

Pharmacogenomics of lipid-lowering therapy is further complicated in that the appropriate response phenotype is unclear. For example, pharmacogenetic studies investigating apolipoprotein E (*APOE*) polymorphisms suggest a gene-dose effect, with $\epsilon 2$ carriers showing greater reductions in LDL cholesterol in response to statins, while $\epsilon 4$ carriers are least responsive.^{2,3} In contrast, when adverse cardiovascular outcomes were examined in a substudy of the Scandinavian Simvastatin Survival Study, $\epsilon 4$ carriers had the greatest reduction in death rates in response to simvastatin compared with non- $\epsilon 4$ carriers.⁴ Therefore, while $\epsilon 2$ carriers may have a better response to statins using a surrogate outcome, $\epsilon 4$ carriers have a better response using mortality as the outcome. Of note, these differences in risk reduction based on *APOE* genotype do not appear to be related to variable LDL cholesterol treatment responses.

Issam Zineh, PharmD
zineh@cop.ufl.edu
College of Pharmacy
Center for Pharmacogenomics
University of Florida
Gainesville

1. Chasman DI, Posada D, Subrahmanyam L, Cook NR, Stanton VP Jr, Ridker PM. Pharmacogenetic study of statin therapy and cholesterol reduction. *JAMA*. 2004;291:2821-2827.
2. Ballantyne CM, Herd JA, Stein EA, et al. Apolipoprotein E genotypes and response of plasma lipids and progression-regression of coronary atherosclerosis to lipid-lowering drug therapy. *J Am Coll Cardiol*. 2000;36:1572-1578.
3. Ordovas JM, Mooser V. The *APOE* locus and the pharmacogenetics of lipid response. *Curr Opin Lipidol*. 2002;13:113-117.
4. Gerdes LU, Gerdes C, Kervinen K, et al. The apolipoprotein $\epsilon 4$ allele determines prognosis and the effect on prognosis of simvastatin in survivors of myocardial infarction: a substudy of the Scandinavian Simvastatin Survival Study. *Circulation*. 2000;101:1366-1371.

This letter was shown to Dr Chasman, who declined to reply on behalf of the authors.—Ed.

Individuals and Global Health Improvement

To the Editor: Many *JAMA* readers practicing in developed nations may have searched in vain for a personal role in global health, the theme of the June 2, 2004, issue of *JAMA*.

Yet I believe there is a call for clinicians in the Commentary by Lee and colleagues.¹ As funding from groups such as the Global Fund and Gates Foundation facilitates basic research and evidence-oriented field trials,² the limiting factor becomes “whether poor countries have the capacity to put additional resources to effective use. . . .”¹ The overarching systemic challenge—scientifically, ethically, and politically—continues to be “going to scale” with what the world already knows. The sine qua non of scaling up is the practicing and teaching of quality clinical and public health care at district/regional hospitals worldwide.³ In dramatic contrast to Chad,¹ which has 1 physician per 40 000 citizens, or even Bangladesh (1:4000), the United States (1:350) has had an abundance of physicians.

Why not forge a new public/private partnership to educationally prepare and logistically support clinical and public

health practitioners, both early and mid-career, to work alongside dedicated but overextended health professionals of developing nations?^{4,5} Putting prepared professionals in the places where the dying goes on daily will finally apply outcomes-based research at the outposts where it ultimately matters. And, much more than money or technology, such collaboration may replace mutual mistrust with insight into our shared humanity.

Ronald Pust, MD
rpust@u.arizona.edu
Department of Family and Community Medicine
University of Arizona College of Medicine
Tucson

1. Lee K, Walt G, Haines A. The challenge to improve global health: financing the Millennium Development Goals. *JAMA*. 2004;291:2636-2638.
2. Buekens P, Keusch G, Belizan J, Bhutta ZA. Evidence-based global health. *JAMA*. 2004;291:2639-2641.
3. English M, Berkeley J, Mwangi I, et al. Hypothetical performance of syndrome-based management of acute paediatric admissions aged over 60 days in a Kenyan district hospital. *Bull World Health Organ*. 2003;81:166-173.
4. Pust RE. US abundance of physicians and international health. *JAMA*. 1984;252:385-388.
5. Educating doctors for world health. *Lancet*. 2001;358:1471.

In Reply: Dr Pust asks how clinicians in high-income countries can contribute to the attainment of the United Nations Millennium Development Goals and the improvement of health more broadly in low-income countries.

He is correct to draw attention to the dramatic contrast between the physician-citizen ratio in a country like the United States and in sub-Saharan Africa. However, it is important to acknowledge that the United States and other high-income countries contribute to the problem by employing and depending on medical and nursing graduates from many low-income countries.¹ For example, between a third and a half of South African medical graduates emigrate.² The situation may be even worse in poorer countries such as Zambia where, some years ago, it was found that only 50 of the 600 physicians trained by the medical school in Lusaka worked in the public sector health service.³ The situation is similar for nurses. In Malawi, two thirds of jobs in the public health system remain vacant, with more nurses emigrating in the past 4 years than the 336 who remain to serve a population of 11.6 million.⁴ Clinicians in countries such as the United States can play an important role by drawing public attention to the problems caused by migration of health professionals and pressing for the development of effective policy responses. These could include encouraging investment in domestic policies to improve the retention of health workers within low-income countries and reduce requirements for overseas recruitment by high-income countries, together with the development, implementation, and enforcement of ethical guidelines on international migration of health professionals.⁵

Collaboration between training and research institutions in low- and high-income countries has produced benefits for decades. Schools of international public health are staffed with dedicated people, many of whom have worked alongside

health professionals in low-income countries, and who have continued to support research and training in developing nations. We would strongly support an initiative that encouraged building on such collaborative efforts, recognizing that strengthening the capacity of local institutions to train health personnel and researchers in low-income countries will require long-term commitment and in-depth knowledge of local disease patterns, available resources, and cultural factors if it is to be successful.

Andy Haines, MBBS, MD
andy.haines@lshtm.ac.uk

Gill Walt, PhD

Kelley Lee, MPA, MA, DPhil
London School of Hygiene and Tropical Medicine
London, England

1. Pang T, Lansang MA, Haines A. Brain drain and health professionals. *BMJ*. 2002; 324:499-500.
2. Weiner R, Mitchell G, Price M. Wits medical graduates: where are they now? *S Afr J Sci*. 1998;94:59-63.
3. Sims P. A medical school in Zambia. *J Public Health Med*. 1997;19:137-138.
4. Dugger CW. An exodus of African nurses puts infants and the ill in peril. *New York Times*. July 12, 2004:A1.
5. Bundred P, Levitt C. Medical migration: who are the real losers? *Lancet*. 2000; 356:245-246.

Compensation for Energy Intake From Fast Food Among Overweight and Lean Adolescents

To the Editor: While 2 recent articles addressed the close relationship between fast food consumption and obesity in both children and adults in the United States,^{1,2} the same phenomenon appears likely to be occurring in China.

Childhood obesity shows an alarming increase in prevalence in recent years. In urban China, it increased from 1.5% in 1989 to 12.6% in 1997, and the prevalence of overweight increased from 14.6% to 28.9% in the same period.³ In a more recent report on urban Chinese children, the prevalence of overweight for children was 27.7% in boys and 14.1% in girls.⁴ At the same time, Chinese children are consuming western fast food more quickly than ever.⁵

Tsung O. Cheng, MD

tcheng@mfa.gwu.edu

Department of Medicine

George Washington University Medical Center
Washington, DC

1. Ebbeling CB, Sinclair KB, Pereira MA, Garcia-Lago E, Feldman HA, Ludwig DS. Compensation for energy intake from fast food among overweight and lean adolescents. *JAMA*. 2004;291:2828-2833.
2. Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. *JAMA*. 2004;291:2847-2850.
3. Luo J, Hu FB. Time trends of obesity in pre-school children in China from 1989 to 1997. *Int J Obes Relat Metab Disord*. 2002;26:553-558.
4. Iwata F, Hara M, Okada T, Harada K, Li S. Body fat ratios in urban Chinese children. *Pediatr Int*. 2003;45:190-192.
5. Cheng TO. Fast food and obesity in China. *J Am Coll Cardiol*. 2003;42:773.

To the Editor: Dr Ebbeling and colleagues¹ reported in study 2 that overweight adolescents did not compensate for the "massive portion sizes characteristic of fast food today" because they

ate 400 more calories on days that they ate fast food compared with days when they did not. However, the overweight adolescents' average caloric intake for both sets of days was 2499, which was similar to the average caloric intake of the lean adolescents (2598), suggesting that although they ate more on fast food days, they also compensated by eating less on nondesignated fast food days.

In addition, study 1 was done in the presumably naturalistic setting of a food court. I am concerned that having the study participants stay for an hour, proceed by eating an extra large meal, and follow by refilling at will encouraged them to overeat. While this method may have been implemented to exaggerate a difference in the amount of food that the 2 groups of adolescents would eat, real world circumstances would have financial and time constraints that could alter the conclusions reached by the investigators.

Paul Pisarik, MD, MPH

ppisarik@bcm.tmc.edu

Department of Family and Community Medicine
Baylor College of Medicine
Houston, Tex

1. Ebbeling CB, Sinclair KB, Pereira MA, Garcia-Lago E, Feldman HA, Ludwig DS. Compensation for energy intake from fast food among overweight and lean adolescents. *JAMA*. 2004;291:2828-2833.

In Reply: We agree with Dr Cheng that fast food may be contributing to the rapidly increasing prevalence of childhood obesity in China and perhaps other developing nations as well.¹

Dr Pisarik addresses 2 points. First he compares energy intake between the lean and overweight subjects in our research (study 2) and concludes that the overweight adolescents compensated for excess energy intake on fast food days by eating less on non-fast food days. As we discussed in the article, we believe that direct comparison of energy intake between groups is problematic because of the well-recognized phenomenon of underreporting among overweight/obese participants.^{2,3} Our comparison between studies provides evidence that this effect was present in study 2. Regarding Pisarik's second point, we agree that the standardized feeding protocol in study 1 did not fully mimic a usual food court experience. However, we note again that the dietary composition, marketing practices, and pricing structure of fast food are specifically designed to foster a maximum of energy consumption in a minimum of time.

Cara B. Ebbeling, PhD

David S. Ludwig, MD, PhD

david.ludwig@childrens.harvard.edu

Department of Medicine

Children's Hospital

Boston, Mass

1. Ebbeling CB, Pawlak DB, Ludwig DS. Childhood obesity: public-health crisis, common sense cure. *Lancet*. 2002;360:473-482.
2. Bandini LG, Schoeller DA, Cyr HN, Dietz WH. Validity of reported energy intake in obese and nonobese adolescents. *Am J Clin Nutr*. 1990;52:421-425.
3. Bandini LG, Vu D, Must A, Cyr H, Goldberg A, Dietz WH. Comparison of high-calorie, low-nutrient-dense food consumption among obese and non-obese adolescents. *Obes Res*. 1999;7:438-443.