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Cancer Expert Working Group
On Cancer Prevention and Screening

Recommendations on Breast Cancer Screening

I. BACKGROUND

In 2004, the Cancer Expert Working Group on Cancer Prevention and Screening (the Working Group) concluded that:

- For the general female population in Hong Kong, routine breast cancer screening by breast self-examination (BSE) and mammography were not recommended, and there was insufficient evidence to recommend clinical breast examination (CBE); and

- For local women with previous history of breast cancer or atypical hyperplasia, or having first-degree relative(s) with breast cancer, there was insufficient evidence to recommend routine mammography screening for breast cancer.[1] These women were advised to be individually assessed by medical professionals to determine the appropriateness of regular surveillance for breast cancer through clinical breast examination and/or mammography.

2. In 2008, the Working Group started another round of discussion on breast cancer screening among the local general female population, taking into consideration studies on breast cancer screening in the general population published after 2004.[2-4] After deliberation, the Working Group maintained that BSE was not recommended as a tool for population-based breast cancer screening while there was insufficient evidence to recommend CBE. On the other hand, the Working Group revised that there was *insufficient evidence* to recommend for or against routine mammography screening for the general female population in Hong Kong. The Working Group agreed that there should be more research on the effectiveness of mammographic screening among Hong Kong women, as well as their attitude.

3. Regarding women at <u>increased risk</u> of breast cancer, in light of new evidence and updated guidelines in other countries[5-8] since 2004, the Working Group started to review the recommendations in high-risk women in Hong Kong in early 2009. In the process, the Working Group drew upon experience from overseas countries, and focused on new studies that bridge the critical evidence gaps identified in the previous review, i.e. the lack of studies linking mammographic screening to improved health outcomes in women at increased risk and a paucity of knowledge about the effectiveness of

supplementary breast cancer screening modalities in these women. This paper focuses on recommendations for women at increased risk.

II. EPIDEMIOLOGY OF FEMALE BREAST CANCER

Local burden of female breast cancer

4. Breast cancer has surpassed lung cancer as the most common cancer among females in Hong Kong since the early 1990's.[9] In 2006, there were 2 584 new cases of female breast cancer, accounting for 23.5% of all new cases of cancer in females.[10] The crude incidence rate was 72.0 per 100 000 female population and the age-standardised incidence rate was 52.1 per 100 000 world standard population. *

5. In 2007, being the third leading cause of cancer deaths among females, breast cancer caused 526 deaths in women and accounted for 11.2% of all cancer deaths. The crude mortality rate was 14.5 per 100 000 female population. The age-standardised mortality rate was 10.0 per 100 000 world standard population.

Local trend

6. Over the past two decades, the number of female breast cancer new cases and deaths are on a rising trend in Hong Kong. The incidence rate of breast cancer is still increasing after adjusting for the aging population. The age-standardised incidence rate has increased by 1.7% per year in females from 1983 to 2006 and is projected to increase to 54.3 per 100 000 world standard population in 2014 to 2018.[11] On the other hand, the age-standardised mortality rate is relatively stable from 1981 to 2007 without any statistically significant trend.

Comparison with other countries

7. According to GLOBOCAN 2002,[12] the world age-standardised incidence rate for breast cancer was 37.4 per 100 000 Segi standard population, while the rate for more developed regions and less developed regions were 67.8 and 23.8 per 100 000 Segi standard population respectively. In the period 1998-2002,[13] the average age-standardised incidence rate of breast cancer in Hong Kong was 41.3 per 100 000 Segi standard population †, which was about three-fifths of those reported in the Western populations.

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* The incidence rate is standardised according to a new world standard population specified in GPE Discussion Paper Series: No.31, EIP/GPE/EBD, World Health Organization, 2001.

† The incidence rate is standardised according to Segi standard population (Segi M 1960. Cancer mortality for selected sites in 24 countries 1950-57. Sendai, Tohoku University School of Public

8. On the other hand, when compared with other Asian countries (e.g. Singapore = 54.1, Japan = 32.0 to 42.5 and Korea = 23.3 per 100 000 Segi standard population †), Hong Kong's incidence rate (41.3 per 100 000 Segi standard population †) was intermediate to high in the region.[13]

III. RISK FACTORS FOR FEMALE BREAST CANCER

9. A range of factors determine a woman's risk of breast cancer. **Family history** is one of the main factors found to be associated with increased risk of breast cancer. Other risk factors include **personal factors** such as increasing age, reproductive and hormonal history, and behavioural factors such as physical inactivity and alcohol consumption. Most studies on the risk factors for breast cancer are carried out in Caucasian populations; however, studies in China have shown that the risk factors in Chinese are similar to those in Caucasians.[14, 15]

Family history

10. A positive family history is the strongest known predictive risk factor for breast cancer after increasing age.[16] For women with a family history of breast cancer, the risk of developing breast cancer increases with: [7, 17]

- increasing degree of relatedness with the affected family member(s) [first-degree relative(s) ‡ affected > second-degree relative(s) § > third-degree relative(s) **];
- increasing number of relative(s) who have developed breast cancer; and
- decreasing age at which the relative(s) developed breast cancer.

For women with a positive family history and especially for those whose relative(s) are diagnosed with breast cancer before 50 years of age, the risk of breast cancer is higher in the younger age groups[17] and the lifetime risk decreases with age (since 20 years of age) until it approaches the population level.[18]

Health), modified by Doll et al. (Doll R, Payne P, Waterhouse J 1966. Cancer incidence in five continents: a technical report. Berlin: Springer-Verlag). The WHO World Standard population has fewer children and notably more adults aged 70 and above than the Segi standard.

‡ First-degree relative(s): mother, father, daughter, son, sister and brother

§ Second-degree relative(s): grandparent, grandchild, aunt, uncle, niece and nephew, half-sister and half-brother

** Third-degree relative(s): great grandparent, great grandchild, great aunt, great uncle, first cousin, grand nephew and grand niece

11. Familial clustering of breast cancer may be the result of chance, a common lifestyle and/or environmental factors, or an increase in genetic susceptibility. Some of familial breast cancers can be explained by specific mutations in single cancer susceptibility genes, BRCA1 and BRCA2, which have been identified in the 1990's. Germline mutations in BRCA1/2 genes are autosomal dominantly inherited and are associated with an approximately 40% to 80% lifetime risk of breast cancer and a 15% to 40% lifetime risk of ovarian and certain other cancers.[6, 16] 50% of women with a BRCA1 mutation develop breast cancer by the age of 50.[19]

Personal risk factors

12. Established personal risk factors for female breast cancer include:[20-23]

- increasing age;
- history of atypical hyperplasia or lobular carcinoma in situ;
- previous breast cancer;
- previous ovarian or endometrial cancer;
- history of radiation therapy to the chest when younger than 30 years of age;
- increased breast density on mammogram;
- early menarche (< 12 years of age) or late menopause (> 55 years of age);
- nulliparity, late first live birth (> 30 years of age);
- obesity after menopause;
- hormone replacement therapy;
- not breastfeeding;
- alcohol consumption; and
- physical inactivity.

Prevalence of risk factors for female breast cancer in Hong Kong

13. In Hong Kong, currently there is no data on the prevalence of family history of breast cancer for the general population. Local prevalence of family history of breast cancer is only available for selected female populations. A study by a private breast care centre in Hong Kong revealed that among 11 408 asymptomatic women screened for breast cancer from 1999 to 2006, 15.0% had a family history of breast cancer.[4] On the other hand, overseas cross-sectional studies[16] have shown that 5% to 10% of women have a mother or sister with breast cancer, and about twice as many have either a first-degree relative or a second-degree relative with breast cancer. With increasing breast cancer incidence, screening and awareness, the proportion of women with a positive family history is expected to increase in Hong Kong.

14. The prevalence of BRCA1/2 mutations in the general population of Hong Kong is unknown. In Western countries, it is estimated that the

genetic mutations contribute to only 5% to 10% of overall breast cancer cases,[16] and these mutations are present in far less than 1% of the general population[24] despite that the prevalence is higher in certain ethnicities such as Ashkenazi Jews. Local studies has reported that there are relatively more BRCA2 mutations among Chinese breast cancer patients, when compared with those from the Western population where the majority of mutations are BRCA1 mutations.[16, 25]

15. Information on other personal risk factors is scarce in Hong Kong. A study performed by a private breast care centre in Hong Kong (the same study mentioned in paragraph 12) reported that among the women screened in their centre, 1.1% had a personal past history of breast cancer, 39.3% had early menarche, 17.2% had late menopause, 5.2% had their first pregnancy after the age of 35 and 28.2% were nulliparous.[4]

IV. OVERSEAS AND LOCAL EXPERIENCE ABOUT BREAST CANCER SCREENING FOR GENERAL WOMEN POPULATION

16. Currently, organized population-based breast cancer screening programme has been introduced in over 20 countries, including Asian countries such as Singapore. Most of the countries have adopted mammography as a screening tool.

17. Experiences from Western countries (e.g. United Kingdom and Australia) suggest that organized screening programmes are effective in terms of detection of tumors at an earlier stage and there is a reduction in mortality in their populations.

18. Nevertheless, mammography screening can also be harmful. Although the sensitivity and specificity of mammography in local studies were comparable to those overseas, the positive predictive value (PPV) in local studies is lower because of a lower prevalence of breast cancer in Hong Kong. The relatively low local PPV would generate more harm related to unnecessary interventions associated with false-positive screening results. It has been estimated that mammography screening resulted in 30% increase in over-diagnosis and over-treatment.

19. Besides clinical effectiveness, other factors like availability of local service, local acceptance and cost-effectiveness of programme should be considered before introducing a population-based screening programme in Hong Kong.

20. Data on its effectiveness in Asian population is not yet available. Furthermore, earlier local studies have concluded that mammography screening is not cost-effective. Nevertheless, given that the incidence rate of breast has increased substantially in the recent years, conclusions of these

earlier studies might no longer be valid. Moreover, local women's wishes should be assessed before making a decision whether or not to implement a population-based screening programme.

V. CEWG RECOMMENDATIONS ON BREAST CANCER SCREENING FOR GENERAL WOMEN POPULATION

Be breast aware

21. *The Working Group advises* that women, whether they are at average-risk or at increased risk of breast cancer, should be aware of the early symptoms of breast cancer[56], such as

- a change in the size or shape of the breast;
- a change in skin texture of the breast;
- a rash around the nipple(s);
- discharge from one or both nipples;
- new and persistent discomfort or pain in one part of the breast or armpit; and
- a new lump or thickening in the breast or armpit.

Women should visit their doctors promptly if these symptoms appear.

Secondary prevention of breast cancer screening for general women population

22. *The Working Group advises* that there is insufficient evidence to recommend for or against routine mammography screening for the general female population in Hong Kong.

VI. OVERSEAS EXPERIENCE ABOUT BREAST CANCER SCREENING IN WOMEN AT INCREASED RISK

A. RISK ASSESSMENT TOOLS OF FEMALE BREAST CANCER

23. The baseline (population) lifetime risk of breast cancer varies among different countries. The lifetime risks of breast cancer among women in Western countries are:

- 1 in 8 (12.3%) in the US,[24]
- 1 in 11 to 1 in 9 (9.1% to 11.1%) in the United Kingdom (UK);[26] and
- 1 in 11 (9.1%) in Australia[8] respectively.

(Hong Kong = 1 in 20 (5.0%)[10])

24. Various algorithms have been developed to predict individual woman's risk of developing breast cancer quantitatively, such as Gail model[27] and Claus model.[28] Different countries adopt different algorithms for assessing risk and also different criteria for stratifying risk.[5-8] While the criteria used in the US[5, 6] also include personal risk factors, the UK and Australia[7, 8] used family history only to estimate and stratify risk levels.

B. GENETIC TESTING FOR BRCA1/2 MUTATIONS IN WOMEN AT INCREASED RISK

25. Genetic testing for deleterious mutations in BRCA1/2 has important implications for the clinical management of individuals and families found to carry a mutation. It serves to identify those at very high risk of developing breast cancer for whom more aggressive surveillance (secondary prevention) or intervention such as chemoprevention or surgery[29] (primary prevention) may be considered.

26. Genetic testing for BRCA1/2 mutations is expensive.[30, 31] Genetic testing may lead to unnecessary investigations and interventions, and potential adverse ethical, legal, and social consequences, such as insurance and employment discrimination. Therefore, genetic counselling should be provided before genetic testing.[5, 32]

27. It has been recommended that genetic testing should only be offered to those most likely to carry clinically important BRCA1/2 mutations[32-34] or those whose family history is associated with an increased risk for BRCA1/2 deleterious mutations.[5] Several algorithms that predict the likelihood of carrying a BRCA1/2 mutation (distinct from the algorithms that predict breast cancer risk) are currently used in clinical practice overseas to identify such individuals;[35] however, there is no empirical evidence concerning the pre-test probability of an individual carrying a BRCA1/2 mutation that merits referral for genetic counseling and testing.[5] Some authors have proposed that genetic testing for BRCA1/2 mutations should only be offered to women who have at least a 10% risk of carrying a mutation.[34]

C. SECONDARY PREVENTION OF BREAST CANCER IN WOMEN AT INCREASED RISK

28. For women identified to be at increased risk of breast cancer, enhanced surveillance for early detection of breast cancer has been suggested as a secondary preventive measure. However, there is as yet no consensus on the:

(i) optimal screening modality or combination of modalities;
(ii) starting age of screening; and
(iii) screening interval.

Modalities of screening

(a) Mammography

29. Mammography has been the standard screening modality for women at increased risk of breast cancer, based on the assumption that early diagnosis and treatment in those at increased risk of breast cancer confers similar benefits of reduced breast cancer mortality as reported from randomised controlled trials of population mammographic screening programmes in average risk women.[36]

30. As yet, there have not been any randomised controlled trials of mammographic screening on women at increased risk. There is also a lack of study that assessed whether enhanced mammographic screening for population at increased risk affects breast cancer mortality.

31. Several observational studies that examined the effectiveness of mammographic screening in population at increased risk as compared with a control group, on the other hand, have concluded that mammographic screening for breast cancer in population at increased risk is effective, despite the differences in their study population, criteria for risk stratification, screening protocols and measures of effectiveness.[26, 37-42]

32. Most studies used surrogate outcomes such as cancer detection rates as the major outcome.[37-42] Only one study used survival as a primary outcome,[26] but the study only reported survival among breast cancer patients detected through enhanced mammographic screening, and whether there was improvement in overall survival of the screened group was not reported.

33. A recent overseas cost-effectiveness analysis[43] of mammographic screening among women less than 50 years of age at increased risk of breast cancer because of a family history reported that for women under the age of 50 even without proven BRCA1/2 mutations, annual mammographic screening was cost-effective in those with at least two relatives with breast cancer including a first-degree relative diagnosed before the age of 50.

(b) MRI

34. Although mammography is a reasonably sensitive test for screening post-menopausal women, it is less sensitive in younger women and those with a genetic predisposition to breast cancer. This has been attributed to increased mammographic density in pre-menopausal women which can obscure the radiological features of early breast cancer.[36] Furthermore, it has been suggested that cancers associated with BRCA mutations, in particular BRCA1, are more likely to have a benign appearance on mammography.[36] Therefore, a supplementary screening modality, contrast-enhanced MRI, has been proposed in addition to mammography in women at increased risk.

35. Emerging evidence that MRI is more sensitive than mammography for the detection of breast cancer, and expert opinion about the potential patient benefits have led to recent overseas guidelines recommending its use for the surveillance of women at increased risk in some countries.[6, 7]

36. In the UK, the National Institute for Health and Clinical Excellence (NICE) guidelines recommended annual screening MRI to women aged 30 – 49 at particularly high risk of developing breast cancer because of a strong family history †† and women aged 20 – 29 who were specific gene mutation carriers.[33]

37. In the US, the American Cancer Society recommended annual screening MRI for women with greater than 20% lifetime risk of breast cancer, including women with a strong family history of breast or ovarian cancer and women who were treated for Hodgkin's disease.[6]

38. It must be noted that although there is evidence that MRI leads to the detection of earlier stage disease, there has not been any study that assessed whether adding MRI reduces patient mortality, interval or advanced breast cancer rates. Conclusions about the value of MRI are therefore based on evidence of improved sensitivity and assumptions about the benefits of early detection in young women at increased risk extrapolated from mammographic screening trials undertaken in older average risk populations. Some overseas authorities, such as The United States Preventive Services Task Force (USPSTF), has thus concluded that the effect of this increased detection on mortality and morbidity remained unclear[32] although they recognised that MRI had higher sensitivity for detecting breast cancer among women with BRCA1/2 mutations.

39. While most of the studies of screening MRI have been carried out in women at increased risk because of a family history of breast cancer, the role of MRI in women at increased risk due to other risk factors is less clear. For example, the American Cancer Society concluded that there were several risk subgroups for which the available data were insufficient to recommend for or against screening MRI, including women with a personal history of breast cancer, carcinoma in situ (ductal and lobular), atypical hyperplasia,[44] and extremely dense breasts on mammography.[6]

40. Currently, MRI is not widely used for breast cancer screening, even in developed countries, because of its high cost, risks associated with injection of contrast, and limited availability of machines and personnel.[45]

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†† According to the degree of relatedness with the affected family member(s), no. of affected family members & the age of relative(s) at which breast cancer was diagnosed as discussed in **paragraph 9.**

(c) Ultrasound

41. Ultrasound, used as an adjunct to mammography in women with radiologically dense breasts, has the potential of depicting small, node-negative breast cancers not seen on mammography.[45] Ultrasound is relatively inexpensive, well tolerated, more widely available than MRI and requires no contrast.

42. However, there are currently few studies that compared the incremental accuracy of breast ultrasound as an addition to conventional screening tests in women at increased risk, and further studies are therefore needed to address the role of ultrasound before it can be promoted as a reasonable alternative to MRI in addition to mammography for screening these women.[46]

Starting age of screening

43. Overseas authorities have recommended that breast cancer screening in women at increased risk needs to start earlier in their lifetime and to repeat in shorter time interval than the general population.[6, 7, 47]

44. However, the age at which screening should be initiated for women at increased risk is not well established.[6] The argument for early screening is based on the higher cumulative risk of breast cancer at a younger age in women with BRCA1 mutations and/or a strong family history of early breast cancer.[7, 19] Some experts have suggested that breast cancer screening should begin 5 to 10 years before the earliest previous breast cancer in the family,[40, 42] or some time between the ages of 25 and 35 years for women with a BRCA1/2 mutation.[48]

45. However, the possibility of radiation-induced breast cancer may limit the starting age of mammographic screening in women at increased risk. Breast cancer susceptibility genes BRCA1/2 are responsible for DNA repair, thus it has been postulated that diagnostic radiation exposure, including mammography, poses more cancer risk in individuals with BRCA1/2 mutations than in women of average risk.[16] In addition, since the risks of radiation-induced breast cancer are age-dependent, younger breasts are also more susceptible to radiation-induced cancers,[49] thus compounding the increased risk even further in women at increased risk. In fact, the NICE guidelines of the UK recommend that mammographic screening should not be started before the age of 30.[7]

46. A recent study[50] determined the reduction in breast cancer mortality required to outweigh the radiation risk from five annual mammographic screenings in young (<40 years) BRCA mutation carriers. Assuming that the mortality reduction from mammography to be 15% – 25% or less for young women (which was extrapolated from studies on older women),

the study results suggested that there would be no net benefit from annual mammographic screening of BRCA mutation carriers at age 25 – 29 years; the net benefit would be zero or small at age 30 – 34 years, but there should be some net benefit at age 35 or older. The finding generally supported the recommendations from NICE.[7] However, it is not known whether the findings could be generalised to young women at increased risk of breast cancer due to risk factors other than BRCA1/2 mutations.

Frequency of screening

47. It has been observed that for women at increased risk of breast cancer, the progression from the preclinical detectable phase (PCDP) to the clinical phase is more rapid than that for women from the general population.[36, 37] The mean sojourn time (the mean duration of the preclinical detectable period) in a study on a group of women at increased risk of breast cancer[37] is 1.9 years, which is shorter than the 3.3 years for women aged 40 to 74 in the Swedish Two-County study,[51] a study on the general population. Therefore, it is generally accepted that surveillance in women at increased risk should be more frequent than that in the general population.

48. The American Cancer Society[6, 47] recommends annual mammography for women at increased risk of breast cancer, with the addition of annual MRI for women at particularly high risk.

49. On the other hand, for women at increased risk of breast cancer, the UK recommends annual mammographic screening before age 50 then every 3 years for those aged 50 and above.[33] However, the UK's recommendation for women aged 50 and above has been challenged by some studies as being too infrequent.[39]

VII. HONG KONG SITUATION OF BREAST CANCER SCREENING IN WOMEN AT INCREASED RISK

50. There are as yet no local studies on the effectiveness or cost-effectiveness of mammographic, MRI or ultrasound screening in women at increased risk of breast cancer in Hong Kong. Moreover, there is also a lack of locally validated tool for assessing the pre-test probability of carrying BRCA1/2 mutations and that for assessing breast cancer risk.

51. In Hong Kong, genetic testing services are limited and are only available in certain specialised centres such as the laboratories of universities and private breast cancer centres. Although criteria for recommendation for genetic testing have been proposed by a local study by the Prince of Wales

Hospital[52] ‡‡ and the Hong Kong Hereditary and High Risk Breast Cancer Programme[53] §§, there is as yet no local consensus on such criteria.

52. In addition, the uncertainty about the spectrum and prevalence of BRCA1/2 mutations in Chinese raises concern about the interpretability of gene testing results in Chinese. Variants of uncertain significance of BRCA1/2 mutations in Chinese may also cause substantial problems in counseling, particularly in terms of cancer risk estimates and risk management.[16]

53. Although certain local non-governmental organisations such as the Hong Kong Cancer Fund[54] and the Hong Kong Breast Cancer Foundation [55] have tried to define the at risk groups for local women, there is currently no consensus on risk stratification criteria. Apart from the Working Group's 2004 recommendations, there is as yet no other local published clinical guideline from medical professional organisations in Hong Kong about breast cancer screening in women at increased risk of breast cancer.

VIII. CEWG RECOMMENDATIONS ON BREAST CANCER SCREENING IN WOMEN AT INCREASED RISK OF BREAST CANCER

Be breast aware

54. *The Working Group advises* that women, whether they are at average-risk or at increased risk of breast cancer, should be aware of the early symptoms of breast cancer[56], such as

- a change in the size or shape of the breast;
- a change in skin texture of the breast;
- a rash around the nipple(s);
- discharge from one or both nipples;
- new and persistent discomfort or pain in one part of the breast or armpit; and
- a new lump or thickening in the breast or armpit.

Women should visit their doctors promptly if these symptoms appear.

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‡‡ The study concluded that the presence of a family history of early onset breast cancer (at age <45 years) in Chinese breast cancer patients may be an adequate indication for BRCA1 mutation analysis and subsequent pre-symptomatic screening of family members at risk.

§§ The Programme recommended genetic testing for the following individuals: multiple cases of early onset breast cancers in the same family; multiple cases of related cancers, especially of early onset, in the same family; ovarian cancer (with family history of breast or ovarian cancer); breast and ovarian cancer in the same woman; bilateral breast cancer; Ashkenazi Jewish heritage; male breast cancer.

Local definition of increased risk of female breast cancer

55. As there are no locally validated tools for breast cancer risk assessment, the Working Group has adopted a set of qualitative risk stratification criteria that include BRCA1/2 deleterious mutations carrier status; characteristics of family history (i.e. the degree of relatedness with the affected family member(s); number of affected family members and the age of relative(s) at which breast cancer was diagnosed; whether their relative(s) has ovarian cancer (as discussed in **paragraph 10 & 11**) and personal risk factors. *The Working Group considers* that local women with **any one** of the following risk factors are at increased risk of developing breast cancer:

High risk

1. A **carrier of BRCA1/2 deleterious mutations** confirmed by genetic testing.

2. **Family history** of
    a. **Any first-degree female relative** being a confirmed carrier of BRCA1/2 deleterious mutations;
    b. **Any first-degree or second-degree female relative** with both breast and ovarian cancer (in the same person) regardless of age at diagnosis;
    c. **Any first-degree female relative** with bilateral breast cancer,
    d. **Any male relative** with a history of breast cancer;
    e. **Two first-degree female relatives** diagnosed to have breast cancer AND one of them being diagnosed at or below 50 years of age;
    f. **Two or more first-degree or second-degree female relatives** with ovarian cancer regardless of age at diagnosis;
    g. **Three or more first-degree or second-degree female relatives** with breast cancer OR a combination of breast cancer and ovarian cancer, regardless of age at diagnosis.

3. Personal risk factors
    a. History of radiation to chest for treatment (not Chest X-Ray) between age 10 and 30 years, e.g. for Hodgkin's disease;
    b. History of breast cancer, including ductal carcinoma in situ (DCIS);
    c. History of lobular carcinoma in situ (LCIS);
    d. History of atypical ductal hyperplasia (ADH) or atypical lobular hyperplasia (ALH).

Moderately increased risk

4. **Family history** of

a. **Only one first-degree female relative** with breast cancer diagnosed at or below 50 years of age; or
b. **Two first-degree female relatives** diagnosed to have breast cancer after the age of 50.

56. First-degree female relatives include mother, daughter and sister. Second-degree female relatives include grandmother, grand-daughter, aunt, niece and half-sister.

Secondary prevention of breast cancer screening in women at increased risk

57. In order to detect breast cancer early and effectively in women at **high risk** of breast cancer because of BRCA1/2 deleterious mutations carrier status, a family history and/or personal risk factors (**55.1**, **55.2.a – 55.2.g** and **55.3.a – 55.3.d**), *the Working Group recommends* that they should see a cancer specialist, and:

- have breast cancer screening by mammography every year;
- begin screening at age 35 or 10 years prior to the age at diagnosis of the youngest affected relative (for those with a family history), whichever is earlier, but not earlier than 30 years of age.

58. For confirmed carriers of BRCA1/2 deleterious mutations (**55.1**) and women with radiation to chest for treatment between age 10 and 30 years, e.g. for Hodgkin's disease (**55**.**3.a**), *the Working Group recommends* that additional annual screening by supplementary MRI should be considered.

59. Women with only one first-degree female relative diagnosed to have breast cancer regardless of age at diagnosis (**55.4.a**), or two first-degree female relatives diagnosed to have breast cancer after the age of 50 (**55.4.b**) are regarded as having a **moderately increased risk** of developing breast cancer. They should discuss with their doctors about the pros and cons of breast cancer screening before deciding whether to start screening by mammography every two to three years. MRI is not recommended for them.

60. Bearing in mind that there is lack of local prevalence of breast cancer risk factors in Hong Kong and assuming a rough estimation of 5% risk factor prevalence[16], the Working Group expects that about 124,000 women aged 30 or above in Hong Kong*** would fulfil the criteria mentioned in **paragraph 55** above.

*** The mid-year population size for female age 30 years or above in 2008 in Hong Kong is 2,487,400.

Genetic testing for BRCA1/2 mutations in women at increased risk

61. *The Working Group recommends that* for women who have any first-degree female relative with confirmed BRCA1/2 deleterious mutations (**55.2.a**), genetic testing should be performed to confirm or refute their carrier status. This could reduce subsequent unnecessary investigations.

62. For women at high risk due to other types of family history (**55.2.b – 55.2.g**) who wish to clarify their genetic risk or that of their family, referral to a specialist cancer clinic for advice, counselling and management should be discussed and considered.

63. Genetic testing should be performed by specialised cancer centres with expertise in genetic counselling, which should be provided before genetic testing. Health care professionals should discuss with their clients in detail about the uncertainties and implications of the test results. Confirmed carriers of BRCA1/2 deleterious mutations who wish to consider prophylactic surgery / chemoprevention should also be referred to a specialist cancer clinic for advice and counselling.

Primary prevention for female breast cancer

64. Primary preventive measures are also important in lowering the risk of developing breast cancer. Women are advised to have regular physical activities, avoid alcohol and maintain a healthy body weight. Moreover, women are recommended to breastfeed each child for longer duration and have childbirth at an earlier age to lower their risk of breast cancer.

65. Health promotion on breast cancer prevention should also be enhanced to raise the awareness of breast cancer in the public.

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