with recent work in the *Journal* by Nathan Herrmann, M.D., F.R.C.P.(C.), et al. (4). Perhaps the alarming reports on risperidone, which could lead to use of nonatypical neuroleptics, should be reconsidered. Previous epidemiological studies (1) have been characterized by a low number of patients, polypharmacy, other diseases, compliance, and/or appropriateness of use. We suggest that additional controlled experimental approaches might better address the safety of psychotropic drugs.

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TO THE EDITOR: Dr. Herrmann et al. reported a retrospective study concerning the risk of stroke among 11,400 patients (age >66 years) who were administered atypical antipsychotics. Use of atypical antipsychotics was not associated with an elevated risk of stroke compared with use of conventional neuroleptics.

We examined the 2-year risk of death among dementia patients who were using atypical antipsychotics or conventional neuroleptics or were nonusers. Originally, 425 patients (age >69 years) in city hospitals and nursing homes in Helsinki, Finland, participated (1); 255 had dementia and 106 had delirium, according to DSM-IV criteria.

One hundred thirty-five (52.9%) of 255 patients were given antipsychotics at baseline, 40.4% took conventional neuroleptics, and 12.5% took atypical antipsychotics. After 2 years, 118 of 255 were deceased. The death rate was 47.6% among those taking conventional antipsychotics, 21.9% among those taking atypical antipsychotics, and 50.0% among nonusers. We performed a logistic regression analysis to clarify which factors had independent prognostic value in mortality. When we entered age, gender, severe stage of dementia (clinical dementia rating=2–3), delirium, high number of comorbidities, impaired physical functioning, use of neuroleptics, use of atypical antipsychotics, and use of restraints into the model, only old age (>85 years) (odds ratio=1.71, 95% confidence interval [CI]=1.00–2.95), high number of comorbid disorders (odds ratio=1.96, 95% CI=1.03–3.73), and use of restraints (odds ratio=2.45, 95% CI=1.06–5.65) predicted mortality. It is surprising that the use of atypical antipsychotics seemed to protect against death (odds ratio=0.40, 95% CI=0.17–0.96). Conventional neuroleptics did not have any effect.

There is a concern that atypical antipsychotics increase the risk of stroke among dementia patients. In the study by Dr. Herrmann et al., there was no evidence of that. Nevertheless, the study also consisted of people without dementia. Patients with dementia are often old and frail and have comorbidities and delirious episodes with acute illnesses that possibly explain the high risk of death. They also have behavioral symptoms that are frightening for the patient and caregiver. These symptoms are the most common reason for admittance to permanent institutional care (1). Thus, these patients urgently need control for their symptoms. There are several randomized trials showing that both atypical antipsychotics and cholinesterase inhibitors are efficient in controlling these symptoms (1). The use of the cholinesterase inhibitors was quite rare—only 3%—among our participants in 1999–2000. Most patients used conventional neuroleptics. To our knowledge, there are no studies concerning the risk of taking neuroleptics among dementia patients. Our study presents that possibility.

It is possible that in our group the frailest patients were administered neuroleptics and the fittest were given atypical antipsychotics even though it would be against any recommendations. Nevertheless, our logistic regression analysis took into account comorbidities, physical functioning, age, and stage of dementia. Rather than showing an elevated risk, atypical antipsychotics had a protective effect.

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Dr. Herrmann and Colleagues Reply

TO THE EDITOR: In response to our administrative health care database study comparing the risks of cerebrovascular accidents in elderly patients treated with either atypical or typical antipsychotics, Dr. Zhao et al. describe the lack of histological damage caused by risperidone treatment in aged rats with preexisting cortical infarcts. We applaud these investigators' "bedside to bench" approach and find the results reassuring in light of the lack of association between the use of atypical antipsychotics and cerebrovascular accidents noted in our population-based cohort study. In the second letter, Dr. Raivio et al. report that in a small group of elderly patients with dementia or delirium, the use of atypical antipsychotics was actually associated with a 60% reduction in the rate of death. Although this study did not address the frequency of cerebrovascular adverse events, it too provides converging evidence that the risk of life-threatening events directly attributable to atypical antipsychotics may be overstated.

Concerns about the association between atypical antipsychotic use and cerebrovascular adverse events in elderly dementia patients based on data from randomized, controlled trials persist (Wooltorton, 2002; reference 1), and prescribing

information for risperidone and olanzapine have been modified to reflect this possibility. Possible biological mechanisms to account for this association might include thromboembolic effects, cardiovascular effects (such as orthostatic hypotension and arrhythmias), hyperprolactinemia leading to atherosclerosis, and excessive sedation, resulting in dehydration and hemoconcentration. To date, there are few data to support these mechanisms (2). Dr. Zhao et al. suggest a number of methodological problems in the previous studies that raise the possibility of an association, including small numbers of patients, the effect of comorbid medical illness (especially preexisting cerebrovascular disease), and concomitant medication use. The latter is particularly poignant given the recent withdrawal of rofecoxib from the market because of higher rates of serious cardiovascular thromboembolic effects, including stroke. It is unclear what role such medications may have played in the randomized, controlled trials of antipsychotics.

Finally, Dr. Zhao et al. raise the concern that warnings such as those of the Committee on Safety of Medicines in the United Kingdom to avoid risperidone and olanzapine use in elderly dementia patients (3) may lead to switching to typical antipsychotics, such as haloperidol. Besides their well-documented tendency to cause both acute and long-term extrapyramidal symptoms (e.g. , tardive dyskinesia), drugs such as haloperidol have been shown to negatively influence motor recovery in poststroke patients (4) and may not confer any reduced risk of cerebrovascular accidents in an elderly population relative to atypical antipsychotics (as in our article).

Further studies focusing on potential mechanisms may help to clarify the association between atypical antipsychotic use and cerebrovascular adverse events and ultimately define subgroups of patients at increased risk in whom benefits of therapy might outweigh the risks.

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Tobacco Use and Cataracts in Patients With Schizophrenia

TO THE EDITOR: We read with great interest the recent report by Stephen R. Marder, M.D., and coauthors on the physical health monitoring of patients with schizophrenia (1). We agree with those authors' concerns that "the health needs of people with schizophrenia…are not adequately addressed by clinicians in specialty mental health programs or in primary care settings." However, we were perplexed to find that tobacco smoking was not considered in the review process, and no recommendations for monitoring and intervening on tobacco smoking were made in the report. There is a real risk that this report may worsen rather than improve the health of people with schizophrenia by advising clinicians to monitor and intervene on factors that have relatively small impact on their patients' health while ignoring the main causes (substance use generally and tobacco use in particular).

Most of the excess mortality in schizophrenia is directly attributable to cigarette smoking (2). There is also an indirect effect of tobacco use on health through the high proportion of total income that people with schizophrenia spend on tobacco (27%) (3). Mental health professionals rarely assess their patients' tobacco use (4), despite the existence of effective treatments (5–7).

We hope that those responsible for the care of people with schizophrenia will strive to improve the physical health of their patients but will target their efforts appropriately to the main causes of ill health and premature death rather than focusing on the side effects of psychotropic medications. Among the most important things clinicians can do for the health of people with schizophrenia is the proper assessment and treatment of nicotine dependence (8).

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TO THE EDITOR: Although implementing many of the specific suggestions of Dr. Marder et al. for expanding the health monitoring of patients with schizophrenia could prove useful, the recommendation for biannual (for patients under age 40) or annual (for patients age 40 or older) slit-lamp examinations is