HARVARD MEDICAL SCHOOL

NURSES' HEALTH STUDY

1984

PLEASE REPLY TO:
Channing Laboratory
180 Longwood Ave.
Boston, Mass. 02115
617-732-2279

Dear Colleague:

I would again like to express my gratitude for your continued and invaluable participation in the Nurses' Health Study. This long-term study provides a unique opportunity to learn about factors related to optimal health. The information you have provided over the last nine years is thus becoming increasingly valuable.

Since last year several preliminary reports have been published as abstracts (see back of letter). In an analysis of oral contraceptive pills and risk of breast cancer, we found no overall association. Similarly, we found no overall association between post-menopausal hormone use and breast cancer risk: however, continued monitoring will be necessary to observe the effects over long periods of time. Women using hormone supplements did experience a reduced risk of coronary heart disease. In addition, those women who had a history of either parent having a heart attack before age 61 have experienced an increased risk of coronary heart disease. Control of blood pressure and avoiding cigarette smoking is advised for all women; this finding emphasizes the particular importance among those with a family history of coronary heart disease.

We found that thinner women had a slightly increased rate of breast cancer during their pre-menopausal years, however, this seemed to be at least in part an artifact due to earlier detection of tumors among lean women. The numbers of breast cancers among post-menopausal women were too few for evaluation; these will be examined in future analyses. We are now in the process of examining the effects of dietary factors, including nail selenium levels, in relation to cancer incidence as well as the long term health effects of hair dyes. In addition, we are currently investigating risk factors for diabetes, rheumatoid arthritis, and gallbladder disease utilizing supplementary information provided by participants who experienced these problems. These will be reported to you as findings develop.

We would like to convey our special appreciation to those who provided permission to review medical records related to diagnoses of high blood pressure or cholesterol, fractures, malignancies, gallbladder disease, and cardiovascular diseases. These record reviews have been extremely important and have documented the accuracy and care with which participants have reported medical events. In addition, an intensive validation study of the Nurses' Health Study dietary questionnaire has demonstrated that accurate information on nutritional practices has been provided by those who completed that questionnaire (to be published in American Journal of Epidemiology in July, 1985). In 1986, we will be sending you another questionnaire to update our information and collect data on new health-related issues.

Again, I am grateful for your invaluable contribution to knowledge of factors that influence the health of women.

Sincerely,

Frank E. Speizer

Frank E. Speizer, M.D.
Principal Investigator

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P.S. As we did not hear from you in response to our 1984 mailing, a very brief questionnaire is enclosed. Since it is extremely important to have up-to-date information on all participants, I would be most grateful if you would complete and return this short form to me.

A PROSPECTIVE COHORT STUDY OF POSTMENOPAUSAL FEMALE HORMONE USE AND RISK OF BREAST CANCER.

Buring, J., Speizer, F., Lipnick, R., Willett, W., Stampfer, M., Rosner, B., Peto, R. and Hennekens, C.

Am. J. Epidemiol 1983; 118 : 416.

The association between female hormone use and the risk of breast cancer was examined in a cohort of 33,335 postmenopausal registered nurses aged 30 to 55 years in 1976. A total of 92% of women in the cohort completed follow-up questionnaires, and mortality was assessed for all non-respondents. After four years, 221 incident breast cancer cases were identified. Compared with those who had never used female hormones, the age-adjusted relative risk of breast cancer for ever use was 1.1 (95% confidence limits (CL), 0.8–1.4) and for current use 1.2 (CL, 0.9–1.7). The relative risk was increased among women using female hormones for 60–119 months, at 1.5 (CL, 1.0–2.2), but not among the small number of women who had used female hormones for longer durations, with a relative risk of 0.9 (CL, 0.4–1.6). These estimates were unchanged after controlling for other known determinants of breast cancer using multiple logistic regression analysis. Furthermore, these risks were not substantially modified by type of menopause, family history of breast cancer, or other breast cancer risk indicators. These findings offer reassuring evidence of no appreciable risk of breast cancer among users of female hormones for less than five years, with a suggestion of a modest increase in risk for use of 5–10 years. Since there are not a large number of women with duration of use of more than 10 years or long intervals since first use, whether there is an increased risk associated with long-term use of female hormones cannot yet be determined.

RELATIVE WEIGHT AND RISK OF BREAST CANCER AMONG PREMENOPAUSAL WOMEN

Willett, W.C., Browne, M.L., Bain, C., Lipnick, R.J., Stampfer, M.J., Rosner, B., Colditz, G.A., Hennekens, C.H., Speizer, F.E.

Am. J. Epidemiol (in press).

Although higher relative weight is generally considered to increase the rick of breast cancer, several case-control studies have suggested that the reverse may be true among premenopausal women. The association between Quetelet's index (a measure of relative weight calculated as weight/height) and the subsequent incidence of breast cancer was therefore examined during four years of follow-up among a cohort of 121,964 U.S. women initially 30-55 years of age in 1976. In contrast to women who had experienced natural menopause or bilateral oophorectomy, the incidence of breast cancer among premenopausal women decreased with higher levels of relative weight. Age-adjusted relative risks for increasing quintiles of Quetelet's index were 1.00, 0.90, 0.90, 0.73, and 0.66 (Mantel Extension test for trend $= -2.82$, $p = 0.005$). This inverse association was not explained by known risk factors for breast cancer and was somewhat stronger when Quetelet's index was computed using reported weight at age 18. However, the excess incidence of breast cancer among lean premenopausal women was limited to tumors that were less than 2.0 cm in diameter, not associated with metastases to lymph nodes, and well-differentiated. These findings suggest that the apparent excess risk of breast cancer among lean premenopausal women may result at least in part from easier, and thus earlier, diagnosis of less aggressive tumors.

PARENTAL HISTORY OF MYOCARDIAL INFARCTION

Colditz, G.A., Stampfer, M.J., Willett, W.C., Rosner, B., Speizer, F.E., Hennekens, C.H.

Am. J. Epidemiol (in press).

Among 121,964 women aged 30 to 55 years in 1976, 117, 156 who were initially free from coronary heart disease provided information on a number of coronary risk factors including parental history of myocardial infarction and were followed prospectively. In 1976, 31,101 (26.5%) reported that at least one parent had suffered a myocardial infarction. Questionnaires in 1978 and 1980 identified women who had developed nonfatal myocardial infarction ($n = 132$) and angina pectoris ($n = 101$). Fatal coronary heart disease cases ($n = 42$) were ascertained by searches of state vital records.

The age-adjusted relative risk of nonfatal myocardial infarction for women with a parental history of myocardial infarction ≤ 60 years of age, compared with women with no family history was 2.8 (95% confidence limits 1.8, 4.3). For those with a parental history of myocardial infarction >60, the age-adjusted relative risk of nonfatal myocardial infarction was 1.0 (0.5, 1.8). The age-adjusted relative risks of fatal coronary heart disease were 5.0 (2.7, 9.2) for parental history before age 61, and 2.6 (1.1, 5.8) for parental history after age 60. The corresponding relative risks of angina pectoris were 3.4 (2.2, 5.2) and 1.9 (1.2, 3.2) respectively. These associations were only slightly altered by adjustment for history of hypertension, diabetes, high cholesterol, the use of oral contraceptives, menopause, postmenopausal hormone use, obesity or smoking, in individual stratified analysis or in multivariate analyses. These data support the hypothesis that parental history of myocardial infarction has an independent effect on risk that is not explained solely by individual risk factors.

REPRODUCIBILITY AND VALIDITY OF A SEMIQUANTITATIVE FOOD FREQUENCY QUESTIONNAIRE

Willett, W.C., Sampson, L., Stampfer, M.J., Rosner, B., Bain, C., Witschi, J., Hennekens, C.H. and Speizer, F.E.

Am. J. Epidemiol, (in press).

The aim of this study was to evaluate the reproducibility and validity of a 61-item semiquantitative food frequency questionnaire used in a large prospective study among women. This form was administered twice to 173 participants at an interval of approximately one year and four one-week diet records for each subject were collected during this period. Intraclass correlation coefficients for nutrient intakes estimated by the one-week diet records (range = 0.41 for total vitamin A without supplements to 0.79 for vitamin B_6 with supplements) were similar to those computed from the questionnaire (range = 0.49 for total vitamin A without supplements to 0.71 for sucrose), indicating that these methods were generally comparable with respect to reproducibility. With the exception of sucrose and total carbohydrate, nutrient intakes from the diet records tended to correlate more strongly with those computed from the questionnaire after adjustment for total caloric intake. Correlation coefficients between the mean calorie-adjusted intakes from the four one-week diet records and those from the questionnaire completed after the diet records ranged from 0.36 for vitamin A without supplements to 0.75 for vitamin C supplements. Overall, 48% of subjects in the lowest quintile of calorie-adjusted intake computed from the diet records were also in the lowest questionnaire quintile and 74% were in the lowest one or two questionnaire quintiles. Similarly, 49% of those in the highest diet record quintile were also in the highest questionnaire quintile and 77% were in the highest one or two questionnaire quintiles. These data indicate that a simple self-administered dietary questionnaire can provide useful information about individual nutrient intakes over a one-year period.

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HARVARD MEDICAL SCHOOL

NURSES' HEALTH QUESTIONNAIRE

Please answer all questions by filling in the appropriate box or writing in the information requested. All information will be regarded as **strictly confidential** and will be used only for medical research purposes.

1. What is your date of birth? ____ / ____ / ____ (month (17) day (19) year (21))

2. Have your menstrual periods ceased permanently? ☐ no or don't know ☐ yes (23)

3. Do you **currently** use female hormone pills (e.g. Premarin)? ☐ no ☐ yes (24)

4. Do you **currently** smoke cigarettes? ☐ no ☐ yes (25)

Since June, 1976 have you had any of the following illnesses diagnosed?
If Yes, please specify date of diagnosis.

		MONTH	YEAR
DIABETES MELLITUS ?	☐ NO ☐ YES (26) →		19
ELEVATED CHOLESTEROL ?	☐ NO ☐ YES (31) →		19
HIGH BLOOD PRESSURE ? (EXCEPT WHILE PREGNANT)	☐ NO ☐ YES (36) →		19
MYOCARDIAL INFARCTION ? (HEART ATTACK)	☐ NO ☐ YES (42) →		19
→ IF YOU HAD AN MI, WERE YOU HOSPITALIZED? →	☐ NO ☐ YES		
ANGINA PECTORIS ?	☐ NO ☐ YES (47) →		19
STROKE (CVA) ?	☐ NO ☐ YES (52) →		19
PULMONARY EMBOLUS ?	☐ NO ☐ YES (57) →		19
PERIPHERAL VENOUS THROMBOSIS ?	☐ NO ☐ YES (62) →		19
FIBROCYSTIC BREAST DISEASE ?	☐ NO ☐ YES (67) →		19
→ IF YES, WAS THIS CONFIRMED BY A BIOPSY? →	☐ NO ☐ YES		
OTHER BENIGN BREAST DISEASE ?	☐ NO ☐ YES (73) →		19
→ IF YES, WAS THIS CONFIRMED BY A BIOPSY? →	☐ NO ☐ YES		
BREAST CANCER ?	☐ NO ☐ YES (15) →		19
CANCER OF CERVIX ? (INCLUDE IN-SITU)	☐ NO ☐ YES (20) →		19
CANCER OF UTERUS ? (ENDOMETRIUM)	☐ NO ☐ YES (25) →		19
CANCER OF OVARY ?	☐ NO ☐ YES (30) →		19
CANCER OF COLON OR RECTUM ?	☐ NO ☐ YES (35) →		19
CANCER OF LUNG ?	☐ NO ☐ YES (40) →		19
MELANOMA ?	☐ NO ☐ YES (45) →		19
BASAL CELL SKIN CANCER ?	☐ NO ☐ YES (50) →		19
SQUAMOUS CELL SKIN CANCER ?	☐ NO ☐ YES (55) →		19
OTHER CANCER ?	☐ NO ☐ YES (60) →		19
→ IF YES, PLEASE SPECIFY SITE			(65)
RHEUMATOID ARTHRITIS ?	☐ NO ☐ YES (68) →		19
GOUT ?	☐ NO ☐ YES (73) →		19
OTHER ARTHRITIS ?	☐ NO ☐ YES (15) →		19
SLE ? (SYSTEMIC LUPUS ERYTHEMATOSIS)	☐ NO ☐ YES (20) →		19
CHOLECYSTECTOMY ? (GALL BLADDER REMOVAL)	☐ NO ☐ YES (25) →		19
→ IF YES, WHEN DID THE GALL STONE SYMPTOMS START?			19 (30)
GALL STONES, NOT REMOVED ?	☐ NO ☐ YES (32) →		19
→ IF YES, HOW WERE GALL STONES DIAGNOSED? →	☐ X-RAYS ☐ ULTRASOUND ☐ SYMPTOMS ONLY ☐ OTHER		
OSTEOPOROSIS ?	☐ NO ☐ YES (40) →		19
FRACTURE OF HIP OR FOREARM ?	☐ NO ☐ YES (45) →		19
GASTRIC OR DUODENAL ULCER ?	☐ NO ☐ YES (50) →		19
ULCERATIVE COLITIS ?	☐ NO ☐ YES (55) →		19
OTHER MAJOR ILLNESS ?	☐ NO ☐ YES (60) →		19
→ IF YES, PLEASE SPECIFY ILLNESS →			

WHEN DID GALL BLADDER SYMPTOMS START? 19 ____ (38)

THANK YOU

Please return completed questionnaire in the pre-paid envelope to:

NURSES HEALTH STUDY
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Harvard Medical School
180 Longwood Avenue
Boston, Massachusetts
02115