

Supplementary Material

Heterogeneity in Reports of Dementia Disease Duration and Severity: A Review of the Literature

Supplementary Table 1. Severity stage duration and total disease duration estimates, sensitivity analysis stratifying by dementia type, study setting (clinical versus population-based) and continent of data collection.

Sensitivity Analysis

| | Articles (n) | Estimates (n) | Stage duration (weighted average, y) | Q-statistic |
|-------------------------------------------|-----------------|------------------|--------------------------------------------|-------------|
| Severity Stage Duration | 15 | 42 | | |
| Severity stage onset to Conversion | 8 | 21 | | |
| MCI/very mild dementia | 8 | 11 | 3.11 | 2.29 |
| Mild | 2 | 4 | 3.32 | 0.39 |
| Moderate | 2 | 4 | 1.99 | 0.42 |
| Severe | 1 | 2 | 1.30 | 0.64 |
| Alzheimer's disease | | | | |
| MCI/very mild dementia | 7 | 9 | 3.74 | 0.82 |
| Mild | 1 | 2 | 3.65 | 0.02 |
| Moderate | 1 | 2 | 2.20 | 0.36 |
| Mixed dementia | | | | |
| MCI/very mild dementia | 1 | 2 | 0.55 | 0.00 |
| Mild | 1 | 2 | 2.25 | 0.06 |
| Moderate | 1 | 2 | 1.30 | 0.00 |
| Severe | 1 | 2 | 1.30 | 0.64 |
| America | | | | |
| MCI/very mild dementia | 3 | 5 | 4.03 | 0.38 |
| Mild | 1 | 2 | 3.65 | 0.02 |
| Moderate | 1 | 2 | 2.20 | 0.36 |
| Europe | | | | |
| MCI/very mild dementia | 6 | 8 | 3.15 | 2.31 |
| Mild | 2 | 4 | 3.32 | 0.39 |
| Moderate | 2 | 4 | 1.99 | 0.42 |
| Severe | 1 | 2 | 1.30 | 0.64 |
| Clinical | | | | |
| MCI/very mild dementia | 7 | 9 | 3.74 | 0.82 |
| Mild | 1 | 2 | 3.65 | 0.02 |
| Moderate | 1 | 2 | 2.20 | 0.36 |

| | | | | |
|--------------------------------------------------------------------------------------|----|-----|------|------|
| Population-based | | | | |
| MCI/very mild dementia | 2 | 4 | 3.30 | 2.44 |
| Mild | 2 | 4 | 3.32 | 0.39 |
| Moderate | 2 | 4 | 1.99 | 0.42 |
| Severe | 1 | 2 | 1.30 | 0.64 |
| Overall disease onset to study entry (clinical) | 5 | 15 | | |
| MCI/very mild dementia | 5 | 5 | 2.27 | 0.25 |
| Mild | 4 | 4 | 2.96 | 0.89 |
| Moderate | 4 | 4 | 4.90 | 0.83 |
| Severe | 2 | 2 | 8.94 | 1.19 |
| Alzheimer's disease | | | | |
| MCI/very mild dementia | 4 | 4 | 2.32 | 0.21 |
| Mild | 3 | 3 | 3.81 | 0.17 |
| Moderate | 3 | 3 | 4.98 | 0.72 |
| Severe | 2 | 2 | 8.94 | 1.19 |
| Dementia with Lewy bodies | | | | |
| MCI/very mild dementia | 1 | 1 | 1.05 | - |
| Mild | 1 | 1 | 2.08 | - |
| Moderate | 1 | 1 | 3.11 | - |
| Asia | | | | |
| MCI/very mild dementia | 3 | 3 | 1.95 | 0.07 |
| Mild | 3 | 3 | 3.87 | 0.40 |
| Moderate | 3 | 3 | 5.14 | 1.17 |
| Severe | 2 | 2 | 8.94 | 1.19 |
| Europe | | | | |
| MCI/very mild dementia | 2 | 2 | 2.59 | 0.24 |
| Mild | 1 | 1 | 3.50 | - |
| Moderate | 1 | 1 | 4.50 | - |
| Diagnosis to death (Mixed dementia, clinical, America) | 1 | 2 | | |
| MCI/very mild or mild dementia | 1 | 1 | 7.17 | - |
| Moderate to severe | 1 | 1 | 6.58 | - |
| Overall disease onset to death (Frontotemporal dementia, clinical, Europe) | 1 | 4 | | |
| MCI/ very mild dementia | 1 | 1 | 12.5 | - |
| Mild | 1 | 1 | 11.6 | - |
| Moderate | 1 | 1 | 11.8 | - |
| Severe | 1 | 1 | 6.7 | - |
| Disease Duration | 93 | 147 | | |
| Overall disease onset to Diagnosis | 5 | 6 | 2.63 | 1.32 |

| | | | | |
|---------------------------------------------|----|----|-------|-------|
| Alzheimer's disease | 3 | 3 | 2.21 | 0.41 |
| Dementia with Lewy bodies | 2 | 2 | 2.09 | 0.17 |
| Mixed dementia | 1 | 1 | 4.90 | 0.00 |
| Clinical | 4 | 5 | 3.04 | 1.35 |
| Population-based | 1 | 1 | 1.70 | - |
| America | 1 | 1 | 1.7 | - |
| Asia | 1 | 1 | 4.9 | - |
| Europe | 3 | 4 | 2.45 | 0.33 |
| Overall disease onset to study entry | 58 | 78 | 3.03 | 2.19 |
| Alzheimer's disease | 40 | 43 | 3.03 | 2.64 |
| Dementia with Lewy bodies | 9 | 9 | 4.32 | 4.06 |
| Frontotemporal dementia | 8 | 8 | 3.27 | 1.24 |
| Vascular dementia | 1 | 1 | 7.30 | - |
| Mixed dementia | 16 | 17 | 2.78 | 0.68 |
| Clinical | 58 | 70 | 3.03 | 2.39 |
| Population-based | 7 | 8 | 2.97 | 0.61 |
| America | 22 | 27 | 3.25 | 1.56 |
| Asia | 9 | 11 | 4.81 | 9.66 |
| Australia | 1 | 1 | 3.10 | - |
| Europe | 35 | 39 | 2.64 | 0.74 |
| South America | 1 | 1 | 4.60 | - |
| Diagnosis to death | 14 | 38 | 5.12 | 1.53 |
| Alzheimer's disease | 7 | 14 | 6.30 | 1.65 |
| Dementia with Lewy bodies | 4 | 4 | 4.00 | 0.73 |
| Frontotemporal dementia | 1 | 1 | 2.94 | - |
| Vascular dementia | 1 | 2 | 4.65 | 0.00 |
| Mixed dementia | 8 | 17 | 4.90 | 1.33 |
| Clinical | 9 | 28 | 5.55 | 1.23 |
| Population-based | 6 | 10 | 4.10 | 0.76 |
| America | 6 | 6 | 4.11 | 0.39 |
| Asia | 2 | 5 | 8.55 | 12.74 |
| Australia | 1 | 2 | 1.16 | 0.06 |
| Europe | 6 | 25 | 5.52 | 1.16 |
| Overall disease onset to death | 14 | 20 | 6.61 | 3.69 |
| Alzheimer's disease | 7 | 12 | 6.87 | 2.31 |
| Dementia with Lewy bodies | 1 | 1 | 8.80 | - |
| Frontotemporal dementia | 2 | 2 | 10.64 | 5.09 |
| Mixed dementia | 5 | 5 | 4.11 | 1.76 |
| Clinical | 11 | 15 | 8.13 | 4.09 |
| Population-based | 3 | 3 | 5.85 | 0.20 |
| Mixed | 1 | 2 | 4.61 | 2.17 |
| America | 12 | 13 | 6.40 | 2.76 |

| | | | | |
|-----------------------------|---|----|------|------|
| Europe | 7 | 10 | 6.59 | 2.98 |
| Study Entry to death | 2 | 2 | 6.77 | 0.06 |
| Alzheimer's disease | 2 | 2 | 6.77 | 0.06 |
| Clinical/Europe | 1 | 1 | 4.30 | - |
| Population-based/Asia | 1 | 1 | 4.30 | - |

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('dementia'/exp/mj OR (dementia OR Alzheimer*):ti) AND ('survival'/mj OR 'life expectancy'/mj OR 'long term survival'/mj OR 'survival time'/mj OR 'staging'/mj OR (duration* NEAR/6 stage*):ab,ti OR (surviv* OR duration* OR life-expect* OR staging):ti)

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(*dementia/ OR (dementia).ti.) AND (exp Longitudinal Studies/ OR (longitudinal* OR prospectiv* OR retrospectiv*).ti.) AND (((0## OR 1## OR 2## OR 3## OR 4## OR 5## OR 6## OR 7## OR 8## OR 9## OR 1### OR 2### OR 3### OR 4### OR 5### OR 6### OR 7### OR 8### OR 9###) ADJ6 (patients OR patient OR subjects OR individuals OR cases OR persons OR men OR women OR participant* OR people OR elderly OR survivor* OR specimen* OR sample* OR episode* OR isolate* OR pediatric OR paediatric OR adult*)) OR ((hundred* OR thousand*) ADJ6 (patients OR patient OR subjects OR individuals OR cases OR persons OR men OR women OR participant* OR people OR elderly OR survivor* OR specimen* OR sample* OR episode* OR isolate* OR pediatric OR paediatric)) OR ((n OR included OR recruited OR randomized OR randomized OR assigned) ADJ2 (0## OR 1## OR 2## OR 3## OR 4## OR 5## OR 6## OR 7## OR 8## OR 9## OR 1### OR 2### OR 3### OR 4### OR 5### OR 6### OR 7### OR 8### OR 9###)) OR large*-cohort*).ab,ti. AND English.la.
Limit 1 to yr="2011-2020"

Supplementary Table 2. Included articles on severity stage durations (in alphabetical order) and review categories.

Articles on severity stage durations

| Article | Population-based or clinical | Dementia Type | Severity Stages and definitions | Sample size | Country | Duration definition |
|-----------------------------------|------------------------------|---------------|------------------------------------------------------------------------------------------------------------------------------------------|-------------|--------------------------------------------|----------------------|
| An et al., 2016 [1] | clinical | AD | MCI (ADNI*) | 83 | US (ADNI) | Onset to conversion |
| Bessi et al., 2018 [2] | clinical | AD | MCI (NIA-AA criteria for MCI due to AD) | 212 | Italy | Onset to conversion |
| Bruun et al., 2019 [3] | clinical | AD | MCI (MMSE \geq 18, CDR \leq 1 and T1-weighted MRI \geq 1.5 Tesla) | 199 | Europe | Onset to study entry |
| Damian et al., 2013 [4] | clinical | AD | MCI (Subjective Cognitive Impairment) | 485 | European (DESCRIPA) | Onset to conversion |
| Duchesne et al., 2015 [5] | clinical | AD | MCI (ADNI*) | 152 | US (ADNI) | Onset to conversion |
| Eldholm et al., 2018 [6] | clinical | AD | Very mild (CDR 0.5), mild (CDR 1), moderate (CDR 2) | 282 | Norway | Onset to study entry |
| Hsu et al., 2017 [7] | clinical | AD | Very mild (CDR 0.5), mild (CDR 1), moderate (CDR 2), severe (CDR 3) | 322 | Taiwan | Onset to study entry |
| Lichtenstein et al., 2018 [8] | clinical | Mixed | Normal to mild (FRS 8-23), moderate to severe (FRS 24-40) | 168 | Canada | Diagnosis to death |
| Niemantsverdriet et al., 2018 [9] | clinical | AD | MCI (NIA-AA criteria for MCI due to AD) | 379 | Belgium | Onset to conversion |
| Nunemann et al., 2011 [10] | clinical | FTD | Very mild (CDR 0.5), mild (CDR 1), moderate (CDR 2), severe (CDR 3) | 124 | Germany | Onset to death |
| Park et al., 2018 [11] | clinical | LBD | Very mild (CDR 0.5), mild (CDR 1), moderate (CDR 2) | 33 | Korea | Onset to study entry |
| Rizzuto et al., 2012 [12] | population based | Mixed | Very mild (MMSE 24-30), mild (MMSE 18-23), moderate (MMSE 10-17), severe (MMSE 0-9) | 1014 | Sweden | Onset to conversion |
| Van der Mussele et al., 2014 [13] | clinical | AD | MCI (Petersen's diagnostic criteria) | 183 | Belgium | Onset to conversion |
| Vermunt et al., 2019 [14] | mixed | AD | MCI (amyloid accumulation and a diagnosis of MCI, NIA-AA, Petersen's or Winblad criteria), mild (CDR $<$ 2), moderate/severe (CDR $>$ 1) | 3268 | Netherlands, US, Australia, Sweden, Europe | Onset to conversion |

| | | | | | | |
|----------------------------|----------|----|--------------------------------------------------------------------|-----|--------|-------------------------|
| Yazar et al., 2018 [15] | clinical | AD | MCI (CDR 0.5), mild (CDR 1), moderate (CDR2), severe (CDR 3) | 120 | Turkey | Onset to study entry |
|----------------------------|----------|----|--------------------------------------------------------------------|-----|--------|-------------------------|

*ADNI MCI subjects: MMSE scores between 24-30 (inclusive), a memory complaint, have objective memory loss measured by education adjusted scores on Wechsler Memory Scale Logical Memory II, a CDR of 0.5, absence of significant levels of impairment in other cognitive domains, essentially preserved activities of daily living, and an absence of dementia.

Supplementary Table 3. Included articles on disease durations (in alphabetical order) and review categories. (Onset refers to overall disease onset)

Articles on total disease duration

| Article | Population-based or clinical | Dementia Type | Sample size | Country | Duration definition |
|---------------------------------|------------------------------|---------------|-------------|---------------------------------|----------------------|
| Alladi et al., 2013 [16] | clinical | Mixed | 648 | India | Onset to study entry |
| Armstrong et al., 2016 [17] | clinical | FTD | 84 | US and Canada | Onset to death |
| Behrens et al., 2018 [18] | population-based | AD | 202 | US | Onset to study entry |
| Benussi et al., 2020 [19] | clinical | FTD | 122 | Italy | Onset to study entry |
| Berge et al., 2016 [20] | clinical | AD | 69 | Norway | Onset to study entry |
| Bonanni et al., 2016 [21] | clinical | DLB | 236 | Italy | Onset to Diagnosis |
| Breitve et al., 2018 [22] | clinical | AD, DLB | 119 | Norway | Onset to study entry |
| Chiu et al., 2018 [23] | clinical | DLB | 78 | Taiwan | Onset to study entry |
| Coon et al., 2011 [24] | clinical | FTD | 56 | US | Diagnosis to death |
| Davis et al., 2017 [25] | population-based | Mixed | 179 | Australia | Diagnosis to death |
| Di Stefano et al., 2015 [26] | clinical | AD | 73 | France | Onset to study entry |
| Donovan et al., 2014 [27] | clinical | AD | 812 | US | Onset to study entry |
| Dourado et al., 2016 [28] | clinical | AD | 69 | Brazil | Onset to study entry |
| Drenth et al., 2017 [29] | clinical | Mixed | 144 | Netherlands | Onset to study entry |
| Dufouil et al., 2018 [30] | population-based | Mixed | 5205 | US | Diagnosis to death |
| Dyer et al., 2020 [31] | clinical | AD | 464 | Europe | Onset to study entry |
| Elahi et al., 2017 [32] | clinical | AD, FTD | 14 | US | Onset to study entry |
| Eldholm et al., 2018 [6] | clinical | AD | 282 | Norway | Onset to study entry |
| Fritze et al., 2011 [33] | clinical | AD, DLB | 138 | Norway | Onset to study entry |
| Fujisawa et al., 2015 [34] | clinical | AD | 13 | Japan | Diagnosis to death |
| Garn et al., 2015 [35] | clinical | AD | 118 | Austria | Onset to study entry |
| Graff-Radford et al., 2016 [36] | clinical | DLB | 167 | US | Onset to study entry |
| Graff-Radford et al., 2017 [37] | clinical | DLB | 807 | US | Onset to death |
| Hafkemeijer et al., 2017 [38] | clinical | AD, FTD | 20 | Netherlands | Onset to study entry |
| Harrison et al., 2014 [39] | clinical | AD | 196 | US and Europe | Onset to study entry |
| Hsieh et al., 2012 [40] | clinical | AD | 17 | Australia | Onset to study entry |
| Hsu et al., 2017 [7] | clinical | AD | 322 | Taiwan | Onset to study entry |
| Irwin et al., 2013 [41] | clinical | Mixed | 92 | US | Onset to death |
| Irwin et al., 2017 [42] | clinical | Mixed | 164 | US | Onset to death |
| Josephs et al., 2014 [43] | clinical | AD | 1002 | USA, Germany, Japan, Canada, UK | Onset to death |
| Kawas et al., 2015 [44] | population-based | Mixed | 98 | US | Diagnosis to death |
| Koch et al., 2017 [45] | clinical | AD | 41 | Italy | Onset to death |
| Koseoglu et al., 2017 [46] | clinical | AD | 62 | Turkey | Onset to study entry |
| Kosteniuk et al., 2016 [47] | population-based | Mixed | 13012 | Canada | Diagnosis to death |
| Lemstra et al., 2017 [48] | clinical | DLB, Mixed | 42 | Netherlands | Onset to study entry |
| Leoutsakos et al., 2012 [49] | population-based | AD | 335 | US | Onset to study entry |
| Leoutsakos et al., 2015 [50] | population-based | Mixed | 328 | US | Onset to death |
| Liao et al., 2016 [51] | clinical | Mixed | 331 | Netherlands | Onset to study entry |
| Lichtenstein et al., 2018 [8] | clinical | Mixed | 168 | Canada | Diagnosis to death |
| Liew et al., 2019 [52] | clinical | Mixed | 183 | Singapore | Onset to Diagnosis |
| Lorius et al., 2015 [53] | clinical | AD | 188 | US | Onset to study entry |

| | | | | | |
|----------------------------------|------------------|----------------|------|--------------------------------------------|----------------------|
| Marshall et al., 2014 [54] | clinical | AD | 188 | US | Onset to study entry |
| Millenaar et al., 2016 [55] | clinical | Mixed | 108 | Netherlands | Onset to study entry |
| Murray et al., 2011 [56] | clinical | AD | 97 | US | Onset to death |
| Nazem et al., 2018 [57] | clinical | AD, FTD, Mixed | 10 | Germany | Onset to study entry |
| Nunnemann et al., 2011 [10] | clinical | AD, FTD | 124 | Germany | Onset to death |
| Oesterhus et al., 2014 [58] | clinical | AD, DLB | 53 | Norway | Diagnosis to death |
| Oosterveld et al., 2014 [59] | clinical | AD | 213 | Netherlands | Onset to diagnosis |
| Ornstein et al., 2013 [60] | clinical | Mixed | 160 | US | Onset to study entry |
| Park et al., 2018 [11] | clinical | DLB | 33 | Korea | Onset to study entry |
| Peters et al., 2015 [61] | population-based | AD | 335 | US | Onset to Diagnosis |
| Pirker-Kees et al., 2019 [62] | clinical | Mixed | 309 | Austria | Onset to study entry |
| Price et al., 2017 [63] | clinical | AD, DLB | 251 | UK | Diagnosis to death |
| Pusswald et al., 2015 [64] | clinical | AD | 286 | Austria | Onset to study entry |
| Rafaniello et al., 2014 [65] | clinical | AD | 1618 | Italy | Onset to study entry |
| Ransmayr et al., 2018 [66] | clinical | Mixed | 585 | Austria | Onset to study entry |
| Rattinger et al., 2015 [67] | population-based | Mixed | 287 | US | Onset to study entry |
| Rattinger et al., 2019 [68] | population-based | Mixed | 280 | US | Onset to study entry |
| Rhodus-Meester et al., 2018 [69] | clinical | AD | 213 | Netherlands | Study entry to death |
| Rizzuto et al., 2012 [12] | population-based | Mixed | 293 | Sweden | Diagnosis to death |
| Roehr et al., 2015 [70] | clinical | Mixed | 523 | Germany | Onset to death |
| Rongve et al., 2016 [71] | population-based | AD, DLB | 107 | Norway | Onset to study entry |
| Roy et al., 2014 [72] | clinical | AD | 95 | US | Onset to study entry |
| Russ et al., 2012 [73] | clinical | AD | 657 | Scotland | Diagnosis to death |
| Sanders et al., 2016 [74] | population-based | Mixed | 292 | US | Onset to study entry |
| Seifan et al., 2015 [75] | clinical | AD | 68 | US | Onset to study entry |
| Seiler et al., 2012 [76] | clinical | Mixed | 240 | Austria | Onset to study entry |
| Shea et al., 2019 [77] | clinical | AD | 31 | China | Diagnosis to death |
| Staffaroni et al., 2019 [78] | clinical | FTD | 77 | US | Onset to study entry |
| Strand et al., 2018 [79] | clinical | AD, VaD, Mixed | 4682 | Norway | Diagnosis to death |
| Stubendorff et al., 2011 [80] | clinical | AD, DLB | 79 | Sweden | Onset to diagnosis |
| Stubendorff et al., 2012 [81] | clinical | DLB | 30 | Norway, UK, Sweden | Onset to study entry |
| Stubendorff et al., 2014 [82] | clinical | Mixed | 32 | Norway, UK, Sweden | Onset to study entry |
| Svendsboe et al., 2018 [83] | clinical | AD | 97 | Norway | Onset to study entry |
| Tan et al., 2013 [84] | clinical | AD, FTD | 23 | US | Onset to study entry |
| Thoits et al., 2018 [85] | clinical | Mixed | 95 | US | Onset to study entry |
| Treiber et al., 2011 [86] | population-based | AD | 187 | US | Onset to study entry |
| Trieu et al., 2018 [87] | population-based | Mixed | 134 | US | Diagnosis to death |
| Tropea et al., 2019 [88] | clinical | AD, FTD, Mixed | 380 | US | Onset to study entry |
| van Vliet et al., 2012 [89] | clinical | AD | 123 | Netherlands | Onset to study entry |
| van Vliet et al., 2013 [90] | clinical | AD | 126 | Netherlands | Onset to study entry |
| Vermunt et al., 2019 [14] | mixed | AD | 3268 | Netherlands, US, Australia, Sweden, Europe | Onset to death |
| Wang et al., 2016 [91] | clinical | AD, VaD | 21 | China | Onset to study entry |
| Wang et al., 2019 [92] | clinical | AD | 38 | China | Onset to study entry |
| Wattmo et al., 2011 [93] | clinical | AD | 790 | Sweden | Onset to study entry |
| Wattmo et al., 2014 [94] | clinical | AD | 707 | Sweden | Onset to death |

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|----------------------------------|------------------|---------|-------|--------|----------------------|
| Wattmo et al., 2015 [95] | clinical | AD | 1021 | Sweden | Onset to study entry |
| Wattmo et al., 2016 [96] | clinical | AD | 220 | Sweden | Onset to death |
| Wattmo et al., 2017 [97] | clinical | AD | 874 | Sweden | Onset to study entry |
| Whitwell et al., 2020 [98] | clinical | AD, FTD | 184 | US | Onset to study entry |
| Yazar et al., 2018 [15] | clinical | AD | 120 | Turkey | Onset to study entry |
| Yeh et al., 2020 [99] | population-based | AD | 20358 | Taiwan | Study entry to death |
| Zissimopoulos et al., 2018 [100] | population-based | Mixed | 1030 | US | Onset to death |

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