Dementia Management Act and Death Toll by Dementia Drug

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Research Article

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Abstract

The Dementia Management Act (DMA) came into effect on August 04 2011, South Korea. Medical data on the correlation between Alzheimer's disease (AD) and anti-AD drugs (AAD) groups were observed from 2010 to 2019. This study investigated the increase and decrease of deaths and AAD used to treat AD. It is known that psychotropic medicines should not be administered for dementia patients because they increase all-cause mortality. This study demonstrated that acetylcholinesterase inhibitors also increase the death toll when used to treat dementia.

Main Text

The Dementia Management Act (DMA) purposes are to mitigate personal pain and damage from dementia. The DMA came into effect on August 04 2011, in South Korea. Act amended it No. 15649, June 12 2018. Medical personnel, the psychiatrists or neurologists of medical institutions, and workers engaged in providing medical services under the Medical Service Act became very active in dementia management programs executed by the State and local governments. According to DMA, the Sorokdo National Hospital, established in May 1916 to treat leprosy, also provide Alzheimer's disease (AD) treatment and preventive services.

This study investigated the increase and decrease of deaths and anti-AD drugs (AAD) used to treat AD in South Korea. South Korea is a country where is the most well-computerized. According to the DMA policy, AD patients and AAD prescriptions are increasing rapidly, so it is most suitable for analyzing national medical data.

Results

Compared with South Koreans' increased life expectancy, there was a gradual decline in Hansen's disease (HD) patients' life expectancy. HD patients taking AAD group 2 together with group 1 had a shorter lifespan than those taking AAD group 1 alone (Fig. 1).

The reason is presumed to be because a public health doctor was working 2017–2019 in Sorokdo National Hospital to thoroughly substitute military service to administer psychiatric medication (AAD).

From 2010 to June 2019, the diagnosis of patients with MCI or AD in Korea increased by 3.26 times, and AAD increased by 4.65 times (Fig. 2).

The number of users who took donepezil in Korea increased by 3.48 times, and the deaths increased by 3.88 times from 2010 to June 2019 (Fig. 3).

The number of users who took AAD in Korea increased by 2.16 times, and the deaths increased by 2.51 times from 2010 to June 2019 (Fig. 4).

The number of users who took risperidone in Korea increased 1.26 times, and the deaths increased by 1.35 times from 2010 to June 2019 (Fig. 5).

The number of users who took memantine in Korea increased 2.50 times, and the deaths increased by 2.29 times From 2010 to June 2019 (Fig. 6).

The number of users who took galantamine and the other psychotropic medications in Korea increased 1.55 times, and the death increased by 1.60 times, From 2010 to June 2019 (Fig. 7).

So, regression analysis was always significant when comparing death among AAD users with regression analysis and diverse power series. In addition to psychotropic medications, cholinesterase inhibitors (donepezil, rivastigmine) also increase mortality when used as a treatment for dementia.

Discussion

DMA intended to lighten its burden on society and help enhance national health by establishing and implementing comprehensive policies on preventing dementia, support for dementia patients, and research of finding a cure for dementia. Life expectancy between AD and AAD group 1, 2 were significantly observed (Fig. 1. between 2018 and 2019). It is because the DMA was strengthened on June 12 2018.

However, the neurological side effects of donepezil among AAD are similar to those of dementia [1]. Few people can distinguish whether they are side effects caused by dementia or donepezil drugs: Dizziness, delusions, dream abnormalities, ataxia, convulsive seizures, hemiplegia, hypertonia, salivation [2 3]. Four FDA-approved therapeutics for the management of cognitive impairment diseases and symptomatic AD include three cholinesterase inhibitors (ChEIs; donepezil, rivastigmine, and galantamine) and memantine, an uncompetitive NMDA receptor modulator. Three ChEIs are approved for use in mild-to-moderate AD, and their symptomatic benefit in AD has been confirmed via meta-analyses assessing both cognitive performance and global functioning [4]. However, the data analysis on the number of people who took donepezil and the number of fatalities among the three ChEIs revealed that the number of deaths increased as the number of prescriptions increased (Fig. 5).

All studies from many countries already confirmed that antipsychotic drugs should not be administered for dementia patients because they increase the risk of seizures and all-cause mortality. Deprescribing psychotropic medications are feasible to most people experiencing no withdrawal symptoms in long-term care [5 6].

However, many toxins are cholinesterase inhibitors, and these toxins can cause death if given in high enough dosages. There is no known cumulative effect when taken consistently like humans. Botulinum toxin blocks the release of acetylcholine hormone from the presynaptic terminal by preventing acetylcholine release [7]. Black widow spider venom is thought to be associated with a wide release of neurotransmitters, especially norepinephrine and acetylcholine, due to spider envenomation. If the widow

venom exhausted all acetylcholine supplies as the opposite effect of botulinum toxin, paralysis occurs [8] [9].

Acetylcholine performs various physiologic functions through cholinergic muscarinic receptors, five different types of muscarinic receptors, M1, M2, M3, M4, and M5. The muscarinic receptor M1 is in the cerebral cortex, salivary, and gastric glands. The muscarinic receptor M2 are present in smooth muscle as well as cardiac tissue. The muscarinic receptor M3 are in smooth muscle cells, particularly of the bronchioles, iris, bladder, and small intestines. The muscarinic receptor M4 and M5 have a less clear distribution but have been found in the hippocampus, substantia nigra, and other locations within the brain [10] [11].

The non-neuronal cholinergic system is involved in the pathophysiology of diseases [12]. On the cardiovascular system, it determines generalized vasodilation, negative chronotropic effect, negative inotropic effect. It is a less pronounced negative dromotropic effect in the specialized tissue of the sinoatrial and atrioventricular nodes at the ventricular level than other organs. Muscarinic receptor 2 is not the only functional subtype found within the heart, and muscarinic receptors 1 and 3 mediate both dilation and constriction in the vasculature [13].

When a patient who had been taking dapsone, which is mainly used in clinical studies on inflammasome competitors [3] [14] [15], stopped dapsone for stroke treatment and administered acetylcholine precursors, it rapidly progressed to rapid hypertension and pulmonary hypertension [2]. Patients life expectancy at Sorokdo National Hospital, which is known to live longer [16], is gradually decreasing (Fig. 1).

AADs administered to the elderly are closely related to health insurance policies. If the elderly die early, health insurance companies will benefit. However, health insurance policies have been operated to improve the health of the elderly [17]. Long-term administration of ChEIs to patients with dementia has increased mortality. The effects of ChEIs on cardiovascular systems should be analyzed and studied.

Materials And Methods

Experimental Design

The Seoul study analyzed AD and anti-Alzheimer's disease drug (AAD) use in Hansen subjects according to the Official Information Disclosure Act in Korea,. We searched all medical records of the National Health Insurance Service (NHIS) in Korea when the Korean government computerized the International Classification of Diseases (ICD)-9 (10) code and Electronic Data Interchange (EDI). We also connected to the medical record database of the Sorokdo National Hospital and archived it from January 2005 to June 2020. The Sorokdo National Hospital was established and operated exclusively for Hansen's disease (HD) patients. Since HD patients take therapeutics for leprosy, a Seoul cohort runs to study AD and AAD's correlation.

With the ICD-9 and – 10 codes, medical data on the correlation between AD and AAD were then analyzed for cohort correlational possibility. AAD First group, according to Korea Drug Code Medicine, First Group: For symptomatic relief of Alzheimer's disease (donepezil hydrochloride, rivastigmine, galantamine, N-methyl-D-aspartate (NMDA) receptor antagonist). AAD Second group is according to Korea Drug Code Medicine Second Group: For psychologic symptoms of Alzheimer's disease (haloperidol, Risperidone, Quetiapine, Olanzapine, Aripiprazole, Oxcarbazepine, fluvoxamine, Escitalopram, Trazodone, Sertraline, Escitalopram, Fluoxetine). (Supplement 1. Korea Drug Code Medicine) The mean age of death of AD patients was classified into the First or Second group.

Through the coordination of the Open Data Mediation Committee, data on the number of deaths among people taking AAD from 2010 to 2019 were available from NHIS. We analyzed the entire ICD 9 and 10 code data (from 2010 to 2019) of AAD and Death from NHIS. We used the software programs Object-Relational DBMS and Google spreadsheet for R^2 analysis and power series calculations.

Declarations

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Author Contributions: JL developed the theory of inflammasome competitor, performed the experiments and wrote the manuscript.

Competing Interests

Authors declare that they have no competing interests.

Data and Materials Availability

According to the Official Information Disclosure Act in Korea, it is possible to provide public access to a dataset based on the linkage of data from nationwide public registries. Access to the National Health Insurance Service (NHIS) in Korea and the Sorokdo National Hospital and the Health Insurance Review & Assessment system's registry data can be granted to individual researchers only upon seeking approval, according to the National Agency for Data Protection. We, therefore, cannot place the dataset in a public repository. However, pooling of aggregated data is possible and would be of interest to the research group.

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Figures

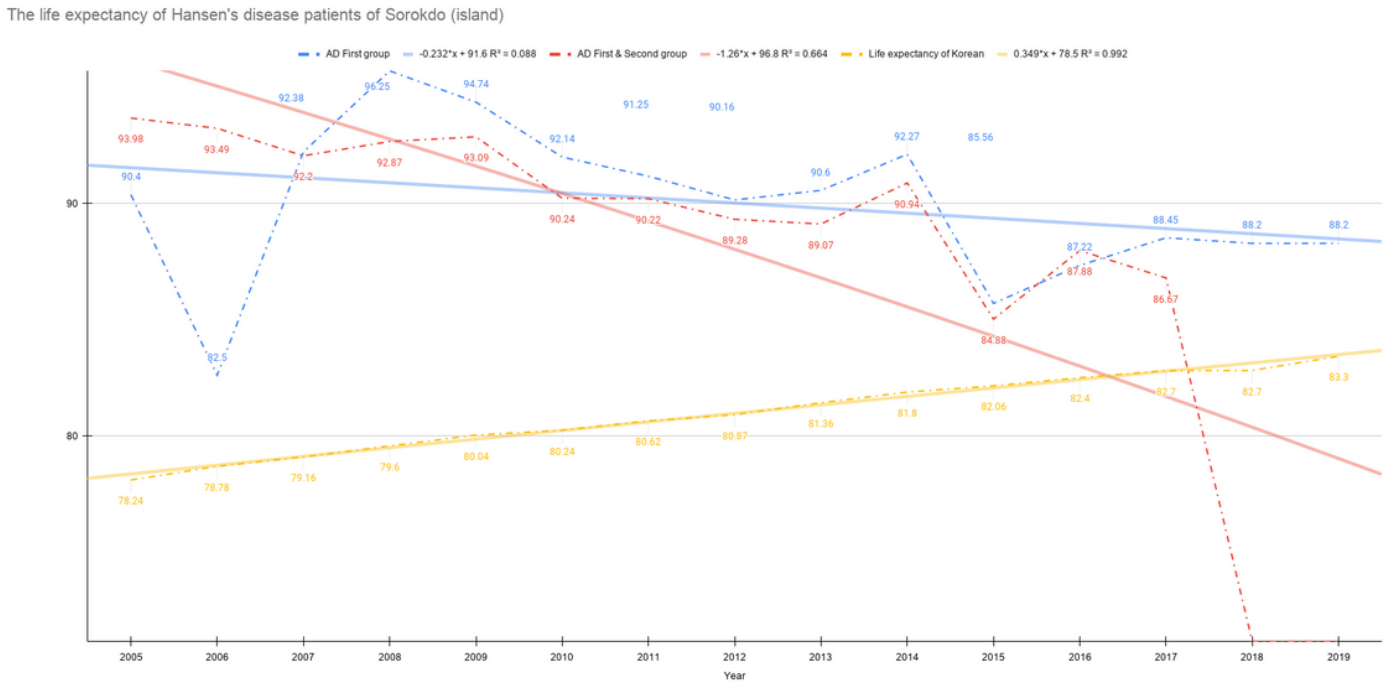

Figure 1

The life expectance of Hansen's disease patients had Alzheimer's disease in the Sorokdo National Hospital. In the group of patients diagnosed with Alzheimer's disease, the mean age of deaths while taking only dementia symptom treatment is blue. The mean age of deaths with taking additional psychiatric drugs is red. In 2018-2019, the life expectancies of Hansen's disease (HD) patients taking additional psychotropic medications were suddenly decreased in the Sorokdo National Hospital. On the other hand, Korean's life expectancy is on the rise (see the yellow). The life expectancies of HD patients taking the AAD first group (blue) were decreased in the Sorokdo National Hospital.

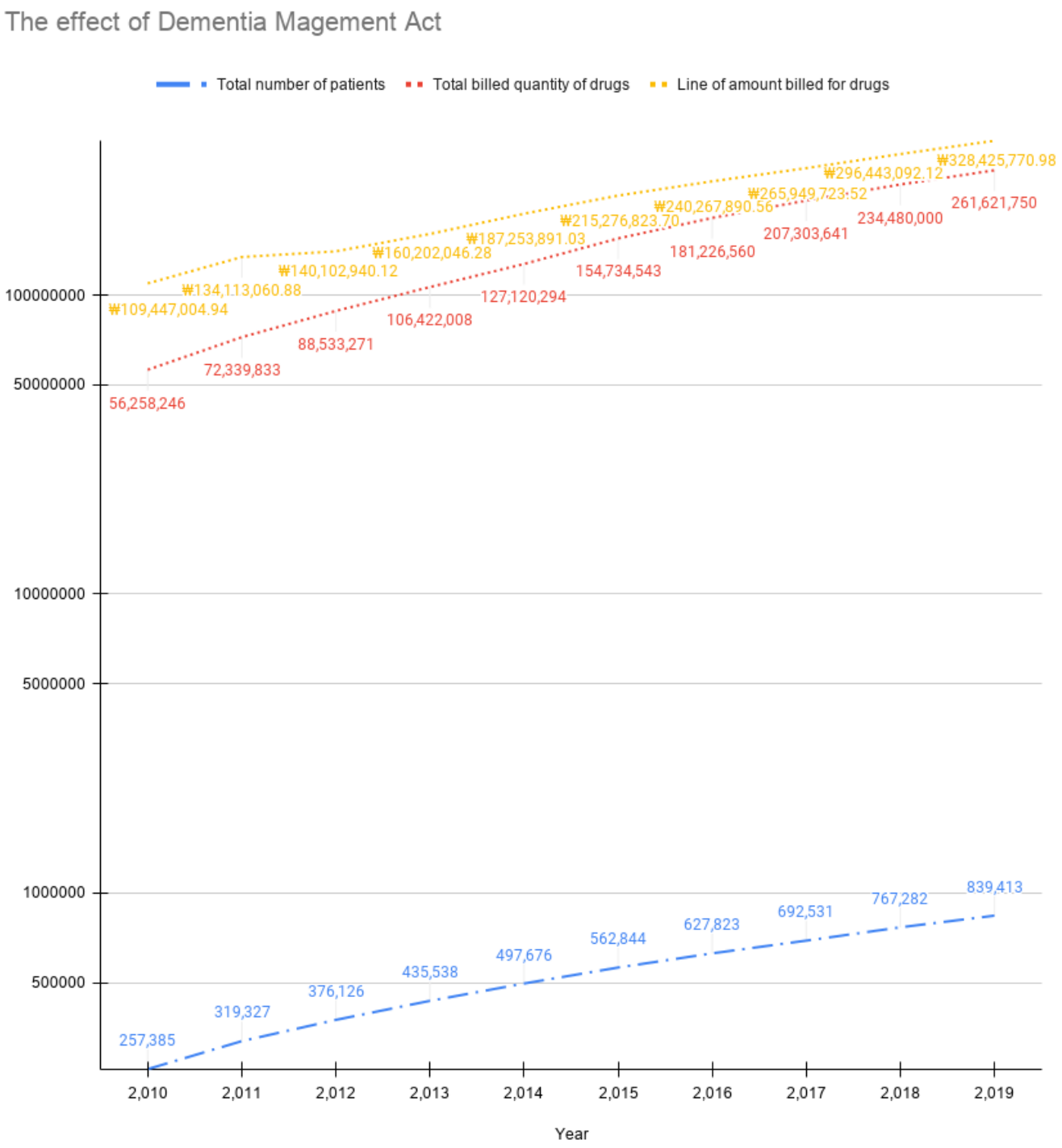

Figure 2

Numbers of drug prescriptions for dementia patients in Korea from 2010 to 2019. The State or a local government subsidizes dementia patients for expenses incurred in the treatment and diagnosis of dementia from its budget, considering each dementia patient's capability to bear such costs. The data of AD and AAD was reported from the Health Insurance Review & Assessment system. From 2010 to June

2020, the diagnosis and prescription of patients with MCI and AD in Korea increased 3.26 times, 4.65 times.

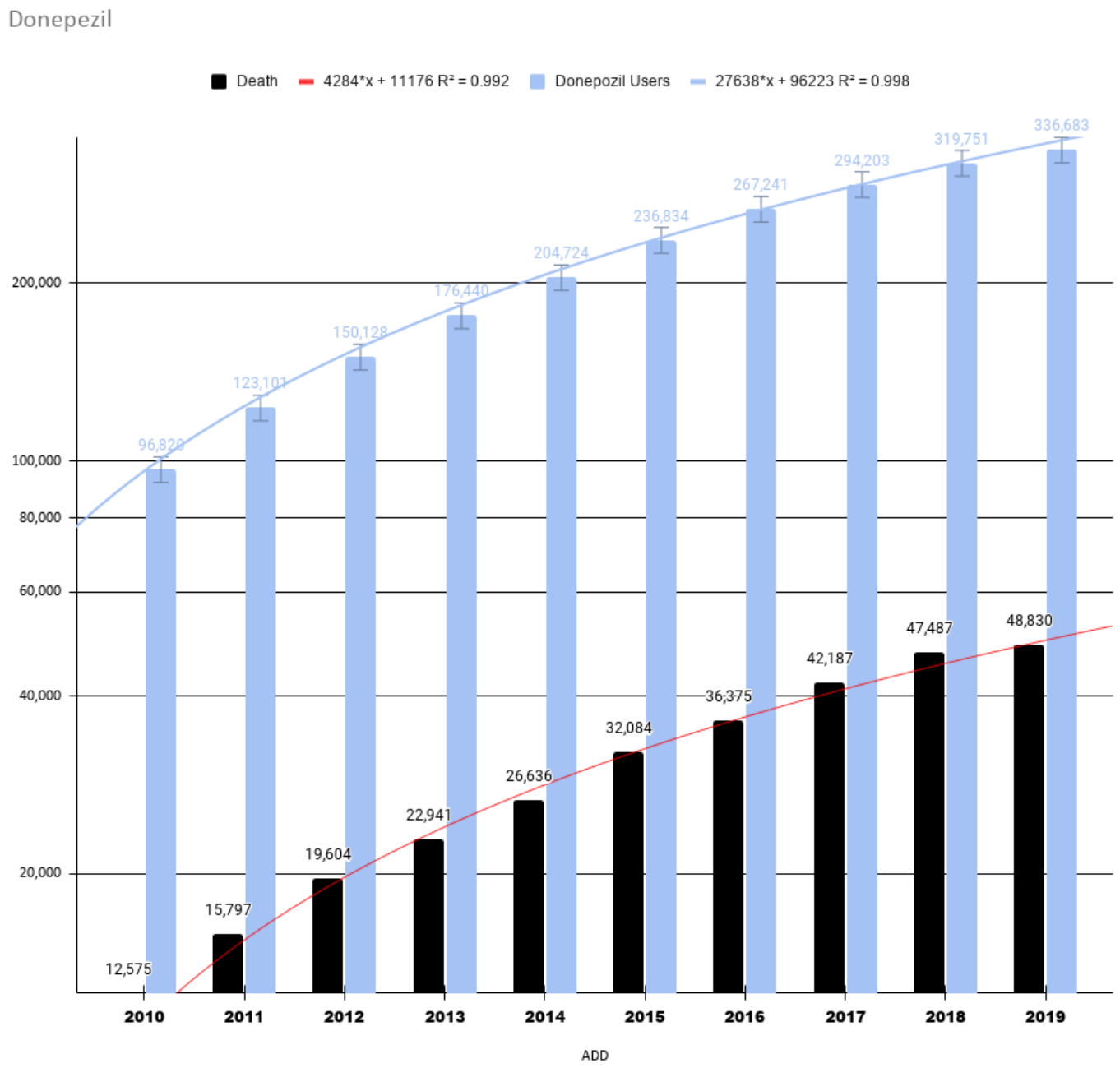

Figure 3

Graph with the 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 deaths increased by 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.

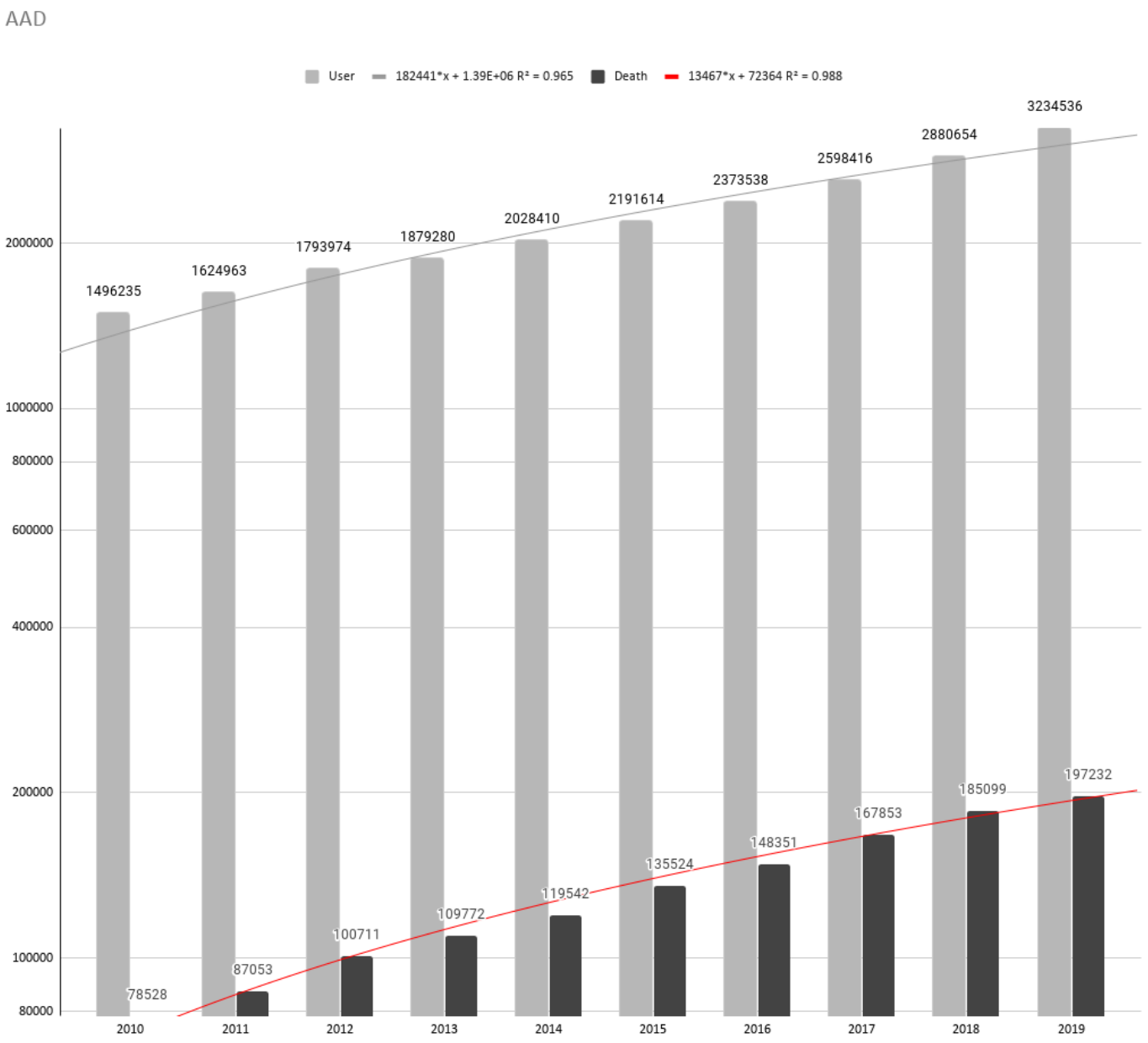

Figure 4

Graph with AAD users and deaths in Korea from 2010 to 2019. The number of users who took AAD in Korea increased 2.16 times, and the deaths increased by 2.51 times From 2010 to June 2019. The life expectancy between AD and AAD were significantly observed between 2017 and 2019. It is because the DMA was strengthened on June 12 2018. The life expectancies of Hansen's disease (HD) patients taking AAD were also decreased in the Sorokdo National Hospital.

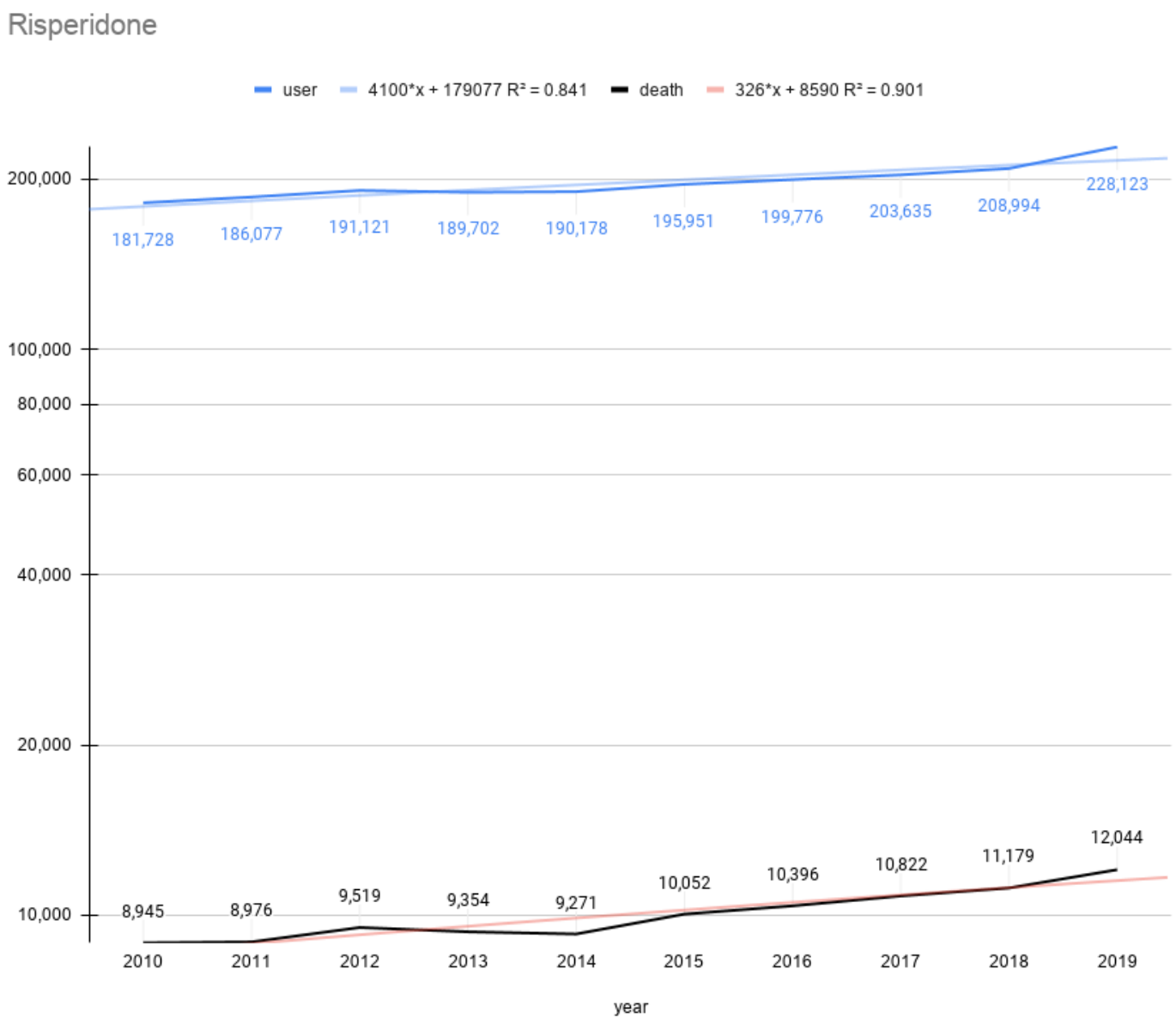

Figure 5

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 deaths increased by 1.35 times from 2010 to June 2019. Risperidone is an antipsychotic medication prescribed to treat schizophrenia and bipolar disorder. It was known to increase the mortality of dementia patients.

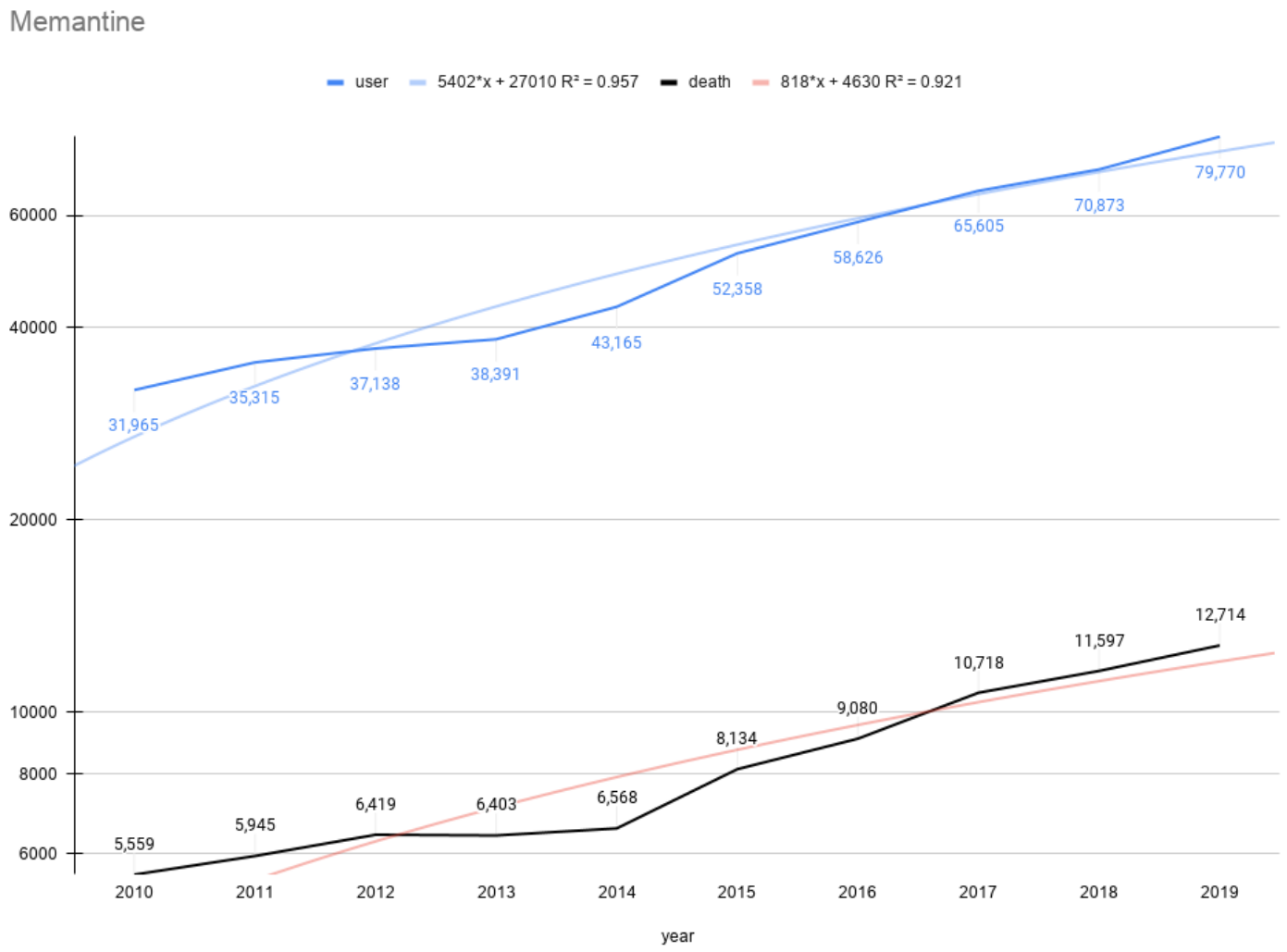

Figure 6

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 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.

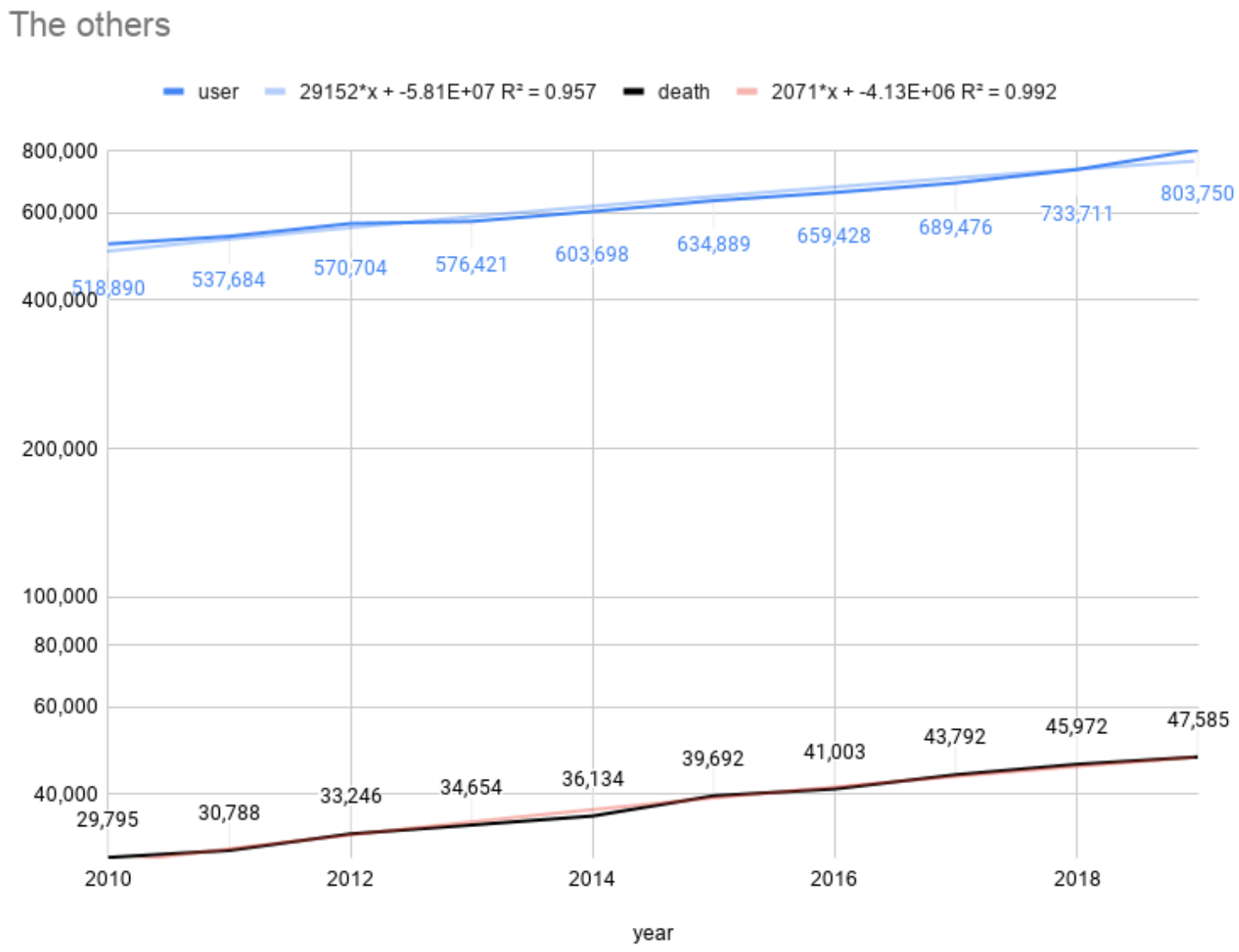

Figure 7

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

Supplementary Files

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- SupplementaryMaterialsfinal.pdf
- 2020029PublicDataProvisionDisputeMediationNotification2.pdf
- KoNIBPIRB20201605001.pdf