BREAST CANCER INITIATIVE 2.5
Making breast health a global priority

PREVENTION

Breast Cancer Risk Factors and Risk Reduction

Knowledge Summary

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Breast Cancer Risk Factors and Risk Reduction

INTRODUCTION

Preventive services are often a lower priority in the spectrum of cancer care and thus receive less funding and attention. However, reducing the incidence of breast cancer can affect quality of life for women as well as reduce health care expenditures. The goal of primary breast cancer prevention is to protect women from developing breast cancer. The goal of secondary breast cancer prevention is to prevent recurrence of breast cancer. Breast cancer prevention should be integrated into comprehensive breast cancer control programs and complement breast cancer awareness and early diagnosis efforts. Experts suggest that if maximal benefit was achieved through prevention programs, 20–50% of breast cancers could be avoided.

Breast cancer is likely caused by a combination of hormonal factors (physiologic and therapeutic), genetic factors, other nonhormonal physiological factors (e.g., age) and environmental and lifestyle factors. Population-based risk assessments can help inform prevention programs in general, whereas, individual risk assessments can help inform patient-centered breast cancer care. Approximately 50% of newly diagnosed breast cancer cases are related to hormonal factors. Only an additional 5–10% of breast cancer cases are associated with genetic factors, although genetic factors are known to significantly increase the risk of breast cancer. Research has identified physiological, environmental and lifestyle factors related to breast cancer incidence, some of which are modifiable through preventive interventions (see Table 2). Research continues to identify other breast cancer risks, and some previously reported risks have been disproven or found to have an inconclusive association with breast cancer risk.

Breast cancer prevention has three components: 1) behavior or lifestyle modifications (e.g., diet, exercise, alcohol consumption); 2) pharmacologic intervention (e.g., tamoxifen) and/or 3) prophylactic surgery (e.g., mastectomy). Although certain breast cancer risk factors cannot be modified (e.g., aging, age at menarche or menopause, family history), and other risk factors—such as not having breastfed—are not necessarily modifiable for all, it is possible to address some risk factors, such as obesity, harmful use of alcohol and physical inactivity, which are known to improve an individual's general health and reduce breast cancer risk.

Studies to date have not evaluated the economics of breast cancer prevention efforts, but as data become available, preventive efforts can be better understood in terms of their long-term cost-effectiveness. Risk assessment is a critical component of cost-effective prevention programs as it can identify higher-risk patients for targeted prevention activities. Thus, health professionals must be well educated in both options—efforts to prevent breast cancer that improve the overall health of patients, and interventions targeting high-risk women, such as surgery to remove breasts and/or ovaries, that may have risks and side effects that are unacceptable for many patients, despite their protective effect against breast cancer.

KEY SUMMARY

Prevention planning

- Integrate prevention programs into breast cancer control programs.
- Use evidence-based guidelines on breast cancer prevention. Update guidelines as new research informs clinical practice.
- Include breast cancer prevention messages in breast health awareness campaigns developed through community and expert consensus building.
- Consider the risks and benefits of various prevention strategies in developing breast cancer prevention programs.
- Assess and address existing barriers and sociocultural beliefs about risk factors and prevention in the target community.

Training and education

- Include breast cancer risk assessment, breast health counseling and breast cancer prevention strategies including general lifestyle modification strategies, as well as potential medical intervention strategies in health professional training.
- Ensure individual preventative interventions include risk assessment and counseling to discuss appropriateness of prevention activities or medical interventions, based on a woman's risk factors and preferences.

Prophylactic approaches

- Include lifestyle modification programs, including weight management and exercise programs, in population-based and individual breast cancer prevention programs.
- Consider prophylactic pharmacologic therapy (e.g., tamoxifen) for inclusion in breast cancer prevention programs for select at-risk women.
- Prophylactic surgery must only be considered for select high-risk women with established susceptibility factors who have completed appropriate counseling.

Resource-stratified pathways across the continuum of care

- Develop programs based on identified needs and barriers, outcome goals and available resources.
- Pursue a defined resource-stratified pathway appropriate for available resources to ensure coordinated investment and incremental program development across the continuum of care.

POINTS FOR POLICYMAKERS:

OVERVIEW

Preplanning

- Identify data sources to estimate disease burden and dominant risk factors.
- Identify who will lead the process as well as stakeholders to be engaged.

Planning Step 1: Where are we now?
Investigate and assess

- Assess existing primary prevention programs.
- Assess existing sociocultural beliefs about breast cancer risk factors and prevention in the target community.
- Identify structural, sociocultural, personal and financial barriers to prevention interventions.
- Examine existing and potential outreach partnerships and collaborations for prevention programs.
- Risk assessment is a critical component of cost-effective approaches to prevention as it can identify high-risk patients for targeted prevention.

Planning Step 2: Where do we want to be?
Set objectives and priorities

- Include preventive lifestyle modification recommendations in breast cancer awareness education efforts.
- Planning effective prevention efforts depends on social, cultural and political acceptability of prevention interventions such as reducing harmful use of alcohol or combating obesity as part of lifestyle modification efforts.
- Prioritize prevention interventions based on population-based risk assessments.

Planning Step 3: How do we get there?
Implement and evaluate

- Integrate breast cancer prevention into existing services.
- Determine the health system primary access point for women seeking counseling on breast cancer prevention and provide educational support and risk assessment tools to health professionals at these access points.
- Monitor and evaluate.

WHAT WE KNOW

Risk Factors

Genetic factors: Genetic factors are known to be involved in increasing the risk of a number of cancers, including breast cancer. A woman's inherited genetic profile affects her risk of developing breast cancer. Approximately 5–10% of breast cancers are attributable to genetic factors. The most common breast cancer susceptibility genes are *BRCA1*, *BRCA2*, *PTEN* (Cowden syndrome) and *TP53* (Li-Fraumeni syndrome). Research continues to explore additional susceptibility genes, as well as gene–environment interactions. Each child of a parent with a mutation has a 50% chance of inheriting the mutation. For persons with *BRCA1* or *BRCA2* mutations, the estimated risk of developing breast cancer by 70 years of age is about 55–65% for *BRCA1* and 45–47% for *BRCA2*. *BRCA1* and *BRCA2* mutations can be inherited from either parent. Genetic mutations may vary by ethnic group (e.g., studies of women in sub-Saharan Africa, Asia and Latin America identified variable rates of *BRCA1* and *BRCA2* mutations ranging from 0.5–18% when testing moderate- to high-risk populations). Genetic testing requires both laboratory expertise and genetic counseling services, which are often not available in low-resource settings.

Family history of breast cancer: One's risk of developing breast cancer increases with the number of affected first-degree relatives. This is thought to be due to a combination of factors, both inherited (although not a specific gene) and environmental.

Personal history of breast cancer: For women with a personal history of breast cancer (ductal carcinoma in situ [DCIS] or invasive breast cancer) there is an increased risk of developing a second breast cancer in either the same breast or the opposite breast (estimates suggest a 4% increase over 7.5 years).

Exposure to therapeutic ionizing radiation: Exposure to ionizing therapeutic radiation of the chest at a young age increases one's risk of developing breast cancer (with highest risk if exposed at 10–14 years of age). The risk decreases dramatically if radiation is administered after age 40. For example, therapeutic radiation at a young age for treatment of Hodgkin's lymphoma is associated with an increased risk of breast cancer. However, there are no data that suggest that current radiation therapy practices administered as part of breast cancer treatment (i.e., radiation therapy after lumpectomy) increases the risk of developing a second breast cancer. In addition, mammography and chest x-rays do not appear to increase breast cancer risk.

Hormonal and reproductive factors: Endogenous hormones (hormones produced within the body's cells), particularly estrogen exposure, play a role in breast cell growth and proliferation. Elevated or prolonged endogenous estrogen levels are associated with an increased risk of breast cancer in postmenopausal women. Known risk factors for breast cancer are associated with reproductive factors that extend natural exposure to hormones produced by the ovaries, such as early onset of menstruation, late onset of menopause, late age at first pregnancy (i.e., more than 30 years of age) and never having given birth. Laboratory evidence also suggests that higher levels of other endogenous hormones (such as insulin and insulin-like growth factor [IGF]), may play a role in breast cancer development.

Therapeutic or exogenous estrogen hormones: The use of prolonged hormone replacement therapy (HRT) after menopause has been associated with an increased risk of breast cancer. In a large randomized trial, women who took the combination of estrogen and progesterone for more than five years after menopause had an increased risk of being diagnosed with breast cancer. It is now recommended that HRT be used only for specific indications (such as significant menopausal symptoms) and duration be limited.

Age: The risk of breast cancer increases with age and in some high-resource settings in populations that have a long life expectancy the lifetime risk could be as high as 1 in 8 women. The impact of age on breast cancer incidence in LMICs is less studied, but becomes increasingly important as life expectancy improves.

Weight (obesity): An association between obesity and breast cancer risk is thought to be at least partially related to the role of fat cells in contributing to levels of circulating hormones. Adiposity (fat cell volume) can affect circulating hormones as

estrogen precursors are converted to estrogen in fat cells. Women's estrogen levels also vary based on their menopausal status, so the effect of obesity on breast cancer risk depends on the menopausal status of the woman, with postmenopausal women being more affected than premenopausal women. Some experts suggest that up to 20% of breast cancer cases could be avoided by increasing physical activity and avoiding weight gain.

Alcohol consumption: Harmful use of alcohol is associated with an increased risk of breast cancer. Experts suggest that up to 14% of breast cancers could be avoided by substantially reducing or eliminating harmful use of alcohol.

Protective Factors

Breastfeeding: Overall, breastfeeding appears to reduce the risk of breast cancer. An expert review found that for every 12 months of breastfeeding, there was a 4.3% reduction in the relative risk for breast cancer, with an additional 7% decrease in the relative risk of developing breast cancer for each child that was breastfed. Experts suggest breastfeeding can reduce breast cancer incidence up to 11%.

Physical activity: Regular exercise appears to provide a protective effect for breast cancer. Studies suggest a 20–40% average risk reduction is possible among physically active women compared to the least active women.

Inconclusive or Disproven Associations

Oral contraceptives and ovarian induction: There is no definitive causative effect between breast cancer and oral contraceptives or between breast cancer and the administration of fertility agents.

HIV/AIDS: Although people infected with HIV have a higher risk of some cancers, including cervical cancer, there is no increased breast cancer risk.

Smoking: Although tobacco smoke contains known breast tissue carcinogens, there is no conclusive association between smoking and an increased breast cancer risk. Ongoing studies include those exploring NAT2 genotypes, long-term/high-pack years smoking and secondhand smoke.

Diet and vitamins: The influence of diet on breast cancer risk is not clear. Dietary patterns high in fat intake, red meat and processed meats may have a weak association with breast cancer, whereas those composed predominantly of fruits and vegetables may have a lower risk of breast cancer. Diet, vitamins and other supplements are being studied but there is little or no definitive evidence available to support risk reduction for specific dietary patterns.

Soy/phytoestrogens: Phytoestrogens have a chemical structure similar to 17 beta-estradiol, and naturally occur in plant substances, predominantly in soybeans, legumes and a variety of fruits, vegetables and cereal products. Studies are ongoing but there is no definitive evidence to support a protective effect of phytoestrogens in the diet that would reduce breast cancer risk.

Statins: Despite earlier reports, a meta-analysis of randomized clinical trials suggests that statins (drugs to reduce cholesterol) do not increase or decrease the risk of breast cancer.

Spontaneous or induced abortion: Despite earlier reports, neither spontaneous abortion (miscarriage) nor induced abortion increase a woman's risk of developing breast cancer.

Trauma or injury to the breast or bruising: There is no evidence that trauma or injury to the breast or bruising causes or increases the risk of cancer. The origin of this belief may be localized pain drawing attention to the breast, making it easier to notice a pre-existing tumor, and/or a woman seeking care following trauma being found, through an exam, to have an unrelated tumor.

Bras: No association has been found between bra use and breast cancer risk.

Deodorant/antiperspirant: There is no evidence linking the use of underarm antiperspirants or deodorants and the subsequent development of breast cancer.

Environmental factors: The data regarding the effect of occupational, environmental and chemical exposures on breast cancer risk are inconclusive.

Lifestyle modifications: Lifestyle recommendations can improve overall health and include increased exercise, avoidance of weight gain (particularly during menopause), encouragement of breastfeeding, avoidance of harmful use of alcohol (more than one drink per day for women) and physical activity. Although not a known breast cancer risk factor, all women should avoid tobacco use. While there are overall health benefits to adopting these lifestyle modifications, prospective data, especially from LMICs, are not available to validate the effects of specific lifestyle modification programs (see Table 3).

Prophylactic interventions

Medical prophylaxis (preventive or protective pharmaceutical therapy): Medical prophylaxis with tamoxifen or raloxifene, which are both selective estrogen receptor modulators (SERMs), has been shown to reduce breast cancer risk in select patients at increased risk of developing breast cancer but this strategy has not been well accepted by health professionals or patients. These therapies require careful consideration and in-depth discussions with patients regarding the benefits and risks of therapy. Tamoxifen, when used as primary prevention, can result in an approximately 50% reduction in the risk of developing breast cancer. However, no studies have shown a decrease in breast cancer mortality rates as a result of this therapy. Side effects may reduce the feasibility of tamoxifen or raloxifene as prevention agents. Side effects of tamoxifen and raloxifene include blood clots in the legs or lungs and an increase in hot flashes, vaginal dryness and the need for cataract surgery. In women with a uterus, tamoxifen also increases the risk of uterine cancer (raloxifene does not increase the risk of uterine cancer). Additional resources are required to manage potential serious complications as well as common side effects that affect quality of life (e.g., vaginal dryness, nonhormonal

hot flashes, vaginal bleeding, lower extremity swelling and shortness of breath).

Guidelines on medical prophylaxis in HICs advise using tamoxifen only in select at-risk women who are not at increased risk for thromboembolic disease or endometrial cancer. For postmenopausal women, raloxifene is an option and does not increase the risk of endometrial cancer.

Additional factors to consider include the risk for vascular events. The general recommended duration of pharmaceutical prevention is five years, but the risk-reducing effects may persist beyond 10 years. The cost of and access to chemoprophylaxis in LMICs has not been studied, but tamoxifen is a WHO essential medicine and is widely available in LMICs.

Surgical prophylaxis (preventive or protective surgery): Surgical interventions such as prophylactic mastectomy and/or oophorectomy (removal of ovaries) are generally only considered for high-risk women with known or highly suspected genetic predisposition to breast cancer. Candidates must understand the irreversible effects of such treatment. The psychological implications can be substantial and include anxiety regarding body appearance, sexual relationships and psychosocial issues. Total mastectomy with breast reconstruction is currently the procedure of choice in HICs among high-risk women with a lifetime risk of developing breast cancer of over 25% (generally those with a *BRCA1* or *BRCA2* mutation or who received therapeutic chest irradiation at a young age). Bilateral prophylactic mastectomy is the complete removal of both breasts, including the nipple-areolar complex (total mastectomy), or as much breast tissue as possible while leaving the nipple-areolar complex intact (nipple-sparing or subcutaneous mastectomy). In HICs, in moderate- to high-risk women, this reduces the risk of breast cancer by 90–95%. Immediate breast reconstruction, if available and desired, should be performed after adequate preoperative counseling. Patient regret regarding the decision to undergo prophylactic mastectomy is not common in HICs (approximately 5–6%).

Prophylactic oophorectomy, after age 35, and child bearing has been completed, should be reserved for high-risk women such as those with a known deleterious BRCA mutation. The potential benefits include a reduction in both breast and ovarian cancer. Oophorectomy in women younger than age 35 is associated with about 50% reduction of breast cancer risk and about 85% risk reduction of ovarian cancer. Surgically induced menopause carries its own concomitant risks, including premenopausal symptoms (e.g., hot flashes, night sweats, vaginal dryness), osteoporosis and increased risk of cardiovascular disease. Women with severe menopausal symptoms after salpingo-oophorectomy may want to consider short-term menopausal hormone therapy.

WHAT WORKS

Health provider training: Frontline health professionals need expertise in breast cancer risk assessment and counseling (including prevention counseling) or must be able to refer women for risk assessment and counseling. Frontline health professionals should understand available breast cancer prevention strategies, including lifestyle modification and preventive or protective medical therapy for select moderate- to high-risk women and preventive surgery for select high-risk women. For health professionals, discussing lifestyle risk factors should be a core component of routine patient visits to a primary care provider for all adolescents and adults.

Community education and awareness: Prevention programs for breast cancer require general breast cancer awareness, (see *Early Detection: Breast Health Awareness and Clinical Breast Exam*) population-based breast cancer risk assessment and individual patient breast cancer risk assessment. If a woman's personal breast cancer risk has been established as moderate or high, a personalized prevention and screening plan can be developed. Lifestyle choices in youth (e.g., nutrition) as well as in adulthood (e.g., alcohol consumption) can affect long-term cancer risk.

Risk factor modeling and stratification: Several risk assessment tools are available for estimating the nongenetic risk of breast cancer for women. The Breast Cancer Risk Assessment Tool (BCRAT), also known as the modified Gail model, is a validated, short survey widely used in high income countries (HICs) and some LMICs. Women are classified as high risk if they score an estimated five-year risk of 1.67% or higher. This cutoff is generally accepted and used in research studies and clinical counseling in HICs. The BCRAT collects data on menarche (age at first menstruation), age at first live birth, nulliparity (never bearing children), family history of breast cancer in first-degree relatives, history of breast biopsy and history of breast biopsy with atypical hyperplasia and race-specific determinations. The International Breast Cancer Intervention Study (IBIS) model may be more appropriate for younger women less than 35 years old, with a personal history of lobular carcinoma in situ (LCIS) or DCIS or strong family history of breast cancer. Computer programs based on these models are available (see Table 1). There are limitations to both models and any risk calculation should be interpreted within the context of a patient's overall personal and family medical history.

Standardize risk assessment strategies: Some breast cancer risk assessment strategies require consensus building. For example, genetic testing for high-risk women is not endorsed by all health professionals. Risk assessments should be based on local disease incidence, population-based risk assessments, surveys and other sources of information and require expert clinical guidance. Risk assessment strategies should consider sociocultural norms.

POINTS FOR POLICYMAKERS:

PLANNING STEP 1: WHERE ARE WE NOW?

Investigate and assess

Assess the burden of disease

- Obtain data on incidence of breast cancer and known risk factors within a target population to inform prevention discussions and policies. Primary data on obesity or alcohol consumption may be obtained from hospital databases.
- Consider using the WHO STEPwise approach to surveillance (STEPS), a standardized method for collecting, analyzing and disseminating data on established risk factors (see Table 1).
- The population attributable risk (PAR) estimates the effect of removing a population risk factor on the incidence of breast cancer in that population.

Assess existing prevention programs

- Identify existing lifestyle modification programs and breast awareness programs that could be adapted to include breast cancer prevention education.
- Prioritize prevention interventions that are immediately feasible and likely to have the greatest impact. For example, interventions to increase physical activity or to provide greater access to healthier food choices (fruits and vegetables) may be an appropriate first step for a community with a high incidence of obesity.
- Identify current preventative pharmaceutical and surgery capacity (including personnel trained in risk assessment, breast counseling and preventative breast cancer strategies).

Assess barriers to prevention programs

- Identify structural, sociocultural, personal and financial barriers to prevention interventions.
- Consider sociocultural and political norms when developing breast cancer prevention programs by including breast cancer patients, survivors, advocates and other stakeholders in discussions.

PLANNING STEP 2: WHERE DO WE WANT TO BE?

Set objectives and priorities

Define target population and approach

- Prioritize primary prevention program goals according to at-risk populations, available resources and cultural considerations. For example, lifestyle modifications can be incorporated into early detection efforts or complementary public health programs such as maternal and family health programs.
- In high-risk subpopulations where tamoxifen therapy is already widely used as adjuvant therapy, preventive therapy with tamoxifen could be introduced as a prevention intervention for select moderate- or high-risk patients.
- In high-risk groups where genetic profiles and detailed risk assessments are available, prophylactic surgery may be introduced as a possible option for select patients who have access to high-level resources.

Identify community and health system partnerships

- Identify decision-makers and partners (advocates, trusted public figures, medical associations, public health institutions) who can help put breast cancer prevention on the breast cancer control agenda.
- Determine the health system primary access point for women seeking counseling on breast cancer prevention and provide educational support and risk assessment tools to health professionals at these access points. Include breast cancer risk assessment and counseling as part of routine patient-centered breast care.

Set achievable objectives

- Objectives should promote one common goal: reducing breast cancer incidence and improving overall health through breast cancer prevention efforts.
- Consider interventions that have been shown to be effective in similar populations or modify interventions to meet your target population profile (e.g., lifestyle modification interventions aimed at reducing alcohol and tobacco use—key objectives of WHO) or modify interventions to meet the target audience (see Table 1).
- Educate health professionals through guideline development and continuing education programs. Education should include patient risk assessments; prevention strategies (lifestyle modifications, prophylactic medicine, prophylactic surgery) and breast health counseling, including risk counseling. Continuing education programs should incorporate an evaluation of their effectiveness.
- Prioritize prevention programs based on local breast cancer incidence and known risk factors, cultural and social acceptance of interventions and available resources.

Set priorities and determine feasibility of interventions

- Assess feasibility of primary breast cancer prevention interventions by implementing demonstration or pilot projects with measurable outcomes.
- Follow a resource-stratified pathway for program development that identifies available resources across the continuum of care. Lifestyle modification programs can be implemented at any resource level as they promote healthy diet, reduced obesity, increased physical activity and reduced alcohol consumption, goals that overlap with prevention goals for many noncommunicable diseases.

PLANNING STEP 3: HOW DO WE GET THERE?

Implement and evaluate

Establish financial support and partnerships

- Secure necessary political and financial support for program interventions.
- Use consensus building to garner endorsements for prevention plans.

Launch, disseminate and implement

- Educate the general public through community-based initiatives, media campaigns and legislation.
- Encourage women to seek breast cancer preventative counseling through public education and a patient-centered approach to breast health care.
- Follow guidelines for risk assessment and educate providers in counseling and appropriate use of medical prophylaxis with tamoxifen or raloxifene for moderate to high-risk patients identified through individual risk assessment and counseling.
- Guidelines should include prophylactic mastectomy or oophorectomy for high-risk women identified through individual risk assessment and genetic testing and breast counseling that addresses physiologic and psychosocial risks.
- Address potential health care-generated risk factors.
- Improve awareness of carcinogenic (cancer-creating) effect of ionizing chest radiation among health providers; make documentation of exposure to chest x-rays a standard part of a patient's permanent health record.
- Medical treatments (prophylactic medication and prophylactic surgery) for breast cancer risk reduction for moderate- to high-risk women require additional resource allocations for accurate risk assessment and pretreatment counseling.

Monitor and evaluate

- Establish assessment, process and quality metrics and outcome measures (e.g., assessing provider and patient awareness of breast cancer prevention and risk factors).
- Collect data on breast cancer incidence to inform future program direction.

CONCLUSION

Effective prevention programs have the potential to reduce the incidence of secondary breast cancer as well as primary breast cancer. Preventive efforts should augment, not replace, early detection, timely diagnosis and treatment programs. Breast cancer prevention tools include risk-associated lifestyle modification programs, chemopreventive medications (tamoxifen) for select moderate- to high-risk women and preventive surgery (mastectomy and oophorectomy) for select high-risk women who have received appropriate testing and counseling.

Understanding how risk assessment informs effective prevention strategies for a high-risk subgroup of women and how prevention strategies translate into clinical and public health practice can be challenging. Prophylactic medications and prophylactic surgery 1) should be pursued only after careful and extensive counseling of high-risk patients and 2) requires investment in identifying high-risk patients through genetic testing, which is often not available. It is unlikely, even with high participation rates in preventive programs (such as elimination of obesity or universally implementing pharmaceutical breast cancer prevention in moderate- and high-risk women), that the reduction of breast cancer mortality would be as great as it would be with interventions that optimize treatment or increase breast cancer screening. Adding prevention to the breast cancer program agenda can ensure that health professionals and patients keep up-to-date on breast cancer incidence rates, breast cancer risk assessment strategies and breast cancer prevention research.

Because lifestyle modification interventions are associated with reduced risk of breast cancer and overall improved health, they may offer the most promise in breast cancer risk reduction for many women. However, no specific formal recommendation can be made at this time regarding specific lifestyle interventions until additional data are available. See tables for prevention strategies by level of resources available in a country, links to resources on risk assessment and recommended lifestyle modifications.

Table 1. Suggested resources for risk assessment and lifestyle modifications

Program	Website
NCI Breast Cancer Risk Assessment Tool	http://www.cancer.gov/bcrisktool/
IBIS Breast Cancer Risk Evaluation Tool	http://www.ems-trials.org/riskevaluator/
European Code Against Cancer	http://cancer-code-europe.iarc.fr/index.php/en/
WHO STEPwise approach to noncommunicable disease risk factor surveillance (STEPS)	http://www.who.int/chp/steps/riskfactor/en/index.html
WHO global strategy to reduce harmful use of alcohol	http://www.who.int/substance_abuse/activities/gsrhua/en/
WHO global recommendations on physical activity for health	http://www.who.int/dietphysicalactivity/factsheet_ recommendations/en/

Table 2. Risk factors for breast cancer and approximate strength of association

Reproductive factors	Hormonal factors	Nutritional/lifestyle factors	Other factors
Early age at first period +	OC use (current vs. none) +	Obesity (>30 BMI vs. <25)	Family history (mother and sister)[a] +++
Age at first birth (>35 vs. <20) ++	Estrogen replacement (10+ yrs. vs. none)+	Premenopausal -	Family history (first-degree relative)[b] ++
No. of births (0 vs.1 child) +	Estrogen plus progesterone replacement (>5 yrs. vs.> none) ++	Postmenopausal +	Jewish heritage (yes vs. no) +
Age at menopause	High blood estrogens or androgens (postmenopause) +++	Adult weight gain (postmenopausal) ++	Ionizing radiation (yes vs. no) +
Breastfeeding (>1 yrs. vs. none) -	High blood prolactin ++	Alcohol (1 or more drink/day vs. none) +	Benign breast disease (physician-diagnosed)[d] ++
		Height (>5 feet 7 inches) +	Mammographic density (highest category vs. lowest) +++
		Physical activity (>3 hr/wk) -	
		Monounsaturated fat[c] - (vs. saturated fat)	
		Low intake of fruits and vegetables[c] (specifically for ER- breast cancer) +	

Note: **BMI**, body mass index; **OC**, oral contraceptives; +, relative risk (RR) = 1.1–1.4; ++, RR = 1.5–2.9; +++, RR = 3.0–6.9; -, RR = 0.7–0.8.

a Two first-degree relatives who have a history of breast cancer before age 65 years versus no relative with breast cancer history.

b First-degree relative who has a history of breast cancer before age 65 years versus no relative.

c Upper quartile (top 25%) versus lower quartile (lowest 25%).

d Clinically recognized chronic cystic, fibrocystic, or other benign breast disease versus none.

Source: Willett WC, Tamimi R, Hankinson SE, Hazra A, Eliassen AH, Colditz GA. Chapter 18: Nongenetic Factors in the Causation of Breast Cancer, in Harris JR, Lippman ME, Morrow M, Osborne CK. Diseases of the Breast, 5th edition, Lippincott Williams & Wilkins, 2014.

Table 3. European Code Against Cancer: 12 ways to reduce your cancer risk[a]

1. Do not smoke. Do not use any form of tobacco.
2. Make your home smoke free. Support smoke-free policies in your workplace.
3. Take action to be a healthy body weight.
4. Be physically active in everyday life. Limit the time you spend sitting.
5. Have a healthy diet:
   - Eat plenty of whole grains, pulses, vegetables and fruits.
   - Limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks.
6. If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention.
7. Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds.
8. In the workplace, protect yourself against cancer-causing substances by following health and safety instructions.
9. Find out if you are exposed to radiation from naturally high radon levels in your home. Take action to reduce high radon levels.
10. For women:
    - Breastfeeding reduces the mother's cancer risk. If you can, breastfeed your baby.
    - Hormone replacement therapy (HRT) increases the risk of certain cancers.
    - Limit use of HRT.
11. Ensure your children take part in vaccination programs for:
    - Hepatitis B (for newborns).
    - Human papillomavirus (HPV).
12. Take part in organized cancer screening programs for:
    - Bowel cancer (men and women).
    - Breast cancer (women).
    - Cervical cancer (women).

a These recommendations refer to reducing cancer risk in general and are not specific to breast cancer.

Source: International Agency for Research on Cancer. European Code Against Cancer: 12 ways to reduce your cancer risk. Lyon: IARC, 2013. Available from: http://cancer-code-europe.iarc.fr/index.php/en/

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