Supplementary material to the manuscript "Trends in Benzodiazepine Receptor Agonists use and Associated Factors in the Belgian General Older Population: Analysis of the Belgian Health Interview Survey Data"

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Supplementary table S1. Trends in benzodiazepines and z-drugs use (crude prevalence) in older adults in 2004, 2008 and 2013

Variable	Year 2004 (N= 3594)		Year 2008 (N=2917)		Year 2013 (N=2048)	
	n	Crude prevalence (%) (95% CI)	n	Crude prevalence (%) (95% CI)	n	Crude prevalence (%) (95% CI)
Total BZRA use	840	23.4 (21.8; 25.0)	681	23.3 (21.6; 25.2)	363	17.7 (15.9; 19.6)
Number of BZRA taken						
1	764	21.3 (19.8; 22.8)	600	20.6 (19.0; 22.3)	326	15.9 (14.32; 17.7)
≥2	76	2.1 (1.7; 2.6)	81	2.8 (2.2; 3.5)	37	1.8 (1.3; 2.5)
Total BZRA use by age group						
65-74 years	279	17.7 (15.7; 19.9)	161	18.0 (15.4; 201.0)	148	14.2 (12.0; 16.7)
75-84 years	265	24.6 (21.7; 27.7)	203	22.6 (19.6; 26.0)	154	20.6 (17.5; 24.2)
85 or more years	296	31.5 (28.0; 35.3)	317	28.1 (25.1; 31.4)	61	23.4 (17.9; 30.0)
Total BZRA use by gender						
Female	602	27.8 (25.7; 30.1)	520	28.2 (25.8; 30.7)	237	20.6 (18.0; 23.4)
Male	238	16.6 (14.6; 18.9)	161	15.0 (12.8; 17.5)	126	14.1 (11.7; 16.7)
BZRA use by class						
Benzodiazepine use (N05BA or N05CD)	748	20.8 (19.3; 22.4)	599	20.5 (18.9; 22.2)	302	14.7 (13.1; 16.5)
Z-drugs use (N05CF)	113	3.1 (2.6; 3.8)	104	3.6 (2.9; 4.3)	64	3.1 (2.4; 4.0)
Sedative BZRA use (N05CD or N05CF)	362	10.1 (9.1; 11.2)	304	10.4 (9.3; 11.7)	169	8.3 (7.1; 9.6)
Anxiolytic BZRA use (N05BA)	528	14.7 (13.5 ; 16.0)	429	14.7 (13.3; 16.2)	221	10.8 (9.4; 12.3)
BZRA use at molecule level						
Alprazolam	124	3.5 (2.9; 4.1)	108	3.7 (3.0; 4.5)	72	3.5 (2.8; 4.4)
Bromazepam	97	2.7 (2.2; 3.3)	85	2.9 (2.3; 3.6)	35	1.7 (1.2; 2.4)
Lorazepam	224	6.2 (5.4; 7.1)	190	6.5 (5.6; 7.5)	87	4.2 (3.4; 5.2)
Lormetazepam	169	4.7 (4.0; 5.5)	138	4.7 (4.0; 5.6)	77	3.8 (3.0; 4.7)
Zolpidem	83	2.3 (1.8; 2.9)	80	2.7 (2.2; 3.4)	57	2.8 (2.1; 3.6)
Other	201	5.6 (4.8; 6.4)	155	5.3 (4.5; 6.2)	68	3.3 (2.6; 4.2)
Concomitant use of BZRA & other drugs						
Antidepressants	223	6.2 (5.4; 7.1)	182	6.2 (5.4; 7.2)	98	4.8 (3.9; 5.8)
Opioids	80	2.2 (1.8; 2.8)	93	3.2 (2.6; 3.9)	38	1.9 (1.3; 2.5)

Abbreviations: BZRA, Benzodiazepine Receptor Agonists (ATC N05BA, N05CD and N05CF); 95%CI: 95% Confidence Interval

Supplementary table S2. Factors associated with benzodiazepine and z-drugs use in older adults in 2013 in univariate and multivariable logistic regression (with detailed univariate analysis)

Variables	Univariate model (N=1286)		Multivariable model (N=1225)	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Socio-demographic factors				
Age				
65-74 years	1.00			
75-84 years	1.57 (1.15; 2.15)	0.005		
85 years or more	1.80 (1.09; 2.90)	0.017		
Female	1.68 (1.25; 2.28)	<0.001	1.62 (1.14; 2.29)	0.007
Region				
Flanders	1.00			
Brussels	0.73 (0.46; 1.12)	0.162		
Wallonia	1.12 (0.81; 1.53)	0.498		
Civil status				
Married or legally cohabiting	1.00			
Single (never married)	0.99 (0.51; 1.79)	0.980		
Widow(er) (not remarried)	1.67 (1.20; 2.31)	0.002		
Divorced (not remarried)	1.25 (0.75; 2.00)	0.373		
Educational level*				
Higher	1.00			
Higher secondary	2.05 (1.31; 3.26)	0.002		
Lower secondary	2.07 (1.30; 3.32)	0.002		
No diploma or primary education	2.43 (1.57; 3.82)	<0.001		
Other	1.81 (0.27; 7.22)	0.457		
Country of birth				
Belgian	1.00			
Non-Belgian EU	1.02 (0.55; 1.77)	0.941		
Non-Belgian Non EU	1.39 (0.55; 3.10)	0.446		
Household income				
Quintile 5 (highest quintile)	1.00			
Quintile 4	1.44 (0.80; 2.64)	0.233		
Quintile 3	2.36 (1.39; 4.14)	0.002		
Quintile 2	2.05 (1.22; 3.57)	0.008		
Quintile 1 (lowest quintile)	1.41 (0.78; 2.62)	0.261		
Missing data (n=141)	1.53 (0.80; 2.93)	0.193		
Geriatric factors				
Number of chronic conditions [a]				
0 to 1	1.00			
2 to 5	2.03 (1.47; 2.81)	<0.001		
6 or more	3.82 (2.20; 6.52)	<0.001		
Low Body Mass Index (<21 kg/m²)	1.64 (0.98; 2.64)	0.051	2.02 (1.13; 3.50)	0.015
Urinary incontinence	1.82 (1.16; 2.77)	0.007		

Osteoporosis in the past 12 months [a]	1.80 (1.19; 2.67)	0.004		
Fall in the past 12 months	2.48 (1.77; 3.46)	<0.001	1.52 (1.02; 2.26)	0.037
Broken hip in the past 12 months	1.14 (0.26; 3.57)	0.840		
Parkinson's disease in the past 12 months	2.14 (0.75; 5.41)	0.123		
Handicap in mobility				
None	1.00			
Limited to house or garden	3.64 (2.22; 5.88)	<0.001		
Limited to a seat	2.65 (1.30; 5.11)	0.005		
Limited to a bed	0.71 (0.04; 3.91)	0.750		
Handicap in performing daily activities [b]				
No restrictions	1.00			
Moderate restrictions	2.64 (1.78; 3.87)	<0.001		
Severe restrictions	2.57 (1.66; 3.91)	<0.001		
Handicap in performing household activities [c]				
No restrictions	1.00			
Moderate restrictions	1.64 (1.01; 2.59)	0.039		
Severe restrictions	3.36 (2.44; 4.64)	<0.001		
Comorbidities				
Low back disorder in the past 12 months	1.99 (1.47; 2.68)	<0.001		
Osteoarthritis in the past 12 months [a]	2.13 (1.59; 2.87)	<0.001		
Diabetes in the past 12 months	1.52 (1.01; 2.24)	0.038		
Myocardial infarction in the past 12 months	2.00 (0.82; 4.46)	0.101		
Coronary heart disease (angina pectoris) in the past 12 months	1.16 (0.50; 2.43)	0.704		
High blood pressure (hypertension) in the past 12 months	1.15 (0.85; 1.56)	0.349		
Pain (SF-36 Bodily pain scale score)				
<30	1.00			
30-49	1.80 (1.22; 2.64)	0.003		
50-74	2.47 (1.64; 3.69)	<0.001		
>75	4.08 (2.58; 6.40)	<0.001		
(Mental) health indicators				
Reporting anxiety disorder	2.39 (1.54; 3.66)	<0.001		
Reporting sleeping disorder	2.58 (1.91; 3.48)	<0.001	1.92 (1.35; 2.72)	<0.001
Reporting depressive disorder [a]	2.86 (2.04; 4.00)	<0.001		
Mean GHQ-12 score				
<2	1.00			
[2-4[	1.92 (1.25; 2.89)	0.002		
[4-7[	3.22 (2.02; 5.06)	<0.001		
>7	2.85 (1.76; 4.51)	<0.001		
Missing data (n=25)	2.19 (0.78; 5.30)	0.102		
Mean score of positive mental health (SF-36 Vitality Index)				
≥50	1.00		1.00	
<50	3.23 (2.32; 4.50)	<0.001	1.73 (1.13; 2.69)	0.011

Missing data (n=163)	1.46 (0.91; 2.28)	0.101	1.18 (0.68; 1.98)	0.552
EQ-5D-5L score	0.05 (0.02; 0.09)	<0.001	0.35 (0.14; 0.84)	0.019
Social Health				
Appreciation of social contacts [a] : rather unsatisfied vs rather satisfied	2.11 (1.34 ; 3.26)	<0.001		
Frequency of social contacts [a] : < 1 a week	1.28 (0.64; 2.37)	0.465		
Perceived quality of social support				
Strong/Intermediate support	1.00			
Poor support	1.59 (1.12; 2.22)	0.008		
Missing data (n=28)	1.50 (0.55; 3.55)	0.384		
Medication use				
Number of medication BZRA excluded				
0-4	1.00		1.00	
5-9 (polypharmacy)	3.24 (2.36; 4.46)	<0.001	2.51 (1.75; 3.60)	<0.001
≥10 (severe polypharmacy)	5.73 (2.98; 10.86)	<0.001	2.82 (1.30; 6.04)	0.008
Opioid use	2.41 (1.25; 4.45)	0.006		
Antipsychotic use	2.88 (1.14; 6.82)	0.018		
Antidepressant use	4.61 (3.10; 6.83)	<0.001		
SSRI use	3.96 (2.34; 6.64)	<0.001		
Trazodone use	7.01 (3.28; 15.37)	<0.001	4.05 (1.64; 10.21)	0.003
Tricyclic antidepressant or mirtazapine use	3.26 (1.34; 7.53)	0.006		
Other antidepressants use (antidepressants except trazodone, SSRI and tricyclic antidepressants or mirtazapine)	4.80 (2.20; 4.42)	<0.001	2.91 (1.16; 7.39)	0.022
Healthcare services use				
Regular GP	1.71 (0.59; 7.22)	0.384		
Number of contacts with GP in the past 2 months				
0	1.00		1.00	
1	2.39 (1.60; 3.64)	<0.001	1.89 (1.22; 2.98)	0.005
≥2	4.69 (3.11; 7.22)	<0.001	2.15 (1.33; 3.51)	0.002
Inpatient hospitalization in the past 12 months	1.40 (0.96; 2.02)	0.075		
Contact with emergency department in the past year	1.63 (1.08; 2.41)	0.018		
Visiting a psychologist or psychotherapist in the past 12 months	1.78 (0.57; 4.70)	0.275		

Abbreviations: BZRA, Benzodiazepines Receptors Agonists (ATC N05BA, N05CD and N05CF); 95%CI, 95% Confidence Interval; EQ-5D-5L, EuroQol 5 dimensions, 5 levels; EU, European Union; GHQ-12, General Health Questionnaire 12 items; GP, General Practitioner; OR, Odds Ratio; SSRI, Selective Serotonin Reuptake Inhibitors

[a] missing values: educational level (16); number of chronic conditions (5), osteoporosis in the past 12 months (4), reporting depressive disorder (2), osteoarthritis (1), appreciation of social support (21), EQ-5D-5L score (52), frequency of social contacts (22)

[b] Getting in and out a bed; getting in and out a seat; getting dressed/undressed; able to take a shower or a bath; eating/cutting food, able to use toilets

[c] Prepare meals, use the phone, able to shop, manage medications, do light housework, do occasionally heavy housework, take care of finance and everyday administrative tasks

Supplementary table S3. Factors candidate for the final multivariable model[a]

Socio-demographic factors
Age
Gender
Civil status
Educational level
Household income
Geriatric factors
Multimorbidity
Urinary incontinence, problems in controlling the bladder in the past 12 months
Osteoporosis in the past 12 months
Fall in the past 12 months
Parkinson's disease in the past 12 months
Risk of underweight (Body Mass Index < 21 kg/m²)
Severity of the handicap in mobility
Severity of restrictions in performing daily activities
Severity of restrictions in performing household activities
Comorbidities
Low back disorder or other chronic back defect in the past 12 months
Osteoarthritis in the past 12 months
Diabetes in the past 12 months
Myocardial infarction in the past 12 months
Pain (MOS 36-item Short-Form Health Survey (SF-36) Bodily pain score)
Mental health indicators and subjective health indicators
Mean score to the General Health Questionnaire (GHQ-12)
Mean score to the Vitality Index (MOS 36-item Short-Form Health Survey (SF-36))
Reporting sleeping disorder (subscale of Symptoms Checklist-90-Revised questionnaire (SCL-90-R))
Reporting anxiety disorder (subscale of Symptoms Checklist-90-Revised questionnaire (SCL-90-R))
Reporting depressive disorder (subscale of Symptoms Checklist-90-Revised questionnaire (SCL-90-R))
EuroQol-5D-5L scale (EQ5D-5L) score
Social health
Appreciation of social contacts
Perceived quality of social support (Oslo Social Support Scale)
Medication use
Number of medications excluding BZRA
Opioid use
SSRI use
Tricyclic antidepressants or mirtazapine use
Trazodone use
Other antidepressant use (antidepressants except SSRI, trazodone and tricyclic antidepressant or mirtazapine)
Antipsychotic use
Healthcare services use
Number of contacts with the GP in the past 2 months
Inpatient hospitalization in the past 12 months
Contact with emergency department in the past 12 months
Abbreviations: BZRA, Benzodiazepine Receptor Agonists (ATC N05BA, N05CD and N05CF); GP, General Practitioner; SSRI: Selective Serotonin Reuptake Inhibitors [a] Candidate variables included in the multivariable model before stepwise selection (= all variables with a p-value <0.15 in the univariate model)

Supplementary table S4. Characteristics of the included and excluded observations

Variable	Included N=1286 n (%)	Excluded N=762 n (%)	p-value [a]
Age			<0.001
65-74 years	115 (8.94)	146 (19.16)	
75-84 years	732 (56.92)	309 (40.55)	
85 years or more	439 (34.14)	307 (40.29)	
Gender			<0.001
Female	683 (53.11)	469 (61.55)	
Male	603 (46.89)	293 (38.45)	
Civil status			0.025
Single (not married)	90 (7.00)	68 (8.92)	
Married or legally cohabiting	715 (55.60)	399 (52.36)	
Widow(er) (not remarried)	344 (26.75)	234 (30.71)	
Divorced (not remarried)	137 (10.65)	61 (8.01)	
Region			<0.001
Flanders	543 (42.22)	208 (27.30)	
Brussels	225 (17.50)	208 (27.30)	
Wallonia	518 (40.28)	346 (45.41)	
Education level			<0.001
No diploma or primary education	330 (25.66)	306 (40.16)	
Lower secondary	274 (21.31)	145 (19.03)	
Higher secondary	313 (24.34)	156 (20.47)	
Higher	341 (26.52)	110 (14.44)	
Other	12 (0.93)	4 (0.52)	
Missing	16 (1.24)	41 (5.38)	
Country of birth			<0.001
Belgian	1218 (94.71)	656 (86.09)	
Non Belgian EU	59 (4.59)	54 (7.09)	
Non Belgian non EU	9 (0.70)	26 (3.41)	
Missing	0 (0.00)	26 (3.41)	
Household income			<0.001
Quintile 1 (lowest income)	192 (14.93)	154 (20.21)	
Quintile 2	307 (23.87)	170 (22.31)	
Quintile 3	248 (19.28)	97 (12.73)	
Quintile 4	203 (15.79)	95 (12.47)	
Quintile 5 (highest income)	195 (15.16)	41 (5.38)	
Missing	141 (10.96)	205 (26.90)	
BZRA use			0.211
Yes	217 (16.87)	146 (19.16)	

Abbreviations: EU, European Union; BZRA, Benzodiazepines Receptors Agonists (ATC N05BA, N05CD and N05CF)

[a] Pearson chi-square test or Fisher exact test