

Correspondence



Retraction: Absence of Human T-Cell Lymphotropic Virus Type I in Cutaneous T-Cell Lymphoma

To the Editor: Most of the data in our letter to the editor on the absence of human T-cell lymphotropic virus type I in cutaneous T-cell lymphoma (Jan. 23, 1997, issue)¹ cannot be verified. The letter is therefore invalid, and we wish to retract it. We apologize to the *Journal* and its readers for reporting these results.

TAKEJI NISHIKAWA, M.D.

Professor of Dermatology
Keio University School of Medicine
Tokyo 160-8582, Japan

KAZUNARI YAMAGUCHI, M.D.

Associate Professor of Blood Transfusion Service
Kumamoto University School of Medicine
Kumamoto 860-0811, Japan

TAKAO SARUTA, M.D.

Dean
Keio University School of Medicine
Tokyo 160-8582, Japan

1. Kikuchi A, Nishikawa T, Yamaguchi K. Absence of human T-cell lymphotropic virus type I in cutaneous T-cell lymphoma. *N Engl J Med* 1997; 336:296-7.

Prophylactic Mastectomy in Women with a High Risk of Breast Cancer

To the Editor: When Hartmann and colleagues (Jan. 14 issue)¹ analyzed the outcomes of prophylactic mastectomies, they expressed the results as a relative risk reduction. They reported that prophylactic mastectomy reduces the incidence of breast cancer by about 90 percent among both moderate-risk and high-risk women. The relative risk reduction allows the reader to judge the magnitude of the association, but it does not express the clinical implications of the findings as clearly as the number of patients who would need to be treated to prevent a bad outcome (referred to as the number needed to treat).² This distinction can make a difference in care, because it has been shown that results expressed as the relative risk reduction and those expressed as the number needed to treat have different influences on decisions about treatment.^{3,4}

The number needed to treat makes clear the proportion of people who would be treated unnecessarily (Table 1)

TABLE 1. RELATIVE RISK REDUCTION AND NUMBER NEEDED TO TREAT FOR THE OUTCOMES OF BREAST CANCER AND DEATH IN HIGH-RISK AND MODERATE-RISK WOMEN WHO UNDERWENT PROPHYLACTIC MASTECTOMY.*

RISK AND OUTCOME	OUTCOME RATE WITHOUT MASTECTOMY	OUTCOME RATE WITH MASTECTOMY	ABSOLUTE RISK REDUCTION	RELATIVE RISK REDUCTION	NUMBER NEEDED TO TREAT
High					
Breast cancer	0.175	0.014	0.161	0.920	6
Death	0.049	0.009	0.040	0.816	25
Moderate					
Breast cancer	0.088	0.009	0.079	0.898	13
Death	0.024	0.000	0.024	1.000	42

*The outcome rate is the proportion of women with the indicated outcome, on the basis of the data reported by Hartmann et al. The absolute risk reduction is calculated as the outcome rate without treatment minus the outcome rate with treatment, the relative risk reduction is calculated as the absolute risk reduction divided by the outcome rate without treatment, and the number needed to treat is calculated as 1 divided by the absolute risk reduction.

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and highlights the differences between the moderate-risk and high-risk groups. Thus, it would be necessary to treat 6 women at high risk to prevent one case of breast cancer, but it would be necessary to treat 13 women at moderate risk to prevent one case. To prevent one death from breast cancer, it would be necessary to treat more women at moderate risk (42) than women at high risk (25).

ROBERT M. HAMM, PH.D.
FRANK LAWLER, M.D.
DEWEY SCHEID, M.D.

University of Oklahoma Health Sciences Center
Oklahoma City, OK 73104

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2. Cook RJ, Sackett DL. The number needed to treat: a clinically useful measure of treatment effect. *BMJ* 1995;310:452-4. [Erratum, *BMJ* 1995; 310:1056.]
3. Bucher HC, Weinbacher M, Gyr K. Influence of method of reporting study results on decision of physicians to prescribe drugs to lower cholesterol concentration. *BMJ* 1994;309:761-4.
4. Forrow L, Taylor WC, Arnold RM. Absolutely relative: how research results are summarized can affect treatment decisions. *Am J Med* 1992;92: 121-4.

To the Editor: In their informative analysis, Hartmann et al. note a dramatic reduction in cases of breast cancer among women who underwent prophylactic mastectomy. Most of the women, however, did not benefit from prophylactic mastectomy in terms of mortality associated with breast cancer. Among the 214 high-risk women, the estimated number of deaths from breast cancer that were averted ranged from 28.6 to 8.5. The higher estimate means that prophylactic mastectomy prevented one death from breast cancer for every 7.5 women who underwent the procedure and made no difference in terms of mortality associated with breast cancer for 87 percent of these women. The lower estimate means that prophylactic mastectomy prevented one death from breast cancer for every 25 women and made no difference in mortality for 96 percent. Similarly, among the 425 moderate-risk women, 10.4 deaths from breast cancer were averted; one death from breast cancer was prevented for every 41 women, but for 98 percent of these women, there was no benefit in terms of reduced mortality.

Providing data in relative terms (e.g., a 90 percent reduction in deaths from breast cancer) and in absolute terms (e.g., 1 in 25 women benefit) will help women who are contemplating prophylactic mastectomy make more informed decisions. Despite the marked reduction in the risk of breast cancer, we need to make it clear that prophylactic mastectomy would not save the vast majority of women from death due to breast cancer, because most women would not die of breast cancer even if they kept their breasts, and a few would die of breast cancer even if they had their breasts removed.

VIRGINIA L. ERNSTER, PH.D.
University of California, San Francisco
San Francisco, CA 94143

To the Editor: The landmark report by Hartmann and colleagues provides sound evidence that bilateral prophylactic

TABLE 1. INSURANCE COVERAGE FOR BILATERAL PROPHYLACTIC MASTECTOMY, WITH OR WITHOUT RECONSTRUCTION, AMONG 100 PATIENTS.

POLICY ON COVERAGE	STRONG FAMILY HISTORY	BRCA MUTATION
	% of patients	
No policy (case referred for review by medical director)	38	91
Noncoverage	17	0
Coverage	45	9

lactic mastectomy can reduce the risk of breast cancer in women with a strong family history of the disease. For many women who consider undergoing this procedure, financial factors are a pivotal issue. We evaluated insurance coverage for prophylactic mastectomy in a university-based breast-care center in northern California.

We contacted the insurance carriers for our most recent 100 patients to determine the current policy on coverage for prophylactic bilateral mastectomy, with or without reconstruction, if the patient had one or more first-degree relatives with breast cancer or a known mutation in the *BRCA* gene (Table 1). Our data show that the insurance carriers for more than half our patients may not cover bilateral prophylactic mastectomy. The lack of a universal policy for insurance coverage has made health care decisions like this one subject to arbitrary criteria.¹

Recent federal legislation² requires insurance companies to cover the cost of breast reconstruction for any woman who undergoes mastectomy, but it does not include a requirement to cover the cost of prophylactic mastectomy. As genetic testing becomes widespread, our health care system has a responsibility to provide all appropriate candidates with access to prophylactic mastectomy.

HENRY MARK KUERER, M.D., PH.D.
E. SHELLEY HWANG, M.D.
LAURA J. ESSERMAN, M.D., M.B.A.
University of California, San Francisco
San Francisco, CA 94143

1. Rosenbaum S, Frankford DM, Moore B, Borzi P. Who should determine when health care is medically necessary? *N Engl J Med* 1999;340: 229-32.

2. House of Representatives, 105th Congress. Omnibus appropriations bill for fiscal year 1999. Title IX — women's health and cancer rights. Conference report to accompany H.R. 4328, 452-54, 1998.

To the Editor: Hartmann et al. report a 90 percent reduction in the risk of breast cancer among 639 women with a family history of breast cancer who underwent bilateral prophylactic mastectomy at the Mayo Clinic. In another study, women with breast hypertrophy who had undergone breast-reduction surgery were reported to have a 39 to 50 percent reduction in the risk of breast cancer; however, the protective effect was apparent only among

women over the age of 40 years at the time of surgery.^{1,2} It would be interesting to know whether the protective effect noted by Hartmann et al. for the overall group of women in their study was found among those who were 40 years old or younger when the surgery was performed.

JOHN D. BOICE, JR., SC.D.
International Epidemiology Institute
Rockville, MD 20853

JØRGEN H. OLSEN, M.D.
Danish Cancer Society
Copenhagen, Denmark

1. Boice JD Jr, Friis S, McLaughlin JK, et al. Cancer following breast reduction surgery in Denmark. *Cancer Causes Control* 1997;8:253-8.
2. Baasch M, Nielsen SF, Engholm G, Lund K. Breast cancer incidence subsequent to surgical reduction of the female breast. *Br J Cancer* 1996;73:961-3.

The authors reply:

To the Editor: Hamm et al. and Ernster raise two key questions. First, what is the appropriate end point in studies of cancer prevention: incidence, mortality, or both? Second, what is the best way to express an effect on these end points?

For trials of cancer treatment, mortality is an essential end point. For prevention studies, we believe incidence is a valid end point. For this disease, a significant reduction in incidence should subsequently translate into a reduction in mortality.

Measurements of relative risk are currently the standard for reporting the results of trials of screening, treatment, and prevention. The number needed to treat has some advantages but important limitations as well.¹ This number is not static but changes with the duration of follow-up, if the intervention has a durable effect. Table 1 shows the number needed to treat in our high-risk group at 5 years, 10 years, and 14 years (the current duration of follow-up).

The median age of the women in our cohort at the time of prophylactic surgery was 42 years. With 14 years of follow-up, their median age is now 56 years. If the protective effect of the procedure is durable, the number needed to treat will continue to decline as the women's remaining life expectancy declines. Expressing the results as the number needed to treat — 6 to prevent one case of breast cancer or 25 to prevent one death from breast cancer — conveys an effect over a period of 14 years, not an entire lifetime.

In our retrospective study, we included all women with any family history of breast cancer who had undergone bilateral prophylactic mastectomy between 1960 and 1993. Many of the women in our moderate-risk group would not now be considered to have a markedly elevated risk of breast cancer. Today, as we emphasized in our article, prophylactic mastectomy would generally be considered only for women with a family history that put them at high risk for breast cancer — namely, a history suggestive of an autosomal dominant predisposition to the disease.

With regard to Boice and Olsen's question about the degree of protection in the younger women, all seven of the breast cancers that occurred after prophylactic mastectomy were in women who were over the age of 40 years at the time of surgery.

TABLE 1. NUMBER NEEDED TO TREAT ACCORDING TO YEARS OF FOLLOW-UP.

OUTCOME	NUMBER NEEDED TO TREAT		
	5 YR	10 YR	14 YR
Diagnosis of breast cancer	13.5	9.0	6.2
Death from breast cancer	136.9	44.8	25.0

We appreciate the comments of Kuerer et al. about inconsistencies in insurance coverage for prophylactic mastectomy. We have only anecdotal information to add to the data they have provided. It has been our experience that coverage for this procedure is by no means ensured and consistent.

LYNN C. HARTMANN, M.D.
DANIEL J. SCHAID, PH.D.
THOMAS A. SELLERS, PH.D.
Mayo Clinic
Rochester, MN 55905

1. Rajkumar SV, Sampathkumar P, Gustafson AB. Number needed to treat is a simple measure of treatment efficacy for clinicians. *J Gen Intern Med* 1996;11:357-9.

The One-in-Nine Risk of Breast Cancer

To the Editor: Phillips et al. (Jan. 14 issue)¹ are to be commended for their lucid deconstruction of the “one in nine” statistic, a figure seized on by the lay and medical media and one that has aroused concern that we are facing an unprecedented increase in breast cancer since it was first reported. However, missing from their discussion is any acknowledgment that life-table analysis of risk, such as that presented in Table 1 and Figure 1 of their article, applies only to the population from which the data were collected.

To the extent that breast cancer and cardiovascular disease are not genetically mediated, there is reason to suspect that the cohort of North American women currently in their 40s may not conform to the incidence and mortality profiles of the cohort currently in their 70s. For example, even if the possible effect of improved therapies on future mortality rates is not considered, these cohorts can be equivalent only if there has been no shift toward healthier lifestyles, if patterns of childbearing (e.g., maternal age at birth of a first child) have not changed, and if the rates of exposure to mammary carcinogens have remained stable over the past 40 years. None of these underlying assumptions seem sustainable. Thus, as several of my well-informed patients have pointed out, it is misleading to tell a group of 970 perimenopausal women that, on average, 105 of them will die of cardiovascular disease between the ages of 60 and 70 and 18 of them will die of breast cancer at that age. In truth, nobody knows what the figures will be.

In my experience, the typical 45-year-old woman whom one counsels about the risks of breast cancer and atherosclerosis has no familial risk factors and is already leading an

active, semivegetarian lifestyle designed to promote cardiovascular fitness. Since life-table data, though imperfect as a predictive tool, are the best we have to go on, it would be helpful to see the numbers for the subgroup consisting of physically active women with good cholesterol values and no history of smoking. Perhaps the authors of this useful and widely quoted discussion can provide us with such statistics.

BARBARA B. HARRELL, M.D.
8009 40th Ave., NE
Seattle, WA 98115-4928

1. Phillips K-A, Glendon G, Knight JA. Putting the risk of breast cancer in perspective. *N Engl J Med* 1999;340:141-4.

The authors reply:

To the Editor: Dr. Harrell is correct in pointing out that the statistics we presented are derived from a snapshot of the general population, which varies with respect to exposure to risk factors and protective factors (both known and unknown) for various diseases. It was not our intent to imply that a life table based on data from the general population can be used to determine an individual woman's exact risk of breast cancer or of death from breast cancer. In fact, given our imperfect understanding of the cause of breast cancer, it is currently not possible to provide a completely accurate estimate of an individual woman's risk, although attempts have been made.^{1,2}

Analysis according to birth cohort is a useful way to assess variations in risk that may occur because of changes in exposure to risk factors over time. In keeping with Harrell's comments, it is interesting that Tarone et al.,³ contrary to their expectations based on trends in reproductive factors, found that the risk of death from breast cancer decreased among women born after 1950.

When educating a population of women, it is appropriate to use estimates of the risk of breast cancer that are derived from that population. Of course, we agree that when counseling an individual woman, one should supplement these general estimates of risk with a discussion of the specific risk factors relevant to that person.

We included the life table in order to convey general concepts about the age distribution and relative magnitude of the risk of breast cancer as compared with the risk of cardiovascular disease. Any estimate of the risk associated with a complex, multifactorial disease has inherent limitations. This fact only serves to highlight our concern about the extensive use of the one-in-nine statistic without any elaboration. This is the only information on the risk of breast cancer that many women receive, and we believe that it is inadequate and potentially misleading.

KELLY-ANNE PHILLIPS, M.B., B.S.
Peter MacCallum Cancer Institute
Melbourne 3000, Australia

GORDON GLENDON, M.Sc.
Ontario Cancer Genetics Network

JULIA KNIGHT, Ph.D.
Cancer Care Ontario
Toronto, ON M5G 2L7, Canada

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3. Tarone RE, Chu KC, Gaudette LA. Birth cohort and calendar period trends in breast cancer mortality in the United States and Canada. *J Natl Cancer Inst* 1997;89:251-6.

Hypovitaminosis D in a Sunny Country

To the Editor: Some normal subjects and a substantial proportion of patients with various illnesses in the United States and northern Europe have vitamin D insufficiency,¹⁻⁴ but information from countries located in more southern latitudes is scarce.

We measured serum 25-hydroxyvitamin D and parathyroid hormone during the summer (August through October) in 465 women from the village of Nabi-Shit (latitude, 33.5 degrees north) in central Lebanon. We studied a random sample of women, most of whom were of reproductive age, who were eating a regular Middle Eastern diet, including dairy products. The dress code requires the head, arms, and legs to be covered. None of the women were taking medication known to affect the metabolism of vitamin D. Serum 25-hydroxyvitamin D was measured by a competitive protein-binding assay with use of the Diasoren Incstar kit (Incstar, Stillwater, Minn.), and serum parathyroid hormone was measured with use of the ELSA-PTH immunoradiometric assay (Cis Bio International, Gif-sur-Yvette, France). The mean (\pm SD) serum concentration of 25-hydroxyvitamin D was 11 ± 14 ng per milliliter (28 ± 35 nmol per liter). Sixty percent of the women had concentrations of less than 10 ng per milliliter (25 nmol per liter), 35 percent had concentrations between 10 and 20 ng per milliliter (25 and 50 nmol per liter), and 5 percent had concentrations greater than 20 ng per milliliter (50 nmol per liter). There was a trend toward a decrease in the mean concentration of 25-hydroxyvitamin D with age (Table 1). The mean serum

TABLE 1. MEAN SERUM CONCENTRATIONS OF 25-HYDROXYVITAMIN D AND PARATHYROID HORMONE IN 465 WOMEN FROM THE VILLAGE OF NABI-SHIT IN THE BEKAA VALLEY, LEBANON.*

AGE GROUP	NO. OF WOMEN	MEAN AGE	BODY-MASS INDEX†	SERUM 25(OH)D	SERUM PTH
		yr		ng/ml	pg/ml
15-19	8	18 \pm 1	22.7 \pm 3.1	8 \pm 4	28 \pm 13
20-29	132	25 \pm 3	25.4 \pm 4.1	13 \pm 25	30 \pm 20
30-39	170	34 \pm 3	27.2 \pm 4.7	11 \pm 6	30 \pm 15
40-49	95	44 \pm 3	30.4 \pm 4.6	10 \pm 5	29 \pm 13
50-59	60	54 \pm 3	32.6 \pm 5.5	9 \pm 7	39 \pm 61

*25(OH)D denotes 25-hydroxyvitamin D, and PTH parathyroid hormone. The normal range for 25-hydroxyvitamin D is 16 to 36 ng per milliliter (40 to 90 nmol per liter), and for parathyroid hormone it is 8 to 76 pg per milliliter. To convert values for 25-hydroxyvitamin D to nanomoles per liter, multiply by 2.5.

†The body-mass index is the weight in kilograms divided by the square of the height in meters.