Supplementary material

Title: Population prevalence and incidence of dementia and associated neuropsychiatric symptoms from real-world data.

Calculation of incidence and prevalence of dementia, and dementia-related NPS.

Given the dynamic nature of populations with specific health problems, to measure the incidence and prevalence of dementia, and dementia-related NPS, we conducted a retrospective study with two cross-sectional datasets (December 31, 2018, and 2019). By "dynamic population", we mean one in which the members vary over time with individuals entering or leaving as a function of the occurrence of events [22]. In our case, over time, individuals in the population may die, which affects both healthy people (denominator of the incidence rate), and sick people (numerator of the rate). In addition, during the observation period there are also state transitions from healthy to sick. This last factor determines the numerator (incident cases of NPS), and the denominator (incident cases of dementia) of the incidence rate of NPS. The analysis of the status of the entire population at the beginning , and end of 2019 aimed to identify, on the one hand, diagnoses of dementia, and on the other hand, the existence of NPS in those cases of dementia. This analysis allowed us to measure the dynamic components of the population under study to calculate incidence, and prevalence.

The prevalence of dementia disaggregated by age as of December 31, 2019 was calculated by dividing the number of cases by the population obtained from the Basque Institute of Statistics (EUSTAT). The cases identified as of December 31, 2019 that were not present in the 2018 dataset were used as numerator of the incidence of dementia. To calculate the rate per 1000 person-years, the denominator was estimated beginning with the population in 2018 from which we subtracted the years of observation lost due to deaths , and the cases of dementia already identified in 2018 [22,24]. It was assumed that both events occurred uniformly throughout the year, and hence, they were assigned a duration of 0·5 years. The results were validated by comparing them with RWD population , and door-to-door survey data on prevalence [9,25,26], and incidence [9,11,25,27] in the literature.

Criteria for the diagnosis of dementia in the population electronic Registry

The search for diagnoses was carried out following validated criteria with a positive predictive value of 95.1% and a negative value of 99.4%. The dementia codes included were in ICD9 (290xx; 2941x; 331xx) and ICD10 (F01.5x; F02.8x; F03.9x; G30.0x; G30.1x; G30.8x; G30.9x; G31.0x; G31.1x; G31.2x; G31.8x; G31.9x). The dementia codes with BPS used were searched in CIE9 (294.11. 290.11. 290.12. 290.13. 290.2x. 290.3. 290.41. 290.42. 290.43. 290.9) and CIE10 (F02.81. F03.90. F05). ICD 10 was added to the searches because from 1 January 2016 it is the official ICD. The identification of dementia also included the prescription of specific drugs for Alzheimer's disease (ATC Group N06D) such as acetylcholinesterase inhibitors (donepezil. rivastigmine and galantamine). memantine and rivastigmine.

Table SM1. Sedative capacity of all the drugs included in the dataset.

	ATC	Drug name	Sedative capacity (0:absent; 1:minimum; 2:mild; 3:moderate; 4:important)
Antipsychotic drugs	N05AA01	Chlorpromazine	3
	N05AA02	Levomepromazine	3
	N05AD01	Haloperidol	2
	N05AH02	Clozapine	4
	N05AH03	Olanzapine	3
	N05AH04	Quetiapine	3
	N05AL01	Sulpiride	1
	N05AL03	Tiapride	1
	N05AN01	Lithium	
	N05AX08	Risperidone	2
	N05AX12	Aripiprazole	1
	N05AX13	Paliperidone	2
Antidepressive drugs	N06AA04	Clomipramine	2
	N06AA09	Amitriptyline	2
	N06AA10	Nortriptyline	2
	N06AA21	Maprotiline	2
	N06AB03	Fluoxetine	0
	N06AB04	Citalopram	0
	N06AB05	Paroxetine	0
	N06AB06	Sertraline	0
	N06AB08	Fluvoxamine	1
	N06AB10	Escitalopram	0
	N06AX03	Mianserin	2
	N06AX05	Trazodone	2
	N06AX11	Mirtazapine	2
	N06AX12	Bupropion	0
	N06AX16	Venlafaxine	0
	N06AX21	Duloxetine	0
	N06AX22	Agomelatine	
	N06AX23	Desvenlafaxine	0
	N06AX26	Vortioxetine	0

Table SM2. Dementia prevalence with confidence intervals (CI).

Age group	Prevalence %	Lower CI	Upper CI
Total	4·5	4·5	4·6
[60;65)	0·3	0·2	0·3
[65;70)	0·6	0·6	0·7
[70;75)	1·7	1·6	1·7
[75;80)	4·8	4·6	4·9
[80;85)	8·9	8·7	9·1
[85;90)	15·6	15·3	16·0
[90;105)	21·3	20·9	21·8

Table MS3. Dementia incidence with confidence intervals (CI)

Age group	Numerator	Denominator	Incidence x 1000	Lower CI	Upper CI
Total	4,028	593,486	6·8	6·6	7·0
[60;65)	54	144,079	0·4	0·3	0·5
[65;70)	123	125,316	1·0	0·8	1·2
[70;75)	413	113,731	3·6	3·3	4·0
[75;80)	756	79,419	9·5	8·8	10·2
[80;85)	1,028	62,998	16·3	15·3	17·3
[85;90)	1,068	44,710	23·9	22·5	25·3
[90;105)	586	23,234	25·2	23·2	27·3

Table MS4. Prevalence of neuropsychiatric symptoms with confidence intervals (CI).

Psychotic Cluster	Prevalence (%)	Lower CI	Upper CI
Total	55·4	54·8	56·0
[60;65)	53·3	48·3	58·3
[65;70)	51·9	48·4	55·4
[70;75)	50·6	48·4	52·8
[75;80)	49·9	48·3	51·4
[80;85)	50·9	49·7	52·1
[85;90)	56·0	54·9	57·0
[90;105)	64·8	63·6	65·9
Depressive Cluster	Prevalence (%)	Lower CI	Upper CI
Total	68·1	67·6	68·7
[60;65)	78·9	74·8	82·9
[65;70)	75·3	72·2	78·3
[70;75)	73·7	71·7	75·6
[75;80)	75·8	74·5	77·1
[80;85)	74·9	73·9	76·0
[85;90)	66·3	65·3	67·3
[90;105)	55·6	54·4	56·8

Table MS5. Incidence of neuropsychiatric symptoms with confidence intervals (CI)

Depressive cluster	Numerator	Denominator	Incidence x 100	Lower CI	Upper CI
Total	3,355	9,247	36·3	35·1	37·5
[60;65)	48	152	31·6	22·7	40·5
[65;70)	106	299	35·4	28·7	42·2
[70;75)	342	763	44·8	40·1	49·6
[75;80)	698	1,168	59·8	55·3	64·2
[80;85)	820	2,320	35·3	32·9	37·8
[85;90)	840	2,807	29·9	27·9	32·0
[90;105)	501	1,738	28·8	26·3	31·3
Psychotic cluster	Numerator	Denominator	Incidence x 100	Lower CI	Upper CI
Total	3,161	12,916	24·5	23·6	25·3
[60;65)	32	332	9·6	6·3	13·0
[65;70)	87	572	15·2	12·0	18·4
[70;75)	248	1,416	17·5	15·3	19·7
[75;80)	504	2,485	20·3	18·5	22·1
[80;85)	697	4,035	17·3	16·0	18·6
[85;90)	919	2,968	31·0	29·0	33·0
[90;105)	674	1,108	60·8	56·2	65·4

Table MS6. Percentage of dementia patients treated with each type of antidepressant

	Age group						
Drug	60-65	65-70	70-75	75-80	80-85	85-90	90-105
Trazodone	127	231	628	1,449	2,595	3,837	3,306
%	13·01%	12·99%	14·09%	16·01%	17·63%	19·9%	22·96%
Mirtazapine	54	113	298	598	976	1,296	817
%	5·53%	6·36%	6·69%	6·61%	6·63%	6·72%	5·67%
Duloxetine	43	108	231	422	654	722	346
%	4·41%	6·07%	5·18%	4·66%	4·44%	3·74%	2·51%
Sertraline	36	98	258	520	889	1045	687
%	3·69%	5·51%	5·79%	5·75%	6·04%	5·42%	4·84%
Escitalopram	103	159	403	885	1,223	1,371	835
%	10·55%	8·94%	9·04%	9·78%	8·31%	7·11%	5·84%

%: percentage for each age-group.