Prevention of breast cancer

Knowledge and attitudes about genetic testing and mammography

Dina Aresvik

Thesis submitted as a part of the Master Thesis

Department of Health Management and Health Economics
The Faculty of Medicine

UNIVERSITY OF OSLO

June 2016
© Dina Mikhailovna Aresvik

2016

Prevention of breast cancer- Knowledge and attitudes about genetic testing and mammography

Dina Mikhailovna Aresvik

http://www.duo.uio.no/
Abstract

Breast cancer is the second most common cancer worldwide, and the second leading cause of cancer death in women. The greatest risk factor for breast cancer is inheritance of a mutation in one of the breast cancer susceptibility genes, BRCA1 and BRCA2. Mutation in those genes is also a risk factor for developing ovarian cancer. Early detection of cancer is associated with earlier intervention and more successful outcomes. The aim of our study was to access knowledge and attitudes about genetic testing and mammography screening among supporters of Norwegian Breast Cancer Association.

A cross-sectional design was employed. An internet based questionnaire that assessed knowledge of genes and genetic testing, use of genetic testing, personal breast cancer history, attitudes about genetic testing as well as attitudes about mammography screening and sociodemographic characteristics was distributed by Norwegian Breast Cancer Association on their home- and Facebook pages. Two hundred and twenty-five people responded to the survey.

On average, respondents answered 7 (IQR 5-8) of 11 items on knowledge about BRCA testing correctly. The percentage of correct responses on the knowledge instrument ranged from 18% to 98%, with the lowest knowledge on risk of ovarian cancer after a prophylactic surgery. Responders who had undergone BRCA1/2 testing had significantly higher knowledge than those who had not undergone testing (p<0.001). In those who had not undergone genetic testing, there was no difference (p=0.856) in total score BRCA knowledge between those with personal history of breast cancer (median 6, IQR 4-7) and those with no personal history of breast cancer (median 6, IQR 5-7). In those who have undergone gene testing, responders with a personal history of breast cancer had significantly lower (p<0.001) levels of overall knowledge compared to individuals with no personal history of breast cancer. Personal history of genetic testing (beta=-0.332, p<0.001), age (beta=0.174, p=0.007) and educational level (beta=0.153, p=0.016) predicted total hereditary breast and ovarian cancer knowledge.

Our study demonstrates less than expected knowledge about hereditary breast and ovarian cancer in a group with personal history of genetic testing, which was expected to have a high knowledge. Our results underline the importance of genetic counseling.
Disclaimer

The author planned the study under supervision of Eli Feiring and in collaboration with Eline Aas and Norwegian Breast Cancer Association. Based on survey developed at Department of Health Management and Health Economics, Faculty of Medicine, University of Oslo in 2009, the new questionnaire was developed further by the author. The author also developed internet based survey, which was distributed by the Norwegian Breast Cancer Association. All statistical analysis was performed by the author, who also was responsible for writing the manuscript.
Acknowledgements

The present work was carried out at the Department of Health Management and Health Economics, Faculty of Medicine, University of Oslo during the years 2015-2016.

I want to thank all persons who have supported me through this period.

First, I want to thank my supervisor Eli Feiring for giving me support and liberty to explore different aspects of this thesis. I appreciate all our discussions throughout this period and believe it has matured my mind. Your support and positive attitude is much appreciated.

Second, I want to express gratitude to Eline Aas who initiated the project and stimulated my interest for this particular project.

I am also very thankful to Norwegian Breast Cancer Association for valuable feedbacks on the questionnaire and for distributing the survey.

Finally, I am deeply grateful all participants who took the time and effort to complete the survey.
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA</td>
<td>Breast cancer, early onset</td>
</tr>
<tr>
<td>CA-125</td>
<td>Cancer antigen 125</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>HBOC</td>
<td>Hereditary breast and ovarian cancer syndrome</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile range</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>NBCA</td>
<td>Norwegian Breast Cancer Association</td>
</tr>
<tr>
<td>NCHGR</td>
<td>National Center for Human Genomic Research</td>
</tr>
<tr>
<td>PTEN</td>
<td>Phosphatase and tensin homolog</td>
</tr>
<tr>
<td>TP53</td>
<td>Tumor protein p53</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
Publications included

I. Aresvik DM, Feiring E.

Knowledge about hereditary breast and ovarian cancer among women who underwent BRCA testing.

Manuscript
# Table of contents

1  Introduction........................................................................................................ 1

1.1  Cancer.............................................................................................................. 1

1.1.1  Benign and Malignant Tumors................................................................. 1

1.1.2  Cause of Cancer......................................................................................... 1

1.2  BRCA 1 and BRCA 2..................................................................................... 3

1.3.  Breast Cancer............................................................................................... 4

1.3.1  Cause of Breast Cancer............................................................................. 4

1.3.2  Treatment of Breast Cancer....................................................................... 5

1.3.3  Prognosis of Breast Cancer....................................................................... 5

1.4  Ovarian Cancer............................................................................................... 6

1.4.1  Cause of Ovarian Cancer........................................................................... 6

1.4.2  Treatment of Ovarian Cancer.................................................................... 6

1.4.3  Prognosis of Ovarian Cancer.................................................................... 6

1.5  Cancer Screening............................................................................................. 7

1.5.1  Criteria for Population Screening.............................................................. 7

1.5.2  Screening for Breast Cancer...................................................................... 8

1.5.3  Screening for Ovarian Cancer................................................................... 10

1.6  Hereditary Breast and Ovarian Cancer and Genetic Testing..................... 10

1.6.1  History of BRCA Testing......................................................................... 11

1.6.2  Challenges of BRCA Testing..................................................................... 11

1.6.3  Genetic Counseling in Norway................................................................. 12

1.6.4  Prevention of Hereditary Breast and Ovarian Cancer............................ 12

2  Aims.................................................................................................................. 14

3  Methods........................................................................................................... 15

3.1  Design and Setting......................................................................................... 15

3.2  Measures....................................................................................................... 15

3.2.1  Sociodemographic and medical characteristics....................................... 15

3.2.2  Knowledge about HBOC......................................................................... 15

3.2.3  Attitudes towards Genetic Testing........................................................... 16

3.2.4  Attitudes towards Mammography Screening........................................... 16

3.2.5  Translation of International Scales........................................................... 16

3.3  Data analysis................................................................................................ 16

4  Summary of the Results.................................................................................... 18
<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Discussion</td>
<td>19</td>
</tr>
<tr>
<td>5.1</td>
<td>Methodological Aspects</td>
<td>19</td>
</tr>
<tr>
<td>5.2</td>
<td>Recall of Medical Information</td>
<td>21</td>
</tr>
<tr>
<td>6</td>
<td>Conclusions</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>Reference List</td>
<td>24</td>
</tr>
<tr>
<td>8</td>
<td>Paper I</td>
<td>27</td>
</tr>
<tr>
<td>9</td>
<td>Appendix: Questionnaires</td>
<td>49</td>
</tr>
<tr>
<td>9.1</td>
<td>Questionnaire to Breast Cancer Survivors – 2009</td>
<td>50</td>
</tr>
<tr>
<td>9.2</td>
<td>Questionnaire Genetic Testing and Mammography</td>
<td>55</td>
</tr>
</tbody>
</table>
1 Introduction

1.1 Cancer

Cancer is one of the leading causes of morbidity and mortality worldwide [1] and the second leading cause of death in Norway [2]. The incidence of cancer is increasing and it is estimated that annual cancer cases worldwide will rise from 14 million in 2012 to 22 within the next 2 decades [1].

Neoplasia means “new growth” and is defined as an abnormal mass of tissue the growth of which exceeds and is uncoordinated with that of the normal tissues [3]. Neoplasms are referred to as tumors, and are divided into benign or malignant tumors. Interestingly, already Hippocrates reported to have distinguished benign from malignant growths. He was also the first to describe breast cancer [4].

1.1.1 Benign and Malignant Tumors

Benign tumors are well differentiated, slow progressive, well-demarcated masses that do not invade or infiltrate the surrounding normal tissue or spread to other sites. They are generally amenable to local surgical removal and patients generally survives [3].

Malignant tumors are collectively referred as cancers. The word cancer is derived from the Latin word for crab and the term was first introduced w by Hippocrates, who named tumors karkinos, because tumor cells adhere to any part that they seize on in an obstinate manner, similar to the crab [3, 4]. Malignant tumors are not well differentiated, they are locally invasive, infiltrating the surrounding normal tissues and they can spread to distant sites (metastasize). Not all cancers lead to death, when discovered early, some cancers can be successfully treated [3]

1.1.2 Cause of Cancer

The incidence of neoplastic disease increase with age, and most cancer mortality occurs between age 55 and 75 years [3]. The greater longevity in modern times necessarily enlarges the population at risk. In previous generations humans did not live long enough to develop many cancers that are particularly common in middle and old age [4]. The rising incidence with age may be explained by a combination of decline in immune competence
and the accumulation of somatic mutation [3]. Other main cancer risk factors worldwide are tobacco smoking, chronic alcohol consumption, unhealthy diet and physical inactivity. In addition, some chronic infections, such as Hepatitis virus B and C, as well as some types of Human Papilloma Virus and Epstein-Barr Virus, increase the risk for certain type of cancer [1, 3, 4]. Ultraviolet radiation, exposure to radiation carcinogens, such as therapeutic and diagnostic use of x-ray, exposure to physical carcinogens such as asbestos or chemical carcinogens such as aromatic amines or nitrosamines are other cancer risk factors [4].

Many type of cancers, among the most common forms such as breast cancer, exist not only environmental influences but also hereditary predispositions [3]. Hereditary forms of cancer can be divided into three categories: Inherited Cancer Syndromes, Familial cancers and Autosomal Recessive Syndromes of Defective DNA Repair. About 5% to 10% of all human cancers will fall into one of the three aforementioned categories [3].

_Inherited cancer syndromes_

Inherited cancer syndromes are uncommon cancers, such as familial retinoblastoma, in which inheritance of a single mutant gene significantly increases the risk of a person’s developing a tumor. These tumors often are associated with a specific marker phenotype and show an autosomal dominant pattern of inheritance [3].

_Autosomal Recessive Syndromes of Defective DNA Repair_

Autosomal Recessive Syndromes of Defective DNA Repair are a small group of familial disorders, such as xeroderma pigmentosum, which are characterized by chromosomal DNA instability leading defective DNA repair and, thus, to cancer development [3].

_Familial cancers_

Virtually all the common type of cancers that occur sporadically, for example breast, ovarian and colon cancers, have been reported to occur in familial forms [3]. Features that characterize those tumors include early age at onset, cancers arising in two or more close relatives, and often multiple or bilateral neoplasms. In contrast to inherited cancer syndromes, the familial cancers are not associated with specific marker phenotypes. Further, the transmission pattern of familial cancers is not clear. Research has shown that predisposition to the tumors is dominant, but multifactorial inheritance can not be easily
ruled out. Certain familial cancers can be linked to the inheritance of mutant genes, for example breast cancer 1, early onset (BRCA1) and breast cancer 2, early onset (BRCA2) genes are associated with familial breast and ovarian cancer [3].

1.2 BRCA 1 and BRCA2

The greatest risk factor for breast and ovarian cancer is inheritance of a mutation in one of the breast cancer susceptibility genes, BRCA1 and BRCA2 (BRCA1/2) [5]. Both BRCA1 and BRCA2 are large, complex genes which act as tumor suppressor genes. BRCA1 is located on chromosome 17q21.3 while BRCA2 is located on chromosome 13q12.13, and their coding region show no homology to each other, nor to other known genes [3, 5, 6]. The function of BRCA1/2 genes is to regulate DNA repair, but proteins encoded but those genes work at different stages in the DNA damage response. The links between the two proteins are not well understood, but because the marked similarity of human cancer susceptibility that arises with germline mutations in those genes, it is hypothesized that such links must exist [5]. The role of those genes in nonhereditary sporadic breast cancer is less clear, because mutations are infrequent in those tumors [6]. Mutations in BRCA1/2 are inherited in an autosomal dominant pattern. This means that only one mutated copy of the gene is necessary for a person to be affected, it may originate from maternal or paternal side and the chance a child will inherit the mutated gene is 50% [7, 8]. If one copy of either gene is mutated in the germ line, the result is hereditary breast and ovarian cancer (HBOC) syndrome [5]. Approximately 3%-5% of breast cancer and 4%-11% of ovarian cancer are due to germline mutations in BRCA1 and BRCA2 genes [7, 9]. Less than 1% of the general population is estimated to carry a mutation in BRCA1/2 [7, 10]. Carriers of BRCA mutations have a relative increased lifetime risk of breast cancer of 2.7-6.4 times, and a relative lifetime risk of ovarian cancer of 9.3-35.3 times greater than average risk women, with the greatest proportions in cancers diagnosed before 50 years of age [7, 10]. Moreover, carriers of BRCA1/2 mutation have a higher risk of developing cancer in prostate, pancreas, bile ducts, stomach, larynx, fallopian tube and melanocytes [5, 6]. The estimated frequency of developing other common malignancies associated with a mutation in BRCA genes is only 0.1% for prostate cancer and 0.5% for pancreatic cancer. However, the relative risk is significantly increased, up to 20-fold for prostate cancer and 10-fold for pancreatic cancer [5]. However, the penetrance, or the lifetime risk of developing cancer up to the age of 70 years, of BRCA mutations is still a matter of research [11].
1.3 Breast Cancer

Breast cancer is the second most common cancer worldwide, after lung cancer. In Norway and worldwide, breast cancer is the most common malignancy diagnosed in women, and the second leading cause of cancer death in women [10, 12, 13].

1.3.1 Cause of Breast Cancer

The risk of breast cancer is multifactorial and is an interaction between environmental, lifestyle, hormonal and genetic factors [8, 12]. A large number of risk factors that modify a woman’s likelihood of developing breast cancer have been identified [6, 8]. The incidence of breast cancer increases with age, doubling about every 10 years until the menopause, after menopause a flatterning of the age-incidence curve is seen. Reproductive patterns have been shown to play an important role. Nulliparity and first live birth at late age both increase the lifetime incidence of the breast cancer [6, 8]. Age at menarche and menopause influence the breast cancer risk as well. Thus, women who start menstruating early in life or who have a late menopause have an increased risk of developing breast cancer [8]. There is an interaction between development of breast cancer and nursing habits, as breastfeeding for over six months protects from breast cancer [6]. Further, prolonged exposure to exogenous estrogens postmenopausal, oral contraceptives, ionizing radiation, obesity, alcohol consumption, diet high in fat and cigarette smoking have been shown to increase the risk of breast cancer. There are geographic variations in the incidence and mortality rates from breast cancer. Thus, the risk of breast cancer is significantly higher in North America and northern Europe than in Asia and Africa. These differences appear to be environmental rather than genetic as migrants from low to high incidence countries tend to acquire the rates of their adoptive countries, and vice versa [3, 8].

Heredity breast cancer

About 80% of hereditary breast cancer are due to mutations in BRCA1/2, where is about half of women have mutations in BRCA1 and an additional one third have mutations on BRCA2 [6]. Less common genetic diseases associated with breast cancer are the Li-Freumeni syndrome which is caused by germ-line mutations in TP53, Cauden disease caused by germline mutations in PTEN, and carriers of ataxia teleangiectasia gene [6, 14]. In order to explain increased prevalence of breast cancer in some families who do not carry
mutations in neither BRCA1 nor BRCA2, researchers have tried to identify BRCA3 gene. BRCA3 have not been discovered, however, it can be due to the low penetrance of the mutations [11]. Woman are more likely to carry a breast cancer susceptibility gene if they develop breast cancer before menopause, have bilateral cancer, have other associated cancers such as ovarian cancer, have a significant family history, or belong to a certain ethnic groups. Studies of BRCA1/2 mutation frequencies have identified great differences in population from different geographic regions and ethnicities [15]. For example, Ashkenazi Jewish population have an unusually high prevalence of germline BRCA1/2 mutations [15], while in Norway BRCA1 mutation have been shown to be more frequent in South-West Norway [16].

1.3.2 Treatment of Breast Cancer
Treatment of breast cancer depends on the stage and the type of the cancer [17]. Mastectomy is recommended for multifocal or large tumors, while smaller single tumors are suitable for breast conservation surgery. For those requiring mastectomy, both immediate and delayed breast reconstructions are available. Postoperative radiotherapy is always recommended as it reduces the risk of local recurrence and has a beneficial effect on survival. Primary systemic therapy is indicated for locally advanced breast cancer and for large operable tumors for reducing tumor size in order to possibly perform surgery. Patients with endocrine responsive tumors may receive endocrine treatment alone or in a combination with chemotherapy [17].

1.3.3 Prognosis of Breast Cancer
Breast cancer typically spreads to the lymph nodes, than lungs, skeleton, liver, adrenals and brain. However, breast cancer may metastasize almost to any organ or tissue in the body. Unfortunately, metastasis may appear many years after apparent therapeutic control of the primary lesion [6].

The most important prognostic factors for breast cancer are the size of the primary tumor, presence of the lymph node (local) metastasis as well as distant metastasis. In addition, invasion of the chest wall, ulceration of the skin and the clinical appearance of inflammatory carcinoma are associated with poor prognosis. These features are used to
classify women into prognostic groups (stages). The 5-year survival for woman ranges from 92% to 13%, depending on the stage of the disease [6, 18].

### 1.4 Ovarian Cancer

Cancer of the ovary accounts for approximately 225 000 cases each year worldwide, causing over 140 000 deaths [14]. In Norway, 424 women were diagnosed with cancer of the ovary in 2014 [13], and 292 died of ovarian cancer the same year [2]. It is the second most frequent gynecological malignancy after endometrial cancer, but it carries a higher mortality rate than all other genital cancers combined [14].

#### 1.4.1 Cause of Ovarian Cancer

Several risk factors for ovarian cancers have been recognized. Two of the most important ones are nulliparity and family history of breast and ovarian cancer, but use of hormone replacement therapy have also been shown to increase the risk [6, 19]. As for breast cancer, there is a higher incidence of carcinoma in unmarried women and married women with low parity [6]. The research has shown that the number of ovulatory cycles a women has in her lifetime is proportional to her risk of developing ovarian cancer. Thus, reduced numbers of ovulatory cycles such as from pregnancy are sought to protect from ovarian cancer. For the same reason, use of contraceptive pill is associated with protective effect [19]. Approximately 10% of ovarian cancers are hereditary and 90% of these hereditary tumors are associated with BRCA mutations, while the remainder are predominantly related predominantly to aforementioned Lynch syndrome, associated with germline mutations in the DNA mismatch repair genes [20, 21]. Further, ovarian cancer is much more common after the menopause [19].

#### 1.4.2 Treatment of Ovarian Cancer

The cornerstone to the management of ovarian cancer is surgery. Adjuvant chemotherapy is used to treat distance occult sites of tumor spread. Later recurrences are seen, and even in the most favorable group treated for advanced disease as many as 70% have been shown to relapse within 18 months [19, 22]. Unfortunately, even in women with long remissions, the management of relapse is palliative rather than curative [19].

### 1.4.3 Prognosis of Ovarian Cancer
Ovarian cancer is difficult to detect early as ovarian masses rarely cause symptoms until they are large. More than three fourths of patients already have metastasis to the pelvis, abdominal organs or bladder at the time of diagnosis [22]. Survival for patients with malignant ovarian tumors is poor in general and the single most important prognostic sign is the stage of the tumor at the time of diagnosis. Overall, the 10-year survival is only 35% [19, 22].

1.5 Cancer Screening

Early detection of cancer is associated with better outcome [23]. Thus, the proximal goal of cancer screening is the identification of precancerous lesions or early stages of cancer, before a person develops symptoms and at a point in the disease when treatment is likely to result in cure [24].

1.5.1 Criteria for Population Screening

World Health Organization (WHO) criteria for population screening were developed in 1968 by James Maxwell Glover Wilson and Gunner Junger [25] and those a still considered the gold standard in screening policy-making [24, 26]. Criteria for population screening are:

- The condition sought should be an important health problem
- There should be an accepted treatment for patients with recognized disease
- Facilities for diagnosis and treatment should be available
- There should be a recognizable latent or early symptomatic stage
- There should be suitable test or examination
- The test should be acceptable to the population
- The natural history of the condition, including development from latent to declared disease, should be adequately understood
- There should be an agreed policy on whom to treat as patients
- The cost of case-finding should be economically balanced in relation to possible expenditure on medical care as a whole
- Case-finding should be a continuing process and not a “once and for all” project
Due to growing interest in genetic screening, increased focused on evidence-based medicine, the rise of managed care models that emphasize cost-effectiveness, the shift towards informed choices et cetera, some adoptions to the classical Wilson and Jungner criteria have been proposed over the past years [26]. Those include:

- The screening program should respond to a recognized need
- The objectives of screening should be defined at the outset
- There should be defined target population
- There should be scientific evidence of screening program effectiveness
- The programmed should integrate education, testing, clinical services and programmed management
- There should be quality assurance, with mechanisms to minimize potential risks of screening
- There programmed should ensure informed choice, confidentiality and respect for autonomy
- The programmed should promote equality and access to screening for the entire target population
- Programmed evaluation should be planned from the outset
- The overall benefits of screening should outweigh the harm

However, despite attempts to modify or reinvent the classic screening criteria, the criteria developed by Wilson and Jungner still remains undisputed [26].

1.5.2 Screening for Breast Cancer

*Mammography*

Mammography is the most widely used screening modality for breast cancer [27]. For woman aged 40 to 74 years, screening with mammography has been associated with 15% to 20%
relative reduction in mortality from breast cancer. However, the research indicates that invitation to modern mammography screening may reduce deaths from breast cancer by as many as 28% [28].

The Norwegian breast cancer screening program was initiated by the Norwegian government in 1995. The program was gradually implemented in all counties and complete national coverage was achieved in 2005. The screening program is administered by the Norwegian Cancer Registry, and all women aged 50–69 are invited to screening every two years [28]. In comparison, in Sweden, as in Norway, all women aged 50–69 years are invited to be screened, but in addition in half of Swedish counties women aged 40–49 years as well as women aged 70–74 years are invited to participate in the mammography screening program [29]. Attendance for screening in Norway has been relatively stable, at approximately 76% [28].

Despite obvious positive effects of mammography on breast cancer survival, mammography screening have been shown to have some adverse effects as well [27]. It has been shown that up to 6% of women with invasive cancer will have negative mammograms. Such false negative results may give false sense of security and lead to potential delay in cancer diagnosis. On the other side, false positive results may lead to additional testing and anxiety among patients. It is estimated that approximately 10% of women will be recalled for further testing and only 5% of women recalled will have cancer. Further, mammography screening may lead to over diagnosis and, as a consequence, result in treatment of insignificant cancers that would otherwise never have caused symptoms or death in a woman’s lifetime. Research has shown that at least 20% of screen-detected breast cancers are over diagnosed. Moreover, there is a theoretical possibility that annual mammograms in women aged 40 to 80 years may cause up to one breast cancer per 1000 women because of radiation. However the radiation dose used in mammography is extremely low and unlikely to cause cancer [27].

**Clinical breast examination**

Clinical breast examination can also detect breast cancer, and research has shown equivalent benefit from high-quality clinical breast examination and mammography. However, sensitivity depends on the training of the personnel performing breast examination, and it has also been shown that 17% to 43% of women with cancer have been shown to have a negative breast examination. A false positive rate vary between 1% and 12% [27].
Breast self-examination

Breast self-examination have not been shown to reduce breast cancer mortality compared to no screening activity [27].

Other modalities

Magnetic resonance imaging, ultrasound as well as tomosynthesis and molecular breast imaging can also detect breast cancer early. However, those technologies are usually used as adjuncts to mammography [27].

1.5.3 Screening for Ovarian Cancer

As previously mentioned, ovarian cancer is difficult to detect early.

Ca-125

CA-125 is the most frequent used biomarker for ovarian cancer detection. However, CA-125 has low specificity for ovarian cancer, because it may also be elevated in other cancers, including breast, lung and gastrointestinal cancers, as well in benign conditions such as endometriosis. Further, CA-125 has particular low specificity in premenopausal woman because CA-125 has been shown to be increased during menstruation. Moreover, CA125 is not very sensitive for detecting ovarian cancer as not every patient with cancer will have elevated levels of CA-125 in their blood. For example only 50% of patients with stage 1 ovarian cancer will have increased levels of CA-125 [19].

Ultrasound

Ultrasound can be used to detect adnexal masses, but currently there is no universally agreed scoring system to triage woman with suspected benign or malign masses detected by ultrasound at primary care level [19]. A study which compared annual screening using CA125 and ultrasound with no investigation did not find any stage shift or mortality benefit from this screening strategy in ovarian cancer [19].

1.6 Hereditary Breast and Ovarian Cancer and Genetic Testing
The important aspect of hereditary cancer risk is that it can be significantly modified [21]. For individuals at risk for hereditary breast or ovarian cancer, genetic testing promises earlier intervention and more successful outcomes, as carriers can choose to engage in surveillance or undergo prophylactic surgery [30]. Based on that, genetic testing for BRCA mutations is offered to the women with a family history suggestive of genetic predisposition to the cancer [12].

1.6.1 History of BRCA Testing

BRCA1 was cloned in 1994 by Mark Skolnick and his colleagues at Myriad Genetics in USA [11]. In fact, BRCA1 had been named three years earlier by Mary-Claire King when she and her group studied a large group of families with cases of early-onset breast cancer and, by linkage analysis, localized BRCA1 gene to chromosome 17, but the identification of truncating mutations in the coding sequence of BRCA1 by Skolnick was the conclusive step. However, families with a high incidence of male breast cancer were found not to carry BRCA1 mutations, leading to the search for other breast cancer genes. As a result, in 1994 Wooster and his research group assigned BRCA2 to chromosome 13. BRCA2 was cloned one year after by the same group [11]. Genetic testing for cancer susceptibility quickly followed, and since then patients with strong personal history of breast and/or ovarian cancer have been counseled to seek genetic testing for germline mutations in those genes [11, 15].

1.6.2 Challenges of BRCA Testing

Genetic testing for BRCA1/2 mutations is complicated by the hundreds of different mutations detected, only some of which confer cancer susceptibility. The degree of penetrance, the age of cancer onset, and the association to other types of cancers can vary with the type of mutations [3]. Due to variable expressivity, it is not possible to predict when an individual carrier will manifest breast or ovarian cancer (or both) [21].

Ethical considerations of BRCA testing are widely discussed in the health care society. A number of research studies addressed the main ethical and social implications of genetic testing for cancer in general, including informed consent, privacy and confidentiality, a person’s right to know or not to know their genetic information, carriers responsibility to share genetic information with relatives at risk, physicians’ duty to warn relatives about
familial risk, reproductive choices, appropriate testing of children and adolescents, equitable access to testing and genetic discrimination [10, 30].

1.6.3 Genetic Counseling in Norway

In Norway, genetic counseling is regulated by law [31]. The Biotechnology Act governs the application of biotechnology in medicine, such as assisted fertilization, embryonic diagnostics, pre-implantation genetic diagnosis and aforementioned genetic examinations. The act is administered by the Ministry of Health and Care Services, and medical use of biotechnology is supervised by the Norwegian Directorate of Health. License to perform predictive testing is granted to regional medical genetics departments and a few other units for defined disorders [31].

Practice of predictive BRCA1/2 testing is based on referral of suspected high-risk patients to clinical genetics services for specialized face-to-face genetic counseling [32]. This procedure includes collection and confirmation of family history, risk assessment and eventually BRCA1/2 testing followed by a post-test counseling with dissemination of test results and advice concerning surveillance and follow-up. Further, women diagnosed with breast or ovarian cancer are offered genetic testing for germline BRCA1/2 mutations at the time of the diagnosis if they meet criteria which point to a mutation. Referral criteria include the following: women with breast cancer who have a known mutation for a breast cancer susceptibility gene within the family, women diagnosed with breast cancer at 50 years old or younger or woman diagnosed with ovarian cancer at 70 years old or younger, women with bilateral breast cancer at the diagnosis, or with a history of ovarian cancer, woman with a “triple negative” breast cancer, woman with a strong family history, if the patient comes from an ethnic background of increased risk or in case of male breast cancer. It is also recommended that women at the age of 40 years old or younger should be referred to genetic counseling prior to genetic testing. Women older than 40 years of age receive information about genetic testing from the physician responsible for the treatment of the patient. Only in case of a positive result, patients are referred to genetic counseling [32].

1.6.4 Prevention of Hereditary Breast and Ovarian Cancer

Cancer risk for developing breast or ovarian cancer can be significantly modified for BRCA1/2 mutation carriers. The three available options to mitigate risk are surveillance, chemoprevention, and risk-reducing surgery [12, 21].
Breast cancer surveillance, such as mammography or magnetic resonance imaging (MRI), is non-invasive, has few adverse long-term effects and does not interfere with child bearing [12]. However, mammographic screening is less effective in younger than in older woman due to increased breast density. MRI is more sensitive and detects more cancers in high risk woman compared to mammography. However, MRI can only detect breast cancer early, not prevent the disease, and there is no evidence, that breast screening reduces the risk of breast cancer death in high risk women [12]. Surveillance with annual CA-125 and ultrasound has low impact on early detection of ovarian cancer [21], as earlier discussed.

Chemoprevention can be used to prevent estrogen receptor positive cancers. However, the uptake of chemoprevention worldwide is low and no study has yet shown an overall survival advantage of chemoprevention in BRCA carriers [7, 12].

Risk reducing surgical removal of both breasts has been shown to reduce the risk of breast cancer by 90%-95% and surgical removal of both ovaries not only reduce the risk of ovarian cancer by up to 90%, but has also been shown to reduce breast cancer by up to 50% in BRCA1/2 mutation carriers [12, 21]. In fact, risk reducing salpingo-oophorectomy is a key component of breast and ovarian cancer risk reduction for BRCA1/2 mutation carriers once they have completed their families [19].
2. Aims of the Study

The general aims of the study were to access knowledge about BRCA testing, attitudes towards genetic testing and knowledge and attitudes about mammography screening among supporters of Norwegian Breast Cancer Association. In addition, we wanted to order to investigate if preferences for genetic testing have changed from 2009 to 2015 as a result of increased public awareness.

We hypothesized that knowledge about BRCA testing will be high in our study group.
3. Methods

3.1 Design and Setting

A cross-sectional design was employed. We collaborated with Norwegian Breast Cancer Association (NBCA) and an internet based survey was distributed by NBCA on their home and Facebook pages. This survey was available for the participants during the summer 2015. Because of concerns about confidentiality and respondent burden, the survey was anonymous. The study was conducted according to the guidelines at University of Oslo. No ethical considerations requiring approval of Regional Committee for Research Ethics apply.

3.2 Measures

In 2009, Department of Health Management and Health Economics, Faculty of Medicine, University of Oslo, in collaboration with NBCA, performed a cross sectional study on women exposed to breast cancer treatment. Questions about personal breast cancer history, demographic and socioeconomic status, preferences for genetic testing, information channels and preferences for having their children tested were included in that questionnaire.

Based on questionnaire from 2009 we developed a new questionnaire which, in addition to aforementioned questions, also assessed knowledge of genes and genetic testing, attitudes towards genetic testing, as well as attitudes about mammography screening. No question from 2009 survey was changed in order to be able to compare those to studies.

3.2.1 Sociodemographic and medical characteristics

The following sociodemographic and medical characteristic were assessed via a self-report questionnaire: age, ethnicity, marital status, number of children, education, employment status, income, personal history of breast cancer, personal history of genetic testing and membership in NBCA.

3.2.2 Knowledge about HBOC

Knowledge about HBOC is a primary outcome variable of the study and was measured with an 11-item National Center for Human Genomic Research (NCHGR) Cancer Genetic Studies Consortium Knowledge Scale [33, 34]. This scale was validated in previous research and
measures four aspects of HBOC genetics knowledge: prevalence of the BRCA gene mutations, patterns of inheritance, cancer risk associated with BRCA mutations and risk management options for woman with a BRCA mutation.

As previously described [34], to calculate an overall knowledge score, all items were scored as 1 if the respondent provided the correct answer and 0 if they gave an incorrect or do not know response. Thus, an overall knowledge score could range from 0 to 11.

3.2.3 Attitudes towards Genetic Testing

A 12-item scale developed and validated in previous research was used to assess precipitations of the importance of the benefits, limitations and risks of BRCA testing [33]. Participants were asked to indicate whatever each item was “not at all important”, “somewhat important” or “very important” for them.

3.2.4 Attitudes towards Mammography Screening

A widely used 11-item scale for breast cancer screening beliefs developed by V. Champion was employed [35]. The Champion Breast Health Survey has an established reliability and validity and explores perceived susceptibility, perceived benefits, perceived self-efficacy and perceived barriers towards mammography screening. In addition, we added four more questions to the scale and asked participants about perceived harms of the mammography screening.

3.2.5 Translation of International Scales

11-item knowledge scale developed by NCHGR, 12-item knowledge scale developed by Lerman and 11-item scale developed by Champion are not available in Norwegian. Therefore, a multistep approach was used to develop Norwegian translation. The instrument was forward translated and back translated by four independent people. Any issues were discussed by team members until consensus was reached.

3.3 Data Analysis

SPSS for Windows release 21 (Chicago, IL,) was used for the statistical analysis. When more than two groups of individuals were compared, the non-parametric Kruskall-Wallis test was used. If a significant difference was found, Mann-Whitney U test was used to calculate the
difference between each pair of groups. Data are given as median and 25th to 75th percentiles unless otherwise stated. Association between HBOC and different sociodemographic factors was accessed using backward linear regression analysis. Figures were generated using GraphPad Prism version 6.04 for Windows (GraphPad Software, La Jolla, CA).
4. Summary of the Results

Two hundred twenty-five people participated in the study. On average, respondents answered 7 (IQR 5-8) out of 11 questions on BRCA knowledge scale correctly. Responders who had undergone BRCA1/2 testing had significantly higher knowledge than those who had not undergone testing (p<0.001). In those who had not undergone genetic testing, there was no difference in total score BRCA knowledge between those with personal history of breast cancer and those with no personal history of breast cancer (6 (IQR 4-7) versus 6 (IQR 5-7), p=0.856). However, in those who have undergone gene testing, responders with a personal history of breast cancer had significantly lower levels of overall knowledge compared to individuals with no personal history of breast cancer (8 (IQR 8-9.5) versus 7 (IQR 6-8), p<0.001). There was a considerable variability in the specific questions that were answered correctly. Only 26% of responders answered correctly on question related to the prevalence of BRCA mutations in general population, and only 18% of responders correctly answered question concerning residual risk of ovarian cancer after a risk reducing salpingo-oophorectomy. Notably, between those who had undergone genetic testing, there was no difference in percentages correct answers between responders with no personal history of breast cancer and those with personal history of breast cancer (p=0.026). Among those who had undergone genetic testing, as many as 80% of those with no personal history of breast cancer and 48% with a personal history of breast cancer answered the question about the residual risk of breast cancer after a prophylactic mastectomy correctly (p<0.001).
5. Discussion

5.1 Methodological Aspects

In this section methodological limitations, strengths and possible sources of bias in the present thesis will be discussed.

We have conducted a cross-sectional study and described knowledge about hereditary breast and ovarian cancer among women who underwent BRCA testing. In general, cross-sectional studies are prevalence studies where all the measurements on each person are made at one point in time [36]. Cross-sectional studies can also be used to infer causation, as at one point in time the subjects are asked to determine whether they were exposed to the relevant intervention or a risk factor and whether they have the outcome of interest [36, 37]. However, these kinds of studies are mainly descriptive and do not provide an explanation for the findings as differentiating cause and effect from simple association is difficult [36]. On the other hand, cross-sectional studies are cheap, take little time to conduct and allow to collect a lot of information, thus giving an opportunity to gain a broad base of knowledge [37].

This study design has several limitations. Because of selection bias, results obtained in our study can not be generalized to a general population. The choice of study population affects the generalizability and usefulness of research findings. As it is not possible to study an entire population of interest, the most appropriate study sample is one that most closely reflects the characteristics of this population [38]. A selection bias comes from any error in selecting the study population and/or from factors affecting the study participation [39]. Participation in our study was voluntary, leading to a possible self-selection (volunteer) bias. Differences may exist between those who refuse to participate and those who volunteer, and volunteers are unlikely to be representative to a study population [36, 38, 39]. Volunteers may be more health conscious [38] or, in our situation, have a higher knowledge related to breast cancer and/or genetic testing. Further, our study was based on an anonymous internet based questionnaire which was distributed by NBCA on their home-and Facebook pages. As a consequence, the response rate could not be calculated. Non-response (participation) bias is important to take into consideration as studies with low response rate can miss significant differences in the responders and non-responders [36, 38].
Moreover, information bias should also be considered. Information (observation) bias occurs during data collection about or from study subjects [38, 39]. Due to retrospective design of our study we have to rely on the memory of our participants, which leads to a potential recall bias. Recall of medical information is discussed in more details in next section.

We should also be aware of confounding factors in our study. Confounding arises when additional factors are independently associated with both exposure and outcome [38]. Common confounding variables are age and sex, however, confounding variables may not be known. In our study, we found higher HBOC knowledge in younger participants with personal history of genetic testing and university degree. One may hypothesize that younger responders are better educated and, thus, have a higher HBOC knowledge. We may also speculate that those with an university degree are more likely to ask for a genetic test. At the same time, the fact that not all patients diagnosed with breast cancer who undergo genetic testing receive genetic counseling, and the fact that younger patients are referred to genetic counseling prior to genetic testing, may explain an association between younger age and higher HBOC knowledge.

Due to economical restrictions, we could not conduct a postal survey. Therefore, an internet based survey was chosen. It have been suggested that use of internet surveys can be considered as an alternative to a traditional epidemiologic mode of data collection, such as postal survey [40]. Web-based questionnaires have been shown to improve data quality and are they are returned more rapidly compared to written questionnaire [40, 41]. Although the researchers disagree whatever the use of electronic surveys results in cost reductions [40], the use of internet based survey resulted in a substantial cost reduction and time saving in our study. On the other hand, a number of disadvantages of this type of data collection have been suggested. Initially, response rates for internet surveys have been lower than for postal questionnaires, leading to a concern of selection bias [40, 42]. However, this tendency may reverse as recent studies reported that the majority of respondents preferred the internet based version to postal survey [40]. As already mentioned, we were unable to calculate the response rate in our study. This problem could be avoided if the survey was distributed by an email with a direct hyperlink to the questionnaire. However, the lack of such email lists makes distribution of the web-based surveys challenging [41]. Further, the researchers are concerned about the reliability and validity of the data obtained through web-based questionnaires. But studies in various areas of health research demonstrated that traditional
epidemiologic risk factors can be collected with better or equal reliability in internet surveys as in traditional questionnaires. Moreover, there are indications that internet based questionnaires are more suitable for research on sensitive topics [40].

5.2 Recall of Medical Information

In order to make decisions about treatment options, the patient must receive detailed information about the disease [43]. Despite increased public awareness about HBOC during last years, the research has shown that increased awareness is not associated with increased knowledge [44]. Our results support those findings, as the responders in our study, who were expected to have a high knowledge about HBOC, answered on average only 7 of 11 questions correctly.

It is well known that about 40-80% of medical information provided to the patient is forgotten immediately and almost half of the information that is remembered is incorrect [43]. Number of factors can influence patients memory for medical information. First, use of difficult medical terminology by the healthcare practitioner can explain poor understanding and, thus, poor recall and knowledge about the disease. The way the information is given is also important. In general, medical information is often spoken. However, spoken information should be supported with written information as is better remembered[43]. Second, age affects our memory and an inverse relation between age and amount of correct information recalled has been reported [43]. We found that the total knowledge was associated with younger age. But, as already discussed, age can be a confounder. Further, the greater the amount of information presented to the patient, the lower the proportion correctly recalled [43]. The amount of correctly recalled information is closely related to the subjective importance of the material. Thus, for a patient with a breast cancer diagnosis or with a family history of breast cancer, information about the ovarian cancer can be too abstract. However, as many as 77% of responders recognized an association between BRCA mutations and increased risk of ovarian cancer. Interestingly, it has been shown that the recall is worse when the medical information is related to the participant’s own illness and thus had personal relevance. Moreover, anxiety and distress can affect the ability to perceive given information. For patients diagnosed with breast cancer, the central message and the primary focus will be the diagnosis, limiting patients attention for peripheral information, such as prevention strategies for ovarian cancer. Moreover, researchers suggests that statements about the
diagnosis tend to be viewed by patients as more important, while those related to treatment less so [43].
6. Conclusions

We found impaired knowledge about hereditary breast and ovarian cancer syndrome in a group who has undergone genetic testing for BRCA mutations.

Our findings are of concern in that a sizable proportion of high-risk women in this study appear to be falsely reassured about the effectiveness of prophylactic salpingo-oophorectomy, as well as prophylactic mastectomy. It may theoretically lead to less awareness of cancer symptoms or poor participation in surveillance.

Further studies are needed in order to compare HBOC knowledge in groups which receive different modes of genetic counseling, such as prior face to face genetic counseling as well as those who receive written, digital or telephone based information.

Our results underlines that it is necessary to update the genetic counseling model in order to offer a high quality genetic testing and counseling in a situation with an increased demand.
7. Reference List

REFERENCES

31 Lov om humanmedisinsk bruk av bioteknologi m.m. (bioteknologiloven). Helse- og omsorgsdepartement: Lovdata 2004.


8. Paper I
Knowledge about hereditary breast and ovarian cancer among women who underwent BRCA testing

D.M. Aresvik and E. Feiring

aDepartment of Health Management and Health Economics, Institute of Health and Society, University of Oslo, Norway

Corresponding author: D.M. Aresvik, MD, Phone: +47 23072986. E-mail: dina.aresvik@rr-research.no

Keywords: Patient knowledge, genetic testing, BRCA1/2, breast cancer, ovarian cancer, HBOC
Abstract

Objective: To examine knowledge about hereditary breast and ovarian cancer (HBOC) among Norwegian Breast Cancer Association (NBCA) supporters. Methods: A cross-sectional design was employed. An internet based questionnaire that assessed knowledge of genes and genetic testing, use of genetic testing, personal breast cancer history, attitudes about genetic testing as well as attitudes about mammography screening and sociodemographic characteristics was distributed by NBCA on their home- and Facebook pages. Two hundred and twenty-five people responded to the survey.

Results: On average, respondents answered 7 (IQR 5-8) of 11 items correctly. The percentage of correct responses on the knowledge instrument ranged from 18% to 98%, with the lowest knowledge on risk of ovarian cancer after a prophylactic surgery. Responders who had undergone BRCA1/2 testing had significantly higher knowledge than those who had not undergone testing (p<0.001). In those who had not undergone genetic testing, there was no difference (p=0.856) in total score BRCA knowledge between those with personal history of breast cancer (median 6, IQR 4-7) and those with no personal history of breast cancer (median 6, IQR 5-7). In those who have undergone gene testing, responders with a personal history of breast cancer had significantly lower (p<0.001) levels of overall knowledge compared to individuals with no personal history of breast cancer. Personal history of genetic testing (beta=-0.332, p<0.001), age (beta=0.174, p=0.007) and educational level (beta=0.153, p=0.016) predicted total HBOC knowledge.

Conclusion: Our study demonstrates diminished HBOC knowledge in a group which was expected to have a high knowledge, and underlines the importance of genetic counseling.
1. Introduction

Approximately 3%-5% of breast cancer and 4%-11% of ovarian cancer are due to germline mutations in breast cancer 1, early onset (BRCA1) and breast cancer 2, early onset (BRCA2) genes [1, 2]. Less than 1% of the general population is estimated to carry a mutation in BRCA1/2. Carriers of BRCA mutations have a relative increased lifetime risk of breast cancer of 2.7-6.4 times, and a relative lifetime risk of ovarian cancer of 9.3-35.3 times greater than average risk women, with the greatest proportions in cancers diagnosed before 50 years of age [2, 3]. Mutations in BRCA1/2 are inherited in an autosomal dominant pattern. This means that only one mutated copy of the gene is necessary for a person to be affected, it may originate from maternal or paternal side and the chance a child will inherit the mutated gene is 50% [2, 4].

Cancer risk can be significantly modified and for BRCA1/2 carriers the three options to mitigate risk are surveillance, chemoprevention, and risk-reducing surgery [5, 6]. Breast cancer surveillance is non-invasive, has few adverse long-term effects and does not interfere with child bearing. However, MRI can only detect breast cancer early, not prevent the disease, and there is no evidence, that breast screening reduces the risk of breast cancer death in high risk women [6]. Surveillance with annual CA-125 and ultrasound has low impact on early detection of ovarian cancer [5]. Chemoprevention can be used to prevent estrogen receptor positive cancers. However, the uptake of chemoprevention worldwide is low and no study has yet shown an overall survival advantage of chemoprevention in BRCA carriers [2, 6]. Risk reducing surgical removal of both breasts has been shown to reduce the risk of breast cancer by 90%-95% and surgical removal of both ovaries not only reduce the risk of ovarian cancer by up to 90%, but has also been shown to reduce breast cancer by up to 50% in BRCA1/2 mutation carriers [5, 6].

Consequences of genetic testing vary according to the disease area. For individuals at risk for hereditary breast or ovarian cancer, genetic testing promises earlier intervention and more successful outcomes, as carriers can choose to engage in surveillance or undergo prophylactic surgery [7]. Based on that, genetic testing for BRCA mutations is offered to the women with a family history suggestive of genetic predisposition to the cancer [6]. However, it has been argued that many women with
mutations in those genes are identified as carriers only after their first cancer
diagnosis because their family history of cancer was not sufficient to suggest genetic
testing [8]. It is internationally discussed whether genetic screening for the genes
associated with hereditary breast and ovarian cancer should be offered to all women
around age 30, in the course of routine medical care. It has been argued that women
do not benefit by practices that “protect” them from information regarding their own
health, and that they should have the choice to learn if they carry a mutation [8].
Interest for the genetic testing for the hereditary breast cancer is growing among both
the medical and the patient community. Thus, in past years, referrals for genetic
testing for hereditary breast and ovarian cancer increased substantially, the pattern of
referral has moved to earlier phases of the disease and closer to the time of diagnosis
and the ratio of relatives tested has increased [9, 10]. Research indicates that
BRCA1/2 testing is not only used for early detection and prevention of breast cancer
among healthy individuals, but also to guide therapeutic decision making at the time
of cancer diagnosis [10]. As a result of the increase of the referrals, and since
traditional approach for BRCA1/2 testing is time consuming and resource demanding,
the need for an update of the genetic counseling model have been raised and
BRCA1/2 mutation testing without prior face-to-face genetic counseling have been
studied [11, 12]. Moreover, direct-to-consumer personal genomic tests which do not
require the participation of health-care provider are now available [13]. However, it
has been shown that increased public awareness of genetic testing for hereditary
breast cancer is not associated with greater knowledge of breast cancer risk [14].

The aim of our study was to investigate knowledge about hereditary breast and
ovarian cancer (HBOC) among women who underwent BRCA1/2 mutation testing.
2. Methods

2.1. Design and setting
A cross-sectional design was employed. We collaborated with Norwegian Breast Cancer Association (NBCA) and an internet based survey was distributed by NBCA on their home and Facebook pages. This survey was available for the participants during the summer 2015. Because of concerns about confidentiality and respondent burden, the survey was anonymous.

The Norwegian healthcare system is founded on the principles of universal access. It is financed by taxation and all residents are covered by the National Insurance Scheme. Private medical insurance is limited [15]. NBCA provide support, education, and outreach for breast cancer patients, survivors, families/friends and others interested in breast cancer[16]. Genetic counselling is regulated by law in Norway. License to perform predictive testing is granted to regional medical genetics departments and a few other units for defined disorders [17].

The study was conducted according to the guidelines at University of Oslo. According to Norwegian law no ethical considerations requiring approval of Regional Committee for Research Ethics apply.

2.2. Measures
In collaboration with NBCA we developed a questionnaire that assessed knowledge of genes and genetic testing, use of genetic testing, personal breast cancer history, attitudes about genetic testing as well as attitudes about mammography screening and sociodemographic characteristics.

2.2.1 Sociodemographic and medical characteristics
The following sociodemographic and medical characteristic were assessed via a self-report questionnaire: age, ethnicity, marital status, number of children, education, employment status, income, personal history of breast cancer, personal history of genetic testing and membership in Norwegian Breast Cancer Association.

2.2.2. Knowledge about HBOC
Knowledge about HBOC is a primary outcome variable of the study and was measured with an 11-item National Center for Human Genomic Research (NCHGR) Cancer Genetic Studies Consortium Knowledge Scale [18, 19]. This scale measures four aspects of HBOC genetics knowledge: prevalence of the BRCA gene mutations, patterns of inheritance, cancer risk associated with BRCA mutations and risk management options for woman with a BRCA mutation.

As previously described [19], to calculate an overall knowledge score, all items were scored as 1 if the respondent provided the correct answer and 0 if they gave an incorrect or do not know response. Thus, an overall knowledge score could range from 0 to 11.

2.2.2.1 Translation of Research (NCHGR) Cancer Genetic Studies Consortium Knowledge Scale

11-item knowledge scale developed by NCHGR Cancer Genetic Studies Consortium is not available in Norwegian. Therefore, a multistep approach was used to develop Norwegian translation. First, the instrument was forward translated and back translated by four independent people. Any issues were discussed by team members until consensus was reached.

2.3. Data analysis

SPSS for Windows release 21 (Chicago, IL,) was used for the statistical analysis. When more than two groups of individuals were compared, the non-parametric Kruskall-Wallis test was used. If a significant difference was found, Mann-Whitney U test was used to calculate the difference between each pair of groups. Data are given as median and 25th to 75th percentiles unless otherwise stated. Association between HBOC and different sociodemographic factors was accessed using backward linear regression analysis. Figures were generated using GraphPad Prism version 6.04 for Windows (GraphPad Software, La Jolla, CA).
3. Results

3.1. Cohort
Two hundred twenty-five people responded to the survey in a period of three months. Demographic and medical characteristics of the sample are shown in Table 1. The majority of the responders was Norwegian (94%), married or living as married (77%), had children (88%) and had a university degree (67%). Seventy percent of the sample was employed at least part time. The sample was approximately equally distributed across income and age categories. Among the responders, 52% were members of NBCA, 59% had a personal history of breast cancer and 60% had undergone genetic testing.

3.2. HBOC knowledge in the study population
Table 2 shows the overall frequency of correct responses across the 11 items of the knowledge questionnaire. On average, respondents answered 7 (IQR 5-8) of the items correctly. As shown in Figure 1, responders who had undergone BRCA1/2 testing had significantly higher knowledge than those who had not undergone testing (p<0.001). In those who had not undergone genetic testing, there was no difference in total score BRCA knowledge between those with personal history of breast cancer and those with no personal history of breast cancer (6 (IQR 4-7) versus 6 (IQR 5-7), p=0.856). However, in those who have undergone gene testing, responders with a personal history of breast cancer had significantly lower levels of overall knowledge compared to individuals with no personal history of breast cancer (8 (IQR 8-9.5) versus 7 (IQR 6-8), p<0.001).

3.3. Difference in HBOC knowledge
As shown in Table 3, there was considerable variability in the specific questions that were answered correctly. Only 26% of responders answered correctly on question related to the prevalence of BRCA mutations in general population. Among those who had undergone genetic testing, the correct response rate was 39% in the group with personal history of breast cancer (group four) while in the group with no personal history of breast cancer (group three) the correct response rate was only 22% (p=0.049). However, 59% correctly answered on question related to prevalence of BRCA mutation in breast cancer. With respect to patterns of inheritance, the majority
appeared to recognize paternal inheritance (73%), but the knowledge were significantly lower (p=0.004) in group four (81%) compared to group three (98%). Responders also recognized the risk of inheriting a BRCA mutation among first-degree relatives (80%). Similarly, knowledge were significantly lower (p<0.001) in group four (98%) than in group three (72%). The majority of responders appeared to differentiate cancer risks for sporadic versus suspected hereditary based on the presence of a mutation (98%) and age of onset (63%), again with a slightly lower knowledge in group 4 compared to group three. As many as 89% correctly answered the question related to penetrance of BRCA mutations. Further, 77% of responders recognized an association between BRCA mutations and increased risk of ovarian cancer. However, only 18% of responders correctly answered question concerning residual risk of ovarian cancer after a risk reducing salpingo-oophorectomy. Notably, there was no difference in percentages correct answers between the four groups (p=0.066) and among those who had undergone genetic testing, only 30% of those with no personal history of breast cancer and 14% of those with personal history of breast cancer answered the question correct (p=0.026). In contrast, as many as 49% of responders recognized the residual risk of breast cancer after prophylactic surgery. However, among those who had undergone genetic testing, as many as 80% of those with no personal history of breast cancer and 48% with personal history of breast cancer answered the question correctly (p<0.001).

3.4 HBOC knowledge and sociodemographic factors
In order to examine whether overall knowledge varied as a function of the demographic characteristics listed, we performed backward multiple regression analysis with total HBOC knowledge as dependent variable. Personal history of genetic testing (beta=-0.332, p<0.001), age (beta=0.174, p=0.007) and educational level (beta=0.153, p=0.016) predicted total HBOC knowledge in our model. HBOC knowledge was higher in younger patients with personal history of genetic testing and university degree.
4. Discussion and conclusion

4.1. Discussion

In this sample of 225 participants we found that responders who had undergone BRCA1/2 testing had significantly higher knowledge than those who had not undergone testing. In those who have undergone gene testing, responders with a personal history of breast cancer had significantly lower levels of overall knowledge compared to individuals with no personal history of breast cancer. Among those who had undergone genetic testing, only 30% of those with no personal history of breast cancer and 14% of those with personal history of breast cancer recognized residual risk of ovarian cancer after prophylactic salpingo-oophorectomy, while 80% and 48% recognized residual risk of breast cancer after risk reducing mastectomy respectively.

Despite increased public awareness about HBOC during last years, the research has shown that increased awareness is not associated with increased knowledge [14]. Our results support those findings, as the responders in our study answered on average only 7 of 11 questions correctly. We recruited participants through NBCA and our results may not be generalized to other populations. However, our study group would be expected to have a high knowledge about HBOC, which makes results even more surprising.

The total knowledge was associated with higher education, younger age and personal history of genetic testing. This in conjunction with previous findings of Petters et al who demonstrated that woman who had undergone BRCA1/2 testing had significantly higher knowledge than woman who had not undergone testing [20] and Katapodi et al who have shown that education is significantly associated with knowledge of breast cancer risk factors [21].

Among those who have undergone genetic testing, we found that total HBOC knowledge was higher in those without previous history of breast cancer. This in conjunction with findings of Vadaparampil et al who have shown lower HBOC knowledge in women with a personal history of cancer [19]. Authors discuss that woman may not regard personal cancer history as a risk factor for HBOC. In Norway, the practice of predictive BRCA1/2 testing is based on referral of suspected high-risk
patients to clinical genetics services for specialized face-to-face genetic counseling. This procedure includes collection and confirmation of family history, risk assessment and eventually BRCA1/2 testing followed by a post-test counseling with dissemination of test results and advice concerning surveillance and follow-up. Women diagnosed with breast or ovarian cancer are offered genetic testing for germline BRCA1/2 mutations at the time of the diagnosis if they meet criteria which point to a mutation. Referral criteria include the following: women with breast cancer who have a known mutation for a breast cancer susceptibility gene within the family, women diagnosed with breast cancer at 50 years old or younger or woman diagnosed with ovarian cancer at 70 years old or younger, women with bilateral breast cancer at the diagnosis, or with a history of ovarian cancer, woman with a “triple negative” breast cancer, woman with a strong family history, if the patient comes from an ethnic background of increased risk or in case of male breast cancer. Further it is recommended that women at the age of 40 years old or younger should be referred to genetic counseling prior to genetic testing. Women older than 40 years of age receive information about genetic testing from the physician responsible for the treatment of the patient. Only in case of a positive result, patients are referred to genetic counseling [22]. The fact that not all patients diagnosed with breast cancer who undergo genetic testing receive genetic counseling can explain differences between those two groups. Since younger patients are referred to genetic counseling prior to genetic testing may also explain why we found an association between younger age and higher HBOC knowledge. However, we can not confirm this hypothesis as we do not know patients test results or whatever they have received face to face genetic counseling or not. In our study, the knowledge about risk reduction management options was lower for ovarian than for breast cancer, while majority of participants recognized that woman with an altered breast cancer gene has a higher ovarian cancer risk. This study did not assessed what information was actually given during counseling, but one may speculate that patients who undergo genetic testing receive more information about risk management of breast than ovarian cancer. A different type of study, such as a qualitative study, is needed to investigate this hypothesis.

Referrals to genetic testing for HBOC increased dramatically during past years [9, 10]. Traditionally, BRCA1/2 testing was used for cancer risk assessment and to indicate early detection and prevention strategies for breast and ovarian cancer among
healthy individuals at risk. Today it is used not only for risk assessment, but also to guide therapeutic decision making at the time of cancer diagnosis. Moreno et al. reported that the pattern of referral among patients with breast cancer and ovarian cancer has moved towards early phases of their disease and close to the time of diagnosis, and the detection criteria has slightly decreased with the use of less strength criteria based on family history [10]. Lokich et al [1] have shown that 70% of women who were BRCA mutation carriers changed their surgical plan after learning their BRCA status. Most changed from planning a wide local excision to choosing a bilateral mastectomy and some also chose to undergo concurrent bilateral salpingo-oophorectomy. Taking into account a very low knowledge regarding residual risk of ovarian cancer in our study group, as well as low knowledge of residual risk of breast cancer after risk reducing mastectomy among participants with personal history of breast cancer and genetic testing, we are concerned that patients may have a false sense of security. Believe that risk reducing surgery protects from developing breast or ovarian cancer, may theoretically lead to less awareness of cancer symptoms or poor participation in surveillance.

As traditional genetic counseling procedure is resource demanding, Høberg-Vetti et al [11] argue that alternative approaches are needed when treatment-driven genetic testing is offered to larger patients groups with lower probability of carrying a pathogenic BRCA1/2 variant. Authors discuss that written, telephone-based or digital information provided by a clinical geneticist or genetic counselor, together with adequate information from the oncologist or surgeon, could be considered as an alternative for some patients. Taking into account our results, which demonstrate diminished HBOC knowledge in a group which was expected to have a high knowledge, we underlines that it is necessary to update the genetic counseling model in order to offer a high quality genetic testing and counseling in a situation with an increased demand.

Further studies are needed in order to compare HBOC knowledge in groups with and without prior face to face genetic counseling and compare knowledge between groups who receive written, digital or telephone based information.
Conflict of interest
The authors have no conflict of interest to declare.

Funding
No competing financial interests exist.

Acknowledgments
The authors would like to thank all participants who took the time and effort to complete the survey and Norwegian Breast Cancer Association for assisting with the survey.
REFERENCES

**Figure legends:**

Fig. 1 Total HBOC knowledge between groups based on history of breast cancer and history of genetic testing. The * marks the p-value <0.001. Group 1 – No personal history of breast cancer, did not undergo genetic testing. Group 2 – Personal history of breast cancer, did not undergo genetic testing. Group 3 – No personal history of breast cancer, undergo genetic testing. Group 4 - Personal history of breast cancer, undergo genetic testing
Table 1 Sociodemographic and medical characteristics of study participants (n=255)

<table>
<thead>
<tr>
<th>Sociodemographic characteristics</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, IQR)</td>
<td>50 (IQR 42-56)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td>220 (98%)</td>
</tr>
<tr>
<td>Norway</td>
<td>212 (94%)</td>
</tr>
<tr>
<td>Asia</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>North America</td>
<td>3 (1.3%)</td>
</tr>
<tr>
<td>Middle East</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Africa</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>South America</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Married/living as married</td>
<td>174 (77%)</td>
</tr>
<tr>
<td>Single/separated/widowed</td>
<td>42 (19%)</td>
</tr>
<tr>
<td>In a relationship</td>
<td>8 (3.6%)</td>
</tr>
<tr>
<td>Have children</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>198 (88%)</td>
</tr>
<tr>
<td>No</td>
<td>26 (12%)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Primary school</td>
<td>15 (7%)</td>
</tr>
<tr>
<td>High school</td>
<td>60 (27%)</td>
</tr>
<tr>
<td>University</td>
<td>150 (67%)</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
</tr>
<tr>
<td>Full or part time</td>
<td>156 (69%)</td>
</tr>
<tr>
<td>Retired/disabled/unemployed</td>
<td>69 (31%)</td>
</tr>
<tr>
<td>----------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Income, NOK per year</td>
<td></td>
</tr>
<tr>
<td>0-99999</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>100000-199999</td>
<td>19 (8%)</td>
</tr>
<tr>
<td>200000-399999</td>
<td>78 (35%)</td>
</tr>
<tr>
<td>400000-599999</td>
<td>98 (44%)</td>
</tr>
<tr>
<td>600000-999999</td>
<td>22 (10%)</td>
</tr>
<tr>
<td>1000000+</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Member of NBCA</td>
<td>118 (52%)</td>
</tr>
</tbody>
</table>

Medical characteristics

| Personal history of breast cancer | 132 (59%) |
| Personal history of genetic testing | 136 (60%) |

n for each variable may not equal 225 due to missing data; percentage may not add up to 100% due to rounding error
### Table 2: Frequency and percentage of correct responses on the knowledge scale

<table>
<thead>
<tr>
<th>Number of items correct</th>
<th>n</th>
<th>Sample (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>12</td>
</tr>
<tr>
<td>6</td>
<td>32</td>
<td>15</td>
</tr>
<tr>
<td>7</td>
<td>42</td>
<td>20</td>
</tr>
<tr>
<td>8</td>
<td>40</td>
<td>18</td>
</tr>
<tr>
<td>9</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td>10</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>11</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

Percentages may not add up to 100% due to rounding error
**Table 3** Percent correct for items from the National Centre for Human Genome Research Cancer Genetics Studies Consortium Knowledge Scale

<table>
<thead>
<tr>
<th>Item</th>
<th>Total</th>
<th>1&lt;sup&gt;b&lt;/sup&gt;</th>
<th>2&lt;sup&gt;c&lt;/sup&gt;</th>
<th>3&lt;sup&gt;d&lt;/sup&gt;</th>
<th>4&lt;sup&gt;e&lt;/sup&gt;</th>
<th>p&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevalence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 in 10 women has an altered breast cancer gene. (False)</td>
<td>26</td>
<td>7</td>
<td>22</td>
<td>22</td>
<td>39</td>
<td>0.049*</td>
</tr>
<tr>
<td>One half of all breast cancer cases occur in women who have an altered breast cancer gene. (False)</td>
<td>59</td>
<td>33</td>
<td>59</td>
<td>62</td>
<td>70</td>
<td>0.351</td>
</tr>
<tr>
<td><strong>Patterns of inheritance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A father can pass down an altered breast cancer gene to his children. (True)</td>
<td>73</td>
<td>42</td>
<td>59</td>
<td>98</td>
<td>81</td>
<td>0.004*</td>
</tr>
<tr>
<td>The sister of woman with an altered breast cancer gene has a 50% risk of having the altered gene. (True)</td>
<td>80</td>
<td>79</td>
<td>76</td>
<td>98</td>
<td>72</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td><strong>Cancer risks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A woman who does not have an altered breast cancer gene can still get breast or ovarian cancer. (True)</td>
<td>98</td>
<td>98</td>
<td>96</td>
<td>100</td>
<td>98</td>
<td>0.276</td>
</tr>
<tr>
<td>Early onset breast cancer is more likely due to an altered breast cancer gene than is late onset breast cancer. (True)</td>
<td>63</td>
<td>68</td>
<td>46</td>
<td>78</td>
<td>61</td>
<td>0.045*</td>
</tr>
</tbody>
</table>
a p-values are calculated using Mann-Whitney U-test for group 3 and group 4
b Group 1 – No personal history of breast cancer, did not undergo genetic testing
c Group 2 – Personal history of breast cancer, did not undergo genetic testing
d Group 3 – No personal history of breast cancer, undergo genetic testing
e Group 4 - Personal history of breast cancer, undergo genetic testing
Total HBOC knowledge

Group 1 | Group 2 | Group 3 | Group 4

NS

* * *
9. Appendix
9.1 Questionnaire to Breast Cancer Survivors - 2009

Foreningen for brystkreftopererte

Rehabilitering, arbeidsevne, mammografi og gentest for kvinner med brystkreft: Fokus på sosial ulikhet

Screening
1. Hvilket år er du født? __________________________
2. Hvilket fylke bor du i? __________________________

3. Før du ble diagnostisert med brystkreft, deltok du noen gang på mammografiscreening?
   □ Ingen (gå til spørsmål 11)
   □ Offentlig (gå til spørsmål 4)
   □ Privat (gå til spørsmål 6)
   □ Begge deler (gå til spørsmål 4)

4. Hvilket år var du første gang på offentlig mammografi screening? _____ år

5. Hvor mange ganger har du vært på offentlig mammografi screening? Antall _____

6. Hvilket år var du første gang på privat mammografi screening? _____ år

7. Hvor mange ganger har du tatt privat mammografi screening? Antall _____

8. Hvis du deltok på privat mammografi screening, hvordan fikk du informasjon om tilbudet?
   □ Venner/familie
   □ Anbefalt av lege eller annet helsepersonell
   □ Aviser, radio eller TV
   □ Reklame i posten
   □ Annet, spesifiser

9. Hvor lang reisetid har du til offentlig mammografi screening? _____ minutter en vei

10. Hvor lang reisetid har du til privat mammografi screening? _____ minutter en vei

Diagnostisering
11. Tidspunkt for diagnose: År _____ Måned _____________

12. Hva var årsaken til at du ble diagnostisert?
   □ Kjente selv en kul i brystet eller hadde andre symptomer og oppsokte lege
   □ Min fastlege (allmennlege) oppdaget en kul og henviste til undersøkelse
   □ Ved screening

13. Da du hadde fått diagnosen, hvilken behandling fikk du (ett eller flere kryss)?
   □ Brystbevarende kirurgi
   □ Kirurgi med fjerning av bryst
   □ Fjernet mer enn to lympekjertler
   □ Cellergift
   □ Stråling
   □ Langvarig behandling med medisiner
   □ Annet behandling, spesifiser: __________________________

14. Har du fått påvist spredning etter at du hadde avsluttet behandlingen?
   □ Ja (gå til spørsmål 15)
   □ Nei (gå til spørsmål 17)

15. Hvilket år fikk du påvist spredning? Årstall: _______ Måned: _______
16. Da du fikk påvist spredning, hvilken behandling fikk du (ett eller flere kryss)?
□ Brystbevarende kirurgi
□ Kirurgi med fjerning av bryst
□ Fjernet mer enn to lympekjertler
□ Celleggift
□ Stråling
□ Langvarig behandling med medisiner
□ Annen behandling, spesifiser:

Rehabilitering
17. Har du ønske om rekonstruksjon av brystet?
□ Ja (gå til spørsmål 18)
□ Nei (gå til spørsmål 19)

18. Har du fått rekonstruksjon?
□ Ja
□ Nei

19. Har du deltatt på en eller flere av disse typene med rehabilitering (ett eller flere kryss)?
□ Fysioterapi
□ Annen form for trening
□ Haugelandssenteret
□ Selvhjelpsgrupper (tilbud i lokalforeningen)
□ Hjemmedebek
□ Kurs (for eksempel Catosenteret, Halvorsbøle, Montebello, Røros)
□ Oppfølgingsgrupper på sykehuset
□ Annet, spesifiser:

20. Hvis du ikke har hatt noen form for rehabilitering, hva er den viktigste årsaken (kun ett kryss):
□ Fikk ikke tilbud om rehabilitering
□ Ønsket ikke
□ Ønsket, men fant ikke noe opplegg som passet for meg
□ Prisen var for høy
□ Fikk nok hjelp og støtte fra venner og familie
□ Lang reisevei
□ Vanskkelig å få det til på grunn av familieforpliktelser
□ Andre årsaker:

Utdanning og arbeid
21. Hva er din høyeste fullførte utdanning (kun ett kryss)?
□ Grunnskole (inkluderer folkeskole og realskole)
□ Videregående skole
□ Høyskole og universitet kort utdanning (t.o.m 4 år)
□ Høyskole og universitet lang utdanning (mer enn 4 år)

22. Var du i arbeid før du fikk brystkreft?
□ Ja, heltid (gå til spørsmål 23)
□ Ja, deltids, angi stillingsandel: __ __% (gå til spørsmål 23)
□ Hjemmeværende (gå til spørsmål 32)
□ Nei, aldrepensjonist, inkl AFP (gå til spørsmål 32)
□ Nei, uforepensjonist (gå til spørsmål 32)
□ Nei, annen årsak (gå til spørsmål 32)

23. Er du fortsatt sykmeldt (helt eller delvis)?
□ Ja
□ Nei
24. Hvor lenge var du eller har du vært sykmeldt (helt eller delvis) etter du ble behandlet (Hvis du har hatt tilbakefall, tenk på første gangen du ble behandlet)?
Angi totalt antall måneder fra diagnose: __ __

25. Hvor mange måneder etter du fikk brystkreft begynte du å jobbe igjen?
Antall: __ __ måneder

26. Når du begynte å jobbe igjen, gikk du tilbake til:
☐ En mindre stillingsandel enn før sykmeldingen?
☐ Tilsvarende stillingsandelen før sykmeldingen?

27. Hvor mange måneder etter at du fikk brystkreft kom du tilbake i tilsvarende stillingsandel som før du fikk brystkreft?
Antall _______ måneder

For deg som har hatt tilbakefall (også inkludert spredning)
(Hvis dette ikke er relevant for deg, gå til spørsmål 32)

28. Hvor lenge var du eller har du vært sykmeldt (helt eller delvis) etter at du fikk tilbakefall?
Angi totalt antall måneder fra diagnose: __ __

29. Hvor mange måneder etter du fikk tilbakefall begynte du å jobbe igjen?
Antall: __ __ måneder

30. Når du begynte å jobbe igjen, gikk du tilbake til:
☐ En mindre stillingsandel enn før sykmeldingen?
☐ Tilsvarende stillingsandelen før sykmeldingen?

31. Hvor mange måneder etter at du fikk tilbakefall kom du tilbake i tilsvarende stillingsandel som før du fikk brystkreft?
Antall _______ måneder

Inntekt
32. Hva var din bruttoinntekt (inklusive skatt, sosiale stønader og andre bidrag) det året du ble diagnostisert med brystkreft?
☐ Under 100 000 kr
☐ 100 000 – 199 999 kr
☐ 200 000 – 399 999 kr
☐ 400 000 – 599 999 kr
☐ 600 000 – 999 999 kr
☐ 1 million og over

33. Kan du anslå husholdningens totale bruttoinntekt samme året? ___________ kr

34. Hva er din bruttoinntekt forrige måned? ____________ kr

Bruk av helsetjenester
35. Hvor mange ganger har du vært hos fastlegen (allmennlege) eller annen lege de siste 12 måneder?
(ikke inkluder besøk hos fastlege og legevakt som følge av syke barn, gamle foreldre, o.l.)
☐ Ingen
☐ 1 – 2
☐ 3 – 4
☐ 5 +
36. Hvor mange ganger har du (bortsett fra for behandling av din brystkreft) vært på sykehus (innlagt eller poliklinisk) de siste 3 årene?
- Ingen
- 1 – 2
- 3 – 4
- 5 +

**Helsetilstand**
37. Hvordan opplever du din helsetilstand for tiden?
- Meget god
- God
- Verken god eller dårlig
- Dårlig
- Veldig dårlig

38. Har du i løpet av de to siste ukene vært plaget med noe av det følgende?
*(Kryss for hver linje)*

<table>
<thead>
<tr>
<th>Ikke plaget</th>
<th>Litt plaget</th>
<th>Ganske mye plaget</th>
<th>Veldig mye plaget</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stadig redd eller engstelig</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Nervøsitet, indre uro</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Følelse av håploshet med hensyn til fremtiden</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Nedtrykt, tungsynlig</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Mye bekymret eller urolig</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

**Familie og venner**
39. Da du ble diagnostisert med brystkreft, bodde du sammen med noen?
- Ja (gå til spørsmål 40)
- Nei (gå til spørsmål 41)

40. Hvem bodde du i så fall sammen med?
- Ektefelle/samboer: ☐ Ja ☐ Nei
- Andre personer, 18 år og eldre: ☐ Ja ☐ Nei
- Personer under 18 år: ☐ Ja ☐ Nei

41. Hvor mange gode venner har du? Antall venner: __ __
*(Regn med de du kan snakke fortrøstelig med og som kan gi deg hjelp dersom du trenger det. Tell ikke med de du bor sammen med, men ta med andre slektnings).*

42. Hvor mange foreninger, lag, grupper, kirkesamfunn e.l. deltar du i på fritiden? *(skriv 0 hvis ingen)*
Antall: __ __

**Gentesting**
43. Kjenner du til at kvinner med brystkreft kan tilbys en genetisk test for å finne ut om man er arvelig disponert?
- Ja (gå til spørsmål 44)
- Nei (gå til spørsmål 46)

44. Hvor fikk du informasjon om denne testen?
- Faslegen/allmennlege?
- Helsepersonell på sykehus
- Brystkreftforeningen
- Media (avisen, TV og radio)
- Venner og familie
- Annet, spesifiser ____________________________
45. Har du tatt en gentest?
- Ja
- Nei
- Har ikke fått tilbud

46. Mener du at kvinner med brystkreft skal tilbys en gentest?
- Ja
- Nei
- Vet ikke

47. Mener du at også kvinner uten brystkreft, men med en mistanke om arvelig disposisjon skal tilbys en gentest?
- Ja
- Nei
- Vet ikke

48. Ville du selv tatt en gentest hvis du fikk tilbud?
- Ja
- Nei
- Vet ikke

49. Vil du anbefalt din datter å ta en gentest?
- Har ingen datter
- Ja
- Nei
- Vet ikke

50. Vil du anbefalt din sønn å ta en gentest?
- Har ingen sønn
- Ja
- Nei
- Vet ikke

Kommentarer
Hvis du har noen kommentarer til for eksempel uklarheter ved skjemaet eller viktige faktorer vi ikke har spurt om, er det fint om du kommenterer dette under:

Tusen takk!
Velkommen til en spørreundersøkelse om gentesting og mammografi!

Først vil vi stille deg noen bakgrunnsspørsmål

Hvilket år er du født?

Er du medlem av Brystkreftforeningen?
- Ja
- Nei

Har du hatt brystkreft?
- Ja
- Nei

Hvilket år fikk du diagnosen?

Da du hadde fått diagnosen, hvilken behandling fikk du?
- Brystbevarende kirurgi
- Kirurgi med fjerning av bryst
- Fjernet mer enn to lymfeknuter
- Cellegift
- Stråling
- Langvarig behandling med medisiner
- Annen behandling
Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Da du hadde fått diagnosen, hvilken behandling fikk du?»: Annen behandling

- Spesifiser hva slags behandling

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Har du hatt brystkreft?»: Ja

- Har du fått påvist spredning etter at du hadde avsluttet behandling?
  - Ja
  - Nei

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Har du fått påvist spredning etter at du hadde avsluttet behandling?»: Ja

- Hvilket år fikk du påvist spredning?

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Har du fått påvist spredning etter at du hadde avsluttet behandling?»: Ja

- Da du fikk påvist spredning, hvilken behandling fikk du?
  ett eller flere kryss
  - Brystbevarende kirurgi
  - Kirurgi med fjerning av bryst
  - Fjernet mer enn to lymfeknuter
  - Cellegift
  - Stråling
  - Langvarig behandling med medisiner
  - Annen behandling

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Da du fikk påvist spredning, hvilken behandling fikk du?»: Annen behandling

- Spesifiser hva slags behandling

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Hva er din høyeste fullførte utdanning?»

- Grunnskole
- Videregående skole
- Høyskole og universitet, kort utdanning (inntil 4 år)
- Høyskole og universitet, lang utdanning (mer enn 4 år)
• **Hva er din nåværende jobbsituasjon?**
  - Heltidsansatt
  - Deltidsansatt
  - Hjemmeværende
  - Alderspensjonist, inkl AFP
  - Uførepensjonist
  - Annet

  Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Hva er din nåværende jobbsituasjon?»: Annet

• **Spesifiser**

• **Hva var din årlige bruttoinntekt siste år (inkludert skatt, sosiale stønader og andre bidrag)?**
  - Under 100 000 kr
  - 100 000 – 199 999 kr
  - 200 000 – 399 999 kr
  - 400 000 – 599 999 kr
  - 600 000 – 999 999 kr
  - 1 million og over

• **Hva er din sivilstatus?**
  - Gift/Samboer
  - Separert
  - Enke
  - I et forhold
  - Singel

• **Har du barn?**
  - Ja
Hvor er du og din mor født?

<table>
<thead>
<tr>
<th></th>
<th>Du</th>
<th>Din mor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norge</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Europa, unntatt Norge</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nord-Amerika</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sør-Amerika</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midtøsten</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afrika</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nå vil vi stille deg noen spørsmål om gentesting og brystkreft

Her kommer noen påstander om gener og brystkreft. Sett et kryss for det du tror er sant/usant for hver påstand

<table>
<thead>
<tr>
<th>Påstand</th>
<th>Sant</th>
<th>Usant</th>
<th>Vet ikke</th>
</tr>
</thead>
<tbody>
<tr>
<td>I av 10 kvinner er arvelig disponert for brystkreft</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Halvparten av alle brystkrefttilfeller skyldes arvelig disposisjon for brystkreft</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>En far kan bringe videre arvelig disposisjon for brystkreft til sine barn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Søsteren til en kvinne som er arvelig disponert for brystkreft, har selv</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
50% sjanse for å være arvelig disponert for brystkreft

<table>
<thead>
<tr>
<th>Sant</th>
<th>Usant</th>
<th>Vet ikke</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

En kvinne som ikke er arvelig disponert for brystkreft kan fremdeles få bryst – eller eggstokkpreft

Brystkreft før fylte 50 år i livet skyldes mer sannsynlig en arvelig disposisjon for brystkreft, enn brystkreft sent i livet

<table>
<thead>
<tr>
<th>Sant</th>
<th>Usant</th>
<th>Vet ikke</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

En kvinne som er arvelig disponert for brystkreft har større risiko for å utvikle eggstokkpreft

Alle kvinner som er arvelig disponert for brystkreft vil få brystkreft

<table>
<thead>
<tr>
<th>Sant</th>
<th>Usant</th>
<th>Vet ikke</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

En kvinne som fjerner brystene kan fortsatt få brystkreft

Det er vanskelig å oppdage eggstokkpreft før etter at den har spredd seg

<table>
<thead>
<tr>
<th>Sant</th>
<th>Usant</th>
<th>Vet ikke</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

Fjerning av eggstokkene vil garantert forhindre eggstokkpreft

Kjenner du til at kvinner med brystkreft kan tilbys en genetisk test for å finne ut om man er arvelig disponert?

- Ja
- Nei

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Kjenner du til at kvinner med brystkreft kan tilbys en genetisk test for å finne ut om man er arvelig disponert?»: Ja

Hvor fikk du informasjon om denne testen?

- Fastlegen/allmennlege
- Helsepersonell på sykehus
- Brystkreftforeningen
- Media (aviser, TV og radio)
- Internett
- Venner og familie
Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Hvor fikk du informasjon om denne testen?»: Annet

- **Spesifiser**

Side 15

- **Har du tatt en gentest?**
  - Ja
  - Nei
  - Har ikke fått tilbud

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Har du tatt en gentest?»: Har ikke fått tilbud, Nei

- **Ville du selv tatt en gentest hvis du fikk tilbud?**
  - Ja
  - Nei
  - Vet ikke

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Ville du selv tatt en gentest hvis du fikk tilbud?»: Nei

- **Hvorfor ikke?**
  - Ønsker ikke å vite
  - Ikke relevant
  - Annet

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Hvorfor ikke?»: Annet

- **Spesifiser**

Side 16

- **Mener du at kvinner med brystkreft skal tilbys en gentest?**
  - Ja
  - Nei
  - Vet ikke

Side 17

- **Mener du at også kvinner uten brystkreft, men med mistanke om arvelig disposisjon skal tilbys en gentest?**
  - Ja
  - Nei
Vet ikke

Side 18

- **Vil du anbefale din datter å ta en gentest?**
  - Har ingen datter
  - Ja
  - Nei
  - Vet ikke

Side 19

- **Vil du anbefale din sønn å ta en gentest?**
  - Har ingen sønn
  - Ja
  - Nei
  - Vet ikke

Side 20

- **Har du deltatt i en spørreundersøkelse via Brystkreftforeningen om rehabilitering, arbeidsevne, mammografi og gentest for kvinner med brystkreft i 2009?**
  - Ja
  - Nei
  - Husker ikke

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Har du deltatt i en spørreundersøkelse via Brystkreftforeningen om rehabilitering, arbeidsevne, mammografi og gentest for kvinner med brystkreft i 2009?»: Ja

- **Har du endret din mening når det gjelder genetisk testing fra 2009?**
  - Ja
  - Nei
  - Husker ikke

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmål «Har du endret din mening når det gjelder genetisk testing fra 2009?»: Ja

- **Hvilken mening har du endret?**
### Hva mener du er fordeler med å ta en gentest? Kryss av for hver linje

<table>
<thead>
<tr>
<th>Mulighet for å planlegge fremtiden</th>
<th>Sterkt enig</th>
<th>Enig</th>
<th>Verken enig eller uenig</th>
<th>Uenig</th>
<th>Sterkt uenig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Å lære om mitt barns risiko</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Å vite om det er behov for å øke screening</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Side 22

### Hva mener du er ulemper med å ta en gentest? Kryss av for hver linje

<table>
<thead>
<tr>
<th>Bekymret for å miste forsikring</th>
<th>Sterkt enig</th>
<th>Enig</th>
<th>Verken enig eller uenig</th>
<th>Uenig</th>
<th>Sterkt uenig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bekymringer om hvordan familien påvirkes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tror ikke at det kan forhindre kreft</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tungt å håndtere det følelsesmessig</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testresultatet kan være unøyaktig</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Til slutt, noen spørsmål om mammografi

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmålet «Har du hatt brystkreft?»: Ja

- **Før du ble diagnostisert med brystkreft, tok du noen gang mammografi?**
  - Ingen
  - Offentlig
  - Privat
  - Begge deler

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmålet «Har du hatt brystkreft?»: Ja

- **Har du vært på mammografi etter at du ble operert?**
  - Ja
  - Nei

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmålet «Har du vært på mammografi etter at du ble operert?»: Ja

- **Hvor mange ganger har du vært på mammografi, både mammografi-screening og mammografi ved etterkontroll, etter at du ble operert?**

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmålet «Har du hatt brystkreft?»: Nei

- **Tok du noen gang mammografi?**
  - Ingen
  - Offentlig
  - Privat
  - Begge deler

Dette elementet vises dersom et av følgende alternativer er valgt på spørsmålet «Tok du noen gang mammografi?»: Ingen

- **Hvorfor ikke?**

Kjenner du til hvem det er som tilbys offentlig mammografi-screening (Mammografiprogrammet) i Norge?

- Alle kvinner i aldersgruppen 40-69 år
- Alle kvinner i aldersgruppen 45-69 år
Alle kvinner i aldersgruppen 50-69 år

- Synes du at offentlig mammografi-screening skal tilbys kvinner fra:
  - Fylte 40 år
  - Fylte 45 år
  - Fylte 50 år

- Synes du at man bør ha en henvisning fra lege hvis man ønsker å ta mammografi privat/utenfor det offentlige Mammografiprogrammet?
  - Ja
  - Nei
  - Vet ikke

- Synes du at mammografi-screening bør være gratis?
  - Ja, mammografi-screening bør være gratis
  - Nei, det er ok å betale en egenandel som kan føres opp på egenandelskort
  - Nei, det er ok å betale en egenandel som ikke føres opp på egenandelskort
  - Nei, kostnaden er ikke viktig
  - Vet ikke

Kryss av for hver linje om du er enig eller uenig i følgende påstander

<table>
<thead>
<tr>
<th>Sterkt enig</th>
<th>Enig</th>
<th>Verken enig eller uenig</th>
<th>Uenig</th>
<th>Sterkt uenig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Det gir meg god selvfølelse å ta mammografi</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Det å ta mammografi reduserer mine bekymringer om brystkreft</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mammografi gjør det mulig å oppdage svulster på et tidlig tidspunkt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Mammografi reduserer risiko for å dø av brystkreft**

**Mammografi reduserer risiko for å trenge radikal kirurgi hvis brystkreft oppdages**

**Mammografi gjør det mulig å oppdage svulster før jeg eller helsepersonell kan kjenne forandringer**

**Rutinemessig mammografi vil gjøre meg bekymret for brystkreft**

**Det er pinlig å ta mammografi**

**Det tar for mye tid å ta mammografi**

**Det er smertefullt å ta mammografi**

**Det er dyrt å ta mammografi**

**Mammografi er skadelig på grunn av stråling og/eller trykk**

**Mammografi kan føre til overdiagnostikk/overbehandling**

**Det kan være vanskelig ved mammografi alene å skille mellom uskyldige forandringer og forandringer som kan være brystkreft eller forstadijer.**

**Noen tilfeller av brystkreft oppdages ikke ved mammografi, eller oppstår i tiden mellom to mammografiundersøkelser**

---

Tusen takk for deltagelse!
Klikk "Send" for å sende inn din besvarelse.