**Supplementary Material for**

**Death Toll by Dementia Drug**

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Supplemental Section 1. Korea Drug Code Medicine

Korean Standard Classification of Diseases (KCD) code for "Alzheimer's disease."

(1) KCD code for Alzheimer's disease.

**Supplementary Table1.** Mental and Behavioural Disorders, F00-F09, G30

|  |  |
| --- | --- |
| F00 code | Dementia in Alzheimer's disease (G30.-+) |
| F01 code | Vascular dementia |
| F02 code | Dementia in other diseases classified elsewhere |
| F03 code | Unspecified dementia |
| F04 code | Organic amnesic syndrome, not induced by alcohol and other psychoactive substances |
| F05 code | Delirium, not induced by alcohol and other psychoactive substances |
| F06 code | Other mental disorders due to brain damage and dysfunction and to physical disease |
| F07 code | Personality and behavioural disorders due to brain disease, damage and dysfunction |
| F09 code | Unspecified organic or symptomatic mental disorder |
| G30 code | Alzheimer's disease |

(2) For symptomatic relief of Alzheimer's disease

**Supplementary Table2.** First Group: For Symptomatic Relief of Alzheimer’s Disease

|  |  |
| --- | --- |
| donepezil hydrochloride | 148603ATB 148602ATD 148602ATB 148601ATD 148601ATB 643401ATD 643402ATD |
| rivastigmine | 224501ACH 224503ACH 224504ACH 224505ACH 224506CPC 224507CPC 224508CPC |
| galantamine | 385203ACR 385203ATR 385204ACR 385204ATR 385205ACR 385205ATR |
| N-methyl-D-aspartate (NMDA) receptor antagonist | 190031ALQ 190001ATB 190003ATD 190004ATB 190004ATD |

**Supplementary Table3.** Second Group: For Psychologic Symptoms of Alzheimer’s Disease

|  |  |
| --- | --- |
| haloperidol | 167903ATB 167904ATB 167905ATB 167906ATB 167908ATB 167908ATB 168030BIJ |
| Risperidone | 224201ATB 224201ATD 224202ATB 224202ATD 224203ATB 224204ATB 224205BIJ 224206BIJ |
| Quetiapine | 378601ATB 378602ATB 378603ATB 378604ATB 378605ATB 378605ATR 378606ATR 378607ATR 378608ATR 378608ATR 378610ATB |
| Olanzapine | 204001ATB 204001ATD 204002ATB 204002ATD 204004ATB 204005ATB |
| Aripiprazole | 451501ATB 451501ATD 451502ATB 451502ATD 451503ATB 451504ATB 451505ATB 451506BIJ 451507BIJ |
| Oxcarbazepine | 206330ASS 206301ATB 206302ATB 206303ATB |
| fluvoxamine | 162501ATB 162502ATB |
| Escitalopram | 474801ATB 474802ATB 474803ATB 474804ATB |
| Trazodone | 242901ACH 242901ATB 242902ATB 242903ATR |
| Sertraline | 227001ATB 227002ATB 227003ATB |
| Escitalopram | 474801ATB 474802ATB 474803ATB 474804ATB |
| Fluoxetine | 161501ACH 161501ATB 161502ACH 161502ATB 161502ATD |

Supplemental Section 2. Data

The National Agency approved this study for Management of Life-sustaining Treatment, which certified that the life-sustaining treatments were managed properly (Korea National Institute for Bioethics Policy (KoNIBP) approval number P01-202007-22-006).

According to the Official Information Disclosure Act in Korea, the Seoul study analyzed AD and anti-Alzheimer's disease drug (AAD) use in Hansen subjects. We searched all medical records of the National Health Insurance Service (NHIS) in Korea and the Sorokdo National Hospital from the time when the International Classification of Diseases (ICD)-9 code and Electronic Data Interchange (EDI) were computerized.

The Sorokdo National Hospital was established in May 1916 to treat leprosy. We connected to the medical record database of the Sorokdo National Hospital and archived it from January 2005 to June 2020. With the ICD-9 and -10 codes, medical data on the correlation between DDS and AD were then analyzed. In the group of patients diagnosed with Alzheimer's disease, the average age of deaths while taking only drugs for dementia treatment (group 1) and the mean age of deaths with taking psychiatric drugs (group 1 & group 2) (Supplementary Table1).

**Supplementary Table4.** The Life expectancy of Hansen's disease patients in the Sorokdo National Hospital

|  |  |  |  |
| --- | --- | --- | --- |
| year | AD First group | AD First & Second group | The life expectancy of Korean |
| 2005 | 90.4 | 93.98 | 78.24 |
| 2006 | 82.5 | 93.49 | 78.78 |
| 2007 | 92.38 | 92.2 | 79.16 |
| 2008 | 96.25 | 92.87 | 79.6 |
| 2009 | 94.74 | 93.09 | 80.04 |
| 2010 | 92.14 | 90.24 | 80.24 |
| 2011 | 91.25 | 90.22 | 80.62 |
| 2012 | 90.16 | 89.28 | 80.87 |
| 2013 | 90.6 | 89.07 | 81.36 |
| 2014 | 92.27 | 90.94 | 81.8 |
| 2015 | 85.56 | 84.88 | 82.06 |
| 2016 | 87.22 | 87.88 | 82.4 |
| 2017 | 88.45 | 86.67 | 82.7 |
| 2018 | 88.2 | 72.1 | 82.7 |
| 2019 | 88.2 | 72.1 | 83.3 |

According to the Official Information Disclosure Act in Korea, we also requested and analyzed the entire ICD 9 and 10 code data (from 2010 to 2019) of AD and AAD from the Health Insurance Review & Assessment system. From 2010 to June 2020, the diagnosis of patients with MCI and AD in Korea increased dramatically (Supplementary Table2).

**Supplementary Table5**. Numbers of drug prescriptions for dementia patients in Korea from 2010 to 2019

|  |  |  |  |
| --- | --- | --- | --- |
| Year | Total billed quantity of drugs | Line of amount billed for drugs | Total number of patients |
| 2,010 | 56,258,246 | 109,447,005 | 257,385 |
| 2,011 | 72,339,833 | 134,113,061 | 319,327 |
| 2,012 | 88,533,271 | 140,102,940 | 376,126 |
| 2,013 | 106,422,008 | 160,202,046 | 435,538 |
| 2,014 | 127,120,294 | 187,253,891 | 497,676 |
| 2,015 | 154,734,543 | 215,276,824 | 562,844 |
| 2,016 | 181,226,560 | 240,267,891 | 627,823 |
| 2,017 | 207,303,641 | 265,949,724 | 692,531 |
| 2,018 | 234,480,000 | 296,443,092 | 767,282 |
| 2,019 | 261,621,750 | 328,425,771 | 839,413 |

(Currency data provided by Morningstar on February 7, 12:58 AM UTC)

|  |
| --- |
| Datalink & processing sheet – Supplementary Tables 4 and 5 |
| https://docs.google.com/spreadsheets/d/1\_L1Q59DNHpod2RdXnZMu\_96utTpIpBugCPZKSZEXJ-E/edit?usp=sharing |

NHIS refused to provide information according to the Official Information Disclosure Act in Korea. The reason was that there was an obligation to protect the business information of pharmaceutical companies. So, the Open Data Mediation Committee should do its best to provide a more efficient and prompt dispute mediation service, intervening in the dispute between NHIS and researchers. Eventually, it was agreed to provide the number of users and deaths for code like this. There were duplicate users and deaths for each code because there might have been a defect in the NHIS database relationships. We decided to accept it and draw a power series to analyze the correlation between the Dementia Management Act trends in 2018 through regression (R2 ) analysis.

**Supplementary Table6.** NHIS Masked Code and ICD-9, -10 Code

|  |  |  |
| --- | --- | --- |
| Masked code | ICD 9, 10 code | Drug  |
| 1486 | 148603ATB 148602ATD 148602ATB 148601ATD 148601ATB 643401ATD 643402ATD | donepezil hydrochloride |
| 1615 | 161501ACH 161501ATB 161502ACH 161502ATB 161502ATD | Fluoxetine |
| 1900 | 190031ALQ 190001ATB 190003ATD 190004ATB 190004ATD | N-methyl-D-aspartate (NMDA) receptor antagonist |
| 2040 | 204001ATB 204001ATD 204002ATB 204002ATD 204004ATB 204005ATB | Olanzapine |
| 2242 | 224201ATB 224201ATD 224202ATB 224202ATD 224203ATB 224204ATB 224205BIJ 224206BIJ | Risperidone |
| 2245 | 224501ACH 224503ACH 224504ACH 224505ACH 224506CPC 224507CPC 224508CPC | Rivastigmine |
| 2270 | 227001ATB 227002ATB 227003ATB | Sertraline |
| 3786 | 378601ATB 378602ATB 378603ATB 378604ATB 378605ATB 378605ATR 378606ATR 378607ATR 378608ATR 378608ATR 378610ATB | Quetiapine |
| 4515 | 451501ATB 451501ATD 451502ATB 451502ATD 451503ATB 451504ATB 451505ATB 451506BIJ 451507BIJ | Aripiprazole |
| 4748 | 474801ATB 474802ATB 474803ATB 474804ATB | Escitalopram |
| 9999 | The others | The others |

**Supplementary Table7.** Anti-Alzheimer's drug (AAD) and User and the Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| Year | AAD | AAD Users | Death |
| 2010 | all | 1496235 | 78528 |
| 2011 | all | 1624963 | 87053 |
| 2012 | all | 1793974 | 100711 |
| 2013 | all | 1879280 | 109772 |
| 2014 | all | 2028410 | 119542 |
| 2015 | all | 2191614 | 135524 |
| 2016 | all | 2373538 | 148351 |
| 2017 | all | 2598416 | 167853 |
| 2018 | all | 2880654 | 185099 |
| 2019 | all | 3234536 | 197232 |

**Supplementary Fig.1.** AAD Trend line. -3.41E-03\*x + 0.0884 R2 = 0.248

**Supplementary Table8.** Donepezil code and User and the Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| Year | Donepezil | Donepezil Users | Death |
| 2010 | 1486 | 96,820 | 12,575 |
| 2011 | 1486 | 123,101 | 15,797 |
| 2012 | 1486 | 150,128 | 19,604 |
| 2013 | 1486 | 176,440 | 22,941 |
| 2014 | 1486 | 204,724 | 26,636 |
| 2015 | 1486 | 236,834 | 32,084 |
| 2016 | 1486 | 267,241 | 36,375 |
| 2017 | 1486 | 294,203 | 42,187 |
| 2018 | 1486 | 319,751 | 47,487 |
| 2019 | 1486 | 336,683 | 48,830 |

**Supplementary Fig.2.** Donepezil Trend line. 2.43E-03\*x + 0.137 R2 = 0.033



**Supplementary Fig.2-1.** Graph of donepezil users and deaths in Korea from 2010 to 2019

The number of users who took donepezil in Korea increased 3.48 times, and the number of deaths increased 3.88 times from 2010 to June 2019. Donepezil users' life expectancies were significantly observed between 2017 and 2019. The DMA was strengthened on June 12 2018.

**Supplementary Table9.** Rivastigmine and User and Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | Rivastigmine user | death |
| 2010 | 2245 | 8,070 | 780 |
| 2011 | 2245 | 9,788 | 850 |
| 2012 | 2245 | 11,218 | 1,103 |
| 2013 | 2245 | 11,935 | 1,170 |
| 2014 | 2245 | 13,705 | 1,291 |
| 2015 | 2245 | 15,542 | 1,847 |
| 2016 | 2245 | 15,103 | 1,682 |
| 2017 | 2245 | 14,443 | 1,716 |
| 2018 | 2245 | 14,777 | 1,839 |
| 2019 | 2245 | 14,964 | 1,840 |



**Supplementary Fig.3.** Rivastigmine Trend line. 3.8E-03\*x + 0.133 R2 = 0.006



**Supplementary Fig.3-1.** Rivastigmine Trend line. The number of users who took rivastigmine in Korea increased 1.84 times, and the number of deaths increased by 2.36 times from 2010 to June 2019

**Supplementary Table10.** Memantine and User and the Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | Memantine user | death |
| 2010 | 1900 | 31,965 | 5,559 |
| 2011 | 1900 | 35,315 | 5,945 |
| 2012 | 1900 | 37,138 | 6,419 |
| 2013 | 1900 | 38,391 | 6,403 |
| 2014 | 1900 | 43,165 | 6,568 |
| 2015 | 1900 | 52,358 | 8,134 |
| 2016 | 1900 | 58,626 | 9,080 |
| 2017 | 1900 | 65,605 | 10,718 |
| 2018 | 1900 | 70,873 | 11,597 |
| 2019 | 1900 | 79,770 | 12,714 |



**Supplementary Fig.4.** Memantine Trend line. 5.67E-03\*x + 0.115 R2 = 0.044



**Supplementary Fig.4-1.** Graph with memantine users and deaths in Korea from 2010 to 2019

The number of users who took memantine in Korea increased 2.50 times, and the number of deaths increased by 2.29 times from 2010 to June 2019. Memantine is an uncompetitive NMDA receptor modulator. It is prescribed to treat moderate-to-severe AD.

**Supplementary Table11.** Risperidone and User and Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | Risperidone user | death |
| 2010 | 2242 | 181,728 | 8,945 |
| 2011 | 2242 | 186,077 | 8,976 |
| 2012 | 2242 | 191,121 | 9,519 |
| 2013 | 2242 | 189,702 | 9,354 |
| 2014 | 2242 | 190,178 | 9,271 |
| 2015 | 2242 | 195,951 | 10,052 |
| 2016 | 2242 | 199,776 | 10,396 |
| 2017 | 2242 | 203,635 | 10,822 |
| 2018 | 2242 | 208,994 | 11,179 |
| 2019 | 2242 | 228,123 | 12,044 |



**Supplementary Fig.5.** Risperidone Trend line. 3.24E-03\*x + 0.0411 R2 = 0.012



**Supplementary Fig.5-1.** Graph with risperidone users and deaths in Korea from 2010 to 2019

The number of users who took risperidone in Korea increased 1.26 times, and the number of deaths increased by 1.35 times from 2010 to June 2019. Risperidone is an antipsychotic medication prescribed to treat schizophrenia and bipolar disorder. It is known to increase the mortality of dementia patients.

**Supplementary Table12.** Fluoxetine and User and Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | Fluoxetine user | death |
| 2010 | 1802 | 156,899 | 1,802 |
| 2011 | 1802 | 151,252 | 1,580 |
| 2012 | 1802 | 150,654 | 1,582 |
| 2013 | 1802 | 140,194 | 1,439 |
| 2014 | 1802 | 134,013 | 1,395 |
| 2015 | 1802 | 133,262 | 1,373 |
| 2016 | 1802 | 137,846 | 1,329 |
| 2017 | 1802 | 144,496 | 1,268 |
| 2018 | 1802 | 157,170 | 1,369 |
| 2019 | 1802 | 173,284 | 1,405 |



**Supplementary Fig.6.** Fluoxetine Trend line. -2.17E-03\*x + 0.0183 R2 = 0.174

**Supplementary Table13.** Olanzapine and User and Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | Olanzapine user | death |
| 2010 | 2040 | 37,810 | 1,654 |
| 2011 | 2040 | 45,177 | 2,001 |
| 2012 | 2040 | 54,344 | 2,681 |
| 2013 | 2040 | 59,184 | 3,112 |
| 2014 | 2040 | 63,444 | 3,276 |
| 2015 | 2040 | 64,123 | 3,036 |
| 2016 | 2040 | 66,902 | 3,368 |
| 2017 | 2040 | 75,153 | 3,700 |
| 2018 | 2040 | 81,868 | 4,042 |
| 2019 | 2040 | 87,565 | 4,359 |



**Supplementary Fig.7.** Olanzapine Trend line. 1.1E-03\*x + 0.0162 R2 = 0.001

**Supplementary Table14.** Sertaline and User and Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | Sertaline user | death |
| 2010 | 2270 | 71,494 | 1,341 |
| 2011 | 2270 | 76,809 | 1,319 |
| 2012 | 2270 | 85,193 | 1,377 |
| 2013 | 2270 | 86,931 | 1,427 |
| 2014 | 2270 | 89,114 | 1,565 |
| 2015 | 2270 | 92,676 | 1,522 |
| 2016 | 2270 | 103,099 | 1,684 |
| 2017 | 2270 | 115,370 | 1,853 |
| 2018 | 2270 | 129,710 | 1,982 |
| 2019 | 2270 | 142,660 | 2,005 |



**Supplementary Fig.8.** Sertaline Trend line. -5.57E-04\*x + 0.0162 R2 = 0.007

**Supplementary Table15.** Quetiapine and User and Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | Quetiapine user | death |
| 2010 | 3786 | 140,218 | 10,654 |
| 2011 | 3786 | 172,218 | 13,466 |
| 2012 | 3786 | 202,486 | 17,654 |
| 2013 | 3786 | 228,140 | 21,117 |
| 2014 | 3786 | 259,635 | 24,520 |
| 2015 | 3786 | 290,105 | 27,972 |
| 2016 | 3786 | 331,811 | 32,972 |
| 2017 | 3786 | 384,209 | 39,984 |
| 2018 | 3786 | 439,704 | 46,257 |
| 2019 | 3786 | 540,397 | 51,767 |



**Supplementary Fig.9.** Quetiapine Trend line. -3.27E-03\*x + 0.125 R2 = 0.151

**Supplementary Table16.** Aripiprazone and User and Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | Ariprprazone | death |
| 2010 | 4515 | 25,155 | 330 |
| 2011 | 4515 | 28,561 | 382 |
| 2012 | 4515 | 37,290 | 466 |
| 2013 | 4515 | 45,297 | 570 |
| 2014 | 4515 | 67,152 | 768 |
| 2015 | 4515 | 84,102 | 1,086 |
| 2016 | 4515 | 102,241 | 1,164 |
| 2017 | 4515 | 133,075 | 1,448 |
| 2018 | 4515 | 174,861 | 1,895 |
| 2019 | 4515 | 214,761 | 2,211 |



**Supplementary Fig.10.** Aripiprazone Trend line. -4.98E-04\*x + 0.0131 R2 = 0.14

**Supplementary Table17.** Escitalopram and User and the Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | Escitalopram | death |
| 2010 | 4748 | 227,186 | 5,093 |
| 2011 | 4748 | 258,981 | 5,949 |
| 2012 | 4748 | 303,698 | 7,060 |
| 2013 | 4748 | 326,645 | 7,585 |
| 2014 | 4748 | 359,582 | 8,118 |
| 2015 | 4748 | 391,772 | 8,726 |
| 2016 | 4748 | 431,465 | 9,298 |
| 2017 | 4748 | 478,751 | 10,365 |
| 2018 | 4748 | 549,235 | 11,480 |
| 2019 | 4748 | 612,579 | 12,472 |



**Supplementary Fig.11.** Escitalopram Trend line. -8.73E-04\*x + 0.0238 R2 = 0.371

**Supplementary Table18.** The others and User and the Death Toll

|  |  |  |  |
| --- | --- | --- | --- |
| year | code | The others user | death |
| 2010 | 9999 | 518,890 | 29,795 |
| 2011 | 9999 | 537,684 | 30,788 |
| 2012 | 9999 | 570,704 | 33,246 |
| 2013 | 9999 | 576,421 | 34,654 |
| 2014 | 9999 | 603,698 | 36,134 |
| 2015 | 9999 | 634,889 | 39,692 |
| 2016 | 9999 | 659,428 | 41,003 |
| 2017 | 9999 | 689,476 | 43,792 |
| 2018 | 9999 | 733,711 | 45,972 |
| 2019 | 9999 | 803,750 | 47,585 |



**Supplementary Fig.12.** AAD The others line. -7.47E-03\*x + 0.116 R2 = 0.129



**Supplementary Fig. 12-1.** Graph with the other users (including galantamine) and deaths in Korea from 2010 to 2019

The number of users who took galantamine and other psychotropic medications in Korea increased 1.55 times, and the number of deaths increased by 1.60 times from 2010 to June 2019.

|  |
| --- |
| Datalink & processing sheet – Supplementary Table7 and S8 |
| https://docs.google.com/spreadsheets/d/1I7WbRVIs4ZKZLCHbpytiOsQlZ8KIgRG55tzKKv1P8U8/edit?usp=sharing |

|  |
| --- |
| Datalink & processing sheet – Supplementary Table9~S18 |
| https://docs.google.com/spreadsheets/d/1gKivXeY7M\_Jp7E\_QP7YlDZSav2s6DCOcTY3i90-ubt0/edit?usp=sharing |

|  |
| --- |
| Datalink & processing sheet – Figure 9 |
| https://docs.google.com/spreadsheets/d/1cWk1adwRFXXynmRPkIMnj1rGghZRAPfK9OHKhcEi8kU/edit?usp=sharing |

Supplemental Section 3. Statistics

The number of deaths is the independent variable, the group of independent variables is five, and the dependent variable is Lee's hidden data.

**Supplementary Table 19.** NHIS Dementia Medicines: Users and Deaths Toll

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Year | AAD | Fluoxetine | Olanzapine | Sertraline | Quetiapine | Aripiprazole | Escitalopram | The others |
|  | User | Death | user | death | user | death | user | death | user | death | user | death | user | death | user | death |
| 2010 | 1,496,235 | 78,528 | 156,899 | 1,802 | 37,810 | 1,654 | 71,494 | 1,341 | 140,218 | 10,654 | 25,155 | 330 | 227,186 | 5,093 | 518,890 | 29,795 |
| 2011 | 1,624,963 | 87,053 | 151,252 | 1,580 | 45,177 | 2,001 | 76,809 | 1,319 | 172,218 | 13,466 | 28,561 | 382 | 258,981 | 5,949 | 537,684 | 30,788 |
| 2012 | 1,793,974 | 100,711 | 150,654 | 1,582 | 54,344 | 2,681 | 85,193 | 1,377 | 202,486 | 17,654 | 37,290 | 466 | 303,698 | 7,060 | 570,704 | 33,246 |
| 2013 | 1,879,280 | 109,772 | 140,194 | 1,439 | 59,184 | 3,112 | 86,931 | 1,427 | 228,140 | 21,117 | 45,297 | 570 | 326,645 | 7,585 | 576,421 | 34,654 |
| 2014 | 2,028,410 | 119,542 | 134,013 | 1,395 | 63,444 | 3,276 | 89,114 | 1,565 | 259,635 | 24,520 | 67,152 | 768 | 359,582 | 8,118 | 603,698 | 36,134 |
| 2015 | 2,191,614 | 135,524 | 133,262 | 1,373 | 64,123 | 3,036 | 92,676 | 1,522 | 290,105 | 27,972 | 84,102 | 1,086 | 391,772 | 8,726 | 634,889 | 39,692 |
| 2016 | 2,373,538 | 148,351 | 137,846 | 1,329 | 66,902 | 3,368 | 103,099 | 1,684 | 331,811 | 32,972 | 102,241 | 1,164 | 431,465 | 9,298 | 659,428 | 41,003 |
| 2017 | 2,598,416 | 167,853 | 144,496 | 1,268 | 75,153 | 3,700 | 115,370 | 1,853 | 384,209 | 39,984 | 133,075 | 1,448 | 478,751 | 10,365 | 689,476 | 43,792 |
| 2018 | 2,880,654 | 185,099 | 157,170 | 1,369 | 81,868 | 4,042 | 129,710 | 1,982 | 439,704 | 46,257 | 174,861 | 1,895 | 549,235 | 11,480 | 733,711 | 45,972 |
| 2019 | 3,234,536 | 197,232 | 173,284 | 1,405 | 87,565 | 4,359 | 142,660 | 2,005 | 540,397 | 51,767 | 214,761 | 2,211 | 612,579 | 12,472 | 803,750 | 47,585 |

Supplementary Table 19-1. NHIS Dementia Medicines: Users and Deaths Toll

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Year | AAD group 1 excluding galantamine | Donepezil | Rivastigmine | Memantine |
|  | User | Death | User | Death | User | Death | user | death |
| 2010 | 136,855 | 18,914 | 96,820 | 12,575 | 8,070 | 780 | 31,965 | 5,559 |
| 2011 | 168,204 | 22,592 | 123,101 | 15,797 | 9,788 | 850 | 35,315 | 5,945 |
| 2012 | 198,484 | 27,126 | 150,128 | 19,604 | 11,218 | 1,103 | 37,138 | 6,419 |
| 2013 | 226,766 | 30,514 | 176,440 | 22,941 | 11,935 | 1,170 | 38,391 | 6,403 |
| 2014 | 261,594 | 34,495 | 204,724 | 26,636 | 13,705 | 1,291 | 43,165 | 6,568 |
| 2015 | 304,734 | 42,065 | 236,834 | 32,084 | 15,542 | 1,847 | 52,358 | 8,134 |
| 2016 | 340,970 | 47,137 | 267,241 | 36,375 | 15,103 | 1,682 | 58,626 | 9,080 |
| 2017 | 374,251 | 54,621 | 294,203 | 42,187 | 14,443 | 1,716 | 65,605 | 10,718 |
| 2018 | 405,401 | 60,923 | 319,751 | 47,487 | 14,777 | 1,839 | 70,873 | 11,597 |
| 2019 | 431,417 | 63,384 | 336,683 | 48,830 | 14,964 | 1,840 | 79,770 | 12,714 |
|  | Results of mortality |
| Year | AAD group 1 excluding galantamine | Donepezil | Rivastigmine | Memantine |
|  | User | Death | User | Death | User | Death | user | death |
| 2010 |  | 0.1382 |  | 0.1299 |  | 0.0967 |  | 0.1739 |
| 2011 |  | 0.1343 |  | 0.1283 |  | 0.0868 |  | 0.1683 |
| 2012 |  | 0.1367 |  | 0.1306 |  | 0.0983 |  | 0.1728 |
| 2013 |  | 0.1346 |  | 0.1300 |  | 0.0980 |  | 0.1668 |
| 2014 |  | 0.1319 |  | 0.1301 |  | 0.0942 |  | 0.1522 |
| 2015 |  | 0.1380 |  | 0.1355 |  | 0.1188 |  | 0.1554 |
| 2016 |  | 0.1382 |  | 0.1361 |  | 0.1114 |  | 0.1549 |
| 2017 |  | 0.1459 |  | 0.1434 |  | 0.1188 |  | 0.1634 |
| 2018 |  | 0.1503 |  | 0.1485 |  | 0.1245 |  | 0.1636 |
| 2019 |  | 0.1469 |  | 0.1450 |  | 0.1230 |  | 0.1594 |

One-Way ANOVA Calculator

|  |
| --- |
| **Summary of Data** |
|  | ***Treatments*** |
| 1 | 2 | 3 | 4 | 5 | Total |
| N | 10 | 10 | 10 | 10 |  | 40 |
| ∑X | 1.395 | 1.3574 | 1.0705 | 1.6307 |  | 5.4536 |
| Mean | 0.1395 | 0.1357 | 0.1071 | 0.1631 |  | 0.136 |
| ∑X2 | 0.1949 | 0.1847 | 0.1163 | 0.2664 |  | 0.7624 |
| Std.Dev. | 0.0061 | 0.0074 | 0.0137 | 0.0075 |  | 0.022 |
| **Result Details** |
| ***Source*** | ***SS*** | ***df*** | ***MS*** |   |
| Between-treatments | 0.0158 | 3 | 0.0053 | *F* = 62.7191 |
| Within-treatments | 0.003 | 36 | 0.0001 |   |
| Total | 0.0189 | 39 |   |   |

The *f*-ratio value is 62.7191. The *p*-value is < .00001. The result is significant at *p* < .05.

The values of the Friedman X2r statistic and p appear



**Supplementary Table 20.** NHIS Dementia Medicines: Users and Deaths Toll

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Year | AAD | Donepezil | Rivastigmine | Memantine | Risperidone |
|  | User | Death | User | Death | User | Death | user | death | user | death |
| 2010 | 1,496,235 | 78,528 | 96,820 | 12,575 | 8,070 | 780 | 31,965 | 5,559 | 181728 | 8945 |
| 2011 | 1,624,963 | 87,053 | 123,101 | 15,797 | 9,788 | 850 | 35,315 | 5,945 | 186077 | 8976 |
| 2012 | 1,793,974 | 100,711 | 150,128 | 19,604 | 11,218 | 1,103 | 37,138 | 6,419 | 191121 | 9519 |
| 2013 | 1,879,280 | 109,772 | 176,440 | 22,941 | 11,935 | 1,170 | 38,391 | 6,403 | 189702 | 9354 |
| 2014 | 2,028,410 | 119,542 | 204,724 | 26,636 | 13,705 | 1,291 | 43,165 | 6,568 | 190178 | 9271 |
| 2015 | 2,191,614 | 135,524 | 236,834 | 32,084 | 15,542 | 1,847 | 52,358 | 8,134 | 195951 | 10052 |
| 2016 | 2,373,538 | 148,351 | 267,241 | 36,375 | 15,103 | 1,682 | 58,626 | 9,080 | 199776 | 10396 |
| 2017 | 2,598,416 | 167,853 | 294,203 | 42,187 | 14,443 | 1,716 | 65,605 | 10,718 | 203635 | 10822 |
| 2018 | 2,880,654 | 185,099 | 319,751 | 47,487 | 14,777 | 1,839 | 70,873 | 11,597 | 208994 | 11179 |
| 2019 | 3,234,536 | 197,232 | 336,683 | 48,830 | 14,964 | 1,840 | 79,770 | 12,714 | 228123 | 12044 |

Supplementary Table20-1. Lee's hidden equation for a comparison graph of five independent variables

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Year | AAD | Donepezil | Rivastigmine | Memantine | Risperidone |
|  |  |  |  |  |  |
| 2010 | 0.0662 | 0.1226 | 0.0407 | 0.1152 | 0.0071 |
| 2011 | 0.0808 | 0.1409 | 0.1769 | 0.2600 | 0.1077 |
| 2012 | 0.1062 | 0.1268 | 0.0934 | -0.0128 | 0.1163 |
| 2013 | 0.0655 | 0.1306 | 0.0684 | 0.0346 | -0.1744 |
| 2014 | 0.0979 | 0.1697 | 0.3027 | 0.1703 | 0.1353 |
| 2015 | 0.0705 | 0.1411 | 0.3759 | 0.1509 | 0.0899 |
| 2016 | 0.0867 | 0.2156 | -0.0515 | 0.2347 | 0.1104 |
| 2017 | 0.0611 | 0.2075 | 0.3683 | 0.1669 | 0.0666 |
| 2018 | 0.0343 | 0.0793 | 0.0053 | 0.1255 | 0.0452 |
| 2019 | 0.0610 | 0.1450 | 0.1230 | 0.1594 | 0.0528 |

One-Way Repeated Measures ANOVA Calculator

|  |
| --- |
| Summary of Data |
|  | *Treatments* |
| AAD | Donepezil | Rivastigmine | Memantine | Risperidone | Total |
| N | 10 | 10 | 10 | 10 | 10 | 50 |
| ∑X | 0.7302 | 1.4791 | 1.5031 | 1.4047 | 0.5569 | 5.674 |
| Mean | 0.073 | 0.1479 | 0.1503 | 0.1405 | 0.0557 | 0.113 |
| ∑X2 | 0.0572 | 0.2336 | 0.4327 | 0.2581 | 0.1034 | 1.085 |
| Std.Dev. | 0.0207 | 0.0406 | 0.1516 | 0.0822 | 0.0897 | 0.0949 |
| Result Details |
| *Source* | *SS* | *df* | *MS* |   |
| Between-treatments | 0.0825 | 4 | 0.0206 | *F* = 3.2028 |
| Within-treatments | 0.3587 | 45 | 0.008 |   |
| Error | 0.2317 | 36 | 0.0064 |   |

The *F*-ratio value is 3.2028. The *p*-value is .023868. The result is significant at *p* < .05.

(https://www.socscistatistics.com/tests/anovarepeated/default.aspx)

The values of F and p appear significant.