# Supplemental Materials

## Prevalence of MCI-AD

**Table 1**: Prevalence of mild cognitive impairment from any cause, by age category

|  |  |  |
| --- | --- | --- |
| **Age categories** | **Prevalence of MCI**  | **Source** |
| 80+ | 25.2% | (1) |
| 75 to 79 | 14.8% |
| 70 to 74 | 10.1% |
| 65 to 69 | 8.4% |
| 60 to 64 | 6.7% |

MCI, Mild cognitive impairment

**Table 2**: Calculated prevalence figures for people aged 65 and above receiving a diagnosis of MCI-AD, per country

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|   | **2022** | **2030** | **2040** | **2050** | **2060** | **2070** | **2080** | **2090** | **2100** |
| **Germany** |  2,088,290  |  2,361,180  |  2,731,099  |  2,952,428  |  2,878,112  |  2,954,620  |  3,031,635  |  3,097,274  |  3,240,576  |
| **UK** |  1,378,895  |  1,711,098  |  1,998,191  |  2,234,254  |  2,366,972  |  2,508,977  |  2,671,675  |  2,810,482  |  2,967,131  |
| **France** |  1,540,055  |  1,899,539  |  2,257,808  |  2,439,217  |  2,515,342  |  2,571,602  |  2,639,821  |  2,735,653  |  2,801,655  |
| **Italy** |  1,609,897  |  1,870,185  |  2,213,099  |  2,481,282  |  2,462,315  |  2,316,836  |  2,317,950  |  2,350,903  |  2,312,022  |
| **Spain** |  1,058,023  |  1,313,766  |  1,659,931  |  1,980,875  |  2,083,951  |  1,978,852  |  1,934,512  |  1,993,244  |  2,003,166  |
| **Sweden** |  225,496  |  277,868  |  313,822  |  350,592  |  392,265  |  431,142  |  467,566  |  495,273  |  525,841  |
| **Canada \*** |  722,230  |  1,023,190  |  1,274,456  |  1,407,560  |  1,533,389  |  1,727,445  |  1,899,293  |  2,014,206  |  2,158,173  |
| **US \*** |  5,774,579  |  7,772,714  |  9,522,764  |  10,419,007  |  11,354,438  |  12,775,042  |  14,069,318  |  14,863,375  |  15,584,140  |

MCI-AD, Mild cognitive impairment due to Alzheimer’s disease, UK, United Kingdom; US, United States of America.

\* In addition to the results included in the main manuscript, further analyses were conducted for Canada and the US which were included as Supplemental Materials for the interested reader. The authors were not able to identify publications reporting population projections by single year of age to 2100 for Canada and the US. Population projections up to 2100 for broad age categories (5-year age categories) were sourced from (2). Single year frequencies were derived using weights calculated from population projections by single year of age available for Canada up to 2068 (3) and the US up to 2060 (4).

The prevalence of MCI was calculated by multiplying the number of individuals aged 65 and older by the country and age specific prevalence figures reported by Petersen and colleagues (1). The resulting values were multiplied by 75% to reflect the number of MCI cases that are due to Alzheimer’s disease (5).

## Model inputs

**Table 3:** Mean model inputs and sources of evidence

|  |  |  |
| --- | --- | --- |
| **Input description** | **Mean input** | **Source** |
| **Demographic characteristics** |  |  |
| Age (years) | 65 | Assumption |
| Males (%) | 50% | Assumption |
| **Natural history** |  |  |
| From MCI-AD to AD-dementia (annual transition probabilities) |
| Year 0 to 1 | 0.190 | (6) |
| Year 1 to 2 | 0.140 |
| Year 2 to 3 | 0.120 |
| Year 3 to 4 | 0.110 |
| Year 4 to 5 | 0.110 |
| Year 5 to 6 | 0.100 |
| Year 6 to 7 | 0.100 |
| Year 7 to 8 | 0.100 |
| Year 8 to 9 | 0.090 |
| Year 9 to 10 | 0.090 |
| Landing spot  |   |   |
| Mild AD  | 72.5% | (6) |
| Moderate AD | 26.7% |
| Severe AD | 0.8% |
| **AD-dementia progression** |   |   |
| From mild AD to: |   | (7) |
| MCI-AD | 0 |
| Moderate AD | 0.293 |
| Severe AD | 0.001 |
| From moderate AD to:  |   |
| MCI-AD | 0 |
| Mild AD | 0.087 |
| Severe AD | 0.109 |
| From severe AD to:  |   |
| MCI-AD | 0 |
| Mild AD | 0 |
| Moderate AD | 0.196 |
| **Probability of institutionalization by AD severity** |   |
| MCI-AD | 0.017 | (8) |
| Mild AD  | 0.043 |
| Moderate AD | 0.116 |
| Severe AD | 0.432 |
| **Mortality** |   |   |
| MCI-AD (HR) | 1.200 | (9) |
| Mild AD (HR) | 2.920 | (10) |
| Moderate AD (HR) | 3.850 |
| Severe AD (HR) | 9.520 |

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

**Table 4:** Cost inputs identified through a targeted literature review, disaggregated by AD severity and type of cost

|  |  |  |  |
| --- | --- | --- | --- |
|   | **France** |   | **Germany** |
| **Type of costs** | **Community** | *Sources* | **Institution** | **Sources** |  | **Community** | *Sources* | **Institution** | *Sources* |
| **Direct medical costs**  |   |   |   |   |   |   |   |   |
| MCI-AD | € 4,648 | ‡ | € 2,435 | \* |   | € 4,577 | ‡ | € 4,977 | \* |
| Mild AD | € 5,453 | (11) | € 2,435 | (11) |   | € 5,369 | (11) | € 4,977 | (11) |
| Moderate AD | € 11,922 | € 9,882 |   | € 6,728 | € 6,558 |
| Severe AD | € 12,089 | € 2,580 |   | € 15,343 | € 7,132 |
| **Direct non-medical costs** |   |   |   |   |   |   |   |   |
| MCI-AD | € 6,701 | ‡ | € 64,714 | \* |   | € 5,322 | ‡ | € 61,760 | \* |
| Mild AD | € 12,400 | (11) | € 64,714 | (11) |   | € 9,848 | (11) | € 61,760 | (11) |
| Moderate AD | € 13,799 | € 64,631 |   | € 16,290 | € 61,745 |
| Severe AD | € 19,981 | € 64,607 |   | € 15,467 | € 62,226 |
| **Informal care costs**  |   |   |   |   |   |   |   |   |
| MCI-AD | € 4,187 | ‡ | € 4,054 | \* |   | € 6,247 | ‡ | € 4,780 | \* |
| Mild AD | € 9,255 | (11) | € 4,054 | || |   | € 13,808 | (11) | € 4,780 | || |
| Moderate AD | € 10,714 | € 4,054 |   | € 19,386 | € 4,780 |
| Severe AD | € 10,941 | € 4,054 |   | € 23,697 | € 4,780 |
|   |   |   |   |   |   |   |   |   |   |
|   | **Italy** |   | **Spain** |
| **Type of costs** | **Community** | *Sources* | **Institution** | *Sources* |  | **Community** | *Sources* | **Institution** | *Sources* |
| **Direct medical costs**  |   |   |   |   |   |   |   |   |
| MCI-AD | € 2,274 | ‡ | € 2,967 | \* |   | € 1,587 | (12) | € 3,467 | \* |
| Mild AD | € 2,667 | (13) | € 2,967 | † |   | € 3,117 | (11) | € 3,467 | (11) |
| Moderate AD | € 1,651 | € 4,925 |   | € 2,361 | € 7,043 |
| Severe AD | € 1,346 | € 4,890 |   | € 1,943 | € 7,056 |
| **Direct non-medical costs** |   |   |   |   |   |   |   |   |
| MCI-AD | € 1,853 | ‡ | € 46,889 | \* |   | € 4,121 | (12) | € 37,601 | \* |
| Mild AD | € 3,429 | (13) | € 46,889 | (14) |   | € 6,071 | (11) | € 37,601 | (11) |
| Moderate AD | € 2,527 | € 46,889 |   | € 6,257 | € 37,609 |
| Severe AD | € 5,068 | € 46,889 |   | € 12,074 | € 37,601 |
| **Informal care costs**  |   |   |   |   |   |   |   |   |
| MCI-AD | € 7,872 | ‡ | € 3,359 | \* |   | € 5,774 | (12) | € 1,401 | \* |
| Mild AD | € 17,400 | (13) | € 3,359 | || |   | € 12,763 | (11) | € 1,401 | § |
| Moderate AD | € 15,533 | € 3,359 |   | € 17,539 | € 3,810 | (15) |
| Severe AD | € 28,234 | € 3,359 |   | € 19,549 | € 4,383 |

|  |  |  |  |
| --- | --- | --- | --- |
|   | **Sweden** |   | **UK** |
| **Type of costs** | **Community** | *Sources* | **Institution** | *Sources* |  | **Community** | *Sources* | **Institution** | *Sources* |
| **Direct medical costs**  |   |   |   |   |   |   |   |   |
| MCI-AD | € 962 | ‡ | € 1,588 | \* |   | € 3,196 | ‡ | € 6,138 | \* |
| Mild AD | € 1,129 | (11) | € 1,588 | (11) |   | € 3,749 | (16) | € 6,138 | (16) |
| Moderate AD | € 1,562 | € 2,428 |   | € 3,673 | € 12,862 |
| Severe AD | € 1,930 | € 3,255 |   | € 15,343 | € 11,841 |
| **Direct non-medical costs** |   |   |   |   |   |   |   |   |
| MCI-AD | € 7,228 | ‡ | € 74,353 | \* |   | € 3,317 | ‡ | € 33,712 | \* |
| Mild AD | € 13,376 | (11) | € 74,353 | (11) |   | € 4,253 | (16) | € 33,712 | (16) |
| Moderate AD | € 14,427 | € 74,369 |   | € 10,592 | € 35,045 |
| Severe AD | € 12,797 | € 74,387 |   | € 14,066 | € 35,261 |
| **Informal care costs**  |   |   |   |   |   |   |   |   |
| MCI-AD | € 4,430 | ‡ | € 403 | \* |   | € 12,155 | ‡ | € 1,454 | \* |
| Mild AD | € 9,793 | (11) | € 403 | § |   | € 26,866 | (16) | € 1,454 | (16) |
| Moderate AD | € 12,589 | € 1,096 | (15) |   | € 43,933 | € 3,954 |
| Severe AD | € 20,019 | € 1,022 |   | € 45,630 | € 2,888 |
|   |   |   |   |   |   |   |   |   |   |
|   | **Canada\*\*** |   | **US\*\*** |
| **Type of costs** | **Community** | *Sources* | **Institution** | *Sources* |  | **Community** | *Sources* | **Institution** | *Sources* |
| **Direct medical costs**  |   |   |   |   |   |   |   |   |
| MCI-AD | € 4,383 | ‡ | € 27,098 | \* |   | € 6,024 | \* | € 7,789 | \* |
| Mild AD | € 5,141 | (17) | € 27,098 | (18) |   | € 7,067 | (15) | € 9,137 | # |
| Moderate AD | € 4,285 | € 27,098 |   | € 6,904 | € 8,926 | (15) |
| Severe AD | € 5,998 | € 27,098 |   | € 6,579 | € 8,996 |
| **Direct non-medical costs** |   |   |   |   |   |   |   |   |
| MCI-AD | € 309 | ‡ | € 47,139 | \* |   | € 1,909 | ‡ | € 95,703 | \* |
| Mild AD | € 571 | (17) | € 47,139 | (19) { |   | € 3,533 | (15) | € 95,703 | # |
| Moderate AD | € 3,570 | € 47,139 |   | € 3,812 | € 95,703 | (15) |
| Severe AD | € 10,854 | € 47,139 |   | € 5,300 | € 98,492 |
| **Informal care costs**  |   |   |   |   |   |   |   |   |
| MCI-AD | € 4,394 | ‡ | € 4,922 | \* |   | € 6,625 | ‡ | € 3,542 | \* |
| Mild AD | € 9,712 | (17) | € 4,922 | || |   | € 14,645 | (15) | € 7,828 | # |
| Moderate AD | € 19,709 | € 4,922 |   | € 19,178 | € 10,251 | (15) |
| Severe AD | € 19,995 | € 4,922 |   | € 27,151 | € 8,833 |

Sources: (11–21)

AD, Alzheimer’s disease; MCI-AD, mild cognitive impairment due to AD; RAMQ, Régie de l’Assurance Maladie du Québec.

\* Cost assumed to be the same as for a person with mild AD who was institutionalized.

† Direct medical costs for community-based individuals with mild AD, moderate AD and severe AD in Italy were 14.42%, 30.07% and 30.70% lower than for their counterparties in Spain. We have used these values to extrapolate direct medical care costs for institutionalized people in Italy based on direct medical costs for institutionalized people in Spain (11).

‡ Calculated from costs for people with mild AD for the same country and cost category by extrapolating from Robinson 2020 (21). Robinson et al. reported that people with MCI-AD had 14.75%, 45.96% and 54.76% lower direct medical, direct non-medical and informal care costs than people with mild AD, respectively.

§ Calculated from informal care costs in people with moderate AD in an institutionalized setting by extrapolating from Prince et al. (2014). Prince reported informal care costs for people with mild AD to be 63.22% lower than for people with moderate AD who were also institutionalized.

|| Assumed that informal carers would visit relatives for 3 hours a week, over 52 weeks. Each hour was valued using country-specific average hourly wages (22).

{ Calculated using average accommodation fee rates for individual, 2 -bed and 3-bed rooms (19).

# Calculated based on values for US individuals with the same AD severity in the community. People with mild AD were associated with 2.31% and 7.32% lower direct medical and direct non-medical costs than people with moderate AD, respectively.

\*\* Model structure used to also produce results for the US and Canada.

## Disaggregated results

**Figure 1:** Three scenarios assessing the impact of Hypothetical DMT on the present value of the lifetime AD-related costs for a cohort aged 65 and over with prevalent MCI-AD in 2022 for France (A), Germany (B), Italy (C), Spain (D), Sweden (E), and the UK (F).

**A) France**

**D) Spain**

**E) Sweden**

## Additional analyses

The existing framework and model structure was utilized to expand the analysis to Canada and the US. The additional data inputs utilized for these countries were described below.

For inflation and currency conversion, we have used Canadian (23, 24) and US (25, 26) publicly available sources, respectively. Country official lifetables were obtained from Statistics Canada (27) and the work published by Arias & Xu, 2020 (28).

The input informing AD-related direct medical, direct non-medical and indirect costs are summarized in Table 3.

**Figure 2:** Three scenarios assessing the impact of a Hypothetical DMT (25% and 50% reduction in progression) and potential lifestyle-based interventions (3 year delay in progression) on the present value of the lifetime AD-related costs for a cohort aged 65 and over with prevalent MCI-AD in 2022 for Canada (A) and the USA (B).

**B) USA**

## References for Supplemental Materials

1. Petersen RC, Lopez O, Armstrong MJ, et al. Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology 2018;90:126-35.

2. United Nations. World Population Prospects 2019 - Population Dynamics. Affairs D of E and S, editor. 2019. Accessed 4 February 2022.

3. Statistics Canada. Projected population, by projection scenario, age and sex, as of July 1 (x 1,000) - Table 17-10-0057-01. 2021. Accessed 21 December 2021.

4. US Census. 2017 National Population Projections Datasets. 2017. Accessed 21, 2021.

5. Knopman DS, Gottesman RF, Sharrett AR, et al. Mild Cognitive Impairment and Dementia Prevalence: The Atherosclerosis Risk in Communities Neurocognitive Study (ARIC-NCS). Alzheimers Dement (Amst) 2016;2:1-11.

6. Green C, Handels R, Gustavsson A, et al. Assessing cost-effectiveness of early intervention in Alzheimer’s disease: An open-source modeling framework. Alzheimers Dement 2019;15:1309-21.

7. Wimo A, Handels R, Winblad B, et al. Quantifying and Describing the Natural History and Costs of Alzheimer’s Disease and Effects of Hypothetical Interventions. J Alzheimers Dis 2020;75:891-902.

8. Davis M, Thomas OC, Johnson S, et al. Estimating Alzheimer’s Disease Progression Rates from Normal Cognition Through Mild Cognitive Impairment and Stages of Dementia. Curr Alzheimer Res 2018;15:777-88.

9. Santabárbara J, Gracia-García P, Pírez G, et al. 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 2016;24:977-86.

10. Andersen K, Lolk A, Martinussen T, Kragh-Sørensen P. Very mild to severe dementia and mortality: A 14-year follow-up - The Odense study. Dement Geriatr Cogn Disord 2010;29:61-7.

11. Wübker A, Zwakhalen SMG, Challis D, et al. Costs of care for people with dementia just before and after nursing home placement: primary data from eight European countries. Eur J Heal Econ 2015;16:689-707.

12. Darbà J, Kaskens L, Lacey L. Relationship between global severity of patients with Alzheimer’s disease and costs of care in Spain; results from the co-dependence study in Spain. Eur J Heal Econ 2015;16:895-905.

13. Bruno G, Mancini M, Bruti G, Dell’Agnello G, Reed C. Costs and Resource Use Associated with Alzheimer’s Disease in Italy: Results from an Observational Study. J Prev Alzheimer’s Dis 2018;5.

14. Pasaresi Franco [TBC by Biogen]. Tariffa giornaliera. 2019. Accessed 20 December 2021.

15. Gustavsson A, Brinck P, Bergvall N, et al. Predictors of costs of care in Alzheimer’s disease: A multinational sample of 1222 patients. Alzheimer’s Dement 2011;7:318-27.

16. Prince M, Knapp M, Guerchet M, et al. Dementia UK Update. 2014; Accessed 4 February 2022.

17. Herrmann N, Tam DY, Balshaw R, Sambrook R, Lesnikova N, Lanctôt KL. The relation between disease severity and cost of caring for patients with Alzheimer disease in Canada. Can J Psychiatry 2010;55:768-75.

18. Ministry of Health and Long-term Care. LTCH Level-of-Care Per Diem Funding Summary. 2019. Accessed 4 February 2022.

19. RAMQ. Accommodation in a public facility. 2021. Accessed 14 December 2021.

20. Robinson RL, Rentz DM, Andrews JS, et al. 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 2020;75:437-50.

21. Leibson CL, Long KH, Ransom JE, et al. Direct medical costs and source of cost differences across the spectrum of cognitive decline: a population-based study. Alzheimers Dement 2015;11:917-32.

22. OECD. Average annual wages. 2021. Accessed 14 December 2021.

23. Statistics Canada. Consumer Price Index, annual average, not seasonally adjusted. 2021. Accessed 25 January 2022.

24. Bank of Canada. Currency Converter, Daily Exchange Rates Lookup (Canadia dollars to Euros). 2021. Accessed 13 December 2021.

25. US Bureau of Labor Statistics. All urban consumers CPI-U, Medical care. 2021. Accessed 25 January 2022.

26. Bank of America. Currency Calculator: Rates for Ordering Foreign Currency (US dollars to Euros). 2021. Accessed 13 December 2021.

27. Statistics Canada. Life Tables, Canada, Provinces and Territories, 1980/1982 to 2017/2019. 2021.. Accessed 27 October 2021.

28. Arias E, Xu J. United States Life Tables, 2018. Rep NVS, editor. Natl Vital Stat Rep; 2020. Accessed 20 December 2021.