Demographics and medication use of patients with late-onset Alzheimer's disease in Hong Kong

Running title: Alzheimer's disease in Hong Kong

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Abstract:

Background: Alzheimer's disease (AD) is the commonest cause of dementia in the elderly population. However, epidemiological studies on the demographics of AD in Hong Kong population are lacking.

Objectives: We investigated the demographics, comorbidities, mortality rates, and medication use of patients with AD in Hong Kong to understand how the disease has been managed locally.

Methods: This was a collaborative study of The Hong Kong University of Science and Technology and the Hospital Authority Data Collaboration Lab. We analyzed the demographic data, clinical records, diagnoses and medication records of patients with AD under the care of the Hospital Authority between January 1, 2007 and December 31, 2017.

Results: We identified 23,467 patients diagnosed with AD. The median age at diagnosis was 84 years old, and 71% of patients were female. The commonest comorbidity was hypertension (52.6%). 39.9% of patients received medications for dementia; of those, 68.4% had taken those medications for >1 year. Compared to nonusers, long-term AD medication users had a significantly younger age of AD onset and were taking more lipid-regulating medication, diabetes medication, or antidepressants. Surprisingly, the use of antipsychotics in patients with AD was quite common; 50.7% of patients had received any type of antipsychotic during disease progression.

Conclusion: This study provides detailed information on the demographics and medication use of patients with AD in Hong Kong. The data from this AD cohort will

aid our future research aiming to identify potential AD risk factors and associations between AD and other diseases.

Keywords: Alzheimer’s disease, demographics, medication use, epidemiological study

Introduction

Alzheimer's disease (AD) is the most common cause of dementia in the elderly population. By 2040, an estimated 80 million people worldwide will have dementia [1]. In 2018, more than 7 million elderly people in China had AD. In 2020, the estimated total costs of managing AD in China exceeded 200 billion USD, highlighting the disease's immense burden on society [2]. In Hong Kong, the elderly population (≥65 years old) has grown 4.3% annually over the past decade, reaching 1 million people in 2016 [3]. A 2018 meta-analysis based on 2 studies published in 1998 and 2008 estimated the prevalence of dementia in Hong Kong to be 7.2% [4-6]. However, studies on the prevalence of AD specifically in Hong Kong are lacking. Moreover, few studies have investigated the demographics or medication use of patients with AD in Hong Kong. There is an urgent need to study patients with AD in Hong Kong to improve patient care, guide government planning, estimate the social and economic costs of AD, and provide valuable information for research on AD pathogenesis and novel treatment strategies.

To understand the demographics and medication use of local patients with AD, The Hong Kong University of Science and Technology and Data Collaboration Lab of the Hospital Authority (HA) in Hong Kong conducted a collaborative study. The Data Collaboration Lab, which provides the 'Big Data Analytics Platform' to researchers for clinical data analysis, granted our team access to the demographic data, clinical records, diagnoses, investigations, and medication records of patients under the care of the HA. Data provided by the Big Data Analytics Platform is generated based on both written medical records and the electronic medical system, which hosts and manages the medical records in the public healthcare system under the Hospital Authority in Hong Kong. To identify patients with AD, we made the clinical diagnosis

based on the ICD-10 codes. Using the Big Data Analytics Platform, we identified patients documented as having AD over a 10-year period and investigated their demographics, comorbidities, medication use, and mortality rates. As the public healthcare services under the HA cover more than 90% of the secondary and tertiary services in Hong Kong [7], this cohort is representative of patients with AD in the Hong Kong elderly population.

Materials and Methods

Subject selection

Using the Big Data Analytics Platform, we identified subjects who were ≥65 years old and had at least one inpatient or outpatient record of an AD-related ICD-10 code between January 1, 2007 and December 31, 2017 (*n* = 28,838). Meanwhile, we excluded subjects with documented neurodegenerative disorders other than AD (*n* = 2,572) since the underlying pathological changes in non-AD dementia differ from those in AD (Supplementary Table 1–2). We subsequently applied a case filter according to the patients' drug dispensing histories and clinical notes (Supplementary Figure 1).

Data analysis

We then analyzed the demographic characteristics, comorbidities, clinical notes, and medication use of the AD cohort. We determined the presence of comorbidities by identifying diagnoses based on ICD-10 codes (Supplementary Table 3). We used the keyword 'death' to search the clinical notes for records relating to the episode of death. Two neurologists determined each subject's principal cause of death based on the

clinical notes. We subsequently calculated annual mortality rates based on the cumulative number of mortalities and the cumulative number of AD cases per year.

Medication use

We defined medication use as a single medication-dispensing episode for at least 21 consecutive days after a diagnosis of AD was made. British National Formulary codes were used to identify the different types of medication dispensed (Supplementary Table 4). We excluded prescription records from when a patient was <65 years old and/or before an AD diagnosis was made. From the prescription records, we identified patients who had at least one dispensing episode of a medication for dementia. Next, we determined the duration of each dispensing record. If the record of one dispensing episode overlapped with the subsequent dispensing record, the interval between the earliest start date and latest end date was used as the drug-dispensing duration of those consecutive prescriptions. Finally, we calculated the total duration of medication use by summing the duration of all dispensing episodes for each patient (Supplementary Figure 2). We also identified those patients who had at least one dispensing record of antipsychotics, antidepressants, or hypnotics.

Protection of personal health information

All personal health information (i.e., names, Hong Kong Identity Card numbers, hospital record numbers, etc.) was removed from the study dataset. All information from the Big Data Analytics Platform was de-identified and encrypted to ensure confidentiality. Access to the platform was restricted to researchers involved in this

study. This project was approved by the Committee on Research Practices of The Hong Kong University of Science and Technology.

Statistical analysis

Continuous variables were compared using 2-sided Student's *t*-tests, whereas categorical variables were compared using Yates' χ^2-test. *P*-values < 0.05 were considered statistically significant. We performed all analyses using RStudio Desktop version 1.4.1106 (Boston, MA, USA).

Results

Demographics and comorbidities

The AD cohort comprised 23,467 patients diagnosed with AD between January 1, 2007 and December 31, 2017; of these patients, 71% (*n* = 16,703) were female and 29% (*n* = 6,764) were male (Figure 1A). The median age at AD diagnosis was 84 years old (range: 77–91). Regarding age at diagnosis, 90% of patients (*n* = 21,134) were ≥75 years old, 47.4% (*n* = 11,129) were ≥85 years old, and 10% (*n* = 2,333) were <75 years old (Figure 1B).

The most common comorbidity among patients with AD was hypertension (52.6%, *n* = 12,343) followed by diabetes mellitus (46.7%, *n* = 10,969) and chronic renal diseases (18.8%, *n* = 4,409) (Table 1). Approximately 17% of patients had a history of cerebrovascular accidents (*n* = 4,148), the majority of which were ischaemic strokes (*n* = 3,463), and 12% had a history of coronary heart disease (*n* = 2,833). In addition,

11.4% of patients (*n* = 2,682) had a history of cancer, with colorectal cancers being the most common type (2.5%, *n* = 576) followed by lung cancers (1.6%, *n* = 369).

Mortality rates

Between 2007 and 2017, 15.3% of patients with AD (*n* = 3,599) died. Annual mortality rates gradually increased from 80 deaths (3.2%) in 2007 to 427 deaths (15.4%) in 2017 (Figure 2). The most common principal cause of death was pneumonia (54.3%, *n* = 1,954) followed by acute myocardial infarction (5.6%, *n* = 203) and cancers (5.3%, *n* = 192). Over 70% of patients passed away at an age of ≥85 (73.4%, *n* = 2,643). Lung cancers accounted for most cancer-related deaths (*n* = 55) followed by colorectal cancers (*n* = 31) and hepatocellular carcinoma (*n* = 16). Septicaemia (3.5%, *n* = 125), urinary tract infections (2.9%, *n* = 104), and bedsores (1.8%, *n* = 65) were causes of death in patients with AD (Table 2).

Medication use

The most commonly prescribed medications for patients with AD are listed in Table 3. The most dispensed medications were those for hypertension (67.4%, *n* = 15,813) including calcium-channel blockers (52.3%, *n* = 12,275), angiotensin-converting enzyme inhibitors (27.3%, *n* = 6,395), and beta-adrenoceptor blocking drugs (23.7%, *n* = 5,570). Antiplatelet medications, which serve as both treatment and prophylaxis for atherosclerotic arterial diseases, were also commonly prescribed (42%, *n* = 9,856). Meanwhile, 26.5% of patients (*n* = 6,216) took lipid-regulating medications. Surprisingly, only 22.2% of patients (*n* = 5,215) took medications for diabetes.

In addition, 39.9% of patients with AD (*n* = 9,351) received medications for dementia. Antipsychotic drug use was common: 50.7% of patients (*n* = 11,895) had taken antipsychotics at least once, with haloperidol being the most prescribed type (25.2%, *n* = 5,908). Antidepressant use was also common (40.3%, *n* = 9,457), and 29.1% of patients (*n* = 6,819) used hypnotics.

Among patients who received medications for dementia ('AD medication users'), 68.4% (*n* = 6,395) did so for >1 year—half of whom (*n* = 3,241) did so for >3 years (Figure 3). Accordingly, we found several significant differences between patients who did not take any medications for dementia ('AD medication nonusers') (*n* = 13,077) with those who took such medications for >1 year ('long-term AD medication users') (*n* = 6,395) (Table 4). First, long-term AD medication users had a younger median age at AD diagnosis than nonusers (82 vs. 86 years, respectively; $p < 0.001$). In addition, more long-term AD medication users than nonusers used lipid-regulating medications (37.6% vs. 21.7%, respectively; $p < 0.001$), diabetes medications (25.5% vs. 21.9%, respectively; $p < 0.001$), and antidepressants (45.1% vs. 41.1%, respectively; $p < 0.001$). However, antipsychotic use was less common in long-term AD medication users than nonusers (49.0% vs. 56.3%, respectively; $p < 0.001$).

As patients with moderate-to-severe AD can present with neuropsychiatric symptoms, we examined patients' simultaneous use of medications for dementia, antipsychotics, antidepressants, and hypnotics (Table 5). Combining antipsychotics and hypnotics was significantly lower among long-term AD medication users than nonusers (16.3% vs. 19%, respectively; $p < 0.001$). Approximately 14–20% of patients with AD required more than one type of medication to control neuropsychiatric symptoms, while 6–7% had a history of simultaneously using antipsychotics, antidepressants, and hypnotics.

Discussion

Our study is the first to provide detailed information about the demographics, comorbidities, mortality rates, and medication use of patients with AD in the Hong Kong elderly population over a 10-year period (2007–2017). While several local studies have focused on patients with dementia, AD-focused studies are limited and mostly single-center studies; therefore, those studies may not be representative of the whole Hong Kong population. Accordingly, in this study, we used the Big Data Analytics Platform of the HA Data Collaboration Lab to examine medical records from public healthcare services in Hong Kong. Specifically, we investigated the demographics, comorbidities, mortality rates, and medication use of patients with AD in Hong Kong. These data may help our local authorities, clinicians, scientists, and the public become more aware of how AD has been managed locally.

Our AD cohort was predominantly female (71%), which may be related to the longer life expectancy of the female population in Hong Kong. In 2016, the female-to-male ratio in the Hong Kong population aged >85 years was 1.9:1 [3]. In 2019, the life expectancy of females and males was 88.1 and 82.2 years, respectively (the Hong Kong Census and Statistics Department). Since the risk of developing AD increases with age, a high female-to-male sex ratio is expected among patients with AD. A comparison of our cohort with 2 previous local studies indicates that the sex ratio of AD has remained stable over the past decade [8, 9].

Most patients with AD were diagnosed after age 85, with a median age at diagnosis of 84 years. Our cohort was older than those of studies conducted in mainland China, Taiwan, the United Kingdom, and the United States, in which most patients were 75–

84 years old [10-13]. It is difficult to postulate the reason for the more advanced age for AD diagnosis in our study, as our study is retrospective and lacked a control population. One possible reason is that we only included subjects with an AD diagnosis made at age ≥65. We applied an age filter to ensure a fair comparison with the general elderly population in Hong Kong, which is defined as people aged ≥65 [3]. However, a previous cross-sectional survey revealed that there is insufficient public education about dementia in Hong Kong; as dementia is the second-most feared disease among the elderly, people tend to seek medical advice only when cognitive decline is advanced [14]. Another possible cause is related to APOE ε4 genotype in Chinese population. Our group has published a study on the genetics of an AD cohort in the Hong Kong Chinese population. Compared to the European-descent population, the Hong Kong population exhibits a lower allele frequency of APOE ε4 (frequency = 0.089 and 0.149, in the Hong Kong Chinese and European populations, respectively) [15]. The lower APOE ε4 frequency may explain, at least in part, the onset of AD in the Hong Kong Chinese population.

The number of patients taking hypertension and lipid-regulating medications exceeded the number of patients documented with comorbidities (Table 1). There are two possibilities for this finding. First, some hypertension medications are also used for treatment of heart failure and coronary heart diseases. Lipid-regulating medications can also be used as a primary prevention for atherosclerotic artery diseases. Second, comorbidities were defined based on the clinical records with ICD-10 codes; the numbers of patients with comorbidities may be underestimated if attending physicians had not used ICD-10 codes in their documentation.

In our study, the mortality rate of AD patients increased for more than three-fold over the past ten years. Similar observation is seen in other demographic studies [13, 16,

17]. The improvement of medical care quality in the past decade may improve the survival duration of AD patients, other than the overall mortalities. Pneumonia was the leading cause of death for more than half of the patients with AD in our study. Meanwhile, malignancy is the leading cause of death in the general Hong Kong population. Pneumonia is the most commonly identified immediate cause of death among older adults with Alzheimer's or other dementias [13]. Our findings are concordant with those of a recent meta-analysis in which autopsy-confirmed pneumonia accounted for approximately 50% of deaths in patients with dementia. The risk of pneumonia-associated death in patients with dementia is double that of patients without dementia [18]. Loss of muscle mass and skeletal muscle strength, reduced physical activity, and immune dysregulation are common during aging, and the impaired cognitive function in AD patients further increases the risk of infection. These findings collectively highlight the need for clinicians to pay careful attention to pneumonia-related symptoms in patients with AD, especially those with difficulty in swallowing and prolonged immobilization in advanced-stage AD. A recent review on the aging population in China summarizes a number of challenges and strategies for ensuring the wellbeing of our elderly population [19]. It will be important to educate our AD patients on maintaining a healthy lifestyle, including a balanced diet and regular exercise; encouraging social engagement especially for patients who live alone; and implementing multidimensional geriatric care including palliative care programs for end-stage AD patients.

This study focused on medication use by patients with AD in Hong Kong. Medication use is closely related to disease control, specifically the control of dementia and comorbidities. Elderly patients with AD have more comorbidities than elderly people without dementia [20]. In this study, drugs for hypertension were the most commonly

prescribed medication among patients with AD, which is concordant with our observation that hypertension was the most common comorbidity among these patients. Antiplatelet drug use was also common, as 12.1–18.8% of patients with AD had chronic kidney diseases, cerebrovascular accidents, or coronary artery diseases.

In our study, approximately 40% of patients with AD received medications for dementia. We compared our cohort with other large-scale studies on medication use in patients with AD. A Swedish study revealed that 73% of patients with AD took cholinesterase inhibitors and 9.8% of patients took NMDA (*N*-methyl-D-aspartate) antagonists [21], while a study in Taiwan found that 7.6% of patients with AD took drugs for dementia [22]. The large variation in medication use for dementia across studies is multifactorial. In Hong Kong, medications for dementia were introduced to the HA drug formulary as 'special drugs' between 1999 and 2011; special drugs could only be prescribed by a certain group of specialists. However, donepezil and rivastigmine were changed from 'special drugs' to 'general drugs' in 2015, while memantine became a 'general drug' in 2017. Therefore, these drugs would have had limited availability before 2015, which may explain why only 40% of the patients in our cohort received medications for dementia.

Meanwhile, the use of antipsychotics in our local AD cohort was high; half of the patients had taken antipsychotics at least once during the disease progression. Antipsychotics are prescribed to patients with AD to manage symptoms related to psychosis, behavioral problems, and euphoria. One local study examining the patterns of hospitalization and emergency room use of long-term care facility residents with AD revealed that psychotropic medication use was negatively associated with acute medical care, especially emergency services [8]. Another local study of Hong Kong Chinese patients with AD also identified that psychosis, behavioral problems, and

mood disturbance were strongly associated with caregiver stress [23]. Thus, prescribing antipsychotics is a common local practice for treating neuropsychiatric symptoms in AD.

Moreover, we compared medication use between patients who had taken medication for dementia for >1 year (i.e., long-term AD medication users) and those who had never been prescribed medication for dementia (i.e., AD medication nonusers). Interestingly, long-term AD medication users used lipid-regulating drugs, diabetes drugs, and antidepressants significantly more than nonusers; in particular, the difference between these 2 subgroups in the use of lipid-lowering drugs exceeded 15%. On the other hand, long-term AD medication users had much lower antipsychotic use. The variable medication use among the AD patient subgroups reflects the diversity of disease management practices. Furthermore, long-term AD medication users had a significantly lower rate of simultaneous use of antipsychotics and hypnotics than AD medication nonusers. Hypnotics are prescribed to patients with AD with sleep disturbances. The effects of medications for controlling behavioral and psychological symptoms of dementia in AD remains controversial. One meta-analysis on the pharmacological management of agitation in dementia supports the use of cholinesterase inhibitors for behavioral and psychological symptoms [24], but such benefits have not been observed in the Chinese population [25].

Nevertheless, our study has a few limitations. First, we included subjects who were documented as having AD. In previous years when advanced imaging modalities (e.g., positron emission tomography scanning) and plasma assays for biomarkers were unavailable, AD diagnoses were mainly made clinically and by exclusion. Second, in conducting a retrospective study, we were unable to extract subgroups among patients with AD for further comparison. Moreover, although all patients suffering from

dementia underwent the Mini–Mental State Examination (MMSE), some of the MMSE records were not in electronic forms; The data quality of some of the hand-written forms was not clear to the Data Lab so the data were not included in Data Catalogue. Therefore, we were unable to retrieve full MMSE records for all patients with AD through the Big Data Analytics Platform. Although we tried to find the related clinical notes by searching the keyword 'MMSE,' we could only retrieve MMSE records for approximately half of the patients. As a result, we did not present any data on MMSE scores here. In collaboration with Data Collaboration Lab, this is the first systematic analysis of AD in the elderly population in Hong Kong. To optimize the data collection and better utilize the Platform database, it has been suggested that data, including case and medication record filtering, and details of death statistics, should be collected and included in the Platform. We believe this will benefit future studies of diseases and medications associated with the elderly in Hong Kong.

Conclusion

Our study provides previously unreported, detailed information about the demographics, comorbidities, mortality rates, and medication use of patients with AD in the Hong Kong elderly population who were under the care of the HA between January 1, 2007 and December 31, 2017. The advanced age at AD diagnosis and increasing mortality rates we observed among patients with AD deserve further attention. Moreover, many patients with AD required antipsychotics and antidepressants to control neuropsychiatric symptoms, while only 40% of patients with AD used medications for dementia. Accordingly, the following should be enhanced to improve the management of AD: (1) the availability of medications for dementia; (2)

healthcare support for prompt diagnosis; (3) AD awareness among the general public; and (4) support to patients and family members. Moreover, greater resources should be allocated to AD research, as studies on AD-related plasma biomarkers and genomics in our local population will contribute to the development of new diagnostic tools and therapies.

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Conflicts of interest/Disclosure Statement

The authors have no conflicts of interest to report.

References

[1] Ballard C, Gauthier S, Corbett A, Brayne C, Aarsland D, Jones E (2011) Alzheimer's disease. *Lancet* **377(9770)**, 1019-1031.

[2] Jia J, Wei C, Chen S, Li F, Tang Y, Qin W, Zhao L, Jin H, Xu H, Wang F, Zhou A, Zuo X, Wu L, Han Y, Han Y, Huang L, Wang Q, Li D, Chu C, Shi L, Gong M, Du Y, Zhang J, Zhang J, Zhou C, Lv J, Lv Y, Xie H, Ji Y, Li F, Yu E, Luo B, Wang Y, Yang S, Qu Q, Guo Q, Liang F, Zhang J, Tan L, Shen L, Zhang K, Zhang J, Peng D, Tang M, Lv P, Fang B, Chu L, Jia L, Gauthier S (2018) The cost of Alzheimer's disease in China and re-estimation of costs worldwide. *Alzheimers Dement* **14(4)**, 483-491.

[3] 2016 Population By-census Thematic Report: Older Persons. *Census and Statistics Department, Hong Kong Special Administrative Region*.

[4] Wu YT, Ali GC, Guerchet M, Prina AM, Chan KY, Prince M, Brayne C (2018) Prevalence of dementia in mainland China, Hong Kong and Taiwan: an updated systematic review and meta-analysis. *Int J Epidemiol* **47(3)**, 709-719.

[5] Chiu HF, Lam LC, Chi I, Leung T, Li SW, Law WT, Chung DW, Fung HH, Kan PS, Lum CM, Ng J, Lau J (1998) Prevalence of dementia in Chinese elderly in Hong Kong. *Neurology* **50(4)**, 1002-1009.

[6] Lam LC, Tam CW, Lui VW, Chan WC, Chan SS, Wong S, Wong A, Tham MK, Ho KS, Chan WM, Chiu HF (2008) Prevalence of very mild and mild dementia in community-dwelling older Chinese people in Hong Kong. *Int Psychogeriatr* **20(1)**, 135-148.

[7] Hospital Authority Statistical Report 2016 - 2017. *Hospital Authority, Hong Kong Special Administrative Region*.

[8] Leung AY, Kwan CW, Chi I (2013) Residents with Alzheimer's disease in long-term care facilities in Hong Kong: patterns of hospitalization and emergency room use. *Aging Ment Health* **17(8)**, 959-965.

[9] Yang YH, Wang H, Lam L, Chan WC, Yu X, Li T, Wang WF, Chiu PY, Lin YT, Hu CJ, Fuh JL, Morris JC (2014) Characteristics of Alzheimer's disease among patients in Taiwan, Hong Kong, and Beijing. *J Alzheimers Dis* **42(1)**, 193-200.

[10] Jia J, Wang F, Wei C, Zhou A, Jia X, Li F, Tang M, Chu L, Zhou Y, Zhou C, Cui Y, Wang Q, Wang W, Yin P, Hu N, Zuo X, Song H, Qin W, Wu L, Li D, Jia L, Song J, Han Y, Xing Y, Yang P, Li Y, Qiao Y, Tang Y, Lv J, Dong X (2014) The prevalence of dementia in urban and rural areas of China. *Alzheimers Dement* **10(1)**, 1-9.

[11] Hung YN, Kadziola Z, Brnabic AJ, Yeh JF, Fuh JL, Hwang JP, Montgomery W (2016) The epidemiology and burden of Alzheimer's disease in Taiwan utilizing data from the National Health Insurance Research Database. *Clinicoecon Outcomes Res* **8**, 387-395.

[12] Imfeld P, Brauchli Pernus YB, Jick SS, Meier CR (2013) Epidemiology, co-morbidities, and medication use of patients with Alzheimer's disease or vascular dementia in the UK. *J Alzheimers Dis* **35(3)**, 565-573.

[13] (2020) 2020 Alzheimer's disease facts and figures. *Alzheimers Dement*.

[14] Lam TP, Sun KS, Chan HY, Lau CS, Lam KF, Sanson-Fisher R (2019) Perceptions of Chinese Towards Dementia in Hong Kong-Diagnosis, Symptoms and Impacts. *Int J Environ Res Public Health* **16(1):**, 128.

[15] Zhou X, Chen Y, Ip FCF, Lai NCH, Li YYT, Jiang Y, Zhong H, Chen Y, Zhang Y, Ma S, Lo RMN, Cheung K, Tong EPS, Ko H, Shoai M, Mok KY, Hardy J, Mok VCT, Kwok TCY, Fu AKY, Ip NY (2020) Genetic and polygenic risk score analysis for Alzheimer's disease in the Chinese population. *Alzheimers Dement (Amst)* **12(1)**, e12074.

[16] Niu H, Alvarez-Alvarez I, Guillen-Grima F, Al-Rahamneh MJ, Aguinaga-Ontoso I (2017) Trends of mortality from Alzheimer's disease in the European Union, 1994-2013. *Eur J Neurol* **24(6)**, 858-866.

[17] Darbà J, A M (2021) Hospital incidence, mortality and costs of Alzheimer's disease in Spain: a retrospective multicenter study. *Expert Rev Pharmacoecon Outcomes Res* **21(5)**, 1101-1106.

[18] Manabe T, Fujikura Y, Mizukami K, Akatsu H, Kudo K (2019) Pneumonia-associated death in patients with dementia: A systematic review and meta-analysis. *PLoS One* **14(3)**, e0213825.

[19] Fang EF, Xie C, Schenkel JA, Wu C, Long Q, Cui H, Aman Y, Frank J, Liao J, Zou H, Wang NY, Wu J, Liu X, Li T, Fang Y, Niu Z, Yang G, Hong J, Wang Q, Chen G, Li J, Chen HZ, Kang L, Su H, Gilmour BC, Zhu X, Jiang H, He N, Tao J, Leng SX, Tong T, Woo J (2020) A research agenda for ageing in China in the 21st century (2nd edition): Focusing on basic and translational research, long-term care, policy and social networks. *Ageing Res Rev* **64**, 101174.

[20] Wang JH, Wu YJ, Tee BL, Lo RY (2018) Medical Comorbidity in Alzheimer's Disease: A Nested Case-Control Study. *J Alzheimers Dis* **63(2)**, 773-781.

[21] Cermakova P, Fereshtehnejad SM, Johnell K, Winblad B, Eriksdotter M, Religa D (2014) Cardiovascular medication burden in dementia disorders: a nationwide study of 19,743 dementia patients in the Swedish Dementia Registry. *Alzheimers Res Ther* **6(3):**, 34.

[22] Lin SK, Tsai YT, Lai JN, Wu CT (2015) Demographic and medication characteristics of traditional Chinese medicine users among dementia patients in Taiwan: a nationwide database study. *J Ethnopharmacol* **161**, 108-115.

[23] Cheng ST, Lam LC, Kwok T (2013) Neuropsychiatric symptom clusters of Alzheimer disease in Hong Kong Chinese: correlates with caregiver burden and depression. *Am J Geriatr Psychiatry* **21(10)**, 1029-1037.

[24] McDermott CL, Gruenewald DA (2019) Pharmacologic Management of Agitation in Patients with Dementia. *Curr Geriatr Rep* **8(1)**, 1-11.

[25] Leung KC, Li V, Ng YZ, Chan TT, Chang RS, Wong RY (2017) Systematic Review of Cholinesterase Inhibitors on Cognition and Behavioral Symptoms in Patients of Chinese Descent with Alzheimer's Disease, Vascular Dementia, or Mixed Dementia. *Geriatrics (Basel)* **2(3)**, 29.

Table 1. Comorbidities of patients with Alzheimer's disease

Comorbidities	Number (%)
Hypertension	12,343 (52.6)
Diabetes Mellitus	10,969 (46.7)
Hyperlipidemia	2,501 (10.7)
Cerebrovascular accident	4,148 (17.7)
Ischaemic stroke	3,463 (14.8)
Haemorrhagic stroke	685 (2.9)
Coronary heart diseases	2,833 (12.1)
Cancers	2,682 (11.4)
Colorectal	576 (2.5)
Lung	369 (1.6)
Breast	320 (1.4)
Chronic renal diseases	4,409 (18.8)
Chronic respiratory diseases	2,650 (11.3)
Asthma	573 (2.4)
COAD	2,077 (8.9)
Chronic liver diseases	1,039 (4.4)

Abbreviation: COAD: chronic obstructive airway diseases

Table 2. Top ten causes of death in Alzheimer's disease

Causes of death (Top 10)	Number (%)
Pneumonia	1,954 (54.3)
Acute myocardial infarction	203 (5.6)
Cancers	192 (5.3)
Sepsis	125 (3.5)
Congestive heart failure	116 (3.2)
Cerebrovascular accident	112 (3.1)
Urinary tract infections	104 (2.9)
Renal failure	72 (2.0)
Infected bedsores	65 (1.8)
Gastrointestinal bleeding	55 (1.5)

Table 3. Medication use in patients with Alzheimer's disease

Medication	Number (%)
Drugs for dementia	
Total	9,351 (39.9)
Donezepil	4,879 (20.8)
Galantamine	4,013 (17.1)
Memantine	4,024 (17.2)
Rivastigmine	2,529 (10.8)
Drugs for hypertension	
Total	15,813 (67.4)
Calcium-channel blockers	12,275 (52.3)
ACEI	6,395 (27.3)
Beta-adrenoceptor blocking drugs	5,570 (23.7)
Drugs for diabetes	
Total	5,215 (22.2)
Sulphonyureas	3,184 (13.6)
Metformin	3,526 (15.0)
Short acting insulins	1,709 (7.3)
Intermediate and long acting insulins	1,238 (5.3)
Lipid-regulating drugs	
Total	6,216 (26.5)
Simvastatin	5,682 (24.2)
Atorvastatin	500 (2.1)
Gemfibrosil	194 (0.8)
Antiplatelets	
Total	9.856 (42.0)
Antipsychotics	
Total	11,895 (50.7)
Haloperidol	5,908 (25.2)
Quetiapine	5,128 (21.9)
Risperidone	2,333 (9.9)
Antidepressants	
Total	9,457 (40.3)
TCA and related anti-depressants	5,697 (24.3)
Selective serotonin reuptake inhibitors	5,231 (22.3)
Hypnotics	
Total	6,819 (29.1)

Abbreviation: ACEI: angiotensin-converting enzyme inhibitors, TCA: tricyclic anti-depressants

Table 4. Comparison between patients who had not taking medication for Alzheimer's disease and those who took medication for longer than one year

	AD medication nonusers Number (%)	**AD medication long-term users Number (%)**	***p* values**
Total	13,077	6,395	
Male	3,692 (28.2)	1,815 (28.4)	0.84
Female	9,385 (71.8)	4,580 (71.6)	
Median age at diagnosis	86	82	**<0.001**
Medication			
Drugs for hypertension	9,273 (70.9)	4,570 (71.5)	0.44
Calcium-channel blockers	7,098 (54.3)	3,678 (57.5)	**<0.001**
ACEI	3,748 (28.7)	1,873 (29.3)	0.37
Beta-adrenoceptor blocking drugs	3,307 (25.3)	1,566 (24.5)	0.23
Drugs for diabetes	2,863 (21.9)	1,633 (25.5)	**<0.001**
Oral hypoglycemic drugs	2,416 (18.5)	1,548 (24.2)	**<0.001**
Insulins	1,416 (10.8)	580 (9.1)	**<0.001**
Lipid regulating drugs	2,832 (21.7)	2,405 (37.6)	**<0.001**
Antiplatelets	5,763 (44.1)	2,865 (44.8)	0.34
Antipsychotics	7,366 (56.3)	3,133 (49.0)	**<0.001**
Antidepressants	5,375 (41.1)	2,886 (45.1)	**<0.001**
Hypnotics	4,113 (31.5)	1,938 (30.3)	0.11

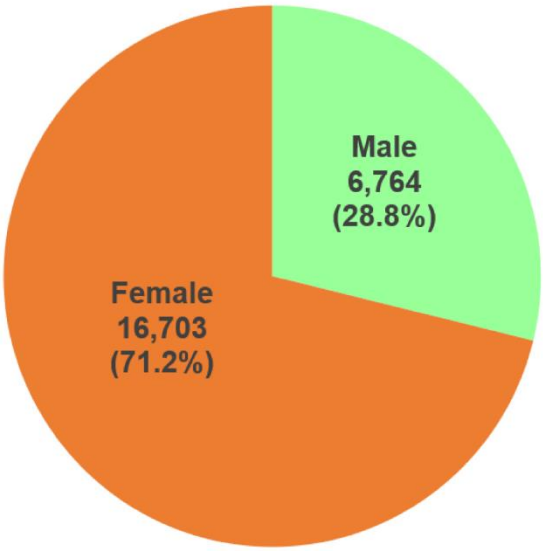
Abbreviation: ACEI: angiotensin-converting enzyme inhibitors

Table 5. Combination of medication use in patients with Alzheimer's disease

	AD medication nonusers Number (%)	AD medication long-term users Number (%)	*p* values
Total	13,077	6,395	
Medication combination			
Antipsychotics + Antidepressants	2,528 (19.3)	1,275 (19.9)	0.33
Antipsychotics + Hypnotics	2,481 (19.0)	1,040 (16.3)	**<0.001**
Antidepressants + Hypnotics	1,801 (13.8)	902 (14.1)	0.25
All three drugs	908 (6.9)	417 (6.5)	0.28

Figure 1. Sex and age at Alzheimer's disease diagnosis in the Hong Kong population from 2007–2017. A total of 23,467 patients with documented Alzheimer's disease (AD) were selected from the Big Data Analytics Platform of the Hospital Authority Data Collaboration Lab from 2007–2017. (A) Sex and (B) age at the time of AD diagnosis.

A



B

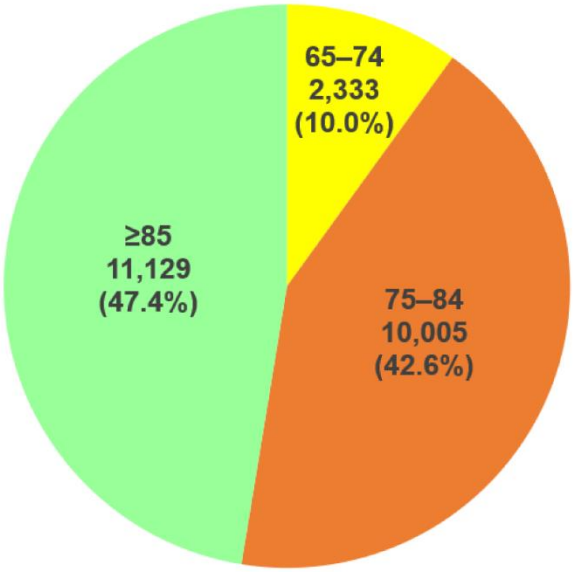


Figure 2. Alzheimer's disease mortality in Hong Kong from 2007–2017. (A) Cumulative Alzheimer's disease (AD) cases (blue bars) and cumulative mortality of patients with AD (black line with triangles) between January 1, 2007 and December 31, 2017. (B) Cumulative AD cases (blue bars) and annual mortality rates (yellow line with circles).

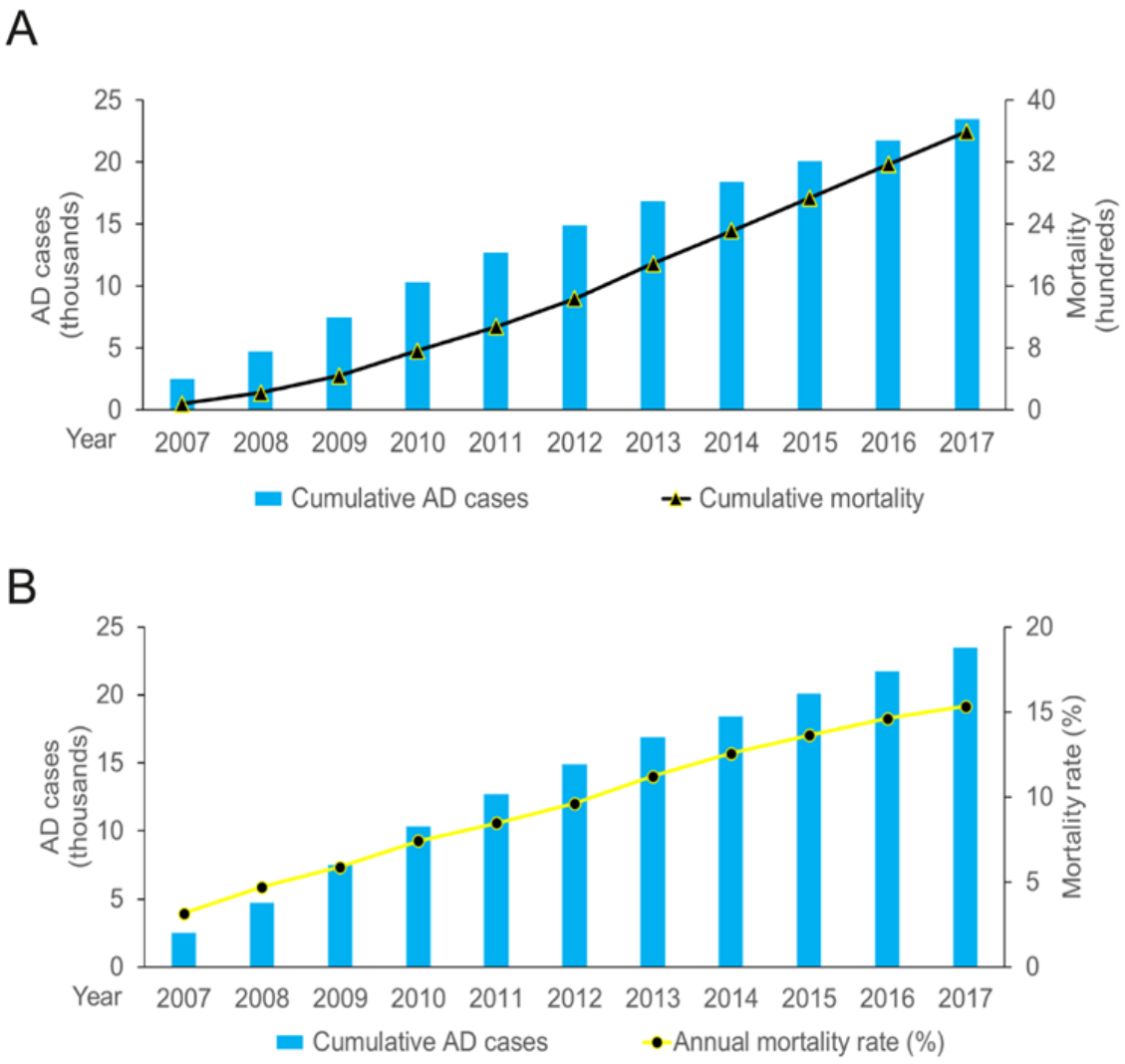
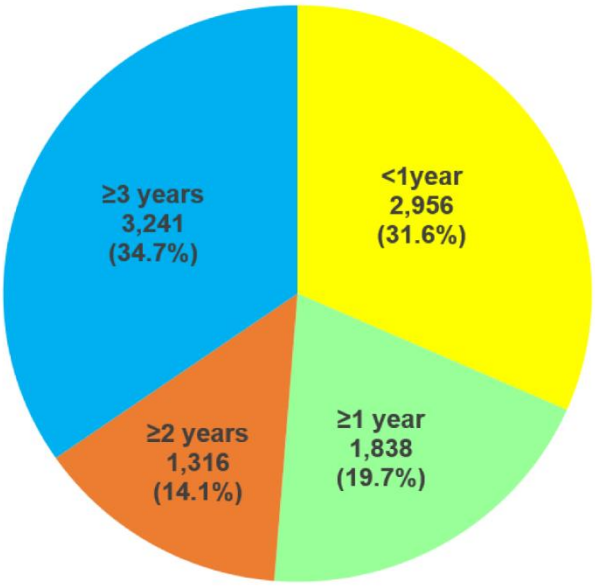
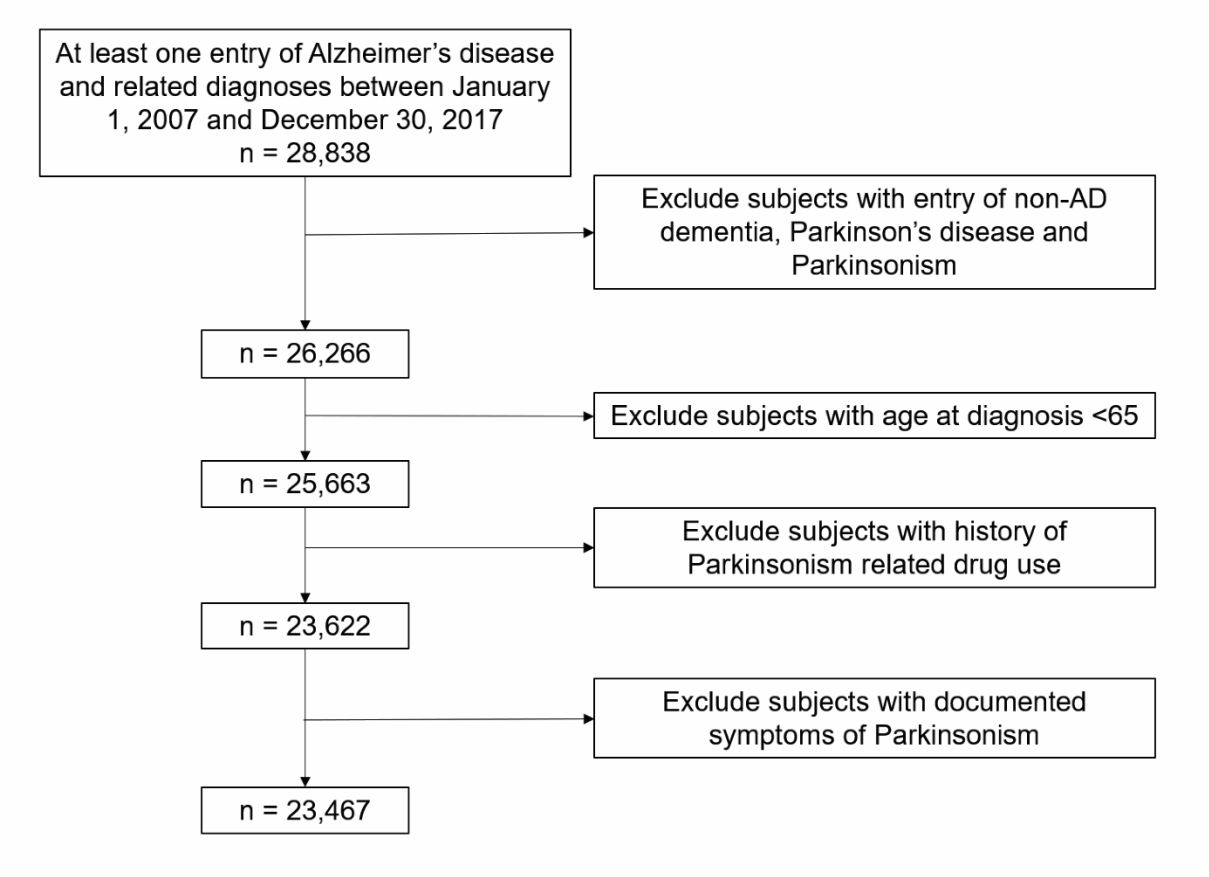


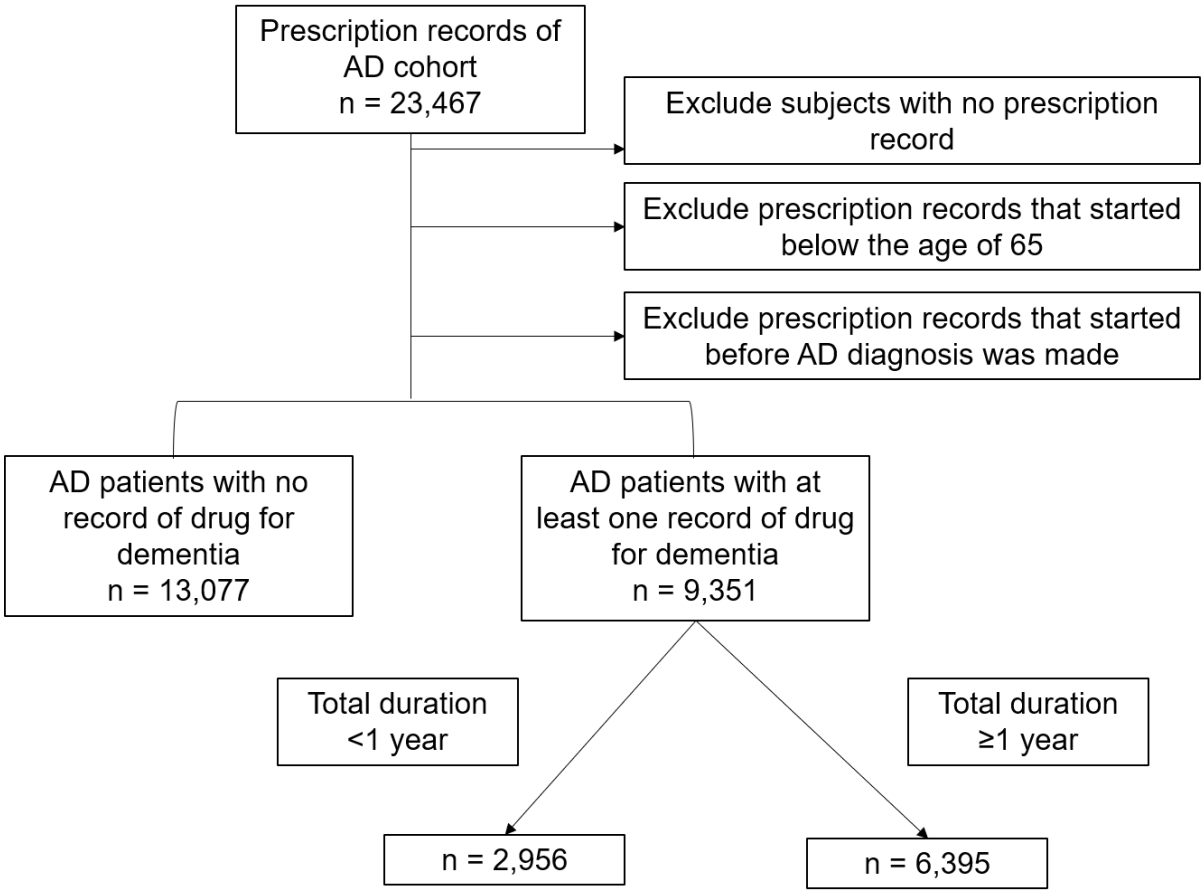
Figure 3. Duration of medication use for dementia in patients with Alzheimer's disease in Hong Kong from 2007–2017. A total of 9,351 patients received medication for dementia during the study period.



Supplementary Figure 1. Selection algorithm for patients with Alzheimer's disease.



Supplementary Figure 2. Selection algorithm of patients with Alzheimer's disease with a history of medication use for dementia.



Supplementary Table 1. Alzheimer’s disease-related diagnoses used for subject selection.

AD-related diagnoses
Alzheimer's disease
Alzheimer"s disease with early onset
Alzheimer"s disease with late onset
Dementia in Alzheimer"s disease atypical or mixed type

Supplementary Table 2. Neurodegenerative disorders other than Alzheimer's disease used for subject selection.

Non-AD dementia, Parkinson's disease and Parkinsonism
Dementia due to Creutzfeldt-Jacob disease
Arteoriosclerotic dementia
Arteoriosclerotic dementia with delirium
Post infarct dementia
Arteoriosclerotic dementia with delusional feature
Arteoriosclerotic dementia with depressive feature
Mixed cortical and subcortical vascular dementia
Mixed cortical and subcortical vascular dementia,without additional symptoms
Mixed cortical and subcortical vascular dementia, with predominant delusional symptom
Mixed cortical and subcortical vascular dementia, with predominantly hallucinatory symptom
Mixed cortical and subcortical vascular dementia , with predominantly depressive symptom
Mixed cortical and subcortical vascular dementia, with mixed symptoms
Multi-infarct dementia
Multi-infarct dementia, without additional symptoms
Multi-infarct dementia, with predominant delusional symptom
Multi-infarct dementia, with predominantly hallucinatory symptom
Multi-infarct dementia, with predominant depressive symptom
Multi-infarct dementia,with mixed symptoms
Subcortical vascular dementia
Subcortical vascular dementia, without additional symptoms
Subcortical vascular dementia, with predominant delusional symptom
Subcortical vascular dementia, with predominantly hallucinatory symptom
Subcortical vascular dementia, with predominant depressive symptom
Subcortical vascular dementia, with mixed symptoms
Vascular dementia
Vascular dementia, acute onset
Vascular dementia of acute onset , without additional symptoms
Vascular dementia of acute onset, with predominant delusional symptom
Vascular dementia of acute onset, with predominantly hallucinatory symptom
Vascular dementia of acute onset, with predominant depressive symptom
Vascular dementia of acute onset, with mixed symptoms
Vascular dementia, without additional symptoms
Vascular dementia with behavioral disturbance
Vascular dementia,uncomplicated
Vascular dementia with hallucination
Vascular dementia with mixed symptoms
Vascular dementia with delirium
Vascular dementia with delirum, with behavioral disturbance
Vascular dementia with delusion, with behavioral disturbance
Vascular dementia with predominantly delusional
Vascular dementia with depressed mood, with behavioral disturbance

Vascular dementia with predominantly depressive
Paralysis agitans
Parkinsonian syndrome
Neuroleptic-induced Parkinsonism
Secondary Parkinsonism
Secondary Parkinsonism
Drug-induced Parkinsonism
Secondary Parkinsonism due to non-drug agents
Postencephalitic Parkinsonism
Dementia in Pick’s disease
Fronto-temporal dementia

Supplementary Table 3. List of diagnoses for determining comorbidities of patients with Alzheimer's disease.

Comorbidities	Disease full description
Hypertension and related diagnoses	Benign essential hypertension
	Essential hypertension
	Hypertension
	Hypertensive encephalopathy
	Hypertensive heart and renal disease
	Hypertensive heart and renal disease, malignant
	Hypertensive heart and renal disease, malignant, with congestive heart failure
	Hypertensive heart and renal disease, with congestive heart failure
	Hypertensive heart and renal disease, with congestive heart failure and renal failure
	Hypertensive heart and renal disease, with renal failure
	Hypertensive heart disease
	Hypertensive heart disease with congestive heart failure
	Hypertensive renal disease
	Hypertensive renal disease with renal failure
	Hypertensive renal disease, malignant
	Hypertensive renal disease, malignant, with renal failure
	Malignant hypertension
	Malignant hypertensive heart disease with congestive heart failure
	Renovascular hypertension
Diabetes Mellitus	Diabetes mellitus
	Diabetes mellitus with autonomic neuropathy
	Diabetes mellitus with background retinopathy
	Diabetes mellitus with drug induced hypoglycaemia
	Diabetes mellitus with hyperglycaemia
	Diabetes mellitus with hyperosmolarity
	Diabetes mellitus with hypoglycaemia
	Diabetes mellitus with maculopathy
	Diabetes mellitus with mononeuropathy
	Diabetes mellitus with overt nephropathy (macroalbuminuria)
	Diabetes mellitus with peripheral angiopathy
	Diabetes mellitus with proliferative retinopathy
	Diabetes mellitus, uncontrolled with gangrene foot
	Diabetes mellitus, uncontrolled with hyperglycaemia
	Diabetes mellitus, uncontrolled with hyperosmolar coma
	Diabetes mellitus, uncontrolled with hyperosmolarity
	Diabetes mellitus, uncontrolled with ketoacidosis
	Diabetic ketoacidosis
	Diabetic retinopathy
	NIDDM with neurological manifestations, uncontrolled
	NIDDM with ophthalmic manifestations, uncontrolled

	Non-insulin dependent diabetes mellitus with neuropathy
	Polyneuropathy in diabetes
	Proliferative diabetic retinopathy
	Type I diabetes mellitus
	Type I diabetes mellitus with background retinopathy
	Type I diabetes mellitus with drug induced hypoglycaemia
	Type I diabetes mellitus with hyperglycaemia
	Type I diabetes mellitus with hypoglycaemia
	Type I diabetes mellitus with leg ulcer
	Type I diabetes mellitus with maculopathy
	Type I diabetes mellitus with neurological manifestations
	Type I diabetes mellitus with overt nephropathy (macroalbuminuria)
	Type I diabetes mellitus with peripheral neuropathy
	Type I diabetes mellitus with pre-proliferative retinopathy
	Type I diabetes mellitus with proliferative retinopathy
	Type I diabetes mellitus with retinopathy
	Type I diabetes mellitus with triopathy
	Type I diabetes mellitus, uncontrolled with hyperglycaemia
	Type I diabetes mellitus, uncontrolled with hyperosmolarity
	Type II diabetes mellitus
	Type II diabetes mellitus uncontrolled with autonomic neuropathy
	Type II diabetes mellitus uncontrolled with nephrotic syndrome
	Type II diabetes mellitus uncontrolled with peripheral neuropathy
	Type II diabetes mellitus with amyotrophy
	Type II diabetes mellitus with arthropathy
	Type II diabetes mellitus with autonomic neuropathy
	Type II diabetes mellitus with background retinopathy
	Type II diabetes mellitus with complication
	Type II diabetes mellitus with foot ulcer
	Type II diabetes mellitus with gangrene foot
	Type II diabetes mellitus with hyperosmolarity
	Type II diabetes mellitus with hypoglycaemia
	Type II diabetes mellitus with hypoglycaemia, drug induced
	Type II diabetes mellitus with hypoglycaemic coma
	Type II diabetes mellitus with incipient nephropathy
	Type II diabetes mellitus with ischaemic heart disease
	Type II diabetes mellitus with ketoacidosis
	Type II diabetes mellitus with ketoacidotic coma
	Type II diabetes mellitus with leg ulcer
	Type II diabetes mellitus with maculopathy
	Type II diabetes mellitus with mononeuropathy
	Type II diabetes mellitus with nephrotic syndrome
	Type II diabetes mellitus with overt nephropathy (macroalbuminuria)
	Type II diabetes mellitus with peripheral neuropathy
	Type II diabetes mellitus with peripheral vascular disease

	Type II diabetes mellitus with polyneuropathy
	Type II diabetes mellitus with pre-proliferative retinopathy
	Type II diabetes mellitus with proliferative retinopathy
	Type II diabetes mellitus with triopathy
	Type II diabetes mellitus, uncontrolled with amyotrophy
	Type II diabetes mellitus, uncontrolled with background retinopathy
	Type II diabetes mellitus, uncontrolled with complication
	Type II diabetes mellitus, uncontrolled with drug induced hypoglycaemia
	Type II diabetes mellitus, uncontrolled with foot ulcer
	Type II diabetes mellitus, uncontrolled with gangrene foot
	Type II diabetes mellitus, uncontrolled with hyperglycaemia
	Type II diabetes mellitus, uncontrolled with hyperosmolar coma
	Type II diabetes mellitus, uncontrolled with hyperosmolarity
	Type II diabetes mellitus, uncontrolled with hypoglycaemia
	Type II diabetes mellitus, uncontrolled with incipient nephropathy
	Type II diabetes mellitus, uncontrolled with ischaemic heart disease
	Type II diabetes mellitus, uncontrolled with ketoacidosis
	Type II diabetes mellitus, uncontrolled with ketoacidotic coma
	Type II diabetes mellitus, uncontrolled with leg ulcer
	Type II diabetes mellitus, uncontrolled with maculopathy
	Type II diabetes mellitus, uncontrolled with mononeuropathy
	Type II diabetes mellitus, uncontrolled with overt nephropathy (macroalbuminuria)
	Type II diabetes mellitus, uncontrolled with peripheral vascular disease
	Type II diabetes mellitus, uncontrolled with polyneuropathy
	Type II diabetes mellitus, uncontrolled with pre-proliferative retinopathy
	Type II diabetes mellitus, uncontrolled with proliferative retinopathy
	Type II diabetes mellitus, uncontrolled with triopathy
	Type II DM with hyperglycaemia
	Type II DM with hyperosmolar coma
Hyperlipidemia	Familial hyperlipidaemia
	Hypercholesterolaemia
	Hyperlipidaemia
	Mixed hyperlipidaemia
	Pure hypercholesterolaemia
	Pure hyperglyceridaemia
Cerebrovascular accident	Acute cerebrovascular disease
	Basilar artery syndrome
	Cerebral artery occlusion with cerebral infarction
	Cerebral embolism with infarction
	Cerebrovascular disease
	Chronic cerebral ischaemia
	Generalized ischaemic cerebrovascular disease
	Haemorrhagic conversion of cerebral infarction
	Occlusion and stenosis of carotid artery
	Occlusion and stenosis of carotid artery with cerebral infarction

	Occlusion and stenosis of multiple arteries with cerebral infarct
	Occlusion and stenosis of precerebral artery with cerebral infarction
	Occlusion and stenosis of vertebral artery
	Transient cerebral ischaemia
	Transient ischaemic attack
	Vertebral artery syndrome
	Cerebral haemorrhage
	Intracerebral haemorrhage - intra-ventricular, non-traumatic
	Intracerebral haemorrhage, non-traumatic
	Intracranial haemorrhage, non-traumatic
Coronary heart disease	Acute ischaemic heart disease
	Chronic ischaemic heart disease
	Free wall rupture - post-myocardial infarction
	Ischaemic heart disease
	Sequelae of myocardial infarction
	Subacute ischaemic heart disease
Cancers	Acute leukaemia
	Acute myeloid leukaemia
	Acute myeloid leukaemia in complete remission
	Anorectal adenocarcinoma
	B-cell lymphoma
	Cancer of ampulla of Vater
	Cancer of anal canal
	Cancer of anterior mediastinum
	Cancer of anus
	Cancer of appendix vermiformis
	Cancer of ascending colon
	Cancer of biliary tract
	Cancer of body of uterus
	Cancer of brain - parietal lobe
	Cancer of brain - temporal lobe
	Cancer of bronchus and lung
	Cancer of caecum
	Cancer of cervix
	Cancer of cervix uteri
	Cancer of cheek mucosa
	Cancer of colon
	Cancer of connective and soft tissue
	Cancer of connective and soft tissue of head, face, and neck
	Cancer of connective and soft tissue of lower limb, including hip
	Cancer of connective and soft tissue of thorax
	Cancer of connective and soft tissue of upper limb, including shoulder
	Cancer of corpus uteri, not involve isthmus
	Cancer of descending colon
	Cancer of digestive organs and peritoneum

	Cancer of digestive system and intra-abdominal organs
	Cancer of duodenum
	Cancer of exocervix
	Cancer of extrahepatic bile ducts
	Cancer of female breast
	Cancer of female breast - central
	Cancer of female breast - lower-inner quadrant
	Cancer of female breast - lower-outer quadrant
	Cancer of female breast - upper-inner quadrant
	Cancer of female breast - upper-outer quadrant
	Cancer of female breast, other site
	Cancer of floor of mouth
	Cancer of gallbladder
	Cancer of hard palate
	Cancer of hepatic flexure of colon
	Cancer of hypopharynx, other site
	Cancer of kidney and ureter
	Cancer of kidney, bilateral
	Cancer of kidney, left
	Cancer of kidney, right
	Cancer of labia majora
	Cancer of labia minora
	Cancer of larynx - glottis
	Cancer of larynx - subglottis
	Cancer of larynx - supraglottis
	Cancer of liver - intrahepatic bile duct
	Cancer of liver, primary
	Cancer of lower gum
	Cancer of lower lip, vermilion border
	Cancer of lower lobe, bronchus or lung
	Cancer of main bronchus
	Cancer of male breast
	Cancer of male breast, left
	Cancer of mediastinum
	Cancer of middle lobe, bronchus or lung
	Cancer of mouth
	Cancer of nasal cavity
	Cancer of nasopharynx
	Cancer of oesophagus
	Cancer of oesophagus - abdominal
	Cancer of oesophagus - cervical
	Cancer of oesophagus - thoracic
	Cancer of oropharynx
	Cancer of ovary
	Cancer of pancreas

	Cancer of pancreas - body
	Cancer of pancreas - head
	Cancer of pancreas - tail
	Cancer of pancreatic duct
	Cancer of parotid gland
	Cancer of pelvic bones, sacrum, and coccyx
	Cancer of penis
	Cancer of peritoneum
	Cancer of pharynx
	Cancer of posterior hypopharyngeal wall
	Cancer of prepuce
	Cancer of prostate
	Cancer of pyloric antrum
	Cancer of pyriform sinus
	Cancer of rectosigmoid junction
	Cancer of rectum
	Cancer of rectum or anus
	Cancer of renal pelvis
	Cancer of renal pelvis, left
	Cancer of renal pelvis, right
	Cancer of retroperitoneum
	Cancer of scalp and skin of neck
	Cancer of sigmoid colon
	Cancer of skin
	Cancer of skin - eyelid, including canthus
	Cancer of skin - face
	Cancer of skin - lip
	Cancer of skin - lower limb, hip
	Cancer of skin of ear and external auditory canal
	Cancer of skin of trunk, not involve scrotum
	Cancer of skin of upper limb including shoulder
	Cancer of splenic flexure of colon
	Cancer of stomach
	Cancer of stomach - body
	Cancer of stomach - cardia
	Cancer of stomach - greater curvature
	Cancer of stomach - lesser curvature
	Cancer of stomach - pylorus
	Cancer of the lip, oral cavity and pharynx
	Cancer of thyroid gland
	Cancer of tip and lateral border of tongue
	Cancer of tongue
	Cancer of tongue - base
	Cancer of tongue - dorsal surface
	Cancer of trachea

	Cancer of transverse colon
	Cancer of upper lobe, bronchus or lung
	Cancer of ureter, left
	Cancer of ureter, right
	Cancer of ureteric orifice
	Cancer of urinary bladder
	Cancer of urinary bladder - anterior wall
	Cancer of urinary bladder - dome
	Cancer of urinary bladder - lateral wall
	Cancer of urinary bladder - neck
	Cancer of urinary bladder - posterior wall
	Cancer of urinary bladder - trigone
	Cancer of urinary bladder, other site
	Cancer of vagina
	Cancer of vallecula
	Cancer of vulva
	Carcinoma in situ of breast
	Carcinoma in situ of cervix uteri
	Carcinoma in situ of female genital organs
	Carcinoma in situ of rectum
	Carcinoma in situ of scalp and skin of neck
	Carcinoma in situ of skin of face
	Carcinoma in situ of skin of lower limb, including hip
	Carcinoma in situ of stomach
	Carcinoma of kidney
	Carcinoma of penis
	Carcinoma of peritoneum
	Carcinoma of prostate
	Carcinoma of prostate with bony metastasis
	Carcinoma of renal pelvis
	Carcinoma of ureter
	Carcinoma of urinary bladder
	Carcinoma with liver metastasis
	Cholangiocarcinoma
	Chronic lymphocytic leukaemia
	Chronic lymphocytic leukaemia in remission
	Chronic myeloid leukaemia
	Chronic myelomonocytic leukaemia
	Invasive transitional cell carcinoma
	Leukaemia
	Lymphoma
	Lymphosarcoma
	Lymphosarcoma involving lymph nodes of head, face, and neck
	Lymphosarcoma involving lymph nodes of multiple sites
	Lymphosarcoma involving spleen

	Malignant ascites
	Malignant lymphoma involving lymph nodes of inguinal region and lower limb
	Malignant lymphoma involving lymph nodes of multiple sites
	Malignant lymphoma, extranodal and solid organ
	Malignant neoplasm of colon
	Malignant neoplasm of female breast
	Malignant neoplasm of nipple and areola of female breast
	Malignant neoplasm of trachea, bronchus, and lung
	Malignant pleural effusion
	Multiple myeloma
	Multiple myeloma in remission
	Myeloma
	Neoplasm of ear
	Neoplasm of skin
	Nodular lymphoma
	Nodular lymphoma involving lymph nodes of multiple sites
	Plasma cell leukaemia
	Renal cell carcinoma
	Skin melanoma
	Skin melanoma - face
	Skin melanoma - foot
	Skin melanoma - hip
	Skin melanoma - lower limb, not involving hip
	Skin melanoma of trunk, not involving scrotum
	Skin melanoma of upper limb, not involving shoulder
	Squamous cell carcinoma
	Transitional cell carcinoma of urinary bladder
Chronic renal diseases	Bilateral renal impairment
	Chronic kidney disease
	Chronic kidney disease, stage 4
	Chronic kidney disease, stage 5
	Chronic renal failure
	Chronic renal impairment
	Chronic renal parenchymal disease
	Diabetes mellitus with overt nephropathy (macroalbuminuria)
	End stage renal failure admitted for haemodialysis
	End stage renal failure admitted for peritoneal dialysis
	Hypertensive heart and renal disease
	Hypertensive heart and renal disease, malignant
	Hypertensive heart and renal disease, malignant, with congestive heart failure
	Hypertensive heart and renal disease, with congestive heart failure
	Hypertensive heart and renal disease, with congestive heart failure and renal failure
	Hypertensive heart and renal disease, with renal failure
	Hypertensive renal disease

	Hypertensive renal disease with renal failure
	Hypertensive renal disease, malignant, with renal failure
	Impaired renal function
	Renal failure
	Secondary hypertension due to renal disorder
	Type I diabetes mellitus with overt nephropathy (macroalbuminuria)
	Type II diabetes mellitus uncontrolled with nephrotic syndrome
	Type II diabetes mellitus with incipient nephropathy
	Type II diabetes mellitus with nephrotic syndrome
	Type II diabetes mellitus with overt nephropathy (macroalbuminuria)
	Type II diabetes mellitus, uncontrolled with incipient nephropathy
	Type II diabetes mellitus, uncontrolled with overt nephropathy (macroalbuminuria)
	Uraemia
Chronic respiratory diseases	Asthma
	Asthma, with status asthmaticus
	Bronchiectasis
	Bronchiolitis obliterans
	Chronic airway obstruction
	Chronic bronchitis
	Chronic obstructive bronchitis
	Chronic obstructive bronchitis with acute exacerbation
	Chronic obstructive pulmonary disease
	Extrinsic asthma
Chronic liver diseases	Acute hepatic failure
	Alcoholic chronic liver disease
	Alcoholic cirrhosis of liver
	'"Alcoholic cirrhosis of liver, Child"s A"'
	'"Alcoholic cirrhosis of liver, Child"s C"'
	Alcoholic liver damage
	Alcoholic liver disease
	Biliary cirrhosis
	Biliary cirrhosis, primary
	Chronic hepatic failure
	Cryptogenic cirrhosis
	Hepatic coma
	Hepatic encephalopathy
	Hepatic fibrosis
	Impaired liver function
	Liver cirrhosis
	'"Non-alcoholic cirrhosis of liver - Child"s A"'
	'"Non-alcoholic cirrhosis of liver - Child"s B"'
	'"Non-alcoholic cirrhosis of liver - child"s C"'
	'"Non-alcoholic cirrhosis of liver - Child"s C"'
	Oesophageal varices due to cirrhosis

Supplementary Table 4. List of British National Formulary codes used to identify the different types of medication dispensed to patients with Alzheimer's disease.

Medication	BNF codes	Medication full description
Drugs for dementia	4.11	Drugs for dementia
Drugs for Parkinsonism	4.9	Drugs used in Parkinsonism and related disorders
Drugs for hypertension	2.4	Beta-adrenoceptor blocking drugs
	2.5	Hypertension and heart failure
	2.6	Calcium-channel blockers
Drugs for diabetes	6.1	Drugs used in diabetes
Lipid-regulating drugs	2.12	Lipid-regulating drugs
Anti-platelets	2.9	Antiplatelet drugs
Anti-psychotics	4.2	Drugs used in psychoses and related disorders
Anti-depressants	4.3	Antidepressant drugs
Hypnotics	4.1	Hypnotics and anxiolytics