
Global trends in symptomatic medication use against dementia in 66 countries/regions from 2008 to 2018

Running title: Global use of medications against dementia

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Structured abstract

Introduction: We aimed to determine trends and patterns of symptomatic medication used against dementia in 66 countries and regions.

Methods: This was a cross-sectional study that used the wholesale data from the IQVIA-Multinational Integrated Data Analysis System database. Sale data for symptomatic medication against dementia from 66 countries and regions from 2008 to 2018 were analyzed, and stratified by income level (Low/Middle-income countries (LMICs), $n=27$; High-income countries (HICs), $n=37$; regions, $n=2$). The medication use volume was estimated by Defined Daily Dose per 1000 inhabitants per day (DDDTID)(WHO DDD, harmonized the size, strength and form of each pack and reflects average dosing). Changes in medication use over time were quantified as percentage changes in compound annual growth rates (CAGR).

Results: Total symptomatic medication against dementia sales increased from 0.85 to 1.33 DDDTID between 2008 and 2018 (LMICs: 0.094 to 0.396; HICs: 3.88 to 5.04), which is an increase of CAGR of 4.53% per year. The increase was mainly driven by the LMICs (CAGR=15.42%) in comparison to the HICs (CAGR=2.65%). The overall medication use from 2008 to 2018 increased for all four agents: memantine (CAGR=8.51%), rivastigmine (CAGR=6.91%), donepezil (CAGR=2.72%), and galantamine (CAGR=0.695%). In 2018, the most commonly used medications globally was donepezil contributed to 49.8% of total use volume, followed by memantine (32.7%), rivastigmine (11.24%) and galantamine (6.36%).

Conclusion: There was an increasing trend in use of symptomatic medications against dementia globally, but the use remained low in LMICs. Interventions may be needed to support the medication use in some countries.

Keywords: Alzheimer's disease; Dementia; Acetylcholinesterase inhibitor; Memantine; Epidemiology; Global neurology.

1 **Background**

2 Dementia is a major cause of comorbidities, disabilities and mortality, making it a major
3 concern for public health.(1) With an ageing population, the burden of dementia is increasing.
4 Globally, the number of people aged 60 years and above have more than doubled in the last
5 forty years(2) from 382 million in 1980 to 962 million in 2017.(3) It was estimated the number
6 of people with dementia in 2015 would be over 46 million worldwide and was predicted to
7 increase to 74.7 million in 2030 and 131.5 million in 2050.(3, 4) Currently, around 60% of all
8 patients with dementia live in low/middle-income countries (LMICs), and this proportion was
9 expected to rise.(4, 5) The total estimated worldwide cost of dementia was US\$818 billion in
10 2015, which accounted for more than one percent of the global gross domestic product
11 (GDP).(4, 6)

12 To date, there is no treatment to cure dementia, and the current pharmacological
13 management aims at managing the cognitive symptoms through the use of the centrally acting
14 acetylcholinesterase inhibitors (AChEIs), consisting of donepezil, galantamine and
15 rivastigmine, or the N-methyl-D-aspartate (NMDA) receptor antagonist, memantine. The
16 medications have the indication of managing dementia caused by Alzheimer's disease (and
17 Parkinson's disease dementia for rivastigmine), while they are also widely off-license used for
18 patients with Lewy body dementia or vascular dementia in practice. (1, 7) The medications for
19 the dementia symptomatic treatments have been shown to produce small to modest
20 improvement but consistent cognitive benefits in Alzheimer dementia by both randomized
21 controlled trials and real-world data.(8-12) In addition, emerging evidence also suggested the
22 long-term drug use can bring other benefits to patients with dementia, such as reduced risk of

1 cardiovascular events and mortality.(8, 13, 14) However, due to the non-curative nature, the
2 exact clinical impact of the symptomatic medications against dementia is still a matter of debate,
3 as reflected by disparities between guidelines for dementia treatment across countries.(15-17)
4 Nevertheless, these medications are widely-used in multiple countries.(18-20)

5 Previous studies that investigate the utilization of symptomatic medications against
6 dementia are very limited, and the majority of these studies were either conducted in high-
7 income countries (HICs) or restricted to the setting of a single country or region.(1, 19-21)
8 However, only few studies investigated the trends of medications use for dementia
9 symptomatic treatments in LMICs.(21, 22) Furthermore, the global trend of the medication use
10 for dementia symptomatic treatments has remained unknown as no study has directly
11 investigated between-country/region differences. Given the above unknowns, understanding
12 the global utilization patterns of symptomatic medications against dementia is of paramount
13 importance to understand the current state of policy and practice on pharmacological
14 management of dementia across countries and regions.

15 Using wholesale data on the medications over an 11-year period, this study aimed to
16 describe the global trends of symptomatic medications against dementia and to compare the
17 utilization patterns between countries for the use of each individual medication.

18

19 **Methods**

20 *Data sources*

21 We conducted a cross-sectional study nested within the wholesale data from the IQVIA-
22 Multinational Integrated Data Analysis System (MIDAS) database. The IQVIA-MIDAS

1 database provides long-term sales data from a large number of countries. Global
2 pharmaceutical sales data on symptomatic medications used against dementia (donepezil,
3 galantamine, rivastigmine and memantine) sales during the period of 2008-2018 were analyzed.
4 The IQVIA-MIDAS database contains annual pharmacy sales data in retail and hospital
5 pharmacies collected from wholesalers in different countries. In the case not all wholesalers of
6 the included countries/regions (23/66 countries/regions) contribute to the MIDAS database,
7 adjustments were made by IQVIA to estimate the probable total sales volume based on
8 knowledge of the market share of participating wholesalers.(23) **Table A1 (Supplementary**
9 **material)** summarizes the sectors covered in each included country/region and the data
10 availability. The IQVIA-MIDAS database has been validated against external data sources(24)
11 and used to produce high-quality epidemiological studies.(25, 26)

12 The annual sales volumes of symptomatic medications used against dementia were
13 from 66 countries/regions [27 countries from LMICs, 37 from HICs, and two regions, namely
14 Central America (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama) and
15 French West Africa (Benin, Burkina Faso, Cameroon, Chad, Côte d’Ivoire, Gabon, Guinea,
16 Mali, Republic of Congo, Senegal, Togo)]. The 64 countries were stratified based on the
17 income levels for further analyses. The two regions were excluded from the analyses after
18 stratification by income levels due to the heterogeneity of the constituent countries.

19 We obtained additional country-level variables during the study period from other
20 data sources. The income levels and mid-year population estimates of each country were
21 obtained from the World Bank.(27) The estimates of the national prevalence of dementia within
22 the study period were obtained from the Global Burden of Diseases, Injuries, and Risk Factors

1 (GBD) Study.(28)

2

3 *Outcome measurements*

4 The outcome of this study was the population-standardized rate of the symptomatic medication
5 use against dementia. The use of the medications was estimated from the sales volume
6 measured in the standard unit (SU) with one SU defined by IQVIA as a single tablet, capsule
7 or ampoule/vial or 5 mL oral suspension. In order to better estimate the use by patients, sales
8 data were also converted into the Defined Daily Dose (DDD) using the World Health
9 Organization (WHO) Anatomical Therapeutic Chemical Classification System, which
10 harmonized the differences in size, strength and form of each pack and accounted for the
11 differences between recommended dosage.

12

13 *Analysis*

14 We first described the overall global trend of symptomatic medication used against dementia
15 over the period of 2008-2018 for each medication. We then stratified the sales data of each
16 medication based on the income level of each country to investigate how trends in use varied
17 with the national income level. The medication use was standardized according to the total
18 population in each country and region. The sales volume was expressed in DDD per 1,000
19 inhabitants per day (DDDTID). This metric provides an estimate of the proportion of the
20 population receiving a particular medicine daily in a specific year, accounting for the
21 differences in population between countries and differences in standard dosages across
22 individual drugs in the same drug class. The sales volume was also expressed in Standard Units

1 per capita (SU/person) to give a more complete picture of the use of the medicines. The global
2 and national secular trends of medication use were calculated in both DDDTID and SU/person.

3 To better quantify the trends in medication utilization, the compound annual growth
4 rate (CAGR) was calculated to demonstrate the average yearly change in use from 2008 to
5 2013, 2013-2018 and 2008-2018, at both the global and country/regional levels. Countries with
6 data in 2008 unavailable were excluded from this analysis. CAGR is defined as:

$$7 \quad CAGR = \left(\sqrt[N]{\frac{\text{Annual sales volume final}}{\text{Annual sales volume initial}}} - 1 \right) \times 100\%.$$

8 The national sales volume of each country and region and the percentage of each
9 medication use over the total symptomatic medication use against dementia in 2018 were used
10 to assess the between country or region differences in use patterns.

11 All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

12 *Sensitivity analysis*

13 To account for the differences in the population structure and the prevalence of dementia
14 between countries, we conducted an additional analysis standardizing the medication use to the
15 estimated counts of dementia cases for each country and region. The use was measured in DDD
16 per patient per day (DDDPD).
17

18 *Ethics approval*

19 This study was exempt from ethics approval by the UCL Research Ethics Committee as the
20 patient-level data are not available in the IQVIA-MIDAS database.
21

1 **Results**

2 *Global trends for symptomatic medication use against dementia*

3 The overall symptomatic medication against dementia sales increased from 0.85 DDDTID in
4 2008 to 1.33 DDDTID in 2018, which was equivalent to an overall increase of 55.74% and a
5 CAGR of 4.53%. The increases were higher from 2008 to 2013 (CARG=6.59%) than from
6 2013 to 2018 (CARG=2.51%). Donepezil was the most commonly used (0.506 DDDTID in
7 2008 to 0.662 DDDTID in 2018, CAGR=2.72%), memantine had the second-highest rate of
8 use and the greatest increase over the study period (0.192 DDDTID in 2008 to 0.43 DDDTID
9 in 2018, CAGR=8.51%). Sales of galantamine and rivastigmine also increased with an overall
10 CARG of 0.70% and 6.91%, respectively. However, the sales of galantamine started to decrease
11 from 2014 (CAGR 2013-2018=-1.57%), and for rivastigmine, it dropped from 2016 onwards
12 (CAGR 2013-2018=-0.26%) (**Table 1**).

13 The symptomatic medication use against dementia was higher in HICs than LMICs.
14 In HICs, the sales of all four medications varied from 3.88 to 5.17 DDDTID, while in LMICs,
15 it ranged from 0.09 to 0.40 DDDTID. The rate of increase by the average CAGR was higher
16 in LMICs (15.43%) than HICs (2.65%). However, HICs had a higher increase by an absolute
17 percentage of 1.16% than that in LMICs, which was 0.30% (**Table 1**). All four medications
18 had overall increases in use from 2008 to 2018 in both HICs and LMICs. Donepezil is the most
19 commonly used in HICs throughout the study period and in LMICs from 2008 to 2014. The
20 use of memantine surpassed donepezil in LMICs from 2015 onwards. In HICs, the greatest
21 increase was observed for the sales of rivastigmine with a CAGR of 6.18%, which was mainly
22 driven by the increase between 2008 to 2013 (CARG 2008-2013=13.53% vs CARG 2013-

2018=-0.67%). In LMICs, memantine had the greatest increase in sales with a CAGR of 18.10%. The sales volumes of galantamine were the lowest with the slowest rate of growth, regardless of the income level (HICs, CAGR=0.04%; LMICs, CAGR=7.70%) (**Table 1**).

The sales volumes measured in SU/person were mostly consistent with the results in DDDTID (**Table 2**).

Trends in between country or region medication use from 2008 to 2018

After excluding countries with unavailable data in 2008, CAGRs from 2008 to 2018 were analyzed for 58 countries/regions. The median CARG was 11.43% per country (IQR 6.48-19.20) [19.43% (IQR 10.69-22.26) for LMICs, and 8.11% (IQR 2.78-12.71) for HICs]. The top two countries with the highest CAGR were HICs (Croatia, 38.09%; Estonia, 31.39%). There were six countries with negative CAGR, 5 of them were HICs (Switzerland, Canada, Luxembourg, the United States and France), and only 1 was LMIC (Bolivarian Republic of Venezuela) (**Figure 1**).

Patterns in within country or region use in 2018

In 2018, the overall sales volume per person of symptomatic medication used against dementia was 1.33 worldwide, and 0.40 for LMICs and 5.04 for HICs. The median sales of all included countries was 1.44 DDDTID (IQR 0.26-4.26) [0.33 DDDTID (IQR 0.14-1.05) in LMICs and 3.63 DDDTID (IQR 1.45-5.94) in HICs]. The top five countries with the highest use are all HICs (Finland, Greece, Portugal, Puerto Rico and Japan). The LMIC with the highest use was Romania with 7.66 DDDTID (**Figure 2**).

1 In 2018, the most commonly used medication for dementia symptomatic treatments
2 was donepezil, with 49.75% of total symptomatic medications against dementia measured in
3 DDD, followed by memantine with 32.65% of all uses rivastigmine with 11.24% and
4 galantamine with 6.36%. Donepezil use was more common than other medications in 39
5 (59.09%) countries and regions. The median use of donepezil across all countries was 44.65%
6 (IQR 33.94-62.62). Twenty-five (37.88%) countries/regions used memantine as the most
7 common agent, and two (0.03%) countries (Slovenia and Netherlands) used rivastigmine as the
8 most used symptomatic medication against dementia (**Figure 3**).

9 10 *Sensitivity analysis with prevalence-standardized use rates*

11 The rankings of each country vary when the medication usage in 2018 was adjusted according
12 to the prevalence of dementia. In general, the differences between the usage in LMICs to HICs
13 became smaller (**Figure A1, supplementary material**). The overall sales volume was 0.20,
14 0.09 and 0.35 DDDPD for all countries, LMICs and HICs, respectively. Two HICs used more
15 than one DDDPDs of symptomatic medications against dementia: Puerto Rico with 1.14 DDDPD
16 and Finland with 1.08 DDDPD. Three LMICs were ranked in top 10 highest national
17 medication usage: Romania, 0.82 DDDPD, 3rd; Argentina, 0.64 DDDPD, 9th; Turkey, 0.53
18 DDDPD, 10th.

19 20 **Discussion**

21 In this study, we found an overall increasing trend in the global use of symptomatic medication
22 against dementia from 2008 to 2018, with an average annual raise of 4.5%. The increase was

1 greater in between 2008 to 2013 than from 2013 to 2018. The rate of increase was six-fold
2 higher in LMICs compared to HICs. Among the four symptomatic medications used against
3 dementia, memantine had the highest increase in its use. Donepezil or memantine was more
4 commonly used than rivastigmine or galantamine in most countries and regions.

5 The increase in symptomatic medication use against dementia, coupled with the
6 rising prevalence of dementia,(4) may reflect a growing demand for pharmacological
7 treatments for the management of dementia. However, the observed rate of increased
8 medication use exceeded the reported annual increase in the global prevalence of dementia,
9 which was around 3%.(4) This may suggest an increasing proportion of patients with dementia
10 or cognitive impairment received pharmacological treatment. Other than a growing number of
11 patients with dementia, the apparent increase in use of the symptomatic medications against
12 dementia was potentially driven by other factors such as changes in prescribing practices and
13 improved access to drug treatment.(17, 29) The same factors may also explain the differences
14 in the increase in rates between LMICs and HICs. From 2015 to 2020, the annual increase of
15 people with dementia was predicted to be 1.5 times higher in LMICs than HICs, which
16 indicates a more rapid increase in the demand for symptomatic medications against dementia
17 in LMICs.(2, 4) In addition, economic development and several global initiatives towards
18 prevention and treatment of dementia in the developing world, for example, the formation of
19 the 10/66 Dementia Research Group, may have facilitated increasing the dementia awareness
20 among the public, policymakers and health professionals, thus improved access to healthcare
21 and medications and contributed to the observed increased use in LMICs.(4, 30, 31) Conversely,
22 in HICs, inequality to the access of the symptomatic medication against dementia has been

1 reported within countries, but there was inconsistent evidence suggesting an improvement in
2 access over the years.(32, 33) Nevertheless, despite the more rapid growth in the use of
3 symptomatic medications against dementia, the population-standardized use rate was 13-fold
4 higher in HICs than LMICs in 2018. This same magnitude of the difference was not seen in the
5 numbers of patients with dementia or life-expectancies between LMICs and HICs.(3, 4) In our
6 prevalence-standardized analysis in 2018, patients with dementia in HICs still used the
7 medications four times higher than the patients in LMICs. A previous study identified
8 significant affordability gaps of the symptomatic medications used against dementia
9 internationally, with the purchasing-power adjusted prices being 100 times higher in certain
10 LMICs than HICs.(34) Therefore, medication uptake is not only a matter of practical
11 availability and accessibility, but may also be profoundly affected by the differential
12 affordability between countries.

13 The use of all four medications experienced varied extents of increase from 2008 to
14 2018. The highest increase was observed in the use of memantine, with an 8.51% increase per
15 year. The increased memantine use has been reported by previous British and Chinese
16 studies.(1, 21) The NMDA receptor antagonist memantine can be used as the first-line
17 treatment for a patient with moderate to severe dementia or a patient who cannot tolerate an
18 AChEI. It has been reported that memantine was more commonly used in older patients with
19 more severe Alzheimer dementia in practice.(35) The increasing use of memantine hence may
20 reflect the growing proportion of ageing individuals with severe dementia globally.(4)
21 Furthermore, there has been some data suggesting the combination use of memantine and an
22 AChEI.(36) Although the additive benefit was not replicated in the DOMINO-AD trial,(9) a

1 fixed-dose combination polypill of donepezil and memantine had been marketed for use,(37)
2 which could partially explain the gaining popularity of memantine. In terms of the overall
3 global use volumes, donepezil was the most commonly used medication. Donepezil was the
4 first licensed symptomatic medication for the management of dementia and has been available
5 for the longest time with prescriber familiarity. The generic donepezil product became
6 available since 2010 and was covered by most health insurance plans.(38, 39) Additionally, the
7 simplicity of once-daily dosing regimen is a unique strength of donepezil treatment in
8 comparison to other symptomatic medications against dementia,(29) of which the medication
9 adherence is particularly tricky and essential.(40) Notably, the use volume estimated by SU
10 was lower than the estimation by DDD for donepezil relative to the other three agents, as fewer
11 SUs would be consumed in one DDD for the once-daily donepezil treatment. On the contrary,
12 galantamine was the least favored medication with little rise in its usage over the study period.
13 Although there was no evidence suggesting the inferiority of galantamine to other AChEIs
14 clinically, the popularization of galantamine might be hindered by its relatively higher
15 acquisition cost.(29)

16 The trends and patterns of symptomatic medication use against dementia varied
17 significantly between countries. Apart from development status, the variations may be driven
18 by the differences in clinical guidelines and subsidy restrictions across countries. France is the
19 only country with a reduction in medication use at an average annual rate of > 10%, as the
20 French minister of health removed state funding for dementia drugs with the concerns over
21 their limited effectiveness, following a long campaign since 2014 led by the French journal
22 *Prescrire*, which is influential among French prescribers.(41, 42) The same drastic reduction

1 in use was also observed in Venezuela at the average annual rate of 7.28%. The reduction
2 occurred after the collapse of the Venezuelan healthcare system as the government reduced the
3 annual expenditure to public healthcare from 9.1% in 2010 to 5.8% in 2014.(43) A number of
4 the most developed countries, such as Canada and the US, also had small reductions of around
5 1% per year in the use. The reductions in these countries, rather than being caused by the
6 reimbursement policy change, were more likely to be associated with the reduced prevalence
7 of dementia as the result of effective risk reduction and early intervention.(44, 45) In contrast,
8 the symptomatic medication use against dementia in the UK increased at 8% per year over the
9 study period. The use of these medications in the UK has been further promoted by the National
10 Institute for Health and Care Excellence (NICE) guidelines updates in 2018, and a series of
11 government dementia strategies,(17, 46) the growth rate in use in the UK may be expected to
12 increase further. Interestingly, the symptomatic medication used against dementia in Romania,
13 which is a less-developed European country, was consistently higher than other LMICs with
14 more than 20% increase per year and was comparable or even higher than most HICs. The high
15 use rate in Romania may be due to the fact that all symptomatic medications against dementia
16 were available and reimbursable in Romania.(47)

17 The differences in the prescribing practices between countries were also reflected in
18 the varied use patterns between four medications. Certain drugs were not reimbursable or
19 available in some countries; thus the use may be restricted. We summarized the availability of
20 the four medications from various data sources in **Supplementary Table A2**. For instance, in
21 the Netherlands, the use of rivastigmine plus galantamine constituted 92% of total medication
22 use volume in 2018, as donepezil, which is more favored in most other countries, was not

1 available.(48) Another example is New Zealand, 94.5% of symptomatic medication against
2 dementia was donepezil, as donepezil was the only medication funded by The Pharmaceutical
3 Management Agency New Zealand for the management of dementia.(49) Furthermore, the
4 prescribing behaviour of physicians might be profoundly influenced by local sources of
5 information on evidence-based medicine. For example, memantine was the most frequently
6 prescribed symptomatic medication against dementia in Russia as supported by several studies
7 published on Russian journals.(22) The differences between guidelines existed not only
8 between countries and regions but also across specialties. Previous studies have reported that
9 the drug management for dementia was more likely to be prescribed by specialists than general
10 practitioners and among different types of specialists. For example, a neurologist would
11 prescribe more symptomatic medications to manage dementia than a psychiatrist or a
12 geriatrician.(19, 50) All of these variations may suggest that there has not been a consensus on
13 the best practice on the pharmacological intervention for dementia with the existing evidence.
14 In the absence of well-recognized guidance on the clinical practice, factors shaping the
15 prescription and use patterns include, but are not limited to, the availability, affordability,
16 accessibility of the drugs, awareness of and attitudes towards dementia and the medications
17 among physicians, patients, and their caregivers and policymakers. This study provides an
18 overview of the symptomatic medication use against dementia at the global scale, further
19 studies to investigate the specific impediments for the drug use in individual countries are
20 warranted.

21 This is the first study describing the utilization of symptomatic medications against
22 dementia at a global scale. We found the trends for use volumes of medications and compared

1 them between LMICs and HICs. We presented the detailed patterns of the utilization of
2 symptomatic medications against dementia in 2018 at the national level. The sales volumes
3 were measured in both the Defined Daily Dose and Standard Unit, and we showed consistency
4 in both results.

5 There are several limitations to our study. Firstly, we extrapolated pharmaceutical
6 sales data to infer the use of the medications, which could lead to an overestimation of the use
7 at a patient-level if not all the sold medications were taken by the patients. Secondly, the
8 external validation of the IQVIA-MIDAS database was not specific to the study medications,
9 the exact validity of the sales data used in the current study is unknown. Thirdly, although we
10 included 66 countries and regions in our study, there was no data on any individual low-income
11 countries (LICs); only five LICs had aggregate data as part of the region French West Africa,
12 which was excluded from the analyses stratified by income levels. Therefore, LICs might be
13 underrepresented in our study. Furthermore, we were not able to obtain patient-level
14 information on the prescribing of symptomatic medication against dementia, which restricted
15 us from making more comprehensive analyses on gender, age, or diagnosis-specific use of the
16 drugs. Lastly, the current study only evaluated the use of AChEIs and the NMDA receptor
17 antagonist, which is one perspective of dementia management. Individuals with dementia are
18 often co-prescribed with medications from other therapeutic classes to manage non-cognitive
19 symptoms.(17)

20 In conclusion, global symptomatic medication use against dementia increased
21 substantially from 2008 to 2018. The medication use patterns varied considerably across
22 countries and regions which may be due to disparities between treatment guidelines and

1 reimbursement policies. The exact causes of the inconsistency remain to be determined by
2 further studies in order to support the appropriate use of symptomatic medications against
3 dementia globally.

4

1 **Conflicts of Interest**

2 ICKW has received research funding outside the submitted work from Amgen, Bristol-Myers
3 Squibb, Pfizer, Janssen, Bayer, GSK, Novartis, the Hong Kong Research Grants Council, and
4 the Hong Kong Health and Medical Research Fund, National Institute for Health Research in
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1 **Author Contributions**

2 CJ, ICKW and LW conceptualized the study. IWCK and LW provided resources and acquired
3 the data. CJ conducted the data analysis and wrote the original draft under the supervision of
4 LW. All authors critically reviewed, commented and edited on all other drafts.

5

6 **Data Sharing and Data Accessibility**

7 No additional data available.

8

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Figure Legends

Figure 1. Compound annual growth rate in symptomatic medication use against dementia measured in DDDTID of each country and region, 2008-2018. Blue bars, HICs; green bars, LMICs; grey bars, pooled regions.

Figure 2. Total use volume in symptomatic medication against dementia measured in DDDTID of each country and region in 2018. Blue bars, HICs; green bars, LMICs; grey bars, pooled regions.

Figure 3. Proportion of each symptomatic medication use against dementia in each country and region in 2018.

Table 1. Global trends of symptomatic medication use against dementia by medication class and country income level from 2008-2018, measured in DDDTID.

Medication class	DDDTID											CAGR	CAGR	CAGR
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2008-2013 (%)	2013-2018 (%)	2008-2018 (%)
All medications	0.85	0.93	1.02	1.07	1.12	1.18	1.22	1.28	1.32	1.33	1.33	6.59	2.51	4.53
LMIC	0.09	0.11	0.136	0.166	0.19	0.22	0.24	0.30	0.34	0.38	0.40	18.32	12.68	15.43
HIC	3.88	4.21	4.57	4.74	4.66	4.84	4.97	5.08	5.17	5.10	5.04	4.55	0.79	2.65
Donepezil	0.51	0.54	0.59	0.60	0.60	0.61	0.61	0.63	0.65	0.66	0.66	3.71	1.75	2.72
LMIC	0.04	0.05	0.06	0.07	0.08	0.09	0.10	0.12	0.14	0.15	0.16	16.72	12.50	14.64
HIC	2.35	2.51	2.70	2.75	2.55	2.58	2.56	2.59	2.67	2.64	2.63	1.86	0.38	1.12
Galantamine	0.08	0.08	0.08	0.08	0.09	0.09	0.09	0.09	0.09	0.09	0.09	3.09	-1.57	0.7
LMIC	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	12.47	4.10	7.7
HIC	0.37	0.37	0.38	0.39	0.39	0.41	0.40	0.40	0.39	0.38	0.37	1.97	-1.83	0.04
Memantine	0.19	0.22	0.24	0.26	0.30	0.32	0.36	0.40	0.42	0.44	0.43	11.03	6.02	8.51
LMIC	0.04	0.04	0.05	0.07	0.08	0.09	0.10	0.14	0.16	0.19	0.19	20.90	15.24	18.1

HIC	0.82	0.91	0.99	1.06	1.14	1.21	1.34	1.42	1.45	1.44	1.42	8.32	3.13	5.7
Rivastigmine	0.08	0.10	0.11	0.12	0.14	0.15	0.16	0.16	0.16	0.16	0.15	14.57	-0.26	6.91
LMIC	0.01	0.01	0.02	0.02	0.02	0.03	0.03	0.03	0.03	0.03	0.04	15.81	9.30	10.75
HIC	0.34	0.42	0.49	0.54	0.58	0.63	0.66	0.67	0.66	0.64	0.61	13.54	-0.67	6.18

DDDTID, Defined Daily Dose per 1000 inhabitant per day; CAGR, Compound Annual Growth Rate; LMIC, Low-middle income country; HIC, High-income country.

Table 2. Global trends of symptomatic medication use against dementia by medication class and country income level from 2008-2018, measured in SU/person.

Medication class	SU/person											CAGR	CAGR	CAGR
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2008-2013 (%)	2013-2018 (%)	2008-2018 (%)
All medications	0.44	0.47	0.51	0.53	0.56	0.59	0.59	0.61	0.63	0.65	0.66	5.81	2.44	4.11
LMIC	0.06	0.07	0.08	0.10	0.12	0.13	0.14	0.16	0.18	0.19	0.21	17.38	10.24	13.75
HIC	1.89	2.01	2.15	2.21	2.16	2.23	2.23	2.23	2.29	2.31	2.32	3.36	0.79	2.07
Donepezil	0.19	0.20	0.22	0.22	0.22	0.23	0.23	0.24	0.25	0.26	0.26	4.02	2.73	3.37
LMIC	0.016	0.02	0.02	0.03	0.03	0.04	0.05	0.05	0.06	0.07	0.08	19.21	13.97	16.58
HIC	0.84	0.90	0.96	0.98	0.90	0.91	0.91	0.92	0.95	0.95	0.95	1.78	0.80	1.29
Galantamine	0.04	0.04	0.04	0.04	0.04	0.05	0.05	0.05	0.05	0.05	0.05	4.78	1.22	3.03
LMIC	<0.01	<0.01	<0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	5.42	3.71	4.41
HIC	0.17	0.16	0.16	0.17	0.18	0.20	0.21	0.22	0.22	0.22	0.22	3.88	1.54	2.7
Memantine	0.16	0.17	0.19	0.20	0.22	0.23	0.23	0.24	0.25	0.26	0.27	8.07	3.41	5.72
LMIC	0.03	0.03	0.04	0.05	0.06	0.07	0.08	0.09	0.09	0.11	0.11	20.89	9.74	15.18
HIC	0.64	0.70	0.74	0.77	0.78	0.80	0.80	0.78	0.81	0.84	0.86	4.70	1.40	3.04

Rivastigmine	0.06	0.06	0.07	0.07	0.08	0.08	0.08	0.08	0.08	0.08	0.07	5.66	-1.30	2.13
LMIC	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.02	0.02	0.02	0.02	6.33	3.96	4.95
HIC	0.25	0.27	0.29	0.29	0.30	0.31	0.31	0.31	0.31	0.30	0.29	4.56	-1.60	1.44

SU, Standard Units; CAGR, Compound Annual Growth Rate; LMIC, Low-middle income country; HIC, High-income country.