Supplementary Material

Mayo Normative Studies: Amyloid and Neurodegeneration Negative Normative Data for the Auditory Verbal Learning Test and Sex-Specific Sensitivity to Mild Cognitive Impairment/Dementia

Supplementary Table 1. Demographic and AVLT variables for A-N- sample; mean (SD) or count (percent).

	30-49 (N=419)	50-59 (N=238)	60-69 (N=262)	70-90 (N=140)	Total A-N- (N=1059)	Total Conventional (N=4428)
Age	40.1 (5.5)	55.0 (2.7)	64.6 (2.7)	74.0 (3.6)	54.0 (13.2)	68.3 (13.1)
Sex (Male)	220 (52.5%)	124 (52.1%)	138 (52.7%)	66 (47.1%)	548 (51.7%)	2,211 (49.9%)
Education (y)	15.8 (2.1)	15.4 (2.2)	15.3 (2.2)	14.7 (2.7)	15.4 (2.3)	14.7 (2.6)
White	389 (92.8%)	231 (97.1%)	259 (98.9%)	136 (97.1%)	1,015 (95.8%)	4,333 (97.9%)
AVLT						
1-5 Total	51.3 (8.4)	48.9 (8.8)	46.6 (8.6)	41.3 (9.0)	48.3 (9.2)	42.3 (10.0)
30-min Recall	10.8 (3.1)	9.9 (3.3)	9.1 (3.2)	7.5 (3.3)	9.7 (3.4)	8.0 (3.5)
Sum of Trials	73.0 (13.4)	69.2 (14.3)	65.2 (13.9)	57.1 (14.4)	68.1 (14.8)	58.7 (15.9)
Recogn PC	93.1 (8.3)	92.5 (8.3)	91.5 (8.6)	89.2 (8.9)	92.0 (8.5)	89.6 (9.6)

Sum of Trials = Trials 1-5 Total + Short Delay (Trial 6) + Delayed recall (30-min). PC, Percent Correct [Recognition hits + (15 - false positives) / 30] × 100.

Supplementary Table 2. Percentage variance explained (pearson correlation coefficient, squared) for each demographic variable and the full regression model (combined)[a]

AVLT Measure (Raw)	Age	Age Squared	Sex	Education	Combined
A-N- Normative Sample					
Trials 1-5 total	13.43	13.91	9.69	6.92	29.35
30-min recall (long delay)	11.11	11.48	9.39	3.46	23.76
Sum of trials[b]	13.57	14.05	10.17	6.22	29.38
Recognition percentage correct[c]	2.54	2.69	6.34	1.52	10.61
Conventional normative sample					
Trials 1-5 total	26.56	27.41	9.08	5.93	40.74
30-min recall (long delay)	17.28	17.56	8.50	2.75	28.31
Sum of trials[b]	25.50	26.19	9.39	5.21	39.37
Recognition percentage correct[c]	4.73	4.91	7.17	0.97	13.37

AVLT, Auditory Verbal Learning Test.

[a] Pearson Correlation Coefficients, Squared is equivalent to R^2. All p values for Pearson correlation coefficients (before squaring) are $p<0.001$.

[b] Trials 1-5 total + trial 6 + 30-min recall.

[c] ([Recognition hits + {15–recognition errors}]/30) × 100.

Supplementary Table 3. AVLT 30-min delayed recall using age-adjusted MOANS: Proportion (%) and 95% Confidence Interval (CI) of low test performance (< -1 SD) in CU validation sample (base rates) and in the MCI/Dementia sample (sensitivity).

CU Validation Sample (*n*=261)	**Female (*n* = 130)**	**Male (*n* = 131)**	**Total (*n* = 261)**
Age-adjusted MOANS [a], % (CI)	3.1 (1.2, 7.6)	13.0 (8.3, 19.8)	8.0 (5.3, 12.0)
MCI/Dementia Sample (*n*=392)	**Female (*n* = 171)**	**Male (*n* = 221)**	**Total (*n* = 392)**
Age-adjusted MOANS [b], % (CI)	36.3 (29.4, 43.7) [c]	56.6 (50.0, 62.9) [c]	47.7 (42.8, 52.6)

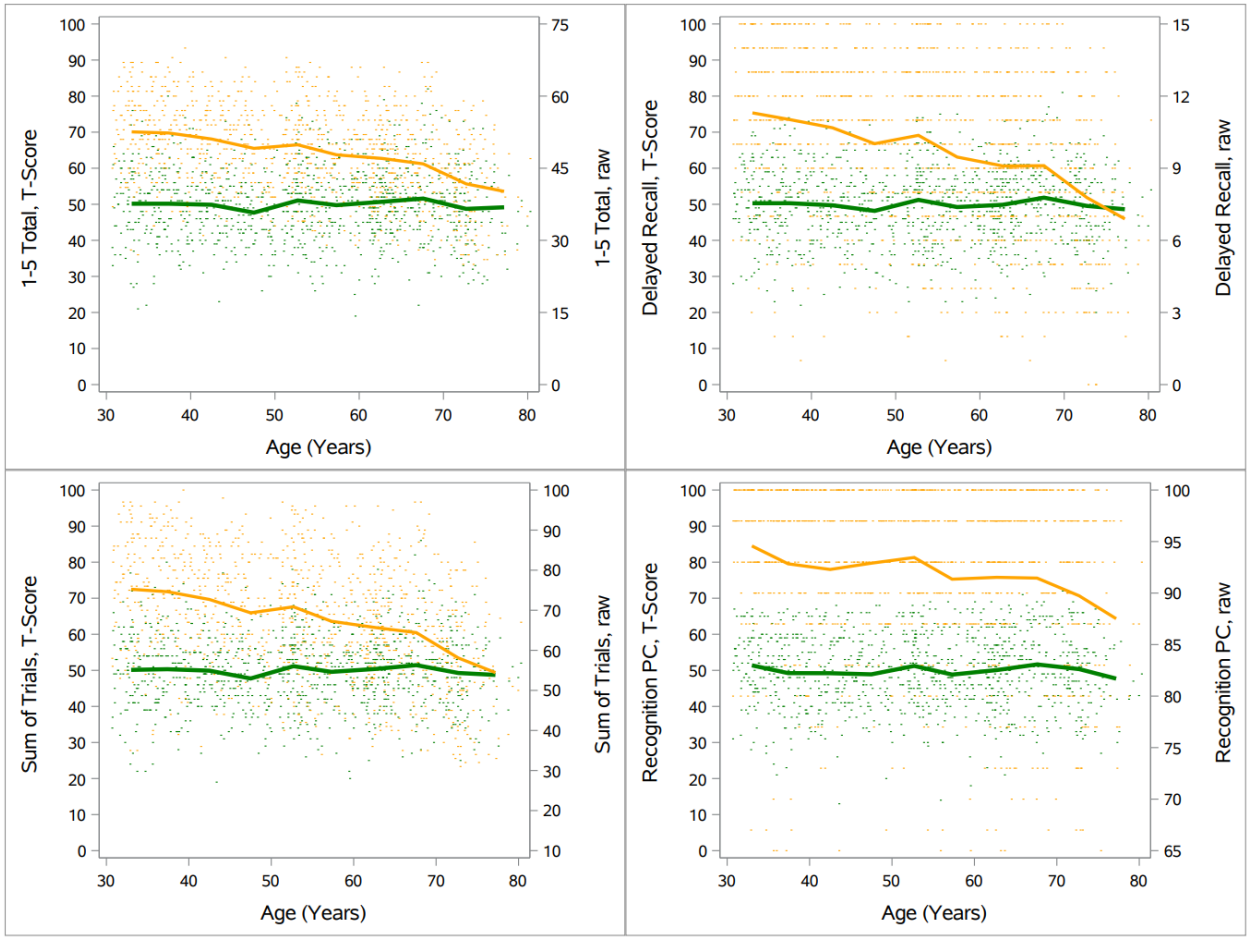
MCI, mild cognitive impairment; AVLT, Auditory Verbal Learning Test; CU, cognitively unimpaired; MOANS, Mayo's Older Americans Normative Studies; MNS, Mayo Normative Studies; A-, amyloid negative; N-, neurodegeneration negative; Sum of Trials, Trials 1-5 total + trial 6 + 30-min recall; PC, percent correct. Fully-adjusted MNS adjusts for age, age squared, sex, and education.

[a] Confidence intervals that do not contain the 14.7% expected base rate value are significantly different than expected. Thus, within the CU validation sample, women had significantly lower base rates of low test performance than expected. The total sample also had significantly lower base rates of low test performance than expected.

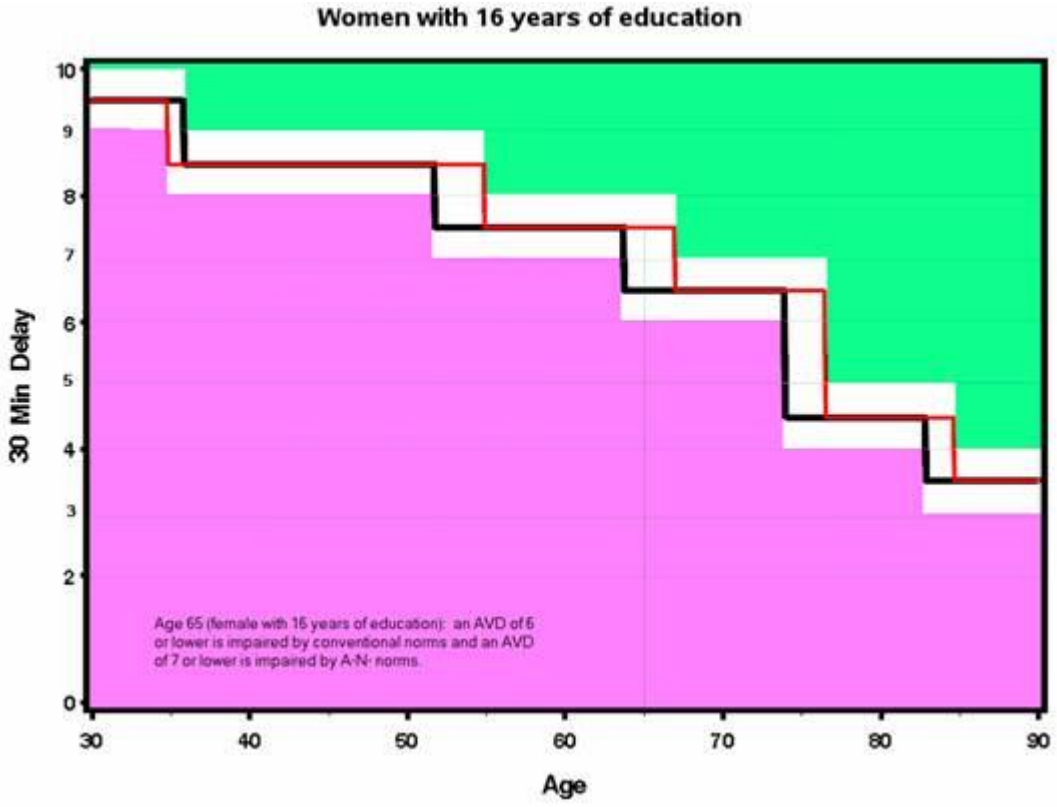
[b] All MNS norms (each of the four MNS variations; see manuscript Table 4) were significantly more sensitive ($p < 0.001$) than MOANS based on McNemar analyses examining for significant differences in frequencies of low test scores across different norms (i.e., different sensitivity in the same individuals when different norms are applied).

[c] Chi-square comparison of females and males $p < 0.05$. In other words, Age-adjusted MOANS norms showed significantly different ($p < 0.05$) sensitivity between females and males.

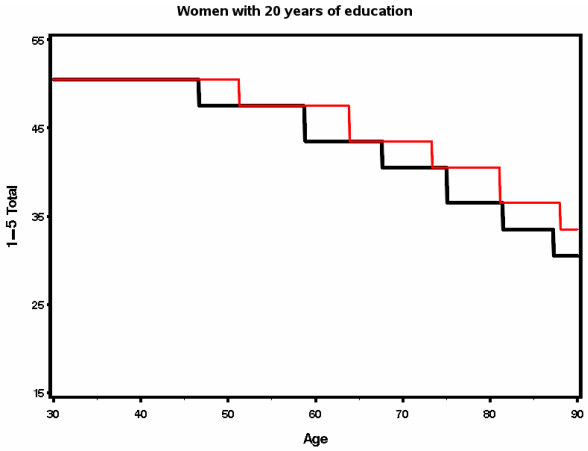
Supplemental Figure 1. Raw AVLT scores (in orange; right side of Y-axis) and demographically corrected AVLT scores (in green; left side of Y-axis) demonstrating that A-N- fully-corrected MNS T-scores correct for age effects.

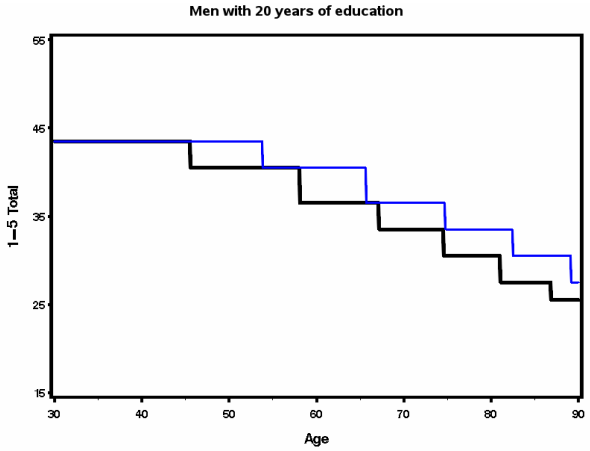


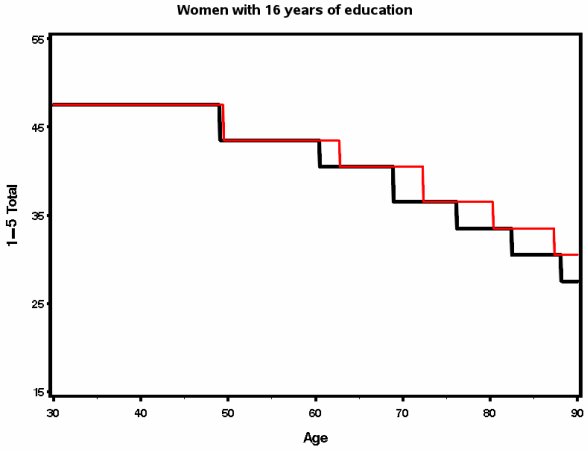
Supplemental Figure 2 Series. The following figure series compares cut-offs for fully adjusted MNS conventional norms and fully adjusted MNS A-N- norms. In instances where the black line is above the line presented in color, the norms are not behaving as expected (e.g., the conventional norms suggest lower performance than the A-N- norms, which is the opposite pattern of that expected). While there are not many instances of this, there are a few occurrences. Therefore, clinically we recommend using both norms together, with preference for the conventional norms in the rare instance where these provide a more stringent normative value. In general, clinical judgment is needed to select the most appropriate norm for the circumstance at hand. The example figure below helps to illustrate how to read this series of figures. This figure example shows 30-minute delay raw score on the y-axis and age on the x-axis for women with 16 years of education (model-generated data). The lines show the cut-off between impaired and intact (≤ 39 also known as <40 for the T-Scores) by illustrating the raw score's highest impaired value + 0.5 (or alternatively the raw score's lowest non-impaired value - 0.5). The black line represents fully-adjusted conventional norms and the red line indicates fully-adjusted A-N- norms. For a 65-year-old woman with 16 years of education, a delayed recall score of 6 or lower is impaired by MNS fully-adjusted conventional norms and a delayed recall score of 7 or lower is impaired by MNS fully-adjusted A-N- norms. A-N- norms are generally performing as expected for this example, with the exception of ages 35-36 where the conventional norm cut-off is 1 raw score point higher than the A-N- cut-off. A score of 10 or above was normal at all levels of demographic variables (age, sex and education), regardless of biomarker status, thus the 0-15 range of this variable was truncated at 10 for easier viewing.

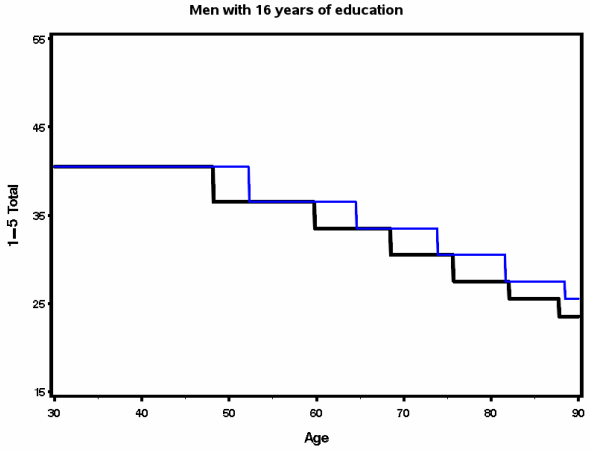


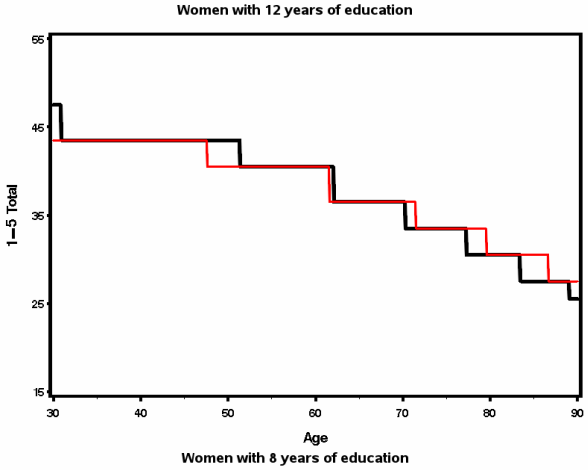
In the following figure series, black lines are Fully-Adjusted Conventional Norms, A-N- Fully-Adjusted Norms are shown in red & blue, for women and men, respectively.

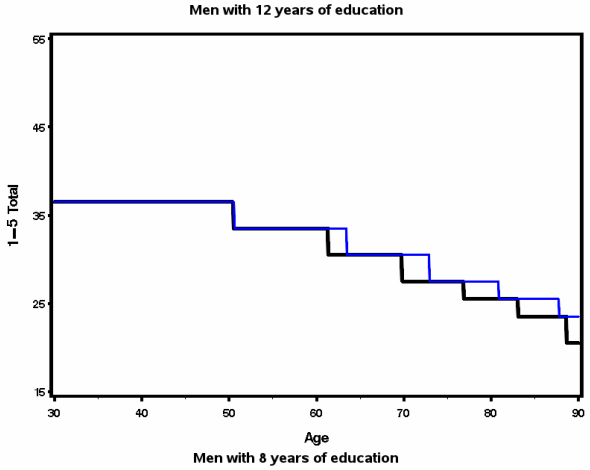

Women with 20 years of education
1−5 Total
55
45
35
25
15
30
40
50
60
70
80
90
Age


Men with 20 years of education
1−5 Total
55
45
35
25
15
30
40
50
60
70
80
90
Age


Women with 16 years of education
1−5 Total
55
45
35
25
15
30
40
50
60
70
80
90
Age


Men with 16 years of education
1−5 Total
55
45
35
25
15
30
40
50
60
70
80
90
Age


Women with 12 years of education
1−5 Total
55
45
35
25
15
30
40
50
60
70
80
90
Age


Men with 12 years of education
1−5 Total
55
45
35
25
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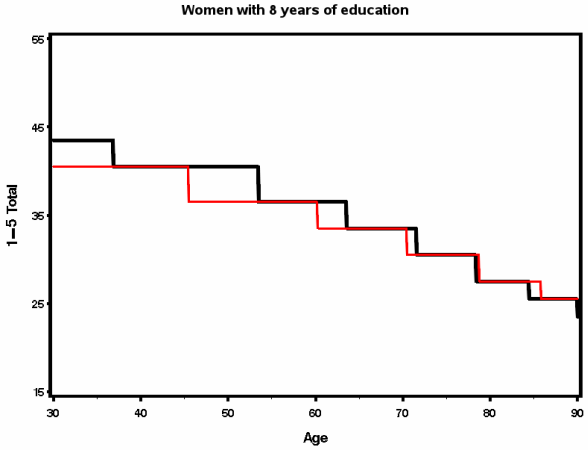
80
90
Age


Women with 8 years of education
1−5 Total
55
45
35
25
15
30
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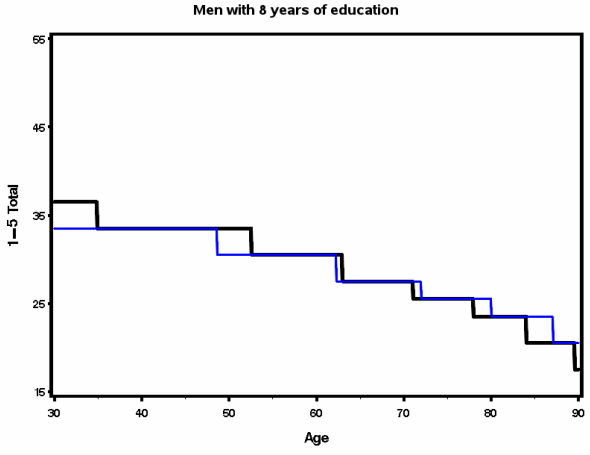
70
80
90
Age


Men with 8 years of education
1−5 Total
55
45
35
25
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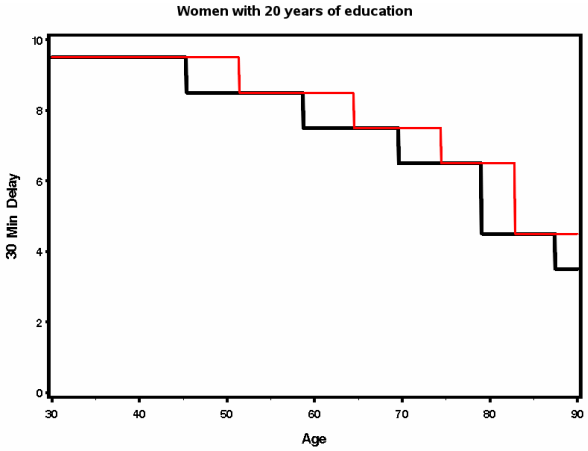
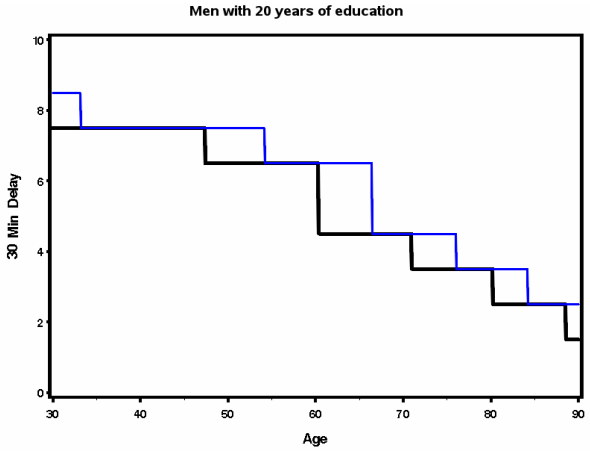
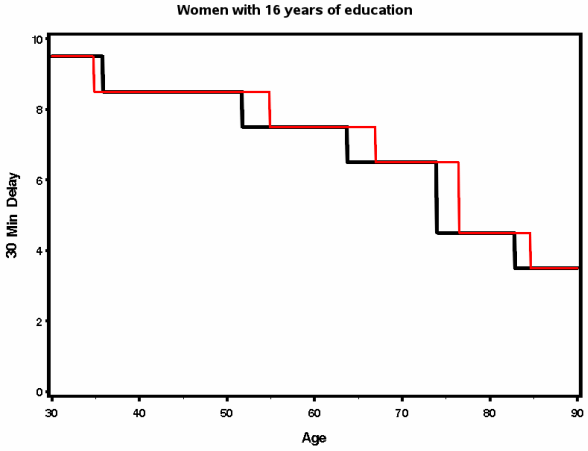
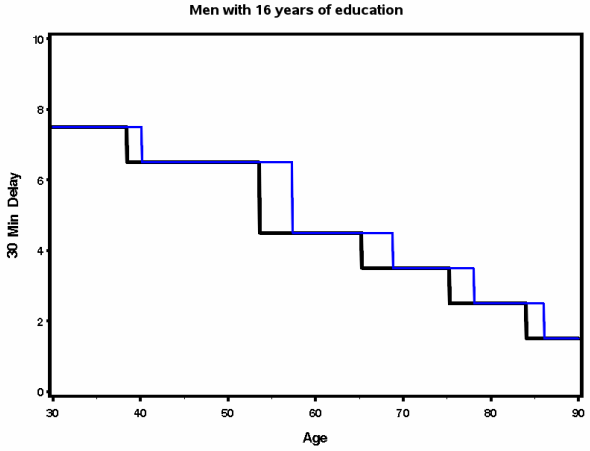
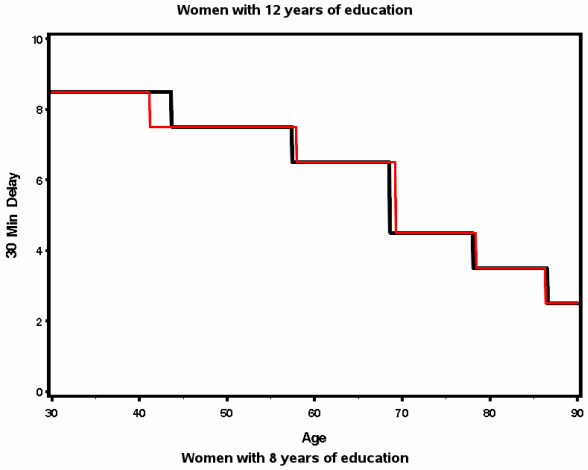
70
80
90
Age

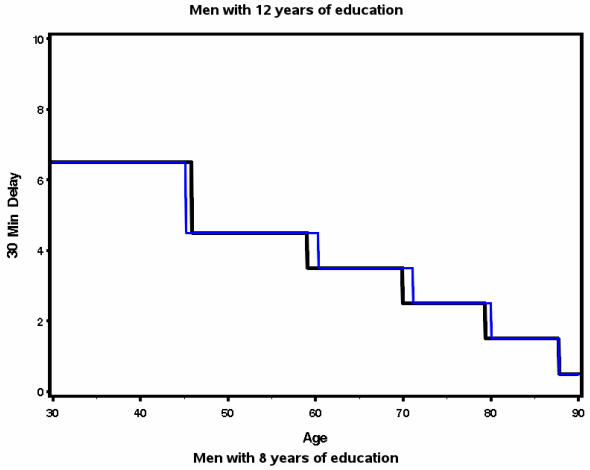

Women with 20 years of education
30 Min Delay
Age

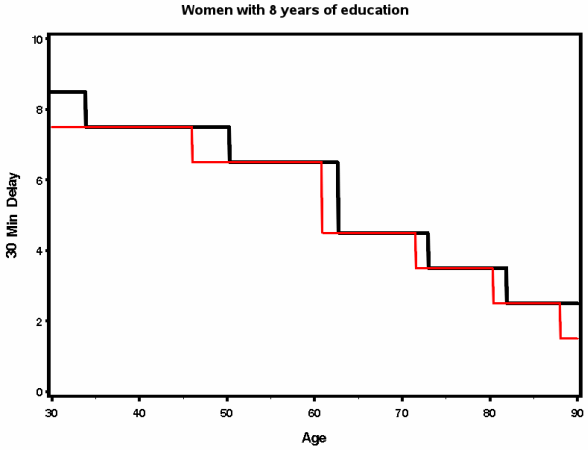

Men with 20 years of education
30 Min Delay
Age

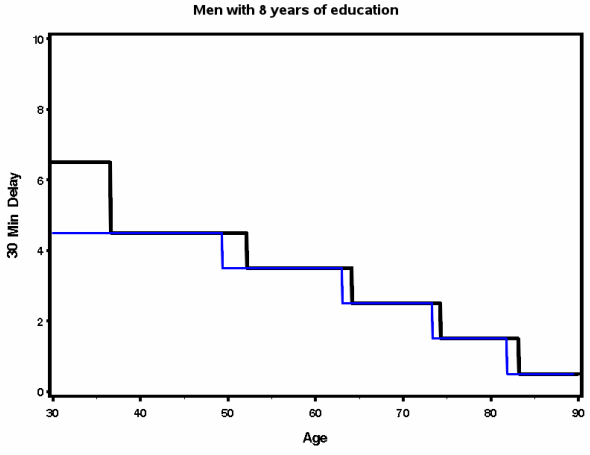

Women with 16 years of education
30 Min Delay
Age

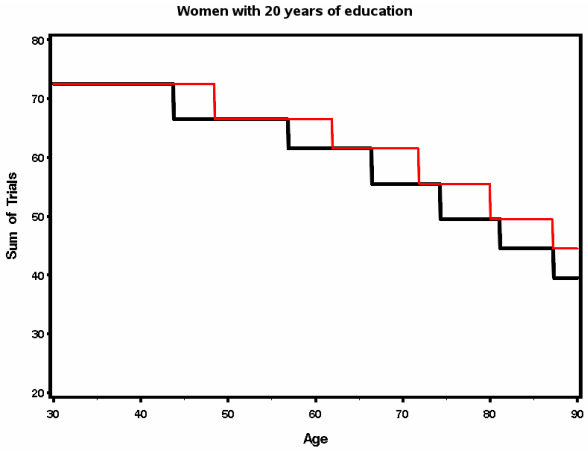

Men with 16 years of education
30 Min Delay
Age

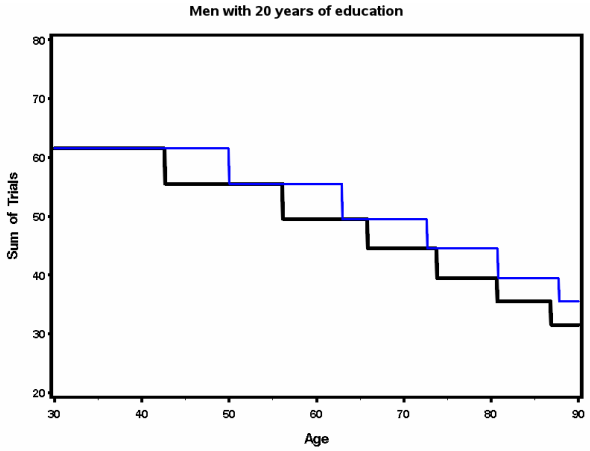

Women with 12 years of education
30 Min Delay
Age

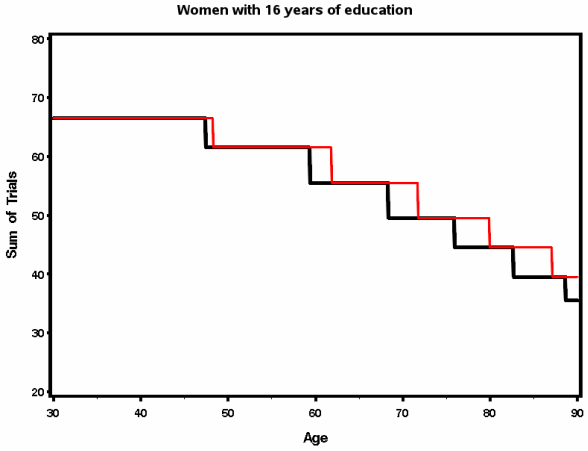

Men with 12 years of education
30 Min Delay
Age

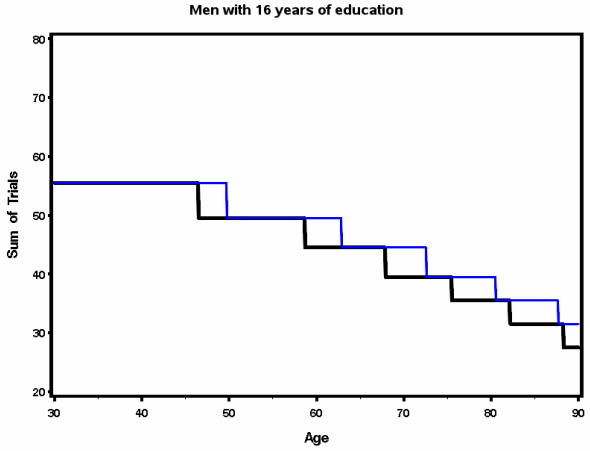

Women with 8 years of education
30 Min Delay
Age

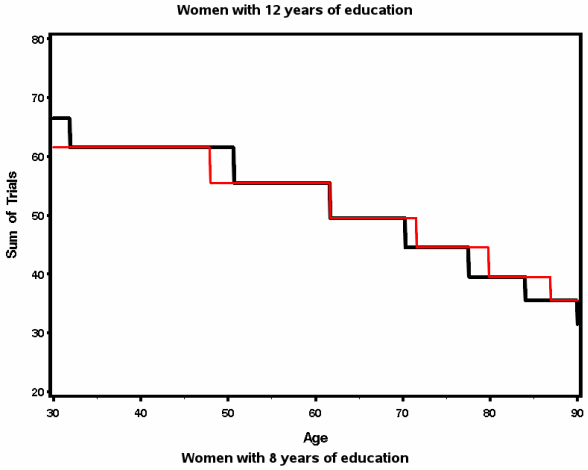

Men with 8 years of education
30 Min Delay
Age

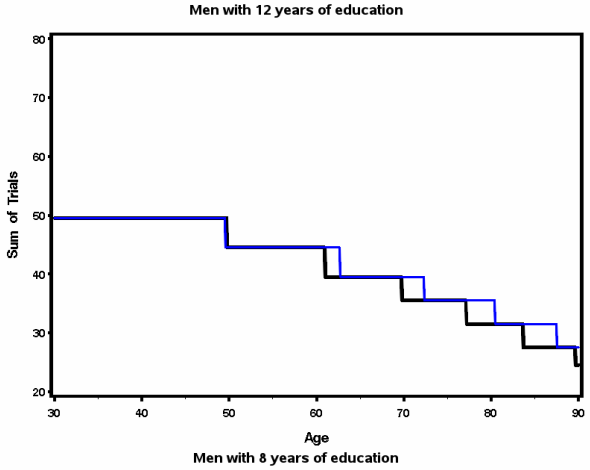

Women with 20 years of education
Sum of Trials
Age

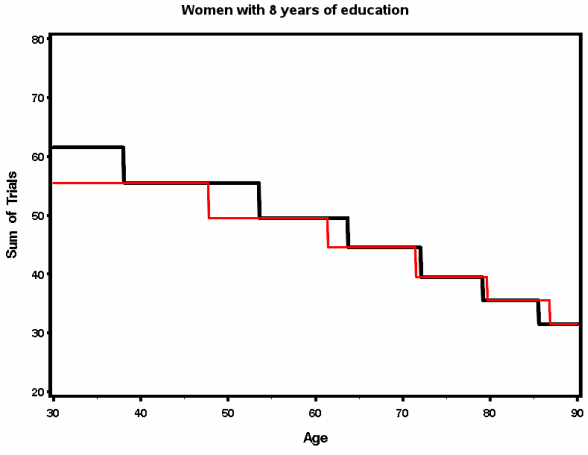

Men with 20 years of education
Sum of Trials
Age

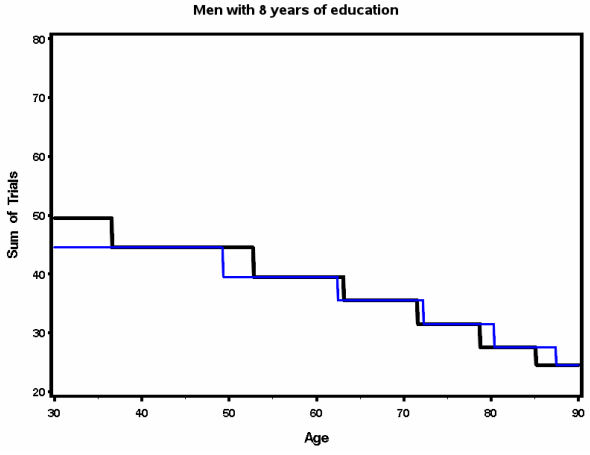

Women with 16 years of education
Sum of Trials
Age

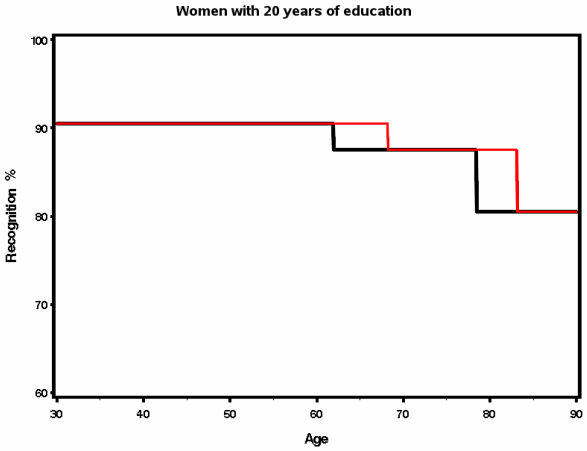

Men with 16 years of education
Sum of Trials
Age

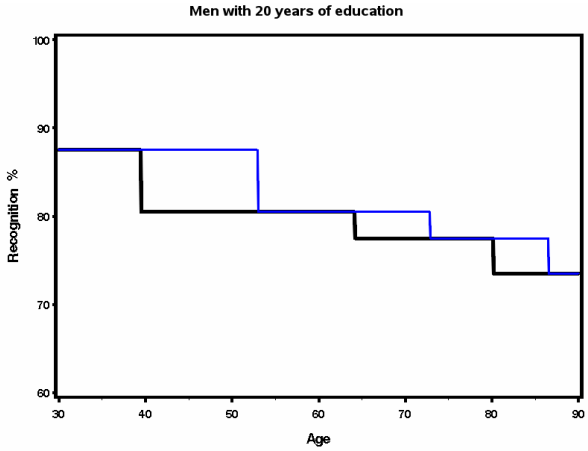

Women with 12 years of education
Sum of Trials
Age

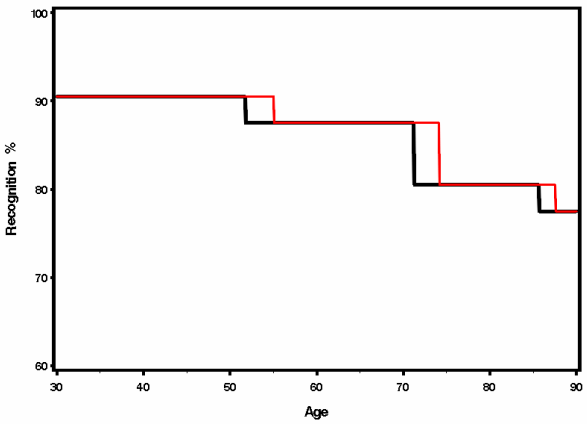

Men with 12 years of education
Sum of Trials
Age

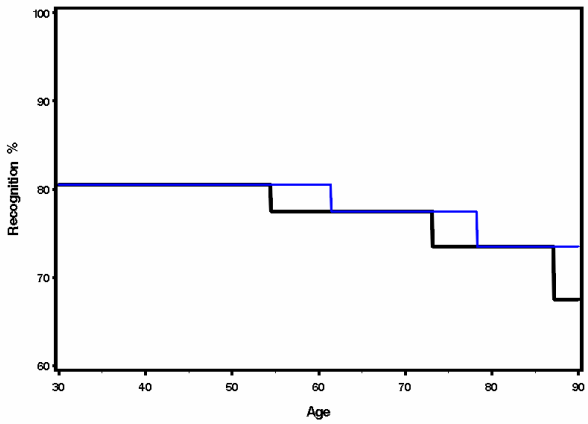

Women with 8 years of education
Sum of Trials
Age

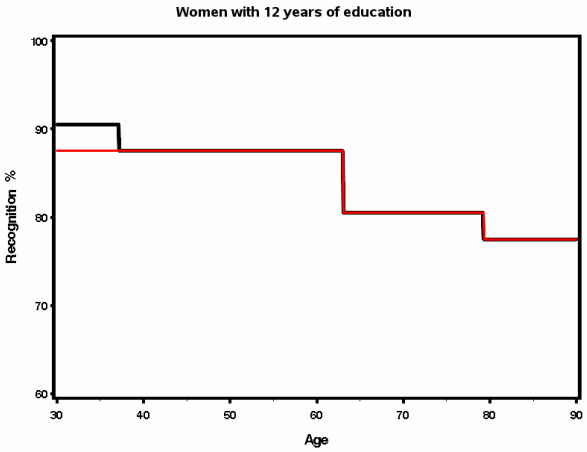

Men with 8 years of education
Sum of Trials
Age

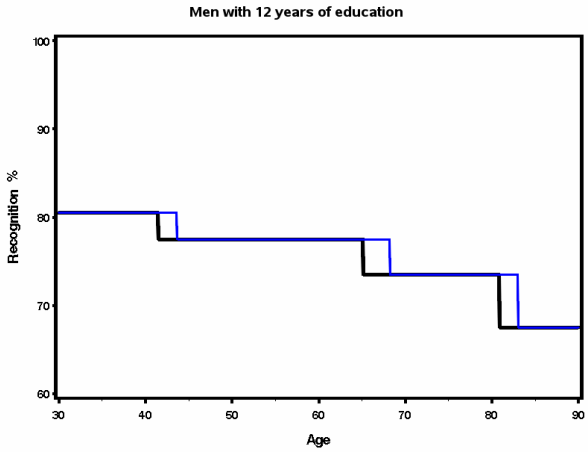

Women with 20 years of education
Recognition %
100
90
80
70
60
30
40
50
60
70
80
90
Age

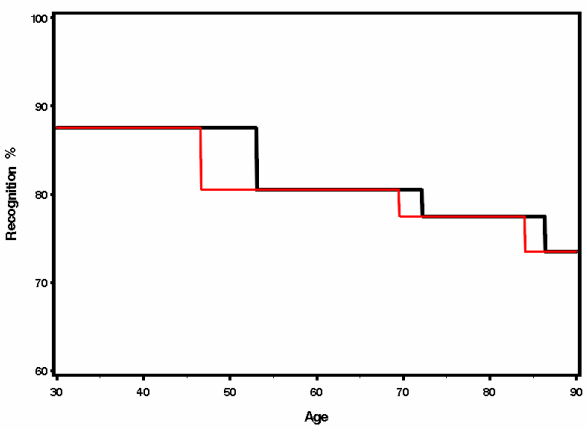

Men with 20 years of education
Recognition %
100
90
80
70
60
30
40
50
60
70
80
90
Age

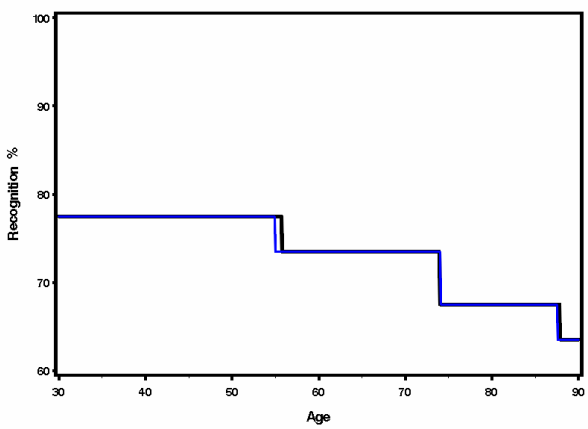

Women with 16 years of education
Recognition %
100
90
80
70
60
30
40
50
60
70
80
90
Age


Men with 16 years of education
Recognition %
100
90
80
70
60
30
40
50
60
70
80
90
Age


Women with 12 years of education
Recognition %
100
90
80
70
60
30
40
50
60
70
80
90
Age


Men with 12 years of education
Recognition %
100
90
80
70
60
30
40
50
60
70
80
90
Age


Women with 8 years of education
Recognition %
100
90
80
70
60
30
40
50
60
70
80
90
Age


Men with 8 years of education
Recognition %
100
90
80
70
60
30
40
50
60
70
80
90
Age