Knowledge, attitude and practice of breast cancer screening among female general practitioners in Riyadh, Saudi Arabia

Mohammed Yehia Saeedi[1], Fahad Al Amri[1], Ahmed Khair Ibrahim[2, *], Kassim Kassim[1]

[1]Deputy Ministry for Public Health, Assistant Deputy for Primary Health Care, Ministry of Health, Riyadh, Saudi Arabia
[2]Public Health & Community Medicine School, Faculty of Medicine, Assiut University, Asyut, Egypt

Email address:
ahmed.ibrahim7@med.au.edu.eg (A. K. Ibrahim), ahmed.khair@yahoo.com (A. K. Ibrahim)

Abstract: *Background:* Breast cancer has been ranked as the 1st cancer in women in Kingdom of Saudi Arabia. Screening, early detection and proper treatment of Breast Cancer was associated with more chances of better prognosis and long-term survival. The role general practitioner's role is to provide professional knowledge, skills and support for patients as well as their caregiver about screening and prevention. This study aimed to investigate the level of knowledge of Breast Cancer risk factors, beliefs, diagnosis and practice of Breast Self Examination, Clinical Breast Examination and mammography among female General Practitioners who are currently working in primary health care center in Riyadh city, Kingdom of Saudi Arabia. *Methods:* A cross-sectional study was conducted using a self-administered questionnaire among female physicians, currently working as General Practitioners in Primary Health Care centers were invited. Descriptive statistics: mean, standard deviation, frequencies, percentage were calculated. *Results:* The majority (90%) of the respondents believed that Breast Cancer is a major health problem and 96% were aware of the importance of mammography as a screening method. But only 19% of the studied physicians requested mammogram as screening tool for women aged 40 years or more. *Conclusion:* The current study demonstrated that knowledge about breast cancer screening was satisfactory and highlighted the need for the provision of continuing medical education programs to improve the general practitioners' practice on cancer screening tools.

Keywords: Breast Cancer, Mammography, Screening and General Practitioner

1. Introduction

Breast cancer (BC) is considered to be one of the most common malignancies and the second leading cause of cancer deaths in women after lung cancer, worldwide. It forms about 23% of all female cancers [1-3]. Breast cancer has become a significant problem in both developed and developing countries and the incidence rates are high in most of the developed areas [4]. The American Cancer Society (ACS) reported that one in eight women (12.3%) in the USA will develop breast cancer once in her lifetime and about 232,340 new cases of invasive BC discovered annually. Moreover, around 39 thousand BC deaths were expected among American women in 2013 [5].

The Kingdom of Saudi Arabia (KSA) is no exception, where BC has been ranked as the most common cancer in

females according to the Saudi Cancer Registry (SCR) in 2012 [6]. It has been reported that BC accounted for 25% of all newly diagnosed female cancers (5,205) in 2009. The median age at diagnosis was 48 years (19-99 years) with age-standardized rate (ASR) 22.7/100,000 [6, 7]. The highest ASR was recorded in five regions, Eastern region at 33.1/100,000, Riyadh region at 29.4/100, 000, Makah region at 26.4/100,000, Qassim region at 25/100,000 and Jouf region at 22.5/100,000 [6, 7].

Gulf Cooperation Council (GCC) countries reported that about 4480 BC cases were diagnosed during the period 1998-2002. BC represented 16.1% of all female cancers in Oman and 35.4% in Bahrain. The ASR per 100,000 was highest in Bahrain (46.4), followed by Kuwait (44.3), Qatar (35.5),

United Arab Emirates (19.2), Oman (14.4) and Saudi Arabia (12.9). These rates were lower compared with those of the most industrialized Western countries [7, 8]. The incidence increased after the introduction of mammography screening and continues to do so with the aging of the population [9]. Despite the low rate in the KSA, it was estimated that, by 2025, BC rate will be increased by around 350% and BC specific mortality by around 160% [10, 11].

ACS guidelines for early detection of BC in average-risk women consisted of a combination of regular clinical breast examination (CBE), counseling to raise awareness about BC symptoms beginning in the early twentieth and annual mammography beginning at the age of 40 [12, 13]. Women should undergo CBE every 3 years between the ages of 20 and 39 and annually after the age of 40 [14]. It should be part of the periodic health examinations [13, 14]. Breast self-examination (BSE) as a screening method is controversial. Data from a large randomized trial on BSE screening in Shanghai, china revealed that instruction in BSE has no effect on reducing breast cancer mortality [15].

Early detection and proper treatment of BC was associated with more chances for better prognosis and long-term survival [16]. The aim of BC screening is to advance the time of diagnosis so for earlier intervention leading to better prognosis [17]. However, earlier diagnosis leads to an increase in the apparent incidence of BC and resulted in lead-time bias, even if screening does not confer any benefit [18].

The role of the general practitioner (GP) is to provide professional knowledge, skills and support for patients as well as their caregiver about screening and prevention. Advocating for the patient and coordination of care is considered to be vital roles for GPs [19]. Consonant evidence showed that higher cancer screening participation rates were associated with greater involvement of primary care. Primary care providers are pivotal in reducing diagnostic delay, particularly in health systems that have long waiting times for outpatient diagnostic services. Several randomized controlled trials have shown primary care-led follow-up care to be equivalent to hospital-led care in terms of patient wellbeing, recurrence rates and survival, and might be less costly [20].

1.1. Aim

The current work aimed to investigate the level of knowledge of BC risk factors, beliefs concerning BC diagnosis and practice of BSE, CBE and mammography among female GPs, working in primary health care centers in Riyadh city, KSA.

2. Materials and Methods

2.1. Study Design and Study Population

A cross-sectional stud protocol was approved by Institutional Review Board (IRB) of the King Saud University (KSU) No. 14/4048/IRB. All female primary health (PHC) physician (N=180), who are currently working as GPs in PHC centers.

2.2. Data Collection

A pre-coded designed questionnaire was used to collect information from all participants. An invitation letter was attached to the questionnaire to explain the research objective, methods and expected benefits. The questionnaire was distributed then collected via the Cancer program coordinators in Riyadh city. All female GPs working in PHC centers of Riyadh city (n= 180) were invited and they were completely free to opt to participate or withdraw, without any consequence at any time prior to or at any point during or after the activity. They were informed that any information provided will be kept confidential and will be used only for the research purposes and will not be used in any way that can identify them.

2.3. Survey Instrument

The study questionnaire was adapted, after modification, from questionnaires used in similar studies carried out in the KSA and other countries. Literature review was used to add items on information of BC prevention and screening for questionnaire modification. Our study questionnaire is composed of 30 questions distributed over four sections as follows;

1 *Socio-demographic data:* age, marital status, job title, nationality and category of PHC
2 *Knowledge of BC screening:* different risk for BC were included; family history of BC, number of 1st degree relative with BC [14], Chest exposure to radiation, previous history of BC, breast feeding, age at first live birth, use of hormonal replacement therapy, obesity, benign breast disease [21], parity, early age at menarche, late age of menopause, begin a female and age at married [22]
3 *Attitude of GPs regarding BC screening and diagnosis*
4 *The last section addressed* the topic of GPs practice and was designed to elicit similar response of always, infrequent and never

2.4. Statistical Analysis

Data was verified and coded by the researcher. Analysis was carried out using the Statistical Package for Social Sciences (SPSS/PC/VER 21) [23]. To minimize data entry errors, check codes were incorporated into the database and the data were cleaned to ensure consistency of responses. Again, Frequency tables were examined to explore missing data, errors in the data and data consistency.

For questions that were unanswered, responses were left blank during data entry and treated as missing in the final analysis. Similarly, if more than one answer was selected, this was left blank during data entry and treated also as missing. Ten participants who failed to complete the majority of items were not included in the final analysis.

It has been proposed that for purposes of analysis replacing missing values can reduce bias and often is used

for this purpose if data are missing at random [24]. Descriptive statistics: mean, standard deviation, frequencies, percentage were calculated to the differences in KAP among the study participants.

3. Results

The study was carried out in Riyadh city for four months. All female PHC physicians were invited to participate (n=180). The response rate was 73.8% (n=133) and the completeness rate after excluding incomplete questionnaires was 91.7% (n=123).

Socio-demographic characteristics of the study participants were summarized in Table 1. Age ranged between 24 and 63 years (Mean = 40.2 ± 7.8), and a total (92.7%) were currently married. All participants possessed basic professional certificate while(48%) had additional post-graduate qualification in internal medicine, pediatric and Gynecology. Average length of practicing after graduation was (17.6 ± 6.7).
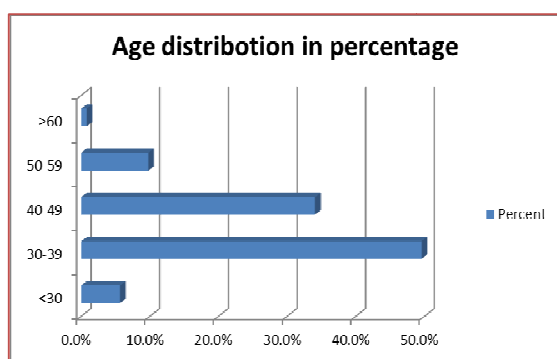

Figure (1). *Percentage of participant's age groups in the current study*

Table 2 depicted the participants' knowledge of breast cancer risk factors, signs and symptoms of BC and screening methods. The majority of respondents (90%) believed that BC is a major health problem and the most common cancer among female in the KSA. For the knowledge of BC risk factors, 82.1% of the participants identified increasing age as

a risk factors while 113 (91.9%) recognized family history of breast cancer as BC risk factor. Other risk factors were recognized by less than 60% of participants. The least recognized risk factor was being non-married (48.8%). More than (86%) participants were aware of the signs and symptoms that may be suggestive for BC. About 96% were aware of the importance of mammography as a screening method for breast cancer and 84.6% knew that the recommended age to start annual screening by mammography is 40. Ninety percent believed that BSE is an effective tool for BC diagnosis. Around 71% believed that regular CBE should be started at the age of 40 and annually.

Table (1). *Socio-demographic characteristics of participants*

Variable		Frequency	%
Age in years	<30	7	5.7%
	33-39	61	49.6%
	40-49	42	34.1%
	50- 59	12	9.8%
	≥60	1	0.8%
Marital status	Single	3	2.4%
	married	114	92.7%
	Divorced	4	3.3%
	Window	1	0.8%
	missing	1	0.8%
Nationality	Saudi	9	7.3%
	Non Saudi	112	91.1%
	Missing	2	1.6%
Practice after graduation	≤10 years	46	37.4%
	11 - 20	60	48.8%
	21 - 30	15	12.2%
	>30	2	1.6%
Professional qualification	Basic	58	47%
	Postgraduate	59	48%
	Missing	6	4.9%
Category of the PHC center	A	28	35.0%
	B	35	43.8%
	C	14	17.5%
	D	3	3.8%
Specialty	Internal medicine	11	8.9%
	Family medicine	64	52%
	Others	48	39%

Table (2). *Knowledge of BC risk factors*

Variable	Frequency	%
BC is the most common cancer among female in KSA	**111**	**90.2**
Risk factor		
Old age	101	82.1%
Early age of menarche	76	61.7%
late age at menopause	93	75.6%
Increase breast density	107	78%
Begin a female	75	61%
Being non married	60	48.8%
Nulliparity	90	73.1%
Hormonal replacement therapy	71	57.7%
Family history of breast cancer	113	91.9%
Radiation exposure to chest	79	64.2%
Signs and symptoms that may be suggestive BC		
Breast lump	106	86.2%
Recent nipple retraction	111	90.2%
Bloody discharge from nipple	116	94.3%
Skin discoloration	107	87%

Variable	Frequency	%
BC is the most common cancer among female in KSA	**111**	**90.2**
Mammography is the best way for screening method for breast cancer	118	95.9.%
The recommended age for mammography to started at the age of 40 and annually	104	84.6%
The breast clinical examination is recommended annually after age of 40	88	71.5%
Breast self-examination is an effective tool for diagnosis of breast cancer	111	90.2%

Participants' responses to inquires about attitude regarding BC screening were illustrated in tables 3. Ninety one participants (91%) have advised at least one member of their families to undergo BC screening. About 85% believed that BC can be diagnosed by PHC physician. About two thirds of the study cohort thought that their patients are aware of BC screening. Less than half (45.5%) were subscribed in at least one international medical journal and only 59% were aware about Saudi guideline for BC management.
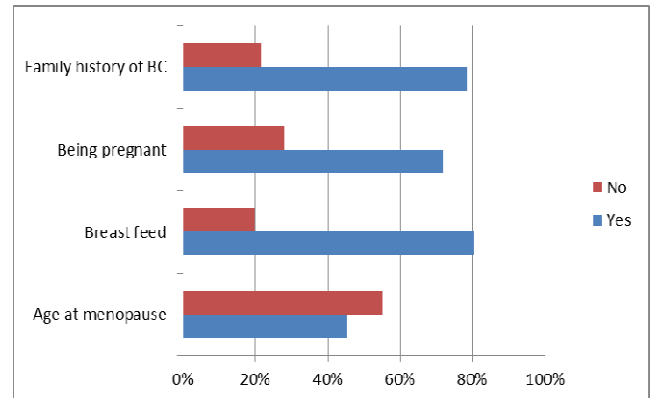
Table (3). Attitude regarding BC screening

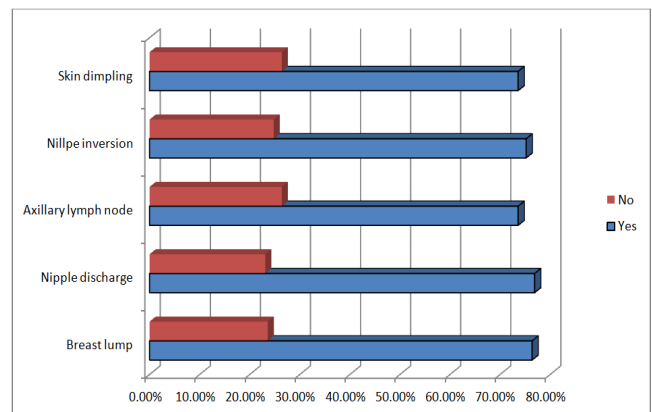| Variable	Frequency	%
Breast cancer can be diagnosed by primary health care physician?	104	84.6%
Do you think that your patients are aware of breast cancer?	79	64.2%
Did you aware of Saudi guideline for breast cancer management?	73	59.3%
Do you have any subscription in any medical journal or medical website?	56	45.5%
Have you ever advised a family member to undergo a mammogram	91	74%
Early diagnosis of BC affects survival.	118	95.9%

Tables 4 summarized the results of the questionnaire bout GPs practices. It showed that more than 70% of doctors were looking for the clinical signs of BC during CBE and less than 30% do not. Moreover, 69% asked about the most common risk factors as part of their routine medical history taking. Around 83.7% advised women to perform SBE. Only 19% of the studied physicians requested routine mammogram screening for all patients aged 40 years or more.

Table (4). Practice of physicians regarding history taking, CBE and mammography

	Yes	No
Did you ask about the following during medical history taking?		
Age at menopause	45%	55%
Breast feed	80.2%	19.8%
Being pregnant	71.9%	28.1%
Family history of BC	78.5%	21.5%
Did you often look for the following signs of breast cancer during clinical examination		
Breast lump	76.4%	23.6%
Nipple discharge	76.9%	23.1%
Axillary lymph node	73.6%	26.4%
Nillpe inversion	75.2%	24.8%
Skin dimpling	73.6%	26.4%
Did you request mammogram screening for all patients 40 years and above		
	19.1	80.9%
Did you advise your patients regularly to perform self-breast examination?		
	83.7%	16.3%

Figure 2. Identified risk factors during medical history taking

Figure 3. Percentage of looking for signs of BC during clinical examination

4. Discussion

The main goal of BC screening program is to detect cancers cases at early stage or even before starting of symptoms. The patient's survival and line of treatment depend heavily on early diagnosis. BCE, BSE and mammography were recognized as effective screening methods for BC and the adoption of mammography screening has led to reduction in mortality from the disease in women over 50 years [25]. Knowledge level, attitude and practice of health care providers toward BCS are important factors in the control of breast cancer. It was proposed that health will be improve in a society in which health personnel play an active role in health education and peruse a good role model in the society [26]. GPs should be aware of the BC risk factors in order to guide the patients for the necessary screenings modalities [3].

The current work was carried out to know the level of knowledge, beliefs and practice among all female GPs (n=123) who are working in PHC in Riyadh city toward BCS

from Feb. to June 2014. The majority of participants (90.2%) believed that BC is the most common cancer among female in KSA, this was consistent with study in Morocco published in 2011, in which all doctors (n=44) believed that BC is a major health problem in their country [27]. Another study in Nigeria in 2009 reported that 86.7% had the same believe [28].

The most common risk factors for BC identified by participants were; family history of BC (91.9%), old age (82.1%), increase breast density (78%), late age at menopause (75.6%) and radiation exposure (64.2%). The least known were: hormonal replacement therapy (57.7%) and nulliparity (48.8%). A similar study in Morocco showed that the all participants (100%) identified the fallowing as risk factors for BC, family history of BC, late age at menopause, nulliparity, early menarche at the age of less 12 years, history of previous benign breast lump and use of oral contraceptive pills. The least known were old age and first childbirth at the age of 30 years (44%)[27]. In contrast, the Nigerian study showed that (95.6%) of doctors identified increasing age as a risk factor while (80%) recognized current use of oral contraceptive pills as breast cancer risk factor. Other risk factors were recognized by less than three-quarters of participants. The least recognized risk factors were nulliparity (73.3%) and advanced age at first childbirth (57.8%) [28]. An Australian study revealed that GPs have limited knowledge about some aspects of BC risk factors with only quarter of them recognized increasing age as breast cancer risk factor [29]. In the United Kingdom, a study of General Practitioner's knowledge about BC risk factors showed that more than half of the participants were able to correctly identify risk factors assessed [30].

The American cancer society guidelines for cancer screening recommended annual mammogram and CBE for women above the age of 40 years. Furthermore, monthly BSE is made optional with emphasis on the importance of breast self-awareness outside a structured BSE [30]. In the current study the majority of participants (96%) were aware of the importance of mammography as a screening tool for BC and 84.6% knew that the recommended age to start screening is 40 years and annually but only 19.1% requested mammogram as screening for all patients 40 years and above due to unavailability of mammogram in PHC center or lack of cooperation and social and cultural barrier. Similar results reported in 2011 by Meissner, et al., in the USA where 94.6% of general Practitioner recommended mammography to women aged 40 to 49 years on an annual basis and 99.5% recommended annual mammography to women aged > 50 years [31].

Ninety percent of participants knew that BSE is an effective tool for diagnosis of BC while 71.5% believed that regular CBE should be started at age of 40 and should be carried annually. Cockburn et al., reported that 95% of general practitioners believed that BSE and BCE were important for asymptomatic women of more than 45 years of age compared with the 75% of respondents who viewed mammography in the same way as a screening method for

early breast cancer[29]. In Meissner's study, the majority of primary care physicians (96.5%) recommended annual CBE to all women aged > 40 years [31]. Ghanem, et al., in 2011 found that all participated physician were aware of BSE and CBE [32]. In current study 95.9 % of participants believed that early detection and treatment of breast cancer affects survival. Also, all participants (100%) in Ghanem, et al., study believed that BC is curable if detected early [27] and 91.1% in Ibrahim et al., [28].

Primary care physicians played a key role in performing and referring patients for cancer screening and previous research indicated that the practices of physicians and other healthcare providers were not necessarily consistent with clinical guidelines [32]. Furthermore, it is unknown to what extent clinical guidelines motivate physician's practice or which barriers or facilitators to implementation of clinical guidelines were associated with changes in practice recommendations [31, 33]. In the current study, 45.5% subscribed in at least one of the international medical journal and only 59.3% of participants were aware about Saudi guideline for breast cancer management. But, in a study by Meissner et al., most of the PHC (82.5%) identified at least one BC screening guideline as being very influential in their practice [31]. About 75% of participants of the current study have advised at least one member of their families to undergo a mammogram and 83.7% have advised their patients regularly to perform SBE which is higher than that of Al-Amoudi's study where only 63.5 % did [10].

The National Comprehensive Cancer Network (NCCNI) group continues to recommend CBE for BC screening [14]. More importantly, preliminary results from a new cluster randomized trial from Mumbai, India suggested that CBE, in fact, facilitates the down-staging of breast cancer in countries where women were commonly presented with advanced stage disease at time of diagnosis [10]. In the current study more than 70% of doctors looked for the clinical signs of BC during CBE but in Al-Amoudi 's study 78.4% perform breast examination if there is a complaint and 11.3% for every patient [10].

5. Conclusion

Up to our knowledge this is the first study to investigate the knowledge, attitude and practice of female GPs in PHC centers regarding BC in Riyadh, KSA. We anticipated that it will provide a baseline to monitor changes over time. The results demonstrated that the knowledge of breast cancer risk factors was satisfactory. A bigger study is recommended to cover all GPs in the KSA to monitoring their beliefs, attitude, and practices and understand how best to incorporate the latest scientific evidence regarding breast cancer prevention and early detection into healthcare practice. Also, a future survey should be conducted to compare the level of knowledge among GPs with different socio-demographic and professional characters.

References

[1]   Bray, F., et al., Global estimates of cancer prevalence for 27 sites in the adult population in 2008. Int J Cancer, 2013. 132(5): p. 1133-45.

[2]   Soerjomataram, I., et al., Global burden of cancer in 2008: a systematic analysis of disability-adjusted life-years in 12 world regions. Lancet, 2012. 380(9856): p. 1840-50.

[3]   Stojadinovic, A., et al., Consensus recommendations for advancing breast cancer: risk identification and screening in ethnically diverse younger women. J Cancer, 2011. 2: p. 210-27.

[4]   Cancer Facts &Figures. Atlanta: American Cancer Society, in2012.

[5]   DeSantis, C., et al., Breast cancer statistics, 2013. CA Cancer J Clin, 2014. 64(1): p. 52-62.

[6]   Al-Eid , H., Cancer Incidence Report Saudi Arabia 2009 S. Bazarbashi and A. Al-Zahrani, Editors. decemcer 2012.

[7]   Ravichandran, K. and A.S. Al-Zahrani, Association of reproductive factors with the incidence of breast cancer in Gulf Cooperation Council countries. East Mediterr Health J, 2009. 15(3): p. 612-21.

[8]   Abdurrahman Al Diab, S.Q., Khalid A. Al Saleh,, A.A. Farjah H. Al Qahtani, Mohammed A. Alghamdi, A. Alsaif,, and V.F.Q.a.M.R.Q. Areej A. Bokhari, Review on Breast Cancer in the Kingdom of Saudi Arabia. Middle-East Journal of Scientific Research, 2013. 14 ((4)): p. 532-543.

[9]   E. Senkus1, S.K., F. Penault-Llorca3,4, P. Poortmans5, A. Thompson6, S. Zackrisson7 & F. Cardoso8,9, on behalf of the ESMO Guidelines Working Group*, Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Annals of Oncology, August 2013. 24 ((Supplement 6)): p. vi7–vi23.

[10] Al-Amoudi, S.M., W.A. Sait, and H.S. Abduljabbar, Health care provider's role in facing the future burden of breast cancer in Saudi. Saudi Med J, 2010. 31(12): p. 1359-62.

[11] Ibrahim, E.M., et al., The present and the future of breast cancer burden in the Kingdom of Saudi Arabia. Med Oncol, 2008. 25(4): p. 387-93.

[12] Chiarelli, A.M., et al., The contribution of clinical breast examination to the accuracy of breast screening. J Natl Cancer Inst, 2009. 101(18): p. 1236-43.

[13] Smith, R.A., et al., Cancer screening in the United States, 2010: a review of current American Cancer Society guidelines and issues in cancer screening. CA Cancer J Clin, 2010. 60(2): p. 99-119.

[14] Bevers, T.B., et al., NCCN clinical practice guidelines in oncology: breast cancer screening and diagnosis. J Natl Compr Canc Netw, 2009. 7(10): p. 1060-96.

[15] Thomas, D.B., et al., Randomized trial of breast self-examination in Shanghai: final results. J Natl Cancer Inst, 2002. 94(19): p. 1445-57.

[16] Mittra, I., et al., A cluster randomized, controlled trial of breast and cervix cancer screening in Mumbai, India: methodology and interim results after three rounds of screening. Int J Cancer, 2010. 126(4): p. 976-84.

[17] Independent, U.K.P.o.B.C.S., The benefits and harms of breast cancer screening: an independent review. Lancet, 2012. 380(9855): p. 1778-86.

[18] Marmot, M.G., et al., The benefits and harms of breast cancer screening: an independent review. Br J Cancer, 2013. 108(11): p. 2205-40.

[19] Group., N.Z.G., Suspected Cancer in Primary Care: Guidelines for investigation, referral and reducing ethnic disparities. Ministry of Health, Wellington, 2009.

[20] Emery, J.D., et al., The role of primary care in early detection and follow-up of cancer. Nat Rev Clin Oncol, 2014. 11(1): p. 38-48.

[21] Singletary, S.E., Rating the risk factors for breast cancer. Ann Surg, 2003. 237(4): p. 474-82.

[22] Richie, R.C. and J.O. Swanson, Breast cancer: a review of the literature. J Insur Med, 2003. 35(2): p. 85-101.

[23] IBM-SPSS. Statistical package for social science. Ver.21. Standard version. SPSS Inc.; 2012, .

[24] P, A., Missing data, Sage University Series on Quantative Applications in the Social Sciences. . 2001: Sage Publications, Thousand Oaks, CA.

[25] Olsen, A.H., et al., Breast cancer mortality in Copenhagen after introduction of mammography screening: cohort study. BMJ, 2005. 330(7485): p. 220.

[26] Koçak S, Ç.L., Özbaş S, et al, Risk factors in breast cancer, risk assessment and prevention: 2010 Istanbul consensus meeeting report. The J of Breast Health, 2011. 7: p. 47-67.

[27] Ghanem, S., et al., Knowledge of risk factors, beliefs and practices of female healthcare professionals towards breast cancer, Morocco. Pan Afr Med J, 2011. 10: p. 21.

[28] Ibrahim, N.A. and O.O. Odusanya, Knowledge of risk factors, beliefs and practices of female healthcare professionals towards breast cancer in a tertiary institution in Lagos, Nigeria. BMC Cancer, 2009. 9: p. 76.

[29] Cockburn, J., et al., Encouraging attendance at screening mammography: knowledge, attitudes and intentions of general practitioners. Med J Aust, 1989. 151(7): p. 391-6.

[30] Bekker, H., L. Morrison, and T.M. Marteau, Breast screening: GPs' beliefs, attitudes and practices. Fam Pract, 1999. 16(1): p. 60-5.

[31] Meissner, H.I., et al., Breast cancer screening beliefs, recommendations and practices: primary care physicians in the United States. Cancer, 2011. 117(14): p. 3101-11.

[32] Richards, M.A., et al., Influence of delay on survival in patients with breast cancer: a systematic review. Lancet, 1999. 353(9159): p. 1119-26.

[33] Klabunde, C.N., M.S. O'Malley, and A.D. Kaluzny, Physicians' reactions to change in recommendations for mammography screening. Am J Prev Med, 1997. 13(6): p. 432-8.