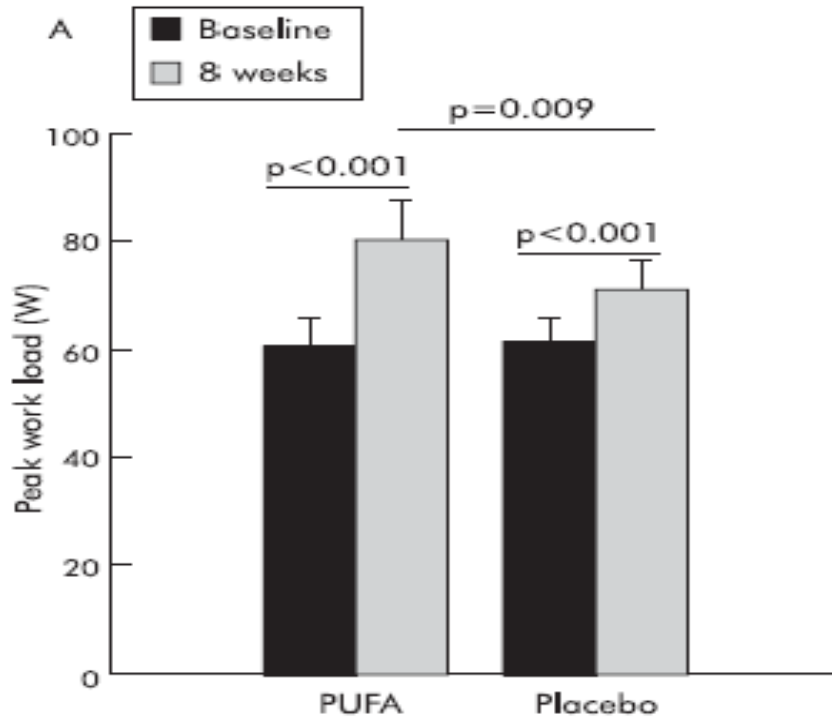
Casaburi *et al.* Am J Crit Care Med 2004;170;870-8

47 male patients with COPD, mean FEV₁ = 40% randomized, double blind, controlled 4 groups, resistance exercise, 100 mg testosterone IM/week, 10 weeks



AGIR

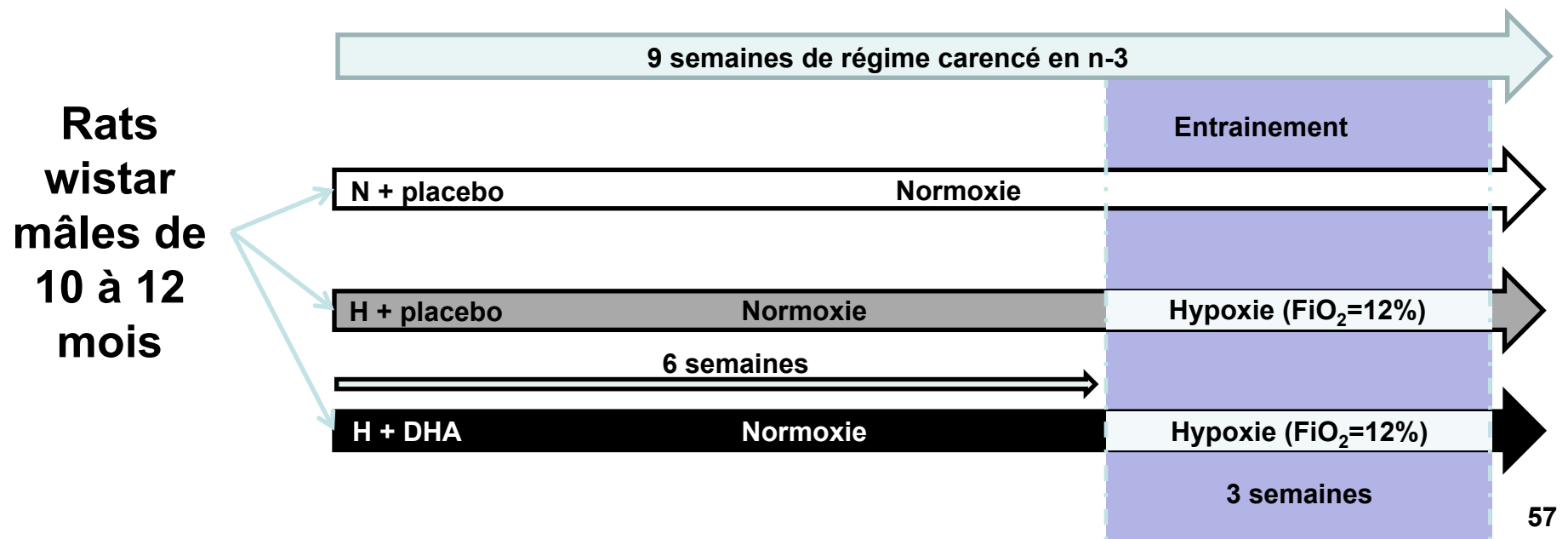
Brokhuizen *et al.* Thorax 2003;124:1733-42



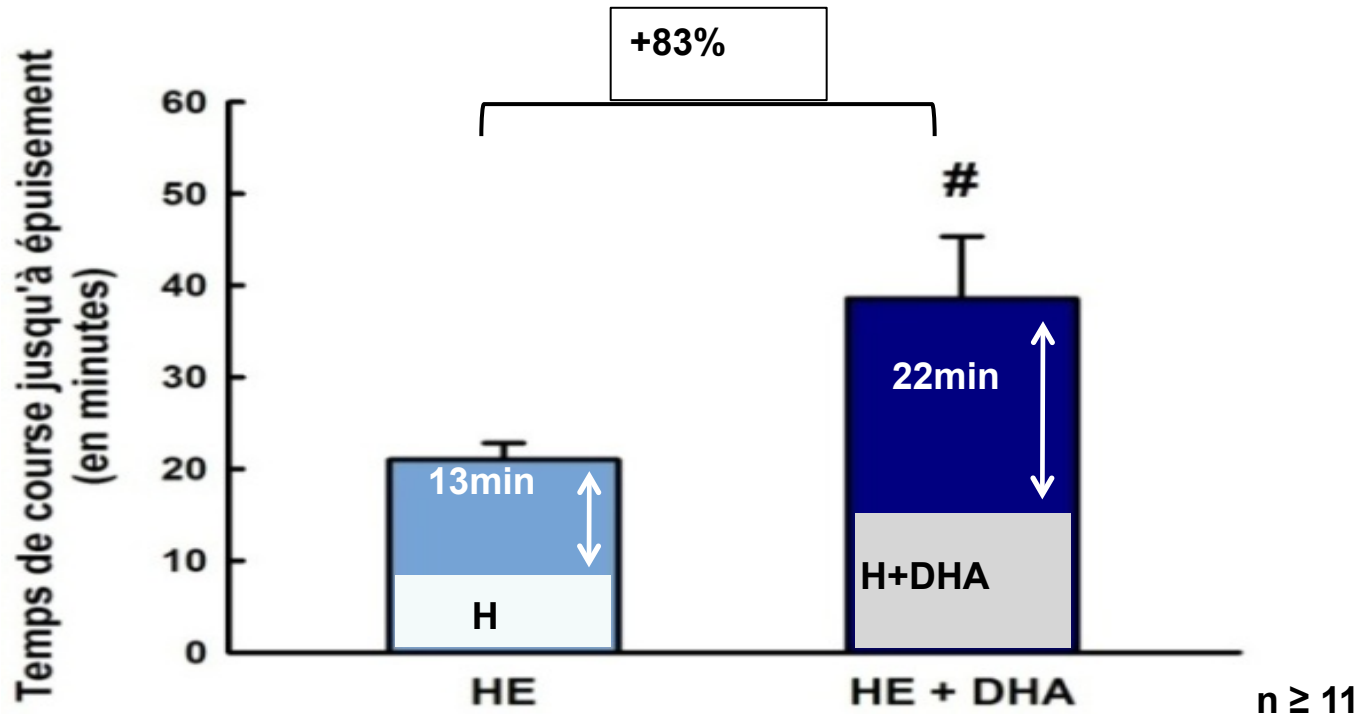
80 COPD, 8 weeks rehabilitation plus oral nutritional supplement (Respifor®)
Double blind, controlled design: oral n-3 PUFA, 9 g/day during 8 weeks

AGIR

Effets d'une supplémentation en DHA sur la tolérance à l'effort lorsqu'elle est combinée à un entraînement en endurance



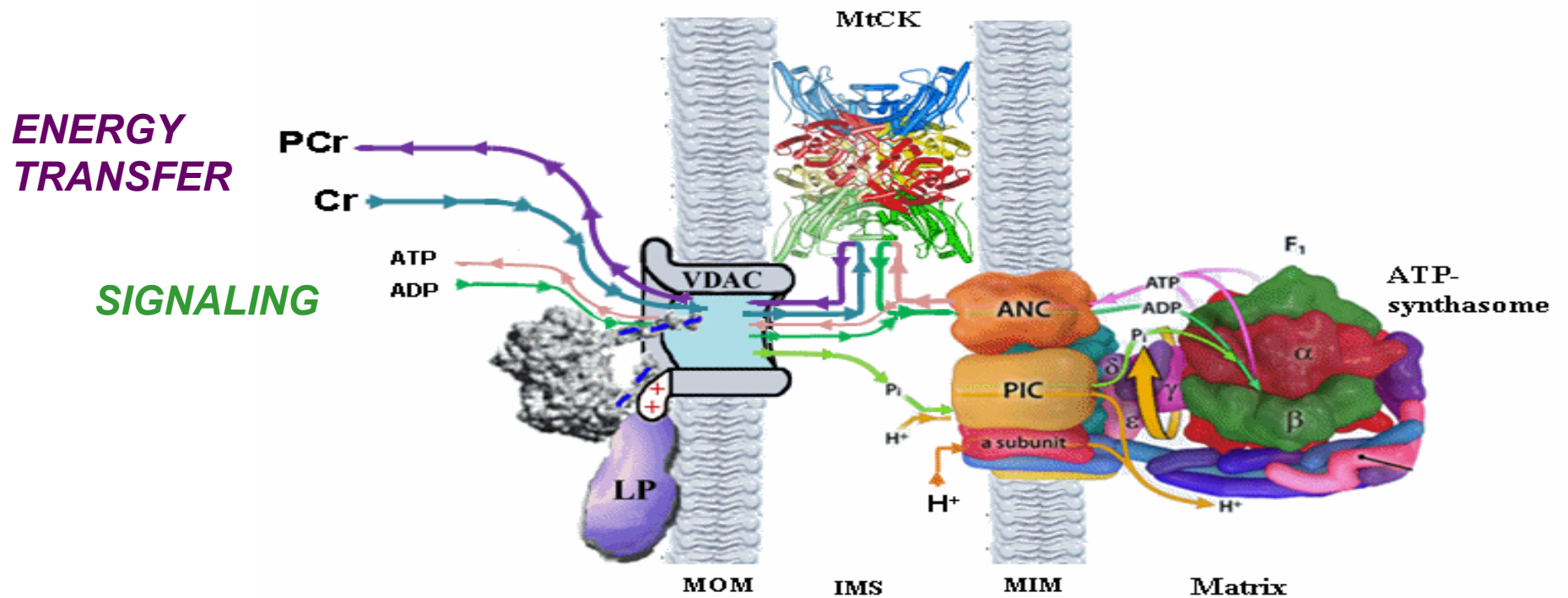
AGIR



Amélioration de la tolérance à l'effort avec effet cumulatif de l'entraînement et de la supplémentation en DHA

AGIR

DHA favorise le couplage ANT-MtCK et conduit à une endurance accrue ?



AGIR

ALIMENTATION ET INSUFFISANCE RESPIRATOIRE : INTERACTIONS EXERCICE-OMEGA N-3
(AIRIEO).

UNE ETUDE PROSPECTIVE CONTROLEE EN DOUBLE INSU CONTRE PLACEBO

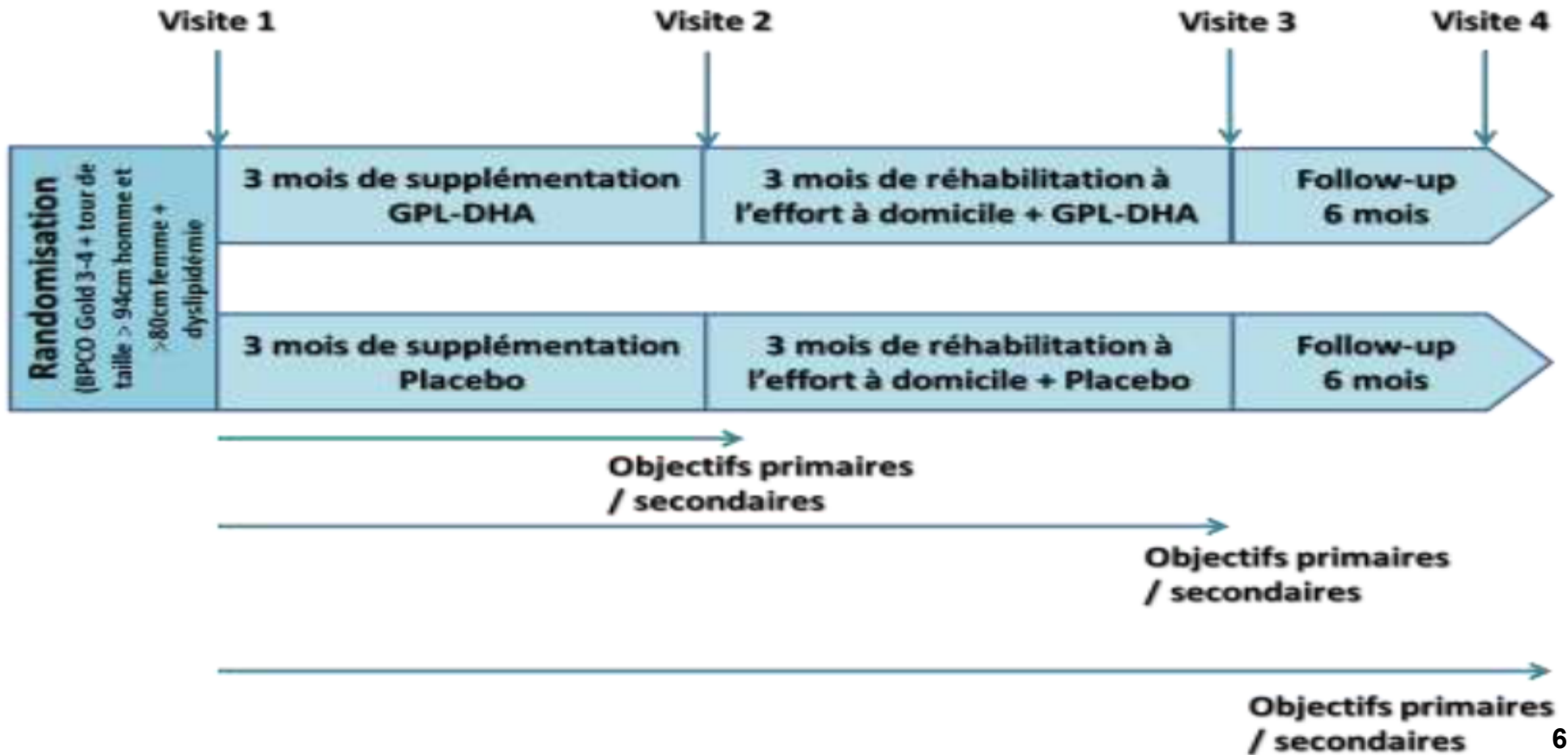
INVESTIGATEUR PRINCIPAL : PR. C. PISON CHU DE GRENOBLE

Objectifs de l'essai :

Objectif principal : Evaluer l'effet d'une supplémentation en Acides Gras PolyInsaturés de la série n-3 (GPL-DHA) et l'effet additif d'une réhabilitation à l'effort à domicile et d'une supplémentation en AGPI sur la tolérance à l'effort de patients BPCO sévères et très sévères à risques cardiométaboliques.

Objectifs secondaires : Evaluer la sensibilité à l'insuline, le profil lipidique, la composition corporelle et la quantité de graisse viscérale, le profil systémique inflammatoire, la dyspnée, l'actimétrie et la qualité de vie.

AGIR



AGIR

IRAD2, Pison, Cano *et al.* Thorax 2011;66:953-60

- **Patients** 60, 66,6 ± 9,6 ans, IMC 21,5 ± 3,8
 62, 65,1 ± 9,6 ans, IMC 21,4 ± 4,0

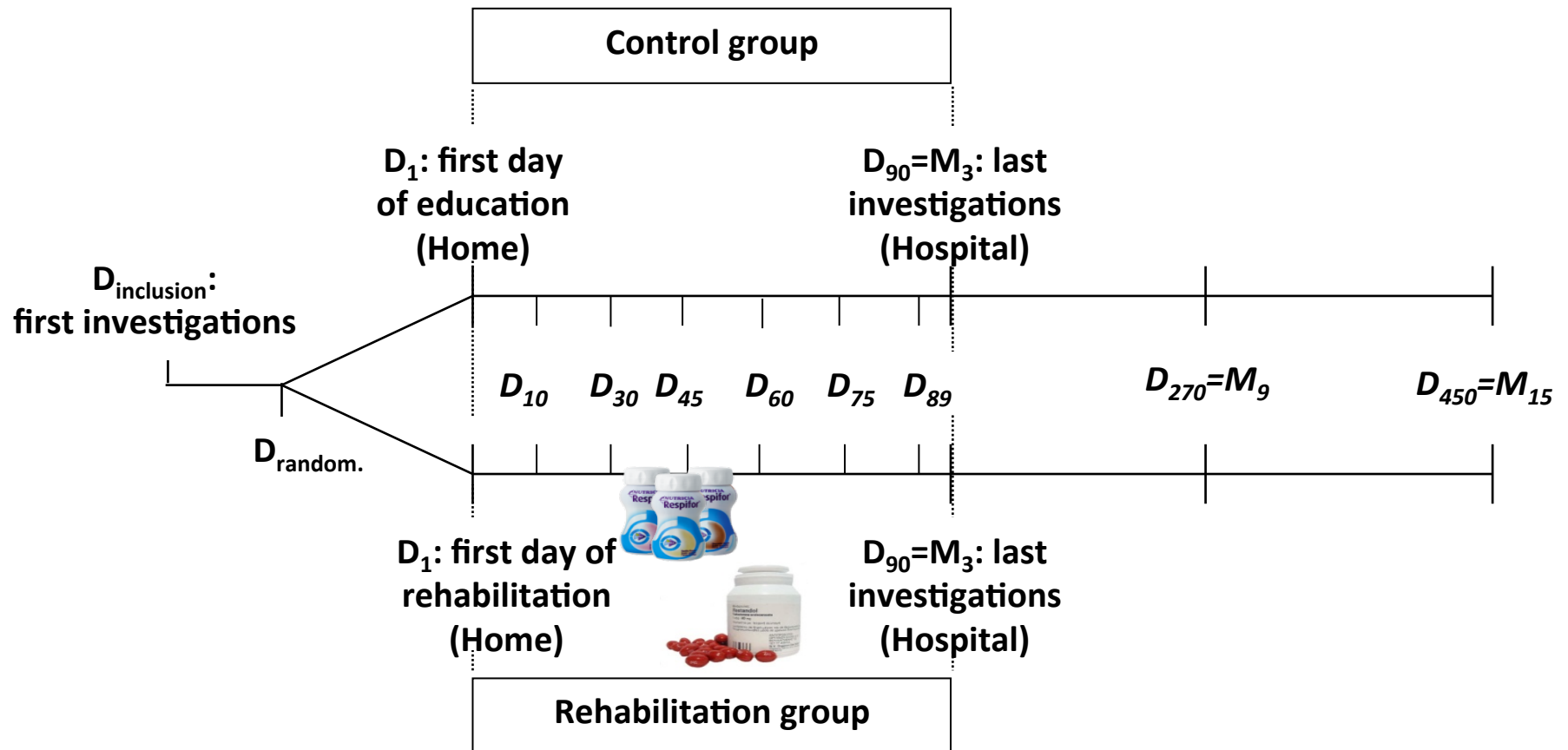
- **Duration** 12 semaines, 12 mois de suivis

- **Intervention** - Education + Exercice + ONS + testostérone orale
 - Education

- **Résultats**
 - 3 mois: augmentation poids, masse non grasse, force quadriceps, hémoglobine, endurance, W_{max} , QdV chez les femmes
 - 15 mois : meilleure survie en per-protocole

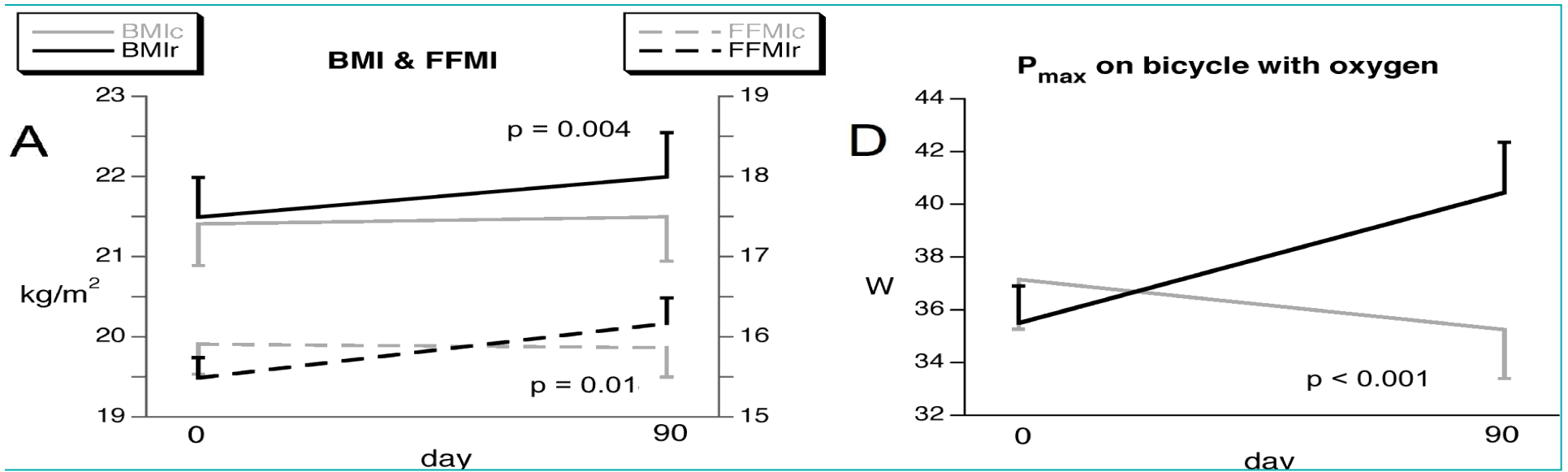
AGIR

IRAD2, Pison, Cano *et al.* Thorax 2011;66:953-60



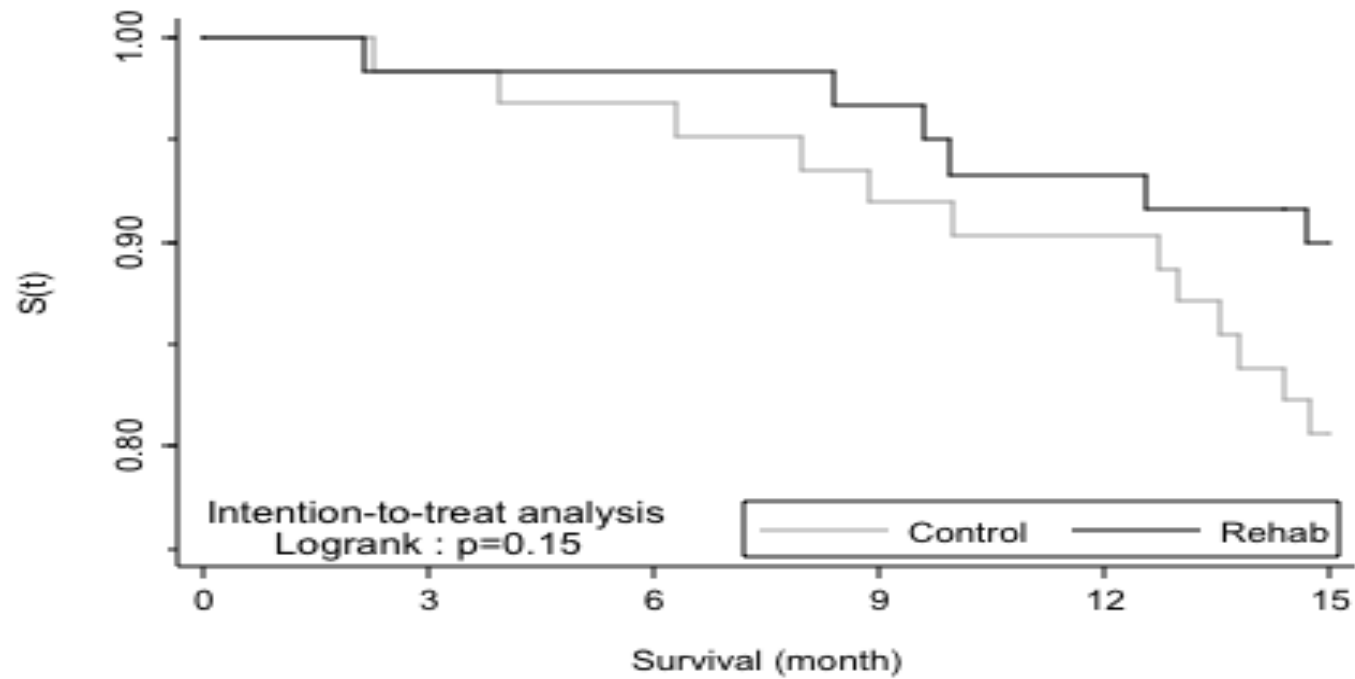
AGIR

IRAD2, Pison, Cano *et al.* Thorax 2011;66:953-60



AGIR

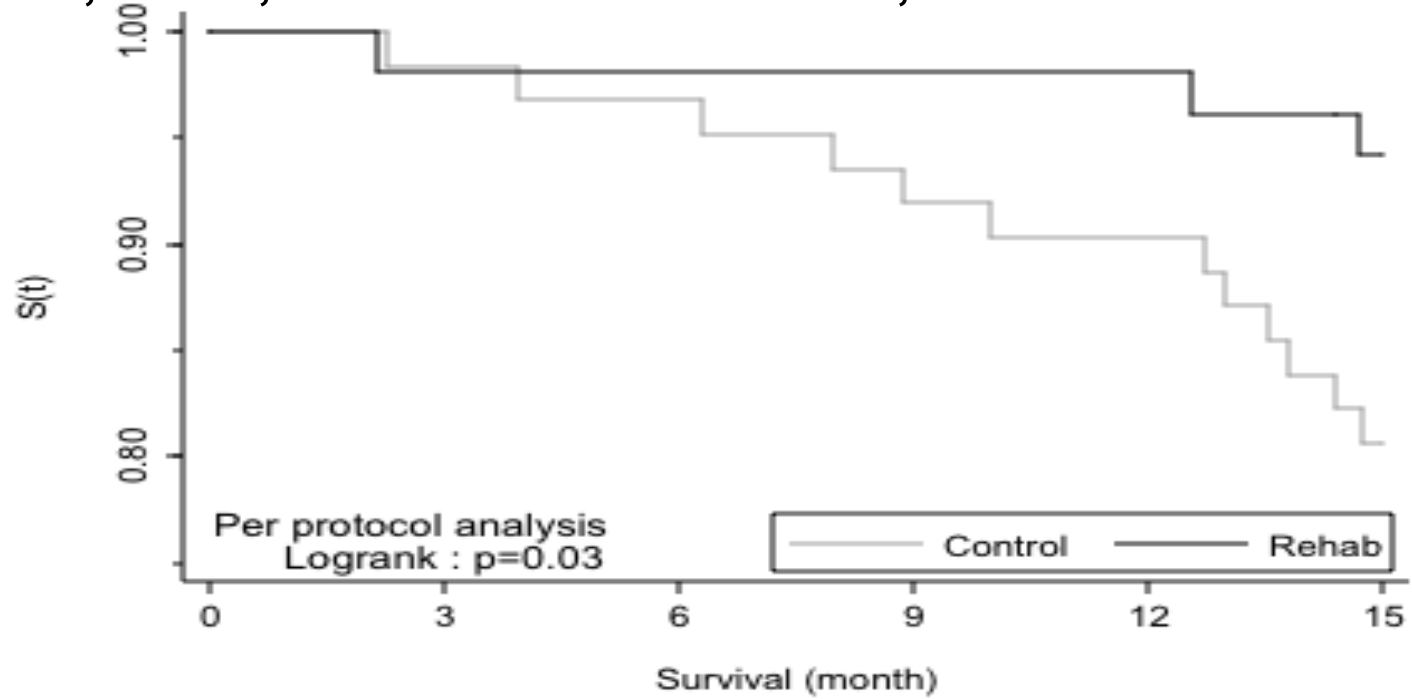
IRAD2, Pison, Cano *et al.* Thorax 2011;66:953-60



Number at risk		0	3	6	9	12	15
Control		62	61	60	57	56	50
Rehabilitation		60	59	59	58	56	53

AGIR

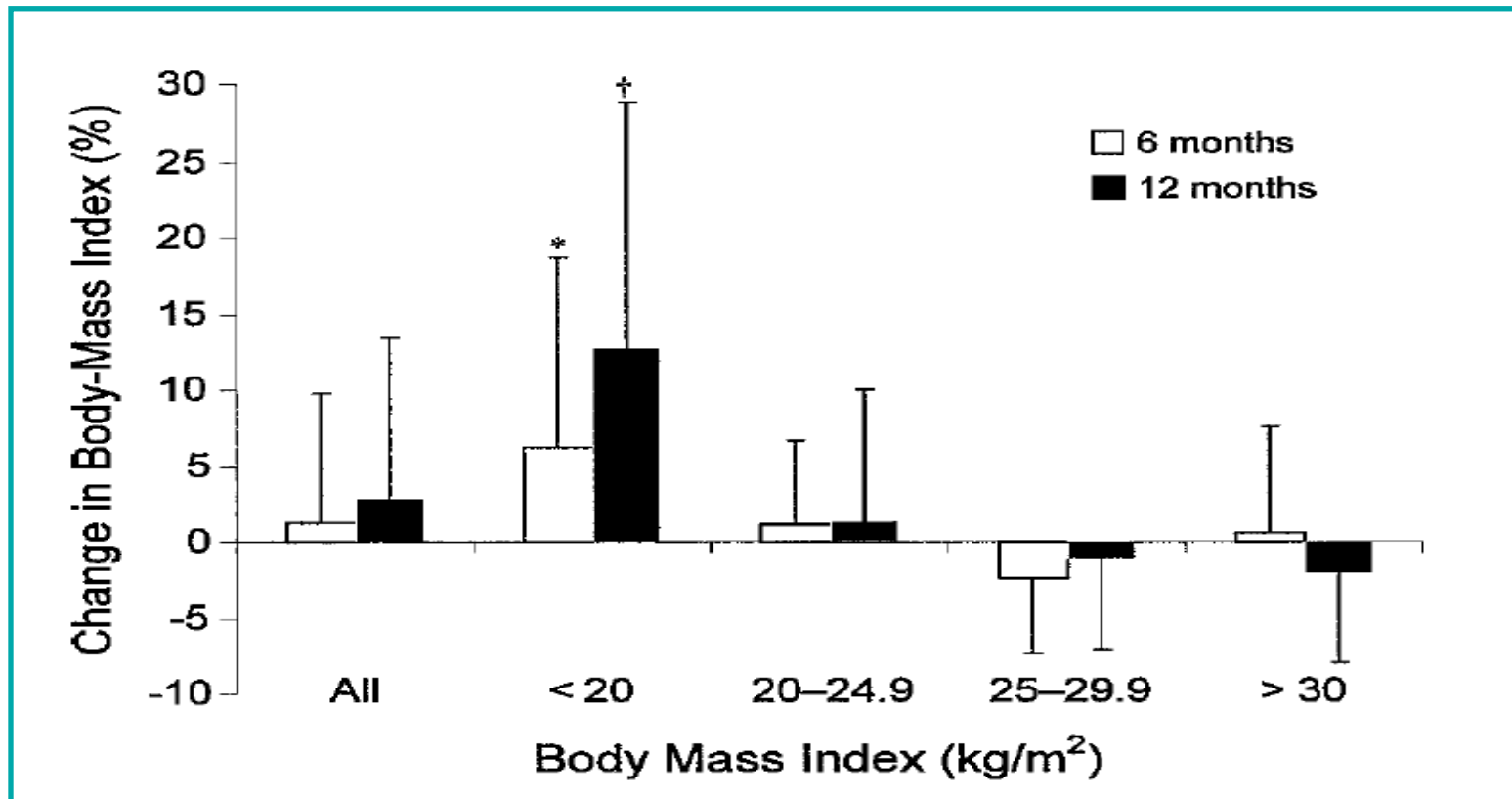
IRAD2, Pison, Cano *et al.* Thorax 2011;66:953-60



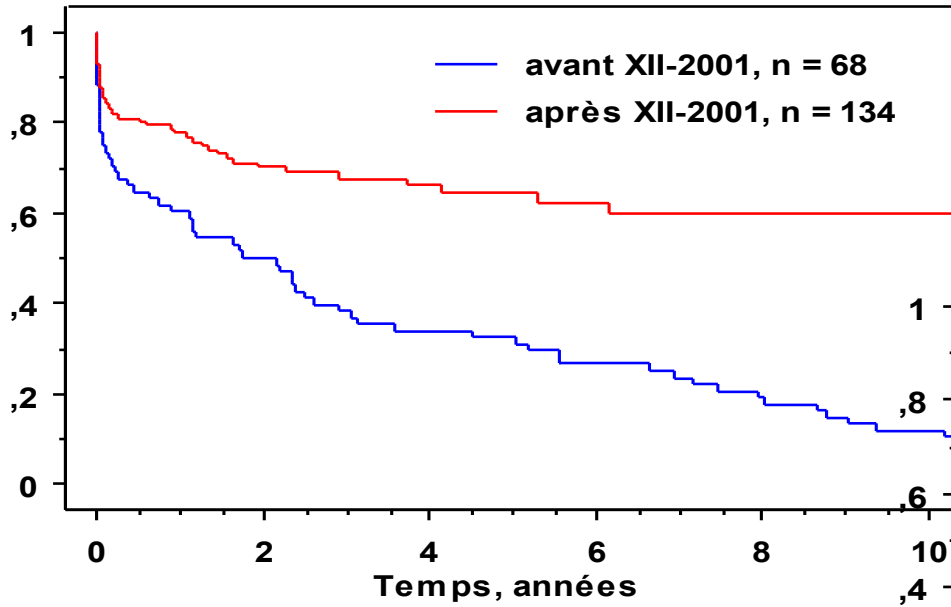
Number at risk	0	3	6	9	12	15
Control	62	61	60	57	56	50
Rehabilitation	52	51	51	51	51	48

AGIR

Budweiser *et al.* Respir Care 2006;51:126-32

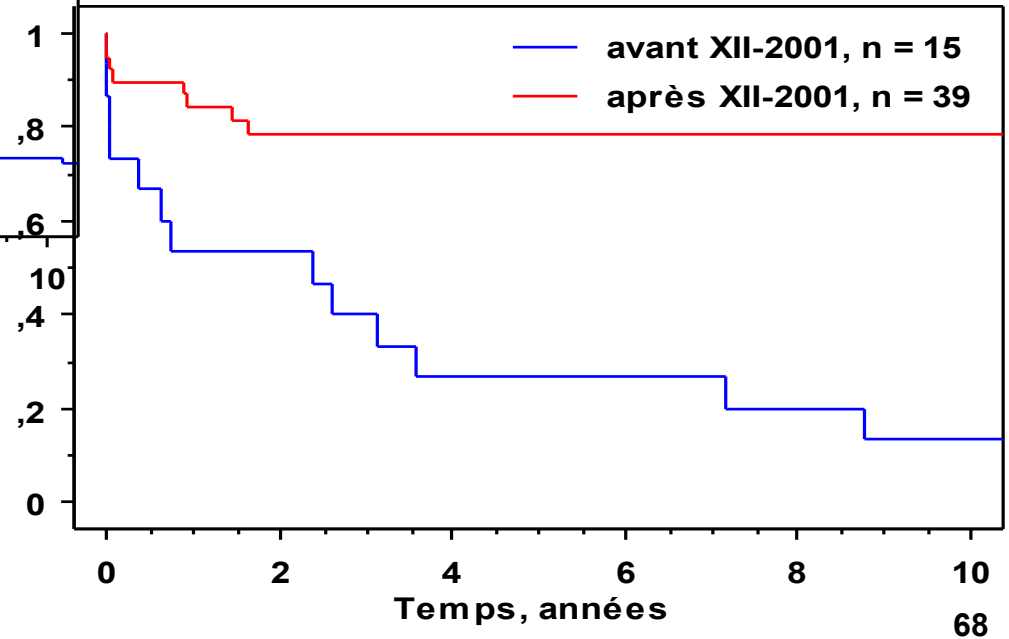


AGIR



Toutes indications, n = 204

Mucoviscidoses, n = 54



AGIR

Programme depuis 2009, J.-C. Borel, F. Frumy



ASSISTANCE MÉDICO-TECHNIQUE À DOMICILE

Compte rendu de la réhabilitation à la nutrition et à l'activité physique

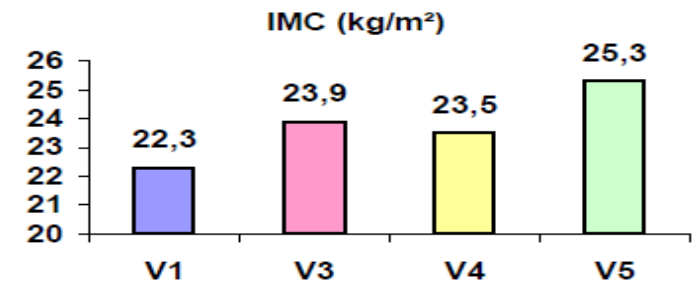
Nom : Pneumologue : Pr. PISON/Dr. JEANJEAN/Dr. F
Prénom : Roland Kinésithérapeute :
Age : 64 ans Médecin traitant : Dr. HADI

Planning des visites

V1 : 04/03/2010 V2 : 23/03/2010 pas de mesures prévues lors de cette visite
V3 : 10/06/2010 V4 : 07/10/2010 V5 : 14/04/2011

	V1	V3	V4	V5
Poids (kg) :	71,3	76,6	75	81
IMC (kg/m ²) :	22,3	23,9	23,5	25,3
Risque de dénutrition : (oui/non)	NON	NON	NON	NON

BOD 5a
1 : bon état de santé → 8 : mauvais état de santé
a : PaO₂ ≥ 60 mmHg ; b : PaO₂ < 60 mmHg

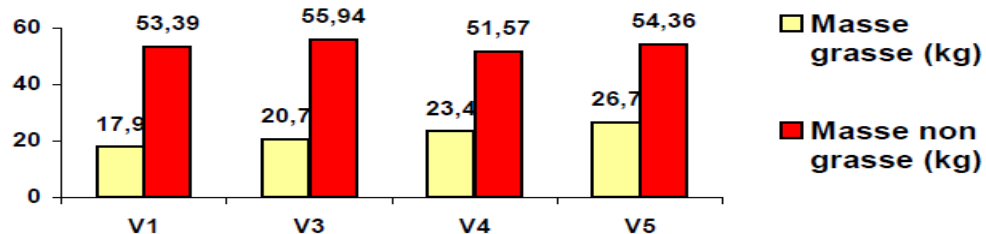


Percentile masse grasse : 50à75 50à75 75à90 75à90
 Percentile masse non grasse : 10à25 25à50 5à10 25à50

Impédancemétrie

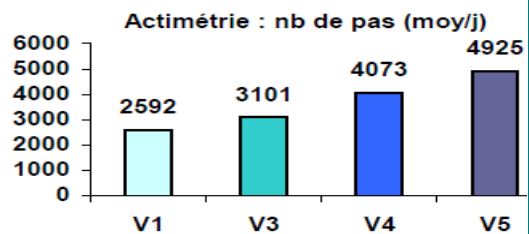
	V1	V3	V4	V5
Masse grasse (Kg) :	17,9	20,7	23,4	26,7
Masse non grasse (Kg) :	53,39	55,94	51,57	54,36

(mucles + os)

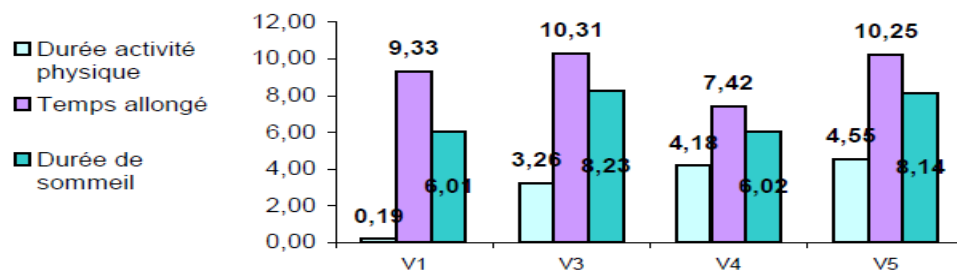


Actimétrie

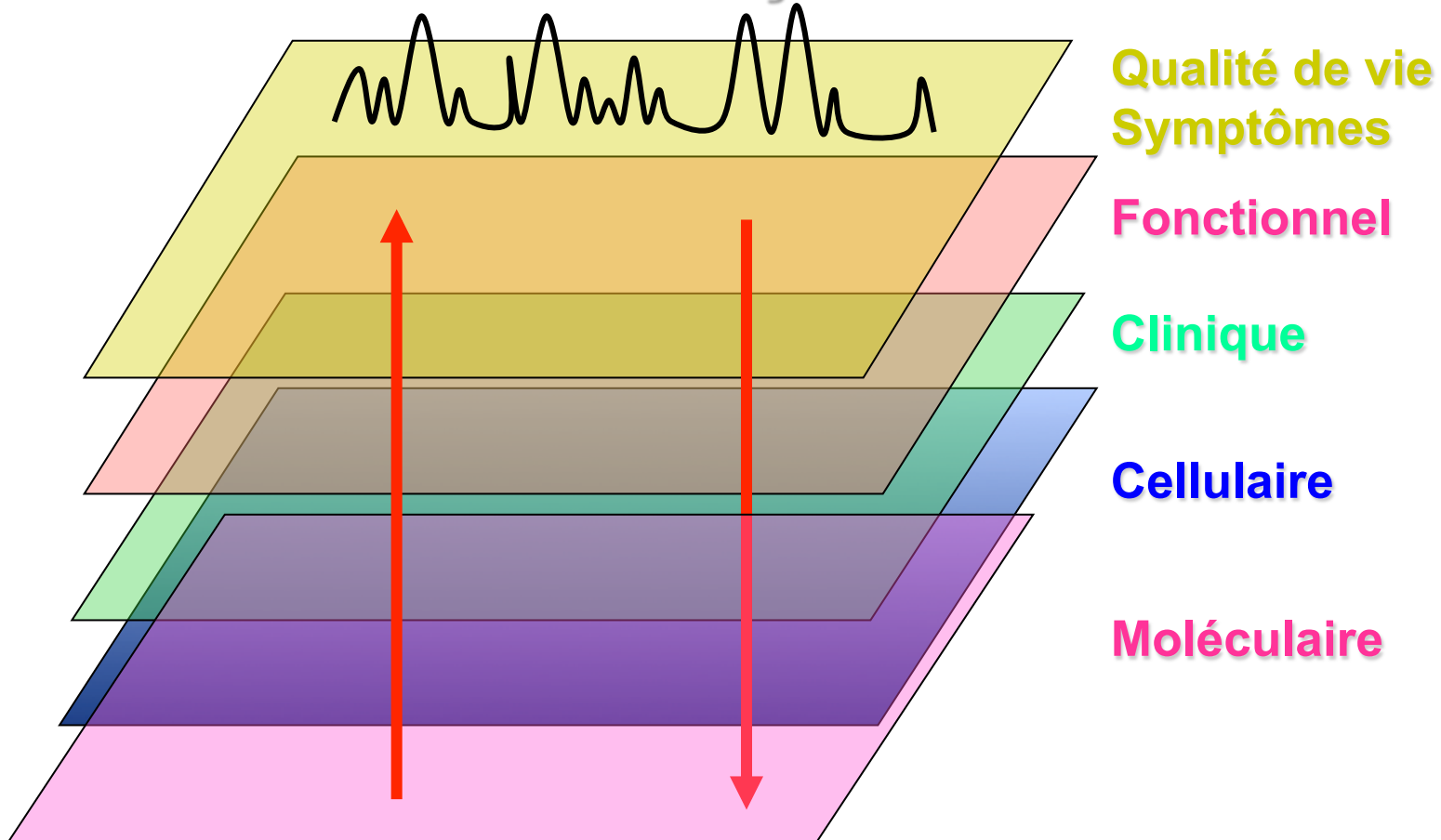
	V1	V3	V4	V5
Durée actimétrie (j) :	3	4	6	4
Durée activité physique : (moy/j, h.min)	0,19	3,26	4,18	4,55
Nb de pas (moy/j) :	2592	3101	4073	4925
Temps allongé : (moy/j, h.min)	9,33	10,31	7,42	10,25
Durée de sommeil : (moy/j, h.min)	6 01	8 23	6 02	8 14



Actimétrie : moy/j, heures et minutes



Leçons



Auffray *et al.* (2009) *Genome Med* 2009;1:2 & *Chest* 2010; 137:1410-6

Leçons

A Systems Biology Approach Identifies Molecular Networks Defining Skeletal Muscle Abnormalities in Chronic Obstructive Pulmonary Disease

Nil Turan¹, Susana Kalko², Anna Stincone¹, Kim Clarke¹, Ayesha Sabah¹, Katherine Howlett³, S. John Curnow³, Diego A. Rodriguez², Marta Cascante⁴, Laura O'Neill³, Stuart Egginton³, Josep Roca², Francesco Falciani^{1*}

18 COPD patients vs 12 age-matched sedentary controls

Effect of a 8-week rehabilitation program on muscle gene expression

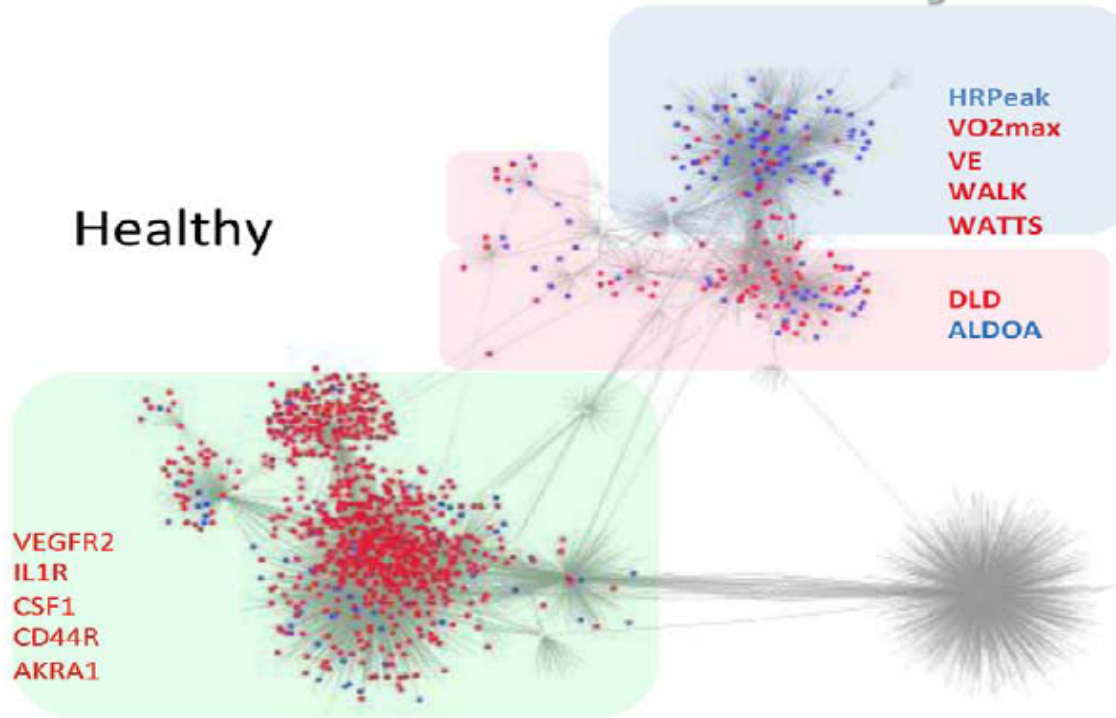
-> altered responses in COPD patients mediated by :

- inflammation
- hypoxia
- nutritional status

Epigenetic control ?

Leçons

Healthy

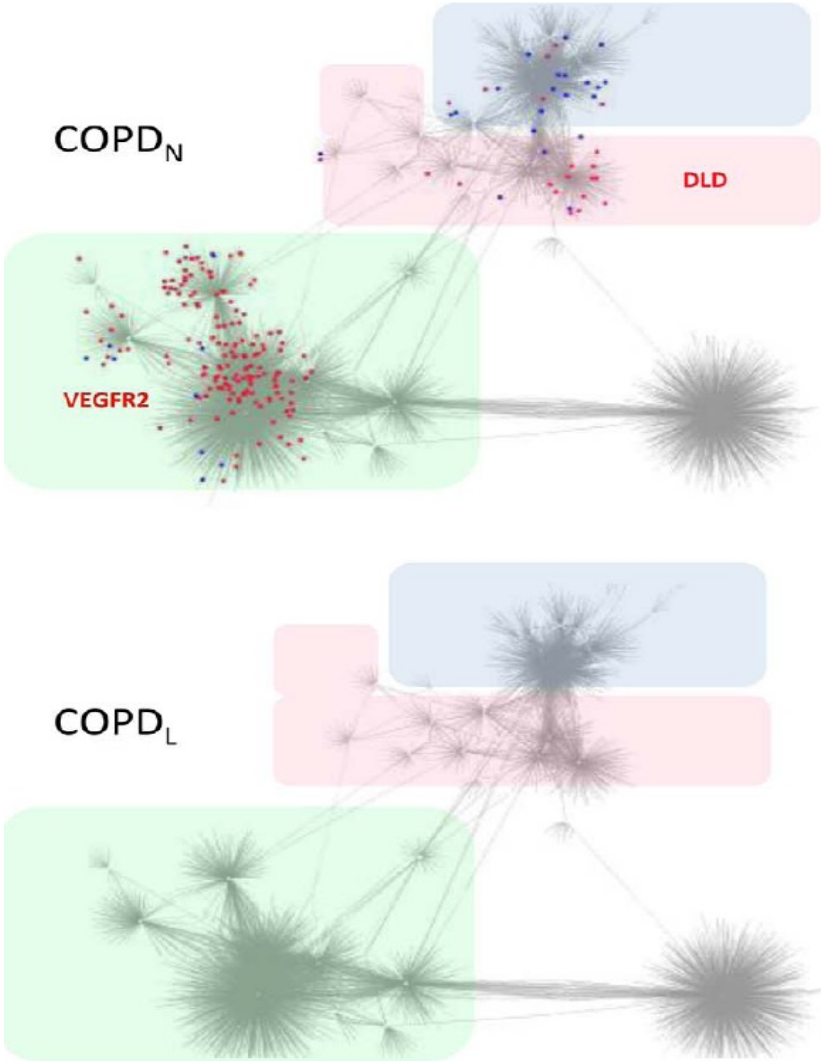


GOBP generation of precursor metabolites and energy (8)
GOCC mitochondrial inner membrane (6)
GOCC respiratory chain complex I (3)
GOCC ribonucleoprotein complex (9)
GOMF Cadmium ion binding (4)

KEGG oxidative phosphorylation (10)
GOCC Mitochondrion (29)

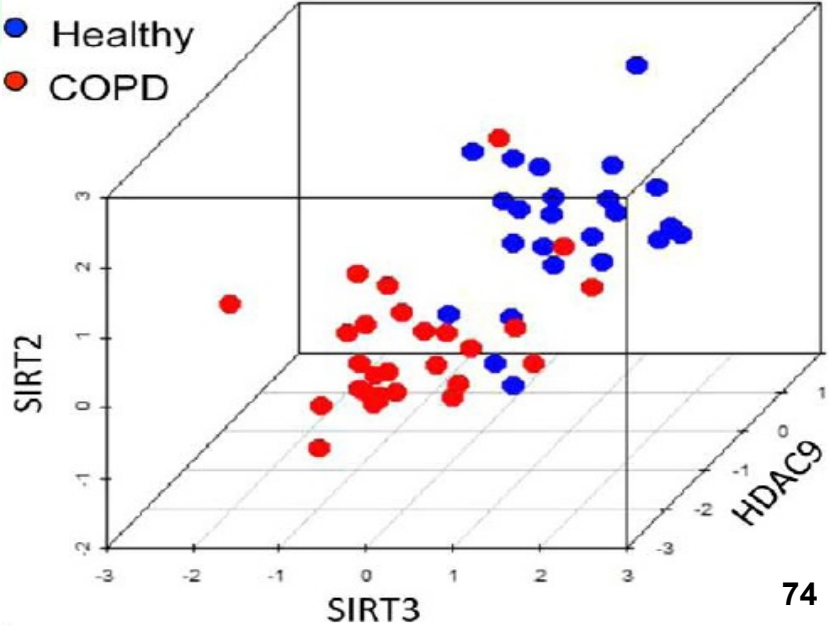
GOBP cell adhesion (85).
GOCC ECM (47).
KEGG Focal adhesion (28).
GOBP cell motility (41).
GOBP development process (173).
GOBP intracellular signalling cascade (86).
GOBP Cell proliferation (53).
GOBP inflammatory response (25)
GOBP blood vessel development (21)

Leçons

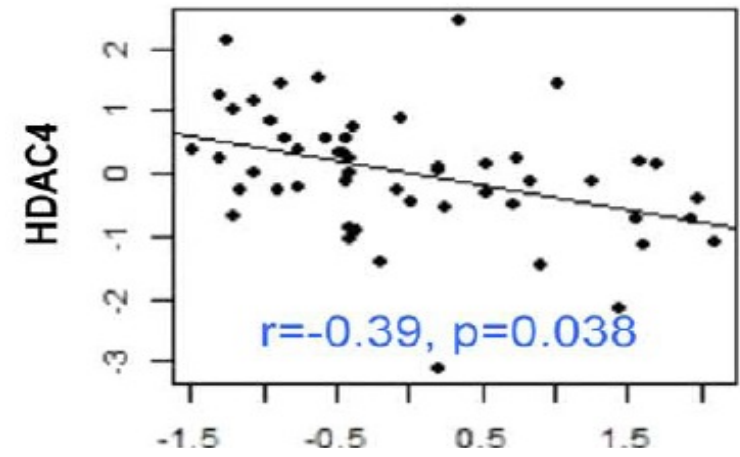
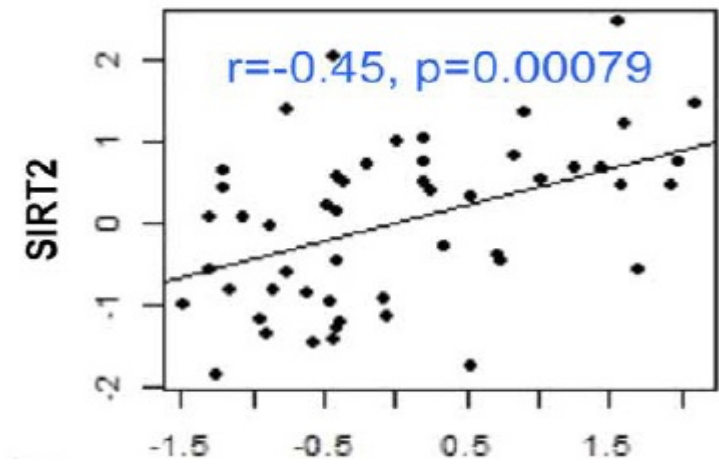
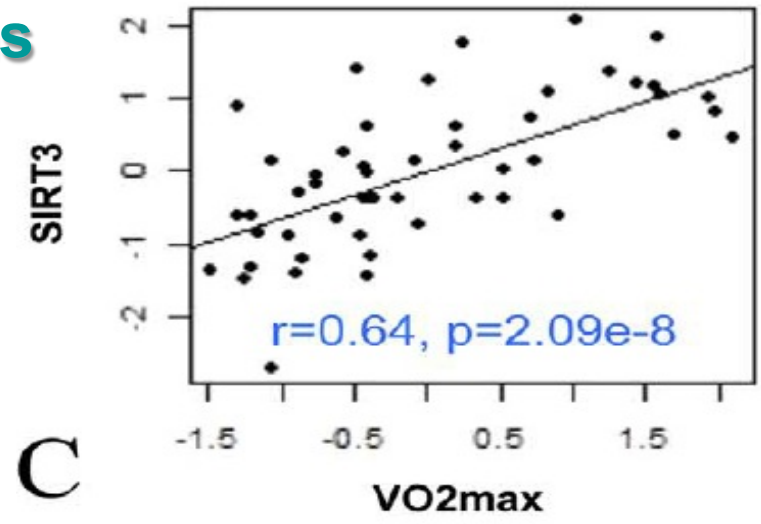
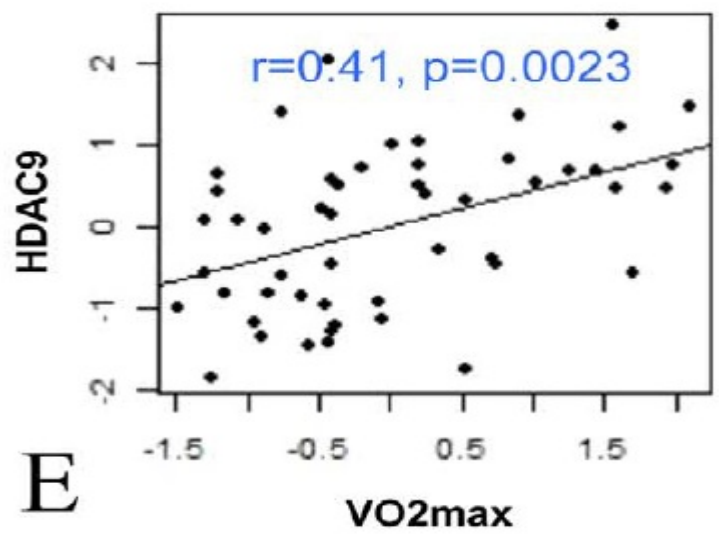


- GOCC ECM (15)
- GOCC collagen (9)
- KEGG Focal adhesion (15)
- GOBP organ development (32)
- GOBP localization of cell (13)
- GOBP Regulation of cell proliferation (16)

● Healthy
● COPD

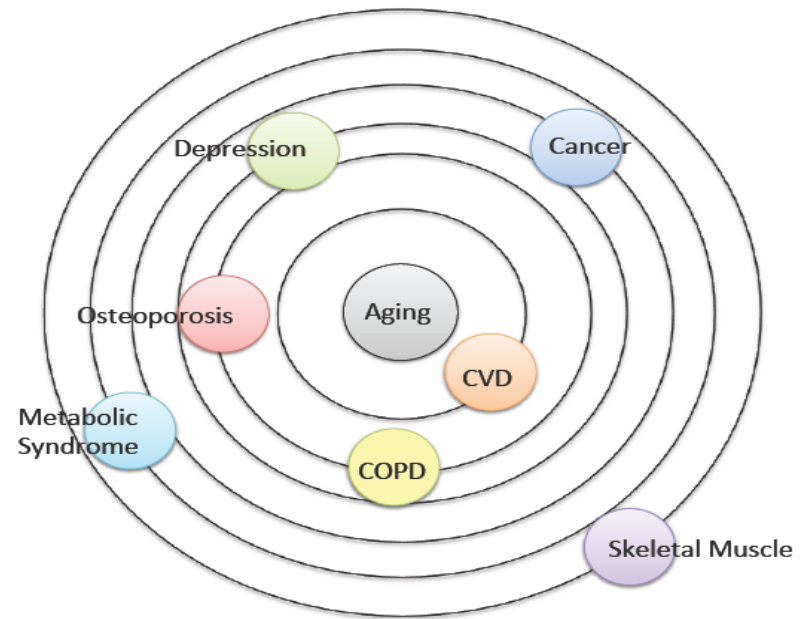
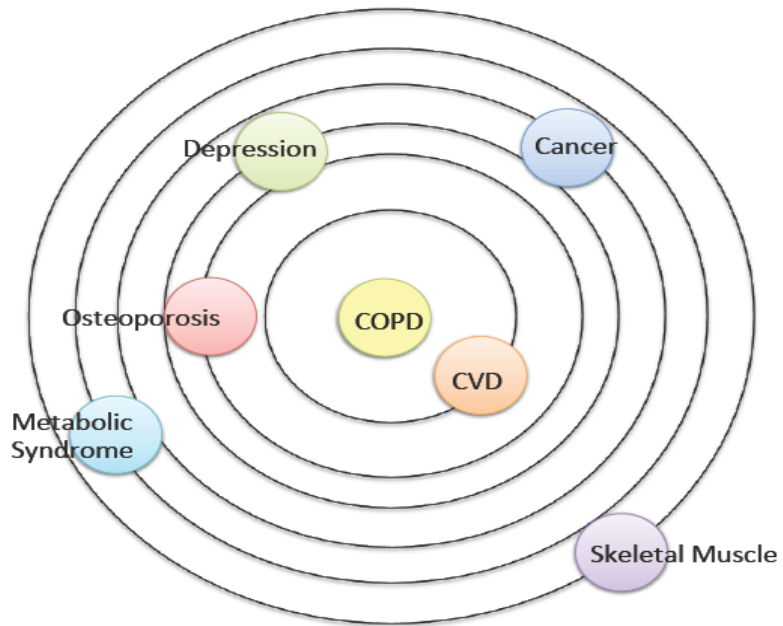


Leçons

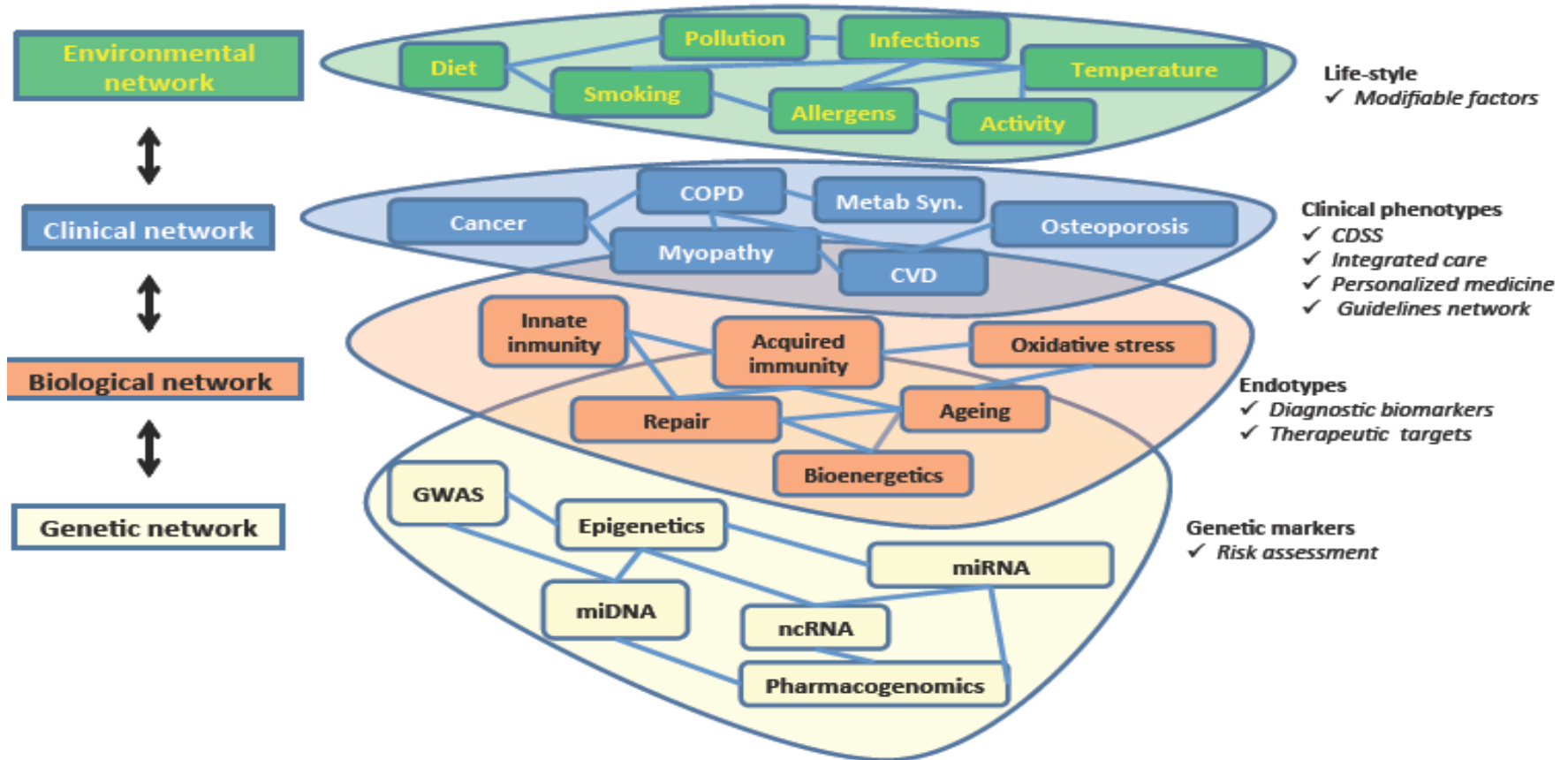


Leçons

The pulmonologist view of comorbidities Moving towards a Copernican view of COPD



Network medicine in COPD



Coordinating Systems Medicine across Europe European Systems Medicine road-map discussions

From Systems Biology to Systems Medicine Workshops June 2010 – December 2013 – Horizon
2020

Predictive, Preventive, Personalized, Participatory Medicine

*Systems biology and personalized medicine - the future is now. Auffray C, Hood L (2012) J Biotech
7:938-939*

*Revolutionizing medicine in the 21st century through systems approaches. Hood L, Balling R,
Auffray C. (2012) Biotechnol J 7:992-1001*

Remerciements



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European Institute of Systems Biology and Medicine, C. Auffray

Cliniques Universitaires de Pneumologie et de Physiologie, Pr. B. Paramelle
Groupe de Transplantation pulmonaire de Grenoble

AGIR@dom

Nutricia, PHRC

