

developing countries are at a disadvantage too. The timely completion and publication of research with limited resources and limited infrastructure already constitute a tall order.^{1,2} A registration process that includes immediate disclosure of research information could further retard the limited competitiveness of the developing world. What might be done is to have trials registered at the outset, but without the information being publicly accessible for a certain grace period. This approach would ensure transparency but would not compromise any competitive edge to which researchers who painstakingly design an innovative study are entitled.

Kittisak Kulwichit, M.D.

Wanla Kulwichit, M.D.

Chulalongkorn University
Bangkok 10330, Thailand
kittisak.k@chula.ac.th

Pisake Lumbiganon, M.D.

Khon Kaen University
Khon Kaen 40002, Thailand

1. Keiser J, Utzinger J, Tanner M, Singer BH. Representation of authors and editors from countries with different human development indexes in the leading literature on tropical medicine: survey of current evidence. *BMJ* 2004;328:1229-32.

2. Smith R. Publishing research from developing countries. *Stat Med* 2002;21:2869-77.

Chronic Renal Disease and Cardiovascular Risk

TO THE EDITOR: Go et al. (Sept. 23 issue)¹ estimated the glomerular filtration rate (GFR) with the simplified four-variable Modification of Diet in Renal Disease (MDRD) formula. Almost half the subjects in their study population (41.7 percent) did not describe themselves as black or white. Despite the important influence of a person's ethnic background on the estimated GFR, the variable "race or ethnic background" allows only factors for "European-American" or "African-American" to be inserted into the MDRD formula.² It can be assumed that if more accurate estimates of the GFR had been obtained with the use of modified ethnicity-specific multiplication factors (e.g., for Asians), the conclusions of the study would probably not have differed. However, it is important to emphasize that the MDRD formula still awaits validation in several nonblack, nonwhite populations living throughout the United States and elsewhere in the world.

Lorenz Risch, M.D.

Markus Sagmeister, M.D.

Academic Teaching Hospital
6800 Feldkirch, Austria
lorenzrisch@hotmail.com

Andreas Huber, M.D.

Kantonsspital
5001 Aarau, Switzerland

1. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004;351:1296-305.

2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002;39:Suppl 1:S1-S266.

death and cardiovascular events. Two issues were not discussed. The first is that the MDRD equation has not been tested in elderly persons or in persons with reduced muscle mass.² Both studies, however, included a high percentage of older adults, and there was no adjustment for body-mass index. Their conclusions may have been weakened as a result. The second is that neither of the two studies showed the size of the effect of mild renal disease on death and cardiovascular events. The size of the effect in an observational study is important.³ Many traditional risk factors, such as hypertension and diabetes, varied significantly according to the GFR, and adjustments for these factors were made. It is still unclear to what extent mild renal disease contributed to death and cardiovascular events. Finally, the GFR tended to decline with increasing age in the study by Anavekar et al. but not in the study by Go et al.

Huai Cheng, M.D., M.P.H.

Columbia University Medical Center
New York, NY 10034-1159
hyc2105@columbia.edu

1. Anavekar NS, McMurray JJV, Velazquez EJ, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med* 2004;351:1285-95.

2. Manjunath G, Sarnak MJ, Levey AS. Estimating the glomerular filtration rate: dos and don'ts for assessing kidney function. *Postgrad Med* 2001;110:55-62.

3. Angell M. The interpretation of epidemiologic studies. *N Engl J Med* 1990;323:823-5.

TO THE EDITOR: In the studies by Go et al. and Anavekar et al.,¹ mild renal disease was associated with

DR. GO AND COLLEAGUES REPLY: Dr. Risch and colleagues note that some members of our cohort could not be determined to be either black or white because either those subjects were of another race

or ethnic group or their race or ethnic group was unknown. This was true primarily for subjects with an estimated GFR of 60 ml per minute per 1.73 m² of body-surface area or higher, so the misclassification of the GFR in those who were not known to be black in this large comparison group should have had minimal effects on our final results. We certainly agree that there is a need to clarify whether being a member of a race or ethnic group other than white or black affects the ability of existing equations to estimate the GFR accurately.

Dr. Cheng raises the question of whether our results were affected by the fact that the MDRD equation was not developed in a population with a large representation of elderly persons or persons with reduced muscle mass. As we note in our article, the relative risks of adverse outcomes associated with a reduced estimated GFR were consistent among all age categories studied (20 to 49, 50 to 59, 60 to 69, 70 to 79, and 80 years or older). In addition, although we did not have body-mass-index values, we adjusted for the presence of serum albumin levels of 3.5 g per deciliter or less as a proxy for malnutrition. As noted by Dr. Cheng, we adjusted for the presence of diagnosed hypertension and diabetes mellitus at entry and for the development of these conditions during follow-up. Since reduced kidney function contributes to the development and exacerbation of hypertension, adjusting for hypertension in our analyses may actually have led to an underestimation of the effect of renal insufficiency on outcomes. Even after adjustment for these and other potential explanatory factors, an estimated GFR of less than 60 ml per minute per 1.73 m² (especially a value below 45 ml per minute per 1.73 m²) remained a graded, independent risk factor for death, cardiovascular events, and hospitalization.

Alan S. Go, M.D.

Kaiser Permanente of Northern California
Oakland, CA 94612-2304
alan.s.go@kp.org

Glenn M. Chertow, M.D., M.P.H.

Chi-yuan Hsu, M.D.

University of California, San Francisco
San Francisco, CA 94143

DR. ANAVEKAR AND COLLEAGUES REPLY: In response to Dr. Cheng: the MDRD equation, though not perfect, is considered to be reliable for estimating the GFR.^{1,2} We acknowledge its limitations, in that serum creatinine is influenced by nonrenal factors, such as muscle mass, and in that its validation in several populations has been limited.¹ In our study, we did take the body-mass index into account. This variable was one of many baseline characteristics used in our adjustment models; it did not attain statistical significance and thus was not entered into the final models presented in our article.

With regard to the effect of mild renal disease on events, we analyzed renal function as a categorical variable and presented proportions of events and hazard ratios for mild, moderate, and severe renal impairment. As compared with an estimated GFR of 75.0 ml per minute per 1.73 m² or higher, mild renal disease (estimated GFR, 60.0 to 74.9 ml per minute per 1.73 m²) was associated with 14 percent and 10 percent increases in the risks of death and composite cardiovascular outcomes, respectively. Each 10-unit decrement in the estimated GFR below 81.0 ml per minute per 1.73 m² portended a 10 percent increase in the risk of cardiovascular events, reinforcing the concept that even mild renal impairment should not be ignored.

Nagesh S. Anavekar, M.D.

Brigham and Women's Hospital
Boston, MA 02115

John J.V. McMurray, M.D.

Western Infirmary
Glasgow G11 6NT, Scotland

Marc A. Pfeffer, M.D., Ph.D.

Brigham and Women's Hospital
Boston, MA 02115
mpfeffer@rics.bwh.harvard.edu

1. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Ann Intern Med* 1999; 130:461-70.
2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002;39:Suppl 1:S1-S266.

Chemotherapy for Advanced Prostate Cancer

TO THE EDITOR: Petrylak et al. (Oct. 7 issue)¹ conclude that combination treatment with docetaxel and estramustine should be used as initial therapy

for androgen-independent metastatic prostate cancer. Several key points that are necessary to reach this conclusion are missing. First, no Gleason scores