



**CONGRESSO  
NAZIONALE SIGG**

**GLI ANZIANI:  
LE RADICI DA PRESERVARE**  
**ROMA** 28 novembre  
01 dicembre 2018 Auditorium della Tecnica, Roma

**Simposio  
Interprofessional Education su Depressione e Demenza**

**DEPRESSIONE DEL TONO DELL'UMORE NEL GRANDE  
VECCHIO: SOTTOSTIMA O SOVRASTIMA?**

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# Solving the Geriatric Mental Health Crisis in the 21st Century

Eric J. Lenze, MD

**JAMA Psychiatry. 2015;72(10):967-968.**

- We are in the midst of an unprecedented demographic trend: we are aging. By 2050, the population aged 65 years and older in the United States will be 84 million.
- .... the unfolding crisis of our health care system lacking the capacity to help a growing elderly population in which 1 in 5 individuals has a mental disorder.

# Burden of Depressive Disorders by Country, Sex, Age, and Year: Findings from the Global Burden of Disease Study 2010

Alize J. Ferrari<sup>1,2\*</sup>, Fiona J. Charlson<sup>1,2</sup>, Rosana E. Norman<sup>1,3</sup>, Scott B. Patten<sup>4</sup>, Greg Freedman<sup>5</sup>, Christopher J.L. Murray<sup>5</sup>, Theo Vos<sup>1,5</sup>, Harvey A. Whiteford<sup>1,2</sup>

**Table 3.** Change in depressive disorder YLDs between 1990 and 2010.

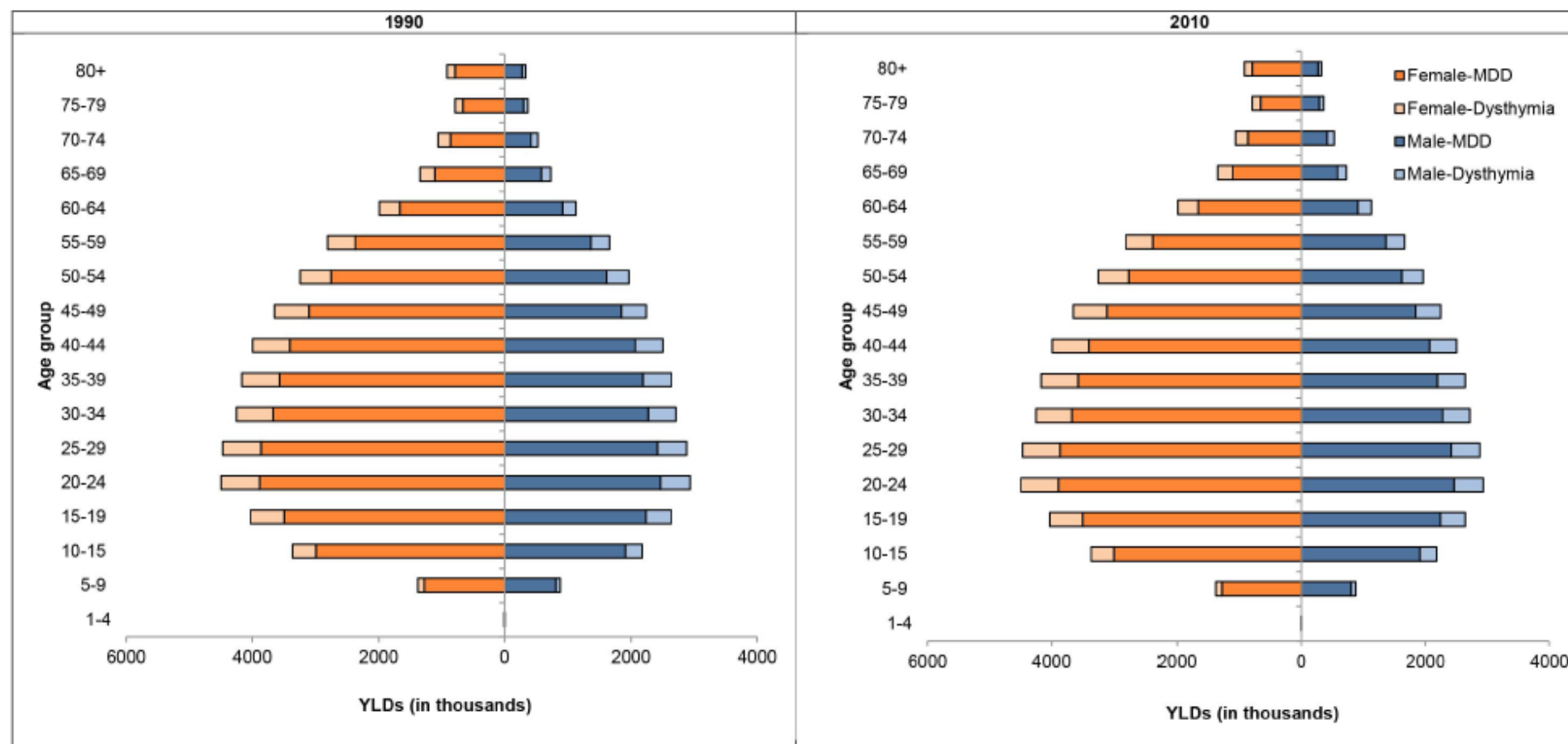
Total YLDs in 1990 and 2010	MDD	Dysthymia	Depressive Disorders
Total YLDs in 1990	46,138,600	7,870,700	54,009,300
Total YLDs in 2010	63,179,247	11,084,100	74,261,500
Total YLDs generated from 2010 population, 1990 population age structure, 1990 YLD rates (step 1)	59,904,870	10,067,939	69,972,809
Total YLDs generated from 2010 population, 2010 population age structure, 1990 YLD rates (step 2)	64,537,300	11,061,231	75,598,531
Total change in YLDs between 1990 and 2010	36.9%	40.8%	37.5%
Change in YLDs between 1990 and 2010 due to population growth	29.8%	27.9%	29.6%
Change in YLDs between 1990 and 2010 due to population aging	10.0%	12.6%	10.4%
Change in YLDs between 1990 and 2010 due to prevalence increase	−2.9%	0.3%	−2.5%

The difference between total YLDs in 1990 and YLDs at step 1 represents the change in YLDs due to population growth; the difference between YLDs at step 1 and YLDs at step 2 represents the change in YLDs due to population aging; the difference between total YLDs in 2010 and YLDs at step 2 represents the change in YLDs due to changes in prevalence.

doi:10.1371/journal.pmed.1001547.t003

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**Figure 1. YLDs by age and sex for MDD and dysthymia in 1990 and 2010.**

doi:10.1371/journal.pmed.1001547.g001



a cura di:  
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Raffaella Antonelli Incalzi, Giuseppe Bellelli, Pietro Gareri, Antonio  
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Pirfo, Francesco Scapatti, Osvaldo Scarpino, Carlo Serrati, Flavio Viscchia

Testo approvato dal Consiglio Direttivo dell'Associazione Italiana di  
Psicogeriatrics nella riunione tenutasi a Martina Franca (TA) il 30-31  
gennaio 2015

La depressione nell'anziano si presenta come la più biologica, ma anche la più "spirituale" delle depressioni, la più impenetrabile e resistente all'accesso farmacologico, come il più immateriale tra disturbi psichici della persona che invecchia. È un disturbo misterioso: lo sguardo di un anziano depresso e forse anche un po' demente, la sua presenza-assenza, il suo smarrimento, la sua corporeità visibilmente alla deriva sono una delle più intense rappresentazioni del mistero dell'uomo e della sua mente. Spesso la depressione nell'anziano è un'evocazione della morte temuta e desiderata da chi sente prossimo nel proprio orizzonte il fine vita.

Questa prossimità alla morte non è solo una conferma delle comorbidità che la letteratura ci dice quanto pesi nella prognosi dei soggetti colpiti, ma ci suggerisce anche quanto tenue sia la tenuta della dimensione stessa di "soggetto" in questi ammalati. Tuttavia la depressione nell'anziano può rappresentare uno degli ambiti diagnostici e terapeutici nei quali si ottengono i maggiori successi, sebbene a tutt'oggi non si disponga di uno schema definitivo per la classificazione dei disturbi depressivi in età avanzata. Quanto differisce da quella che si manifesta in età giovane-adulta? Quali sono le cause dell'eterogeneità della depressione nella vecchiaia? Quali sono i tassi di prevalenza e quali i fattori di rischio? È più elevata la prevalenza della depressione in vecchiaia? È più difficile da diagnosticare? Quale depressione trova vantaggi dalla terapia farmacologica e quale dalla psicoterapia? È più difficile da trattare? (Williams et al., 2000; 2002).



CLINICAL PRACTICE

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

## Depression in the Elderly

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

Late-life depression is the occurrence of major depressive disorder in adults 60 years of age or older. Major depressive disorder occurs in up to 5% of community-dwelling older adults, and 8 to 16% of older adults have clinically significant depressive symptoms.<sup>1</sup> Rates of major depressive disorder rise with increasing medical morbidity, with reported rates of 5 to 10% in primary care<sup>2</sup> and as high as 37% after critical care hospitalizations.<sup>3</sup>

Patients with late-life depression are heterogeneous in terms of clinical history and coexisting medical conditions. As compared with older adults reporting an initial depressive episode early in life, those with late-onset depression are more likely to have neurologic abnormalities, including deficits on neuropsychological tests and age-related changes on neuroimaging that are greater than normal; they are also at higher risk for subsequent dementia.<sup>4</sup> Such observations informed the hypothesis that vascular disease may contribute to depression in some older adults.<sup>5,6</sup>

# Late life depression

- Community sample > age 65
  - 1-5% Major depression
  - 2% Dysthymia
  - 4-10% Adjustment Disorder with depressed mood
  - 15% Sub-syndromal Depression
- Both the prevalence and the incidence of major depression double after age 70–85 years.
- Late-onset depression are frequently associated with medical conditions, medications, and neurological diseases

# Late life depression in special population

- 10-25% in Primary Care
  - 30% of these have major depression
- 25-60% of hospitalized patients
  - 11% have major depression
- 16-50% of NH residents are depressed



# Categoria diagnostica del disturbo depressivo ed età

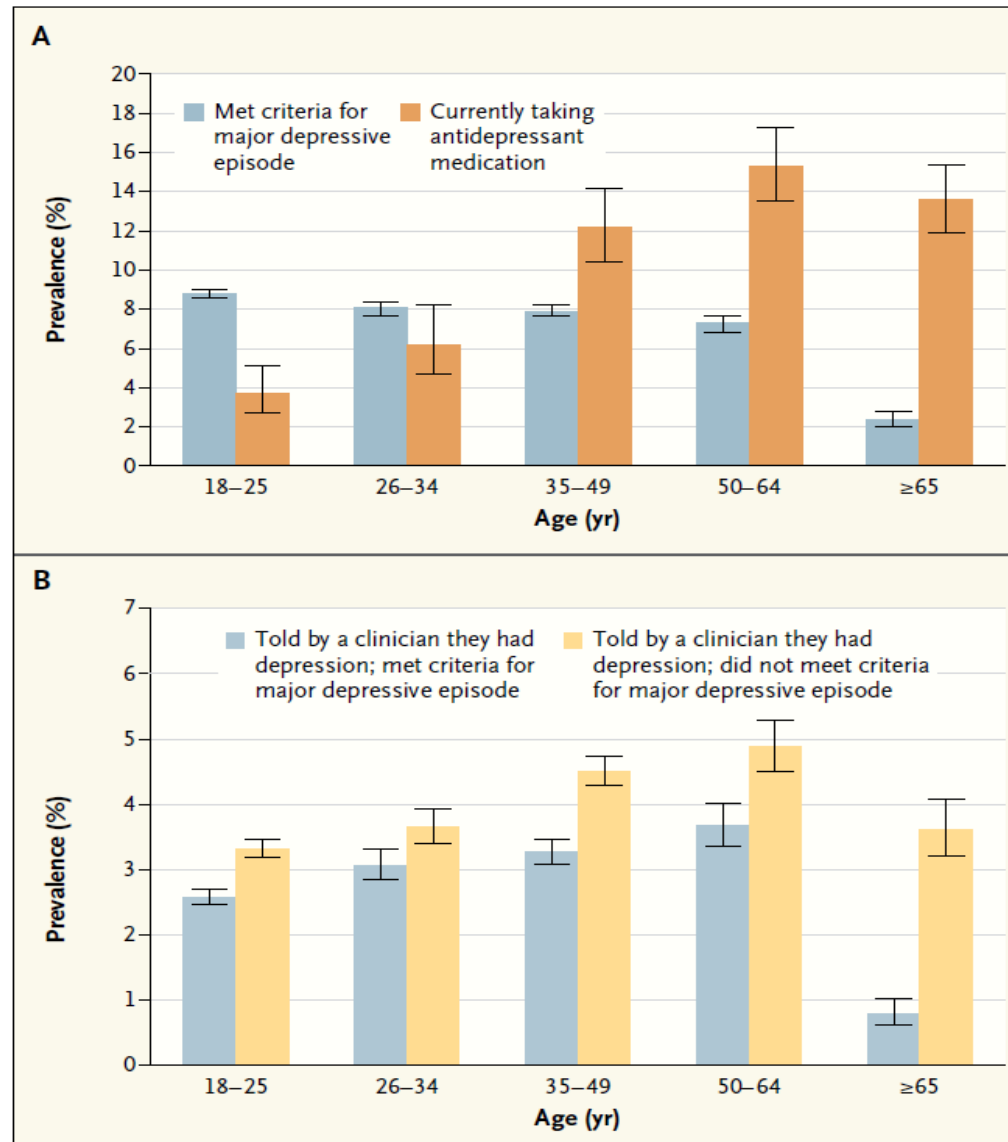
(studio EpiDei – AIP – 995 casi)

• < 65 anni	• DM	55%
	• Distimia	17%
	• Dist. Adatt.	14%
	• Depr. NAS	9%
• 65-75 anni	• DM	44%
	• Distimia	21%
	• Dist. Adatt.	25%
	• Depr. NAS	9%
• >75 anni	• DM	26%
	• Distimia	21%
	• Dist. Adatt.	33%
	• Depr. NAS	15%

# 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



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

# Twenty-Year Depressive Trajectories Among Older Women

Amy L. Byers, PhD, MPH; Eric Vittinghoff, PhD, MPH; Li-Yung Lui, MA, MS; Tina Hoang, MPH; Dan G. Blazer, MD; Kenneth E. Covinsky, MD, MPH; Kristine E. Ensrud, MD, MPH; Jane A. Cauley, DrPH; Teresa A. Hillier, MD, MS; Lisa Fredman, PhD; Kristine Yaffe, MD

**Context:** Despite the frequent occurrence of depressive symptoms among older adults, especially women, little is known about the long-term course of late-life depressive symptoms.

**Objective:** To characterize the natural course of depressive symptoms among older women (from the young old to the oldest old) followed up for almost 20 years.

**Design:** Using latent-class growth-curve analysis, we analyzed women enrolled in an ongoing prospective cohort study (1988 through 2009).

**Setting:** Clinic sites in Baltimore, Maryland; Minneapolis, Minnesota; the Monongahela Valley near Pittsburgh, Pennsylvania; and Portland, Oregon.

**Participants:** We studied 7240 community-dwelling women 65 years or older.

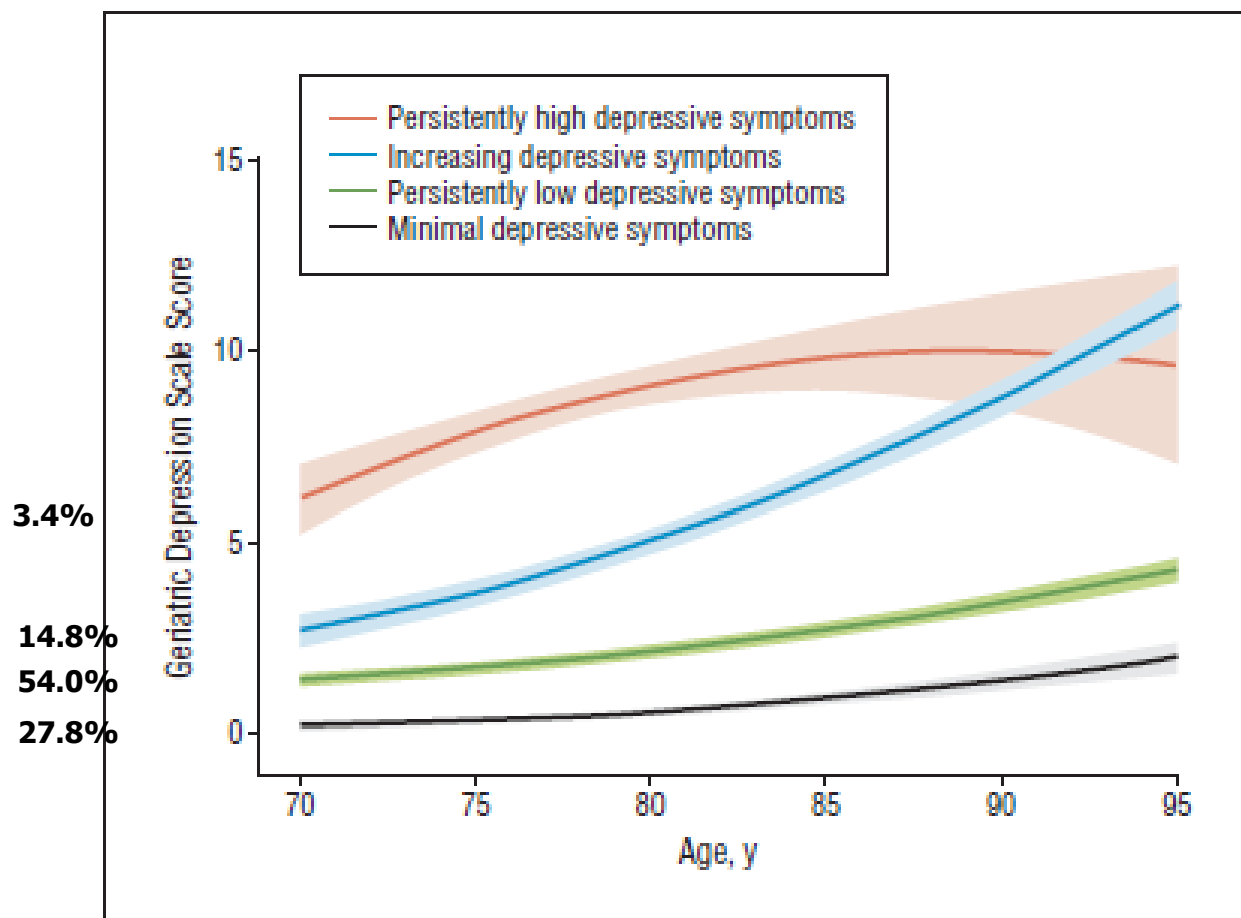
**Main Outcome Measure:** The Geriatric Depression Scale short form (score range, 0-15) was used to routinely assess depressive symptoms during the follow-up period.

**Results:** Among older women, we identified 4 latent classes during 20 years, with the predicted probabilities

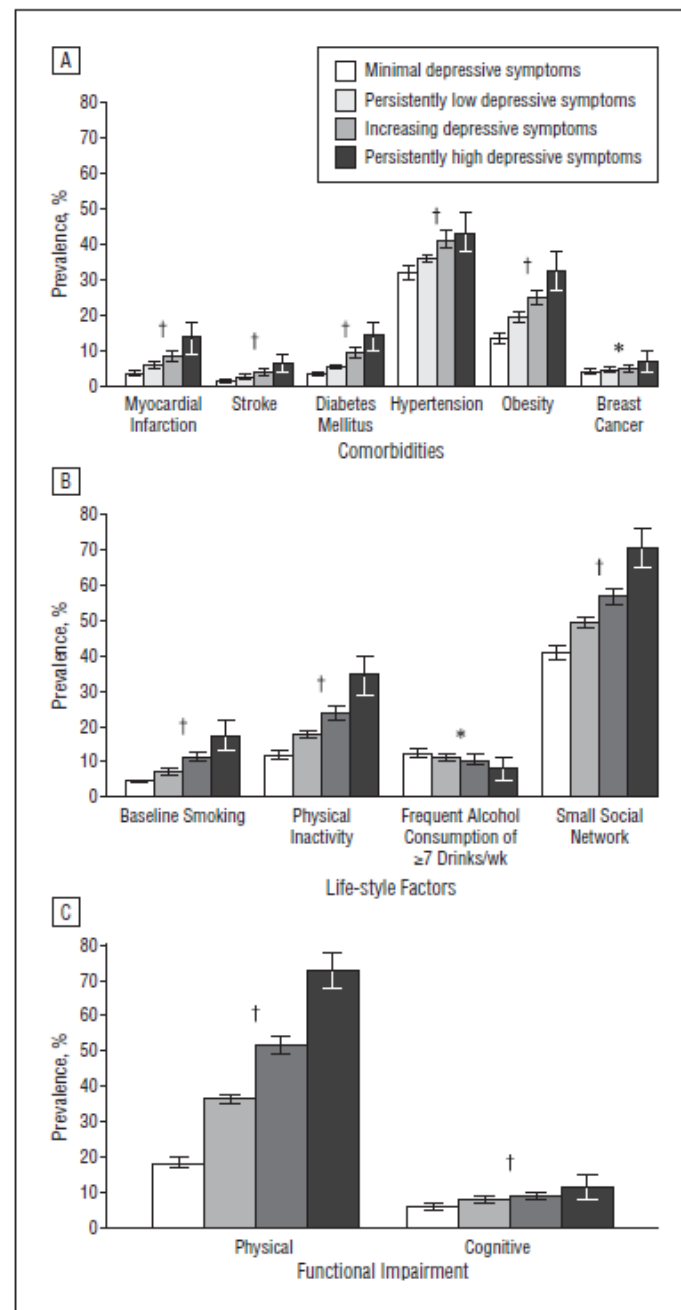
of group membership totaling 27.8% with minimal depressive symptoms, 54.0% with persistently low depressive symptoms, 14.8% with increasing depressive symptoms, and 3.4% with persistently high depressive symptoms. In an adjusted model for latent class membership, odds ratios (ORs) for belonging in the increasing depressive symptoms and persistently high depressive symptoms classes, respectively, compared with a group having minimal depressive symptoms were substantially and significantly ( $P < .05$ ) elevated for the following variables: baseline smoking (ORs, 4.69 and 7.97), physical inactivity (ORs, 2.11 and 2.78), small social network (ORs, 3.24 and 6.75), physical impairment (ORs, 8.11 and 16.43), myocardial infarction (ORs, 2.09 and 2.41), diabetes mellitus (ORs, 2.98 and 3.03), and obesity (ORs, 1.86 and 2.90).

**Conclusions:** During 20 years, almost 20% of older women experienced persistently high depressive symptoms or increasing depressive symptoms. In addition, these women had more comorbidities, physical impairment, and negative lifestyle factors at baseline. These associations support the need for intervention and prevention strategies to reduce depressive symptoms into the oldest-old years.

*Arch Gen Psychiatry.* 2012;69(10):1073-1079



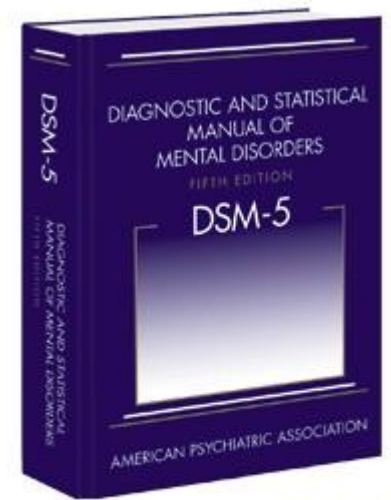
**Figure 1.** Mean trajectories of depressive symptoms by increasing age among older women.



**Figure 2.** Prevalences across trajectory groups of depressive symptoms. A, Comorbidities. B, Lifestyle factors. C, Functional impairment. The I bars indicate 95% CIs. \* $P < .05$ ; † $P < .001$  (test for trend based on orthogonal contrasts in weighted generalized estimating equation models).

# Il problema dell'approccio clinico: olistico o categoriale?

- È più corretto incasellare i disturbi depressivi in **costrutti diagnostici** o misurare l'**entità della sintomatologia depressiva** e definire i trattamenti sulla base di tale misura?



DSM-5  
2013





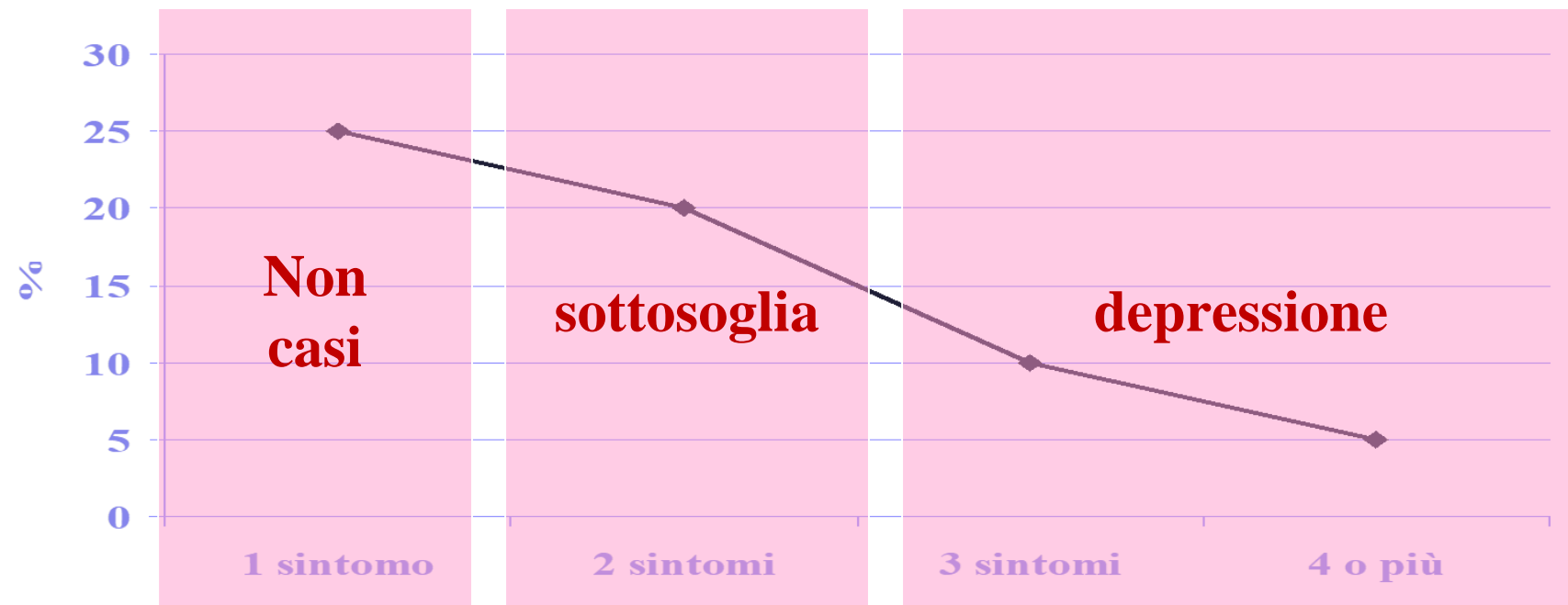
# The geriatric syndrome of late-life depression

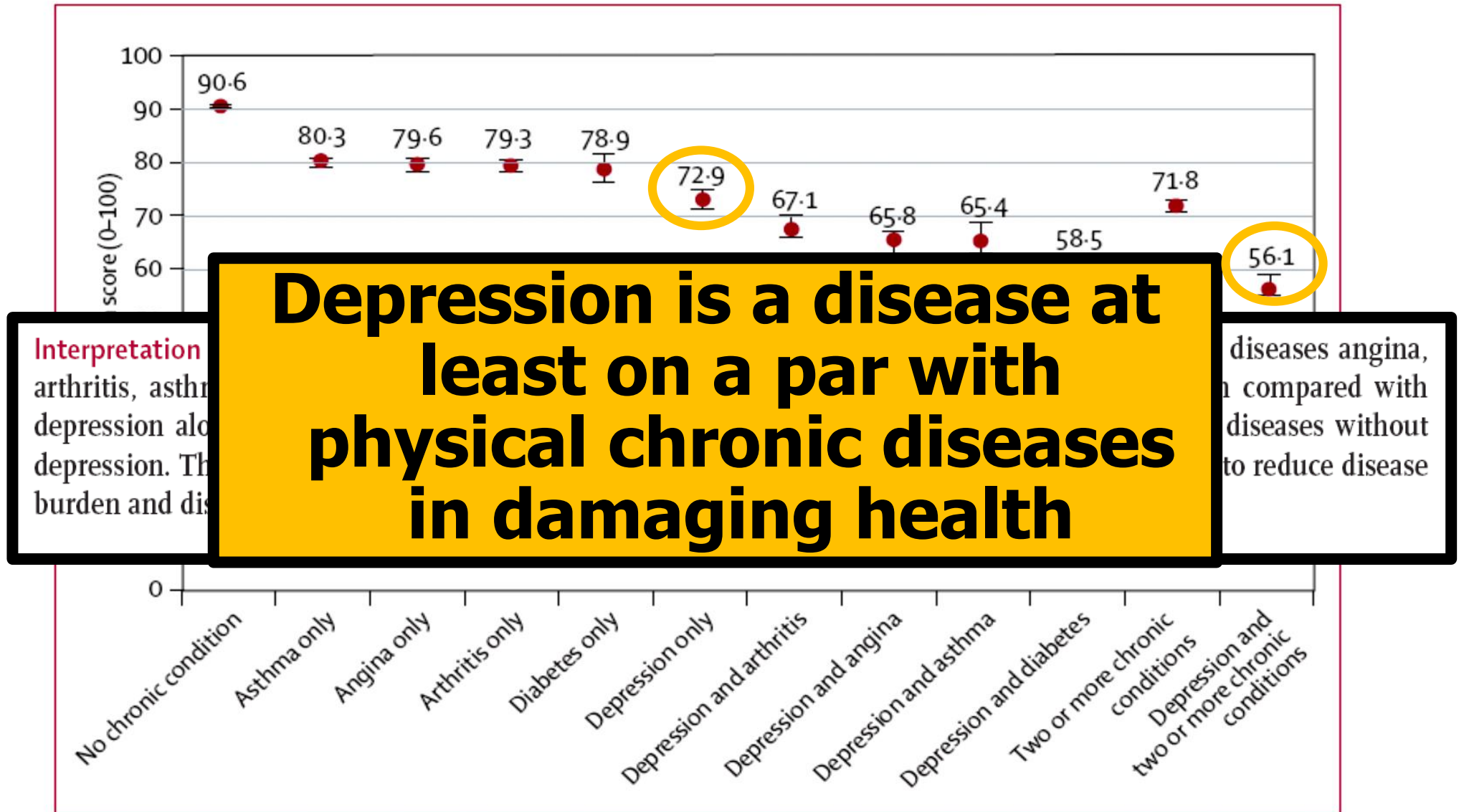
Kennedy GJ.

Psychiatr Serv. 1995 Jan;46(1):43-8.

- Existing data on the treatment, course, and outcome of depression are not representative of the older depressed person who is most frequently encountered in clinical practice.
- If mental health services are to become more effectively applied, **late-life depression should be conceptualized not as a categorical disorder but as a geriatric syndrome with multiple etiologies requiring a combination of treatments.**

# Continuum depressivo





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

***Moussavi S et al, Lancet 2007; 370:851-58***



# Course of Depression and Mortality Among Older Primary Care Patients

*Hillary R. Bogner, M.D., M.S.C.E., Knashawn H. Morales, Sc.D.,  
Charles F. Reynolds, III, M.D., Mark S. Cary, Ph.D., Martha L. Bruce, Ph.D.*

**Context:** Depression is a treatable illness that disproportionately places older adults at increased risk for mortality. **Objective:** We sought to examine whether there are patterns of course of depression severity among older primary care patients that are associated with increased risk for mortality. **Design and Setting:** Our study was a secondary analysis of data from a practice-based randomized controlled trial within 20 primary care practices located in greater New York City, Philadelphia, and Pittsburgh. **Participants:** The study sample consisted of 599 adults aged 60 years and older recruited from primary care settings. Participants were identified through a two-stage, age-stratified (60–74 years; older than 75 years) depression screening of randomly sampled patients. Severity of depression was assessed using the 24-item Hamilton Depression Rating Scale (HDRS). **Measurements:** Longitudinal analysis via growth curve mixture modeling was carried out to classify patterns of course of depression severity across 12 months. Vital status at 5 years was ascertained via the National Death Index Plus. **Results:** Three patterns of change in course of depression severity over 12 months were identified: (1) persistent depressive symptoms, (2) high but declining depressive symptoms, (3) low and declining depressive symptoms. After a median follow-up of 52.0 months, 114 patients had died. Patients with persistent depressive symptoms were more likely to have died compared with patients with a course of high but declining depressive symptoms (adjusted hazard ratio 2.32, 95% confidence interval [1.15–4.69]). **Conclusions:** Persistent depressive symptoms signaled increased risk of dying in older primary care patients, even after adjustment for potentially influential characteristics such as age, smoking status, and medical comorbidity. (Am J Geriatr Psychiatry 2012; 20:895–903)

<sup>b</sup>p < 0.05.



## **Keep Calm and Carry On: Progress in Understanding Depression, Neurocognitive Impairments, and Dementia**

*Am J Geriatr Psychiatry 20:8, August 2012*

- ❑ depression in earlier life does increase the risk of dementia in old age by about twofold and that this risk extends for many years and may be greater with greater distance from the onset of dementia
- ❑ dysthymia at baseline conferred a similar, though reduced, risk of dementia suggesting there may be a dose–response relationship between depression severity and risk of dementia
- ❑ pathophysiologic mechanism(s) makes people with depression or dysthymia more likely to develop dementia are cerebrovascular disease and Alzheimer disease (or more broadly neurodegenerative disease)
- ❑ improvements in depression do not necessarily lead to a similar improvement in cognition, at least not in all domains; attentional and executive impairments tended not to improve with improvements in depression status, whereas those in learning and memory did improve

# Depression, Vascular Factors, and Risk of Dementia in Primary Care: A Retrospective Cohort Study

Sebastian Köhler, PhD,\* Frank Buntinx, MD, PhD,<sup>†‡</sup> Katie Palmer, PhD,<sup>§</sup> and Marjan van den Akker, PhD\*<sup>†</sup>

**OBJECTIVES:** To study the interaction between and timing effects of depression and vascular disorders on dementia risk.

**DESIGN:** Retrospective cohort study.

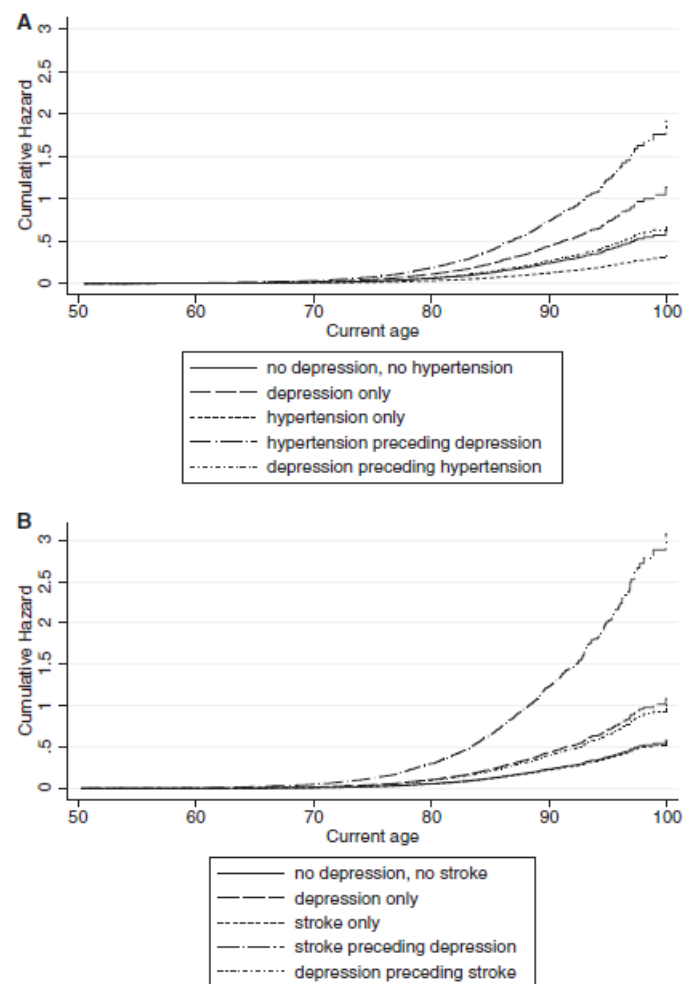
**SETTING:** Primary care practices in the south of the Netherlands.

**PARTICIPANTS:** Individuals in primary care aged 50 to 100 followed for 13 years (N = 35,791).

**MEASUREMENTS:** Medical diagnoses of incident depression, hypertension, obesity, type 2 diabetes mellitus, stroke, and dementia were extracted from a research database. Cox proportional hazards regression was used to test whether incident depression predicted dementia and its putative interactions with vascular factors.

**RESULTS:** In total, 1,680 participants developed dementia. Individuals with depression (n = 978) had a higher risk of dementia (adjusted hazard ratio (HR) = 2.03, 95% confidence interval (CI) = 1.56–2.64). Depression exerted most effect in participants with incident stroke (HR = 5.29, 95% CI = 2.52–11.14) or newly diagnosed hypertension (HR = 3.09, 95% CI = 1.54–6.20).

**CONCLUSION:** Depression in later life increases the risk of dementia. The effect is particularly high in individuals with depression and vascular disorders. Targeting late-onset depression in individuals with vascular disorders might lower dementia risk by preventing cerebrovascular changes. *J Am Geriatr Soc* 63:692–698, 2015.



**Figure 2.** Effect of timing of exposure on the cumulative hazards in those without a diagnosis of (A) hypertension or (B) stroke before the study period.

# Association of Microvascular Dysfunction With Late-Life Depression

## A Systematic Review and Meta-analysis

Marnix J. M. van Agtmaal, MD; Alfons J. H. M. Houben, PhD; Frans Pouwer, PhD;  
Coen D. A. Stehouwer, MD, PhD; Miranda T. Schram, MD

**IMPORTANCE** The etiologic factors of late-life depression are still poorly understood. Recent evidence suggests that microvascular dysfunction is associated with depression, which may have implications for prevention and treatment. However, this association has not been systematically reviewed.

**OBJECTIVE** To examine the associations of peripheral and cerebral microvascular dysfunction with late-life depression.

**DATA SOURCES** A systematic literature search was conducted in MEDLINE and EMBASE for and longitudinal studies published since inception to October 16, 2016, that assessed the associations between microvascular dysfunction and depression.

**STUDY SELECTION** Three independent researchers performed the study selection based on consensus. Inclusion criteria were a study population 40 years of age or older, a validated method of detecting depression, and validated measures of microvascular function.

**DATA EXTRACTION AND SYNTHESIS** This systematic review and meta-analysis has been registered at PROSPERO (CRD42016049158) and is reported in accordance with the PRISMA and MOOSE guidelines. Data extraction was performed by an independent researcher.

**MAIN OUTCOMES AND MEASURES** The following 5 estimates of microvascular dysfunction were considered in participants with or without depression: plasma markers of endothelial function, albuminuria, measurements of skin and muscle microcirculation, retinal arteriolar and venular diameter, and markers for cerebral small vessel disease. Data are reported as pooled odds ratios (ORs) by use of the generic inverse variance method with the use of random-effects models.

**RESULTS** A total of 712 studies were identified; 48 were included in the meta-analysis, of which 8 described longitudinal data. Data from 43 600 participants, 9203 individuals with depression, and 72 441 person-years (mean follow-up, 3.7 years) were available. Higher levels of plasma endothelial biomarkers (soluble intercellular adhesion molecule-1: OR, 1.58; 95% CI, 1.28-1.96), white matter hyperintensities (OR, 1.29; 95% CI, 1.19-1.39), cerebral microbleeds (OR, 1.18; 95% CI, 1.03-1.34), and cerebral (micro)infarctions (OR, 1.30; 95% CI, 1.21-1.39) were associated with depression. Among the studies available, no significant associations of albuminuria and retinal vessel diameters with depression were reported. Longitudinal data showed a significant association of white matter hyperintensities with incident depression (OR, 1.19; 95% CI, 1.09-1.30).

**CONCLUSIONS AND RELEVANCE** This meta-analysis shows that both the peripheral and cerebral forms of microvascular dysfunction are associated with higher odds of (incident) late-life depression. This finding may have clinical implications because microvascular dysfunction might provide a potential target for the prevention and treatment of depression.

## Key Points

**Question** Are both the peripheral and cerebral forms of microvascular dysfunction associated with late-life depression, as suggested by the vascular depression hypothesis?

**Findings** This systematic review and meta-analysis of 48 studies comprising 43 600 participants, including 9203 individuals with depression, shows that the cerebral and peripheral forms of microvascular dysfunction were associated with increased odds for (incident) late-life depression, independent of cardiovascular risk factors.

**Meaning** These findings support the hypothesis that microvascular dysfunction is causally linked to late-life depression. This finding may have clinical implications because microvascular dysfunction might provide a target for the prevention and treatment of depression.

# **“The Depression– Executive Dysfunction Syndrome of Late Life”**

## ***A Specific Target for D<sub>3</sub> Agonists?***

***George S. Alexopoulos, M.D.***

- Executive dysfunction, including disturbances in planning, sequencing, organizing, and abstracting, occurs in at least some patients with major depression.
- Depressed elderly patients often have poor retrieval, with relative preservation of recognition memory.
- These impairments are consistent with disruption of the integrity of striatofrontal pathways.
- White-matter hyperintensities have been reported in geriatric depression and mainly occur in subcortical structures and their frontal projections.
- The depression–executive dysfunction syndrome of late life is characterized by psychomotor retardation, apathy, limited depressive ideation, reduced agitation and insight, prominent disability.
- Executive dysfunction has been found to be associated with, poor or delayed antidepressant response, chronicity, relapse and recurrence of geriatric major depression and with residual depressive symptomatology.



## Depression in the Elderly

**Table 2. Crucial Elements of the History.**

History Component	Rationale
Psychiatric history	
Past psychiatric diagnoses and treatment	Allows confirmation of diagnosis and can guide treatment decisions
Current suicidal thoughts and past suicide attempts	Crucial in assessing safety; past suicide attempts indicate increased risk of future attempts
Substance use	Indicates contributing factors, such as alcohol use, for which additional intervention may be needed
Problems with memory	Initial screen for cognitive problems; should address with both patient and family if possible
Medical history	
Presence of chronic pain	May exacerbate depression and indicate need for additional treatment
Polypharmacy	May complicate antidepressant treatment
Problems with medication adherence	May lead to nonresponse to antidepressant treatment
Review of current medications	To identify any medications that may confer a predisposition to depression (e.g., propranolol, prednisone)
Social history	
Recent stressors or losses	Factors contributing to depression
Available social support	Indicates extent of social engagement or isolation
Access to transportation and ability to drive	Indicates ability to engage socially and to meet basic needs such as shopping for groceries
Access to guns	Indicates increased risk that a suicide attempt would be lethal
Family history	
Dementia	Indicates increased risk of dementia for the patient
Suicide	Indicates increased risk of suicide for the patient



## Depression in the Elderly

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

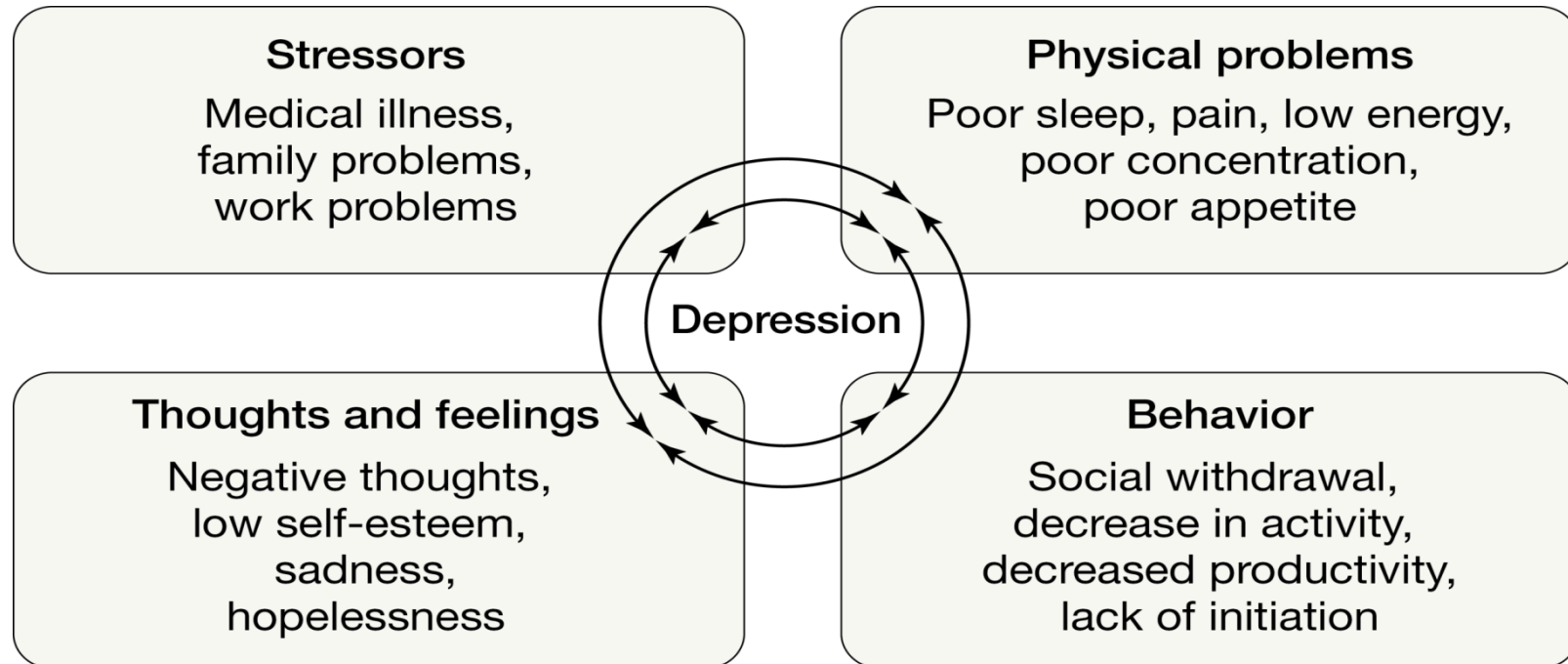
### KEY CLINICAL POINTS

#### DEPRESSION IN THE ELDERLY

- Late-life depression (occurring in persons 60 years of age or older) is common and is often associated with coexisting medical illness, cognitive dysfunction, or both.
- Depressed older adults are at increased risk for suicide.
- Screening for depression is important, but positive screening results should be followed by a thorough evaluation to assess patient safety and ensure that treatment is warranted.
- Either pharmacotherapy or psychotherapy may be used as first-line therapy.
- Currently available antidepressants show efficacy in depressed older populations, but older adults may be at increased risk for medication side effects. Selective serotonin-reuptake inhibitors (SSRIs) are considered first-line pharmacotherapy.
- Standardized psychotherapy techniques are also effective for depression in older adults.

From: **Older Adults With Severe, Treatment-Resistant Depression**

JAMA. 2012;308(9):909-918. doi:10.1001/2012.jama.10690



This conceptual model can help clinicians explain to patients how symptoms of depression may be interrelated.

# Conclusioni

- I disturbi depressivi sono frequenti nei soggetti anziani e si associano ad aumentato rischio di mortalità, morbidità e demenza
- Il carico dei sintomi è più importate della categoria sindromica
- Fattori di rischio vascolari e vascolarità cerebrale si associano spesso ai sintomi depressivi e aumentano il rischio di demenza
- La etiologia dei disturbi depressivi è sempre polifattoriale (fattori intrapsichici, stressor ambientali, comorbidità somatica)