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# Depressione nell'anziano e patologia somatica: una rivisitazione

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### Di cosa voglio parlare

- Depressione: dove eravamo rimasti?
- Il medico (geriatra, psichiatra, neurologo) e la depressione nell'anziano
- "La grammatica della vita interiore" nei medici e nei vecchi d'oggi
- Depressione e mortalità
- Depressione e patologia
- Epidemiologia del trattamento
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- Conclusioni

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#### Psicogeriatria Psicogeriatria Direttore Editoriale Marco Trabucchi Comitato Editoriale Carlo Caltagirone Niccolò Marchionni Elvezio Pirfo Umberto Senin La depressione Coordinatore Comitato Scientifico nella persona che invecchia Luigi Ferrannini Segreteria di Redazione Angelo Bianchetti Vincenzo Canonico Comitato Scientifico Raffaele Antonelli Incalzi Fabrizio Asioli Giuseppe Barbagallo Luisa Bartorelli Giuseppe Bellelli Carlo Adriano Biagini Enrico Brizioli Amalia Cecilia Bruni Fabio Cembrani Alberto Cester Erminio Costanzo Antonino Cotroneo Luc Pieter De Vreese Fabio Di Stefano Andrea Fabbo Antonio Federico Giovanna Ferrandes Nicola Ferrara Giuseppe Fichera Marino Formilan Lodovico Frattola Pietro Gareri Gianluigi Gigli Marcello Giordano Guido Gori Antonio Guaita Marcello Imbriani Cristian Legrin Daniela Leotta Giancarlo Logroscino Maria Lia Lunardelli Alberto March Patrizia Mecocci Fiammetta Monacelli Enrico Mossello Massimo Musicco Leo Nahon Gianfranco Nuvoli Patrizio Odetti Alessandro Padovani Luigi Pernigotti Nicola Renato Pizio Alice Pluderi Paolo Francesco Putzu Renzo Rozzini Michaela Santoro Francesco Scapati. Osvaldo Scarpino Luca Serchisu Carlo Serrati Sandro Sorbi Gianfranco Spalletta Anna Laura Spinelli Orazio Zanetti Documento dell'Associazione Italiana di Psicogeriatria

Gabriele Tripi Claudio Vampini Flavio Vischia

Giovanni Zuliani

## Depression, chronic diseases, and decrements in health: results from the World Health Surveys

Saba Moussavi, Somnath Chatterji, Emese Verdes, Ajay Tandon, Vikram Patel, Bedirhan Ustun

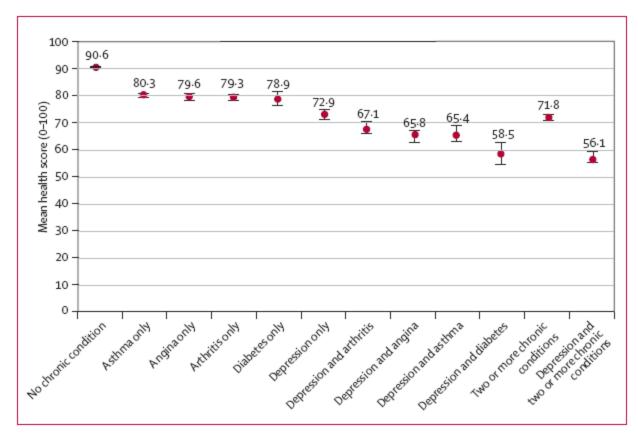


Figure: Global mean health by disease status
Data from WHS 2003.

#### Diagnosing Depression in Older Adults in Primary Care

Ramin Mojtabai, M.D., Ph.D., M.P.H.

N ENGL J MED 370;13 NEJM.ORG MARCH 27, 2014

The prevalence of diagnosed depression in U.S. adults 65 years of age or older doubled from 3% to 6% between 1992 and 2005.¹ A majority of patients with diagnosed depression were treated with antidepressant medications by primary care and other general medical clinicians.

#### The NEW ENGLAND JOURNAL of MEDICINE

#### CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., Editor

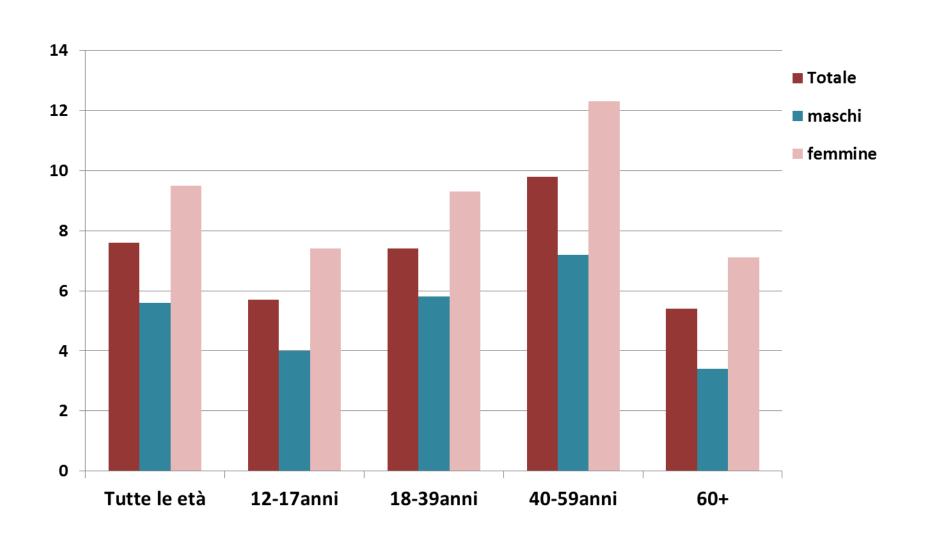
## Depression in the Elderly

Warren D. Taylor, M.D., M.H.Sc.

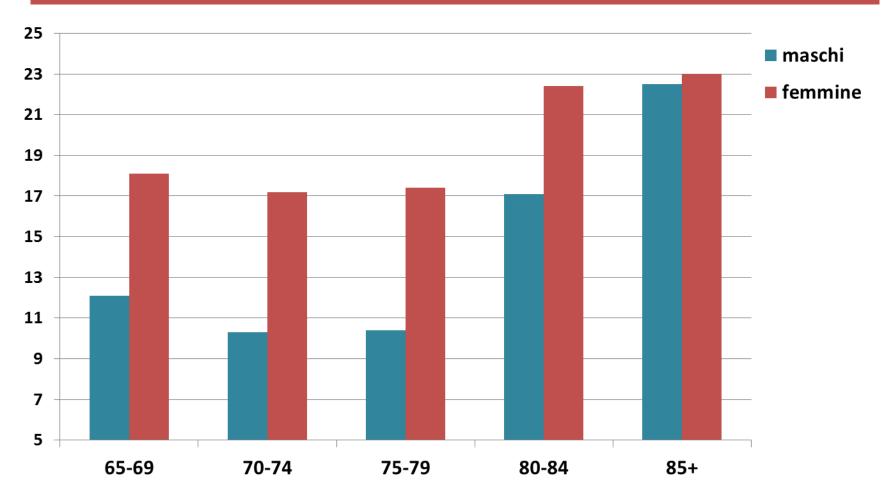
This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

N ENGL J MED 371;13 NEJM.ORG SEPTEMBER 25, 2014

## Percentuale di depressione maggiore stratificata per età e sesso (US, 2009–2012)



#### Prevalenza di sintomatologia depressiva grave (per età e sesso).

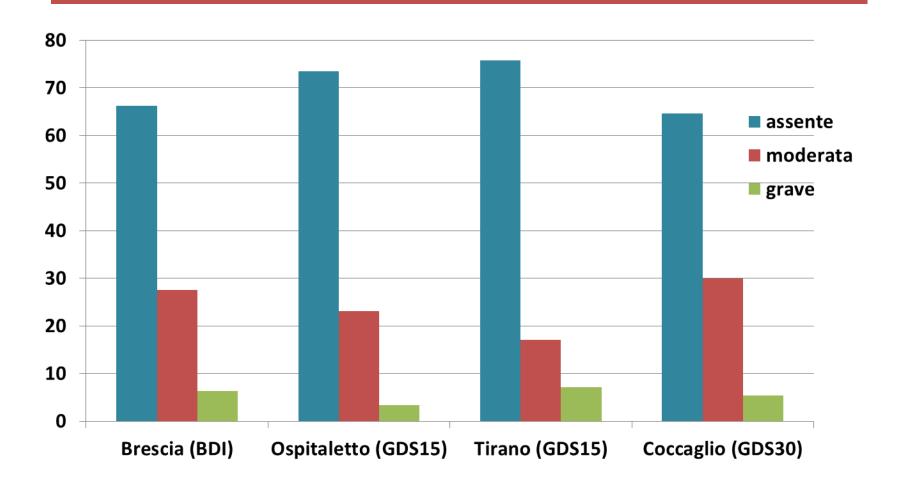


Nota: Definizione di sintomi depressivi gravi: quattro o più sintomi di una serie di otto sintomi depressivi della versione abbreviata del Centro di Studi Epidemiologici Depression Scale (CES-D), adattato dalla Health and Retirement Study.

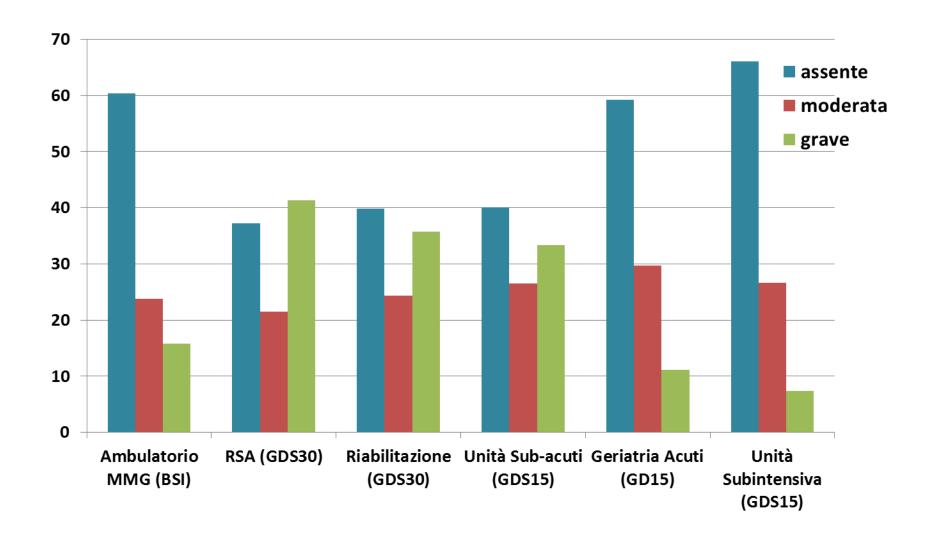
I dati si riferiscono ad una popolazione residente al proprio domicilio (non istituzionalizzata).

Fonte: Health and Retirement Study.

#### Prevalenza di sintomatologia depressiva in anziani residenti al domicilio



Prevalenza di sintomatologia depressiva in pazienti che si rivolgono al medico di medicina generale, residenti in RSA, ricoverati in ospedale (Riabilitazione, Sub-acuti, Geriatria Acuti, Sub-Intensiva) (GDS30)



### **Epidemiology**

1–4% of the general elderly population has <u>major depression</u>, equivalent to an incidence of 0·15% per year. Twice as many women as men are affected. Both the prevalence and the incidence of major depression double after age 70–85 years. (The prevalence of major depression among older adults actually decreases with age, with this rate being approximately 5 to 10% of older person living in community; MD is found in 16 to 50% of older adults in NH or acute care setting). Similarly, the number of elderly people with <u>bipolar disorder</u> is increasing, because the absolute number of old people is rising and, possibly, because the proportion of elderly individuals with this illness is increasing. These disorders account for 10 to 25% of all geriatric patients with mood disorders.

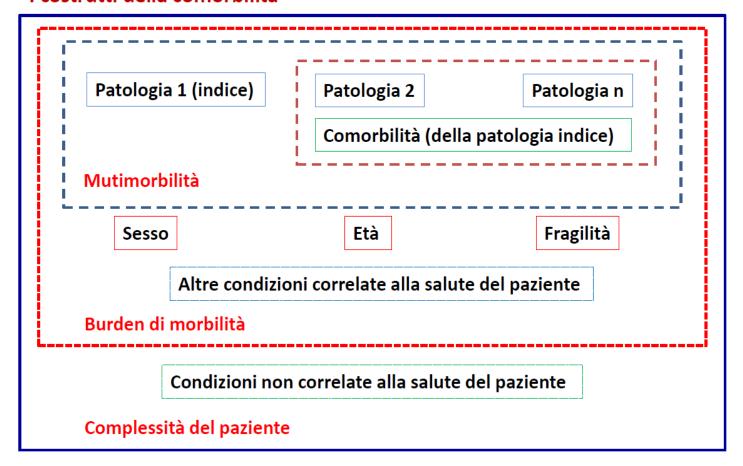
Minor depression has a prevalence of 4–10%. (The prevalence of subsyndromal depression, i.e. symptoms of depression that do not meet standard criteria for MD, however, steadily increases with age and ranges from 10 to 25% among community-dwelling adults and increases to 50% among those in NH or acute care setting). Dysthymic disorder, characterized by low-intensity symptoms of depression that last 2 years or longer, occurs in about 2% of elderly people.

Persons age 65 and over account for 25% of all suicides.

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#### I costrutti della comorbilità



<u>Cormorbilità</u>: presenza di una patologia aggiuntiva rispetto ad una patologia indice in un paziente <u>Multimorbilità</u>: presenza di più patologie in uno stesso paziente

<u>Burden di morbilità</u>: impatto complessivo di diverse patologie in un individuo che tiene in conto della loro gravità <u>Complessità del paziente</u>: impatto complessivo di diverse patologie in un individuo che tiene in conto della loro gravità e di altri fattori correlati alla salute

### Il geriatra e la depressione

- Il geriatra e la modificazione della domanda.
- Oggi il geriatra cura la depressione dei nati nel 1940 o prima («storia della depressione»: dalla «felicità che viene dal sapersi uniformare ai propri doveri» alla «capacità di sapersi uniformare ai propri desideri»; ognuno è il proprietario della propria vita; tutti hanno il diritto di sentirsi psicologicamente male).

### Il geriatra e la depressione

- Dalla psichiatria alla medicina del territorio; il disturbo mentale non è «follia», è parte dei problemi quotidiani; dalla malattia ai problemi psicologici.
- Gli antidepressivi (1960→); l'FDA e il DSM.
- Il geriatra deve conoscere la depressione (il geriatra viene in contatto con la maggior parte delle depressioni, la sua competenza ed esperienza possono facilitare la comprensione dei correlati, ma solo con una parte dello spettro delle depressioni).
- Un geriatra non è uno psichiatra!
- Il geriatra prescrive farmaci antidepressivi: una molecola basta a curare?

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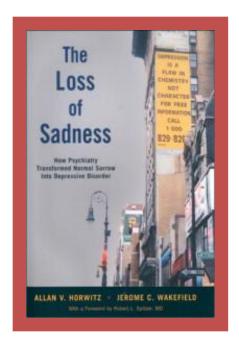
#### La grammatica della vita interiore ad uso pubblico

Traduzioni di opere americane intrise di psicologia, modernizzazione della retorica della posta del cuore, promozione radiotelevisiva del dettaglio intimo, ecc.: tutto concorre a creare spazi pubblici destinati alla trasmissione del linguaggio interiore.

I media fanno emergere una domanda per formulare la quale sanno suggerire le parole convenienti; creano in tal modo uno spazio pubblico per la realtà psichica e modellano una sorta di linguaggio psicologico per le masse (circa '65-'70).

L'interiorità non è tanto dentro la testa delle persone che sono incapace di inventarsi da sole il proprio linguaggio, ma è simultaneamente nel mondo e in noi: presuppone l'azione di interpreti che sappiano formulare significati comuni, che ciascuno può comprendere e far propri per poter esprimere ciò che avverte dentro di sé.

La fatica di essere sé stessi - A. Ehrenberg, 1998



Allan Horwitz and Jerome Wakefield's important book, *The Loss of Sadness: How Psychiatry Transformed Normal Sorrow into Depressive Disorder*, is part of a gathering blowback against the pathologisation and medicalisation of the ordinary human condition of sadness after loss.

There are many things in life to make one feel sad. Losses abound. Relationships go to pieces. People get sacked from a decent job. Career fail. Aesthetic or moral projects are checked. Families fall down the class and status ladder. A myriad of disappointments can demoralize and defeat any of us. And, as we age, we sense death coming. Researchers and clinicians (even the general public) have come to use the euphemism "stress" to stand for the routine and extraordinary dangers that each of us experience. These run from financial crisis to health catastrophes; from serious accidents to disabling chronic disorders; and, especially among the truly poor, from incidental to structural violence. In most societies the popular culture's wisdom makes the point that life is difficult, uncertain, and only poorly predicted or controlled.

For thousands of years of recorded medical history, it is well documented that physicians understood that symptoms cannot be interpreted outside of the actual context of the patient's life. No master clinician, in the past, would confuse depressive disorder with normal grief, unless the symptoms of grief lasted such a disproportionately long time and were dangerously dysfunctional to the patient and his or her world as to indicate pathology. Horwitz and Wakefield suggest that the same professional common sense informed the diagnostic systems from Hippocrates and Galen to pre-1980 medicine in the West for other losses from jobs and status to lovers.

Then came the cultural revolution of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III, 1980). To improve clinical reliability, DSM-III simply added up symptoms. With the exception of bereavement—which the latest version (DSM-IV) grudgingly regards as normally lasting 2 months—DSM-III recognized no contextual events, besides other diseases, that might qualify the depressive syndrome as a normal response to serious life events. A modern Romeo might experience sadness after the break-up of a consuming love affair and would have several weeks or a month of sadness, sleeplessness, exhaustion, difficulty concentrating on his work, agitation, and lack of interest in eating and other previously valued things. In the DSM-III, the symptom count would easily make the cut off for depressive disorder, never mind the obvious social source of the problem or even the fact that, left to his own devices, our young man might no longer experience symptoms as he got over his loss and found a new love.

The elderly are at high risk for depression because they are more likely than younger people to have experienced illness, death of loved ones, impaired function and loss of independence. The cumulative effect of negative life experiences may be overwhelming to an older person.

Fattori precipitanti una malattia depressiva o eventi che inducono una "ragionevole" risposta maladattativa?

Qual'è il loro significato clinico?

Is replacing the medicalisation of depression with the biologisation of sadness a useful trade-off?

## Is depression overdiagnosed?

Gordon Parker scientia professor School of Psychiatry, University of New South Wales, Randwick NSW 2031, Australia g.parker@unsw.edu.au

YES It is normal to feel depressed. In our study of 242 teachers, the 1978 baseline questionblue ...down in the dumps." Criterion B (mandating four of eight listed items) could be met by appetite change, sleep disturbance, drop in libido, and fatigue. Trials confirmed the low reliability of these criteria, 4 and studies showed variable

#### Does overdiagnosis matter?

Does current looseness matter if a low diagnostic threshold destigmatises depression, encouraging people to seek help? After all, breast screening programmes may lead to detecting more malignant lumps. However,

BMJ | 18 AUGUST 2007 | VOLUME 335

Meta-analyses show striking gradients favouring antidepressant drugs over placebo for melancholic depression. Yet trials in major depression show minimal differences between antidepressant drugs, evidence based psychotherapies, and placebo. The benefit of treatment for minor and subsyndromal depression is even more unclear. Extrapolating management of the more severe biological conditions to minor symptom states reflects marketing prowess rather than evidence.

Depression will remain a non-specific "catch all" diagnosis until common sense prevails.

As American journalist Ed Murrow said: "Anyone who isn't confused doesn't really understand the situation."

## Is depression overdiagnosed?

Ian Hickie executive director, Brain and Mind Research Institute, University of Sydney, Camperdown NSW 2050, Sydney, Australia Ianh@med.usyd.edu.au

It is appropriate for the wider community to ask if the benefit of increased treatment of depresof mental hospital environments. Without diagnosis of these conditions, we would still distance ourselves, our families, and our communities from the benefits of receiving mental health care.

The promotion of safer antidepressants in

antidepressants. In fact, substantive personal, demographic, geographical, professional, training, and health system barriers remain in place. The net result is that diagnosis of major depression is largely restricted to people with severe or persistent disorders, It is appropriate for the wider community to ask if the benefit of increased treatment of depression over the past 15 years has outweighed any harm. If increased treatment has led to demonstrable benefits, and is cost effective, then depression is not being overdiagnosed. From a health and economic perspective, we can give a clear answer—more adults are alive and well, and we can easily afford to treat more. Increased treatment of depression reduces suicides and increases productivity. The provision of appropriate medical and psychological care is also cost effective.

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## Depressione e mortalità

#### **Article**

#### Medical Illness, Past Depression, and Present Depression: A Predictive Triad for In-Hospital Mortality

Stephanie von Ammon Cavanaugh, M.D.

Leticia M. Furlanetto, M.D., Ph.D.

Steven D. Creech, M.S.

Lynda H. Powell, Ph.D.

Objective: The authors' objectives were to determine 1) whether major depressive disorder diagnosed according to DSM-IV criteria modified for the medically ill predicted in-hospital mortality better than major depressive disorder diagnosed according to inclusive DSM-IV criteria and 2) whether a history of depression and current depression predicted mortality independent of severity of physical illness.

Method: Of 392 consecutive medical inpatients, 241 were interviewed within the first 3 days of admission and 151 were excluded from the study. Chart review and a clinical interview that included the Schedule for Affective Disorders and Schizophrenia were used to determine demographic variables, past psychiatric history, psychiatric diagnoses, and illness measures. Diagnoses included major depressive disorder and minor depression diagnosed according to DSM-IV criteria that included all symptoms regardless of etiology and according to criteria modified for the medically ill (hopelessness, depression, or anhedonia were used as the qualifying affective symptoms; depressive symptoms were eliminated if easily explained by medical illness, treatments, or hospitalization). The Charlson combined age-comorbidity index was used to measure severity of illness.

Results: A diagnosis of major depressive disorder based on criteria modified for patients with medical illness better predicted mortality than a diagnosis based on inclusive criteria. A past history of depression and the Charlson combined agecomorbidity index predicted in-hospital mortality, but demographic variables. pain, discomfort, length of stay, medical diagnoses, and minor depression did not. In the final multivariate logistic regression model, the Charlson combined age-comorbidity index, a modified diagnosis of major depressive disorder, and a history of depression were independent predictors of in-hospital death.

Conclusions: Severity of medical illness, a diagnosis of major depressive disorder based on modified criteria, and a past history of depression independently predicted in-hospital mortality in medical inpatients.

## Outcomes of Minor and Subsyndromal Depression among Elderly Patients in Primary Care Settings

Jeffrey M. Lyness, MD; Moonseong Heo, PhD; Catherine J. Datto, MD, MS; Thomas R. Ten Have, PhD; Ira R. Katz, MD, PhD; Rebecca Drayer, MD; Charles F. Reynolds III, MD; George S. Alexopoulos, MD; and Martha L. Bruce, PhD, MPH\*

**Background:** Although depressive conditions in later life are a major public health problem, the outcomes of minor and subsyndromal depression are largely unknown.

**Objective:** To compare outcomes among patients with minor and subsyndromal depression, major depression, and no depression, and to examine putative outcome predictors.

Design: Cohort study.

**Setting:** Patients from primary care practices in greater New York City, and Philadelphia and Pittsburgh, Pennsylvania.

Patients: 622 patients who were at least 60 years of age and presented for treatment in primary care practices that provided usual care in a randomized, controlled trial of suicide prevention. Of the 441 (70.9%) patients who completed 1 year of follow-up, 122 had major depression, 205 had minor or subsyndromal depression, and 114 did not have depression at baseline.

Measurements: One year after a baseline evaluation, data were collected by using the following tools: Hamilton Depression Rating Scale, the depressive disorders section of the Structured Clinical Interview for DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders*, fourth edition), Charlson Comorbidity Index, Multilevel Assessment Instrument for measuring instrumental activities of daily living, Physical Component Summary of the Medical Outcomes Study Short Form-36, and Duke Social Support Index.

Results: Patients with minor or subsyndromal depression had intermediate depressive and functional outcomes. Mean adjusted

1-year Hamilton depression score was 10.9 (95% CI, 9.6 to 12.2) for those with initial major depression, 7.0 (CI, 5.9 to 8.1) for those with minor or subsyndromal depression, and 2.9 (CI, 1.6 to 4.2) for those without depression (P < 0.001 for each paired comparison). Compared with patients who were not depressed, those who had minor or subsyndromal depression had a 5.5-fold risk (CI, 3.1-fold to 10.0-fold) for major depression at 1 year after controlling for demographic characteristics (P < 0.001). Cerebrovascular risk factors were not associated with a diagnosis of depression at 1 year after controlling for overall medical burden. Initial medical burden, self-rated health, and subjective social support were significant independent predictors of depression outcome.

**Limitations:** Participants received care at practices that had personnel who had been given enhanced education about depression treatment; 29.1% of participants withdrew from the study before completing 1 year of follow-up.

Conclusions: The intermediate outcomes of minor and subsyndromal depression demonstrate the clinical significance of these conditions and suggest that they are part of a spectrum of depressive illness. Greater medical burden, poor subjective health status, and poorer subjective social support confer a higher risk for poor outcome.

Ann Intern Med. 2006;144:496-504.

www.annals.org

For author affiliations, see end of text.

\*Additional information regarding the authors' roles as study coordinators is available in the Appendix. Crude and adjusted associations of GDS score with 60-month mortality in a community-dwelling population aged 70 and over.

	n/deaths	RR <sup>a</sup>	95% C.I.	$RR^b$	95% C.I.
GDS					
0-2	227/35	1.0		1.0	
3-5	159/41	1.7	1.1-2.8	1.5	0.9-2.4
6-15	136/53	3.0	1.9-4.6	1.9	1.2-3.1
			p<0.0001 a		p<0.005 b

A: crude analysis.

B: adjusted for age, gender, education (years of schooling), cognitive status (MMSE), number of diseases, disability (BADL).

(Rozzini et al., Arch. Int. Med., 2000)

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#### ORIGINAL INVESTIGATION

## Relationship of Depression to Death or Hospitalization in Patients With Heart Failure

Andrew Sherwood, PhD; James A. Blumenthal, PhD; Ranak Trivedi, PhD; Kristy S. Johnson, MPH; Christopher M. O'Connor, MD; Kirkwood F. Adams, Jr, MD; Carla Sueta Dupree, MD; Robert A. Waugh, MD; Daniel R. Bensimhon, MD; Laura Gaulden, MS; Robert H. Christenson, PhD; Gary G. Koch, PhD; Alan L. Hinderliter, MD

Arch Intern Med. 2007;167:367-373

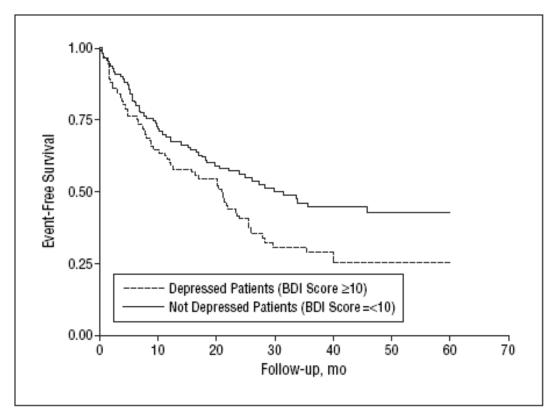


Figure. Kaplan-Meier curves indicate the composite end point of death or hospitalization because of cardiovascular disease in 94 patients with heart failure (HF) with clinically significant symptoms of depression (BDI score ≥10) compared with 110 patients with HF without depression (BDI score <10). Note: P = .02 comparing patients with and without depression, based on proportional hazards models including adjustment for age, HF etiology, left ventricular ejection fraction, N-terminal pro—B-type natriuretic peptide, and antidepressant medication use. BDI indicates Beck Depression Inventory.

Table 2. Cox Proportional Hazards Regression Analyses for Death and Hospitalizations Because of Cardiovascular Disease

	Deaths or Hospita (n = 120		All-Cause Do or Hospitaliza (n = 145	ations	Deaths (n = 54)		
Variable*	HR (95% CI)	<i>P</i> Value	HR (95% CI)	<i>P</i> Value	HR (95% CI)	<i>P</i> Value	
Age/10 y†	1.11 (0.94-1.32)	.22	1.18 (1.00-1.39)	.045	0.92 (0.71-1.18)	.49	
HF etiology	1.05 (0.71-1.55)	.82	0.90 (0.64-1.28)	.57	1.37 (0.75-2.52)	.31	
LVEF, %	0.99 (0.97-1.01)	.27	0.99 (0.98-1.01)	.60	0.97 (0.94-1.00)	.06	
NT-ProBNP/1000 pg/mL	1.28 (1.16-1.42)	<.001	1.23 (1.12-1.35)	<.001	1.42 (1.24-1.64)	<.001	
BDI score	1.06 (1.03-1.09)	<.001	1.06 (1.03-1.09)	<.001	1.05 (1.00-1.10)	.06	
Antidepressant medication	1.75 (1.14-2.68)	.01	1.57 (1.06-2.34)	.02	1.79 (0.96-3.34)	.07	

Abbreviations: BDI, Beck Depression Inventory; CI, confidence interval; HF, heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro—B-type natriuretic peptide.

Arch Intern Med. 2007;167:367-373

<sup>\*</sup>Values for each variable in the model are adjusted for all other variables in the model.

<sup>†</sup>Age divided by 10 indicates the heart rate values associated with age reflect a decade.

**Conclusions:** Symptoms of depression were associated with an adverse prognosis in patients with HF after controlling for HF severity. The unexpected association of antidepressant medications with worse clinical outcome suggests that patients with HF requiring an antidepressant medication may need to be monitored more closely.

Arch Intern Med. 2007;167:367-373

# Depressione e outcome in pazienti anziani con scompenso cardiaco

## Depression and major outcomes in older patients with heart failure

Renzo Rozzini, MD, Tony Sabatini, MD, Giovanni B. Frisoni, MD, Marco Trabucchi, MD Arch Int Med, 2002; 162:362-363

In our study, 6-month mortality was 8%, and the rate of rehospitalization was 29%. Mortality in patients with neither HF nor depression was 4%; in patients without HF and with depression, 7%; in patients with HF and without depression, 15%; and in those with both HF and depression, 21% (differential survival on log rank test, P<.01). In the same groups, the rate of rehospitalization was 35%, 38%, 44%, and 67%, respectively (chi- square test, P<.01).

# Association of groups of risk with 6-month mortality in hospitalized elderly patients

		Α		В	
	N/events	RR	95% C.I.	RR	95% C.I.
No HF and no depression	353/14	1.0	Ref.	1.0	Ref.
No HF and yes depression	361/23	1.9	0.9-4.0	1.8	0.8-4.3
Yes HF and no depression	47/7	3.2	1.0-10.3	3.1	1.0-10.4
Yes HF and yes depression	39/8	6.9	2.6-18.3	5.8	2.1-16.6
Disability in BADL	143/22	2.8	1.6-4.9	2.2	1.1-4.6
Serum albumin (<3.5 g/dl)	112/16	2.4	1.3-4.4	2.0	0.9-4.1
APACHE (APS score >5)	76/14	3.3	1.7-6.2	2.3	1.1-5.0

A: crude analysis. B: adjusted for potential confounders (disability, serum albumin, and APACHE) RR: risk ratio. C.I.: confidence interval.

Variables failing to qualify for entering the multivariate regression model were: age, male gender, cognitive impairment, anemia (Hem<8g/dl), diabetes mellitus, COPD, and GI diseases.

Rozzini R, Sabatini T, Frisoni GB, Trabucchi M. Arch Intern Med (2002).



(\$)SAGE

# The association of depressive symptoms with cardiovascular and all-cause mortality in Central and Eastern Europe: Prospective results of the HAPIEE study

Magdalena Kozela<sup>1</sup>, Martin Bobak<sup>2</sup>, Agnieszka Besala<sup>1</sup>, Agnieszka Micek<sup>1</sup>, Ruzena Kubinova<sup>3</sup>, Sofia Malyutina<sup>4,5</sup>, Diana Denisova<sup>4</sup>, Marcus Richards<sup>6</sup>, Hynek Pikhart<sup>2</sup>, Anne Peasey<sup>2</sup>, Michael Marmot<sup>2</sup> and Andrzej Pająk<sup>1</sup>

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#### Abstract

**Background:** Studies in western populations have shown a positive association between depression and cardiovascular disease (CVD) and all-cause mortality. The association with depressive symptoms seems to be graded, rather than limited to the presence versus the absence of depression. Evidence from populations with potentially different patterns of confounders helps to address the consistency of these findings. The objective of the study was to investigate the association between depressive symptoms and all-cause and CVD mortality in populations of Central and Eastern Europe.

Study design: This was a prospective cohort study.

Methods: A total of 24,542 participants aged 45–69 years, randomly selected from populations of Novosibirsk (Russia), Krakow (Poland) and six Czech towns, were included. Depressive symptoms, assessed by the 20-item Center for Epidemiologic Studies Depression (CES-D) scale, were used as both continuous and categorical variables. Data on deaths were obtained from local or national death registers. Associations between depression and mortality were assessed using Cox proportional hazards models.

Results: Over a median of 7 years, 2091 deaths from all causes and 850 CVD deaths occurred in the cohorts. There was a graded association between CES-D score and mortality; the hazard ratio (HR) of CVD mortality for a 1 SD increase in CES-D was 1.20 (95% confidence interval (CI): 1.16–1.24) in men and 1.23 (95% CI: 1.12–1.35) in women; for all-cause mortality, the HRs were 1.13 (95% CI: 1.09–1.18) and 1.17 (95% CI: 1.10–1.25), respectively. The results were similar across countries.

Conclusions: Depressive symptoms predicted CVD and all-cause mortality independently of a wide range of potential confounders. The association followed a gradient and increased mortality risks were associated with scores below the cut-offs that are commonly used to define 'depression'.

#### **Keywords**

Depressive symptoms, mortality, Eastern Europe, cardiovascular disease

Dobbiamo sempre prescrivere farmaci antidepressivi nei pazienti affetti da malattia fisica (ad es. scompenso cardiaco) tenuto conto che la depressione peggiora il decorso della malattia? Il problema è chiarire se la depressione sia una comorbilità, la cui rilevanza potrebbe essere smascherata da una malattia fisica, oppure una condizione psicologica indicatore di fragilità spia di un'incapacità a far fronte ad un evento stressante. Nel primo caso il trattamento farmacologico potrebbe essere efficace, nel secondo, inutile o negativo.

Renzo Rozzini & Marco Trabucchi, Arch Int Med, 2003; 163:498-499

## Di cosa voglio parlare

- Depressione: dove eravamo rimasti?
- Il medico (geriatra, psichiatra, neurologo) e la depressione nell'anziano
- "La grammatica della vita interiore" nei medici e nei vecchi d'oggi
- Depressione e mortalità
- Depressione e patologia
- Epidemiologia del trattamento
- La fenomenologia della depressione nell'anziano
- Conclusioni

### JAMA Internal Medicine | Original Investigation

### Treatment of Adult Depression in the United States

Mark Olfson, MD, MPH; Carlos Blanco, MD, PhD; Steven C. Marcus, PhD

IMPORTANCE Despite recent increased use of antidepressants in the United States, concerns persist that many adults with depression do not receive treatment, whereas others receive treatments that do not match their level of illness severity.

OBJECTIVE To characterize the treatment of adult depression in the United States.

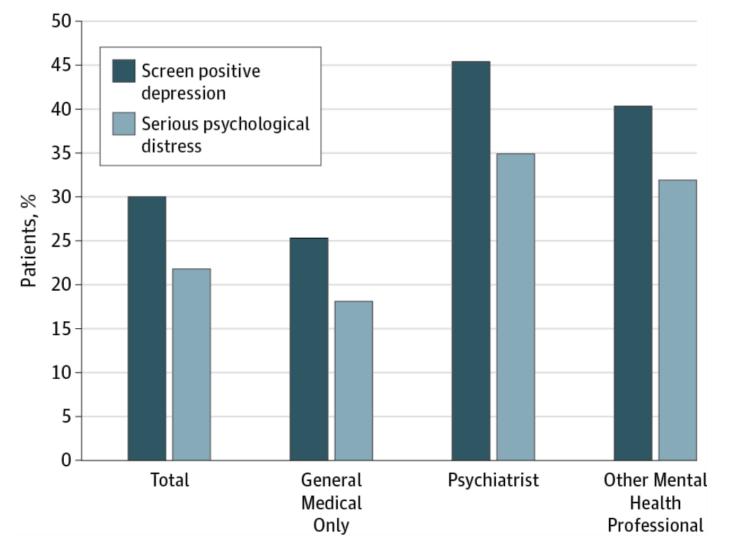
DESIGN, SETTING, AND PARTICIPANTS Analysis of screen-positive depression, psychological distress, and depression treatment data from 46 417 responses to the Medical Expenditure Panel Surveys taken in US households by participants aged 18 years or older in 2012 and 2013.

MAIN OUTCOME AND MEASURES Percentages of adults with screen-positive depression (Patient Health Questionnaire-2 score of  $\geq$  3) and adjusted odds ratios (AORs) of the effects of sociodemographic characteristics on odds of screen-positive depression; percentages with treatment for screen-positive depression and AORs; percentages with any treatment of depression and AORs stratified by presence of serious psychological distress (Kessler 6 scale score of  $\geq$  13); and percentages with depression treatment by health care professional group (psychiatrists, other health care professionals, and general medical providers); and type of depression treatment (antidepressants, psychotherapy, and both) all stratified by distress level

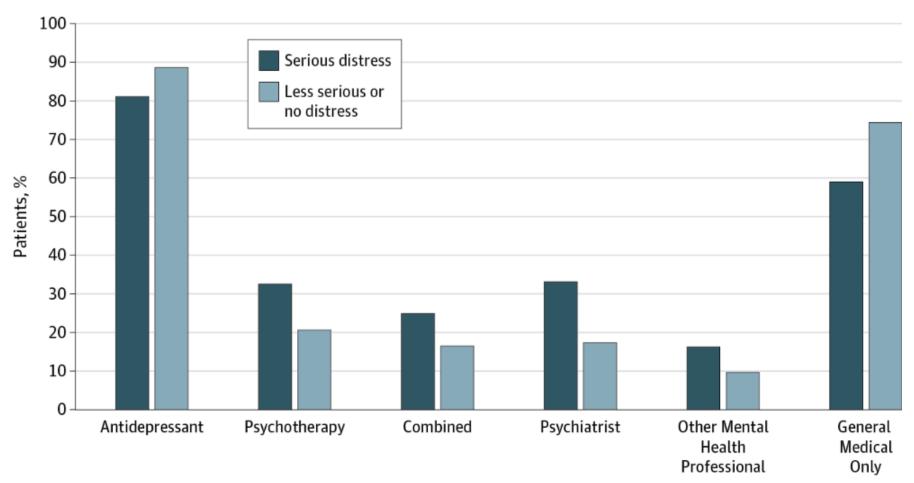
Supplemental content

**RESULTS** Approximately 8.4% (95% CI, 7.9-8.8) of adults screened positive for depression, of which 28.7% received any depression treatment. Conversely, among all adults treated for depression, 29.9% had screen-positive depression and 21.8% had serious psychological distress. Adults with serious compared with less serious psychological distress who were treated for depression were more likely to receive care from psychiatrists (33.4% vs 17.3%, P < .001) or other mental health specialists (16.2% vs 9.6%, P < .001), and less likely to receive depression care exclusively from general medical professionals (59.0% vs 74.4%, P < .001). They were also more likely to receive psychotherapy (32.5% vs 20.6%, P < .001), though not antidepressant medications (81.1% vs 88.6%, P < .001).

conclusions and relevance Most US adults who screen positive for depression did not receive treatment for depression, whereas most who were treated did not screen positive. In light of these findings, it is important to strengthen efforts to align depression care with each patient's clinical needs.



Percentages of Patients With Screen-Positive Depression and Serious Psychological Distress Treated For Depression by Health Care Professional Group Data are from Medical Expenditure Panel Surveys (2012-2013). Analysis limited to ages 18 years or older. Percentages (95% Cls) of adult sample treated for depression with screen-positive depression are: total, 29.9% (27.9-31.9); general medical only, 25.3% (23.0-27.6); psychiatrist, 45.4% (40.5-50.3); and other mental health professional, 40.3% (33.9-46.8). Corresponding percentages for serious psychological distress are: total, 21.8% (19.9-23.6); general medical only, 18.1% (16.0-20.2); psychiatrist, 34.9% (30.1-39.7); and other mental health professional, 31.9% (25.5-38.3).



Percentages of Patients With Screen-Positive Depression and Serious Psychological Distress Treated For Depression by Health Care Professional Group Data are from Medical Expenditure Panel Surveys (2012-2013). Analysis limited to ages 18 years or older. Percentages (95% Cls) of adult sample treated for depression with screen-positive depression are: total, 29.9% (27.9-31.9); general medical only, 25.3% (23.0-27.6); psychiatrist, 45.4% (40.5-50.3); and other mental health professional, 40.3% (33.9-46.8). Corresponding percentages for serious psychological distress are: total, 21.8% (19.9-23.6); general medical only, 18.1% (16.0-20.2); psychiatrist, 34.9% (30.1-39.7); and other mental health professional, 31.9% (25.5-38.3).

Table 1. Percentage of Adults With Screen-Positive Depression, Treatment of Screen-Positive Depression, and Any Treatment for Depression, Total and Stratified by Sociodemographic Characteristics

Characteristic	Adults With Screen-Positive Depression, % (95% CI) (n = 46 417) <sup>a</sup>	Adjusted Odds Ratio (95% CI) <sup>b</sup>	Adults Receiving Treatment for Screen-Positive Depression, % (95% CI) (n = 4430)	Adjusted Odds Ratio (95% CI) <sup>c</sup>	Adults Receiving Any Treatment for Depression, % (95% CI) (n = 46 417)	Adjusted Odds Ratio (95% CI) <sup>c</sup>
Total	8.4 (7.9-8.8)		28.7 (26.9-30.6)		8.1 (7.7-8.6)	
Age, y						
18-34	6.6 (6.0-7.3)	1 [Reference]	20.1 (16.2-24.0)	1 [Reference]	4.4 (3.9-5.0)	1 [Reference]
35-49	8.8 (8.0-9.7)	1.59 (1.36-1.86)	31.0 (26.8-35.1)	1.55 (1.10-2.19)	8.2 (7.4-9.1)	1.81 (1.50-2.19)
50-64	10.0 (9.2-10.7)	1.92 (1.65-2.22)	35.7 (32.2-39.1)	1.96 (1.44-2.68)	11.3 (10.3-12.3)	2.53 (2.10-3.06)
≥65	8.3 (7.4-9.2)	0.98 (0.80-1.20)	25.1 (20.2-30.0)	1.10 (0.72-1.68)	9.5 (8.4-10.6)	1.77 (1.40-2.22)
Sex						
Male	7.3 (6.8-7.9)	0.87 (0.79-0.96)	20.9 (18.2-23.6)	0.52 (0.41-0.66)	5.1 (4.7-5.6)	0.48 (0.42-0.54)
Female	9.3 (8.7-9.9)	1 [Reference]	34.5 (31.9-37.1)	1 [Reference]	10.9 (10.1-11.6)	1 [Reference]
Race/Ethnicity						
White, non-Hispanic <sup>a</sup>	8.1 (7.6-8.6)	1 [Reference]	31.6 (29.2-34.0)	1 [Reference]	9.3 (8.7-9.9)	1 [Reference]
Black, non-Hispanic	10.6 (9.6-11.5)	0.87 (0.78-0.98)	21.7 (18.1-25.2)	0.61 (0.47-0.80)	4.9 (4.2-5.5)	0.42 (0.36-0.48)
Hispanic	8.2 (7.4-8.9)	0.67 (0.59-0.77)	22.1 (18.6-25.6)	0.69 (0.52-0.91)	4.6 (3.9-5.2)	0.54 (0.45-0.65)
Education						
<high graduate<="" school="" td=""><td>12.7 (11.6-13.8)</td><td>1 [Reference]</td><td>22.9 (19.5-26.4)</td><td>1 [Reference]</td><td>6.7 (5.8-7.6)</td><td>1 [Reference]</td></high>	12.7 (11.6-13.8)	1 [Reference]	22.9 (19.5-26.4)	1 [Reference]	6.7 (5.8-7.6)	1 [Reference]
High school graduate	9.1 (8.6-9.6)	0.90 (0.79-1.02)	29.8 (27.4-32.3)	1.39 (1.08-1.78)	8.5 (7.9-9.1)	1.43 (1.19-1.72)
College graduate	4.6 (4.1-5.1)	0.66 (0.56-0.78)	34.6 (29.6-39.6)	1.90 (1.38-2.61)	8.1 (7.3-9.0)	1.62 (1.33-1.99)
Marital status						
Married	6.3 (5.8-6.9)	1 [Reference]	26.9 (23.8-29.9)	1 [Reference]	7.3 (6.7-7.9)	1 [Reference]
Separated/divorced/ widowed	13.3 (12.4-14.2)	1.48 (1.31-1.66)	35.2 (31.5-38.9)	1.29 (0.97-1.72)	12.8 (11.7-13.9)	1.29 (1.13-1.48)
Not married	8.6 (7.8-9.3)	1.18 (1.02-1.37)	23.8 (20.2-27.4)	1.13 (0.82-1.55)	6.2 (5.6-6.8)	1.28 (1.09-1.51)
Income level (% FPL)						
<100	18.2 (16.9-19.5)	1 [Reference]	30.1 (26.7-33.6)	1 [Reference]	11.1 (9.9-12.2)	1 [Reference]
100-200	12.3 (11.3-13.3)	0.76 (0.68-0.86)	29.3 (25.6-33.0)	0.98 (0.78-1.23)	8.8 (7.8-9.8)	0.90 (0.77-1.06)
201-400	7.9 (7.1-8.7)	0.55 (0.47-0.65)	28.5 (25.0-31.9)	0.86 (0.64-1.15)	7.8 (7.2-8.4)	0.88 (0.74-1.04)
>400	3.7 (3.29-4.2)	0.28 (0.24-0.34)	26.1 (21.5-30.8)	0.70 (0.49-1.00)	7.1 (6.4-7.8)	0.84 (0.69-1.03)
Health insurance						
Private, any	5.6 (5.2-5.9)	1 [Reference]	29.8 (26.7-32.9)	1 [Reference]	7.5 (7.0-8.1)	1 [Reference]
Public, only	17.0 (15.8-18.2)	2.17 (1.91-2.47)	32.5 (29.5-35.5)	1.11 (0.86-1.42)	13.4 (12.1-14.6)	1.33 (1.12-1.57)
None	10.5 (9.5-11.5)	1.23 (1.12-1.50)	18.8 (14.2-23.3)	0.56 (0.39-0.80)	4.4 (3.6-5.1)	0.54 (0.44-0.68)

Abbreviation: FPL, federal poverty level.

Data are from Medical Expenditure Panel Surveys (2012-2013). Analysis limited to ages  $\ge$ 18 y.

<sup>&</sup>lt;sup>a</sup> Patient Health Questionaire-2 (PHQ-2) score ≥3.

<sup>&</sup>lt;sup>b</sup> Model controls for age, sex, race/ethnicity, education, marital status, income level, and health insurance.

 $<sup>^{\</sup>rm c}$  Model controls for PHQ-2, age, sex, race/ethnicity, education, marital status, income level, and health insurance.

Table 2. Outpatient Treatments for Depression by Level of Psychological Distress and Treatment Modality Stratified by Sociodemographic Characteristics<sup>a</sup>

	Antidepressant, %				Psychotherapy, %				Antidepressant and Psychotherapy, %			
Characteristic	Serious Distress (n = 4265)	Less Serious or No Distress (n = 42 152)	AOR (95% CI)	P Value <sup>b</sup>	Serious Distress (n = 4265)	Less Serious or No Distress (n = 42 152)	AOR (95% CI)	P Value <sup>b</sup>	Serious Distress (n = 4265)	Less Serious or No Distress (n = 42 152)	AOR (95% CI)	P Value <sup>b</sup>
Total	81.1	88.6	0.65 (0.48-0.90)	<.001	32.5	20.6	1.77 (1.34-2.34)	<.001	24.9	16.5	1.60 (1.17-2.19)	<.001
Age, y				.63				.54				.37
18-34	76.2	77.7	0.78 (0.46-1.31)		39.0	31.2	1.78 (0.91-3.51)		25.5	20.3	1.47 (0.72-3.02)	
35-49	77.4	87.7	0.59 (0.33-1.08)		36.0	24.8	1.53 (0.95-2.46)		26.2	20.1	1.30 (0.78-2.17)	
50-64	83.8	91.9	0.70 (0.41-1.21)		35.6	19.6	2.15 (1.31-3.54)		30.0	16.8	2.21 (1.32-3.72)	
≥65	87.8	92.2	0.87 (0.35-2.15)		9.0	10.2	0.90 (0.30-2.68)		6.8	9.4	0.72 (0.20-2.56)	
Sex				.62				.59				.97
Male	77.7	84.8	0.75 (0.45-1.24)		32.6	21.8	2.07 (1.23-3.50)		21.8	16.2	1.71 (0.99-2.96)	
Female	82.6	90.2	0.62 (0.42-0.91)		32.5	20.1	1.69 (1.22-2.35)		26.1	16.6	1.57 (1.09-2.27)	
Race/ethnicity				.20				.93				.63
White, non-Hispanic	83.4	90.4	0.57 (0.38-0.85)		31.2	19.7	1.82 (1.31-2.54)		25.1	16.3	1.65 (1.14-2.38)	
Black, non-Hispanic	71.8	76.2	0.80 (0.43-1.52)		40.7	29.5	1.39 (0.85-2.28)		24.8	20.3	1.09 (0.62-1.91)	
Hispanic	74.4	76.0	0.91 (0.54-1.53)		34.2	24.4	1.63 (1.00-2.65)		23.5	14.9	1.64 (0.89-3.02)	
Education				.99				.06				.05
<high graduate<="" school="" td=""><td>68.4</td><td>77.0</td><td>0.60 (0.36-1.00)</td><td></td><td>26.0</td><td>21.0</td><td>1.56 (0.90-2.68)</td><td></td><td>17.2</td><td>14.0</td><td>1.18 (0.59-2.37)</td><td></td></high>	68.4	77.0	0.60 (0.36-1.00)		26.0	21.0	1.56 (0.90-2.68)		17.2	14.0	1.18 (0.59-2.37)	
High school graduate	83.5	89.4	0.70 (0.46-1.07)		29.0	18.6	1.44 (1.00-2.08)		21.4	14.9	1.30 (0.89-1.89)	
College graduate	86.7	91.2	0.57 (0.27-1.18)		51.9	24.3	3.52 (1.97-6.28)		45.3	20.2	3.33 (1.78-6.24)	
Marital status				.82				.26				.10
Married	83.5	91.4	0.61 (0.37-0.99)		27.2	14.4	2.61 (1.62-4.19)		23.0	12.3	2.45 (1.50-4.01)	
Separated/divorced/ widowed	84.5	91.1	0.72 (0.40-1.32)		31.5	21.6	1.41 (0.89-2.24)		25.9	18.1	1.43 (0.88-2.32)	
Not married	70.8	77.8	0.71 (0.41-1.24)		43.7	34.8	1.59 (1.00-2.52)		25.9	24.6	1.15 (0.69-1.93)	
Income level (% FPL)				.55				.63				.42
<100	77.8	83.4	0.77 (0.49-1.23)		36.6	27.0	1.48 (1.00-2.20)		28.4	19.8	1.58 (1.00-2.48)	
100-200	81.5	87.4	0.64 (0.38-1.10)		28.0	20.8	1.88 (1.02-3.46)		20.4	17.4	1.45 (0.76-2.75)	
201-400	81.0	90.0	0.43 (0.23-0.82)		27.8	20.6	1.50 (0.87-2.62)		20.1	17.1	1.21 (0.66-2.21)	
>400	88.3	89.8	1.19 (0.43-3.30)		40.9	18.5	2.72 (1.35-5.51)		34.4	14.5	2.95 (1.38-6.29)	
Health insurance				.07				.31				.08
Private, any	88.5	89.1	0.87 (0.51-1.49)		34.1	21.1	2.16 (1.37-3.40)		28.2	16.7	2.06 (1.27-3.36)	
Public, only	73.5	87.8	0.45 (0.29-0.71)		32.6	21.1	1.35 (0.94-1.94)		23.6	17.4	1.04 (0.72-1.50)	
None	84.0	86.4	0.84 (0.35-2.00)		27.6	14.4	1.84 (0.96-3.54)		22.2	10.7	2.08 (0.97-4.47)	

Abbreviations: AOR, adjusted odds ratio; FPL, federal poverty level.

 $Models \ control\ for\ age, sex,\ race/ethnicity,\ education,\ marital\ status,\ education,\ income,\ and\ health\ insurance.$  Serious psychological distress defined as Kessler 6 score of 13 or greater (range: O to 24).

<sup>&</sup>lt;sup>a</sup> Data are from Medical Expenditure Panel Surveys (2012-2013). Analysis limited to ages 18 years and older.

<sup>&</sup>lt;sup>b</sup> *P* values for interaction.

Table 3. Outpatient Treatment of Depression by Level of Psychological Distress and Health Care Professional Stratified by Sociodemographic Characteristics

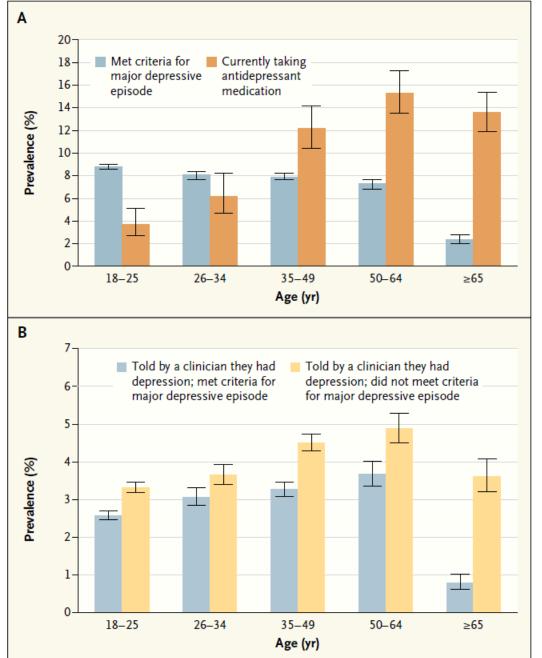
	Treatment by Psychiatrist, %				Treatment by Other Mental Health Professionals, %				Treatment by Only General Medical Professionals, %			
Characteristic	Serious Distress (n = 4265)	Less Serious or No Distress (n = 4252)	AOR (95% CI)	P Value <sup>b</sup>	Serious Distress (n = 4265)	Less Serious or No Distress (n = 4252)	AOR (95% CI)	P Value <sup>b</sup>	Serious Distress (n = 4265)	Less Serious or No Distress (n = 42 152)	AOR (95% CI)	P Value
Total	33.4	17.3	2.37 (1.82-3.08)	<.001	16.2	9.6	1.82 (1.28-2.61)	<.001	59.0	74.4	0.52 (0.42-0.68)	<.001
Age, y, %				.17				.14				.17
18-34	29.7	23.8	1.65 (0.91-2.99)		19.0	18.4	1.44 (0.72-2.89)		55.8	59.1	0.78 (0.45-1.38)	
35-49	35.6	16.6	2.54 (1.60-4.03)		20.8	11.7	1.92 (1.09-3.36)		55.9	72.7	0.57 (0.37-0.88)	
50-64	40.3	19.1	2.84 (1.77-4.56)		16.4	7.7	2.43 (1.16-5.07)		53.7	75.1	0.41 (0.25-0.65)	
≥65	13.9	10.8	1.92 (.73-5.04)		2.0	4.0	0.64 (0.15-2.83)		84.1	85.9	0.63 (0.27-1.48)	
Sex				.45				.70				.63
Male	36.2	23.3	2.27 (1.40-3.69)		12.6	9.5	1.56 (0.73-3.33)		57.4	68.7	0.54 (0.34-0.85)	
Female	32.2	14.7	2.48 (1.78-4.46)		17.7	9.7	1.93 (1.26-2.96)		59.6	76.8	0.52 (0.38-0.69)	
Race/ethnicity				.20				.87				.42
White, non-Hispanic	31.5	16.3	2.55 (1.83-3.56)		15.5	9.4	1.80 (1.17-2.78)		61.6	75.5	0.53 (0.39-0.72)	
Black, non-Hispanic	35.5	24.7	1.33 (0.88-2.11)		18.3	11.3	1.74 (0.96-3.16)		53.2	66.0	0.72 (0.46-1.13)	
Hispanic	43.6	24.1	2.41 (1.42-4.08)		18.9	11.1	2.22 (1.13-4.38)		47.0	67.4	0.40 (0.24-0.66)	
Education				.02				.25				.04
<high graduate<="" school="" td=""><td>31.0</td><td>23.6</td><td>1.72 (1.00-2.97)</td><td></td><td>12.9</td><td>11.7</td><td>2.37 (0.99-5.69)</td><td></td><td>62.9</td><td>67.9</td><td>0.66 (0.41-1.07)</td><td></td></high>	31.0	23.6	1.72 (1.00-2.97)		12.9	11.7	2.37 (0.99-5.69)		62.9	67.9	0.66 (0.41-1.07)	
High school graduate	29.1	14.3	2.03 (1.44-2.87)		13.6	7.9	1.48 (0.91-2.41)		62.6	77.6	0.60 (0.42-0.85)	
College graduate	51.0	20.6	4.74 (2.62-8.59)		28.8	11.9	2.78 (1.43-5.38)		41.8	70.7	0.29 (0.17-0.51)	
Marital status				.06				.03				.17
Married	29.1	12.3	3.57 (2.23-5.72)		15.8	5.9	3.66 (1.88-7.13)		64.8	81.4	0.38 (0.25-0.59)	
Separated/divorced/ widowed	32.8	15.6	2.58 (1.59-4.19)		16.1	10.8	1.45 (0.84-2.49)		59.9	75.1	0.55 (0.37-0.84)	
Not married	41.8	32.5	1.46 (0.94-2.29)		17.0	5.4	1.19 (0.71-1.99)		47.2	55.7	0.72 (0.47-1.09)	
Income level (% FPL)				.48				.33				.92
<100	38.8	21.3	2.34 (1.56-3.50)		17.9	13.9	1.47 (0.90-2.41)		51.6	65.6	0.55 (0.39-0.78)	
100-200	32.2	16.3	3.03 (1.65-5.57)		9.8	8.4	1.46 (0.65-3.28)		65.0	75.8	0.48 (0.28-0.82)	
201-400	24.8	16.6	1.54 (0.96-2.49)		10.6	16.2	1.76 (0.86-3.61)		63.9	75.6	0.61 (0.37-1.00)	
>400	39.5	17.1	3.54 (1.73-7.23)		24.5	8.0	3.57 (1.61-7.91)		54.9	75.7	0.43 (0.21-0.86)	
Health insurance				.49				.04				.12
Private, any	32.5	17.0	2.90 (1.86-4.52)		21.0	10.2	2.52 (1.51-4.20)		59.2	75.0	0.42 (0.28-0.63)	
Public, only	36.0	18.8	2.06 (1.39-3.03)		12.3	8.9	1.00 (0.63-1.59)		59.6	72.6	0.70 (0.49-1.00)	
None	27.4	15.5	1.38 (0.71-2.68)		14.3	5.9	3.52 (1.53-8.10)		56.2	74.4	0.53 (0.30-0.94)	

Abbreviations: AOR, adjusted odds ratio; FPL, federal poverty level.

Serious psychological distress defined as Kessler 6 score of 13 or greater (range: O to 24).

<sup>&</sup>lt;sup>a</sup> Data are from Medical Expenditure Panel Surveys (2012-2013). Analysis limited to ages 18 years and older. Models control for age, sex, race/ethnicity, education, marital status, education, income, and health insurance.

<sup>&</sup>lt;sup>b</sup> P values for interaction.

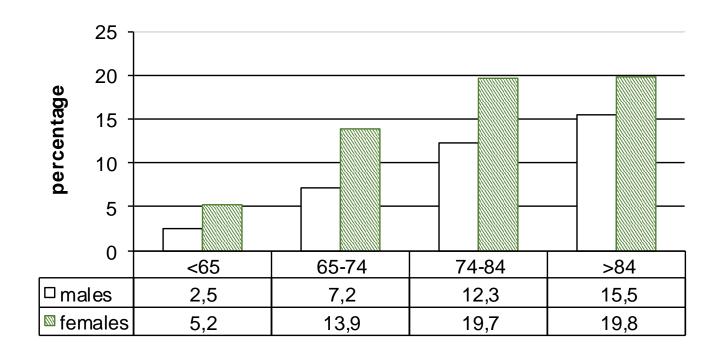


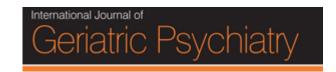
Prevalence of Major Depressive Episodes in Relation to Antidepressant-Medication Use and Clinician-Diagnosed Depression, 2005–2010.



N Engl J Med 2014;370:1180-1182

## Rates of antidepressant prescriptions according to gender and age in elderly patients living at home (Rozzini et al. Int J Geriatr Psychiatry, 2008)





Research

#### Original Investigation

# Effect of Escitalopram on All-Cause Mortality and Hospitalization in Patients With Heart Failure and Depression The MOOD-HF Randomized Clinical Trial

Christiane E. Angermann, MD; Götz Gelbrich, PhD; Stefan Störk, MD, PhD; Hilka Gunold, MD; Frank Edelmann, MD; Rolf Wachter, MD; Heribert Schunkert, MD; Tobias Graf, MD; Ingrid Kindermann, MD; Markus Haass, MD; Stephan Blankenberg, MD; Sabine Pankuweit, MD; Christiane Prettin, PhD; Martin Gottwik, MD; Michael Böhm, MD; Hermann Faller, MD, PhD; Jürgen Deckert, MD; Georg Ertl, MD; for the MOOD-HF Study Investigators and Committee Members

**IMPORTANCE** Depression is frequent in patients with heart failure and is associated with adverse clinical outcomes. Long-term efficacy and safety of selective serotonin reuptake inhibitors in these patients are unknown.

**OBJECTIVE** To determine whether 24 months of treatment with escitalopram improves mortality, morbidity, and mood in patients with chronic systolic heart failure and depression.

DESIGN, SETTING, AND PARTICIPANTS The Effects of Selective Serotonin Re-Uptake Inhibition on Morbidity, Mortality, and Mood in Depressed Heart Failure Patients (MOOD-HF) study was a double-blind, placebo-controlled randomized clinical trial conducted at 16 tertiary medical centers in Germany. Between March 2009 and February 2014, patients at outpatient clinics with New York Heart Association class II-IV heart failure and reduced left ventricular ejection fraction (<45%) were screened for depression using the 9-item Patient Health Questionnaire. Patients with suspected depression were then invited to undergo a Structured Clinical Interview based on the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) to establish the diagnosis.

INTERVENTIONS Patients were randomized 1:1 to receive escitalopram (10-20 mg) or matching placebo in addition to optimal heart failure therapy. Study duration was 24 months.

- Supplemental content at jama.com
- ← CME Quiz at jamanetworkcme.com

MAIN OUTCOMES AND MEASURES The composite primary outcome was time to all-cause death or hospitalization. Prespecified secondary outcomes included safety and depression severity at 12 weeks of treatment (including the titration period), which were determined using the 10-item Montgomery-Åsberg Depression Rating Scale (total possible score, 0 to 60; higher scores indicate more severe depression).

RESULTS A total of 372 patients (mean age, 62 years; 24% female) were randomized and had taken at least 1 dose of study medication when the data and safety monitoring committee recommended the trial be stopped early. During a median participation time of 18.4 months (n = 185) for the escitalopram group and 18.7 months (n = 187) for the placebo group, the primary outcome of death or hospitalization occurred in 116 (63%) patients and 119 (64%) patients, respectively (hazard ratio, 0.99 [95% CI, 0.76 to 1.27]; P = .92). The mean Montgomery-Asberg Depression Rating Scale sum score changed from 20.2 at baseline to 11.2 at 12 weeks in the escitalopram group and from 21.4 to 12.5 in the placebo group (between-group difference, -0.9 [95% CI, -2.6 to 0.7]; P = .26). Safety parameters were comparable between groups.

CONCLUSIONS AND RELEVANCE In patients with chronic heart failure with reduced ejection fraction and depression, 18 months of treatment with escitalopram compared with placebo did not significantly reduce all-cause mortality or hospitalization, and there was no significant improvement in depression. These findings do not support the use of escitalopram in patients with chronic systolic heart failure and depression.

TRIAL REGISTRATION isrctn.com Identifier: ISRCTN33128015

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: A complete list of the MOOD-HF Study Investigators and Committee Members appears in Supplement 1.

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JAMA. 2016;315(24):2683-2693. doi:10.1001/jama.2016.7635

Nighttime heart rate predicts response to depression treatment in patients with coronary heart disease.

J Affect Disord. 2016 Aug;200:165-71. doi: 10.1016/j.jad.2016.04.051. Epub 2016 Apr 25.

Carney RM1, Freedland KE2, Steinmeyer BC2, Rubin EH2, Stein PK3, Rich MW3.

BACKGROUND: Previous studies suggest that patients with coronary heart disease (CHD) who do not respond to treatment for depression are at higher risk of mortality than are treatment responders. The purpose of this study was to determine whether elevated nighttime heart rate (HR) and low heart rate variability (HRV), both of which have been associated with depression and with cardiac events in patients with CHD, predict poor response to depression treatment in patients with CHD. METHODS: Patients with stable CHD and a current major depressive episode completed 24h ambulatory ECG monitoring and were then treated for up to 16 weeks with cognitive behavior therapy (CBT), either alone or in combination with an antidepressant. Pre-treatment HR and HRV were calculated for 124 patients who had continuous ECG from early evening to mid-morning. RESULTS: Following treatment, 64 of the 124 patients (52%) met study criteria for remission (Hamilton Rating Scale for Depression score≤7). Prior to treatment, non-remitters had higher nighttime HR (p=0.03) and lower nighttime HRV (p=0.01) than did the remitters, even after adjusting for potential confounds.

LIMITATIONS: Polysomnography would have provided information about objective sleep characteristics and sleep disorders. More CBT sessions and higher doses of antidepressants may have resulted in more participants in remission.

CONCLUSIONS: High nighttime HR and low nighttime HRV predict a poor response to treatment of major depression in patients with stable CHD. These findings may help explain why patients with CHD who do not respond to treatment are at higher risk for mortality.

## Does Depression in Older Medical Inpatients Predict Mortality?

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Background. Previous studies of the effect of depression on mortality among older medical inpatients have yielded inconsistent results. We examined the effects on mortality of both a diagnosis of depression at hospital admission and a history of previous depression, taking into account potential sources of bias (sample selection and confounding).

Methods. Medical inpatients aged 65+ with at most mild cognitive impairment were recruited at two Montreal hospitals and were screened for depression. All those with a diagnosis of major or minor depression (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV] criteria) and a random sample of nondepressed patients were invited to participate. Baseline data included: history of previous depression, severity of physical illness, comorbidity, and health services utilization. Cox proportional hazards methods were used to analyze survival during the 16- to 52-month follow-up period.

Results. Five hundred patients were enrolled; 116 (23.2%) had a history of previous depression. After adjustment for demographic factors, physical illness, cognitive impairment, and prior service utilization, the only depression group with significantly different mortality was patients with both current major depression and a history of depression, who had lower mortality than all other patient groups (hazard ratio 0.42; 95% confidence interval: 0.25, 0.70).

Conclusions. Among patients with no history of depression, a diagnosis of depression was not associated with mortality after adjustment for confounding by physical illness and other factors. Coincident major depression and history of depression was associated with decreased mortality.

## Characteristics of hospitalized elderly patients according to their mood status: No Depression, Major and Minor Depression.

	Total N=1234 Mean (±SD)	No Depres N=564 Mean (±SD)	Major Depres N=164 Mean (±SD)	P*	Minor Depres N=506 Mean (±SD)	P**	P***
Age (years)	78.8 (±7.4)	77.4 (±7.7)	77.0 (±6.9)	.223	79.5 (±7.0)	.000	.000
Gender (female) n (%)	832 (67.4)	323 (57.3)	143 (87.2)	.000	366 (72.3)	.000	.000
MMSE score	25.2 (±3.9)	25.8 (±3.9)	25.6 (±3.8)	.821	24.3 (±4.1)	.000	.001
GDS score	5.1 (±3.5)	2.2(±1.3)	8.0 (±3.9)	.000	7.4 (±2.5)	.000	.050
Living alonen (%)	385 (31.7)	152 (27.4)	74 (45.7)	.001	159 (31.9)	.800	.008
Barthel Idx (prior hosp)	88.8 (±17.3)	92.2 (±14.2)	90.3 (±14.2)	.170	84.5 (±20.1)	.000	.003
Barthel Idx (at adm)	81.0 (±24.5)	84.1 (±23.7)	86.1 (±18.8)	.360	75.9 (±26.1)	.000	.000
Barthel Idx (at disch)	84.1 (±22.3)	88.1 (±19.7)	87.8 (±16.6)	.665	78.4 (±25.1)	.000	.000
IADLs lost (prior hosp)	2.5 (±2.5)	1.9 (±2.3)	2.6 (±2.3)	.004	3.1 (±2.6)	.000	.103
Charlson Index	2.5 (±2.3)	2.5 (±2.3)	1.7 (±1.9)	.001	2.6 (±2.3)	.234	.000
APACHE II score	7.9 (±4.3)	8.1 (±4.6)	6.6 (±3.0)	.004	8.1 (±4.3)	.608	.007
APACHE II-APS score	1.8 (±2.6)	2.0 (±2.7)	1.2 (±1.9)	.030	1.9 (±2.6)	.684	.050
Serum Albumin (g/dl)	4.0 (±0.8)	4.0 (±0.7)	4.1 (±0.6)	.026	4.1 (±0.9)	.495	.192
6-month mortality n (%)	174 (14.1)	74 (13.1)	12 (7.3)	.048	88 (17.4)	.226	.026

(Rozzini et al., J Gerontol., 2007)

### Cardiac Risk Markers and Response to Depression Treatment in Patients With Coronary Heart Disease

Robert M. Carney, PhD, Kenneth E. Freedland, PhD, Brian Steinmeyer, MS, Eugene H. Rubin, MD, PhD, Douglas L. Mann, MD, and Michael W. Rich, MD

#### **ABSTRACT**

**Background:** Depression is associated with an increased risk of mortality in patients with coronary heart disease. There is evidence that this risk may be reduced in patients who respond to depression treatment. The purpose of this study was to determine whether cardiac risk markers predict poor response to depression treatment and, second, whether they improve with successful treatment.

**Methods:** One hundred fifty-seven patients with stable coronary heart disease who met the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, criteria for a moderate to severe major depressive episode were treated with cognitive behavior therapy, either alone or combined with an antidepressant, for up to 16 weeks. Depression, physical activity, sleep quality, thyroid hormones (total thyroxine [T4] and free T4), and inflammatory blood markers (C-reactive protein, interleukin-6, tumor necrosis factor) were assessed at baseline and after 16 weeks of treatment.

**Results:** The mean (SD) Beck Depression Inventory scores were 30.2 (8.5) at baseline and 8.5 (7.8) at 16 weeks. More than 50% of the participants met the criteria for depression remission (17-item Hamilton Rating Scale for Depression  $\leq$ 7) at 16 weeks. Only free T4 thyroid hormone at baseline predicted poor response to depression treatment after adjustment for potential confounders (p=.004). Improvement in sleep quality (p=.012) and physical activity level (p=.041) correlated with improvement in depression. None of the inflammatory markers predicted posttreatment depression or changed with depression.

Conclusions: Thyroid hormone (T4) level predicted depression treatment outcome, and improvement in depression correlated with improvement in sleep and physical activity. More detailed studies of thyroid function and objective assessments of sleep and physical activity in relation to depression improvement and cardiac outcomes are needed.

Key words: depressive disorder, treatment, cardiac risk markers.

**TABLE 2.** Baseline Risk Markers as Predictors of Depression Improvement (n = 157)

	Unadjusted		Adjusted <sup>a</sup>			
Risk Marker	Estimate (95% CI)	ρ	Estimate (95% CI)	р		
Sleep quality				.14		
PSQI global score	0.12 (-0.06 to 0.28)	.18	0.13 (-0.04 to 0.29)			
Physical functioning						
IPAQ category	0.07 (-0.10 to 0.23)	.40	0.07 (-0.10 to 0.23)	.43		
Inflammatory markers						
CRP	0.04 (-0.14 to 0.22)	.67	0.04 (-0.14 to 0.22)	.65		
IL-6	0.03 (-0.16 to 0.21)	.77	0.03 (-0.16 to 0.21)	.76		
TNF	0.09 (-0.11 to 0.28)	.38	0.10 (-0.10 to 0.29)	.34		
Thyroid hormone levels						
Free T4	0.29 (0.13 to 0.44)	<.001	0.25 (0.08 to 0.40)	.004		
T4 total	0.19 (0.02 to 0.34)	.030	0.16 (-0.01 to 0.32)	.063		

CI = confidence interval; PSQI = Pittsburgh Sleep Quality Index; IPAQ = International Physical Activity Inventory; CRP = C-reactive protein; IL-6 = interleukin-6; TNF = tumor necrosis factor; T4 = thyroxine.

<sup>&</sup>lt;sup>a</sup> Regression coefficients adjusted for age, intercurrent cardiac or other medical events, and antidepressant use at baseline. The presence of a fever or recent infection was added to the models for the inflammatory markers. Thyroid hormone replacement and thyroid disease were added to the models for the thyroid hormone levels.

## Di cosa voglio parlare

- Depressione: dove eravamo rimasti?
- Il medico (geriatra, psichiatra, neurologo) e la depressione nell'anziano
- "La grammatica della vita interiore" nei medici e nei vecchi d'oggi
- Depressione e mortalità
- Depressione e patologia
- Epidemiologia del trattamento
- La fenomenologia della depressione nell'anziano
- Conclusioni

-<u>Insonnia (o ipersonnia) e stanchezza</u> sono sintomi d'esordio frequentemente non interpretati come marcatori di depressione; la loro misclassificazione spesso spiega la sottodiagnosi.

-Nell'episodio depressivo maggiore il paziente descrive il proprio <u>umore come</u> <u>depresso, triste, senza speranza, scoraggiato o "giù di corda</u>". La riduzione dell'umore può essere meno comune nei pazienti molto anziani, mentre lo è maggiormente l'irritabilità, l'ansia e i sintomi somatici.

-Alcuni pazienti enfatizzano i sintomi somatici piuttosto che riferire sentimenti di tristezza. Molti riferiscono facile irritabilità (ad esempio, rabbia persistente, tendenza a rispondere con scoppi d'ira o a incolpare gli altri, esagerato senso di frustrazione per questioni minori). La coesistenza di patologia somatica complica anche la gestione (management) della depressione. Anziani con depressione hanno un tasso di comorbilità e concomitante uso di farmaci maggiore rispetto ai pazienti non depressi. Il rapporto tra depressione e patologia medica può essere bidirezionale: problemi di salute fisica (ad es. il dolore cronico) possono predisporre alla depressione; di contro la depressione può associarsi a esiti peggiori delle malattie somatiche (ad es. patologia cardiaca).

La coesistenza di patologia somatica rende complesso il politrattamento e le modificazioni età-correlate del metabolismo dei farmaci possono aumentare il rischio di effetti collaterali.

-La <u>perdita di interesse</u> o della capacità di provare piacere è quasi sempre presente, almeno in certa misura. I pazienti possono riferire di sentirsi meno interessati alle attività avanzate della vita quotidiana (AADL, i.e.hobby) o non provare alcun gusto nelle attività che in precedenza erano considerate piacevoli.

-Aumento o riduzione dell'appetito: alcuni pazienti dicono di doversi costringere a mangiare mentre altri possono aumentare l'assunzione di cibo o desiderare cibi specifici (ad esempio, dolci o altri carboidrati). Quando alterazioni dell'appetito sono gravi (in entrambe le direzioni), ci può essere una significativa perdita o aumento di peso.

-Le <u>alterazioni psicomotorie</u> includono agitazione (i pazienti sono incapaci a stare fermi, si contorcono le mani, si tirano o sfregano la pelle, i vestiti o altri oggetti) o rallentamento psicomotorio (ad esempio, pensano e parlano molto lentamente, hanno movimenti lenti del corpo, fanno lunghe pause prima di rispondere; parlano a bassa voce; anche la varietà e la quantità dei contenuti è povera).

-Il <u>senso di autosvalutazione o di colpa</u> che accompagna un episodio depressivo può includere sensi di colpa o ruminazioni anche per piccoli errori del passato. I pazienti fraintendono eventi insignificanti della vita quotidiana come prova di disvalore personale e hanno un esagerato senso di responsabilità per eventi spiacevoli occorsi.

-Molti individui riferiscono di avere un <u>declino cognitivo</u>, una ridotta capacità di pensiero, o di concentrazione, come pure di prendere decisioni anche di scarsa rilevanza. Possono apparire facilmente distratti o si lamentano delle difficoltà di memoria. Coloro che sono impegnati in attività che richiedono una cognitività elevata non sono frequentemente in grado di avere performance soddisfacenti. Nei soggetti anziani, la difficoltà di memoria può essere il disturbo principale e può essere interpretata come primo segni di demenza.

-I pensieri di morte, l'ideazione suicidaria o i tentativi di suicidio sono comuni. Possono variare dal desiderio di non svegliarsi la mattina o dalla convinzione che gli altri starebbero meglio se si fosse morti, da pensieri transitori, ma ricorrenti di suicidio, a un piano di suicidio specifico. I soggetti con ideazione suicidaria pervasiva possono aver messo i loro affari in ordine (per esempio, testamenti aggiornati, saldato i debiti), acquistato il materiale necessario per compiere l'atto (ad esempio, una corda o una pistola) e scelto il luogo e tempo per realizzare il suicidio.

## Di cosa voglio parlare

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- Conclusioni

### Aspetti centrali della depressione nell'anziano

- -La depressione nell'anziano è una condizione frequente ed è spesso associata a comorbilità somatiche, deterioramento cognitivo o a entrambi.
- -La depressione nel paziente anziano peggiora la prognosi di qualsiasi condizione medica (e si associa a un elevato rischio suicidario).
- -Lo screening per la depressione è importante, ma alla positività allo screening dovrebbe far seguito una valutazione psichica completa che valuti la sicurezza del paziente e faccia in modo che il trattamento prescritto sia effettuato.
- -Sia la terapia farmacologica che la psicoterapia possono essere utilizzate come terapie di prima linea.
- -Gli antidepressivi disponibili sono efficaci anche nella popolazione anziana; la probabilità di effetti collaterali è più elevata.
- -Anche le tecniche psicoterapeutiche standardizzate sono efficaci nel trattamento della depressione nell'anziano.