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

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THE AUTHORS REPLY: We agree that iodine deficiency was present among women in the United Kingdom and Turin, Italy. We were not specifically diagnosing hypothyroidism but, rather, using thyrotropin and free thyroxine levels in the upper and lower tails of these respective distributions to identify women whose children might benefit from maternal thyroxine supplementation. If we had included more women in the screen-positive group, more women would have been treated, but these women would have had a reduced risk of having a child with hypothyroidism and hence a low IQ. Any effect of screening and treatment would have been diluted.

The correspondents state that the reference range is inaccurately converted for free thyroxine on page 494. This is correct; the values should be 0.65 to 1.13 ng per deciliter. We apologize for this error.

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

Lifetime Risks of Cardiovascular Disease

TO THE EDITOR: In their article (Jan. 26 issue), Berry et al.[1] reported on the lifetime risks of cardiovascular disease in the United States based on a total cohort of 257,384 men and women. Our own research estimating the lifetime risk of cardiovascular disease in England and Wales was based on a cohort of 2,343,759 persons, including 113,925 who were nonwhite.[2] We validated our algorithms in a separate cohort of 1,267,159 people from England and Wales. Like Berry et al., we found that diabetes, smoking, and higher levels of cholesterol and blood pressure were associated with increased lifetime risks of cardiovascular disease. We also took into account body-mass index, socioeconomic variables, family history of heart disease, rheumatoid arthritis, atrial fibrillation, and renal disease, which were associated with increased risk. Unlike Berry et al., we found differences in risk between ethnic groups even after accounting for differing levels of risk factors, with substantially higher risks in South Asians and marginally lower risks in black populations as compared with white ones. Overall estimates were broadly similar in the two studies.

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Dr. Coupland reports being a consultant statistician for ClinRisk. Dr. Hippisley-Cox reports being co-director of QResearch and director of ClinRisk. No other potential conflict of interest relevant to this letter was reported.

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2. Hippisley-Cox J, Coupland C, Robson J, Brindle P. Derivation, validation, and evaluation of a new QRISK model to estimate lifetime risk of cardiovascular disease: cohort study using QResearch database. BMJ 2010;341:c6624.

TO THE EDITOR: Berry et al. present a meta-analysis of lifetime risk for cardiovascular disease, calculated with the use of a Practical Incidence Estimator, which uses "age" as the time scale (as opposed to "calendar period," as used in Kaplan–Meier analyses). It allows the combination of subject information enrolled at different ages, with varied follow-up.[1] However, some germane points remain to be addressed. First, the proportions of risk factors measured at one time point (subject to inaccuracies) versus those averaged over a number of measurements were not reported. Second, given that the average follow-up was just 10 years, most of the data contributing to lifetime-risk estimates at age 55 years were not from the actual 55-year-olds themselves but rather from the 65-year-olds and 75-year-olds initially allocated to the same risk-factor category. Related to this, the allocation to risk-factor categories was (unidirectionally) fixed in this analysis. For example, 70-year-olds initially enrolled in the category "all risk factors optimal" are presumed to have always been in this category throughout their prior lifespan. Clearly this is not always the case in real life. How this consideration influenced the results was not discussed. Finally, would the authors speculate as to why the percentage of men in the all-risk-factors-optimal category remained constant with age (at about 2.9%)?

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

1. Vasan RS, Beiser A, Seshadri S, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: the Framingham Heart Study. JAMA 2002;287:1003-10.

TO THE EDITOR: Berry et al. performed a meta-analysis using data from 18 unique cohort studies that focused on lifetime risks of cardiovascular disease. Their findings convincingly reinforce the importance of traditional coronary risk factors with respect to the lifetime risks of cardiovascular disease. Beside age, sex, and race, risk-factor profiles included diabetes, smoking, total cholesterol level, and systolic blood pressure. In my view it is a real pity that some measures of physical activity consistently remain unconsidered in otherwise large and excellent studies. There is ample evidence that physical activity is an independent and important factor in assessing the risk of cardiovascular disease and that increasing levels of physical fitness protect against elevations in most risk factors in subjects with or without cardiovascular disease, thus reducing mortality.[1,2] Despite these facts, physical activity is often ignored in large epidemiologic studies, as well as in the general cardiovascular risk–assessment profile.[3] A consideration of physical activity would also help focus attention on important nonpharmacologic preventive measures, such as the change from a sedentary to a more active lifestyle.

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

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3. Vasan RS, Kannel WB. Strategies for cardiovascular risk assessment and prevention over the life course: progress amid imperfections. Circulation 2009;120:360-3.

THE AUTHORS REPLY: We are aware of the valuable study by Hippisley-Cox et al., in which information on both traditional and nontraditional risk factors was obtained between 1994 and 2010 and participants were followed for up to 16 years.[1] Their approach should be distinguished from ours, in which we report lifetime risks on the basis of directly measured risk factors and observed outcomes among participants in the United States over the past 50-plus years. Our approach allows us to provide insight into an important clinical question: What is the effect of a given risk-factor profile in middle age on cardiovascular disease events decades later? Cardiovascular disease in later life reflects the cumulative burden of risk factors across the lifespan, and the benefit of a low risk-factor burden is greatest at younger ages. Nevertheless, the findings from the QResearch database and those from our study are, overall, quite similar.

We would like to make several important clarifications with respect to McEvoy's comments about our methodologic approach. The choice of time scale for Kaplan–Meier and other techniques for survival analysis can vary, and it is well established that the "time on study" approach and the "attained age" approach yield similar results when persons who are disease-free are followed after a selected index age.[2] Our approach uses age as the time scale, but we did not average risk-factor levels across the lifespan, as we clearly state in our article: "Participant data were stratified according to risk-factor levels or status as assessed within 5 years of each index age. For example, risk factors measured for participants between 40 and 49 years of age were included in the analyses for the age of 45 years." All reported lifetime-risk estimates for each age group are derived only from the participants with risk factors measured at that reported age. The relatively constant prevalence of low-risk status in men reflects the effects of changes in individual risk factors across the age spectrum. For example, when men with risk factors measured at 45 and 75 years of age are compared, smoking is more prevalent at the younger age (51.0% vs. 20.7%), whereas diabetes is more prevalent at the older age (2.8% vs. 11.7%).

Finally, we appreciate the insightful comments from Burtscher on the importance of physical activity on lifetime risk for cardiovascular disease. Recently, we reported on the association between physical-fitness levels and lifetime risk for cardiovascular disease in the Cooper Center Longitudinal Study using this same analytic approach.[3] We observed that physical fitness represents an important determinant of long-term risk, particularly among persons with established risk factors.

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1. Hippisley-Cox J, Coupland C, Robson J, Brindle P. Derivation, validation, and evaluation of a new QRISK model to estimate lifetime risk of cardiovascular disease: cohort study using QResearch database. BMJ 2010;341:c6624.
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IgG4-Related Disease

TO THE EDITOR: In their review, Stone et al. (Feb. 9 issue)[1] describe clinical features of IgG4-related disease. However, it is critical for physicians to be aware of two additional clinical aspects. First, IgG4-related disease affects joints,[2-4] and second, it can affect children[5] as well as adults. We are currently treating a 15-year-old patient who has had IgG4-related disease for 4 years. He first presented with two episodes of bilateral mastoiditis, which required surgery. Both the clinical course and the histologic findings were compatible with chronic nonspecific inflammation. Two years later, the patient had severe headaches, polyuria and polydipsia due to diabetes insipidus, and ankle arthritis. Magnetic resonance imaging of the brain revealed meningeal inflammation and hypophysitis. A brain biopsy showed hypertrophic pachymeningitis with mixed infiltrates of lymphocytes, plasma cells, and eosinophils. The ratio of IgG4-positive to IgG-positive plasma cells was increased (32 per high-power field). The same findings were present on a synovial biopsy of the talocalcaneal joint (Fig. 1). This case suggests that arthritis should be included in the list of organ manifestations in IgG4-related disease in both adults and children.

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