

results. As such, I fear that subject consent was not truly informed.

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

THE AUTHORS REPLY: Parienti suggests that drug-resistant minority quasi-species present at study entry and not detected by means of consensus sequencing may have contributed to virologic failure. We agree that this is a potential explanation for the findings, and we plan to investigate baseline samples obtained from the patients with virologic failure and controls using allele-specific polymerase-chain-reaction assays¹ and pyrosequencing² to test this hypothesis. Since minority species are probably equally prevalent in both treatment groups because of randomization, we are particularly interested in mutations that may confer different effects on susceptibility to abacavir and tenofovir, such as a substitution of a methionine for a valine at residue 184 in HIV-1 reverse transcriptase (M184V mutation).³ The study started before baseline genotypic resistance testing was recommended in treatment guidelines. It is not readily apparent why having baseline genotypic testing performed at the discretion of the provider was associated with a higher risk of virologic failure to abacavir–lamivudine than to tenofovir DF–emtricitabine. We speculate that physicians who chose to obtain a baseline resistance test may have done so for patients who were perceived to be at a higher risk for resistance.

We agree with Leiner that knowledge of drug-resistance mutations at the time of treatment failure is the standard of care for patient treatment. That information was provided to the study participants and their primary providers as soon as the results were available to guide selection of the next regimen (see the Supplementary Appendix, available with the full text of our article at NEJM.org, for the full study protocol). The data and safety monitoring board request was that the full data on resistance not be released to the protocol team, since the study was ongoing; however, each individual provider did receive the necessary data to make an informed choice about treatment options.

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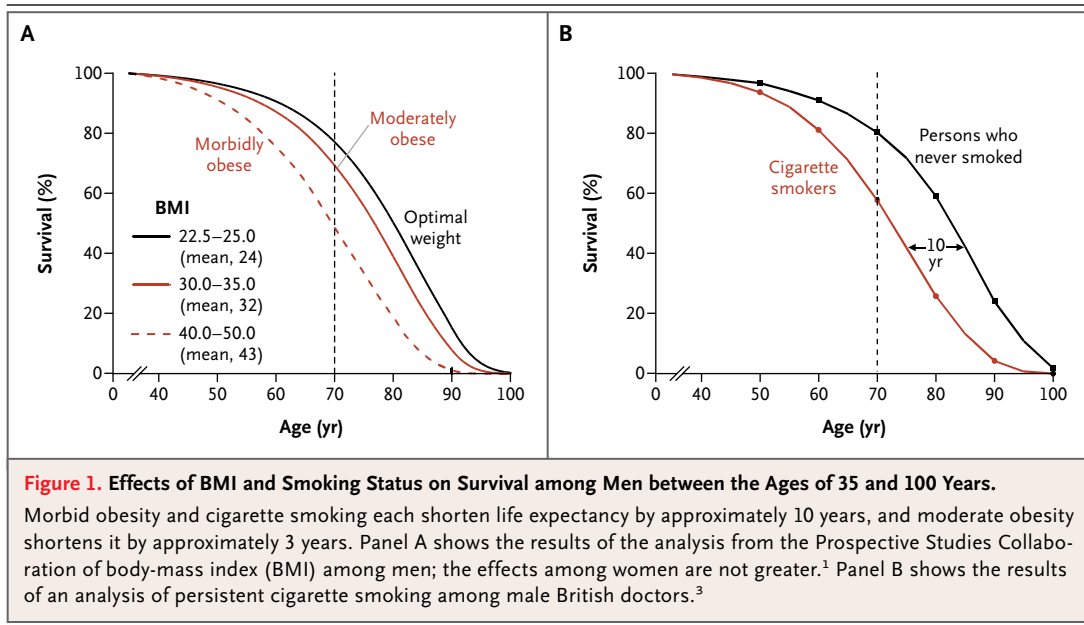
Since publication of their article, the authors report no further potential conflict of interest.

1. Johnson JA, Li JF, Wei X, et al. Minority HIV-1 drug resistance mutations are present in antiretroviral treatment-naive populations and associate with reduced treatment efficacy. *PLoS Med* 2008;(7)5:e158.
2. Wang C, Mitsuya Y, Gharizadeh B, Ronaghi M, Shafer RW. Characterization of mutation spectra with ultra-deep pyrosequencing: application to HIV-1 drug resistance. *Genome Res* 2007;17:1195-201.
3. Whitcomb JM, Parkin NT, Chappey C, Hellmann NS, Petropoulos CJ. Broad nucleoside reverse-transcriptase inhibitor cross-resistance in human immunodeficiency virus type 1 clinical isolates. *J Infect Dis* 2003;188:992-1000.

Effects of Obesity and Smoking on U.S. Life Expectancy

TO THE EDITOR: Mortality from adult obesity and from persistent smoking have already been reliably assessed in studies of tens of thousands of deaths.¹⁻⁴ A common measure of obesity is the body-mass index (BMI, the weight in kilograms divided by the square of the height in meters).² An increase of 2 in the BMI in overweight populations and an increase of 10% in the prevalence of smoking reduce the life span in men comparably, each by about 1 year (Fig. 1). Public debate by

economists should use such assessments. Instead, Stewart et al. (Dec. 3 issue)⁵ overestimate the hazards of obesity and underestimate the hazards of tobacco use. They mainly use data from a study involving only 3000 deaths that were analyzed, without epidemiologically appropriate precautions,¹⁻⁴ in 32 separate subgroups, yielding unreliable relative risks (see Table A3 in the Supplementary Appendix, available with the full text of their article at NEJM.org). Also, they present their



underestimated hazards of tobacco use as the relatively small gain in nationwide life expectancy they forecast if, from 2005 through 2020, the prevalence of smoking in the United States decreases from 24% to 19%. This is their predicted decrease; however, the prevalence may decrease faster, since the federal tax on cigarettes just increased by 150%. Even if the hazards were corrected, such calculations could obscure tobacco's substantial importance for individual smokers.⁴ Stopping smoking can lead to a gain in life expectancy of about 10 years, far more than a smoker could expect to gain from weight control.¹

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1. Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900,000 adults: collaborative analyses of 57 prospective studies. *Lancet* 2009;373:1083-96.
2. Pischon T, Boeing H, Hoffmann K, et al. General and abdominal adiposity and risk of death in Europe. *N Engl J Med* 2008;359:2105-20.
3. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. *BMJ* 2004;328:1519-28.

4. The hazards of smoking and the benefits of stopping: cancer mortality and overall mortality. In: IARC handbooks on cancer prevention: tobacco control. Vol. 11. Reversal of risk after quitting smoking. Lyon, France: International Agency for Research on Cancer, 2007:15-27.

5. Stewart ST, Cutler DM, Rosen AB. Forecasting the effects of obesity and smoking on U.S. life expectancy. *N Engl J Med* 2009; 361:2252-60.

THE AUTHORS REPLY: The relative risks of all-cause mortality in our article are comparable to those from multiple U.S. studies¹⁻⁵ and are broadly consistent with those in the studies cited by Peto and colleagues. They note an approximate 1-year reduction in life expectancy associated with an increase of 2 in the BMI or an increase of 10% in the prevalence of smoking. Our data suggest a reduction in life expectancy of 0.66 years for the BMI increase of 2 and a reduction in life expectancy of 0.77 years for the increased prevalence of smoking of 10%. Thus, the overwhelming effect of obesity in our study was driven not by an underestimation of the hazards of tobacco use relative to those of an elevated BMI, but rather by the greater prevalence of obesity as compared with smoking in the U.S. population. This population perspective should not obscure the large gains that are possible for persons who quit smoking.

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

1. Allison DB, Fontaine KR, Manson JE, Stevens J, VanItallie TB. Annual deaths attributable to obesity in the United States. *JAMA* 1999;282:1530-8.
2. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess

deaths associated with underweight, overweight, and obesity. *JAMA* 2005;293:1861-7.

3. van Baal PH, Hoogenveen RT, de Wit GA, Boshuizen HC. Estimating health-adjusted life expectancy conditional on risk factors: results for smoking and obesity. *Popul Health Metr* 2006;4:14.

4. Freedman DM, Sigurdson AJ, Rajaraman P, Doody MM, Linnet MS, Ron E. The mortality risk of smoking and obesity combined. *Am J Prev Med* 2006;31:355-62.

5. Thun MJ, Day-Lally C, Myers DG, et al. Trends in tobacco smoking and mortality from cigarette use in cancer prevention studies I (1959-1965) and II (1982-1988). In: Changes in cigarette-related disease risks and their implications for prevention and control. NCI monographs. No. 8. Bethesda, MD: National Cancer Institute, 1997. (NIH publication no. 97-4213.)

Repair of Mitral-Valve Prolapse

TO THE EDITOR: In the review article by Verma and Mesana (Dec. 3 issue),¹ mitral-valve prolapse is defined as the displacement of some portion of one or both mitral-valve leaflets into the left atrium during systole. This term was introduced in 1966 by Criley et al.² and has been frequently used as a synonym for “billowing mitral leaflet,” which was used by Barlow et al.³ to describe the same condition. Unfortunately, imprecise terminology may have important implications for mitral-valve repair. According to Carpentier,⁴ the term “prolapse” should be reserved to indicate that the free edge of the leaflet protrudes beyond the mitral annulus level during systole, whereas the term “billowing” should be used when the leaflet body bulges into the left atrium, overriding the mitral annulus plane and usually maintaining the free edge of the leaflets on the ventricular side,^{5,6} although the two conditions may coexist. Agreement on a common terminology may allow a better anatomic correlation of the echocardiographic

findings, which may result in improved treatment for patients.

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

1. Verma S, Mesana TG. Mitral-valve repair for mitral-valve prolapse. *N Engl J Med* 2009;361:2261-9.

2. Criley JM, Lewis KB, Humphries JO, Ross RS. Prolapse of the mitral valve: clinical and cine-angiographic findings. *Br Heart J* 1966;28:488-96.

3. Barlow JB, Bosman CK, Pocock WA, Marchand P. Late systolic murmurs and non-ejection (“mid-late”) systolic clicks: an analysis of 90 patients. *Br Heart J* 1968;30:203-18.

4. Carpentier A. Cardiac valve surgery — the “French correction.” *J Thorac Cardiovasc Surg* 1983;86:323-37.

5. Barlow JB, Pocock WA. Billowing, floppy, prolapsed or flail mitral valves? *Am J Cardiol* 1985;55:501-2.

6. Pellerin D, Brecker S, Veyrat C. Degenerative mitral valve disease with emphasis on mitral valve prolapse. *Heart* 2002;88: Suppl 4:iv20-iv28.

A Crisis in Late Pregnancy

TO THE EDITOR: In the article by Desai et al. (Dec. 3 issue),¹ the electrocardiogram has the characteristics of one with the right-arm and left-arm cables exchanged, resulting in the appearance of lead I as a mirror image and leads aVL and aVR exchanged. The correctly connected electrocardiograph would show an ST-segment elevation only in leads aVR and aVL; this pattern would be more suggestive of diffuse myocardial injury than lo-

calized injury and would be consistent with catecholamine-induced injury.

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

1. Desai AS, Chutkow WA, Edelman E, Economy KE, Dec GW Jr. A crisis in late pregnancy. *N Engl J Med* 2009;361:2271-7.