# 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**

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