

Healthcare burden of cognitive impairment: Evidence from a Singapore Chinese health study

Junxing Chay¹ PhD, Woon-Puay Koh^{2,3} PhD, Kelvin Bryan Tan^{4,5} PhD, Eric A Finkelstein¹ PhD

ABSTRACT

Background: Cognitive impairment (CI) raises risks for unplanned healthcare utilisation and expenditures and for premature mortality. It may also reduce risks for planned expenditures. Therefore, the net cost implications for those with CI remain unknown.

Method: We examined differences in healthcare utilisation and cost between those with and without CI. Using administrative healthcare utilisation and cost data linked to the Singapore Chinese Health Study cohort, we estimated regression-adjusted differences in annual healthcare utilisation and costs by CI status determined by modified Mini-Mental State Exam. Estimates were stratified by ex ante mortality risk constructed from out-of-sample Cox model predictions applied to the full sample, with a separate analysis restricted to decedents. These estimates were used to project differential healthcare costs by CI status over 5 years.

Results: Patients with CI had 17% higher annual cost compared to those without CI (SGD4870 versus SGD4177, $P < 0.01$). Accounting for the greater mortality risk, individuals with CI cost 9% to 17% more over 5 years, or SGD2500 (95% confidence interval 1000–4200) to SGD3600 (95% confidence interval 1300–6000) more, depending on their age. Higher cost was mainly due to more emergency department visits and subsequent admissions (i.e. unplanned). Differences attenuated in the last year of life when costs increased dramatically for both groups.

Conclusion: Ageing populations and higher rates of CI will further strain healthcare resources primarily through greater use of emergency department visits and unplanned admissions. Efforts should be made to identify at risk patients with CI and take appropriate remediation strategies.

Ann Acad Med Singap 2024;53:233-40

Keywords: burden, cognitive impairment, end-of-life, healthcare, healthcare cost, Singapore, survival, utilisation

CLINICAL IMPACT

What is New

- Our study demonstrates that individuals with cognitive impairment tend to experience higher rates of unplanned healthcare utilisation, such as visits to emergency departments and subsequent hospital admissions.
- Additionally, those with cognitive impairment face significantly higher overall healthcare costs when compared to individuals without cognitive impairment.

Clinical Implications

- These findings confirm the growing concern regarding the burden of cognitive impairment on healthcare systems, especially within ageing populations, as evidenced by increased healthcare utilisation and escalating costs.

INTRODUCTION

Individuals with cognitive impairment (CI) are predisposed to injuries, infections and treatment complications,¹ have poorer treatment compliance, and face greater difficulties with post-discharge care.² These challenges, exacerbated by comorbidities,³⁻⁶ lead to poorer ambulatory care management, reduced contacts with primary and outpatient care providers, and greater use of emergency department (ED) visits, more unplanned admissions, and longer length of inpatient stays.⁷⁻⁹ Roughly two-thirds of those with CI will also develop dementia.¹⁰

The above suggests that rising rates of CI will increase health expenditures. Yet, this is not necessarily the case as those with CI have higher mortality risk.^{11,12} Those with CI may also be less aggressively treated and therefore less likely

The Annals is an open access journal, allowing non-commercial use under CC BY-NC-SA 4.0.

¹ Lien Centre for Palliative Care, Duke-NUS Medical School, Singapore

² Healthy Longevity Translational Research Programme, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

³ Singapore Institute for Clinical Sciences, Agency for Science Technology and Research (A*STAR), Singapore

⁴ Chief Health Economist Office, Ministry of Health, Singapore

⁵ Centre for Regulatory Excellence, Duke-NUS Medical School, Singapore

Correspondence: Dr Junxing Chay, Lien Centre for Palliative Care, Duke-NUS Medical School, 8 College Road, Singapore 169857.

Email: junxing.chay@duke-nus.edu.sg

to receive life-extending treatments, such as dialysis, cancer treatments or surgeries.^{13,14} This may result both because these patients face greater difficulty adhering to treatment guidelines, such as post-surgical care and because surrogate decision-makers may be less inclined to pursue life-extending or elective treatments for someone with CI.^{15,16} Hence, while unplanned healthcare utilisation is likely greater for those with CI, planned utilisation may be less due to both the mortality effect and the possible attenuation of planned care. Therefore, whether those with CI have higher or lower expenditures than those without is ultimately an empirical question.

We address this question by quantifying differences in healthcare utilisation and costs for those with and without CI using a retrospective analysis of a population-based cohort, the Singapore Chinese Health Study cohort, linked to administrative healthcare records.¹⁸ Our primary analysis compared utilisation and costs between those with and without CI. We expect that those with CI will have higher utilisation and costs associated with ED visits and unplanned admissions (i.e. through the ED) but will have lower utilisation and costs associated with outpatient visits and planned hospital admissions (i.e. not through the ED). Moreover, we expect that the hypotheses for outpatient visits, ED visits and unplanned admissions are more likely to hold for those at greater ex ante risk of dying because CI complicates treatment for other conditions and ambulatory care management. On the other hand, the hypothesis for planned admissions is more likely to hold for those at lower ex ante risk of dying as these patients face less urgency for life-extending treatment. In the last year of life we expect cost differences between those with and without CI to attenuate, both because those with CI are less likely to receive life-extending treatments and because those without CI are likely to be much more expensive than in non-terminal years.^{7,8,17}

As a secondary analysis, we combined the expenditure and survival estimates to quantify the expected 5-year per capita burden of CI for varying ages between 65 and 90. We hypothesised that the 5-year burden of CI will attenuate with increasing age due to increased mortality risk attributable to CI. These results will help policy-makers better understand drivers for end-of-life costs and budget for future health expenditures that will come with Singapore's ageing population.

METHOD

The Singapore Chinese Health Study is a longitudinal cohort study that recruited 63,257

Chinese residents aged 45–74 years and residing in public housing estates during recruitment from 1993 to 1998; at the time of recruitment, about 86% of Singapore population resided in these estates.¹⁸ Trained interviewers used a structured questionnaire to collect information on usual diet, lifestyle factors and medical history from consenting participants. Our study focused on respondents of the third follow-up interview (n=16,947), conducted from 2014 to 2016, which examined cognitive function among the participants using the Singapore-modified version of the Mini-Mental State Exam (SM-MMSE).¹⁹ Although an MMSE cut-off point of 23 to 24 is usually used to define CI in Western countries,²⁰ previous studies have showed that MMSE score is significantly affected by education level.^{21,22} As education level in our population was generally low, we used education-specific cut-off points from the Shanghai Dementia Survey which had a comparable education level with our study population.²¹ Individuals with CI were identified by SM-MMSE scores <18, <21 and <25 for those with no formal education, with primary school education, and with secondary school or higher education, respectively. Vital status as of 31 December 2019 and date of death were obtained from linkage with the Singapore Registry of Births and Deaths.

Healthcare utilisation and cost

Data on healthcare utilisation and costs from 2014 to 2019 were obtained by linking the Singapore Chinese Health Study (SCHS) cohort to administrative data from the Ministry of Health. The latter captures cost and utilisation data from public and private acute hospitals in Singapore for admissions, day surgeries, hospital outpatient visits and visits to government-run polyclinics.²³

Healthcare utilisation was examined in terms of having any visits, number of visits and length of stay for hospital admissions. We consider all ED visits and all hospital admissions following an ED visit as unplanned. Healthcare costs were taken from the non-subsidised bill amount and adjusted to 2021 Singapore dollars (SGD) using the healthcare consumer price index.

Burden estimation

We used regression analysis to estimate the differences in healthcare utilisation and cost between cognitively impaired and cognitively intact individuals, controlling for potential confounders, including age, gender, education, residence type, whether they lived alone, health conditions (e.g. body mass index and self-reported chronic conditions), and year-fixed effects. Probit regression was used for the probability of having at least 1 visit or

admission. Negative binomial regression was used for number of visits and length of inpatient stay.

A 2-part model was used to quantify healthcare cost a year from the survey date to account for the fact that many individuals do not utilise ED or inpatient services.²⁴ The first part is a probit model which estimated the probability of having a positive cost. The second part is a generalised linear regression model (GLM) with log link function and gamma-distributed errors that estimated non-zero costs.²⁵ For the analysis of cost in the last year of life, we found the GLM with log link function and gamma-distributed errors to be a reasonable fit as the probability of having a positive cost was high.

Since CI was assessed only once for the SCHS cohort in the third follow-up survey, our primary analysis focused on estimating CI burden in the 12-month period immediately after survey to test our hypotheses on differences in utilisation and costs over different healthcare settings as a function of CI status. To investigate the extent to which our hypotheses hold for those with different underlying risk of dying, we conducted a stratified analysis by the 12-month ex ante mortality risk—defined here as the out-of-sample predicted probability of dying as discussed in the following paragraph—running separate regressions for those in the top 25% risk and those in the bottom 75% risk. For comparisons of healthcare utilisation and cost in the last year of life, we assumed that decedents who were cognitively intact during the interview remained so until death.

Survival estimation

A stratified Cox proportional-hazards model, controlling for the same set of predictors used in the burden estimation, was used to estimate survival differences attributed to CI, as well as generate ex ante mortality risk predictions. Stratification was performed over cancer status, which failed the proportional hazards test based on Schoenfeld residuals. To obtain ex ante mortality risk, we implemented a 10-fold out-of-sample prediction procedure that involved randomly partitioning the sample into 10 equal-sized subsamples. For each subsample, the survival model was fitted on the other 9 subsamples and out-of-sample predictions were generated for the withheld subsample.

Expected 5-year cost

We projected the expected total 5-year cost of cognitively impaired and cognitively intact individuals beginning at ages 65, 70, 75, 80, 85 and 90 years to investigate any offsetting effects of increased mortality for older individuals. The projections were based on 3 sets of age-specific predictive margins over CI status: (1) annual

survival probabilities; (2) total end-of-life cost in the last 12 months of life; and (3) annual non-end-of-life cost. Predictive margins were averaged over those whose ages were within 2 years of the reference age to ensure other covariates such as health conditions are representative (e.g. predictive margin for a 70-year-old is averaged over those aged 68 to 72). The expected 5-year cost for an individual is then the probability-weighted sum of end-of-life and non-end-of-life costs in each year, with costs beyond the first year discounted at 3% per annum. Standard errors and 95% confidence intervals were calculated based on 2000 bootstrap replications. Similar to the analysis of the end-of-life costs, the projections assumed CI status remains unchanged throughout this period.

RESULTS

Table 1 presents the demographic and health characteristics of individuals participating in the third SCHS follow-up interviews. Approximately 14% of respondents had evidence of CI based on the SM-MMSE scores. These individuals were more likely to be female, older, less educated, and residing in 3-room flats or smaller. They were also more likely to be unhealthy, have a higher risk of cardiovascular disease, and more likely to have reported being diagnosed with hypertension, diabetes, stroke, arthritis and Parkinson's. However, they were also less likely to have reported having high cholesterol, gout and cancer. By the end of 2019, individuals with CI were more than twice as likely to have died than those without CI.

The first 2 columns of Table 2 report the regression-adjusted healthcare utilisation and costs incurred within a year from interview. Overall, individuals with CI were more likely than those without CI to have at least one visit to the ED (26% versus [vs] 20%, $P<0.01$) and at least 1 unplanned admission (18% vs 13%, $P<0.01$). On average, individuals with CI spent 1.22 more days in the hospital than those without ($P<0.01$), and these days were mostly attributed to unplanned admissions. In terms of total healthcare costs, individuals with CI cost about SGD700 or 17% more per year than those without CI (SGD4870 vs SGD4177, $P<0.01$), which were largely driven by higher costs for unplanned admissions. Costs for outpatient visits were significantly lower for individuals with CI ($P<0.05$). There were no differences in utilisation or costs of planned admissions. Utilisation and cost of ED without admission were significantly higher for individuals with CI ($P<0.05$).

Columns 3 to 6 of Table 2 report results stratified by ex ante mortality risk (see Supplementary

Table 1. Sample characteristics by vital and cognitive impairment status.

Cognitive status	No CI (n=14,504)	CI (n=2443)
Panel A: Demographics		
Men, %	41.4	37.0
Age, mean	72.0	76.7
Level of education, %		
None	18.0	24.0
Primary	45.3	41.6
Secondary and above	36.7	34.4
Living alone, %	7.8	7.9
Housing type, %		
HDB 1-2 room	4.2	6.8
HDB 3-room	30.6	36.4
HDB 4 room	38.1	36.1
HDB 5 room or exec	24.3	19.0
Private or others	2.7	1.7
Panel B: Health measures		
BMI group, %		
≤18.4 (underweight)	6.5	7.2
18.5–22.9 (low CVD risk)	42.2	39.9
23.0–27.4 (moderate CVD risk)	40.6	40.7
≥27.5 (high CVD risk)	10.8	12.2
High blood pressure, %	61.9	66.1
Heart attack/angina/heart failure, %	9.6	10.1
Coronary bypass/angioplasty, %	7.1	7.4
Stroke, %	4.7	8.1
Diabetes, %	22.0	26.1
High cholesterol, %	57.6	53.1
Gout, %	6.2	4.3
Cancer, %	6.8	5.6
Chronic lung disease, %	1.0	0.8
Arthritis, %	18.4	20.1
Kidney failure, %	1.3	1.6
Parkinson's disease, %	0.5	1.2
Deceased by 2019, %	7.1	17.6

BMI: body mass index; CI: cognitive impairment; CVD: cardiovascular disease

Materials Tables S1 and S2 for fitted survival model and its discriminative power). Approximately 35% of those with higher mortality risk had CI, while only 8% of those with lower mortality risk had CI. Individuals with the same CI status but with higher risk of dying over the next year had substantially higher healthcare utilisation and costs in all settings. Among those with lower mortality risk, ED and unplanned inpatient utilisation remained significantly higher for individuals with CI. However, the difference in total costs was smaller and not statistically significant. This is because despite having significantly higher costs for unplanned admissions, individuals with CI had significantly lower costs for planned admissions. Healthcare burden associated with CI was also generally larger in absolute terms for those with higher mortality risk. Incremental ED visits and unplanned admissions associated with CI were relatively greater and more statistically significant in magnitude for this group. Similar results were found for healthcare costs. Additionally, high mortality risk individuals with CI incurred significantly lower outpatient costs than those without (SGD187, $P<0.05$). Total costs associated with CI was SGD1177 ($P<0.01$) for those with higher mortality risk; but for those with lower mortality risk it was only SGD251 and not statistically significant. Alternative estimates restricted to a subsample of those with matched CI propensity scores (Supplementary Materials Table S3) yielded similar findings.

Table 3 reports the regression-adjusted healthcare utilisation and costs incurred in the last year of life. Utilisation of ED and inpatient service settings were substantially higher than Table 2 but were more similar between CI status. Although the lack of statistically significant differences may be partly due to the smaller sample size, we note that the absolute difference between those with and without CI was also smaller. Outpatient visits and planned admissions at the end of life were significantly lower for individuals with CI. Unplanned inpatient costs were also lower for individuals with CI. There was little difference in costs by place of service or overall in the last year of life.

Table 4 presents the expected 5-year total healthcare cost by age and CI status. Costs increase with starting age and were significantly higher for individuals with CI by about SGD2500 to SGD3600 (i.e. SGD500 to SGD720 per year), based on the 95% bootstrapped confidence intervals. The incremental cost associated with CI rose initially with age, peaking at around age 80 before falling. A breakdown of the survival

Table 2. Healthcare utilisation and cost, a year after the interview.

Ex ante mortality risk	All (n=16,939)		Bottom 75% mortality risk (n=12,703)		Top 25% mortality risk (n=4236)	
	No CI	CI	No CI	CI	No CI	CI
Panel A: Any visit/admission, %						
Outpatient	94.1	93.6	93.2	93.2	96.6	96.5
Emergency department	19.7	25.7***	16.0	18.7**	30.9	40.2***
Emergency department without admission	9.6	12.0***	8.6	10.0	12.4	16.1***
Inpatient	16.3	21.9***	12.6	15.0**	27.5	36.1***
Planned inpatient	6.1	6.3	5.2	4.5	8.9	9.7
Unplanned inpatient	12.6	18.2***	9.0	12.3***	23.5	31.8***
Panel B: Number of visits/admissions, mean						
Outpatient	10.4	10.1*	9.76	9.67	12.4	12.0
Emergency department	0.30	0.46***	0.22	0.31***	0.52	0.81***
Emergency department without admission	0.11	0.15***	0.10	0.12	0.16	0.20***
Inpatient	0.27	0.40***	0.19	0.24**	0.49	0.74***
Planned inpatient	0.08	0.08	0.07	0.06	0.13	0.14
Unplanned inpatient	0.18	0.31***	0.12	0.19***	0.36	0.60***
Panel C: Length of inpatient stay, mean days						
All admissions	1.66	2.88***	1.00	1.60**	3.38	5.73***
Planned admissions	0.43	0.50	0.31	0.23	0.78	1.08
Unplanned admissions	1.24	2.45***	0.71	1.41**	2.60	4.86***
Panel D: Costs (2021), SGD						
Total	4177	4870***	3283	3534	6072	7249***
Outpatient	1790	1673**	1623	1631	2265	2078**
Emergency department	74	110***	55	73***	132	196***
Emergency department without admission	30	36**	26	29	43	54**
Inpatient	2292	3118***	1616	1745	4348	5830***
Planned inpatient	986	895	844	458***	1388	1621
Unplanned inpatient	1299	2157***	778	1283**	2910	4327***

CI: cognitive impairment

Estimates are regression-adjusted, controlling for factors listed in Table 1 and time-fixed effects. Statistically significant differences between the cognitively intact and impaired are indicated by asterisks: * $P<0.1$, ** $P<0.05$, *** $P<0.01$.

probability and undiscounted cost for each year reveal what is driving this u-shaped pattern (Supplementary Materials Table S4). The CI burden increased initially with age because incremental costs, both non-end-of-life and end-of-life,

increased with age. However, higher mortality attributable to CI also increased with age, offsetting the additional costs with an increasingly lower probability of surviving. Hence, the projected costs subsequently fell with age.

Table 3. Total healthcare utilisation and cost in the last year of life.

Cognitive status of decedents (n=1454)	No CI	CI
Panel A: Any visit/admission, %		
Outpatient	97.7	94.8**
Emergency department	89.9	92.4
Emergency department without admission	29.0	31.9
Inpatient	89.7	91.1
Planned inpatient	35.0	26.6***
Unplanned inpatient	84.5	85.8
Panel B: Number of visits/admissions, mean		
Outpatient	16.7	13.5***
Emergency department	2.57	2.59
Emergency department without admission	0.41	0.40
Inpatient	2.76	2.65
Planned inpatient	0.63	0.47**
Unplanned inpatient	2.13	2.17
Panel C: Length of inpatient stay, mean days		
All admissions	24.8	26.4
Planned admissions	4.58	4.44
Unplanned admissions	20.3	22.0
Panel D: Costs (2021), SGD		
Total	34,469	33155
Outpatient	3515	2736***
Emergency department	699	697
Emergency department without admission	122	118
Inpatient	30,228	29745
Planned inpatient	7523	6553
Unplanned inpatient	22,847	22927

CI: cognitive impairment.

Estimates are regression-adjusted, controlling for factors listed in Table 1 and time-fixed effects. Statistically significant differences between the cognitively intact and impaired are indicated by asterisks: * $P<0.1$, ** $P<0.05$, *** $P<0.01$.

DISCUSSION

This study quantified the annual and 5-year per capita burden of CI for an elderly Chinese population in Singapore. Using our annual estimates and assuming 44,000 individuals have CI in Singapore,²⁶ the aggregate burden is about

SGD134 million over 5 years, or SGD27 million annually. This figure represents only 0.1% of the nation's total health expenditure today, but it is likely to rise dramatically in the future given the ageing population and rising rate of CI.²⁷ While several cost-of-illness studies have been published for CI,²⁸⁻³³ only 2 studies, both from the US, focused on its impact on healthcare utilisation at the end-of-life.^{7,8} Our findings are largely consistent with results from these studies.

The higher cost among those with CI resulted because these individuals utilised more ED and inpatient services, most of which were unplanned. As hypothesised, those most at risk of dying had the greatest difference. This may result from CI complicating treatment for other health conditions such as end-stage renal disease and cancer, which require good ambulatory care management and high patient adherence. Among the subset with lower mortality risk, those with CI had fewer planned admissions, shorter associated stays, and significantly lower costs. This could be due to efforts on the part of caregivers and providers to avoid costly and invasive discretionary treatments for those with CI. When mortality risk was higher, utilisation patterns did not appear to differ by CI status, perhaps because treatment is less discretionary in these circumstances.

During the last year of life, we found that older adults with CI had fewer outpatient visits and planned admissions but total cost appeared similar between those with and without CI. The similarity in costs is possibly because of the high and variable costs associated with dying, which makes it difficult to tease out costs specifically related to CI.

Our results show that the bulk of the CI burden is from ED visits and unplanned admissions. Common causes for ED visits among those with CI include pneumonia, heart failure, urinary tract infection and fall-related injuries.³⁴ Future research should investigate the extent to which such cases can be avoided or diverted to lower-cost outpatient and community care settings, and whether strategies to do so are cost-effective.

We also found evidence of lower expenditures on planned hospitalisations among those with lower risk of dying, suggesting that doctors or surrogate decision-makers may be less inclined to pursue costly elective treatment for patients with CI. A better understanding of treatment choices and their consequences for patients with CI should be an area of future research.

This study has several limitations. First, our estimates are limited to medical costs. They do not include the cost of private primary care clinics, nursing homes, other non-institutional care (e.g.

Table 4. Expected 5-year total healthcare cost (2021, SGD).

Cognitive status	No CI	CI	Incremental cost
Starting age			
65	15,200 (14,400 to 16,000)	17,800 (16,000 to 19,600)	2500 (1000 to 4200)
70	18,400 (17,600 to 19,200)	21,400 (19,600 to 23,300)	3000 (1200 to 5000)
75	21,600 (20,700 to 22,700)	25,000 (23,100 to 27,000)	3400 (1300 to 5600)
80	25,000 (23,600 to 26,700)	28,500 (26,500 to 30,900)	3600 (1300 to 6000)
85	27,400 (25,400 to 29,900)	30,800 (28,000 to 33,700)	3400 (1000 to 6000)
90	28,700 (25,800 to 32,100)	31,300 (28,400 to 34,800)	2700 (200 to 5200)

CI: cognitive impairment.

The 95% confidence intervals are based on 2000 bootstrap replications, reported in parentheses. Costs beyond the first year were discounted at the rate of 3%.

day care, home care), and large indirect costs associated with informal caregiving.^{35,36} Second, estimates were based on the Chinese population in Singapore only, so results may not generalise to the roughly 25% of the population who is not Chinese.³⁷⁻³⁹ Third, CI status was measured only once at the start of the study. Our analysis assumed those who are cognitively intact remain so until the end of the analysis period. This attenuates the burden of CI because a proportion of those who were cognitively intact during the survey may later become impaired, thus increasing costs. Restricting our ex ante mortality risk analysis to within a year of the survey reduced this bias, but this approach was not feasible for the analysis of the last year of life due to too few deaths. Nevertheless, we argue that this bias is likely small given the short follow-up period. Another potential source of bias is that costly chronic conditions (e.g. cancer) may have a higher likelihood of being under-reported or unobserved by individuals with CI, resulting in overestimating the CI burden. However, it is not clear whether the lower prevalence observed in our sample is due to misreporting or undiagnosed cases due to a lack of health screening.

CONCLUSION

The anticipated increase in burden associated with CI is a concern for many countries with an ageing population. We show that this concern is valid but partly attenuated by greater mortality risk and less use of planned healthcare services. Regardless, ageing populations and higher rates of CI will further strain healthcare resources. Efforts should be made to identify the most at-risk patients with CI, including which components of CI (e.g.

behavioural/psychological issues, physical/functional decline) have the largest impact, and take appropriate remediation strategies.

Funding

This study was funded Singapore Millennium Foundation (2019-SMF-0005). Data collection for Singapore Chinese Health Study was supported by the Singapore National Medical Research Council (NMRC/CSA/0055/2013) and the Saw Swee Hock School of Public Health, National University of Singapore. Woon Puay Koh is supported by the National Medical Research Council, Singapore (CSA-SI [MOH-000434]). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Acknowledgement

We thank Siew-Hong Low of the National University of Singapore for overseeing the fieldwork of the Singapore Chinese Health Study, and the Ministry of Health in Singapore for linkage with the MediClaim database.

REFERENCES

1. Zhao Y, Kuo TC, Weir S, et al. Healthcare costs and utilization for Medicare beneficiaries with Alzheimer's. *BMC Health Serv Res* 2008;8:108.
2. Sachs GA, Shega JW, Cox-Hayley D. Barriers to excellent end-of-life care for patients with dementia. *J Gen Intern Med* 2004;19:1057-63.
3. Zhu CW, Cosentino S, Ornstein KA, et al. Interactive Effects of Dementia Severity and Comorbidities on Medicare Expenditures. *J Alzheimers Dis* 2017;57:305-15.
4. Kuo TC, Zhao Y, Weir S, et al. Implications of comorbidity on costs for patients with Alzheimer disease. *Med Care* 2008;46:839-46.

5. Hill JW, Futterman R, Duttagupta S, et al. Alzheimer's disease and related dementias increase costs of comorbidities in managed Medicare. *Neurology* 2002;58:62-70.
6. Fillit H, Hill JW, Futterman R. Health care utilization and costs of Alzheimer's disease: the role of co-morbid conditions, disease stage, and pharmacotherapy. *Fam Med* 2002;34:528-35.
7. Daras LC, Feng Z, Wiener JM, et al. Medicare Expenditures Associated With Hospital and Emergency Department Use Among Beneficiaries With Dementia. *Inquiry* 2017;54:0046958017696757.
8. Feng Z, Coots LA, Kaganova Y, et al. Hospital And ED Use Among Medicare Beneficiaries With Dementia Varies By Setting And Proximity To Death. *Health Aff (Millwood)* 2014;33:683-90.
9. Fogg C, Griffiths P, Meredith P, et al. Hospital outcomes of older people with cognitive impairment: An integrative review. *Int J Geriatr Psychiatry* 2018;33:1177-97.
10. Busse A, Angermeyer MC, Riedel-Heller SG. Progression of mild cognitive impairment to dementia: a challenge to current thinking. *Br J Psychiatry* 2006;189:399-404.
11. An J, Li H, Tang Z, et al. Cognitive Impairment and Risk of All-Cause and Cardiovascular Disease Mortality Over 20-Year Follow-up: Results From the BLSA. *J Am Heart Assoc* 2018;7:e008252.
12. Hao Q, Dong B, Yang M, et al. Frailty and Cognitive Impairment in Predicting Mortality Among Oldest-Old People. *Front Aging Neurosci* 2018;10.
13. Richardson SS, Sullivan G, Hill A, et al. Use of Aggressive Medical Treatments Near the End of Life: Differences between Patients with and without Dementia. *Health Serv Res* 2007;42:183-200.
14. Morin L, Beaussant Y, Aubry R, et al. Aggressiveness of End-of-Life Care for Hospitalized Individuals with Cancer with and without Dementia: A Nationwide Matched-Cohort Study in France. *J Am Geriatr Soc* 2016;64:1851-57.
15. Gao X, Prigerson HG, Diamond EL, et al. Minor Cognitive Impairments in Cancer Patients Magnify the Effect of Caregiver Preferences on End-of-Life Care. *J Pain Symptom Manage* 2013;45:650-59.
16. Kurita K, Reid MC, Siegler EL, et al. Associations between Mild Cognitive Dysfunction and End-of-Life Outcomes in Patients with Advanced Cancer. *J Palliat Med* 2018;21:536-40.
17. Sallnow L, Smith R, Ahmedzai SH, et al. Report of the Lancet Commission on the Value of Death: bringing death back into life. *Lancet* 2022;399:837-84.
18. Hankin JH, Stram DO, Arakawa K, et al. Singapore Chinese Health Study: Development, Validation, and Calibration of the Quantitative Food Frequency Questionnaire. *Nutr Cancer* 2001;39:187-95.
19. Feng L, Chong MS, Lim WS, et al. The Modified Mini-Mental State Examination test: normative data for Singapore Chinese older adults and its performance in detecting early cognitive impairment. *Singapore Med J* 2012;53:458-62.
20. Mitchell AJ. A meta-analysis of the accuracy of the mini-mental state examination in the detection of dementia and mild cognitive impairment. *J Psychiatr Res* 2009;43:411-31.
21. Katzman R, Zhang MY, Ouang Ya Q, et al. A Chinese version of the Mini-Mental State Examination; impact of illiteracy in a Shanghai dementia survey. *J Clin Epidemiol* 1988;41:971-8.
22. Lipnicki DM, Crawford JD, Dutta R, et al. Age-related cognitive decline and associations with sex, education and apolipoprotein E genotype across ethnocultural groups and geographic regions: a collaborative cohort study. *PLoS Med* 2017;14:e1002261.
23. Ministry of Health Singapore. Terms and conditions of approval under the MediSave scheme and the MediShield Life scheme. <https://www.mediclaim.moh.gov.sg/mmae/OverviewRules.aspx?Tag=TnC>. Accessed 29 November 2022.
24. Duan N, Manning WG, Morris CN, et al. Choosing Between the Sample-Selection Model and the Multi-Part Model. *Journal of Business & Economic Statistics* 1984;2:283-89.
25. Mihaylova B, Briggs A, O'Hagan A, et al. Review of statistical methods for analysing healthcare resources and costs. *Health Econ* 2011;20:897-916.
26. Institute for Health Metrics and Evaluation. Global Burden of Disease Study 2019 (GBD 2019) Data Resources. <https://vizhub.healthdata.org/gbd-results/>. Accessed 29 November 2022.
27. World Health Organization. Global Health Expenditure Database. <https://apps.who.int/nha/database/Home/Index/en>. Accessed 29 November 2022.
28. Rice DP, Fox PJ, Max W, et al. The economic burden of Alzheimer's disease care. *Health Aff (Millwood)* 1993;12:164-76.
29. Joling KJ, Schoppe J, van Hout HP, et al. Predictors of Societal Costs in Dementia Patients and Their Informal Caregivers: A Two-Year Prospective Cohort Study. *Am J Geriatr Psychiatry* 2015;23:1193-203.
30. Jonsson L, Wimo A. The cost of dementia in Europe: a review of the evidence, and methodological considerations. *Pharmacoeconomics* 2009;27:391-403.
31. Gustavsson A, Brinck P, Bergvall N, et al. Predictors of costs of care in Alzheimer's disease: a multinational sample of 1222 patients. *Alzheimers Dement* 2011;7:318-27.
32. Hurd MD, Martorell P, Delavande A, et al. Monetary costs of dementia in the United States. *N Engl J Med* 2013;368:1326-34.
33. Kelley AS, McGarry K, Gorges R, et al. The burden of health care costs for patients with dementia in the last 5 years of life. *Ann Intern Med* 2015;163:729-36.
34. LaMantia MA, Stump TE, Messina FC, et al. Emergency Department Use Among Older Adults With Dementia. *Alzheimer Dis Assoc Disord* 2016;30:35-40.
35. Connors MH, Seeher K, Teixeira-Pinto A, et al. Mild Cognitive Impairment and Caregiver Burden: A 3-Year-Longitudinal Study. *Am J Geriatr Psychiatry* 2019;27:1206-15.
36. Oba H, Kadoya Y, Okamoto H, et al. The Economic Burden of Dementia: Evidence from a Survey of Households of People with Dementia and Their Caregivers. *Int J Environ Res Public Health* 2021;18.
37. Sahadevan S, Saw SM, Gao W, et al. Ethnic Differences in Singapore's Dementia Prevalence: The Stroke, Parkinson's Disease, Epilepsy, and Dementia in Singapore Study. *J Am Geriatr Soc* 2008;56:2061-68.
38. Hilal S, Tan CS, Xin X, et al. Prevalence of Cognitive Impairment and Dementia in Malays - Epidemiology of Dementia in Singapore Study. *Curr Alzheimer Res* 2017;14:620-27.
39. Wong MYZ, Tan CS, Venketasubramanian N, et al. Prevalence and Risk Factors for Cognitive Impairment and Dementia in Indians: A Multiethnic Perspective from a Singaporean Study. *J Alzheimers Dis* 2019;71:341-51.