

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

1. Malempati S, Joshi S, Lai S, Braner DAV, Tegtmeyer K. Videos in clinical medicine: bone marrow aspiration and biopsy. *N Engl J Med* 2009;361(15):e28. (Available at NEJM.org.)

THE AUTHORS REPLY: Focosi points out several appropriate alternatives to the methods depicted in our video of bone marrow aspiration and biopsy. Our experience does not suggest that the degree of pain associated with the procedure is lower when the biopsy is performed first, and the sequence probably does not matter in the sedated patient.

We agree that a frail biopsy specimen may be damaged by collection onto gauze; however, immediate inspection of the biopsy specimen is critical and requires placement onto gauze or a glass slide. It is not uncommon for an extracted biopsy specimen to contain exclusively cortical bone without marrow, which is an inadequate

sample for evaluation. Immediate placement into formalin precludes the ability to inspect the specimen appropriately. In addition, a touch preparation may provide useful information.

Although collecting aspirate into anticoagulated vacuum tubes may be feasible, in certain conditions, marrow can be difficult to aspirate and requires substantial suction. There is no ability to modify the force or pull when using vacuum tubes. In regard to the preparation of slides, we agree that a slide should be appropriately anchored to create an evaluable aspirate smear.

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

Lack of Population Diversity in Commonly Used Human Embryonic Stem-Cell Lines

TO THE EDITOR: Human embryonic stem-cell research may lead to new methods of drug discovery, insights into mechanisms of disease, and eventually, cellular therapies. The potential benefit to patient populations may depend partially on the diversity of the stem-cell lines that are available for research and clinical use. However, investigators have been unable to target their research to diverse subgroups of existing lines or to ensure the inclusion of lines from the human populations most relevant to their diseases of interest, because almost no information has been available on the human population origin of existing stem-cell lines.

Therefore, with the approval of the University of Michigan's Human Pluripotent Stem Cell Research Oversight Committee, we determined the genetic ancestry of a large collection of stem-cell lines, including the most commonly used lines that were approved for federally funded research under the Bush administration's policy, other lines derived in the United States that have been widely distributed,¹ and additional lines derived in other countries (for details, see the table in the Supplementary Appendix, available with the full text of this letter at NEJM.org).

Using the Illumina 660W genotyping platform, we genotyped genomewide single-nucleotide polymorphisms (SNPs) in each stem-cell line. Control experiments showed that the presence of mouse embryonic feeder cells did not affect the SNP genotypes (>99.99% identity of SNP genotypes between stem-cell lines that were grown with or without feeder cells) or the inferred ancestry (data not shown). Genotypes of the stem-cell lines were compared with previously obtained genotypes on a reference set of 2001 subjects from the HapMap Project and the Human Genome Diversity Project,^{2,3} comprising 63 populations with worldwide representation. We analyzed 483,304 high-quality SNPs that had been genotyped in all sets of samples.

A cluster analysis⁴ of combined stem-cell and worldwide reference genotypes showed that nearly all the stem-cell lines clustered exclusively with reference subjects of known European and Middle Eastern origin (Fig. 1). Two stem-cell lines clustered with East Asians. Using a European and Middle Eastern subgroup of the reference data, we found that most lines clustered primarily with subjects of northern and western European an-