

CORRESPONDENCE



Clinical Trial Registration

TO THE EDITOR: The statement from the International Committee of Medical Journal Editors (ICMJE) with respect to the registration of clinical trials (Sept. 16 issue)¹ advocates the use of www.clinicaltrials.gov as a registry. I am astonished by this recommendation because that registry does not fulfill the criteria demanded by the ICMJE. Currently, only the U.S. federal agencies conducting or sponsoring clinical research and holders of an investigational-new-drug application under U.S. Food and Drug Administration regulations may apply for registration. In contrast, www.controlled-trials.com, an international registry, is open to every investigator. That the editors do not mention this registry amazes me even more because several of them are European. The European guidelines on application for approval by competent authorities and ethics committees before commencement of a clinical trial of medicinal products include detailed instructions for application forms that are used in the member states of the European Union. These application forms ask for the International Standard Randomised Controlled Trial Number (ISRCTN), which to my knowledge is given only in the registry at www.controlled-trials.com. The editors should clarify these contradictions.

Guido Grass, M.D.

University of Cologne
50937 Cologne, Germany

1. DeAngelis C, Drazen JM, Frizelle FA, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. *N Engl J Med* 2004;351:1250-1.

Editor's note: Since this letter was written clinicaltrials.gov has been opened to any investigator in the world.

TO THE EDITOR: The ICMJE supports a solution to the selective reporting of clinical studies. Although efforts have been made to encourage investigators to register their trials, registration is still voluntary. Several major barriers to the development of a comprehensive registry of clinical trials have been described.¹ Research involving human subjects poses complex ethical issues. As stated by the ICMJE, patients who volunteer to participate in clinical trials deserve to know that their contribution to the improvement of human health will be available to inform health care decisions. Therefore, prospective trial registration is an ethical obligation and should be a legally required component of written informed consent.

Ludovic Reveiz, M.D.

Clinica Reina Sofia
Bogota 571, Colombia
lureveiz@colsanitas.com

Andres Felipe Cardona, M.D.

Instituto Nacional de Cancerología
Bogota 571, Colombia

Edgar Guillermo Ospina, M.D.

Clinica Reina Sofia
Bogota 571, Colombia

1. Dickersin K, Rennie D. Registering clinical trials. *JAMA* 2003; 290:516-23.

TO THE EDITOR: The trial-registration initiative of the ICMJE is laudable. However, research sponsors are not the only stakeholders who may lose a competitive edge through registration. Researchers from

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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