BRIGHAM AND WOMEN'S HOSPITAL

Harvard Medical School

Department of Medicine
Channing Laboratory

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November 1989

Dear Colleague,

In the past year and a half we have been unable to update information on your health status despite up to five letters sent by regular mail. Our attempts to reach you have now extended to this brief questionnaire sent by certified mail. I apologize for any trouble the certified mailing may have caused. Whether or not you are still active in nursing, your continued participation is critical in furthering our understanding of factors influencing the health of women.

The study would not have been possible without the long-term collaboration of the 121,700 participants, who first provided information in 1976. The continued, high rate of participation makes the Nurses' Health Study the largest of its kind. However, your response is essential to maintain the validity of the follow-up data already provided by over 100,000 of your nursing colleagues.

Many of your fellow participants have called or taken the time to write and tell me how proud they are to be part of such an important study. They feel, and rightly so, that the study is theirs, and that their efforts may help the medical world to better understand the causes, and possibly help prevent, serious illness in women. I hope you share their feelings and will consider continuing your involvement in the study. We are confident that findings during the next several years will provide further important guidance to women for maintaining optimal health.

Enclosed are media stories about the recently published work from the study, and a shortened version of the questionnaire. I hope that you will take the few minutes needed to complete it and send it back to us in the prepaid reply envelope.

Of course, all information will be held in strictest confidence and used for medical statistical purposes only.

Sincerely,

Frank E. Speizer, M.D.

Frank E. Speizer, M.D.
Principal Investigator

Enclosures

Harvard Medical Area

FOCUS

September 21, 1989

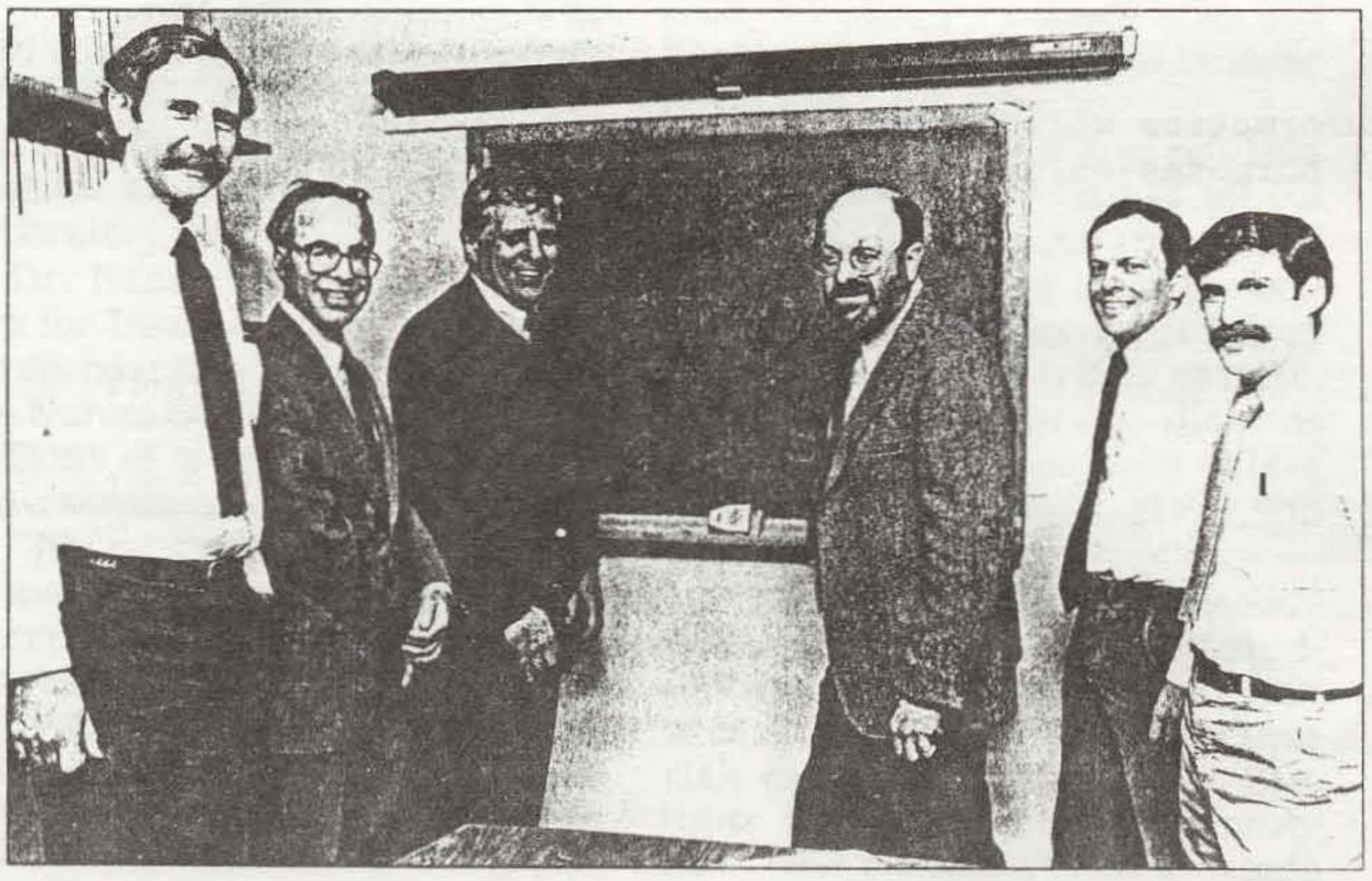
Harvard's Nurses' Health Study Finds Past Use of Oral Contraceptives Not Linked With Breast Cancer Risk

Past use of oral contraceptives is not associated with an increased risk of breast cancer, according to a ten-year epidemiological study of 120,000 women nurses conducted by Harvard researchers.

In this latest finding of the Harvard Nurses' Health Study, women who had used oral contraceptives in the past did not experience any increase in breast cancer, even if they had used these preparations for more than ten years. A modest increase in risk, however, was seen among the small number of women who were still actively using oral contraceptives after the age of 40.

Over the course of ten years, half or about 60,000 of the women had used oral contraceptives, and 1799 cases of breast cancer were diagnosed in the total group. The researchers looked at a wide variety of subgroup categories — duration of contraceptive use, time since first and last use, duration of use at an early age, menopausal status — and in none of the subgroups did they find a suggestion of an adverse effect.

Nurses' Health Study researchers, from left: Drs. Walter Willett, Bernard Rosner, Charles Hennekens, Frank Speizer, Graham Colditz and Meir Stampfer.



Begun in 1976

These results* are the latest to emerge from the Nurses' Health Study, begun in 1976 under the direction of Dr. Frank Speizer at Harvard Medical School's Channing Laboratory and Brigham and Women's Hospital. Approximately 121,700 female registered nurses 30 to 55 years of age, living in eleven larger states, returned questionnaires with information about medical conditions and lifestyle practices. On biennial follow-up questionnaires, women have provided updated information on reproductive variables and reported the occurrence of breast cancer and other major illnesses. The study was funded by the National Cancer Institute.

This recent study provides reassurance to former oral contraceptive users now in their 40s and 50s.

"This study provides reassurance to women who are now in their forties and fifties that use of oral contraceptives in the past is unlikely to have appreciably increased their risk of breast cancer," according to Dr. Walter Willett, Professor of Epidemiology and Nutrition at the Harvard School of Public Health and a coauthor of the study. "However, there does remain an unanswered question about the effects of longer-term contraceptive use in early reproductive life."

Conflicting Evidence

The youngest participants are only now approaching the age when breast cancer risk is high,

continued

Nurses' Health Study on Oral Contraceptives

said Dr. Willett, and several other studies have provided conflicting evidence on the relation of such use to the risk of breast cancer. Several of these other studies have found that women up to 40 and 45 who used oral contraceptives for extended periods are at increased risk for breast cancer. "If those studies are correct, and the risk extends to later years, this would represent a serious public health problem."

New Study To Be Launched

Because of the importance of this issue — whether there is increased risk of breast cancer among long-term oral contraceptive users who began before age 25 — the same group of investigators is about to launch a major new research initiative. Dr. Willett, a principal investigator, and colleagues will mail nearly half a million questionnaires around the country to registered nurses between the ages of 25 to 42 years, inviting users and non-users of oral contraception to participate in the Nurses' Health Study II. Participation will involve completing detailed health and medical questionaires on alternate years.

Dr. Willett noted, "In this study, also funded by the National Cancer Institute, we expect to learn not only much more about the long-term effects of oral contraceptive use, but also about the contributions of diet, physical activity, and other lifestyle factors to long-term health."

**Prospective Study of Oral Contraceptive Use and Risk of Breast Cancer in Women.* I. Romieu, W.C. Willett, G.A. Colditz, M.J. Stampfer, B. Rosner, C.H. Hennekens, F.E. Speizer, Journal of the National Cancer Institute, Vol. 81, No. 17, September 6, 1989.

SEPTEMBER 6, 1989

USA TODAY

Pill study reassures older users

By Kim Painter
USA TODAY

Millions of middle-aged women who used birth control pills in their mid-20s or later don't face an unusually high risk for breast cancer, says a major new study out today.

But the Harvard Medical School study — the largest yet with 118,000 women followed for 10 years — offers no reassurance for younger women.

"Women are in a position where they have to make decisions with incomplete information," says Dr. Walter Willett, a member of the team reporting in the *Journal of the National Cancer Institute*.

The researchers hope to answer questions raised by the study with a new one involving 100,000 to 150,000 nurses, ages 25 to 43. Today's study involved nurses now ages 43 to 68.

Among remaining questions:

▶ Does the pill increase a woman's chance of getting breast cancer before her early 40s? The disease is more common in older women.

One British study showed a 70 percent increase among women under age 36 who took the pill at least eight years.

▶ If there is an effect, does it depend on when a woman starts taking the pill or how long she takes it?

▶ Do today's pills have the same effect as higher-dose pills used in the '60s and early '70s?

Dr. Bruce Stadel, a Food and Drug Administration scientist, believes today's pills are less risky. Also, he says, evidence suggests the higher-dose pills haven't caused overall increases in breast cancer, but may have caused some susceptible women to develop breast cancer earlier.

THE BOSTON GLOBE

AUGUST 31, 1989

Medical Notebook

JUDY FOREMAN

Study adds gallstone risks to burdens of being obese

AS IF FATNESS and fat phobia weren't, well, heavy enough burdens already, consider this depressing item from the latest New England Journal of Medicine: Being even moderately overweight can almost double a woman's risk of gallstones.

And being seriously overweight puts a woman at six times the risk, compared to a skinny woman, of winding up with these chunks of crystallized cholesterol that accumulate in the gallbladder and often, though not always, require surgery.

For the purposes of this research, called the Nurses' Health Study, nearly 90,000 women were followed for four years after detailing their diet and alcohol intake.

Armed with calculations of each woman's weight relative to her height, researchers classified women into groups. An obese woman, for instance, was defined as a 5-foot-6 woman weighing more than 200 pounds, or a 5-foot-2 woman weighing more than 175 pounds. A slightly overweight woman would be 5 foot 6 inches tall and weigh 150-155 pounds, or be 5 foot 2 and weigh 130-135 pounds.

Overall, said the researchers from the Harvard School of Public Health, Brandeis University, Harvard Medical School and Boston's Brigham and Women's Hospital, there's a roughly linear relationship between relative weight and gallstones – the more overweight, the higher the risk.

Also, the more calories you consume per day, the higher your risk of gallstones. No one knows yet if high cholesterol intake per se adds to the risk.

All in all, it's enough to drive a woman to drink, which in fact might not be a bad idea, in moderation, of course. The researchers found that, for unclear reasons, women who drank two to three glasses of wine, beer or hard liquor per week had fewer gallstones than nondrinkers. For what it's worth, they found more or less the same thing in prairie dogs.

MS. MAGAZINE

OCTOBER 1989

AS THE WORLD BURNS

For an adolescent, fun in the sun may turn out to be an oxymoron. A teenage girl, it was recently reported, doubles her risk of skin cancer—the deadly melanoma variety—if she's had five blistering sunburns between age 15 and 20. These findings, based on 130 women with melanoma who participated in Harvard Medical School's Nurses Health Study, confirm the growing belief that severe sunburns in childhood and adolescence have dangerous consequences. These same researchers, for example, turned up no link between skin cancer and blistering sunburns after age 30. Which doesn't mean that older people should not exercise caution in the sun. The incidence of melanoma, in this country, is steeply on the ascent. It may soon exceed colon cancer among people born after 1950.

Pill-cancer study reassures, leaves question unanswered

THE BOSTON GLOBE
WEDNESDAY,
SEPTEMBER 6, 1989

By Richard A. Knox
Globe Staff

Middle-aged women who once used birth control pills do not need to worry about a higher risk of breast cancer, according to a 10-year study published today, the largest ever to examine this issue.

However, the report leaves unanswered a question that increasingly worries researchers: Whether oral contraceptives increase the risk of breast cancer among women who started taking the Pill early in their reproductive lives.

The 118,000 registered nurses who participated in the study were generally too old in the early 1960s, when oral contraceptives became available, to answer that now-urgent question. Those women are now in their 40s, 50s and 60s, and about half used birth control pills earlier in life.

Among the few nurses still using the Pill in their 40s, the study appeared to reveal a slight elevation of breast cancer risk. However, specialists say the association may be false because it was based on very few cancer cases.

"For past users of oral contraceptives who are now 40 years old and older, our study provides a lot of reassurance," said Dr. Walter C. Willett of Brigham and Women's Hospital. Even women who used the Pill for 10 years or longer suffered no more breast cancer than nonusers, Willett and his colleagues at Harvard's Channing Laboratory found.

Dr. Nancy Lee of the US Centers for Disease Control's division of reproductive health agreed that the Nurses Study is reassuring for millions of women who used oral contraceptives.

"It's compatible with what information we have – that oral contraceptives don't seem to increase the risk of getting breast cancer in those ages when most women are likely to get breast cancer," Lee said in a telephone interview. "The evidence is that if birth control pills increase breast cancer risk, it's in women who are premenopausal, when breast cancer is rare. At the same time, there's all kinds of evidence that oral contraceptives prevent women of all ages from getting ovarian and endometrial cancer."

A possible link between oral contraceptives and breast cancer has been intensively studied, with widely conflicting results.

US breast cancer rates have been rising in recent decades, but the increase began before oral contraceptives were introduced. According to a recent review published by Johns Hopkins University, "most of the increase appears to be due to later first births." Having a child at a young age is known to lower a woman's risk of breast cancer.

It is difficult to study a possible association between early Pill use and breast cancer because the disease is unusual in young women and because not enough women now in their postmenopausal years, when the cancer is common, took oral contraceptives when they were teen-agers.

To discern the effect of early Pill use on breast cancer incidence, the Harvard group is embarking on a federally financed study of younger nurses, who are likely to have used the Pill in their teens and early 20s.

Questionnaires will go out this week to more than half of all US female nurses between the ages of 25 and 42, inviting their participation in a new Harvard research project that will track cancer, heart disease, arthritis, diabetes and other diseases and relate them to diet, physical activity, Pill use and other factors.

"The really big question now," Willett said, "is that if recent studies that show a breast cancer risk of early Pill use are right, and that risk extends throughout a lifetime, that's an enormous problem. That's a question that needs to be answered clearly and firmly."

The suggestion of an elevated breast cancer risk among women who started oral contraceptive use early – three years or more before their first pregnancy – has emerged from a half-dozen smaller studies published since 1981.

The most influential of these appeared in May, when British researchers reported that the risk of developing breast cancer before age 36 increased with the duration of oral contraceptive use.

Evidence from such backward-looking studies, which compare the contraceptive histories of women with breast cancer and those without, is not considered conclusive. However, a meeting of leading researchers this summer at Britain's Royal College of Medicine persuaded many that "something is going on in young women up to about the mid-30s," said one participant.

"It seems that if you start to take the Pill in your mid-20s, your risk appears not to be increased. That's the message at the moment," Malcolm Pike, a University of Southern California epidemiologist, said in a telephone interview yesterday.

"If you take the Pill very young, in your late teens and early 20s, there appears to be some increased risk up to about age 35," Pike said. "We don't know what happens to such women afterwards. There are no data on that and the Nurses Study doesn't add any."

Pike recently called on contraceptive researchers to "rethink" the birth control pill, and suggested one way of using other drugs to block ovulation while reducing the estrogen component of contraceptives by 80 percent. Estrogen is thought to be the main culprit in any possible link with breast cancer, possibly by promoting the growth of tumors that arise from other causes.