

NHS News



Dear Colleagues,

As the principal investigators of the Nurses' Health Studies, we would like to thank you for your dedication to this research. When you enrolled, you became part of the largest and longest-running studies of women's health in the world, and we hope that you are as proud of that as we are. No matter what

your age or profession, you continue to be vital to this study, and we look forward to collaborating with you for years to come.

This year, we are excited to be celebrating the 15th anniversary of the Nurses' Health Study II. Our recent application to the National Institutes of Health for continued funding was approved with an outstanding score. This assures another five years of support for NHS II, and we are confident that it will be a productive time for enhancing the health and well-being of women.

Thank you, as always, for your participation in the Nurses' Health Studies.

Sincerely,

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Preventing Osteoporosis

Postmenopausal hormones can strengthen women's bones and lower the risk of osteoporosis. However, with their many risks and benefits, hormones are not right for everyone, and so it's important to be informed about other ways of protecting your bones. Three excellent lifestyle choices are to be physically active, eat a healthy diet, and avoid smoking. Together, these behaviors can offer as much protection against fractures as hormones do, with the added benefit of improving overall health.

Physical Activity

Being physically active is one of the best ways to protect your bones early in life and as you age. Activity forces the bone tissue to absorb calcium and become stronger. It can also improve your balance, muscle strength, and flexibility, which in turn help prevent the falls that often precipitate fractures.



Although weight training and vigorous exercise have long been touted as the most effective activities for preventing osteoporosis, recent data suggest that moderate weight-bearing exercise like walking may also help reduce risk. In the Nurses' Health Study, women who walked for at least four hours a week had a 40 percent reduction in the risk of hip fractures. Among postmenopausal women, walking for at least eight hours a week (or the equivalent amount of another activity) provided the same level of protection against fractures as hormones did, while also lowering the risk of heart disease, diabetes, and stroke.

These data have important implications for all women, regardless of your current activity level. If you're sedentary, becoming more active can lower your risk of fractures. If you're already active, maintaining your current level (or even taking it a notch higher) can help ensure long-term protection for your bones. To learn more about strategies for an active lifestyle, see pages 4 and 5.

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Study Updates

Cheek Cell Collection

We would like to thank the thousands of women who provided us with cheek cell samples over the past two years. These samples are an invaluable resource for investigating the role of possible genetic markers in the development of chronic diseases. Fortunately, collecting the cells is a simple process. We asked NHS participants who had not provided us with a blood sample to swish Scope® mouthwash and then spit into a cup we provided. So far, we've received samples from about 60 percent of the nurses who were invited to participate, for a total of over 30,000 samples. We plan to complete this collection in the next several months and then start a similar collection in the Nurses' Health Study II.



Tissue Block Collection

Understanding the etiology and progression of cancer has always been one of the main goals of the Nurses' Health Studies. To further that goal, we have been collecting and studying samples of cancerous tissue. These paraffin-embedded samples (called tissue blocks) contain molecular information that we combine with questionnaire data on diet, lifestyle, and medical history. By merging these two sources of information, we hope to better understand how cancer develops and how it might be prevented.

The tissue block collection began in the Nurses' Health Studies in the early 1990s with breast cancer and has since been expanded to include ovarian cancer, colorectal cancer, melanoma, pancreatic cancer, and bladder cancer. We also collect specimens of precancerous conditions, such as colon polyps and certain types of benign breast disease. To date, we have received a total of over 6,000 specimens, including both tissue blocks and slides, and we are grateful to the many women who have allowed us access to their specimens.

As always, the information you provide to the Nurses' Health Study is completely confidential. Your tissue samples, DNA, test results, and other personal data are never released to outside parties such as insurance companies, pharmaceutical companies, or employers. For more information on our privacy measures, please see below.

Study of Multiple Sclerosis

Multiple sclerosis (MS) is a chronic demyelinating disease that affects between 250,000 and 350,000 people in the United States. Although there is a strong genetic component in MS susceptibility, there is also convincing evidence for strong environmental factors. The specific causes of this condition, however, are not yet known and are being investigated in the Nurses' Health Studies. Because of the wealth of information that study participants have provided over the years (in the form of questionnaires as well as blood samples), we have been able to examine the possible impact of lifestyle and infection on MS risk. Our ongoing studies have already led to some important findings.

In terms of infectious agents, we found an elevated antibody response against the Epstein-Barr virus (EBV) in women who eventually developed MS and also observed a twofold increase in risk among women with a history of infectious mononucleosis (a condition caused by EBV). Together, these findings support a role for EBV in MS development, and if confirmed, could lead to new preventive and therapeutic strategies.

In terms of lifestyle factors, we found that higher vitamin D intakes may lower MS risk, while smoking increases risk. We also looked at a range of other factors (including dietary fat, antioxidant intake, oral contraceptive use, number of pregnancies, and exposure to the hepatitis B vaccine), but none were associated with MS.

Your Privacy

As an NHS participant, you provide us with very personal information through your questionnaires and biological specimens. We are grateful for the trust you have shown in us and want to assure you that we hold ourselves to the highest standards in the safekeeping and use of your data. For example, only authorized study personnel are granted access to your personal information, and all genetic results are coded so that they are never stored with individual identifying information.* We also have a certificate of confidentiality from the Department of Health and Human Services, which means that under current laws we cannot be forced to disclose information that may identify you in any legal proceedings.

Your trust is essential to the success of the study, and we would never do anything to risk losing your faith in us. Thank you for your continued commitment.



* To learn more about how Brigham and Women's Hospital and its affiliates use protected health information, visit www.partners.org and click on **Patient Privacy**.

As we move forward with our research, we plan to explore these findings in greater detail. For example, we will study the impact of specific EBV strains on risk and will also examine the possible interaction between infection and genetics. We also plan to learn more about the association with vitamin D by studying blood levels of this vitamin. Our hope is that these ongoing studies will help clarify the causes of MS and eventually lead to prevention strategies.



Mothers Study

Several years ago, we asked NHS participants if we could send questionnaires to their mothers to learn what the nurses experienced early in life, such as whether they were breastfed or what they ate as preschoolers. The goal of the study is to better understand how early-life factors might influence women's health later in life. We are thrilled to report that when our data collection

wrapped up, we had received questionnaires from over 40,000 mothers. We appreciate the time that so many mothers took to participate in this study, sometimes with the help of their nurse daughters.

The Growing Up Today Study



For the past eight years, the participants of the Growing Up Today Study (GUTS) have provided us with yearly updates about their lifestyle and body weight. These contributions have helped us to identify determinants of weight gain among adolescents. So far, we have found that physical activity plays a more dominant role in adolescent weight control than diet does. Replacing one hour of TV or video games each day with one hour of physical activity can promote weight loss, while dieting at this age may actually promote weight gain. ♦

Medical Record Review

Participants who report a new diagnosis often receive a letter from our study, requesting permission to review their pertinent medical records. This review is important because it allows us to obtain specific information about treatment and diagnosis that only original records can provide. We want to extend a special thank you to all of the nurses who have helped our work by allowing us to confidentially review their records. We would also like to encourage participants who receive these requests to **complete and sign the release forms and then mail them back to us (not directly to the physician)**. This allows us to keep study information together in an organized and secure manner.

Update on the Health Effects of Postmenopausal Hormones

Evidence continues to mount about the health effects of postmenopausal hormones. As most women know, long-term use of estrogen plus progestin is no longer recommended for the prevention of chronic disease. This therapy has been shown to raise the risk of breast cancer, stroke, and pulmonary embolism, and these risks appear to outweigh potential benefits (for example, reducing osteoporosis).

The latest evidence on hormones comes from the Women's Health Initiative trial and addresses the effects of estrogen alone. In this trial, women with a hysterectomy took daily estrogen or a daily placebo for about seven years. At the end of the trial, women on estrogen had the following outcomes compared to women on placebo:



- A *higher* risk of stroke and deep vein thrombosis (blood clots in the legs)
- A *lower* risk of hip fracture and *possible* lower risk of breast cancer
- *No difference* in the risk of heart disease, colon cancer, pulmonary embolism, or death

Notably, the breast cancer results are inconsistent with previous studies and require more investigation. In addition, many women in the trial started taking hormones at later ages than most women do, and so the overall study results may not apply to those who begin using hormones early in menopause. We will share new information with you as it becomes available.

In the meantime, personal decisions about hormone use should be made with a health care provider. In general, postmenopausal hormones (in the form of estrogen alone or estrogen plus progestin) should not be taken to prevent chronic disease. Safer approaches are available for reducing the risk of osteoporosis, heart disease, and many types of cancer. Hormone use is still reasonable for relieving menopausal symptoms, but the U.S. Food and Drug Administration recommends that it be limited to the lowest effective dose for the shortest possible time. ♦

Healthy Diet

If you ask most people what you should do to lower your risk of osteoporosis, they would probably tell you to get more calcium. While this might be good advice, it doesn't give you the whole picture: you also need sufficient amounts of vitamins D and K, so that your body can take full advantage of its calcium.

Calcium is an essential building block of bone: it helps with the formation of bone mass early in life and then slows the rate of bone loss during adulthood. The question, though, is just how much calcium is needed and whether increasing dairy consumption or calcium supplements will really reduce risk.



For calcium-rich foods, the data are not promising. Most long-term studies have shown no link between these foods and fracture risk. For example, in the Nurses' Health Study, women who drank milk twice a day were just as likely to suffer a fracture as those who drank it once a week. For calcium supplements, there are not yet enough data to make firm conclusions about fracture risk. Several well-designed trials have shown that calcium supplements slightly improve bone mass, but most did not look directly at long-term effects

like fractures. A nine-year trial is currently underway to address this issue, with results due out in 2005.

Despite the somewhat contradictory evidence related to calcium and bone health, the National Academy of Sciences recommends 1,000 milligrams a day for women ages 19–50 and 1,200 milligrams a day for those over age 50. Women who do not get the recommended amount through diet should do so through supplements.

Vitamin D helps in the intestinal absorption of calcium and also plays an important role in maintaining bone mass. As a result, it is probably at least as important, if not more so, than calcium. Among postmenopausal women in the Nurses' Health Study, vitamin D offered protection against hip fractures, even when milk and high-calcium diets didn't: we found a 40 percent lower risk among women who consumed over 500 IU of vitamin D per day. Overall, these results suggest that women can benefit from boosting their vitamin D intake. The easiest way to do this is by taking a daily multivitamin or taking a combined calcium and vitamin D supplement.

Estimating Your Risk

Together with colleagues at Harvard University, we recently launched a new website called **Your Disease Risk** that builds on research from the Nurses' Health Study. This interactive website offers visitors personalized tips for lowering their risk of five major diseases: **cancer, heart disease, stroke, diabetes** and **osteoporosis**.



To learn more, visit

www.YourDiseaseRisk.harvard.edu

PHYSICALLY ACTIVE

Leading an active lifestyle can be challenging in today's world, but the many health benefits make it worth the effort. Below are tips for conquering two of the most common barriers to activity: **lack of time** and **fear of injury**.



Finding time

Most of us are constantly on the run between career obligations, family commitments, and household responsibilities. If you can't find a full 30 minutes for exercise, aim for **shorter intervals throughout the day**.

- Take the stairs instead of the elevator.
- Park your car farther from your destination, and walk the rest of the way.
- Go for a walk instead of taking a coffee break.
- Ride your bike or walk to work.
- Build exercise into your family time. Shoot some baskets, ride bikes, or toss a baseball.
- Take on some of the more active chores in your household, like mowing the lawn or walking the dog.

OSTEOPOROSIS



Vitamin K helps produce one of the main proteins used to build bone, inhibits the production of substances that can break down bone, and also helps regulate the amount of calcium in the blood. Given these critical roles, it is not surprising that vitamin K intake has been found to influence bone mass and possibly fracture risk. In the Nurses' Health Study, we found a 30 percent reduction in the risk of hip fractures among women who consumed at least 100 micrograms of vitamin K a day. Notably, this vitamin is easy to obtain through daily diet. There are about 70 micrograms in a cup of lettuce and 300 micrograms in a cup of broccoli.

Vitamin A, unlike vitamins D and K, may actually be detrimental to bone when consumed in large quantities. We examined two forms of vitamin A (beta-carotene and retinol) among postmenopausal women and found that high intakes of retinol, but not beta-carotene, increased the risk of hip fracture. Women who consumed at least 6,600 IU of retinol per day were nearly twice as likely to suffer hip fractures as those who consumed less than 1,650 IU of retinol per day.

LIFESTYLE



Playing it safe

If you haven't been active for a while, or if you've suffered an injury in the past, you might be hesitant about becoming more active. This is a normal fear, but keep in mind that you can prevent most injuries by using common sense and **listening to your body**.

- No matter how fit you are, be sure to warm up and cool down for at least 5 to 10 minutes.
- If you haven't been active recently, talk to your doctor before you get started. You'll want to begin slowly, with just enough exercise to get your muscles and joints used to the movement. Then slowly increase the length and intensity of your activity over time.
- If you feel any of the following while you're exercising (or any other time), stop and get help: chest pain or pressure; pain in the arms, neck, or jaw; light-headedness or dizziness; palpitations; nausea; blurred vision; breathlessness; or faintness.

(Adapted from U.S. Department of Health and Human Services. *Promoting Physical Activity*. 1999.)

To monitor your retinol intake, look for multivitamins and fortified foods (e.g., cereal) that derive at least half of their vitamin A from beta-carotene. If the label doesn't specify the type of vitamin A, then choose products that contain less than 5,000 IU of vitamin A.

Smoking

Smokers appear to lose more bone mass after menopause than non-smokers do, and this may translate into an increased risk of hip fracture. In the Nurses' Health Study, we found a 30 percent increase in risk among women who smoked. The good news is that quitting smoking appears to reduce this excess risk. About ten years after women quit smoking, their risk of hip fracture drops to that of women who never smoked.

Conclusion

Although clinicians have long focused on diet to prevent osteoporosis, the best way to prevent it is actually through the same combination of behaviors recommended for most other chronic diseases: engage in regular physical activity, eat a diet rich in vitamins and minerals, and avoid smoking. ♦

Diagnosing Osteoporosis

Osteoporosis occurs when the bones lose so much mass and become so brittle that they are prone to fracture. The only way to diagnose osteoporosis is to measure your bone density, which is usually done using dual-energy x-ray absorptiometry (DEXA). Testing is usually recommended for women beginning at age 65, or earlier if you have a personal or family history of fractures.

If you are found to have low bone mass, you have several options for lowering your risk of fracture. Simple lifestyle changes, such as being active, eating a healthy diet, and not smoking, can all help lower fracture risk. In addition, there are several FDA-approved medications for the prevention and treatment of osteoporosis. Examples include bisphosphonates, calcitonin, raloxifene, and parathyroid hormone.



Focus on Our Research Team

After more than a decade with the Nurses' Health Study, **Dr. Diane Feskanich** can be proud of the contributions she's made to women's health, particularly in the area of osteoporosis prevention. Since completing her doctorate in nutrition at the Harvard School of Public Health in 1994, Dr. Feskanich has shown that physical activity and certain vitamins can play an essential role in preventing osteoporotic hip fractures. What she's most excited about, though, is that her findings have influenced real-world change.

The most dramatic example of this occurred in 2002, when Dr. Feskanich's findings led to a change in the reformulation of multivitamins. At that time, she and her colleagues found that high amounts of retinol (a form of vitamin A) were contributing to an increased risk of hip fracture. Based on these results, she suggested that there might be too much retinol available in multivitamins and fortified foods. The multivitamin manufacturers promptly responded by lowering the amount of retinol in their products, a change that will hopefully lead to fewer hip fractures.

Dr. Feskanich's work has also influenced federal recommendations for physical activity. These were traditionally focused on vigorous activity because of its cardiovascular benefits. However, the recommendations have recently been changed, based in part on NHS data, to reflect the broader benefits of moderate activity, including a reduced risk of hip fractures, diabetes, stroke, and some cancers.

Although Dr. Feskanich's work has led to some important large-scale changes, she hasn't let her professional success change her own healthy lifestyle. She made exercise a priority for herself long ago, and she continues to swim and bike regularly. ♦



Nurses' Health Study II Celebrates 15-Year Anniversary

Fifteen years ago, we started the Nurses' Health Study II to better understand the health effects of lifestyle and reproductive factors among younger women. Thanks to the continued collaboration of more than 116,000 study members, we have learned a great deal about many important issues. For example, this was the first study to document a clear relationship between body weight and asthma risk. It was also the first to demonstrate a link among premenopausal women between intake of animal fat (but not vegetable fat) and the risk of breast cancer.

Because of the importance of this ongoing research, we recently received funding from the National Institutes of Health to continue the Nurses' Health Study II for another five years. We will be focusing much of our effort on identifying modifiable risk factors for breast cancer, such as diet, physical activity, and reproductive factors. We also plan to explore genetic markers of disease using cheek cell samples (see page 2). As we move forward with this work, we are excited to continue our partnership with you. Thank you again.

New Directions: Epilepsy Study

Epilepsy is a common condition in women, yet little is known about ways to prevent it. In the Nurses' Health Study II, we are beginning to study possible risk factors for this condition. In the next year, we plan to investigate how exposures like smoking and alcohol might relate to the incidence of seizures and epilepsy. We also plan to expand this research to the original Nurses' Health Study to examine risk factors in older women.

NHS II by the numbers

- 90:** the percentage of study members who respond to any given questionnaire
- 825,000:** the total number of NHS II questionnaires completed since 1989
- 19,000:** the number of study members who completed the most recent NHS II survey online
- 43,000:** the number of study participants who have involved their family members in our research (for example, their children are part of GUTS, or their mothers responded to our recent survey)
- 313:** the number of study members who currently live overseas
- 6 to 7:** the number of hours that study members sleep each night
- 35:** the percentage of participants who eat chocolate at least once a week.

The Nurses' Health Studies produced more than 65 publications on women's health last year. Below is a selection of our findings. To view a complete list of our papers, visit www.NursesHealthStudy.org and click on [Publications](#).

High Fiber, Whole Grains, and Body Weight

Many Americans have recently begun to curb their carbohydrate intake with the hope of losing weight. However, new data from the Nurses' Health Study suggest that cutting back on all carbs might not be the answer. Instead, the focus should probably be on increasing fiber intake and choosing whole grains (such as brown rice and whole wheat bread) over refined grains (such as white rice and white bread). In our study, women who increased their consumption of fiber and whole grains over a 12-year period were half as likely to become obese as women who decreased their intake of these foods. Furthermore, a high intake of whole grains was associated with less weight gain than a high intake of refined grains was. Overall, a diet rich in fiber and whole grains will likely not only help with weight control but also lower the risk of heart disease, diabetes, and possibly some types of cancer. (Liu S et al. *Am J Clin Nutr* 2003;78:920-7)



Fiber, Carbohydrates, and the Risk of Breast Cancer

Fiber and carbohydrates have been hypothesized to influence breast cancer risk through their effects on insulin. We recently examined the link between fiber, carbohydrates, and breast cancer risk among premenopausal women in the Nurses' Health Study II. For fiber, we found no association with breast cancer risk. For carbohydrates, our results varied by body weight: high carbohydrate intakes appeared to lower risk in lean women but raise risk in heavier women. These results are preliminary and need to be confirmed in additional studies. (Cho E et al. *Cancer Epidemiol Biomarkers Prev* 2003;12:1153-8)

Postmenopausal Hormones and the Risk of Urinary Incontinence

For many years, physicians believed that postmenopausal hormones could be used to treat and possibly prevent urinary incontinence. When we examined incontinence prevention in the Nurses' Health Study, however, we found that postmenopausal hormones actually increased women's risk of developing urinary incontinence. The increase in risk was moderate and came down within 10 years after women stopped taking hormones. It was observed for estrogen plus progestin, estrogen alone, and different types of estrogen, including both oral and transdermal. (Grodstein F et al. *Obstet Gynecol* 2004;103:254-60)

Interaction between Genes and Diet May Influence Body Weight



Although obesity is caused by lifestyle factors like diet and physical activity, genetic factors likely influence which individuals will gain weight under specific conditions. In the Nurses' Health Study, we have been studying a genetic polymorphism that appears to modify how dietary fat consumption affects an individual's body weight. We found that a high-fat diet was associated with an increased risk of obesity only among women who did not have this polymorphism. While these types of findings are not yet useful in the clinical setting, they have potential to eventually help clinicians identify which individuals are genetically most likely to respond to particular changes in diet. (Memisoglu A et al. *Human Molecular Genetics* 2003;12:2923-29)

Adolescent Diet, Benign Breast Disease, and Breast Cancer

Researchers have speculated that breast cancer risk may be influenced by early-life exposures, such as physical activity and diet during adolescence. In the Nurses' Health Studies, we recently examined the impact of adolescent diet on two important outcomes: breast cancer itself and proliferative benign breast disease, a marker for increased risk of breast cancer. In both studies, our results suggested that vegetable fat and fiber might lower the risk of breast cancer later in life. Although these findings are preliminary, they will likely spur additional research that could lead to prevention strategies. (Baer H et al. *Cancer Epidemiol Biomarkers Prev* 2003;12:1159-67. Frazier L et al. *Breast Cancer Res* 2003;5:R59-64)

Moderate Alcohol Consumption and Memory

Several small studies—and now the Nurses' Health Study—have suggested that moderate alcohol intake might be related to better memory in older women. We found that women who drank up to one alcoholic beverage a day had slightly better memory than those who never drank alcohol. These women were also less likely to experience any declines in memory over a two-year period. While these results are promising, they must be considered in relation to alcohol's other risks and benefits. Moderate alcohol consumption has been shown to lower the risk of heart disease but raise the risk of breast cancer. (Stampfer MJ et al. *Am J Epidemiol* 2003;S35) ♦



Feedback



We hear you: Important changes in response to your feedback

Questionnaire change

In last year's newsletter, we fielded a long-standing question about why we use the phrase "physician-diagnosed illnesses" in our surveys. Many of you responded with insightful comments about the range of health care professionals who diagnose and treat disease in today's environment. Based on that feedback, we are changing the wording of our new surveys (beginning in 2004) to ask about illnesses that are "**clinician-diagnosed.**"

Authorization for Release of Medical Records

Over the years, many NHS participants have asked us for a document that they can use in the event of disability or death to inform their family and doctor about their NHS participation. In response to this request, we have developed the enclosed Authorization for Release of Medical Records. If you choose to complete and sign this form, please place it with your will or other personal papers. It will make your wishes about the Nurses' Health Study known and provide an easy way for your family or doctor to notify us of your health status.

For additional copies of the form, please visit www.NursesHealthStudy.org.



Q: *When women are diagnosed with benign breast disease, the Nurses' Health Studies request tissue samples that were removed during biopsies. What do you hope to learn from these samples?*

A: There is consistent evidence that having a personal history of benign breast disease increases a woman's risk of breast cancer. However, there are many different types of benign breast disease, and only a small proportion of women with these conditions actually go on to develop breast cancer. By studying the morphology and molecular characteristics of the tissue samples we collect, we hope to get a better sense of which types of disease are most likely to lead to breast cancer. This could help identify women who might benefit most from intensive screening and/or chemoprevention. It could also help alleviate anxiety for women found to be at low risk.

Q: *What is the funding source for NHS?*

A: Since their inception, the Nurses' Health Studies have been continuously funded by the federal government through the National Cancer Institute

(NCI) at the National Institutes of Health (NIH). This funding covers the studies' main activities, including the mailing and processing of questionnaires, the management of data, and the confirmation of any cancers diagnosed. Other institutes at NIH have funded our sub-studies on respiratory disease, diabetes, heart disease, fractures, eye disease, Parkinson's disease, multiple sclerosis, and other conditions. Collectively, the NIH funds about 95 percent of our work.

The remaining 5 percent of our funding is made up of general gifts and project-specific support for non-NIH work. For example, some of our analyses on fruit and vegetable consumption have been funded by the Florida Citrus Growers. Before we accept such funding, we take a number of precautions to ensure that the funder will not interfere with the scientific integrity of our work. For example, we only accept funding for studies that we agree are scientifically justified, and the funder cannot interfere with the publication of results. ♦

Update on the WW II U.S. Cadet Nurse Corps

In previous newsletters, we reported on a bill that had been introduced in the U.S. Congress to grant veteran status and benefits to women who served in the Cadet Nurse Corps during World War II. The bill is still pending but now has 56 cosponsors in the House of Representatives (H.R. 476) and 4 cosponsors in the Senate (S. 1948). If you are interested in helping to promote this legislation, please contact your legislators and ask them to co-sponsor and pass this bill. For more information, send a business-size self-addressed stamped envelope to: **Anne R. Kakos, RN (Retired) ♦ 28 Mulberry St ♦ Yonkers, NY 10701-6004**



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With sincere thanks,
Frank E. Speizer, MD, Founding Principal Investigator

