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TO THE EDITOR: Barrett and colleagues (1) reported a placebo-controlled trial of echinacea for the common cold. The Food and Drug Administration defines a placebo control as "an identical-appearing treatment that does not contain the test drug . . . the placebo control design, by allowing blinding and randomization and including a group that receives an inert treatment, controls for all potential influences on the actual or apparent course of the disease other than those arising from the pharmacologic action of the test drug" (2). Alfalfa does not meet these requirements because it is a potential influence on the course of the disease and therefore must be considered an active control.

Alfalfa is biochemically complex, containing large amounts of vitamins, minerals, phytoestrogens, and saponins. The saponin constituents alone (molecules with a triterpene or steroid moiety) have shown a wide range of biological activity. Alfalfa saponins are fungicidal, bactericidal, and insecticidal and have cholesterol-lowering properties (3). Alfalfa has also been found to contain an abundance of thyrotropin-releasing hormone–like material (4), which may be the basis of its traditional use in thyroid disease (5). Alfalfa tablets, seeds, and sprouts have also been associated with rare instances of the reactivation of systemic lupus erythematosus and the onset of other autoimmune disorders. As with echinacea, alfalfa is part of the herbal pharmacopoeia and has significant known and no doubt unknown biological effects.

Barrett and colleagues' study informed us of the equivalent effect of alfalfa and echinacea on the outcomes measured. However, the results cannot be interpreted because neither herb is considered a standard treatment for the common cold.

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IN RESPONSE: Randomized, controlled trials are designed to test specific hypotheses. While bias can be reduced, generalizability and interpretation are limited. In our trial, a specific echinacea preparation was tested against a specific control as a treatment for the common cold. The choice of echinacea was influenced by the literature and by popular practice. Several trials of *Echinacea purpurea* and *E. angustifolia* preparations had been positively reported (1, 2). Products containing either or both species were in wide use. We chose a capsulized whole plant preparation for its simplicity and ease of manufacture. We avoided a liquid preparation because the taste and tingling sensation of echinacea are notoriously difficult to disguise. We were intent on demonstrating intact blinding, since this had not previously been accomplished. This guided our choice of placebo. Because we used clear gelatin capsules containing the whole plant product, and because some of the herbal taste could leak from the capsules (and was available to participants who opened them), we needed a plant-based product that would be indistinguishable to participants and to research personnel. We settled on whole dried alfalfa because the color and consistency mimicked the echinacea product and no research had reported any effects of alfalfa on the severity or duration of the common cold. However, taste was still distinguishable, so technicians at Shaklee Technica experimented with adding various flavoring agents, eventually finding that a very small amount of thyme and peppermint successfully disguised echinacea's flavor.

We agree that these choices could affect results. Although a bit far-fetched, it is possible that tiny amounts of peppermint or thyme could block a positive effect of echinacea. It is also possible, although unlikely, that a few grams of alfalfa could be an effective treatment for the common cold. If so, the multimillion-dollar cold remedy industry should shudder, as a few grams of alfalfa costs only a few pennies. Perhaps an alfalfa trial will be carried out, and perhaps some benefit will be found. In the meantime, we stand by the results of our trial: The echinacea preparation we used provided no measurable benefit to college students experiencing cold symptoms. Perhaps it would have worked in an older sample. Perhaps a refined extract or liquid preparation would have worked. Perhaps dosing should occur within 12 hours rather than 36 hours of first symptoms. Our results cannot address these important questions, nor can our trial by itself negate the results of the several positively reported trials. More and better research is warranted.

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Alcohol, Postmenopausal Hormones, and Breast Cancer

TO THE EDITOR: In the Nurses' Health Study cohort, Chen and colleagues (1) found an approximately 2-fold excess risk for breast cancer in women who currently used postmenopausal hormones and drank alcohol. However, the researchers were unable to consider high alcohol consumption. To address this issue, we analyzed data from 2 Italian case–control studies. The first was conducted between 1983 and 1991 in greater Milan (2), and the second was conducted between 1991 and 1994 in 6 centers in various regions of Italy (3). The studies involved 3573 postmenopausal women (median age, 61 years [range, 31 to 74 years]) with a histologically confirmed diag-

Table. **Odds Ratios for Breast Cancer in Postmenopausal Women, by Alcohol Intake and Postmenopausal Hormone Use**

Alcohol Intake	Postmenopausal Hormone Use	All Postmenopausal Women			Women Who Reported Natural Menopause
		Women with Breast Cancer	Controls	Odds Ratio (95% CI)*	Odds Ratio (95% CI)*
None (abstainers)	Never	970	1152	1†	1†
	Ever	97	82	1.48 (1.08–2.04)	1.39 (0.95–2.05)
1 drink per day	Never	1140	1133	1.19 (1.05–1.35)	1.21 (1.05–1.39)
	Ever	148	129	1.41 (1.08–1.83)	1.35 (0.99–1.85)
2 drinks per day	Never	792	759	1.23 (1.07–1.41)	1.30 (1.11–1.51)
	Ever	63	45	1.60 (1.07–2.40)	2.32 (1.40–3.82)
≥3 drinks per day	Never	327	252	1.62 (1.33–1.96)	1.56 (1.26–1.93)
	Ever	36	20	2.25 (1.27–3.99)	2.95 (1.43–6.11)

* Derived from multiple logistic regression models including terms for age, study center, calendar year of interview, education, smoking habit, body mass index, age at menarche, type of menopause, parity age at first birth, oral contraceptive use, history of benign breast diseases, and family history of breast cancer in first-degree relatives.
† Reference category.

nosis of incident breast cancer. Controls were 3572 postmenopausal women (median age, 61 years [range, 34 to 74 years]) admitted to the same network of hospitals for acute, non-neoplastic, non–hormone-related conditions. The participation rate exceeded 95% for both case-patients and controls. Information collected on alcohol drinking included the number of days per week that each type of alcoholic beverage (wine, beer, and spirits) was consumed, the average numbers of drinks per day, and the duration of the habit in years. Each drink included approximately 12 g of ethanol.

In comparison with women who did not drink, the multivariate odds ratio (OR) was 1.62 for women who had never used postmenopausal hormones who consumed at least 3 drinks per day. Compared with never-users of postmenopausal hormones, the OR was 1.48 for ever-users who abstained from alcohol. Women exposed to both factors had an OR of 2.25. Among the 2879 case-patients and 2752 controls who reported natural menopause, the OR for women who were exposed to both factors was 2.95 (**Table**).

Moderate alcohol drinking is socially acceptable among Italian women (4), and the information on alcohol consumption was satisfactorily valid and reproducible (5). Our findings, based on a uniquely large data set and comparatively high levels of alcohol drinking, provide further evidence of a substantial excess risk for breast cancer in women who drink alcohol and have ever used postmenopausal hormones.

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Update in Hospital Medicine

TO THE EDITOR: Regarding the section on avoiding femoral line placement in Flansbaum and Huddleston's Update in hospital medicine (1), am I the only one who sees the folly of leaving a femoral line in place for more than 4 days? In the study reviewed (2), femoral lines were used for an average of 9.3 days!

I argue that in the short run a femoral line is far safer than a subclavian line. The complications associated with femoral lines all occur after 72 hours. Line infections are rare in this time window. If short-term access is needed, it makes more sense to use the femoral vein. If access may be needed for more than 72 hours, a subclavian line should be used. I use femoral lines for all of my patients with diabetic ketoacidosis. They don't need the line longer than 72 hours, and they don't get pneumothorax.

I would love to see a study that compares complication rates between subclavian lines left in longer than 5 days and femoral lines pulled in less than 72 hours. We all know that the infection rate and thrombotic rate will both be lower with the femoral line. If central access will be needed for less than 72 hours, I argue that the femoral vein is better.

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