THE AUTHORS REPLY: The details regarding the identification and phytochemical characterization of *E. angustifolia* requested by Mr. Leach were provided as online supplementary material to our publication. This appendix is available on the *Journal*'s Web site (www.nejm.org) and provides detailed information about the "strength" of the three formulations as defined according to the concentrations of various polysaccharides and alkamides.

The use of a single rhinovirus serotype in the challenge model is one of many variables that were controlled in the study, as compared with studies performed in the natural setting. The controlled conditions of our model have generally resulted in larger effect sizes and increased sensitivity in the detection of treatment effects than have studies involving the use of natural-infection models.[1-4] We are not aware of examples of treatments that were effective in natural models but had negative results in adequately designed studies involving the experimental model. It is possible, however, that different treatment effects might have been detected under different experimental conditions.

The suggestion that a higher dose of echinacea might have produced different results raises important issues about the study and the use of herbal products. The dosage recommendations cited by Mr. Blumenthal and Dr. Farnsworth do not appear to be based on experimental or pharmacokinetic data. Furthermore, it is not clear how the dose of echinacea should be measured and interpreted. As demonstrated in our study, the same root-equivalent dose of echinacea can be extracted in different ways to produce dramatically different "doses" of the different phytochemical constituents. The lack of standardization of products, the absence of definitive information about the mechanism of action or the active constituents, and the limited pharmacokinetic data regarding the various constituents preclude a meaningful discussion of an appropriate dosing regimen.

Implicit in the comments of these correspondents is an assumption that, had the study been designed or executed differently, a beneficial effect of echinacea would have been demonstrated. Given the available data, we believe it is most reasonable to conclude that echinacea is not useful as a treatment for the common cold. This conclusion should stand until those who promote, manufacture, and sell these products produce convincing evidence of a clinically meaningful benefit.

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Adherence to Medication

TO THE EDITOR: Osterberg and Blaschke (Aug. 4 issue)[1] discuss interventions that can be used to improve adherence to medication regimens. However, I am surprised that they do not include interventions by pharmacists among the recommendations in Table 3 of their article, which listed strategies for improving adherence.

The article does highlight pharmacist-led interventions for HIV infection as a promising area. The involvement of pharmacists has also been demonstrated to improve adherence or compliance in the management of hypertension,[2] lowering of lipid levels,[3] and the treatment of depression in patients.[4] Furthermore, a set of billing codes, which are in compliance with the Health Insurance Portability and Accountability Act, for pharmacists to use in billing third-party payers when providing Medication Therapy Management Services (MTMS) has been recently approved in the United States. The Current Procedural Terminology Editorial Panel of the American Medical Association has approved three codes effective as of January 1, 2006.[5] Pharmacists can use MTMS to communicate with patients and physicians in a concerted effort to improve adherence to medication.

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TO THE EDITOR: The article by Osterberg and Blaschke is a nice review of how to increase adherence once a patient has a medication in his or her possession. What the article mentions but fails to address is how to deal with patients who do not adhere to the regimens because they cannot afford their medications. This is a problem especially for patients on multiple medication regimens. A mention of possible solutions to this ever-increasing cause of nonadherence would be useful.

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TO THE EDITOR: Many of the complexities associated with adherence to medication are laid out by Osterberg and Blaschke. However, the authors do not consider the role of sex in their discussion of both barriers to and interventions for appropriate drug use. For example, women are often poorer than men and, for cost reasons alone, may split pills or skip taking them — and then be judged as "lacking" in terms of adherence. In fact, all items on the authors' list of major predictors of poor adherence are relevant to sex differences. Consequently, interventions that assume a one-size-fits-all approach are likely to be too generalized and, thereby, potentially ineffective.[1]

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1. Broyles LM, Colbert AM, Erlen JA. Medication practice and feminist thought: a theoretical and ethical response to adherence in HIV/AIDS. Bioethics 2005;19:362-78.

TO THE EDITOR: Osterberg and Blaschke provide a stimulating description of the importance of taking medication and the barriers that may impede adherence, thereby influencing clinical outcome. One barrier the authors highlight is inadequate communication between patient and provider, the remedy for which is at the heart of a recent philosophical move toward concordance — the process, as described by Marinker et al., of forming a therapeutic alliance to "optimise health gain from the best use of medicines, compatible with what the patient desires and is capable of achieving."[1] In this setting, the prescription is replaced by a "concordat," which is broken only if communication fails. In the United Kingdom, this terminology is gradually replacing the terms "compliance" and "adherence,"[2] which Osterberg and Blaschke agree are troublesome. We praise their suggestions for nonjudgmental inquiry about the consumption of medication, but further steps (especially training in communication)[3,4] may be needed to facilitate full concordance and thus better streamline personal and health care system costs through optimal health. The article's epigraph should perhaps be reconsidered in terms of the patient's perspective: patients take drugs only if they agree that these agents are more beneficial than disruptive.

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THE AUTHORS REPLY: We agree with Dr. Campbell that pharmacist-led interventions have proved successful in improving patient adherence to medications. However, these resources are not readily avail-

able to all providers. In the first paragraph under the section on interventions in our article, we did mention the benefits of interventions that involve pharmacists to improve adherence to medication, but we did not include this information in Table 3, which we limited to simple strategies that providers can use in general-practice settings. It is important that any intervention used to improve adherence, such as pharmacist-led interventions, include an evaluation of the cost and benefits of the approach.

We agree with Dr. Lippman's point that the role of sex should be considered in terms of the barriers and interventions related to medication-taking behavior and that more studies are needed in this area of medication adherence. We did not address the role of sex, since available data have not been consistent among all studies.[1] We agree that adherence to antiretroviral medication is generally poorer in women than in men, as shown in studies on adherence to treatment regimens for HIV, and a recent study involving microelectronic monitors supports Dr. Lippman's argument about poorer adherence to medication among women with HIV.[2]

We addressed the need for physicians to be aware of the cost of medications, since expensive medications can be a barrier to adherence, but we did not explicitly include interventions that providers can use to overcome nonadherence that results from a patient's inability to afford the medication. The rising cost of prescription drugs, in addition to the increasing cost of insurance copayments, clearly contributes to poor adherence in many patients, but solutions to this problem were beyond the scope of our article.

We agree with Dr. Treharne and colleagues regarding the advantage of using the term "concordance" in describing the medication-taking behavior of a patient, since this implies an equal responsibility of patient and physician in the therapeutic relationship. We hope this term will become prevalent in the United States as well.

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Postmenopausal Osteoporosis

TO THE EDITOR: In discussing vitamin D deficiency, Rosen (Aug. 11 issue)[1] refers to a serum level of 25-hydroxyvitamin D below 15 ng per milliliter (37.4 nmol per liter). I believe that this level is too low. Studies have shown increases in serum parathyroid hormone levels[2] and decreases in bone mineral density[3] at approximately 20 ng per milliliter (50 nmol per liter) and below. In addition, levels below 20 ng per milliliter have been associated with decreases in intestinal calcium absorption and lower-extremity function. Therefore, vitamin D deficiency should be considered if the serum 25-hydroxyvitamin D level is below 20 ng per milliliter, and perhaps even below 30 ng per milliliter (75 nmol per liter).[4]

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DR. ROSEN REPLIES: Dr. Chan raises an important point: At what level of 25-hydroxyvitamin D should the patient be considered to have vitamin D deficiency? In my review article, I cited a report that up to two of every three women with hip fracture had vitamin D levels of less than 15 ng per milliliter.[1] More recently, Gaugris et al., in a meta-analysis of 30 studies, found that up to 70 percent of all postmenopausal women with a history of any frac-