1. We know patients respond better to specific recommendations regarding lifestyle modification goals. Are there any evidence-based recommendations for alcohol use, reduction of body fat or body mass index, or duration and frequency of exercise that would yield a decreased risk of breast cancer?

Response from Dr. Pearlman:
Numerous studies have demonstrated that the intake of moderate amounts of alcohol (1–2 drinks daily) is associated with a 30–50% increase in the incidence of breast cancer. A population-based study of 51,847 postmenopausal women provided evidence to support an association between increased alcohol consumption and an increased likelihood of development of estrogen receptor positive breast cancer.¹ Though the effect of reduction in alcohol consumption on the incidence of breast cancer has not been well studied, many experts recommend that alcohol consumption should be limited to less than 1 drink daily.²

Diet and exercise have demonstrated effects on cardiovascular disease, but they may also have an effect on breast cancer risk. An increased level of physical activity has been associated with a decreased risk of breast cancer. In one study, the effect of exercise on risk of breast cancer was evaluated in a population-based design involving 90,509 women aged between 40 years and 65 years. A relative risk of 0.62 (0.49–0.78) was observed for women who

reported more than five hours of vigorous exercise per week compared to women who did not participate in regular exercise. \(^3\) The Women’s Health Initiative (WHI) study also evaluated 48,835 postmenopausal women and the interventional effect of a low-fat diet (i.e., fat intake < 20% of total calories, and increased consumption of fruit, vegetables, grains) on breast cancer. The results did not show a statistical difference in invasive breast cancer in women who followed a low-fat diet over an average of 8.1 years (HR 0.91, 95% CI 0.83–1.01). \(^4\) There were several limitations to this study including how compliant the study participants were, recall biases, short duration of follow-up, and the older age of onset of intervention. While diet interventions have not been proven to decrease the risk of breast cancer, there is a substantial amount of evidence indicating that overweight or obese women have a higher risk of postmenopausal breast cancer. \(^5\) Recent results from the Nurses’ Health Study evaluating the effect of weight change on the incidence of invasive breast cancer suggested that women experiencing a weight gain of 25 kg or more since age 18 have an increased risk of breast cancer when compared with women who have maintained their body weight (RR=1.45, 1.27–1.66). \(^6\) Women who have never used hormone therapy and lost 10 kg or more since menopause and kept the weight off had a significantly lower risk of breast cancer than women who had maintained their weight (RR 0.43, 0.21–0.86). \(^7\) Results from a case-control study of 1,073 pairs of women with BRCA 1/2 mutations indicated that a weight loss of 10 or more pounds in women with BRCA1 mutation between age 18 to 30 years was associated with a decreased risk for developing breast cancer between the ages of 30 and 40 years (OR 0.35, 0.18–0.67). \(^8\)

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2. A major question for most gynecologists is when to refer a patient to a breast specialist. Using the algorithm in Figure 2, at what points should a recently trained gynecologist refer the patient to a breast specialist?

Response from Dr. Pearlman:
The answer to this question really depends on the type and quality of breast education training during one’s residency, in practice, and in other postgraduate education venues. The basic work-up and evaluation of the breast mass should be within the educational comfort zone of a properly trained ob–gyn specialist. Appropriate history, physical examination, and ordering and interpreting the results of breast imaging are part of the Residency Review Committee (RRC) requirements for ob–gyn training programs in the United States. Moreover, women are very likely to present with breast complaints to their ob–gyn physician. The majority of breast lesions that are visible on breast imaging are typically sampled by a radiology specialist using either a fine needle aspiration (FNA) or core biopsy. These results are then sent to the referring physician (ob–gyn). A benign diagnosis should be able to be managed by an ob–gyn (see article), whereas a diagnosis of cancer should prompt the gynecologist to refer to the patient to appropriate specialists for management. More complex or “gray area” cases should be sent to a breast specialist consultant. If the breast imaging results suggest the need for excisional biopsy of the breast, the gynecologist in practice should either 1) proceed with the biopsy if appropriately trained and if (s)he has privileges to perform the procedure or 2) refer the patient to an appropriate breast specialist. Office-based procedures such as FNA and core biopsy are relatively straightforward, but appropriate training in residency or postresidency should be in place prior to doing these. If office-based procedures of the breast are performed, appropriate handling of the specimen, interpretation, and follow-up of the results should be the responsibility of the clinician performing the procedure. While the properly trained ob–gyn is capable of doing all of these things (office-based and operating room diagnostic breast procedures), many ob–gyn residency training programs do not teach all of these skills. The performance of these procedures should be done based on the training and demonstrated competency of the individual clinician, irrespective of specialty. At our facility, all of these procedures are performed by me as well as many of my surgical colleagues.
3. How do you use the information about breast cancer risk associated with the use of postmenopausal estrogen plus progestin therapy? Would you recommend that patients keep hormone therapy use to 4 years or less regardless of symptoms in order to prevent increasing breast cancer risk? Would your answer differ according to the presence or absence of other risk factors? Should there be increased surveillance of women with greater than 4 years of hormone therapy while they remain at increased risk?

**Response from Dr. Pearlman:**

The Women’s Health Initiative (WHI) provides great insight into the changed breast cancer risk when menopausal hormone therapy is prescribed. While women who were enrolled in the WHI and placed on estrogen plus progestin (E+P) were about a decade older in the WHI study than the onset of menopause in the United States, there was a statistically significant increase in breast cancer in women placed on E+P compared to placebo (Hazard Ratio=1.26, 95% CI 1.00–1.59). However, there was no increased risk in breast cancer in women taking estrogen alone. The increased risk in E+P users declines rapidly after cessation of use. The increased risk of breast cancer in E+P users is somewhat time dependent and is not significantly higher in the first two years of use. In average-risk women, this slight elevation in risk does not change my recommendations for using hormone therapy. Typically, I only prescribe E+P in women with significant symptomatology related to estrogen deprivation (e.g., troubling vasomotor symptoms, symptomatic vulvovaginal atrophy, etc.). I do discuss discontinuation/weaning off hormone therapy in women after 2 years of use. The guide for that discussion is the timeframe in which the WHI study identified an increased risk for breast cancer. That discussion is both a reminder for the patient of what we discussed 2 years earlier, and often a helpful motivating assist to wean off hormone therapy at that point.

There are certain circumstances in which I avoid the use of E+P altogether, such as women with a personal history of estrogen or progesterone receptor positive breast cancer. Women with an elevated risk for breast cancer are counseled specifically about the findings of increased risk of breast cancer when E+P is used, and individual decisions are made typically based on the severity of the symptoms. In other words, the threshold for use of E+P in women with an elevated lifetime risk of breast cancer is higher than for women at average risk. There are no direct data to guide the practitioner as to the actual percent elevation in breast cancer risk in a high-risk woman using E+P, but it is reasonable to assume that it is likely a higher elevation in risk (i.e., number of incremental breast cancers per 10,000 women-years) compared to average risk women.

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4. With a 30% risk of current or future breast cancer, multiple peripheral intraductal papillomas convey a risk comparable to BRCA carriers. Should these women be offered medical treatment or bilateral mastectomy for risk reduction?

Response from Dr. Griffin:

*Multiple intraductal papilloma syndrome describes a relatively rare occurrence of multiple large papillomas in a single duct system that are located in the extreme periphery of the ductal system, the terminal duct lobular unit. In some cases, these papillomas are palpable. Two small series reported an increased lifetime risk of cancer (greater than 30%) in these patients, although others have suggested that the increased cancer risk may be due to associated atypical epithelial hyperplasia rather than the papillomas themselves. This is somewhat less than the risk of breast cancer in BRCA gene mutation carriers that are in the 40–75% range (depending on the specific gene mutation).

This should be distinguished from the much more common central papillomas that are subareolar and frequently cause nipple discharge. In approximately 10% of cases, more than one papilloma is present (usually 2–3). These do not appear to increase breast cancer risk, unless atypia is present.

For the few women who would fall into the former category, based on limited data, these women could be offered enhanced screening and risk-reduction options as are available to women with other breast pathology that confers increased cancer risk (atypical hyperplasias or lobular carcinoma in situ).


5. If a patient is diagnosed with mild hyperplasia of the usual type, should they continue routine screening?

Response from Dr. Pearlman:

*Yes, mild hyperplasia of the uterine type conveys very little increased future risk of breast cancer, and routine breast cancer surveillance for women at average risk is recommended.*
6. What methods do you use for breast cancer surveillance or risk reduction in women with moderate hyperplasia?

Response from Dr. Pearlman: 
Unlike the context of cervical cancer preinvasive lesions (frequently thought of as a progression from mild to moderate to severe hyperplasia prior to invasive disease), breast cancer is generally not thought to progress in the same way. Florid hyperplasia (severe hyperplasia) of the breast confers a relatively small incremental risk of breast cancer compared to atypical hyperplasias (RR 1.3–1.9 vs 4.1–5.3, respectively). However, because atypical cells within a hyperplastic background do substantially increase the future risk of breast cancer, these women should undergo enhanced surveillance and risk-reduction methods (see article for details).

7. Is excision of lobular carcinoma in situ (LCIS) required—unless for therapy or symptoms—if this condition is not a cancer precursor? With a high likelihood of future cancer seen in patients found to have LCIS, in addition to more intensive surveillance and risk reduction methods, would these patients be candidates for prophylactic mastectomy?

Response from Dr. Pearlman: 
Lobular carcinoma in situ (LCIS) is a noninvasive pathologic finding that predicts an increased risk of bilateral breast cancer. It is nearly always an incidental finding at breast surgery done for some other reason, and LCIS generally cannot be identified on clinical, breast imaging, or gross pathologic examination. Unlike ductal carcinoma in situ (DCIS), it has been generally felt that LCIS does not need to be completely excised or have clear margins. However, there are two studies that demonstrated that follow-up surgical excision when LCIS was identified on core needle biopsy did detect noninvasive or invasive cancer lesions on reexcision in 25% to 31% of cases.10,11

So, while LCIS is not a preinvasive lesion and does not need to have “clear margins,” if LCIS is detected on core biopsy, reexcision of the site is prudent to identify potential coincident DCIS or invasive cancer. The other important factor with LCIS is that it predicts a higher future risk of breast cancer in either breast (see article for further discussion of surveillance and risk reduction methods).

8. How helpful is an ultrasound in a woman older than 30 years with history and physical examination consistent with a benign mass and a BI-RADS 1-3 result? Should the ultrasound be done prior to the mammogram? Are there any sonographic findings that would make the mammogram unnecessary? What does the mammogram add to patient care when the sonogram indicates that the mass is benign?

Response from Dr. Griffin:
Women aged 30 years or older who present with a breast mass or asymmetry that has benign characteristics on clinical breast examination should always be referred for diagnostic breast imaging. In this age group that would include both mammography and ultrasound. Because women in their 30s and 40s frequently have dense breast parenchyma, the appearance of masses may be obscured on mammography, making ultrasound particularly useful in identifying and characterizing masses as opposed to mammography alone. Therefore, the ultrasound should always be included regardless of mammogram results.

In limited cases, ultrasound may be done without mammography. For example, women under 30 years of age who have a mass should have ultrasound alone for breast imaging evaluation. Ultrasound alone would also be appropriate in low-risk patients under 40 years who have not had a mammogram before if the ultrasound demonstrated a specific benign etiology, that is, a BI-RADS 2 result (e.g., simple cyst) that explains the clinical finding. In women 40 years and older, the patient should have a documented normal mammogram within the past year even if there is a specific BI-RADS 2 diagnosis.

When ultrasound identifies a solid mass or complex cyst in women 30 years or older, malignancy remains in the differential diagnosis, and findings such as clustered microcalcifications or asymmetry or the appearance of the mass on mammogram may change the BI-RADS classification of the finding. Therefore, mammography should always be done in these cases. Colleagues in breast imaging are helpful in defining the need for mammography.