



67° CONGRESSO NAZIONALE SIGG

LA LONGEVITÀ DECLINATA AL FEMMINILE

ALESSANDRA COIN

L'uso del trazodone nel real world dell'anziano residente in long-term care



SOCIETÀ ITALIANA
DI GERONTOLOGIA
E GERIATRIA

Roma, 30 novembre - 3 dicembre 2022



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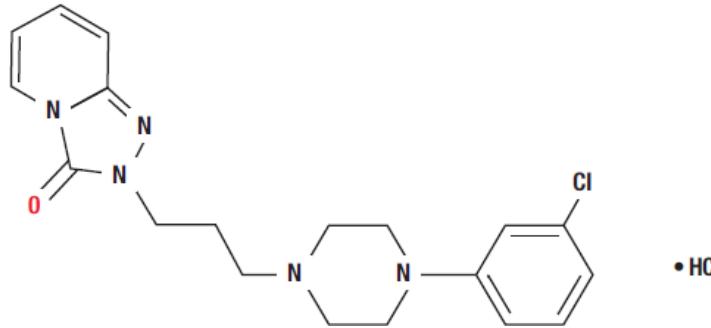
LA LONGEVITÀ DECLINATA AL FEMMINILE



Trazodone



Profilo farmacologico

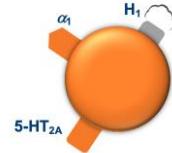


Trazodone cloridrato

- Derivato triazolopiridinico
- Primo **SARI** sviluppato¹
(Serotonin-2 Antagonist/Reuptake Inhibitor)
- Approvato per il Disturbo Depressivo Maggiore²
- **Duplice meccanismo d'azione** (in base al dosaggio)³

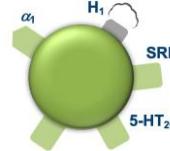


Profilo farmacologico



Dosaggi bassi (50-150mg/die) e rilascio immediato:
blocco $5-HT_{2A/2C}$ e arruolamento progressivo di α_1 e H_1

- rapida efficacia nel miglioramento sintomatico della depressione senile associata ad ansia, insonnia e BPSD

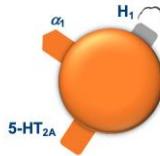


Dosaggi elevati (150-300mg/die) e formulazioni RP:
azione combinata di antagonismo su $5-HT_{2A}$ e di blocco del SERT

- approccio farmacologico appropriato sul nucleo serotoninergico della depressione con migliorata tollerabilità

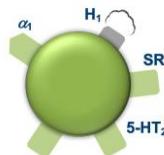


Profilo farmacologico



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blocco 5-HT_{2A/2C} e arruolamento progressivo di a₁ e H₁

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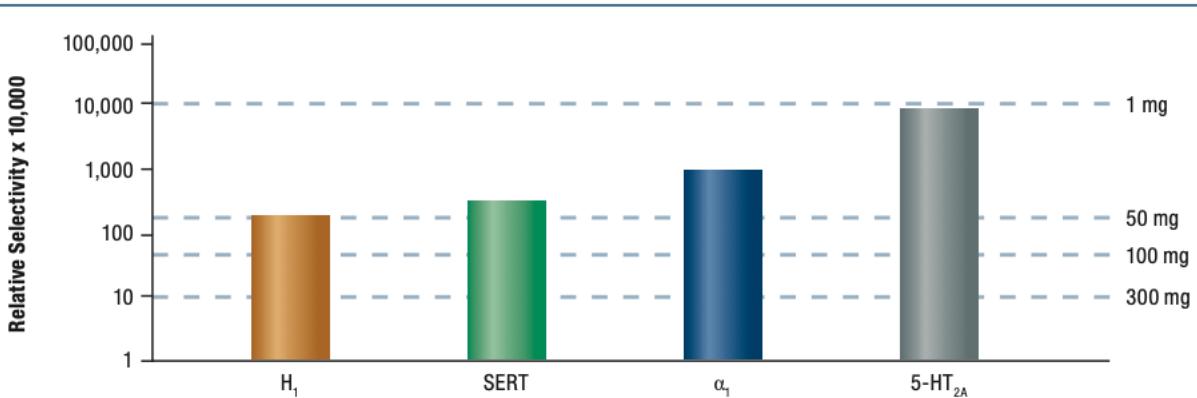


Figure 1. Relative receptor selectivity for four key receptors. Adapted from^[2].



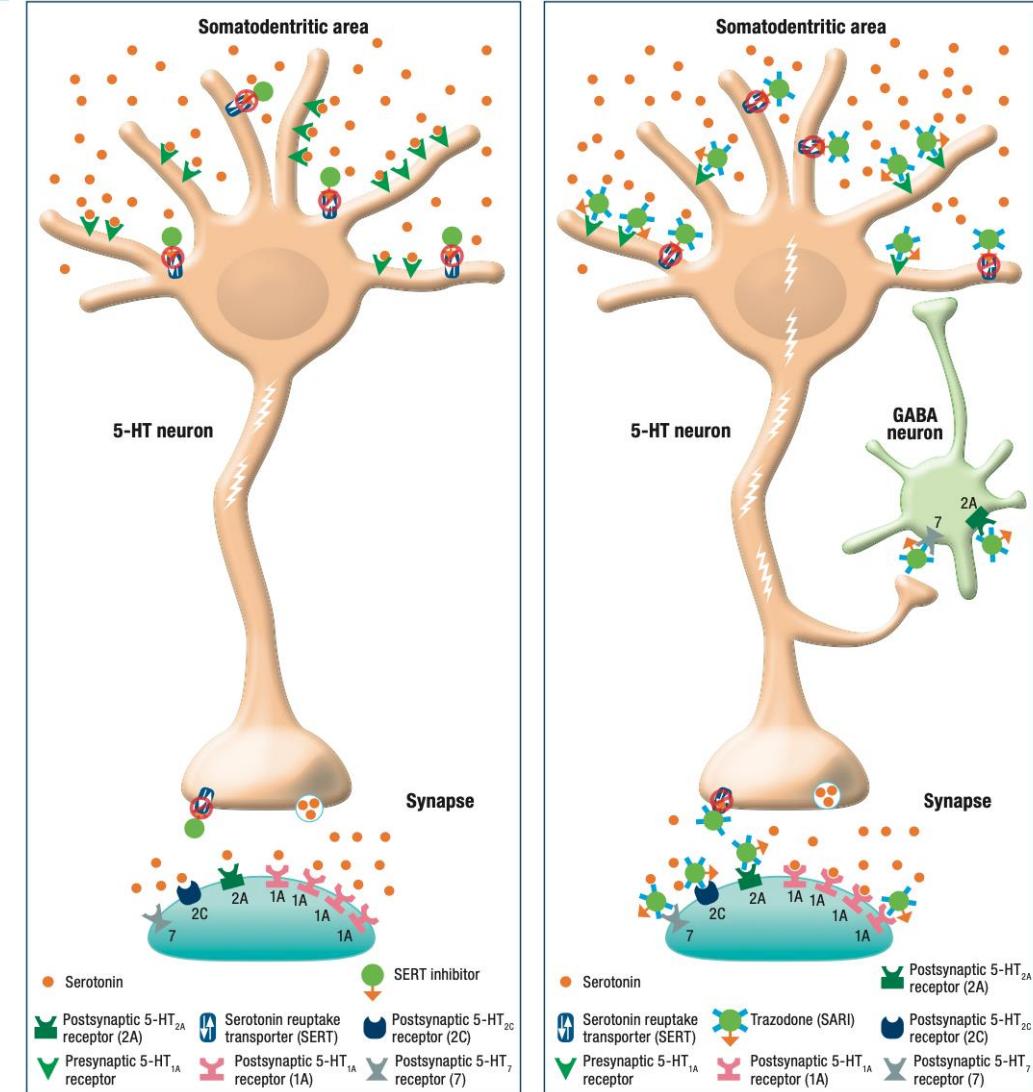
Profilo farmacologico

- Stessa efficacia degli antidepressivi di seconda generazione
- Migliore tollerabilità
- Poche interazioni farmacologiche



Profilo farmacologico

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Profilo farmacologico

- Stessa efficacia degli antidepressivi di seconda generazione

- Migliore tollerabilità
- Poche interazioni farm

Sheehan et al. (2009)¹ and
Fagiolini et al. (2020)²

Efficacia superiore e più rapida di trazodone OAD
rispetto al placebo¹ e rispetto a venlafaxina XR²

Kasper et al. (2005)³

Nessuna differenza significativa a livello
di endpoint di efficacia e tassi di risposta e remissione
fra trazodone RP e paroxetina

Munizza et al. (2006)⁴

Trazodone RP e sertralina sono risultati
ugualmente efficaci nel ridurre i sintomi
depressivi e nel promuovere la remissione

Buoli et al. (2017)⁵

Trazodone OAD e clomipramina sono risultati opzioni
rapide ed efficaci nel migliorare i sintomi depressivi

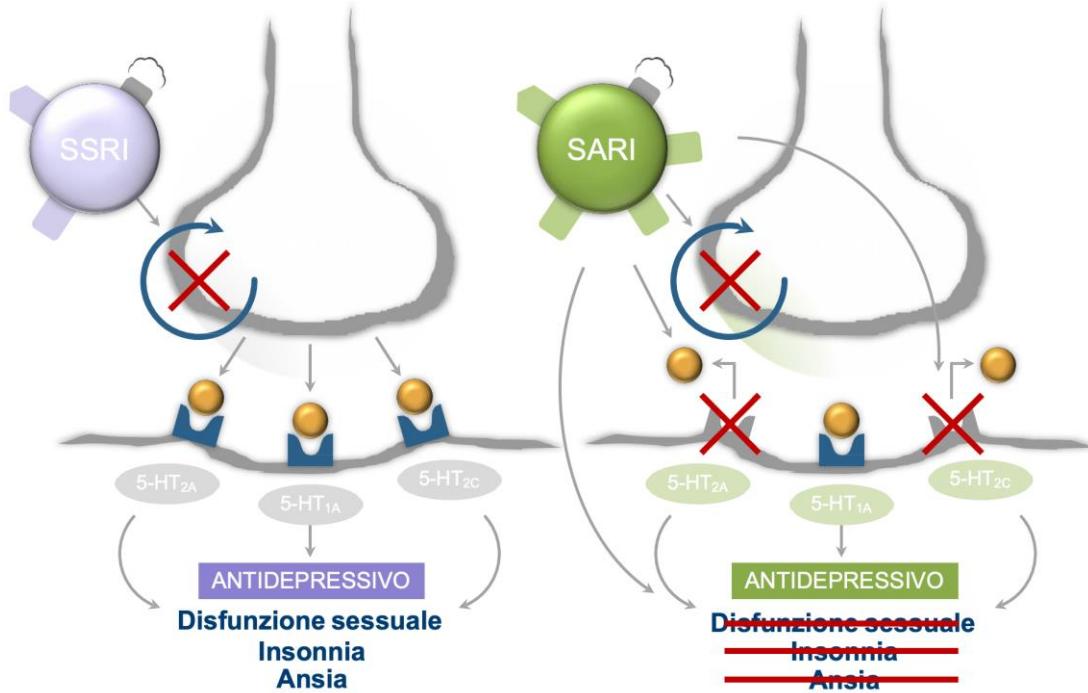
Češková et al. (2018)⁶

Diminuzione statisticamente significativa
del MADRS score dopo la prima settimana
di trattamento con trazodone OAD



Profilo farmacologico

- Stessa efficacia degli antidepressivi di seconda generazione
- **Migliore tollerabilità¹**
- Poche interazioni farmacologiche
 - Eventi avversi più comuni: sonnolenza e sedazione, ipotensione, mal di testa, vertigini, secchezza delle fauci
 - Raramente disfunzione sessuale, aumento di peso, attivazione e/o viraggi maniacali
 - Non causa effetti extrapiramidali o anticolinergici
 - Non è controindicato nel glaucoma e nei disturbi minzionali
 - Non c'è evidenza che possa dare origine a fenomeni di abuso/assuefazione
 - Tollerabilità cardiologica²: non associato ad allungamento del QT (studio ECG Screening Outcome in Psychiatry, ESOP)





Profilo farmacologico

- Stessa efficacia degli antidepressivi di seconda generazione
- Migliore tollerabilità
- Poche interazioni farmacologiche

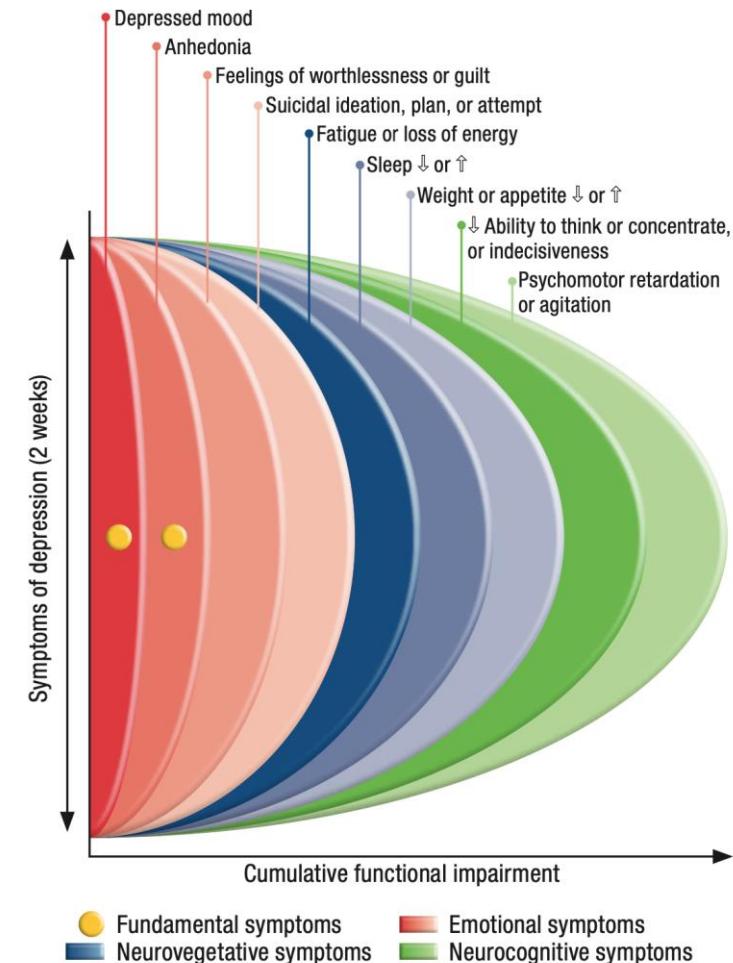
Inibitori del CYP3A4	Possono causare un sostanziale aumento della concentrazione plasmatica di trazodone
Carbamazepina	La co-somministrazione in associazione con trazodone ne riduce la concentrazione plasmatica
Antidepressivi triciclici	Evitare l'uso concomitante con trazodone per il rischio di interazione
Fluoxetina	Sono stati riportati casi rari di aumento dei livelli plasmatici di trazodone e l'insorgere di effetti avversi quando trazodone è somministrato con fluoxetina
Inibitori delle mono aminossidasi (IMAO)	Occasionalmente sono stati riportati casi di interazione con IMAO
Fenotiazine	È stata osservata ipotensione ortostatica severa in caso di somministrazione concomitante di fenotiazine
Anestetici e miorilassanti	Trazodone cloridrato può aumentare gli effetti dei miorilassanti e degli anestetici volatili
Alcool	Trazodone potenzia gli effetti sedativi dell'alcool
Levodopa	Gli antidepressivi possono accelerare il metabolismo della levodopa
Altro	L'uso concomitante di trazodone con farmaci noti per prolungare l'intervallo QT può aumentare il rischio di aritmia ventricolare, incluse "torsioni di punta"



Profilo terapeutico

Disturbo Depressivo Maggiore (DMM) nell'anziano¹

- Prevalenza in aumento negli over 65
- Si associa ad alta comorbosità, con polipatologia nell'88% dei casi
- Frequenti copresenza di depressione e decadimento cognitivo, rendendone difficile la diagnosi come patologie autonome
 - > 30% degli anziani affetti da demenza manifesta sintomi di depressione
 - Frequenti alterazioni comportamentali in anziani con disturbo depressivo ma senza una diagnosi di deficit cognitivo (che possono migliorare dopo la remissione dell'episodio depressivo)²
- Variabilità clinica della depressione, soprattutto nelle prime fasi³



1. Biggio G. Depressione dell'anziano nell'ambulatorio del medico di medicina generale: dai sintomi alla terapia. Soc. Italiana di Med. Generale 2017. 2. Ulbricht CM et al. Depression and cognitive impairment among newly admitted nursing home residents in the USA: Depression and cognitive impairment. Int J Geriatr Psychiatry. 2017. 3. Neviani F. La complessità dell'esperienza depressiva nell'anziano: diagnosi e terapia, una chimera? Psicogeriatría 2013. Image: Stahl SM. Mechanism of action of trazodone: a multifunctional drug. CNS Spectr 2009



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- Variabilità clinica della depressione, soprattutto nelle prime frasi²

	Anziano	Adulto giovane
Tristezza espressa	+ (+)	+++
Anedonia	+++	+++
Ansia	+++	++
Rallentamento	++	+
Sintomi cognitivi	+++	+
Sintomi somatici (GI)	+++	+
Ipocondria	++	+
Sintomi psicotici	++	+
Alterazioni del carattere	++	(+)
Ridotto interesse sessuale	++	+
Suicidalità	+++	++

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Profilo terapeutico

Due to this sedative action, trazodone is often used (off label) in older people with dementia or delirium to manage **agitation or aggression, insomnia, anxiety** and other **BPSD**



Profilo terapeutico

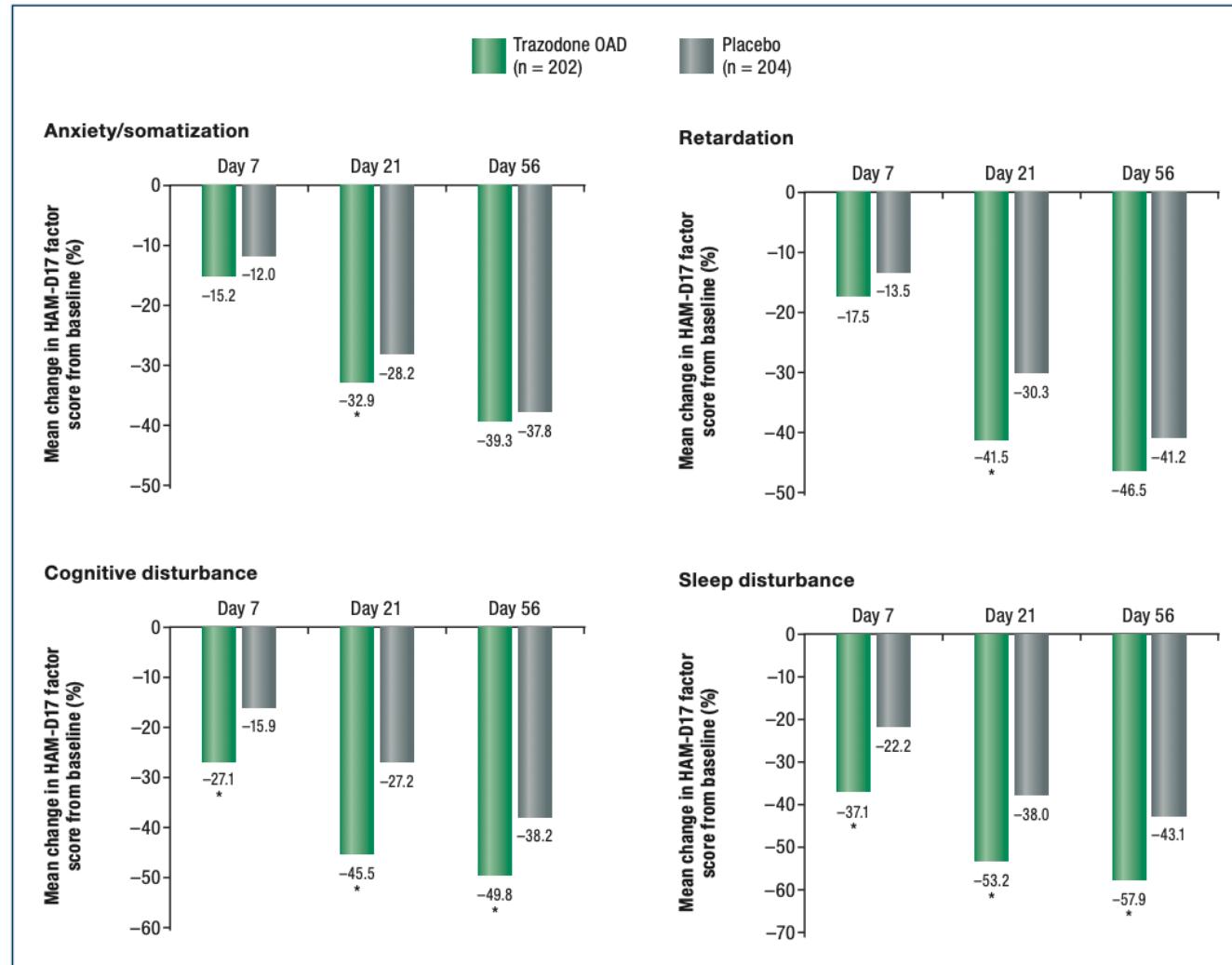
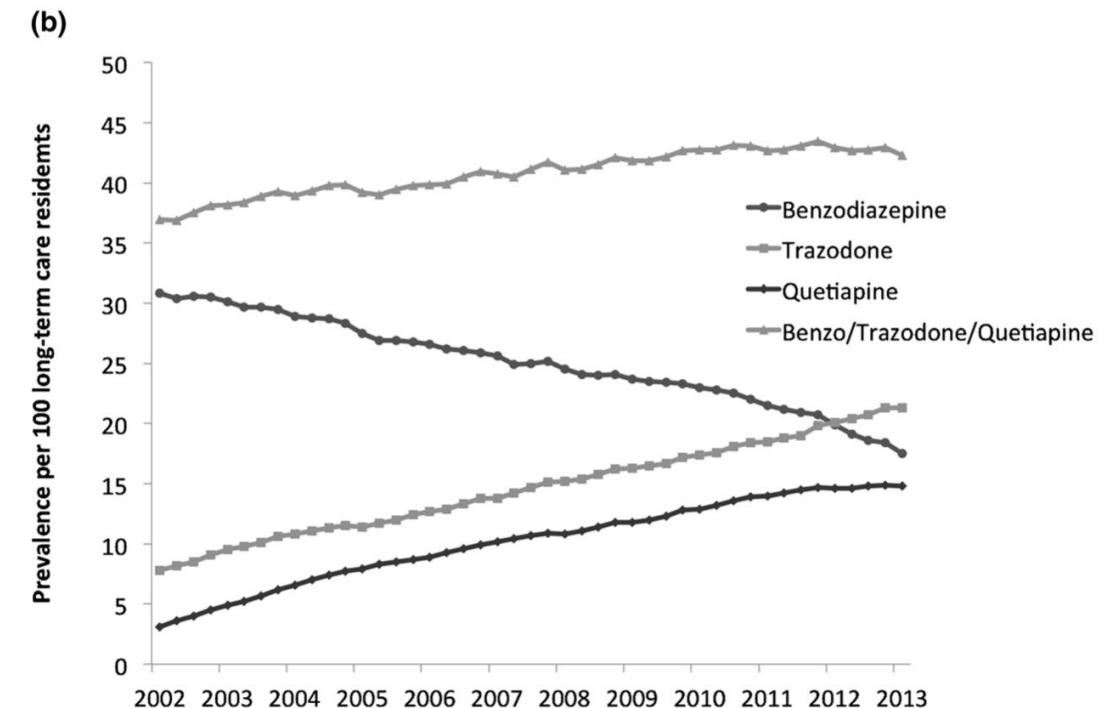
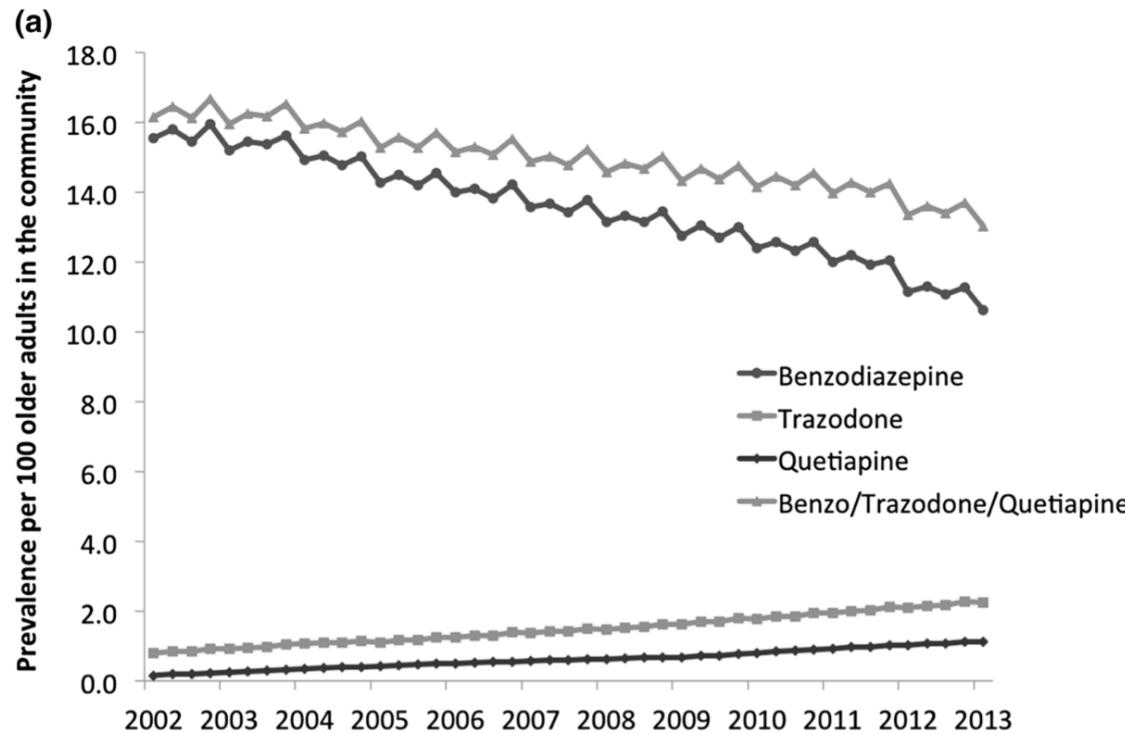


Figure 5. Reduction at day 7, 21 and 56 in the mean HAM-D factors in the trazodone OAD versus placebo^[8] study. * $P < 0.05$.





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CLINICAL GERIATRICS - REVIEW

Trazodone: a multifunctional antidepressant. Evaluation of its properties and real-world use

Alessandro Cuomo¹, Angelo Bianchetti², Annachiara Cagnin³,

Fazio⁵, Raffaele Antonelli Incalzi⁶,
Pier Francesco Laurenzi¹,

In elderly patients, trazodone has reported excellent results, keeping high-quality standards for safety and tolerability. It can help to improve insomnia and anxiety without resorting to benzodiazepines. In patients with neurological conditions, trazodone helps to treat anxiety-depressive symptoms. In patients with Alzheimer's disease or frontotemporal dementia, trazodone can help to handle behavioural symptoms, also acting as a putative neuroprotective agent.



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Clinical profile of trazodone users in a multi-setting older population: data from the Italian GeroCovid Observational study

Alessandra Coin, Marianna Noale, Pietro Gareri, Caterina Trevisan, Andrea Bellio, Filippo Fini, Angela Marie
Abbatecola, Stefania Del Signore, Alba Malara, Enrico Mossello, Stefano Fumagalli, Stefano Volpato, Fabio
Monzani, Giuseppe Bellelli, Gianluca Zia, Raffaele Antonelli Incalzi & the GeroCovid Observational Working Group



Italian GeroCovid Observational study

- Multicenter and multi-setting study
- Designed by the Italian Society of Gerontology and Geriatrics;
approved by the Campus Bio-Medico University Ethical Committee in April 2020
- Involved adults aged ≥60 years evaluated during the Covid-19 pandemic
- Assessment of the impact of the Covid-19 pandemic on the health of older people in different care settings
- Also included data collection related to chronic diseases and treatments
→ secondary analyses exploring the current management of some common conditions.



Aim

- Characterize the **prescription patterns** of trazodone in comparison with other antidepressants in older people across different settings of care (scant literature)
- Due to its **versatility**, trazodone may be also prescribed in frail older patients affected by dementia and BPSD



Materials and methods → Results

- Cross-sectional study
- Data from GeroCovid Observational: COVID-19 related data, demographic characteristics, lifestyle, mobility, social determinants, chronic diseases, functional status, pharmacotherapy
- Study participants were grouped according to the use of **antidepressants** (TRAZ, AnDep, No AnDep)

n = 3396

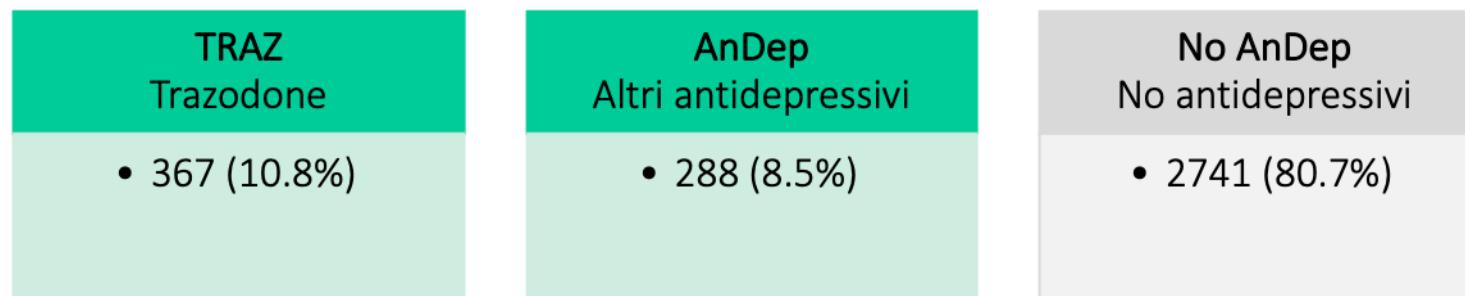




Table 1. Demographic, lifestyle and social characteristics of the GeroCovid population according to TRAZ, AnDep and No AnDep groups.

	All (n=3396)	TRAZ (n=367)	AnDep (n=288)	No AnDep (n=2741)	p-value		All (n=3396)	TRAZ (n=367)	AnDep (n=288)	No AnDep (n=2741)	p-value
<u>Demographic characteristics</u>											
Age (years)											
Age (years)	80.6±9.1	84.3±6.6	82.5±7.2	80.0±9.4	<0.0001						
Gender (Female)	1938 (57.1)	251 (68.4)	191 (66.3)	1496 (54.6)	<0.0001						
<u>Lifestyle</u>											
Smoking habits (available for n=1830)											
Current smoker	86 (4.7)	10 (4.9)	8 (4.7)	68 (4.7)	0.0077						
Former smoker	371 (20.3)	26 (12.8)	24 (14.2)	321 (22.0)							
Never smoker	1373 (75.0)	168 (82.4)	137 (81.1)	1068 (73.3)							
Alcohol consumption (available for n=1707)											
Walks independently	1615 (51.0)	112 (32.4)	99 (36.4)	1404 (55.0)							
Walks with help (cane or walker)	613 (19.3)	95 (27.4)	79 (29.0)	439 (17.2)	<0.0001						
Wheelchair (autonomous or pushed)	334 (10.5)	57 (16.5)	43 (15.8)	234 (9.2)							
Bed-rest condition	608 (19.2)	82 (23.7)	51 (18.8)	475 (18.6)							
<u>Social determinants</u>											
Care setting (available for n=2974)											
Outpatients	918 (30.9)	114 (33.8)	60 (22.6)	744 (31.4)							
Nursing Home	559 (18.8)	72 (21.4)	63 (23.7)	424 (17.9)							
In-patient	1113 (37.4)	89 (26.4)	91 (34.2)	933 (39.3)							
Home-based	384 (12.9)	62 (18.4)	52 (19.6)	270 (11.4)							
Household (available for n=2763)											
Lives at home alone, autonomous	160 (5.8)	11 (3.2)	11 (4.3)	138 (6.3)							
Lives at home alone, regularly assisted	195 (7.1)	25 (7.4)	29 (11.3)	141 (6.5)							
Lives at home alone, informal caregiver	528 (19.1)	125 (37.0)	67 (26.3)	336 (15.5)							
Lives at home with family, autonomous	1057 (38.2)	52 (15.4)	66 (25.9)	939 (43.3)							
Lives in a Nursing Home	823 (29.8)	125 (37.0)	82 (32.2)	616 (28.4)							
Social distancing impact (available for n=1477)											
Major impact	543 (36.8)	64 (27.7)	51 (33.3)	428 (39.2)							
No or moderate impact	934 (63.2)	167 (72.3)	102 (66.7)	665 (60.8)							

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Former smoker	371 (20.3)	26 (12.8)	24 (14.2)	321 (22.0)	<u>Household</u> (available for n=2763)													
Never smoker	1373 (75.0)	168 (82.4)	137 (81.1)	1068 (73.3)	Lives at home alone, autonomous													
Alcohol consumption (available for n=1707)	158 (9.3)	9 (3.8)	6 (3.6)	143 (11.0)	<0.0001	Lives at home alone, regularly assisted	195 (7.1)	25 (7.4)	29 (11.3)	141 (6.5)								
<u>Mobility</u> (available for n=3170)																		
Walks independently	1615 (51.0)	112 (32.4)	99 (36.4)	1404 (55.0)	Lives at home alone, informal caregiver													
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					Major impact													
					No or moderate impact													

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Table 2. Health-related, functional and frailty characteristics of the GeroCovid population according to TRAZ, AnDep and No AnDep groups.

	All (n=3396)	TRAZ (n=367)	AnDep (n=288)	No AnDep (n=2741)	p-value
Hypertension * (available for n=3236)	1972 (60.9)	262 (72.2)	210 (72.9)	1500 (58.0)	<0.0001
Cardiovascular diseases * (available for n=3219)	1371 (42.6)	177 (48.8)	136 (47.6)	1058 (41.2)	0.0048
Stroke (available for n=3212)	305 (9.5)	44 (12.3)	35 (12.2)	226 (8.8)	0.0285
Diabetes mellitus (available for n=3217)	684 (21.3)	76 (21.1)	61 (21.3)	547 (21.3)	0.9970
Osteoarthritis * (available for n=3213)	806 (25.1)	131 (36.5)	102 (35.5)	573 (22.3)	<0.0001
Chronic Obstructive Pulmonary Disease (available for n=3211)	426 (13.3)	52 (14.5)	36 (12.5)	338 (13.2)	0.7367
Chronic renal failure (available for n=3213)	384 (12.0)	49 (13.7)	40 (13.9)	295 (11.5)	0.2691
Obesity (available for n=3224)	254 (7.9)	25 (7.0)	24 (8.4)	205 (8.0)	0.7689
Depression (available for n=3213)	564 (17.6)	101 (27.9)	155 (54.0)	308 (12.0)	<0.0001
Mild Cognitive Impairment	140 (4.1)	15 (4.1)	10 (3.5)	115 (4.2)	0.8410
Dementia	978 (28.8)	245 (66.8)	141 (49.0)	592 (21.6)	<0.0001
Comorbidities, 3+ *	1546 (45.5)	245 (66.8)	205 (71.2)	1096 (40.0)	<0.0001
Functional status					
Activities of Daily Living, (available for n=1668)	4 (1, 6)	2 (1, 4)	3 (1, 5)	4 (1, 6)	<0.0001
Instrumental Activities of Daily Living, (available for n=1444)	1 (0, 5)	0 (0, 1)	1 (0, 4)	2 (0, 6)	<0.0001



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Obesity (available for n=3224)	254 (7.9)	25 (7.0)	24 (8.4)	205 (8.0)	0.7689
Depression (available for n=3213)	564 (17.6)	101 (27.9)	155 (54.0)	308 (12.0)	<0.0001
Mild Cognitive Impairment	140 (4.1)	15 (4.1)	10 (3.5)	115 (4.2)	0.8410
Dementia	978 (28.8)	245 (66.8)	141 (49.0)	592 (21.6)	<0.0001
Comorbidities, 3+ *	1546 (45.5)	245 (66.8)	205 (71.2)	1096 (40.0)	<0.0001
Functional status					
Activities of Daily Living, (available for n=1668)	4 (1, 6)	2 (1, 4)	3 (1, 5)	4 (1, 6)	<0.0001
Instrumental Activities of Daily Living, (available for n=1444)	1 (0, 5)	0 (0, 1)	1 (0, 4)	2 (0, 6)	<0.0001



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	All (n=3396)	TRAZ (n=367)	AnDep (n=288)	No AnDep (n=2741)	p-value
If dementia, specify					
Alzheimer's disease	402 (11.8)	119 (32.4)	62 (21.5)	221 (8.1)	<0.0001
Vascular dementia	151 (4.5)	33 (9.0)	14 (4.9)	104 (3.8)	<0.0001
Dementia with Lewy bodies	18 (0.5)	6 (1.6)	3 (1.0)	9 (0.3)	0.0039
Frontotemporal dementia	10 (0.3)	3 (0.8)	2 (0.7)	5 (0.2)	0.0311
Mixed dementia	105 (3.1)	24 (6.5)	19 (6.6)	62 (2.3)	<0.0001
Other	253 (7.5)	46 (12.5)	40 (13.9)	167 (6.1)	<0.0001
Dementia due to Parkinson's disease	11 (0.3)	2 (0.5)	0 (0.0)	9 (0.3)	0.5098
Dementia due to other medical condition	10 (0.3)	4 (1.1)	0 (0.0)	6 (0.2)	0.0389
Dementia with BPSD	270 (8.0)	127 (34.6)	40 (13.9)	103 (3.8)	<0.0001



Table 2. Health-related, functional and frailty characteristics of the GeroCovid population according to TRAZ, AnDep and No AnDep groups.

	All (n=3396)	TRAZ (n=367)	AnDep (n=288)	No AnDep (n=2741)	p-value
Antipsychotic drugs use, n (%)	545 (16.1)	164 (44.7)	89 (30.9)	292 (10.7)	<0.000
Trazodone dose, n (%)					
>100 mg/die		19 (7.8)	--	--	
≤100 mg/die	226 (92.2)				



Table 3. Multinomial logistic regression model with outcome “Trazodone”, “Other antidepressants” or “No Antidepressants” use in the GeroCovid population

	TRAZ vs No AnDep			AnDep vs No AnDep			TRAZ vs AnDep		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Study participants with depression									
Dementia no BPSD, vs no dementia	2.29	1.26-4.16	0.0066	1.53	0.92-2.56	0.1037	1.50	0.78-2.89	0.2305
Dementia with BPSD, vs no dementia	4.97	2.52-9.80	<0.0001	1.96	0.99-3.78	0.0560	2.54	1.22-5.29	0.0128
Dementia with BPSD, vs dementia no BPSD	2.17	1.05-4.49	0.0365	1.28	0.63-2.60	0.4988	1.70	0.78-3.68	0.1797
Study participants without depression									
Dementia no BPSD, vs no dementia	3.87	2.66-5.62	<0.0001	3.25	2.12-4.98	<0.0001	1.19	0.70-2.03	0.5254
Dementia with BPSD, vs no dementia	28.4	18.0-44.7	<0.0001	5.68	2.94-10.9	<0.0001	5.00	2.48-10.1	<0.0001
Dementia with BPSD, vs dementia no BPSD	7.34	4.72-11.4	<0.0001	1.75	0.90-3.38	0.0974	4.20	2.12-8.32	<0.0001



Figure 1. Depression, dementia and BPSD prevalence by clusters identified among TRAZ users

	Cluster 1	Cluster 2	Cluster 3
Demographic characteristics	Female dominance Older participants	Female dominance Older participants	Male dominance Younger participants
Mobility	Walk with help	Bed-rest conditions	Walk independently
Social determinant	Living at home	Institutionalized	Living at home with family
Chronic Condition	Multimorbidity (hypertension, dementia and BPSD)	Multimorbidity (hypertension, osteoarthritis, diabetes mellitus, COPD, obesity)	Fewer chronic diseases
Dementia	82% (BPSD: 62%)	55% (BPSD: 5%)	58% (BPSD: 36%)
Depression	25%	>30%	21%

The dose of TRAZ was mainly <100 mg/day and > 40% were using antipsychotics with a slightly higher frequency in cluster 1



Discussion

- 18.5% persons received an antidepressant, with **trazodone** being the most prescribed drug (10.8% vs 8.5%)
- Lower use of antidepressants compared with data from LTCF¹, yet higher use of trazodone than those reported in other studies^{1,2}
- Trazodone-users “profile”
 - Users were more likely to be **functionally dependent** and to have several **comorbidities**
 - Independently of a depression, **BPSD** was associated with an increased use of trazodone
 - Its prescription in older adults with dementia may be intended to **improve BPSD** than to treat depression alone

Limitations

- Cross sectional study, no information about reason of prescription, efficacy and tolerability



67° CONGRESSO NAZIONALE SIGG

LA LONGEVITÀ DECLINATA AL FEMMINILE



Real world use of Trazodone in older persons in Long Term Care setting: an analysis database study



Aim

- **Clinical characteristics** leading to trazodone prescription
- Therapeutic effects in different **care settings** → Long Term Care (LCT)



Results

- Preliminary data: 920 subjects in treatment with trazodone; 427 completed the study
- Descriptive statistics → clustering analysis

n = 427

DEM (143)	BPSD (58)	DEP (29)	DEMDEP (182)	ALTRO (15)
• Demenza senza BPSD	• Demenza con BPSD	• Depressione	• Demenza + depressione	• No demenza, no BPSD, no depressione

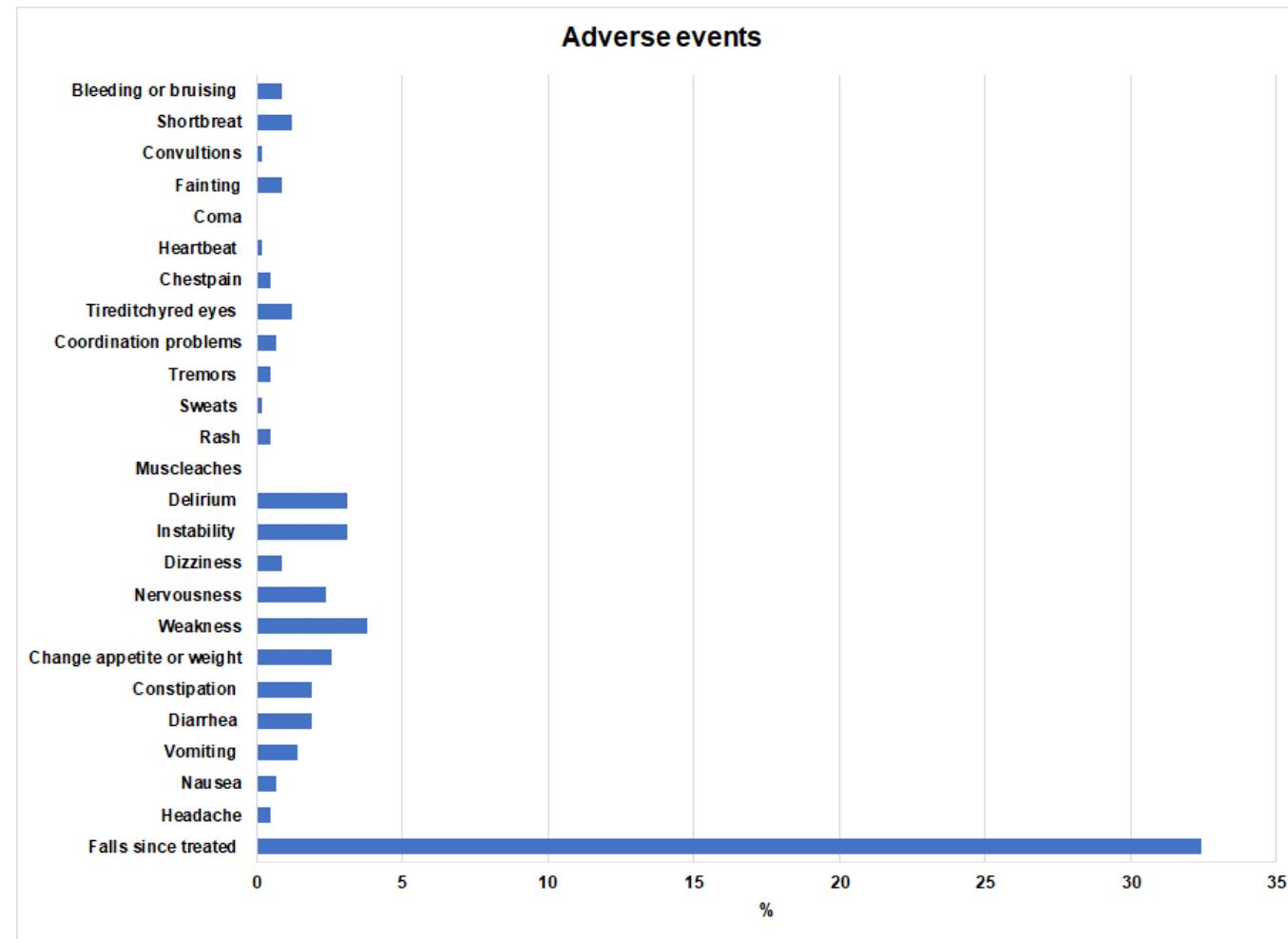


Table 2. Indications

	TUTTI 427	ALTRO 15	DEM 143	BPSD 58	DEP 29	DEMDEP 182	p
AGITATION = 1 (%)	241 (56.4)	9 (60.0)	92 (64.3)	33 (56.9)	18 (62.1)	89 (48.9)	0,1
INSOMNIA = 1 (%)	184 (43.1)	12 (80.0)	60 (42.0)	31 (53.4)	9 (31.0)	72 (39.6)	0
WANDERING = 1 (%)	47 (11.0)	0 (0.0)	23 (16.1)	6 (10.3)	0 (0.0)	18 (9.9)	0,1
DEPRESSION = 1 (%)	127 (29.7)	0 (0.0)	0 (0.0)	0 (0.0)	24 (82.8)	103 (56.6)	<0.001
APATHY = 1 (%)	45 (10.5)	0 (0.0)	7 (4.9)	6 (10.3)	2 (6.9)	30 (16.5)	0
PHYSICAL AGGRESSION = 1 (%)	36 (8.4)	2 (13.3)	13 (9.1)	11 (19.0)	1 (3.4)	9 (4.9)	0
VERBAL AGGRESSION = 1 (%)	82 (19.2)	2 (13.3)	36 (25.2)	18 (31.0)	0 (0.0)	26 (14.3)	0
ANXIETY = 1 (%)	124 (29.0)	1 (6.7)	27 (18.9)	19 (32.8)	11 (37.9)	66 (36.3)	0
ECOLALIA = 1 (%)	8 (1.9)	0 (0.0)	6 (4.2)	0 (0.0)	0 (0.0)	2 (1.1)	0,2
GRUMBLE = 1 (%)	25 (5.9)	0 (0.0)	11 (7.7)	7 (12.1)	1 (3.4)	6 (3.3)	0,1
DELUSIONS = 1 (%)	40 (9.4)	0 (0.0)	10 (7.0)	15 (25.9)	1 (3.4)	14 (7.7)	<0.001
HALLUCINATIONS = 1 (%)	55 (12.9)	0 (0.0)	17 (11.9)	17 (29.3)	2 (6.9)	19 (10.4)	0
OPPOSING ATTITUDE = 1 (%)	82 (19.2)	0 (0.0)	35 (24.5)	19 (32.8)	2 (6.9)	26 (14.3)	0
OTHER BPSD = 1 (%)	3 (100.0)	0 (NaN)	1 (100.0)	0 (NaN)	0 (NaN)	2 (100.0)	NA
At least one symptom among BPSD list = 1 (%)	395 (92.5)	15 (100.0)	143 (100.0)	58 (100.0)	23 (79.3)	156 (85.7)	<0.001



Figure 1. Adverse Events





	OR	95% CI	p-value
Sex, female vs male	0.77	0.40-1.47	0.425
Age, year	1.01	0.96-1.05	0.831
Cancer	2.50	1.18-5.27	0.016
Apathy	2.24	0.94-5.35	0.068
Physical aggression	3.68	1.46-9.25	0.006
Grumble	2.82	0.98-8.19	0.056

Table 5. Characteristics associated with falls since treated among those with no falls before treatment (multivariable logistic regression*)
 OR (Odds Ratio); CI (Confidence Interval). *: stepwise selection (p-entry 0.15, p-stay 0.20) among variables associated with the outcome with $p \leq 0.20$ at the univariable level; sex and age forced into the model

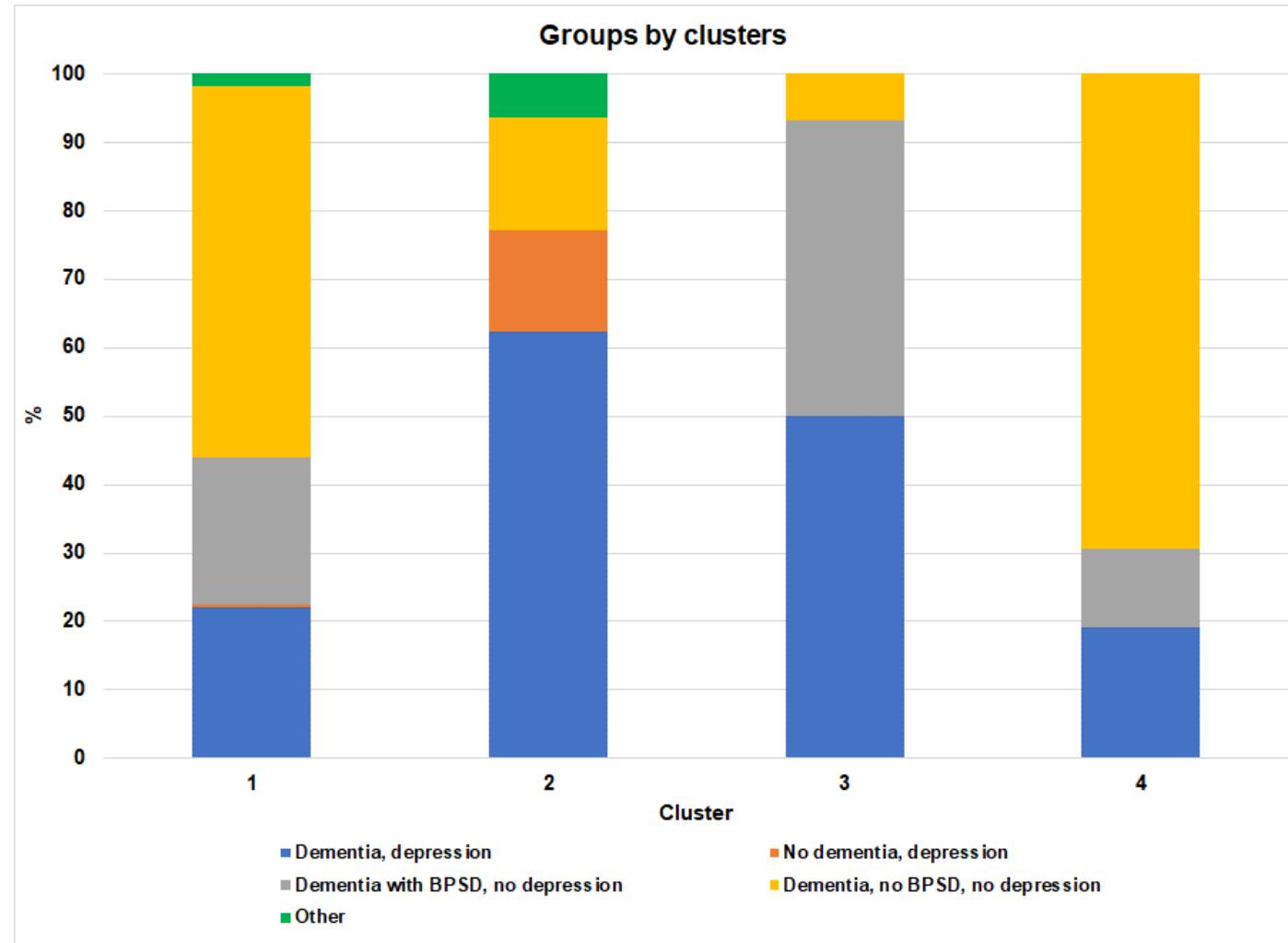


Table 4. Reasons for interruption

	TUTTI 427	ALTRO 15	DEM 143	BPSD 58	DEP 29	DEMDEP 182	p
NEW UNRELATED CONDITIONS = 1 (%)	16 (3.8)	1 (6.7)	6 (4.2)	2 (3.4)	0 (0.0)	7 (3.9)	0,8
First choice = 1 (%)	283 (67.7)	9 (69.2)	105 (75.0)	39 (70.9)	13 (44.8)	117 (64.6)	0
benefit (%)							0
No	40 (9.4)	0 (0.0)	17 (11.9)	7 (12.1)	3 (10.3)	13 (7.2)	
A bit	143 (33.6)	0 (0.0)	44 (30.8)	26 (44.8)	10 (34.5)	63 (35.0)	
Yes	242 (56.9)	15 (100.0)	82 (57.3)	25 (43.1)	16 (55.2)	104 (57.8)	
INEFFICACY = 1 (%)	47 (11.1)	0 (0.0)	15 (10.5)	8 (13.8)	5 (17.2)	19 (10.6)	0,5
ADVERSE REACTION = 1 (%)	9 (2.1)	0 (0.0)	3 (2.1)	1 (1.7)	0 (0.0)	5 (2.8)	0,8
EFFECTIVE BUT NO MORE NECESSARY = 1 (%)	21 (5.0)	1 (6.7)	7 (4.9)	0 (0.0)	1 (3.4)	12 (6.7)	0,4
FEAR OF DRUG INTERACTION = 1 (%)	1 (0.2)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0,7



Figure 2. Groups by clusters





Reason for prescription, n (%)	Cluster 1 (n=168)	Cluster 2 (n=189)	Cluster 3 (n=44)	Cluster 4 (n=26)	p-value
Agitation	103 (61.3)	97 (51.3)	22 (50.0)	19 (73.1)	0.063
Insomnia	60 (35.7)	91 (48.2)	21 (47.7)	12 (46.2)	0.103
Wandering	31 (18.5)	7 (3.7)	6 (13.6)	3 (11.5)	<0.001
Depression	9 (5.4)	103 (54.5)	15 (34.1)	0 (0.0)	<0.001
Apathy	12 (7.1)	18 (9.5)	12 (27.3)	3 (11.5)	0.004
Physical aggression	24 (14.3)	8 (4.2)	3 (6.8)	1 (3.9)	0.006
Verbal aggression	44 (26.2)	19 (10.1)	11 (25.0)	8 (30.8)	<0.001
Anxiety	31 (18.5)	61 (32.3)	32 (72.7)	0 (0.0)	<0.001
Ecolalia	5 (3.0)	2 (1.1)	0 (0.0)	1 (3.9)	0.295
Grumble	16 (9.5)	6 (3.2)	3 (6.8)	0 (0.0)	0.041
Delusions	17 (10.1)	6 (3.2)	15 (34.1)	2 (7.7)	<0.001
Hallucinations	30 (17.9)	13 (6.9)	8 (18.2)	4 (15.4)	0.012
Opposing attitudes	47 (28.0)	18 (9.5)	9 (20.5)	8 (30.8)	<0.001



Adverse events, n (%)	Cluster 1 (n=168)	Cluster 2 (n=189)	Cluster 3 (n=44)	Cluster 4 (n=26)	p-value
Headache	0 (0.0)	1 (0.5)	1 (2.3)	0 (0.0)	0.302
Nausea	1 (0.6)	1 (0.5)	0 (0.0)	1 (3.9)	0.368
Vomiting	2 (1.2)	3 (1.6)	0 (0.0)	1 (3.9)	0.578
Diarrhea	1 (0.6)	6 (3.2)	0 (0.0)	1 (3.9)	0.185
Constipation	1 (0.6)	5 (2.7)	0 (0.0)	2 (7.7)	0.068
Change appetite or weight	3 (1.8)	2 (1.1)	1 (2.3)	5 (19.2)	<0.001
Weakness	2 (1.2)	11 (5.8)	2 (4.6)	1 (3.9)	0.090
Nervousness	4 (2.4)	4 (2.1)	1 (2.3)	1 (3.9)	0.819
Dizziness	1 (0.6)	2 (1.1)	1 (2.3)	0 (0.0)	0.575
Instability	2 (1.2)	4 (2.1)	4 (9.1)	3 (11.5)	0.005
Delirium	3 (1.8)	6 (3.2)	1 (2.3)	3 (11.5)	0.094
Muscleaches	-	-	-	-	
Rash	1 (0.6)	1 (0.5)	0 (0.0)	0 (0.0)	1.000
Sweats	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0.556
Tremors	1 (0.6)	1 (0.5)	0 (0.0)	0 (0.0)	1.000
Coordination problems	1 (0.6)	2 (1.1)	0 (0.0)	0 (0.0)	1.000
Tireditchyred eyes	1 (0.6)	3 (1.6)	0 (0.0)	1 (3.9)	0.342
Chestpain	1 (0.6)	1 (0.5)	0 (0.0)	0 (0.0)	1.000
Heartbeat	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.9)	0.061
Coma	-	-	-	-	
Fainting	1 (0.6)	3 (1.6)	0 (0.0)	0 (0.0)	0.818
Convulsions	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0.556
Shortbreath	1 (0.6)	1 (0.5)	0 (0.0)	3 (11.5)	0.004
Bleeding or bruising	0 (0.0)	3 (1.6)	0 (0.0)	1 (3.9)	0.115



Prescription and benefit	Cluster 1 (n=168)	Cluster 2 (n=189)	Cluster 3 (n=44)	Cluster 4 (n=26)	p-value
First choice	127 (77.4)	107 (57.5)	29 (69.1)	20 (76.9)	<0.001
Benefit					
No	21 (12.5)	14 (7.5)	3 (7.7)	2 (7.7)	
Partially	57 (33.9)	54 (28.7)	21 (48.8)	11 (42.3)	0.086
Yes	90 (53.6)	120 (63.8)	19 (44.2)	13 (50.0)	
Reason for discontinuation, n (%)					
New unrelated conditions	4 (2.4)	10 (5.4)	2 (4.7)	0 (0.0)	0.383
Inefficacy	17 (10.1)	22 (11.8)	6 (14.0)	2 (7.7)	0.845
Adverse reaction	3 (1.8)	6 (3.2)	0 (0.0)	0 (0.0)	0.706
Effective but no more necessary	7 (4.2)	10 (5.4)	2 (4.7)	2 (7.7)	0.799
Fear of drug interactions	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0.559



Conclusioni

- ✓ Si conferma l'uso non convenzionale del trazodone nella pratica clinica dell'anziano in long term care, particolarmente affetto da demenza, con o senza BPSD.
- ✓ Tra gli effetti avversi rilevati le cadute sono quelle più descritte
- ✓ In generale è ben tollerato ed efficace
- ✓ Sono necessari studi ad hoc che includano le ragioni di prescrizione e aggiungano dati sull'efficacia e la tollerabilità di trazodone e altri antidepressivi nell'anziano fragile.
- ✓ Sono necessari studi clinici per fornire ai clinici specifiche opzioni terapeutiche nel campo dei disturbi psico-comportamentali delle demenze in considerazione del numero in crescita di persone affette da questa patologia particolarmente nel mondo delle cure croniche che è una sfida dei nostri tempi