ADNI 2 Enrollment by Cohort

Total at initial entry (includes 276 ADNI 1 + 120 ADNI GO rollovers): **1180**
Current total (minus reported withdrawals): **917**
# ADNI GO + 2 Baseline

<table>
<thead>
<tr>
<th></th>
<th>CN n=184</th>
<th>SMC n=103</th>
<th>EMCI n=301</th>
<th>LMCI n=160</th>
<th>AD n=145</th>
<th>Combined n=893</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>73.4 (6.3)</td>
<td>72.2 (5.6)</td>
<td>71.3 (7.4)</td>
<td>72.2 (7.5)</td>
<td>74.6 (8.1)</td>
<td>72.5 (7.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>94 (51%)</td>
<td>61 (59%)</td>
<td>132 (44%)</td>
<td>74 (46%)</td>
<td>59 (41%)</td>
<td>420 (47%)</td>
<td>0.027</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td>16.5 (2.5)</td>
<td>16.7 (2.6)</td>
<td>16.0 (2.7)</td>
<td>16.5 (2.6)</td>
<td>15.8 (2.7)</td>
<td>16.3 (2.6)</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>CDR-SB</strong></td>
<td>0.0 (0.1)</td>
<td>0.01 (0.2)</td>
<td>1.3 (0.8)</td>
<td>1.7 (1.0)</td>
<td>4.5 (1.7)</td>
<td>1.5 (1.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>ADAS 13</strong></td>
<td>9.2 (4.5)</td>
<td>8.9 (4.3)</td>
<td>12.7 (5.4)</td>
<td>18.7 (7.1)</td>
<td>31.0 (8.4)</td>
<td>15.5 (9.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>MMSE</strong></td>
<td>29.0 (1.3)</td>
<td>29.0 (1.2)</td>
<td>28.3 (1.6)</td>
<td>27.6 (1.8)</td>
<td>23.1 (2.1)</td>
<td>27.6 (2.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Part. ECog</strong></td>
<td>1.3 (0.3)</td>
<td>1.6 (0.3)</td>
<td>1.8 (0.5)</td>
<td>1.8 (0.5)</td>
<td>1.9 (0.6)</td>
<td>1.7 (0.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Study Part. Ecog</strong></td>
<td>1.2 (0.3)</td>
<td>1.3 (0.3)</td>
<td>1.6 (0.5)</td>
<td>1.9 (0.7)</td>
<td>2.7 (0.7)</td>
<td>1.7 (0.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Dropout Rate

p < 0.0001

Drop out (%)

0  25  50  75  100

0  2  4  6  8
Years

AD  333  165  0  0  0
LMCI  550  446  199  147  64
EMCI  301  232  49  0  0
SMC  103  3  0  0  0
CN  410  335  155  132  49

Number active

dropout = reported withdrawals

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dropout = reported withdrawals or no new data in last 18 months
Instrument sensitivity to \textit{APOE} related change

• The following slides summarize MMRM estimates of the \textit{APOE}-\textepsilon 4 group difference in change from baseline at 24 months.

• Estimated differences are reported on a common scale (mean:SD).

• CN, EMCI, LMCI, and AD are modeled separately.
NC APOE group diff. in 2-yr change
EMCI *APOE* group diff. in 2-yr change
LMCI APOE group diff. in 2-yr change
AD APOE group diff. in 2-yr change
NC Amyloid group diff. in 2-yr change

![Graph showing the mean and standard deviation of various cognitive measures for NC Amyloid group. The x-axis represents the mean, and the y-axis lists different cognitive tests such as MMSE, Digit, Trails B, Animal Fl, RAVLT, Ecog Pt, Trails A, Log Mem Del, Log Mem Imm, CDRSB, Ecog SP, FAQ, MOCA, Boston Naming, ADAS13, ADAS DWR, Clock, Vegetable Fl. The graph indicates differences in 2-year change for each measure.]
EMCI Amyloid group diff. in 2-yr change
LMCI Amyloid group diff. in 2-yr change
AD Amyloid group diff. in 2-yr change
Transitions from MCI

Graph showing the probability of transitioning from MCI to different states over years.
Transitions from “de novo” MCI

Transition
- MCI to Dementia
- MCI to NL

Probability

Year
ADNI 3 CLINICAL CORE PLANS

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Ron Petersen
Mike Donohue
Mike Weiner
The aims of the ADNI3 Clinical Core will include:

- Oversight of ADNI3 clinical activities, data management, tracking and quality control, recruitment and retention of participants, regulatory oversight and financial management.

- Characterization of the cross-sectional features and longitudinal trajectories of cognitively normal older individuals and mild cognitive impairment.

- Study of the relationships among clinical/demographic, cognitive, genetic, biochemical and neuroimaging features of AD from the preclinical through dementia stages.

- Assessment of genetic, biomarker and clinical predictors of decline.

- Refinement of clinical trial designs, including secondary prevention, slowing of progression in symptomatic disease, and cognitive/behavioral management.
Key hypotheses of ADNI3 Clinical Core

- All or almost all normal participants with brain amyloidosis will show cognitive decline compared to those without amyloidosis, and will progress to MCI.

- Confirmation of this hypothesis is critical to early stage trial design and regulatory support.

- MCI participants who are biomarker positive (amyloid and tau) will progress more rapidly than those who are negative
Other hypotheses

- Amyloid-related cognitive decline involves episodic memory, executive function and orientation across the spectrum of AD
- AD-related cognitive decline can be captured by unsupervised web-based testing
- Early stage AD cognitive decline predicts later functional and clinical decline
- Web-based registries will facilitate recruitment for ADNI (and therapeutic trials)
ADNI3 cohorts

- ADNI3 will carry forward roughly 300 normals (w/wo subjective concerns) and 300 MCI (EMCI+LMCI)
- ADNI3 will enroll modest numbers of new normal and MCI participants
- ADNI3 will follow MCI participants who progress to AD dementia
Possible adjustments to assessments

- Drop RAVLT, add FCSRT.
- Drop Boston Naming.
- Drop Clock Drawing.
- Add web-based cognitive testing.
- CFI instead of eCOG?
- Other subjective concerns measures?

- Reaching a consensus will be challenging, but we need to begin the discussion even as we work on additional analyses.