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Fiscal consequences of Alzheimer's disease and informal care provision in the UK: A "government perspective" microsimulation

Ana T. Paquete [a], Rui Martins [a,b], Nikolaos Kotsopoulos [a,c], Michael Urbich [d], Colin Green [e], Mark P. Connolly [a,b,*]

[a] *Global Market Access Solutions, Health Economics Unit, St-Prex, Switzerland*
[b] *Unit of PharmacoEpidemiology & PharmacoEconomics, Department of Pharmacy, University of Groningen, Groningen, The Netherlands*
[c] *Department of Economics, University of Athens, Athens, Greece*
[d] *Biogen International GmbH, Baar, Switzerland*
[e] *Biogen UK & Ireland, Berkshire, United Kingdom*

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ABSTRACT

Objectives: Estimating the fiscal consequences of Alzheimer's disease (AD) on patients and informal carers using a UK public economic perspective.
Methods: A simulated cohort of 1,000 pairs of people with AD and informal carers was compared with 1,000 demographically identical pairs in the general population. Both cohorts enter the model at the mean age of mild cognitive impairment onset. Time to AD onset was based on the literature and AD progression was modelled using published equations and a state-transition microsimulation. Labour participation, financial support, and paid taxes were linked to cognitive decline and caregiving needs using UK labour statistics and tax rates. Healthcare costs were based on published literature. Future costs and life-years were discounted at 3.5%. Results were reported as incremental differences in total tax revenue, financial support, and healthcare costs, over the AD continuum, between cohorts affected and unaffected by AD.
Results: Each AD-affected pair was associated with estimated incremental fiscal losses of £73,749 to the UK government. Financial support and healthcare costs were responsible for 59.3% and 22.2% of AD's fiscal burden, respectively. Total lost tax revenue due to PwAD and carers' reduced earnings represented 18.5% of total government losses. Sensitivity analyses confirmed the robustness of the results. Assuming mild cognitive impairment onset at age 60 let to incremental fiscal losses of £141,323 per AD-affected pair. Fiscal costs for entire UK population with AD were predicted to be £16 billion annually.
Conclusions: Alzheimer's disease strongly impacts UK's public economy and should be considered to inform healthcare policymaking.

Introduction

The prevalence of dementia worldwide has more than doubled in the last 30 years and the trend is expected to continue (Nichols et al., 2019, Cao et al., 2020). In the UK, about 850 thousand cases of dementia were estimated in 2015 (NHS England, 2021). Published projections predict prevalence to increase 80.1 % by 2040, with severe dementia accounting for more than 67.0 % of cases (Wittenberg et al., 2019a). Alzheimer's disease (AD) is the most common cause of dementia (Prince, 2014, Cao et al., 2020). The prevalence of AD has been historically higher among women and in developed countries (Nichols et al., 2019, Cao et al., 2020, Niu et al., 2017). In the UK, 62.0 % of dementia cases are estimated to be related to AD (Prince, 2014).

Dementia progressively decreases cognitive function and autonomy in daily life activities, mostly affecting elderly adults (Alzheimer's Association, 2020). People with dementia become highly dependent on

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Abbreviations: AA, Attendance Allowance; AD, Alzheimer's disease; ADL, Activities of Daily Living; CA, Carer's Allowance; ESA, Employment and Support Allowance; HR, hazard ratio; INC, Incremental Net Consequence; MCI, mild cognitive impairment; MCI-AD, mild cognitive impairment due to Alzheimer's disease; MMSE, Mini-Mental State Examination; NHS, National Health Service; NPV, Net Present Value; OWSA, one-way sensitivity analysis; PIP, Personal Independence Payment; PwAD, people/person with Alzheimer's disease; SD, standard deviation; SPA, state pension age; UK, United Kingdom.

* Corresponding author at: Global Market Access Solutions, St-Prex 1162, Switzerland.
E-mail address: mark@gmasoln.com (M.P. Connolly).

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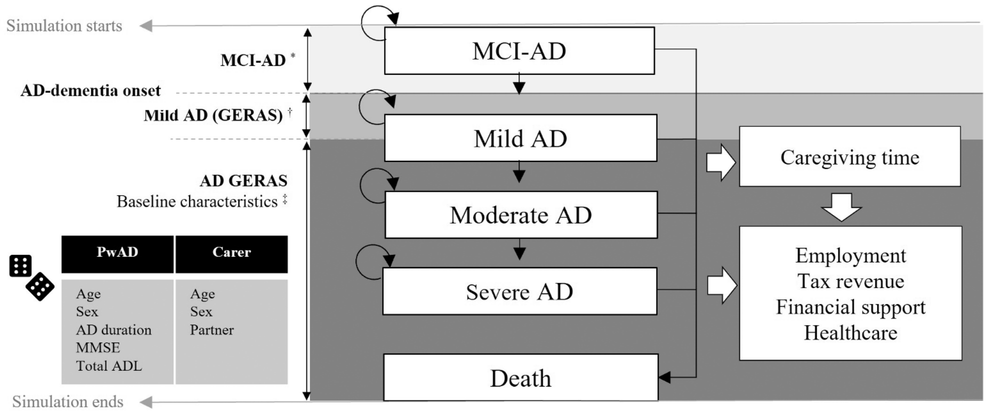

Fig. 1. Model structure. AD, Alzheimer's disease; ADL, Activities of Daily Living; MCI-AD, mild cognitive impairment due to Alzheimer's disease; MMSE, Mini-Mental-State-Examination. * Assumed to last 3.4 years (Vermunt et al., 2019). † The minimum duration of mild AD was assumed to be 1.8 years based on GERAS UK data (Lenox-Smith et al., 2016, Wimo et al., 2013). ‡ The progression in AD-severity was predicted using baseline characteristics from the GERAS UK study (Lenox-Smith et al., 2016, Wimo et al., 2013).

carers as the disease progresses (Alzheimer's Association, 2020, Alzheimer Europe, 2019, Prince, 2014). In 2015, 540,000 people were deemed to provide dementia-related informal care in the UK (NHS England, 2021). Informal care, mostly provided by family members, has a major importance as most people with dementia live in the community (El-Hayek et al., 2019, Lenox-Smith et al., 2016, Wimo et al., 2013, Reed et al., 2017).

In high income countries, 37.9 % of dementia costs were related to informal care costs with direct social and health care costs accounting for 43.1 % and 19.0 % of overall costs, respectively (Prince, 2015). In England, total annual costs of dementia were estimated at £24.2 billion in 2015, of which unpaid care represented £10.1 billion and £3.8 billion that were related to healthcare costs (Wittenberg et al., 2019b). It is estimated that 39.4 % of overall social care costs are funded by the government (Wittenberg et al., 2019b). The findings from this study illustrate the importance of the government perspective applied to AD. In this regard, reduced work activity translates to lower tax revenue for government, and increased dependency on tax-financed public support programmes.

To the best of our knowledge, there is no publication estimating the fiscal burden of AD in the UK. Commonly, burden of disease studies take a societal perspective, focusing on direct medical and non-medical care costs, such as social care costs and unpaid care costs. Financial support as state benefits or transfers provided by the government and foregone tax contributions due to lower labour participation are rarely considered in evaluations of health programmes (Kotsopoulos and Connolly, 2014).

The current study uses a public economic perspective (Connolly et al., 2017) to estimate the impact of AD on public finances by simulating the fiscal life of people with AD (PwAD) and their informal caregivers since the diagnosis of mild cognitive impairment due to AD (MCI-AD) to death. This cohort was compared to pairs with identical demographic characteristics unaffected by AD in UK's general population.

Materials and methods

Health and labour market outcomes

Model overview

The goal of the analysis is to estimate the fiscal burden of AD to the UK government. This is achieved by modelling the AD-related decrease in cognitive function, associated informal care requirements, and link these to labour force participation, earnings, tax contributions, healthcare costs, and financial support from disability benefits in PwAD and their main informal carer. Because of the demographic variability in both patients and carers, the analysis uses distributions of published PwAD/carer characteristics to simulate their unique fiscal pathways from the diagnosis of MCI-AD to death. We report the average costs of 1,000 unique pathways in a cohort affected by AD. This cohort was compared to 1,000 pairs with identical demographic characteristics unaffected by AD in UK's general population. For clarity, the equivalent of an informal caregiver in the general population (cohort unaffected by AD), is a person demographically identical to those providing care in the AD cohort, but it does not necessarily imply they are providing care. In the cohort unaffected by AD, the rate of fiscal outcomes was informed by the UK national average.

We have developed a Microsoft Excel microsimulation to model AD progression and AD-related events in PwAD and their carers. A microsimulation structure was preferred, allowing for care requirements and costs to be modelled continuously, considering multiple combination of PwAD/carer's sex and age whilst avoiding memoryless Markovian states (Drummond et al., 2015, DSU, 2014, Siebert et al., 2012).

We have not identified a UK publication reporting MMSE and activities of daily living (ADL) scores for people across the full AD spectrum, required to estimate independence and informal care requirements. Data were particularly scarce at the MCI-AD stage. Alternatively, we have modelled MMSE and ADL scores over time, to determine disease severity and individual care requirements, using predictive equations at the AD-dementia stage and applied average AD metrics at the MCI-AD and part of the mild AD (AD onset) stages.

Health states were categorized using Mini-Mental State Examination (MMSE) scores (Green and Zhang, 2016, Folstein et al., 1975, Eftychios et al., 2021). Scores of 27 to 29 corresponded to MCI-AD, 21 to 26 to mild AD, 10 to 20 to moderate AD, and scores below 10 were linked to the severe AD state. Cognitively normal individuals were assumed to have the maximum MMSE score of 30. The description of day-to-day functioning per MMSE categories is presented in Table A1. The model structure is shown in Fig. 1.

Simulation events were deemed to occur if its likelihood (e.g., probability of death, institutionalization) at each cycle was greater than an evenly distributed random probability of the event. We have followed the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) recommendations for state transition modelling (Siebert et al., 2012). The model used 6-monthly cycles, granular enough to capture expected changes in disease progression, and the costs and consequences of AD. Future costs and life-years (LY) were discounted at 3.5 % annually (NICE, 2022).

Baseline characteristics and disease progression

The model started when PwAD and their comparators were 70 years (Winblad et al., 2008, van Maurik et al., 2021, Moodley et al., 2015). The carer cohorts entered the model with a mean age of 60.5 years, considering mean age differences between people with mild AD and their carers reported by the UK GERAS I study (Wimo et al., 2013, Lenox-Smith et al., 2016). The GERAS I observational cohort followed people with AD-dementia (people with MCI-AD were not recruited) and their

Table 1
Demographic characteristics used to generate the simulated cohorts.

Attributes	PwAD		Informal carers		Sampling distribution
	Mean	SD	Mean	SD	
Age (years)	75.2[*]	7.5[†]	65.7	6.6[†]	Lognormal[‡]
Spouse (%)	–	–	72.0 %	–	Beta
Females (%)	50.0 %	–	64.5 %	–	Beta
Disease Duration (years)	1.8	2.1	–	–	Gamma
MMSE score	23.1	1.6	–	–	Normal
Total ADL	58.5	0.6	–	–	Normal

AD, Alzheimer's disease; ADL, activities of daily living; MMSE, Mini-Mental State Examination; PwAD, people with Alzheimer's disease; SD, standard deviation.
Baseline characteristics of the GERAS cohort with mild AD-dementia sourced from the publications by Lenox-Smith et al. and Wimo et al. (Lenox-Smith et al., 2016, Wimo et al., 2013), (n = 200).

[*] Estimated as the sum of the mean age at model entry for MCI-AD of 70 years old (Winblad et al., 2008, van Maurik et al., 2021, Moodley et al., 2015), mean duration of MCI-AD of 3.4 years (Vermunt et al., 2019) and the mean disease duration in people with mild AD in the UK GERAS I study of 1.8 years (Wimo et al., 2013, Lenox-Smith et al., 2016).

[†] Assumed a standard deviation of 10%.

[‡] The age distribution for both PwAD and informal carers is shown in Appendix (Fig. A1).

primary carers in France, Germany, and the UK over an 18-month period. We have sampled carer's age using mean and standard deviation inputs from Table 1. The spouse/partner or adult child status was inferred based on age difference to PwAD to achieve 72 % of carers who are spouses/partners. The proportion of carers who are a spouse/partner will impact the estimated total hours of informal care. The remaining consequences were based on carer's age. The average length of MCI-AD duration (3.4 years) was based on Vermunt et al. (Vermunt et al., 2019), after which all PwAD were assumed to progress to mild AD.

With exception of age at MCI-AD onset, most individual characteristics were randomly sampled from common probability distributions, parameterized using baseline mean and standard deviation inputs from the mild AD cohort recruited as part of the UK GERAS I study (Wimo et al., 2013, Lenox-Smith et al., 2016). These inputs are reported in Table 1.

The minimum duration of mild AD was informed by the disease duration value sampled using data from the UK GERAS I study (Table 1). From this point, disease progression to moderate and severe AD, was informed by equations published by Getsios et al (2010). The published equations are/were derived from data taken from the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) and control arms of seven clinical trials (Getsios et al., 2010). The equations allowed MMSE and total ADL scores to be updated every cycle, which influenced disease severity and individual care requirements (total hours of informal care), respectively. Changes in MMSE scores were predicted by age and previous changes in MMSE scores (Equation A.1 to Equation A.4 in Appendix). Changes in total ADL scores were predicted by MMSE and ADL scores at baseline and on the previous cycle, age, and time (Equation A.5 and Equation A.6 in Appendix). The model does not allow returning to a state of lower AD severity.

As data for MMSE and ADL scores were not available from the onset of mild AD to enrolment in the GERAS I study, we have assumed that during this period, MMSE and ADL scores were identical to those reported at GERAS I baseline (Table 1). Functional ability was assessed using the Alzheimer's Disease Co-operative Study Activities of Daily Living Inventory (ADCS-ADL), with higher scores indicating lower functional impairment (Wimo et al., 2013, Lenox-Smith et al., 2016).

Mortality

Baseline mortality data for both cohorts was based on published UK lifetables for 2018–2020 (ONS, 2021e). Excess mortality due to MCI-AD was applied to the baseline sex and age-specific mortality rates of PwAD, based on a Spanish longitudinal study with an 11.2 years follow-up (hazard ratio [HR] of 1.2, adjusted for age, sex and educational level, with MCI-AD defined by the Petersen criteria (Santabarbara et al., 2016, Petersen et al., 1999). After AD onset, excess AD-mortality HRs were applied to the sex and age-specific mortality rates, sourced from a commonly utilized study (Lin et al., 2021, Green et al., 2019) using a Danish population-based cohort (Andersen et al., 2010). Parameters informing excess AD mortality are presented in Table 2.

Death was possible at any time in the model. The death of a PwAD released the carers from caring responsibilities, allowing them to return

Table 2
Modelled inputs for disease progression and demographical characteristics, by cohort affected or unaffected by AD.

Input	Cohort affected by AD	Cohort unaffected by AD
Start age for MCI-AD	**PwAD**: 70 years old (Winblad et al., 2008, van Maurik et al., 2021, Moodley et al., 2015) **Carers**: 9.5 years younger than the PwAD (60.5 years old) (Wimo et al., 2013, Lenox-Smith et al., 2016)	**Equivalent to PwAD:** assumed to be demographically identical to the cohort affected by AD (same age and sex); **Equivalent to carers**: assumed to be demographically identical to the cohort affected by AD (same age and sex).
Other baseline characteristics	**PwAD**: % females; disease duration; MMSE scores; total ADL. (Lenox-Smith et al., 2016) **Carers**: % females (Wimo et al., 2013, Lenox-Smith et al., 2016)	
Time in MCI-AD	3.4 years (Vermunt 2019)	N/A
Progression of AD-dementia	Minimum time on mild AD: 1.8 years (Wimo et al., 2013, Lenox-Smith et al., 2016). AD-dementia severity progression: predicted by equations using MMSE and total ADL scores, time, and sex data (Getsios et al., 2010).	N/A
Mortality	Sex and age-specific survival data based on life tables from UK's general population (ONS, 2021e). Excess mortality due to MCI-AD excess mortality: HR 1.20 (Santabarbara et al., 2016). AD-dementia excess mortality: HR 2.92 mild AD; HR 3.85 moderate AD; HR 9.52 severe AD (Andersen et al., 2010).	Sex and age-specific survival data based on life tables from UK's general population (ONS, 2021e).
Institutionalization	People with MCI-AD were assumed not to require institutionalization. **PwAD-dementia:** Absolute probabilities of institutionalization (6 months): 3.0 % in mild AD; 8.0 % in moderate AD; 10.0 % in severe AD (Knapp et al., 2016).	**Equivalent to PwAD at MCI-AD:** assumed not to require institutionalization. **Equivalent to PwAD at AD-dementia:** The age-specific prevalence of institutionalization values for England and Wales was applied (0.0 % if < 65 years old; 0.4 % if 65 to 74 years old; 2.8 % if 75 to 84 years old; 13.6 % if ≥ 85 years old) (ONS, 2014).

AA, Attendance Allowance; AD, Alzheimer's disease; ADL, Activities of Daily Living; CA, Carer's Allowance; ESA, Employment and Support Allowance; HR, hazard ratio; MCI-AD, mild cognitive impairment due to Alzheimer's disease; MMSE, Mini-Mental State Examination; N/A, not applicable, PIP, Personal Independence Payment; PwAD, people with Alzheimer's Disease; UK, United Kingdom.

Table 3
Modelled earnings from employment, by cohort affected or unaffected by AD.

Input	Cohort affected by AD	Cohort unaffected by AD
Baseline rates of employment	Age-specific employment rates based in the UK's general population (ONS, 2021b).	
Employment discontinuation due to disability or informal caregiving	**PwAD at the MCI-AD stage**: risk ratio 2.0 higher disability compared to general population (Artero et al., 2001). **Carers of PwAD at MCI-AD stage**: assumed not to have higher employment discontinuation rates. **PwAD-dementia**: higher risk of not being employed, HR 2.26 (Sakata and Okumura, 2017). **Carers of PwAD-dementia:** higher risk of not being employed, HR 1.19 (Sakata and Okumura, 2017). **Full-time work reduction by employed carers**: estimated using equations based on time spent caring for PwAD, carer's age, and family relationship to the PwAD (Lilly et al., 2010). Informal care requirements (hours) in community-based PwAD were predicted by equations using individual MMSE and total ADL scores (Reed et al., 2016). If a PwAD becomes institutionalized or dies, carers aged under 75 years can return to work, subject to employment rates in the general UK population (assumption).	N/A[*]
Earnings from employment	Baseline sex and age-specific gross earnings from employees in the UK's general population (ONS, 2021d). Carers returning to the labour force after ≥ 2 years will have reduced earnings from employment (Speiser, 2021).	Sex and age-specific gross earnings from employees in the UK's general population (ONS, 2021d).

AD, Alzheimer's disease; HR, hazard ratio; MCI, mild cognitive impairment; N/A, not applicable, PwAD, people with Alzheimer's disease; UK, United Kingdom.

[*] Because people with mild cognitive impairment were twice as likely not to be employed than the general population, we have applied the AD-related excess likelihood of employment discontinuation to the cohort with AD alone.

to employment. Any form of AD-related financial support was also discontinued. Carer's death was assumed not to affect the probability of employment of the PwAD or the amount of financial support they would be receiving. After carer's death, PwAD having an MMSE score below 20 were assumed to require institutionalization as 24-hour supervision is often required at this AD severity (Table A1).

Institutionalization and informal care

The likelihood of PwAD being institutionalized was sourced from a large London case register, specific to AD severity (Knapp et al., 2016). In the cohort without AD, institutionalization was based on age-specific prevalence values for England and Wales (ONS, 2014). We have assumed that cognitive deficits associated with MCI-AD alone would not justify institutionalization (Green et al., 2019). Data informing the likelihood of institutionalization are presented in Table 2. In the event of institutionalization, carers were assumed to be able to return to work and would stop receiving financial support.

Informal care needs of community based PwAD were estimated using an equation sourced from the GERAS I study. The equation predicts total hours of informal care based on age, individual MMSE and ADL scores, if the carer is the spouse, and on the country-origin of the PwAD (Reed et al., 2016) Equation A.7 in the Appendix.

Labour market participation

Sex and age-specific probabilities of employment and annual earnings from employment in the general population were sourced from UK national statistics (ONS, 2021b, ONS, 2021d). We assumed that PwAD having an MMSE score below 25, living in an institutional setting or above the age of 75 (the maximum age of employment) would not be in employment.

We were not able to identify a publication linking MCI-AD to the likelihood of maintaining a job, which is supported by the systematic review by Silvaggi and colleagues (Silvaggi et al., 2020). For this reason, the prevalence of disability was considered a proxy for work discontinuation in those with MCI-AD. Disability in the UK population was based on nationally available data (ONS, 2021c). The risk of disability in people with MCI-AD was sourced from a French longitudinal study, reporting it to be twice as high as in the general population (Artero et al., 2001). The risk ratio of 2.0 was applied to the sex and age-specific disability rates from the UK's general population to estimate work discontinuation of people with MCI-AD.

The effect of AD-dementia on employment discontinuation was informed by a Japanese cohort study of employees with a diagnosis of dementia under the age of 65. Participants were each matched to 5 controls without dementia. People in the cohort with dementia were more likely to be out of employment, and so were their primary carers (Sakata and Okumura, 2017). Sex and age-specific employment rates applied on the model are presented in the Appendix (Table A1).

Some employed carers were estimated to have a reduction on full-time working hours as consequence of the time spent caring for PwAD (Lilly et al., 2010). This was implemented using a published sex-specific equation that estimated labour participation based on survey data by Statistics Canada, according to carer's age and family relationship to the PwAD (Equation A.8 to Equation A.11 in the Appendix) (Lilly et al., 2010, Martins et al., 2022). Sustained periods of absence from the labour market are likely to influence future earnings from employment. Consequently, we reduced gross earnings in carers returning to work after 2 or more years of informal care provision using a 7.2 % rate

Table 4
Annual healthcare and formal social care costs.

	Cohort with AD		Cohort without AD	
	Healthcare	**Social care**	**Healthcare**	**Social care**
People living in the community				
MCI-AD	£2,560 [*]	£1,105 [*]	£2,003 [*]	£228 [*]
Mild AD	£3,003 [†]	£2,044 [‡]	£2,350 [§]	£422 [§]
Moderate AD	£2,942 [†]	£5,091 [‡]	£1,874 [§]	£922 [§]
Severe AD	£12,290 [†]	£6,760 [‡]	£5,719 [§]	£1,461 [§]
People living in residential care				
MCI-AD	–	–	–	–
Mild AD	£4,917 [†]	£9,452 [‡]	£3,847 [§]	£1,731 [§]
Moderate AD	£10,304 [†]	£9,826 [‡]	£6,562 [§]	£737 [§]
Severe AD	£9,486 [†]	£9,886 [‡]	£4,414 [§]	£477 [§]

AD, Alzheimer's disease; MCI-AD, mild cognitive impairment due to Alzheimer's disease.

[*] Costs based on the ratio of care costs of MCI and mild AD patients (Robinson et al., 2020).

[†] Sourced from Dementia UK update (Prince, 2014, Curtis, 2017, Curtis, 2020).

[‡] Sourced from Dementia UK update, including the 60.0% of costs of people living in the community and the 35.0% of costs of people living in the residential care that are paid by the government (Prince, 2014, Curtis, 2017, Curtis, 2020).

[§] Costs based on the ratio of care costs of patients with and without dementia, by severity (Leicht et al., 2011).

Table 5
Modelled fiscal consequences, by cohort affected or unaffected by AD.

	Cohort affected by AD	Cohort unaffected by AD
Taxes		
Direct taxes	UK's tax wedge (OECD, 2021) applied to the earnings from employment: 30.8 %	
Indirect taxes	UK's indirect tax rates as a percentage of gross income (ONS, 2021f): 12.4 %	
Financial support and healthcare costs		
Transfers to PwAD and carers (proportion receiving transfers)	**PwAD and carers at the MCI-AD stage**: Sex and age-specific prevalence of people receiving ESA, PIP or AA in the UK's general population (DWP, 2021c, DWP, 2021d, DWP, 2021e, DWP, 2021a) **PwAD-dementia:** proportion receiving ESA or PIP based on the German GERAS I study (Boess et al., 2016), adjusted for the UK (HR 0.35) (Reed et al., 2017): 28.6 % mild AD, 56.7 % moderate AD, 73.2 % severe AD. **PwAD-dementia with carers:** proportion of unpaid care needs by AD severity (29.8 % mild AD, 47.6 % moderate AD, 20.0 % severe AD) (Wittenberg et al., 2019b) used to estimate the proportion of PwAD receiving AA and of carers receiving CA. [*]	**Equivalent to PwAD:** Sex and age-specific prevalence of people receiving ESA, PIP or AA in the UK's general population (DWP, 2021c, DWP, 2021d, DWP, 2021e, DWP, 2021a) **Equivalent to carers:** Age-specific prevalence of people receiving CA in the UK's general population (DWP, 2021b).
Transfers to PwAD, carers, and cohort unaffected by AD (amount)	Sex and age-specific mean amount provided to entitled individuals in the UK for: **PwAD and Equivalent**: ESA due to diseases of the nervous system (DWP, 2021c, DWP, 2021a); PIP due to dementia (DWP, 2021d, DWP, 2021e); AA due to dementia (DWP, 2021a). [†] **Carers and Equivalent**: CA (not disease/condition-specific) (DWP, 2021b).	
Health and social care provided by the government	**PwAD at MCI-AD stage**: based on the ratio of care costs of MCI and mild AD patients from the US GERAS II study: 85.2 % for direct medical costs and 54.0 % for direct non-medical costs (Robinson et al., 2020). **PwAD-dementia:** Mean annual costs per patient for health and social care, in the societal perspective, by AD-severity (Prince, 2014) inflated to £2019/2020 prices (Curtis, 2017, Curtis, 2020). Healthcare costs are totally paid by the government (assumption). The proportion of social care costs paid by the government was considered according to patients living in residential care or in the community (35.0 % and 60.0 %, respectively) (Prince, 2014). No costs were applied to carers.	**Equivalent to PwAD at MCI-AD stage**: Assumed the same ratio of care costs applied to the cohort affected by AD (Robinson et al., 2020) (assumption). **Equivalent to PwAD-dementia:** based on the ratio of care costs compared to those affected by dementia. [‡] Medical care costs: 78.2 %, 63.7 %, and 46.5 % Institutionalized: 18.3 %, 7.5 %, and 4.8 % [§] Community-based: 20.6 %, 18.1 %, and 21.6 % [₸] compared to mild, moderate, and severe dementia, respectively (Leicht et al., 2011). **Equivalent to carers:** No costs were applied.

AA, Attendance Allowance; AD, Alzheimer's disease; CA, Carer's Allowance; ESA, Employment and Support Allowance; MCI, mild cognitive impairment; PIP, Personal Independence Payment; PwAD, people with Alzheimer's disease UK, United Kingdom.

[*] Carers are entitled to Carer's Allowance (CA) if PwAD receive AA, if the carer provides care for at least 35 h per week and if the carer's disposable income is less than £129 per week.

[†] Data was unavailable for AD so we have used values reported for the closest diagnosis available (ESA due to diseases of the nervous system, PIP due to dementia, AA due to dementia).

[‡] These ratios were applied to healthcare costs and formal social care costs of PwAD to estimate the costs of people unaffected by AD.

[§] Nursing home care.

[₸] Professional home care.

(Speiser, 2021). Conservatively, we have assumed that MCI-AD had no effect on the carer's employment status, but carers could in fact decide to retire earlier or may find it difficult to return to employment. Baseline sex and age-specific annual gross earnings based on the UK's official data are presented in the Appendix (Table A2) (ONS, 2021d).

The modelled inputs on labour market participation and earnings from employment, for both cohorts compared, are summarised in Table 3.

Fiscal consequences

Fiscal consequences consist of tax revenue, transfer payments to individuals and government expenditure on social and healthcare provision that affect government finances. AD-dementia severity and care requirements is linked to the likelihood of receiving transfers from the government. Direct taxes paid on earnings and indirect consumption taxes weigh positively on government budgets. Transfers used to support disabled individuals and formal social and medical healthcare provision costs were considered public expenses.

Direct and indirect taxes

Employment related taxes consisted of direct tax on earnings falling on employees and social security contributions incurred by employees and employers, often referred to as the tax wedge. Total direct tax on employment was calculated by multiplying the UK tax wedge (OECD, 2021) by the gross earnings stratified by age (ONS, 2021d) (Table A2). Indirect taxes were calculated using consumption tax rates reported as a percentage of gross income from employment or any other sources such as transfers (ONS, 2021f).

Financial support: transfers to PwAD and carers

Several forms of financial support provided by the UK government are available to PwAD and carers according to individual needs and age. These were implemented in the model following national rules outlined below. Working age individuals whose condition affects how much they can work are entitled to an Employment and Support Allowance (ESA). The amount received depends on individual's ability to return to work (work-related activity group) or permanent inability to work (support group). People under state pension age (SPA) maintaining a long-term illness status are entitled to Personal Independence Payment (PIP) if they have limited ability to complete daily living tasks (daily living part) and/or on getting around (mobility part). People above SPA who are not autonomous, and therefore rely on carers, are eligible to receive an Attendance Allowance (AA). The amount received depends on supervision being needed only during the day/night or both (UK Government, 2021b). Carers might be eligible to Carer's Allowance (CA) (UK Government, 2021a).

The proportions of PwAD receiving financial support were based on severity specific values reported for the GERAS I German cohort (Boess et al., 2016), which were adjusted to the UK using a published HR of the difference of people affected by AD receiving financial support in Germany vs the UK (Reed et al., 2017). People with AD entitled to government financial support were assumed to receive the average amount provided to sex and age-specific individuals in the UK (Table A3 and Table A4) (DWP, 2021c, DWP, 2021d, DWP, 2021e, DWP, 2021a).

The proportion of PwAD receiving AA and carers receiving CA was based on the proportion of adults with dementia having unpaid care needs (Wittenberg et al., 2019b). The CA amount provided per carer was based on the average amount of CA provided to age-specific entitled individuals in the UK (DWP, 2021b).

We have calculated the amount of financial support received by the general population as the average monetary values of ESA, PIP, AA, and CA. The average monetary values were weighted using the national entitlement frequencies by age and sex (DWP, 2021c, DWP, 2021d, DWP, 2021e, DWP, 2021a, DWP, 2021b). Data on proportion of people receiving each transfer and the average biannual amount received is reported in the Appendix (Table A5-A12).

Because we found no information on the prevalence of financial support in people with MCI-AD, the support received by the same age-group in the general population was applied.

There is limited evidence about the impact of AD on state pensions. Also, AD-excess mortality may lead to perverse incentives from a government fiscal perspective as longevity will lead to a greater use of government resources in the form of state benefits, which is not offset unless LY gained are monetized. For simplicity we have excluded state pensions from the model base case under the assumption these would not be differential between cohorts. We challenge this assumption in scenario analysis.

Financial support on social care provision and expenditure on health care provision

Our analysis considers the costs of social and health care required by PwAD to be part of the fiscal burden if these were incurred by the government. We have sourced the severity-specific costs of health and social care for community-based and institutionalized PwAD from the Alzheimer's Society UK study, which collected costs on total care and support used, but did not disaggregate comorbidity-related costs (Prince, 2014). Because the standard of care for AD-dementia has not substantially changed since, these costs were considered representative of current UK clinical practice. The proportion of residential social care costs and of community-based social care costs paid by the government, respectively 35 % and 60.0 %, was based on Prince *et al.* (Prince, 2014). We have assessed uncertainty around these inputs in sensitivity analysis. It was assumed that healthcare costs were totally supported by the government.

Due to paucity of data on costs of people with MCI-AD, these were based on the relative difference between people with MCI-AD and mild AD in the US GERAS II study (Robinson et al., 2020). These proportions were applied to the social and healthcare costs of people with mild AD reported by Prince et al. (Prince, 2014) to estimate costs at the MCI-AD stage.

The health and social care costs in the general UK population compared to AD-affected individuals were based on a ratio of care costs from a German study, for each cost category, by disease severity. Leicht et al. estimated medical care costs and formal nursing care costs (in nursing home care and in professional home care) in people with dementia and non-demented controls (Leicht et al., 2011). Ratios between the costs in the controls and cohort with dementia were applied to the previously determined costs of PwAD to derive the corresponding costs in the general population. The proportional difference in costs in MCI-AD and mild AD patients from Robinson et al. was also applied to the cohort unaffected by AD to estimate costs for people with no MCI-AD. Although no AD-dementia severity states exist in the cohort without AD, dummy states were assumed for modelling purposes, so that costs in the same category were applied to individuals of the same age in the comparator arm. As social and healthcare costs of PwAD differ by AD severity, we have modelled costs of people unaffected by AD to change with ageing.

Caring for a PwAD was assumed not to impact carers' consumption of healthcare resources so we excluded healthcare costs for carers from the model calculations in both cohorts. Formal social care and healthcare costs considered in the model are presented in Table 4.

We have included formal social care costs in the total amount for financial support but have reported healthcare costs separately. Reporting healthcare costs separately allows us to estimate its proportion among overall costs for comparison with other publications.

The modelled inputs on fiscal consequences, by cohort affected or unaffected by AD, are summarized in Table 5.

Model results calculations

We have calculated the net present value (NPV) of tax revenue, financial support and healthcare costs for each cohort using the equations shown below. The difference between NPV summarizes the overall consequences of AD on public finances, compared to the non-AD cohort, and was expressed as an Incremental net consequence (INC). Lifetime earnings from employment were also reported but not included in the INC value as they represent a loss to individuals. The equations used in the calculations are shown below.

$$INC = NPV_{cohort\ affected\ by\ AD} - NPV_{cohort\ unaffected\ by\ AD} \tag{1}$$

$$NPV_j = \sum_{t_0}^{t} \frac{Tax_t - Financial\ support_t - Healthcare\ costs_t}{(1+r)^t} \tag{2}$$

$$Tax_t = Direct\ tax_t + Indirect\ tax_t + Social\ security\ contributions_t \tag{3}$$

$$Financial\ support_t = Financial\ support_{PwAD_j} + Financial\ support_{Carers_j} \tag{4}$$

Where *j* is AD status (cohort affected by AD vs cohort unaffected by AD), *r* is the annual discount rate of 3.5 %, and *t* is time.

All costs were reported in 2020 lb sterling (£). When required, costs were inflated to current values using the National Health Service (NHS) cost inflation index (Curtis, 2017, Curtis, 2020).

Additional results

We have also estimated the annual fiscal loss associated to the entire AD population in the UK by combining the INC with prevalence data. The mean annual fiscal loss per pair affected by AD was calculated as the ratio of the NPV to PwAD's LY.

To estimate the prevalence of AD we considered both people living with MCI-AD and those for which the disease has already progressed to AD-dementia. The age-specific prevalence of MCI from any cause was based on Petersen et al. (Petersen et al., 2018) (Table A14) and applied to the demographic projections of the UK population older than the minimum age simulated at model baseline (52 years old) in 2021 (ONS, 2022). AD has shown to be in the aetiology of 75 % of MCI cases (Knopman et al., 2016). Based on this, 1.79 million people in the UK were estimated to have MCI-AD. Wittenberg et al. (Wittenberg et al., 2019a) have estimated that in 2019, 883,100 older people would have dementia in the UK. Assuming the population growth of people aged over 50 years old between 2019 and 2021 (3.1 %) and that 62 % of dementia cases are caused by AD (Prince, 2014), 564,532 people were estimated to live with AD-dementia in the UK, in 2021.

Sensitivity analysis

We have identified uncertainty surrounding several parameters and base case assumptions. These were challenged in sensitivity analyses.

We have conducted one-way scenarios to challenge uncertainty around some model inputs including varying the age at MCI-AD onset (to 60 years old) and reducing the carers' age accordingly, considering the average hours of care from the UK GERAS I study (Lenox-Smith et al., 2016), varying the proportion of formal social care paid by the government to 39.4 % of the total social care costs (Wittenberg et al., 2019b), and assuming 72.0 % of institutionalization costs are paid by the government (Bond et al., 2012).

We have also challenged some base case assumptions in separate scenarios including removing any impact from MCI-AD (employment reduction in people with MCI–AD or carers, and excess mortality), and assuming all PwAD and carers would receive financial support.

We have also assessed the impact of attributing state pensions to all living PwAD and equivalents over the age of retirement (66 years), assuming its value would not be influenced by other financial support already being received. For simplicity and due to the lack of data, we have not considered the possibility of a partner receiving part of the deceased spouse pension, which would reduce the incremental difference between cohorts. Private pensions were not modelled. The monetary value of state pensions was included in Table A15.

One-way sensitivity analyses (OWSA) were conducted using 95 % confidence intervals (CI) bounds of all mean inputs to identify the most influential parameters. Resulting findings were summarized in a tornado diagram.

Results

The model estimates an average life-expectancy of 10.3 LY after MCI-AD (standard-deviation [SD] 2.7 years) with 37.9 % of time spent on MCI-AD, 22.2 % in mild AD, 24.2 % in moderate AD, and 15.7 % in severe AD. After discounting, the model predicted an average of 8.46 LY until death with 5.3 LY in AD–dementia. Over the same time horizon, the model estimated 11.7 and 15.6 discounted LY for people without AD and carers, respectively. We have not modelled the effect of caregiving on mortality so carers for PwAD averaged the same LY as their comparator cohort.

Base case

Fiscal burden of AD over PwAD's lifetime

Base case results were reported as discounted INC calculated from MCI-AD onset to PwAD's death. The model estimates that the UK government will lose £73,749 (95 % credible intervals [CrI] -£77,150 to -£70,347) per pairing of PwAD and informal carer, compared to an identical pair unaffected by AD (Table 6). A PwAD was estimated to earn £11,141 less, leading to an 41.1 % reduction in direct taxes paid. Each PwAD was also predicted to require additional £42,786 on financial support and to incur £16,395 more on healthcare, compared to people without AD. Carers of a PwAD were predicted to earn £27,189 less, with a 28.3 % reduction of direct taxes paid. Each PwAD's carer was predicted to cost £942 more on financial support than their comparators unaffected by AD. The overall fiscal loss (INC) was mostly due to the increase in financial support (59.3 % of total INC), 22.2 % was due to healthcare costs and 18.5 % due to loss tax revenue (Table 6).

Total fiscal burden of AD in the entire UK population

The burden of AD on the entire UK population was based on prevalence estimates of 1.79 million people living with MCI-AD and 564.5 thousand people living with AD-dementia in 2021. The fiscal burden to the UK government could reach £50 billion over the lifetime of the cohort with AD (£12 billion for people at MCI-AD and £38 billion for people with AD-dementia).

Incremental results per health state (MCI-AD and AD-dementia) and mean annual fiscal balance values are presented in Appendix (Table A16). The mean annual fiscal loss per pair affected by AD was estimated at £2,128 per person with MCI-AD and at £21,070 per person with AD-dementia (Table A16 in the Appendix).

The mean annual fiscal loss due to AD to the UK government in 2021 was then assessed at £16 billion (£4 billion with people with MCI-AD and £12 billion with people with AD-dementia).

Figures depicting the gross earnings, tax revenue and financial support provided to people affected and unaffected by AD since MCI-AD diagnosis to death are presented in Fig. A2 and Fig. A3 in the Appendix.

Sensitivity analysis

Scenario analyses

Results of scenario analyses are presented in Table 7. The scenario with most impact on results is the one leading to a higher PwAD's life expectancy with AD. Naturally, these individuals would receive financial support and have increased healthcare costs for longer periods. If MCI-AD was diagnosed earlier in life (at a mean age of 60 years old), PwAD and carers would be younger and most likely be in the labour force. Consequently, lost tax revenue would be higher when compared to the cohort unaffected by AD, with INC increasing by 91.6 %, representing a loss of £141,323 per patient and carer to UK government.

Any parameter that estimates an increase in public funding leads to higher fiscal losses. If all PwAD would get financial support, the INC would increase by 24.8 %. If the proportion of institutionalization costs paid by the government was 72.0 %, as assumed by Bond and colleagues (Bond et al., 2012), the INC would increase by 21.2 %.

If MCI had no impact on PwAD and carer's employment likelihood, the overall fiscal burden would hardly be affected (-4.6 %), as most PwAD and carers are above the SPA. For the same reason, using a different source for the average hours of care (Lenox-Smith et al., 2016) would slightly increase the INC (5.5 %).

The scenario modelling the impact of pensions led to a 11.7 % reduction of the overall fiscal loss to £65,108 mostly due to a greater increase in financial support to individuals unaffected by AD, due to their longer life-expectancy. Those unaffected by AD receive the state pension for a longer period. All remaining scenarios varied the INC by

Table 6
Base case results from the UK government perspective[*].

		Cohort affected by AD	Cohort unaffected AD	Difference[†]	Fiscal effect	% of INC
Person with/without AD	**Direct tax**	£4,927	£8,358	**-£3,432**	Fiscal loss	4.7 %
	Indirect tax	£4,986	£3,552	**£1,434**	Fiscal gain	−1.9 %
	Financial support[*]	-£50,507	-£7,721	**-£42,786**	Fiscal loss	58.0 %
	Healthcare costs	-£42,459	-£26,064	**-£16,395**	Fiscal loss	22.2 %
Carer of a person with/without AD	**Direct tax**	£21,200	£29,574	**-£8,374**	Fiscal loss	11.4 %
	Indirect tax	£8,707	£11,962	**-£3,255**	Fiscal loss	4.4 %
	Financial support[*]	-£1,390	-£447	**-£942**	Fiscal loss	1.3 %
Sum		**-£54,535**	**£19,214**	**-£73,749**[‡] (95 % CrI -£77,150 to -£70,347)	**Overall fiscal loss (INC)**	100.0 %

AD, Alzheimer's disease; CrI, credible interval; INC, Incremental net consequence.

[*] Financial support includes transfers to people with Alzheimer's disease and carers and costs on formal social care provision.

[†] Negative costs represent a fiscal loss to the UK Government; positive values represent a fiscal gain to the UK Government.

[‡] Incremental Net Consequence (INC).

Table 7
Scenario analyses.

	Cohort	**Person with AD/without AD**				**Carer of a person with/without AD**			**Sum**
Scenarios	**AD status**	**Direct tax**	**Financial support**	**Indirect tax**	**Healthcare costs**	**Direct tax**	**Financial support**	**Indirect tax**	
Base case	Affected by AD	£4,927	-£50,507	£4,986	-£42,459	£21,200	-£1,390	£8,707	-£54,535
	Unaffected by AD	£8,358	-£7,721	£3,552	-£26,064	£29,574	-£447	£11,962	£19,214
	Incremental[*]	**-£3,432**	**-£42,786**	**£1,434**	**-£16,395**	**-£8,374**	**-£942**	**-£3,255**	**-£73,749**[†]
PwAD's age: early MCI-AD diagnosis (60 years old)	Affected by AD	£17,792	-£78,135	£12,226	-£56,888	£50,316	-£2,290	£20,541	-£36,437
	Unaffected by AD	£33,753	-£9,456	£13,729	-£33,971	£72,254	-£586	£29,162	£104,885
	Incremental[*]	**-£15,961**	**-£68,679**	**-£1,502**	**-£22,917**	**-£21,938**	**-£1,705**	**-£8,621**	**-£141,323**[†]
Monthly mean hours of care from UK GERAS I study	Affected by AD	£4,638	-£50,922	£4,881	-£42,643	£18,850	-£1,548	£7,781	-£58,962
	Unaffected by AD	£8,175	-£7,748	£3,478	-£26,093	£29,553	-£447	£11,954	£18,871
	Incremental[*]	**-£3,537**	**-£43,173**	**£1,402**	**-£16,550**	**-£10,703**	**-£1,100**	**-£4,173**	**-£77,833**[†]
39.4 % formal social care costs paid by the government (Wittenberg et al., 2019b)	Affected by AD	£4,661	-£46,543	£4,872	-£42,503	£20,917	-£1,353	£8,589	-£51,359
	Unaffected by AD	£8,370	-£5,638	£3,557	-£26,137	£29,743	-£447	£12,030	£21,476
	Incremental[*]	**-£3,709**	**-£40,905**	**£1,315**	**-£16,365**	**-£8,825**	**-£906**	**-£3,441**	**-£72,835**[†]
72.0 % institutionalization costs paid by the government (Bond et al., 2012)	Affected by AD	£4,728	-£66,047	£4,923	-£42,676	£21,488	-£1,388	£8,823	-£70,148
	Unaffected by AD	£8,473	-£7,845	£3,598	-£26,047	£29,552	-£447	£11,953	£19,238
	Incremental[*]	**-£3,745**	**-£58,201**	**£1,325**	**-£16,629**	**-£8,064**	**-£941**	**-£3,130**	**-£89,385**[†]
No impact due to MCI-AD (No reduction in employment of PwAD or carer's and no excess mortality)	Affected by AD	£7,055	-£49,658	£5,777	-£42,330	£22,519	-£1,367	£9,236	-£48,768
	Unaffected by AD	£8,274	-£7,719	£3,518	-£25,927	£29,641	-£447	£11,989	£19,327
	Incremental[*]	**-£1,218**	**-£41,940**	**£2,259**	**-£16,403**	**-£7,121**	**-£920**	**-£2,753**	**-£68,096**[†]
All people affected by AD get financial support	Affected by AD	£4,489	-£71,024	£7,290	-£42,427	£21,413	-£1,408	£8,795	-£72,872
	Unaffected by AD	£8,387	-£7,721	£3,564	-£26,022	£29,467	-£447	£11,919	£19,147
	Incremental[*]	**-£3,898**	**-£63,303**	**£3,726**	**-£16,405**	**-£8,054**	**-£961**	**-£3,123**	**-£92,019**[†]
State pensions included	Affected by AD	£4,784	-£54,064	£4,906	-£42,323	£21,574	-£1,305	£8,848	-£57,580
	Unaffected by AD	£8,290	-£19,174	£3,525	-£25,990	£29,424	-£447	£11,902	£7,529
	Incremental[*]	**-£3,506**	**-£34,890**	**£1,381**	**-£16,333**	**-£7,850**	**-£858**	**-£3,054**	**-£65,108**[†]

AD, Alzheimer's disease; MCI, mild cognitive impairment; PwAD, Person with Alzheimer's disease, UK, United Kingdom.

[*] Incremental results calculated by subtracting values from people not affected by AD from the values for people affected by AD.

[†] Incremental Net Consequence (INC).

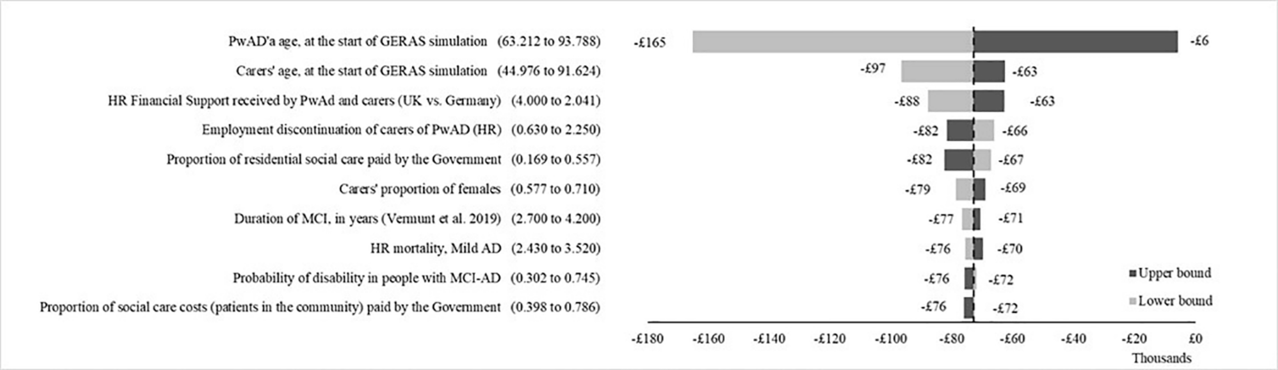

Fig. 2. Tornado diagram of the 10 most sensitive input parameters. PwAD, people with Alzheimer's disease; HR, hazard ratio; UK, United Kingdom; MCI, mild cognitive impairment; MCI-AD, mild cognitive impairment due to Alzheimer's disease.

less than 10 %. Overall, model results were robust to the one-way sensitivity analyses.

One-way sensitivity analyses

The ten model inputs with a higher impact on the INC are presented in Fig. 2. The age of PwAD is the most influential parameter, as younger PwAD can cost 126.7 % more to the government and older PwAD cost 92.0 % less. Even so, older PwAD represent a fiscal loss of -£5,813 per PwAD to the UK's government. The carers' age is the second input with a higher impact on the overall fiscal impact, with younger carers costing more 32.5 % and older carers costing less 14.1 %. The proportion of people receiving financial support, based on the comparison of people from Germany and the UK in the GERAS I study, is the third parameter that led to a higher uncertainty on the magnitude of the overall fiscal loss. All other parameters do not affect the results considerably (changes lower than 10 %).

Discussion

The current study estimates the economic consequences of AD from the UK government perspective, reported in 2020 lb sterling (£). The impact of the disease on PwAD and informal carers' fiscal pathways was considered incrementally to a demographically identical cohort unaffected by AD. Over the PwAD's lifetime, we estimated a fiscal loss of £73,749 per average pair of PwAD and main informal carer. The financial support provided to PwAD and carers accounted for 59.3 % of the total fiscal loss. This comprised transfers, as well as formal social care and institutionalization services' costs. The lost tax revenue from reduced PwAD and carers employment participation represented 18.5 % of total fiscal losses. Carers themselves accounted for 17.0 % of the total fiscal loss. Their tax contributions were reduced by £11,629 compared to their comparators, unaffected by AD, over the expected PwAD's lifetime. This highlights the importance of including informal care costs in the analysis. Healthcare costs corresponded to 22.2 % of total fiscal losses.

The total fiscal burden of AD could be estimated using our model's results and the projected AD prevalence in 2021. Over a lifetime, all pairs of PwAD and their informal carers affected by AD would cost the UK government £50 billion. Annually, it is expected a mean fiscal burden of £16 billion for all pairs of PwAD and carers affected by AD. Our study is unique as it captures the fiscal consequences of AD to the UK government across economic sectors. Our approach adds to the existing literature by considering the burden of AD over a PwAD's lifetime, focusing on externalities solely falling on the government, namely forgone tax revenue from employment, government transfer payments and indirect taxes.

There are several studies reporting the economic burden of dementia in the UK (Lowin et al., 2001, Maresova et al., 2019, Prince, 2014) or specifically to England (Wittenberg et al., 2019b). These studies differ in their perspectives, methodological approach, included cost components, and format chosen to communicate the results. Publications reporting the overall annual burden of dementia in the UK suggest values between £11.3 and £25.7 billion (Lowin et al., 2001, Prince, 2014) (costs inflated to 2020) (Curtis, 2020). Considering Alzheimer's represents 62.0 % of all cases of dementia (Prince, 2014), AD could be expected to cost society between £7.0 to £15.9 billion annually. Our analysis estimated an annual fiscal burden of £16 billion to the UK government but directly comparing these values can be misleading. Firstly, our analysis considers only costs falling on the government, excluding private losses which include foregone earnings from employment in people with AD and their informal careers. Secondly, this analysis considers the cost of MCI-AD which has historically been excluded from burden of disease publications (Lenox-Smith et al., 2016, Maresova et al., 2019, Prince, 2014, Wittenberg et al., 2019b). Finally, the annual UK burden of AD reported by this fiscal analysis is derived using the UK prevalence of MCI-AD and AD-dementia and the average results of a microsimulation considering costs across the AD continuum, which may differ from cross-sectional analyses (Prince, 2014, Wittenberg et al., 2019b). A systematic review by Maresova and colleagues (Maresova et al., 2019) reports the UK per capita economic burden by AD-dementia severity to range from £12,473 to £30,123 (2018 euros converted to lb sterling using 0.885 rate (European Central Bank, 2022) and inflated to 2020 (Curtis, 2020). Our analysis estimated an average fiscal burden of £21,070 per pair affected by AD, which numerically falls within the range presented by Maresova and colleagues. Once more, comparing these monetary values is misleading as they were obtained using different methodologies in populations with a different distribution of AD-dementia severity, and importantly, using a different perspective. The original results presented here should preferably be seen as complementary to other published economic burden of dementia or AD. Much like other publications, our analysis does suggest that direct healthcare costs represent only a small share of the overall economic burden of dementia (22.2 %). Despite the different denominator, this is somewhat comparable to the 14 % to 16 % suggested by important studies (Klieβ et al., 2021, Prince, 2014, Wittenberg et al., 2019b).

The current analysis is not without uncertainty and limitations. We identified uncertainty around the mean age of MCI-AD onset and on excess mortality due to AD, as no robust data for the UK is available. Intuitively, sensitivity analyses indicated that model results were sensitive to the mean age at AD onset, as it strongly impacts longevity and disease progression. Nonetheless, our model predicted a life-expectancy of 10.3 years from MCI-AD onset to death. This value is comparable to those reported in a publication by Vermunt and colleagues (Vermunt et al., 2019) who predicted an AD duration of 11.8 for people experiencing MCI-AD at the age of 70 years old.

Uncertainty around model conclusions was assessed in scenario analysis and OWSA, showing the influence of specific parameters on government expenditure. The age at diagnosis of MCI-AD, as well as the carer's age, had a major impact on government costs. Patients with a long-term disease and informal care requirements will incur higher costs to society and the government. Uncertainty about the share of public funding also leads to significant variation in results. A higher fiscal loss was obtained when more transfers were provided and/or if a higher proportion of formal social care and institutionalization costs were incurred by the government. As there is no perfect source to inform these inputs, we are left with exploring a meaningful range of parameters in the hope these produce a likely range of public costs.

For simplicity, the current model took a conservative approach when modelling the impact on carers' earnings. Return to employment with a lower income was considered possible after PwAD's death or institutionalization. However, carers can decide retiring earlier or may find it difficult to return to employment (Michaud et al., 2010). Lower earnings during the caring period or afterwards may also affect personal savings and pension arrangements. Also, uncertainty exists on the eligibility to CA or any other additional allowances, which could impact the costs to the government. Excess healthcare costs due to caregiving were also not included, although an increase could be expected (Chiao et al., 2015, Alzheimer's Association, 2020). We predict that modelling the above would contribute to increasing the overall fiscal loss to the government.

Modelling AD progression accurately is also essential to estimate government expenditure. The equations used to estimate disease severity and individual care requirements (Getsios et al., 2010) have been previously discussed in the literature (Martins et al., 2022).

Moreover, due to the lack of specific data for PwAD in the UK some assumptions were required to link the AD to labour participation in people with the disease and their informal carers. We have drawn this evidence from international studies, under the assumption that the AD affects employment with similar intensities across countries. Further data would be needed to tackle uncertainty on the impact of AD and MCI-AD on employment. The difference in healthcare costs of people affected and unaffected by AD in the UK would also be highly valued for the analysis. It is unlikely that such parameters would lead to significantly different conclusions, but they would mostly likely contribute to greater precision in estimating the different sources of public expenditure.

Conclusion

The present research uses a broad public economic perspective, considering the effects of AD to the UK government across economic sectors. As AD progresses, decreased labour participation by PwAD and informal carers will invariably reduce earnings and tax contributions. Subsequently, the UK government faces increased costs with transfers (financial support, welfare benefits) provided to people affected by AD. We have shown that the fiscal losses are substantial, far surpassing commonly estimated medical and formal social care costs of people affected by AD. Accordingly, it seems imperative that the estimation of the fiscal consequences of diseases is considered to inform health policy and healthcare resource allocation. These findings should be used to characterize the severity of diseases and should be considered in parallel or combined with evidence on cost-effectiveness by bodies assessing new health technologies. The monetary value of our results can be used to offset the costs of public policies tackling preventable risk factors for AD. This type of analysis is particularly relevant for countries such as the UK because the government directly finances health, social care and other forms of support to individuals with chronic diseases.

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Disclosures

During the peer review process, Biogen had the opportunity to review and comment on the manuscript. The authors retained full editorial control of the manuscript and provided their final approval on all content to be published.

CRediT authorship contribution statement

Ana T. Paquete: Conceptualization, Validation, Formal analysis, Methodology, Writing - original draft, Writing - review & editing. **Rui Martins:** Conceptualization, Validation, Formal analysis, Methodology, Writing - original draft, Writing - review & editing. **Nikolaos Kotsopoulos:** Conceptualization, Validation, Writing – review & editing. **Michael Urbich:** Conceptualization, Validation, Writing – review & editing. **Colin Green:** Conceptualization, Writing – review & editing. **Mark P. Connolly:** Conceptualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix

Cognition scores ranges defined by the Mini-Mental State Examination (MMSE)

Table A1

Cognition score ranges and interpretation of day-to-day functioning.

Clinical Disease Stage	MMSE*	Day-to-day functioning†
MCI-AD	27–29	May have clinically significant but mild deficits. Likely to affect only most demanding ADL.
Mild AD	21–26	Significant effect. May require some supervision, support, and assistance.
Moderate AD	10–20	Clear impairment. May require 24-hour supervision.
Severe AD	< 10	Marked impairment. Likely to require 24-hour supervision and assistance with ADL.

AD, Alzheimer's disease; ADL, Activities of daily living; MCI-AD, mild cognitive impairment due to AD; MMSE, Mini-Mental State Examination.

[*] Individuals with an MMSE score of 30 were assumed to be cognitively normal. The same MMSE categories were based on previously published model (Green and Zhang, 2016, Martins et al., 2022).

[†] Adapted from Eftychios et al. (Eftychios et al., 2021).

Age distribution at mild AD in the simulated cohorts

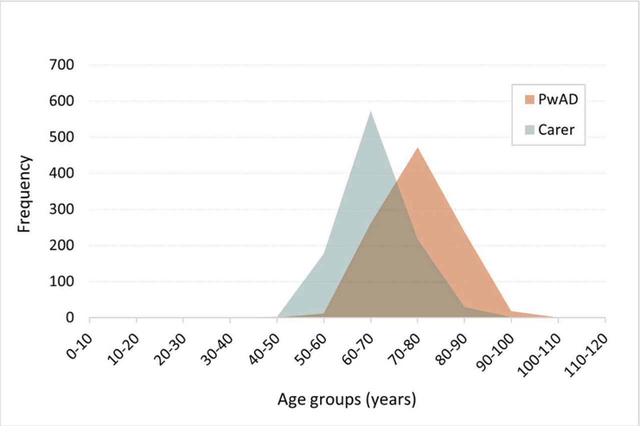

Fig. A1. Age distribution at AD GERAS simulation: PwAD and informal carers. PwAD, people with Alzheimer's disease.

Equations predicting Alzheimer's Disease progression

Progression of AD from the GERAS enrolment onwards was modelling using published equations that predict changes in the MMSE and the ADL scores (Getsios et al., 2010).

Equation A.1 to A.4 were used to predict changes in the MMSE scores:

$$Change\ in\ MMSE_{Treated} = \left(\left[(T)\right]_{eff} - 5.4663 - 0.429PM_1 - 0.004PM_2 + 0.1415PM_3 - 0.079PrevMMSEChange + 0.0747Age + \delta_i\right) \times \mathrm{CycleLength} \tag{A.1}$$

$$\mathrm{PM}_1 = \min(\mathrm{PrevMMSE}, 9) \tag{A.2}$$

$$\mathrm{PM}_2 = \max(0,\ \min[\mathrm{PrevMMSE} - 9, 9]) \tag{A.3}$$

$$\mathrm{PM}_3 = \max(0, \min[\mathrm{PrevMMSE} - 18, 12]\,) \tag{A.4}$$

Where T_{eff} is the treatment effect (assumed to take the value of 0 for standard of care), *PrevMMSEChange* is the value of MMSE change in the previous cycle, *Age* is current age in years, and *CycleLength* is the simulation cycle length. Between patient variability was introduced using δ_i, implemented as a random draw from a normal distribution with mean zero and standard deviation of 0.5.

Equation A.5 was used to predict changed in ADL scores:

$$\text{Change in ADL} = \mathrm{Base}_{\mathrm{ADL}} + 1.35 + 0.06\mathrm{weeks} - 0.79\mathrm{ADL}_{\mathrm{baseline}} + 0.71\mathrm{ADL}_{\mathrm{recent}} + 0.12\mathrm{MMSE}_{\mathrm{baseline}} + 0.09\mathrm{age} - 0.49\mathrm{MMSE}_{\mathrm{recent}} + \delta_{\mathrm{i}} \tag{A.5}$$

Where *weeks* is the simulation time in weeks, $ADL_{baseline/recent}$ and $MMSE_{baseline/recent}$ are the ADL and MMSE scores at baseline or in the previous cycle, respectively.

Variability between patients was included using the δ_i parameter implemented by sampling from a normal distribution with mean 0 and standard deviation 2.48. The coefficients for race (-3.05) and psychiatric medication (0.81) used in the original publication were left out of the analysis as data was not available in the synthesized cohort. A full explanation of how these equations were obtained is explained in the original publication (Getsios et al., 2010).

The range for the total Alzheimer's Disease Cooperative Study (ADCS) ADL score used in GERAS study ranged from 0 to 78 (with high scores representing less dependency). Getsios and colleagues have standardized ADL scores to range from 0 to 100. In the model the ADL scores sampled from average GERAS scores were rescaled using Equation A.6.

$$\mathrm{S}_{\mathrm{t}} = \frac{\mathrm{Max}_{\mathrm{Target}} - \mathrm{Min}_{\mathrm{Target}}}{\mathrm{Max}_{\mathrm{Source}} - \mathrm{Min}_{\mathrm{Source}}} \times (\mathrm{S}_{\mathrm{i}} - \mathrm{Max}_{\mathrm{Source}}) + \mathrm{Max}_{\mathrm{Target}} \tag{A.6}$$

Where S_t is the desired value, S_i is the value score to be converted, *Max* and *Min* represent the maximum and minimum of the original (*Source*) and desired score (*Target*).

Equation predicting total hours of informal care

The following equation was used to predict total hours of informal care based on individual MMSE and ADL scores, based on the GERAS I study (Reed et al., 2016):

$$\text{Total carer time} = 7.0706 - 0.3727\mathrm{Country} - 0.1411\mathrm{MMSE}_{\mathrm{Severity}} + 0.0029\mathrm{Age} - 0.3600\mathrm{Spouse} - 0.403\mathrm{ADL} + \mathrm{Scale} \tag{A.7}$$

Where *Country* referred to GERAS I cohort location (0 for the UK). $MMSE_{Severity}$ was −0.1411 for mild AD, 0.0168 for moderate AD and 0 for severe AD. *Age* was the current age in the model, *Spouse* took the value of −0.36 for spouses of PwAD and 0 otherwise, *ADL* was the individual ADL score, and *Scale* took the value of 0.5438. The predicted hours of informal care were used to calculate the proportion of carers able to maintain employment. We have explored uncertainty around the estimation of total carer time by utilizing severity-specific estimates from the UK cohort in the GERAS study (Lenox-Smith et al., 2016).

Probabilities of employment and disability

Table A2

Probabilities of employment and disability in the general population, adjusted probability of employment in PwAD and their informal carers.

Age band (years)	Employment in the general population		Employment in MCI-AD[*]		Employment of PwAD[†]		Employment of carers of PwAD[‡]	
	Males	Females	Males	Females	Males	Females	Males	Females
75 to 79	–	–	0.49	0.53	–	–	–	–
70 to 74	0.12	0.07	0.42	0.45	0.01	0.00	0.08	0.04
65 to 69	0.27	0.21	0.35	0.39	0.05	0.3	0.21	0.15
60 to 64	0.60	0.50	0.30	0.33	0.32	0.21	0.55	0.44
55 to 59	0.78	0.70	0.25	0.29	0.56	0.45	0.74	0.66
50 to 54	0.86	0.79	0.21	0.24	0.71	0.58	0.83	0.75
45 to 49	0.88	0.80	0.17	0.21	0.75	0.60	0.86	0.77
40 to 44	0.89	0.80	0.14	0.18	0.77	0.60	0.87	0.77
35 to 39	0.91	0.79	0.12	0.15	0.80	0.59	0.89	0.76
30 to 34	0.90	0.80	0.10	0.13	0.79	0.60	0.88	0.76
25 to 29	0.85	0.81	0.09	0.11	0.69	0.62	0.82	0.78
20 to 24	0.65	0.68	0.09	0.10	0.38	0.42	0.60	0.63

AD, Alzheimer's disease; MCI-AD, mild cognitive impairment due to AD; PwAD, people with Alzheimer's disease.

Sources: (ONS, 2021b, ONS, 2021c, Sakata and Okumura, 2017).

[*] Prevalence of disability in the UK.

[†] Calculated by applying the HR 2.26 to the sex-specific rate of employment in the general population.

[‡] Calculated by applying the HR 1.19 to the sex-specific rate of employment in the general population.

Equation predicting carer's labour participation

Carer's labour participation was estimated using a published equation, based on an analysis of survey data by Statistics Canada (Lilly et al., 2010, Martins et al., 2022):

$$\mathrm{P(LFP)}_{\mathrm{Males}} = -0.308 - 0.275\mathrm{Age}_{50-54} - 0.843\mathrm{Age}_{55-59} - 1.531\mathrm{Age}_{60-75} + 0.339\mathrm{Spouse} \tag{A.8}$$

$$\mathrm{P(LFP)}_{\mathrm{Females}} = -0.661 - 0.249\mathrm{Age}_{50-54} - 0.781\mathrm{Age}_{55-59} - 1.470\mathrm{Age}_{60-75} - 0.113\mathrm{Spouse} \tag{A.9}$$

Where $Age_{Min\text{-}Max}$ took the value of 1 if the carers' age would fall in that range and 0 otherwise. The upper limit of $Age_{60\text{-}75}$ was assumed to equal the maximum age of employment. *Spouse* would take the value of 1 for spouses and 0 for child caregivers. Other parameters from the original probit equations (primary/secondary carers, region of birth, education, and the number of children below the age of 15) were excluded as no data were available from the GERAS I study. Higher uncertainty is acknowledged due to the lack of these data.

The proportion of full-time equivalent (FTE) among employed carers was based on the following equations, also sourced from the same publication (Lilly et al., 2010).

$$\mathrm{Proportion}_{\mathrm{FTE\,Males}} = \exp(-0.045\mathrm{Primary}_{\mathrm{CG}} - 0.032\mathrm{Care}_{10} - 0.089\mathrm{Care}_{15} - 0.156\mathrm{Care}_{20}) \tag{A.10}$$

$$\mathrm{Proportion}_{\mathrm{FTE\,Females}} = \exp(-0.037\mathrm{Primary}_{\mathrm{CG}} + 0.023\mathrm{Care}_{10} - 0.022\mathrm{Care}_{15} - 0.018\mathrm{Care}_{20}) \tag{A.11}$$

Where $Primary_{CG}$ took the value of 1 for primary carer and 0 otherwise, and $Care_{10}$, $Care_{15}$ and $Care_{20}$ took the value of 1 if informal care was provided for more than 10, 15 or 20 h weekly, respectively, and took the value of 0 otherwise.

Fiscal consequences

Gross income from employment

Table A3
Annual gross earnings by age (per capita).

	Annual gross earnings*	
Age bands (years)	**Males**	**Females**
60+	£31,715	£18,973
50 to 59	£42,305	£26,137
40 to 49	£44,552	£28,043
30 to 39	£38,093	£27,076
22 to 29	£28,932	£23,001
18 to 21	£14,034	£10,680

Source: (ONS, 2021d).
* Weighted for the distribution of full-time and part-time in the general population.

Financial support received by the cohort affected by AD

Table A4
Average biannual financial support provided to PwAD (per capita): ESA, PIP, AA.

	Biannual financial support (per capita)			
Age bands (years)	**ESA due to Diseases of the Nervous System**	**PIP due to Dementia**		**AA due to Dementia**
		Daily Living Award	**Mobility Award**	
80+	–	–	–	£2,079
75–79	–	–	–	£2,052
70–74	–	£3,748	£3,362	£2,056
65–69	£2,457	£3,805	£3,337	£2,058
60–64	£2,614	£3,812	£3,284	–
55–59	£2,858	£3,820	£3,292	–
50–54	£3,069	£3,775	£3,320	–
45–49	£3,203	£3,784	£3,153	–
40–44	£3,309	£3,747	£3,090	–
35–39	£3,309	£3,900	£1,980	–
30–34	£3,306	£3,828	£1,911	–
25–29	£3,306	£1,416	£0	–
18–24	£3,151	£0	£0	–

AA, Attendance Allowance; ESA, Employment and Support Allowance; PIP, Personal Independence Payment; PwAD, people with Alzheimer's disease.
Sources: (DWP, 2021c, DWP, 2021d, DWP, 2021e, DWP, 2021a).

Table A5
Average biannual financial support provided to carers of PwAD (per capita): Carer's Allowance.

Age bands (years)	Carer's Allowance
65+	£1,580
60–64	£1,753
55–59	£1,754
50–54	£1,754
45–49	£1,754
40–44	£1,754
35–39	£1,754
30–34	£1,754
25–29	£1,754
18–24	£1,753

PwAD, people with Alzheimer's disease.
Source: (DWP, 2021b).

Financial support received by the comparator cohort

Table A6
Proportion of people receiving ESA due to Disease of the Nervous System (PwAD's comparator cohort).

	Males		**Females**	
Age band (years)	**Work Related Activity group**	**Support group**	**Work Related Activity group**	**Support group**
65+	0.00 %	0.03 %	0.00 %	0.03 %
60–64	0.06 %	0.49 %	0.06 %	0.60 %
55–59	0.06 %	0.43 %	0.05 %	0.54 %
50–54	0.05 %	0.36 %	0.05 %	0.45 %
45–49	0.05 %	0.30 %	0.04 %	0.37 %
35–44	0.04 %	0.23 %	0.03 %	0.25 %
25–34	0.03 %	0.22 %	0.02 %	0.19 %
18–24	0.01 %	0.13 %	0.01 %	0.11 %

ESA, Employment and Support Allowance; PwAD, people with Alzheimer's disease.
Source: (DWP, 2021c).

Table A7
Average biannual amount of ESA due to diseases of the nervous system (PwAD's comparator cohort).

	Males		**Females**	
Age band (years)	**Work Related Activity group**	**Support group**	**Work Related Activity group**	**Support group**
65+	£2,014	£1,473	£3,442	£3,382
60–64	£2,362	£1,680	£3,546	£3,470
55–59	£2,641	£2,100	£3,694	£3,540
50–54	£2,875	£2,422	£3,813	£3,641
45–49	£2,997	£2,615	£3,880	£3,722
35–44	£2,999	£2,799	£3,839	£3,784
25–34	£2,994	£2,886	£3,718	£3,715
18–24	£2,744	£2,721	£3,567	£3,581

ESA, Employment and Support Allowance; PwAD, people with Alzheimer's disease.
Source: (DWP, 2021c).

Table A8
Proportion of people receiving PIP due to dementia (PwAD's comparator cohort).

	Males		Females		Males		Females	
Age band (years)	**Daily Living - Enhanced**	**Daily Living - Standard**	**Daily Living - Enhanced**	**Daily Living - Standard**	**Mobility Award - Enhanced**	**Mobility Award - Standard**	**Mobility Award - Enhanced**	**Mobility Award - Standard**
70+	0.03 %	0.00 %	0.02 %	0.00 %	0.03 %	0.00 %	0.02 %	0.00 %
65–69	0.17 %	0.01 %	0.14 %	0.01 %	0.16 %	0.02 %	0.13 %	0.01 %
60–64	0.12 %	0.01 %	0.10 %	0.00 %	0.11 %	0.01 %	0.09 %	0.01 %
55–59	0.04 %	0.00 %	0.04 %	0.00 %	0.04 %	0.01 %	0.04 %	0.00 %
50–54	0.01 %	0.00 %	0.01 %	0.00 %	0.01 %	0.00 %	0.01 %	0.00 %
45–49	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %
40–44	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %
35–39	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %
30–34	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %
25–29	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %
20–24	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %

PIP, Personal Independence Payment; PwAD, people with Alzheimer's disease.
Source: (DWP, 2021d, DWP, 2021e).

Table A9
Average biannual amount of PIP due to dementia (PwAD's comparator cohort).

	Males		Females		Males		Females	
Age band (years)	**Daily Living - Enhanced**	**Daily Living - Standard**	**Daily Living - Enhanced**	**Daily Living - Standard**	**Mobility Award - Enhanced**	**Mobility Award - Standard**	**Mobility Award - Enhanced**	**Mobility Award - Standard**
70+	£3,779	£2,378	£3,813	£2,471	£3,950	£3,949	£2,764	£2,848
65–69	£3,849	£2,476	£3,879	£2,554	£3,941	£3,939	£2,738	£2,671
60–64	£3,871	£2,451	£3,902	£2,454	£3,934	£3,934	£2,637	£2,592
55–59	£3,867	£2,218	£3,898	£2,596	£3,950	£3,937	£2,637	£2,606
50–54	£3,865	£2,397	£3,887	£2,273	£3,942	£3,932	£2,715	£2,562
45–49	£3,823	£2,284	£3,843	–	£3,940	£3,961	£2,332	£2,617
40–44	£3,895	£2,278	£3,854	–	£3,935	£3,961	£2,168	£2,694
35–39	£3,847	–	£3,953	–	£3,961	£3,953	–	–
30–34	£3,962	–	£3,694	–	£3,823	–	–	–
25–29	£2,831	–	–	–	–	–	–	–
20–24	–	–	–	–	–	–	–	–

PIP, Personal Independence Payment; PwAD, people with Alzheimer's disease.
Source: (DWP, 2021d, DWP, 2021e).

Table A10
Proportion of people receiving AA due to dementia (PwAD's comparator cohort).

	Males		Females	
Age band (years)	**Lower Rate**	**Higher Rate**	**Lower Rate**	**Higher Rate**
80+	0.97 %	1.90 %	1.43 %	2.67 %
75–79	0.40 %	0.75 %	0.65 %	1.13 %
70–74	0.30 %	0.58 %	0.44 %	0.77 %
65–69	0.19 %	0.38 %	0.27 %	0.46 %

AA, Attendance allowance; PwAD, people with Alzheimer's disease.
Source: (DWP, 2021a).

Table A11
Average biannual amount of AA due to dementia (PwAD's comparator cohort).

	Males		Females	
Age band (years)	**Lower Rate**	**Higher Rate**	**Lower Rate**	**Higher Rate**
80+	£1,558	£2,326	£1,558	£2,326
75–79	£1,558	£2,326	£1,558	£2,326
70–74	£1,558	£2,326	£1,558	£2,326
65–69	£1,558	£2,326	£1,558	£2,326

AA, Attendance allowance; PwAD, people with Alzheimer's disease.
Source: (DWP, 2021a).

Table A12
Proportion of people receiving CA (Carer's comparator cohort).

Age band (years)	Males	Females
65+	0.34 %	0.67 %
60–64	2.16 %	4.15 %
55–59	1.75 %	3.70 %
50–54	1.52 %	3.59 %
45–49	1.35 %	3.83 %
40–44	1.18 %	4.06 %
35–39	1.04 %	4.14 %
30–34	0.89 %	3.54 %
25–29	0.74 %	1.96 %
18–24	0.87 %	1.22 %

CA, Carer's Allowance.
Source:(DWP, 2021b).

Table A13
Average biannual amount of CA (Carer's comparator cohort).

Age bands (years)	Males	Females
65+	£1,646	£1,515
60–64	£1,754	£1,753
55–59	£1,754	£1,754
50–54	£1,754	£1,754
45–49	£1,754	£1,754
40–44	£1,755	£1,754
35–39	£1,755	£1,754
30–34	£1,755	£1,754
25–29	£1,754	£1,754
18–24	£1,753	£1,753

CA, Carer's Allowance.
Source:(DWP, 2021b).

Prevalence of MCI-AD

Table A14
Age-specific prevalence of MCI in the overall population.

Age band (years)	MCI %
80+	25.2 %
75–79	14.8 %
70–74	10.1 %
65–69	8.4 %
60–64	6.7 %
50–59	3.4 %*

MCI, mild cognitive impairment.

* Assumed to be half the prevalence for those aged 60–64 years old.
Source: (Petersen et al., 2018).

Pensions

Table A15
Monetary value of state pensions.

Age bands (years	Weekly amount (£)
90+	£158
85–89	£164
80–84	£158
75–79	£150
70–74	£151
65–69	£159

Source:(ONS, 2021a).

Additional results

Table A16
Incremental base case results disaggregated by health state and mean annual costs.

			Total Earnings	Total direct tax	Total Indirect tax	Healthcare costs	Total Financial support	Total transfers	Incremental results	Life-years (PwAD)	Weighted cost per life year lived with AD	
Cohort unaffected by AD	**MCI-AD**		£61,184	£18,845	£7,664	-£6,718	-£1,390	-£8,108	£18,401	3.18	£5,786*	£5,786†
	AD-dementia	AD onset	£22,640	£6,973	£2,853	-£4,302	-£1,192	-£5,494	£4,332	1.49	£2,908*	£2,410‡
		GERAS	£39,333	£12,115	£4,997	-£15,044	-£5,587	-£20,631	-£3,520	7.07	-£498*	
Cohort affected by AD	**MCI-AD**		£56,616	£17,438	£7,099	-£8,573	-£4,329	-£12,902	£11,635	3.18	£3,658*	£3,658†
	AD-dementia	AD onset	£12,494	£3,848	£1,833	-£5,264	-£3,938	-£9,201	-£3,520	1.40	-£2,519*	-£18,660‡
		GERAS	£15,718	£4,841	£4,762	-£28,622	-£43,630	-£72,252	-£62,649	3.88	-£16,142*	
									Incremental annual cost per capita		**MCI-AD**	**-£2,128†**
											AD-dementia	**-£21,070‡**

AD, Alzheimer's disease; PwAD, person with Alzheimer's disease; MCI-AD, mild cognitive impairment due to Alzheimer's disease.
* Incremental results divided by life-years of the person with AD life-years.
† Mean annual fiscal burden per person with MCI-AD.
‡ Mean annual fiscal burden per person with AD-dementia.

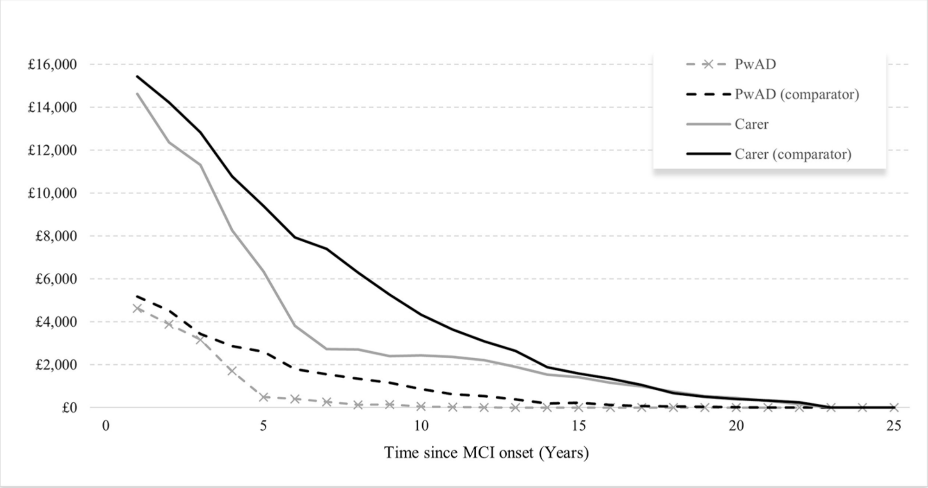

Fig. A2. Gross earnings from employment in PwAD and carer vs comparators unaffected by AD (per capita). MCI, mild cognitive impairment; PwAD, people with Alzheimer's disease.

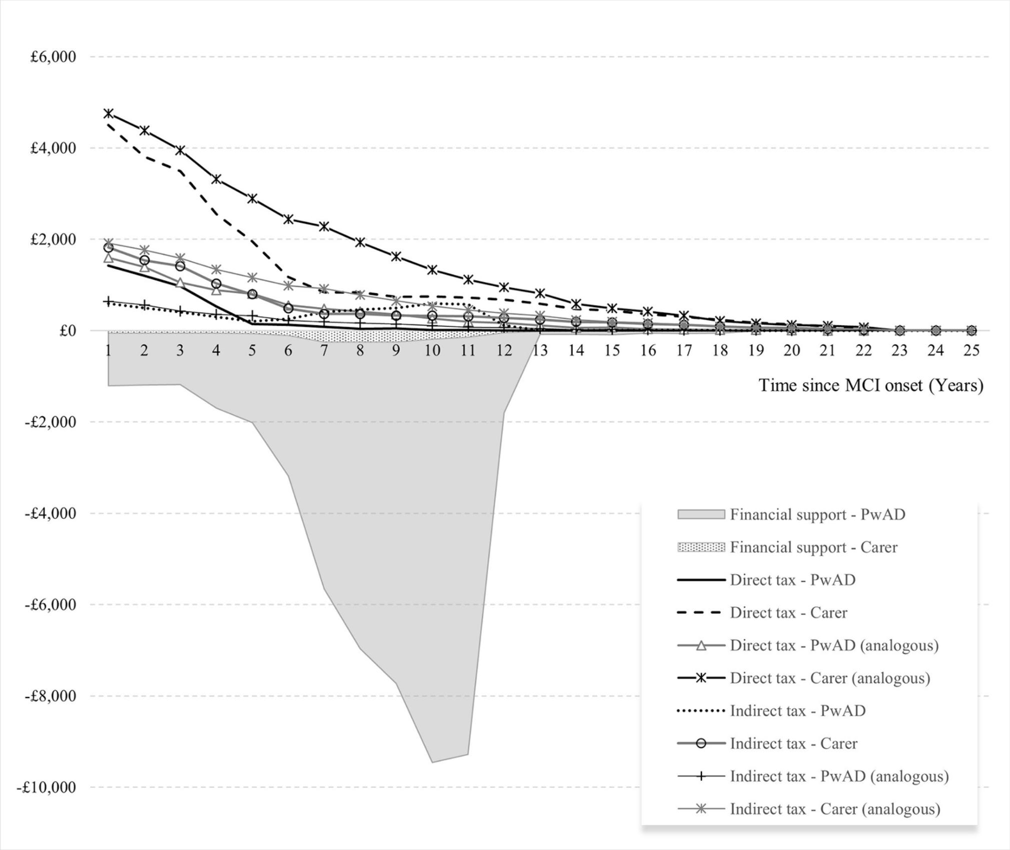

Fig. A3. Tax and financial support to PwAD and carer vs comparators unaffected by AD (per capita). MCI, mild cognitive impairment; PwAD, people with Alzheimer's disease.

References

Alzheimer Europe. 2019. *Alzheimer's disease and Alzheimer's dementia* [Online]. Available: https://www.alzheimer-europe.org/Dementia/Alzheimer-s-disease-and-Alzheimer-s-dementia [Accessed 04/06/2021].

Alzheimer's Association 2020. 2020 Alzheimer's disease facts and figures. *Alzheimers Dement.*.

Andersen, K., Lolk, A., Martinussen, T., Kragh-Sorensen, P., 2010. Very mild to severe dementia and mortality: A 14-year follow-up - The Odense study. Dement. Geriatr. Cogn. Disord. 29, 61–67.

Artero, S., Touchon, J., Ritchie, K., 2001. Disability and mild cognitive impairment: a longitudinal population-based study. Int. J. Geriatric Psychiatry 16, 1092–1097.

Boess, F., Lieb, M., Schneider, E., Zimmermann, T., Dodel, R., Belger, M., 2016. Kosten der Alzheimer-Erkrankung in Deutschland – aktuelle Ergebnisse der GERAS-Beobachtungsstudie. Gesundheitsökonomie & Qualitätsmanagement 21, 232–241.

Bond, M., Rogers, G., Peters, J., Anderson, R., Hoyle, M., Miners, A., Moxham, T., Davis, S., Thokala, P., Wailoo, A., Jeffreys, M., Hyde, C., 2012. The effectiveness and cost-effectiveness of donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review of Technology Appraisal No. 111): a systematic review and economic model. Health Technol. Assess. 16, 1–470.

Cao, Q., Tan, C.C., Xu, W., Hu, H., Cao, X.P., Dong, Q., Tan, L., Yu, J.T., 2020. The Prevalence of Dementia: A Systematic Review and Meta-Analysis. J. Alzheimers Dis. 73, 1157–1166.

Chiao, C.Y., Wu, H.S., Hsiao, C.Y., 2015. Caregiver burden for informal caregivers of patients with dementia: A systematic review. Int. Nurs. Rev. 62, 340–350.

Connolly, M.P., Kotsopoulos, N., Postma, M.J., Bhatt, A., 2017. The Fiscal Consequences Attributed to Changes in Morbidity and Mortality Linked to Investments in Health Care: A Government Perspective Analytic Framework. Value Health 20, 273–277.

Curtis, L., Burns, A 2017. Unit Costs of Health and Social Care 2017. *Kent Academic Repository*.

Curtis, L., Burns, A 2020. Unit Costs of Health & Social Care 2020. *Kent Academic Repository*.

Drummond, M. F., Sculpher, M. J., Claxton, K., Stoddart, G. L. & Torrance, G. W. 2015. *Methods for the Economic Evaluation of Health Care Programmes,* Great Clarendon Street, Oxford, OX2 6DP.

DSU 2014. NICE DSU Technical support document 15: Cost-effectiveness modelling using patient-level simulation.

DWP, D. F. W. A. P. 2021c. *Employment and Support Allowance due to Diseases of the Nervous System* [Online]. Available: https://stat-xplore.dwp.gov.uk/webapi/jsf/tableView/tableView.xhtml# [Accessed 10/11/2021 2021].

DWP, D. F. W. A. P. 2021a. *Attendance Allowance due to Dementia* [Online]. Available: https://stat-xplore.dwp.gov.uk/webapi/jsf/tableView/tableView.xhtml [Accessed 10/11/2021 2021].

DWP, D. F. W. A. P. 2021b. *Carer's Allowance* [Online]. Available: https://stat-xplore.dwp.gov.uk/webapi/jsf/tableView/tableView.xhtml [Accessed 10/11/2021 2021].

DWP, D. F. W. A. P. 2021d. *Personal Independence Payment Cases with Entitlement due to Dementia - Daily living award* [Online]. Available: https://stat-xplore.dwp.gov.uk/webapi/jsf/tableView/tableView.xhtml [Accessed 10/15/2021 2021].

DWP, D. F. W. A. P. 2021e. *Personal Independence Payment Cases with Entitlement due to Dementia - Mobility award* [Online]. Available: https://stat-xplore.dwp.gov.uk/webapi/jsf/tableView/tableView.xhtml [Accessed 10/15/2021 2021].

Eftychios, A., Nektarios, S., Nikoleta, G., 2021. Alzheimer Disease and Music-Therapy: An Interesting Therapeutic Challenge and Proposal. Adv. Alzheimer's Disease 10, 1–18.

El-Hayek, Y.H., Wiley, R.E., Khoury, C.P., Daya, R.P., Ballard, C., Evans, A.R., Karran, M., Molinuevo, J.L., Norton, M., Atri, A., 2019. Tip of the Iceberg: Assessing the Global Socioeconomic Costs of Alzheimer's Disease and Related Dementias and Strategic Implications for Stakeholders. J. Alzheimer's Dis. : JAD 70, 323–341.

European Central Bank. 2022. *Euro foreign exchange reference rates, Euros to Sterling 01/01/2018 to 31/12/2018* [Online]. Available: https://www.ecb.europa.eu/stats/policy_and_exchange_rates/euro_reference_exchange_rates/html/eurofxref-graph-gbp.en.html [Accessed 07/09/2022].

Folstein, M., Folstein, S., McHugh, P., 1975. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 12, 189–198.

Getsios, D., Blume, S., Ishak, K.J., Maclaine, G.D., 2010. Cost effectiveness of donepezil in the treatment of mild to moderate Alzheimer's disease: A UK evaluation using discrete-event simulation. Pharmacoeconomics 28, 411–427.

Green, C., Handels, R., Gustavsson, A., Wimo, A., Winblad, B., Sköldunger, A., Jönsson, L., 2019. Assessing cost-effectiveness of early intervention in Alzheimer's disease: An open-source modeling framework. Alzheimers Dement 15, 1309–1321.

Green, C., Zhang, S., 2016. Predicting the progression of Alzheimer's disease dementia: A multidomain health policy model. Alzheimer's & Dementia 12, 776–785.

Kließ, M.K., Martins, R., Connolly, M.P., 2021. Major Cost Drivers in Assessing the Economic Burden of Alzheimer's Disease: A Structured, Rapid Review. J. Prevent. Alzheimer's Dis.

Knapp, M., Chua, K.C., Broadbent, M., Chang, C.K., Fernandez, J.L., Milea, D., Romeo, R., Lovestone, S., Spencer, M., Thompson, G., Stewart, R., Hayes, R.D., 2016. Predictors of care home and hospital admissions and their costs for older people with

Alzheimer's disease: findings from a large London case register. BMJ Open 6, e013591.

Knopman, D.S., Gottesman, R.F., Sharrett, A.R., Wruck, L.M., Windham, B.G., Coker, L., Schneider, A.L., Hengrui, S., Alonso, A., Coresh, J., Albert, M.S., Mosley, T.H., 2016. Mild Cognitive Impairment and Dementia Prevalence: The Atherosclerosis Risk in Communities Neurocognitive Study (ARIC-NCS). Alzheimers Dement (Amst) 2, 1–11.

Kotsopoulos, N., Connolly, M.P., 2014. Is the gap between micro- and macroeconomic assessments in health care well understood? The case of vaccination and potential remedies. Journal of Market Access & Health Policy 2, 23897.

Leicht, H., Heinrich, S., Heider, D., Bachmann, C., Bickel, H., van den Bussche, H., Fuchs, A., Luppa, M., Maier, W., Mosch, E., Pentzek, M., Rieder-Heller, S.G., Tebarth, F., Werle, J., Weyerer, S., Wiese, B., Zimmermann, T., Konig, H.H., Agecode Study, G., 2011. Net costs of dementia by disease stage. Acta Psychiatr. Scand. 124, 384–395.

Lenox-Smith, A., Reed, C., Lebrec, J., Belger, M., Jones, R.W., 2016. Resource utilisation, costs and clinical outcomes in non-institutionalised patients with Alzheimer's disease: 18-month UK results from the GERAS observational study. BMC Geriatr 16, 195.

Lilly, M.B., Laporte, A., Coyte, P.C., 2010. Do they care too much to work? The influence of caregiving intensity on the labour force participation of unpaid caregivers in Canada. J Health Econ 29, 895–903.

Lin GA, Whittington MD, Synnott PG, Mckenna A, Campbell J, Pearson SD & DM, R. 2021. *Aducanumab for Alzheimer's Disease: Effectiveness and Value; ; Draft Evidence Report.* [Online]. Institute for Clinical and Economic Review. Available: https://icer.org/wp-content/uploads/2020/10/ICER_ALZ_Draft_Evidence_Report_050521.pdf [Accessed 05/08/2021].

Lowin, A., Knapp, M., McCrone, P., 2001. Alzheimer's disease in the UK: comparative evidence on cost of illness and volume of health services research funding. Int J Geriatr Psychiatry 16, 1143–1148.

Maresova, P., Dolejs, J., Mohelska, H., Bryan, L.K., 2019. Cost of Treatment and Care for People with Alzheimer's Disease: A Meta- Analysis. Curr. Alzheimer Res. 16, 1245–1253.

Martins, R., Kotsopoulos, N., Michalowsky, B., Pemberton-Ross, P., Urbich, M., Connolly, M., 2022. Economic evaluation of the fiscal costs and consequences of Alzheimer's disease in Germany: Microsimulation of patients' and caregivers' pathways. *J Prev Alzheimers Dis,* under review 1–11.

Michaud, P.-C., Heitmueller, A., Nazarov, Z., 2010. A dynamic analysis of informal care and employment in England. Labour Economics 17, 455–465.

Moodley, K., Minati, L., Contarino, V., Prioni, S., Wood, R., Cooper, R., D'Incerti, L., Tagliavini, F., Chan, D., 2015. Diagnostic differentiation of mild cognitive impairment due to Alzheimer's disease using a hippocampus-dependent test of spatial memory. Hippocampus 25, 939–951.

NHS England. 2021. *Dementia* [Online]. Available: https://www.england.nhs.uk/mental-health/dementia/ [Accessed 12/10/2021 2021].

NICE. 2022. *NICE health technology evaluations: the manual* [Online]. Available: www.nice.org.uk/process/pmg36 [Accessed].

Nichols, E., Szoeke, C.E.I., Vollset, S.E., Abbasi, N., 2019. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 18, 88–106.

Niu, H., Álvarez-Álvarez, I., Guillén-Grima, F., Aguinaga-Ontoso, I., 2017. Prevalence and incidence of Alzheimer's disease in Europe: A meta-analysis. Neurología (English Edition) 32, 523–532.

OECD 2021. Taxing Wages 2021 - The United Kingdom.

ONS. 2021a. *Pensions by age (bands and single year) by Quarter by Mean of Weekly Amount of Benefit* [Online]. Available: https://stat-xplore.dwp.gov.uk/webapi/jsf/tableView/tableView.xhtml [Accessed 01/07/2022].

ONS. 2022. *National Population projections by single year of age* [Online]. NOMIS. Available: https://www.nomisweb.co.uk/datasets/ppsyoa [Accessed 01/07/2022].

ONS, O. F. N. S. 2014. *Changes in the Older Resident Care Home Population between 2001 and 2011* [Online]. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/ageing/articles/changesintheolderresidentcarehomepopulationbetween2001and2011/2014-08-01 [Accessed 12/07/2021 2021].

ONS, O. F. N. S. 2021f. *Taxes as a percentage of gross income, disposable income and expenditure for all individuals, 2019/20* [Online]. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/personalandhouseholdfinances/incomeandwealth/datasets/theeffectsoftaxesandbenefitsonhouseholdincomefinancialyearending2014 [Accessed 10/08/2021].

ONS, O. F. N. S. 2021b. *Annual population survey - regional - labour market status by age* [Online]. Available: https://www.nomisweb.co.uk/datasets/aps170 [Accessed 10/07/2021 2021].

ONS, O. F. N. S. 2021c. *Disability-free prevalence rates and disability-free life expectancy by method, sex, geographical area and period* [Online]. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandlifeexpectancies/datasets/disabilityfreeprevalenceratesanddisabilityfreelifeexpectancybymethodsexgeographicalareaandperiod [Accessed 10/04/2021 2021].

ONS, O. F. N. S. 2021d. *Earnings - Annual pay per age group (Table 6.7a)* [Online]. Available: https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/datasets/agegroupashetable6 [Accessed 11/05/2021 2021].

ONS, O. F. N. S. 2021e. *National life tables: UK, based on data for the years 2018-2020* [Online]. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/nationallifetablesunitedkingdomreferencetables [Accessed 10/07/2021 2021].

Petersen, R.C., Smith, G.E., Waring, S.C., Ivnik, R.J., Tangalos, E.G., Kokmen, E., 1999. Mild cognitive impairment: clinical characterization and outcome. Arch. Neurol. 56, 303–308.

Petersen, R.C., Lopez, O., Armstrong, M.J., Getchius, T.S.D., Ganguli, M., Gloss, D., Gronseth, G.S., Marson, D., Pringsheim, T., Day, G.S., Sager, M., Stevens, J., Rae-Grant, A., 2018. Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology 90, 126–135.

Prince, M., Knapp, M, Guerchet, M, Mccrone, P, Prina, M, Comas-Herrera, A, Wittenberg, R, Adelaja, B, Hu, B, king, D, Rehill, A and Salimkumar, D. 2014. Dementia UK Update.

Prince, M., Wimo, A., Guerchet, M., Ali, G.C., Wu, Y.T., Prina, M., 2015. World Alzheimer Report 2015 - The Global impact of Dementia - Analysis of prevalence, incidence, costs and trends. Alzheimer's disease International.

Reed, C., Belger, M., Vellas, B., Andrews, J.S., Argimon, J.M., Bruno, G., Dodel, R., Jones, R.W., Wimo, A., Haro, J.M., 2016. Identifying factors of activities of daily living important for cost and caregiver outcomes in Alzheimer's disease. Int. Psychogeriatr. 28, 247–259.

Reed, C., Happich, M., Argimon, J.M., Haro, J.M., Wimo, A., Bruno, G., Dodel, R., Jones, R.W., Vellas, B., Belger, M., 2017. What Drives Country Differences in Cost of Alzheimer's Disease? An Explanation from Resource Use in the GERAS Study. J. Alzheimers Dis. 57, 797–812.

Robinson, R.L., Rentz, D.M., Andrews, J.S., Zagar, A., Kim, Y., Bruemmer, V., Schwartz, R.L., Ye, W., Fillit, H.M., 2020. Costs of Early Stage Alzheimer's Disease in the United States: Cross-Sectional Analysis of a Prospective Cohort Study (GERAS-US)1. J. Alzheimers Dis. 75, 437–450.

Sakata, N., Okumura, Y., 2017. Job Loss After Diagnosis of Early-Onset Dementia: A Matched Cohort Study. J. Alzheimers Dis. 60, 1231–1235.

Santabarbara, J., Gracia-Garcia, P., Pirez, G., Lopez-Anton, R., de la Camara, C., Ventura, T., Perez-Sastre, M., Lobo, E., Saz, P., Marcos, G., Lobo, A., 2016. Mortality in Mild Cognitive Impairment Diagnosed with DSM-5 Criteria and with Petersen's Criteria: A 17-Year Follow-Up in a Community Study. Am J Geriatr Psychiatry 24, 977–986.

Siebert, U., Alagoz, O., Bayoumi, A.M., Jahn, B., Owens, D.K., Cohen, D.J., Kuntz, K.M., 2012. State-transition modeling: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force–3. Value Health 15, 812–820.

Silvaggi, F., Leonardi, M., Tiraboschi, P., Muscio, C., Toppo, C., Raggi, A., 2020. Keeping People with Dementia or Mild Cognitive Impairment in Employment: A Literature Review on Its Determinants. Int. J. Environ. Res. Public Health 17, 842.

Speiser, A., 2021. Back to work: the effect of a long-term career interruption on subsequent wages in Switzerland. Swiss J. Econ. Stat. 157.

UK Government. 2021a. *Benefits and financial support if you're caring for someone* [Online]. Available: https://www.gov.uk/browse/benefits/help-for-carers [Accessed 12/02/2021 2021].

UK Government. 2021b. *Benefits and financial support if you're disabled or have a health condition* [Online]. Available: https://www.gov.uk/browse/benefits/disability [Accessed 12/02/2021 2021].

van Maurik, I.S., Rhodius-Meester, H.F.M., Teunissen, C.E., Scheltens, P., Barkhof, F., Palmqvist, S., Hansson, O., van der Flier, W.M., Berkhof, J., 2021. Biomarker testing in MCI patients-deciding who to test. Alzheimers Res Ther 13, 14.

Vermunt, L., Sikkes, S.A.M., van den Hout, A., Handels, R., 2019. Duration of preclinical, prodromal, and dementia stages of Alzheimer's disease in relation to age, sex, and APOE genotype. Alzheimers Dement 15, 888–898.

Wimo, A., Reed, C.C., Dodel, R., Belger, M., Jones, R.W., Happich, M., Argimon, J.M., Bruno, G., Novick, D., Vellas, B., Haro, J.M., 2013. The GERAS Study: A Prospective Observational Study of Costs and Resource Use in Community Dwellers with Alzheimer's Disease in Three European Countries – Study Design and Baseline Findings. J. Alzheimers Dis. 36, 385–399.

Winblad, B., Gauthier, S., Scinto, L., Feldman, H., Wilcock, G.K., Truyen, L., Mayorga, A. J., Wang, D., Brashear, H.R., Nye, J.S., 2008. Safety and efficacy of galantamine in subjects with mild cognitive impairmentGraphic. Neurology 70, 2024–2035.

Wittenberg, R., Hu, B., Barraza-Araiza, L. & Rehill, A. 2019a. Projections of older people with dementia and costs of dementia care in the United Kingdom, 2019–2040. *Care Policy and Evaluation Centre, London School of Economics and Political Science,* CPEC Working Paper 5.

Wittenberg, R., Knapp, M., Hu, B., Comas-Herrera, A., King, D., Rehill, A., Shi, C., Banerjee, S., Patel, A., Jagger, C., Kingston, A., 2019. The costs of dementia in England. Int. J. Geriatr. Psychiatry 34, 1095–1103.