

# Commentary for the Elderly in the Pandemic Era

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In Korea, research into geriatric medicines started the Seoul Longitudinal Study on Aging from 1996 to 1999 [1] at the WHO Collaborating Center of Physical Culture and Aging Research for Health Promotion, Medical Research Center, Seoul National University, Seoul, Republic of Korea. The Seoul Longitudinal Study studied subjects (centenarians) older than 95 years of age [2]. Since 2001, various members of the Faculties of Medicine, Nutrition, Psychology, Family and Environmental Medicine, Demography, and Anthropology have participated in the nation-wide Korean Centenarian Study.

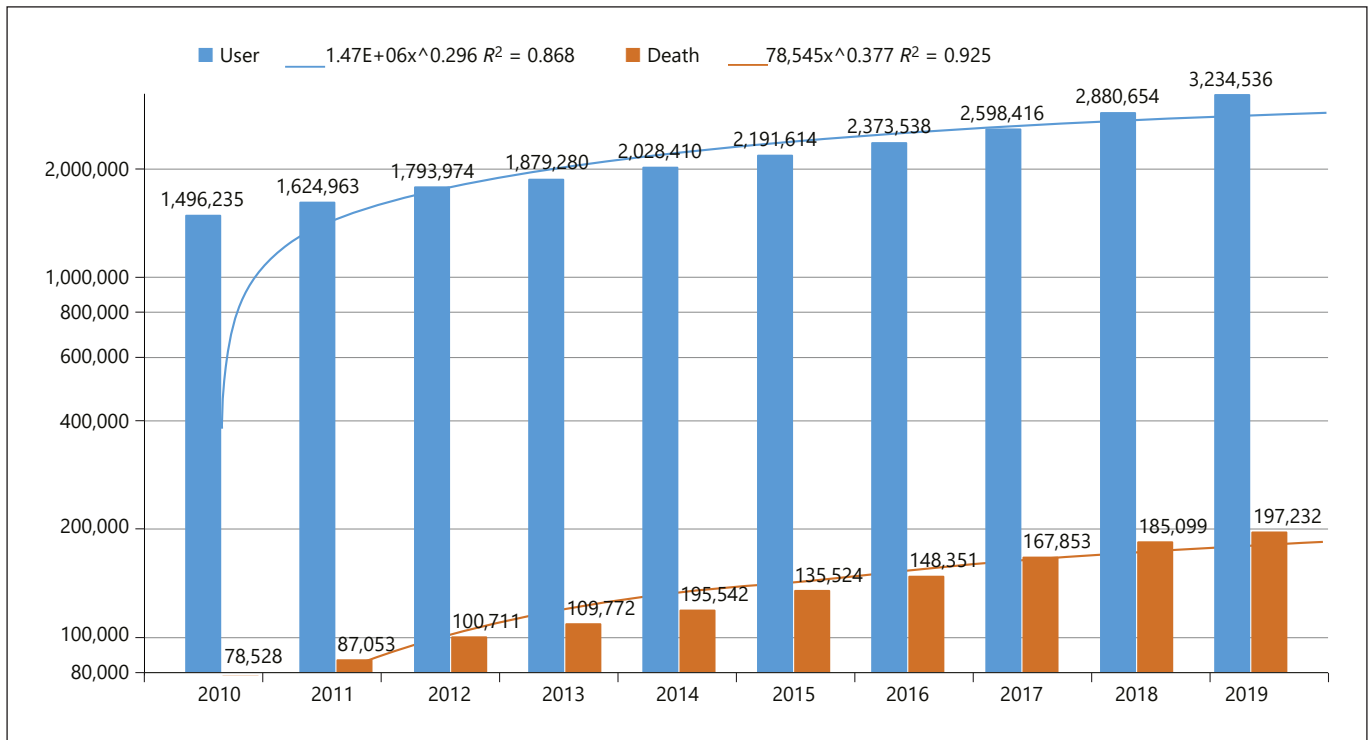
Some places in the world like Okinawa, Japan, and Sardinia, Italy, have an unusual number of individuals older than 100 years. There is a longevity village, Sunchang, in Korea. Centenarians living in mountainous regions have better health than those living near the sea. Similar findings have been noted in Sardinia, Italy. Habitat might influence gender differences in longevity, mainly via the influence of diet and physical activity [3].

One of the Centenarian Study researchers, S.C. Park, visited Sorok Island, where Hansen's disease (HD) pa-

tients live, and found that the population had a long life expectancy [4–7]. He hypothesized that one of the reasons for this long life expectancy is that dapsone, a medicine for HD, acts as an antioxidant. This investigation into whether dapsone contributes to longevity is ongoing.

J.L., who was conducting a study on the elderly diagnosed with mild cognitive impairment in 2008, began researching Alzheimer's disease and Parkinson's disease [8]. He created the Seoul cohort to study the action of the sulfone group of dapsone (under the assumption that this drug would expand cerebrovascular blood vessels). In December 2020, the study confirmed the action of dapsone on the neuroinflammasome [9, 10]. In addition to the research into Alzheimer's disease, the findings of the HD studies are currently being clinically implemented to treat COVID-19 patients for acute respiratory distress syndrome (ARDS). Dapsone is also used to treat sequelae.

Dapsone binds noncovalently to the minor groove of DNA [11, 12]. Until now, scientists regarded dapsone as an adjuvant [13], alternative [14], augmentation [15, 16], or active ingredient [6, 17] for improved outcomes for



**Fig. 1.** Graph of total dementia drug prescriptions and deaths of Alzheimer's disease patients in Korea. The trend line is a power series. Around the revision of the Dementia Act in 2018, the prescription of dementia drugs and deaths increased together. Psychiatric drugs: aripiprazole, olanzapine, risperidone, quetiapine, hal-

operidol, selective serotonin reuptake inhibitors, and carbamazepine. Dementia symptom-improving drugs: donepezil, galantamine, rivastigmine, and memantine. These data are from an entire database of the Korea Health Insurance Corporation.

patients. Newly developed drugs are used to treat significant diseases, but dapsones improve treatment efficiency.

To date, dapsones are used as a treatment and preventive drug for mild cognitive impairment [8, 18], Alzheimer's disease [10], Parkinson's disease [19, 20], seizure [21], stroke [9, 22, 23], and COVID-19 ARDS [11, 13].

We present the data on the increase and decrease in deaths and the psychiatric drugs administered with 4 types of dementia symptom-improving drugs from 2010 to 2019 (Fig. 1).

The medicines mainly administered to the elderly are closely related to health insurance policies. Of course, if the elderly die quickly, health insurance companies benefit. However, health insurance policies are operated to maintain the health of the elderly. If dapsones were used for the early symptoms of cognitive impairment or stroke, many earlier deaths could be prevented. Recently, the team of B.K. at the Hunt Regional Hospital reported a study that drastically reduced mortality by administering dapsones to patients with COVID-19 ARDS in the intensive care unit [11, 13]. J.M.'s

research team, who studied brain autopsy findings of COVID-19 patients, supported the findings of B.K.'s team by demonstrating the impact of SARS-CoV-2 infection in the medulla oblongata's pre-Bötzinger complex [24].

## Methods

We connected to the Korea Health Insurance Corporation's medical records database and archived it from 2010 to 2019. With the ICD-9 and ICD-10 codes, medical data on the correlation between Alzheimer's disease and dementia drugs were then analyzed for cohort correlational possibility.

### List of ICD Codes and Diseases

F00, dementia in Alzheimer's disease (G30.-+); F01, vascular dementia, F02, dementia in other diseases classified elsewhere; F03, unspecified dementia; F04, organic amnesic syndrome, not induced by alcohol and other psychoactive substances; F05, delirium, not induced by alcohol and other psychoactive substances; F06, other mental disorders due to brain damage and dysfunction, and to physical disease; F07, personality and behavioral disorders

due to brain disease, damage, and dysfunction; F09, unspecified organic or symptomatic mental disorder; G30, Alzheimer's disease.

#### *Dementia Drugs according to the Korea Drug Code of Medicines*

First-group dementia drugs are administered for symptomatic relief in Alzheimer's disease. Examples are: donepezil hydrochloride (148603ATB 148602ATD 148602ATB 148601ATD 148601ATB 643401ATD 643402ATD), rivastigmine (224501ACH 224503ACH 224504ACH 224505ACH 224506CPC 224507CPC 224508CPC), galantamine (385203ACR 385203ATR 385204ACR 385204ATR 385205ACR 385205ATR), and N-methyl-D-aspartate [NMDA] receptor antagonist (190031ALQ 190001ATB 190003ATD 190004ATB 190004ATD).

Second-group drugs are administered for psychological symptoms of Alzheimer's disease. Examples are: haloperidol (167903ATB 167904ATB 167905ATB 167906ATB 167908ATB 167908ATB 168030BI), 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), and fluoxetine (161501ACH 161501ATB 161502ACH 161502ATB 161502ATD).

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## Statement of Ethics

The Bioethics Committee, a central institution designated by the Ministry of Health and Welfare, approved the observational study of patients ethically based on FDA guidelines following the World Medical Association Declaration of Helsinki (P01-202007-22-006). We carried out all methods following relevant ethics guidelines and regulations.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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## Author Contributions

J.L. discussed with C.J.L., J.P., S.J.L., and S.-H.C., who studied Alzheimer's disease and stroke to write this paper. J.L. discussed SAR-CoV-2 treatment with A.K., B.K., C.S., and J.B. The contents and conclusions of this paper were reviewed by all authors. J.L. wrote the paper.

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