To the Editor:

In their Research Letter, Ms Stjernberg and Dr Berglund1 documented a repellent effect of garlic against an unnamed species of tick and stated that daily consumption of 1200 mg of garlic was an alternative to "other agents that might have more adverse effects." Based on the design of their study, any conclusions concerning the relative effectiveness and safety of garlic as a tick repellent are unfounded. They compared garlic to a placebo, not to other currently available repellents, and they did not present any data on the comparative safety of garlic vs other repellents.

In fact, consumption of garlic appeared to be only marginally better than doing nothing at all to prevent tick bites. By contrast, treatment of clothing with permethrin, a synthetic pyrethroid, has been shown to be 100% effective against *Ixodes scapularis,*2 the vector of *Borrelia burgdorferi* in the northeastern United States, and to provide nearly 100% protection against *Amblyomma americanum* and *Dermacentor variabilis.*3 Diethyltoluamide (DEET)-based repellents also are effective in repelling ticks2 and can be applied to skin, as well as to clothing. The US Department of Defense (DoD) promotes the concurrent use of a 33% DEET-based lotion on exposed skin, treatment of uniforms with permethrin, and proper wearing of the uniform. This strategy has been termed the DoD Repellent System and is believed to be the most effective method for reducing the risk of arthropod bites.4

Brown and Hebert5 were cited as the source of information on adverse effects of repellents other than garlic. In fact, they concluded that appropriate use of repellents was a "safe means of minimizing the risk of bites and vector-borne diseases." In additional reviews, DEET has been associated with "remarkably few problems"6 while the concurrent use of DEET and permethrin was judged "safe and effective."4

The study by Stjernberg and Berglund raises 2 additional questions. First, does garlic effectively repel other arthropods of medical importance? Troops frequently are at risk of attack by several arthropod taxa and need a repellent that is broadly effective. The DoD Repellent System is extremely effective in repelling a number of arthropods in addition to ticks.4 Second, how difficult is it to ensure compliance with a daily regimen of 1200 mg garlic? That is, do troops find garlic acceptable, and can they be relied on to remember to take daily doses? Treatment of uniforms with permethrin can provide repellency for the life of the garment while requiring no action on the part of the wearer.4 For troops and other populations at high risk for arthropod bites, the use of DEET and permethrin remains the most effective and safe method of protection.

Chad P. McHugh, MPH, PhD Air Force Institute for Environment, Safety and Occupational Health Risk Analysis Brooks Air Force Base, Tex

1. Stjernberg L, Berglund J. Garlic as an insect repellent. *JAMA*. 2000;284:831. **2.** Schreck CE, Snoddy EL, Spielman A. Pressurized sprays of permethrin or DEET on military clothing for personal protection against *Ixodes dammini* (Acari: Ixodidae). *J Med Entomol*. 1986;23:396-399. **3.** Evans SR, Korch GW, Lawson MA. Comparative field evaluation of permethrin and DEET-treated military uniforms for personal protection against ticks (Acari). *J Med Entomol*. 1990;27:829-834. **4.** Young GD, Evans S. Safety and efficacy of DEET and permethrin in the prevention of arthropod attack. *Mil Med*. 1998;163:324-330. **5.** Brown M, Hebert AA. Insect repellents: an overview. *J AmAcad Dermatol*. 1997; 36:243-249. **6.** Goodyear L, Behrens RH. Short report: the safety and toxicity of insect repellents. *Am J Trop Med Hyg.* 1998;59:323-324.

To the Editor:

Ms Stjernberg and Dr Berglund1 reported that garlic may be an effective tick repellent. However, the content of sulfuric compounds in garlic is subject to large variations that influence pharmacological effects and the only information about the garlic preparation in their study is "1200 mg/d *Allium sativum* in capsule form." There was no information about whether the plant material was fresh, dried, or treated in any way. Herbal preparations containing garlic are normally prepared in several different ways, such as dried, fermented, oil macerated, or solvent extracted.

Stjernberg and Berglund also state that "diethyltoluamide is the best repellent against insect vectors." DEET is the most commonly used mosquito repellent and has activity against other insects. However, several other compounds and even plant extracts have a mosquito-repellent effect of the same magnitude as that of DEET.2,3 Furthermore, permethrin is a synthetic pyrethroid, ie, insecticide and acaricide, and not a true repellent.

Ha°kan Tuno´n, PhD Swedish Biodiversity Centre Swedish Agricultural University Uppsala, Sweden

1. Stjernberg L. Berglund J. Garlic as an insect repellent. *JAMA*. 2000;284:831. **2.** Tuno´ n H, Thorsell W, Bohlin L. Mosquito-repelling activity of compounds occurring in *Achillea millefolium L*. (Asteraceae). *Econ Bot*. 1994;48:111-120. **3.** Thorsell W, Mikiver A, Malander I, Tuno´ n H. Efficacy of plant extracts and oils as mosquito repellents. *Phytomedicine*. 1998;5:311-323.

To the Editor:

Ms Stjernberg and Dr Berglund1 recently presented a randomized, double-blind, crossover trial of garlic to prevent tick bites among Swedish military conscripts. Fifty subjects were treated with garlic first and placebo second while another 50 were given placebo first and then garlic. The total number of subjects was thus 100. Of these, 66 were reported to have been bitten by ticks. The authors presented a relative risk (RR) of 0.79 with the 95% confidence interval (CI) 0.65-0.96. They did not reveal the number of bitten subjects per sequence.

In a crossover trial the RR is calculated from discordant pairs, ie, the number of subjects with more events on active treatment than on placebo is compared with the number of subjects with more events on placebo than on active treatment. The more effective the treatment is the lower ratio between the 2 numbers. In this trial, a discordant pair is a subject with at least 1 bite while receiving either active or placebo treatment. The number of subjects entering the analysis could therefore be lower, but not greater, than 66. Several possible sets of discordant pairs among these 66 conscripts could give a RR of approximately 0.79, but the *P* value could not be lower than .39 (exact McNemar test using maximum possible sample size, 37+29=66 discordant pairs). The corresponding CI is 0.46-1.31.

The authors also present a *P* value of .04 for the difference in number of tick bites between treatments. However, using tick bite as analysis unit instead of conscript is incorrect since the risk of a tick bite differs between conscripts; counting tick bites instead of conscripts in a traditional single-level analysis exaggerates the statistical significance of the findings.2

Jonas Ranstam, PhD School of Health and Society Malmo¨ University Malmo¨ , Sweden

1. Stjernberg L, Berglund J. Garlic as an insect repellent. *JAMA*. 2000;284:831. **2.** Ranstam J. Repeated measurement and analysis units. *Acta Orthop Scand*. 1998; 69:345-346.

In Reply:

In response to Dr McHugh, our study specifically assessed the effectiveness of garlic as a repellent for tick bites. We did not measure its effectiveness for other arthropods or insects, nor did we compare it with other repellents. We choose military personnel because their behavior is relatively consistent.

Both McHugh and Dr Tuno´n point out that there are other effective insecticides and repellents. However, the adverse effects of DEET and permethrin are a subject of recurrent debate. Swedish regulations concerning the use of these products are very strict, for permethrin because of toxicity in aquatic organisms1 and for DEET because of studies showing adverse effects in humans.2,3 Thus, Swedish troops cannot use permethrin- or DEET-treated uniforms. In Sweden, garlic might be considered as an alternative to other repellents for people staying in tick endemic areas. Of course, treatment of clothes with permethrin guarantees amuch higher level of protection as long as the clothing are worn. Garlic should certainly not be substituted for more effective protective measurements in areas that are endemic to other vector borne diseases, such as malaria.

In response to Dr Ranstam, all participants in our trial recorded in a diary the time of exposure and observed tick bites. This allowed us to standardize for time of exposure. Our statements were related to per protocol analysis only, which lead us to be conservative in our conclusions. Per protocol statements included all individuals fulfilling the study requirements and describes the time the study drug was taken as directed; all episodes with deviating compliance were excluded.

The 2 periods of observation differed in length, and some units spent different amounts of time within each period. Therefore, we considered the Wilcoxon test for paired observations a more appropriate method to test our hypothesis. This test for paired samples compared the individual number of tick bites per unit of time (days) between placebo and active treatment.

However, when presenting the RRs we compared (standardized for time of exposure) the number of bitten participants in the placebo groups with the number of bitten participants in the garlic groups and did not take into consideration the crossover design when comparing paired samples. We agree that this is inappropriate and that CIs should not have been presented.

Louise Stjernberg, RN, MPH Department of Science and Health Blekinge Institute of Technology Karlskrona, Sweden Johan Berglund, MD, PhD Department of Community Medicine Lund University Malmo¨ , Sweden

1. Torstensson L. *Ecotoxicity Evaluation of Permethrin*. Uppsala: Swedish Agricultural University; 1989. **2.** Brown M, Hebert AA. Insect repellents: an overview. *J AmAcad Dermatol*. 1997; 36:243-249. **3.** Clem JR, Havemann DF, Raebel MA. Insect repellent (N,N-diethyl-m-toluamide) cardiovascular toxicity in an adult. *Ann Pharmacother*. 1993;27:289-293.