COSTS OF ALZHEIMER'S DISEASE IN CZECHIA

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Abstract

This study investigates the economic burden of Alzheimer's disease in Czechia. We use decision analytic framework to estimate lifetime costs per patient. These costs are modeled for several patient profiles defined by gender and age of disease onset with the help of Monte Carlo simulation. The parameters entering the model are subject to careful scrutiny in this study. As decision analytic modelling combines multiple data sources, we debate the reliability of each source both with respect to the quality of the data and their representativeness of the Czech context. The resulting figures are broken down into the following three categories of care provided to patients suffering from Alzheimer's disease: Health care includes costs of outpatient treatment and inpatient care. Social care costs consist of home services and stays in a nursing institution. Informal care costs refer to the lost productivity of caregivers. We also break the costs down according to who pays them, discussing thus the extent of the burden for different budgets. Differences among profiles are evaluated.

Key words: costs of Alzheimer's disease, decision analytic modelling, Monte Carlo simulation, health economics

JEL Code: C15, I10, I18

Introduction

This study attempts to estimate lifetime costs of patients suffering from Alzheimer's disease (AD) in Czechia. Worldwide, AD and the associated economic burden represent a major threat to the ageing population (Prince et al., 2016). Successful management of the disease, including closing of the existing treatment gap, requires that the current treatment situation be understood accurately. For this reason, our paper gathers existing epidemiological, medical and economic evidence (Holmerová et al., 2017; Luzny et al., 2014; Marešová & Zahálková, 2016; Mátl et al., 2016;

Mohelska et al., 2015) to describe and cost the care as usual (CAU) provided in Czechia. Beside health care costs we consider also costs of informal care provided mainly by the family.

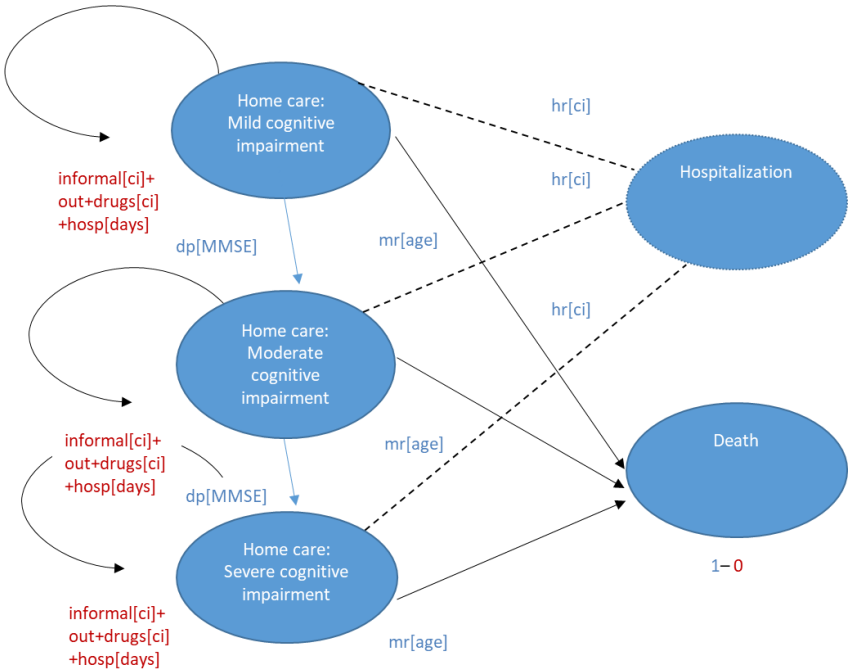
We build a decision analytic model and employ Monte Carlo simulation (1000 trials) as an estimation method. The model arises from a study of (Weimer & Sager, 2009) and (Broulikova et al., 2017). The great advantage of decision analytic modelling is that it provides a framework for combining multiple data inputs in order to answer complex questions that cannot be addressed by using a single data source (e.g. trial or database) (Briggs et al., 2006). Since validity of results provided by this approach depends on the quality of data sources, we investigate the quality of Czech sources available for each relevant parameter and suggest possible improvements where appropriate. Several nationwide health care registers were identified as data sources that shall be exploited in the future for the purposes of decision analytic modelling in (mental) health care.

The contribution of this study is three-fold. First, we provide information on what CAU for people with AD looks like. Second, we estimate the lifelong economic burden per one patient and show who pays for the care. Third, we explore the quality of input data and identify how the knowledge about the Czech AD patients could be extended by using routinely collected data.

1 The Model

Figure 1 depicts the structure of the model and Table 1 describes its parameters. A patient migrates through five health states: home care with mild cognitive impairment, home care with moderate cognitive impairment, home care with severe cognitive impairment, hospitalization, and death. The length of one cycle is one year. The patient´s characteristics – gender and age at the time of the disease onset – are choice variables of this model. Disease progression is represented by three stages of cognitive impairment: mild, moderate and severe. The pace of disease progression depends on whether treatment is available to the patient. According to Mátl et al. (2016), only 26% of patients in Czechia receive treatment. Any patient in our model may be hospitalized. Hospitalization is a temporary state in which the patient cannot stay after the cycle ends; i.e. the maximum length of one hospitalization is 365 days. Death is the absorbing state of the model with no transition back. The order of steps in each cycle is as follows: death risk and subsequently hospitalization risk is imposed at the beginning of cycle, cognitive decline risk is imposed at the end of the cycle.

Fig. 1: Model scheme



Source: own illustration

Tab. 1: Model parameters

Transition probabilities are in blue	
dp[MMSE]	Pace of disease progression from current severity of cognitive impairment to worse state (dependent on the MMSE score)
hr[ci]	Hospitalization risk (dependent on the severity of cognitive impairment)
mr[age]	Mortality risk adjusted for AD (dependent on age)

State costs are in red	
informal[ci]	Costs of informal care at home (dependent on the severity of cognitive impairment)
out	Costs of outpatient treatment
drugs[ci]	Costs of drugs (dependent on the severity of cognitive impairment)
hosp[days]	Costs of hospitalization (dependent on its length in days)

Note: *dp* stands for disease progression, *hr* for hospitalization risk, *ci* for cognitive impairment and *mr* for mortality risk. Source: own illustration

1.1 Parameters

Decline scheme. The backbone of the analysis is a decline scheme used to model disease progression. Following the existing literature (Weimer & Sager, 2009) we use a decline scheme based on the annual decrease in the Mini Mental Examination (MMSE) score. MMSE is a simple instrument measuring cognitive impairment. The maximum number of points to be reached is 30 and any score below 29 points is considered to represent a cognitive deficit. Scores within the range 28-21 points indicate mild, 20-11 moderate, and 10-0 severe cognitive impairment (Weimer & Sager, 2009). Biostatistical research (Lopez et al., 2005) conceptualizes the pace of the disease progression as an annual random draw from the given probability distribution. The decline scheme used in our model relies on normal distribution with negative truncation. The distribution has a mean of 3.5, and a standard deviation of 1.5 for untreated patients. For treated patients the mean drops to 1.5 but standard deviation stays same. The treatment strategy modeled by this scheme pertains to medication based on cholinesterase inhibitors (donepezil) and memantine. To model the situation in Czechia where patients are usually diagnosed already with moderate or severe cognitive impairment (Mátl et al., 2016), we consider 19 points as the score at which treatment is initiated for 26% of the patients. It is noteworthy that this modelling approach relying on a decline scheme does not directly use transition probabilities as usual in Markov models.

There are three potentially relevant concerns associated with the used cognitive decline scheme. First, the assumption of linear cognitive decline might be oversimplifying as the rate of decline likely has an inverse S-shaped curve; i.e. the cognitive capacity declines fast early on but decline slows down in the more progressed stages of the disease (Stern et al., 1996). Second, treatment initiated at different stages of cognitive impairment might be differently effective. Third, it is not clear whether treatment strategies in Czechia rely mainly on cholinesterase inhibitors and memantine.

Investigation of clinical data in Czechia could help to address these three concerns. First, usual treatment strategies shall be identified. Second, heterogeneity in the treatment initiation among patients would help to determine treatment effect dependency on the duration of untreated AD. Third, methods such as growth curve modelling (Stern et al., 1996) allow for non-linearity and its application to Czech clinical data would lead to more accurate context-specific decline scheme.

Hospitalization risk. Hospitalization risk (*hr*) and length are derived from the epidemiological data published by the Czech Institute of Health Information and Statistics as well as from the primary data coming from the National Register of Hospitalizations operated by this institute. The annual hospitalization rate reaches six percent of the estimated size of population suffering from dementia in Czechia (IHIS, 2013; Mátl et al., 2016). This figure is relatively difficult to use in a decision analytic model as it refers to the whole heterogeneous population rather than to the hospitalization risk faced by an individual. Another available piece of information are the shares of cognitive impairment severity among patients admitted for hospitalization. According to Luzny et al. (2014) 3.8% of patients admitted for hospitalization suffer from mild, 39.6% from moderate and 56.6% from severe cognitive impairment.

To convert these two known parameters into (rough) individual and group-specific estimates, three assumptions are required. The first two assumptions are strong: the disease needs to onset at the same age for all patients, and all the birth cohorts need to have the same size. The third assumption is non-controversial as it requires the same probability of hospitalization for women and men. Under these three assumptions, the cross-sectional snapshot of a population looks comparable in terms of number of people living with mild, moderate and severe cognitive impairment to the cumulative number of people-years lived by one cohort from the disease onset to death of the last patient; i.e. the population consists of cohorts of people aged 70 entering at time t_0, aged $71_{t(-1)}$, $72_{t(-2)}$. A cohort enters aged 70 at time t_0 and lives aged 71_{t0}, 72_{t0} etc. When the size of all cohorts of patients entering a population is identical, number of patients-years annually lived by a population is equal to sum of years that all patients from one cohort lived within each of the three health states.

We simulate the disease progression for a cohort of homogeneous patients and summarize their years-lived according to the disease severity (*ly(ci)*) and total years-lived (*tly*). Equation 1 show that individual risk of hospitalization for the given disease severity (*hr(ci)*) is equal to admission share for that severity (*as(ci)*) divided by the share of years-lived with that severity and multiplied by an annual hospitalization rate (*hr*)

$$hr(ci) = \frac{as(ci)}{ly(ci)/tly} \cdot hr \ . \qquad (1)$$

Although this approach gives a basic idea as to the number of hospitalizations and their costliness, it is apparently cumbersome. More valid estimates of hospitalization risk dependent on

age and/or disease severity could be derived from clinical data complemented by the newly established National Register of Paid Health Care Services (Národní registr placených zdravotnických služeb, NRHZS), which contains individual data about all health services provided to a patient including both ambulatory and inpatient care.

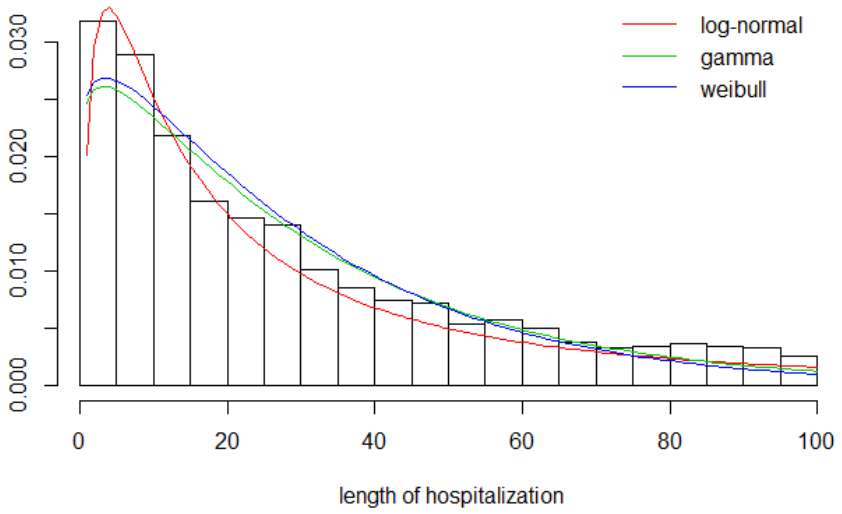
Probability distribution used to model hospitalization length is derived from the National Register of Hospitalizations that contains an individual record of each hospitalization including basic information about patient (AD diagnosis, hospitalization length, age of patient etc.). The dataset contains records about 13,194 patients relevant for estimation. Average hospitalization length for patients is 93.7 days and median is 29 days. Based on numerical and graphical analysis we assume that hospitalization length is a positively skewed continuous random variable with a long-tail distribution. Three possible types of distributions were considered: lognormal, Gamma and Weibull distribution and robust method of estimation parameters should be used. We estimated its parameters with robust quantile matching estimator to account for the presence of extreme values. The results are shown in Table 2 and Figure 2. Real number of hospitalization with specific length and its estimation are shown in Table 2. Lognormal distribution, with the mean value 21.9 and standard deviation 3.74 days, describes the hospitalization lengths best even for values in the right tail. We have found no effect of demographic characteristics on the hospitalization length.

Tab. 2: Comparison on considered distributions

Hospitalization length	<=10 days	<=20 days	<=50 days	<=70 days	<=100 days	<=150 days	<=200 days	<=300 days	<=365 days
reality	3,271	5,308	8,636	9,707	10,754	11,568	11,950	12,384	12,558
lognormal	3,658	6,236	9,671	10,678	11,528	12,223	12,563	12,873	12,969
gamma	3,297	6,017	10,575	11,876	12,728	13,113	13,180	13,193	13,194
weibull	3,403	6,237	10,913	12,155	12,888	13,157	13,190	13,194	13,194

Source: own illustration

Fig. 2: Histogram of hospitalization length and theoretical densities for chosen distributions



Source: own illustration

Mortality risk. Mortality risk is derived from Czech lifetables and adjusted for the higher risk faced by AD patients compared to the general population. Fitzpatrick et al. (2005) used the sample of 3602 participants of the Cardiovascular Health (CHS) Cognition Study to estimate the risk to be 2.1 times higher. Similarly, to the disease progression pace, a constantly higher mortality risk of AD patients seems as an oversimplification. There is an available data source on the mortality of AD patients in Czechia: lifetables of patients who died from AD (IHIS, 2016). These figures are derived from the National Register of Death Causes. However, it includes only a very limited number of patients as AD is only rarely recorded as the primary cause of death. Consequently, the results are likely suffering from a survival bias and only the most severe AD cases are included in these statistics. The ideal approach to address the issue of mortality risk is to construct lifetables from the combination of clinical and NHRZS data.

Costs. There are two main categories of costs considered by this model: health care and informal care costs. Health care costs are further divided into costs of medication, outpatient care and hospitalization. The treatment strategy modelled by the decline scheme involves the use of cholinesterase inhibitors. Specifically, we model indication of donepezil for patients suffering from mild and moderate dementia and memantine for severely impaired patients. Costs of donepezil (memantine) are reported by the by the Medicinal Product Database of the State Institute for Drug Control and annually amount to €187 (€579.4) per patient (SUKL, 2015). The outpatient

care usually provided to treated patients has been specified by the published research as two visits of neurologist, twice blood sampling and once sampling of the cerebrospinal fluid per year (Mohelska et al., 2015). The associated costs amounted to €94 in the year 2014. The costs of these procedures are based on reimbursement to their providers regulated by the Ministry of Health of Czechia. A survey of psychiatric hospitals determined costs of inpatient day to be €63 (National Institute of Mental Health, unpublished).

Costs of informal care are defined as replacement and opportunity costs of the main caregiver providing home care to the patient. Based on the sample of 119 patient-caregiver dyads, Holmerová et al. (2017) calculated the annual costs of care amount to €11,412/22,470/25,867 for patients with mild/moderate/severe dementia. These costs are usually incurred by the family of the patient and might be partially covered by social transfers provided by the Ministry of Labor and Social Affairs. Although the presented cost data comes from reliable sources, it considers homogeneous (median) value for patients suffering from a given disease severity. NRHZS contains both service and cost-related information and shall be exploited in order to incorporate heterogeneity in the model and to make costs conditional on the wider range of patient's characteristics.

2 Results

We estimate the average lifetime costs for a woman with the disease onset at age of 70 to reach €223 thousand (no discounting or cost increase considered). For a man, the lifetime costs amount €156 thousand as a result of his shorter life span. According to AD-adjusted life tables, the woman lives another 10.5 years after the disease onset while the man survives only 7.5 years. The time they spent living with mild and moderate dementia is comparable (2.5 vs. 2.4, and 2.9 vs. 2.3 years respectively). But because the men die earlier, they spend a shorter (4.9 vs. 2.9 years) time living with the severe, and most expensive, disease stage. In addition, 45% of women and one third of men experience (in most cases one) hospitalization lasting about 45 days as a direct consequence of AD.

Although a part of informal costs can by covered by a social transfer from public budgets, the heaviest economic burden is likely born by patients and their caregivers. Costs of informal care provided to patients reach almost 99% of all lifetime expenses. The rest is allocated to hospitalizations (0.8%), outpatient care and medication.

Comparing treated and untreated patients, lifetime costs for treated woman (man) is lower by 5 (11)%. A treated woman (man) spends 2.8 (2.6)/ 4.5 (3.2)/ 3.0 (1.4) years living with mild/ moderate/ severe dementia in comparison to 2.4 (2.3)/ 2.4 (2)/ 5.5 (3.4) years for an untreated woman (man). The relative shift of time towards the less severe dementia means a shorter time requiring more intensive informal care. Thus, lower costs emerge as a direct economic consequence of a slower cognitive decline. Nevertheless, informal care remains the highest cost entry even for treated patients. Health care costs amount to slightly less than 3% (outpatient care, medication, hospitalization) of total lifetime costs for treated and to 0.8% (hospitalization) for untreated patients.

Conclusion

This study estimated the lifetime economic burden per patient suffering from AD. According to our analysis, most of the burden is carried by the patient and his/her family caregivers in the form informal care costs. We discussed the validity of the parameters the entering decision analytic model and identified better data sources where appropriate. Future research shall involve analysis based on Czech clinical data as well as the data from the newly established National Register of Paid Health Care Services.

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