

## PREVENTION: BREAST CANCER RISK FACTORS AND PREVENTION



### About this Knowledge Summary (KS):

This summary covers the preventive approach to breast cancer control and includes prophylactic medications, prophylactic surgery and lifestyle modifications for breast cancer prevention. Health professional training and individual risk assessments and counseling are also discussed.

## KEY POLICY SUMMARY

### Planning

- Prevention should be integrated into breast cancer control programs.
- Guidelines on breast cancer prevention should be evidence-based and updated as new research informs clinical practice.
- Breast cancer prevention messages should be included in breast awareness campaigns and developed through community and expert consensus building. Preventive programs should include an evaluation component that informs future programs.
- Breast cancer prevention programs should include the risks/benefits of prevention strategies.
- Programs should assess and address existing sociocultural beliefs about risk factors and prevention in the target community.

### Training and Information

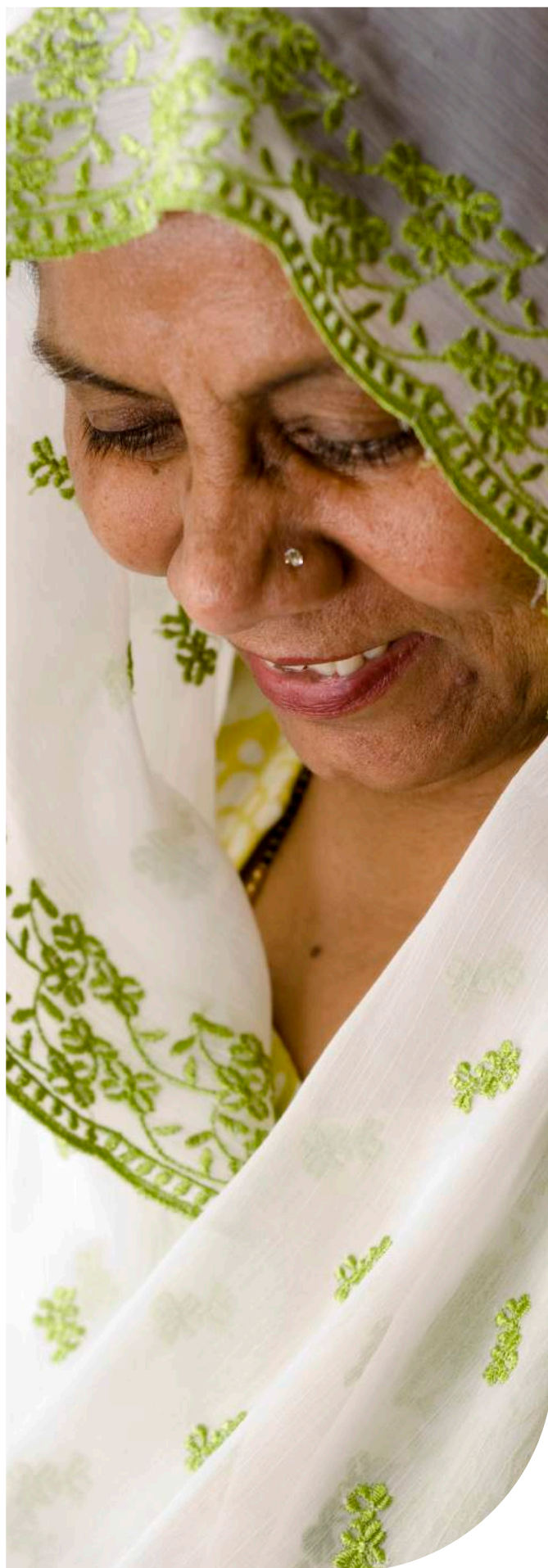
- Health professional training should include breast cancer risk assessment, breast health counseling and breast cancer prevention strategies including general lifestyle modification strategies as well as potential medical intervention strategies based on patient risk assessment.
- Individual patient preventative interventions should 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

- Lifestyle modification programs, including weight management and exercise programs, should be part of population-based and individual breast cancer prevention programs.
- Prophylactic pharmacologic therapy (e.g., tamoxifen) should be considered 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 sessions.

### Resource-stratified pathways across the continuum of care

- Breast cancer programs in LMICs should follow a defined resource-stratified pathway to allow for coordinated incremental program improvement across the continuum of care.
  - A pathway is a progression of resource investment, program development and interval health gains.
  - Program design and improvements should be based on outcome goals, identified barriers and needs and available resources.



## INTRODUCTION & THE CHALLENGE

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. Primary prevention offers the greatest public health potential and most cost-effective long-term cancer control program. Breast cancer prevention should be integrated into comprehensive breast cancer control programs, and complement breast cancer awareness and early detection efforts. Experts suggest that if maximal benefit was achieved through prevention programs, up to 50% of breast cancers could be avoided. 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 breast fed – are not necessarily modifiable for all, it is possible to take responsibility at both an individual and a policy level for some risk factors, such as obesity, harmful use of alcohol and physical inactivity, which are known to also improve an individual's general health as well as reduce breast cancer risk.

There are currently no studies evaluating the cost effectiveness of breast cancer prevention efforts; however, as data become available, preventive efforts can be better understood in terms of 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 - preventive options for breast cancer which improve the overall health of patients, as well as more targeted interventions for high risk women, such as surgery to remove breasts and/or ovaries, that may have unacceptable risks and side-effects for many women, despite their protective effect against breasts cancer.

## POLICY ACTION OVERVIEW

### *Preplanning*

- Is a new prevention strategy needed?
- If so, who will lead the process?

### *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 approach to prevention programs as it can identify higher-risk patients for targeted prevention programs.

### *Planning Step 2: Where do we want to be? (Set objectives and priorities)*

- Preventive lifestyle modifications recommendations should be included in breast cancer awareness and education efforts.
- Planning effective preventative efforts depends on social, cultural and political acceptability of prevention interventions such as reducing harmful use of alcohol or combatting obesity as part of lifestyle modifications 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.
- Medical treatments (prophylactic medication and prophylactic surgery) for breast cancer risk reduction for moderate to high at-risk women require additional resource allocations for accurate risk assessment and pretreatment counseling.

## WHAT WE KNOW

Breast cancer is likely caused by a combination of hormonal factors (physiologic and therapeutic), genetic factors, other non-hormonal 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 3). 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.

### 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 impacts 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 risks of developing breast cancer by 70 years of age is about 55-65% (BRCA1) and 45-47% (BRCA2). BRCA1 and BRCA2 mutations can be inherited from either parent. Genetic mutations may vary by ethnic group, for example, 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 (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 (highest risk if exposed at 10-14 years of age) increases one's risk; however, the risk of developing decreases dramatically if radiation is administered after age 40. For example, therapeutic radiation at a young age for treatment of Hodgkin lymphoma is associated with an increased risk of breast cancer. However, there are no data to suggest that current radiation therapy practices administered as part of breast cancer treatment, (i.e., radiation therapy after lumpectomy) increases the risk for developing a second breast cancer. Additionally, 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 increase risk of breast cancer in post-menopausal women. Known risk factors for breast cancer are associated with reproductive factors which extend natural exposure to hormones produced by the ovaries such as early onset of menstruation, late onset of menopause, later age of first pregnancy (i.e., over 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 5 years after menopause had an increased risk of being diagnosed with breast cancer. It is now recommended that HRT should be used only for specific indications (such as significant menopausal symptoms) and the duration of treatment should 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 well 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 and other factors. 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 may depend on the menopausal status of the woman, with post-menopausal 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 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 25-40% average risk reduction is possible amongst physically active women as 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 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. Studies are ongoing, including studies exploring NAT2 genotypes, long-time, high pack-years smoking and second-hand 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 one 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 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 (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 is possibly that localized pain draws attention to the breast making it easier to notice a pre-existing tumor, or a woman who seeks care following trauma is 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 conclusive evidence linking the use of underarm antiperspirants or deodorants and the subsequent development of breast cancer.

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

### Risk Factor Modeling and Stratification

Several risk assessment tools are available to estimate the non-genetic risk of breast cancer for women. The Breast Cancer Risk Assessment Tool (BCRAT), also known as the modified Gail Model, is a validated, widely used form in HICs and some LMICs. Women are classified as high risk if they score an estimated 5-year risk of 1.67% or higher. This cutoff is generally accepted and used in research studies and clinical counseling in HICs. The BCRAT includes age at first menstruation (menarche), 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 as well as race-specific determinations. The International Breast Cancer Intervention Study (IBIS) model may be more appropriate for younger women (under 35), who have a personal history of lobular (LCIS) or ductal carcinoma in situ (DCIS), or strong family history of breast cancer. Computer programs based on these models are available (see Table 2). 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.



### **PLANNING STEP 1:** WHERE ARE WE NOW?

#### **POLICY ACTION:** INVESTIGATE AND ASSESS

##### ***Assess the need for primary prevention***

- The incidence of breast cancer and the known risk factors within a target population should inform prevention discussions and policies. For example, data on obesity or alcohol consumption may be available for extraction through hospital data bases.
- Consider using the WHO STEPwise approach to surveillance (STEPS), a standardized method for collecting, analyzing and disseminating data on established risk factors (see Table 2).
- The population attributable risk (PAR) estimates the effect of removing a risk factor from the population on the incidence of breast cancer in that population.

##### ***Assess current or available prevention policies or interventions***

- Identify existing lifestyle modification programs and breast awareness programs that could be adapted to include breast cancer prevention education.
- Identify current preventive pharmaceutical and surgery capacity (including personnel trained in risk assessment, breast counseling and preventive breast cancer strategies).

- 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.

##### ***Anticipate and address obstacles to program activities***

- Consider local social, cultural and political norms when developing breast cancer prevention programs by including stakeholders in discussions. Educate the general public through community-based initiatives, media campaigns and legislation.

##### ***Use a resource-stratified pathway approach to planning***

- Prioritize prevention programs based on local breast cancer incidence and known risk factors, cultural and social acceptance of intervention and available resources.

## WHAT WORKS

Prevention programs for breast cancer require general breast cancer awareness (see Early Detection: Breast Health Awareness and Clinical Breast Exam KS) 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. 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, or preventive or protective medical therapy for select moderate- to high-risk women or preventive surgery for select high-risk women.

### 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, is not available to validate specific lifestyle modification programs (see Table 4).

### Medical prophylaxis (preventive or protective pharmaceutical therapy)

Medical prophylaxis with tamoxifen and raloxifene, both selective estrogen receptor modulators (SERMs), has been shown to reduce breast cancer risk in select patients, but has not been well-accepted by health professionals or patients. It requires careful consideration and in-depth discussions regarding the benefits and risks of therapy. Tamoxifen, when used as primary prevention, can result in a 38% reduction in breast cancer incidence. However, studies did not report a decrease in breast cancer mortality rates. 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, increase in hot flashes and vaginal dryness and an increase in 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 impact quality of life (e.g., vaginal dryness, non-hormonal hot flashes, vaginal bleeding, lower extremity swelling and shortness of breath).

Guidelines used in HICs are available on medical prophylaxis and generally advise medical prophylaxis with tamoxifen only in select at-risk women who do not have a past history of, or who are not at increased risk for, thromboembolic disease or endometrial cancer. For post-menopausal women, raloxifene is also an option.

Additional factors to consider include risk for vascular events. The general recommended duration of pharmaceutical prevention is 5 years; although, the risk-reducing effects may persist beyond 10 years. Guidelines vary with regards to the exact patient inclusion criteria, as well as the duration of recommended therapy. The cost and access to chemoprophylaxis in LMICs has not been studied, although tamoxifen is a WHO essential medicine and is widely available in LMICs, the cost charged to the patient varies by region.

### Surgical prophylaxis (preventive or protective surgery)

Surgical interventions, such as prophylactic mastectomy and/or oophorectomy (removal of ovaries), should only be considered for high-risk women with known or highly suspected genetic predisposition to breast cancer. Candidates must understand the irreversible effects of such treatment.

Total mastectomy with breast reconstruction is currently the procedure of choice in HICs among some high-risk women. The psychological implications can be substantial and include anxiety regarding body appearance, sexual relationships and psychosocial issues. 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 pre-operative 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 35 years old is associated with an approximately 50% reduction of breast cancer risk and an 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.

**PLANNING STEP 2:**

WHERE DO WE WANT TO BE?

**POLICY ACTION:**

SET OBJECTIVES AND PRIORITIES

**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. 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 impact quality of life for women as well as reduce healthcare expenditures.

**Identify target population(s) and strategy**

- Prioritize primary prevention program goals based on 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 could be introduced as a possible option for select patients who have access to high level resources.

**Set achievable objectives**

- Objectives should promote a common goal: reducing breast cancer incidence and improving overall health through breast cancer prevention efforts.
- Educate health professionals through guideline development and continuing education programs. Education should include patient risk-assessments, prevention strategies (lifestyle modifications, prophylactic medicine, prophylactic surgery), breast health counseling, including risk counseling. Continuing education programs should incorporate an evaluation of their effectiveness.
- Include breast cancer risk assessment and counseling as part of routine patient-centered breast care.

**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. For example, lifestyle modification programs can be implemented at any resource level as they promote healthy diet, reduced obesity, increased physical activity, and reduced alcohol consumption. These goals overlap with prevention goals for many non-communicable diseases.

**HOW DO WE GET THERE?**

**Set a goal for prevention**

Prevention of primary and secondary breast cancer should be a goal for policymakers, health professionals and patients. Although considerable progress has been made in reducing mortality from breast cancer through improved early detection and treatment, effective programs to prevent the onset of breast cancer have not been a priority for health systems. Data and expert observations now suggest that breast cancer prevention efforts targeted at population-based modifiable risk factors, such as obesity, physical inactivity and reduced alcohol consumption can reduce breast cancer incidence and improve overall health. Prophylactic medicine and prophylactic surgery can further reduce breast cancer risks in select patients.

**Start the prevention discussion early**

Lifestyle choices in youth (e.g., nutrition) as well as in adulthood (e.g., alcohol consumption) can affect long-term cancer risks. 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.

**Standardize risk assessment strategies using consensus building**

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, other sources of information, and require expert clinical guidance. Risk assessment strategies should consider sociocultural norms.

**Health professionals should keep up-to-date on breast cancer prevention research and guidelines**

Health professionals should be prepared to answer questions from patients regarding breast cancer risk and breast cancer prevention strategies for select women identified as high-risk. Health professionals should be able to discuss the benefits and risks of preventive therapy, including the adverse events associated with tamoxifen use and the physiological, and psychosocial impact of prophylactic mastectomy, as well as the ongoing studies related to lifestyle modifications that continue to expand the list of both potential interventions and inconclusive or disproven associations with breast cancer risk. Research continues to inform prevention guidelines regarding risk factors for breast cancer.





### PLANNING STEP 3: HOW DO WE GET THERE?

#### POLICY ACTION: IMPLEMENT AND EVALUATE

##### *Establish political and financial support for prevention*

- Integrate 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.
- Use consensus building to garner endorsements for prevention plans.

##### *Launch, disseminate and implement*

- Prioritize prevention interventions based on population-based risk assessments.
- Consider interventions that have been shown to be effective in similar populations or modify interventions to meet your target population profile. For example lifestyle modification interventions aimed at reducing alcohol and tobacco use are available and are key objectives supported by the World Health Organization (see Table 2).
- Encourage women to seek breast cancer preventive counseling through public education and a patient-centered approach to breast health care.

- Develop 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 healthcare-generated risk factors.
- Improve awareness of the 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.

##### *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).

## CONCLUSION

Prevention must be a core component of any breast cancer program; effective programs have the potential to significantly reduce the incidence of secondary breast cancer as well as primary breast cancer. 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.

Preventive efforts should augment, not replace, early detection, timely diagnosis and treatment programs. It is unlikely, even with high participation rates in preventive programs (such as elimination of obesity or universally implementing pharmaceutical prevention in moderate- and high-risk women), that the reduction of breast cancer mortality would be as great as 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.

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 should be pursued only after careful and extensive counseling of high-risk patients, and requires investment in identifying high-risk patients through genetic testing, which is often not available.

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 Appendix for prevention strategies by level of resources available in a country, links to resources on risk assessment and general lifestyle modifications.

**Table 1. Prevention strategies for noncommunicable diseases (NCDs) based on level of resources available in a country. (WHO 2002)**

All countries	Implement integrated health promotion and prevention strategies for non-communicable diseases that include legislative/regulatory and environmental measures as well as education for the general public, targeted communities and individuals.
Low level of resources	Focus on areas where there are great needs and potential for success. Ensure that priority prevention strategies are targeted to those groups that are influential and can spearhead the process (e.g., policymakers, and teachers). In areas endemic for liver cancer, integrate HBV and other vaccination programs.
Medium level of resources	Develop integrated clinical preventive services for counseling on risk factors in primary healthcare settings, schools, and workplaces. Develop model community programs for an integrated approach to prevention of noncommunicable diseases.
High level of resources	Strengthen comprehensive evidence-based health promotion and prevention programs and ensure nationwide implementation in collaboration with other sectors Establish routine monitoring of ultraviolet radiation levels if the risk of skin cancer is high.

**Table 2. Useful Resources for risk assessment and lifestyle modifications**

Program	Website
NCI Breast Cancer Risk Assessment Tool	<a href="http://www.cancer.gov/bcrisktool/">http://www.cancer.gov/bcrisktool/</a>
IBIS Breast Cancer Risk Evaluation Tool	<a href="http://www.ems-trials.org/riskevaluator/">http://www.ems-trials.org/riskevaluator/</a>
European Code Against Cancer	<a href="http://cancer-code-europe.iarc.fr/index.php/en/">http://cancer-code-europe.iarc.fr/index.php/en/</a>
WHO STEPwise approach to noncommunicable disease risk factor surveillance (STEPS):	<a href="http://www.who.int/chp/steps/riskfactor/en/index.html">http://www.who.int/chp/steps/riskfactor/en/index.html</a>
WHO Global strategy to reduce harmful use of alcohol	<a href="http://www.who.int/substance_abuse/activities/gsrhua/en/">http://www.who.int/substance_abuse/activities/gsrhua/en/</a>
WHO Global Recommendations on Physical Activity for Health	<a href="http://www.who.int/dietphysicalactivity/factsheet_recommendations/en/">http://www.who.int/dietphysicalactivity/factsheet_recommendations/en/</a>

**Table 3. 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) <sup>a</sup> +++
Age at first birth (>35 vs. <20) ++	Estrogen replacment (10+ yr vs. none) +	Premenopausal - Postmenopausal +	Family history (first-degree relative) <sup>b</sup> ++
No. of births (0 vs. 1 child) +	Estrogen plus progesterone replacment (>5 yr vs> none) ++	Adult weight gain (postmenopausal) ++	Jewish heritage (yes vs. no) +
Age at menopause (5-yr increment)	High blood estrogens or androgens (postmenopause) +++	Alcohol (1 or more drink/day vs. none) +	Ionizing radiation (yes vs. no) +
Breast-feeding (>1 yr vs. none) -	High blood prolactin ++	Height (>5 feet 7 inches) +	Benign breast disease (MD diagnosed) <sup>d</sup> ++
		Physical activity (>3 hr/wk) -	Mammographic denisty (highest category vs. lowest) +++
		Monounsaturated fat <sup>c</sup> - (vs. saturated fat)	
		Low intake of fruits and vegetables <sup>c</sup> (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.

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

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

<sup>c</sup>Upper quartile (top 25%) versus lower quartile (lowest 25%).

<sup>d</sup>Clinically recognized chronic cystic, fibrocystic, or other benign breast disease versus none.

Willett et al., *Diseases of the Breast* 5th edition p.250, 2014

**Table 4. European Code Against Cancer: 12 ways to reduce your cancer risk\***

- 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 programmes for:
  - Hepatitis B (for newborns)
  - Human papillomavirus (HPV) (for girls).
- 12 Take part in organised cancer screening programmes for:
  - Bowel cancer (men and women)
  - Breast cancer (women)
  - Cervical cancer (women).

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

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