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PALAZZO DEI CONGRESSI

L'insonnia: la patologia delle 24 ore

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Fondazione IRCCS San Gerardo dei Tintori
Quocumque modo faciemus
Sistema Socio Sanitario
Regione Lombardia
UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA
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1998 | 2023

My talk today

- Epidemiologia
- Insonnia e patologie
- Insonnia e farmaci
- Conclusioni

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Diagnostic criteria for chronic ID according to ICSD-3 (AASM, 2014)

A. The patient reports, or the patient's parent or caregiver observes, one or more of the following:
   1. Difficulty initiating sleep; 2. Difficulty maintaining sleep; 3. Waking up earlier than desired; 4. Resistance to going to bed on appropriate schedule; 5. Difficulty sleeping without parent or caregiver intervention.

B. The patient reports, or the patient's parent or caregiver observes, one or more of the following related to the night-time sleep difficulty:
   1. Fatigue/malaise; 2. Attention, concentration or memory impairment; 3. Impaired social, family, occupational or academic performance; 4. Mood disturbance/irritability; 5. Daytime sleepiness; 6. Behavioural problems (e.g. hyperactivity, impulsivity, aggression); 7. Reduced motivation/energy /initiative; 8. Proneness for errors/accidents; 9. Concerns about or dissatisfaction with sleep.

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Diagnostic criteria for chronic ID according to ICSD-3 (AASM, 2014)

C. The reported sleep/wake complaints cannot be explained purely by inadequate opportunity (i.e. enough time is allotted for sleep) or inadequate circumstances (i.e. the environment is safe, dark, quiet and comfortable) for sleep.

D. The sleep disturbance and associated daytime symptoms occur at least three times per week.

E. The sleep disturbance and associated daytime symptoms have been present for at least 3 months.

F. The sleep/wake difficulty is not better explained by another sleep disorder.

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F. The sleep/wake difficulty is not better explained by another sleep disorder.

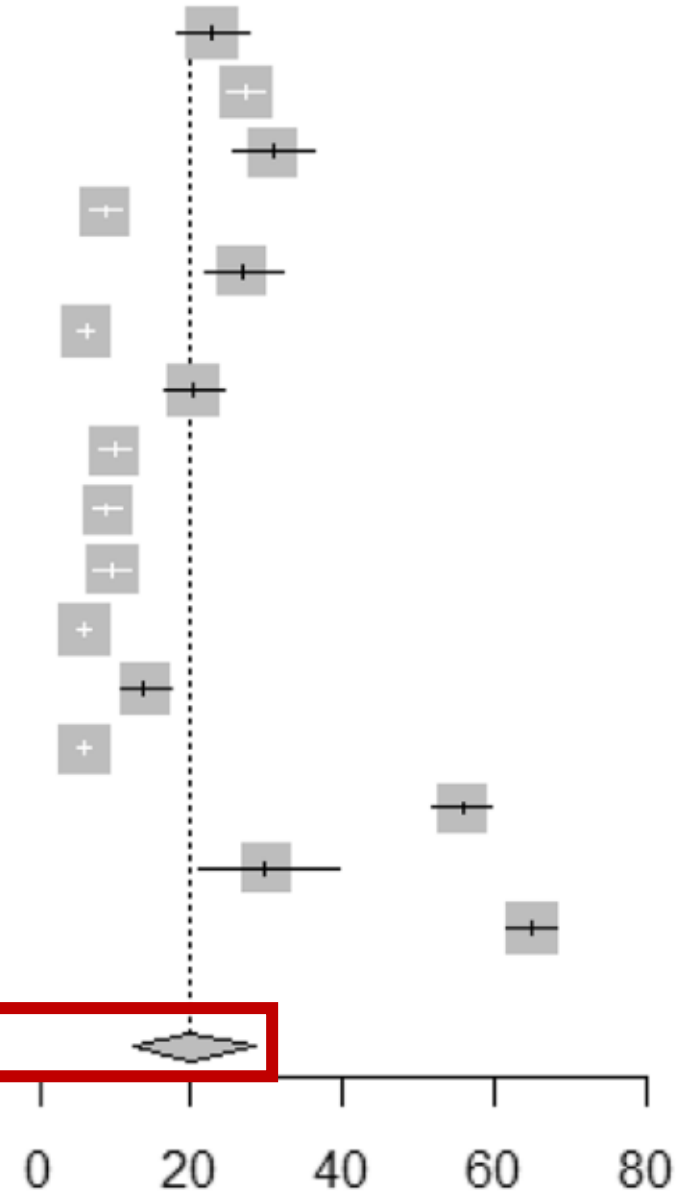
Epidemiology of insomnia disorder in older persons according to the Diagnostic and Statistical Manual of Mental Disorders: a systematic review and meta-analysis

Francky Teddy Endomba[1,2] · Patrick Yvan Tchebegna[3] · Edmond Chiabi[4] · Dominic Leandry Angong Wouna[4] · Clément Guillet[5] · Jean Christophe Chauvet-Gélinier[6,7]

Systematic review and meta-analysis of 16 studies (18,270 participants) published before June 2023.
The male/female ratio was 0.89 (12 studies), and the mean age varied from 65.9 to 83.1 years (8 studies)

European Geriatric Medicine, 2023

Study	Cases	Total	Prevalence,%	[95% CI]	Weight
Hohagen,1994	75	330	22.7	[18.3; 27.6]	6.2%
Roberts,2000	407	1497	27.2	[24.9; 29.5]	6.3%
Redondo-Martínez,2000	95	309	30.7	[25.6; 36.2]	6.2%
Ohayon (b),2001	63	728	8.7	[6.7; 10.9]	6.3%
Ohayon (a),2002	84	314	26.8	[21.9; 32.0]	6.2%
Voyer,2006	144	2324	6.2	[5.3; 7.3]	6.3%
Boix Gras,2009	86	424	20.3	[16.6; 24.4]	6.2%
Ohayon (c),2010	71	723	9.8	[7.7; 12.2]	6.3%
López-Torres Hidalgo,2011	83	926	9.0	[7.2; 11.0]	6.3%
Morin,2011	56	585	9.6	[7.3; 12.3]	6.3%
Chen,2013	240	4064	5.9	[5.2; 6.7]	6.3%
Benbir,2015	58	418	13.9	[10.7; 17.6]	6.2%
Chiou,2016	238	4047	5.9	[5.2; 6.7]	6.3%
Zou,2019	333	597	55.8	[51.7; 59.8]	6.3%
Boyle,2020	31	104	29.8	[21.2; 39.6]	6.0%
Sanjay,2022	571	880	64.9	[61.6; 68.0]	6.3%
Pooled Prevalence		**18270**	**19.6**	**[12.3; 28.3]**	**100.0%**



Endomba et al, European Geriatric Medicine, 2023

Sleep Quality and Factors Influencing Self-Reported Sleep Duration and Quality in the General Internal Medicine Inpatient Population

Selina Dobing[1], Natalia Frolova[2], Finlay McAlister[2], Jennifer Ringrose[2]*

- Patients reported **significantly worse nighttime sleep duration in hospital** compared with home (mean 5.5 versus 7.0 hours per night, $p < 0.0001$). **Sleep quality was poor**, as measured by the VSH disturbance, effectiveness, and supplementation subscales.
- The most frequently reported **reasons for poor sleep included noise (59%), nursing interruptions (30%), uncomfortable beds (18%), bright lights (16%), unfamiliar surroundings (14%), and pain (9%).**

PLOS ONE | DOI:10.1371/journal.pone.0156735 June 9, 2016

My talk today

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Insomnia and the Risk of Acute Myocardial Infarction

A Population Study

Lars E. Laugsand, MD; Lars J. Vatten, MD, PhD; Carl Platou, MD; Imre Janszky, MD, PhD

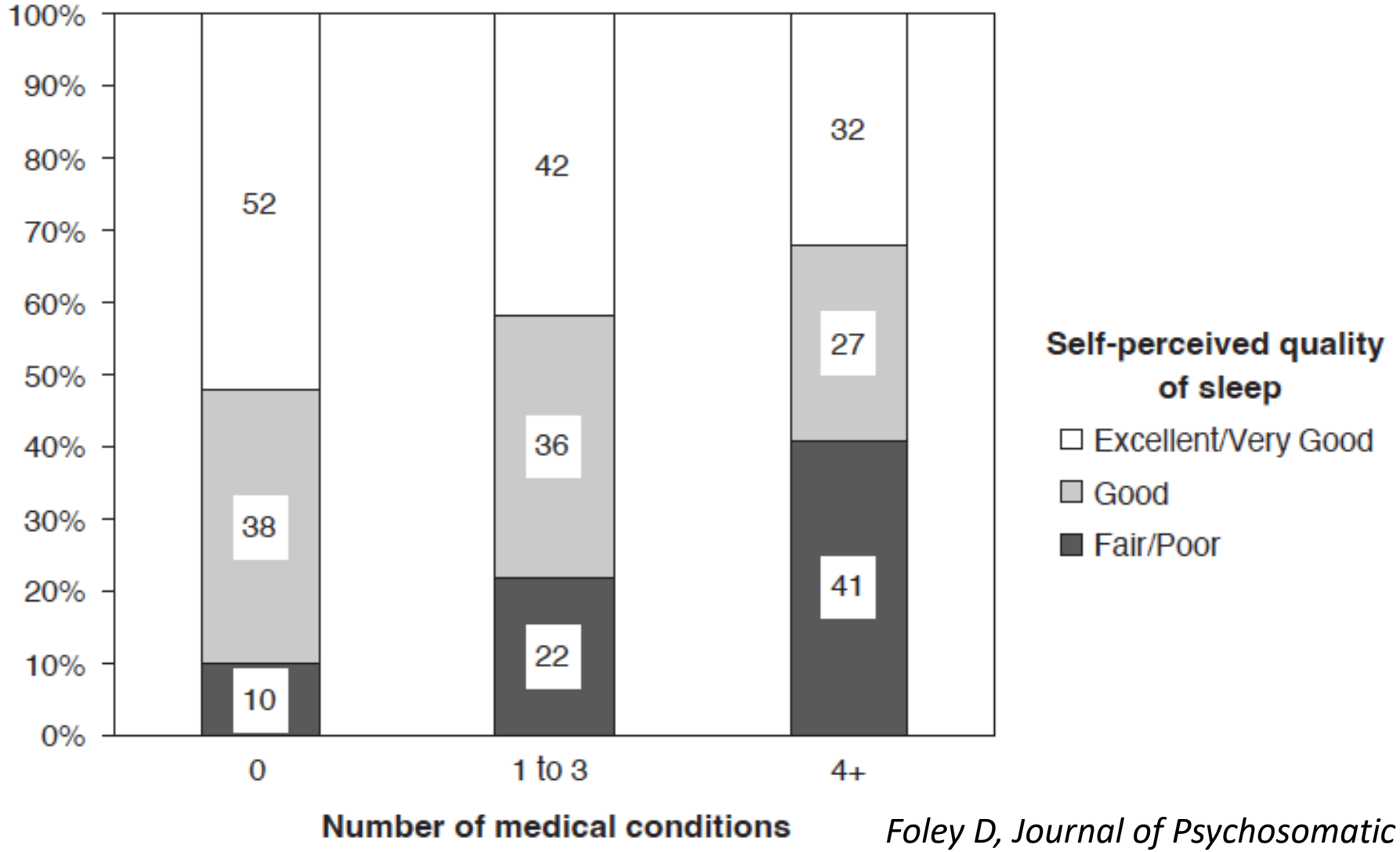
Table 3. HRs (95% CIs) for AMI According to Number of Insomnia Symptoms

	Events/Person-Time	Model 1	Model 2	Model 3	Model 4	Model 5
No. of symptoms						
0	997/463131	Reference	Reference	Reference	Reference	Reference
1	212/37710	1.24 (1.00–1.54)	1.28 (1.03–1.59)	1.19 (0.94–1.50)	1.19 (0.94–1.51)	1.30 (1.02–1.65)
2	81/12727	1.47 (1.07–2.02)	1.44 (1.04–2.00)	1.39 (0.98–1.97)	1.34 (0.94–1.93)	1.47 (1.02–2.13)
3	13/2417	1.92 (1.11–3.33)	1.73 (0.98–3.06)	1.89 (1.04–3.44)	1.73 (0.92–3.25)	2.12 (1.13–4.00)
HR for each symptom increase		1.24 (1.11–1.38)	1.22 (1.10–1.37)	1.20 (1.06–1.35)	1.18 (1.04–1.34)	1.25 (1.08–1.45)
P for trend		<0.0001	<0.001	0.003	0.011	0.001

HR indicates hazard ratio; CI, confidence interval; and AMI, acute myocardial infarction.

Circulation 2011

Sleep disturbances and chronic disease in older adults
Results of the 2003 National Sleep Foundation *Sleep in America* Survey



Foley D, Journal of Psychosomatic Research 2004

Sleep disturbances and chronic disease in older adults
Results of the 2003 National Sleep Foundation *Sleep in America* Survey

Odds ratios[a] for symptoms of insomnia according to major medical conditions: 2003 National Sleep Foundation Survey

Medical condition	Insomnia symptom (%) Difficulty falling asleep (9%), OR (95% CI)	Awake a lot during the night (22%), OR (95% CI)	Wake too early (11%), OR (95% CI)	Wake unrefreshed (14%), OR (95% CI)
Obesity	NS	1.36 (1.02–1.82)	NS	1.45 (1.04–2.03)
Bodily pain	1.89 (1.28–2.78)	2.68 (2.06–3.49)	1.88 (1.32–2.66)	2.11 (1.54–2.90)
Depression	2.44 (1.59–3.73)	1.59(1.14–2.22)	2.21 (1.49–3.29)	2.18 (1.53–3.13)
Heart disease	1.99 (1.29–3.07)	1.67 (1.23–2.31)	1.87 (1.27–2.78)	NS
Arthritis	NS	NS	NS	NS
Diabetes	NS	NS	NS	NS
Stroke	NS	NS	NS	NS
Lung disease	NS	NS	NS	1.50 (1.01–2.24)
Osteoporosis	NS	NS	NS	NS
Memory problems	1.76 (1.08–2.87)	1.56 (1.07–2.27)	NS	NS

[a] Each column is logistic regression model ($N = 1506$) that includes age, gender and diagnosis of a sleep disorder followed by a stepwise entry of significantly associated medical conditions.

Foley D, Journal of Psychosomatic Research 2004

Connections between sleep and cognition in older adults

Kristine Yaffe, Cherie M Falvey, Tina Hoang

Lancet Neurol 2014; 13: 1017–28

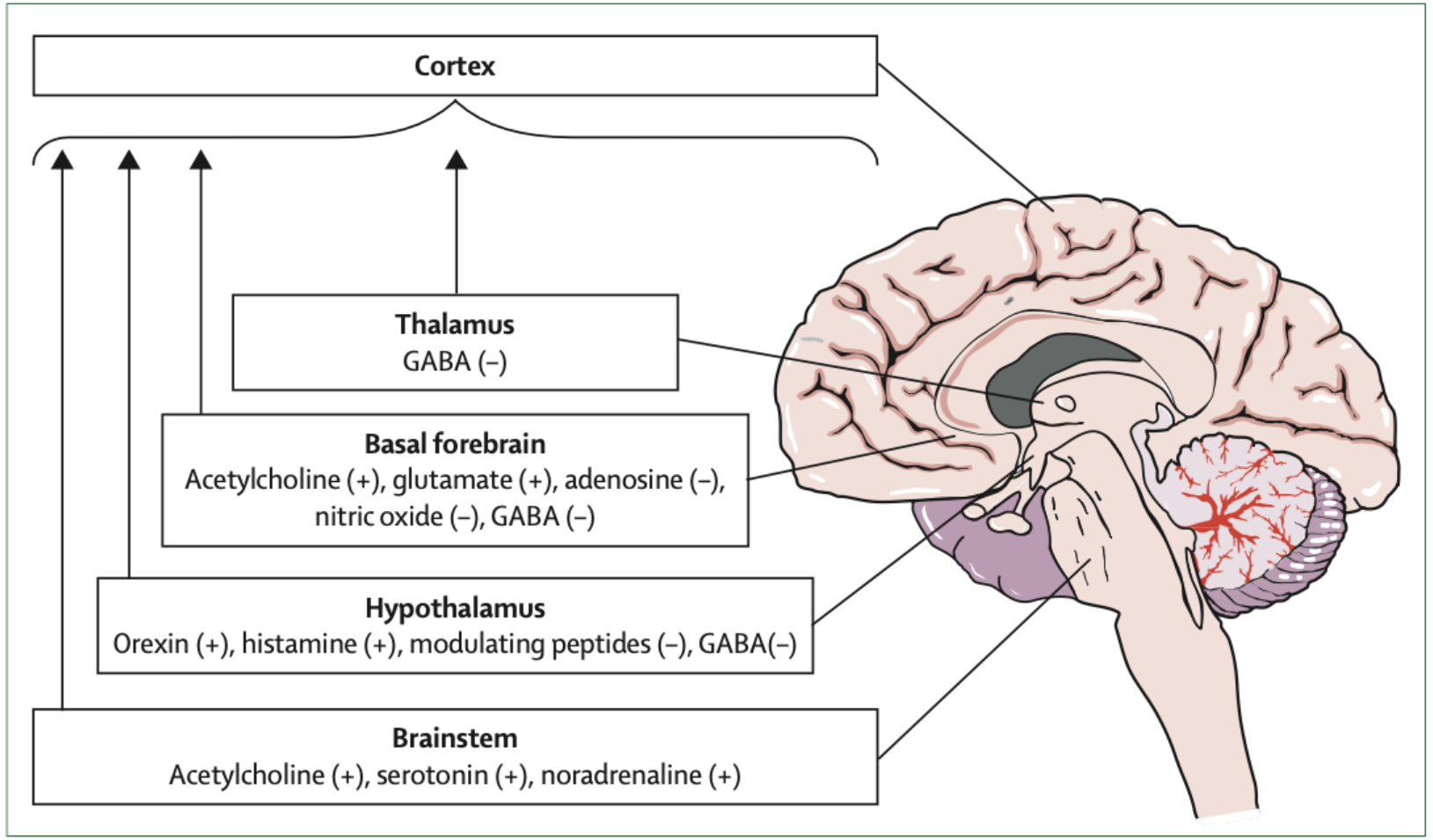


Figure 1: **Brain regions and neurotransmitter systems involved in sleep regulation**

Panel: **Prevalent sleep disturbances in people with dementia**

Alzheimer's disease

- Circadian rhythm dysfunction:
  - Fragmented nocturnal sleep
  - Excessive daytime sleepiness
  - Phase delay in activity rhythms
  - Amplitude of melatonin rhythms
  - Sundowning
- Changes in sleep architecture:
  - Wake after sleep onset
  - Latency to onset of first rapid eye movement episode
  - Total sleep time
  - Sleep efficiency
  - Rapid eye movement and slow wave sleep
  - Indeterminate non-rapid eye movement sleep patterns
- Sleep-disordered breathing

Dementia with Lewy bodies

- Rapid eye movement behavioural sleep disorder
- Hypersomnia
- Periodic limb movements in sleep

Vascular dementia

- Sleep-disordered breathing

Frontotemporal dementia

Few studies have reported on sleep disorders in those with frontotemporal dementia; however, there is some evidence to suggest that patients might have a phase advance or an increased prevalence of excessive daytime sleepiness

	Sample	Sleep measure	Cognitive measure	Results
Cross-sectional studies				
Merlino et al, 2010[25]	750 adults aged ≥65 years	Insomnia was determined by interview and defined as reporting ≥1 insomnia symptoms ≥3 times per week	Cognition was measured with the MMSE; those with score <24 or with clinical signs of dementia were assessed by a panel of experts to diagnose dementia (DSM-IV criteria)	No association
Retrospective case–control studies				
Chen et al, 2012[26]	34 158 adults aged ≥50 years	Insomnia was determined by ICD-9 codes	Dementia was determined by ICD-9 codes	Participants with insomnia and prescribed hypnotics had a higher risk of dementia (HR 2·34, 95% CI 1·92–2·85); adjusted for cardiovascular risk factors
Prospective studies				
Cricco et al, 2001[27]	6444 adults aged ≥65 years	Insomnia was determined by self-reported questionnaire	Global cognition was measured with the 9-item version of the SPMSQ; cognitive decline was defined as ≥2 errors over follow-up	Chronic insomnia was associated with a greater risk of cognitive decline in men with (OR 1·49, 95% CI 1·03–2·14) and without depression (2·18, 1·30–3·67) and in women with chronic insomnia and depression (1·36, 1·01–1·84), adjusted for baseline SPMSQ, demographics, physical function, vascular disease, health behaviours, and prescription sleep medication
Foley et al, 2001[28]	2346 men aged ≥71 years	Insomnia was determined by self-reported questionnaire	Cognition was measured with CASI; cognitive decline was defined as >9 point drop in CASI score; dementia was assessed by specialist physicians	No association

MMSE=Mini-Mental State Examination. DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. ICD-9=International Classification of Diseases, Ninth Revision. HR=hazard ratio. SPMSQ=Pfeiffer's Short Portable Mental Status Questionnaire. OR=odds ratio. CASI=Cognitive Abilities Screening Instrument.

Table 1: **Observational studies of insomnia and cognitive function in older adults**

Lancet Neurol 2014; 13: 1017–28

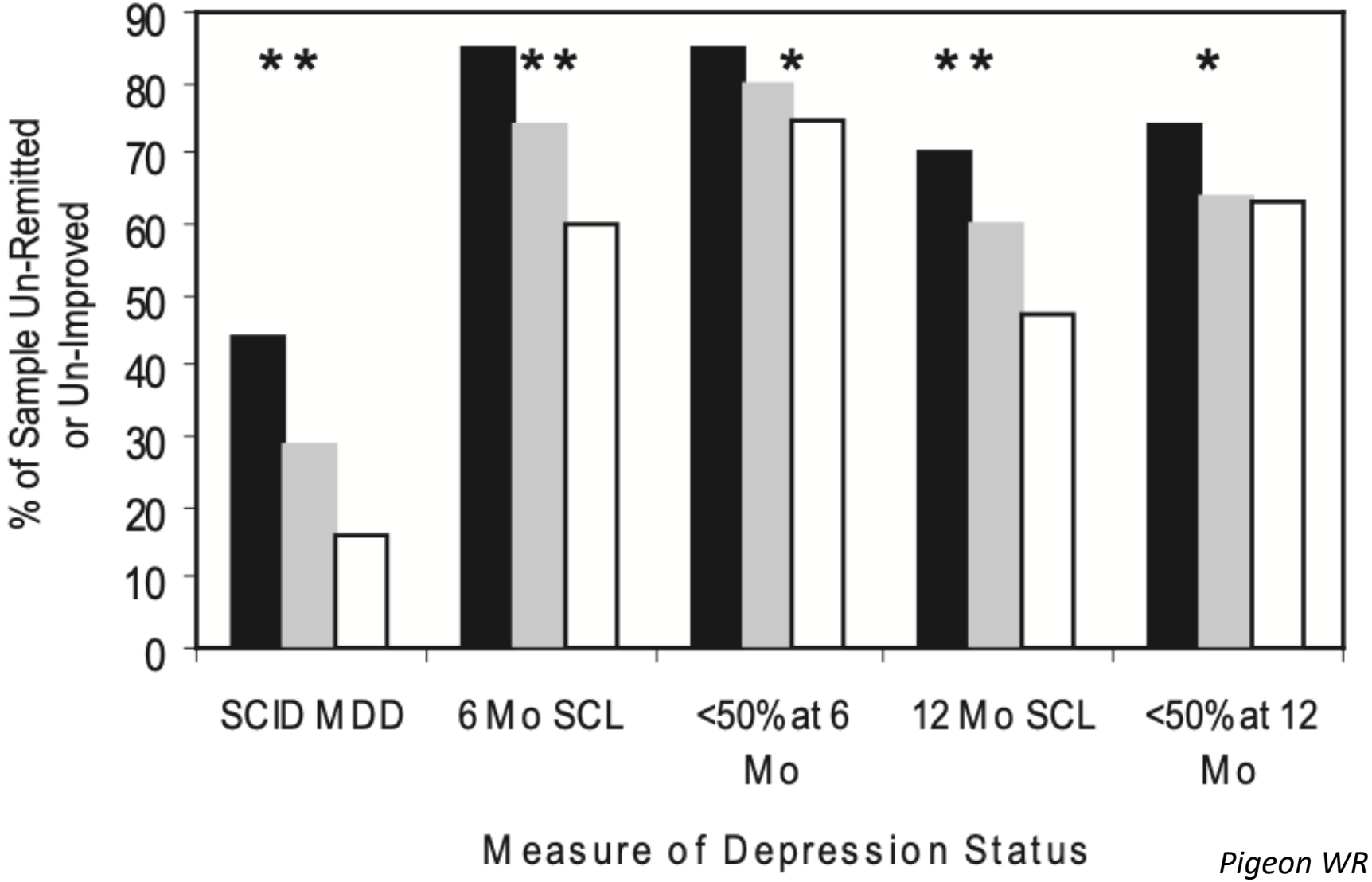
Insomnia and Daytime Sleepiness Are Risk Factors for Depressive Symptoms in the Elderly

	OR*	95% CI*	P**
Component symptoms of insomnia			
Insomnia symptoms			
No	1		0.0144
Yes	1.27	1.05-1.54	
Sleep quality (SQ)			
Good	1		< 0.0001
Average	1.62	1.32-1.98	
Poor	1.71	1.26-2.32	
Difficulty initiating sleep (DIS)			
Never	1		< 0.0001
Rarely	1.05	0.79-1.39	
Frequently	1.65	1.19-2.28	
Often	1.88	1.35-2.62	
Difficulty maintaining sleep (DMS)			
Never	1		< 0.0001
Rarely	1.09	0.67-1.78	
Frequently	1.63	1.01-2.62	
Often	1.92	1.18-3.13	

	OR*	95% CI*	P**
Early morning awakening (EMA)			
Never	1		0.0023
Rarely	1.31	1.01-1.70	
Frequently	1.55	1.14-2.09	
Often	1.58	1.16-2.15	
Number of insomnia symptoms			
0	1		< 0.0001
1	1.00	0.78-1.27	
2	1.56	1.15-2.11	
3-4	1.75	1.28-2.40	
Excessive daytime sleepiness (EDS)			
Never	1		< 0.0001
Rarely	1.29	1.04-1.60	
Frequently	1.74	1.30-2.34	
Often	2.15	1.36-3.38	

Jaussent I et al., SLEEP 2011;34(8):1103-1110.

Dose-Response Relationship of Insomnia Status Across Depression Outcomes

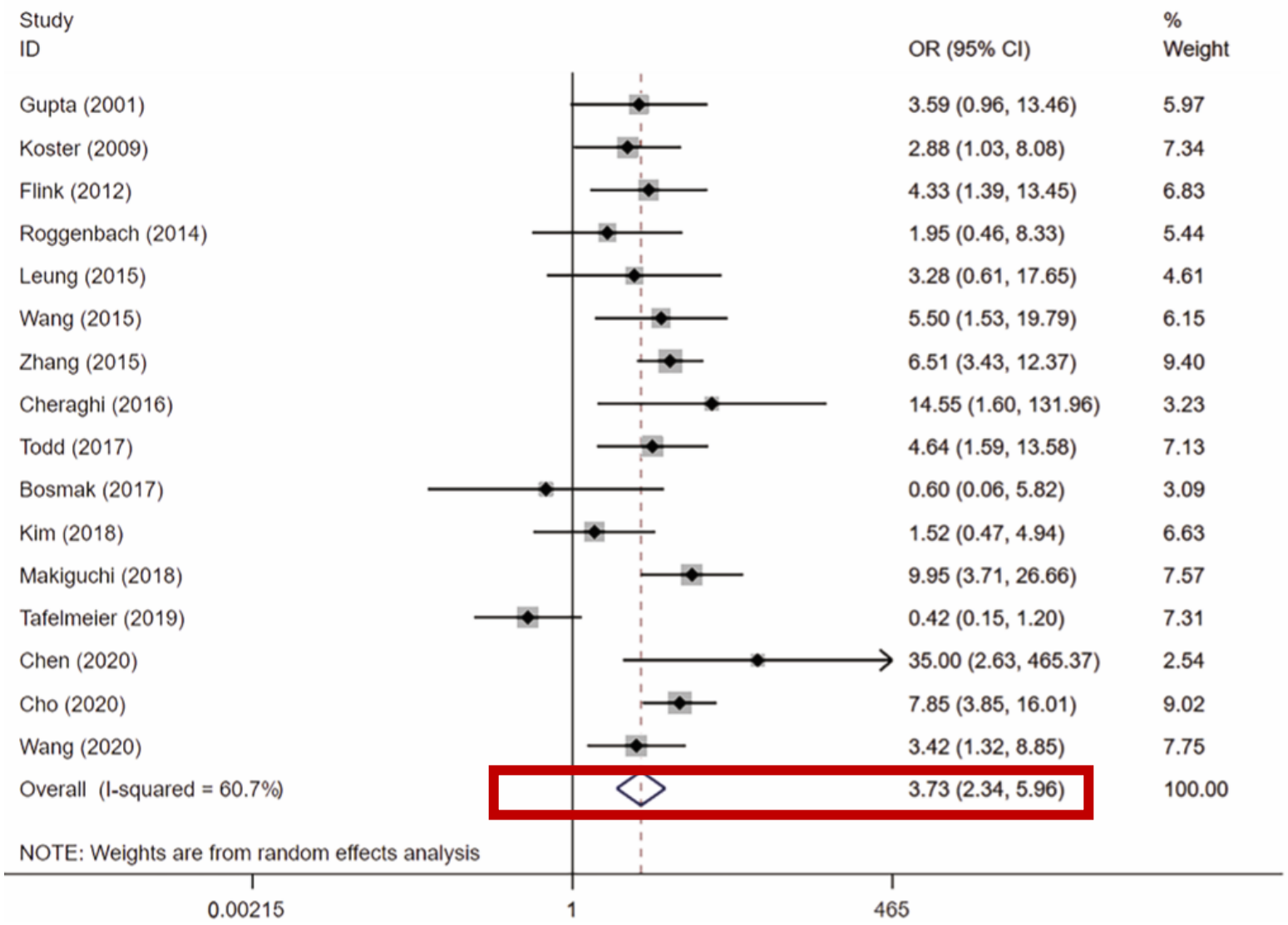


1801 older pts (71 yr mean age) with MDD and/or dyshtymia from 18 primary clinics in 5 US states

Black bars= persistent
Grey bars= intermediate
White bars= no insomnia

Pigeon WR et al., SLEEP 2008;31(4):481-488

Relationship of sleep disturbance and postoperative delirium: a systematic review and meta-analysis

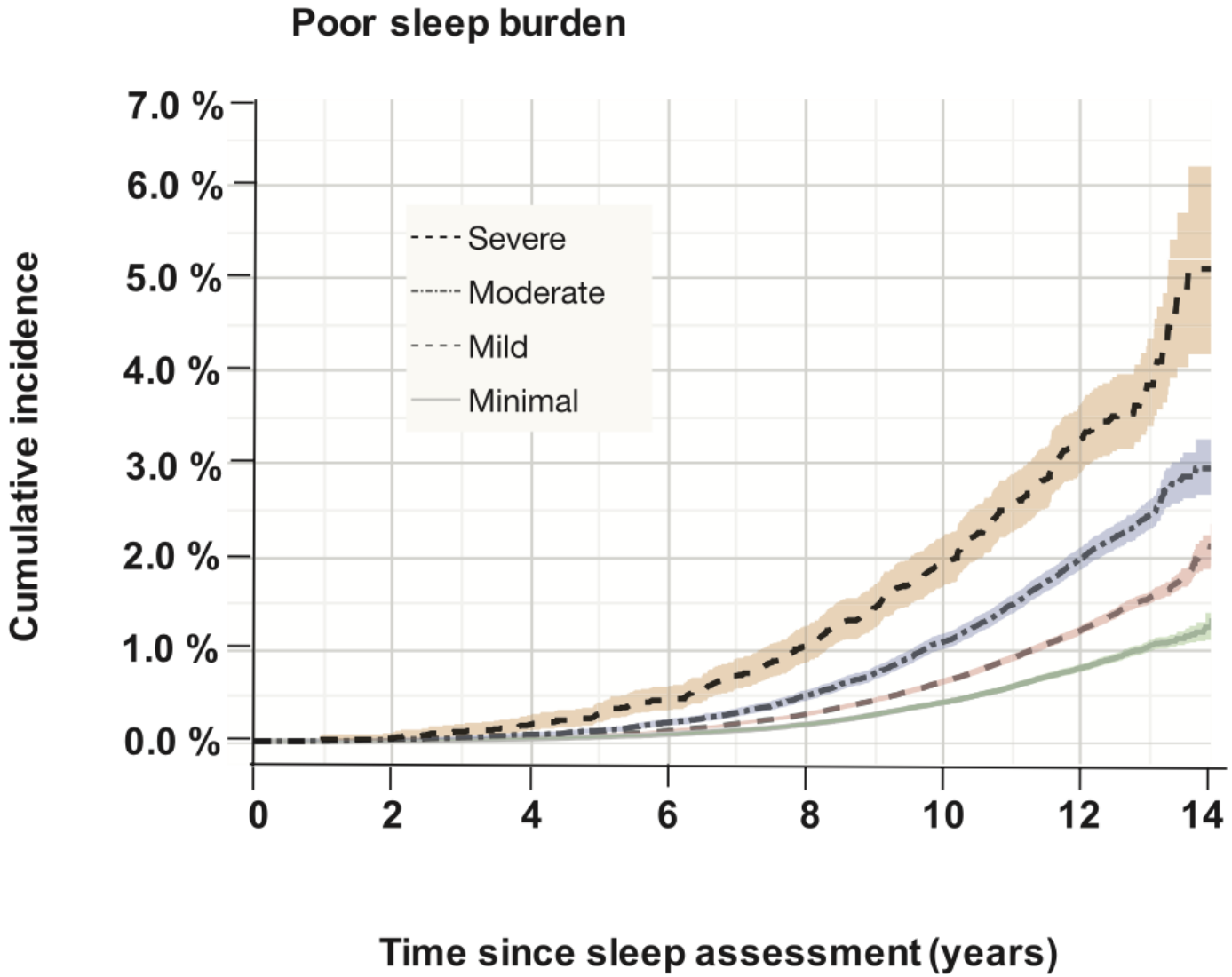


- PubMed, Embase, Cochrane Library, and WOS databases were searched for relevant studies from inception to April 28, 2021
- 18 articles (2,714 patients), (most of the included literature of moderate to high quality)

He E et al, Gland Surg 2022;11(7):1192-1203

Association of Poor Sleep Burden in Middle Age and Older Adults With Risk for Delirium During Hospitalization

321 818 participants from the UK Biobank (mean age 58±8 years; 2006–2010)



Cherrysse Ulsa M et al, JGMS 2022

My talk today

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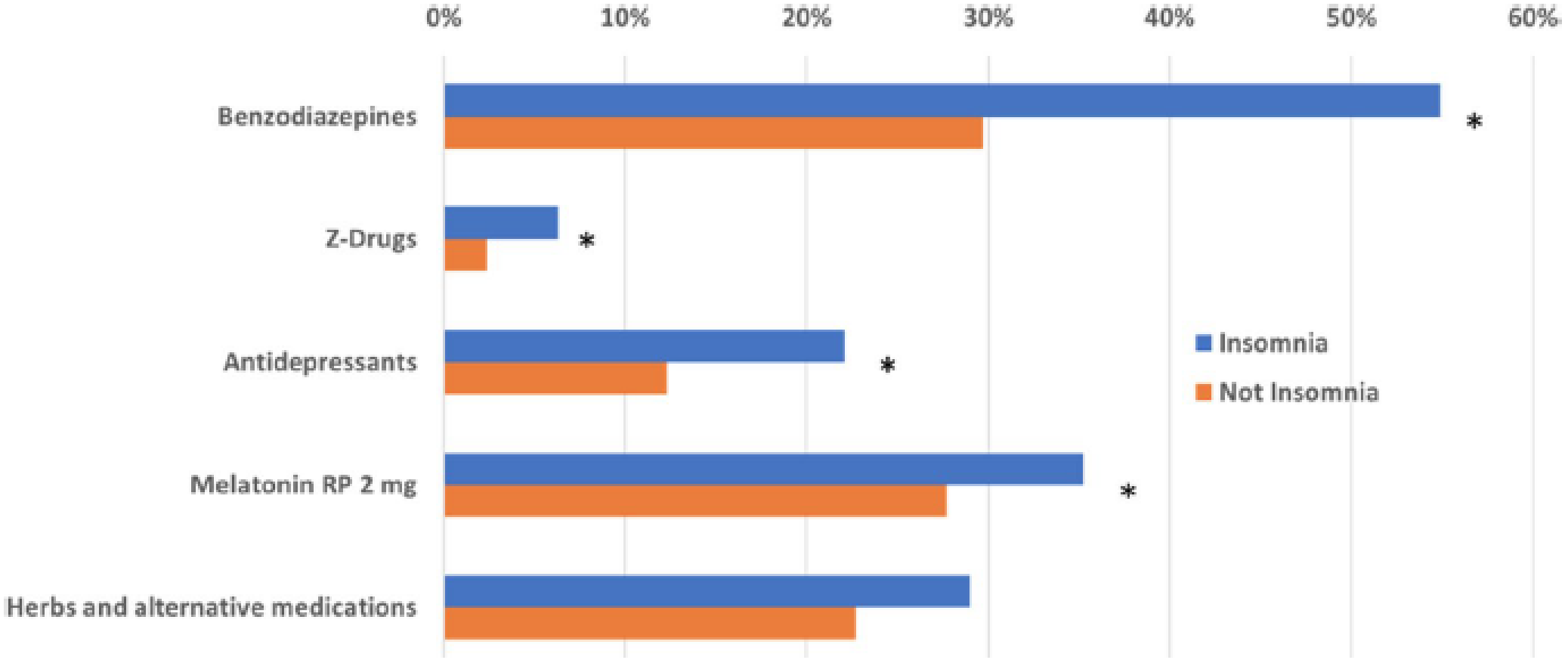
Uso di farmaci psicotropi negli ospedali italiani- Dati dell'Italian Delirium Day

	Total (n=4133)	Delirium 969 (23.4)	No delirium 3164 (76.6)	p
Age, yrs, mean (SD)	81.6 (7.6)	84.4 (7.0)	80.8 (7.6)	<.001
Female, n (%)	2284 (55.2)	540 (55.7)	1774 (55.1)	.73
Medical wards, n (%)	3770 (91.8)	906 (93.5)	2864 (90.5)	.004
Surgical wards, n (%)	363 (8.8)	63 (6.5%)	300 (9.5)	
Charlson Index, mean (SD)	6.4 (2.4)	6.7 (2.4)	6.3 (2.5)	<.001
Dementia, n (%)	977 (23.6)	566 (58.4)	505 (16.0)	.03
Number of drugs, median (SD)	5.3 (2.2)	5.5 (2.2)	5.3 (2.2)	.001
Benzodiazepines	1014 (24.5)	242 (25.0)	772 (24.4)	.071
Typical antipsychotics	335 (8.1)	177 (18.3)	158 (5.0)	<.001
Atypical antipsychotics	310 (7.5)	177 (18.3)	133 (4.2)	<.001

Aloisi G et al, J Clin Psych, 2019. doi: 10.4088/JCP.18m12430.

Disturbi del sonno e farmaci

748 patients (mean age 65.12 ± 9.45 years) enrolled by 149 GPs. Sleep Condition Indicator (SCI) and a visual analogic scale (VAS) used to evaluate daytime sleepiness.



Proserpio P, et al. Neurol Sci. 2022 Nov;43(11):6487-6494

Association between benzodiazepines use and risk of hip fracture in the elderly people: A meta-analysis of observational studies

Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Bakken-2014	1.200	1.104	1.305	4.278	0.000	18.66
Chang-2008	1.000	0.400	2.500	0.000	1.000	0.43
Cummings-1995.	1.200	0.688	2.093	0.642	0.521	1.15
Golden-2010.	1.330	1.146	1.544	3.745	0.000	10.53
Herings-1995	1.300	0.702	2.407	0.835	0.404	0.94
Perreault-2008	1.020	0.872	1.193	0.248	0.804	9.89
Ray-1989.	1.100	0.898	1.347	0.921	0.357	6.85
Sgadari-2000	1.100	1.004	1.205	2.049	0.040	17.48
Wagner-2004	1.130	0.822	1.554	0.752	0.452	3.24
Wang-2001	1.300	1.163	1.453	4.609	0.000	14.62
Zint-2010	1.050	0.950	1.160	0.958	0.338	16.21
Random model:	1.155	1.087	1.227	4.643	0.000	

Heterogeneity (I^2): 37.76, **Q** = 16.06, **tau-squared** = 0.003

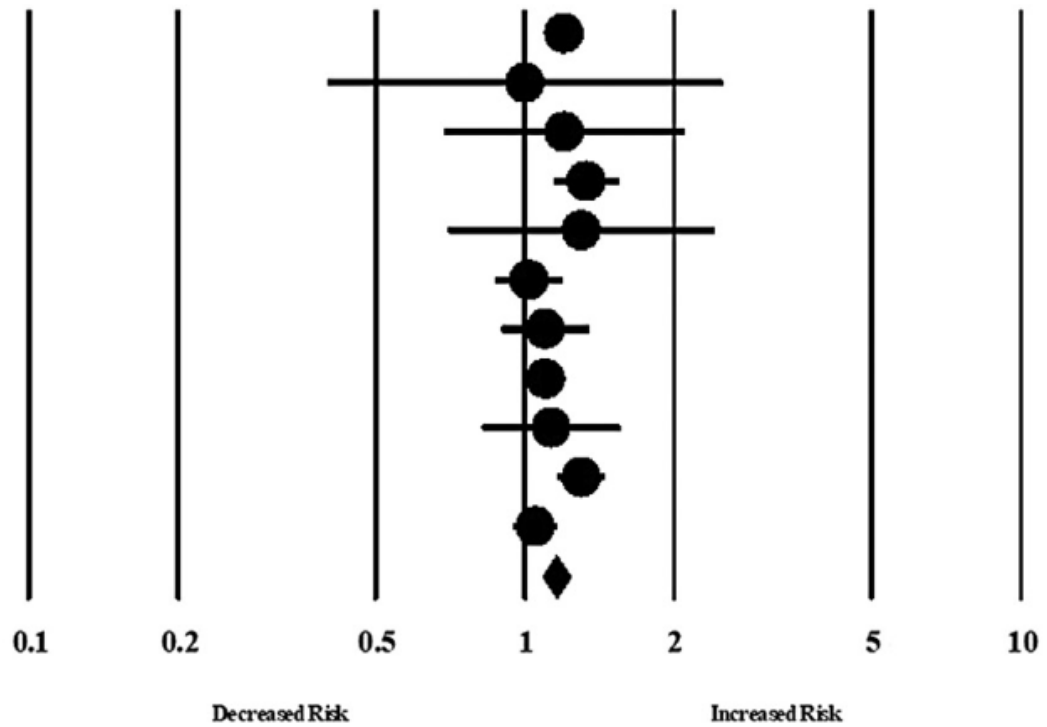


Fig. 3. Long-acting BDZs use and hip fracture risk.

Association between benzodiazepines use and risk of hip fracture in the elderly people: A meta-analysis of observational studies

Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Bakken-2014	1.500	1.403	1.604	11.903	0.000	14.79
Chang-2008	1.800	1.283	2.526	3.400	0.001	5.78
Cummings-1995.	1.200	0.688	2.093	0.642	0.521	2.79
Golden-2010.	1.330	1.146	1.544	3.745	0.000	11.82
Herings-1995	1.500	1.112	2.023	2.659	0.008	6.73
Ray-1989.	1.100	0.898	1.347	0.921	0.357	9.75
Sgadari-2000	1.100	1.004	1.205	2.049	0.040	14.03
Wagner-2004	1.270	1.012	1.593	2.065	0.039	8.89
Wang-2001	1.500	1.240	1.815	4.174	0.000	10.21
Zint-2010	1.190	1.131	1.252	6.756	0.000	15.20
Random effect:	1.312	1.185	1.454	5.204	0.000	

Heterogeneity (I^2): 82.11, Q = 50.31, tau-squared = 0.01

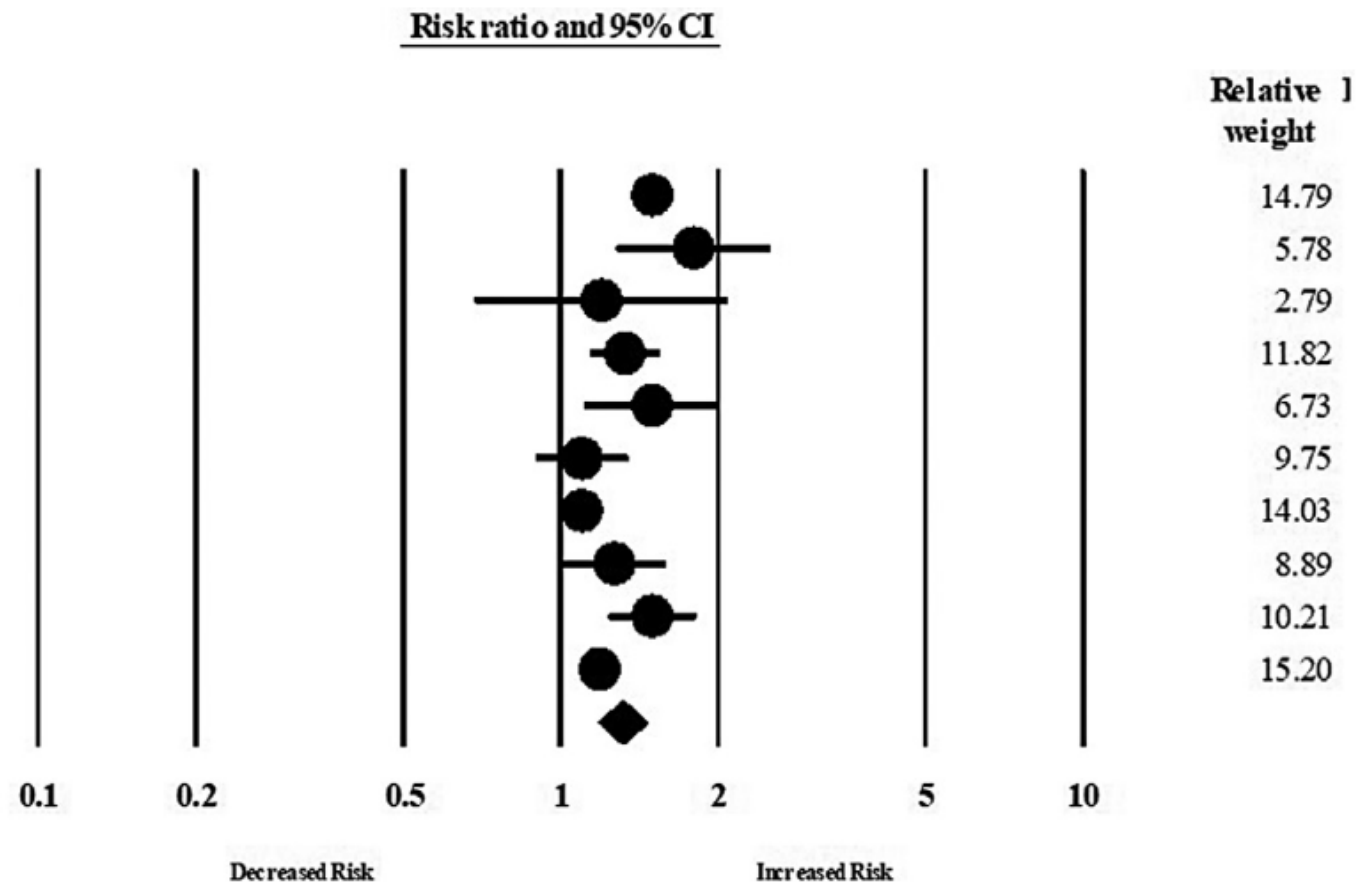


Fig. 2. Short-acting BDZs use and hip fracture risk.

Risk of Falls Associated with Long-Acting Benzodiazepines or Tricyclic Antidepressants Use in Community-Dwelling Older Adults: A Nationwide Population-Based Case–Crossover Study

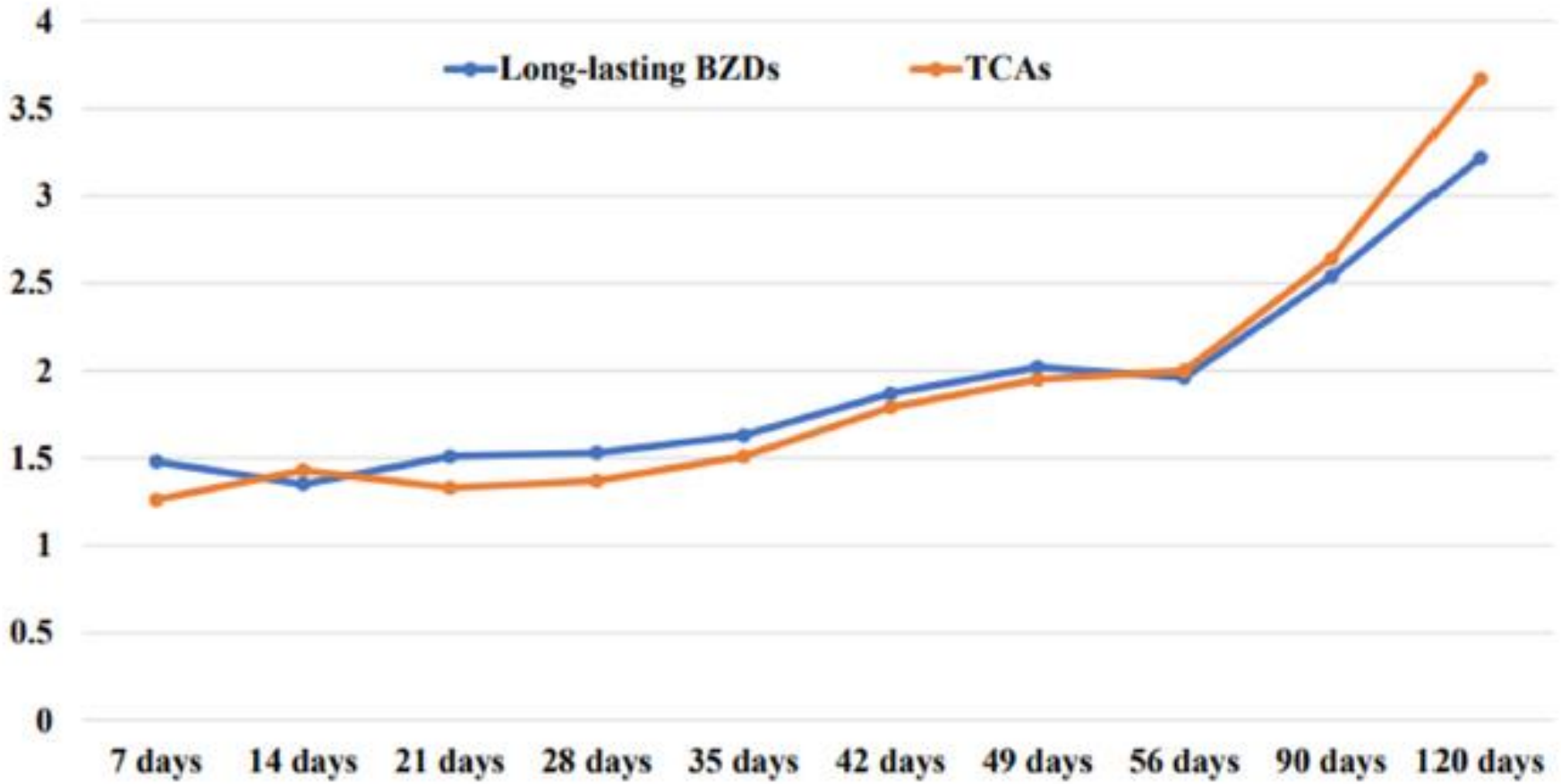


Figure 2. The relationship between the cumulative time of drug prescription and the increase in the risk of falls.

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Take home messages

- L’insonnia è una problematica molto comune e «pervasiva»
- Vi è una forte relazione tra:
  - percezione della qualità del sonno e comorbilità
  - insonnia e demenza, depressione e delirium
- La gestione dell’insonnia è prevalentemente di tipo farmacologico, utilizzando principi che impattano sulla termini di qualità del sonno e sul rischio di complicanze