

Supplementary Material

Comparative Value of Cholinesterase Inhibitors and Memantine in Persons with Moderate-to-Severe Alzheimer's Disease in the United States: A Cost-Effectiveness Analysis

Supplementary Table 1. 2015 US Life Table (General Population) [1]

| Age | Probability of Death | Number Alive | Life expectancy |
|------------|-----------------------------|---------------------|------------------------|
| 1 | 0.005894 | 100,000 | 78.7 |
| 2 | 0.000403 | 99,411 | 78.2 |
| 3 | 0.000252 | 99,371 | 77.2 |
| 4 | 0.000193 | 99,345 | 76.2 |
| 5 | 0.000145 | 99,326 | 75.3 |
| 6 | 0.000143 | 99,312 | 74.3 |
| 7 | 0.000128 | 99,298 | 73.3 |
| 8 | 0.000116 | 99,285 | 72.3 |
| 9 | 0.000104 | 99,273 | 71.3 |
| 10 | 0.000095 | 99,263 | 70.3 |
| 11 | 0.000091 | 99,254 | 69.3 |
| 12 | 0.000098 | 99,245 | 68.3 |
| 13 | 0.000125 | 99,235 | 67.3 |
| 14 | 0.000174 | 99,222 | 66.3 |
| 15 | 0.000241 | 99,205 | 65.3 |
| 16 | 0.000314 | 99,181 | 64.4 |
| 17 | 0.000388 | 99,150 | 63.4 |
| 18 | 0.000473 | 99,112 | 62.4 |
| 19 | 0.000566 | 99,065 | 61.4 |
| 20 | 0.000660 | 99,009 | 60.5 |
| 21 | 0.000757 | 98,943 | 59.5 |
| 22 | 0.000846 | 98,868 | 58.5 |
| 23 | 0.000914 | 98,785 | 57.6 |
| 24 | 0.000958 | 98,694 | 56.6 |
| 25 | 0.000984 | 98,600 | 55.7 |
| 26 | 0.001004 | 98,503 | 54.8 |
| 27 | 0.001028 | 98,404 | 53.8 |
| 28 | 0.001056 | 98,303 | 52.9 |
| 29 | 0.001094 | 98,199 | 51.9 |
| 30 | 0.001138 | 98,092 | 51.0 |
| 31 | 0.001185 | 97,980 | 50.0 |
| 32 | 0.001232 | 97,864 | 49.1 |

| Age | Probability of Death | Number Alive | Life expectancy |
|------------|-----------------------------|---------------------|------------------------|
| 33 | 0.001277 | 97,743 | 48.2 |
| 34 | 0.001318 | 97,619 | 47.2 |
| 35 | 0.001359 | 97,490 | 46.3 |
| 36 | 0.001408 | 97,357 | 45.3 |
| 37 | 0.001468 | 97,220 | 44.4 |
| 38 | 0.001535 | 97,077 | 43.5 |
| 39 | 0.001608 | 96,928 | 42.5 |
| 40 | 0.001690 | 96,773 | 41.6 |
| 41 | 0.001790 | 96,609 | 40.7 |
| 42 | 0.001909 | 96,436 | 39.7 |
| 43 | 0.002043 | 96,252 | 38.8 |
| 44 | 0.002191 | 96,055 | 37.9 |
| 45 | 0.002360 | 95,845 | 37.0 |
| 46 | 0.002541 | 95,619 | 36.1 |
| 47 | 0.002752 | 95,376 | 35.2 |
| 48 | 0.003018 | 95,113 | 34.3 |
| 49 | 0.003346 | 94,826 | 33.4 |
| 50 | 0.003717 | 94,509 | 32.5 |
| 51 | 0.004098 | 94,158 | 31.6 |
| 52 | 0.004481 | 93,772 | 30.7 |
| 53 | 0.004885 | 93,352 | 29.8 |
| 54 | 0.005319 | 92,896 | 29.0 |
| 55 | 0.005781 | 92,402 | 28.1 |
| 56 | 0.006271 | 91,867 | 27.3 |
| 57 | 0.006775 | 91,291 | 26.5 |
| 58 | 0.007291 | 90,673 | 25.6 |
| 59 | 0.007824 | 90,012 | 24.8 |
| 60 | 0.008383 | 89,307 | 24.0 |
| 61 | 0.008991 | 88,559 | 23.2 |
| 62 | 0.009652 | 87,763 | 22.4 |
| 63 | 0.010353 | 86,915 | 21.6 |
| 64 | 0.011081 | 86,016 | 20.9 |
| 65 | 0.011838 | 85,062 | 20.1 |
| 66 | 0.012634 | 84,055 | 19.3 |
| 67 | 0.013510 | 82,994 | 18.6 |
| 68 | 0.014504 | 81,872 | 17.8 |
| 69 | 0.015664 | 80,685 | 17.1 |
| 70 | 0.017059 | 79,421 | 16.3 |
| 71 | 0.018766 | 78,066 | 15.6 |
| 72 | 0.020689 | 76,601 | 14.9 |

| Age | Probability of Death | Number Alive | Life expectancy |
|------------|-----------------------------|---------------------|------------------------|
| 73 | 0.022709 | 75,016 | 14.2 |
| 74 | 0.024795 | 73,313 | 13.5 |
| 75 | 0.027078 | 71,495 | 12.9 |
| 76 | 0.029614 | 69,559 | 12.2 |
| 77 | 0.032507 | 67,499 | 11.6 |
| 78 | 0.035786 | 65,305 | 10.9 |
| 79 | 0.039616 | 62,968 | 10.3 |
| 80 | 0.044017 | 60,473 | 9.7 |
| 81 | 0.048899 | 57,811 | 9.1 |
| 82 | 0.054283 | 54,985 | 8.6 |
| 83 | 0.060367 | 52,000 | 8.1 |
| 84 | 0.066954 | 48,861 | 7.5 |
| 85 | 0.074533 | 45,589 | 7.0 |
| 86 | 0.082695 | 42,192 | 6.6 |
| 87 | 0.092575 | 38,702 | 6.1 |
| 88 | 0.103427 | 35,120 | 5.7 |
| 89 | 0.115296 | 31,487 | 5.3 |
| 90 | 0.128216 | 27,857 | 4.9 |
| 91 | 0.142211 | 24,285 | 4.6 |
| 92 | 0.157287 | 20,832 | 4.2 |
| 93 | 0.173433 | 17,555 | 3.9 |
| 94 | 0.190616 | 14,510 | 3.6 |
| 95 | 0.208781 | 11,744 | 3.4 |
| 96 | 0.227849 | 9,292 | 3.2 |
| 97 | 0.247715 | 7,175 | 2.9 |
| 98 | 0.268255 | 5,398 | 2.7 |
| 99 | 0.289322 | 3,950 | 2.6 |
| 100 | 0.310753 | 2,807 | 2.4 |
| 101 | 1.000000 | 1,935 | 2.2 |

Supplementary Table 2. 2015 US Life Table by Sex [1]

| Male | | | | Female | | | |
|------|----------------------|--------------|-----------------|--------|----------------------|--------------|-----------------|
| Age | Probability of Death | Number Alive | Life expectancy | Age | Probability of Death | Number Alive | Life expectancy |
| 1 | 0.00639 | 100000 | 76.3 | 1 | 0.005377 | 100000 | 81.1 |
| 2 | 0.00045 | 99361 | 75.8 | 2 | 0.000352 | 99462 | 80.5 |
| 3 | 0.00028 | 99316 | 74.8 | 3 | 0.000227 | 99427 | 79.6 |
| 4 | 0.00022 | 99289 | 73.8 | 4 | 0.000160 | 99405 | 78.6 |
| 5 | 0.00016 | 99267 | 72.9 | 5 | 0.000125 | 99389 | 77.6 |
| 6 | 0.00016 | 99250 | 71.9 | 6 | 0.000122 | 99376 | 76.6 |
| 7 | 0.00015 | 99234 | 70.9 | 7 | 0.000109 | 99364 | 75.6 |
| 8 | 0.00013 | 99219 | 69.9 | 8 | 0.000099 | 99354 | 74.6 |
| 9 | 0.00012 | 99206 | 68.9 | 9 | 0.000093 | 99344 | 73.6 |
| 10 | 0.00010 | 99195 | 67.9 | 10 | 0.000089 | 99334 | 72.6 |
| 11 | 0.00009 | 99185 | 66.9 | 11 | 0.000089 | 99326 | 71.7 |
| 12 | 0.00010 | 99176 | 65.9 | 12 | 0.000096 | 99317 | 70.7 |
| 13 | 0.00014 | 99166 | 64.9 | 13 | 0.000112 | 99307 | 69.7 |
| 14 | 0.00021 | 99152 | 63.9 | 14 | 0.000139 | 99296 | 68.7 |
| 15 | 0.00031 | 99132 | 63.0 | 15 | 0.000173 | 99282 | 67.7 |
| 16 | 0.00041 | 99101 | 62.0 | 16 | 0.000212 | 99265 | 66.7 |
| 17 | 0.00052 | 99061 | 61.0 | 17 | 0.000252 | 99244 | 65.7 |
| 18 | 0.00065 | 99009 | 60.0 | 18 | 0.000292 | 99219 | 64.7 |
| 19 | 0.00079 | 98945 | 59.1 | 19 | 0.000330 | 99190 | 63.7 |
| 20 | 0.00094 | 98867 | 58.1 | 20 | 0.000365 | 99157 | 62.8 |
| 21 | 0.00109 | 98774 | 57.2 | 21 | 0.000401 | 99121 | 61.8 |
| 22 | 0.00123 | 98666 | 56.2 | 22 | 0.000437 | 99081 | 60.8 |
| 23 | 0.00134 | 98544 | 55.3 | 23 | 0.000469 | 99038 | 59.8 |
| 24 | 0.00140 | 98412 | 54.4 | 24 | 0.000496 | 98992 | 58.9 |
| 25 | 0.00143 | 98275 | 53.4 | 25 | 0.000520 | 98943 | 57.9 |
| 26 | 0.00145 | 98135 | 52.5 | 26 | 0.000543 | 98891 | 56.9 |
| 27 | 0.00147 | 97993 | 51.6 | 27 | 0.000569 | 98838 | 56.0 |
| 28 | 0.00150 | 97849 | 50.7 | 28 | 0.000601 | 98781 | 55.0 |
| 29 | 0.00153 | 97702 | 49.7 | 29 | 0.000641 | 98722 | 54.0 |
| 30 | 0.00158 | 97553 | 48.8 | 30 | 0.000688 | 98659 | 53.1 |
| 31 | 0.00162 | 97399 | 47.9 | 31 | 0.000739 | 98591 | 52.1 |
| 32 | 0.00167 | 97241 | 47.0 | 32 | 0.000792 | 98518 | 51.1 |
| 33 | 0.00171 | 97079 | 46.1 | 33 | 0.000841 | 98440 | 50.2 |
| 34 | 0.00175 | 96913 | 45.1 | 34 | 0.000884 | 98357 | 49.2 |
| 35 | 0.00179 | 96743 | 44.2 | 35 | 0.000924 | 98270 | 48.3 |
| 36 | 0.00185 | 96569 | 43.3 | 36 | 0.000970 | 98179 | 47.3 |
| 37 | 0.00191 | 96391 | 42.4 | 37 | 0.001027 | 98084 | 46.3 |
| 38 | 0.00198 | 96207 | 41.4 | 38 | 0.001092 | 97983 | 45.4 |
| 39 | 0.00205 | 96017 | 40.5 | 39 | 0.001166 | 97876 | 44.4 |

| Male | | | | Female | | | |
|------|----------------------|--------------|-----------------|--------|----------------------|--------------|-----------------|
| Age | Probability of Death | Number Alive | Life expectancy | Age | Probability of Death | Number Alive | Life expectancy |
| 40 | 0.00213 | 95820 | 39.6 | 40 | 0.001250 | 97762 | 43.5 |
| 41 | 0.00224 | 95615 | 38.7 | 41 | 0.001347 | 97640 | 42.5 |
| 42 | 0.00237 | 95401 | 37.8 | 42 | 0.001458 | 97508 | 41.6 |
| 43 | 0.00252 | 95175 | 36.9 | 43 | 0.001578 | 97366 | 40.7 |
| 44 | 0.00268 | 94936 | 36.0 | 44 | 0.001707 | 97213 | 39.7 |
| 45 | 0.00288 | 94681 | 35.1 | 45 | 0.001849 | 97047 | 38.8 |
| 46 | 0.00309 | 94409 | 34.2 | 46 | 0.002000 | 96867 | 37.9 |
| 47 | 0.00334 | 94117 | 33.3 | 47 | 0.002173 | 96674 | 36.9 |
| 48 | 0.00366 | 93803 | 32.4 | 48 | 0.002384 | 96464 | 36.0 |
| 49 | 0.00407 | 93459 | 31.5 | 49 | 0.002636 | 96234 | 35.1 |
| 50 | 0.00454 | 93079 | 30.6 | 50 | 0.002915 | 95980 | 34.2 |
| 51 | 0.00502 | 92657 | 29.8 | 51 | 0.003199 | 95700 | 33.3 |
| 52 | 0.00551 | 92191 | 28.9 | 52 | 0.003484 | 95394 | 32.4 |
| 53 | 0.00603 | 91683 | 28.1 | 53 | 0.003783 | 95062 | 31.5 |
| 54 | 0.00658 | 91131 | 27.2 | 54 | 0.004103 | 94702 | 30.6 |
| 55 | 0.00718 | 90531 | 26.4 | 55 | 0.004443 | 94314 | 29.8 |
| 56 | 0.00780 | 89881 | 25.6 | 56 | 0.004808 | 93895 | 28.9 |
| 57 | 0.00844 | 89180 | 24.8 | 57 | 0.005185 | 93443 | 28.0 |
| 58 | 0.00912 | 88427 | 24.0 | 58 | 0.005562 | 92958 | 27.2 |
| 59 | 0.00983 | 87621 | 23.2 | 59 | 0.005936 | 92441 | 26.3 |
| 60 | 0.01058 | 86760 | 22.4 | 60 | 0.006323 | 91893 | 25.5 |
| 61 | 0.01141 | 85842 | 21.7 | 61 | 0.006739 | 91312 | 24.6 |
| 62 | 0.01230 | 84862 | 20.9 | 62 | 0.007208 | 90696 | 23.8 |
| 63 | 0.01320 | 83818 | 20.2 | 63 | 0.007742 | 90043 | 23.0 |
| 64 | 0.01407 | 82711 | 19.4 | 64 | 0.008349 | 89345 | 22.1 |
| 65 | 0.01493 | 81547 | 18.7 | 65 | 0.009024 | 88599 | 21.3 |
| 66 | 0.01581 | 80330 | 18.0 | 66 | 0.009754 | 87800 | 20.5 |
| 67 | 0.01678 | 79060 | 17.3 | 67 | 0.010550 | 86944 | 19.7 |
| 68 | 0.01789 | 77733 | 16.5 | 68 | 0.011452 | 86026 | 18.9 |
| 69 | 0.01920 | 76342 | 15.8 | 69 | 0.012489 | 85041 | 18.1 |
| 70 | 0.02082 | 74876 | 15.1 | 70 | 0.013714 | 83979 | 17.3 |
| 71 | 0.02280 | 73317 | 14.4 | 71 | 0.015204 | 82827 | 16.6 |
| 72 | 0.02503 | 71646 | 13.8 | 72 | 0.016900 | 81568 | 15.8 |
| 73 | 0.02735 | 69852 | 13.1 | 73 | 0.018696 | 80190 | 15.1 |
| 74 | 0.02980 | 67942 | 12.5 | 74 | 0.020515 | 78690 | 14.4 |
| 75 | 0.03246 | 65917 | 11.8 | 75 | 0.022528 | 77076 | 13.7 |
| 76 | 0.03540 | 63777 | 11.2 | 76 | 0.024780 | 75340 | 13.0 |
| 77 | 0.03881 | 61520 | 10.6 | 77 | 0.027308 | 73473 | 12.3 |
| 78 | 0.04253 | 59133 | 10.0 | 78 | 0.030300 | 71466 | 11.6 |
| 79 | 0.04685 | 56618 | 9.4 | 79 | 0.033840 | 69301 | 11.0 |

| Male | | | | Female | | | |
|------|----------------------|--------------|-----------------|--------|----------------------|--------------|-----------------|
| Age | Probability of Death | Number Alive | Life expectancy | Age | Probability of Death | Number Alive | Life expectancy |
| 80 | 0.05192 | 53965 | 8.9 | 80 | 0.037844 | 66956 | 10.3 |
| 81 | 0.05763 | 51163 | 8.3 | 81 | 0.042223 | 64422 | 9.7 |
| 82 | 0.06403 | 48215 | 7.8 | 82 | 0.047002 | 61702 | 9.1 |
| 83 | 0.07087 | 45128 | 7.3 | 83 | 0.052739 | 58802 | 8.5 |
| 84 | 0.07822 | 41929 | 6.8 | 84 | 0.059026 | 55701 | 8.0 |
| 85 | 0.08692 | 38650 | 6.4 | 85 | 0.066100 | 52413 | 7.5 |
| 86 | 0.09624 | 35290 | 5.9 | 86 | 0.073764 | 48948 | 7.0 |
| 87 | 0.10764 | 31894 | 5.5 | 87 | 0.083117 | 45338 | 6.5 |
| 88 | 0.12012 | 28461 | 5.1 | 88 | 0.093469 | 41569 | 6.0 |
| 89 | 0.13369 | 25042 | 4.7 | 89 | 0.104878 | 37684 | 5.6 |
| 90 | 0.14838 | 21694 | 4.4 | 90 | 0.117395 | 33732 | 5.2 |
| 91 | 0.16419 | 18475 | 4.1 | 91 | 0.131057 | 29772 | 4.8 |
| 92 | 0.18109 | 15442 | 3.8 | 92 | 0.145887 | 25870 | 4.4 |
| 93 | 0.19905 | 12646 | 3.5 | 93 | 0.161887 | 22096 | 4.1 |
| 94 | 0.21798 | 10128 | 3.3 | 94 | 0.179040 | 18519 | 3.8 |
| 95 | 0.23780 | 7921 | 3.0 | 95 | 0.197299 | 15203 | 3.5 |
| 96 | 0.25839 | 6037 | 2.8 | 96 | 0.216593 | 12204 | 3.3 |
| 97 | 0.27959 | 4477 | 2.6 | 97 | 0.236822 | 9560 | 3.0 |
| 98 | 0.30125 | 3225 | 2.5 | 98 | 0.257858 | 7296 | 2.8 |
| 99 | 0.32319 | 2254 | 2.3 | 99 | 0.279548 | 5415 | 2.6 |
| 100 | 0.34522 | 1525 | 2.2 | 100 | 0.301715 | 3901 | 2.4 |
| 101 | 1.00000 | 999 | 2.0 | 101 | 1.000000 | 2724 | 2.3 |

Supplementary Table 3. Transition Matrices

| Best Supportive Care | | | | |
|--|---------|-------------|-----------|----------|
| From | To_Mild | To_Moderate | To_Severe | To_Death |
| Mild | 0.954 | 0.033 | 0.008 | 0.005 |
| Moderate | 0.046 | 0.570 | 0.292 | 0.092 |
| Severe | 0.000 | 0.000 | 0.701 | 0.299 |
| Death | 0.000 | 0.000 | 0.000 | 1.000 |
| Donepezil/Memantine Combination | | | | |
| From | To_Mild | To_Moderate | To_Severe | To_Death |
| Mild | 0.955 | 0.033 | 0.008 | 0.004 |
| Moderate | 0.092 | 0.570 | 0.292 | 0.046 |
| Severe | 0.000 | 0.000 | 0.849 | 0.151 |
| Death | 0.000 | 0.000 | 0.000 | 1.000 |
| Rivastigmine Monotherapy (Oral) | | | | |
| From | To_Mild | To_Moderate | To_Severe | To_Death |
| Mild | 0.874 | 0.103 | 0.019 | 0.004 |
| Moderate | 0.052 | 0.619 | 0.250 | 0.079 |
| Severe | 0.000 | 0.000 | 0.742 | 0.258 |
| Death | 0.000 | 0.000 | 0.000 | 1.000 |
| Donepezil Monotherapy | | | | |
| From | To_Mild | To_Moderate | To_Severe | To_Death |
| Mild | 0.874 | 0.103 | 0.019 | 0.004 |
| Moderate | 0.061 | 0.619 | 0.250 | 0.070 |
| Severe | 0.000 | 0.000 | 0.772 | 0.228 |
| Death | 0.000 | 0.000 | 0.000 | 1.000 |
| Galantamine/Memantine Combination | | | | |
| From | To_Mild | To_Moderate | To_Severe | To_Death |
| Mild | 0.956 | 0.033 | 0.008 | 0.003 |
| Moderate | 0.000 | 0.470 | 0.247 | 0.283 |
| Severe | 0.000 | 0.000 | 0.076 | 0.924 |
| Death | 0.000 | 0.000 | 0.000 | 1.000 |
| Rivastigmine Transdermal Patch | | | | |
| From | To_Mild | To_Moderate | To_Severe | To_Death |
| Mild | 0.876 | 0.103 | 0.019 | 0.002 |
| Moderate | 0.097 | 0.619 | 0.250 | 0.033 |
| Severe | 0.000 | 0.000 | 0.891 | 0.109 |
| Death | 0.000 | 0.000 | 0.000 | 1.000 |
| Memantine Monotherapy | | | | |
| From | To_Mild | To_Moderate | To_Severe | To_Death |
| Mild | 0.955 | 0.033 | 0.008 | 0.004 |
| Moderate | 0.042 | 0.570 | 0.292 | 0.096 |

| | | | | |
|---|---------|-------------|-----------|----------|
| Severe | 0.000 | 0.000 | 0.687 | 0.313 |
| Death | 0.000 | 0.000 | 0.000 | 1.000 |
| Rivastigmine/Memantine Combination | | | | |
| From | To_Mild | To_Moderate | To_Severe | To_Death |
| Mild | 0.874 | 0.103 | 0.019 | 0.004 |
| Moderate | 0.078 | 0.619 | 0.250 | 0.053 |
| Severe | 0.000 | 0.000 | 0.828 | 0.172 |
| Death | 0.000 | 0.000 | 0.000 | 1.000 |
| Galantamine Monotherapy | | | | |
| From | To_Mild | To_Moderate | To_Severe | To_Death |
| Mild | 0.875 | 0.103 | 0.019 | 0.003 |
| Moderate | 0.079 | 0.619 | 0.250 | 0.052 |
| Severe | 0.000 | 0.000 | 0.831 | 0.169 |
| Death | 0.000 | 0.000 | 0.000 | 1.000 |

Supplementary Table 4. Effect of Drug Therapy on Mortality

| Strategy | Odds Ratio (95% Confidence Interval) |
|-----------------------------------|---|
| Donepezil monotherapy | 0.76 (0.47-1.24) |
| Galantamine monotherapy | 0.56 (0.36-0.87) |
| Rivastigmine monotherapy (Oral) | 0.86 (0.28-2.46) |
| Rivastigmine transdermal patch | 0.36 (0.05-1.86) |
| Memantine monotherapy | 1.05 (0.63-1.70) |
| Donepezil/memantine combination | 0.50 (0.13-1.78) |
| Galantamine/memantine combination | 3.23 (0.10-28.64) |

Supplementary Table 5. Cost and Utility Inputs

| Parameter | Value, mean (SE) | Distribution | Source |
|---|-------------------------|---------------------|---|
| Direct medical care cost, \$^a | | | |
| Moderate | 11,442 (1,126) | Normal | Saint-Laurent Thibault et al., 2015 [2] |
| Severe | 12,779 (1,258) | Normal | Saint-Laurent Thibault et al., 2015 [2] |
| Drug Costs, \$^a | | | |
| Donepezil monotherapy | 182 (14) | Normal | CMS [3] |
| Galantamine monotherapy | 968 (78) | Normal | CMS [3] |
| Rivastigmine oral monotherapy | 3,866 (278) | Normal | CMS [3] |
| Rivastigmine transdermal patch | 6,307 (610) | Normal | RED BOOK [4] |
| Memantine monotherapy | 3,626 (467) | Normal | CMS [3] |
| Donepezil/Memantine | 3,674 (491) | Normal | CMS [3] |
| Galantamine/Memantine | 4,595 (545) | Normal | CMS [3] |
| Rivastigmine/Memantine | 7,493 (745) | Normal | CMS [3] |
| Patient Utility | | | |
| Moderate | 0.54 (0.06) | Lognormal | Saint-Laurent Thibault et al., 2015 [2] |
| Severe | 0.37 (0.04) | Lognormal | Saint-Laurent Thibault et al., 2015 [2] |

^a annual cost based on 2020 dollar

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