Correspondence

The American Health Care System

To the Editor: Iglehart (Jan. 7 issue)[1] has undertaken the admittedly difficult exercise of tracking how Americans spend money on health care. In Table 2 of his article, which shows expenditures in 1970, 1980, and 1990 and projected expenditures in 1998 and 2007, Iglehart indicates that about 18 to 20 percent of national health care expenditures are for physicians' services, and about 4 to 7 percent are for program administration. The expenditures that he cites for physicians' services probably reflect gross payments, including overhead, not physicians' take-home income. Overhead is much higher in the United States than in other countries and is related, at least in part, to the costs of dealing with the requirements of regulatory agencies that are unique to the American health care system. These requirements affect expenditures in most of the categories shown under "personal health care" in Table 2. Inasmuch as this portion of overhead is related to administrative costs, it can be argued that these costs belong more appropriately in the category of "program administration and net cost." The high cost of dealing with regulatory issues may be an additional reason why health care expenditures in the United States are higher than per capita income would predict. Iglehart's calculations may underestimate these costs. Are data available to allocate administrative costs more accurately? If not, perhaps an additional category — overhead — should be included in an analysis of health care expenditures, so that the interested reader can have a better understanding of how the health care dollar is being spent.

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1. Iglehart JK. The American health care system — expenditures. N Engl J Med 1999;340:70-6.

To the Editor: Kuttner's assessment of this country's health insurance coverage (Jan. 14 issue)[1] illustrates why the American Academy of Pediatrics has been calling for the adoption of a national health care policy to cover all children and adolescents and, eventually, all Americans.

Programs such as the Children's Health Insurance Program continue to be a priority for the American Academy of Pediatrics. However, as Kuttner points out, even with this program, millions of children will remain uninsured. Since 1989, children have lost private health insurance coverage at twice the rate that adults have.[2]

Health insurance coverage for all infants, children, and adolescents in this country should be a right, regardless of their economic situation. Such coverage must offer high-quality care that is accessible, continuous, comprehensive, family-centered, coordinated, and compassionate. We should expect no less for our children.

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1. Kuttner R. The American health care system — health insurance coverage. N Engl J Med 1999;340:163-8.
2. Current population survey. Washington, D.C.: Bureau of the Census, March 1990, March 1997.

INSTRUCTIONS FOR LETTERS TO THE EDITOR

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To the Editor: We enjoyed reading Kuttner's article on employer-sponsored health coverage (Jan. 21 issue).[1] However, we disagree with Kuttner on several points. First, he states that employers contracting with a single health plan prevent market forces from disciplining suppliers. However, employers listen to their employees and insurance brokers, as well as paying attention to published information, such as the insurance commissioner's ranking of complaints and National Committee for Quality Assurance status, when deciding whether to contract with a health plan. There are many competitors that are eagerly willing to pitch their products to employers. Thus, we believe that market forces are at play. For example, in Chicago during the second half of 1998, at least five health maintenance organizations (HMOs) and one indemnity-insurance carrier closed operations or merged.

Second, it is in the best interest of an employer to contract with as few health plans as possible, because doing so results in easier collection of premiums, fewer benefits packages to understand, and economies of scale for purchasing the coverage. This approach greatly eases the administration of health care benefits.

Finally, why is it so bad that employees have some out-of-pocket expenses? Consumers pay deductibles when they have claims involving their automobile insurance, home insurance, property insurance, and other insurance policies. We agree that workers unfortunately drop their health care coverage as their share of the premium increases, and this results in increased numbers of uninsured people. However, a policy of no out-of-pocket expenses would defeat the purpose of any insurance plan: to prevent catastrophic losses.

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1. Kuttner R. The American health care system — employer-sponsored health coverage. N Engl J Med 1999;340:248-52.

To the Editor: Kuttner predicts a "shifting of costs to employees, paring of benefits, and resulting increases in the number of the uninsured and underinsured . . . as long as the basic system of employer-provided health insurance continues." True, business is focused on price, but with his glum vision, Kuttner fails to ask, "Why?" The simple answer is that medicine has not quantitatively demonstrated the value of health care. How can corporations buy health care if no one can measure it?

Shopping for a complex product only on the basis of price is a poor strategy.[1] Businesses know this and have attempted value-based purchasing (e.g., using measures from the National Committee for Quality Assurance). But only we in medicine can truly measure health and define quality. We have failed miserably because we have no systems to aggregate clinical data. Aggregated claims data, a poor substitute but the best available, now drive health care. However, if we in medicine can credibly measure health, businesses will, for two powerful reasons, buy on the basis of value. The obvious reason for businesses to buy wisely is to provide employees with the benefit of excellent health care. Measurably better health plans will attract and retain high-quality work forces, which are now in great demand. The less obvious but more compelling reason to buy wisely is productivity. Healthy people produce more, make better decisions, have better morale, and make fewer mistakes than do people who are not healthy.

Current ignorance about the relation of corporate expenditures for medical care to economic success is profound. The United States spends twice as much per capita on health care as other nations, yet economists cannot agree whether this expenditure is a drain on the competitiveness of America's corporations or a major reason for their global preeminence. At the core of this ignorance is the failure of the medical community to measure the health of the populations it serves. Physicians who practice occupational medicine believe that the potential value of gains in health-related productivity is huge — at least twice the amount of corporate spending for medical care.[2] When better data confirm this, businesses will buy more health care, on the basis of the return on the investment. The return on the investment will result in a greater emphasis on prevention-based approaches to health care, which dovetail beautifully with population-based systems of clinical data. Doctors will once again focus on improving health rather than rationing care.

We are the problem, not our business customers. Physicians must unite and invest now in the data infrastructure. The electronic medical record will improve health more than penicillin will.

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1. Rubin PH. Managing business transactions: controlling the cost of coordinating, communicating, and decision making. New York: Free Press, 1990.
2. Brady W, Bass J, Moser R Jr, Anstadt GW, Loeppke RR, Leopold R. Defining total corporate health and safety costs — significance and impact: review and recommendations. J Occup Environ Med 1997;39:224-31.

To the Editor: Iglehart's report on Medicare (Jan. 28 issue)[1] contains a surprising inaccuracy that obscures both an important shortcoming in Medicare coverage and an injustice to Medicare beneficiaries with mental disorders. The author states, "Under Part B, Medicare pays 80 percent of the approved amount (according to a fee schedule) for covered services in excess of an annual deductible of $100." In fact, for most outpatient mental health services, Medicare pays only 50 percent of approved charges in excess of the deductible.

This discrimination against beneficiaries with mental disorders has been part of the Medicare program since its inception, and it creates a financial barrier to mental health care for many elderly and disabled persons. In spite of continued efforts to secure parity in coverage for physical and mental health care, this inequity persists. Although not mentioned by Iglehart, it is one of the inadequacies of Medicare's current benefits package, which Congress would do well to correct.

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1. Iglehart JK. The American health care system — Medicare. N Engl J Med 1999;340:327-32.

To the Editor: The cutbacks in Medicare support for graduate medical education and reimbursements for physicians' services will soon limit medical school applicants to the well-to-do. It is not reasonable for Congress or the American public to expect physicians to bear the entire cost of their education in an era of declining income expectations, when they may already have incurred a large debt for undergraduate education and have, on average, 5 to 10 fewer working years than persons in other professions that require less education and training. Ultimately, the taxpayers are going to have to ante up.

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To the Editor: In your thoughtful series "The American Health Care System," two issues that have important policy implications were not emphasized in Iglehart's article on Medicare[1] or in Bodenheimer's article on measuring and monitoring quality in health care (Feb. 11 issue).[2] The first issue is the finding that race and socioeconomic status are associated with the use of many Medicare services, which my colleagues and I reported in 1996.[3] For example, in 1993, the rate of immunization against influenza was 31 percent for black beneficiaries and 52 percent for white beneficiaries; for the least affluent whites, the rate was 26 percent lower than it was for the most affluent whites, and for the least affluent blacks, the rate was 39 percent lower than it was for the most affluent blacks. As compared with whites and the most affluent members of both races, blacks and the least affluent undergo fewer common surgeries (e.g., hip and knee replacements) but strikingly more of certain procedures associated with poor outcomes of chronic diseases (e.g., amputation of all or part of a lower limb).[3] Biologic differences do not explain these disparities. The association of beneficiaries' characteristics, such as race and income, with use of Medicare services was unexpected. It is clear now that the implementation of Medicare was a necessary condition for improving access to care on the part of the elderly, but Medicare alone is not sufficient to ensure equity in the use of Medicare services.

The second issue that was not underscored is the magnitude of the difficulty ahead in obtaining valid and reliable data from HMOs and other managed-care organizations. Several data problems must be acknowledged and solved to develop a useful monitoring system such as that which the Health Plan Employer Data and Information Set is intended to be. Data must be generated to monitor the use of specific services according to the race and socioeconomic status of the enrollees — including rates of preventive services, common elective procedures, diagnostic tests, and procedures associated with less than optimal outcomes of chronic conditions. Unless information is generated for vulnerable subgroups, inequalities in health care will go unrecognized in the managed-care environment. The next difficult problem is to implement methods to ensure that the data are reliable and comparable among HMOs and other managed-care systems. Another challenge is to deal with the problem of small samples, because the rates of use of many common procedures are relatively low.

Disparities in use of Medicare services remained undetected for the first 25 years of the program. It required the large Medicare administrative data base from the fee-for-service sector and the monitoring of many different services — on the basis of race and socioeconomic status — to discover disparities in patterns of care. Without adequate monitoring of the changing health care delivery system, the disparities may increase if vulnerable subgroups have more difficulties than others in dealing with the growing managed-care marketplace. This issue is especially important today because disparities in health are growing larger.[4]

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1. Iglehart JK. The American health care system — Medicare. N Engl J Med 1999;340:327-32.
2. Bodenheimer T. The American health care system — the movement for improved quality in health care. N Engl J Med 1999;340:488-92.
3. Gornick ME, Eggers PW, Reilly TW, et al. Effects of race and income on mortality and use of services among Medicare beneficiaries. N Engl J Med 1996;335:791-9.
4. Pappas G, Queen S, Hadden W, Fisher G. The increasing disparity in mortality between socioeconomic groups in the United States, 1960 and 1986. N Engl J Med 1993;329:103-9. [Erratum, N Engl J Med 1993;329:1139.]

To the Editor: I see no hope for the future of health insurance as long as the fiction is maintained that the employees of a company receive health care but do not pay for it. We must be certain that patients know they are responsible for their own health care. Giving businesses a tax deduction is not acceptable.

Since people do not wish to pay for health care, bottom-line, basic care might also be funded by taxes (through Medicaid). Physicians, patients, and companies must understand that they ultimately pay for their own health care.

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To the Editor: In her editorial "The American Health Care System Revisited — A New Series," Angell (Jan. 7 issue)[1] compares the American health care system with the systems in other developed countries. This is not a reasonable comparison. Medical care in the United States is molded by many factors that are not present in other developed countries.

These factors include the wide availability of guns and the trauma caused by them, the high rate of infection with the human immunodeficiency virus, and the high rate of pregnancy among teenagers, with little prenatal care. In addition, the United States allows over 1 million immigrants to enter the country each year — more than the number of immigrants to all other countries combined. Many of these people come from Third World countries, bringing with them many medical problems. Millions more have entered the country illegally and receive medical treatment. Add to these factors the American legal system and bureaucracy, which account for untold billions of dollars in costs to avoid litigation and keep records, respectively. The American diet and lack of exercise have been cited for years as major causes of cardiovascular-related deaths.

These are just a few of the many factors that add greatly to the costs of health care in the United States. Comparing the costs of American health care with the costs of care in other developed countries without noting these and other differences does not provide a realistic picture of the unique problems the American health care system has to deal with.

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1. Angell M. The American health care system revisited — a new series. N Engl J Med 1999;340:48.

The authors reply:

To the Editor: Dr. Leeman is correct. Medicare pays only 50 percent of approved charges (above the deductible) for most outpatient mental health services. The payment differential for services that treat physical and mental illnesses was adopted by Congress when it initially designed Medicare and reflected most private insurance policies in the 1960s. Because it was difficult for actuaries to determine the necessity of mental health services, insurers decided the market would be the best determinant of need. This payment differential is likely to receive greater attention from Congress in the future, because the number of disabled persons who are under 65 years of age, eligible for Medicare, and afflicted with problems treatable by mental health services is growing. Nevertheless, despite the improved treatments that are available and the demonstrated interest of legislators in achieving parity of payment for services that treat mental and physical illnesses, the discrimination against beneficiaries with mental disorders is not likely to be eliminated soon, because of the lack of understanding about these disorders.

Drs. Menon and Vickers ask a useful question. Unfortunately, not many data exist to allow an accurate estimation of regulatory costs. Woolhandler et al. attempted to estimate these costs for the hospital sector.[1] They estimated that, nationally, administration accounted for an average of 24.8 percent of each hospital's spending in fiscal year 1990. They based their analysis on Medicare cost reports, one of the regulatory requirements that becomes a cost for a hospital. To my knowledge, similar data do not exist for the physician sector. Conceivably, a designated agency could solicit such information from physicians' offices. But the additional expense incurred by physicians in order to comply with the request for information would only add to the paperwork burden, thus increasing "administrative overhead" beyond current requirements. Without the broad-based collection of such data, estimates of regulatory costs could be gleaned only from in-depth interviews with a sample of physicians. Beyond the investment of time this would require of physicians and their office staffs, it is not clear who would pay for such an undertaking.

Dr. Rosenblatt asserts that reductions in the growth of Medicare's support of graduate medical education and reimbursements for physicians' services will limit the pursuit of a medical education to the affluent. The rising debt that many medical students incur as a result of higher educational expenses must certainly present a problem for young people who come from families of limited means. But despite the high cost of education, the uncertainty of changes in the system, and reports that many practicing physicians would choose a different career if they had a chance to start over, a large number of people (although a proportionately smaller number who are members of minority groups) continue to apply to medical school. One approach to this issue was suggested recently by Mullan, who urged the federal government to link educational subsidies for students to the requirement that, in return, they provide professional service for a specified period in geographic areas deemed to be medically underserved.[2]

JOHN K. IGLEHART

1. Woolhandler S, Himmelstein DU, Lewontin JP. Administrative costs in U.S. hospitals. N Engl J Med 1993;329:400-3.
2. Mullan F. The muscular Samaritan: the National Health Service Corps in the new century. Health Aff (Millwood) 1999;18(2):168-75.

To the Editor: Gornick's letter about the influence of race and socioeconomic status on quality of care in the Medicare program is on target. Sadly, the situation may soon get far worse.

Senator John Breaux (D-La.) and Representative Bill Thomas (R-Calif.), who cochaired the now defunct National Bipartisan Commission on the Future of Medicare, are moving swiftly to push their Medicare-voucher proposal through Congress. If this proposal for what they call "premium support" passes, the quality of care for lower-income Medicare beneficiaries is likely to fall precipitously.

Under a voucher program, the government would pay a certain amount each year to assist Medicare beneficiaries in purchasing health care coverage.[1] Beneficiaries would have to pay the remainder of the premium out of pocket. Those who could afford more expensive, higher-quality coverage would generally purchase it. Lower-income beneficiaries would be able to afford only the lowest-cost plans, which would probably be lacking in quality and access. The Breaux–Thomas proposal would divide the Medicare population into those with higher incomes, who could buy high-quality care, and those with lower incomes, who would be forced to buy lower-quality care. The result would be a worsening of the inequities so clearly described by Gornick.

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1. Vladeck BC. Plenty of nothing — a report from the Medicare commission. N Engl J Med 1999;340:1503-6.

Dr. Angell replies:

Dr. LaPorta suggests that the American health care system is more expensive than systems in other developed countries because Americans are sicker. I know of no evidence to support that claim. In particular, there is no evidence that an early death from trauma is more expensive than a late one from Alzheimer's disease; the tragedy of the former is not economic.

Indeed, most measures of health status show that the United States is near the bottom of the list of developed

countries but is not an outlier. It is certainly an outlier in terms of health care expenditures. The only reasonable explanation is that the extraordinary costs of health care in the United States stem largely from the system in which it is delivered, not from the health care needs of its citizens.

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Valacyclovir to Prevent Cytomegalovirus Disease after Renal Transplantation

To the Editor: In their placebo-controlled study, Lowance et al. (May 13 issue)[1] found that treatment with valacyclovir markedly reduced the incidence of cytomegalovirus (CMV) disease after renal transplantation. The reduction in CMV disease among CMV-seronegative recipients was accompanied by a 50 percent reduction in the rate of acute graft rejection. Of concern, however, is the fact that this study was performed with a placebo control. The authors state that this approach was acceptable because "there was no accepted standard regimen of prophylaxis at the inception of the study." At the time the study began — July 7, 1992 — there were prophylactic regimens with demonstrated efficacy against CMV in renal-transplant recipients. In fact, the use of both CMV immune globulin[2,3] and acyclovir[4] had been reported in the *Journal* and elsewhere to reduce the incidence of CMV disease significantly after renal transplantation. Thus, the use of a placebo control in seronegative recipients of kidneys from CMV-seropositive donors subjected these patients to an unnecessary and unacceptable risk. It would have been more appropriate to use acyclovir prophylaxis as the control treatment, as was recently done in a controlled trial of oral ganciclovir.[5]

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1. Lowance D, Neumayer H-H, Legendre CM, et al. Valacyclovir for the prevention of cytomegalovirus disease after renal transplantation. N Engl J Med 1999;340:1462-70.
2. Snydman DR, Werner BG, Heinze-Lacey B, et al. Use of cytomegalovirus immune globulin to prevent cytomegalovirus disease in renal-transplant recipients. N Engl J Med 1987;317:1049-54.
3. Snydman DR, Werner BG, Tilney NL, et al. Final analysis of primary cytomegalovirus disease prevention in renal transplant recipients with a cytomegalovirus-immune globulin: comparison of the randomized and open-label trials. Transplant Proc 1991;23:1357-60.
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5. Flechner SM, Avery RK, Fisher R, et al. A randomized prospective controlled trial of oral acyclovir versus oral ganciclovir for cytomegalovirus prophylaxis in high-risk kidney transplant recipients. Transplantation 1998; 66:1682-8.

The authors reply:

To the Editor: We appreciate the concern of Shapiro and Abrams, and we are well aware of the studies they cited. Although many renal-transplant physicians now consider high-dose oral acyclovir to be the gold standard for CMV prophylaxis after kidney transplantation, this was not uniformly the case when our study was designed.

The study by Balfour et al.[1] was small and has been criticized by many because of its size and the unusually high rate of disease (100 percent) reported in the CMV-negative group receiving placebo. In the absence of a confirmatory study with sufficient numbers of patients, many transplant physicians were reluctant to consider acyclovir therapy as a routine CMV prophylactic strategy. CMV hyperimmune globulin has been shown to be effective, but it must be administered intravenously, is very costly, and still has not gained wide acceptance in the transplantation community.

At the time our study was designed, we thought that it was imperative to answer the question regarding the efficacy of valacyclovir as a preventive treatment and at the same time to avoid exposing any of our patients to undue risk. The protocol stipulated that the investigator at each center was allowed to stop the study drug if CMV infection was suspected and to intervene with the most appropriate therapy. The centers that participated in the study did not use prophylaxis as the routine strategy for the prevention of CMV; most relied on the preemptive approach.[2] The protocol was approved at all the study centers by institutional review boards or ethics committees. The question of the efficacy of valacyclovir was answered and the safety of the study validated by the outcomes. We do not agree that the study design entailed unacceptable risks to the patients.

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1. Balfour HH Jr, Chace BA, Stapleton JT, Simmons RL, Fryd DS. A randomized, placebo-controlled trial of oral acyclovir for the prevention of cytomegalovirus disease in recipients of renal allografts. N Engl J Med 1989; 320:1381-7.
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Death after Transplantation of a Liver from a Donor with Unrecognized Ornithine Transcarbamylase Deficiency

To the Editor: Ornithine transcarbamylase deficiency is the most common inherited disorder of the urea cycle.[1,2] It is an X-linked disease that can range in severity from hyperammonemic coma in neonates to the absence of symptoms in adults.[1,2] Liver transplantation is an effective treatment for patients with this disease.[3] However, this disease has another implication for liver transplantation, as demonstrated by the following case.

In December 1998, a 65-year-old woman underwent orthotopic liver transplantation for liver cirrhosis related to hepatitis C infection and hepatocellular carcinoma. She was extubated on the first postoperative day and initially did well (Table 1). However, on the third day after surgery, she had nausea and became somnolent. Initially, a computed tomographic (CT) scan of the brain was normal. Twenty-four hours later, a CT scan showed severe cerebral edema. Laboratory investigations showed extremely high blood levels of ammonia (Table 1). All other laboratory values and the

TABLE 1. CLINICAL COURSE OF THE LIVER-TRANSPLANT RECIPIENT AND ASSOCIATED LABORATORY VALUES.*

DAY	CLINICAL EVENT	ALANINE AMINOTRANSFERASE	ASPARTATE AMINOTRANSFERASE	LACTATE DEHYDROGENASE	PROTHROMBIN ACTIVITY	AMMONIA
			U/liter		%	μmol/liter
0	Orthotopic liver transplantation	7120	3090	4460	39	
1	Extubation	4970	2970	1350	29	
2		3780	917	353	31	
3	Nausea, somnolence, normal CT scan, coma	2860	285	335	36	
4	Brain edema on CT scan, hemofiltration	1680	103	359	32	3793
5	Multiorgan failure	659	127	513	25	1513
6	Death	6420	5990	8510	<5	199

*Normal values are as follows: alanine aminotransferase, 1 to 23 U per liter; aspartate aminotransferase, 1 to 19 U per liter; lactate dehydrogenase, 120 to 240 U per liter; prothrombin activity, 70 to 130 percent; and ammonia, less than 50 μmol per liter.

results of diagnostic tests for hepatic perfusion (Doppler ultrasonography and clearance of indocyanine green[4]) were normal or within the range expected after liver transplantation. The blood level of ammonia was reduced by continuous hemofiltration. However, multiorgan failure developed, and the patient died six days after the surgery.

The isolated finding of high ammonia levels suggested a disorder of the urea cycle. We hypothesized that a liver deficient in ornithine transcarbamylase had been transplanted. Subsequently, the diagnosis of ornithine transcarbamylase deficiency was established by enzyme analysis of a biopsy specimen of the transplanted liver.[1] The activity of ornithine transcarbamylase measured in the liver tissue was approximately 10 percent of normal, whereas the activity of other enzymes of the urea cycle was normal. Molecular analysis revealed a point mutation at codon 40 of exon 2 of the ornithine transcarbamylase gene (CGT to CAT, resulting in a change from arginine to histidine), which is associated with late-onset symptoms in males.[1] This finding established that an ornithine transcarbamylase–deficient liver had been transplanted. Further evaluation of the donor's history lent support to the diagnosis. He was a 26-year-old man who had died of brain edema of unknown origin. A maternal uncle of the donor had also died from coma of unknown origin.

Although rare, transplantation of a liver from a donor with unrecognized ornithine transcarbamylase deficiency is a potential hazard to the recipient and may lead to the recipient's death.

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Folic Acid Fortification

To the Editor: Jacques and colleagues (May 13 issue)[1] report data showing that the 30 percent of the Framingham Offspring Study cohort who took B vitamin supplements had a substantially lower mean plasma homocysteine concentration that the members of the cohort who did not take such vitamins, even after the fortification of grain products with folic acid was introduced by the Food and Drug Administration (FDA). Furthermore, the upper tail of the distribution of homocysteine concentrations remained skewed in those who did not take supplements after fortification as compared with those who did take them. This distribution suggests that the homocysteine concentration remains too high in those who do not take supplements. Thus, approximately 70 percent of the adult population in the United States is exposed to a risk factor for cardiovascular disease — an elevated plasma homocysteine concentration — that can be easily avoided simply by consuming a B vitamin supplement. It seems strange that the authors suggest neither supplements nor increased fortification of food.

Ward and colleagues gave male hospital workers 100, 200, or 400 μg of synthetic folic acid daily.[2] They reported that in order for the one third with the highest plasma homocysteine concentrations (those who were the most vitamin deficient) to reduce their plasma homocysteine con-

centrations to a level as low as the one third with the lowest concentration (those with enough vitamins), 400 μg of synthetic folic acid daily was required. Thus, Americans who are not taking supplements should begin taking 400 μg of synthetic folic acid daily. Since the Framingham Offspring Study cohort is middle-aged or older, it is likely that some of the increased homocysteine concentrations among those not taking supplements were due to the fact that they did not consume enough synthetic vitamin B_{12}. In April 1998, the Institute of Medicine recommended that adults 50 years of age or older consume 2.4 μg of synthetic vitamin B_{12} daily.[3]

Most Americans who consume B vitamin supplements take a multivitamin that contains 400 μg of synthetic folic acid and 6 μg of synthetic vitamin B_{12}. The studies by Jacques et al.[1] and Ward et al.[2] suggest that hundreds of thousands of Americans who do not take B vitamin supplements will be exposed unnecessarily to a cardiovascular risk factor until the FDA increases the amount of synthetic folic acid in the diet so that almost all Americans — not just the average American — are consuming 400 μg of synthetic folic acid and 2.4 μg of synthetic vitamin B_{12} daily.[4] Until the FDA gets the amount of fortification right, adults can largely avoid the cardiovascular risk associated with high plasma homocysteine concentrations by eating well and taking a multivitamin.

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To the Editor: In their article on the effect of folic acid fortification on plasma folate and total homocysteine concentrations, Jacques et al. concluded that the recent introduction of folic acid fortification was associated with a substantial improvement in folate status in a population of middle-aged or older adults.

In order to evaluate the effect of folic acid fortification on the risk of neural-tube defects, vascular diseases, and cancer, however, researchers will need to conduct additional studies that relate these outcomes to changes in concentrations of blood folate.

One key point in the evaluation of the success of the national folic acid fortification program is the ability to compare serum and whole-blood folate results obtained by different laboratories and methods. In an international, interlaboratory study, Gunter et al.[1] reported that folate concentrations measured by different methods varied by factors of two to nine, with the greatest variation occurring at critical, low concentrations of folate.

If we want to be able to use data on folate generated by many studies and laboratories in a meaningful way, we need to ensure the comparability and accuracy of folate measurements. This can be achieved only if high-quality reference methods and definitive means of analyzing serum and whole-blood folate are developed and validated and if properly characterized reference materials are introduced through a standardization program. The need for such a standardization program has been recognized,[1,2] but no such program has been established. The emerging understanding of the relation between folate concentrations and the risks of vascular disease and cancer makes it imperative that we begin to establish a standardization program now. This program will be essential for ensuring the comparability of data from future studies and for evaluating the effectiveness and safety of folic acid fortification and supplementation as a public health intervention.

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To the Editor: The increases in blood folate concentrations and the declines in homocysteine values attributed to the fortification of cereal-grain products with folic acid presented by Jacques et al. are encouraging. However, we urge caution in concluding that "the job is done," as many in the media imply, by claiming, for example, that "folic acid deficiency has all but vanished."[1] Folate "deficiency" was defined on the basis of megaloblastic anemia, not on the prevention of neural-tube defects. The mechanism by which folic acid prevents neural-tube defects is unknown but could be related to compensating for individual variations in folate metabolism rather than to correcting a folate "deficiency." In addition, it is premature to interpret the findings as proof that the intake of folic acid among women of childbearing age is currently optimal and will maximize reductions in the occurrence of neural-tube defects. Higher red-cell folate concentrations have been shown to be associated with lower rates of neural-tube defects, with continuous rate decreases well past clinically normal folate concentrations.[2]

Ultimately, the effectiveness of folic acid fortification will be determined by its effect on the occurrence of neural-tube defects independent of the effects of the increasing use of prenatal diagnosis and termination of pregnancy, which has already lowered the birth prevalence of neural-tube defects by at least 32 percent.[3] The Centers for Disease Control and Prevention monitors the rates of neural-tube defects closely. It is too early to assess the effect of fortification on the occurrence of neural-tube defects. Although many targeted foods were probably fortified with folic acid before the FDA's January 1998 deadline,[4] there may have been some lag time owing to the consumption

of products that were stored before the fortification requirement was in place. If most targeted items consumed in January 1998 were fortified, the earliest term infants of mothers who were "exposed" to fortification early in pregnancy would be those born in late 1998.

If the increase in folate concentrations found among older adults in the Framingham Offspring Study applies to women of childbearing age, and if this increase translates to more healthy babies born without major disabling birth defects, we will have strong evidence that fortification is successful. In the meantime, we think it is most appropriate to continue to advocate that all women capable of becoming pregnant take 400 μg of a synthetic folic acid supplement daily. Achieving the recommended 400 μg daily by consuming fortified grains alone requires a substantial change in behavior; the estimated average daily intake of folic acid from fortified grains by women is 100 μg.[4]

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The authors reply:

To the Editor: Dr. Oakley blurs the distinction between the effect of folic acid fortification on folate status and the effect of vitamin-supplement use on vitamin B_{12} status. Rather than consider all the evidence that we presented relating fortification to the improved folate status of Americans, he chooses to select a single confounded observation to support his belief that fortification levels are too low. Dr. Oakley considers only the difference in mean homocysteine concentrations after fortification between the participants who used multivitamin supplements and those who did not. However, he ignores the evidence presented in our paper that showed that this difference was due to a better vitamin B_{12} status among those who used supplements. Furthermore, Dr. Oakley ignores the finding that the prevalence of homocysteine concentrations of more than 13 μmol per liter after fortification among those who did not use multivitamin supplements was not significantly different from the prevalence among those who did. Finally, he ignores the observation that the prevalence of folate concentrations of less than 3 ng per milliliter dropped from greater than 20 percent before fortification to 1.7 percent after fortification in those who did not use supplements and that this latter prevalence was not significantly different from that for those who used vitamin supplements.

We also believe that Dr. Oakley's comment that approximately 70 percent of the adult population of the United States has an elevated risk of cardiovascular disease as a result of increased plasma homocysteine concentrations is unsupported by any evidence. Furthermore, his recommendation that the entire population use multivitamin supplements to protect against elevated homocysteine concentrations seems unwarranted in the absence of any data from randomized, controlled clinical trials indicating that treatment of mild hyperhomocysteinemia with B vitamins actually reduces the incidence of cardiovascular disease.

Pfeiffer and colleagues present their case for the standardization of folate measures, but the lack of standardization had no effect on our results, since all the measurements were performed in the same laboratory with the use of the same methods.

In response to the comments of Watkins and colleagues: we did not conclude or intend to imply that the job is done. Since folic acid fortification was mandated by the FDA as a means of reducing the incidence of neural-tube defects, we agree that the effectiveness of fortification will only be demonstrated through its effect on the prevention of such defects. Given that fortification has been largely in place for almost two years, we anticipate that such evidence will soon be forthcoming. In the meantime, it seems only prudent to await the data before deciding on the adequacy of the current fortification level.

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Hot-Tub Therapy for Type 2 Diabetes Mellitus

To the Editor: Physical exercise is effective therapy for patients with type 2 diabetes mellitus. Therefore, my colleagues and I asked the following question: Would the effects of partial immersion in a hot tub simulate the beneficial effects of exercise? We asked eight patients (five men and three women; age range, 43 to 68 years; mean [±SD] weight, 104.7±53.2 kg) to sit in a hot tub at an athletic facility with water up to their shoulders. They used the hot tub for 30 minutes a day, six days a week, for three weeks between September 1998 and April 1999 (Table 1). The patients' diets, exercise routines, and therapy (three patients were taking insulin, and all were taking various oral hypoglycemic drugs) were stable for eight weeks before the study and while the study took place.

The temperature of the water in the tub ranged from 37.8°C to 41.0°C, and the patients' oral temperature rose an average of 0.8°C during each session. After 10 days, one patient reduced his dose of insulin by 18 percent to prevent hypoglycemic reactions. During the three-week period, the patients' weight decreased by a mean of 1.7±2.7 kg ($P=0.08$). Their mean fasting plasma glucose level decreased from 182±37 mg per deciliter (10.1±2.0 mmol per liter) to 159±42 mg per deciliter (8.8±2.3 mmol per liter) ($P=0.02$), and their mean glycosylated hemoglobin

TABLE 1. CHARACTERISTICS OF THE EIGHT PATIENTS AND RESULTS OF THREE WEEKS OF EXPOSURE TO A HOT TUB.

AGE	SEX	DURATION OF DIABETES	MEDICATIONS	BODY WEIGHT (BEFORE/AFTER EXPOSURE)	FASTING PLASMA GLUCOSE (BEFORE/AFTER EXPOSURE)*	GLYCOSYLATED HEMOGLOBIN (BEFORE/AFTER EXPOSURE)†
yr		yr		kg	mg/dl	%
43	M	14	Glyburide, metformin hydrochloride	83.2/80.9	190/186	13.6/12.7
50	M	13	Glyburide, troglitazone, insulin	201.8/199.1	109/66	8.6/7.7
51	M	9	Glyburide, metformin hydrochloride, insulin	175.0/168.2	231/181	12.2/11.1
54	F	9	Metformin hydrochloride, insulin	60.9/61.8	207/156	17.4/14.8
57	F	8	Glipizide, metformin hydrochloride	64.5/64.5	197/155	11.0/11.1
57	M	3	Glyburide, troglitazone	75.0/73.6	165/162	8.6/7.6
63	M	11	Glipizide, metformin hydrochloride	91.8/91.8	158/160	9.1/8.1
68	F	9	Glyburide, metformin hydrochloride, troglitazone	85.5/84.1	197/203	9.5/8.9

*To convert the values to millimoles per liter, multiply by 0.05551.

†The normal range was 4 to 8 percent.

levels decreased from 11.3±3.1 percent to 10.3±2.6 percent ($P=0.004$).

When the water temperature was greater than 40°C, the patients reported feeling hot. Patients became dizzy on exiting the tub when they hurried to stand. Therefore, they were routinely helped from the tub and seated until they could safely walk. As the study progressed, they reported improved sleep and an increased general sense of well-being. Our results suggest that hot-tub therapy should be further evaluated as a therapy for patients with type 2 diabetes mellitus. It may be especially helpful for patients who are unable to exercise. The benefits could result from increased blood flow to skeletal muscles.[1]

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