

more severe than symptom-eligible but unconfirmed cases, but we³ and other investigators have examined this question previously.

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Since publication of their article, the authors report no further potential conflict of interest.

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Disclosure of the Genetic Risk of Alzheimer's Disease

TO THE EDITOR: Green et al. (July 16 issue)¹ report that the disclosure of a positive apolipoprotein E (APOE) genotyping result to adult children of patients with Alzheimer's disease led to no short-term increases in depression or anxiety relative to a control group of subjects who underwent testing but to whom results were not disclosed. These findings are based on a flawed comparison. From a policy perspective, one would wish to compare persons who were tested and provided results with those who were not tested at all; no one advocates testing and withholding results. The study's use of an inappropriate control group created bias in favor of its null finding: the experience of being tested and coming close to learn-

ing one's susceptibility to Alzheimer's disease could "prime" subjects' awareness of their risk of the disease, artificially elevating levels of anxiety or depression after testing in the control group.

A reasonable approximation of the appropriate counterfactual condition is the full group of subjects at baseline (before testing). Table 1 shows the effects of testing with the use of the revised control group. The mean scores and variances for all subjects at baseline were calculated from the data in Table 1 of the article by Green et al., whereas the means for other measures (adjusted for covariates) were based on the values reported in Table 3 of their article. Variances were imputed from reported standard errors and sample sizes.

Table 1. Differences in Measures of Anxiety and Depression after Testing with a Revised Control Group of All Subjects at Baseline.*

Measure	Difference between Nondisclosure Group and All Subjects at Baseline (95% CI)		Difference between ε4-Positive Subgroup and All Subjects at Baseline (95% CI)		Difference between ε4-Negative Subgroup and All Subjects at Baseline (95% CI)	
		P Value		P Value		P Value
BAI score†						
At 6 wk	0.1 (-1.5 to 1.7)	0.91	0.9 (-0.7 to 2.5)	0.27	0.2 (-1.2 to 1.6)	0.79
At 6 mo	0.3 (-1.1 to 1.7)	0.69	0.3 (-1.1 to 1.7)	0.69	-0.4 (-1.8 to 1)	0.56
At 12 mo	-0.1 (-1.5 to 1.3)	0.88	0.1 (-1.3 to 1.5)	0.9	-0.1 (-1.5 to 1.3)	0.88
CES-D score‡						
At 6 wk	3.1 (0.9 to 5.2)	0.01	2.8 (0.6 to 4.9)	0.01	2.3 (0.3 to 4.3)	0.03
At 6 mo	2.5 (0.3 to 4.6)	0.02	3.4 (1.2 to 5.5)	<0.01	2.7 (0.5 to 4.8)	0.02
At 12 mo	1.8 (-0.2 to 3.7)	0.08	2.1 (0.1 to 4.1)	0.04	2.3 (0.3 to 4.3)	0.03

* CI denotes confidence interval.

† Scores on the Beck Anxiety Inventory (BAI) range from 0 to 63, with higher scores indicating greater anxiety.

‡ Scores on the Center for Epidemiological Studies Depression Scale (CES-D) range from 0 to 60, with higher scores indicating greater depression. Eight of nine CES-D differences are statistically significant at the conventional level (two-sided P<0.05). The 95% confidence intervals cover the standard threshold for clinical significance (a 5-point difference) for two of those eight depression measures and come within a fraction of a point of that threshold for the remaining six measures.

We found significant increases in depression in eight of nine measures. Given self-selection and the counseling and education included in the authors' study, the true psychological consequences were probably even greater.

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No potential conflict of interest relevant to this letter was reported.

1. Green RC, Roberts JS, Cupples LA, et al. Disclosure of *APOE* genotype for risk of Alzheimer's disease. *N Engl J Med* 2009;361:245-54.

THE AUTHORS REPLY: Gordon and Landa raise an interesting point, but we disagree that our control group was the wrong one. Our design was focused on isolating the effect of disclosure of genetic risk on persons who were motivated to learn about their own risk of Alzheimer's disease. A comparison group of persons who did not have an interest in their own risk of Alzheimer's disease would therefore be inappropriate, and a comparison group of persons who had such an interest and who received no information at all would have measured the effect of risk disclosure without reference to the genetic component. Gordon

and Landa also suggest that our choice biased results in favor of the null hypothesis by priming subjects with an increased awareness of risk. This bias seems unlikely, because most of our subjects entered the study with an inflated sense of their risk of disease (i.e., their perceived risk was higher than that warranted by their status as first-degree relatives). After testing, clinically insignificant, minor elevations were observed in scales of depression symptoms, but not anxiety symptoms. In-depth interviews of subjects whose scores changed the most did not reveal any priming but instead referenced stressors that were not related to the risk of Alzheimer's disease. We agree that our results do not generalize to contexts in which *APOE* information is provided without the support of genetic counseling.

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Since publication of their article, the authors report no further potential conflict of interest.

Bone Marrow Aspiration and Biopsy

TO THE EDITOR: In their Video in Clinical Medicine, Malempati et al. (Oct. 8 issue)¹ provide an excellent overview of bone marrow aspiration and biopsy procedures. However, I differ with some of their recommendations.

First, the practice of rolling and smearing the extracted bone marrow trephine-biopsy specimen on sterile gauze can cause disruption of a frail specimen and exposes it to a chance of loss. In my experience, placing the specimen directly into a formalin-filled tube with the use of a trephine-biopsy needle that will trap the specimen into a needle cannula is less risky.

Second, collecting bone marrow directly into vacuum tubes (rather than using manually heparinized syringes and aspirating the bone marrow by hand) may provide a more standardized operating procedure.

Third, when smears of the aspirate are made while holding both slides in the hands (as shown in the video), there is a risk of dropping a slide. I would suggest leaving one of the slides on a flat surface and anchoring it by finger pressure. I also find that smearing bone debris that has been isolated after absorbing serum (e.g., with a wooden match) can sometimes provide better cellularity than the normal bone marrow smear.

Finally, whenever a trephine-biopsy specimen is needed, I think it is less painful for the patient if the clinician performs the biopsy first and then uses the emptied trephine needle to aspirate blood.

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