Dear Colleague:

This note is to bring you up to date on the progress of the Nurses' Health Study and to ask for your continued assistance in the study.

We have now published a number of articles from information that you and others have provided. This information has made a valuable contribution to our understanding of several important diseases. Abstracts from some of these publications are printed on the back of this letter. We have also enclosed a reprint from the American Journal of Nursing to bring you up to date on the progress of the NHS and our future plans.

In addition, I hope you will take a few moments to complete the attached short questionnaire. I realize it is sometimes hard to find the time to complete our longer form. However, to maintain the validity of data in the NHS it is critical to have complete information on the health experience of all those who completed our original questionnaire in 1976. Therefore, completing and returning this form would be an important contribution for learning how common practices of daily life affect health in women. As always, your responses will be held strictly confidential and stored in our files by identification number only.

Thank you for your assistance.

Sincerely,

Frank E. Speizer, M.D.
Principal Investigator
EARLY MENOPAUSE AND THE RISK OF MYOCARDIAL INFARCTION
Lynn Rosenberg, Charles H. Hennekens, Bernard Rosner, Charlene Belanger, Kenneth J. Rothman, and Frank E. Speizer
We evaluated the relation between age at menopause and the risk of nonfatal myocardial infarction (MI) among 121,964 nurses who responded to a mail questionnaire. Of 279 women who reported having been hospitalized for MI, 123 (44%) were postmenopausal (i.e., no longer menstruating) at the time of hospitalization, compared with 1,859 (33%) of 5,580 age-matched control subjects. Among women who became menopausal because of bilateral oophorectomy, the estimated relative risk of MI increased with decreasing age at menopause, and women who underwent bilateral oophorectomy before age 35 were estimated to have a risk of hospitalization for MI approximately 7.2 times (95% confidence interval, 4.5 to 11.4) that of premenopausal women. Hysterectomy without the removal of both ovaries was only weakly associated with an increased risk. The data support the hypothesis that premature cessation of ovarian function increases the risk of nonfatal MI. (Am J Obstet Gynecol 1981; 139:47)

ORAL CONTRACEPTIVES AND RISK OF OVARIAN CANCER
Walter C. Willett, Christopher Bain, Charles H. Hennekens, Bernard Rosner, and Frank E. Speizer
Among a large cohort of married, female, registered nurses under 55 years of age, oral contraceptive (OC) use was examined in women with ovarian cancer and 470 age-matched controls. Use of OCs before the diagnosis of cancer was reported by 28% of the women with ovarian cancer and 33% of the controls, yielding a relative risk of 0.8 (95% confidence limits 0.4-1.5). This apparent inverse relationship was attributable to a large effect in women 35 years of age or younger (relative risk = 0.2, 95% confidence limits 0.1-1.0). Patients with ovarian cancer were 2.2 times more likely than controls to be nulliparous. These data provide reassurance that OC use is not likely to be associated with any major increase in risk of ovarian cancer, but suggest that future studies of this relationship need to consider the possible confounding effect of infertility. (Cancer 1981; 48:1684)

EARLY AGE AT FIRST BIRTH AND DECREASED RISK OF BREAST CANCER
Christopher Bain, Walter Willett, Bernard Rosner, Frank E. Speizer, Charlene Belanger and Charles H. Hennekens
The relationship between age at birth of a first child and breast cancer was evaluated for 1159 affected women and 11,590 women without cancer in data collected in 1976 among married female registered nurses residing in 11 states in the United States. A positive trend of increasing risk of breast cancer with later ages at first birth was found (x² for trend in proportions = 30.9, p < 0.01). Adjustment for potential confounding variables by multiple logistic regression did not affect this trend. The presence of this relationship using non-hospitalized controls of similar social status to cases supports the reality of this association, which has recently been challenged as an artifact due to inappropriate choice of hospitalized controls. (Am J Epidemiol 1981; 114:705)

ORAL CONTRACEPTIVE USE IN RELATION TO NONFATAL MYOCARDIAL INFARCTION
Lynn Rosenberg, Charles H. Hennekens, Bernard Rosner, Charlene Belanger, Kenneth J. Rothman, and Frank E. Speizer
The relation of oral contraceptive (OC) use to the risk of hospitalization for myocardial infarction (MI) was evaluated among 121,964 US nurses who responded to a mail questionnaire. There were 156 women who reported having been hospitalized for MI before the menopause, and 23 (15%) were OC users at the time of the MI. Of 3120 controls matched to the cases for menopausal status at the time of the MI and for age, 304 (10%) were using OCs at the time of the MI. The apparent increase in the risk of MI for current OC users was not explained by cigarette smoking, hypertension, elevated cholesterol or other identified risk factors for MI. We estimated that OC use increased MI risk 1.8-fold overall and 2.8-fold among nonsmokers without other risk factors. The increase in risk attributed to the combined effect of current OC use, smoking and hypertension was considerably greater than what would be predicted from the sum of the separate effects of these factors. (Am J Epidemiol 1980; 111:59)

ORAL CONTRACEPTIVE USE AND MALIGNANT MELANOMA
Christopher Bain, Charles H. Hennekens, Frank E. Speizer, Bernard Rosner, Walter Willett, and Charlene Belanger
There was no overall relationship between a prior history of oral contraceptive (OC) use and the development of melanoma among 141 cases of nonfatal malignant melanoma and 2,820 age-matched controls drawn from respondents to a large postal survey of registered U.S. nurses; crude relative risk (RR) was 0.93 and 95% confidence limits (CL) were between 0.64 and 1.36. Adjustment for a number of additional variables did not alter this estimate materially. Duration of OC use and interval since first use were similarly unrelated to the occurrence of melanoma. For women diagnosed before age 40, there was a crude positive association of ‘ever’ use of OC and melanoma (RR = 1.78;95% CL, 1.11-2.86). However, adjustment for geography and other variables diminished this association and rendered it statistically not significant (RR = 1.43; 95% CL, 0.83-2.46). These data do not support the hypothesis that OC use is an independent risk factor for melanoma.—(JNCI 1982; 68:537)

CIGARETTE SMOKING AND NON-FATAL MYOCARDIAL INFARCTION IN WOMEN
Walter C. Willett, Charles H. Hennekens, Christopher Bain, Bernard Rosner and Frank E. Speizer
The relationship between smoking and the risk of hospitalization for acute myocardialinfarction (MI) was evaluated among 121,964 nurses aged 30-55 years who resided in 11 of the larger US states and who responded to a mail questionnaire. Among 249 women who experienced an MI, 159 (64%) were smokers at the time of hospitalization. Of 4977 controls matched to the cases on the basis of age, 1850 (37%) were smoking at the corresponding time. Smokers experienced a three-fold increase in risk of MI relative to individuals who never smoked, which was not explained by history of hypertension, diabetes, high cholesterol or familial MI. Women who had stopped smoking experienced a risk of MI no greater than women who had never smoked. (Am J Epidemiol 1981; 113:575)
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)

5. Since June 1976 have you been diagnosed to have any of the following conditions?  
   If yes, please specify date of diagnosis.

   PLEASE MARK IF DIAGNOSED  
   MONTH  
   YEAR

   □ HIGH BLOOD PRESSURE (EXCEPT WHILE PREGNANT)  
   □ DIABETES MELLITUS  
   □ ELEVATED CHOLESTEROL  
   □ MYOCARDIAL INFARCTION (HEART ATTACK)  
   □ WERE YOU HOSPITALIZED FOR THIS HEART ATTACK?  
   □ ANGINA PECTORIS  
   □ PERIPHERAL VENOUS THROMBOSIS  
   □ FIBROCYSTIC BREAST DISEASE  
   □ WAS THIS CONFIRMED BY A BREAST BIOPSY?  
   □ OTHER BENIGN BREAST DISEASE  
   □ WAS THIS CONFIRMED BY A BREAST BIOPSY?  
   □ BREAST CANCER  
   □ CANCER OF THE CERVIX – IN SITU ONLY  
   □ CANCER OF THE CERVIX – ALL OTHER  
   □ CANCER OF THE UTERUS (ENDOMETRIUM)  
   □ CANCER OF THE OVARY  
   □ CANCER OF THE COLON OR RECTUM (LARGE BOWEL)  
   □ CANCER OF THE LUNG  
   □ MELANOMA  
   □ OTHER CANCER (SPECIFY)  
   □ OTHER MAJOR ILLNESS

6. Have you ever had any of the following conditions?  

   PLEASE MARK IF DIAGNOSED  

   YEAR OF DIAGNOSIS

   □ RHEUMATOID ARTHRITIS  
   □ GOUT  
   □ OTHER ARTHRITIS  
   □ SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)  
   □ CHOLECYSTECTOMY (GALL BLADDER REMOVAL)  
   □ GALL STONES, NOT REMOVED  
   □ STROKE (CVA)  
   □ PULMONARY EMBOLUS  
   □ OSTEOPOROSIS  
   □ FRACTURE OF HIP OR FOREARM  
   □ GASTRIC OR DUODENAL ULCER  
   □ ULCERATIVE COLITIS

THANK YOU.

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

NURSES HEALTH STUDY
Frank E. Speizer, M.D.
Harvard Medical School
180 Longwood Avenue
Boston, Massachusetts 02115