

BPCO: focus sull'anziano

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Sequenza

- Cenni di epidemiologia
- Comorbilità, età e BPCO
- Il malato reale e quello dei trial
- La diagnosi fisiopatologica
- Terapia: fattori ostativi
- Terapia: che cosa fare e che cosa no
- Dalla valutazione multidimensionale al trattamento multidisciplinare

Tra il 1978-80 e il 2000-1 la prevalenza media
 immo modificata, ma aumenta nell'anziano (Vasankari TM
 et al Eur Respir J 2010; 36: 766)

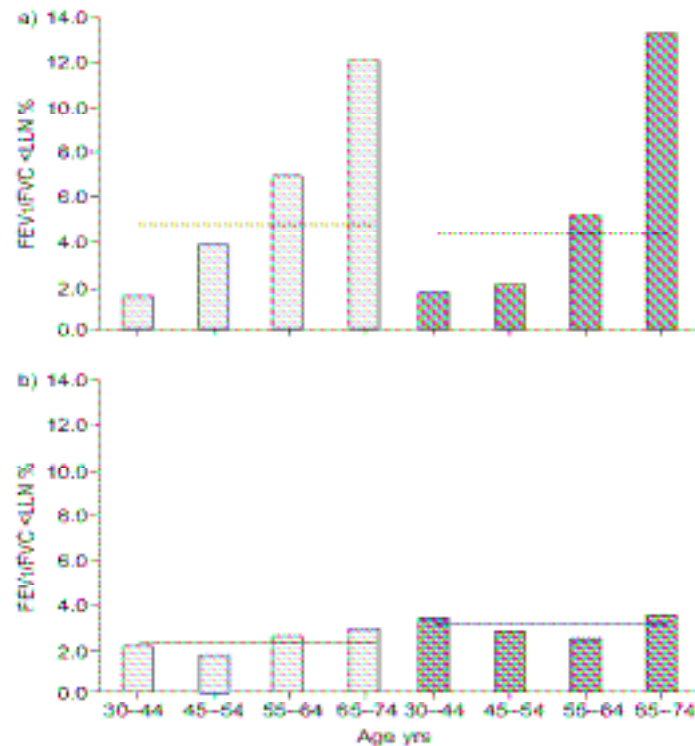


FIGURE 1. Prevalence of bronchial obstruction defined as forced expiratory volume in 1 s (FEV₁)/forced vital capacity (FVC) below the lower limit of normal (<LLN) in a) males and b) females in the Men Finland Health Survey (performed in 1978-1980; □) and in the Health 2000 Survey (performed in 2000-2001; ▨).

Il rapporto con l'età: effetto cumulativo o base biologica? (Gould NS et al Am J Respir Crit Care Med 2010; 182: 1114)

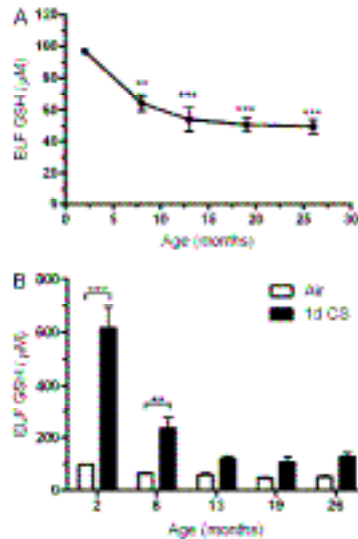


Figure 7. Age decreases both basal and the adaptive epithelial lining fluid (ELF) glutathione (GSH) levels. (A) Basal levels of GSH in the ELF were measured in mice 2, 8, 13, 19, or 26 months of age. All age groups have significantly reduced ELF GSH compared with the 2-month-old mice. (B) Both young and aged mice were exposed to air (open bars) or cigarette smoke (closed bars) for 1 day and the GSH adaptive response was examined. Data represented as mean \pm SEM with **P < 0.01, and ***P < 0.001; n = 4–6 compared with control.

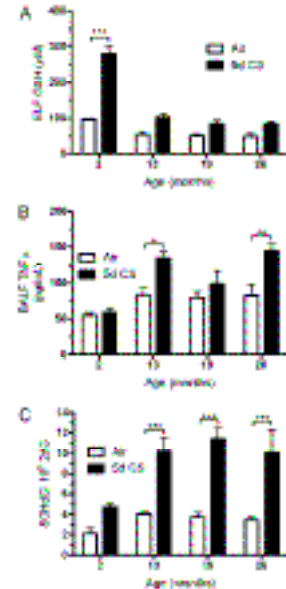


Figure 8. Inflammation and oxidation are increased in the aged airway. 5 days of cigarette smoke (CS) exposure. (A) Epithelial lining fluid (ELF) glutathione was measured after exposure to air (open bars) or (closed bars) for 5 days in the 2-, 13-, 19-, and 26-month-old mice. (B) Bronchoalveolar lavage fluid (BALF) TNF- α and (C) 8-hydroxydeoxyguanosine (8OHdG) were measured in the aged mice in the young mice with CS exposure. Data represented as mean \pm SEM with *P < 0.05, **P < 0.01, ***P < 0.001 compared between air and CS; n = 4–6.

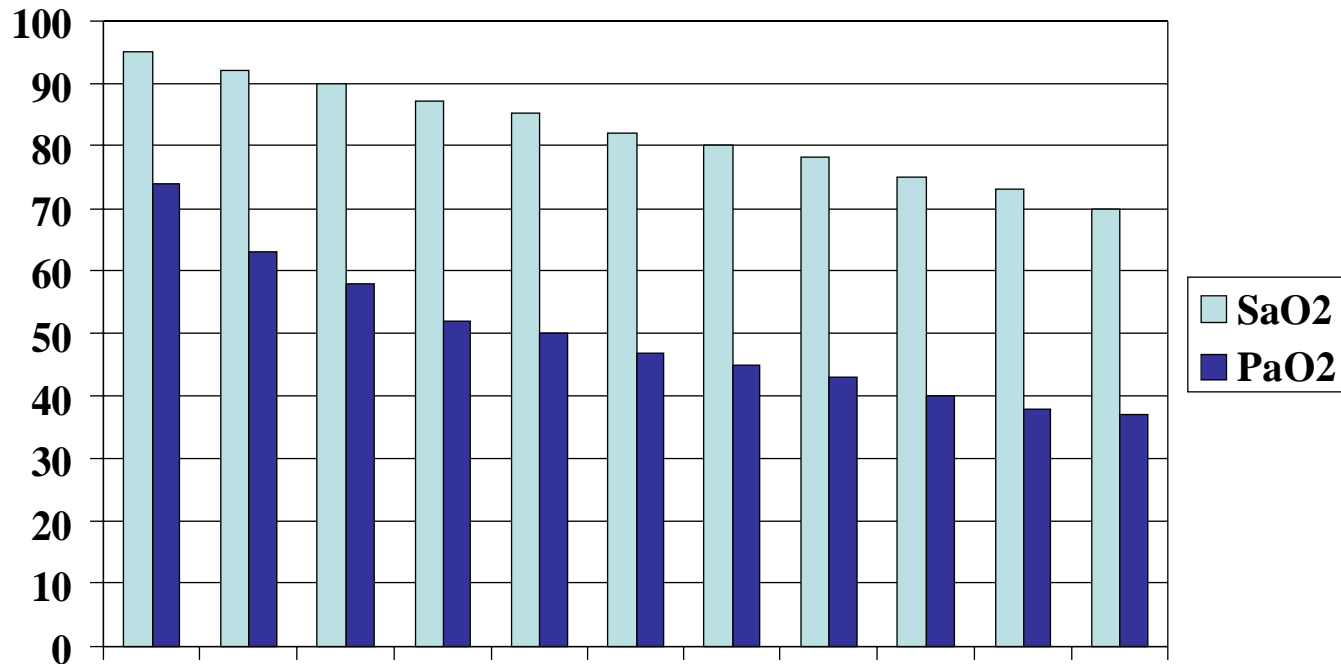
...ma la BPCO resta spesso misconosciuta

- Sintomi “atipici”
- Impropria interpretazione degli edemi
- Limiti della SaO₂
- Comorbilità o multimorbilità
- Incertezze in merito ai valori normali di PaO₂ e PA-aO₂

La dispnea può mancare anche in malati respiratori gravi
(Antonelli Incalzi et al, J Int Med 252 (1): 48-55, 2002)

	Diagnosi corretta, n: 67	Diagnosi errata, n: 13	p
Dispnea	60	3	<.001
Astenia	21	10	.002
Edemi	14	6	.06
Toracoalgia	6	3	.14
Confusione	3	1	.63
Vertigini	4	2	.24

L'ipossiemia è spesso tardiva: rapporto tra SaO₂ e PaO₂



PaO₂ e DA-aO₂ in funzione dell'età

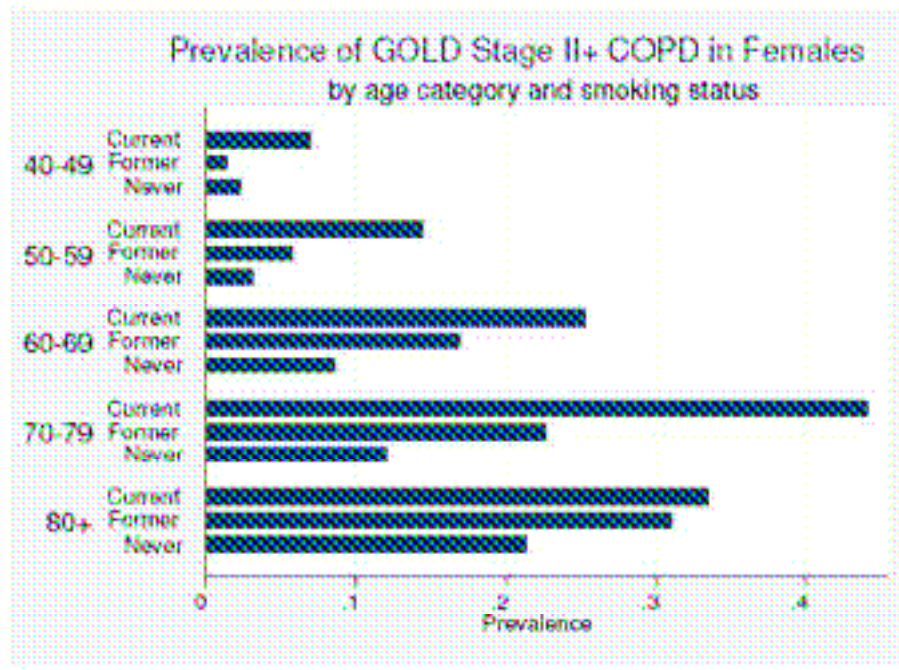
- PaO₂=110 - (0.4 x età). In pratica un 50enne avrà PaO₂= 86 mm Hg, un 80enne PaO₂= 78 mm Hg.
- La PA-aO₂ in media è compresa tra 7 e 14 mm Hg, ma sono accettabili valori più alti in funzione dell'età secondo la formula:
PA-aO₂=(età/4)+4.
- Così a 80 anni è considerato normale un valore di PA-aO₂=24. Questo valore è compatibile con una buona efficienza degli scambi gassosi.

COPD: a frequently unrecognized condition

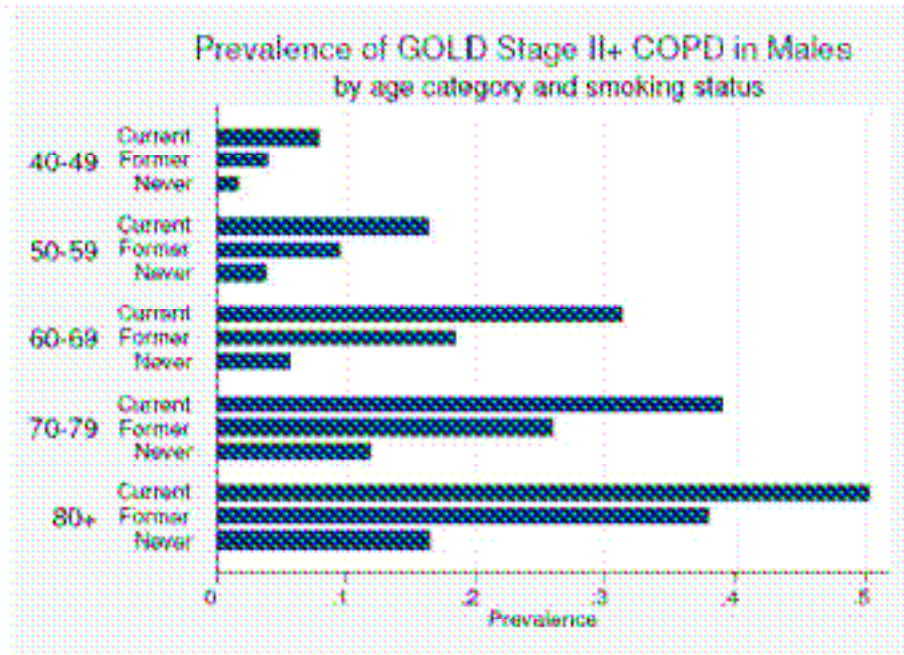
	<u>Criteria of COPD</u>	<u>Diagnosed (%)</u>
NHANES III, USA	(BTS)	37
IBERPOC, Spain	ERS	22
DIMCA, Netherlands	(CNSLD)	35
OLIN, Sweden	BTS	31
	GOLD	18
An European assumption	(clinical)	25

Though being symptomatic, only a half of the subjects with severe COPD are properly labelled Lindberg A. et al., Respir. Med., 2005; 100: 264-72

L'anziana spesso ha BPCO senza essere (stato) un fumatore (Lamprecht B et al Chest 2010, on line)



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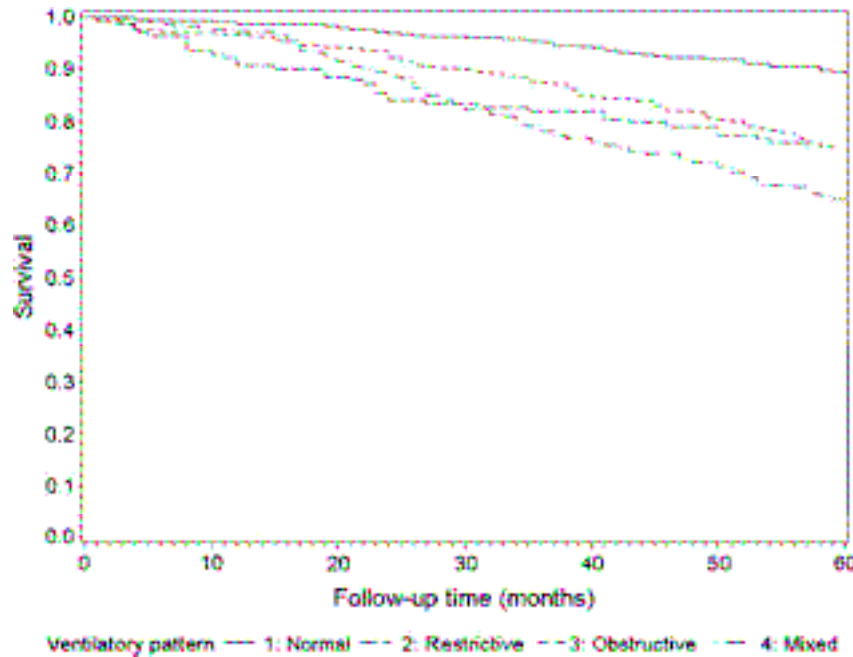


...e spesso ha forme miste (Scarlata S et al Respir Med 2008; 102: 1349)

Table 1 Demographic, clinical and anthropometric characteristics.

	Respiratory pattern				P
	Normal (586) %	Restrictive (138) % (OR; 95% CI)	Obstructive (322) % (OR; 95% CI)	Mixed (219) % (OR; 95% CI)	
Age over 80	18.1 (1.00)	26.8 (1.66; 1.08–2.55)	18.6 (1.03; 0.73–1.47)	17.8 (0.98; 0.65–1.47)	0.11
Gender (male)	35.8 (1.00)	49.3 (1.74; 1.20–2.53)	65.2 (3.36; 2.52–4.46)	76.3 (5.75; 4.03–8.19)	<0.001
Smoking status					
Never	55.1 (1.00)	58.4 (1.14; 0.78–1.67)	27.4 (0.30; 0.23–0.42)	23.7 (0.25; 0.17–0.36)	<0.001
Former	32.4 (1.00)	34.1 (1.09; 0.73–1.61)	52.2 (2.29; 1.72–3.04)	63.0 (3.55; 2.53–4.98)	<0.001
Current	12.5 (1.00)	7.3 (0.55; 0.27–1.10)	20.2 (1.78; 1.23–2.58)	13.2 (1.07; 0.68–1.70)	<0.001
Disability in at least 1 ADL	10.1 (1.00)	19.6 (2.17; 1.32–3.58)	12.1 (1.23; 0.80–1.89)	24.7 (2.92; 1.94–4.40)	<0.001
Poor physical performance ^a	21.4 (1.00)	32.3 (1.75; 1.15–2.67)	24.3 (1.18; 0.85–1.65)	36.0 (2.06; 1.45–2.93)	<0.001
Cognitive impairment ^b	11.5 (1.00)	21.0 (2.05; 1.27–3.32)	10.6 (0.91; 0.59–1.41)	15.2 (1.38; 0.88–2.17)	0.009
Depression ^c	35.1 (1.00)	36.9 (1.08; 0.73–1.60)	30.2 (0.80; 0.59–1.08)	41.4 (1.31; 0.94–1.80)	0.068
Body mass index <20	3.8 (1.00)	5.1 (1.37; 0.57–3.27)	5.0 (1.34; 0.69–2.59)	5.9 (1.62; 0.80–3.27)	0.570
Body mass index >30	18.6 (1.00)	23.9 (1.37; 0.88–2.14)	15.5 (0.80; 0.56–1.16)	16.9 (0.89; 0.59–1.34)	0.180
Increased waist circumference ^d	56.8 (1.00)	62.1 (1.24; 0.84–1.83)	44.1 (0.60; 0.45–0.79)	51.2 (0.80; 0.58–1.09)	<0.001

..e le forme miste hanno la
prognosi peggiore



Self reported comorbidity: COPD patients (no=200, age>70 y)

(Paladini L et al Respir Med. 2010; 104: 1027-34)

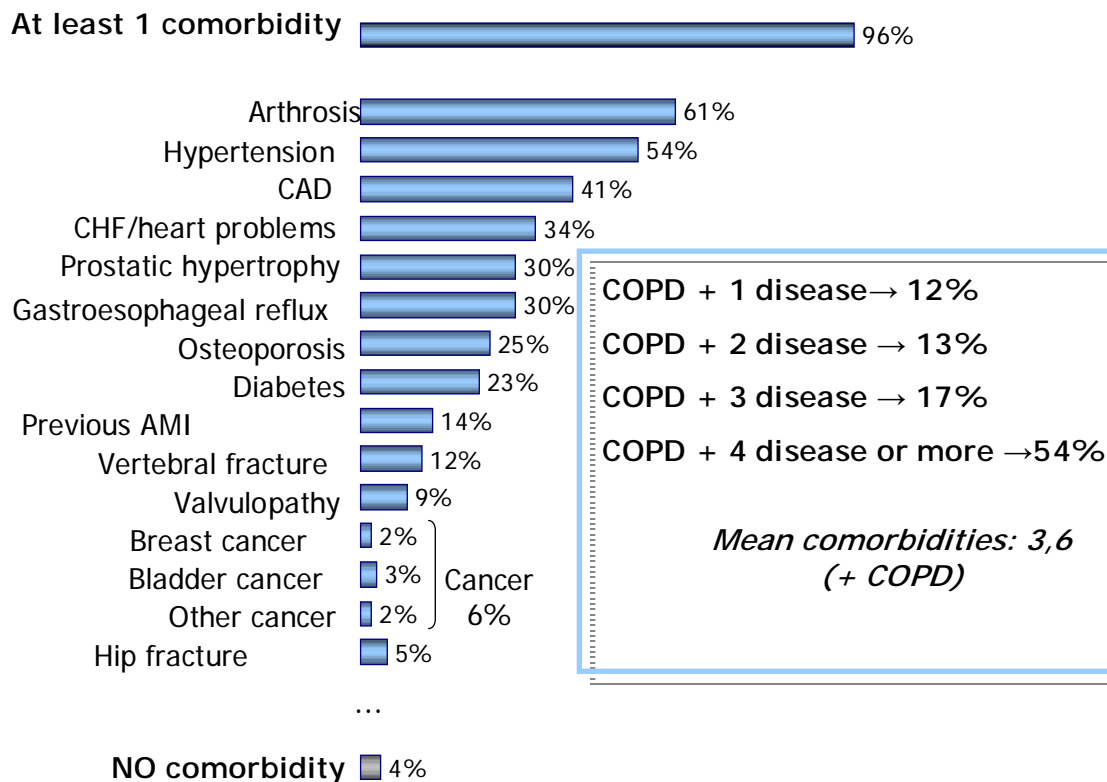


Figure 2 – Distribution of concomitant diseases. Total patients with at least 1 concomitant disease = 380

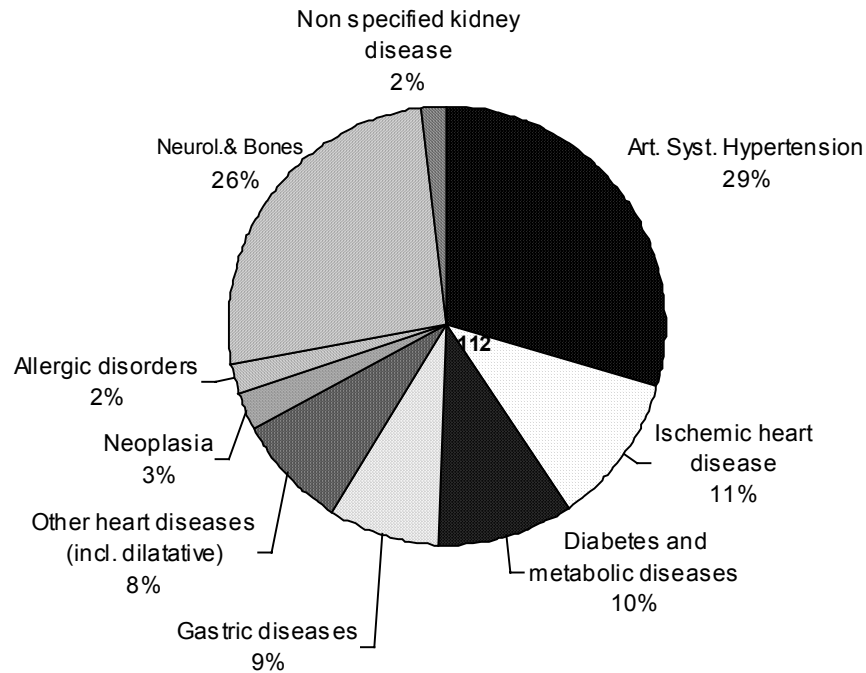
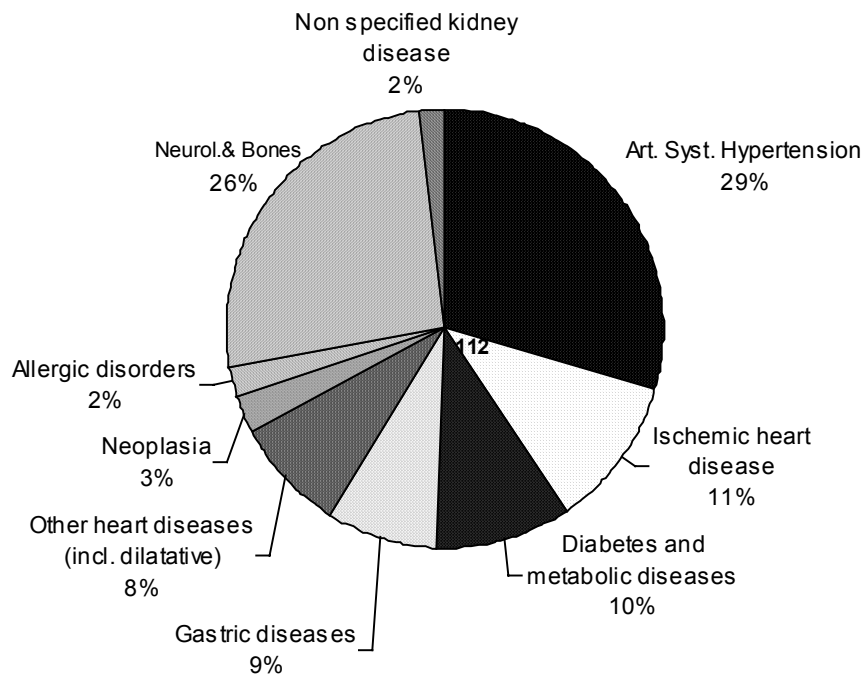


Figure 2 – Distribution of concomitant diseases. Total patients with at least 1 concomitant disease = 380

COPD mean age = 70.3y ± 9.2 sd



Tre esempi di comorbidità della BPCO

- Insufficienza renale: spesso misconosciuta
- Aneurisma aortico: una base biologica comune alla BPCO?
- Disfagia: l'interazione età-BPCO-fumo

Correlates of concealed and overt renal failure in an elderly population

Antonelli Incalzi R et al. Chest 2010; 137: 831

Table 4—Backward Stepwise Logistic Regression Models of Selected Variables to Concealed or Overt Renal Dysfunction vs Normal Renal Function

Variables	OR	95% CI
Concealed renal dysfunction^a		
Age, y (for each 1-y increase)	1.06	1.04-1.09
COPD	2.19	1.17-4.12
Serum albumin < 3.5 g/dL	2.83	1.70-4.73
Muscle-skeletal disease	1.78	1.01-3.16
Diabetes	1.96	1.02-3.76
Overt renal dysfunction^b		
Age, y (for each 1-y increase)	1.06	1.04-1.10
BMI	1.05	1.01-1.10
COPD	1.94	1.01-4.66
Diabetes	2.25	1.26-4.03

COPD-related or smoke-related renal failure? The nephrotoxic effects of smoke

Nephrotoxic agent	Mechanism	Reference
Pb, Cd	Glomerulosclerosis, Glomerulonephritis-IgA	Toxicology 2004; 204: 161 Occup Med 2004; 54: 265
Nicotine	+Proteinuria in diabetic patients	Scand J Clin Lab Invest 1996; 56: 393
Nicotine et al	Arteriolosclerosis	
Nicotine et al	+ Sympathetic tone Hypertension	Nephrol Dial Transplant 1998; 13: 940 J Am Soc Nephrol 1996; 7: 158
Nicotine	+ Lipid peroxidation (++ with alcohol)	Nephron 2002; 92: 772

COPD and aortic aneurysm: a very strong association

(Lederle FA et al. J Vasc Surg 2003; 38: 329)

Table III. Pooled estimates of smokers' relative risk for death from aortic aneurysm divided by smokers' relative risk for death from other smoking-related diseases

	<i>Pooled estimates* of ratio of smokers' relative risk</i>			
	<i>Aortic aneurysm to coronary artery disease</i>	<i>Aortic aneurysm to cerebrovascular disease</i>	<i>Aortic aneurysm to COPD</i>	<i>Aortic aneurysm to lung cancer</i>
Men				
Ever vs never	2.5 (2.2, 2.8) [‡]	3.5 (2.4, 5.3) [‡]	0.56 (.36, .86) [‡]	0.38 (.29, .50) [‡]
Current vs never	3.0 (2.5, 3.4) [‡]	4.7 (3.1, 7.2) [‡]	0.62 (.40, .98) [§]	0.34 (.23, .49) [‡]
Current vs not current [†]	2.0 (1.7, 2.3) [‡]	2.7 (1.9, 3.8) [‡]	0.93 (.75, 1.1)	0.54 (.47, .62) [‡]
Women				
Ever vs never	2.5 (1.7, 3.6) [‡]	2.8 (2.0, 3.8) [‡]	0.39 (.33, .47) [‡]	0.36 (.31, .43) [‡]
Current vs never	3.0 (2.0, 4.6) [‡]	3.5 (2.4, 5.2) [‡]	0.43 (.36, .52) [‡]	0.37 (.31, .43) [‡]
Current vs not current [†]	2.9 (2.1, 4.0) [‡]	3.3 (2.4, 4.5) [‡]	0.58 (.40, .83) [‡]	0.51 (.44, .59) [‡]

From overestimated to neglected comorbidities: the case of dysphagia

(Diez Gross R et al. Am J Respir Crit Care Med 2009;
179: 559)

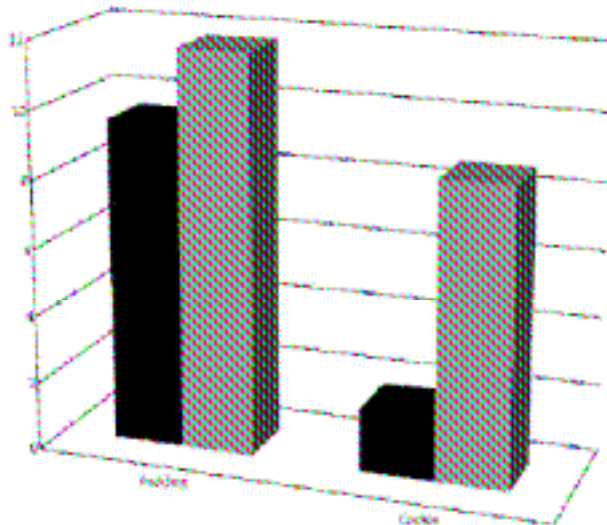


Figure 3. Graphic display of the percentage of swallows for each consistency that occurred during inhalation. Black bars, control subjects; gray bars, patients with chronic obstructive pulmonary disease.

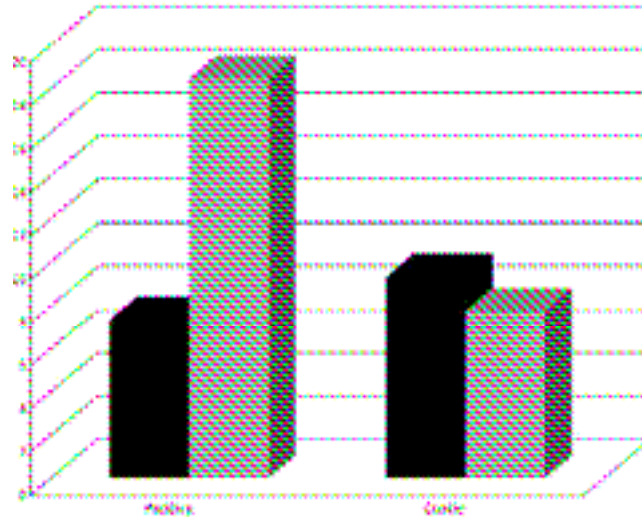


Figure 4. Graphic display of the percentage of swallows for each consistency that were followed by inhalation (postswallow inhalation). Black bars, control subjects; gray bars, patients with chronic obstructive pulmonary disease.

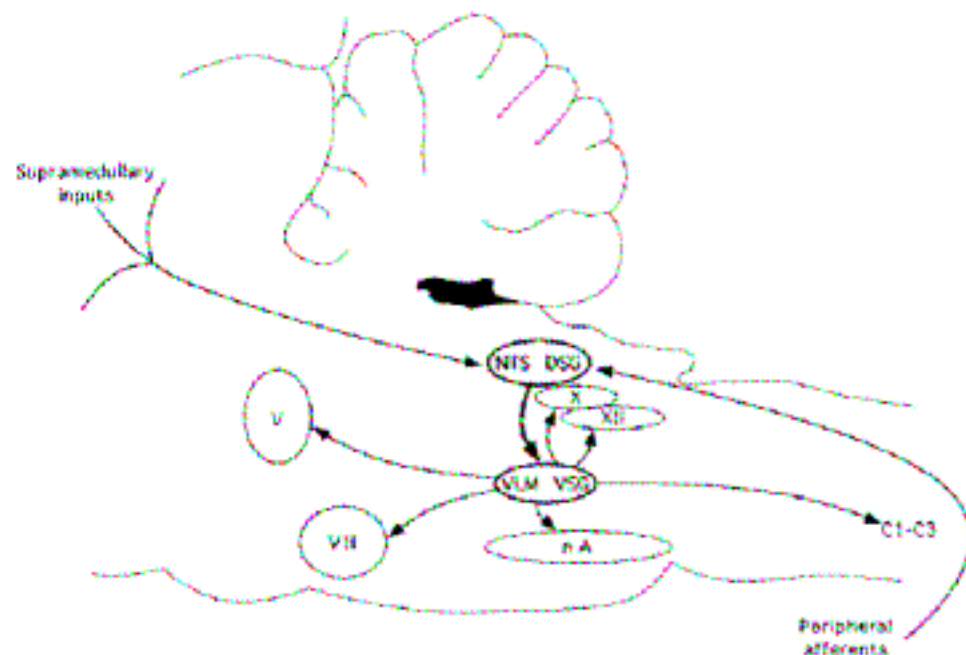


FIG. 5. Diagram of the swallowing central pattern generator (CPG). The CPG includes two main groups of neurons located within the medulla oblongata: a dorsal swallowing group (DSG) located within the nucleus tractus solitarius (NTS) and the adjacent reticular formation and a ventral swallowing group (VSG) located in the ventrolateral medulla (VLM) adjacent to the nucleus ambiguus (nA). The DSG contains the generator neurons involved in triggering, shaping, and timing the sequential or rhythmic swallowing pattern. The VSG contains the switching neurons, which distribute the swallowing drive to the various pools of motoneurons involved in swallowing. It should be noted that the pathway including the peripheral afferent fibers, neurons in the DSG and VSG, and motoneurons forms an oligosynaptic loop involved in swallowing and the elementary reflexes (see text for additional information). [Adapted from Jeun (150).]

Prognostic implications of comorbidity in a COPD population

Variabile	Hazard Rate	95% CI	p
Età (per anno)	1.04	1.02 - 1.05	0.00001
Segni ECG di cuore polmonare cronico	1.76	1.30 - 2.38	0.0003
Insufficienza renale cronica	1.79	1.05 - 3.02	0.032
Cardiopatìa ischemica	1.42	1.02 - 1.96	0.037
FEV1 < 590 mL	1.49	0.97 - 2.27	0.049

Antonelli Incalzi R et al. Eur Respir J 1997;10:2794

Il malato dei trial

Criteri di selezione dei pazienti

Sara	Torch	Uplift	Ecce
≥65 y	40-80 y ≥10 packyears	≥40 y ≥10 packyears	≥65 y
No: neoplasia, CHF NYHA>2, creatinina≥2 mg/dl, deficit sensoriale o cognitivo che impedisce VMD	No: comorbilità respiratoria, LTOT	No: comorbilità capace di ostacolare la partecipazione o interferire nei risultati	No: cancro

Design of Clinical Trials

	UPLIFT Decramer 2004	TORCH Calverley 2007	INSPIRE Wedzicha 2008
Duration	4 yrs	3 yrs	2yrs
Run in	Anticholinergic stopped	All medications stopped	Patients received oral steroids
n	5993	6184	1323
Post BD FEV₁	47%	44%	39 %
Primary end- point	FEV1 decline	Mortality	Exacerbations rate
Reversibility	80 µg Ipratropium + 400 µg Salbutamol	400 µg Salbutamol	400 µg Salbutamol
	Value after BDs	≤ 10 % pred FEV ₁	≤ 10 % pred FEV ₁

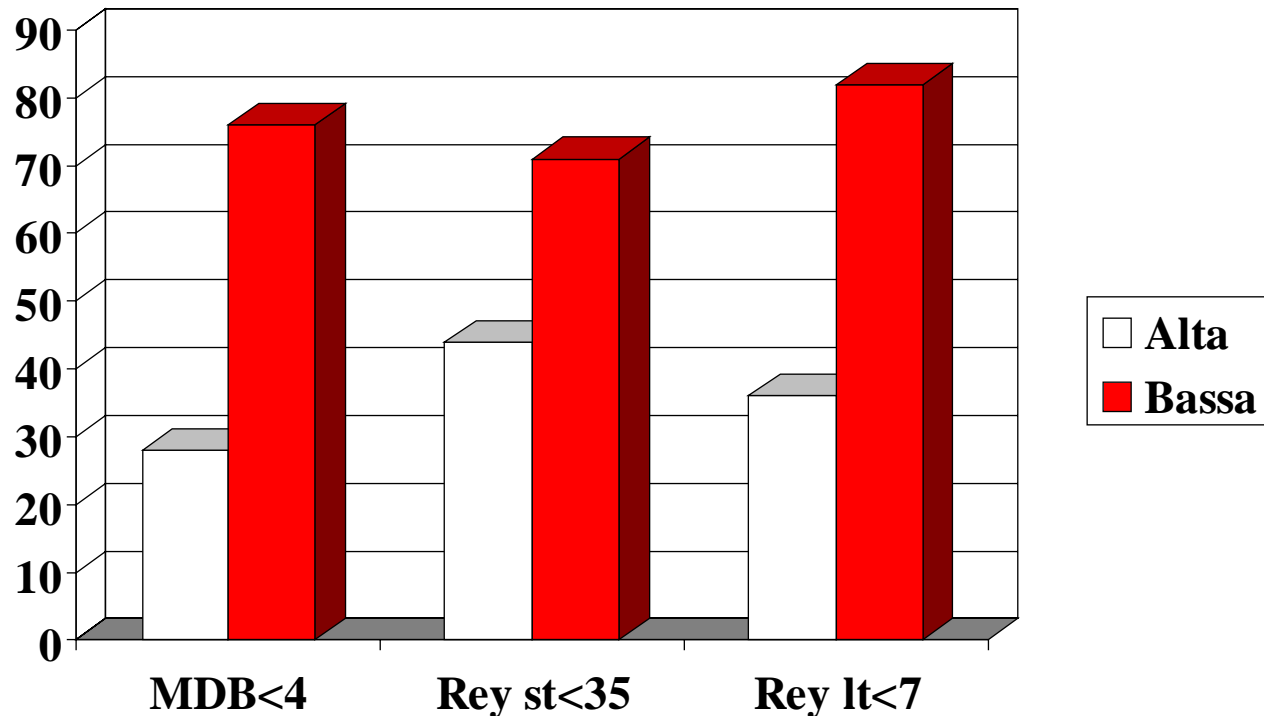
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Nessun trial tiene conto della capacità di aderire alla terapia e dei suoi correlati

- ... ma questa condiziona i risultati nella pratica quotidiana
- La selezione di un campione conveniente collide con l'applicabilità dei risultati più che garantirne l'affidabilità

Cognitive impairment and adherence to therapy in COPD



*Low compliance: the patient omits to take the drug at least twice for week

Cognitive impairment is the main risk factor for improper use of inhaler devices

Table 3 Number of subjects with adequate or inadequate Turbohaler technique when retested the day after training in comparison with their performance on the pentagon copying test ($n = 50$)

	<i>Adequate technique</i>	<i>Inadequate technique</i>	<i>p-value</i>
IP-	2	13	<0.0001
		1	
IP+	26	9	1

IP- = unable to copy intersecting pentagons. IP+ = able to copy intersecting pentagons.

Sistemi di erogazione a confronto

	Vantaggi	Svantaggi
MDI	Elevata riproducibilità da dose a dose	Necessità di coordinare il respiro con l'attivazione dell'inalatore
DPI	Attivato dal respiro, non richiede collaborazione	Può essere difficoltoso per le persone con deficit cognitivo. Richiede un maggior sforzo respiratorio
Aerosol	Elevata riproducibilità da dose a dose	Richiede maggior tempo e (spesso) assistenza per la preparazione

Declino della pressione inspiratoria con l'età

Age Group (yr)	Gender	Entire Cohort				Healthy Subjects			
		No.	Mean Age (Range) (yr)	Mean MIP \pm SD (cm H ₂ O)	Mean FEV ₁ % Predicted \pm SD	No.	Mean Age (Range) (yr)	Mean MIP \pm SD (cm H ₂ O)	Mean FEV ₁ % Predicted \pm SD
Age < 39.9	Men	56	30.5 (22-39)	117.6 \pm 28.8	96.5 \pm 14.6	38	30.4 (23-39)	120.5 \pm 26.9	100.3 \pm 9.9
	Women	68	29.9 (20-39)	79.5 \pm 20.4	98.6 \pm 10.5	40	29.6 (20-39)	79.7 \pm 17.6	98.0 \pm 10.3
40 < Age < 54.9	Men	89	46.4 (40-54)	107.4 \pm 23.7	95.8 \pm 11.9	40	46.4 (40-53)	111.6 \pm 22.6	97.1 \pm 22.6
	Women	89	47.0 (40-54)	73.7 \pm 20.3	99.9 \pm 12.8	50	46.9 (40-53)	75.8 \pm 23.1	105.7 \pm 11.7
55 < Age < 64.9	Men	72	60.0 (55-64)	94.4 \pm 27.3	92.4 \pm 14.1	22	60.2 (55-64)	91.7 \pm 23.4	91.7 \pm 12.0
	Women	46	59.2 (55-64)	64.6 \pm 17.9	101.3 \pm 15.7	17	57.8 (55-63)	68.3 \pm 20.9	102.9 \pm 17.3
65 < Age < 74.9	Men	95	68.9 (65-74)	81.9 \pm 21.4	92.2 \pm 14.9	24	69.3 (65-74)	84.1 \pm 19.9	96.5 \pm 12.9
	Women	45	69.5 (65-74)	55.7 \pm 17.4	100.3 \pm 17.9	11	67.1 (65-72)	60.8 \pm 16.5	101.1 \pm 18.8
Age > 74.9	Men	69	80.1 (75-90)	66.0 \pm 19.4	89.6 \pm 23.2	15	80.3 (75-90)	65.4 \pm 19.4	105.7 \pm 20.0
	Women	39	80.0 (75-90)	45.5 \pm 17.5	99.5 \pm 16.4	10	78.6 (75-83)	46.0 \pm 20.0	99.5 \pm 20.0

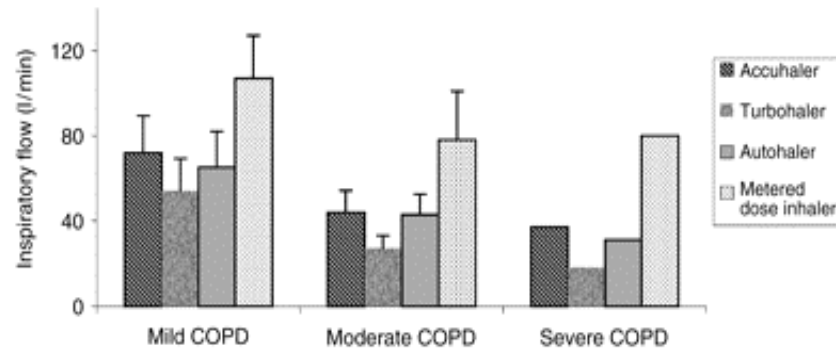
Harik-Khan R et al. Am J Respir Crit Care Med 1998; 158:1459–1464.

Flussi necessari per attivare gli inalatori

- In genere i DPI richiedono un flusso di 25 L/min per essere efficaci (Goodman DE et al. J Am Respir Crit Care Med 1994; 150:1256-1261);
- La maggior parte dei DPI richiede un flusso di 30 – 60 L/min, e 60 L/min è considerata la soglia per il costo/beneficio (Payne N et al. NICE 2000);
- Il picco di flusso espiratorio in persone anziane con BPCO, misurato contro resistenza di 60 L/min è di (Jarvis S et al. Age Ageing 2007; 36:213-218):
 - 54 L/min nella BPCO lieve
 - 27 L/min nella BPCO moderata
 - 18 L/min nella BPCO grave

Flussi inspiratori in pazienti con BPCO

Table 1. Inspiratory flow in elderly COPD patients according to different degrees of resistance



	Accuhaler* (l/min)	Turbohaler* (l/min)	Autohaler* (l/min)	pMDI* (l/min)
Mild	72 ± 17	54 ± 15	65 ± 16	107 ± 20
Moderate	44 ± 10	27 ± 6	43 ± 10	78 ± 22
Severe	37	18	31	80
All Patients	63 ± 20	44 ± 19	58 ± 18	98 ± 25

* Minimum required inspiratory flow rate: MDI, 25 l/min; Autohaler, 30 l/min; Accuhaler, 30 l/min; Turbohaler, 60 l/min

Limiti alla diagnosi funzionale

- Spirometria di difficile esecuzione nell'anziano malato: FVC spesso non disponibile
- FEV6: alternativa affidabile, ma non universale, alla FVC
- FVC6 o sFVC: possibile ultima spiaggia della diagnosi spirometrica

La spirometria nell'anziano: nel SaRA 508/638 casi e 747/984 controlli non produssero tre curve ripetibili (Bellia V et al. Am J Respir Crit Care Med 2000; 161: 1094)

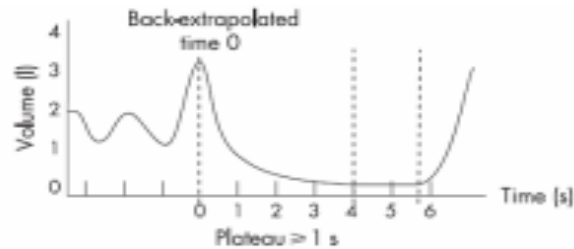
TABLE 5
STEPWISE LOGISTIC ANALYSIS

Outcomes	Predictors	Odds Ratio	Confidence Interval	p Value
Poor acceptability	MMSE	1.59	1.07–2.37	< 0.05
	< 75th percentile			
	6MWT	1.57	1.09–2.26	< 0.05
Poor FEV ₁ reproducibility	< 75th percentile			
	Educational level ≤ 5 yr	1.54	1.08–2.20	< 0.05
Poor FVC reproducibility	Male sex	3.04	1.44–6.42	< 0.001
	Age	1.05	1.01–1.10	< 0.05
Poor FEV ₁ repr + accept	Respiratory drugs, n	1.40	1.21–1.62	< 0.001
	Male sex	1.99	1.26–3.12	< 0.005
	Age	1.04	1.01–1.07	< 0.01
Poor FEV ₁ repr + accept	Age	1.04	1.02–1.06	< 0.001
	Respiratory drugs, n	1.17	1.05–1.32	< 0.01
	Male sex	1.63	1.22–2.16	< 0.01
	MMSE	1.54	1.08–2.20	< 0.05
	< 75th percentile			
	Educational level ≤ 5 yr	1.39	1.04–1.87	< 0.05

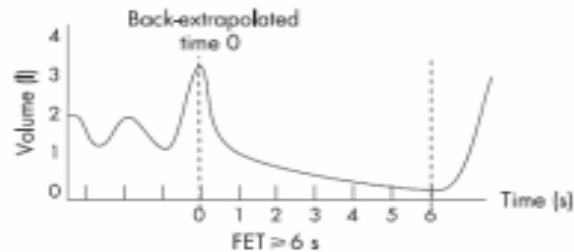
For definition of abbreviations, see Table 2.

La diagnosi funzionale: un serio problema

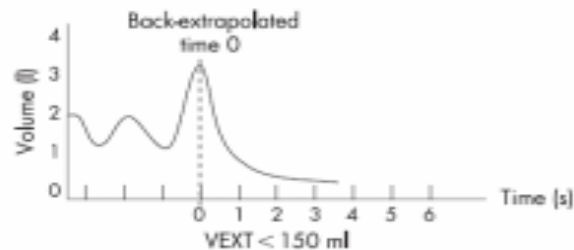
(Bellia V et al Thorax 2008; 66: 60)



VEXT	< 150 ml
FET	≥ 6 s
Plateau	≥ 1 s
Measurable FEV ₁ , FVC ₆ , FEV ₆ , FVC	



VEXT	< 150 ml
FET	≥ 6 s
Plateau	Any
Measurable FEV ₁ , FVC ₆ , FEV ₆	



VEXT	< 150 ml
FET	≥ 2 s
Plateau	Any
Measurable FEV ₁ , FVC ₆	

E il FEV6 non è una soluzione universale (Bellia

V et al Thorax 2008; 66: 60)

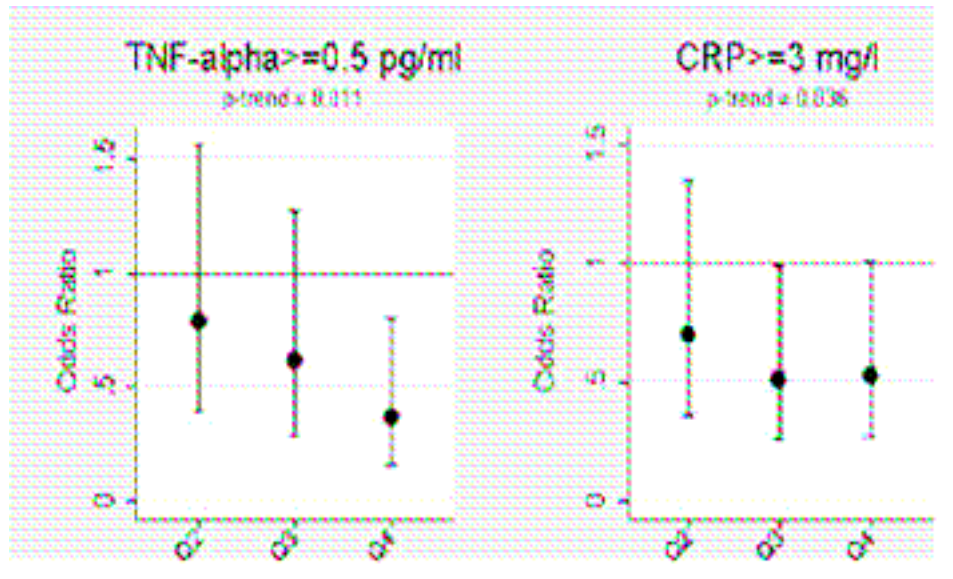
Table 3 Factors negatively influencing achievement of valid FEV₆ measurement: multivariable logistic analysis on 1531 subjects with a satisfactory start-of-test criterion

	Odds ratio	p Value	95% confidence interval
Older age (every 5 years)	1.42	<0.001	1.25 to 1.59
Female sex	1.58	0.022	1.08 to 2.31
Lower education*	1.77	0.001	1.25 to 2.51
Depression†	1.54	0.045	1.12 to 2.13
Cognitive impairment‡	1.61	0.009	1.09 to 2.37
Spirometric restriction§	1.98	<0.001	1.37 to 2.86

Principi di terapia

- Che cosa fare
 - Lotta al fumo et al.
 - Esercizio fisico – FKT
 - Educazione
 - Vaccinazioni
 - Farmaci
 - Prevenzione e terapia complicanze
 - Correzione deficit nutrizionali selettivi
 - O2 terapia se $SaO_2 < 90\%$
- Che cosa non fare
 - O2 terapia “iperbolica”
 - Supporto nutrizionale
 - Riattivazione cognitiva
 - (Antidepressivi)
 - Correzione sovrappeso moderato

Physical activity: an antiinflammatory “drug” in COPD? (Garcia_Aymerich J et al. Chest 2009;136: 62)



Rehabilitation: a safe antidepressive drug

Rehabilitation Study	No. of Patients Mean Age	Type of Study/Intervention	Main Results
Garrod <i>et al.</i> [63]	51 68.0 years	Observational study/Pulmonary rehabilitation	77% had a clinically significant benefit. Depression was a risk factor for subject drop-out
Trappenburg <i>et al.</i> [64]	81 63.0 years	Observational study/Pulmonary rehabilitation	Significant improvement in exercise performance, functional status, anxiety, and depression (HADS depression score -3 ± 3 points, $p<0.001$)
Goldberg <i>et al.</i> [65]	45 67.4 years	Observational study/Pulmonary rehabilitation	Significant improvement in anxiety ($p<0.001$), depression ($p<0.001$), and dyspnoea ($p<0.001$)
de Godoy <i>et al.</i> [66]	30 60.3 years	Randomized controlled trial/Pulmonary rehabilitation vs pulmonary rehabilitation + psychotherapy	Patients undergoing pulmonary rehabilitation + psychotherapy had a significant improvement of anxiety ($p<0.001$), and depression ($p<0.001$) with respect to patient treated with pulmonary rehabilitation alone. Both groups had a significant functional improvement

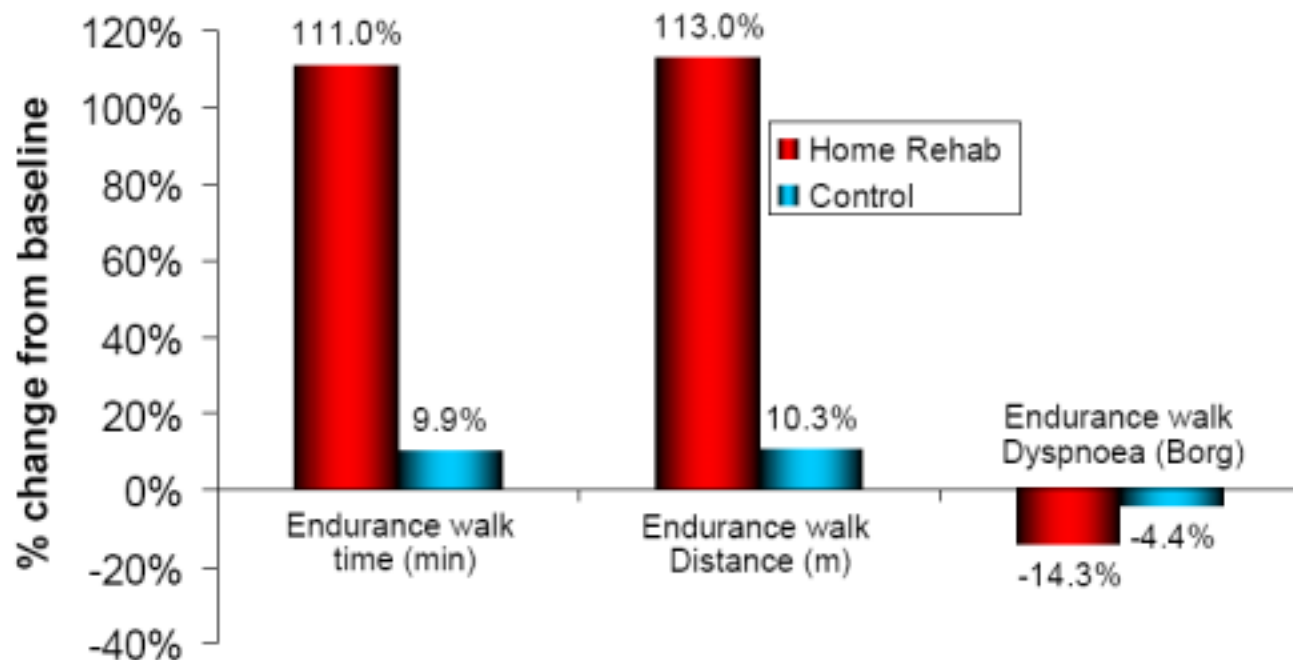
HADS, Hospital Anxiety and Depression Score.

Results of a home-based training program for patients with COPD

Henandez MTE et al. CHEST 2000; 118: 106-114

Home Program:

Shuttle walk test daily, 6 days/week for 12 weeks



Pulmonary rehabilitation is beneficial even in severe COPD

The Maugeri Study

MRF: Maugeri Respiratory Failure Questionnaire

**Chronic
Respiratory
Failure**

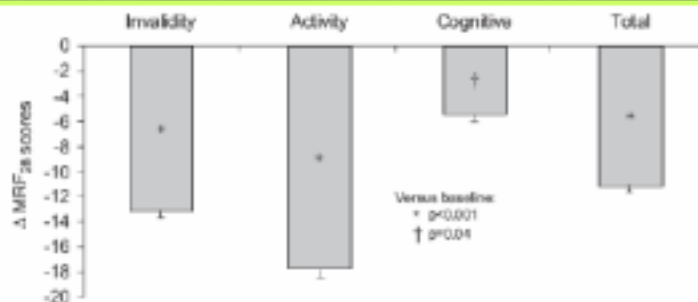


Figure 1 Improvement in MRF₂₈ scores (patients with CRF) (mean value \pm SE) after PR programme.

**No
Chronic
Respiratory
Failure**

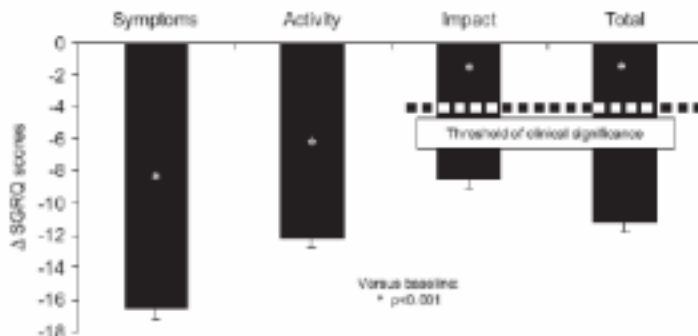


Figure 2 Improvement in SGRQ scores (patients without CRF) (mean value \pm SE) after PR programme.



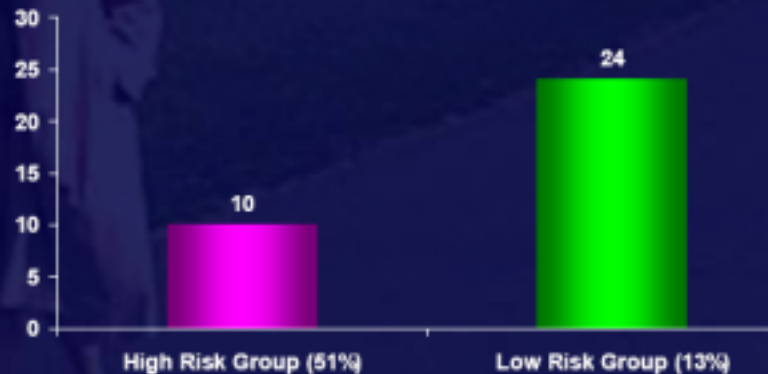
Self-management Education for Patients with COPD (Cochrane Review)

Effing T et al. Cochrane Reviews 2007

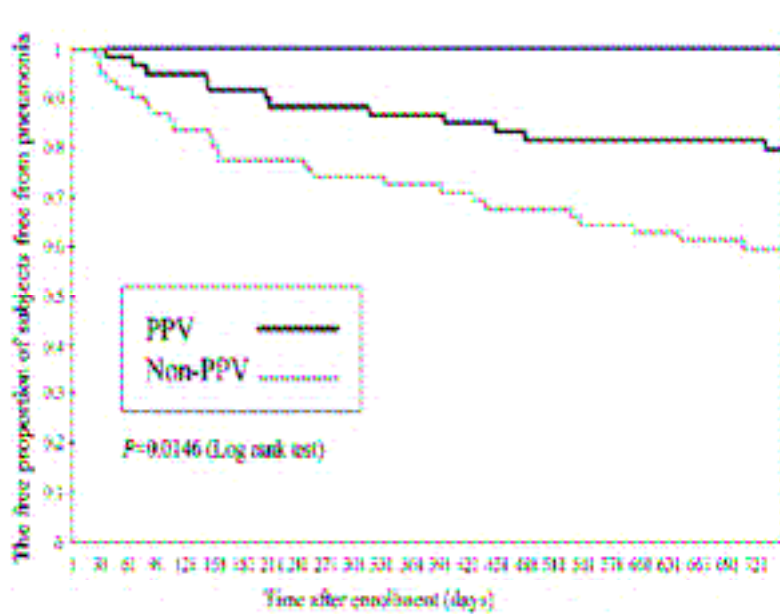
Odds ratio for hospitalization

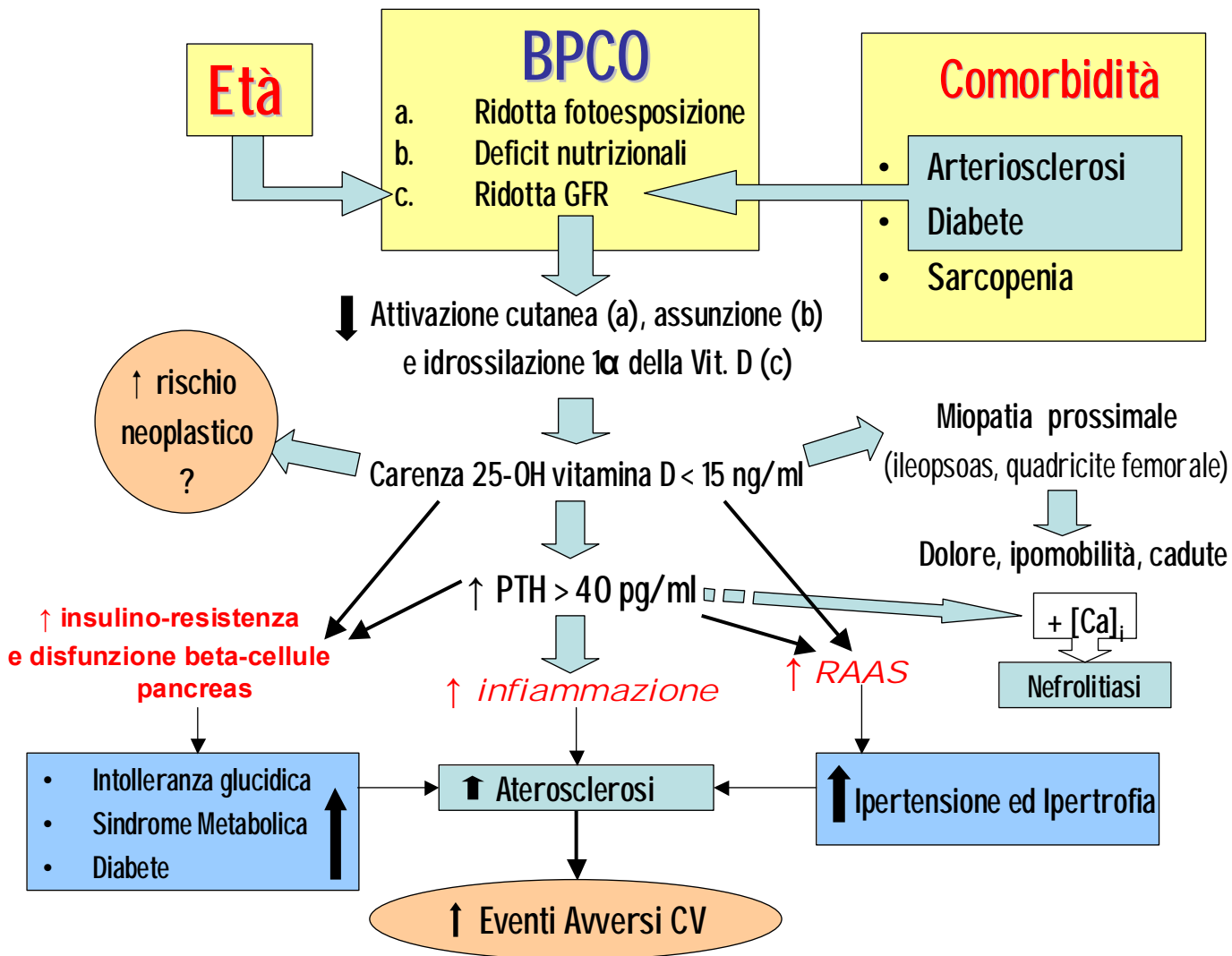


One year Number Needed to Treat



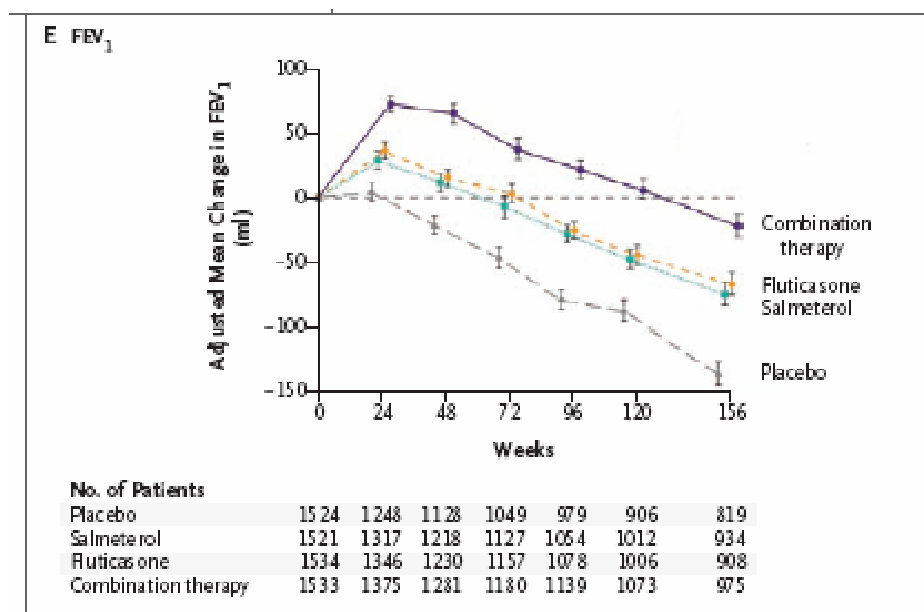
Efficacia del vaccino-23 anti PN in soggetti >65 anni immunizzati verso l'influenza e con difficoltà nella deambulazione (Kawakami K et al. Vaccine 2010, in press)



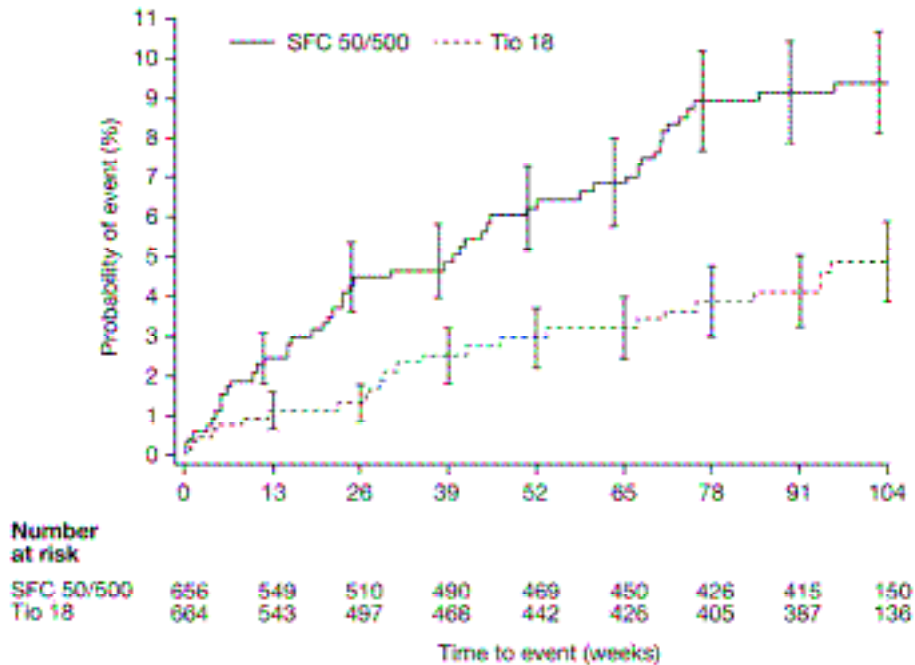


Different therapies differently affect the early gain in and not rate of decline of FEV₁

TORCH study N Engl J Med 2007;356:775-89.



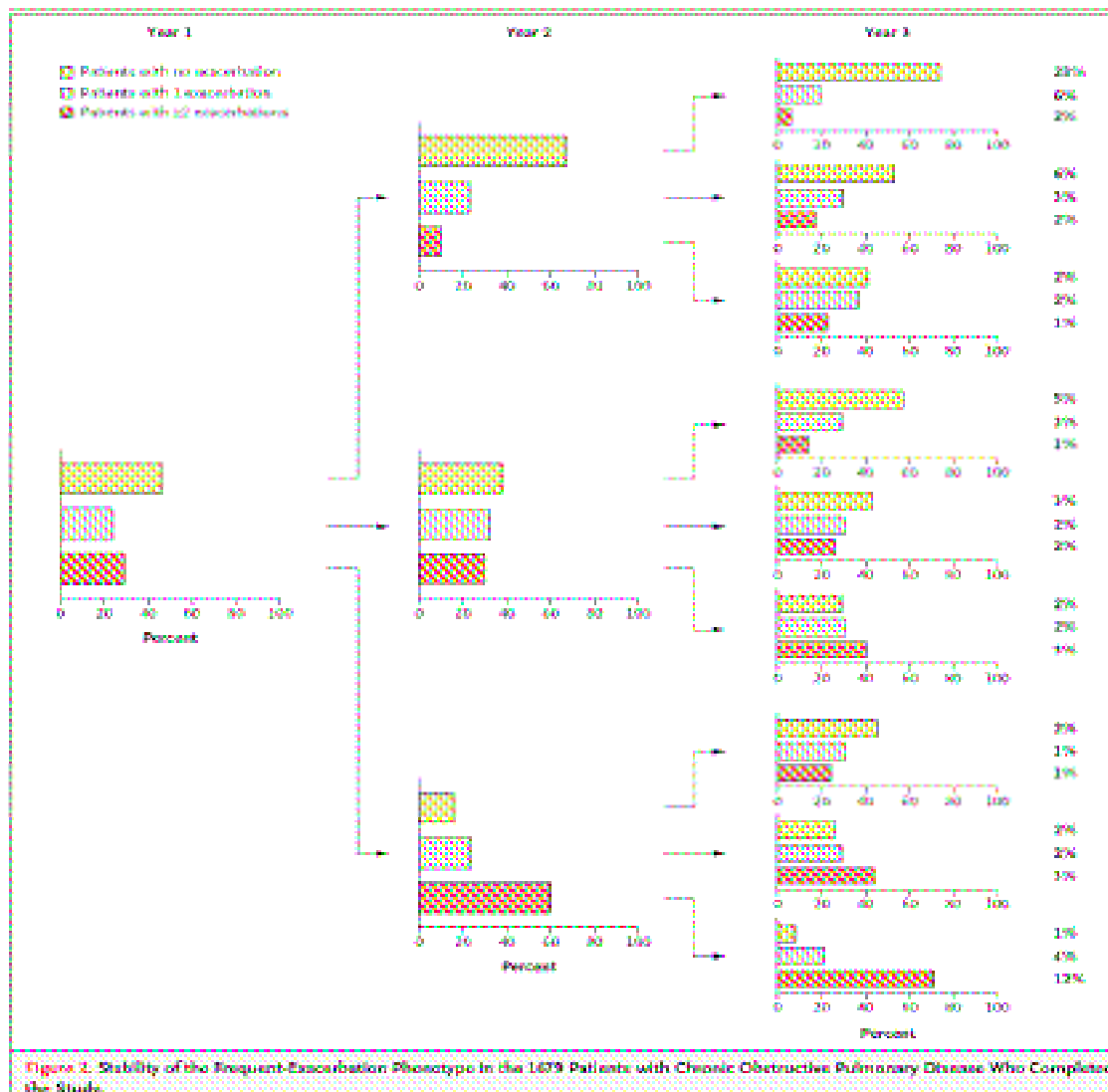
Inhaled steroids and risk of pneumonia (The Inspire study)



Time to first pneumonia; SFC: salmeterol/fluticasone propionate 50/500 µg BID; TIO: tiotropium.
90x66mm (600 x 600 DPI)

..ma il rischio di polmonite non motiva l'astensione dagli steroidi inalatori

- Basandoci sui dati Torch, 1000 pazienti BPCO incorrono annualmente in circa 1300 riacutizzazioni.
- La combinazione fluticasone-salmeterolo è in grado di prevenire circa 300 riacutizzazioni al prezzo di 36 polmoniti extra.
- Le polmoniti sono non fatali.
- La mortalità nei tre anni seguenti la riacutizzazione è del 38% (Almagro P et al Thorax 2010; 65: 298).

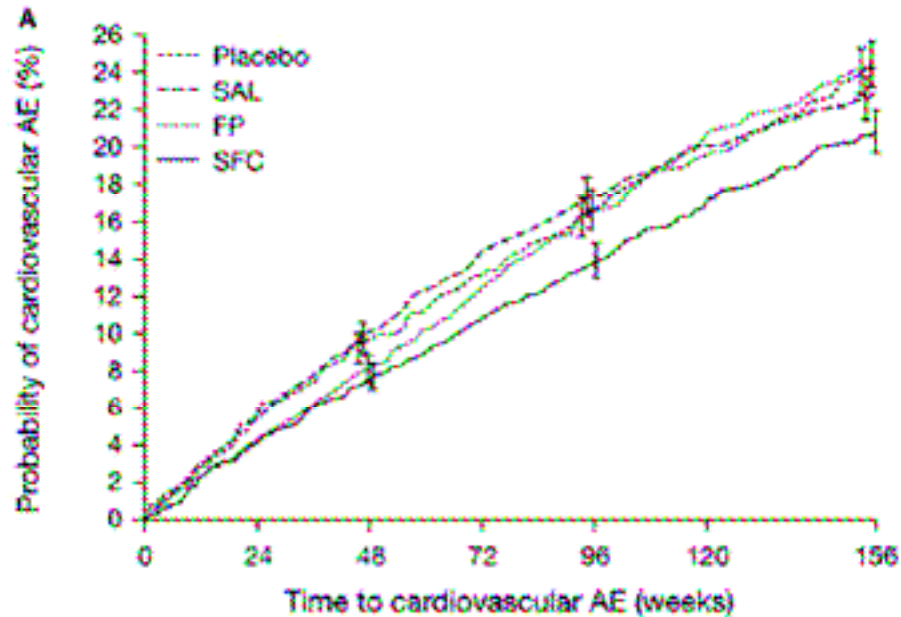


La scelta del broncodilatatore

- I farmaci inalati vengono considerati “topici”, ma:
- La frazione di dose inalata di formoterolo che viene deglutita varia tra il 60% ed il 90%.
Almeno il 65% della dose deglutita è assorbita, il farmaco è eliminato per via renale. Non ci sono dati disponibili sull'uso di formoterolo nei pazienti con GFR ridotta;
- Anche il tiotropio ha un assorbimento sistemico e viene eliminato per via renale. Nei pazienti con insufficienza renale da moderata a grave deve essere utilizzato solo se i benefici attesi superano i potenziali rischi.

Il Torch attesta che salmeterolo e fluticasone non aumentano il rischio cardiovascolare

Thorax 2010;65:719—725.



No. of patients							
Placebo	1544	1231	1074	974	883	805	521
SAL	1542	1293	1150	1035	945	878	593
FP	1552	1323	1175	1074	981	884	565
SFC	1548	1364	1228	1127	1039	963	644

The Safety of Tiotropium — The FDA's Conclusions

Theresa M. Michele, M.D., Simone Pinheiro, Sc.D., and Solomon Iyasu, M.D., M.P.H.

N ENGL J MED 363:12 NEJM.ORG SEPTEMBER 16, 2010

Safety Data from Pooled Analysis of Tiotropium Trials and UPLIFT.*		
Attribute	29 Pooled Trials (N = 13,544)	UPLIFT (N = 5992)
Study duration	1–12 mo	48 mo
Patient-years (placebo group)	3065	8499
Patient-years (tiotropium group)	4571	9222
Relative risk (95% CI)		
Stroke	1.37 (0.73–15.6)	0.95 (0.70–1.29)
Myocardial infarction		0.71 (0.51–0.99)
Death from cardiovascular causes†	0.97 (0.54–1.75)	0.73 (0.56–0.95)
Death from any cause		0.85 (0.74–0.98)

...can we improve deglutition in COPD?

Manovra	Modalità di esecuzione
Deglutizione sopraglottica	<ul style="list-style-type: none">- Trattenere il respiro durante la deglutizione- Mantenerlo durante tutta la deglutizione- Effettuare un colpo di tosse alla fine della deglutizione
Deglutizione superglottica	<ul style="list-style-type: none">- Inspirare profondamente e mantenere l'apnea- Deglutire eseguendo contemporaneamente la manovra di Valsalva- Eseguire espirazione forzata e un nuovo atto deglutitorio
Deglutizione doppia	<ul style="list-style-type: none">- Inspirazione prima della deglutizione- Deglutizione in apnea- Espirazione con un colpo di tosse- Nuova deglutizione
Manovra Mendelsohn	di <ul style="list-style-type: none">- Mantenere manualmente o pronunciando il suono "ch" muto, l'elevazione laringea per 2-3 secondi dopo la deglutizione

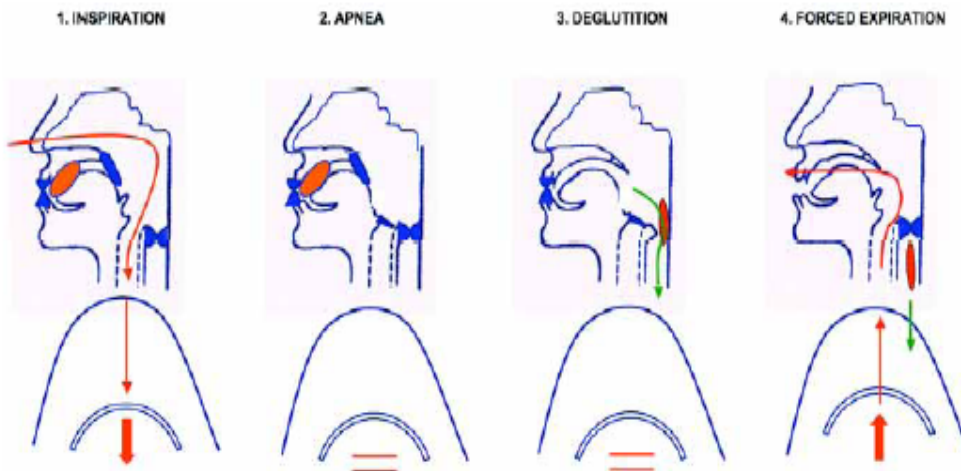
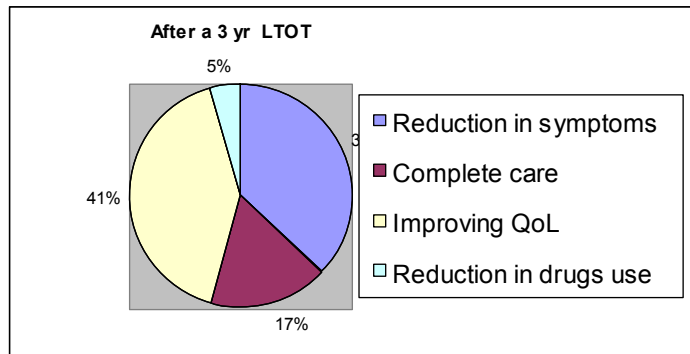
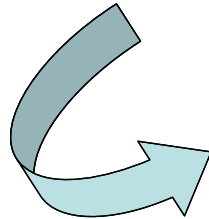
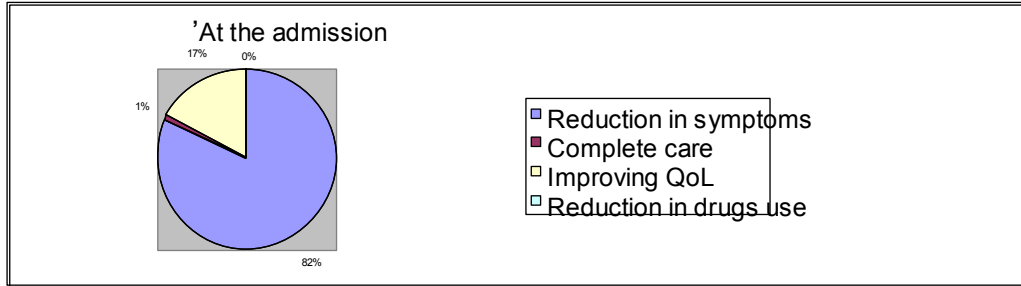


Figure 6. Diagrams showing the 4 steps of supraglottic swallow to protect the airway from aspiration. Commands for the patient are: 1) take a deep breath; 2) hold your breath; 3) hold your breath while swallowing; and 4) cough immediately after you swallow.

Patients' perspective after a 3 yr period of telemetric LTOT



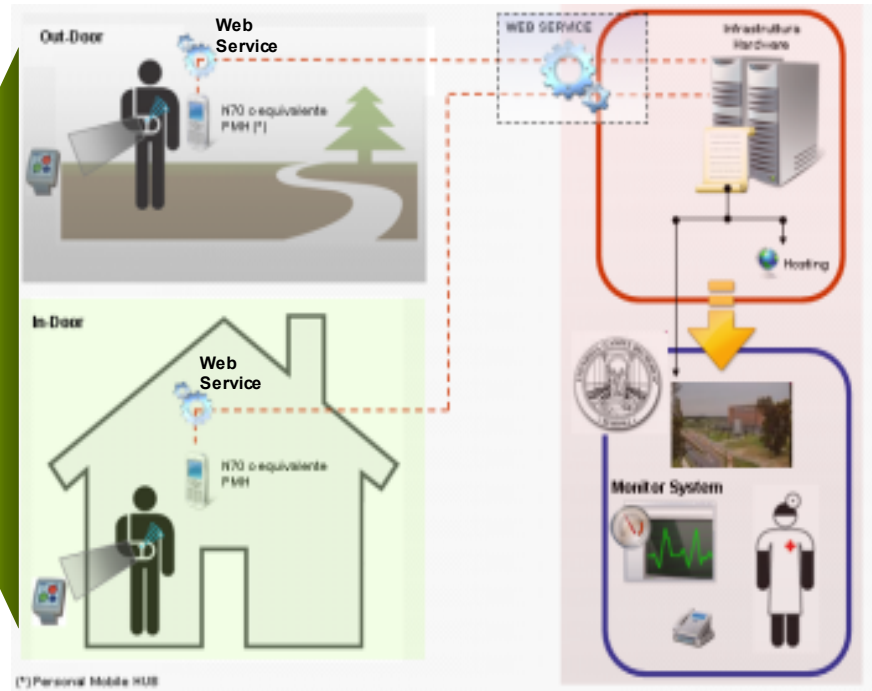


Il Controllo Telemetrico e gli strumenti disponibili R Antonelli Incalzi et al.





Il Controllo Telemetrico e gli strumenti disponibili R Antonelli Incalzi et al.

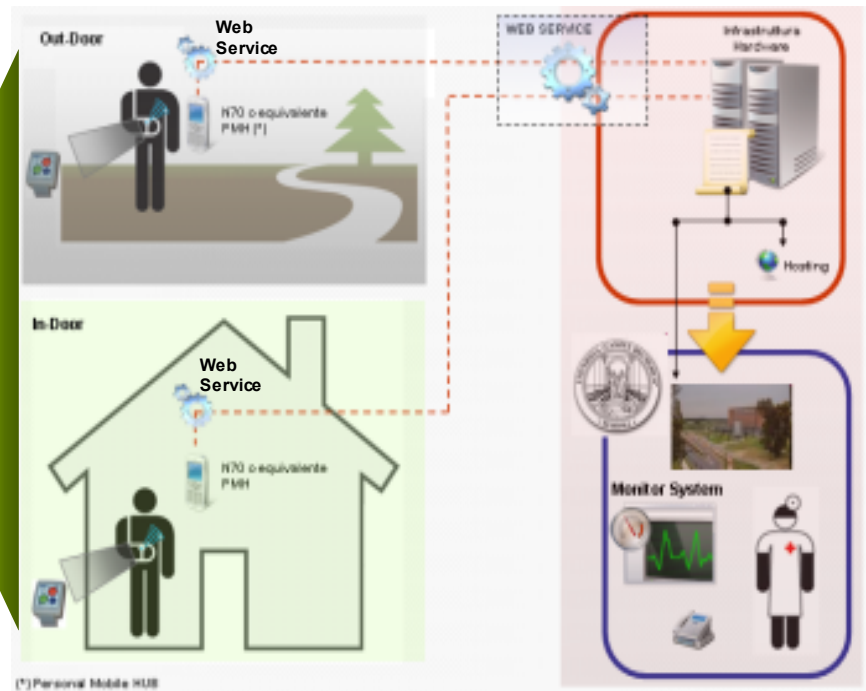




Il Controllo Telemetrico e gli strumenti disponibili R Antonelli Incalzi et al.

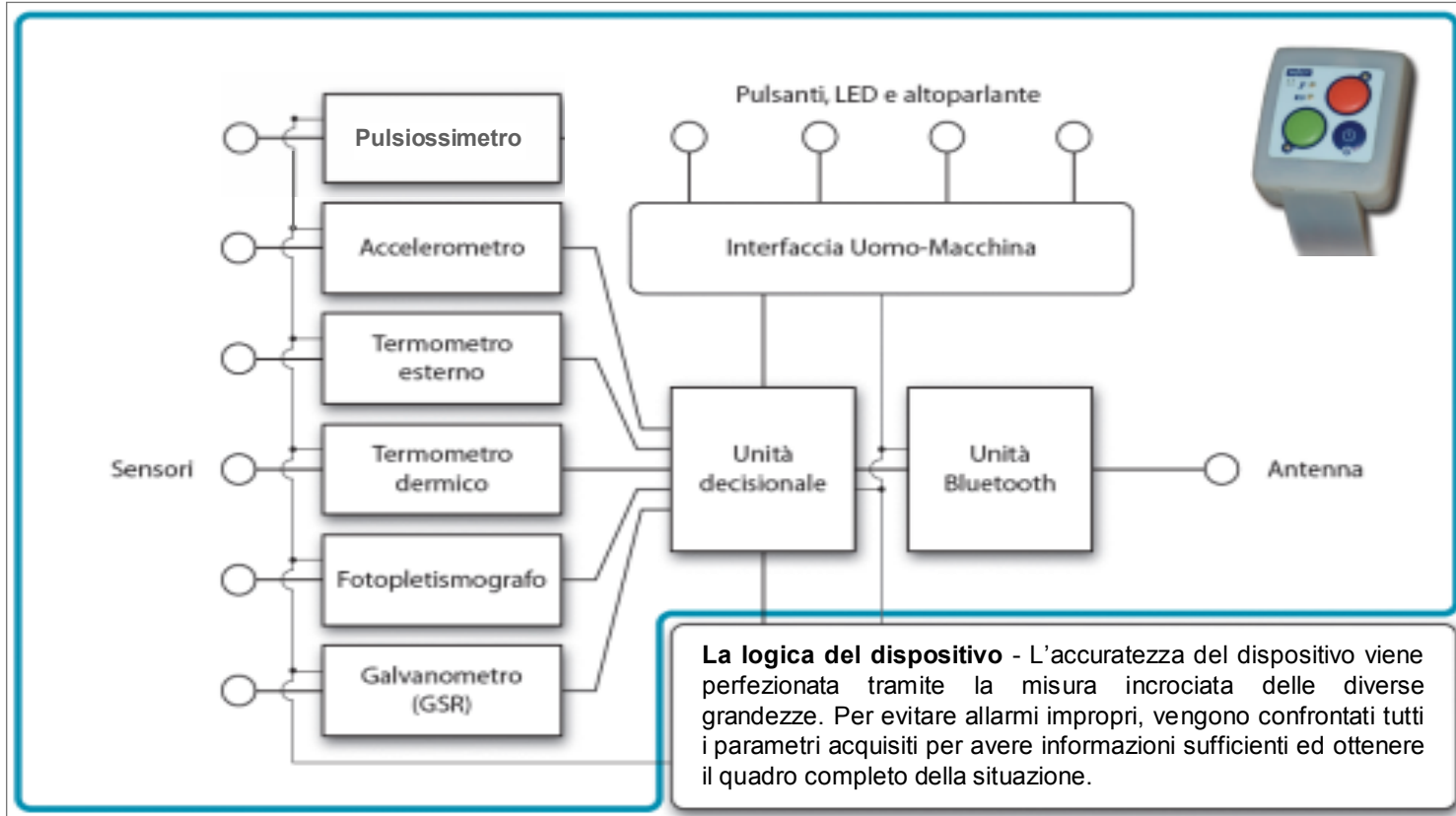
Il sistema rileva:

- ⇒ Attività motoria
- ⇒ Frequenza Cardiaca
- ⇒ Frequenza Respiratoria
- ⇒ Ossimetria
- ⇒ Galvanic Skin Response
- ⇒ Temperatura Epidermica





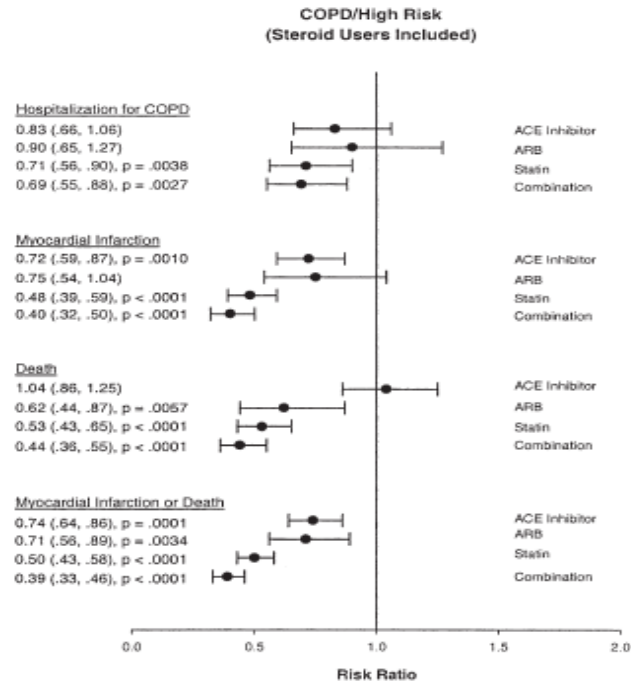
Il Controllo Telemetrico e gli strumenti disponibili R Antonelli Incalzi et al.



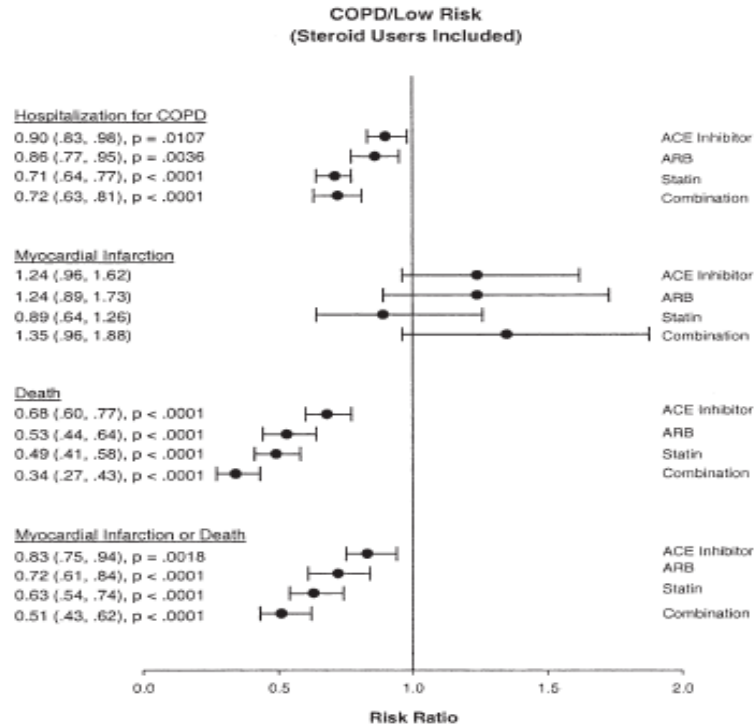
Palliative care, the neglected

- provides relief from pain and other distressing symptoms;
- affirms life and regards dying as a normal process;
- intends neither to hasten nor to postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death;
- offers a support system to help the family cope during the patient's illness and in their own bereavement;
- uses a team approach to address the needs of patients and their families, including bereavement counseling, if indicated;
- will enhance quality of life, and may also positively influence the course of illness;
- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy;
- includes the investigations needed to better understand and manage distressing clinical complications.

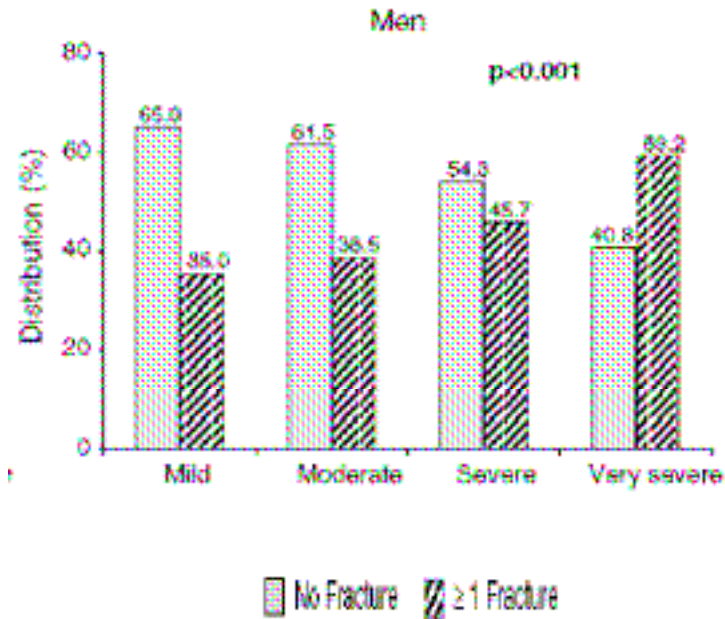
Do statins, ACE-I and ARBs affect survival of COPD patients?



Do statins, ACE-I and ARBs affect survival of COPD patients?



COPD-osteoporosi: un rapporto precoce (Nuti P et al. Osteop Int 2009; 20: 989), in assenza di indicazioni terapeutiche..



- Meccanismi COPD-correlati variamente contribuiscono a causare osteoporosi, ma la terapia si basa su linee guida generali

Il rischio di fratture vertebrali aumenta per
 beclometasone >1500 mcg/die (Gonnelli S et al Calcif Tissue Int 2010; 87:
 137)

Table 3 Association of selected clinical variables with vertebral fractures: Wald chi-squared statistics (degrees of freedom [DF] and *P* values)

	Fractures vs. no fractures			
	OR	95% CI	<i>P</i>	DF
Age (years)	1.03	1.02–1.05	<0.001	1
Gender (M/F)	0.93	0.78–1.13	n.s.	1
BMI (<26.7 kg/m ²)	1.28	1.07–1.54	0.008	1
COPD severity				
Very severe	2.05	1.28–3.28	0.003	
Severe	1.40	1.06–1.82	0.017	
Moderate	1.29	1.01–1.62	0.03	
Mild	1.00			3
Inhaled GCs (µg/day)				
GCs > 1,500	1.40	1.04–1.89	0.03	
750 < GCs ≤ 1,500	1.36	0.93–1.72	n.s.	
GCs ≤ 750	1.26	0.98–1.89	n.s.	
No treatment	1.00			3
Inhaled β ₂ agonists (µg/day)				
>400	0.93	0.69–1.25	n.s.	
≤400	1.00			1

This model includes 2,073 patients

Multiple logistic model adjusted for age, gender, BMI, and COPD severity

..ma lo studio Torch ci rassicura

Chest 2009;136;1456-1465;

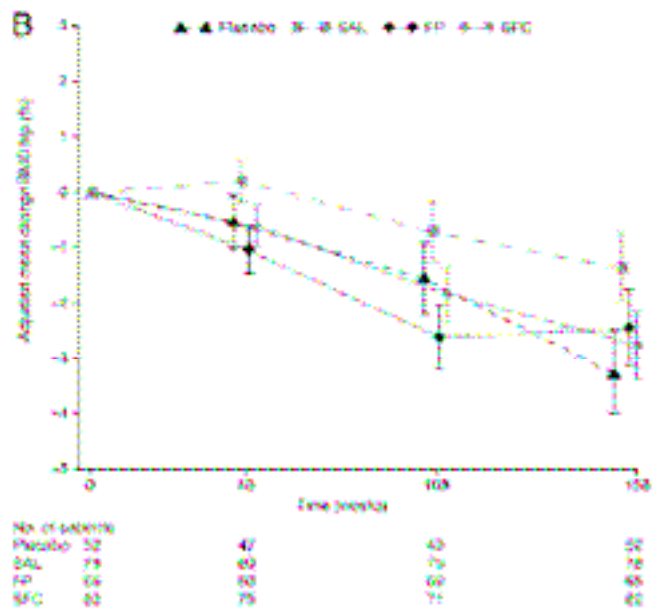


FIGURE 2. Adjusted mean percent change in BMD at the total hip (A) in all patients over the course of the study and (B) in patients who completed all 3 years of therapy. Vertical bars represent SEs.

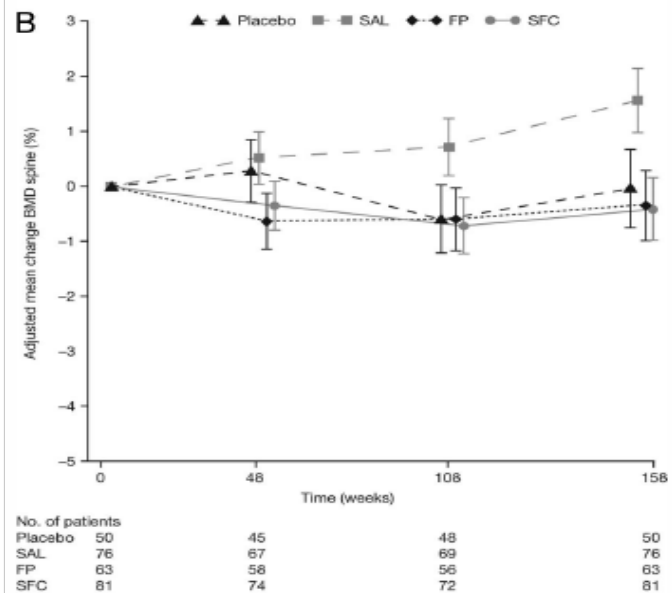


FIGURE 3. Adjusted mean percent change in BMD at the lumbar spine (A) in all patients over the course of the study and (B) in patients who completed all 3 years of therapy. Vertical bars represent SEs.

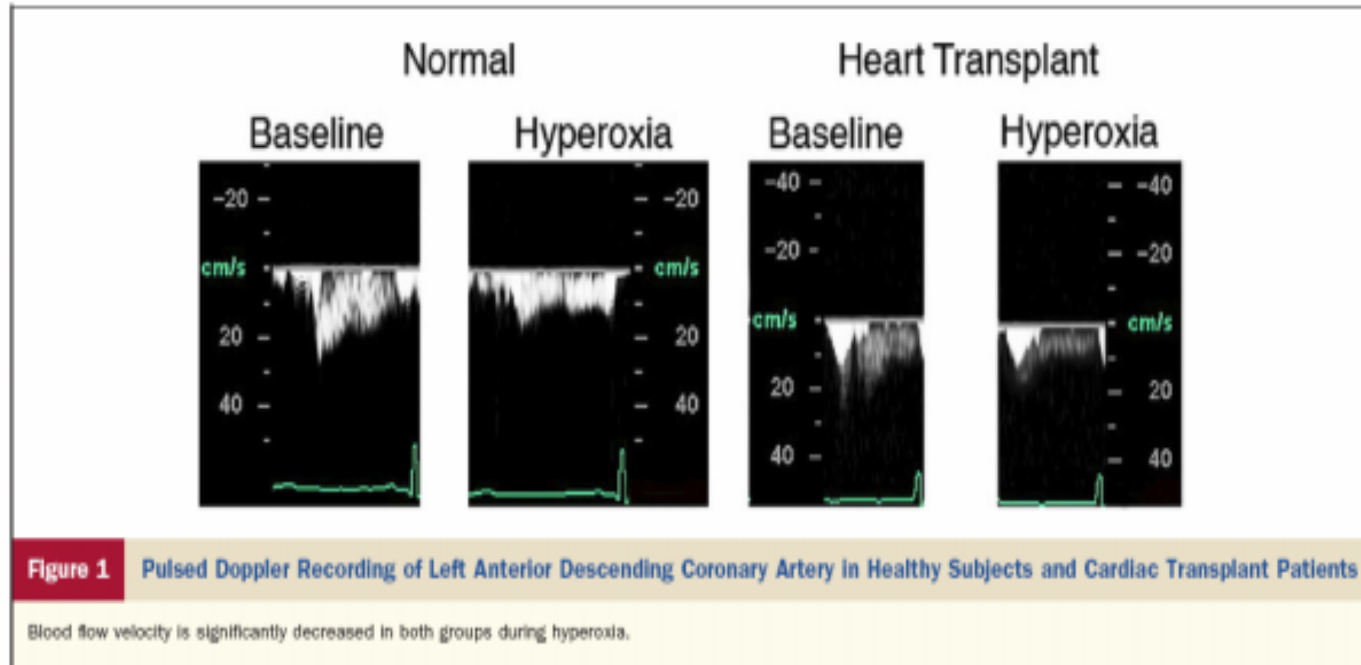
Attenzione alle ADRs, anche inattese

(Afonso ASM et al. BJUI 2010, on line)

- L'uso di anticolinergici, specie nebulizzati e in soggetti con IPB, aumenta del 40% il rischio di ritenzione urinaria acuta.
- L'effetto è maggiore all'inizio della terapia e non è dose dipendente.
- Non v'è differenza tra ipratropio e tiotropio

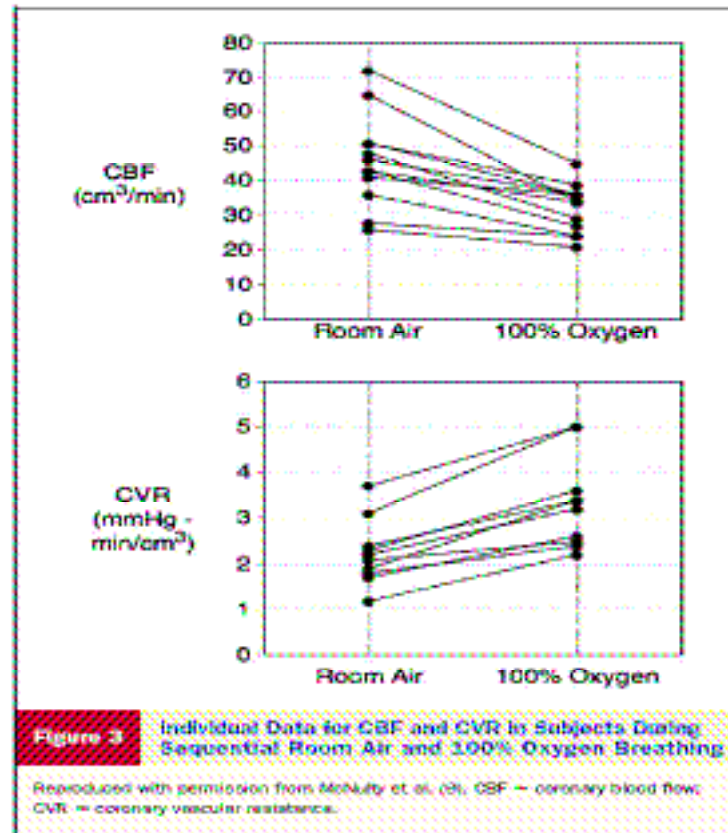
Che cosa non fare: O₂-terapia incongrua

(Moradkhan R et al. JACC 2010; 56: 1013)



Che cosa non fare: O₂-terapia incongrua

(Moradkhan R et al. JACC 2010; 56: 1013)



Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial

BMJ 2010;341:c5462

Michael A Austin, honorary associate,¹ emergency medicine registrar,² wilderness helicopter, intensive care paramedic,³ Karen E Wills, biostatistician,³ Leigh Blizzard, senior biostatistician,¹ Eugene H Walters, professorial fellow,³ Richard Wood-Baker, honorary fellow,³ director²

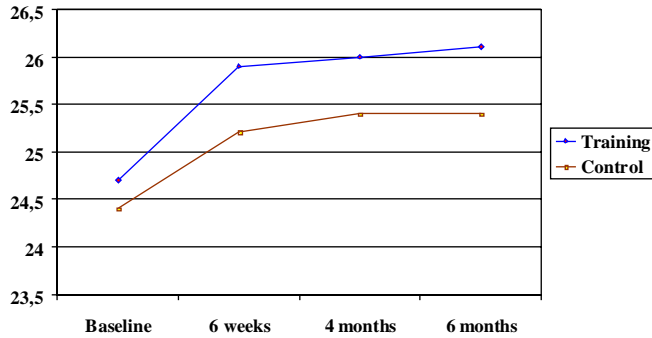
Table 3 | Intention to treat analysis. Values are numbers (percentages) unless stated otherwise

	Control (high flow oxygen)	Active (titrated oxygen)	Treatment effect	P value
Mortality				
All patients	21/226 (9)	7/179 (4)	0.42 (0.20 to 0.89)*	0.02
Confirmed COPD	11/117 (9)	2/97 (2)	0.22 (0.05 to 0.91)*	0.04
Incidence of ventilation				
All patients	19/213 (9)	13/166 (8)	0.88 (0.45 to 1.72)*	0.70
Non-invasive ventilation	7	8		
Invasive ventilation	12	5		
Confirmed COPD	15/105 (14)	8/84 (10)	0.67 (0.29 to 1.54)*	0.34
Non-invasive ventilation	6	5		
Invasive ventilation	9	3		
Length of hospital stay (mean (SD) days)				
All patients	5.9 (5.6) (n=226)	5.5 (5.9) (n=179)	-0.45 (0.57)†	0.19
Confirmed COPD	6.3 (5.8) (n=117)	5.4 (4.1) (n=97)	-0.88 (0.70)†	0.37

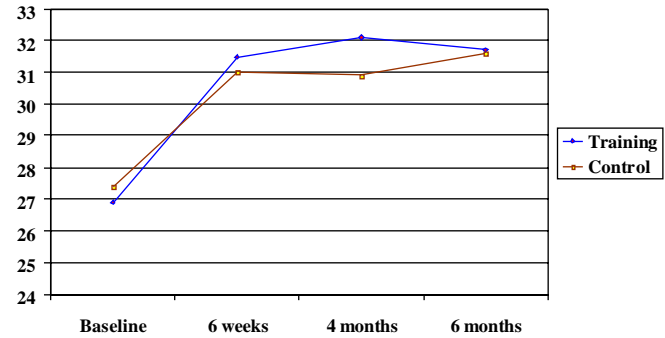
Cognitive training is ineffective in hypoxemic COPD: a 6-months randomized controlled trial.

(Antonelli Incalzi et al. Rejuv Res 2008; 11: 1-12)

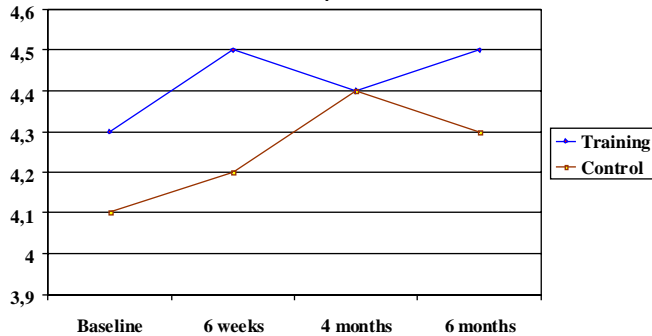
Raven's Progressive Matrices



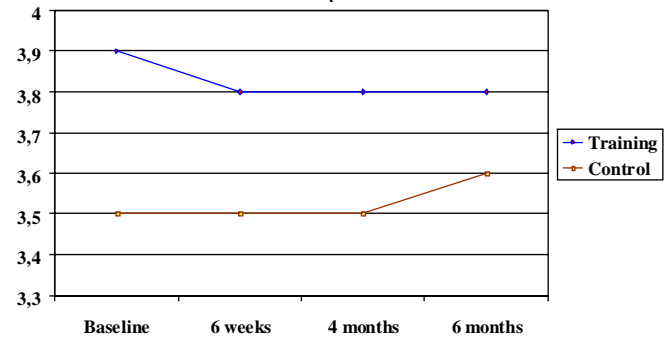
Verbal fluency



Visual Span



Verbal span



Che cosa non fare: un'assistenza domiciliare nurse-based

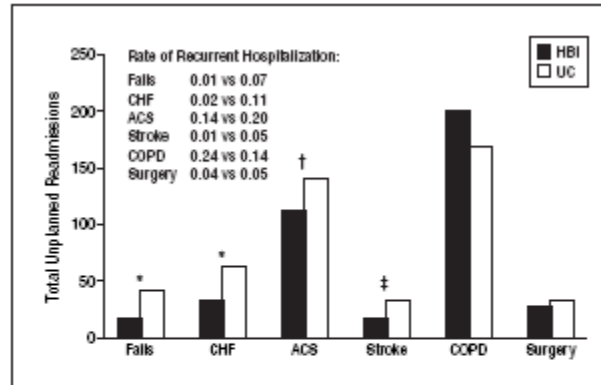


Figure 4. Comparison of the total number and frequency of unplanned hospitalizations according to treatment group in high-risk patients during long-term follow-up. The most frequent contributors are shown. ACS indicates acute coronary syndrome; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; HBI, home-based intervention; and UC, usual postdischarge care. Asterisk indicates $P \leq .01$; dagger, $P \leq .05$; and double dagger, $P \leq .001$.

Conclusioni

- BPCO: una malattia dell'anziano, ma eterogenea per fenotipo e gravità.
- Rischio di misconoscimento e di impropria diagnosi.
- Terapia non solo farmacologica.
- Terapia farmacologica efficace.
- Strategie di CGE: da sviluppare.