and observational studies is required to select appropriate subjects and to create a protocol that controls for confounding variables. Megatrials should therefore be conducted only at the end of a long process of therapeutic development.[3] Paradoxically, megatrials may be superfluous once a significant treatment effect is evident from meta-analysis of existing trials,[4] as indicated by studies demonstrating agreement of statistical conclusions among megatrials.[5]

Observational studies can recruit a broader range of patients and are often cheaper, quicker and less difficult to carry out than RCTs. Moreover, high-quality observational studies and RCTs usually produce similar results.[6] Hence, observational studies may be preferable for identifying rare side effects and when RCTs would be impractical.[7]

Michal R. Pijak
Consultant in Rheumatology, Allergy and Clinical Immunology
Division of Clinical Immunology
Department of Internal Medicine
Frantisek Gazdik
Associate Professor
Institute of Preventive and Clinical Medicine
Stefan Hrusovsky
Associate Professor of Gastroenterology
Head, Department of Internal Medicine
Slovak Medical University
Bratislava, Slovakia

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Competing interests: Michal Pijak has received speaker fees from local branches of Pharmacia and Fournier.

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[The author responds:]

Chris Delaney and Michal Pijak and associates argue that observational studies are preferable to the large simple RCTs recommended in my commentary[1] because they sometimes yield the same results as RCTs. That is true, but the problem is that often they do not. Therefore, without confirmatory RCT data, we risk making serious mistakes if we advise or prescribe solely on the basis of observational studies. Because of the Women's Health Initiative RCT, we can advise women that the harms of long-term estrogen–progesterone combination therapy outweigh the benefits,[2] but on the basis of observational data, physicians were advising the opposite. The details of this debate are well covered in 2 recent articles.[3,4]

I agree with Delaney that the key to research is to ask the right question, find out if the question has been answered and, if not, use the appropriate study to answer it. Because of the inability to draw conclusions from observational data alone, the appropriate study is almost always an RCT. Unfortunately, this type of study is too infrequently conducted. The ALLHAT trial[5] is an exception to this general pattern. As a result of that trial, we can advise patients, with a high degree of certainty, that chlorthalidone, a thiazide-like diuretic, is preferable to amlodipine, a calcium-channel blocker (CCB), as first-line therapy for hypertension; for every 61 patients treated, using a thiazide rather than a CCB prevents one death or hospital admission for heart failure. This finding would not have been discovered from observational data.

Barton,[6] in the editorial cited by Pijak and associates, stated that "If high quality randomized trials exist for a clinical question then they trump any number of observational studies." We need to appreciate that well-designed, large, simple RCTs are not that difficult or expensive to conduct and are highly preferable to widespread empiri-

cal prescription of drugs, from which we can learn little or nothing.

James M. Wright
Departments of Pharmacology and of Therapeutics and Medicine
University of British Columbia
Vancouver, BC

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Physicians with depression

We commend Mark Bernstein for his brave yet disturbing description of a neurosurgeon in an advanced state of burnout and depression.[1] Physicians have an increased risk of depression, suicide and substance abuse.[2] They are especially vulnerable because of the demands of caring for the ill, managing a practice, pursuing lifelong education in a rapidly changing field, and the litigious environment in which they work. Physicians in distress face emotional exhaustion, cynicism, feelings of ineffectiveness and depersonalization.[3] Studies have revealed that two-thirds of Canada's physicians consider their workload too heavy, and more than half say that personal and family life has suffered because of their career choice.[4] In a recent CMA survey of 2251 doctors, 45.7% of the respondents reported an advanced state of burnout.[5] The profession is aware that mental health problems can begin in medical school and worsen during residency, when fatigue and emotional exhaustion are often the norm.[2] Yet the topics of burnout, stress and poor mental health are not easy to discuss openly. The stigma of mental illness and the potential impact on professional status inhibit disclosure. We therefore strongly support the CMA initiative on Physician Health and Well-Being[6] and the need to change the culture to address the barriers to disclosure.

Sarita Verma
Associate Dean, Medical Education
Leslie Flynn
Assistant Dean, Postgraduate Medical Education
Queen's University
Kingston, Ont.

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[Dr. Bernstein replies:]

I thank Drs. Verma and Flynn, as we all should, for their thoughtful and very appropriate letter. Their message is vitally important: doctors are at high risk for depression, and when it affects us we must confront it and treat it as we would any other illness. After the *CMAJ* article was published,[1] I received a small number (under 10) of private letters from doctors who bravely described their own experience with depression, expressed concern for my well being, and made suggestions about how I could seek help. However, I feel like a bit of a fraud. I have published extensively in the peer-reviewed medical literature, and in the last few years have tried my hand at nonmedical writing, in the nonfiction genre. The piece in *CMAJ* was but my bravest to date, and apparently was quite effective in painting the picture I set out to paint. But I am not depressed and I am not burned out. Perhaps the development of new pursuits in my life like creative writing is one of the very reasons why I have not suffered burnout. At the risk of stating the obvious, it is terribly important for hard-working doctors to develop diverse outside interests as passionately as possible. Again I thank Drs. Verma and Flynn, and the other doctors who wrote me, and the many others who must have silently worried about me. But please allow me to assure all of you that I am very well and happy, and apparently my creative writing is improving!

Mark Bernstein
Division of Neurosurgery
University Health Network
Professor
Department of Surgery
University of Toronto
Toronto, Ont.

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1. Bernstein M. Neurosurgical depression. *CMAJ* 2003;169(9):943-4.

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[The senior deputy editor responds:]

Articles published under the Room for a View heading in The Left Atrium, like those penned by "Dr. Ursus" for our back-page column, occupy a liminal territory between fact and fiction. Authors are required to change details to protect confidentiality, and are at liberty to refine, embellish or reinvent reality for narrative effect. Some pieces are inspired by experience, and thus lay claim to authenticity. But a ring of truth can arise from other things, such as empathy, insight and imagination. Mark Twain knew the craft of storytelling. A saying attributed to him (by Rudyard Kipling) goes like this: "Get your facts first, and then you can distort them as much as you please."

Anne Marie Todkill
CMAJ

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