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Projecting Individualized Absolute Breast Cancer Risk in Iranian women

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Abstract

Background: Iranian breast cancer patients are relatively younger than their Western counterparts. The objective of the present study was to investigate risk factors for breast cancer in Iranian women. Method: A case-control study was conducted from 2013 to 2014 in Iran. Demographical data and risk factor related information collected using a short structured questionnaire. Odds ratios (ORs) and 95% confidence intervals (CIs) were derived from logistic regression analysis. We used SAS 9.2 program to estimate risks and 95 % confidence intervals. Gail's model used to estimate within 5 years interval of age for the study participants.

Results: In all, 417 women with breast cancer and 823 control women were interviewed. In multivariate analysis, those women 40 – 49 years were less likely to get breast cancer than those were in older age groups, (OR=.147; CI, .041 -.524, OR=.183; CI, .048-.694 and OR=.156; CI, .029-.833 respectively). Menopause women more than 45 years than those less than 45 years had greater chance to having breast cancer (OR= 1.86; CI, 0.1.30-

2.67). There was not significant differences across the groups (case & control), according to married status. Odds ratio to having breast cancer in women used hormone was .75 more compare with those not using. Odds ratio women with having problem in breast than those without history to having breast cancer to having breast cancer was 1.94 more than those have not experience problem. Odds ratio women without having history of natural biopsy results than those with history to having breast cancer were 207 times greater. Odds ratio women with having history of unnatural biopsy results than those with no history were more likely to get breast cancer. The other variables did not exhibit a significant association with breast cancer. According to Gail's model relative risk (RR) for women less than 50 years compared to those who had all the risk factors than to those woman at the same age and without risk factors was 4.71 (SD=2.87). Relative risk women more than 50 years compared to those who had all the risk factors than to those woman at the same age and without risk factors was 3.77 (SD=2.47). Results of this study found absolute risk mean of developing breast cancer at for those who had risk factors was 1.27 (SD = .90).

Conclusion: The findings of the present study suggest that relative risk women less than 50 years was greater than those more than 50 years (OR = 4.71±2.87 versus OR = 3.77±2.47).

1. Background

The global context of breast cancer is complex. Although breast cancer incidence is lower in developing countries, the prognosis and survival are poorer relative to developed countries. For example, Iranian women are more likely be diagnosed with locally advanced disease [1]. Disparities in stage detection and survival may be related to differences in health behaviors. Early detection has been thought to be a key factor in reducing mortality from breast cancer: increased use of mammography is viewed as a promising way to reduce 65% of breast cancer deaths [2]. Although implementing mammography use has increased dramatically in developed countries, there are the challenges to find ways to enhance continuous, regular screening practices in developing countries like Iran. Results of several studies showed that, among women 40- year and older range of mammogram was and 5.7% to 12% [3], [4]. In order to improve breast health among women living in developing countries, it is imperative to address factors influencing screening practices. It is assumed that individuals act to prevent or control a disease when they believe it is likely they are at risk develop a disease (perceived estimated risk). Individualized Breast Cancer risk may contribute to elevated breast cancer screening behaviors [5, 6].

Absolute risk is used to describe an individual's likelihood of developing breast cancer. Some factors contribute to increase including the older age, family history, reproductive history (such as menstrual and childbearing history), race/ethnicity, and other factors. The absolute risk of breast cancer is much higher for women who have inherited mutations in the

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genes known as BRCA 1 or BRCA 2. For women with a BRCA 1 mutation, the risk of developing breast cancer by age 70 ranges from 55-65%. This means that out of every 100 women who have this mutation, anywhere from about 55 to 65 of them can expect to develop breast cancer should they live to age 70. For women with a BRCA 2 mutation, the risk is a bit lower, at 45%[7]. Relative risk is a number or percentage that compares one group's risk of developing breast cancer to another's. There known risk factors that increase relative risk for breast cancer. For example, age at menarche, age at first delivery, family history of breast cancer, and body mass index (BMI) (in post-menopausal women) [7]. Estimates of absolute risk can be used more correctly to estimate the risks and assistances of an intervention to prevent breast cancer if that intervention has side effects that increase the risks of other unfavorable health outcomes. For example, tamoxifen not only prevents breast cancer, but it also causes certain adverse events [8]. Many women have unrealistic concepts of their risks that can lead to poor management decisions. A woman with an overestimate of risk might take an extreme preventive action, such as prophylactic mastectomy, that is not necessary by her exact risk[8]. If the estimated risk is less than the actual value may prevent women from adopting appropriate screening. This has important implications for clinical cases [9]. Women at risk for breast cancer was estimated to be less than the actual value are less likely to follow medical advice and access in early detection and prevention methods [10]. It is likely that women with moderate size risk suffer unnecessary anxiety by overestimated risk [8]. Health care providers can use risk assessment tool to estimate a person's risk of developing breast cancer and provide advice

tailored to the risk factors on and screening behaviors. Absolute risk models may also play a role in the productive allocation of prevention resources under cost constraints [11]. Disease prevention attempts are often inhibited by restricted resources, and one approach to assign those resources is to direct them to those who stand to help the most, who are usually those at the highest risk of the disease[8, 12]. It is more important when there is not sufficient money to support a program of screening mammography for an entire population [11].

The models of absolute breast cancer risk are beneficial in clinical management and disease prevention [9, 13, 14]. In addition to giving important overall viewpoint to patients, such models can be used to assess risks and benefits of a preventive outcome formally [15, 16]. In the context of disease prevention, these models are useful for planning intervention trials, and for measuring the potential absolute reductions in disease risk that might result from reductions in modifiable exposures in the population [8, 17].

Rayna K. Matsuno showed by using the Data from 589 Asian and Pacific Islander American (APA) women with breast cancer and 952 women without breast cancer (control subjects) computed relative and attributable risks based on the age at menarche, number of affected mothers, sisters, and daughters, and number of previous benign biopsies. Relative and attributable risks for APA women were comparable to those in Breast Cancer Risk Assessment Tool (BCRAT). The authors concluded their developed model was calibrated to ethnicity-

specific incidence rates can be used for projecting absolute invasive breast cancer risk and for counseling APA women[16].

Mitchell H. Gail developed a model for projecting absolute risk of invasive breast cancer in African American women. Data from 1607 women with invasive breast cancer and 1647 control subjects were used to compute relative and attributable risks that were based on age at menarche, number of affected mother or sisters, and number of previous benign biopsy examinations. Results showed that 30.3% of African American women would have had 5-year invasive breast cancer risk. Using The Tool is recommended for counseling African American women regarding their risk of breast cancer[18].

Mitchell H. Gail de*nes absolute risk and some of its properties, and presents applications in breast cancer counseling and prevention. In these applications, it is important that the risk model be well calibrated, namely that it accurately predicts the numbers of women who will develop breast cancer in various subsets of the population. It also is discussed the potential use of risk models in allocating prevention resources under cost constraints and the risk assessment should not be expensive in comparison with the intervention [8].

Mitchell H. Gail suggested Absolute Risk Models for Subtypes of Breast Cancer can project the absolute risks of breast cancer subtypes may help identify women who could benefit from specific preventive interventions and improve estimates of total breast cancer risk [10].

Kimiko Ueda made individualized tool of developing breast cancer within 10-20 years and until life expectancy for Japanese women by multiplying the relative risk for each risk factor combination by the cumulative risk for the

reference group. The risk factors used were age at menarche, age at first delivery, family history of breast cancer, and body mass index (BMI) (in post-menopausal women). The relative risk by menopausal status for each risk factor combination was estimated from a case control study. Results indicated the highest risk group had about a 5 times higher risk probability of developing breast cancer than the general population at initial age 40, within 10- 20 years, and until life expectancy. The cumulative risk of breast cancer varied according to individuals' risk factors among Japanese women. The availability of concrete individualized risk estimation figures will be of use to health care providers in encouraging Japanese women to seek counseling and to adopt self-control of body weight as a primary preventive measure, as well as to have breast cancer screening [16].

2. Rationale:

Absolute risk' is the likelihood that an individual with a given set of risk factors and free of the disease of interest at age x will develop disease before a subsequent age x+ t, where t is the period of the interval over which risk is projected. Breast Cancer Absolute Risk Assessment Tools (BCARAT) has been used for counseling women and designing breast cancer prevention trials. Although BCARAT includes separate risk-prediction models for American and African American women, projections of absolute risk for Iranian women are based on data from those women only. Therefore, BCARAT includes a disclaimer for Iranian women. Inaccurate projections could result in misleading counseling of Iranian women and might mistakenly render some of them as eligible or ineligible for participation in breast cancer prevention

trials. As a result, It seems developing a model for Iranian women with variety of ethnicities include Kurdish, Balouch, Arab, Azeri Turkish, Turkmens, and Persians would provide a plenty of information for developing cancer prevention strategies.

3. Objectives:

3.1 General objective: Developing Individualized Absolute Invasive Breast Cancer Risk in Iranian women

3.2 Specific objectives:

1. Calculate of breast cancer relative risk among Iranian women across age groups.
2. Calculate of breast cancer ethnicity-specific relative risk in Iranian women.
3. Calculate of breast cancer attributable risk in Iranian women across age groups.
4. Calculate of breast cancer ethnicity-specific attributable risk in Iranian women.

4. Methodology

4.1 Study design

This research conducted as a Nested Case Control Study. Other estimates obtained using data from the cancer registry system in Iran, Iranian death registration system, and other studies, which had determined the burden of

breast cancer in the country.

4.2 Study setting / data sources

The data required for the nested case control study collected from Gilan, Kurdistan, Alborz, Hormozgan, Kermanshah provinces, which selected based on sampling methods. Absolute risk estimated on the basis of this information and through combining this information with other data which collected from the cancer registry data of Iran, the Iranian death registration system, and studies which determined the burden of breast cancer in the country [8, 18, 19].

4.3 Study population

The populations of this study were Iranian women. To select cases, the population of this study included the cancer patients; moreover, to choose the controls, sampling conducted among neighbors of the selected cases. The cases with breast cancer included those who pathologically diagnosed with cancer, as defined by the cancer care system of the country. The controls selected from among the neighbors of selected cases, who were at the same age.

4.4 Sampling method

This study designed so that to meet the study requirements in Iran. Accordingly, sampling method followed:

Country divided into five regions, including North, South, West, East, and the center. From each region, one province selected at random. The research team studied the list of patients with breast cancer, levied in each

city, who had been registered by the cancer registry system over the past two years. In proportion to the contribution of each province in each region, a specified number of patients selected from the list. For each case, two matched controls selected from among the neighbors of the selected cases who were the same age group [8, 16].

4.5 Sample size (sample size assumptions / estimation / size)

According to data from cancer registries in 1392 -1393 the fellow provinces selected in the following table:

	The selected provinces	The number of breast cancer cases in 1392-93	The needed number of cases in 1392-93	The needed number of controls in 1392-93
1	Gilan	350	120	240
2	Kurdistan	145	52	104
3	Alborz	314	108	216
4	Hormozgan	150	51	102
5	Kermanshah	200	69	138
Total	-	1159	400	800

The sample size, considering the number of cases of breast cancer in selected provinces in 1392-93, the sample size of patients and controls were as follows.

The procedures operated as follows:

1. A list of patients in 1392 to 1393 prepared in which the order were numbered from 1 to the last patients.

2. From the list of patients, the numbers of patients for each province based on the above table specified cases (patients with breast cancer) were randomized selected.
3. Based on the address of patents, visited and the questionnaire was completed.
4. For each case, two controls of the same age group were selected from their neighbors.

4.6 Data collection

Data collection method

Data collected via interviews, and using the questionnaire designed for this purpose (Appendix file No 1). The designed questionnaire assessed demographic factors and breast cancer risk factors. Breast cancer defined consistent with the definitions by the cancer registration system and pathologic diagnosis methods.

4.7 Data management plan

We used the data collected from 417 women with breast cancer and 823 women without breast cancer to calculate the relative and attribute risks by age at menarche, race, number of affected mothers, sisters and daughters, and number of previous benign biopsies.

4.8 Coordination, monitoring and quality control

The research team involved individuals with different specialties. At first, they wrote a protocol for the implementation of the project. In this protocol, the interviews and data collection methods determined. The research team considered advantage of all possible tools that would improve the quality of the study outcomes.

4.9 Ethical considerations:

As this research involved human subjects, the research ethics committee reviewed research on human subjects. We received an ethical approval for this research (Appendix file No 2).The written informed consent from human subjects needed in this research. Therefore, "informed consent form" used in our research. A copy of the "informed consent" form "used in the research is attached (Appendix file No 3).

4.10 Data Analysis

All follow steps were performed using SPSS version 22 and the significance level of 5% was reported. In the first stage descriptive results as frequencies and percentages for categorical variables and as mean and standard deviation for continuous variables reported (Tables 1 to 18), the quantitative and qualitative variables associated with breast cancer, were

classified on the basis of documents found in previous studies [9]. The quantitative variables were woman's age in year, age at the start of menstruation, age at the first live birth of a child, woman's age at menopause in year and number of previous breast biopsies. The qualitative variables included individual's race, the presence of atypical hyperplasia in any previous breast biopsy specimen, and the history of breast cancer among her first-degree relatives (mother, sisters, and daughters). The other variable contained use of hormone and married status (Tables 1-18).

Univariate logistic regression analysis was performed to calculate odds ratios (ORs) and to examine the predictive effect of each factor on risk for breast cancer, $P < 0.05$ was considered statistically significant. Those risk factors that were significantly associated with breast cancer were entered into a forward selection multivariate logistic regression analysis.

5. Results

5.1 Descriptive results

In the first stage descriptive results as frequencies and percentages for categorical variables and as mean and standard deviation for continuous variables have reported in tables 1-18.

5.2 Univariate and Multivariate logistic regression results

The results of univariate logistic regression analysis are shown in Tables 19 to 28. Those lived in rural areas were less likely to get breast cancer than urban citizens (OR= 1.52; CI, 0.1.08-2.15). Those women 40 – 49 and ≥ 70 years than those less than 40 years were less likely to get breast cancer than urban citizens (OR= 1.32; CI, 0.1.01-1.85 and OR= 1.78; CI,

0.1.00- 3.18 respectively). Menopause women more than 45 years than those less than 45 years had greater chance to having breast cancer (OR= 1.86; CI, 0.1.30-2.67). The comparison results was not significant across the groups (case & control), according to BMI categories [20]. BMI index values categorized below 18.5 (underweight), 18.5-24.9 (normal), 25.0-29.9 (Overweight) and 30.0 and above Menopause women more likely to get breast cancer than those no menopause (OR= 2.47; CI, 1.94-3.14). There was not significant differences across the groups (case & control), according to married status. Odds ratio to having breast cancer in women used hormone was .75 more compare to those not using. Odds ratio women with having problem in breast than those without history to having breast cancer to having breast cancer was 1.94 more than women have not had problem. Odds ratio women without having history of natural biopsy results than those with history to having breast cancer were 207 times greater. Odds ratio women with having history of unnatural biopsy results than those with no history were more likely to get breast cancer. The other variables did not exhibit a significant association with breast cancer.

The results of forward selection multivariate logistic regression displayed in Table 29, for variable location, city classification, for age in categories of 5 years, age less than 45 years as basis class considered as basis class. In terms of age of menopause, age less than 45 years, for marital status, single status, not having history of natural biopsy for the history of hyperplasia biopsy, having history of unnatural biopsy and for hormone use, not using were considered as basic class. The BMI index 18.5-24.9 range considered as basic class. The odds ratio of other classes

compared to basic class calculated reported. In addition, a 95% confidence interval for the odds ratio associated with the probability value detected. In order to provide more precise the estimates of the parameters using 1000 bootstrap subsamples re-estimation of parameters, Orthogonabias and the probability value have been reported (Tables 19 to 28). Results of logistic regression used for all variable are presented in Table 29 was similar univariate logistic regression used for all variables except location, BMI status, married status, hormone using, having problem history in breast.

5.3 Gail's model

Absolute risks calculated via combining this information with ethnicity-specific data so that to create Iranian Breast Cancer Study model (IBCS model). In addition, we used a multivariable relative risk model such as that described by Gail and Logistic Regression to find log odds parameters for the covariates.

We used SAS 9.2 program to estimate risks and 95 % confidence intervals. In this model, if data on national incidence required we used the data from the National Cancer Registry System, and if data on deaths by breast cancer required we used the data from national mortality registry system. In the next phase, Gail's model used to estimate within 5 years interval of age for the study participants. In Gail's model, eight variables entered as follow: early age and projection age. The should be in between 20 and 90 years, in current study a range of 5 years considered as projection age. Information having biopsy history and biopsy with atypical hyperplasia was coded as Yes and No. Next variables included age at first menarche and age at first live birth that were numbers correct. The last variable, in Gail's model there are 11 levels for race. Level 1 to 4 including white, black, Hispanic and American. The other races including Japanese, Chinese, Filipino, and other Asian races. In this study, the eleventh level (the other Asian races) considered for the participants (SAS output tables).

Based on the above risk factors and categorization, the total number of possible combinations (groups) is ⁄ = 3×2×3×4×3=216. The baseline age-specific hazard rate defined as the hazard rate for a patient who does not have identified risk factors. It is computed as the product of the observed age-specific composite hazard rate times the quantity of 1 minus the absolute risk[21]. Then, mean and standard deviation relative risk age and more than 50 years calculated (Table 30). According to Gail's model relative risk (RR) for women less than 50 years compared to those who had all the risk

factors than to those woman at the same age and without risk factors was 4.71 (SD=2.87). Relative risk women more than 50 years compared to those who had all the risk factors than to those woman at the same age and without risk factors was 3.77 (SD=2.47). Results of this study found absolute risk mean of developing breast cancer at for those who had risk factors was 1.27 (SD = .90) (Table 30). Given to reporting the errors in the 216 class required to spend more time, value this index has reported for the first 100 people. As well, absolute risk index and the average of the first women to 100 cases have reported.

6. Discussion

The mean age of patients with breast cancer in this study was 48.07± (12.15) years, which is consistent with the findings of previous studies in Iran and confirms a young age for breast cancer development in Iranian women [22].

The results showed high proportion of young breast cancer cases (31%). With regard to the findings from the current study, one may dispute that the relatively high proportion of young breast cancer cases in Iran is most likely due a to a young population structure and to a combination of high age at menarche and low age at first pregnancy, which are protective in later life [23]. Evidence from the USA [24] also suggests that, in some Asian subgroups such as the Vietnamese, women diagnosed with breast cancer tend to be younger than those from other racial or ethnic groups, with half of the diagnoses occurring in women younger than 50 years; this needs further exploration.

The findings of the present study are inconsistent with the published reports related to BMI and its association with breast cancer [25-27]. In the present study, the daily intake of fat was not assessed but an evaluation of fat intake was made through questions regarding the consumption of fatty food, such as fried food, high-fat dairy products, and mayonnaise, and the predominant method of cooking in the home. It appears that further research is needed on this issue.

There was no significant link between BMI and breast cancer incidence. One possible reason for the lack of a significant relationship in the present study is the measuring of BMI when a patient is already suffering from breast cancer; future studies should consider this matter. In the literature results of association between increased BMI and breast cancer incidence is mixed. For example in a study observed significantly stronger association between increased BMI and breast cancer incidence in the Asia-Pacific group (RR 1.18:1.11-1.26) than in European-Australian (1.05:1.00-1.09) and North-American group (1.06:1.03-1.08) (meta-regression $p<0.05$). No association between increased BMI and pancreatic cancer incidence (0.94:0.71-1.24) was shown in the Asia-Pacific group (meta-regression $p<0.05$), whereas positive associations were found in other two groups [28]. In a meta-analysis including 15 cohort studies involving 2,104,203 subjects and 3,414,806 person-years and 35 case-control studies involving 71,216 subjects. There was an inverse non-significant correlation between BMI and breast cancer risk during premenopausal period : OR = 0.93 (95% CI 0.86, 1.02); RR(i) = 0.97 (95% CI 0.82, 1.16); and RR(a) = 0.99 (95% CI 0.94, 1.05), but a direct and significant correlation during

postmenopausal period: OR = 1.15 (95% CI 1.07, 1.24); RR(i) = 1.16 (95% CI 1.08, 1.25); and RR(a) = 0.98 (95% CI 0.88, 1.09) [29].

Breast cancer patients in Iran are relatively young, and the findings presented here suggest that women 60 – 69 years than those less than 40 years were the most likely to get breast cancer (OR=.183; CI, 0.48 - 0.69). This is in accordance with other research findings indicating that older age as a strong risk factor to develop breast cancer [30].

Our results supported early menopause has been linked with a lower risk of breast cancer [31, 32]. Considerable research effort has been directed to understanding how the process of aging is linked to breast cancer development. Of note, the greatest increase in rate of breast cancer occurs during the pre- and early postmenopausal years [33].

The previous investigations revealed that breast cancer risk is concentrated in the 40 % of postmenopausal women for whom the process of lobular involution (LI) is delayed [34]. Our findings presented here reveal that women without having history of natural biopsy results than those with history to having breast cancer were 25 times greater. Radisky's study found among women with multiple biopsies, there was a significant association of higher breast cancer risk among those with involution stasis (lack of progression, HR 1.63) as compared with those with involution progression, p = 0.036. The majority of women in the multiple biopsy cohort showed progression of lobular involution (LI) status between benign biopsies, and extent of progression was highest for women who were in the pre-menopausal age range at initial biopsy. Progression of LI status between initial and subsequent biopsy was associated with decreased breast cancer

risk [32].

The lack of significant relations between breast cancer and the other variables studied was unexpected. For example, studies have shown that past oral contraceptive use is associated with a somewhat higher OR women who have a family history of breast cancer [23].

The proposed SAS macro makes it easy to implement the Gail model to assess the risk of breast cancer. By using several basic key risk factors, we can estimate a patient's breast cancer risk over a pre-determined time interval.

Absolute risk is used to describe an individual's likelihood of developing breast cancer. It is based on the number of people who will develop breast cancer within a certain time period. Absolute risk also can be stated as a percentage. Our results showed absolute risk mean of developing breast cancer at for those who had risk factors was 1.27 (SD = .90). Absolute risk cannot specify likelihood of developing breast cancer in individuals not exposed to risk factors. In facts, it does not indicate that exposure to risk factors increased risk of developing breast cancer or not. In total absolute risk does not help to carry out an explicit comparison.

The relative risk (RR) for women less than 50 years compared to those who had all the risk factors than to those woman at the same age and without risk factors was 4.71 (SD=2.87). while relative risk women more than 50 years compared to those who had all the risk factors than to those woman at the same age and without risk factors was 3.77 (SD=2.47). Our results suggested that women at age < 50 years had more chance of developing breast cancer than those who were > 50 years. Relative risk is a number or percentage that

compares one group's risk of developing breast cancer to another's. This is the type of risk frequently reported by research studies, which often compare groups of women with different characteristics or behaviors to determine whether one group has a higher or lower risk of breast cancer than the other (either as a first-time diagnosis or recurrence). Understanding relative risk can help to answer an important question: If a woman make certain lifestyle choices or have certain treatments, how much will she increase or decrease her risk of developing breast cancer or having a recurrence?

Conclusion

The study revealed that the risk factors for breast cancer among women in Iran are related to the relative risk women less than 50 years was greater than those more than 50 years (OR = 4.71±2.87 versus OR = 3.77±2.47).
The findings of the present study suggest menopause age more than 45 years may have an impact on the incidence of breast cancer in Iranian women (OR= 1.86; CI, 0.1.30-2.67). Therefore, the provision of menopause age more than 45 years for early breast cancer detection is recommended. The lack of significant associations between BMI status breast cancer and the other variables studied was unexpected. The daily intake of fat was not assessed but an evaluation of fat intake was made through questions regarding the consumption of fatty food, such as fried food, high-fat dairy products, and mayonnaise, and the predominant method of cooking in the home. It appears that further research is needed on this issue. Although the results cannot be generalized, the findings suggest that the association between some risk factors for breast cancer may differ in Iran as compared with western countries and familial breast cancer in young breast cancer patients deserves

further investigation.

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Appendix No 1.

Questionnaire

1. woman's age in year.

2. woman's age at the time of her first menstrual period in year.

3. woman's age at the time of her first live birth of a child in year.

4. woman's age at menopause in year.

5.Useofbirthcontrol Yes

No

If yes, how long (in month/year)

6. Use of hormone replacement therapy: Yes No

If yes, how long (in month/year)

7. Drinking alcohol: Yes No

8. Smoking: Yes No

9. Status of Married: Married Unmarried

10. History of breast-feeding: Yes No

If yes: how many

If yes: Long time in each time (in month/year)

11. Number of full pregnancy:

12. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?

13. Has the woman ever had a breast biopsy?

13 a. How many breast biopsies (positive or negative) has the woman had?

13 b. Has the woman had at least one breast biopsy with atypical hyperplasia?

14. woman's race/ethnicity?

14 a. What is the sub race/ethnicity?

15. Body mass index (BMI):

Weight:

Height:

Appendix No 2.

- Kurdistan University of Medical Sciences
Chancellor in Research Affair

14/5217/4100 Apr 26, 2015

To whom it may concern;

Kurdistan University of Medical Sciences Review Board confirms that the research entitled “Projecting Individualized Absolute Breast Cancer Risk in Iranian women” has been approved, and monitored scientifically and ethically in *Institutional Review Board* (IRB) of this university (MUK.REC.1394.4).

Farzin Rezaie

Kurdistan University of Medical Sciences

Vice-Chancellor in Research Affair

Kurdistan University of Medical Sciences

Vice-Chancellor in Research Affair

66177-13446 Pasdaran Ave,

Sanandaj, Iran. www.muk.ac.ir

Appendix No 3.

INFORMATION CONSENT

KURDISTAN UNIVERSITY OF MEDICAL SCIENCES

دانشگاه علوم پزشکی و خدمات بهداشتی درمانی کردستان

This Informed Consent Form is for the women we are inviting to participate in research on Estimate Individualized Absolute Breast Cancer Risk in Iranian women. The title of our research project is " Projecting Individualized Absolute Breast Cancer Risk in Iranian women".

Name of Principal Investigator: Dr Parvaneh Taymoori

Name of Organization: Kurdistan University of Medical Sciences

Name of Sponsor: world health organization

Name of Proposal and version: Projecting Individualized Absolute Breast Cancer Risk in Iranian women

Introduction

I am Dr Parvaneh Taymoori, working for the Kurdistan University Of Medical Sciences Research Institute. We are doing research on Breast Cancer disease, which is very common in this country. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, or the study staffs.

Purpose of the research

Absolute risk' is the likelihood that an individual with a given set of risk factors and free of the disease of interest at age x will develop disease. Breast Cancer Absolute Risk Assessment Tools (BCARAT) has been used for counseling women and designing breast cancer prevention trials. Although BCARAT includes separate risk-prediction models for American and African American women, projections of absolute risk for Iranian women are based on data from those women only. Therefore, BCARAT includes a disclaimer for Iranian women. Inaccurate projections could result in misleading counseling of Iranian women and might mistakenly render some of them as eligible or ineligible for participation in breast cancer prevention trials. The reason we are doing this research is to calculate BCARAT for Iranian women

Benefits

If you participate in this research, there may not be any benefit for you but your participation is likely to help us find the answer to the research question. There may not be any benefit to the society at this stage of the research, but future generations are likely to benefit.

Reimbursements

We will give you 3.5 $ for lost work time. You will not be given any other money or gifts to take part in this research.

Confidentiality

With this research, something out of the ordinary is being done in your community. It is possible that if others in the community are aware that you are participating, they may ask you questions. We will not be sharing the identity of those participating in the research.

The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except World Health Organization.

Sharing the Results

The knowledge that we get from doing this research will be shared with you through community meetings before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. After these meetings, we will publish the results in order that other interested people may learn from our research.

Right to Refuse or Withdraw

You do not have to take part in this research if you do not wish to do so and refusing to participate will not affect your treatment at this clinic in any way. You will still have all the benefits that you would otherwise have at this clinic. You may stop participating in the research at any time that you wish without losing any of your rights as a patient here. Your treatment at this clinic will not be affected in any way.

Who to Contact

1.1.1 If you have any questions, you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following:

1.1.2 Dr Parvaneh Taymoori: POSTAL ADDRESS:

1.1.3 Kurdistan University of Medical Sciences, Sanandaj,Iran, PO Box 66177-13391, Pasdaran Street, Sanandaj, Iran (Parvaneh.tay@gmail.com).

1.1.4 TEL: 98- 08731827468 09183737303

FAX: 98-87-33625131

This proposal has been reviewed and approved by Ref.WR/IRN/11/63, which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact

1.2 *WORLD HEALTH ORGANIZATIONREGIONAL OFFICE FOR THE EASTERN MEDITERRANEAN,*

(WHO/EMRO). 12TH Floor, building of the Minstary Of Health & Medical Education, Simaye-Iran street, phase 5, Shahrak-e-Qods,Tehran . 1467664951

P.O.Box: 1465-1565

Tel: +9821(88363979, 88363980, 88363718

Fax: +9821 88364100

E-mail:whoteh@ira.emro.who.int

It has also been reviewed by the Ethics Review Committee of the World Health Organization (WHO), which is funding/sponsoring/supporting the study.

Certificate of Consent

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant_____

Signature of Participant _____

Date _____

Day/month/year

If illiterate

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____ ***AND*** ***Thumb print of participant***

Signature of witness _____

Date _____

Day/month/year

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____

Day/month/year

Table 1. Number of cases and controls across selected provinces

XXX

	Case		Control	
	N	%	N	%
Kermanshah	106	25.4	210	25.5
Alborz	110	26.4	213	25.9
Kurdistan	52	12.5	103	12.5
Hormozgan	28	6.7	57	6.9
Gilan	121	29.0	240	29.2
Total	417	100.0	823	100.0

Table 2. Number and age percent groups across cases and control groups

Age groups	Case		Control	
	N	%	N	%
<40	130	31.2	313	38.0
40-49	126	30.2	221	26.9
50-59	82	19.7	163	19.8
60-69	56	13.4	93	11.3
>=70	23	5.5	31	3.8
Total	130	31.2	821	99.8

Table 3. Mean and SD of participant's age across case and control groups

	Mean (SD)
Control	45.82 (12.12)
Case	48.07(12.15)
Total	45.0 (14.14)

Table 4. Number and age percent groups across case and control groups and selected provinces

group(case or control)			City					Total
			Kermanshah	Alborz	Kurdistan	Hormozgan	Gilan	
control	<40	Count	137	59	23	44	50	313
		% within City	65.2%	28.0%	22.3%	77.2%	20.8%	38.1%
	40-49	Count	73	58	30	8	52	221
		% within City	34.8%	27.5%	29.1%	14.0%	21.7%	26.9%
	50-59	Count	0	57	26	4	76	163
		% within City	.0%	27.0%	25.2%	7.0%	31.7%	19.9%
	60-69	Count	0	32	16	0	45	93
		% within City	.0%	15.2%	15.5%	.0%	18.8%	11.3%
	>=70	Count	0	5	8	1	17	31
		% within City	.0%	2.4%	7.8%	1.8%	7.1%	3.8%

Total		Count	210	211	103	57	240	821
		% within City	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
case	<40	Count	68	19	11	8	24	130
		% within City	64.2%	17.3%	21.2%	28.6%	19.8%	31.2%
	40-49	Count	38	36	17	7	28	126
		% within City	35.8%	32.7%	32.7%	25.0%	23.1%	30.2%
	50-59	Count	0	26	12	7	37	82
		% within City	.0%	23.6%	23.1%	25.0%	30.6%	19.7%
	60-69	Count	0	22	8	3	23	56
		% within City	.0%	20.0%	15.4%	10.7%	19.0%	13.4%
	>=70	Count	0	7	4	3	9	23
		% within City	.0%	6.4%	7.7%	10.7%	7.4%	5.5%
Total		Count	106	110	52	28	121	417
		% within City	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Table 5. Education level of participants across case and control groups

Education level	Case		Control	
	N	Percent	N	Percent
lower diploma	271	65.0	543	66.0
diploma	93	22.3	185	22.5
undergraduate	42	10.1	85	10.3
post graduate	8	1.9	5	.6
Total	414	99.3	818	99.4

Table 6. Mean and SD of participant's age first menstrual period across case and control groups

group	Mean (SD)
Control	14.50 (.707)
Case	13.32 (1.42)
Total	13.28 (1.65)

Table 7. Mean and SD of participant's age at the time diagnosis breast cancer

	Mean (SD)
N	393
Case	45.53 (12.54)

Table 8. Mean and SD of woman's age at menopause across case and control groups

Group	Mean (SD)
Control	47.78 (4.96)
Case	45.86 (6.13)
Total	46.92 (5.59)

Table 9. Mean and SD of woman's age age at first live birth across case and control groups

Group	Mean (SD)
Control	21.66 (4.85)
Case	21.91 (5.32)

Total	19.50 (6.36)

Table 10. Number and percent BMI across cases and control groups

BMI	Case N & %		Control N & %	
<18.4	10	2.4	10	1.2
18.5-24.9	92	22.1	209	25.4
25-29.9	178	42.7	321	39.0
>30	102	24.5	231	28.1
Total	382	91.6	771	93.7

BMI >19.1= Low Weight, 19.1-26 = Natural Weight, < 26= Hipper Weight

Table 11. Number and percent hormone using across cases and control groups

Group			Frequency	Percent
Control		have/had	455	55.3
		not have/had	325	39.5
		Total	780	94.8
	Missing	System	43	5.2
	Total		823	100.0
Case		have/had	257	61.6
		not have/had	138	33.1
		Total	395	94.7
	Missing	System	22	5.3
	Total		417	100.0

Table 12. Number and percent duration of hormone using in year across cases and control groups

Group			Frequency	Percent
Control		lower one year	201	24.4
		1-2 years	89	10.8
		more than 2 years	211	25.6
		Total	501	60.9
	Missing	System	322	39.1
	Total		823	100.0
Case		lower one year	97	23.3
		1-2 years	55	13.2
		more than 2 years	125	30.0
		Total	277	66.4
	Missing	System	140	33.6
	Total		417	100.0

Table 13. Number and percent type of hormone used across cases and control groups

Group			Frequency	Percent
Control		0	74	9.0
		estrogen	29	3.5
		Composite (estrogen+ progestin)	328	39.9

		progestin	1	.1
		Estrogen + composite	4	.5
		Projection +composite	48	5.8
		Total	484	58.8
	Missing	System	339	41.2
	Total		823	100.0
Case		0	33	7.9
		estrogen	19	4.6
		Composite (estrogen+ progestin)	186	44.6
		Estrogen +composite	3	.7
		Projection +composite	35	8.4
		all types	1	.2
		Total	277	66.4
	Missing	System	140	33.6
	Total		417	100.0

Table 14.Number and percent alcohol using across cases and control groups

Group			Frequency	Percent
Control		yes	4	.5
		no	606	73.6
		Total	610	74.1
	Missing	System	213	25.9
	Total		823	100.0
Case		yes	2	.5
		no	306	73.4

		Total	308	73.9
	Missing	System	109	26.1
	Total		417	100.0

Table 15.Number and percent smoking across cases and control groups

group(case or control)			Frequency	Percent
Control		yes	16	1.9
		no	596	72.4
		Total	612	74.4
	Missing	System	211	25.6
	Total		823	100.0
Case	Valid	yes	11	2.6
		no	296	71.0
		Total	307	73.6
	Missing	System	110	26.4
	Total		417	100.0

Table 16. Number and percent family history breast cancer in first degree family across cases and control groups				
Group			Frequency	Percent
Control		yes	1	50.0
		no	1	50.0
		Total	2	100.0
		yes	277	33.7
		no	541	65.7
		Total	818	99.4
	Missing	System	5	.6
	Total		823	100.0
Case		yes	152	36.5
		no	264	63.3
		Total	416	99.8
	Missing	System	1	.2
	Total		417	100.0

Table 17. Number and percent married status across cases and control groups

Group			Frequency	Percent
Control		Unmarried	56	6.8
		Married	687	83.5
		Widow	78	9.5
		Total	821	99.8
	Missing	System	2	.2
	Total		823	100.0
Case		Unmarried	39	9.4
		Married	326	78.2
		Widow	50	12.0
		Total	415	99.5
	Missing	System	2	.5
	Total		417	100.0

Table 18. Number and percent biopsy history with breast across cases and control groups

Group			Frequency	Percent
		yes	1	50.0
		no	1	50.0
		Total	2	100.0
Control		yes	20	2.4
		no	787	95.6
		Total	807	98.1
	Missing	System	16	1.9
	Total		823	100.0
Case	Valid	yes	348	83.5
		no	66	15.8
		Total	414	99.3
	Missing	System	3	.7
	Total		417	100.0

Pairwise comparison results across the groups (case & control), are shown in Tables 19 to 29. Estimated ORs and 95% CIs are presented for each 2-level comparison.

Table 19. Odds ratio rural than urban area to having breast cancer

Logistic regression — Number of obs = 1031; LR chi2(1) = 5.71; Prob > chi2 = 0.0169; Log likelihood = -654.9958; Pseudo R2 = 0.0043

group	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
2.Location	1.528655	.2689367	2.41	0.016	1.082822	2.15805
_cons	.4712838	.0342238	-10.36	0.000	.4087612	.5433696

Those lived in rural areas were less likely to get breast cancer than urban citizens (OR= 1.52; CI, 0.1.08-2.15).

Table 20. Odds ratio women more than 40 years than those less than 40 years to having breast cancer

```
. logistic group ib(1).n_age

Logistic regression                             Number of obs   =       1238
                                                LR chi2(4)      =       7.73
                                                Prob > chi2     =     0.1019
Log likelihood = -787.10827                     Pseudo R2       =     0.0049

------------------------------------------------------------------------------
       group | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       n_age |
          2 |   1.372711   .2097537     2.07   0.038     1.017451    1.852017
          3 |   1.211232   .2070366     1.12   0.262     .8664247     1.69326
          4 |   1.449793   .2881299     1.87   0.062     .9820633     2.14029
          5 |   1.786352    .525757     1.97   0.049     1.003327    3.180473
            |
      _cons |   .4153355   .0433368    -8.42   0.000     .3385191    .5095829
------------------------------------------------------------------------------
```

Those women 40 - 49 and ≥ 70 years than those less than 40 years were less likely to get breast cancer than urban citizens (OR= 1.32; CI, 0.1.01-1.85 and OR= 1.78; CI, 0.1.00- 3.18 respectively).

Table 21. Odds ratio menopaused women more than 45 years than those less than 45 years to having breast cancer

```
. logistic group ib(2).age_mo

Logistic regression                                     Number of obs   =        543
                                                        LR chi2(1)      =      11.78
                                                        Prob > chi2     =     0.0006
Log likelihood = -367.69806                             Pseudo R2       =     0.0158

------------------------------------------------------------------------------
       group | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
   1.age_mo |   1.869337   .3422673     3.42   0.001     1.305678    2.676324
       _cons |   .6574074    .071024    -3.88   0.000     .5319536    .8124477
------------------------------------------------------------------------------
```

Menopaused women more than 45 years than those less than 45 years had greater chance to having breast cancer (OR= 1.86; CI, 0.1.30-2.67)

Table 22. Odds ratio women's BMI more than 18.5 – 24.9 than those were underweight (<18.5) and overweight to having breast cancer

```
Logistic regression                                     Number of obs   =       1153
                                                        LR chi2(3)      =       5.71
                                                        Prob > chi2     =     0.1265
Log likelihood = -729.41683                             Pseudo R2       =     0.0039

------------------------------------------------------------------------------
       group | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       N_BMI |
          1 |   2.271739   1.054964     1.77   0.077     .9142658    5.644747
          3 |   1.259718   .1967239     1.48   0.139     .9275676    1.710808
          4 |   1.003106   .1731256     0.02   0.986     .7152174    1.406874
            |
       _cons |   .4401914   .0550754    -6.56   0.000     .3444624    .5625243
------------------------------------------------------------------------------
```

The comparison results not significant across the groups (case & control), according to BMI.

Table 23. Odds ratio menopaused women than those less than no menopaused to having breast cancer

```
Logistic regression                               Number of obs   =       1240
                                                  LR chi2(1)      =      55.28
                                                  Prob > chi2     =     0.0000
Log likelihood = -764.15703                       Pseudo R2       =     0.0349

------------------------------------------------------------------------------
       group | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
1.n_age_mono~e |   2.471746   .3040507     7.36   0.000     1.942214    3.145651
       _cons |   .3301527   .0289496   -12.64   0.000      .2780205    .3920603
------------------------------------------------------------------------------
```

Menopaused women more likely to get breast cancer than those no menopaused (OR= 2.47; CI, 1.94-3.14)

Table 24. Odds ratio married women than no married to having breast cancer

```
Logistic regression                               Number of obs   =       1236
                                                  LR chi2(2)      =       4.88
                                                  Prob > chi2     =     0.0870
Log likelihood = -786.35317                       Pseudo R2       =     0.0031

------------------------------------------------------------------------------
       group | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     married |
           2 |   .681372   .1493142    -1.75   0.080      .4434596    1.046922
           3 |   .9204471   .2542812    -0.30   0.764      .5356083    1.581796
             |
       _cons |   .6964286   .1452486    -1.73   0.083      .4627518    1.048106
------------------------------------------------------------------------------
```

The comparison results not significant across the groups (case & control), according to married status.

Table 25. Odds ratio women used hormone than those without using to having breast cancer

```
Logistic regression                               Number of obs   =       1175
                                                  LR chi2(1)      =       5.01
                                                  Prob > chi2     =     0.0252
Log likelihood = -747.68703                       Pseudo R2       =     0.0033

------------------------------------------------------------------------------
       group | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
2.using_hor~e |    .751751   .0963068    -2.23   0.026     .5848259    .9663209
       _cons |   .5648352   .0440747    -7.32   0.000     .4847318    .6581758
------------------------------------------------------------------------------
```

Odds ratio to having breast cancer in women used hormone was .75 more than those without using.

Table 26. Odds ratio women with having problem in breast than those without history to having breast cancer

```
Logistic regression                               Number of obs   =       1233
                                                  LR chi2(1)      =      16.25
                                                  Prob > chi2     =     0.0001
Log likelihood = -780.78958                       Pseudo R2       =     0.0103

------------------------------------------------------------------------------
       group | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
1.problem_his~y |   1.943088   .3174439     4.07   0.000     1.410688    2.676418
       _cons |   .4604716   .0305408   -11.69   0.000     .4043401    .5243953
------------------------------------------------------------------------------
```

Odds ratio women with having problem in breast than those without history to having breast cancer to having breast cancer was 1.94 more than those without problem

Table 27. Odds ratio women without having history of natural biopsy

results than those with history to having breast cancer

Logistic regression				Number of obs	= 1221
				LR chi2(1)	= 943.95
				Prob > chi2	= 0.0000
Log likelihood = -309.97246				Pseudo R2	= 0.6036

group	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
1.biopsy_hi~y	207.4818	54.61768	20.27	0.000	123.8537	347.577
_cons	.0838628	.0107469	-19.34	0.000	.0652362	.1078077

Odds ratio women without having history of natural biopsy results than those with history to having breast cancer were 207 times greater

Table 28. Odds ratio women with having history of unnatural biopsy results than those without history to having breast cancer

Logistic regression	Number of obs	=	907
	LR chi2(1)	=	712.24
	Prob > chi2	=	0.0000
Log likelihood = -263.06917	Pseudo R2	=	0.5751

group	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
2.biopsy_history_unnat~l	.0041589	.0014982	-15.22	0.000	.0020528	.0084257
_cons	34.88889	11.79512	10.51	0.000	17.98522	67.67971

Odds ratio women with having history of unnatural biopsy results than those without history were more likely to get breast cancer.

Table 29. Multivariate logistic

Logistic regression

Number of obs	617
LR chi2(16)	515.48
Prob > chi2	0.0000
Log likelihood = -163.4924	
Pseudo R2	0.6119

group	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
2.Location	.5846062	.2481372	-1.26	0.206	.2544305	1.343252
n_age						
2	.6883744	.3507273	-0.73	0.464	.2535928	1.868584
3	.1473456	.0954475	-2.96	0.003	.0413948	.5244791
4	.1833129	.1245584	-2.50	0.013	.0483965	.6943396
5	.1568081	.1336541	-2.17	0.030	.0295022	.8334566
1.age_m	.9351648	.3854087	-0.16	0.871	.4169492	2.097458
N_BMI						
1	.8380636	1.071444	-0.14	0.890	.0683969	10.26875
3	2.29194	1.017544	1.87	0.062	.9600607	5.471519
4	2.20509	1.007547	1.73	0.084	.9005267	5.399533
1.n_age_monopose	11.75813	6.320678	4.58	0.000	4.099848	33.72163
married						
2	.3145771	.3110188	-1.17	0.242	.0453058	2.184241
3	.4116624	.4342621	-0.84	0.400	.0520727	3.254412
2.using_hormone	.6651931	.2077751	-1.31	0.192	.3606387	1.22694
1.problem_history	.8774781	.4360825	-0.26	0.793	.3312932	2.324128
1.biopsy_hisory	25.04022	13.97282	5.77	0.000	8.387931	74.75177
2.biopsy_history_unnat~l	.0582893	.0357584	-4.63	0.000	.0175148	.1939864
_cons	2.861862	3.402082	0.88	0.376	.2784646	29.41219

regression.

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BrCa_RAM, sas macro to project for BrCa absolute risk
Listing of All constants required for BrCa absolute risk projections

Ln Relative Risk: Beta

Beta	Gail lnRR White	CARE lnRR AfrnAmrcn	Gail lnRR Hispanic	Gail lnRR NativAmrcn	AABCS lnRR AsianAmrcn
N_Biop	0.529264	0.182212	0.529264	0.529264	0.552636
AgeMen	0.094010	0.267253	0.094010	0.094010	0.074993
AgeFst	0.218626	0	0.218626	0.218626	0.276383
N_Rels	0.958303	0.475724	0.958303	0.958303	0.791856
A50*NB	-0.288042	-0.111941	-0.288042	-0.288042	0
AF*NR	-0.190811	0	-0.190811	-0.190811	0

1-Attributable Risk: F(t)

AgeGrp	White	AfrnAmrcn	Hispanic	NativAmrcn	AsianAmrcn
Age< 50	0.578841	0.729499	0.578841	0.578841	0.475198
Age>=50	0.578841	0.743971	0.578841	0.578841	0.503164

Breast cancer composite incidences: h1*

5yr AgeGrp	SEER 1983:87 White	SEER 1995:03 White	1994:98 Afrn-Amrcn	1990:96 Hispanic	1983:87 NativAmrcn
[20:25)	0.0000100	0.0000120	0.0000270	0.0000200	0.0000100
[25:30)	0.0000760	0.0000747	0.0001130	0.0000710	0.0000760
[30:35)	0.0002660	0.0002438	0.0003109	0.0001970	0.0002660
[35:40)	0.0006610	0.0005878	0.0006764	0.0004380	0.0006610
[40:45)	0.0012650	0.0012070	0.0011944	0.0008110	0.0012650
[45:50)	0.0018660	0.0019762	0.0018739	0.0013070	0.0018660
[50:55)	0.0022110	0.0026201	0.0024150	0.0015740	0.0022110
[55:60)	0.0027210	0.0033402	0.0029111	0.0018570	0.0027210
[60:65)	0.0033480	0.0039744	0.0031013	0.0021510	0.0033480
[65:70)	0.0039230	0.0044876	0.0036656	0.0025120	0.0039230
[70:75)	0.0041780	0.0048945	0.0039313	0.0028460	0.0041780
[75:80)	0.0044390	0.0051611	0.0040895	0.0027570	0.0044390
[80:85)	0.0044210	0.0048268	0.0039679	0.0025230	0.0044210
[85:90)	0.0041090	0.0040407	0.0036371	0.0020390	0.0041090

Competing mortality excluding death from BrCa: h2

5yr AgeGrp	SEER 1985:87 White	SEER 1995:03 White	1996-00 Afrn-Amrcn	1990:96 Hispanic	1985:87 NativAmrcn
[20:25)	0.0004930	0.0004000	0.0007435	0.0004370	0.0004930
[25:30)	0.0005310	0.0004280	0.0010170	0.0005330	0.0005310
[30:35)	0.0006250	0.0005657	0.0014594	0.0007000	0.0006250
[35:40)	0.0008250	0.0008474	0.0021593	0.0008970	0.0008250
[40:45)	0.0013070	0.0012753	0.0031508	0.0011630	0.0013070
[45:50)	0.0021810	0.0018601	0.0044878	0.0017020	0.0021810
[50:55)	0.0036550	0.0028781	0.0063228	0.0026460	0.0036550
[55:60)	0.0058520	0.0046903	0.0096304	0.0042160	0.0058520
[60:65)	0.0094390	0.0078835	0.0147182	0.0069600	0.0094390
[65:70)	0.0150280	0.0127434	0.0211630	0.0108670	0.0150280
[70:75)	0.0238390	0.0208586	0.0326604	0.0168580	0.0238390
[75:80)	0.0388320	0.0335901	0.0456409	0.0251560	0.0388320
[80:85)	0.0668280	0.0575791	0.0683519	0.0418660	0.0668280
[85:90)	0.1449080	0.1377327	0.1327126	0.0894760	0.1449080

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BrCa_RAM, sas macro to project for BrCa absolute risk
Listing of All constants required for BrCa absolute risk projections

Breast cancer composite incidences: h1*

5yr AgeGrp	SEER 18 1998:2002 Chinese	SEER 18 1998:2002 Japanese	SEER 18 1998:2002 Filipino	SEER 18 1998:2002 Hawaiian	SEER 18 1998:2002 OtrPacIsl	SEER 18 1998:2002 OtrAsian
[20:25)	0.0000041	0.0000000	0.0000075	0.0000451	0.0000000	0.0000124
[25:30)	0.0000459	0.0000995	0.0000811	0.0000986	0.0000715	0.0000595
[30:35)	0.0001883	0.0002870	0.0002275	0.0003400	0.0002888	0.0001843
[35:40)	0.0004929	0.0005453	0.0005498	0.0008526	0.0006023	0.0004547
[40:45)	0.0009136	0.0011522	0.0011294	0.0016686	0.0007556	0.0007913
[45:50)	0.0014715	0.0018592	0.0018139	0.0025527	0.0007664	0.0010485
[50:55)	0.0014213	0.0026063	0.0022237	0.0033218	0.0018931	0.0013725
[55:60)	0.0019709	0.0032218	0.0026803	0.0053730	0.0023656	0.0014955
[60:65)	0.0016747	0.0040070	0.0028912	0.0052378	0.0028439	0.0016467
[65:70)	0.0018216	0.0035217	0.0025344	0.0055817	0.0029209	0.0014784
[70:75)	0.0018345	0.0035930	0.0024572	0.0056774	0.0023304	0.0012160
[75:80)	0.0019199	0.0035893	0.0022866	0.0065134	0.0020363	0.0010677
[80:85)	0.0022334	0.0035385	0.0018148	0.0038895	0.0014827	0.0013761
[85:90)	0.0022473	0.0020516	0.0017509	0.0029491	0.0010122	0.0006616

Competing mortality excluding death from BrCa: h2

5yr AgeGrp	SEER 18 1998:2002 Chinese	SEER 18 1998:2002 Japanese	SEER 18 1998:2002 Filipino	SEER 18 1998:2002 Hawaiian	SEER 18 1998:2002 OtrPacIsl	SEER 18 1998:2002 OtrAsian
[20:25)	0.0002106	0.0001736	0.0002291	0.0005635	0.0004655	0.0002126
[25:30)	0.0001926	0.0002958	0.0002630	0.0003696	0.0006005	0.0002422
[30:35)	0.0002444	0.0002283	0.0003148	0.0010199	0.0008511	0.0003016
[35:40)	0.0003179	0.0003632	0.0003945	0.0012340	0.0014783	0.0003691
[40:45)	0.0004733	0.0005906	0.0006476	0.0020983	0.0019315	0.0005430
[45:50)	0.0008003	0.0010861	0.0011702	0.0029829	0.0038666	0.0008939
[50:55)	0.0012175	0.0018600	0.0018094	0.0054024	0.0049249	0.0015152
[55:60)	0.0020998	0.0032166	0.0026142	0.0095915	0.0081771	0.0025747
[60:65)	0.0034369	0.0047194	0.0044833	0.0163155	0.0086382	0.0043244
[65:70)	0.0060974	0.0085353	0.0073937	0.0201522	0.0189747	0.0074196
[70:75)	0.0106645	0.0124335	0.0122331	0.0273548	0.0292576	0.0132518
[75:80)	0.0201487	0.0202302	0.0211271	0.0504470	0.0384090	0.0222914
[80:85)	0.0379908	0.0377255	0.0379370	0.0722620	0.0528696	0.0417466
[85:90)	0.0983339	0.1061491	0.0851385	0.1458445	0.0747457	0.0874858

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Table 30. Relative Risk for women less than 50 years compared to those woman ≥ 50 years

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BrCa_RAM, sas macro to project for BrCa absolute risk
Quick check for erromous records on input file

(# of records with errors is the # listed under the NMiss column in the 'AbsRsk' line)

The MEANS Procedure

Variable	Label	Mean	Std Dev
RR_Star1	Relative risk age lt 50	4.71722	2.87444
RR_Star2	Relative risk age ge 50	3.77483	2.47894

Table 31 . Relative risk for women less than 50 years compared to those woman ≥ 50 years

BrCa_RAM, sas macro to project for BrCa absolute risk
Quick check for erromous records on input file

IF MEAN OF 'Error_Ind' EQUALS 0, ERROR FREE. ERROR LISTING BELOW WILL BE EMPTY.
IF MEAN OF 'Error_Ind' IS NOT 0, ERRORS EXISTS. CHECK ERROR LISTING BELOW.

(# of records with errors is the # listed under the NMiss column in the 'AbsRsk' line)

The MEANS Procedure

Variable	Label	Mean	Std Dev
Absolute_Risk	Abs risk(%) of BrCa in age interval [T1,T2)	1.27744	0.90747

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The MEANS Procedure

Variable	Label	N	Sum	Mean
Absolute_Risk	Abs risk(%) of BrCa in age interval [T1,T2)	346	441.9953875	1.2774433
AbsRisk_Avg	Abs risk(%) of BrCa in age interval [T1,T2) for an Average Women	346	175.5685198	0.5074235

Variable	Label	Std Error	Minimum
Absolute_Risk	Abs risk(%) of BrCa in age interval [T1,T2)	0.0487857	0.0446964
AbsRisk_Avg	Abs risk(%) of BrCa in age interval [T1,T2) for an Average Women	0.0116270	0.0297408

Variable	Label	Maximum	Median
Absolute_Risk	Abs risk(%) of BrCa in age interval [T1,T2)	6.5965000	1.0820557
AbsRisk_Avg	Abs risk(%) of BrCa in age interval [T1,T2) for an Average Women	0.8112034	0.5537483

BrCa_RAM, sas macro to project for BrCa absolute risk
Listing of All constants required for BrCa absolute risk projections

Ln Relative Risk: Beta

Beta	Gail lnRR White	CARE lnRR AfrnAmrcn	Gail lnRR Hispanic	Gail lnRR NativAmrcn	AABCS lnRR AsianAmrcn
N_Biop	0.529264	0.182212	0.529264	0.529264	0.552636
AgeMen	0.094010	0.267253	0.094010	0.094010	0.074993
AgeFst	0.218626	0	0.218626	0.218626	0.276383
N_Rels	0.958303	0.475724	0.958303	0.958303	0.791856
A50*NB	-0.288042	-0.111941	-0.288042	-0.288042	0
AF*NR	-0.190811	0	-0.190811	-0.190811	0

1-Attributable Risk: F(t)

AgeGrp	White	AfrnAmrcn	Hispanic	NativAmrcn	AsianAmrcn
Age< 50	0.578841	0.729499	0.578841	0.578841	0.475198
Age>=50	0.578841	0.743971	0.578841	0.578841	0.503164