APOE-ε4 count predicts age when prevalence of AD increases, then declines

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Our recent article¹ on the prevalence of AD and other dementias in Cache County, Utah, reported a series of analyses that were erroneous. Our described multiple logistic regression models for π , the age-specific population probability of prevalent AD, mistakenly employed each demented individual's estimated age at onset rather than current age at time of examination. A revised table 3 and figures 5 and 6, reflecting correction of this error, appear below.

The best-estimate odds ratios (OR) for association of AD with one or two $\epsilon 4$ alleles at the *APOE* locus (table 3, Models 4 and 5) are increased substantially, reflecting a strong influence of *APOE* at ages near the population mean centering value of 76.8 years.

The modest but previously “statistically significant” inverse association of education with AD is slightly attenuated such that the OR confidence interval now includes the null value of 1. The apparent interaction of sex with two $\epsilon 4$ s is also reduced but remains within our published confidence interval.

The revised figure 5 shows shifts in the means of all estimated prevalence distributions, with substantial change in the subjects having one or, especially, two $\epsilon 4$ alleles. Notably, with exception of the very late onset no- $\epsilon 4$ distribution, the amplitudes of the sex-specific curves are similar, suggesting that comparable proportions with one or two $\epsilon 4$ s are likely to develop AD. The lower-amplitude curve for men may reflect shorter average duration of illness (shorter life expectancy) for men with AD. Likewise, owing to the force of mortality for those in their 90s (regardless of sex or presence of dementia), the average duration of disease is shorter in no- $\epsilon 4$ subjects. The revised figure 6 suggests that age-specific curves depicting the estimated prevalence OR for AD with one or two $\epsilon 4$ s cross over at age 91, or 9 years later than previously estimated.

Table 3 (revised) Multiple logistic regression models from the Cache County sample (n = 4917) for π , the probability that an individual is a prevalent case of AD

Variable	Model 1	Model 2	Model 3	Model 4	Model 5
Age at baseline	1.145 (1.124–1.166)	1.170 (1.147–1.194)	1.226 (1.180–1.274)	1.334 (1.250–1.423)	1.335 (1.251–1.424)
Sex*	1.201 (0.900–1.604)	1.140 (0.846–1.536)	1.140 (0.847–1.535)	1.165 (0.867–1.566)	0.919 (0.577–1.465)
Education, y	0.992 (0.946–1.040)	0.979 (0.931–1.023)	0.978 (0.930–1.028)	0.981 (0.934–1.031)	0.982 (0.935–1.032)
One $\epsilon 4$	—	5.310 (3.900–7.234)	5.060 (3.730–6.865)	9.904 (5.677–17.277)	7.954 (4.081–15.500)
Two $\epsilon 4$ s	—	15.361 (8.887–26.551)	14.838 (8.527–25.822)	34.430 (16.892–70.174)	24.714 (9.070–67.343)
(Age at baseline) [†]	—	—	0.997 (0.994–0.999)	0.994 (0.992–0.997)	0.994 (0.992–0.997)
Age by one $\epsilon 4$	—	—	—	0.923 (0.876–0.973)	0.922 (0.874–0.972)
Age by two $\epsilon 4$ s	—	—	—	0.852 (0.776–0.935)	0.847 (0.771–0.930)
Sex by one $\epsilon 4$	—	—	—	—	1.438 (0.772–2.678)
Sex by two $\epsilon 4$ s	—	—	—	—	1.720 (0.570–5.197)
LR χ^2	—	160.89 (df = 2, p < 0.001)	9.96 (df = 1, p < 0.001)	15.28 (df = 2, p < 0.001)	1.71 (df = 2, p = 0.42)

Odds ratios (95% CI), likelihood ratio (LR) χ^2 (with df, p value).

* Men = 0, women = 1.
† Age at baseline centered at 76.8 years.

Figure 5, revised. Probability by age (π) that subjects will have prevalent AD, predicted from a multiple logistic regression model (Model 5 from table 3). Squares represent men; circles represent women. Black symbols indicate no $\epsilon 4$; gray symbols, one $\epsilon 4$; open symbols, two $\epsilon 4$ s. The curves indicate predicted prevalence among individuals with the mean population value of 13 years of schooling. There is no apparent difference in π between men and women with no $\epsilon 4$. Significant interaction terms for age by one $\epsilon 4$ and age by two $\epsilon 4$ s result in distributions around younger mean ages for these groups. Inclusion of interaction terms for sex by one $\epsilon 4$ and sex by two $\epsilon 4$ s suggests higher prevalence among women in these groups, especially $\epsilon 4$ homozygotes. In all groups, π reaches a maximum and then declines at later ages.

Reference

1. Breitner JCS, Wyse BW, Anthony JC, et al. APOE- $\epsilon 4$ count predicts age when prevalence of AD increases, then declines. The Cache County Study. *Neurology* 1999;53:321–331.

Figure 6, revised. Odds ratios for AD by age with one $\epsilon 4$ (open circles) and with two $\epsilon 4$ s (black squares) versus individuals with no $\epsilon 4$ as the reference group. The odds ratios were derived from multiple regression Model 5, table 3. Age-related heterogeneity in the risk estimates is marked, especially for the group with two $\epsilon 4$ s.

A phase II trial of nerve growth factor for sensory neuropathy associated with HIV infection

In the article “A phase II trial of nerve growth factor for sensory neuropathy associated with HIV infection” (*Neurology* 2000;54:1080–1088) by McArthur et al., one author was inadvertently omitted. Igor J. Karalnik, MD, Beth Israel Deaconess Medical Center, Boston, MA should have been included. Also, several investigators were omitted from the Appendix, including the following: Beth Israel Deaconess Medical Center, Boston, MA (T. Sandson, C. Crumpacker, B. Chapman); University of Washington, Seattle (N.J. Conley). The authors apologize for these errors.

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