



60° CONGRESSO NAZIONALE



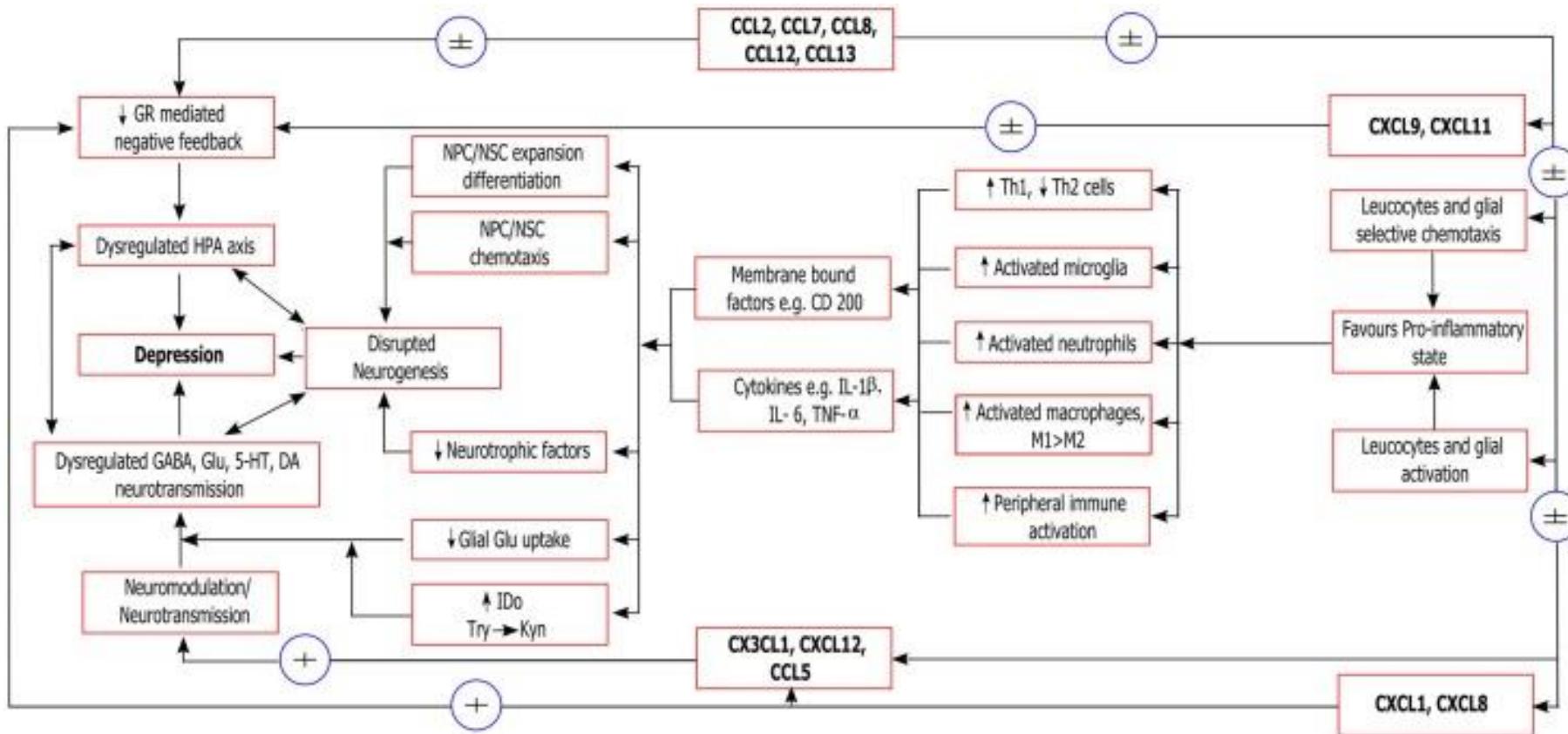
BPCO e depressione

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Aging and depression: neurobiology



Systemic effects and comorbidities of COPD

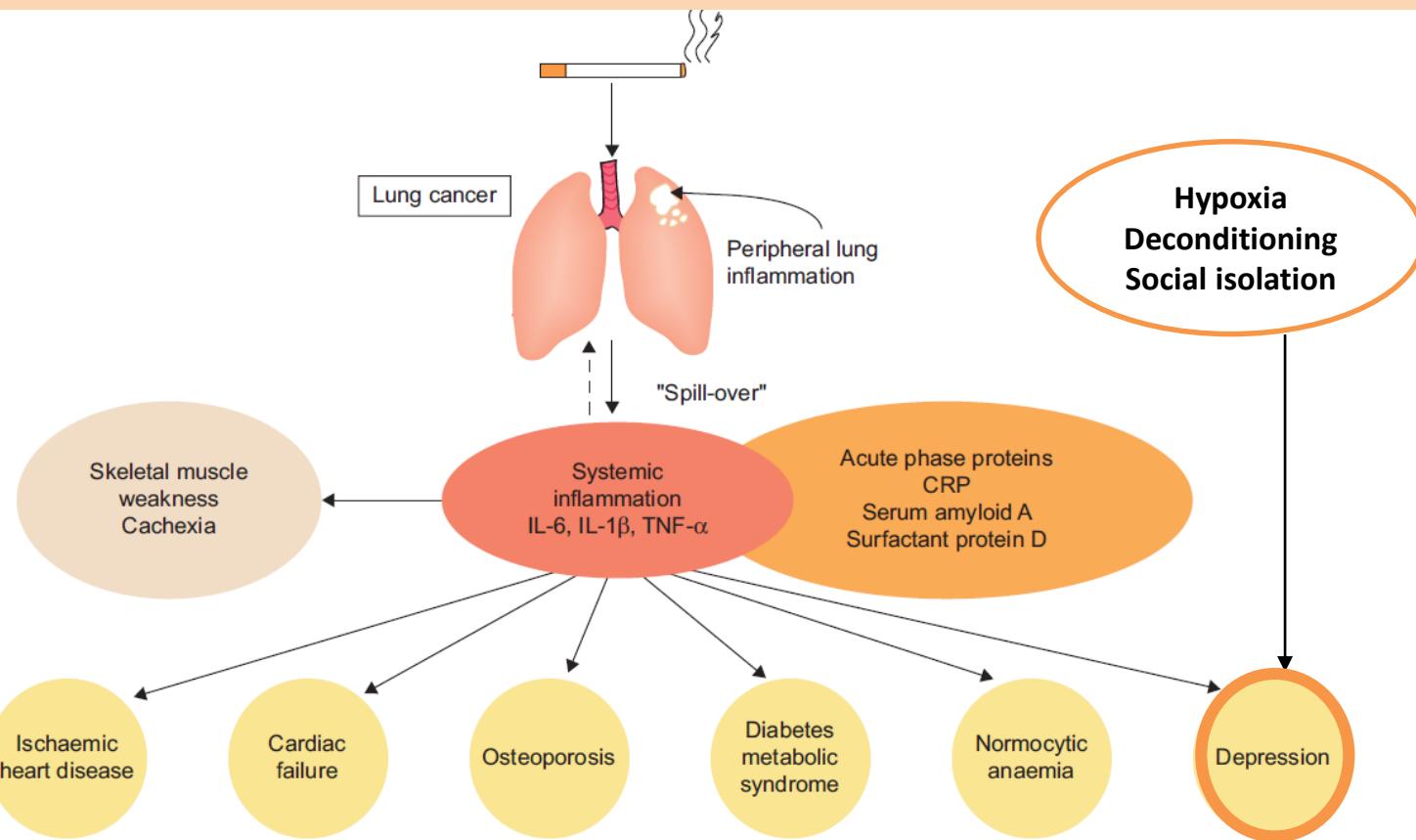
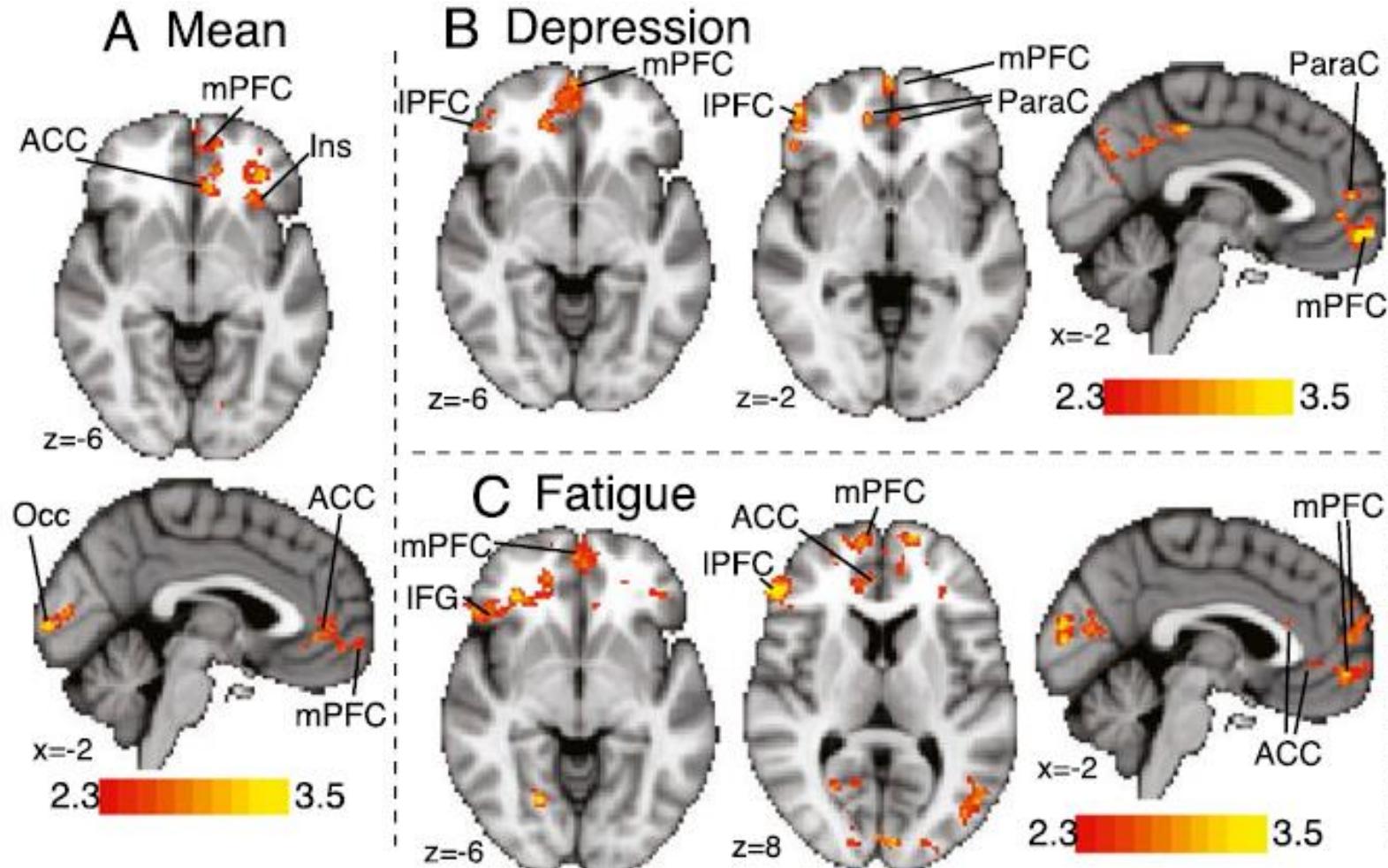


FIGURE 1. Systemic effects and comorbidities of chronic obstructive pulmonary disease (COPD). Peripheral lung inflammation may cause a "spill-over" of cytokines, such as interleukin (IL)-6, IL-1 β and tumour necrosis factor (TNF)- α , into the systemic circulation, which may increase acute-phase proteins such as C-reactive protein (CRP). Systemic inflammation may then lead to skeletal muscle atrophy and cachexia and may initiate and worsen comorbid conditions. Systemic inflammation may also accelerate lung cancer. An alternative view is that systemic inflammation causes several inflammatory diseases, including COPD.

Modified from Barnes, ERJ 2009

Dyspnea-Related Cues Engage the Prefrontal Cortex



BPCO e depressione

- Epidemiologia ed impatto sugli outcomes
- Implicazioni gestionali
- Problemi diagnostici
- Problemi terapeutici
- Conclusioni

Prevalence of depression among COPD patients

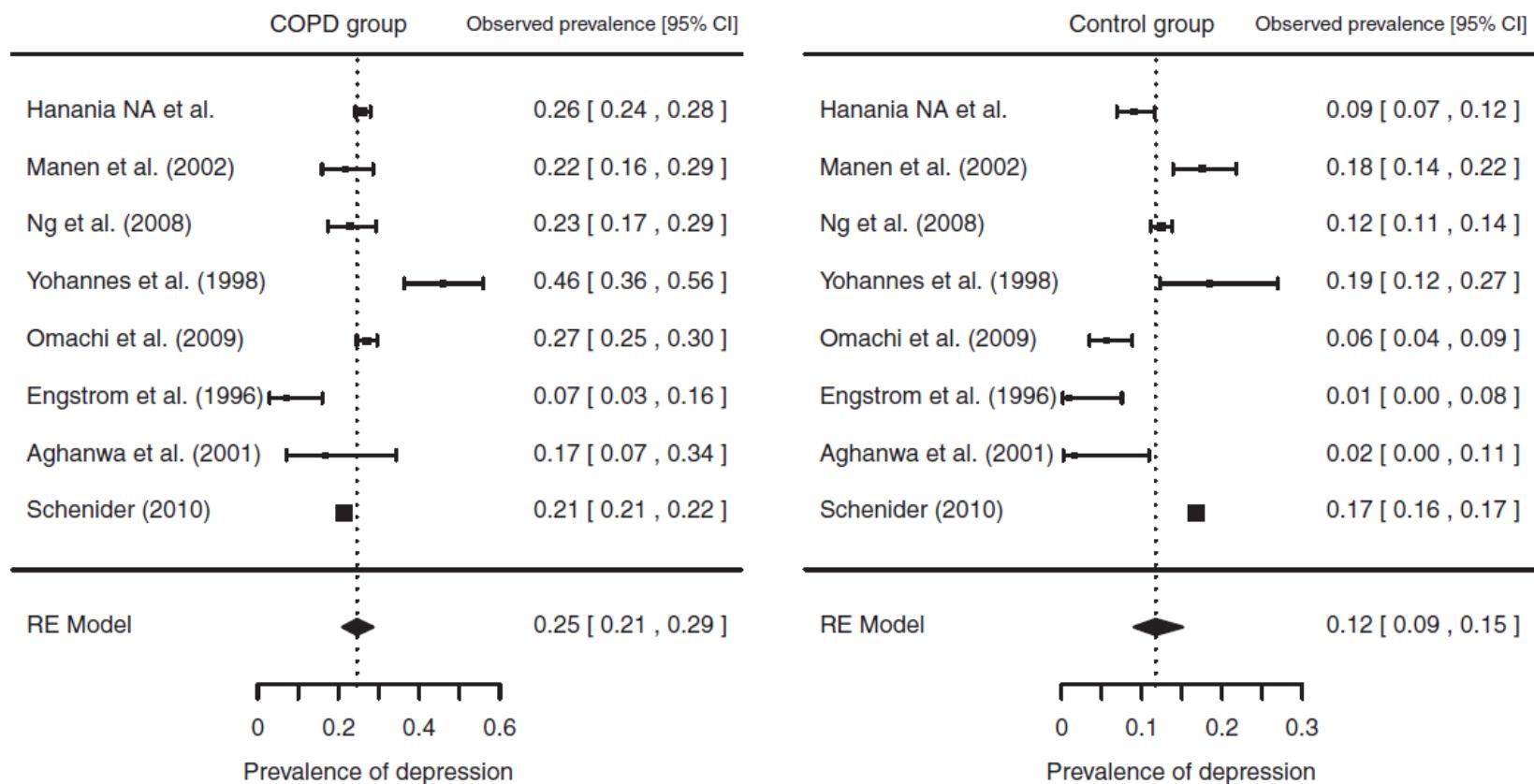
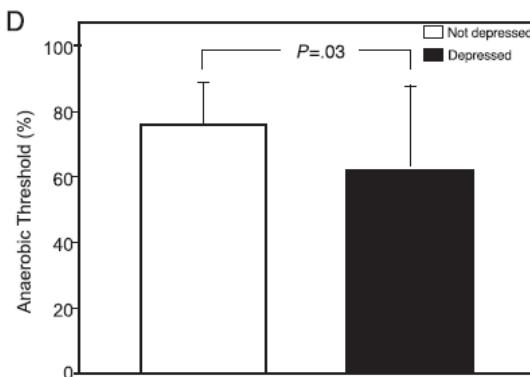
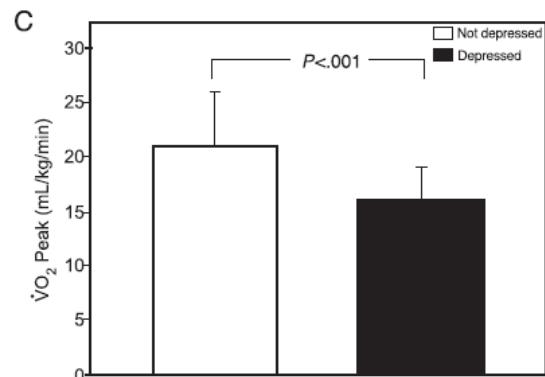
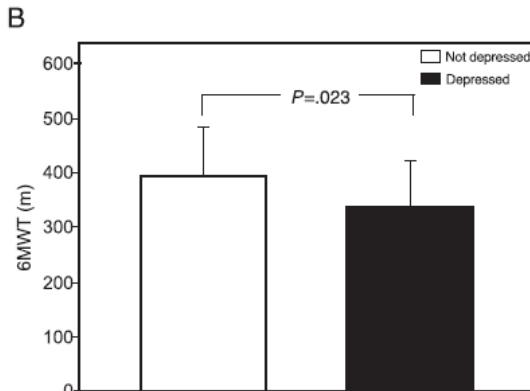
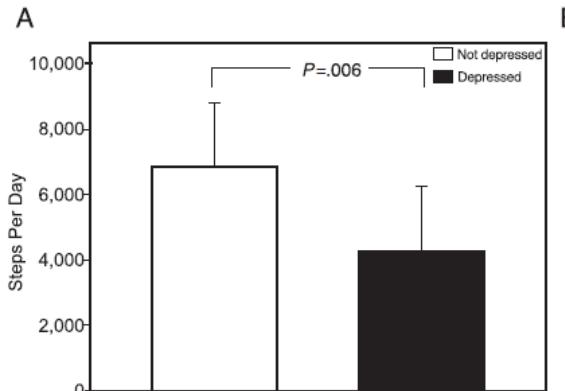


Fig. 2. Forest plot comparing the prevalence of depressive symptoms among COPD patients versus controls without COPD.

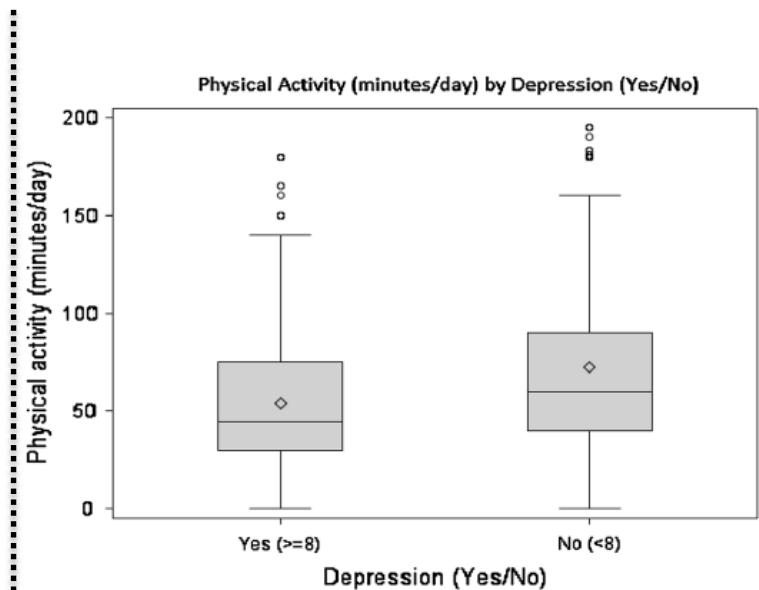
Summary of prospective studies investigating the relationship between depression and mortality in COPD

Study	Patients	Age	COPD type	F.U. yrs	Diagnosis	% depression	HR (95%CI)
Abrams et al, USA, 2011	26,591	69	COPD admission	0.08	ICD9	11.6	1.53(1.28-1.82)
Lou et al, China, 2014	7,787	62	Stable COPD	4	HADS	35	1.35 (1.02-1.68)
Fan et al, USA, 2007	603	67	Emphysema	3	BDI	41	2.26(1.30-3.93)
Ng et al, Singapore, 2007	376	72	COPD admission	0.86	HADS	44	2.26(1.30-4.0)
Gudmundsson et al, Scandinavia, 2012	256	69	COPD admission	8.7	HADS	N.A.	N.S.
Yohannes et al, UK, 2002	137	73	Stable COPD	2.5	BASDEC MADRS	N.A.	N.S.
Almagro et al, Spain, 2002	135	72	COPD admission	1.9	YESAVAGE/ GDS-SF	N.A.	3.60(1.46-6.59)
De Voogd et al, Netherland, 2009	121	62	Stable COPD, Rehab	8.5	BDI	33	1.93(1.12-3.33)
Yohannes et al, UK, 2005	100	73	COPD admission	1	BASDEC	56	1.13(1.02-1.26)
Stage et al, Denmark, 2005	49	71	Stable COPD	2.2	ICD10	47	0.20(0.09-0.82)

Impact on outcomes: physical performance



Di Marco et al, Respiratory Care 2014



Independent predictors	Dependent variable		
	Odds ratio	95 % CI for OR	p value*
EQ-5D	0.23	0.15–0.35	<0.0001
COPDSS (per one-point increase)	1.04	1.02–1.07	<0.0001
Depression (HAD ≥8, ref. HAD <8)	1.58	1.25–2.01	<0.0001

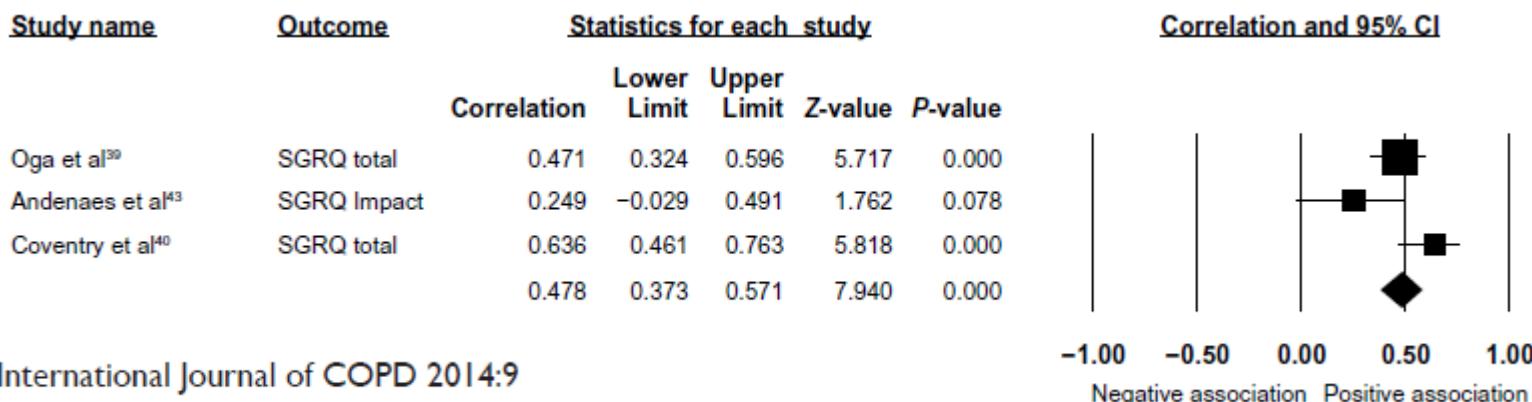
Miravitles et al, Lung 2014

Impact on outcomes: HRQoL

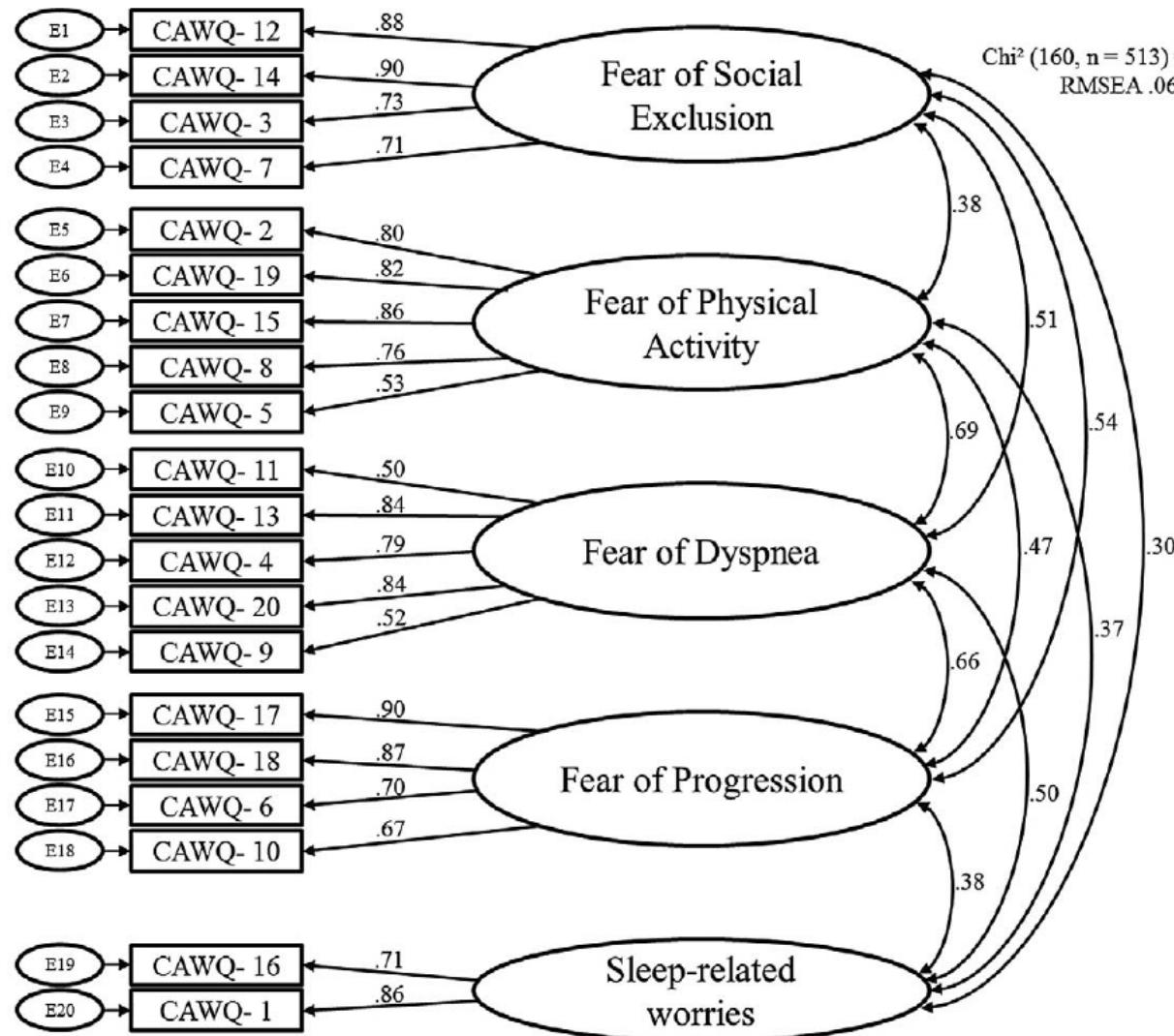
Table 3 Longitudinal correlations between depression and HRQoL in chronic obstructive pulmonary disease

Reference	Depression measure	HRQoL measure	Length of follow-up	Sample size	Correlation (<i>r</i>)	P-value
Andenaes et al ⁴³	HSCL-25	SGRQ symptoms	9 months	51	-0.079	NS
	HSCL-25	SGRQ impact	9 months	51	0.279	<0.05
	HSCL-25	SGRQ activities	9 months	51	-0.138	NS
	HSCL-25	WHOQOL physical	9 months	51	-0.638	<0.001
	HSCL-25	WHOQOL psychiatric	9 months	51	-0.622	<0.001
	HSCL-25	WHOQOL social	9 months	51	-0.225	NS
	HSCL-25	WHOQOL environment	9 months	51	-0.405	<0.01
Oga et al ³⁹	HAD-D	SGRQ total	1 year	128	0.471	<0.001
	HAD-D	CRQ total	1 year	128	-0.581	<0.001
	HAD-D	SGRQ total	5 years	72	0.473	<0.001
	HAD-D	CRQ total	5 years	72	-0.549	<0.001
Coventry et al ⁴⁰	HAD-D	SGRQ total	3 months	79	0.517	<0.001
	HAD-D	SGRQ total	1 year	62	0.636	<0.001

Abbreviations: HSCL-25, Hopkins Symptoms Checklist; SGRQ, St George's Respiratory Questionnaire; CRQ, Chronic Respiratory Questionnaire; HAD-D, Hospital Anxiety and Depression Scale depression subscale; HRQoL, health-related quality of life; NS, not significant; WHOQOL-BREF, World Health Organization Quality of Life Instrument.



COPD-specific fears and COPD-specific disability

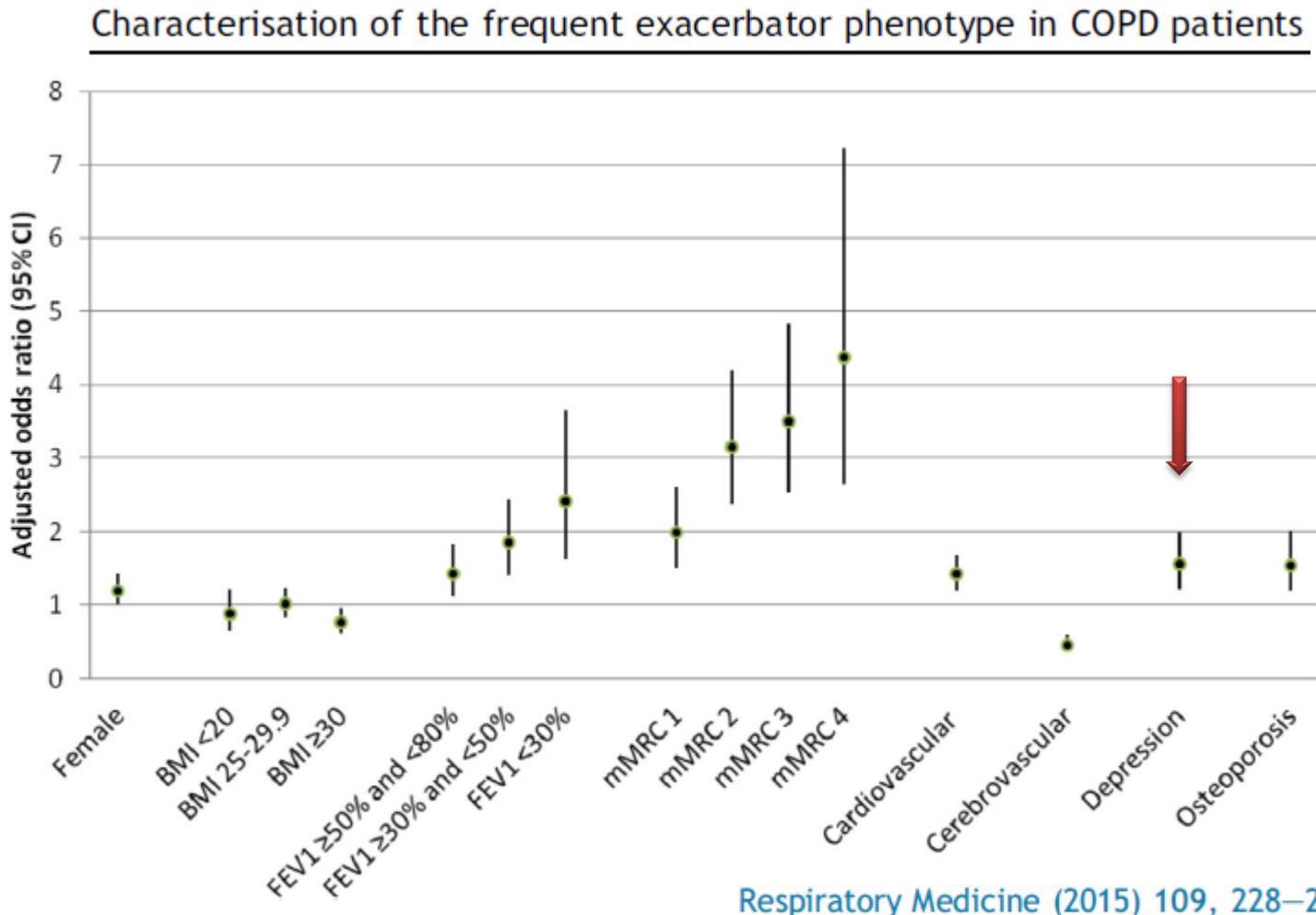


Chronic Respiratory Disease
2014, Vol 11(1) 31–40

$B=1.61, SE(B)=0.23, p<0.01$

$B=2.29, SE(B)=0.19, p<0.01$

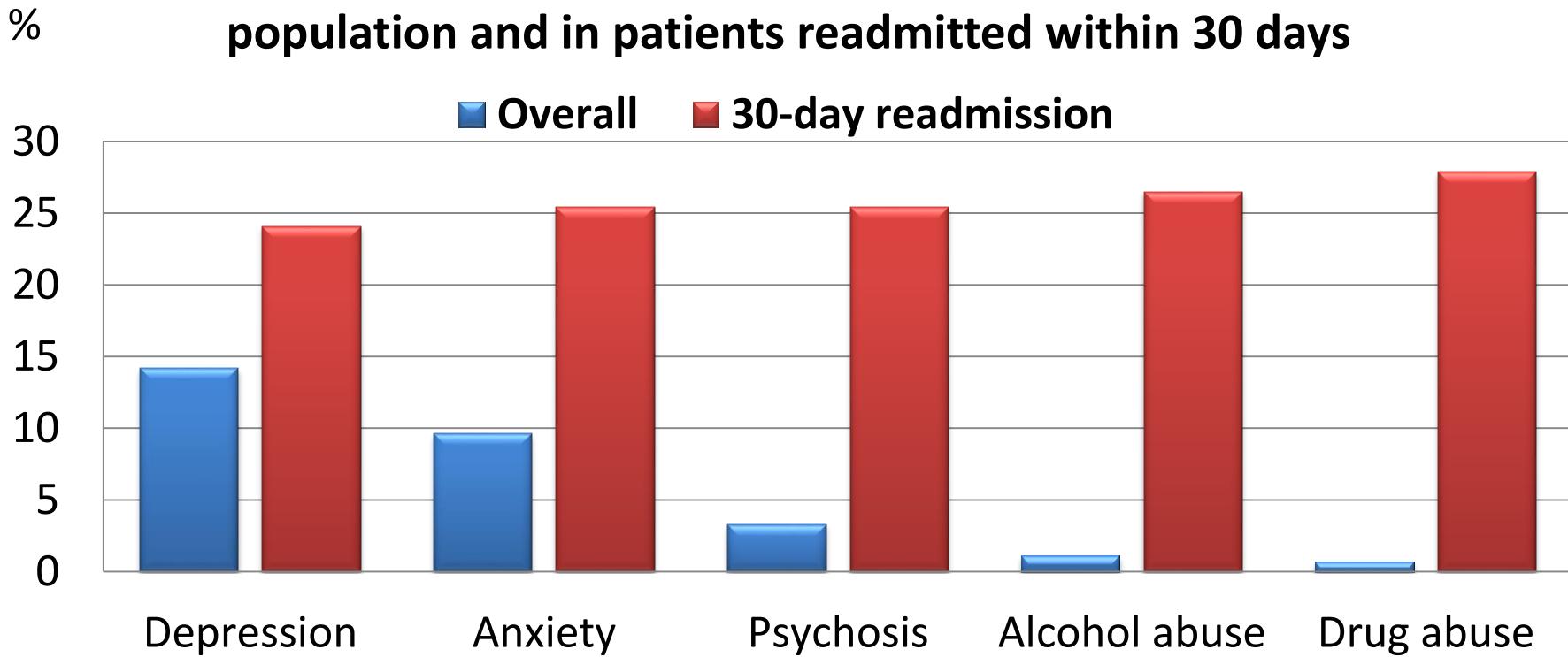
Management implications: exacerbations



Management implications: 30-day readmission

Singh et al, Chest 2015 online first

Prevalence of psychological disorders in the overall COPD population and in patients readmitted within 30 days



Adj OR (95%CI)	1.34 1.29-1.39	1.43 1.37-1.50	1.18 1.10-1.27	1.30 1.15-1.47	1.29 1.11-1.50
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Management implications: medication adherence

Medicare beneficiaries enrolled in Parts A, B, and D plans with diagnosed COPD (n=74,863).

COPD MM adherence was measured as medication discontinuation and proportion of days covered (PDC).

Depression was identified through the ICD-9CM codes

	Discontinuation		PDC>0.80	
	PR	95%CI	PR	95%CI
Depression (crude)	1.16	1.12-1.21	0.82	0.79-0.84
Depression (adjusted)*	1.09	1.04-1.14	0.89	0.86-0.92

*After adjusting for age, gender, race, income, comorbidities, and COPD severity

The COPD/depression vicious cycle

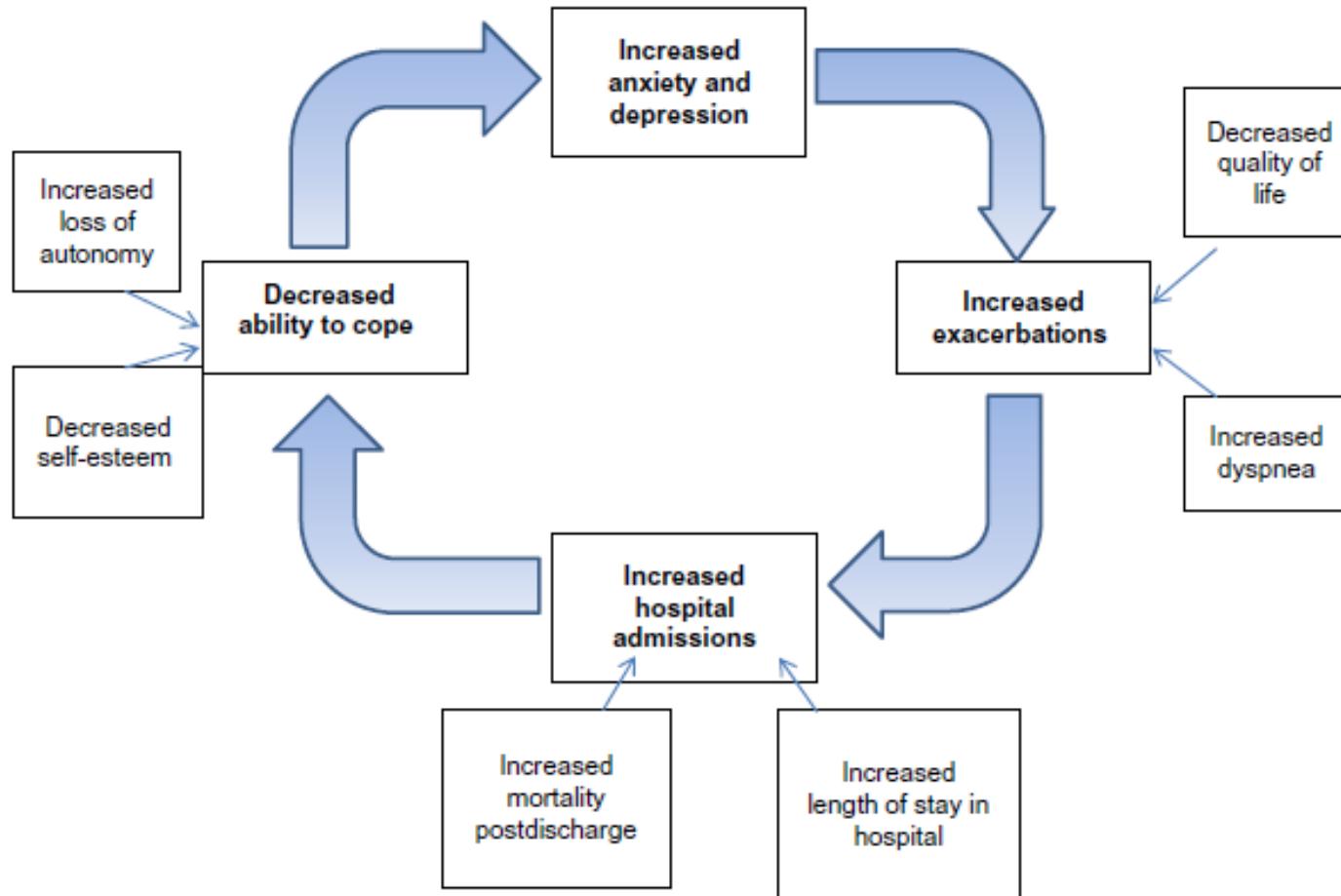


Tabella 2 Criteri diagnostici per l'episodio depressivo maggiore.

DSM-IV

A	Cinque (o più) dei seguenti sintomi sono stati contemporaneamente presenti durante un periodo di 2 settimane e rappresentano un cambiamento rispetto al precedente livello di funzionamento; almeno uno dei sintomi è costituito da 1) umore depresso o 2) perdita di interesse o piacere
	Umore depresso per la maggior parte del giorno, quasi ogni giorno, come riportato dal soggetto (per esempio, si sente triste o vuoto) o come osservato dagli altri (per esempio, appare lamentoso)
	Marcata diminuzione di interesse o piacere per tutte, o quasi tutte, le attività quasi ogni giorno (come riportato dal soggetto o come osservato dagli altri)
	Significativa perdita di peso, senza essere a dieta, o aumento di peso (per almeno 5% del peso corporeo in un mese) oppure diminuzione o aumento dell'appetito
	Insomnia o ipersonnia quasi ogni giorno
	Agitazione o rallentamento psicomotorio quasi ogni giorno (osservabile da altri) o sentimenti soggettivi di essere irrequieto o rallentato
	Faticabilità o mancanza di energia quasi ogni giorno
	Sentimenti di autosvalutazione o di colpa eccessivi o inappropriati (che quasi ogni giorno (non semplicemente autoaccusa o sentimenti di colpa o osservata dagli altri)
	Ridotta capacità di pensare o di concentrarsi, o indecisione, quasi ogni giorno (osservata dagli altri)
	Pensieri ricorrenti di morte (non solo paura di morire), ricorrente ideazione di un suicidio o un tentativo di suicidio, o l'ideazione di un piano specifico per commettere suicidio
B	I sintomi non soddisfano i criteri per un episodio misto
C	I sintomi causano disagio clinicamente significativo o compromissione del funzionamento sociale, lavorativo o di altre aree importanti
D	I sintomi non sono dovuti agli effetti fisiologici diretti di una sostanza (per esempio una droga di abuso, un medicamento) o di una condizione medica generale (per esempio, ipotiroidismo)
E	I sintomi non sono meglio giustificati da lutto, cioè, dopo la perdita di una persona amata, i sintomi persistono per più di 2 mesi o sono caratterizzati da compromissione funzionale marcata, autosvalutazione patologica, ideazione suicidaria, sintomi psicotici o rallentamento psicomotorio

List of Depression Disorders According to DSM-5



- Premenstrual Dysphoric Disorder
- Unspecified Depressive Disorder
- Other Specified Depressive Disorder
- Disruptive Mood Dysregulation Disorder
- Persistent Depressive Disorder (Dysthymia)
- Substance/Medication-induced Depressive Disorder
- Major Depressive Disorder
(single and recurrent episodes)

Tabella 4 Questionari per lo screening di depressione/ansia in pazienti con BPCO.

Strumenti per lo screening di massa

Patient Health Questionnaire-2 (PHQ2):

Depression screening [34]

Patient Health Questionnaire-3 (PHQ3):

Anxiety screening [34]

Strumenti per lo screening mirato

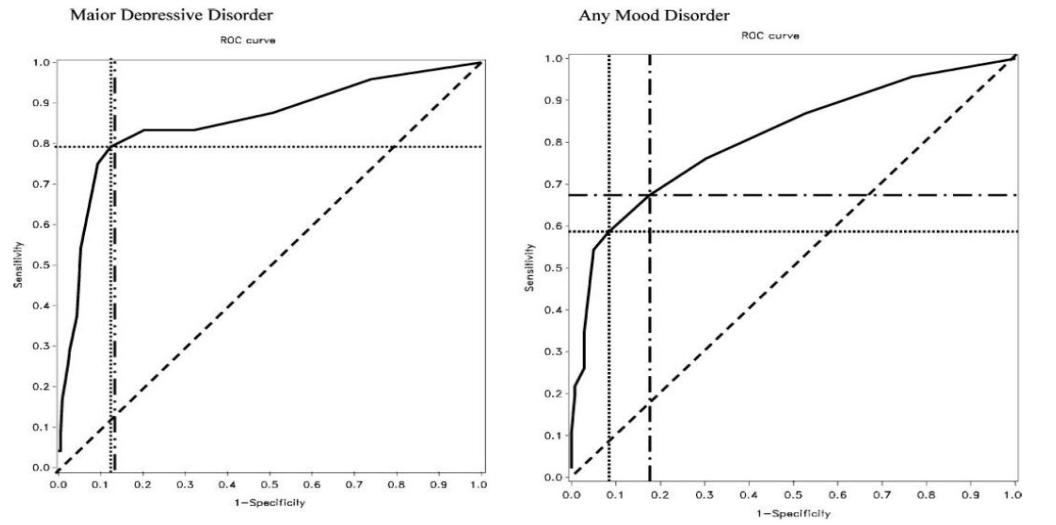
Depressione

1. Patient Health Questionnaire-9 (PHQ-9) [35]
2. Center for Epidemiologic Studies – Depression (CES-D) scale [36]
3. Geriatric Depression Scale (GDS-30 o GDS-15) [37]
4. Zung Self-Rating Depression Scale [38]
5. Beck Depression Inventory [39]
6. Hamilton Depression Scale [40]

Ansia

1. Hospital Anxiety and Depression Scale (HADS) [41]
2. Depression Anxiety Stress Scale [42]
3. Beck Anxiety Inventory [39]
4. Hamilton Anxiety Rating Scale [43]
5. Spielberg State Trait Anxiety Inventory [44]

Accuracy of GDS



	Major Depressive Disorder Cut-point 5 and above		Total n = 188	Any mood disorder Cut-point 4 and above		Total n = 188
	<65 yrs n = 78	≥65 yrs n = 110		<65 yrs n = 78	≥65 yrs n = 110	
Stratified by age						
Prevalence n(%)	8 (10.3%)	13 (11.8%)	21 (11.2%)	20(25.6%)	26(23.6%)	46(24.5%)
Sensitivity	0.75	0.85	0.81	0.75	0.62	0.67
Specificity	0.84	0.89	0.87	0.83	0.82	0.82
Positive Predictive Value	0.35	0.50	0.44	0.60	0.52	0.55
Negative Predictive Value	0.97	0.98	0.97	0.91	0.87	0.89
Correctly Classified (%)	83%	88%	86%	73%	77%	79%
Stratified by disease severity	GOLD<2 n = 84	GOLD≥2 n = 82	Total n = 166	GOLD<2 n = 84	GOLD≥2 n = 82	Total n = 166
Prevalence n(%)	8(9.5%)	7(8.5%)	15(9.0%)	18 (21.4%)	17(20.7%)	35 (21.1%)
Sensitivity	0.88	0.71	0.80	0.61	0.59	0.60
Specificity	0.90	0.85	0.87	0.85	0.79	0.82
Positive Predictive Value	0.47	0.31	0.39	0.52	0.42	0.47
Negative Predictive Value	0.99	0.97	0.98	0.89	0.88	0.88
Correctly Classified (%)	89%	84%	87%	80%	74%	77%

Accuracy of HADS

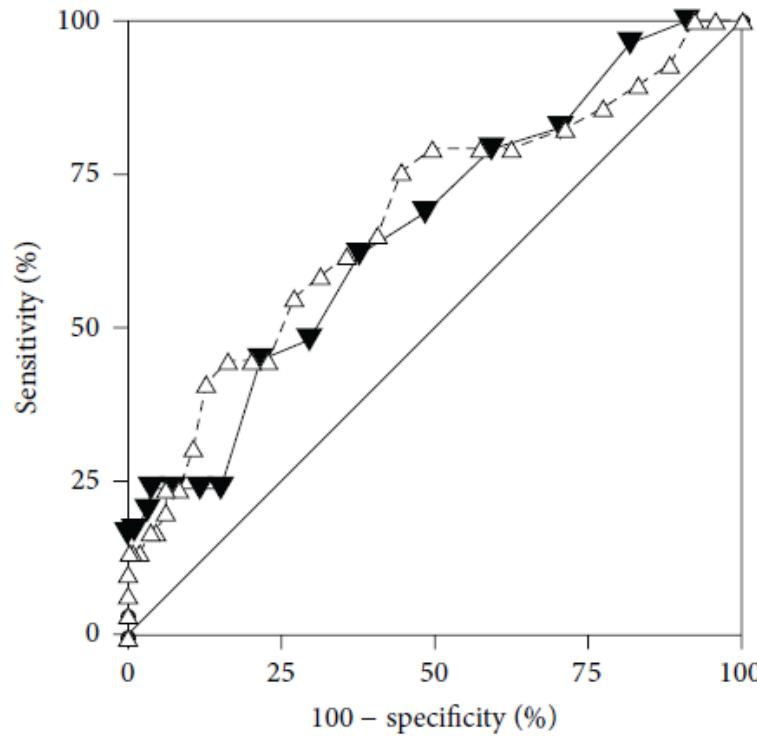


FIGURE 3: Comparative receiver operating characteristic (ROC) curves for HADS-depression (solid triangles) and HADS-total (white triangles).

Terapia farmacologica della depressione in BPCO

-Evidenze-

Triciclici

Notriptilina
Desipramina
Doxepin
Imipramine + diazepam
Protriptilina

Risultati non univoci (in alcuni studi non sono stati rilevati miglioramenti dei sintomi depressivi superiori al controllo)
Eventi avversi frequenti

SSRI

Citalopram
Fluoxetina
Paroxetina
Sertralina

Risultati non univoci (in alcuni studi non sono stati rilevati miglioramenti dei sintomi depressivi superiori al controllo)
Generalmente ben tollerati

Gordon GH, Psychiatry Res 1985
Light RW Arch Intern Med 1986
Sharma TN Indian J Chest Dis Allied Sci 1988
Borson S, Psychosomatics 1992
Ström K, Eur Respir J 1995
Papp LA, Psychiatry 1995
Evans M, Int J Geriatr Psychiatry 1997
Smoller JW; Psychosomatics 1998
Lacasse Y, Monaldi Arch Chest Dis 2004
Eiser N, COPD 2005
Fritzsche A, Resp Med 2011
Hegerl & Mergl, Eur Respir J 2014 (Review)

SSRIs: safety in COPD

Theophylline



Fluvoxamine

Inhibits
theophylline
metabolism

Inhaled bronchodilators
Steroids
Leukotriene antagonists

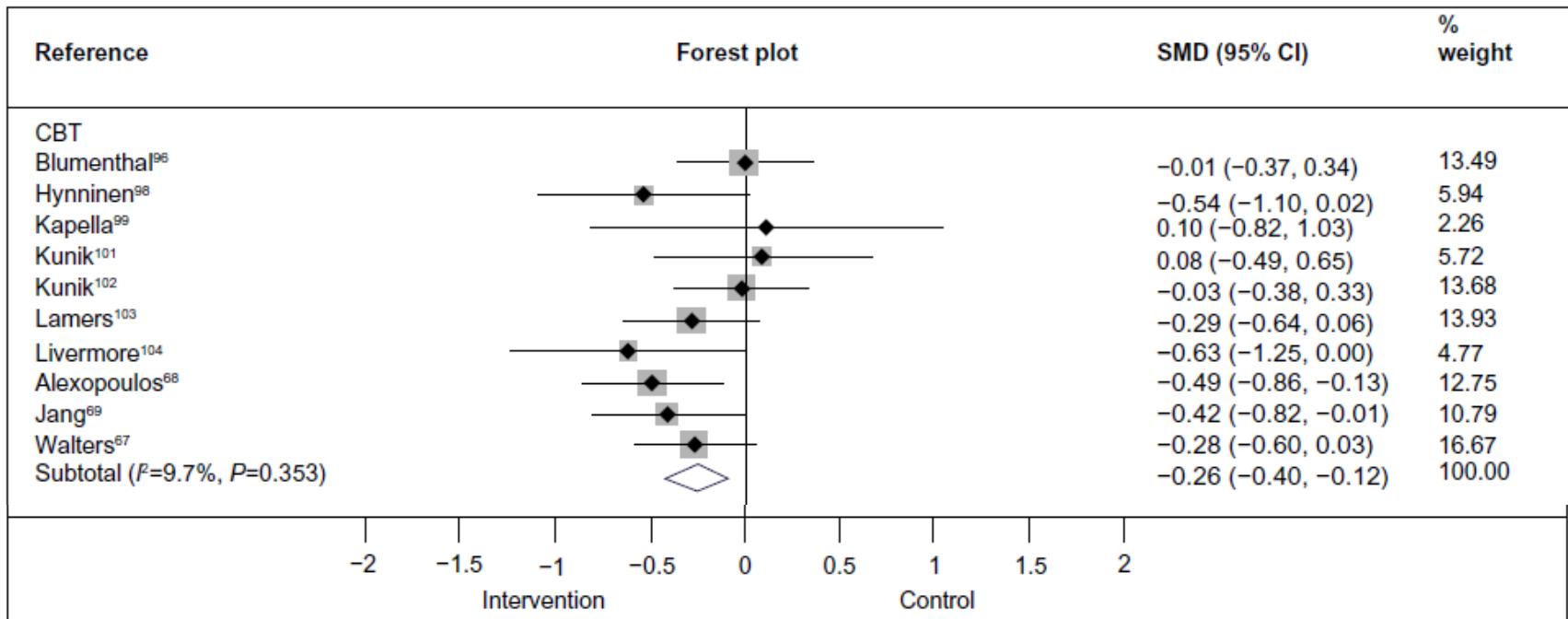


SSRIs
No specific
contraindications

Cognitive-behavioral therapy



Efficacy of cognitive-behavioral therapy



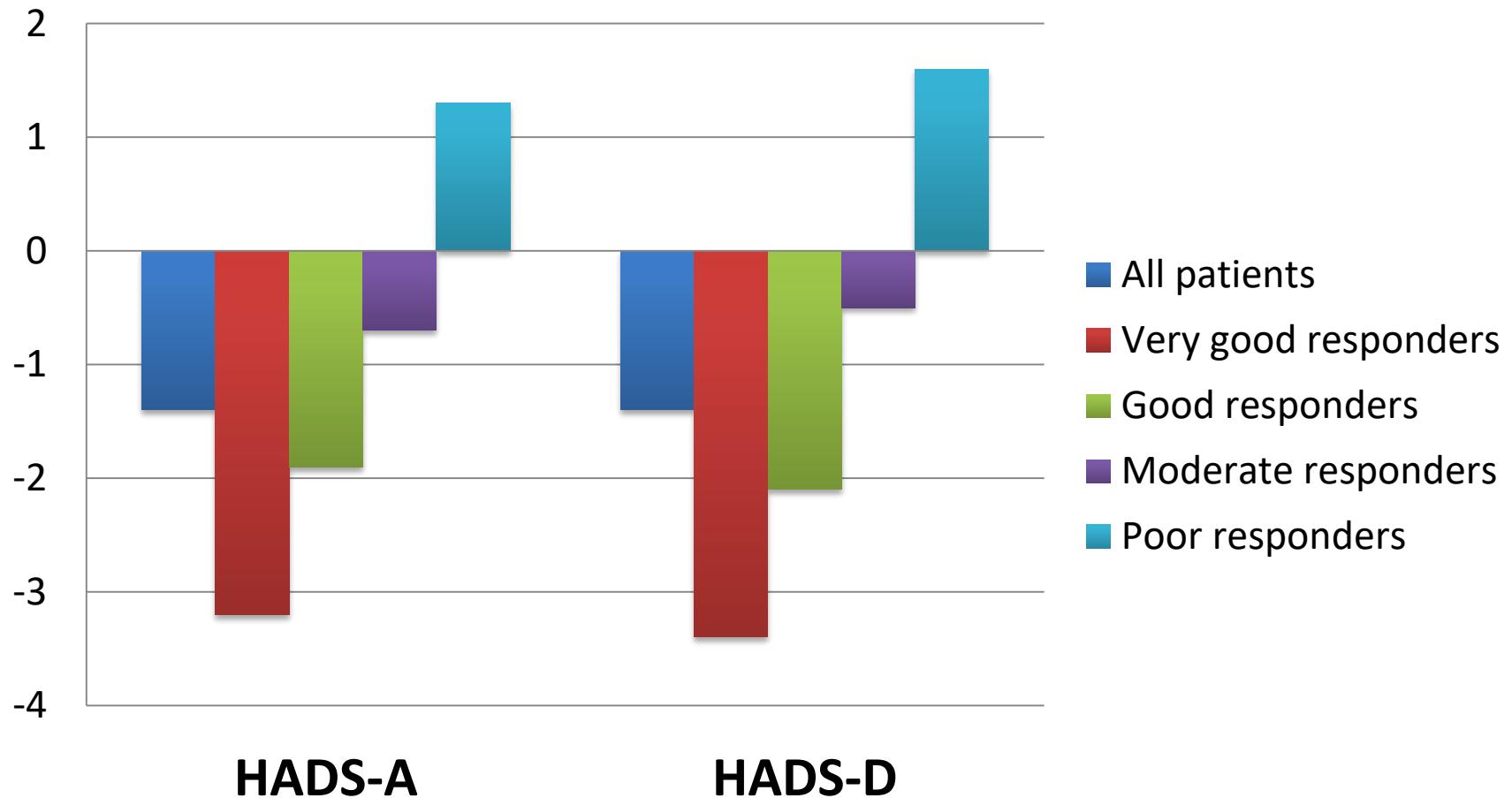
Efficacy of pulmonary rehabilitation

Depression is associated with lower response to PR in terms of

Depression is associated with lower rate of PR completion



Multidimensional profiling of response to pulmonary rehabilitation



Take home messages

