I disturbi dello spettro ansioso nella terza età

Claudio Mencacci, Virginio Salvi

Sistema Socio Sanitario
Ospedale Fatebenefratelli e Oftalmico
Ospedale Macedonio Melloni
Regione Lombardia
ASST Fatebenefratelli Sacco

Dipartimento di Neuroscienze DSMD
ASST Fatebenefratelli Sacco
Milano

Outline

- Prevalenza dei disturbi d’ansia nell’anziano
- Evoluzione dei disturbi d’ansia
- Trattamento
  - Efficacia
  - Rischi

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La prevalenza dei disturbi d'ansia nella popolazione anziana

	Paese	N	Strumento	% qualsiasi disturbo d'ansia
Bland et al., 1988	Canada	199	DSM-III	5.0
Check et al., 1996	Australia	107	DSM-III	3.7
Forsell e Winblad, 1997	Sweden	966	CPRS	3.2
Pamelee et al., 1993	USA	451	DSM-III R	3.3
Smallbrugge et al., 2005	Netherlands	333	DSM-IV	5.7

da: Craighton et al., Int J Geriatr Psychiatry 2016:31:555-66

Anxiety disorders in old age: psychiatric comorbidities, quality of life, and prevalence according to age, gender, and country

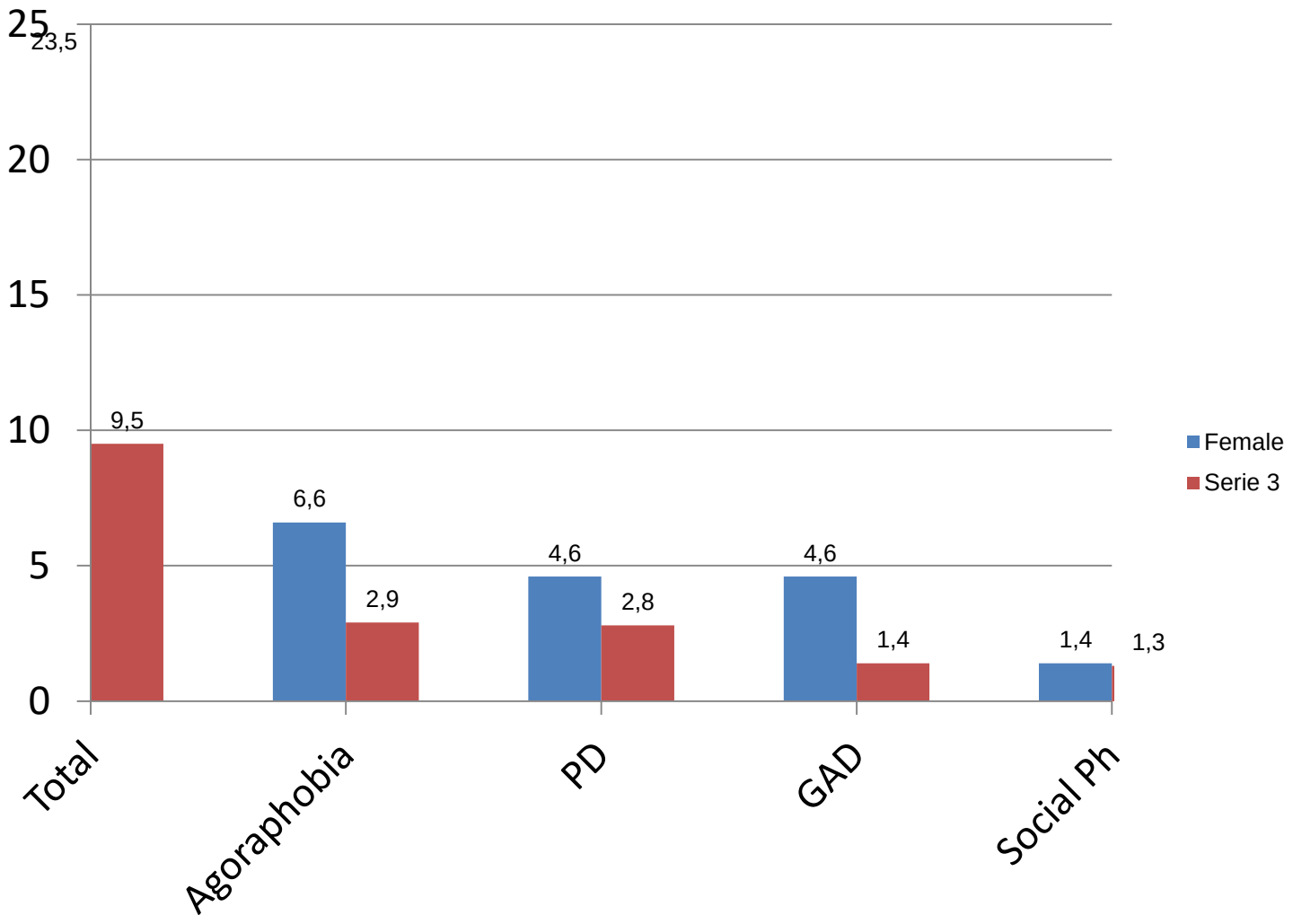
N=3142

	Adj. prev.	95% CI
Hamburg (GE)	16.8	14.4 -19.2
Ferrara (IT)	14.4	11.6 -17.3
London (EN)	20.8	15.6 -26.0
Madrid (ES)	18.3	14.4 -22.3
Geneva (CH)	14.1	10.4 -17.8
Jerusalem (IL)	14.7	10.7 -18.7
Total	17.2	14.0-20.4

12-months prevalence of any anxiety disorder

Canuto et al., Am J Geriatr Psychiatry 2018:26(2):164-85

Prevalence of Anxiety Disorders in old age



Canuto et al., Am J Geriatr Psychiatry 2018:26(2):164-85

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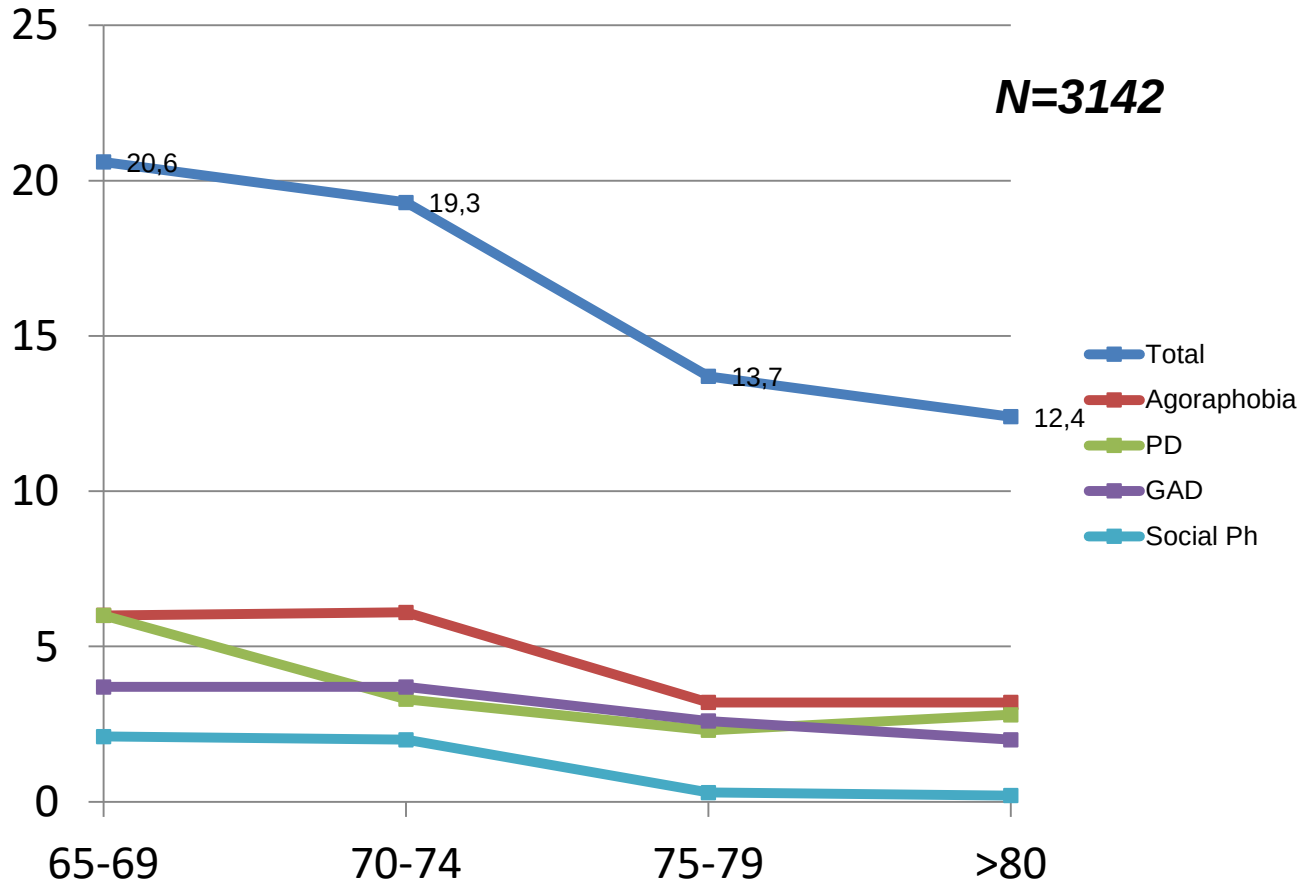
Prevalence of Anxiety Disorders in old age



Canuto et al., Am J Geriatr Psychiatry 2018:26(2):164-85

Anxiety, depression, and comorbid anxiety and depression: risk factors and outcome over two years

	CLINICAL STATUS AFTER 24 MONTHS				
STATUS AT BASELINE	NO ANXIETY OR DEPRESSION $N = 14,825$ *n* (%) OR [95% CI]	ANXIETY $N = 585$ *n* (%) OR [95% CI]	DEPRESSION $N = 224$ *n* (%) OR [95% CI]	DEPRESSION & ANXIETY $N = 231$ *n* (%) OR [95% CI]	LOST $N = 4,171$ *n* (%) OR [95% CI]
No anxiety or depression	14,274 (96.3)	298 (50.9)	137 (61.2)	77 (33.3)	3,679 (88.2)
	1	1	1	1	1
Anxiety	377 (2.5)	204 (34.9)	24 (10.7)	59 (25.5)	272 (6.5)
	1	**12.1 [9.3–15.7]**	**2.1 [1.2–3.7]**	**11.1 [7.1–17.5]**	**1.9 [1.6–2.3]**
Depression	107 (0.7)	19 (3.2)	40 (17.9)	11 (4.8)	98 (2.3)
	1	**3.9 [2.2–7.1]**	**10.7 [6.5–17.8]**	**6.2 [2.8–13.9]**	**1.9 [1.3–2.6]**
Depression & Anxiety	67 (0.4)	64 (10.9)	23 (10.3)	84 (36.4)	122 (2.9)
	1	**15.1 [9.4–24.5]**	**8.7 [4.5–16.7]**	**54.5 [31.4–94.5]**	**4.5 [3.1–6.6]**

Almeida et al., Int Psychogeriatr 2012;24(10):1622-32

The natural course of anxiety disorders in the elderly: a systematic review of longitudinal trials

- Mortalità → **nessun effetto**[1]
- Cognitività → **perdita di memoria**[2]

[1] Tre studi, due negativi e uno di più piccole dimensioni positivo
[2] Due studi, entrambi positivi per deficit mnesici. Riduzione di 4 punti MMSE a 4 anni

Sami et al., Int Psychogeriatr 2015;27(7):1061-9

Amyloid-β, Anxiety, and Cognitive Decline in Preclinical Alzheimer Disease

Figure 1. Slopes of Change in Verbal Memory Composite Score by Amyloid-β (Aβ) and Anxiety Levels

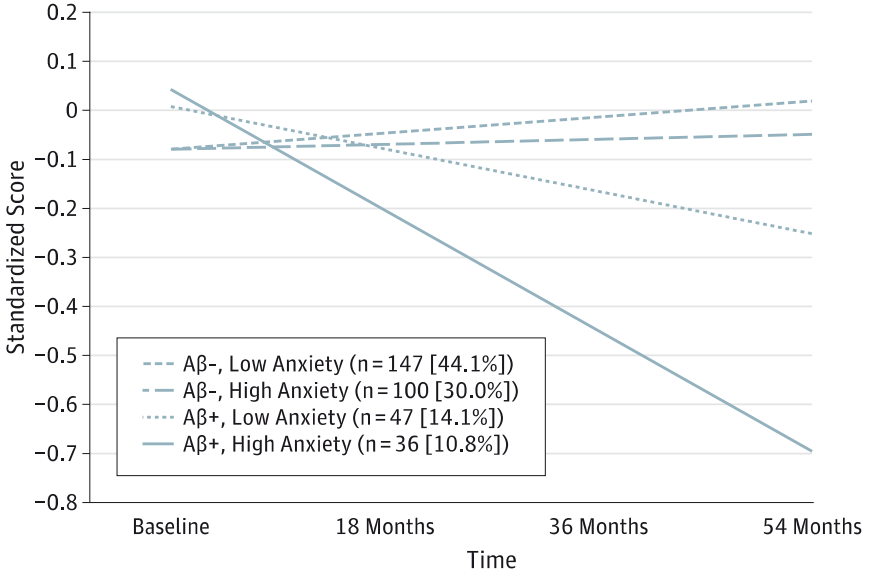
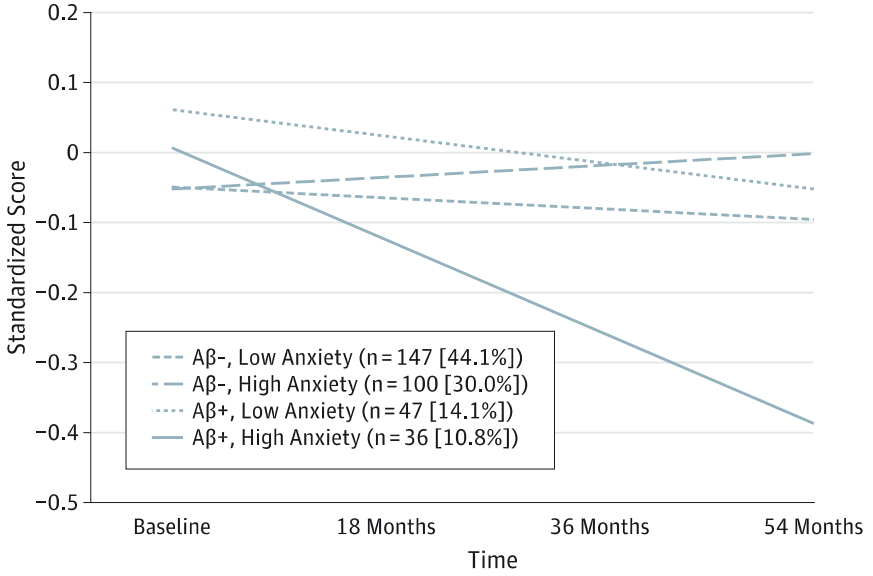


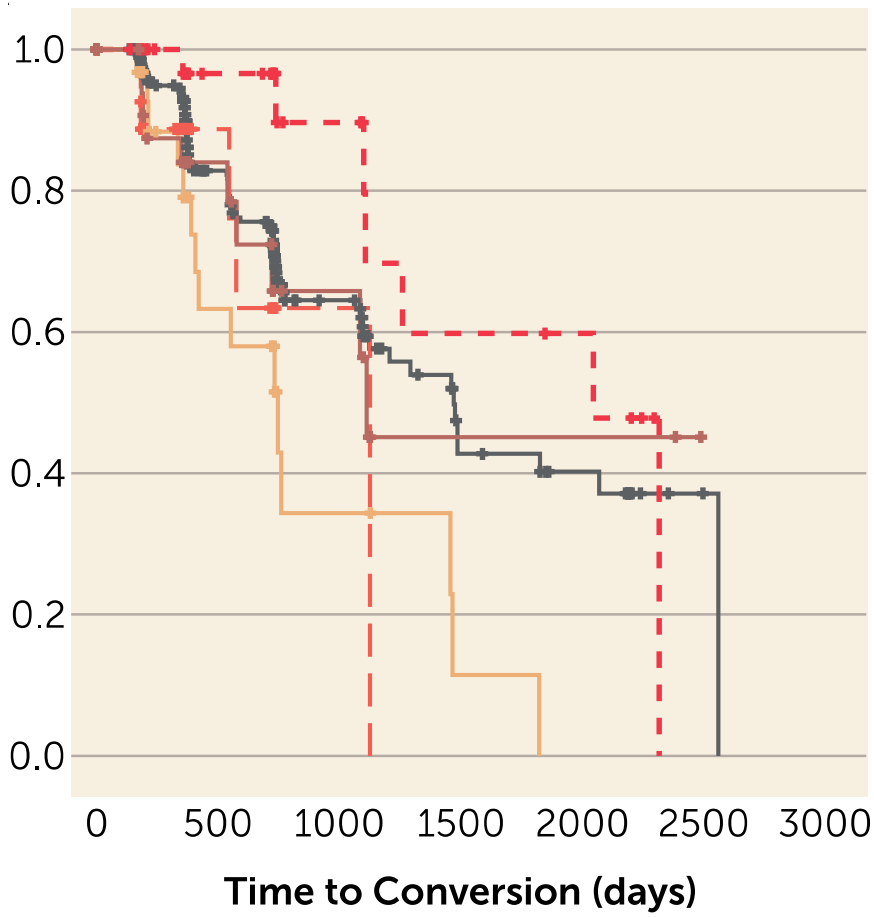
Figure 3. Slopes of Change in Executive Function Composite Score by Amyloid-β (Aβ) and Anxiety Levels



333 cognitively normal elders (≥70) followed for 4 years

Pietrzak et al., JAMA Psychiatry 2015;72(3):284-91

Impact of SSRI Therapy on Risk of Conversion From Mild Cognitive Impairment to Alzheimer's Dementia in Individuals With Previous Depression



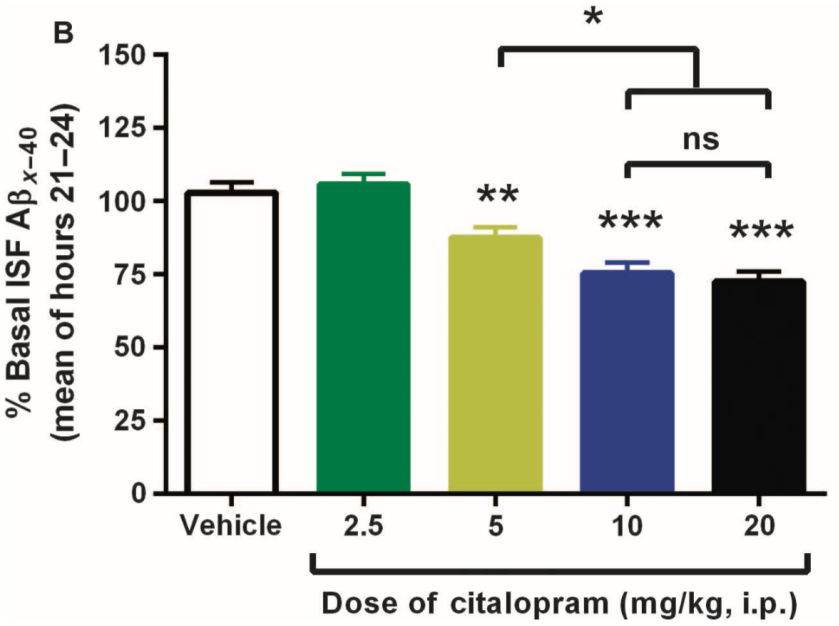
No prior depression–no antidepressants (N=301)
Prior depression–no antidepressants (N=37)
Prior depression–short-term SSRI (N=29)
Prior depression–long-term SSRI (N=38)
Prior depression–other antidepressants (N=33)

438 patients with MCI followed-up until conversion to dementia

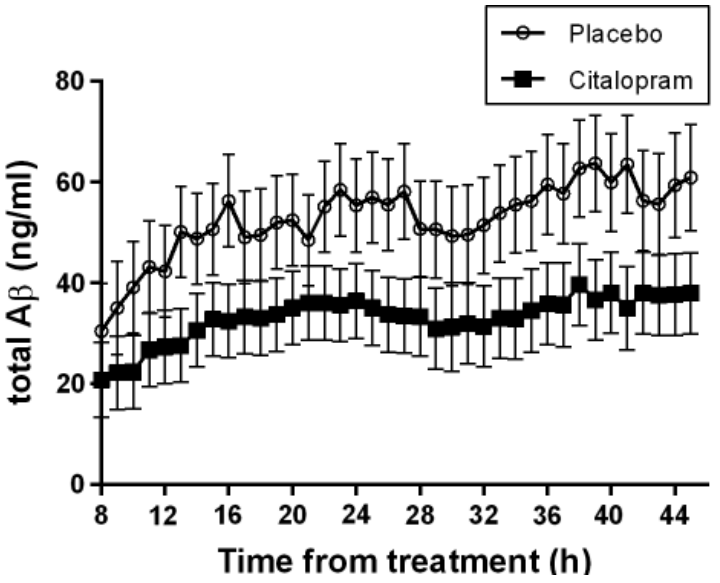
Bartels et al., Am J Psychiatry 2018;175(3):232-41

ALZHEIMER'S DISEASE

An Antidepressant Decreases CSF Aβ Production in Healthy Individuals and in Transgenic AD Mice



Effect of citalopram administration on amyloid-beta in mice



Citalopram reduces CSF Ab concentrations and production rate in healthy humans

Sheline et al., Sci Transl Med 2014;6(236):236re4

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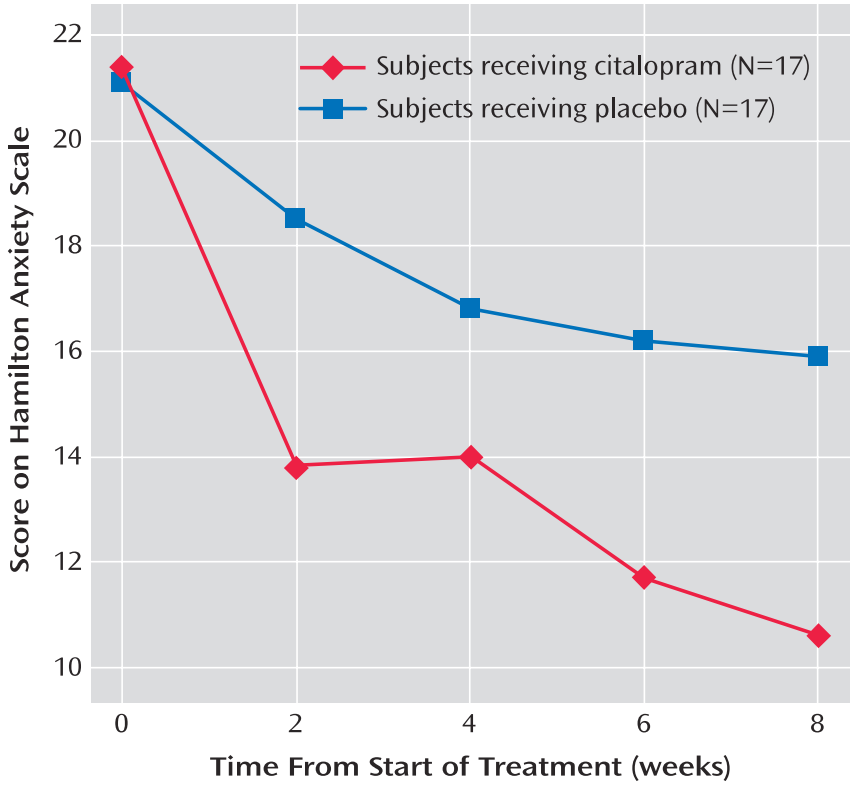
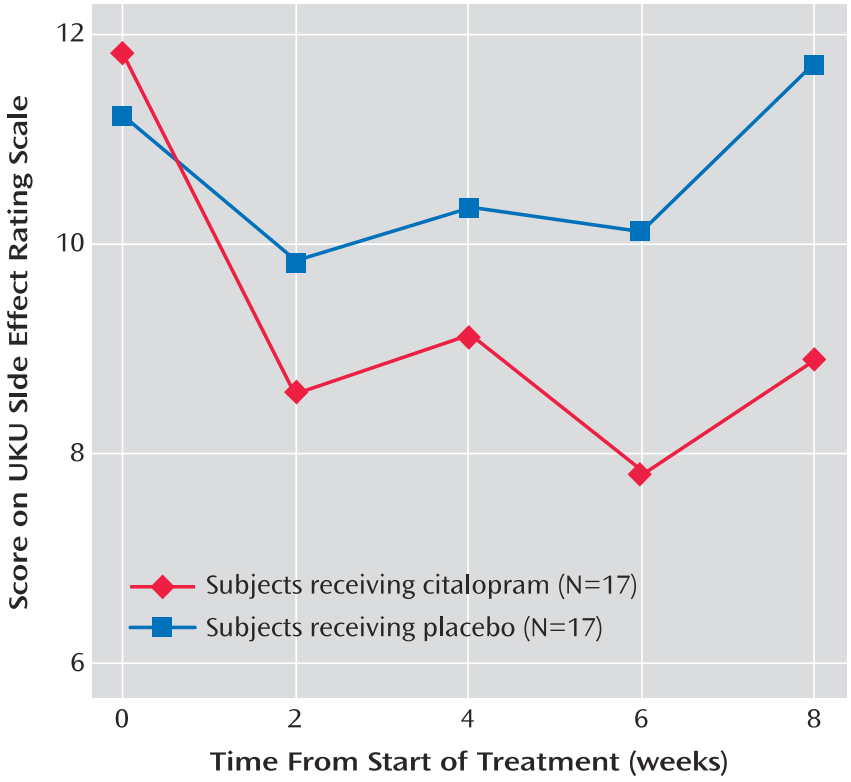
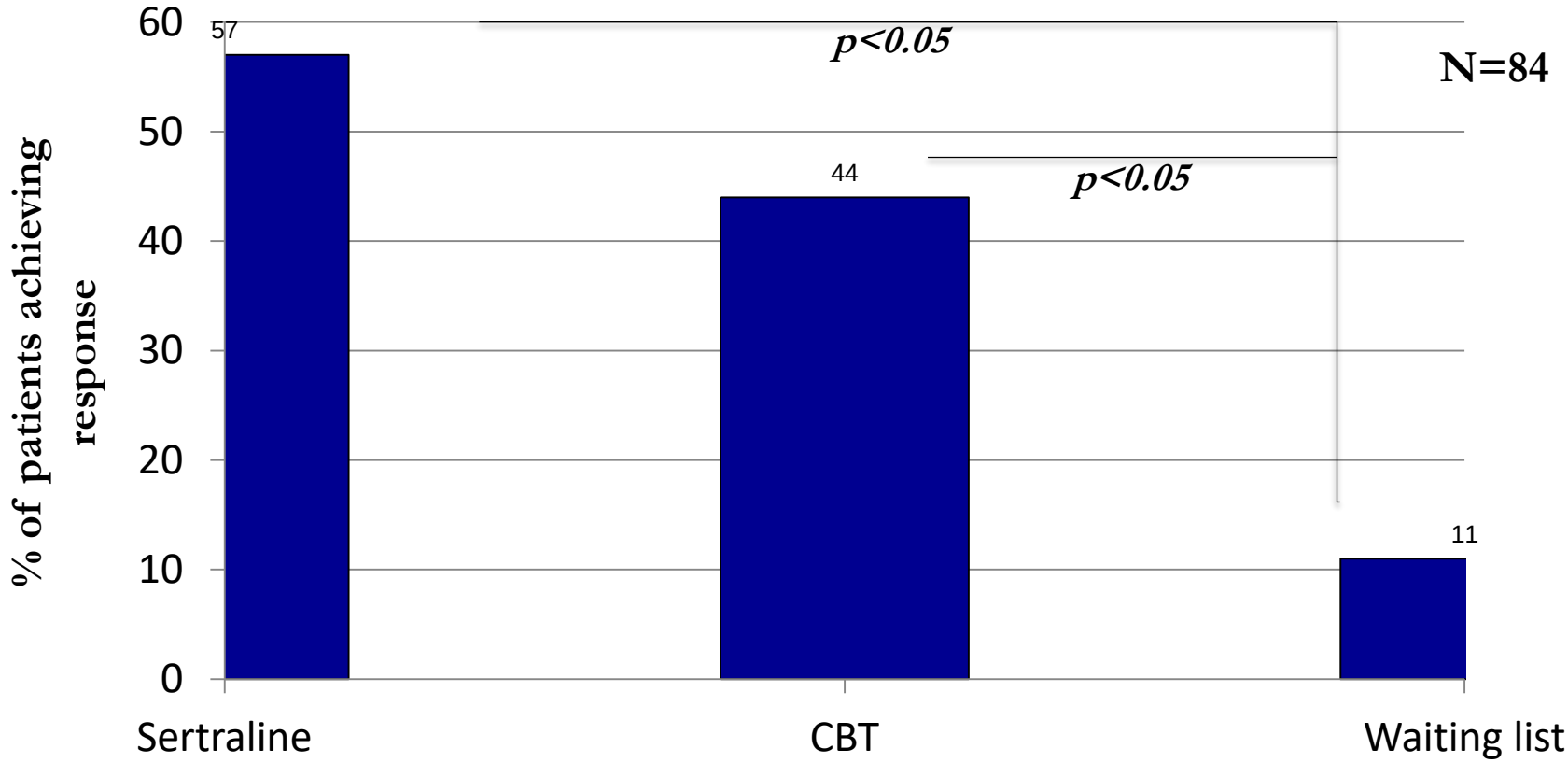
Efficacy and Tolerability of Citalopram in the Treatment of Late-Life Anxiety Disorders: Results From an 8-Week Randomized, Placebo-Controlled Trial





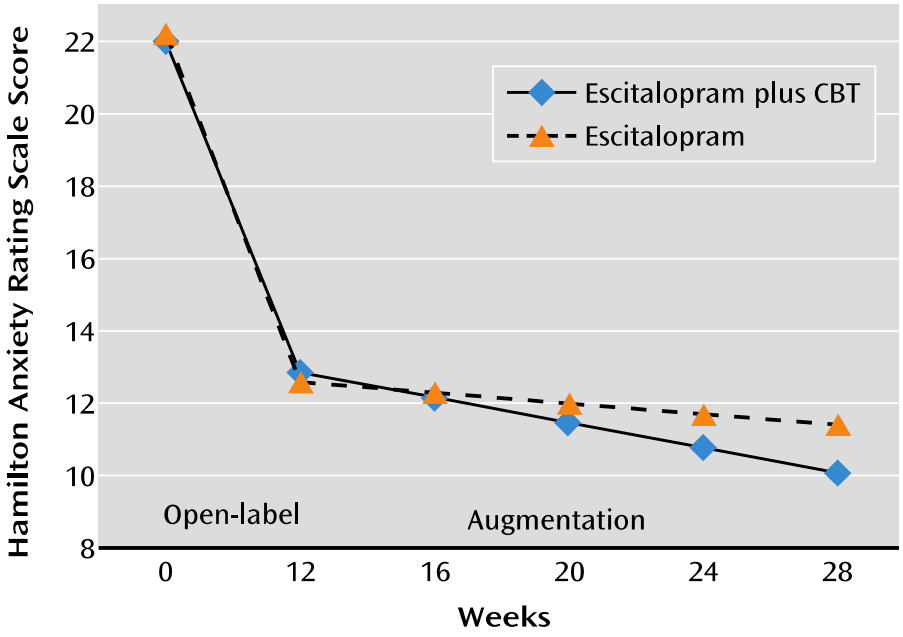
Lenze et al., Am J Psychiatry 2005;162:146-50

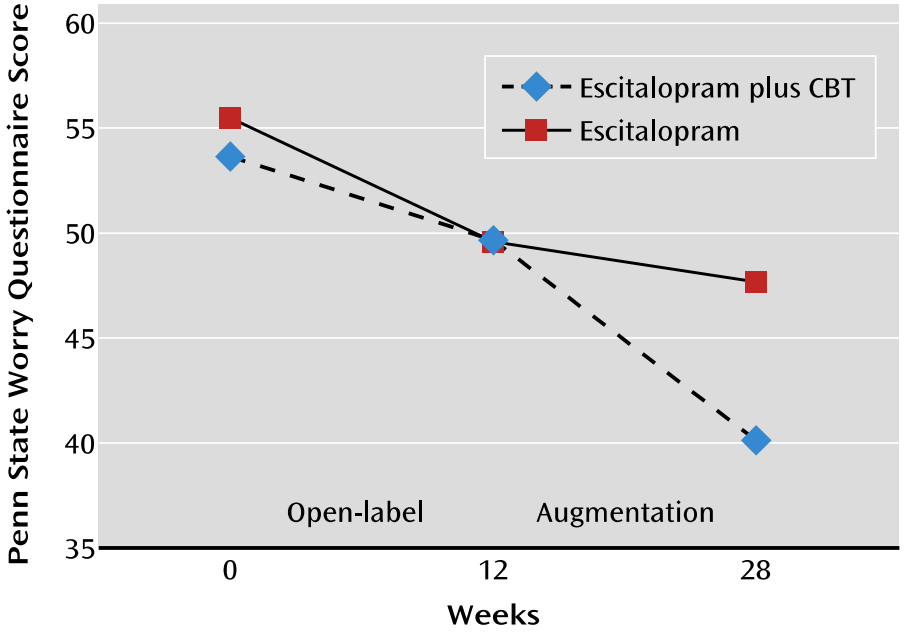
Effectiveness of Cognitive–Behavioral Therapy and Sertraline versus a Waitlist Control Group for Anxiety Disorders in Older Adults



Schuurmans et al., Am J Geriatr Psychiatry 2006;14:255–63

Antidepressant Medication Augmented With Cognitive-Behavioral Therapy for Generalized Anxiety Disorder in Older Adults

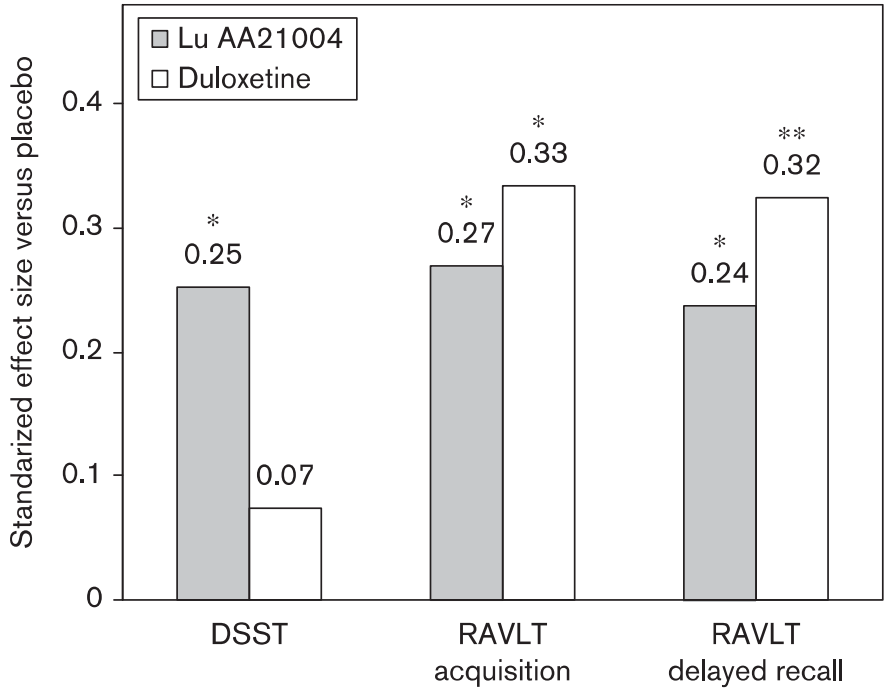




Wetherell et al., Am J Psychiatry 2013;170:782–9

Vortioxetine has specific effects on cognition compared to duloxetine in elderly patients with major depression

	n (%)		
Response/remission criterion	PBO	Lu AA21004	DUL
Response			
HAM-D_{24}[a]	51 (35.2%)	82 (53.2%)**	93 (63.3%)***
MADRS[a]	52 (35.9%)	92 (59.7%)***	104 (70.7%)***
CGI-I $\leq$ 2	55 (38.0%)	95 (61.7%)***	106 (72.1%)***
Remission			
HAM-D_{17} $\leq$ 7	28 (19.3%)	45 (29.2%)*	51 (34.7%)**
MADRS $\leq$ 10	30 (20.7%)	52 (33.8%)*	69 (46.9%)***
CGI-S $\leq$ 2	28 (19.3%)	51 (33.1%)**	60 (40.8%)***



456 patients ≥ 65 yo with Major Depressive Episode

Katona et al., Int Clin Psychopharmacol 2012;27:215-23

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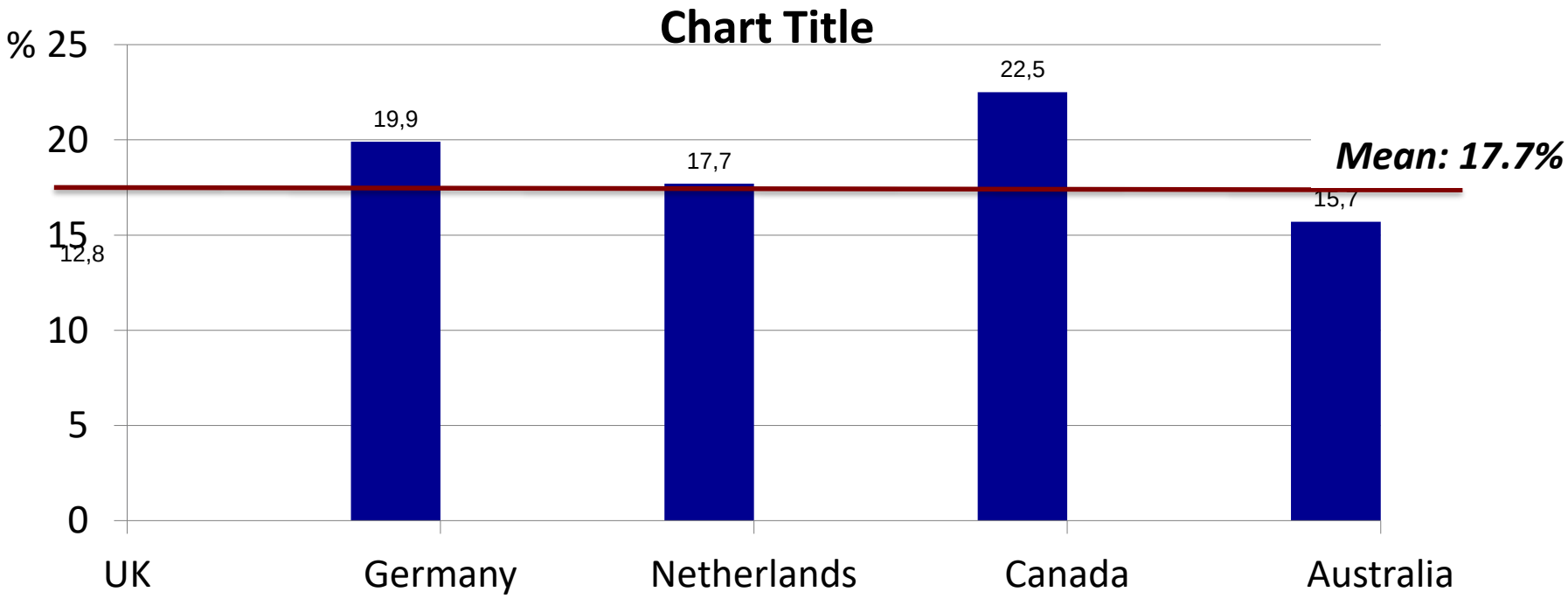
Benzodiazepines in the elderly

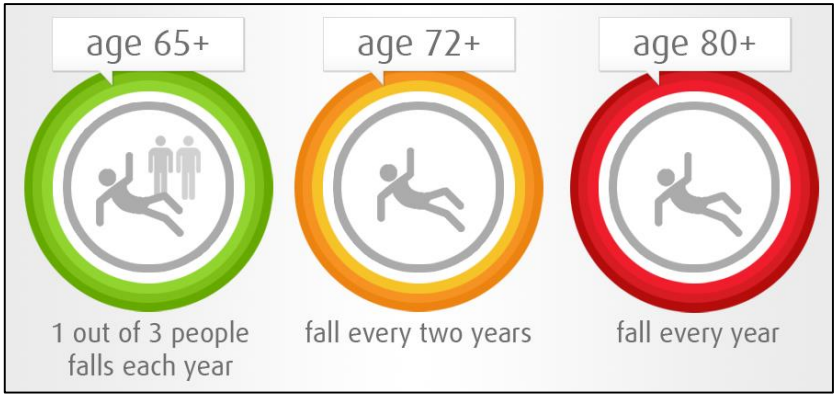
- Insomnia
- Generalized anxiety disorder
- Acute grief reactions

Survey of benzodiazepine usage in elderly population



Dell'Osso and Lader. Eur Psychiatry 2013;28(1):7-20

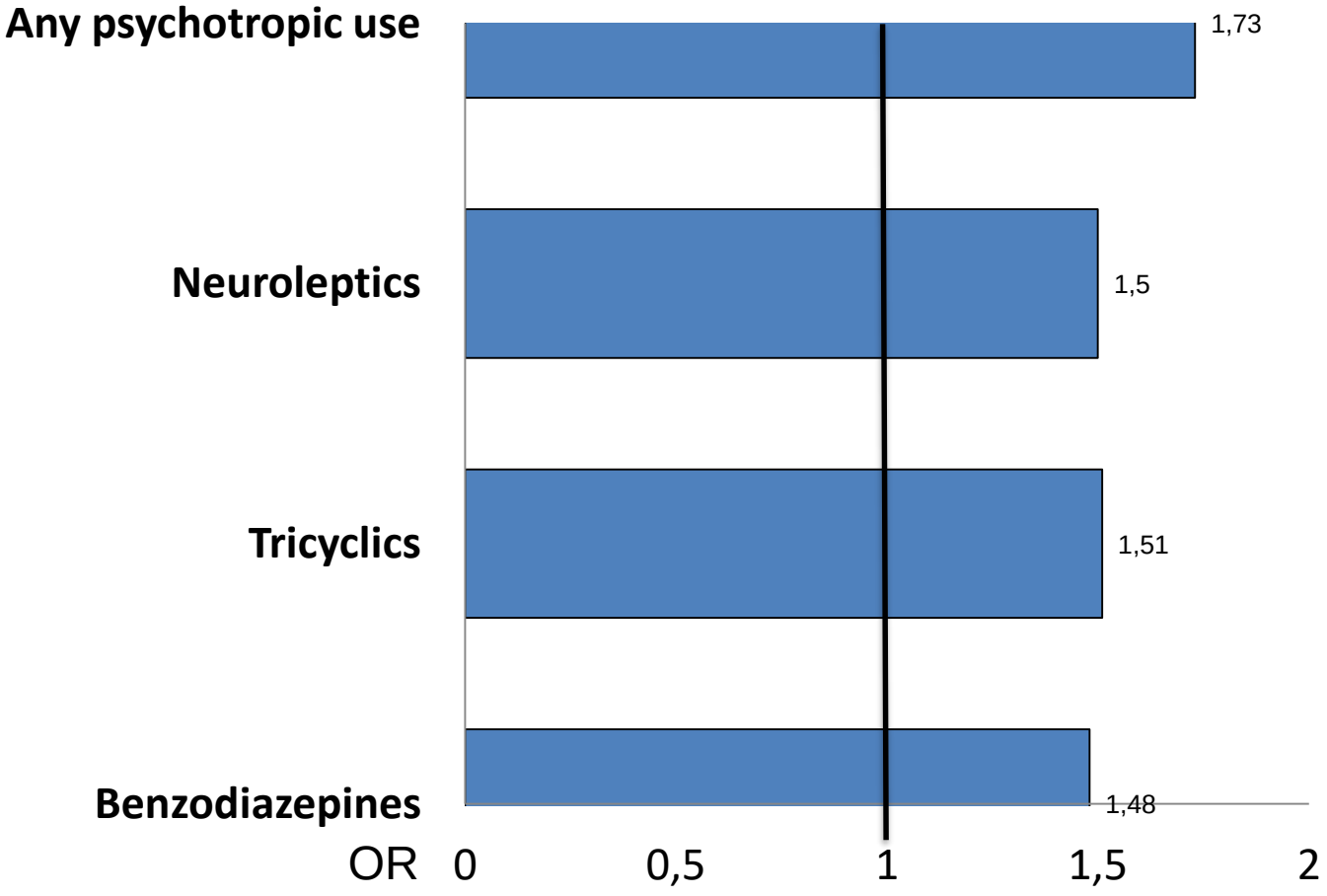
Le cadute nell'anziano



- **40% non ritorna a casa**
- **25% muore entro l'anno dalla caduta**

da: https://goldage.com.au/preventing-falls-elderly/

Drugs and falls in older people: a systematic review and meta-analysis



40 studies, patients >60 years old

Leipzig et al., J Am Ger Soc 1999;47(1):30-9

A 5-year prospective assessment of the risk associated with individual benzodiazepines and doses in elderly users

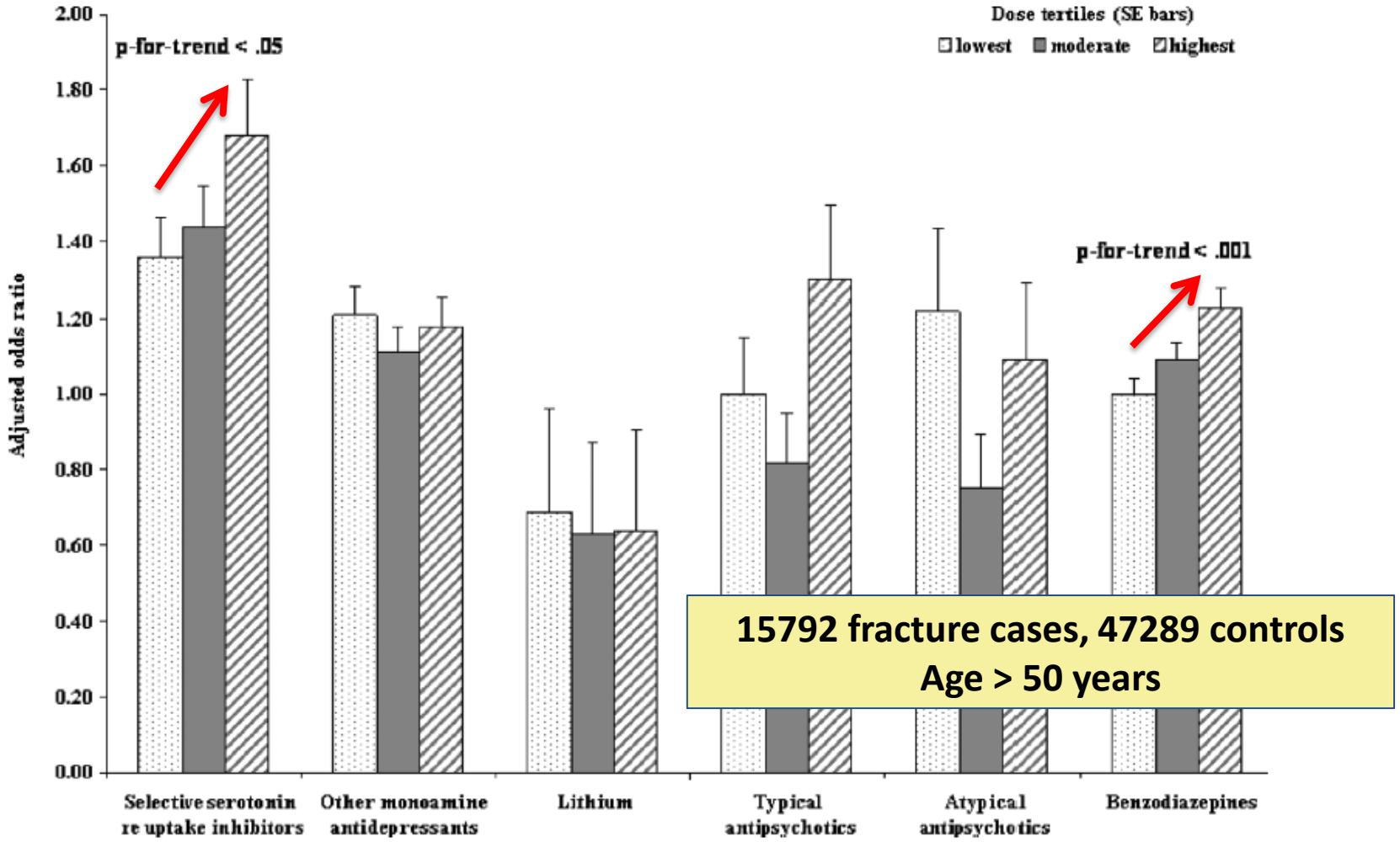
Benzodiazepine Exposure*	WHO-Defined Daily Dose mg† (1)	Mean ± SD‡ (2)	Effect of Current Use Adjusted for Past Use§ (Model 2) (3)	Effect of Current Use Adjusted for Past Use + Dose‖ (Model 3) (4)	Drug-Specific Effect of Current Dose Adjusted for Past Use¶ (Model 4) (5)
Short half-life products					
Triazolam	0.25	0.92 ± 0.38	1.34 (0.95–1.90)	1.31 (0.93–1.85)	1.20 (0.85–1.70)
Temazepam	20	1.04 ± 0.45	1.29 (1.01–1.65)	1.22 (0.94–1.57)	1.23 (1.01–1.51)
Oxazepam	50	0.41 ± 0.25	1.14 (1.01–1.28)	1.19 (1.05–1.35)	1.46 (1.17–1.81)
Intermediate half-life products					
Alprazolam	1	0.54 ± 0.36	1.10 (0.84–1.42)	1.13 (0.87–1.47)	0.92 (0.60–1.42)
Nitrazepam	5	1.29 ± 0.52	1.12 (0.77–1.63)	1.02 (0.69–1.49)	1.06 (0.81–1.38)
Bromazepam	10	0.44 ± 0.26	1.08 (0.81–1.43)	1.14 (0.86–1.52)	1.29 (0.79–2.11)
Lorazepam	2.5	0.49 ± 0.29	1.15 (1.06–1.24)	1.19 (1.09–1.30)	1.29 (1.14–1.46)
Long half-life products					
Chlordiazepoxide	30	0.65 ± 0.51	1.55 (0.83–2.90)	1.55 (0.83–2.90)	2.20 (1.39–3.47)
Flurazepam	30	0.74 ± 0.31	1.61 (1.31–1.99)	1.62 (1.31–1.99)	1.93 (1.53–2.44)
Diazepam	10	0.63 ± 0.45	1.01 (0.77–1.33)	1.03 (0.78–1.36)	1.03 (0.71–1.48)

253244 elderly patients followed-up for 5-years
Mean age 72 years

Tamblyn et al., J Am Ger Soc 2005;53:233-41

Fracture risk from psychotropic medications

a population-based analysis



Bolton et al., J Clin Psychopharmacol 2008;28:384-91

Use of Selective Serotonin Reuptake Inhibitors and Bone Mineral Density Change

A Population-Based Longitudinal Study in Middle-Aged and Elderly Individuals

TABLE 2. Association Between Current SSRI and TCA Use and Mean FN BMD in Men and Postmenopausal Women

	Model 1				Model 2				Model 3‡			
	n*	Mean Difference, g/cm^2	95% CI	$P^\dagger$	n*	Mean Difference, g/cm^2	95% CI	$P^\dagger$	n*	Mean Difference, g/cm^2	95% CI	$P^\dagger$
Men												
Nonuse	8748	Ref			8498	Ref			6287	Ref		
SSRI use	130	−0.001	−0.014 to 0.013	0.922	126	−0.001	−0.014 to 0.013	0.899	111	0.004	−0.012 to 0.020	0.598
TCA use	131	0.008	−0.005 to 0.022	0.205	126	0.010	−0.004 to 0.023	0.149	98	0.002	−0.016 to 0.019	0.848
Women												
Nonuse	10,250	Ref			9719	Ref			6788	Ref		
SSRI use	286	0.007	−0.002 to 0.017	0.123	266	0.005	−0.004 to 0.015	0.294	237	0.007	−0.004 to 0.018	0.209
TCA use	266	0.003	−0.007 to 0.012	0.568	254	0.0003	−0.009 to 0.010	0.947	185	0.005	−0.007 to 0.017	0.427

Model 1: adjusted for age. Model 2: adjusted for age, BMI, MMSE score, hypertension, and age at menopause (in women only). Model 3: adjusted for age, BMI, MMSE score, hypertension, age at menopause (in women only), and presence of depressive symptoms.

10746 elders followed-up for 4-years

Ham et al., J Clin Psychopharmacol 2017;37:524-30

Benzodiazepine Use and Risk of Dementia in the Elderly Population: A Systematic Review and Meta-Analysis

First author, year	Study country	Study period	Study design	Benzodiazepine users/non-users, cases/control	Adjustment
Shash, 2016	France	1999–	Prospective cohort	1,246/5,884	Age, gender, BMI, alcohol consumption, hypertension, cardiac disease, smoking, insomnia, anxiety
Gray, 2016	United states	1994–2003	Prospective cohort	1,018/2,416	Age, gender, obesity, hypertension, diabetics, stroke, heart disease
Imfeld, 2015	United Kingdom	1998–2013	Case–control	9,636/9,636	Age, gender, BMI, smoking status, hypertension, diabetics, dyslipidemia, heart failure, depression, statins, antihypertensives, etc.
Shih, 2015	Taiwan	2006–2010	Case–control	8,406/16,812	Age, gender, hypertension, diabetics, stroke, CAD, hyperlipidemia, depression, anxiety, statin, antihypertensive, psychotics, etc.
Billioti de Gage, 2014	Canada	2000–2009	Case–control	1,796/7,184	Age, gender, stroke, high blood pressure, myocardial infarction, diabetics, hypercholesterolemia, platelets inhibitors, anxiety, depression, insomnia
Billioti de Gage, 2012	France	1988–2006	Prospective cohort	95/968	Age, gender, high blood pressure, diabetics, statin users, platelet inhibitors
Wu, 2011	Taiwan	1997–2007	Nested case–control	8,434/16,706	Age, gender, diabetics, cardiac disease, epilepsy, dyslipidemia, alcoholism, hypertension, insomnia
Gallacher, 2012	United Kingdom	1983–2004	Prospective cohort	103/1,085	Age, gender, smoking, alcohol, BMI, anxiety, depression
Wu, 2009	Taiwan	1997–2004	Nested case–control	779/4,626	Age, gender, hypertension, diabetics, dyslipidemia, cardiac disease, anxiety, mood disorder, psychotic disorder
Lagnaoui, 2002	France	1989–1997	Case–control	150/3,519	Age, gender, depression symptoms, living status, alcohol consumption

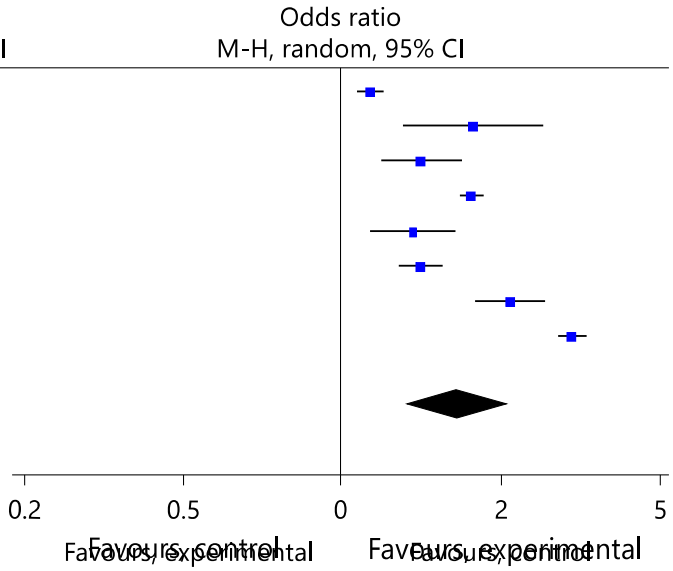
Islam et al., Neuroepidemiology 2016;47:181-91

Benzodiazepine Use and Risk of Dementia in the Elderly Population: A Systematic Review and Meta-Analysis

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M-H, random, 95% CI
Imfeld, 2015	2,872	9,636	2,576	9,636	13.0%	1.16 [1.09, 1.24]
Lagnaoui, 2002	97	150	1,714	3,519	11.1%	1.93 [1.37, 2.71]
Shash, 2016	151	1,246	496	5,884	12.3%	1.50 [1.23, 1.82]
Shih, 2015	3,682	8,406	4,870	16,812	13.0%	1.91 [1.81, 2.02]
Billioti de Gage, 2012	233	467	741	1,810	12.3%	1.44 [1.17, 1.76]
Billioti de Gage, 2014	894	1,796	2,873	7,184	12.8%	1.49 [1.34, 1.65]
Wu, 2009	267	779	852	4626	12.5%	2.31 [1.96, 2.73]
Wu, 2011	3,113	8,434	2,628	16,706	13.0%	3.13 [2.95, 3.33]
Total (95% CI)		30,914		66,177	100.0%	1.78 [1.33, 2.38]
Total events	11,309		16,750			

Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 534.13$, df = 7 ($p < 0.00001$); $I^2 = 99\%$

Test for overall effect: Z = 3.84 ($p = 0.0001$)

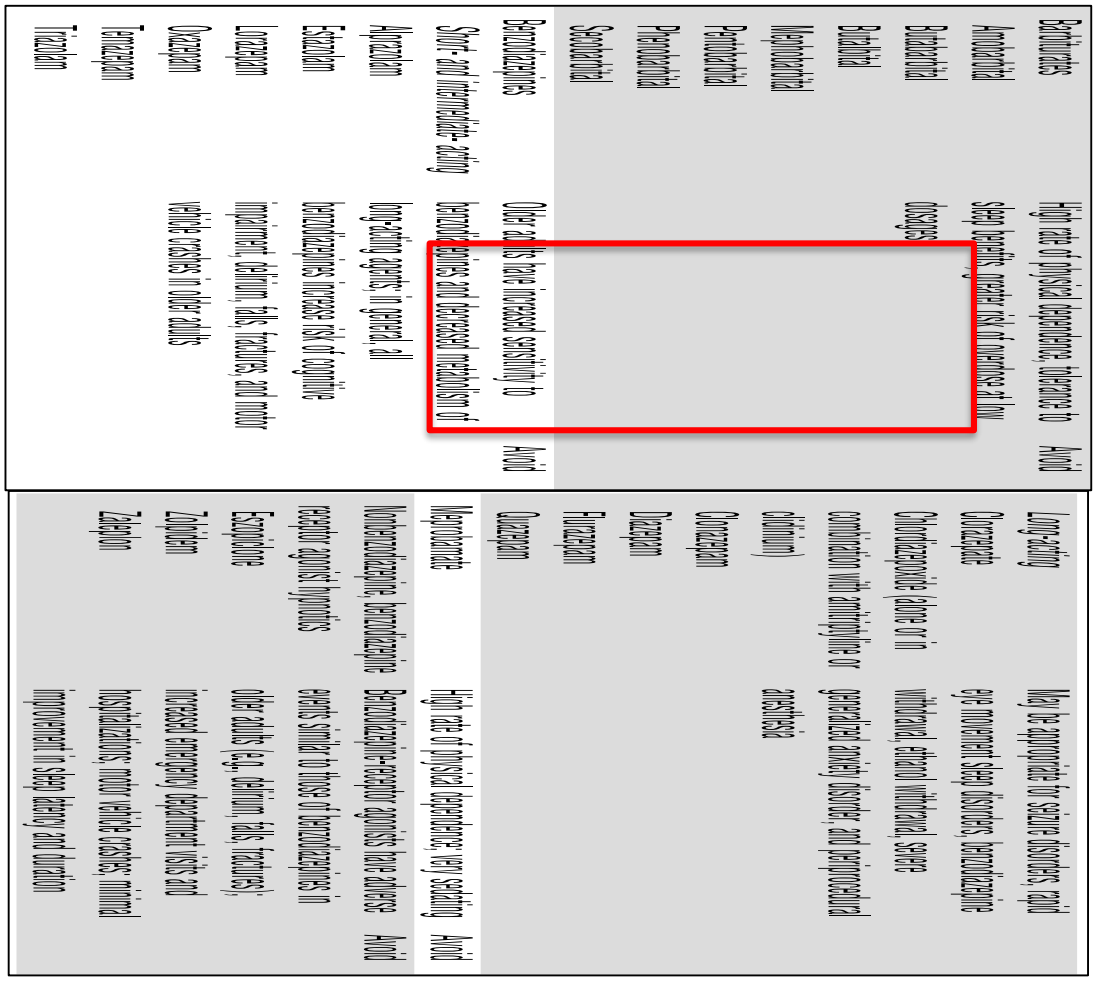


Random-effects meta-analysis of studies of risk of dementia in patients receiving benzodiazepines

OR=1.78

Islam et al., Neuroepidemiology 2016;47:181-91

American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults



American Geriatrics Society Expert Panel. J Am Geriatr Soc. 2015;63(11):2227-46

Conclusioni

- I disturbi d'ansia sono frequenti nella terza età, con una tendenza a ridursi nel grande anziano
- Vanno trattati per ridurre il rischio di evoluzione a **depressione** e **demenze**
- I farmaci più indicati sono gli SSRI, in particolare **citalopram**, **escitalopram**, **sertralina**
- Le benzodiazepine andrebbero evitate per il rischio di cadute e deterioramento cognitivo

Grazie per l’attenzione

claudio.mencacci@gmail.com