# Učinak edukacijske intervencije na točnost samoprocjene rizika obolijevanja od karcinoma dojke i na znanje o kemoprevenciji

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**Doctoral thesis / Disertacija**

**2021**

*Degree Grantor / Ustanova koja je dodijelila akademski / stručni stupanj:* **Josip Juraj Strossmayer University of Osijek, Faculty of Medicine Osijek / Sveučilište Josipa Jurja Strossmayera u Osijeku, Medicinski fakultet Osijek**

*Permanent link / Trajna poveznica:* https://urn.nsk.hr/urn:nbn:hr:152:415144

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*Download date / Datum preuzimanja:* **2024-03-29**

*Repository / Repozitorij:*

Repository of the Faculty of Medicine Osijek

JOSIP JURAJ STROSSMAYER UNIVERSITY OF OSIJEK

FACULTY OF MEDICINE

Sonja Vukadin

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Osijek, 2021.

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The dissertation contains 121 pages.

## PREFACE

This study was the part of the Institutional Project of the Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, titled 'The Development of Educational Intervention and the Assessment of its Effect on Chemoprevention Attitude', project manager Assoc.Prof. Martina Smolic, Ph.D.

Foremost, I would like to thank all the participants of this study, your good will was the main prerequisite for this work.

Thank you Kaja Grgić and Luka Malenica, for all the hard work during the participants regrutation.

I would like to thank Assoc.Prof. Martina Smolic, Ph.D. who trully is a mentor – a carring teacher and a friend.

Thank you Assist. Prof. Kristina Bojanić, Ph.D., for your big contribution to this study.

A heartful thanks to Kristina Kralik, Prof. who was always available for all the advice in relation to data analysis.

The warmest thanks to my family. To my brother Filip who was recruiting the participants and who advised me during this dissertation writing. To my parents and brother Ivan, thank you for teaching me how to be persistent even when it is hard to. Mom, thank you for looking after our little angel whenever I couldn't!

To my Stjepan, thank you for being so supportive, I am so happy to have you.

I dedicate this work to my family, who is my rock, and primarily to our Lucija who is my biggest joy.

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**Abbreviations**

| | |
|---|---|
| **AH** | atypical hyperplasia |
| **AI** | aromatase inhibitor |
| **AJCC TNM** | American Joint Committee on Cancer Tumour Nodes Metastases |
| **AR** | average risk |
| **BC** | breast cancer |
| **BC RF** | breast cancer risk factor |
| **BCPT P-1** | Breast Cancer Prevention Trial |
| **BCRAT** | Breast Cancer Risk Assessment Tool |
| **BD** | breast density |
| **BMD** | bone mineral density |
| **BMI** | body mass index |
| **BOADICEA** | Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm |
| ***BRCA1*** | *Breast Cancer Gene 1* |
| ***BRCA2*** | *Breast Cancer Gene 2* |
| **DCIS** | ductal carcinoma *in situ* |
| **EI** | educational intervention |
| **ER** | estrogene receptor |
| **ER(+) BC** | estrogene receptor positive breast cancer |
| **ER(+) IBC** | estrogene receptor positive invasive breast cancer |

| | |
|---|---|
| **FHS** | family history score |
| **HER2** | human epithelial growth factor receptor 2 |
| **HL** | health literacy |
| **HR** | high risk |
| **HRT** | hormone replacement therapy |
| **IBIS – I** | International Breast Cancer Intervention Study One |
| **IBIS – II** | International Breast Cancer Intervention Study Two |
| **IQR** | interquartile range |
| **Ki67** | proliferating cell nuclear antigen |
| **LCIS** | lobular carcinoma in situ |
| **MAP.3** | Mammary Prevention 3 Trial |
| **OTC** | over-the-counter |
| **PgR** | progesterone receptor |
| **RCT** | randomised controlled trial |
| **RF** | risk factor |
| **SERM** | selective estrogen receptor modulator |
| **SF-36** | Short Form 36 |
| **STAR P-2** | Study of Tamoxifen and Raloxifene |
| **VTE** | venous thromboembolism |

# 1. INTRODUCTION

## 1.1. BREAST CANCER

### 1.1.1 Breast cancer definition and epidemiology

Breast cancer (BC) is malignant tumor originated from epithelial cells in terminal duct-lobular unit (1).

Breast cancer is the most common malignancy in women, with its highest incidence in the developed world. Estimated 2 088 849 women were diagnosed with BC in 2018 throughout the world, accounting for 24.2% of all malignancies in women (2). In 2016, 97 000 people died from BC in the European Union (EU) and among EU Member States, Croatia had the highest standardised death rate for BC, it was 40.4/100 000 inhabitants (3). The world age-standardized incidence rate is 46.3/100 000 (2). In 2018, worldwide age-standardised mortality rate was 13.0/100 000 (2), whereas mortality rate in Croatia in 2017 was 40.0/100 000 (4).

### 1.1.2 Risk factors and protective factors

It is known that certain factors increase the risk of BC. One of them is the length of exposure to estrogen, therefore menarche before the age of 11 and late menopause onset, ie. after age of 54, are associated with increased BC risk (5, 6). Childbearing reduces the BC risk and that reduction is higher in women who had their first full-term pregnancy early, as compared to those who were aged over 30. Nulliparity increases BC risk (6). Obesity in premenopausal women slightly decreases the risk of developing BC, while it increases the risk in postmenopausal women, eg. body mass index (BMI) > 30 kg/$m^2$ leads to a 30% risk increase as compared to women with normal BMI (7). When it comes to alcohol, even moderate intake (1 unit per day) increases the risk, and it further increases it by 7% for intake of each additional unit of alcohol (8). Physical activity showed to reduce BC risk in both premenopausal and postmenopausal women and this benefit remains irrespective of BMI reduction. It is still unclear what dose and intensity of workout should be recommended for BC risk reduction,

but it is encouraging to know that even walking showed to be beneficial (7). One of the most significant risk factors (RF) is age. BC risk increases with age and its incidence throughout the world peaks at the age of 60, while in Croatia the highest incidence of BC is at age 65 to 70 (4, 6, 8). There is significant geographical and ethnical variation in BC incidence, namely in Asian and African countries the peak incidence is between age 40 and 50 (9). Some breast tissue characteristics, like breast density (BD) are positively correlated with BC risk (10). Due to its significance, breast density is being investigated as potential biomarker of efficiency of agents used in BC chemoprevention (11, 12). Another aggravating factor in women with high BD is the difficulty in their mammogram interpretation, leading to increased chance of missing the diagnosis of an early-stage BC (13). Positive family history contributes to the person's own risk, but it is a complex relationship. One study proposed the use of family history score (FHS) to assess individual's risk more accurately. FHS takes into account family's age structure, age at the time of BC diagnosis in family members and national cancer incidence rate (14). *BRCA 1* and *BRCA 2* gene (*Breast Cancer Gene 1* and *2*) mutations are responsible for over 90% of hereditary breast cancers, which are characterised by an early onset, tendency to affect contralateral breast and increased ovarian cancer risk (15). But, several other genes are known to be present in BC tissue and appear to be potential candidates for targeted therapy (8).

### 1.1.3 Primary breast cancer chemoprevention

Primary BC chemoprevention is a method by which the risk of estrogen receptor positive (ER(+)) invasive BC development is reduced by endocrine treatment. To date two different classes of drugs have been investigated in large randomised clinical trials (RCTs), selective estrogen receptor modulators (SERM) and aromatase inhibitors (AI). Both interfere with estrogen activity: SERM by blocking its effect on breast tissue, but preserving agonistic effect on other tissues and organs, while AI inhibit androgen conversion into estrogen in adipose tissue (16).

Primary BC chemoprevention is only recommended for women of high BC risk. Several RCTs were conducted over the years. Breast Cancer Prevention Trial (BCPT P-1) was a double-blind, placebo-controlled RCT in which 13 388 high-risk (HR) women were recruited. HR women were those with predicted 5-year BC risk of at least 1.66% according to Gail model or

with history of lobular carcinoma *in situ* (LCIS). Hormonal replacement therapy was not permitted in this study. Intervention group received 20mg of tamoxifen once a day for 5 years. Results indicated 49% risk reduction in invasive ER(+) BC (IBC) incidence. The subgroup analysis showed 56% risk reduction in women with history of LCIS and 86% risk reduction in women with history of atypical hyperplasia (AH) (17).

IBIS-I study, a randomised, placebo-controlled study enrolled 7154 women aged 35 to 70 (18). The study results showed risk reduction in IBC incidence by about a third in the treatment group, with greatest effect on ER(+) BC and DCIS (ductal carcinoma *in situ)*. Treatment with tamoxifen had no effect on triple negative BC. Long-term follow up showed that this beneficial effect is sustained for at least further 5 years after treatment completion, while side effects were limited to the treatment period (19).

The Study of Tamoxifen and Raloxifene (STAR P-2) trial compared the efficacy of tamoxifen and raloxifene among HR postmenopausal women. The outcome was that raloxifene was 76% as effective as tamoxifen in ER(+) IBC risk reduction, but with favourable side effect profile (20-22).

The fact that neither tamoxifen, nor raloxifene were found to be ideal agents, further trials investigated exemestane and anastrozole, two AIs. Exemestane is irreversible AI of steroid structure, its efficacy in primary BC chemoprevention was investigated in MAP.3 (Mammary Prevention 3 Trial) trial in centres in the USA, Canada, France and Spain. The follow-up was only 3 years and it showed a 65% risk reduction of ER(+) IBC (23). Due to its steroid structure and consequent potentially androgenic effect in bone, exemestane seemed to be a promising candidate for bone mineral density (BMD) preservation. However, MAP.3 trial design did not prospectively include the assessment of bone health and all the bone-related adverse events reports were left to be self-reported. Therefore, no conclusions in that regard could have been drawn (24).

Anastrozole showed to reduce the risk of IBC by 50% and the risk of ER (+) BC by 58% in HR women in IBIS-II trial (25). Overall, 3864 HR postmenopausal women were enrolled in this randomised, placebo-controlled study. The beneficial effect of anastrozole was sustained for at least seven years (19).

As per American Society of Clinical Oncology (ASCO) Clinical Guidelines from 2019, the agents used for primary BC chemoprevention are anastrozole in addition to exemestane, raloxifene or tamoxifen in postmenopausal women. While tamoxifen at the dose of 20 mg daily for 5 years, in women over 35 who have completed childbearing, is considered a standard of care (26). This kind of intervention would be suitable for women at increased risk, as calculated by the BCRAT. All the clinical trials investigating chemoprevention agents considered the 5-year BC risk of >= 1.66% to be elevated and women with such risk to be eligible to engage in such treatment. However, United States Preventive Services Task Force consider a 5-year risk >= 3% being risk/benefit acceptable (27).

In a UK study published in 2018 by Hackett et al, where they investigated the uptake of tamoxifen in women with moderately high or high BC risk, only 14.7% of women commenced tamoxifen. The uptake was higher among women who already had children (28). Even more worrisome is the fact that less than 5% of HR women in the USA who are offered chemoprevention agent decide to take it (20).

There are number of concerns related to implementation of primary BC chemoprevention. The lack of knowledge among health care providers seems to be the major one. Practical guidelines have been created for primary care physicians and they include step-wise approach consisting of: individual's BC risk assessment according to Gail model and discussion about the results, selection of the appropriate chemoprevention drug based on risk-benefit analysis, shared decision-making and follow-up with monitoring and management of side effects that may arise from the treatment (29). However, there seems to be a lot of uncertainty still left and neither health care providers nor HR women are comfortable enough to fully embrace them.

#### 1.1.3.1 Breast cancer risk assessment tools

The first step in deciding about the nature of preventive measures is BC risk assessment. To date several risk assessment tools have been created, however each of them has limitations. The most important one is that they are most relevant for ER(+) BC risk prediction, whereas for more aggressive forms, such as tripple negative BC we still have no appropriate tool, which is mainly due to the lack of knowledge about RFs contributing to its

development (30). It is crucial to develop more relevant risk assessment tools in the future, in order to ensure the optimal candidates selection who would trully benefit from primary BC chemoprevention. Some of the most commonly used BC risk assessment tools are explained below.

In nearly all primary chemoprevention trials eligibility criteria included 5-year BC risk > 1.66% calculated according to Gail model. Breast Cancer Risk Assessment Tool (BCRAT) was designed by Dr Mitchell Gail of National Cancer Institute in 1989 and is used to calculate one's 5-year BC risk and a lifetime BC risk. It compares individual's risk with the risk of a woman of the same age and race who has no particular BC RFs. It, however, should not be used in women who are at risk of developing hereditary BC, such as *BRCA 1* and *BRCA 2* mutation carriers or women diagnosed with syndromes associated with increased risk of BC (31).

International Breast Cancer Intervention Study (IBIS) BC risk evaluation tool calculates the risk in the succeeding 10 years, as well as the lifetime risk and compares it to the average risk (AR). It can be used in women who are *BRCA 1* or *2* mutation carriers. The latest version of IBIS Risk Assessment Tool, v8.0, alongside classical RFs, incorporates BD and also data about family history of BC up to third degree relatives (32).

Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) model calculates the BC risk in known carriers of genes that make an individual more susceptible to breast and ovarian cancer (33).

#### 1.1.3.2 Drugs used as breast cancer chemoprevention agents

As mentioned above, agents used in primary BC chemoprevention belong to two different classes of drugs: SERMs and AIs.

Tamoxifen and raloxifene are SERMs. Tamoxifen exhibits estrogen-like effects on endometrium, bone and lipid metabolism, while it acts as an estrogen antagonist in the breast tissue. The side effect profile includes menopause-like symptoms like hot flashes and night sweats; cataracts, nausea, but also more serious effects like hypercoagulability and consequent venous thromboembolic events (VTE) (34). The increase in VTE risk is by 2 to 7-fold (35). Due to its agonistic effect on endometrium, tamoxifen can cause variety of

endometrial proliferative conditions, including endometrial cancer. The risk of endometrial cancer in postmenopausal women is reported to be 1.5- to 6.9-fold higher than in general population (36). However, interestingly, it was found that 31.3% of women at the time of ER (+) BC diagnosis also suffer from some form of endometrial proliferative pathology for which they are asymptomatic (37, 38). The efficacy of tamoxifen in primary BC risk reduction was observed in several clinical trials. The Royal Marsden Prevention trial was conducted in late 1980s and it recruited 2471 women of increased BC risk. At a twenty-year follow up, the investigators concluded that tamoxifen did not significantly reduce the risk of ER(+) BC during 8-year treatment period, but it did in the long term post treatment period. Additionally, side effects were mainly reported during the treatment period (39). International Breast cancer Intervention Study (IBIS-1) on 7145 women showed a reduction in invasive ER (+) BC by 31% in women with increased BC risk, this reduction was noted not only during the treatment period, which was 5 years, but also at median 16 years follow up after randomisation. The effect size was noted to be higher in women who did not use hormone replacement therapy (HRT) before or during the trial. Importantly, tamoxifen prophylaxis is contraindicated in women at high risk (HR) of thromboembolic events (19, 40). Raloxifene is another SERM, also used for osteoporosis treatment in postmenopausal women. It exerts estrogen agonistic effects on bone and lipid metabolism, while it blocks the effects of estrogen in breast tissue and endometrium, therefore not increasing the risk of endometrial malignancy. However, raloxifene too increases the risk of thromboembolic events (41) Its efficacy in primary BC prevention was investigated in STAR trial, which included nearly 20 000 women. The trial comprised 2 arms, tamoxifen and raloxifene arm. Raloxifene showed to be inferior to tamoxifen in invasive ER(+) BC risk reduction but proved to cause less thromboembolic events and cataracts (21). In addition, raloxifene showed no increase in the risk of endometrial cancer as compared to placebo (42).

AIs used in primary BC chemoprevention are anastrozole and exemestane. The mechanism by which AIs reduce ER(+) BC is by reducing the peripheral conversion of androgens into estrogen, which is the main source of estrogen in postmenopausal women. Anastrozole is the first and most commonly used in this indication. The most concerning side effect is bone mineral density (BMD) reduction, which can lead to osteoporosis (43). It would be ideal to investigate BMD at baseline in every woman and to introduce bone protection

therapy if required. However, the phase III DATA study (Different Durations of Adjuvant Anastrozole Therapy After 2 to 3 Years Tamoxifen Therapy in Breast Cancer) reported that only 48.9% of 1860 patients who were commenced on adjuvant anastrozole had baseline densitometry scan (44). IBIS – II trial included 3864 postmenopausal women with increased BC risk, who were randomised to take either anastrozole 1mg once daily or placebo for 5 years. The results showed about 50% BC risk reduction, which persisted even after 10 years of follow-up. Interestingly, there were no excess fractures in anastrozole group (45). Exemestane is an irreversible AI. Due to its steroid structure it also exhibits some androgenic effects, consequently it causes BMD reduction to lesser extent than anastrozole (46). Some of the other common AI side effects include musculosceletal symptoms, such as artralgia, carpal tunnel syndrome, joint stiffness, vasomotor symptoms, such as night sweats and hot flashes; eye dryness and hypertension (25). In MAP.3 trial, where exemestane efficacy in primary BC risk reduction was compared with placebo on 4560 postmenopausal women with increased BC risk at a median 3-year follow-up the results showed about 50% reduction in ER(+) BC and no serious toxic side effects attributed to exemestane (23).

### 1.1.4 Secondary breast cancer prevention - screening programmes

Screening programs for BC early detection had widely been implemented due to its major public health importance. In Croatia, the national screening program for early detection of BC began in 2006; every two years women aged 50-69 are invited to undergo screening mammography. Unfortunately, the response to invitation to participate has only been about 60% in the first three rounds. The benefit from the screening program lies in the fact that since its initiation, 60-70% of newly diagnosed cases were localized disease, as compared to only 40% of cases before the program had been implemented. Also, the BC mortality rate decreased by 15-20% in 2017 (47). Similarly, national screening programme in the U.S. led to significantly reduced BC mortality rate among women aged 50 to 70. As expected, it did not affect mortality rate among women below 50 years of age (8).

### 1.1.5 Breast cancer diagnosis

Breast cancer diagnosis is based on anamnestic data, physical examination, imaging and pathohistological analysis. Primary tumor is assessed by examination, mammography and breast ultrasound. Oftentimes, MRI breast is also indicated for more detailed tumor assessment. Subsequently, core tissue biopsy is performed and pathology analysis for histology, grade, ER (estrogen receptor), PgR (progesterone receptor) and HER2 (human epidermal growth factor receptor 2) status and Ki67 (proliferating cell nuclear antigen). All these tumor characteristics together are required to establish the tumor subtype, decide about the treatment and estimate the prognosis. Nowdays, with advancements in treatment additional test can be performed in order to assess for certain targeted therapy eligibility (48). An ultrasound of axillae needs to be performed to assess the nodal status, followed by the ultrasound-guided node biopsy if required. More investigations are indicated only in case of high suspicion for metastatic disease (49).

### 1.1.6 Breast cancer treatment and prognosis

The treatment of BC is tailored according to its AJCC TNM (American Joint Committee on Cancer Tumour Node Metastases) stage and tissue characteristics. The regiments consist of variuos combinations of chemotherapy, hormonal therapy, HER2 antibodies, radiation therapy and different surgical interventions. Whereas immune checkpoint inhibitors' efficacy is currently being investigated in treatment of triple negative BC (50).

Breast cancer can be divided into luminal type A, luminal type B, HER2 positive non-luminal type and triple negative BC by its clinicopathological surrogate definition.

Luminal type A tumors are ER-positive, HER2-negative, with low Ki67 (proliferating cell nuclear antigen), high PgR and low-risk molecular signature. This type is a predictor of favourable prognosis (49).

Luminal type B tumors can be HER2-negative, ER-positive and either Ki67 high or PgR low, with HR molecular signature or HER2-positive, ER-positive, with any Ki67 and PgR . This type is characterised by aggressive clinical behaviour (49, 51).

HER2-positive non-luminal BC is HER2-positive, while ER and PgR are absent. Prognosis in this type is similar to luminal type B tumor (52).

In basal-like BC ER and PgR are absent and HER2 is negative (triple negative BC). This type is predictor of a poor prognosis, especially in metastatic disease (49).

Adjuvant hormonal therapy is indicated in women who were diagnosed with early stage ER(+) BC and to reduce the occurence of secondary and contralateral BC. For this purpose tamoxifen is used in premenopausal women, whereas AIs are used in postmenopausal women. Treatment duration is 5 years for low risk recurrence cases and 7-10 years in women with HR of recurrence (53).

## 1.2. HEALTH LITERACY

### 1.2.1 Definition

Health literacy (HL) is defined as “the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions” (54). It is a concept that recognizes that health care system as it is does not suit to every individual and it fails to answer everyone’s needs. As such, it seeks adjustment of health care provision to ensure equally good access to the service to all the people (55).

There are three forms of HL (56). Functional HL involves having the ability to access and process health-related information, which enables informed decision-making about own health. Interactive HL means ability to gain information from interaction with health care workers or other persons and is the most important segment of one’s HL. Critical HL involves retaining, processing and critically appraising health-related information and making a decision based on that, this involves a shared decision-making, too (55-57).

Most HL assessment instruments confine HL to an individual, but van der Heide et al. dispute this kind of approach by saying HL is predicted not only by person’s characteristics but

also the characteristics of the health system and more importantly by the interaction of the two (58).

### 1.2.2 Predictors of health literacy

European Health Literacy Survey, HLS-EU, found that low socio-economic status is the strongest predictor of low HL. Lower educational level also has strong negative correlation with HL, as does older age. In this way vulnerable subsets of population were identified (59) and strong disparities in HL among EU Member States reflected the difference in population structure based on these criteria. Importantly, HL is not definite and can successfully be modified by carefully tailored educational intervention (EI), which in turn can increase the participation in screening programmes (60).

### 1.2.3 Health literacy implications

Sufficient level of HL is required to successfully access and utilize health care services, to care about own health and health of the others, to communicate with health care providers and to participate in health debates and shared decisions about own health (55). To date many HL surveys have been conducted. Published data from studies on different populations suggest that parents with lower HL level, in comparison to parents with higher HL, have lower health knowledge and also practice more disadvantageous behaviours that lead to deleterious effects on their child's health and their worse health outcomes (55). Research to date showed that HL positively correlates with chronic disease outcomes (61), whereas lower HL represents a challenge in disease control, due to poor adherence to medication and lifestyle modifications (58, 62, 63). Another consequence of low HL is it's negative impact on preventive behaviour. It was found that people with low HL are less likely to participate in screening mammography, vaccination and to have Pap smears (64). HL is also a prerequisite for better engagement in shared decision-making, which is the basis for patient-centred care (65). Low HL showed to contribute to poorer disease outcomes and inadequate use of health care services, including inappropriate Emergency Department attendances and unnecessary

hospital admissions and readmissions (66). As a consequence, inappropriate use of health services leads to additional expenses.

### 1.2.4 Assessment tools

To date over one hundred different HL measurement tools have been developed and used in different studies. Part of them is intended for HL examination on different populations and the rest of them can serve as an individual screening instrument (55). European Health Literacy Survey Consortium created European Health Literacy Survey Questionnaire (HLS-EU-Q) which is validated for the use in the European population (67). Interestingly, a study conducted in Australia showed that proportion of people in general population who have inadequate HL ranges from 7% to 60%, depending on the assessment tool (55), which questions the appropriateness and the validity of the tools used.

## 1.3. EDUCATIONAL INTERVENTION

Population education is one of the main instruments that public health service uses in order to ensure improved health-related quality of life. Participation rates in screening programs drastically increase after EI is conducted on a target population (68). There are different types of such interventions: lectures, leaflets, letters or call- and text message-mediated education. In order to accomplish greater success, an educator needs to carefully tailor its intervention to suit his target audience best. There are behavioural theories that advocate different approaches in educating lay people about health-related matters. But, none of them dominates the research or practice of health promotion or education (69). When educating about prevention behaviour, like participation in screening programmes or about vaccines, it is important to keep in mind that one's attitudes toward such interventions and health-related behaviour are affected by so many factors, and not all of them we can influence. For example, according to Health Belief Model, one's beliefs about own susceptibility to certain disease and the perceived benefit of a certain intervention are important determinants of behaviour (69). EI aiming to increase the awareness about BC

incidence can improve the accuacy of someone's perceived BC risk and encourage better screening rates.

## 1.4. BELIEFS ABOUT MEDICINES QUESTIONNAIRE (BMQ)

One of the factors influencing adherence to medicines are person's general and/or specific beliefs about medicines. Back in 1999, authors R. Horne, J. Weinman and M. Hankins created a questionnaire which can be used to assess one's both general and specific beliefs about medicines (70). This questionnaire is comprised of items which are groupped into four subdomains: *necessity* and *concerns* related to specific treatment and general beliefs about medicines *harm* and *overuse* by doctors (70, 71). Answer to each item is marked on a 5-point Likert scale. Overall score in subdomains about general *harm* and *overuse* ranges from 4 to 20, with higher score indicating more negative beliefs. Similar principle is applied in subdomains about necessity and concerns in relation to medicine of interest. Research from Porteous et al., who measured BMQ General responses in two time points on a same population found that BMQ General shows temporal stability (72).

Studies to date have shown that lower overall scores in subdomains of this questionnaire are predictive of poorer adherence to prescribed medicines in different chronic conditions (71, 73). In the study about initiation of prophylactic tamoxifen women's decision was predicted by their beliefs about tamoxifen and about medicines in general, in addition to self-perceived sensitivity to its side effects (74).

In the context of adjuvant endocrine therapy use among BC survivors, intentional non-adherers reported significantly higher concerns and lower perceived necessity of it (75). In the study about beliefs about adjuvant hormonal treatment, the concerns were more accentuated in women who experienced side effects from the drug, who were less satisfied as patients and the ones who were very religious. Whereas higher necessity beliefs expressed women who previously underwent chemotherapy and women with lower educational level (76).

## 1.5. SHORT FORM 36 (SF-36)

A 36-items Short Form questionnaire was used in Medical Outcomes Study as assessment tool for health-related quality of life in patients with certain chronic diseases (77). The questionnaire was developed by Research and Development organisation in the U.S. It taps on different aspects of health status: physical health, emotional well-being, social functioning, general health and health change. This questionnaire relies upon patient reporting of his/her self-perceived health. It is nowdays widely used for assessment of medical care outcomes in adult patients (78).

The majority of studies in which SF-36 was used were examining the effect of a certain illness on the health-related quality of life, such as liver cirrhosis (79), systemic erythematous disease (80), diabetes mellitus (81) and other chronic diseases. It showed good reliability for health-related quality of life assessment in number of health conditions. Some studies were conducted in more time points, in order to assess the effect of certain treatment on the quality of life.

# 2. HYPOTHESIS

Participants with higher level of HL assess own BC risk more accurately, are more informed about primary BC chemoprevention and have more positive attitude towards primary BC chemoprevention. EI will lead to more accurate BC risk self-assessment and improved knowledge about chemoprevention.

# 3. RESEARCH OBJECTIVES

The main objectives of this study were to:

- Examine how participants' HL influenced their accuracy of self-perceived BC risk, knowledge about and attitude towards BC chemoprevention
- Examine how participants' general beliefs about medicines and self-assessed health status correlate with their attitude towards BC chemoprevention
- Conduct EI about BC, BC RFs and BC chemoprevention
- Examine the accuracy of self-perceived BC risk and knowledge about BC chemoprevention after the EI

# 4. PARTICIPANTS AND METHODS

## 4.1. Study design

The proposed study was approved by the Ethical Committte of the Faculty of Medicine at the Josip Juraj Strossmayer University of Osijek (Approval number: 602-04/20-08/07) and by the Health Center Osijek Review Board (Approval number: 03-319-1/19). All research involving human subjects in this study was done in accordance with ethical principles outlined in the World Medical Association Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects (initiated in June 1964, last amendment in October 2000). All participants signed the informed consent form before being included in the study.

The study was structured as a non-randomised controlled study (non-RCT) (82, 83) and was conducted in the Department for Breast Diagnostics in Health Centre Osijek and at the Faculty of Dental Medicine and Health in Osijek.

The study was initially planned to be structured as a randomised controlled trial (RCT) in which the intervention group would have been created by randomly picking the informed consents from the pile of informed consents of all recruited participants. Randomisation process was carried out by the independent person and it was planned to invite 60 participants to the lecture, that would have been the intervention group. However, as the participants were being invited by the phone call many of them immediately excused themselves for not being able to attend. Even after repeated calls it was obvious that the recall was going to be much lower than expected. The most common reasons were fear of coronavirus infection and absence from the town. Consequently, all the 249 participants were invited to the lecture and only 65 of them attended it. Those 65 therefore formed the intervention group, while the rest formed the control group (184 participants).

## 4.2. Participants

For the purpose of this study women who attended Health Centre Osijek's Department for Breast Diagnostics for screening mammography or diagnostic either mammography or breast ultrasound were recruited. At the recruitment stage all the participants were assessed for eligibility. At least 159 participants were required in order to establish mean effect in numerical variables difference, with significance level 0.05 and power 0.8 (G*Power version 3.1.2, Franz Faul, University Kiel, Germany). To test the differences between the participants in control group and intervention group at least 58 participants in the interventional group were required; power 95%, effect 0.5.

Inclusion criteria were the following: signed informed consent, mammography/breast ultrasound result was negative for BC and being 35 or older.

Exclusion criteria were history of breast malignancy (*in situ* or invasive), *BRCA 1* or *BRCA 2* mutation carrier and previous radiotherapy to thorax.

The details of the recruitment process are shown in the Figure 4.1. Overall, we approached to 833 women, of which 267 women were included in the initial survey. The remaining 566 women either declined participation (n=506) or did not meet the inclusion criteria. However, due to the incomplete data obtained, further 18 respondents were excluded and the final analysis included data from 249 women.

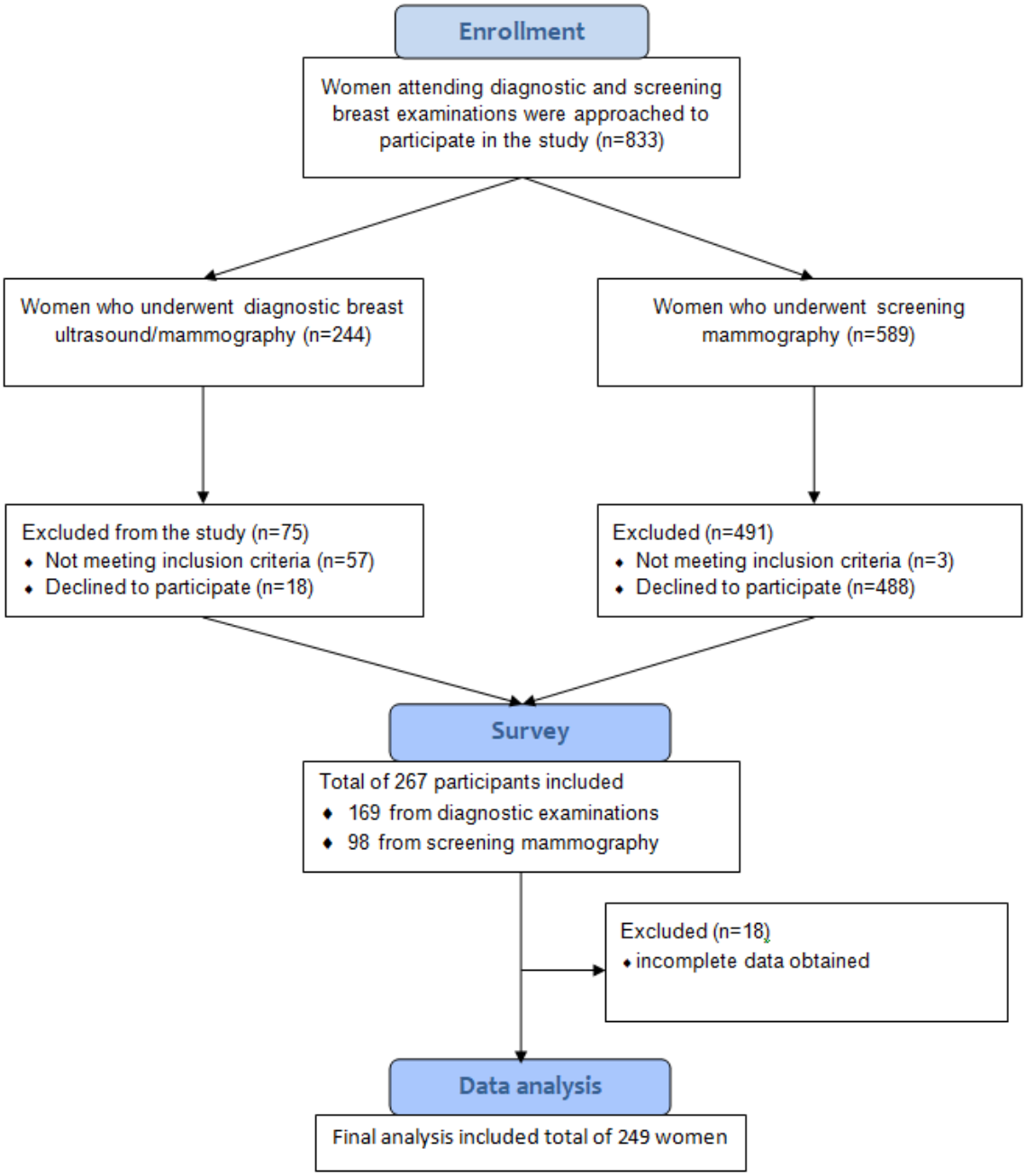



Figure 4. 1. Flow diagram of the recruitment process

The recruitment phase was running from January 2019 until September 2020. At the recruitment point all the participants who consented to participate in the study filled out the questionnaires *Beliefs about medicines General (BMQ – General), Short survey – 36 (SF – 36), Health Literacy Survey European Questionnaire 47 (HLS – EU – Q47), Opinions, knowledge and attitudes towards self-perceived breast cancer risk and chemoprevention.* They were

supported by three trained sixth-year medical school students and the Ph.D. candidate, who were available for any clarification needed.

Following the initial survey, all the participants were invited to the lecture , which was held at the Faculty of Dental Medicine and Health in Osijek by the Ph.D. candidate. Intention was to randomly choose the participants who would undergo survey after the lecture was held and they would have formed the intervention group. However, the recall to our invitation was lower than expected so the intervention group was formed from all the participants who attended the lecture, which was 65 of them. The rest of the participants formed the control group which therefore contained 184 participants.

EI in the form of a lecture was carried out in November 2020. After the lecture the participants were free to ask for any additional information on the topic, which led to a brief discussion after which they filled out the questionnaire ***Opinions, knowledge and attitudes towards self-perceived breast cancer risk and chemoprevention***. At one week after the EI, the participants again filled out the same questionnaire.

## 4.3. Methods

Breast cancer risk was calculated by using the BCRAT. Women were categorised into average-risk group if their calculated 5-year BC risk was 1.66% or lower, otherwise they were considered high-risk.

The survey was performed with the following four different questionnaires.

***Health Literacy Survey European Questionnaire 47 (HLS-EU-Q47)*** is a standardised questionnaire used to assess participants' HL level (59). Permission to use this questionnaire was granted by the head of the European Health Literacy Consortium, Prof Kristine Sorensen. The questionnaire was translated into Croatian language by the Ph.D. candidate; back translation from Croatian version to English was performed by English language translator. The questionnaire consists of 47 items across 12 domains examining person's ability to access, understand, appraise and apply health-related information within three topics: healthcare, disease prevention and health promotion (67). In each item participant rated her perceived

difficulty of a given task on a five-point Likert scale (i.e. 1 - very difficult, 2 - difficult, 3 - easy, 4 - very easy, 5 - don't know – used only by the examiner). We included all the participants who replied to at least of 80% of questions, which was in accordance to how the results were interpreted in previously published study (59).

The level of HL was presented as *Index of Health Literacy* (abbreviation *Index*), which was calculated using the following formula: *Index* = (mean – 1) * (50/3), where mean represents mean of all participating items for each individual; 1 represents minimal possible value of the mean; 3 represents range of the mean; 50 is chosen maximum value of the new metric (84). Consequently, the lowest possible *Index* was 0, and the highest was 50. Higher *Index* means higher HL. Participants were divided into three groups, based on their HL according to their indices: limited HL (*Index* 0 – 33), sufficient HL (*Index* > 33 - 42) and excellent HL (*Index* > 42 - 50).

For the purpose of this study a specific questionnaire ***'Opinions, knowledge and attitudes towards self-perceived breast cancer risk and chemoprevention'*** was created. The questionnaire consisted of 5 sections. Section one examined participants' self-perceived BC risk by asking them to rate own BC risk on a 5-point Likert scale: 1 – very small, 2 – small, 3 – average, 4 – high, 5 – very high. They also rated their BC worry, whereby the grades 1-5 denoted as follows. 1 – not worried at all, 2 – neither worried nor not worried, 3 – worried a little bit, 4 – worried, 5 – very worried. In addition, knowledge of BC RFs was examined by listing 16 different factors that increase BC risk, have protective effect on BC risk or have no influence on BC risk. Participants were required to mark what kind of effect every factor has from those three options offered. Section two was Breast Cancer Risk Assessment Tool (BCRAT), a standardised 9-item questionnaire which examines woman's objective BC risk. The questionnaire was translated into Croatian language by the Ph.D. candidate; back translation from Croatian version to English was performed by English language translator. This tool assesses 5-year BC risk and a lifetime BC risk. Section three consisted of 12 items about participants' demographic characteristics and medical history. Section four, titled 'Knowledge about primary BC chemoprevention' consisted of 6 items examining participants' chemoprevention knowledge. Section five, titled 'Attitudes towards BC chemoprevention' consisted of 20 items, divided further into 2 subsections. Attitudes about BC chemoprevention was examined by 5-item questionnaire, designed for the purpose of this

study. Participants answered questions on a five-point Likert scale (1 – I completely disagree, 2 – I disagree, 3 – Neither agree, nor disagree, 4 – I agree, 5 – I completely agree). Answers of the five questions were summed, so the minimum score was 5 and maximum was 25. Based on the overall score, participants were divided into 3 groups according to their attitudes about BC chemoprevention therapy: negative attitude (score 5-11), neutral attitude (score 12-18) and positive attitude (score 19-25). The succeeding four questions examined the potential concerns associated with use of chemoprevention agents. This questionnaire was validated on a sample of 150 respondents, internal consistency coefficient Alpha=0.707.

The third questionnaire used was ***Beliefs about medicines – General (BMQ – General).*** It comprises two 4-item domains assessing beliefs that medicines are harmful, addictive poisons which should not be taken continuously (*General-Harm*) and that medicines are overused by doctors (*General-Overuse*) (85). Minimal overall score for each domain is 4 and maximal is 20, where higher overall score indicates higher overuse by doctors or stronger harm. The participants graded their level of agreement with each of the items on a five-point Likert scale as follows: 1 – I completely agree, 2 - I agree, 3 – I am not sure, 4 - I disagree, 5 – I completely disagree.

***Short form-36 (SF-36),*** is the a 36-Item Health Survey (Version 1.0) which taps eight health concepts: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. It also includes a single item that provides an indication of perceived change in health (86). There are specific instructions provided how to score this survey (87). In summary, each item is scored on a 0 to 100 range. Higher score defines a more favourable health state. Certain items are grouped together to form 8 different scales reflecting different aspects of one's health. Items that are left blank (missing data) are not taken into account when calculating the scale scores. Hence, scale scores represent the average for all items in the scale that the respondent answered (87).

The **EI** in form of a lecture was titled: 'Breast Cancer: Do I belong to a HR group and can I prevent breast cancer?'. After the lecture the leaflets containing the brief overview of the topic were given to all the participants who attended the lecture. The lecture was

validated by the three university professors and was described as informative and not sugestive.

The lecture was structured in the following way and the Microsoft Power Point was used as a tool for the lecture presentation.

- Explanation of the anatomy of the breast in the following way: in the breast there is glandular tissue surrounded by connective and adipose tissue. BC originates from the glandular tissue, and the more glandular tissue there is, that means higher BD, which is a RF for BC. There will only be an image of breast anatomy on the slide.
- 1 slide showing BC stages. Explaining there are early and advanced BC and the implications for the therapy and prognosis.
- 1 slide showing the BC incidence in Croatia. To make participants more aware of the problem, the Ph.D. candidate asked if there was anyone in the audience who did not know at least 2 persons who were diagnosed with BC in their surroundings. Everyone agreed they knew at least 2 persons with BC diagnosis.
- 5 slides about BC RFs. The factors are listed and briefly explained.
- 1 slide about BC risk reducing factors. The factors are listed and briefly explained.
- 1 slide naming certain factors that make a woman HR, such as positive family history in first degree relative, radiotherapy to thorax, history of AH, LCIS.
- 1 slide for preliminary results of this study indicating that 20% of women underestimated their own BC risk and that one third of participants' with positive family history underestimated own BC risk. Also, 77.1% did not know their BD.
- 4 slides about primary/secondary BC prevention: lifestyle modification, early diagnosis, primary chemoprevention and preventive mastectomy. The mechanism of action of 4 medications used in primary chemoprevention, their side effects and contraindications were briefly explained.
- 5 slides about breast self-examination (BSE): the technique was demonstrated and recommended frequency of BSE was outlined.
- 3 slides about types of radiological examinations used for BC screening and diagnostics.
- 1 slide with the image showing the early signs of BC.

One week after the EI a repeated survey was conducted using the questionnaire ***Opinions, knowledge and attitudes towards self-perceived breast cancer risk and chemoprevention*.**

## 4.4. Statistical methods

Categorical data were represented by absolute and relative frequencies. Differences of categorical variables were tested by $\chi^2$ test and, if necessary, by Fisher's Exact test. Numerical data were described by arithmetic mean and standard deviation in cases of normal distribution and in other cases by the median and the limits of the interquartile range (IQR). The difference in categorical variables between the measurements were tested by McNemar-Bowker test and if needed by Marginal Homogeneity test. Differences in continuous variables in cases of 2 independent groups were tested by Mann-Whitney U Test, and in case of three or more independant groups by Kruskal-Wallis test (Post hoc Conover). Differences in continuous variables given the three measurement points were tested by Friedman's test (Post hoc Conover). The strenght of correlation was expressed with Spearman's correlation coefficient (Rho).

All P values are two-sided. The significance level was set to Alpha = 0.05.

MedCalc Statistical Software version 19.1.7. (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2020) and SPSS Statistics 23 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp) were used for statistical analysis.

# 5. RESULTS

## 5.1. Participants' characteristics and breast cancer risk assessment

Table 5.1. gives an overview of participants' general characteristics. Overall number of participating women was 249. They were aged from 35 to 85, with median age being 57 (IQR 47 – 62). Majority of participants achieved high school diploma, accounting for 58.6% of all participants. Regarding the employment, 85 or 34.1% were retired, while 81 or 32.5% of women were public sector employees. They had 1 to 6 children, with median of 2 (IQR 2-3) children.

Table 5.1. Demographic characteristics

| Participants' characteristics | |
|---|---|
| Age [Median (IQR)] | 57 (47 – 62) |
| Education [n(%)] | |
| Primary school diploma | 38 (15.3) |
| High school diploma | 146 (58.6) |
| Bachelor's degree | 18 (7.2) |
| Master's degree | 43 (17.3) |
| Doctorate | 4 (1.6) |
| Number of children [Median (IQR)] | 2 (2 – 3) |
| Employment [n(%)] | |
| Private Sector Employee | 48 (19.3) |
| Public Sector Employee | 81 (32.5) |
| Free profession | 2 (0.8) |
| Unemployed | 33 (13.3) |
| Retired | 85 (34.1) |
| Active menstrual cycle [n(%)] | 70 (28.1) |

IQR – interquartile range

Table 5.2. gives an overview of participants' family history of malignancies and personal history of chronic disease and treatment. Positive family history for BC in wider family and first-degree relatives had 49 (19.6%) and 46 (18.5%) women, respectively. Slightly above half of all participants had positive family history of malignancy and 131 (52.6%) of

women had comorbidities. Nearly 60% of all participants were taking at least 1 prescription drug on a regular basis. Quarter of all participants smoked cigarettes.

Table 5.2. Family history of malignancy and personal history of chronic illness, treatment and risk-related health behaviour

| Participants' characteristics | n (%) |
|---|---|
| Breast cancer in first degree relatives | 49 (19.6) |
| Breast cancer in wider family | 46 (18.5) |
| Family history of ovarian cancer | 22 (8.8) |
| History of any malignancy in the family | 134 (53.8) |
| Comorbidities | 131 (52.6) |
| Number of regular prescription drugs | |
| 0 | 100 (40.2) |
| 1 | 53 (21.3) |
| 2 | 41 (16.5) |
| 3 | 22 (8.8) |
| 4 or more | 33 (13.3) |
| Number of regular OTC drugs | |
| 0 | 186 (74.7) |
| 1 | 37 (14.9) |
| 2 | 11 (4.4) |
| 3 | 6 (2.4) |
| 4 or more | 3 (1.2) |
| Smoking | 64 (25.7) |
| Alcohol use* | 4 (1.6) |

OTC – over the counter. *equivalent of 2 dl of alcoholic drink per day

The representation of participants' characteristics necessary for objective BC risk calculation is shown in Table 5.3. The median age of participating women was 57 (IQR 47-62). More than half of women had their first menstrual period at the age 12 or 13 and only 29 (11.6%) participants had it at the age considered to be a RF for developing BC (age 11 or younger). Overall 21.6% of participants were childless or had their first child at the age of 30 or later, both of which are known BC RFs. Nearly 20% have 1 or more first-degree relative with history of BC. Among all participating women, only 3 (1.2%) of them had a history of AH.

Table 5.3. Participants' characteristics according to anamnestic data required for BC risk calculation (Gail model)

| Participants' characteristics | n (%) |
|---|---|
| Age [Median (IQR)] | 57 (47 – 62) |
| Age at the time of the first menstrual period | |
| 7 to 11 | 29 (11.6) |
| 12 to 13 | 140 (56.2) |
| 14 or more | 80 (32.1) |
| Age at the time of the first childbirth | |
| Nulliparous | 27 (10.8) |
| < 20 | 31 (12.4) |
| 20 – 24 | 112 (45) |
| 25 – 29 | 52 (20.9) |
| 30 or more | 27 (10.8) |
| First-degree relative with history of BC | |
| Yes, 1 first-degree relative with history of BC | 31 (12.4) |
| Yes, more than 1 first-degree relative with history of BC | 18 (7.2) |
| No | 200 (80.3) |
| History of breast biopsy | |
| Yes, once | 14 (5.6) |
| Yes, more than once | 4 (1.6) |
| No | 231 (92.8) |
| History of AH | |
| Yes | 3 (1.2) |
| No | 14 (5.6) |
| I have never had breast biopsy | 232 (93.2) |

IQR – interquartile range. BC- breast cancer; AH – atypical hyperplasia

In Table 5.4. we can see the distribution of different RFs between AR and HR groups. Women in AR group were significantly older, with median age of 58, compared to 54 in HR (Mann-Whitney U test, P=0.030). There were significantly more women of high BC risk who had their first child at the age of 30 or later ( $\chi^2$ test, P<0.001). There were significantly more participants in HR group with 1, or more than 1 first-degree relative with BC ( $\chi^2$ test, P<0.001). HR women had breast biopsy significantly more times than women of AR and also the diagnosis of AH was only present in HR women (Fisher's exact test, P=0.005 and P=0.020, respectively).

Table 5.4. The representation of different anamnestic data used for BC risk calculation according to Gail model in average-risk and high-risk participants

| | Number (%) of participants according to the objective BC risk | | | P* |
|---|---|---|---|---|
| | Average | High | Total | |
| Age [Median(IQR)] | 58 (49 – 63) | 54 (43 – 61) | 57 (47 – 62) | **0.030‡** |
| Age at the time of the first menstrual period | | | | |
| 7 to 11 | 21 (12) | 8 (12) | 29 (12) | |
| 12 to 13 | 95 (52) | 45 (66) | 140 (56) | 0.100 |
| 14 or more | 65 (36) | 15 (22) | 80 (32) | |
| Age at the time of the first childbirth | | | | |
| Nulliparous | 20 (11) | 7 (10) | 27 (11) | |
| < 20 | 23 (13) | 8 (12) | 31 (12) | |
| 20 – 24 | 89 (49) | 23 (34) | 112 (45) | **<0.001** |
| 25 – 29 | 45 (25) | 7 (10) | 52 (21) | |
| 30 or more | 4 (2) | 23 (34) | 27 (11) | |
| First-degree relative with history of BC? | | | | |
| Yes, 1 first-degree relative with history of BC | 1 (1) | 30 (44) | 31 (12) | |
| Yes, more than 1 first-degree relative with history of BC | 0 | 18 (26) | 18 (7) | **<0.001** |
| No | 180 (99) | 20 (29) | 200 (80) | |
| History of breast biopsy | | | | |
| Yes, once | 9 (5) | 5 (7) | 14 (6) | |
| Yes, more than once | 0 | 4 (6) | 4 (2) | **0.005†** |
| No | 172 (95) | 59 (87) | 231 (93) | |
| History of AH | | | | |
| Yes | 0 | 3 (4) | 3 (1) | |
| No | 9 (5) | 5 (7) | 14 (6) | **0.020†** |
| I have never had breast biopsy | 172 (95) | 60 (88) | 232 (93) | |

* $\chi^2$ Test, †Fisher's Exact Test; ‡Mann Whitney U test
IQR – interquartile range, BC – breast cancer, AH – atypical hyperplasia

Table 5.5. shows the overview of the investigated population with regards to their objective BC risk (calculated with BCRAT). Overall, 184 (73.9%) women were calculated to have average BC risk, based on their predicted 5-year absolute BC risk, while 65 (26.1%) of women were of HR. Of all the participants, 70.7% correctly perceived own risk, while 19.7% underestimated it.

Table 5.5. Five-year and lifetime BC risk and the accuracy of self-perceived risk

| BC risk | |
|---|---|
| Absolute 5-year BC risk [Median (IQR)] | 1.3 (0.9 – 1.7) |
| 5-year absolute BC risk [n(%)] | |
| Average | 184 (73.9) |
| High | 65 (26.1) |
| 5-year relative BC risk [n(%)] | |
| Average | 181 (72.7) |
| High | 68 (27.3) |
| Accuracy of the 5-year absolute BC risk self-assessment [n(%)] | |
| Underestimated | 49 (19.7) |
| Correct | 176 (70.7) |
| Overestimated | 24 (9.6) |
| Accuracy of the 5-year relative BC risk self-assessment [n(%)] | |
| Underestimated | 49 (19.7) |
| Correct | 176 (70.7) |
| Overestimated | 24 (9.6) |
| Absolute lifetime BC risk [Median (IQR)] | 8.5 (6.45 – 11.30) |
| Absolute lifetime BC risk [n(%)] | |
| Average | 230 (92.4) |
| High | 19 (7.6) |
| Relative lifetime BC risk [n(%)] | |
| Average | 181 (72.7) |
| High | 68 (27.3) |
| Accuracy of the absolute lifetime BC risk self-assessment [n(%)] | |
| Underestimated | 10 (4) |
| Correct | 203 (81.5) |
| Overestimated | 36 (14.5) |
| Accuracy of the relative lifetime BC risk self-assessment [n(%)] | |
| Underestimated | 45 (18.1) |
| Correct | 177 (71.1) |
| Overestimated | 27 (10.8) |

IQR – interquartile range , BC – breast risk

Table 5.6. shows that in the group of women with objectively average 5-year BC risk there was significantly higher proportion of women who expressed low level of worry about the possibility of developing BC in the future. In the group of women with HR, they were significantly more worried ( $\chi^2$ test, P=0.008). Interestingly, women who underestimated own BC risk expressed high level of worry and so did women who overestimated own risk ( $\chi^2$ test, P=0.030). The results are the same in women who underestimated and overestimated their lifetime BC risk (Fisher's Exact Test, P=0.010).

Table 5.6. The correlation between the worry about developing breast cancer, objective 5-year and lifetime breast cancer risk and the accuracy of breast cancer risk self-assessment

| | Number (%) of participants according to the level of worry | | | | P* |
|---|---|---|---|---|---|
| | Low | Medium | High | Total | |
| 5-year absolute BC risk | | | | | |
| Average | 85 (81) | 56 (77) | 43 (61) | 184 (73.9) | **0.008** |
| High | 20 (19) | 17 (23) | 28 (39) | 65 (26.1) | |
| Accuracy of the 5-year absolute BC risk self-assessment | | | | | |
| Underestimated | 15 (14) | 17 (23) | 17 (24) | 49 (19.7) | **0.030** |
| Correct | 84 (80) | 50 (68) | 42 (59) | 176 (70.7) | |
| Overestimated | 6 (6) | 6 (8) | 12 (17) | 24 (9.6) | |
| Absolute lifetime BC risk | | | | | |
| Average | 98 (93) | 71 (97) | 61 (86) | 230 (92.4) | **0.030** |
| High | 7 (7) | 2 (3) | 10 (14) | 19 (7.6) | |
| Accuracy of the absolute lifetime BC risk self-assessment | | | | | |
| Underestimated | 4 (4) | 1 (1) | 5 (7) | 10 (4) | **0.010†** |
| Correct | 91 (87) | 64 (88) | 48 (68) | 203 (81.5) | |
| Overestimated | 10 (10) | 8 (11) | 18 (25) | 36 (14.5) | |

* $\chi^2$ Test, †Fisher's exact test
BC – breast cancer

Participants in their generative age significantly overestimated own BC risk ( $\chi^2$ test, P=0.020), while the ones with history of AH significantly underestimated own BC risk (Fisher's exact test, P=0.004), as can be seen in table 5.7., because all three of them were objectively HR.

Table 5.7. The association between different participants' characteristics and the accuracy of breast cancer risk self-assessment

| | Number (%) of participants according to the accuracy of 5-year absolute BC risk self-assessment | | | | P* |
|---|---|---|---|---|---|
| | Underestimated | Correct | Overestimated | Total | |
| Active menstrual cycle | 6 (12.2) | 55 (31.3) | 9 (37.5) | 70 (28.1) | **0.020** |
| First-degree relative with history of BC | 16 (32.7) | 23 (13.1) | 7 (29.2) | 46 (18.5) | **0.003** |
| Chronic disease | 31 (63.3) | 87 (49.7) | 13 (54.2) | 131 (52.8) | 0.240 |
| Smoking | 13 (26.5) | 45 (25.7) | 6 (25) | 64 (25.8) | 0.990 |
| History of breast biopsy | | | | | |
| Yes, once | 6 (12.2) | 7 (4) | 1 (4.2) | 14 (5.6) | 0.090† |
| Yes, more than once | 2 (4.1) | 2 (1.1) | 0 | 4 (1.6) | |
| No | 41 (83.7) | 167 (94.9) | 23 (95.8) | 231 (92.8) | |
| History of AH | | | | | |
| Yes | 3 (6.1) | 0 | 0 | 3 (1.2) | **0.004**† |
| No | 5 (10.2) | 8 (4.5) | 1 (4.2) | 14 (5.6) | |
| I have never had breast biopsy | 41 (83.7) | 168 (95.5) | 23 (95.8) | 232 (93.2) | |
| Chemoprevention attitude | | | | | |
| Negative | 6 (12.2) | 17 (9.7) | 2 (8.3) | 25 (10) | 0.350 |
| Neutral | 26 (53.1) | 73 (41.5) | 8 (33.3) | 107 (43) | |
| Positive | 17 (34.7) | 86 (48.9) | 14 (58.3) | 117 (47) | |

* $\chi^2$ Test; †Fisher's Exact Test. BC – breast cancer, AH – atypical hyperplasia

As shown in table 5.8., participants' age did not have a significant association with the accuracy of BC self-assessment.

Table 5.8. Participants' age and the accuracy of breast cancer risk self-assessment

| | Median (IQR) according to the accuracy of 5-year absolute BC risk self-assesment | | | | P* |
|---|---|---|---|---|---|
| | Underestimated | Correct | Overestimated | Total | |
| Age | 62 (54 – 64) | 56 (46 – 61) | 57 (43 – 62) | 57 (47 – 62) | 0.780 |

*Kruskal-Wallis test. BC – breast cancer.
IQR - interquartile range, BC – breast cancer

## 5.2. Chemoprevention attitude

Women in their generative age showed significantly more negative attitude towards chemoprevention (Fisher's exact test, P=0.010). Within that same group of women there was only less than 20% of them who had positive chemoprevention attitude, as shown in Table 5.9. As for the other demographical data, significant positive correlation was found between the presence of comorbidities and positive attitude towards chemoprevention ($\chi^2$test, P=0.002).

Table 5.9. The correlation between attitudes towards chemoprevention and demographical and other participants' data

| | Number (%) of participants according to the attitude towards chemoprevention | | | | P* |
|---|---|---|---|---|---|
| | Negative | Neutral | Positive | Total | |
| Education status [n(%)] | | | | | |
| Primary school diploma | 2 (8) | 17 (16) | 19 (16) | 38 (15.3) | 0.440† |
| High school diploma | 15 (60) | 57 (53) | 74 (63) | 146 (58.6) | |
| Bachelor's degree | 1 (4) | 8 (7) | 9 (8) | 18 (7.2) | |
| Master's degree | 7 (28) | 22 (21) | 14 (12) | 43 (17.3) | |
| Doctorate | 0 | 3 (3) | 1 (1) | 4 (1.6) | |
| Active menstrual cycle [n(%)] | 11 (44) | 36 (33.6) | 23 (19.7) | 70 (28.1) | 0.010† |
| First-degree relative with history of BC | | | | | |
| Yes, 1 first-degree relative with history of BC | 0 | 17 (16) | 14 (12) | 31 (12.4) | 0.240† |
| Yes, more than 1 first-degree relative with history of BC | 2 (8) | 7 (7) | 9 (8) | 18 (7.2) | |
| No | 23 (92) | 83 (78) | 94 (80) | 200 (80.3) | |

| | | | | | |
|---|---|---|---|---|---|
| BC in wider family | 3 (12) | 25 (23) | 18 (15) | 46 (18.5) | 0.210 |
| History of any malignancy in the family | 15 (60) | 58 (54) | 61 (53) | 134 (54) | 0.800 |
| Comorbidities | 13 (54) | 43 (40) | 75 (64) | 131 (52.8) | 0.002 |
| Number of regular prescription drugs | | | | | |
| 0 | 9 (36) | 59 (55) | 32 (27) | 100 (40.2) | 0.003† |
| 1 | 3 (12) | 20 (19) | 30 (26) | 53 (21.3) | |
| 2 | 6 (24) | 12 (11) | 23 (20) | 41 (16.5) | |
| 3 | 2 (8) | 9 (8) | 11 (9) | 22 (8.8) | |
| 4 or more | 5 (20) | 7 (7) | 21 (18) | 33 (13.3) | |
| Number of regular OTC drugs | | | | | |
| 0 | 20 (83) | 84 (79) | 82 (73) | 186 (76.5) | 0.760† |
| 1 | 4 (17) | 15 (14) | 18 (16) | 37 (15.2) | |
| 2 | 0 | 4 (4) | 7 (6) | 11 (4.5) | |
| 3 | 0 | 3 (3) | 3 (3) | 6 (2.5) | |
| 4 or more | 0 | 0 | 3 (3) | 3 (1.2) | |
| Smoking | 5 (20) | 29 (27) | 30 (26) | 64 (25.8) | 0.810 |
| Alcohol use | 0 | 0 | 4 (3) | 4 (1.6) | 0.210† |

* $\chi^2$ test; †Fisher's exact test

BC – breast cancer; OTC – over the counter

Fisher's exact test showed no significant correlation between the history of breast biopsy and attitude towards chemoprevention (Fisher's exact test, P=0.570). Similarly, the level of BC-specific worry did not have a significant association with chemoprevention attitude (Fisher's exact test, P=0.540) and neither did the other characteristics of participants showed in table 5.10.

Table 5.10. The correlation between attitudes towards chemoprevention and history of breast disease, breast cancer worry and objective breast cancer risk

| | Number (%) of participants according to the attitude towards chemoprevention | | | | P |
|---|---|---|---|---|---|
| | Negative | Neutral | Positive | Total | |
| **History of breast biopsy** | | | | | |
| Yes, once | 3 (12) | 6 (5.6) | 5 (4.3) | 14 (5.6) | 0.570† |
| Yes, more than once | 0 | 2 (1.9) | 2 (1.7) | 4 (1.6) | |
| No | 22 (88) | 99 (92.5) | 110 (94) | 231 (92.8) | |
| **History of AH** | | | | | |
| Yes | 1 (4) | 0 | 2 (1.7) | 3 (1.2) | 0.150† |
| No | 2 (8) | 8 (7.5) | 4 (3.4) | 14 (5.6) | |
| I have never had breast biopsy | 22 (88) | 99 (92.5) | 111 (94.9) | 232 (93.2) | |
| **BC worry** | | | | | |
| Low | 12 (48) | 42 (39.3) | 51 (43.6) | 105 (42.2) | 0.540† |
| Medium | 8 (32) | 36 (33.6) | 29 (24.8) | 73 (29.3) | |
| High | 5 (20) | 29 (27.1) | 37 (31.6) | 71 (28.5) | |
| **Objective absolute 5-year risk** | | | | | |
| Average | 19 (76) | 79 (73.8) | 86 (73.5) | 184 (73.9) | 0.970* |
| High | 6 (24) | 28 (26.2) | 31 (26.5) | 65 (26.1) | |
| Total | 25 (100) | 107 (100) | 117 (100) | 249 (100) | |

AH – atypical hyperplasia; BC – breast cancer

Women with positive attitude towards primary BC chemoprevention were significantly older than ones with neutral attitude, 58 (IQR 51 - 62,5) and 55 (IQR 44 - 61), respectively (Kruskal-Wallis test (Post hoc Conover), P=0.030), as shown in table 5.11.

Table 5.11. Correlation between the attitude about chemoprevention and participants' age and number of children

| | Median (IQR) Age | P* | Median (IQR) Number of children | P* |
|---|---|---|---|---|
| **Attitude towards chemoprevention** | | | | |
| Negative | 54 (44.5 – 62) | **0.03**‡ | 2 (1 – 2) | 0.730 |
| Neutral | 55 (44 – 61) | | 2 (1 – 2) | |
| Positive | 58 (51 – 62.5) | | 2 (2 – 2) | |

*Kruskal-Wallis test (Post hoc Conover). IQR – interquartile range

‡ at the level P<0,05 significant are differences are between *neutral* vs. *positive*

Table 5.12. gives an overview of the correlation between participants' characteristics and certain concerns in relation to chemoprevention drugs. Women of higher age were more worried about the price of such drug in case it was not covered by the health insurance, but the correlation between the two was poor (Spearman's ρ=0.158, P=0.01). Women who were younger were more worried about the effect of such drug on the child in case of unplanned pregnancy. The correlation between the two variables is moderate (Spearman's ρ=-0.466, P<0.001).

Table 5.12. Concerns in relation to primary chemoprevention drugs and participants' age (Spearman's Rho)

| | Spearman's Rho (P value) Age |
|---|---|
| I would worry about the price of the drug in case it was not covered by the health insurance | **0.158 (0.010)** |
| I would worry about the side effects | -0.069 (0.280) |
| I would worry about the drug's effect on the child in case of unplanned pregnancy | **-0.466 (<0.001)** |
| It would be difficult for me to take the drug at the same time every day | -0.074 (0.250) |

By Kruskal-Wallis test it was found that women who had positive chemoprevention attitude marked significantly lower their worry about the drugs' side effects in contrast to others (Kruskal-Wallis test (Post hoc Conover), P<0.001). Also, the worry about drug side effects was significantly lower in women with positive chemoprevention attitude in comparison to ones with neutral attitude (Kruskal-Wallis test (Post hoc Conover), P=0.010), as seen in table 5.13.

Table 5.13. Concerns in relation to chemoprevention drugs and chemoprevention attitude

| | Chemoprevention attitude – Median (IQR) | | | | P* |
|---|---|---|---|---|---|
| | Negative | Neutral | Positive | Total | |
| I would worry about the price of the drug in case it was not covered by the health insurance | 4 (2.25 - 5) | 3 (2 - 4) | 3 (2 - 4) | 3 (2 – 4) | 0.180 |
| I would worry about the side effects | 4 (4 - 5) | 4 (4 - 5) | 3.5 (3 - 4) | 4 (3 – 4) | **<0.001**[†] |
| I would worry about the drug's effect on the child in case of unplanned pregnancy | 1 (1 - 4) | 1.5 (1 - 4) | 1 (1 - 2) | 1 (1 – 3) | **0.010**[‡] |
| It would be difficult for me to take the drug at the same time every day | 1 (1 - 2) | 1 (1 - 3) | 1 (1 - 2) | 1 (1 – 2) | 0.050 |

*Kruskal-Wallis test (Post hoc Conover). Data are presented as medians (IQR) of grades 1 to 5.
IQR – interquartile range
1 - I completely disagree, 2 - I disagree, 3 - I am not sure, 4 - I agree, 5 - I completely agree
[†]at the level P<0,05 significant the differences are between *negative* vs. *positive*, *neutral* vs. *positive*
[‡] at the level P<0,05 significant the differences are between *neutral* vs. *positive*

There was no significant association between self-perceived BC risk and chemoprevention attitude ($\chi^2$ test, P=0.970), table 5.14.

Table 5.14. The relationship between self-perceived BC risk and chemoprevention attitude

| | Number (%) of participants according to chemprevention attitude | | | | P* |
|---|---|---|---|---|---|
| | Negative | Neutral | Positive | Total | |
| **5-year absolute BC risk [n(%)]** | | | | | |
| Average | 19 (76) | 79 (73.8) | 86 (73.5) | 184 (73.9) | 0.970 |
| High | 6 (24) | 28 (26.2) | 31 (26.5) | 65 (26.1) | |
| Total | 25 (100) | 107 (100) | 117 (100) | 249 (100) | |

* $\chi^2$ test.
BC – breast cancer

### 5.2.1 Beliefs about medicines and chemoprevention attitude of the whole studied population

Participants' beliefs about medicines and their correlation with chemoprevention attitude was examined on the whole studied population of 249 women. The more the participants believed that doctors prescribe too many medication the less prescription medicines they were taking, but the analysis showed very weak correlation between the two (Spearman's Rho=-0.130, P=0.040). The more the participants believed that natural drugs are safer than medical ones the younger they were (Spearman's Rho=-0.135, P=0.030). Additionally, the more they believed that drugs do more harm than good the younger they were and the less prescription drugs they were taking (Spearman's Rho=-0.148, P=0.020 and Spearman's Rho= -0.175, P=0.010, respectively). This is shown in table 5.15. Although the above mentioned correlations were significant, they were actually very weak, given the value of the Rho.

Table 5.15. The correlation between participants' age and medication use with their beliefs about medicines (Spearman's Rho)

| | Spearman's Rho (P value) | | |
|---|---|---|---|
| | Age | Prescription drugs | OTC drugs |
| Doctors prescribe too many medicines. | -0.068 (0.290) | **-0.130 (0.040)** | 0.012 (0.860) |
| People who take medicines should stop them from time to time. | 0.005 (0.940) | -0.05 (0.440) | -0.036 (0.570) |
| Most medicines are addictive. | -0.001 (0.990) | -0.035 (0.580) | -0.095 (0.140) |
| Natural remedies are safer than medicines. | **-0.135 (0.03)** | -0.101 (0.110) | -0.092 (0.160) |
| Medicines do more harm than good. | **-0.148 (0.02)** | **-0.175 (0.01)** | -0.025 (0.700) |
| All medicines are poisons. | 0.003 (0.960) | 0.033 (0.610) | -0.063 (0.330) |
| Doctors place too much trust in medicines. | -0.016 (0.800) | -0.103 (0.110) | -0.052 (0.430) |
| If doctors had more time for patients they would prescribe fewer medicines. | 0.020 (0.750) | -0.048 (0.450) | 0.012 (0.860) |
| OVERUSE | -0.059 (0.360) | -0.113 (0.070) | -0.062 (0.340) |
| HARM | -0.041 (0.520) | -0.067 (0.290) | -0.080 (0.210) |

OTC – over the counter

As regards to the relationship between participants' educational level and their general beliefs about medicines, the analysis showed that women of higher educational level had significantly lower median score in the subdomain *medicines harm* (Kruskal-Wallis test,

P=0.010), indicating their more positive beliefs.The correlation between all items from the BMQ questionnaire and chemoprevention attitude are shown in table 5.16.

Table 5.16. The correlation between educational level and beliefs about medicines

| | Median (IQR) | | | | | P* |
|---|---|---|---|---|---|---|
| | Primary School Diploma | High School Diploma | Bachelor's Degree | Master's Degree | Doctorate | |
| Doctors prescribe too many medicines. | 3 (2 - 4) | 3 (2 - 4) | 3 (2.5 - 4.5) | 3 (2 - 4) | 3.5 (2.3 - 4) | 0.910 |
| People who take medicines should stop them from time to time. | 4 (3 - 4) | 4 (3 - 4) | 3 (2 - 4.5) | 3 (2.8 - 4) | 3 (3 - 4.5) | 0.130 |
| Most medicines are addictive. | 4 (2 - 4) | 3 (2.8 - 4) | 3 (2 - 4) | 3 (2 - 4) | 2.5 (1.3 - 4.5) | 0.530 |
| Natural remedies are safer than medicines. | 3 (2 - 4) | 3 (2 - 4) | 3 (2 - 4) | 3 (2 - 3) | 3 (3 - 3.8) | 0.160 |
| Medicines do more harm than good. | 3 (2 - 3) | 3 (2 - 3) | 2 (1.5 - 3) | 2 (1.8 - 3) | 1.5 (1 - 2.8) | **0.020**‡ |
| All medicines are poisons. | 3 (2 - 4) | 2 (2 - 3) | 2 (1 - 4) | 2 (1 - 3) | 2 (1 - 3.8) | **0.040**‡ |
| Doctors place too much trust in medicines. | 4 (3 - 4.3) | 3 (2 - 4) | 3 (2 - 4) | 3 (2 - 3.3) | 4 (2.5 - 4.8) | **0.020**§ |
| If doctors had more time for patients they would prescribe fewer medicines. | 4 (3 - 4.3) | 4 (2.5 - 4) | 3 (2 - 4) | 3 (2.8 - 4) | 4 (3.3 - 4.8) | 0.610 |
| OVERUSE | 14 (11 - 15.3) | 13 (10 - 14) | 13 (10 - 15) | 12 (10 - 13) | 15 (12 - 15.8) | 0.180 |
| HARM | 12 (10 - 15) | 12 (10 - 14) | 11 (7 - 14.3) | 10 (9 - 13) | 9.5 (6.3 - 15) | **0.010**‡ |

*Kruskal-Wallis test. Data are presented as medians (IQR) of grades 1 to 5. IQR – interquartile range
1 - I completely disagree, 2 - I disagree, 3 - I am not sure, 4 - I agree, 5 - I completely agree.
‡ at the level P<0,05 significant are the differences primary school diploma vs. master's degree; high school diploma vs. master's degree
§ at the level P<0,05 significant are the differences *primary school diploma* vs. *high school diploma*; *primary school diploma* vs. *bachelor's degree*; *primary school diploma* vs. *master's degree*

Table 5.17. shows what are beliefs about medicines like in participants with and without existing comorbidities. There was no significant differences in overall median scores

in the two subdomains, but women with no comorbidities believed significantly more that doctors prescribe too many medicines and that medicines do more harm than good (Mann-Whitney U test, P=0.020 and P=0.001, respectively).

Table 5.17. General beliefs about medicines according to presence of comorbidities

| | Median (IQR) according to comorbidities | | P* |
|---|---|---|---|
| | Yes | No | |
| Doctors prescribe too many medicines. | 3 (2 - 4) | 3 (3 - 4) | **0.020** |
| People who take medicines should stop them from time to time. | 4 (3 - 4) | 4 (3 - 4) | 0.270 |
| Most medicines are addictive. | 3 (2 - 4) | 4 (2 - 4) | 0.470 |
| Natural remedies are safer than medicines. | 3 (2 - 4) | 3 (3 - 4) | 0.170 |
| Medicines do more harm than good. | 2 (2 - 3) | 3 (2 - 3) | **0.001** |
| All medicines are poisons. | 2 (1 - 3) | 2 (2 - 3) | 0.750 |
| Doctors place too much trust in medicines. | 3 (2 - 4) | 3 (3 - 4) | 0.180 |
| If doctors had more time for patients they would prescribe fewer medicines. | 3 (2 - 4) | 4 (3 - 4) | 0.480 |
| OVERUSE | 12 (10 - 15) | 13 (11 - 15) | 0.130 |
| HARM | 12 (10 - 14) | 12 (10 - 14.5) | 0.080 |

*Mann-Whitney U test. Data are presented as medians (IQR) of grades 1 to 5. IQR – interquartile range
1 - I completely disagree, 2 - I disagree, 3 - I am not sure, 4 - I agree, 5 - I completely agree.

The association between different HL levels and beliefs about medicines is presented in table 5.18. Women with excellent HL had significantly lower median score in the subdomain *medicines overuse* in comparison to women of limited HL (Kruskal-Wallis test (Post hoc Conover), P=0.020). Similarly, excellent HL was associated with significantly lower median score in the subdomain *medicines harm* in comparison to lower HL levels (Kruskal-Wallis test (Post hoc Conover), P=0.030).

Table 5.18. The association between health literacy and beliefs about medicines

| | Median (IQR) of scores according to HL level | | | P* |
|---|---|---|---|---|
| | Limited | Sufficient | Excellent | |
| Doctors prescribe too many medicines. | 3 (2 - 4) | 3 (2 - 4) | 3 (2 - 3) | 0.300 |
| People who take medicines should stop them from time to time. | 4 (3 - 4) | 4 (3 - 4) | 3 (2 - 4) | **0.020**§ |
| Most medicines are addictive. | 3 (2 - 4) | 3 (2 - 4) | 3 (1 - 4) | 0.260 |
| Natural remedies are safer than medicines. | 3 (2 - 4) | 3 (2 - 4) | 3 (2 - 3) | 0.680 |
| Medicines do more harm than good. | 3 (2 - 3) | 3 (2 - 3) | 2 (1 - 3) | 0.530 |
| All medicines are poisons. | 2 (2 - 3) | 3 (1 - 4) | 2 (1 - 3) | 0.220 |
| Doctors place too much trust in medicines. | 3 (3 - 4) | 3 (2 - 4) | 3 (2 - 3) | **0.004**† |
| If doctors had more time for patients they would prescribe fewer medicines. | 4 (3 - 4) | 3.5 (2 - 4) | 3 (2 - 4) | 0.050 |
| OVERUSE | 13 (11 - 15) | 12 (10 - 15) | 11 (8 - 13) | **0.020**‡ |
| HARM | 12 (10 - 14) | 12 (10 - 15) | 11 (6 - 12) | **0.030**§ |

*Kruskal-Wallis test (Post hoc Conover). Data are presented as medians (IQR) of grades 1 to 5.
1 - I completely disagree, 2 - I disagree, 3 - I am not sure, 4 - I agree, 5 - I completely agree
‡ at the level P<0,05 significant are the differences *limited* vs. *excellent*
§ at the level P<0,05 significant are the differences *limited* vs. *excellent*; *sufficient* vs. *excellent*
† at the level P<0,05 significant are differences *limited* vs. *sufficient, limited* vs. *excellent*; *sufficient* vs. *excellent*
HL- health literacy, IQR – interquartile range

Women who expressed positive chemoprevention attitude had significantly lower median score in subdomain about *medicines overuse* in comparison to ones with neutral attitude (Kruskal-Wallis test (Post hoc Conover), P=0.020). While there was no significant associations in the subdomain of *medicines harm* (Kruskal-Wallis test (Post hoc Conover), P=0.590), as shown in Table 5.19.

Table 5.19. The association between beliefs about medicines and chemoprevention attitude

| | Median (IQR) of scores according to chemoprevention attitude | | | P* |
|---|---|---|---|---|
| | Negative | Neutral | Positive | |
| Doctors prescribe too many medicines. | 3 (2 - 4) | 3 (2.5 - 4) | 3 (2 - 4) | **0.030**‡ |
| People who take medicines should stop them from time to time. | 4 (3 - 4) | 4 (3 - 4) | 4 (3 - 4) | 0.880 |
| Most medicines are addictive. | 4 (2 - 4) | 4 (2 - 4) | 3 (2 - 4) | 0.760 |
| Natural remedies are safer than medicines. | 3 (2.5 - 4) | 3 (3 - 4) | 3 (2 - 3) | **0.004**§ |
| Medicines do more harm than good. | 2 (2 - 3) | 3 (2 - 3) | 2 (2 - 3) | 0.050 |
| All medicines are poisons. | 2 (2 - 3.5) | 2 (2 - 3) | 2 (1 - 3) | 0.760 |
| Doctors place too much trust in medicines. | 3 (2 - 4) | 3 (3 - 4) | 3 (2 - 4) | 0.090 |
| If doctors had more time for patients they would prescribe fewer medicines. | 4 (2 - 5) | 4 (3 - 4) | 4 (2 - 4) | 0.690 |
| OVERUSE | 12 (10 - 15) | 13 (11 - 15) | 12 (10 - 14) | **0.020**‡ |
| HARM | 12 (9 - 14) | 12 (10 - 15) | 12 (10 - 14) | 0.590 |

*Kruskal-Wallis test (Post hoc Conover). Data are presented as medians (IQR) of grades 1 to 5.
1 - I completely disagree, 2 - I disagree, 3 - I am not sure, 4 - I agree, 5 - I completely agree
ta

IQR – interquartile range

The analysis showed that the higher the median score in the subdomain of *medicine overuse* was, the more negative chemoprevention attitude they had. This is a significant correlation, but very weak according to Rho value (Spearman's Rho=-0.136, P=0.030). This means that these participants had more negative beliefs in relation to medicines overuse. Same applied in two items of the questionnaire, in the belief that *natural remedies are safer than medicines* (Spearman's Rho=-0.211, P=0.001) and in *medicines do more harm than good* (Spearman's Rho= -0.125, P=0.040), which again is very weak correlation. These data are shown in Table 5.20.

Table 5.20. The association between beliefs about medicines and chemoprevention attitude, Spearman's Rho

| | Spearman's Rho (P value) |
|---|---|
| | BC chemoprevention attitude |
| Doctors prescribe too many medicines. | -0.116 (0.070) |
| People who take medicines should stop them from time to time. | 0.046 (0.470) |
| Most medicines are addictive. | -0.019 (0.760) |
| Natural remedies are safer than medicines. | **-0.211 (0.001)** |
| Medicines do more harm than good. | **-0.125 (0.040)** |
| All medicines are poisons. | -0.046 (0.470) |
| Doctors place too much trust in medicines. | -0.033 (0.610) |
| If doctors had more time for patients they would prescribe fewer medicines. | -0.068 (0.290) |
| OVERUSE | **-0.136 (0.030)** |
| HARM | -0.049 (0.440) |

BC – breast cancer

### 5.2.2 Self-reported health status and chemoprevention attitude of the whole study population

Table 5.21. shows an overview of correlation between certain participants' characteristics and different domains of their self-reported health, which turned out to be mostly very weak or weak, with the exception of negative correlation between self-perceived physical health and the number of prescription drugs, which was moderate. The analysis showed that *physical functioning* was declining with age (Spearman's ρ=-0.130, P=0,040) and the perception of own *general health* was worse with growing age (Spearman's ρ=-0.187, P=0.004). In this studied group, the more prescription drugs the participants were using the worse their self-perceived, both *physical* and *mental health* were, across all domains (Spearman's ρ= -0.421, P<0.001 and Spearman's ρ=-0.300, P<0.001, respectively). Same applied for the correlation between number of OTC drugs and perceived physical and mental health Spearman's ρ=-0.264, P<0.001 and Spearman's ρ=-0.259, P<0.001, respectively).

Table 5.21. Correlation between age, chronic therapy, over-the-counter drugs and certain domains of self-perceived health status

| | Spearman's Rho (P value) | | |
|---|---|---|---|
| | Age | Prescription drugs | OTC drugs |
| **Physical Health** | | | |
| Physical Functioning | **-0.130 (0.040)** | **-0.286 (<0.001)** | **-0.171 (0.010)** |
| Role limitation due to Physical problems | **-0.167 (0.009)** | **-0.339 (<0.001)** | **-0.209 (0.001)** |
| Pain | -0.061 (0.34) | **-0.281 (<0.001)** | **-0.268 (<0.001)** |
| General Health Perception | **-0.187 (0.004)** | **-0.471 (<0.001)** | **-0.224 (0.001)** |
| **Mental Health** | | | |
| Energy Vitality | 0.009 (0.890) | **-0.274 (0.001)** | **-0.164 (0.010)** |
| Social Functioning | 0.088 (0.180) | **-0.143 (0.030)** | **-0.283 (<0.001)** |
| Role limitation due to Emotional problems | **-0.150 (0.020)** | **-0.288 (<0.001)** | **-0.215 (0.001)** |
| Mental Health | -0.090 (0.170) | **-0.283 (<0.001)** | **-0.182 (0.005)** |
| **Physical Health Summary Scales** | **-0.179 (0.005)** | **-0.421 (<0.001)** | **-0.264 (<0.001)** |
| **Mental Health Summary Scales** | -0.049 (0.440) | **-0.300 (<0.001)** | **-0.259 (<0.001)** |

OTC – over the counter

Women of higher educational level reported better *general* and *physical health* (Kruskal-Wallis test (Post hoc Conover), P=0.003 and P=0.040, respectively) as shown in Table 5.22.

Table 5.22. Health-related quality of life across different educational levels

| | Median (IQR) | | | | | P* |
|---|---|---|---|---|---|---|
| | Primary School Diploma | High School Diploma | Bachelor's Degree | Master's Degree | Doctorate | |
| Physical Functioning | 75 (52.5 - 95) | 80 (52.5 - 92.5) | 75 (38.8 - 86.3) | 85 (51.3 - 100) | 97.5 (87.5 - 100) | 0.090 |
| Role limitation due to Physical problems | 50 (25 - 100) | 75 (0 - 100) | 87.5 (25 - 100) | 100 (50 - 100) | 100 (62.5 - 100) | 0.270 |
| Pain | 65 (30 - 90) | 60 (40 - 90) | 55 (40 - 90) | 70 (55 - 90) | 90 (52.5 - 90) | 0.350 |
| General Health Perception | 57 (37.5 - 71) | 62 (51.5 - 72) | 67 (51.5 - 72.8) | 67 (62 - 76.5) | 83.5 (62.8 - 87) | **0.003**† |
| Energy Vitality | 50 (40 - 71.3) | 60 (40 - 70) | 60 (48.8 - 65) | 60 (50 - 75) | 67.5 (42.5 - 92.5) | 0.490 |
| Social Functioning | 81.3 (50 - 100) | 87.5 (53.1 - 100) | 75 (62.5 - 90.6) | 81.3 (62.5 - 100) | 87.5 (75 - 100) | 0.890 |
| Role limitation due to Emotional problems | 83.3 (0 - 100) | 100 (33.3 - 100) | 100 (66.7 - 100) | 100 (33.3 - 100) | 100 (100 - 100) | 0.270 |
| Mental Health | 56 (44 - 80) | 68 (52 - 76) | 68 (61 - 75) | 68 (58 - 80) | 76 (56 - 96) | 0.180 |
| **Physical Health Summary Scales** | 57.4 (42.3 - 84.3) | 65 (46.4 - 82.3) | 68.8 (47.7 - 75.8) | 74.3 (58.3 - 85.5) | 92.8 (66.6 - 93.9) | **0.040**‡ |
| **Mental Health Summary Scales** | 61.9 (40.1 - 84.3) | 72 (50.2 - 82.8) | 72.6 (62.3 - 80.3) | 72.3 (47.4 - 85.8) | 82.8 (69.9 - 95.6) | 0.310 |

*Kruskal Wallis Test (Post hoc Conover). The data are presented as median (IQR) of score 0-100.

†at the level P<0,05 significant are the differences *Primary School Diploma* vs. *Master's Degree*; *Primary School Diploma* vs. *Doctorate*

‡ at the level P<0,05 significant are the differences *Primary School Diploma* vs. *Master's Degree*; *Primary School Diploma* vs. *Doctorate*; *High School* vs. *Master's Degree*, *High School* vs. *Doctorate*; *Bachelor's Degree* vs. *Doctorate*

IQR – interquartile range

Women with existing comorbidities reported significantly worse quality of life across all domains but *social functioning* (Mann-Whitney U test, P<0.001), Table 5.23.

Table 5.23. Health-related quality of life and comorbidities

| | Median (IQR) - Comorobidities | | P* |
|---|---|---|---|
| | Yes | No | |
| Physical Functioning | 75 (45 - 85) | 85 (70 - 100) | **<0.001** |
| Role limitation due to Physical problems | 50 (0 - 100) | 100 (50 - 100) | **<0.001** |
| Pain | 50 (30 - 80) | 80 (60 - 90) | **<0.001** |
| General Health Perception | 57 (43.8 - 67) | 67 (61.5 - 80) | **<0.001** |
| Energy Vitality | 50 (40 - 65) | 60 (50 - 71.3) | **<0.001** |
| Social Functioning | 75 (50 - 100) | 87.5 (62.5 - 100) | 0.060 |
| Role limitation due to Emotional problems | 66.7 (0 - 100) | 100 (66.7 - 100) | **<0.001** |
| Mental Health | 60 (48 - 72) | 68 (60 - 80) | **<0.001** |
| **Physical Health Summary Scales** | 56.8 (38.9 - 74.5) | 78.6 (60.7 - 88.6) | **<0.001** |
| **Mental Health Summary Scales** | 61.9 (40 - 80.4) | 75.5 (62.8 - 86) | **<0.001** |

*Mann-Whitney U test. The data are presented as median (IQR) of score 0-100.
IQR – interquartile range

Table 5.24. contains data about self-reported health in relation to beliefs about medicines. The better the *overall physical health* was, the more positive beliefs about medicines in the subdomain about *medicines overuse* was, but the correlation is very weak (Spearman's Rho=0.148, P=0.020).

Table 5.24. The association between self-reported health through SF-36 questionnaire and beliefs about medicines (Spearman's Rho)

| | Spearman's Rho (P value) | |
|---|---|---|
| | General harm | General overuse |
| Physical Functioning | 0.036 (0.58) | 0.126 (0.050) |
| Role limitation due to Physical problems | 0.054 (0.40) | **0.148 (0.020)** |
| Pain | 0.066 (0.31) | 0.075 (0.240) |
| General Health Perception | -0.067 (0.30) | 0.051 (0.430) |
| Energy Vitality | 0.025 (0.70) | 0.040 (0.530) |
| Social Functioning | 0.030 (0.65) | 0.035 (0.590) |
| Role limitation due to Emotional problems | -0.015 (0.78) | 0.008 (0.900) |
| Mental Health | -0.018 (0.78) | -0.043 (0.510) |
| **Physical Health Summary Scales** | 0.041 (0.53) | **0.137 (0.030)** |
| **Mental Health Summary Scales** | 0.002 (0.98) | 0.019 (0.770) |

The correlation between self-reported health status and participants' HL can be seen in the Table 5.25. It was found that women of excellent HL perceived own *general health* as significantly better in comparison to women of limited HL, as indicated by the higher median score for this item: 67 (57-85.8) vs. 62 (49.3 – 72) (Kruskal-Wallis test (Post hoc Conover), P=0.030). Significant was also that women of excellent HL reported better *mental health* (Kruskal-Wallis test (Post hoc Conover), P=0.002).

Table 5.25. The association between self-reported health through SF-36 questionnaire and health literacy

| | Median (IQR) HL level | | | P* |
|---|---|---|---|---|
| | Limited | Sufficient | Excellent | |
| Physical Functioning | 80 (55 - 95) | 80 (48.8 - 96.3) | 80 (25 - 95) | 0.630 |
| Role limitation due to Physical problems | 75 (0 - 100) | 100 (43.8 - 100) | 100 (25 - 100) | 0.120 |
| Pain | 60 (40 - 90) | 70 (50 - 90) | 65 (40 - 90) | 0.550 |
| General Health Perception | 62 (49.3 - 72) | 62 (52 - 76) | 67 (57 - 85.8) | **0.030**‡ |
| Energy Vitality | 55 (40 - 70) | 57.5 (45 - 70) | 65 (52.5 - 73.8) | 0.060 |
| Social Functioning | 75 (50 - 100) | 87.5 (62.5 - 100) | 87.5 (62.5 - 100) | 0.160 |
| Role limitation due to Emotional problems | 100 (33.3 - 100) | 100 (33.3 - 100) | 100 (66.7 - 100) | 0.710 |
| Mental Health | 64 (48 - 76) | 68 (60 - 80) | 72 (64 - 80) | **0.002**§ |
| **Physical Health Summary Scales** | 63 (47.5 - 83) | 71.9 (55.8 - 84.6) | 72.8 (49.1 - 83) | 0.340 |
| **Mental Health Summary Scales** | 70.6 (41.9 - 82.3) | 72.6 (56.6 - 84.4) | 79.8 (59.6 - 86.2) | 0.080 |

*Kruskal Wallis Test (Post hoc Conover). The data are presented as median (IQR) of score 0-100.
‡ at the level P<0,05 significant are the differences *limited* vs. *excellent*
§ at the level P<0,05 significant are the differences *limited* vs. *sufficient*; *limited* vs. *excellent*
IQR – interquartile range, HL – health literacy

One of the main objectives of this research was to explore the association between self-reported health status and attitude towards chemoprevention. The data are presented in Table 5.26. It was found that women with positive chemoprevention attitude perceived own *general health* worse in comparison to ones with neutral attitude (Kruskal Wallis Test (Post hoc Conover), P=0.030).

Table 5.26. The association between self-reported health through SF-36 questionnaire and chemoprevention attitude

| | Median (IQR) chemoprevention attitude | | | P* |
|---|---|---|---|---|
| | Negative | Neutral | Positive | |
| Physical Functioning | 80 (70 - 97.5) | 80 (50 - 95) | 80 (50 - 95) | 0.850 |
| Role limitation due to Physical problems | 75 (12.5 - 100) | 100 (25 - 100) | 75 (0 - 100) | 0.070 |
| Pain | 60 (40 - 90) | 60 (50 - 90) | 60 (40 - 90) | 0.240 |
| General Health Perception | 60 (52 - 73.5) | 67 (57 - 75) | 60 (47 - 72) | **0.030**† |
| Energy Vitality | 60 (45 - 70) | 60 (45 - 70) | 55 (40 - 70) | 0.300 |
| Social Functioning | 81.3 (53.1 - 100) | 81.3 (62.5 - 100) | 87.5 (50 - 100) | 0.920 |
| Role limitation due to Emotional problems | 100 (0 - 100) | 100 (58.3 - 100) | 66.7 (0 - 100) | **0.030**† |
| Mental Health | 64 (50 - 76) | 68 (56 - 80) | 64 (52 - 72) | 0.060 |
| **Physical Health Summary Scales** | 69.3 (47.1 - 82.5) | 69.4 (56.1 - 85.8) | 62.1 (43.8 - 80.7) | 0.090 |
| **Mental Health Summary Scales** | 73 (41.8 - 82.8) | 72.3 (58 - 84.5) | 70.5 (41.4 - 81.7) | 0.160 |

*Kruskal Wallis Test (Post hoc Conover). The data are presented as median (IQR) of score 0-100.
† at the level P<0,05 significant are the differences *neutral* vs. *positive*
IQR – interquartile range

### 5.2.3 Health literacy and chemoprevention attitude of the whole study population

HL was examined by the HLS-EU-Q47, a questionnaire validated on the European population. The participants were stratified into three levels, depending on their HL index, which is derived from their responses in the questionnaire as follows: limited HL (*Index* 0 – 33), sufficient HL (*Index* > 33 - 42) and excellent HL (*Index* > 42 - 50). In the studied group which consisted of 249 participants, most of them were of limited HL: 160 of them. There were 59 women with sufficient HL and 28 with excellent HL. This distribution can be seen on the Figure 5.1.

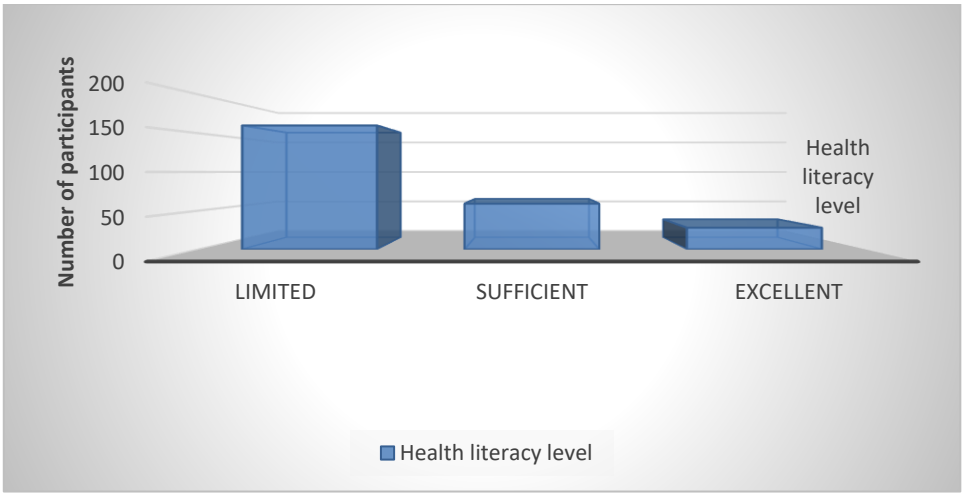



Figure 5.1. The study population's health literacy

The association between different demographic characteristics and HL level was examined (Table 5.27.). $\chi^2$ test showed that participants with excellent HL level had significantly higher educational level, like *Bachelor's degree*, *Master's degree* or *doctorate* ($\chi^2$ test, P<0.001). On the other hand, participants with limited HL had significant proportion of lower educated persons, like *primary* or *high school diploma* ($\chi^2$ test, P<0.001).

Table 5.27. Participants' demographic data and their health literacy

| | Number (%) HL level | | | | P* |
|---|---|---|---|---|---|
| | Limited | Sufficient | Excellent | Total | |
| Age [Median (IQR)] | 58 (50 – 62) | 57 (47 – 63) | 50 (43 – 60) | 57 (47 – 62) | 0.080† |
| Education status [n(%)] | | | | | |
| Primary School Diploma | 31 (19) | 7 (12) | 0 | 38 (15.4) | |
| High School Diploma | 98 (61) | 34 (58) | 12 (43) | 144 (58.3) | |
| Bachelor 's Degree | 4 (3) | 8 (14) | 6 (21) | 18 (7.3) | **<0.001** |
| Master's Degree | 26 (16) | 9 (15) | 8 (29) | 43 (17.4) | |
| Doctorate | 1 (1) | 1 (2) | 2 (7) | 4 (1.6) | |
| Employment status [n(%)] | | | | | |
| Private Sector Employee | 30 (19) | 12 (20) | 5 (18) | 47 (19) | |
| Public Sector Employee | 42 (26) | 23 (39) | 16 (57) | 81 (32.8) | |
| Free profession | 1 (1) | 1 (2) | 0 | 2 (0.8) | **0.030** |
| Unemployed | 27 (17) | 4 (7) | 1 (4) | 32 (13) | |
| Retired | 60 (38) | 19 (32) | 6 (21) | 85 (34.4) | |

*$\chi^2$ test; †Kruskal-Wallis test
HL – health literacy, IQR – interquartile range

In Table 5.28., data about accuracy of BC risk self-assessment across different HL levels are shown. Participants who correctly estimated own lifetime absolute BC risk were significantly more of excellent HL level ($\chi^2$ test, P=0.040)**.** But HL level did not have any significant correlation with the accuracy of 5-year absolute BC risk self-assessment ($\chi^2$ test, P=0.660).

Table 5.28. The correlation between the accuracy of own breast cancer risk assessment and participants' health literacy

| | Number (%) HL level | | | | P* |
|---|---|---|---|---|---|
| | Limited | Sufficient | Excellent | Total | |
| **Accuracy of the 5-year absolute BC risk self-assessment** | | | | | |
| Underestimated | 32 (20) | 13 (22) | 4 (14) | 49 (19.8) | 0.660 |
| Correct | 114 (71) | 38 (64) | 22 (79) | 174 (70.4) | |
| Overestimated | 14 (9) | 8 (14) | 2 (7) | 24 (9.7) | |
| **Accuracy of the absolute lifetime BC risk self-assessment** | | | | | |
| Underestimated | 5 (3) | 2 (3) | 3 (11) | 10 (4) | **0.040** |
| Correct | 134 (84) | 43 (73) | 24 (86) | 201 (81.4) | |
| Overestimated | 21 (13) | 14 (24) | 1 (4) | 36 (14.6) | |
| Total | 160 (100) | 59 (100) | 28 (100) | 247 (100) | |

*$\chi^2$ test
HL- health literacy; BC – breast cancer

At the baseline survey, there was no significant differences in knowledge about BC RFs between the participants of different HL level (Fisher's exact test, P=0.390), as presented in Table 5.29.

Table 5.29. Knowledge about breast cancer risk factors and participants' health literacy

| | Number (%) HL level | | | | P* |
|---|---|---|---|---|---|
| | Limited | Sufficient | Excellent | Total | |
| **Knowledge about BC risk factors** | | | | | |
| Problematic | 127 (79) | 51 (86) | 20 (71) | 198 (80.2) | 0.390 |
| Good | 30 (19) | 8 (14) | 7 (25) | 45 (18.2) | |
| Excellent | 3 (2) | 0 (0) | 1 (4) | 4 (1.6) | |
| Total | 160 (100) | 59 (100) | 28 (100) | 247 (100) | |

* Fisher's exact test
BC –breast cancer; HL – health literacy

At the baseline survey on all 249 participants, the ones with excellent HL had significantly higher median of answers in the item *Have you ever heard of BC chemoprevention*? In comparison to participants with lower levels of HL, indicating their better knowledge (Kruskal Wallis Test (Post hoc Conover), P= 0.009). However, the median 3.5 in the group with excellent HL still indicates that their knowledge was not very good either. The same effect was noted in the item about the knowledge of *Raloxifene* and *Anastrozole* (Kruskal Wallis Test (Post hoc Conover), P=0.009 and P=0.010, respectively), but the later one was observed only as a difference between the groups with limited HL and excellent HL. These data are presented in Table 5.30.

Table 5.30. Knowledge of chemoprevention and chemoprevention drugs and participants' health literacy

| | Median (IQR) HL level | | | | P* |
|---|---|---|---|---|---|
| | Limited | Sufficient | Excellent | Total | |
| **Have you ever heard of BC chemoprevention?** | 2 (1 - 3) | 3 (1 - 4) | 3.5 (1 - 3.8) | 2 (1 - 3) | **0.009**‡ |
| Tamoxifen | 1 (1 - 1) | 1 (1 - 1) | 1 (1 - 1) | 1 (1 - 1) | 0.100 |
| Raloxifene | 1 (1 - 1) | 1 (1 - 1) | 2 (1 - 2) | 1 (1 - 1) | **0.010**§ |
| Exemestane | 1 (1 - 1) | 1 (1 - 1) | 1 (1 - 1) | 1 (1 - 1) | 0.100 |
| Anastrozole | 1 (1 - 1) | 1 (1 - 1) | 1.5 (1 – 1.5) | 1 (1 - 1) | **0.007**§ |

*Kruskal Wallis Test (Post hoc Conover). Data are presented as medians (IQR) of grades 1-5.
Item *Have you ever heard of BC chemoprevention*: 1 – I completely disagree, 2 – I disagree, 3 – Neither agree, nor disagree, 4 – I agree, 5 – I completely agree
Items *Tamoxifen, Raloxifene, Exemestane, Anastrozole*: 1 - No, I have never heard of it, 2 – I may have heard, but am not sure, 3 – I recognize the name of the drug, 4 – I recognize the name of the drug and indication for use, 5 – Yes, I recognise the name of the drug, indication for use and its side effects
‡ at the level P<0,05 significant are the differences between *limited* vs. *sufficient*; *limited* vs. *excellent*
§ at the level P<0,05 significant are the differences between *limited* vs. *excellent*
BC – breast cancer; HL – health literacy, IQR – interquartile range

When we tested if there was any association between the HL level of our overall group of 249 respondents with their BC chemoprevention attitude, we found that there was no significant association between those two variables ($\chi^2$ test, P=0.800). Data are presented in Table 5.31.

Table 5.31. Attitudes towards breast cancer chemoprevention according to health literacy level

| **Chemoprevention attitude** | Number (%) HL level | | | | P* |
|---|---|---|---|---|---|
| | Limited | Sufficient | Excellent | Total | |
| Negative | 17 (11) | 7 (12) | 1 (4) | 25 (10.1) | |
| Neutral | 69 (43) | 24 (41) | 13 (46) | 106 (42.9) | 0.800 |
| Positive | 74 (46) | 28 (47) | 14 (50) | 116 (47) | |
| | 160 (100) | 59 (100) | 28 (100) | 247 (100) | |

*$\chi^2$ test
HL – health literacy

### 5.2.4 The effect of educational intervention on chemoprevention knowledge and other parameters

#### 5.2.4.1 Basic characteristics of the intervention group

Table 5.32. shows an overview of some of the demographic data of the intervention group, which consisted of 65 participants. The median age was 55 (IQR 44-61) and the median number of children was 2 (1-2).

Table 5.32. Demographic characteristics of the interventional group

| | |
|---|---|
| Age [Median (IQR)] | 55 (44 – 61) |
| Education status [n(%)] | |
| Primary School Diploma | 11 (17) |
| High School Diploma | 36 (55) |
| Bachelor's Degree | 6 (9) |
| Master's Degree | 9 (14) |
| Doctorate | 3 (5) |
| Number of children [Median (IQR)] | 2 (1 – 2) |
| Employment status [n(%)] | |
| Private Sector Employee | 16 (25) |
| Public Sector Employee | 20 (31) |
| Free profession | 1 (2) |
| Unemployed | 5 (8) |
| Retired | 23 (35) |
| Active menstrual cycle [n(%)] | 24 (37) |

IQR – interquartile range

As regards to their medical history, 19% had a first-degree relative with BC and an additional 19% in wider family. Fifty-two per cent (52%) of them had existing comorbidities

and 55% of the participants were taking one or more prescription drugs, which is presented in Table 5.33.

Table 5.33. Participants of intervention study group according to family history, comorbidities and risk factors

| | n (%) |
|---|---|
| BC in first degree relatives | 12 (19) |
| Breast cancer in wider family | 12 (19) |
| Family history of ovarian cancer | 2 (31) |
| History of any malignancy in the family | 32 (49) |
| Comorbidities | 34 (52) |
| Number of regular prescription drugs | |
| 0 | 29 (45) |
| 1 | 16 (25) |
| 2 | 8 (12) |
| 3 | 6 (9) |
| 4 or more | 6 (9) |
| Number of regular OTC drugs | |
| 0 | 51 (79) |
| 1 | 8 (12) |
| 2 | 1 (2) |
| 3 | 3 (5) |
| 4 or more | 1 (2) |
| Smoking | 20 (31) |
| Alcohol use* | 0 |

*equivalent of 2 dcl of alcoholic beverage a day
BC – breast cancer, OTC – over the counters

As regards to anamnestic data which are used to calculate the objective BC risk according to Gail model, there was 15% of women with early menarche, a recognised BC RF. Furthermore, women with BC RFs including childlessness and first childbirth after age of 30 accounted for 23% of participants in the intervention group. There were 7 women with history of AH, which is by 4 more than at the baseline survey. The reason is because for some of the participants about 20 months passed between the inital survey and the one after the EI, therefore 4 new cases were diagnosed in that timeframe. These data are presented in Table 5.34.

Table 5.34. Anamnestic data of the interventional group necessary for breast cancer risk calculation according to Gail model

| | n (%) |
|---|---|
| Age [Median (IQR)] | 55 (44 – 61) |
| Age at the time of the first menstrual period | |
| 7 to 11 | 10 (15) |
| 12 to 13 | 43 (66) |
| 14 or more | 12 (19) |
| Age at the time of the first childbirth | |
| Nulliparous | 11 (17) |
| < 20 | 7 (11) |
| 20 – 24 | 27 (42) |
| 25 – 29 | 16 (25) |
| 30 or more | 4 (6) |
| First-degree relative with history of BC | |
| Yes, 1 first-degree relative with history of BC | 4 (6) |
| Yes, more than 1 first-degree relative with history of BC | 8 (12) |
| No | 53 (82) |
| History of breast biopsy | |
| Yes, once | 6 (9) |
| Yes, more than once | 1 (2) |
| No | 58 (89) |
| History of AH | |
| Yes | 7 (11) |
| No | 58 (89) |

BC – breast cancer, IQR – interquartile range, AH – atypical hyperplasia

#### 5.2.4.2 Basic characteristics of the control group

Table 5.35. summarizes demographic characteristics of the control group. Median age was 59 (IQR 49-62) and majority of participants had high school diploma (59.8%) and were postmenopausal (75%).

Table 5.35. Demographic characteristics of the control group

| Participants' characteristics | |
|---|---|
| Age [Median (IQR)] | 58 (49 - 62) |
| Education status [n(%)] | |
| Primary School Diploma | 27 (14.7) |
| High School Diploma | 110 (59.8) |
| Bachelor's Degree | 12 (6.5) |
| Master's Degree | 34 (18.5) |
| Doctorate | 1 (0.5) |
| Number of children [Median (IQR)] | 2 (1 – 2) |
| Employment status [n(%)] | |
| Private Sector Employee | 32 (17.4) |
| Public Sector Employee | 61 (33.2) |
| Free profession | 1 (0.5) |
| Unemployed | 28 (15.2) |
| Retired | 62 (33.7) |
| Active menstrual cycle [n(%)] | 46 (25) |

IQR – interquartile range

As regards to the personal and family history of disease, 39% had positive family history of BC and 20% had first-degree relative with BC. About a half of participants (53%) in the control group had one or more comorbidities and 61% were taking some regular therapy, these data are shown in Table 5.36.

Table 5.36. Participants of control study group according to family history, comorbidities and risk factors

| | n (%) |
|---|---|
| BC in first degree relatives | 37 (20) |
| Breast cancer in wider family | 34 (19) |
| Family history of ovarian cancer | 20 (11) |
| History of any malignancy in the family | 102 (55) |
| Comorbidities | 97 (53) |
| Number of regular prescription drugs | |
| 0 | 71 (39) |
| 1 | 37 (20) |
| 2 | 33 (18) |
| 3 | 16 (9) |
| 4 or more | 27 (15) |
| Number of regular OTC drugs | |
| 0 | 135 (73) |
| 1 | 1 (29) |
| 2 | 10 (5) |
| 3 | 3 (2) |
| 4 or more | 2 (1) |
| Smoking | 44 (24) |
| Alcohol use* | 4 (2) |

*equivalent of 2 dcl of alcoholic beverage a day
BC – breast cancer, OTC – over the counters

In Table 5.37. anamnestic data required for BC risk calculation are presented. There were 10% of participants who had menarche at the age considered to be a BC RF and 21.7% of women with BC RF related to their parity. Eleven participants had one or more breast biopsies and 7 had history of AH.

Table 5.37. Anamnestic data of the control group necessary for breast cancer risk calculation according to Gail model

| | n (%) |
|---|---|
| Age [Median (IQR)] | 58 (49 - 62) |
| Age at the time of the first menstrual period | |
| 7 to 11 | 19 (10) |
| 12 to 13 | 97 (53) |
| 14 or more | 68 (37) |
| Age at the time of the first childbirth | |
| Nulliparous | 16 (8.7) |
| < 20 | 24 (13) |
| 20 – 24 | 85 (46) |
| 25 – 29 | 36 (20) |
| 30 or more | 23 (13) |
| First-degree relative with history of BC | |
| Yes. 1 first-degree relative with history of BC | 27 (15) |
| Yes. more than 1 first-degree relative with history of BC | 10 (5) |
| No | 147 (80) |
| History of breast biopsy | |
| Yes. once | 8 (4) |
| Yes. more than once | 3 (2) |
| No | 173 (94) |
| History of AH | |
| Yes | 7 (11) |
| No | 58 (89) |

BC – breast cancer, IQR – interquartile range, AH – atypical hyperplasia

#### 5.2.4.3. Comparison of different characteristics between the control and the intervention group

Different characteristics like family history of BC, history of breast biopsy, HL and chemoprevention attitudes were compared between the control and intervention group, these data are presented in Tables 5.38., 5.39. and 5.40. No significant differences between the two groups in the tested characteristcis were found, apart from the one that the intervention group had significantly more participants who had their menarche at the age considered to be a BC RF ( $\chi^2$ test, P=0.020).

5.38. The comparison of anamnestic data necessary for breast cancer risk calculation according to Gail model between the control and intervention group

| | Number (%) of participants | | | P* |
|---|---|---|---|---|
| | Control group | Intervention group | Total | |
| Age [Median(IQR)] | 58 (49 62) | 55 (44 – 61) | 57 (47 – 62) | 0.230‡ |
| **Age at the time of the first menstrual period** | | | | |
| 7 to 11 | 19 (10.3) | 10 (15.4) | 29 (12) | |
| 12 to 13 | 97 (52.7) | 43 (66.2) | 140 (56) | **0.020** |
| 14 or more | 68 (37) | 12 (18.5) | 80 (32) | |
| **Age at the time of the first childbirth** | | | | |
| Nulliparous | 16 (8.7) | 11 (16.9) | 27 (11) | |
| < 20 | 24 (13) | 7 (10.8) | 31 (12) | |
| 20 – 24 | 85 (46.2) | 27 (41.5) | 112 (45) | 0.220 |
| 25 – 29 | 36 (19.6) | 16 (24.6) | 52 (21) | |
| 30 or more | 23 (12.5) | 4 (6.2) | 27 (11) | |
| **Malignancy in family** | | | | |
| Yes | 102 (55.7) | 32 (49.2) | 134 (54) | 0.370 |
| No | 81 (44.3) | 33 (50.8) | 114 (46) | |
| **Family history of BC** | | | | |
| Yes | 34 (18.5) | 12 (18.5) | 46 (18.5) | 0.990 |
| No | 150 (81.5) | 53 (81.5) | 203 (81.5) | |
| **BC in first-degree relatives** | | | | |
| Yes, 1 close relative with history of BC | 27 (14.7) | 4 (6.2) | 31 (12.4) | |
| Yes, more than 1 close relative with history of BC | 10 (5.4) | 8 (12.3) | 18 (7.2) | 0.050 |
| No | 147 (79.9) | 53 (81.5) | 200 (80.3) | |
| **History of breast biopsy** | | | | |
| Yes. once | 8 (4.3) | 6 (9.2) | 14 (5.6) | |
| Yes. more than once | 3 (1.6) | 1 (1.5) | 4 (1.6) | 0.340† |
| No | 173 (94) | 58 (89.2) | 231 (92.8) | |
| **History of AH** | | | | |
| Yes | 3 (1.6) | 0 | 3 (1.2) | |
| No | 7 (3.8) | 7 (10.8) | 14 (5.6) | 0.070† |
| History of breast biopsy | 174 (94.6) | 58 (89.2) | 232 (93.2) | |

* $\chi^2$ test, †Fisher's exact test; ‡Mann-Whitney U test

BC – breast cancer, IQR – interquartile range, AH – atypical hyperplasia

5.39. The comparison of chemoprevention attitudes between the control and intervention group

| **Chemoprevention attitude** | Number (%) of participants | | | P* |
|---|---|---|---|---|
| | Control group | Intervention group | Total | |
| Negative | 18 (9.8) | 7 (10.8) | 25 (10) | |
| Neutral | 74 (40.2) | 33 (50.8) | 107 (43) | 0.270 |
| Positive | 92 (50) | 25 (38.5) | 117 (47) | |
| Total | 184 (100) | 65 (100) | 249 (100) | |

* $\chi^2$ test

5.40. The comparison of health literacy between the control and intervention group

| **HL level** | Number (%) of participants | | | P* |
|---|---|---|---|---|
| | Control group | Intervention group | Total | |
| Limited | 117 (63.9) | 43 (67.2) | 160 (64.8) | |
| Sufficient | 45 (24.6) | 14 (21.9) | 59 (23.9) | 0.890 |
| Excellent | 21 (11.5) | 7 (10.9) | 28 (11.3) | |
| Total | 183 (100) | 64 (100) | 247 (100) | |

* $\chi^2$ test
HL – health literacy

By $\chi^2$ test no statistically significant correlation was found between participants' self-perceived BC risk and their attitude towards BC chemoprevention neither in the intervention group ( $\chi^2$ test, P=0.970), as shown in Table 5.41, nor in the control group ($\chi^2$ test, P=0.460), Table 5.42.

Table 5.41. Correlation between the self-perceived breast cancer risk and chemoprevention attitude in the intervention group at the baseline survey

| **Intervention group** | Self-perceived 5-year absolute BC risk [n(%)] | | | P* |
|---|---|---|---|---|
| | Average | High | Total | |
| **Chemoprevention Attitude** | | | | |
| Negative | 19 (10.3) | 6 (9.2) | 25 (10) | 0.970 |
| Neutral | 79 (42.9) | 28 (43.1) | 107 (43) | |
| Positive | 86 (46.7) | 31 (47.7) | 117 (47) | |
| Total | 184 (100) | 65 (100) | 249 (100) | |

* $\chi^2$ test
BC- breast cancer

Table 5.42. Correlation between the self-perceived breast cancer risk and chemoprevention attitude in the control group

| **Control group** | Self-perceived 5-year absolute BC risk [n(%)] | | | P* |
|---|---|---|---|---|
| | Average | High | Total | |
| **Chemoprevention Attitude** | | | | |
| Negative | 15 (10.9) | 3 (6.4) | 18 (9.8) | 0.460 |
| Neutral | 52 (38) | 22 (46.8) | 74 (40.2) | |
| Positive | 70 (51.1) | 22 (46.8) | 92 (50) | |
| Total | 137 (100) | 47 (100) | 184 (100) | |

* $\chi^2$ test
BC- breast cancer

The accuracy of BC risk self-assessments among participants with different HL levels in both the control and the intervention group are shown in Table 5.43. Overall, no statistical significance was observed in the accuracy of BC risk self-assessment between the different HL levels neither in the intervention nor in the control group (Fisher's Exact Test, P>0.050). Due to missing data in the HLS-EU-Q47 questionnaire, in each of the group 1 participant was excluded from the analysis, ie. data from 183 participants are shown in the control group and 64 from the intervention group.

Table 5.43. The accuracy of breast cancer risk self-assessment according to participants' health literacy, in the control and the intervention group

| | Number of participants (%) according to HL level | | | | P* |
|---|---|---|---|---|---|
| | Limited | Sufficient | Excellent | Total | |
| **Control group** | n=117 | n=45 | n=21 | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 24 (20.5) | 10 (22.2) | 2 (9.5) | 36 (19.7) | 0.100 |
| Correct | 82 (70.1) | 27 (60) | 19 (90.5) | 128 (69.9) | |
| Overestimated | 11 (9.4) | 8 (17.8) | 0 | 19 (10.4) | |
| ***Accuracy of the absolute lifetime BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 2 (1.7) | 2 (4.4) | 2 (9.5) | 6 (3.3) | 0.050 |
| Correct | 99 (84.6) | 33 (73.3) | 19 (90.5) | 151 (82.5) | |
| Overestimated | 16 (13.7) | 10 (22.2) | 0 (0) | 26 (14.2) | |
| **At baseline – intervention group** | n=43 | n=14 | n=7 | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 8 (19) | 3 (21) | 2 (29) | 13 (20.3) | 0.200 |
| Correct | 32 (74) | 11 (79) | 3 (43) | 46 (71.9) | |
| Overestimated | 3 (7) | 0 | 2 (29) | 5 (7.8) | |
| ***Accuracy of the absolute lifetime BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 3 (7) | 0 | 1 (14) | 4 (6.3) | 0.350 |
| Correct | 35 (81) | 10 (71) | 5 (71) | 50 (78.1) | |
| Overestimated | 5 (12) | 4 (29) | 1 (14) | 10 (15.6) | |
| **P value (control vs. intervention group)** | | | | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment*** | 0.840 | 0.220 | 0.630 | 0.840 | |
| ***Accuracy of the absolute lifetime BC risk self-assessment*** | 0.230 | 0.670 | 0.560 | 0.550 | |

* Fisher's exact test

BC - breast cancer, HL – health literacy

### 5.2.4.3. Health literacy and the accuracy of breast cancer risk self-assessment in the control and the intervention group

In both the intervention and the control group participants with limited HL level were dominant, 117 in the control group (63.5%) and 43 (66.2%) in the intervention group. This can be seen on the Figure 5.2.

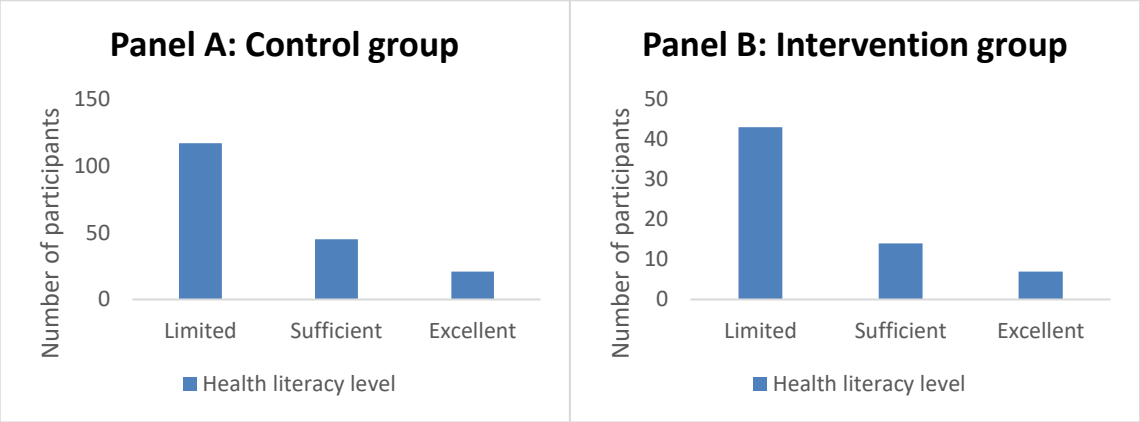



Figure 5.2. Panel A shows health literacy in the control group and Panel B in the intervention group

The analysis of correlation between HL and the accuracy of BC risk self-assessment showed no significant association between the two variables (Fisher's Exact Test, P>0.05), neither in the control, nor the intervention group. Given that in each of the groups 1 respondent had incomplete data in HLS-EU-Q47, in Tables 5.44. and 5.45. control group is represented with 283 and intervention group with 64 individuals.

Table 5.45. shows the comparison between the control group and the intervention group after the EI. It is obvious that in each measurement point there were no significant differences in the accuracy of BC risk self-assessment between the different HL levels. However, in the group with excellent HL, there was significantly less participants who correctly identified own lifetime BC risk immediately after the EI as compared with the control group (Fisher's Exact Test, P=0.04).

Table 5.44. The accuracy of breast cancer risk self-assessment according to participants' health literacy, at baseline survey

| | Number of participants (%) according to HL level | | | | P* |
|---|---|---|---|---|---|
| | Limited | Sufficient | Excellent | Total | |
| **At baseline – control group** | n=117 | n=45 | n=21 | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 24 (20.5) | 10 (22.2) | 2 (9.5) | 36 (19.7) | 0.100 |
| Correct | 82 (70.1) | 27 (60) | 19 (90.5) | 128 (69.9) | |
| Overestimated | 11 (9.4) | 8 (17.8) | 0 | 19 (10.4) | |
| ***Accuracy of the absolute lifetime BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 2 (1.7) | 2 (4.4) | 2 (9.5) | 6 (3.3) | 0.050 |
| Correct | 99 (84.6) | 33 (73.3) | 19 (90.5) | 151 (82.5) | |
| Overestimated | 16 (13.7) | 10 (22.2) | 0 (0) | 26 (14.2) | |
| **At baseline – intervention group** | n=43 | n=14 | n=7 | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 8 (19) | 3 (21) | 2 (29) | 13 (20.3) | 0.200 |
| Correct | 32 (74) | 11 (79) | 3 (43) | 46 (71.9) | |
| Overestimated | 3 (7) | 0 | 2 (29) | 5 (7.8) | |
| ***Accuracy of the absolute lifetime BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 3 (7) | 0 | 1 (14) | 4 (6.3) | 0.350 |
| Correct | 35 (81) | 10 (71) | 5 (71) | 50 (78.1) | |
| Overestimated | 5 (12) | 4 (29) | 1 (14) | 10 (15.6) | |
| **P value (control vs.intervention ntervention group)** | | | | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment*** | 0.840 | 0.220 | 0.630 | 0.840 | |
| ***Accuracy of the absolute lifetime BC risk self-assessment*** | 0.230 | 0.670 | 0.560 | 0.550 | |

* Fisher's exact test

BC - breast cancer, HL – health literacy

Table 5.45. The accuracy of breast cancer risk self-assessment according to participants' health literacy, comparison between the control and the interv group

| | Number of participants (%) according to HL level | | | | P* |
|---|---|---|---|---|---|
| | Limited | Sufficient | Excellent | Total | |
| **Control group** | n=117 | n=45 | n=21 | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 24 (20.5) | 10 (22.2) | 2 (9.5) | 36 (19.7) | 0.100 |
| Correct | 82 (70.1) | 27 (60) | 19 (90.5) | 128 (69.9) | |
| Overestimated | 11 (9.4) | 8 (17.8) | 0 | 19 (10.4) | |
| ***Accuracy of the absolute lifetime BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 2 (1.7) | 2 (4.4) | 2 (9.5) | 6 (3.3) | 0.050 |
| Correct | 99 (84.6) | 33 (73.3) | 19 (90.5) | 151 (82.5) | |
| Overestimated | 16 (13.7) | 10 (22.2) | 0 (0) | 26 (14.2) | |
| **Immediately after the EI – intervention group** | n=43 | n=14 | n=7 | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 7 (16.3) | 2 (14.3) | 3 (42.9) | 12 (18.8) | 0.540 |
| Correct | 31 (72.1) | 11 (78.6) | 4 (57.1) | 46 (71.9) | |
| Overestimated | 5 (11.6) | 1 (7.1) | 0 | 6 (9.4) | |
| ***Accuracy of the absolute lifetime BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 1 (2.3) | 0 (0) | 1 (14.3) | 2 (3.1) | 0.250 |
| Correct | 37 (86) | 12 (85.7) | 4 (57.1) | 53 (82.8) | |
| Overestimated | 5 (11.6) | 2 (14.3) | 2 (28.6) | 9 (14.1) | |
| **1 week after the EI – intervention group** | n=43 | n=14 | n=7 | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 8 (18.6) | 3 (21.4) | 2 (28.6) | 13 (20.3) | |
| Correct | 31 (72.1) | 10 (71.4) | 5 (71.4) | 46 (71.9) | 0.980 |
| Overestimated | 4 (9.3) | 1 (7.1) | 0 (0) | 5 (7.8) | |
| ***Accuracy of the absolute lifetime BC risk self-assessment [n(%)]*** | | | | | |
| Underestimated | 1 (2.3) | 1 (7.7) | 1 (14.3) | 3 (4.8) | |
| Correct | 38 (88.4) | 9 (69.2) | 5 (71.4) | 52 (82.5) | 0.170 |
| Overestimated | 4 (9.3) | 3 (23.1) | 1 (14.3) | 8 (12.7) | |
| **P value (control vs. intervention group – immediately afer the EI /1 week after the EI)** | | | | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment*** | 0.810 / >0.990 | 0.490/ 0.690 | 0.080/ 0.250 | >0.990/ 0.870 | |
| ***Accuracy of the absolute lifetime BC risk self-assessment*** | >0.990 / 0.670 | 0.830/ 0.870 | **0.040/** 0.250 | >0.990/ 0.820 | |

* Fisher's exact test

BC - breast cancer, HL – health literacy

By $\chi^2$ test, no statistically significant differences were found in the accuracy of BC risk self-assessment between the control group and the intervention group. This indicated that the EI did not have an impact on the accuracy of own BC risk perception ($\chi^2$ test, P>0.050), Table 5.46.

Table 5.46. The accuracy of breast cancer risk self-assessment: comparison of the control group and intervention group after the educational intervention

| | Control group - number of participants (%) | Immediately after the EI - number of participants (%) | P* |
|---|---|---|---|
| ***Accuracy of the 5-year absolute BC risk self-assessment [n(%)]*** | | | |
| Underestimated | 36 (19.6) | 12 (18.8) | |
| Correct | 129 (70.1) | 46 (71.9) | 0.940 |
| Overestimated | 19 (10.3) | 6 (9.4) | |
| ***Accuracy of the absolute lifetime BC risk self-assessment [n(%)]*** | | | |
| Underestimated | 2 (1.7) | 2 (3.1) | |
| Correct | 99 (84.6) | 53 (82.8) | 0.820 |
| Overestimated | 16 (13.7) | 9 (14.1) | |
| | Control group - number of participants (%) | One week after the EI - number of participants (%) | P* |
| ***Accuracy of the 5-year absolute BC risk self-assessment [n(%)]*** | | | |
| Underestimated | 36 (19.6) | 13 (20.3) | |
| Correct | 129 (70.1) | 46 (71.9) | 0.840 |
| Overestimated | 19 (10.3) | 5 (7.8) | |
| ***Accuracy of the absolute lifetime BC risk self-assessment [n(%)]*** | | | |
| Underestimated | 2 (1.7) | 3 (4.8) | |
| Correct | 99 (84.6) | 52 (82.5) | 0.490 |
| Overestimated | 16 (13.7) | 8 (12.7) | |

*$\chi^2$ test

BC - breast cancer, EI – educational intervention

After looking at the HLS-EU-Q47 domains *Understanding of information* and *Assessment of information* to see if it might have had an influence on the accuracy of self-perceived BC risk, especially after the EI, again no statistical significance was observed between the measurement points, Tables 5.47. and 5.48.

Table 5.47. Health literacy domain *Assessment of information* and breast cancer risk self-assessment

| | Understanding of information | | | | P† (control vs. intervention group) |
|---|---|---|---|---|---|
| | Intervention group | | Control group | | |
| | Median (IQR) | P* | Median (IQR) | P* | |
| **At baseline** | | | | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment*** | | | | | |
| Underestimated | 3 (2.75 – 3.75) | | 3 (2.75 – 3) | | 0.360 |
| Correct | 3 (2.94 – 3.25) | 0.140 | 3 (2.75 – 3.25) | 0.080 | 0.980 |
| Overestimated | 3.5 (3 – 4) | | 3 (2.5 – 3) | | **0.040** |
| ***Accuracy of the absolute lifetime BC risk self-assessment*** | | | | | |
| Underestimated | 3.13 (2.81 - 3.81) | | 3 (2.88 – 3.81) | | 0.830 |
| Correct | 3 (2.75 – 3.25) | 0.500 | 3 (2.75 – 3) | 0.530 | 0.550 |
| Overestimated | 3.13 (3 – 3.5) | | 3 (2.5 – 3.31) | | 0.200 |
| **Immediately after the EI** | | | | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment*** | | | | | |
| Underestimated | 3 (2.75 – 3.87) | | 3 (2.75 – 3) | | 0.490 |
| Correct | 3 (3 – 3.25) | 0.860 | 3 (2.75 – 3.25) | 0.080 | 0.620 |
| Overestimated | 3 (2.94 – 3.81) | | 3 (2.5 – 3) | | 0.090 |
| ***Accuracy of the absolute lifetime BC risk self-assessment*** | | | | | |
| Underestimated | 3.37 (2.06 – 3) | | 3 (2.88 – 3.81) | | 0.590 |
| Correct | 3 (2.88 – 3.25) | 0.400 | 3 (2.75 – 3) | 0.530 | 0.410 |
| Overestimated | 3 (3 – 3.75) | | 3 (2.5 – 3.31) | | 0.030 |
| **One week after the EI** | | | | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment*** | | | | | |
| Underestimated | 3 (2.75 – 3.38) | | 3 (2.75 – 3) | | 0.530 |
| Correct | 3 (3 – 3.25) | 0.740 | 3 (2.75 – 3.25) | 0.080 | 0.560 |
| Overestimated | 3 (2.88 – 3.88) | | 3 (2.5 – 3) | | 0.090 |
| ***Accuracy of the absolute lifetime BC risk self-assessment*** | | | | | |
| Underestimated | 2.75 (2.75 – 4) | | 3 (2.88 – 3.81) | | 0.220 |
| Correct | 3 (3 – 3.25) | 0.320 | 3 (2.75 – 3) | 0.530 | 0.410 |
| Overestimated | 3.25 (3 – 3.75) | | 3 (2.5 – 3.31) | | 0.030 |

*Kruskal Wallis test; †Mann Whitney U test; Data are presented as medians (IQR) of grades 1-5. 1 - I completely disagree, 2 - I disagree, 3 - I am not sure, 4 - I agree, 5 - I completely agree
BC – breast cancer; EI –educational intervention

The only statistical significance appeared in the comparison of the control group and the intervention group at the baseline survey, so that individuals in the control group who overestimated own BC risk rated lower own ability to understand information (Mann Whitney U test, P=0.040). However medians were 3.5 and 3 for the intervention and the control group, respectively, therefore both standing for the answer 'I am not sure'.

Table 5.48. Health literacy domain *Assessment of information* and breast cancer risk self-assessment

| | Assessment of information | | | | P† (control vs. intervention group) |
|---|---|---|---|---|---|
| | Intervention group | | Control group | | |
| | Median (IQR) | P* | Median (IQR) | P* | |
| **At baseline** | | | | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment*** | | | | | |
| Underestimated | 2.75 (2.25 – 3.13) | 0.210 | 2.75 (2.5 – 3) | 0.220 | 0.840 |
| Correct | 2.75 (2.5 – 3) | | 2.75 (2.5 – 3) | | 0.510 |
| Overestimated | 3 (2.75 – 3.63) | | 2.75 (2.25 – 3.44) | | 0.070 |
| ***Accuracy of the absolute lifetime BC risk self-assessment*** | | | | | |
| Underestimated | 2.63 (2.31 – 3.5) | 0.260 | 2.88 (2.63 – 3.44) | 0.060 | 0.450 |
| Correct | 2.75 (2.37 – 3) | | 2.75 (2.5 – 3) | | 0.450 |
| Overestimated | 3 (2.69 – 3.31) | | 3 (2.25 – 3) | | 0.100 |
| **Immediately after the EI** | | | | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment*** | | | | | |
| Underestimated | 2.63 (2.25 – 3.25) | 0.770 | 2.75 (2.5 – 3) | 0.220 | 0.990 |
| Correct | 2.75 (2.5 – 3) | | 2.75 (2.5 – 3) | | 0.940 |
| Overestimated | 2.75 (2 – 3.13) | | 2.5 (2.25 – 3) | | 0.830 |
| ***Accuracy of the absolute lifetime BC risk self-assessment*** | | | | | |
| Underestimated | 3.25 (2.06 – 2.81) | 0.160 | 2.88 (2.63 – 3.44) | 0.060 | 0.730 |
| Correct | 2.75 (2.5 – 3) | | 2.75 (2.5 – 3) | | 0.400 |
| Overestimated | 3 (2.38 – 3.63) | | 2.5 (2.25 – 3) | | 0.070 |
| **One week after the EI** | | | | | |
| ***Accuracy of the 5-year absolute BC risk self-assessment*** | | | | | |
| Underestimated | 2.75 (2.25 – 3.13) | 0.910 | 2.75 (2.5 – 3) | 0.220 | 0.810 |
| Correct | 2.75 (2.5 – 3) | | 2.75 (2.5 – 3) | | 0.870 |
| Overestimated | 3 (2.25 – 3.25) | | 2.5 (2.25 – 3) | | 0.490 |
| ***Accuracy of the absolute lifetime BC risk self-assessment*** | | | | | |
| Underestimated | 2.75 (2.25 – 3.75) | 0.340 | 2.88 (2.63 – 3.44) | 0.060 | 0.690 |
| Correct | 2.75 (2.5 – 3) | | 2.75 (2.5 – 3) | | 0.430 |
| Overestimated | 3 (2.63 – 3.78) | | 2.5 (2.25 – 3) | | 0.070 |

*Kruskal Wallis test; †Mann Whitney U test; Data are presented as medians (IQR) of grades 1-5. 1 - I completely disagree, 2 - I disagree, 3 - I am not sure, 4 - I agree, 5 - I completely agree;
BC – breast cancer; EI –educational intervention

#### 5.2.4.4. Breast cancer worry

Further, it was examined how much did the participants worry about the possibility of developing BC. By Friedman's test the analysis was performed to clarify if any change in their level of worry appeared after they had been exposed to the EI and also to find out if there were significant differences between the control and the intervention group (Mann Whitney U Test). The data can be seen in Table 5.49. The results showed that their worry significantly increased from baseline survey to the survey immediately after the EI, but it did not persist until the measurement point at one week after the EI (Friedman's test, P=0.02)). In addition, there was no significant difference in the level of worry between the control group and the intervention group in neither of the measurement points.

Table 5.49. Breast cancer worry in the three measurement points: at baseline, immediately after the educational intervention and 1 week after the educational intervention

| **BC worry** | Median (IQR) | | | P* |
|---|---|---|---|---|
| | At baseline | Immediately after the EI | One week after the EI | |
| Intervention group | 2.5 (2 – 3) | 3.25 (2 – 4) | 3 (2 – 3) | **0.02** |
| Control group | 2.5 (2 – 4) | 2.5 (2 – 4) | 2.5 (2 – 4) | - |
| Intervention vs. control group ($P^{\dagger}$ value) | 0.23 | 0.16 | 0.56 | |

*Friedman's test. †Mann Whitney U test; Data are presented as medians (IQR) of grades 1-5.
1 – not worried at all, 2 – neither worried nor not worried, 3 – worried a little bit, 4 – worried, 5 – very worried
†at the level P<0,05 significant is the difference between *at baseline* vs. *Immediately after the EI*
BC – breast cancer, EI – educational intervention

By Spearman's correlation coefficient the association between the self-reported *mental health* (in the SF-36 questionnaire) and the level of BC worry in three measurement points was examined in the both groups. In the control group there was negative correlation between the mental health and BC worry, but Rho=-0.173 shows very weak association. Similarly, in the intervention group there was significant negative correlation between the mental health and the BC worry, but with weak association between the two variables (Spearmen's Rho=-0.287, P=0.020). There was no significant differences in the level of BC worry between the two groups. Data are presented in Table 5.50.

Table 5.50. The correlation between breast cancer worry and domain *Mental health* from the SF-36 questionnaire about own health perception, in three measurement points

| BC worry | Spearman's Rho (P value) | | |
|---|---|---|---|
| | At baseline | Immediately after the EI | One week after the EI |
| Intervention group | -0.010 (0.94) | -0.200 (0.11) | **-0.287 (0.02)** |
| Control group | **-0.173 (0.02)** | **-0.173 (0.02)** | **-0.173 (0.02)** |
| Intervention vs. control group ($P^{+}$ value) | 0.26 | 0.85 | 0.41 |

EI – educational intervention, BC – breast cancer; *comparison of correlation coefficients

#### 5.2.4.5 Breast cancer knowledge

In Table 5.51. we can see what was the knowledge of BC RFs like in each of the measurement points for each HL level in the both studied groups. Overall, in each of the measurement points participants of different HL level exhibited similar level of knowledge (Kruskal Wallis test, P>0.05). In addition, there was no significant difference between the control and the intervention group before the EI (Mann Whitney U test, P>0.05). After the EI, there was significant improvement in BC knowledge so that it was significantly better in comparison to the control group (Mann Whitney U test, P<0.001).

The overall number of recognised BC RFs significantly increased after the EI in all the participants, irrespective of their HL level and was maintained one week later (Friedman's test, P<0.05 in each HL group), as presented in Table 5.52.

Table 5.51. Number of correctly recognised breast cancer risk factors before and after the educational intervention across all health literacy levels

| | Number of correctly recognised risk factors | | | | P† |
|---|---|---|---|---|---|
| | Median (IQR) **Intervention group** | P* | Median (IQR) **Control group** | P* | |
| **At baseline** | | | | | |
| ***HL level*** | | | | | |
| Limited | 8 (5 – 10) | | 8 (6 – 10) | | 0.370 |
| Sufficient | 8 (3 – 10) | 0.770 | 7 (6 – 10) | 0.260 | 0.580 |
| Excellent | 8 (4 – 11) | | 9 (7 – 11) | | 0.530 |
| **Immediately after the EI** | | | | | |
| ***HL level*** | | | | | |
| Limited | 12 (10 – 14) | | 8 (6 – 10) | | **<0.001** |
| Sufficient | 13 (12 – 14) | 0.160 | 7 (6 – 10) | 0.260 | **<0.001** |
| Excellent | 13 (12 – 14) | | 9 (7 – 11) | | **<0.001** |
| **One week after the EI** | | | | | |
| ***HL level*** | | | | | |
| Limited | 12 (11 – 14) | 0.780 | 8 (6 – 10) | 0.260 | **<0.001** |
| Sufficient | 13 (12 – 13) | | 7 (6 – 10) | | **<0.001** |
| Excellent | 12 (12 – 13) | | 9 (7 – 11) | | **<0.001** |

*Kruskal Wallis test. †Mann Whitney U test; The highest possible number of correctly recognised risk factors was 16. HL- health literacy; EI – educational intervention

Table 5.52. Progression of knowledge of breast cancer RFs after the educational intervention within each health literacy level

| **HL level** | Median (IQR) correct answers about BC risk factors | | | P* |
|---|---|---|---|---|
| | At baseline | Immediately after the EI | 1 week after the EI | |
| Limited | 8 (5 – 10) | 12 (10 – 14) | 12 (11 – 14) | **<0.001**† |
| Sufficient | 8 (3 – 10) | 13 (12 – 14) | 13 (12 – 13) | **<0.001**‡ |
| Excellent | 8 (4 – 11) | 13 (12 – 14) | 12 (12 – 13) | **0.003**‡ |

*Friedman's test. The highest possible number of correctly recognised risk factors was 16.
†at the level P<0,05 significant difference is between *at baseline* vs. *immediately after the EI*; *at baseline* vs. *one week after the EI*
‡ at the level P<0,05 significant difference is between *at baseline* vs. *immediately after the EI*; *at baseline* vs. *one week after the EI*
EI – educational intervention; HL – health literacy; BC – breast cancer

Knowledge of BC RFs improved for most of RFs after the EI and remained fairly stable one week post EI. However, it remained low for *BD* and *first childbirth before age of 30* (McNemar test, P>0.050). At the baseline survey, most commonly recognised BC RF was *BC in the close relative*, recognised by 55 (85%) of the respondents. At the measurement point immediately after the EI, it increased to 64 (99%), which was statistically significant increase (McNemar test, P=0.010). And it did not significantly deteriorate by the measurement point at one week after the EI (McNemar test, P=0.070 ). The least recognised was the protective effect of the *first childbirth before the age 30,* only by 9 (14%) of the respondents in the intervention group. Unfortunatelly, it remained exactly at the same level after the EI. This and all the other items our participants were asked to recognise as: RF, protective factor or neither of those, are presented in Table 5.53.

Table 5.53. Recognition of breast cancer risk factors before and after the educational intervention (intervention group)

| | Number (%) correct answers | | | P value – at baseline vs. | | P value – immediately after the EI vs. |
|---|---|---|---|---|---|---|
| | At baseline | Immediately after the EI | One week after the EI | Immediately after EI | One week after the EI | One week after the EI |
| Growing age | 31 (48) | 56 (86) | 59 (91) | **<0.001** | **<0.001** | 0.510 |
| Early menarche | 16 (25) | 55 (85) | 56 (86) | **<0.001** | **<0.001** | >0.990 |
| Late menopause onset | 11 (17) | 49 (75) | 51 (79) | **<0.001** | **<0.001** | 0.770 |
| Nuliparous | 21 (32) | 57 (88) | 57 (88) | **<0.001** | **<0.001** | >0.990 |
| First childbirth before age 30 | 9 (14) | 9 (14) | 9 (14) | > 0.990 | > 0.990 | >0.990 |
| BC in the close relative | 55 (85) | 64 (99) | 62 (95) | **0.010** | 0.070 | 0.630 |
| AH | 47 (72) | 53 (82) | 54 (83) | 0.290 | 0.190 | >0.990 |
| *BRCA1/2* carrier | 49 (75) | 60 (92) | 62 (95) | **0.030** | **0.002** | 0.730 |
| HRT | 36 (55) | 48 (74) | 53 (82) | **0.020** | **<0.001** | 0.300 |
| Alcohol misuse | 31 (48) | 62 (95) | 59 (91) | **<0.001** | **<0.001** | 0.450 |
| Obesity in menopause | 36 (55) | 64 (99) | 60 (92) | **<0.001** | **<0.001** | 0.130 |
| Breastfeeding for long period | 35 (54) | 58 (89) | 57 (88) | **<0.001** | **<0.001** | >0.990 |
| Physical fitness | 41 (63) | 62 (95) | 61 (94) | **<0.001** | **<0.001** | >0.990 |
| Antiperspirants use | 30 (46) | 28 (43) | 34 (52) | 0.880 | 0.630 | 0.240 |
| Breast implants | 20 (31) | 23 (35) | 21 (32) | 0.710 | >0.990 | 0.800 |
| Breast density | 19 (29) | 28 (43) | 27 (42) | 0.230 | 0.290 | >0.990 |

*McNemar test. There were 65 participants in the intervention group.
BC – breast cancer, *BRCA1/2 – breast cancer gene 1 or 2,* HRT – hormonal replacement therapy, EI –educational intervention, AH – atypical hyperplasia

Table 5.54. shows the data about BC RF knowledge in the both studied groups and correlation of knowledge of each BC RF between the control group and the intervention group at baseline and after the EI. The EI significantly improved BC RFs awareness as compared to the control group (McNemar test, P<0.05) with the exception of *breast implants* (which is not the BC RF) and *breast density* (McNemar test, P<0.05).

Table 5.54. Comparison between the control and the intervention group in breast cancer risk factors knowledge

| | Number (%) correct answers | | | | P value – control group vs. intervention group | | |
|---|---|---|---|---|---|---|---|
| | Control group | Intervention group at baseline | Immediately after the EI | One week after the EI | At baseline | Immediately after the EI | One week after the EI |
| Growing age | 98 (53) | 31 (47.7) | 56 (86.2) | 59 (90.8) | 0.470 | **<0.001** | **<0.001** |
| Early menarche | 45 (24.3) | 16 (24.6) | 55 (84.6) | 56 (86.2) | 0.960 | **<0.001** | **<0.001** |
| Late menopause | 51 (27.6) | 11 (16.9) | 49 (75.4) | 51 (78.5) | 0.090 | **<0.001** | **<0.001** |
| Nuliparous | 79 (42.7) | 21 (32.3) | 57 (87.7) | 57 (87.7) | 0.140 | **<0.001** | **<0.001** |
| First childbirth before age of 30 | 67 (36.2) | 9 (13.8) | 9 (13.8) | 9 (13.8) | **0.001** | **0.008** | **0.001** |
| BC in close relative | 159 (85.9) | 55 (84.6) | 64 (98.5) | 62 (95.4) | 0.790 | **0.003** | 0.050 |
| AH | 127 (68.6) | 47 (72.3) | 53 (81.5) | 54 (83.1) | 0.580 | **0.04** | **0.030** |
| *BRCA1/2* | 137 (74.1) | 49 (75.4) | 60 (92.3) | 62 (95.4) | 0.830 | **0.003** | **0.003** |
| HRT | 103 (55.7) | 36 (55.4) | 48 (73.8) | 53 (81.5) | 0.970 | **0.009** | **<0.001** |
| Alcohol misuse | 95 (51.4) | 31 (47.7) | 62 (95.4) | 59 (90.8) | 0.610 | **<0.001** | **<0.001** |
| Obesity in menopause | 97 (52.4) | 36 (55.4) | 64 (98.5) | 60 (92.3) | 0.680 | **<0.001** | **<0.001** |
| Breastfeeding for long period | 80 (43.2) | 35 (53.8) | 58 (89.2) | 57 (87.7) | 0.140 | **<0.001** | **<0.001** |
| Physical fitness | 115 (62.2) | 41 (63.1) | 62 (95.4) | 61 (93.8) | 0.890 | **<0.001** | **<0.001** |
| Antiperspirants use | 112 (60.5) | 30 (46.2) | 28 (43.1) | 34 (52.3) | 0.050 | **0.020** | 0.250 |
| Breast implants | 67 (36.2) | 20 (30.8) | 23 (35.4) | 21 (32.3) | 0.430 | 0.860 | 0.540 |
| Breast density | 71 (38.4) | 21 (32.3) | 28 (43.1) | 27 (41.5) | 0.380 | 0.520 | 0.610 |

*McNemar test. There were 65 participants in the intervention group. BC – breast cancer, *BRCA1/2 – breast cancer gene 1 or 2,* HRT – hormonal replacement therapy, EI –educational intervention

### 5.2.4.6 Breast cancer chemoprevention knowledge and attitudes

Improvement in knowledge of chemoprevention and chemoprevention drugs was achieved after the education and maintained one week later, as shown in Table 5.47. This was achieved in all the participants, irrespective of their HL level.

Table 5.55. shows the correlation of data about chemoprevention knowledge between the control and the intervention group and also postintervention data. The analysis showed no significant difference in knowledge about chemoprevention between the control group and the intervention group at the baseline survey (Friedman's test (Post hoc Conover), P>0.05). As regards to the effect of EI on the BC kemoprevention knowledge, it achieved improvement in each of the HL levels in both measurement points post intervention and in comparison to the control group (Friedman's test (Post hoc Conover), P<0.05).

Table 5.55. Knowledge of chemoprevention and chemoprevention drugs before and after the educational intervention, through all the health literacy levels

| HL level | Median (IQR) of grades | | | | P* value Control vs. Intervention | | |
|---|---|---|---|---|---|---|---|
| | Control group | At baseline | Immediately after the EI | One week after the EI | P*- Intervention group | At baseline | Immediately after the EI | One week after the EI |
| **Limited** | | | | | | | | |
| ***Have you ever heard od BC chemoprevention?*** | 2 (1 – 3) | 3 (1 - 3) | 2 (1 - 3) | 3 (1 - 3) | **<0.001†** | 0.300 | **<0.001** | **<0.001** |
| Tamoxifen | 1 (1 – 1) | 1 (1 - 1) | 1 (1 - 1) | 2 (1 - 3.5) | **<0.001†** | 0.210 | **<0.001** | **<0.001** |
| Raloxifene | 1 (1 – 1) | 1 (1 - 1) | 1 (1 - 1) | 2 (1 - 5) | **<0.001†** | 0.410 | **<0.001** | **<0.001** |
| Eksemestane | 1 (1 – 1) | 1 (1 - 1) | 1 (1 - 1) | 2 (1 - 2) | **<0.001†** | 0.170 | **<0.001** | **<0.001** |
| Anastrozole | 1 (1 – 1) | 1 (1 - 1) | 1 (1 - 1.3) | 1.5 (1 - 2) | **<0.001†** | 0.090 | **<0.001** | **<0.001** |
| **Sufficient** | | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Have you ever heard about BC chemopreventio n?*** | 1 (1 – 3.5) | 2 (1 – 3) | 4 (3 - 4.3) | 4.5 (3 - 5) | **<0.001†** | 0.890 | **<0.001** | **<0.001** |
| Tamoxifen | 1 (1 – 1) | 1 (1 – 1) | 4.5 (2 - 5) | 4 (1 - 5) | **<0.001†** | 0.230 | **<0.001** | **<0.001** |
| Raloxifene | 1 (1 – 1) | 1 (1 – 1) | 4.5(2 - 5) | 4 (1 - 5) | **<0.001†** | 0.240 | **<0.001** | **<0.001** |
| Exemestane | 1 (1 – 1) | 1 (1 – 1) | 4 (2 - 5) | 3 (1 - 4) | **<0.001†** | 0.730 | **<0.001** | **<0.001** |
| Anastrozole | 1 (1 – 1) | 1 (1 – 1) | 3.5 (2 - 5) | 3 (2 - 5) | **<0.001†** | 0.060 | **<0.001** | **<0.001** |
| **Excellent** | | | | | | | | |
| ***Have you ever heard about BC chemopreventio n?*** | 1 (1 – 3) | 3 (1 – 3) | 4 (3.8 - 4.3) | 4 (3 - 5) | 0.400 | 0.260 | **0.005** | **0.005** |
| Tamoxifen | 1 (1 – 1) | 1 (1 – 3.5) | 4 (3 - 5) | 4 (3 - 5) | 0.150 | 0.190 | **0.003** | **<0.001** |
| Raloxifene | 1 (1 – 1) | 1 (1 – 5) | 4 (3 - 5) | 4 (3 - 5) | 0.570 | 0.130 | **0.002** | **<0.001** |
| Exemestane | 1 (1 – 1) | 1 (1 – 2) | 4 (3 - 5) | 4 (2 - 5) | 0.080 | 0.590 | **0.003** | **<0.001** |
| Anastrozole | 1 (1 – 1) | 1 (1 – 2) | 4.5 (3 - 5) | 4 (2 - 5) | 0.007† | 0.810 | **0.001** | **0.001** |

*Friedman's test (Post hoc Conover). †at the level P<0,05 significant is the difference *at baseline* vs *immediately after the EI*; *at baseline* vs. *one week after the EI*

Data are presented as medians (IQR) of grades 1-5. 1 – I completely disagree, 2 – I disagree, 3 – Neither agree, nor disagree, 4 – I agree, 5 – I completely agree

EI – educational intervention, HL – health literacy, BC – breast cancer

No significant differences in knowledge of chemoprevention and chemoprevention drugs when comparing the participants of different HL level was observed in neither of the three measurement points, as seen in table 5.56.

Table 5.56. Knowledge of chemoprevention before and after the educational intervention, according to participants' health literacy

| | Median (IQR) HL level | | | | P* |
|---|---|---|---|---|---|
| | Limited | Sufficient | Excellent | Total | |
| **At baseline** | | | | | |
| ***Have you ever heard od BC chemoprevention?*** | 3 (1 – 3) | 2 (1 – 3) | 3 (1 – 3) | 3 (1 – 3) | 0.550 |
| Tamoxifen | 1 (1 – 1) | 1 (1 – 1) | 1 (1 – 4) | 1 (1 – 1) | 0.120 |
| Raloxifene | 1 (1 – 1) | 1 (1 – 1) | 1 (1 – 5) | 1 (1 – 1) | 0.100 |
| Exemestane | 1 (1 – 1) | 1 (1 – 1) | 1 (1 – 2) | 1 (1 – 1) | 0.490 |
| Anastrozole | 1 (1 – 1) | 1 (1 – 1) | 1 (1 – 2) | 1 (1 – 1) | 0.060 |
| **Immediately after the EI** | | | | | |
| ***Have you ever heard od BC chemoprevention?*** | 4 (3 – 4) | 4 (3 – 4) | 4 (3 – 5) | 4 (3 – 4) | 0.830 |
| Tamoxifen | 4 (2 – 4) | 4 (2 – 5) | 4 (1 – 5) | 4 (2 – 5) | 0.860 |
| Raloxifene | 4 (2 – 5) | 4 (2 – 5) | 4 (1 – 5) | 4 (2 – 5) | 0.810 |
| Exemestane | 4 (2 – 5) | 4 (2 – 5) | 3 (1 – 4) | 4 (2 – 5) | 0.560 |
| Anastrozole | 3 (2 – 5) | 3.5 (2 – 5) | 3 (2 – 5) | 3 (2 – 5) | 0.910 |
| **One week after the EI** | | | | | |
| ***Have you ever heard od BC chemoprevention?*** | 4 (4 – 4) | 4 (4 – 4) | 4 (3 – 5) | 4 (4 – 4) | 0.990 |
| Tamoxifen | 4 (2 – 4) | 4 (3 – 5) | 4 (3 – 5) | 4 (3 – 4) | 0.450 |
| Raloxifene | 3 (2 – 4) | 4 (3 – 5) | 4 (3 – 5) | 4 (3 – 4) | 0.180 |
| Exemestane | 3 (2 – 4) | 4 (3 – 5) | 4 (2 – 5) | 3 (3 – 4) | 0.260 |
| Anastrozole | 3 (2 – 4) | 4 (3 – 5) | 4 (2 – 5) | 3 (3 – 4) | 0.340 |

*Kruskal-Wallis test. Data are presented as medians (IQR) of grades 1-5. 1 – I completely disagree, 2 – I disagree, 3 – Neither agree, nor disagree, 4 – I agree, 5 – I completely agree.
BC – breast cancer, EI – educational intervention

The EI significantly shifted the chemoprevention attitude towards more positive, as indicated by the data presented in Table 5.57. In comparison to the baseline survey, at one week after the EI there was significantly more participants with positive chemoprevention attitude: 17% vs 45% (Marginal homogeneity test, P<0.001). Also, significantly less participants had neutral attitude one week after the EI, in comparison to baseline survey: 71% vs 55% (Marginal homogeneity test, P<0.001). Interestingly, before the EI there was 12% of women with negative attitude, but 0% one week after the EI.

Table 5.57. Chemoprevention attitude before and after the educational intervention

| | Number (%) according to the chemoprevention attitude **at baseline** | | | | P |
|---|---|---|---|---|---|
| | Negative | Neutral | Positive | Total | |
| **Immediately after the EI** | | | | | |
| Negative | 1 | 1 | 0 | 2 (3) | |
| Neutral | 7 | 38 | 10 | 55 (85) | 0.080† |
| Positive | 0 | 7 | 1 | 8 (12) | |
| Total | 8 (12) | 46 (71) | 11 (17) | 65 (100) | |
| **One week after the EI** | | | | | |
| Negative | 0 | 0 | 0 | 0 | |
| Neutral | 6 | 27 | 3 | 36 (55) | **<0.001*** |
| Positive | 2 | 19 | 8 | 29 (45) | |
| Total | 8 (12) | 46 (71) | 11 (17) | 65 (100) | |

*Marginal homogeneity test; †McNemar-Bowker test
EI – educational intervention

There were no significant differences in chemoprevention attitude between the control group and the intervention group at the initial survey, as seen in Table 5.58.

Table 5.58. Correlation of chemoprevention attitude between the control group and the intervention group

| | Number (%) according to the chemoprevention attitude | | | P* |
|---|---|---|---|---|
| | Control group | Intervention group | Total | |
| **Chemoprevention Attitude** | | | | |
| Negative | 18 (9,8) | 7 (10,8) | 25 (10) | 0,27 |
| Neutral | 74 (40,2) | 33 (50,8) | 107 (43) | |
| Positive | 92 (50) | 25 (38,5) | 117 (47) | |
| Total | 184 (100) | 65 (100) | 249 (100) | |

*$\chi^2$ test

Table 5.59. shows the correlation between the chemoprevention attitude of the control group and the intervention group after the intervention. There was significant difference in all types of chemoprevention attitudes. In the intervention group, there were significantly less individuals with negative attitude after the EI ($\chi^2$ test, P<0.001), interestingly there was no one with negative attitude 1 week after the intervention ($\chi^2$ test, P=0.010). There were significantly more participants with neutral attitude after the EI in comparison to the control group, however, in both measurement points after the EI there

were significantly less individuals with positive attitude when comparing to the control group ($\chi^2$ test, P>0.050).

Table 5.59. Chemoprevention attitude of the control group and the intervention group after the educational intervention

| | Control | Immediately after the EI | P* |
|---|---|---|---|
| **Chemoprevention attitude [n(%)]** | | | |
| Negative | 18 (9.8) | 2 (3) | |
| Neutral | 74 (40.2) | 55 (85) | **<0.001** |
| Positive | 92 (50) | 8 (12) | |
| | **Control** | **One week after the EI** | **P*** |
| **Chemoprevention attitude [n(%)]** | | | |
| Negative | 18 (9.8) | 0 | |
| Neutral | 74 (40.2) | 36 (55) | **0.010** |
| Positive | 92 (50) | 29 (45) | |

*$\chi^2$ test
EI – educational intervention

# 6. DISCUSSION

## 6.1. Breast cancer risk self-assessment

There were 249 women who participated in this study, aged 35 to 85, of which 70 women (28.1%) were premenopausal. Overall, 95 (38.1%) had positive family history of BC, of which about half in first-degree relative.

One of the study's main objectives was to investigate the accuracy of self-perceived BC risk, regarding it to be one of the key motivators for enrolment in health-related preventive behaviours. The influence of certain participants' characteristics on their own risk perception was also explored, like their HL, their worry about BC and emotional attributes.

BC risk can be defined in several ways: absolute and relative BC risk, or short- and long-term risk. In nearly all large RCTs about the efficacy of chemoprevention drugs, the eligibility for initiation of chemoprevention drug was based on the elevated absolute 5-year BC risk calculated according to Gail model, with BCRAT (23, 30, 88, 89). Likewise, the participants in this study were categorised into HR group if their 5-year absolute BC risk was >1.66%. Based on such calculation, 184 (73.9%) had average 5-year absolute BC risk (AR), while 65 (26.1%) belonged to HR group. Literature data suggest that HR women are also ones with absolute lifetime Gail BC risk of >= 20% (90), however, only the 5-year absolute BC risk was implemented in inclusion criteria in earlier mentioned RCTs, as referenced above.

The results of this study show that majority of participants thought they had an average BC risk and 179 (70.7%) were accurate in their estimation, while nearly one-fifth underestimated own risk. Such self-perceived estimates are in line with published data (91). There is also a group of women who overestimated own risk, 24 (9.6%) of them. As for the intervention group (64 participants), baseline survey showed comparable results to the control group regarding the accuracy of BC risk self-assessment. EI did not lead to any improvement in the accuracy of perception of own absolute 5-year BC risk, irrespective of participant's HL level. The lack of effect of EI in this case can partly be explained by the fact that during the EI participants were not individually informed about their objective BC risk, but were rather informed about all the BC RFs and BC epidemiological data. Indeed, the

recognition of BC RFs significantly improved after the EI and was maintained one week after the EI, through all the HL levels. In order to accurately recognize own susceptibility to BC based on learning about the BC RFs, the participant was required to process those information and apply in own case of BC risk assessment. Therefore, it was not a direct reproduction of received information. For this reason, the relationship between participants' HL and the accuracy of BC risk self-assessment was investigated. At the baseline survey in the whole study population, most women (81.4 %) gave an accurate estimation of own lifetime absolute BC risk, which was an average BC risk. In the group who correctly estimated own lifetime absolute BC risk, most of them had excellent HL. Regarding the estimation of their 5-year absolute BC risk, there was no significant association with HL level. In the intervention group there was no significant association between HL level and accuracy of self-perceived BC risk neither at baseline, nor immediately or 1 week after the EI. In the intervention group, the relationship between 2 items of HLS-EU-Q47: *understanding of information* and *information assessment* and self-perceived BC risk was analysed and it showed no significant correlation with the accuracy of personal BC risk assessment. The same holds true for the control group. Overall, no significant association between HL and accuracy of BC risk perception was seen. Although a negative result, it contributes to existing literature about predictors of risk assessment. However, in the future it would be useful to examine does one's numeracy add up to accuracy of BC risk perception, since it has been established to be a contributing factor in understanding probability (92).

Due to the fact that health behaviour oftentimes changes when risk perception changes (93), factors that influence risk perception were explored.

Perception of own risk of developing certain serious and life-threatening disease, such is BC, certainly is not purely rational and aligned with the objective health risk, but is affected by psychological component also. In addition, lived experiences play a significant role in risk perception, too (88). Some research even suggests that emotions play a crucial role in risk assessment and statistical probabilities are in turn neglected (94), while other are more cautious and contradict it by saying that neither of elements are superior to each other but rather both contribute to the formation of risk perception (92). As per literature review by Ferrer R. and Klein W. M. there are three components of risk perception: deliberative, affective and experiential or intuitive (95). This is so called Tripartite Model of Risk Perception

(TRIRISK) (96). All three components play part in the formation of perceived risk, interactions between them are fairly complex and outcome of that interaction is hardly predictable, if even so. While deliberative risk perceptions are based on reason-derived judgements, affect associated with the risk plays significant role in risk-judgement and decision-making (95). Experiential risk perception is based on previous experiences and a 'gut'-feeling or intuition and belief about own vulnerability to certain disease (95). The later one is the main predictor of risk-related behaviour (95). Therefore, by the EI deliberative risk perception could have been influenced and possibly participants' affect, but certainly the participants' intuition could not have been affected. This is in line with previously reported results of a study on women who continue to underestimate own BC risk after attending genetic counselling clinic (97). Because people tend to estimate the risk not only on the basis of what they think about it, but maybe the crucial element is how they feel about it (88, 92, 98). Another phenomenon, known as 'unrealistic optimism' is a fairly common bias in general population (95) adds to explanation of risk underestimation in about 20% of the participants. It would be interesting to correlate the findings with participants' numeracy, since it has been found that in highly numerate individuals affect plays less significant role in overall risk perception (99).

In this study, worrisome findings are that women with positive family history in close relatives and women with personal history of AH significantly underestimated own BC risk. This finding points to the fact that those two RFs are not recognised enough and in turn women are not aware of own increased BC risk. This is supported by the finding that 85% of participants recognised BC in close relative as a BC RF in the survey questionnaire, which is in line with recently published similarly designed study (100). Meanwhile, 72% of surveyed women recognised AH as BC RF. The knowledge of both of them increased to some extent after the EI and was maintained one week later. The study by Morere J. F. et al. from 2018, which was designed in a way that participants were asked to name BC RFs, showed that most frequently recalled RF was positive family history, a little more than 50% of women reported it. On the other hand, mastopathy and benign breast conditions were not reported at all (101). In other studies, too, positive family history is most commonly known BC RF (91, 102, 103). The discrepancies in results regarding the prevalence of RF knowledge in comparison to the study are a consequence of differently designed study, meaning that in this study some participants may have guessed rather than actually be familiar with certain RFs, which is

known principle (104). In baseline survey, only 3 women had the history of AH, but all three perceived own BC risk to be average and therefore underestimated it. In the subgroup of women with positive family history in close relatives, one-third of them underestimated own risk. This is comparable to the research performed by Watson M. et al. (97), while Spector D. et al. found that 16% of women with BC in close relative considered themselves to be at low or AR although they recognised it to be a RF (105). Similarly, the study by Poehls et al reported that 75.1% of women with positive family history reported to have increased BC risk (91).

### 6.1.1 Breast cancer worry

No significant correlation between BC cancer worry and attitude towards chemoprevention drug usage was found, however this survey was placed in the context of a hypothetical situation and the results may have differed in a real life situation where chemoprevention drug would have been offered to a HR woman. Studies about chemoprevention uptake report distinct behavioural outcome measures, such as intention to seek more information about the drug, intention to take and actual drug uptake. The later one being always the least represented option among HR women (109).

The EI significantly increased BC worry of the intervention group as obvious from the survey immediately after the EI. But this effect faded with time and it did not persist by the measurement point at one week post EI. Comparing to results of the prospective study by Bish A. et al. on women who were attending family cancer clinic, these results are the opposite. However, in the mentioned study some of the women were given good news and they were worried about their risk being certainly high beforehand (107). Importantly, the intervention group was not stratified according to their objective BC risk, neither were they precisely informed about their calculated risk. Similarly, in the study by Xie Z. et al., who investigated the effect of personalized counselling on BC risk perception and level of distress, they found that after the counselling participants worry became more aligned with their objective BC risk (110). This finding points to the necessity of a personalized counselling and psychological support as a complementary measure to BC risk communication, thereby avoiding unnecessary distress in susceptible individuals and also in order to avoid their tendency to insist on needless screening tests in case they misjudged own risk of disease.

When the analysis of how cancer worry influenced own BC risk perception was performed, it was found that high level of BC worry showed both women who overestimated and underestimated own BC risk. While women who correctly perceived own susceptibility to BC expressed low level of worry. The finding of high level of worry in women who overestimated own BC risk is in accordance with the findings of Rondanina et al. in their study incorporated in a chemoprevention trial in Italy (108). But the relationship between cancer worry and cancer risk perception goes in both directions, so that higher level of psychological distress was found in women with known high BC risk due to positive family history (107). In psychology it is known that certain emotions are linked to the way person perceives the risk. Accordingly, the feeling of fear is associated with more pessimistic risk perception (95, 98, 111). The feelings of worry and fear are both caused by low certainty and low control over situation and as such associated with higher risk estimates. In addition, it is known that high level of distress can lead to excessive self examination (107) and insisting on unnecessary investigations (97). It seems counterintuitive for someone to be highly worried and at the same time grade own risk as being lower than it is, but perhaps it is a self defense mechanism of not wanting to accept what is actually known deep inside.

Literature data suggest that high cancer worry is associated with seemingly counterintuitive inverse correlation between risk perception and behaviour. So that people who are anxious about developing cancer, if they conclude that their concerns are reasonable, are less likely to seek medical advice in fear of their worry became true (108) and also to participate in cancer screening programs (112) or prevention trials (108). Another possibility for such behaviour is the belief that such health problem is beyond anyone's control and that fate cannot be influenced (106). In this study, there was a trend towards positive attitude towards chemoprevention in women with high BC worry and negative attitude in women with low BC worry, but it did not reach statistical significance. The major difference between the existing data on this topic and the ones presented here is in the studied population from which data were derived from. While for this study healthy women of diverse BC risk in a setting of their radiology department attendance for breast examination (screening or diagnostic) were recruited, other studies were performed on HR women who either attended HR breast clinic for consultation or were offered participation in a chemoprevention trial. Therefore, those women might have reflected on it in more depth, due to more personal approach and possibly

better awareness and knowledge about chemoprevention. Similar to this one, study by Bastian L. A. et al. was performed on women of different BC risk and were asked about their interest in taking tamoxifen in a hypothetical situation, the results showed that their interest positively correlated with BC worry, but not with their objective BC risk (113).

## 6.2. Chemoprevention attitude

Another study objective was to explore what was the attitude towards BC risk-reducing hormonal treatment in a population of healthy women in one health centre in Croatia. Breast cancer is the leading malignancy in women in developed world, including Croatia where every eleventh woman is at risk of developing the disease in her lifetime. Given its high prevalence and significant mortality as a consequence, it was interesting to find out whether the studied group had heard of the principle of chemoprevention and what did they think about such option. Based on so far published literature, the uptake has been extremely low in countries with developed web of breast clinics where counselling of HR women takes place (20, 28, 30, 114-116). ASCO has published guidelines in 2019 (26), but in addition reminds of a personalized approach. Decision to involve in this type of treatment is complex and influenced by many factors (63). It was the goal of this study to identify ones that would further contribute to current knowledge, with the hope that some of them are modifiable in a way to increase uptake in women who would benefit from it. For this purpose the relationship between demographical data, cancer worry, self-perceived BC risk, objective BC risk, HL, history of breast disease, beliefs about medicines and attitudes towards chemoprevention was explored. In the intervention group, the effect of EI on knowledge about and attitude towards chemoprevention was examined and compared to the control group. The worries associated with chemoprevention agents use were also explored. Given that the whole study was performed on healthy women of variable BC risk, all survey items about chemoprevention uptake refer to a hypothetical situation.

### 6.2.1 Demographic data

It was found that premenopausal women expressed negative opinion about chemoprevention, while women with existing comorbidities were dominantly of positive attitude. Also, women who expressed positive opinion were significantly older than the ones who had neutral opinion, with median age 58 and IQR being 51-62.5, which again confirmed that postmenopausal women were more open to this option. Given the known side effects of hormonal treatment like fertility impairment, it was unsurprising to learn that younger women would preferentially avoid it. This is consistent with so far published data (117, 118). The fact that women with poorer health had dominantly positive opinion about chemoprevention could be interpreted in a way that those women are more aware of own frailty. But this might also be a reflection of personal positive experience with health services and reliability on same.

Interestingly, previous breast biopsy and even history of AH did not show any significant correlation with certain attitude. This is in contrast to the earlier published data (119, 120). One might think that the anxiety related to undergoing biopsy might trigger the feeling of vulnerability in affected person which in return could encourage preventive behaviour. On the other hand, it seems that AH is not widely known RF (101) and this might have contributed to this result. However, we should keep in mind that even women treated with hormonal therapy for known BC showed not to always be compliant, even after being an actual victim of a disease (75, 121). This leads to the conclusion that even awareness of a certain risk does not always trigger preventive behaviour.

Objective BC risk did not significantly correlate with attitude towards chemoprevention. In the setting of this study, where the participants did not find out their objective risk, because there was no individualised approach in their education, this finding is not surprising. This is in line with findings of Bastian L. A. et al. (113) and Melnikow et al. (122). Although we know about the importance of a personalized approach in BC risk communication, studies have shown that risk perception oftentimes differs between the affected person and a health care provider which is discussed earlier. However, due to the fact that women who perceive own risk higher decide more often to start chemoprevention drug (119), we need to at least ensure proper risk communication.

There was no statistically significant association between self-perceived BC risk and chemoprevention attitude. This is in contrast to the published data about actual uptake (119, 120) and attitude towards chemoprevention expressed by healthy women of variable risk (103). But, in line with the findings of Heisey et al (123). The reason for such finding in this study could be the fact that nearly 90% of surveyed women were neutral or positive in their attitude towards chemoprevention and only a tiny proportion had negative attitude, therefore the sample with negative attitude was too small.

Participants were asked about possible concerns in relation to hormonal treatment. On a 5-point Likert scale they rated how much concern would a medicine cost, possibility of adverse events, effect on a child in case of unplanned pregnancy and daily medicine intake cause. It was discovered that the most worrisome was the possibility of drug's side effects, which is consistent with previous research (108, 109, 116). The same issue is linked to non-adherence to adjuvant endocrine therapy following BC diagnosis (124). In the group of women who formed a negative attitude towards chemoprevention they rated their worry about side effects to be significantly higher than ones with neutral or positive attitude. The question here is how accurate the perceptions about the risk of drugs' side effects are and if they aren't, how much we could modify them. It is reasonable to assume that same as the BC risk, the perception of risk of drugs' side effects is complex and highly influenced by previous life experiences, emotions and affect. Earlier research by Holmberg C. et al. embedded into STAR trial showed that women formed decision about participation in the chemoprevention trial based on their already subjectively established risk perception and probabilistic risk estimation they have received from trial investigators did not seem to influence their final decision, nor did the information about possible side effects (88). For example, if they have already perceived own risk to be high and then heard about the risk of endometrial cancer with tamoxifen treatment, they gave a rationale that they were almost certain that they would develop BC and they were willing to accept the possibility of adverse events of a drug. On the contrary, if they did not believe their BC risk to be high, they expressed high worry about serious drug side effects (88). In psychology, a phenomenon called the "affect heuristic" is the principle by which a person judges upon benefits and risks based on how he feels about a certain thing, rather than by a probabilistic approach. In addition, the risks and benefits are negatively correlated in person's mind (98). Applied on the example of BC chemoprevention,

it means that if a woman has negative opinion about chemoprevention drug because she perceives a significant threat of serious side effects, she will also attribute a low benefit to this medicine. Additionally, people tend to overweight small probabilities and underweight medium and high probabilities (92), and this mechanism might have impacted their worry about possible side effects, and contributed to overall stance.

### 6.2.2 Beliefs about medicines and chemoprevention attitude

There are numerous factors that intertwine and interact between each other before one makes decision whether to engage in chemoprevention measures for BC and also to adhere to them once she has commenced them. One of the significant factors are woman's beliefs about medicines in general and beliefs about such treatment's necessity and concerns (124-126). Given that the participants could not have been exposed to endocrine treatment for the purpose of a primary BC prevention, their general beliefs about medicines were examined to see if there was a significant correlation to their chemoprevention attitudes.

It was found that women who expressed positive attitude to chemoprevention had significantly lower median score on the scale of medicines *overuse* in comparison to ones with neutral attitude. The change in perception of why medicines are necessary may contribute to the overall more positive perception of hormonal treatment, too. One of the interventions to increase the adherence is motivational interviewing (127) and same can be applied for the initiation of the treatment. This accentuates the importance of a good relationship between patient and a doctor, because it is more likely that woman will adhere to hormonal treatment if she feels supported and safe (76, 121, 124), but also if she has better opinion about the drug in her particular case (124). Importantly, in the setting of endocrine treatment for BC risk reduction it is crucial to predict the obstacles in 5-year adherence to treatment and to establish a service that will support the woman throughout that journey.

As for the predictors of more positive beliefs about medicines, it was found that participants of higher HL were neutral in opinion that *people should take a break from medicines from time to time* in contrast to the group with lower level of HL who actually agreed with this statement. Significant differences in opinion that doctors rely too much on medicines

were also observed across different HL levels, with participants with higher HL less agreed to this. Overall, women with lower HL believed significantly more in both medicines overuse and harm as compared to women with better HL. This is consistent with findings that lower HL level is associated with poorer health outcomes due to weaker adherence to prescribed medicines, among other reasons (128). Lower HL is also known to predict beliefs about illness and medicines that are associated with poorer medicines adherence, such as belief that their chronic illness will not persist long term (128).

Educational level showed to be positively correlated with general beliefs about medicines, so that in the studied population women of higher educational grade, had lower median score in the subdomain of medicines *harm*, indicating their more positive beliefs. This result is also in line with previous research findings (73, 129). Women with lower level of education were also dominantly neutral in opinion about *medicines doing more harm than good* and that *all medicines are poisons*, while women with master's degree were disagreeable with such statement. Similar were results for the statement that *doctors rely too much on medicines*. This finding is hardly surprising and reflects another disadvantage of insufficient education. It has been established earlier that BMQ is a good predictor of medication adherence (71, 73) and this finding should warn us to carefully tailor our communication with patients, to increase their understanding of the medication necessity. In the context of chemoprevention drug use, again a tailored approach is crucial, thereby trying to fill the gaps of inadequate education and ensuring informed decision-making and obtaining appropriate health care.

Women without comorbidities believed significantly more that *doctors prescribe too many medicines* and that *medicines do more harm than good* and same believed women who take less prescription medicines or none, this is in comparison to women with no known illnesses or chronic therapy. The median overall scores in subdomains *harm* and *overuse* showed trend towards negative correlation with women's medicines use and existing comorbidities, but it did not reach statistical significance.

This result goes in favour of the findings that women with existing comorbidities and more prescription drugs have more positive beliefs about medicines. For example, in the study by Lash et al. about adherence to adjuvant tamoxifen, women who were already taking

prescription drugs showed to be more adherent (124). Furthermore, the research on general population showed that people with chronic illness and if already taking medicines have more positive general beliefs about medicines (73, 85, 129). People tend to become aware of medication benefit and necessity usually when they become ill and require them to feel better, which is the most likely explanation of this result.

### 6.2.3 Association between health-related quality of life and attitude towards chemoprevention

In the studies about adjuvant hormonal treatment use it was found that women with existing comorbidities had more positive beliefs about medicines, which was then associated with better adherence to the treatment. It was found that self-reported health was significantly associated with certain chemoprevention attitude.

As for the predictors of the health status, it was found that *overall physical health* aspect is inversely correlated with the number of prescription and OTC drugs used. Women with no comorbidities reported better *overall physical* and *mental health*, which was expected.

It was also observed that women of higher educational level reported significantly better *overall physical health*. This is consistent with previous research on European population by Sorensen K. (59). Given that better educational level is usually linked to better socio-economic status and better HL, this allows better access to health care and consequently better health status, therefore this finding is unsurprising. A study on general population in Sweden also found the positive correlation between socioeconomic position and self-reported health (130). Similar were the findings of Mujčić K. A. and Mujčić A. in their study (131).

With regards to relationship between HL and self-reported health, there was a trend towards positive correlation between the *overall mental health scale* and HL, but it did not reach statistical significance. However, subscales of g*eneral health perception* and *mental health* showed to be significantly positively correlated with HL. This finding is in line with previous research by Sorensen K. et al. (59) and Hersh L. et al. (62). It was already discussed how low HL is associated with poorer medical outcomes and that it has adverse influence on

the health due to lack of understanding of health-related messages, more difficult navigation through health system and inadequate health services use. Altogether, the findings from this study are expected and confirm this connection.

The *summary scale of physical health* showed trend towards negative correlation with chemoprevention attitude, similarly to *mental health summary scale*, but neither reached statistical significance. Two items from SF-36 questionnaire showed significant correlation with chemoprevention attitude: women with worse *general health perception* and stronger *role limitation due to emotional problems* had significantly more positive attitude towards chemoprevention. However, in their review, Lerner S. J. et al., interpret the existing evidence as not mature as yet to clarify the exact influence of emotion on decision-making (132).

In a study about predictors of participation in risk-based prostate cancer (PC) screening study, the decliners reported to feel less vulnerable to PC and also to be less worried, but also showed poor knowledge about PC (133). In contrast to this study results, the participants of PC screening study reported to have better general health as compared to decliners (133). Usually the worse health status is linked with greater medicines use. It was already discussed earlier that women with existing comorbidities have more positive beliefs about medicines, which is likely the explanation for this result.

### 6.2.4 Association between health literacy and attitude towards chemoprevention

HL is a prerequisite for understanding and critical analysis of received health-related information, enabling informed decision-making. Literature data suggest that limited HL is linked with unfavourable health outcomes (62, 66, 134, 135) and inappropriate use of health services (136). In the studied group, 64.8% of participants had limited HL, 23.9% had sufficient HL and only 11.3% had excellent HL. The European Health Literacy Survey (HLS-EU), conducted in eight European countries, showed significant disparities in HL among citizens of different countries. For example, the prevalence of limited HL was 28.7% in Netherlands, whereas it was more than 62% in Bulgaria (137). In the U.S., more than one-third of adults have limited HL (62). This studied population is not representative of our nation, but this finding gives us an insight into one of the studied population's characteristics. Due to the fact that HL is

modifiable (138), carefully tailored educational campaigns for the target groups should be one of the priorities of public health medicine. However, this would require better staffing and financial resources that are likely currently the major limiting factors in our country for such interventions.

A number of studies found the positive correlation between educational level and HL (62, 128, 139), however the study by Wilson and McLemore in 1997 on 26 patients who had hip- or knee-replacement surgery found that HL actually was inversely associated with highest grade of education completed (140). In the studied group, among participants with primary and high school diploma there was significantly more ones with limited HL, while among participants with higher level of education (i.e. Bachelor's or Master's degree and doctorate) dominated participants with excellent HL. Low social status has proved to be determinant of worse HL level, which is an additional factor contributing to vulnerability of this particular subpopulation (137). Although there was no direct investigation of the participants' socioeconomic status, the results show that unemployed and retired participants, who can reasonably be presumed to have lower socioeconomic status rather than higher, were significantly more often of limited HL. From the above mentioned results we can conclude that persons with low education and social status, which usually follow each other, belong to vulnerable subsets of population. Efforts from the government need to be made to improve the quality of education and to make it accessible and affordable to all citizens, which would make the basis for more successful health care provision, among other benefits.

One of the strong predictors of HL level is age (135, 137, 139, 141), namely geriatric population has been found to be highly vulnerable in that perspective. In this study, median participant's age was 57, with IQR range of 47 to 62. No correlation between lower HL and older age was found, which can be explained by the fact that vast majority of the participants did not belong to geriatric population, meaning they were aged below 65. Therefore, it was found that in population of middle-aged participants growing age was not the predictor of lower HL level.

Given that HL is thought to be an important factor in health-related decision-making, I explored if there was any significant association with the attitude towards chemoprevention drug use in a hypothetical situation. The analysis showed no significant correlation between

the two variables, neither at baseline or after the EI. To the best of my knowledge, there was no research done to date to assess the relationship between HL and attitude towards hormonal treatment for primary BC risk reduction. Also, very little research is done on the population of BC patients in relation to their HL, although it is thought that it might help to elucidate the reasons for non-adherence to chemotherapy and that personalized interventions in that field might help to improve it (142). However, multiple studies have been done across the world to investigate the relationship between HL and BC and other malignancy screening rates (143, 144). There have been mixed findings and some of them found a positive correlation between the HL level and BC and/or cervical cancer screening rates (60, 143, 145, 146). The study on nationally representative U.S. sample by Kim K. and Han H. R. found significant correlation between oral and listening literacies with BC screening rates, however, the overall HL had no significant impact on screening rates observed (147). A study in Japan also did not find significant correlation between HL and adherence to recommendations to undergo cancer screening, but rather that health care provider support positively influenced preventive behaviour (144). The differences in the observed data are likely a consequence of different HL assessment tools used, which was previously documented (55).

A project of the Cancer Research Network, called 'Health Literacy and cancer Prevention: Do people understand what they hear?' has three major objectives. Firstly, to create and validate an assessment tool for oral HL, secondly, to examine how oral HL relate to different types of preventive behaviour, including primary BC chemoprevention with tamoxifen and lastly, to develop and test the recommendation for improving oral communication between health care provider and a patient and consequently improve preventive behaviour. The project is still under way, but some of the research findings have been published. A nested study within this project was examining the relationship between oral HL and patient engagement in discussion about preventive behaviour with the doctor. The strength of engagement was measured by the number of questions asked by the participants. The analysis showed that there was no significant difference in number of question asked between the different oral HL levels. But, what they have found was that participants with lower oral HL were asking for the information that would apply directly to them, rather than generalised information about screening programmes. On the other hand,

participants with higher oral HL were more enquiring about the risks and benefits of the certain procedure or medicine (tamoxifen) (65). We are yet to see from this project how oral HL influenced the participation in tamoxifen uptake.

It can be concluded that HL literacy is not a key determinant for making decision about chemoprevention initiation, but it may contribute to informed decision-making. It would be also useful to assess cancer-specific HL and provide lay people with information about benefits and risks of this treatment in a way they can easily understand.

### 6.2.5 Effect of educational intervention on the chemoprevention attitude

In interaction with lay people it is important to adjust the way of conveying health-related information, so that all the individuals can appraise what they have heard or read (148, 149). EI in the shape of a lecture was conduced, performed by one individual, therefore avoiding the interindividual variability in lecture delivery. In addition, participants were given an information leaflet containing a brief summary of what they were presented at the lecture. Data analysis showed that this kind of EI offered a valuable material that women of different HL levels could have successfully absorbed and learnt about this topic.

EI not only increased knowledge of the principle of chemoprevention and knowledge about chemoprevention agents, but it also significantly increased the interest in taking chemoprevention drug in a hypothetical situation, even more so with time passed. This was observed in the intervention group. This is in contrast to the results of literature data to date, in other studies EI reduced the chemoprevention uptake (109, 150) or did not have any significant influence (151). When comparing the control group with postintervention data it transpired that there were significantly less participants with negative chemopevention attitude, especially one week after the EI (0%) in the intervention group. In both measurement points after the EI, there were significantly more participants with neutral attitude. Whereas there were more ones with positive attitude in the control group. Which overall means that the majority had neutral opinion after the EI, while the control group dominantly expressed positive opinion. Given that individuals with neutral opinion can ultimatively go either way, these results are difficult to compare to some of the previously published data mentioned

above. But it certainly leaves room for intervention which can improve chemoprevention uptake in women who would benefit from it.

With the EI, it was also aimed to increase the knowledge about this topic and drugs used in this indication rather than suggest its use. However, both was achieved - improvement in knowledge about chemoprevention, but also increased interest in using such agent. The most likely explanation for this is the difference in approach in estimation of women' stance about chemoprevention. In this study, women were asked if they would have taken such agent in case doctor advised them to, if doctor presented clear evidence about BC risk reduction, in case doctor estimated their BC risk being very high, if they would take it irrespective of possible side effects or if they would have never taken such drug. Meaning, three of the five questions would be the reflection of a joint decision between the doctor and the participant, meanwhile the later two would be purely woman's decision. In the study by Fagerlin A et al., they ascertained woman's willingness to take tamoxifen by directly asking how likely were they to take tamoxifen in the next year and followed up in three months to assess the actual uptake (109). The current study's contribution is this element of suggestion by the medical professional. This points to the fact that knowledgeable physician who can appropriately recommend chemoprevention drug with confidence is likely to convince woman to start it. In complex decision-making, many factors play role and sometimes other person's opinion is the key one to decide between the options (28, 63). Therefore, experienced and knowledgeable doctors who can counsel women about their personal BC risk and offer a personalized chemoprevention option may be the key to increase its uptake. The importance of a skilled professional is also confirmed in the study by Bober et al. (120). Knowing that physicians' barriers to chemoprevention prescribing are insufficient knowledge and side effects, whereas the strongest facilitators were clear guidelines, strong family history and better tools for patient selection (116) this gives us an opportunity to overcome these barriers by targeting them by appropriate measures. The study on beliefs about adjuvant hormonal treatment in BC survivors found that women who were more satisfied with their interaction with health care provider reported lower concerns and higher *necessity* beliefs in relation to tamoxifen (76). In addition, women who felt unsupported during the length of their adjuvant hormonal treatment for BC were more likely to disrupt their treatment (75), therefore it confirms the importance of personalised approach (109), together with continuity of care the patients

thrive for. Similarly, confidence in the physician was found to increase the adherence to prescribed antiretroviral medicines in AIDS patients, but this was also mediated by positive beliefs about these particular medication *necessity* (71).

The study by Fagerlin A. et al. showed that in real life situation, after having used personalized decision aid consisting of individual's BC risk report and information about benefits and risks of tamoxifen use, HR women engage in chemoprevention extremely rarely (less than 1% of 632 women) (109). In contrast to this study, where EI shifted the attitude about chemoprevention towards more positive in the intervention group and significantly reduced the number of participants with negative attitude in comparison to the control group. The reason for such difference can partly be explained by the fact that, again this was a hypothetical situation and usually less women actually engage in chemoprevention than they have expressed intention to (152). Overall, the EIs alone do not seem to increase chemoprevention uptake (153) and other factors need to be considered, as already discussed.

## 6.3. Chemoprevention and breast cancer risk factors knowledge

A lot of attention is given to informed decision-making in medicine. Lay people oftentimes have difficulty understanding health-related information. Before an important decision is made, it is crucial that the affected person is fully informed and able to comprehend information of interest. As already mentioned, primary BC chemoprevention is yet unavailable in Croatia, but the national screening programme for BC early detection exists for over a decade. The participant's knowledge about BC RFs and their familiarity with endocrine treatment for BC risk reduction was examined.

### 6.3.1 Knowledge of breast cancer risk factors

The participants were asked to mark if certain factors increase, decrease or have no effect on BC risk. Overall, 16 different items were proposed. All the correct answers were counted and analysed if there was any association between HL and their BC knowledge and the effect of the EI on BC RF knowledge was also analysed.

At the baseline survey, most commonly known RF was family history of BC in close relative, recognised by about 85% of participants in both the intervention and the control group. This was followed by *BRCA 1/2 gene* mutation, recognised by about 75 % and history of AH, recognised by about 70 % of participants in both groups. A study on German population of women found similar level of awareness of benign breast disease as a RF (91).

At the baseline survey, 43% and 53% of participants recognised the protective effect of prolonged breastfeeding on BC risk in control and intervention group, respectively and the effect of HRT on BC risk. This result is almost identical to results from the study by Poehls published in 2019 (102) and better than some of earlier published data (91).

Women in both groups were least familiar with factors like late menopause (17%) and early menarche (25%). This is in line with previous research (91, 102, 103).

The majority of factors were significantly more accurately recongised after the EI and maintained one week later. But not the knowledge of protective effect of the first chilbirth before the age of 30 or RFs such as AH or BD.

The study by Morere J. F. et al. was examining awarness of BC RFs in lay people and medical professionals. With regards to study population, it was extracted from the general population and the data were obtained by respondents' self-reporting. The results showed that postive family history was most commonly known RF, which is in line with results of this study (101). Interestingly, benign breast conditions were not reported at all, neither by lay people nor medical professionals (101). The study by Fasching P. A. et al. which measured the chemoprevention attitude of women with variable BC risk also showed that women were most commonly aware of a positive family history as a BC RF (103).

The analysis showed that the significant improvement in knowledge of BC RFs after the EI was achieved across all HL levels, indicating that the EI was successfully tailored to meet everyone's needs, irrespective of their HL. Interestingly, there was no significant difference in knowledge about BC RFs between the women of different HL levels in neither of measurements.

In the studies which aimed to improve BC knowledge and screening rates by different EI s this was successfully achieved (154, 155), indicating the importance and usefulness of

tailored education. In Croatia, the recall in national BC screening programme is about 60%. In order to increase the screening rates, public campaigns should be organised to increase awareness of BC, including the RFs, early BC symptoms and also to present the good results of early BC detection in the previous years withing the programme. Same holds for primary breast cancer chemoprevention, in order to contribute to informed decision-making.

Worrisome finding is the low prevalence of awareness of BD as a BC RF. This EI did not lead to significant improvement in that regard. In Croatia, health care workers are not legaly obliged to report the type of BD the woman has and more importantly the implications of high BD. The written report though contains the Breast Imaging Reporting and Data System (BI-RADS) score, but again with no detailed explanation. In the U.S., a national BD notification law was passed and adopted by 21 states, with Connecticut being the first one, in 2009 (156). In comparison to U.S. women, this studied population had lower BD knowledge (as in identifying it a BC RF). Interestingly, the study by Rhodes et al. found that less than three quarters of women who were aware of the term BD actually knew its implications (156). Moreover, it found that women from Connecticut were more than three times likely to know the masking effect of BD, but not that BD is a BC RF. This means that written mammography reports serve as good educational material for raising awareness, because information about masking effect is a part of the report, whereas BD implications on BC are not. Similar approach would be beneficial for raising BD awareness in our country, too.

### 6.3.2 Effect of health literacy and educational intervention on the knowledge about chemoprevention

The knowledge about chemoprevention was examined by asking the participants if they have ever heard of this principle of BC risk reduction and by asking them to mark how much do they know about tamoxifen, raloxifene, anastrazole and exemestane.

As expected, the overall chemoprevention knowledge at baseline survey in both groups was poor. With regards to chemoprevention drugs, median of answers across all the items, irrespective of participants' HL level was 1 – *I have never heard of the drug or 2 – I may have heard of the drug, but am not sure.* In comparison, a study on HR Australian women

found that about 50% of them were unaware of chemoprevention (116). The same study found that the main barriers among women are the fear of side effects and inadequate information (116), therefore targeted EIs such as this one may contribute to greater chemoprevention uptake.

Knowledge about chemoprevention and drugs significantly increased after the EI and was maintained one week later. In the group with excellent HL, in some of the items a positive trend was observed in knowledge improvement after the EI, but it did not reach statistical significance. However, it turned out that the whole intervention group in the end had very similar level of knowledge about chemoprevention, which was better than in the control group.

Based on the above findings, it can be concluded that EI of this type improved knowledge of BC RFs and chemoprevention knowledge and therefore contributed to the better informed decision-making, which was its purpose. Studies to date also managed to improve informed decision-making with interventions such as personalised decision aids (109, 157).

This study had several limitations. HL level was based on a self-report. There are established downsides of subjective HL assessment, not having the ground truth being the most important one (158). Therefore, I relied on respondents' honesty and accuracy of self-assessment. However, HLS-EU-Q47 was chosen because it was validated on a population of BC patients and is recommended to be used to assess HL, which is close to the topic investigated here (159). Some of the other objective HL assessment tools have shown not to have association with health-related decision-making in cancer patients (160). It would have been useful if participants' numeracy had also been assessed, because it might have had contributed to their accuracy of BC risk self-perception, especially after the EI. A third limitation was the context of a hypothetical situation, because the results from previous studies have shown that there was a difference between intention and actual behaviour, as already discussed before. However, due to the lack of primary BC chemoprevention opportunities in our country, this was the only feasible way of study design. And lastly, this EI was not tailored to each individual, but rather the given information were applicable to the general population of women. The reason behind this was to avoid anxiety in susceptible

women. Because it is beyond my control to enable a personalised preventive approach. For example, there are no designated breast clinics for HR women to where I may have referred the HR participants to, but it is up to every woman herself to privately undergo breast examinations at intervals as wished or as per advice of gynecologist or radiologist interpreting their breast exam.

# 7. CONCLUSIONS

Based on this study results, the following conclusions can be drawn:

- Nearly one-fifth of the participants underestimated own BC risk. In the subgroup of women with positive family history in close relatives, one-third of them underestimated own risk and so did all three participants with history of AH.
- There was no significant association between the accuracy of 5-year absolute BC risk self-assessment and participants' HL level, but women who correctly estimated own lifetime BC risk were dominantly of excellent HL.
- EI did not lead to any improvement in the accuracy of perception of own BC risk, irrespective of participant's HL level.
- EI significantly increased BC worry, but this effect faded with time.
- Previous breast biopsy or personal history of AH did not contribute to higher interest in taking chemoprevention drug.
- Women of higher age had more positive attitude towards chemoprevention.
- Women with worse *general health perception* and stronger *role limitation due to emotional problems* had significantly more positive attitude towards chemoprevention.
- Neither objective nor subjective BC risk significantly correlated with attitude towards chemoprevention.
- The most common concern in relation to chemoprevention drug was the fear of side effects and it mostly contributed to negative chemoprevention attitude
- It was found that women who expressed positive attitude to chemoprevention had significantly lower median score on the scale of medicines *overuse* in comparison to ones with neutral attitude, indicating their more positive beliefs about medicines
- Women with lower HL believed significantly more in both medicines *overuse* and *harm* as compared to women with better HL.
- Educational level showed to be positively correlated with general beliefs about medicines.

- Education was positively correlated with HL
- The analysis showed no significant correlation between HL level and chemoprevention attitude, neither at baseline nor after the EI.
- At the baseline survey, most commonly known BC RF was family history of BC in close relative, recognised by 85% of participants, followed by *BRCA 1/2 gene* mutation, recognised by 75% and history of AH, recognised by 72% of participants, while about 50% of participants recognised the protective effect of prolonged breastfeeding and the effect of HRT on BC risk.
- Women were least familiar with risk factors like late menopause and early menarche, recognised by 14%, 17% and 25%, respectively.
- EI significantly improved the knowledge of the majority of BC RFs, but not BD. This was achieved in all HL levels.
- The overall chemoprevention knowledge at baseline survey was poor. There were no significant disparities between the HL levels in neither of measurement points for the intervention group.
- Knowledge about chemoprevention and chemoprevention drugs significantly increased after the EI and was maintained one week later. The whole intervention group in the end had very similar level of knowledge about chemoprevention.
- Based on the above findings, it can be concluded that EI of this type improved knowledge of BC RFs and chemoprevention knowledge and therefore contributed to the better informed decision-making, which was its purpose.
- EI also significantly increased the interest in taking chemoprevention drug of the intervention group in a hypothetical situation, even more so with time passed. As compared to the control group, there were less individuals with negative and positive attitudes and more ones with neutral

# 8. SUMMARY

**Objectives:** The effect of educational intervention (EI) on the accuracy of breast cancer (BC) risk self-assessment and knowledge about chemoprevention was investigated. In addition, it was investigated how different participants' characteristics like HL, general beliefs about medicines and self-reported health status influenced BC risk perception and BC chemoprevention knowledge and attitudes. Chemoprevention attitude was examined in a hypothetical situation.

**Study design:** This was non-randomised controlled trial conducted in a single health centre in Croatia.

**Participants and Methods**: 249 healthy women who attended Health Centre Osijek's Department for Breast Diagnostics for screening mammography or diagnostic either mammography or breast ultrasound were recruited. Standardised questionnaires Health Literacy European Questionnaire 47, Beliefs about Medicines Questionnaire General, Short Form-36 were used. With questionnaire created for the purpose of this study (and validated) BC risk perception, knowledge about BC and chemoprevention and chemoprevention attitudes were examined at the recruitment point, immediately after the EI and one week after the EI. Educational interventervention in a form of a lecture was conducted and information leaflet was given to the participants.

**Results:** Nearly 20% of participants underestimated own BC risk, including one-third of women with positive family history of BC in the close relative. Women who correctly estimated own lifetime BC risk were dominantly of excellent HL. Women with positive chemoprevention attitude had significantly more positive beliefs about medicines in the subdomain *medicines overuse*, worse *general health perception* and stronger *role limitation due to emotional problems*. Previous breast biopsy or personal history of AH did not contribute to higher interest in taking chemoprevention drug. No significant correlation between HL level and chemoprevention attitude was noted. Knowledge about chemoprevention and chemoprevention drugs significantly increased after the EI and was maintained one week later. In comparison to the control group, after the EI there was significantly more participants with neutral chemoprevention attitude: 40.2% vs 85% ($\chi^2$test, P<0.001). Also, significantly less participants had positive attitude immediately after the EI, in comparison to the control group:

12% vs 50% ($\chi^2$test, P=0.010, P<0.001). Interestingly, in the control group there were 12% of women with negative attitude, but 0% one week after the EI.

**Conclusion:** The EI significantly increased knowledge about BC and chemoprevention. And it shifted the chemoprevention attitude towards more neutral. The EI did not have an impact on the accuracy of BC risk self-assessment.

**Key words:** breast cancer risk; beliefs about medicines; chemoprevention; educational intervention; health literacy

# 9. SAŽETAK

**Učinak edukacijske intervencije na točnost samoprocjene rizika obolijevanja od karcinoma dojke i na znanje o kemoprevenciji**

**Cilj istraživanja**: Ispitan je učinak edukacijske intervencije na točnost samoprocjene rizika obolijevanja od raka dojke, te na znanje i stav o kemoprevenciji raka dojke. Uz to, ispitan je utjecaj zdravstvene pismenosti, općenitog vjerovanja o lijekovima i kvalitete zdravlja na viđenje vlastitog rizika obolijevanja, te na znanje i stav prema kemoprevenciji. Stav o kemoprevenciji je ispitivan u hipotetskoj situaciji.

**Nacrt studije**: Nerandomizirana klinička studija.

**Ispitanici i metode:** Uključeno je 249 zdravih žena koje su posjetile Zavod za dijagnostiku dojke Doma zdravlja Osijek radi probirne (eng. *screening*) mamografije ili dijagnostičke mamografije ili ultrazvuka dojke. U istraživanju su korišteni standardizirani upitnici: *Europski upitnik o zdravstvenoj pismenosti* s 47 pitanja, *Vjerovanja o lijekovima – Općenito* i *Zdravstveni upitnik*. Za potrebe istraživanja napisan je i validiran upitnik kojim smo ispitali samoprocjenu rizika obolijevanja od raka dojke, znanje o raku dojke i kemoprevenciji te stav o kemoprevenciji, i to tijekom uključivanja u studiju, odmah nakon edukacijske intervencije, te tjedan dana nakon edukacijske intervencije.

**Rezultati:** Gotovo 20 % ispitanica je podcijenilo vlastiti rizik, uključujući i trećinu žena s pozitivnom obiteljskom anamnezom raka dojke kod bliskih srodnika. Žene odlične zdravstvene pismenosti značajno su točnije procijenile svoj cijeloživotni rizik od obolijevanja. Žene pozitivnog stava prema kemoprevenciji manje su vjerovale u *pretjeranu upotrebu lijekova*, te su vlastito *opće zdravlje* vidjele lošijim i imale snažnija *ograničenja radi emocionalnih problema*. Prijašnja biopsija dojke i dijagnoza stanične atipije nisu pridonijele pozitivnijem stavu prema kemoprevenciji. Nije bilo značajne povezanosti zdravstvene pismenosti i stava prema kemoprevenciji. Znanje o kemoprevenciji značajno se poboljšalo nakon edukcijske intervencije. U odnosu na kontrolnu skupinu, tjedan dana nakon edukacijske intervencije značajno više sudionica imalo je neutralan stav prema kemoprevenciji: 40.2 % prema 85 % ($\chi^2$test, $P < 0{,}001$). Također, značajno je manje bilo sudionica pozitivnoga odmah nakon

edukacije u odnosu na kontrolnu grupu. Zanimljivo je i da je u početnom ispitivanju bilo 12 % sudionica s negativnim stavom, dok tjedan dana nakon edukacije nije bilo niti jedne.

**Zaključak**: Edukacijska intervencija značajno je poboljšala znanje o raku dojke i o kemoprevenciji. Također je stav prema kemoprevenciji pomaknula prema prevladavajuće neutralnom. Istovremeno, nije imala utjecaj na točnost samoprocjene vlastitog rizika oboljenja od raka dojke.

**Ključne riječi:** edukcijska intervencija; karcinom dojke; kemoprevencija; vjerovanja o lijekovima; zdravstvena pismenost

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# 11. CURRICULUM VITAE

**Name and surname:** **Sonja Vukadin (born Šarčević)**

**Date and place of birth:** September 19th 1986., Osijek, Croatia

**Nationality:** Croatian

**Home address:** 15, The Radic Brothers' Street 15, Bizovac

**E-mail:** sonya.sarcevic@gmail.com, sonja.vukadin@fdmz.hr

**Education:**

| | |
|---|---|
| 2017 - 2019 | Basic specialist training in General internal medicine, Royal College of Physicians of Ireland |
| 2012 – 2013 | Postgraduate doctoral study of Biomedicine and health |
| 2005 – 2011 | Medical doctor, Faculty of Medicine Osijek, University of J.J. Strossmayer in Osijek |

**Work experience:**

| | |
|---|---|
| June 2020 - now | Teaching assistant at the Department of Pharmacology and biochemistry, Faculty of Dental Medicine and Health, Osijek |
| July 2017 - July 2019 | SHO in Basic Specialist Training in General Internal Medicine, Mater Misericodiae University Hospital, Dublin, Republic of Ireland |
| January 2017 – July 2017 | SHO in Medical Oncology, Beaumont Hospital, Dublin, Republic of Ireland |
| July 2016 – January 2017 | SHO in General Internal Medicine, St. Columcille's Hospital, Loughlinstown, Dublin, Republic of Ireland |

| | |
|---|---|
| September 2015 – July 2016 | Registrar in Palliative Care, Our Lady of Lourdes Hospital, Drogheda, Republic of Ireland |
| September 2012 – July 2015 | Teaching assistant at the Department of Pharmacology, Faculty of Medicine Osijek,University of J. J. Strossmayer in Osijek |
| March 2014 – July 2015 | Resident of Clinical pharmacology and toxicology at the Department of Pharmacology, Faculty of Medicine Osijek,University of J. J. Strossmayer in Osijek |
| November 2011 – October 2012 | Intern, University Hospital Osijek |

**Book chapters:**

- Banić, Erceg et al. Drug Interactions in Gastroenterology, Springer, 2020.; poglavlje Antisecretory drugs – in press
- Roguljic, Hrvoje; **Sarcevic, Sonja**; Smolic, Robert; Lucic Raguz, Nikola; Vcev, Aleksandar; Smolic, Martina. Current Management and Novel Therapeutic Strategies to Combat Chronic Delta Hepatitis // Drug Discovery and Development - From Molecules to Medicine / Valisuta, O ; Olimat, S (ur.). Rijeka : INTECH EUROPE, 2015. Str. 183-200.

**Scientific articles:**

- Bojanic K[§], **Vukadin S**[§], Grgic K, Malenica L, Sarcevic F, Smolic R, Kralik K, Včev A, Wu GY, Smolic M. The accuracy of breast cancer risk self-assessment does not correlate with knowledge about breast cancer and knowledge and attitudes towards primary chemoprevention. Prev Med Rep. 2020 Oct 20;20:101229. doi: 10.1016/j.pmedr.2020.101229. PMID: 33145151; PMCID:PMC7593623 (IF=2.40, Q1).
  **§ Both authors contributed equally to this work**
- Bojanic K, **Vukadin S**, Sarcevic F, Malenica L, Grgic K, Smolic R, Kralik K, Bilic Curcic I, Ivanac G, Wu GY, Smolic M. Impact of Breast Density Awareness on Knowledge about Breast Cancer Risk Factors and the Self-Perceived Risk of Breast Cancer. Diagnostics (Basel). 2020

Jul 20;10(7):496. doi: 10.3390/diagnostics10070496. PMID: 32698375; PMCID: PMC7399945. (IF 4.717, Q1)

**Congressional abstracts:**

- Debeljak Ž, **Šarčević S**, Raguž-Lučić N, Ismailovski L, Šahinović I, Samardžija G, Zibar L: Therapeutic Monitoring of Mycophenolate Mofetil – A Case Report. Ninth ISABS Conference on Forensic and Anthropologic Genetics and Mayo Clinic Lectures in Individualized Medicine, Bol, Croatia, June 2015.
- **Šarčević S**, Debeljak Ž, Čulig J: Association Between Cyclosporine Concentration in Blood and Side Effects in Renal Transplant Patients. Eight ISABS Conference on Forensic and Antropologic Genetics and Mayo Clinic Lectures in Individualized Medicine, ,Croatia, June 2013.

**Scientific projects:**

- 2020. – now: *Razvoj i procjena učinka edukacijske intervencije na stavove o kemoprevenciji raka dojke*. IP project of the Faculty of Medicine, University J. J. Strossmayer in Osijek. - Project member. Project manager: assoc.prof.dr.sc. Martina Smolić.

**Membership in scientific and professional societies:**

- Croatian Medical Chamber; 2013.-now, member
- Irish Medical Council; 2015.-now, member
- Royal College of Physicians of Ireland; 2018.-now, member
- American Society of Clinical Oncology (ASCO); 2017.-now, member

**Certified laboratory skills:**

- Laboratory Animal Science Course, FELASA cat C equivalent, Zagreb, Croatia, March 2013.

**Participation in exchange programmes as a guest scientist or student**

- Erasmus study exchange, University of Pecs, September 2013 – January 2014

**Foreign languages:**

- English - IELTS speech 7.0, writing 7.0. listening 7.0, reading 7.5.
  CEFR level C1
- German – B1 level

# 12. SUPPLEMENTARY MATERIAL

1. Informed consent
2. Health Literacy Survey European Questionnaire 47 (HLS-EU-Q47)
3. Short form – 36 (SF-36)
4. Questionnaire ‘Opinions, knowledge and attitudes towards self-perceived breast cancer risk and chemoprevention’
5. Information leaflet

**1. Informed consent**

Naslov (naziv) istraživanja:

**Stavovi žena o vlastitom riziku oboljevanja od karcinoma dojke i prevenciji karcinoma dojke lijekovima**

Mjesto istraživanja:

Osijek

Ime i prezime voditelja istraživanja (ispitivača)

Kristina Bojanić, dr. med., spec. radiologije

Poštovana,

Pozivamo Vas da u svojstvu ispitanika sudjelujete u znanstvenom istraživanju u kojem se ispituju stavovi žena o njihovom riziku oboljevanja od karcinoma dojke i preventivnim lijekovima koji se koriste u svrhu sprječavanja pojave karcinoma dojke kod žena s visokim rizikom oboljevanja od karcinoma dojke.

Voditelj istraživanja je Kristina Bojanić, dr. med. Istraživanje će se provesti u Osijeku. Istraživanje se provodi u svrhu izrade doktorskog rada. Molimo Vas pažljivo pročitajte ovaj Informirani pristanak za sudjelovanje u istraživanju u kojem se objašnjava zašto se ispitivanje provodi.

U slučaju da ne razumijete bilo koji dio Informiranog pristanka molimo Vas da se za objašenjenje obratite ispitivaču u istraživanju. Vaše sudjelovanje u ovom ispitivanju je

dobrovoljno i možete se u bilo kojem trenutku odustati od istraživanja. Ukoliko odlučite sudjelovati u ovom istraživanju od Vas će se tražiti da potpišete Informirani pristanak uz naznaku datuma. Informirani pristanak potpisuje i istraživač, a potpisan preslik Informiranog pristanka dobit ćete osobno prije početka navedenog istraživanja. Original Informiranog pristanka nalazi se kod voditelja ovog ispitivanja.

Liječnik - istraživač koji provodi ovo istraživanje neće primiti nikakvu financijsku naknadu za ovo istraživanje.

Svrha istraživanja je istražiti svijesnost žena o njihovom riziku oboljevanja od karcinoma dojke, usporediti njihov stav o riziku oboljevanja s njihovom medicinskom dokumentacijom i na temelju medicinske dokumentacije pomoću modela za procjenu rizika oboljevanja od karcinoma dojke procjeniti njihov stvaran rizik oboljevanja.

Kao ispitanica ćete kroz upitnik u pisanoj formi biti upitana o tome što smatrate koliko je velik vaš rizik oboljevanja od karcinoma dojke i zašto smatrate da je vaš rizik manji ili veći nego u ostalih žena. Drugi dio upitnika odnosi se na pitanja o preventivnom uzimanju lijekova koji smanjuju mogućnost pojave karcinoma dojke. Pitanja u drugom dijelu upitnika su o tome jeste li ikada čuli za neki od lijekova koji se mogu primjenjivati u svrhu prevencije karcinoma dojke, biste li uzimali takav lijek, iako može imati vrlo izražene neželjene učinke. Osim upitnika o znanju i stavovima vezanim uz kemoprevenciju, molimo Vas da ispunite i upitnike: Upitnik o vjerovanjima o lijekovima (BMQ), Upitnik o zdravstvenoj pismenosti (HLS-EU-Q47) i Zdravstveni upitnik (SF-36).

Od Vas, kao ispitanice očekuje se popunjavanje pisanig upitnika uz prisustvo suradnika na istraživanju koji će Vam detaljno objasniti i pomoći Vam u odgovoru na sva pitanja, s detaljnim pojašnjenjem pitanja vezanih uz prevenciju karcinoma dojke pomoću lijekova.

Dobiveni podaci bit će korišteni isključivo u ovom istraživanju i za ranije navedenu svrhu.

Vaše sudjelovanje u ovome istraživanju je u potpunosti dobrovoljno. Vaša odluka o tome da li želite ili ne želite sudjelovati u ovom istraživanju ni na koji način neće utjecati na način, postupke i tijek Vašeg liječenja. Ukoliko se odlučite sudjelovati u istraživanju, možete u bilo kojem trenutku prekinuti svoje sudjelovanje u njemu. Vaša odluka o prekidanju sudjelovanja u istraživanju ni na koji način neće utjecati na način, postupke i tijek Vašeg liječenja. Za dodatna pitanja o samom istraživanju možete se obratiti Kristini Bojanić, dr.med., spec. radiologije na mail kristina.bojanic@dzo.hr

Svojim potpisom potvrđujem da sam informiran/a o ciljevima, prednostima i rizicima ovog istraživanja i pristajem u njemu sudjelovati.

U Osijeku,_____.

_____

Potpis sudionice

Ja, liječnik istraživač potvrđujem da sam usmeno pružio/pružila potrebne informacije o ovom ispitivanju i dao/dala preslik Informiranog pristanka potpisanog od strane ispitanika i istraživača.

_____

Potpis voditelja istraživanja
Kristina Bojanić, dr.med., spec. radiologije

## 2. Health literacy Survey European Questionnaire 47 (HLS-EU-Q47©)

| Broj čestice | | *Na ljestvici od vrlo jednostavno do vrlo teško, koliko jednostavno Vam je:* | 1 Vrlo teško | 2 Teško | 3 Jednostavno | 4 Vrlo jednostavno | 5 Ne znam (koristi samo ispitivač) |
|---|---|---|---|---|---|---|---|
| 1 | Zdravstvo / Pristup informacijama | pronaći informacije o simptomima bolesti koja vas zanima? | | | | | |
| 2 | Zdravstvo / Pristup informacijama | pronaći informacije o liječenju bolesti koja vas zanima? | | | | | |
| 3 | Zdravstvo / Pristup informacijama | pronaći što učiniti u slučaju hitnog medicinskog slučaja? | | | | | |
| 4 | Zdravstvo / Pristup informacijama | pronaći gdje možete dobiti stručnu pomoć kada ste bolesni? | | | | | |
| 5 | Zdravstvo/ Razumijevanje | razumjeti što Vam liječnik govori? | | | | | |
| 6 | Zdravstvo/ Razumijevanje | razumjeti letak uputa o lijeku koje dobijete uz Vaš lijek? | | | | | |
| 7 | Zdravstvo/ Razumijevanje | razumjeti što učiniti u slučaju hitnog medicinskog slučaja? | | | | | |
| 8 | Zdravstvo/ Razumijevanje | razumjeti upute liječnika ili ljekarnika kako uzimati lijek koji Vam je prepisan? | | | | | |
| 9 | Zdravstvo/ Procjena informacija | procijeniti kako su informacije liječnika primjenjive na Vaš slučaj? | | | | | |
| 10 | Zdravstvo/ Procjena informacija | procijeniti prednosti i nedostatke različitih mogućnosti liječenja? | | | | | |
| 11 | Zdravstvo/ Procjena informacija | procijeniti kada trebate tražiti drugo mišljenje od drugog liječnika? | | | | | |
| 12 | Zdravstvo/ Procjena informacija | procijeniti jesu li informacije o bolestima iz medija pouzdane? | | | | | |
| 13 | Zdravstvo/ Primjena informacija | koristiti informacije koje dobijete od liječnika da biste napravili odluke o svojoj bolesti? | | | | | |
| 14 | Zdravstvo/ Primjena informacija | slijediti upute o lijeku? | | | | | |
| 15 | Zdravstvo/ Primjena informacija | nazvati Hitnu pomoć kod hitnog medicinskog slučaja? | | | | | |
| 16 | Zdravstvo/ Primjena informacija | slijediti upute liječnika ili ljekarnika? | | | | | |
| 17 | Prevencija bolesti / Pristup informacijama | pronaći informacije o tome kako mijenjati nezdravo ponašanje kao što je pušenje, premalo fizičke aktivnosti i pretjerano pijenje alkohola? | | | | | |
| 18 | Prevencija bolesti / Pristup informacijama | pronaći informacije o tome kako utjecati na zdravstvene probleme kao što su stres i depresija? | | | | | |
| 19 | Prevencija bolesti / Pristup informacijama | pronaći informacije o cijepljenju i preventivnim pregledima na koje biste trebali ići? | | | | | |
| 20 | Prevencija bolesti / Pristup informacijama | pronaći informacije o tome kako spriječiti ili kontrolirati pretjeranu tjelesna težina, visok krvni tlak ili visoki | | | | | |
| 21 | Prevencija bolesti / Razumijevanje informacija | razumjeti zdravstvena upozorenja o ponašanju kao što je pušenje, premalo fizičke aktivnosti i pretjerano pijenje alkohola? | | | | | |
| 22 | Prevencija bolesti / Razumijevanje | razumjeti zašto Vam je potrebno cijepljenje? | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 23 | Prevencija bolesti / Razumijevanje informacija | razumjeti zašto je potrebno obavljati preventivne preglede? | | | | | |
| 24 | Prevencija bolesti / Procjena informacija | procijeniti koliko su pouzdana zdravstvena upozorenja o pušenju, premalo fizičke aktivnosti i pretjeranom pijenju | | | | | |
| 25 | Prevencija bolesti / Procjena informacija | procijeniti kada trebate otići liječniku na kontrolni pregled? | | | | | |

| Broj čestice | | *Na ljestvici od vrlo lagano do vrlo teško, koliko jednostavno Vam je:* | 1 Vrlo teško | 2 Teško | 3 Jednostavno | 4 Vrlo Jednostavno | 5 Ne znam (koristi samo ispitivač) |
|---|---|---|---|---|---|---|---|
| 26 | Prevencija bolesti / Procjena informacija | procijeniti koje cijepljenje Vam je potrebno? | | | | | |
| 27 | Prevencija bolesti / Procjena informacija | procijeniti koji preventivni pregled Vam je potreban? | | | | | |
| 28 | Prevencija bolesti / Procjena informacija | procijeniti je li informacija o zdravstvenom riziku u medijima pouzdana? | | | | | |
| 29 | Prevencija bolesti / Primjena informacija | odlučiti je li Vam potrebno cijepljenje protiv gripe? | | | | | |
| 30 | Prevencija bolesti / Primjena informacija | donijeti odluku kako se možete zaštiti od bolesti na temelju savjeta prijatelja i obitelji? | | | | | |
| 31 | Prevencija bolesti / Primjena informacija | donijeti odluku kako se možete zaštiti od bolesti na temelju informacija iz medija? | | | | | |
| 32 | Promocija zdravlja/ Pristup informacijama | pronaći informacije o zdravim aktivnostima kao što je vježbanje i zdrava prehrana? | | | | | |
| 33 | Promocija zdravlja/ Pristup informacijama | informirati se o aktivnostima koja su dobre za Vaše mentalno zdravlje? | | | | | |
| 34 | Promocija zdravlja/ Pristup informacijama | informirati se kako Vaše susjedstvo može pozitivno utjecati na zdravlje? | | | | | |
| 35 | Promocija zdravlja/ Pristup informacijama | Informirati se o političkim promjenama koje mogu utjecati na zdravlje? | | | | | |
| 36 | Promocija zdravlja/ Pristup informacijama | informirati se o mjerama za poboljšanje vašeg zdravlja na radnom mjestu? | | | | | |
| 37 | Promocija zdravlja/ Razumijevanje informacija | razumjeti savjete o zdravlju od članova obitelji ili prijatelja? | | | | | |
| 38 | Promocija zdravlja/ Razumijevanje informacija | razumjeti informacije na pakiranjima hrane? | | | | | |
| 39 | Promocija zdravlja/ Razumijevanje informacija | razumjeti informacije u medijima o tome kako postati zdraviji? | | | | | |
| 40 | Promocija zdravlja/ Razumijevanje informacija | razumjeti informacije o tome kako očuvati psihičko zdravlje? | | | | | |
| 41 | Promocija zdravlja/ Procjena informacija | prosuđivati o tome kako Vaš način života utječe na zdravlje i blagostanje? | | | | | |
| 42 | Promocija zdravlja/ Procjena informacija | prosuđivati koji uvjeti stanovanja pomažu da biste ostali zdravi? | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 43 | Promocija zdravlja/ Procjena informacija | procijeniti koja svakodnevna ponašanja su u vezi s vašim zdravljem? | | | | | |
| 44 | Promocija zdravlja/ Primjena informacija | donijeti odluke kako bi poboljšali zdravlje? | | | | | |
| 45 | Promocija zdravlja/ Primjena informacija | priključiti se sportskom klubu ili grupi za vježbanje ako to želite? | | | | | |
| 46 | Promocija zdravlja/ Primjena informacija | utjecati na uvjete u kojima živite, a koji utječu na vaše zdravlje i blagostanje? | | | | | |
| 47 | Promocija zdravlja/ Primjena informacija | sudjelovati u aktivnostima u Vašoj zajednici koje poboljšavaju zdravlje? | | | | | |

**3. Short form (SF-36)**

Ovom se anketom ispituje Vaše *mišljenje o vlastitom zdravlju*. Ti će podaci pokazati kako se osjećate i koliko ste u stanju obavljati svoje uobičajene aktivnosti. Odgovorite na svako pitanje tako da označite odgovor onako kako je navedeno. Ako niste sigurni kako odgovoriti na neko pitanje, molimo Vas da odgovorite najbolje što možete.

| | |
|---|---|
| SF_01 | Općenito, da li biste rekli da je Vaše zdravlje: (zaokružite jedan odgovor) |
| | 1 – odlično |
| | 2 - vrlo dobro |
| | 3 – dobro |
| | 4 – zadovoljavajuće |
| | 5 – loše |
| SF_02 | U usporedbi s prošlom godinom, kako biste sada ocijenili svoje zdravlje? (zaokružite jedan odgovor) |
| | 1 - puno bolje nego prije godinu dana |
| | 2 - malo bolje nego prije godinu dana |
| | 3 - otprilike isto kao i prije godinu dana |
| | 4 - malo lošije nego prije godinu dana |
| | 5 - puno lošije nego prije godinu dana |

Sljedeća pitanja se odnose na aktivnosti kojima se možda bavite tijekom jednog tipičnog dana.
Da li Vas trenutačno Vaše zdravlje ograničava u obavljanju tih aktivnosti? Ako da, u kojoj mjeri? (zaokružite jedan broj u svakom redu)

| AKTIVNOST | | DA Puno | DA Malo | NE Nimalo |
|---|---|---|---|---|
| SF_03a | fizički naporne aktivnosti, kao što su trčanje, podizanje teških predmeta, sudjelovanje u napornim portovima | 1 | 2 | 3 |
| SF_03b | pomicanje stola, vožnja biciklom, boćanje i sl. | 1 | 2 | 3 |
| SF_03c | podizanje ili nošenje torbe s namirnicama | 1 | 2 | 3 |
| SF_03d | uspinjanje uz stepenice (nekoliko katova) | 1 | 2 | 3 |
| SF_03e | uspinjanje uz stepenice (jedan kat) | 1 | 2 | 3 |

| | | | | |
|---|---|---|---|---|
| SF_03f | saginjanje, klečanje ili pregibanje | 1 | 2 | 3 |
| SF_03g | hodanje više od 1 kilometra | 1 | 2 | 3 |
| SF_03h | hodanje oko pola kilometra | 1 | 2 | 3 |
| SF_03i | hodanje 100 metara | 1 | 2 | 3 |
| SF_03j | kupanje ili oblačenje | 1 | 2 | 3 |

Jeste li u protekla 4 tjedna u svom radu ili drugim redovitim dnevnim aktivnostima imali neki od sljedećih problema zbog svog fizičkog zdravlja? (zaokružite jedan broj u svakom redu)

| | AKTIVNOST | DA | NE |
|---|---|---|---|
| SF_04a | Skratili ste vrijeme provedeno u radu ili drugim aktivnostima | 1 | 2 |
| SF_04b | Obavili ste manje nego što ste željeli | 1 | 2 |
| SF_04c | Niste mogli obavljati neke poslove ili druge aktivnosti | 1 | 2 |
| SF_04d | Imali ste poteškoća pri obavljanju posla ili nekih drugih aktivnosti (npr. morali ste uložiti dodatni trud) | 1 | 2 |

Jeste li u protekla 4 tjedna imali neke od dolje navedenih problema na poslu ili pri obavljanju nekih drugih svakodnevnih aktivnosti zbog bilo kakvih emocionalnih problema (npr. osjećaj depresije ili tjeskobe)? (zaokružite jedan broj u svakom redu)

| | AKTIVNOST | DA | NE |
|---|---|---|---|
| SF_05a | Skratili ste vrijeme provedeno u radu ili drugim aktivnostima | 1 | 2 |
| SF_05b | Obavili ste manje nego što ste željeli | 1 | 2 |
| SF_05c | Niste obavili posao ili neke druge aktivnosti onako pažljivo kao obično | 1 | 2 |

| | |
|---|---|
| SF_06 | U kojoj su mjeri u protekla 4 tjedna Vaše fizičko zdravlje ili Vaši emocionalni problemi utjecali na Vaše uobičajene društvene aktivnosti u obitelji, s prijateljima, susjedima ili drugim ljudima?<br>(zaokružite jedan odgovor) |
| | 1 - uopće ne |
| | 2 - u manjoj mjeri |
| | 3 – umjereno |
| | 4 – prilično |
| | 5 – izrazito |
| SF_07 | Kakve ste tjelesne bolove imali u protekla 4 tjedna?<br>(zaokružite jedan odgovor) |
| | 1 – nikakve |
| | 2 - vrlo blage |
| | 3 – blage |
| | 4 – umjerene |
| | 5 – teške |
| | 6 - vrlo teške |
| SF_08 | U kojoj su Vas mjeri ti bolovi u protekla 4 tjedna ometali u Vašem uobičajenom radu (uključujući rad izvan kuće i kućne poslove)? (zaokružite jedan odgovor) |
| | 1 - uopće ne |
| | 2 – malo |
| | 3 – umjereno |
| | 4 – prilično |
| | 5 – izrazito |

Sljedeća pitanje govore o tome kako se osjećate i kako ste se osjećali u protekla 4 tjedna. Molim Vas da za svako pitanje odaberete po jedan odgovor koji će najbliže odrediti kako ste se osjećali.

| Koliko ste (se) vremena u protekla 4 tjedna: (zaokružite jedan odgovor u svakom redu). | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | stalno | skoro uvijek | dobar dio vremena | povre-meno | rijetko | nikada |
| SF_09a | osjećali puni života? | 1 | 2 | 3 | 4 | 5 | 6 |
| SF_09b | bili vrlo nervozni? | 1 | 2 | 3 | 4 | 5 | 6 |
| SF_09c | osjećali tako potištenim da Vas ništa nije moglo razvedriti? | 1 | 2 | 3 | 4 | 5 | 6 |
| SF_09d | osjećali spokojnim i mirnim? | 1 | 2 | 3 | 4 | 5 | 6 |
| SF_09e | bili puni energije? | 1 | 2 | 3 | 4 | 5 | 6 |
| SF_09f | osjećali malodušnim i tužnim? | 1 | 2 | 3 | 4 | 5 | 6 |
| SF_09g | osjećali iscrpljenim? | 1 | 2 | 3 | 4 | 5 | 6 |
| SF_09h | bili sretni? | 1 | 2 | 3 | 4 | 5 | 6 |
| SF_09i | osjećali umornim? | 1 | 2 | 3 | 4 | 5 | 6 |

SF_10 Koliko su Vas vremena u protekla 4 tjedna Vaše fizičko zdravlje ili emocionalni problemi ometali u društvenim aktivnostima (npr. posjete prijateljima, rodbini itd.) (zaokružite jedan odgovor)

1 - stalno
2 - skoro uvijek
3 - povremeno
4 - rijetko
5 - nikada

Koliko je u Vašem slučaju TOČNA ili NETOČNA svaka od dolje navedenih tvrdnji? (zaokružite jedan odgovor u svakom redu)

| | | potpuno točno | uglavnom točno | ne znam | uglavnom netočno | potpuno netočno |
|---|---|---|---|---|---|---|
| SF_11a | Čini mi se da se razbolim lakše nego drugi ljudi | 1 | 2 | 3 | 4 | 5 |
| SF_11b | Zdrav sam kao i bilo tko drugi koga poznajem | 1 | 2 | 3 | 4 | 5 |
| SF_11c | Mislim da će mi se zdravlje pogoršati | 1 | 2 | 3 | 4 | 5 |
| SF_11d | Zdravlje mi je odlično | 1 | 2 | 3 | 4 | 5 |

**4. Opinions, knowledge and attitudes towards self-perceived breast cancer risk and chemoprevention**

**IME I PREZIME:**

**DANAŠNJI DATUM:**
**DATUM ROĐENJA:**
**MJESTO STANOVANJA:**

**TELEFON/MOBITEL:**

**Mišljenja, znanje i stavovi žena o vlastitom riziku obolijevanja od raka dojke i sprječavanju nastanka raka dojke lijekovima**

**Zainteresirani smo za Vaše mišljenje o Vašem vlastitom riziku obolijevanja od raka dojke. Nema točnih i pogrešnih odgovora. Zanima nas Vaše mišljenje o sljedećim tvrdnjama:**

| ZAOKRUŽIVANJEM JEDNOG BROJA (OD 1 DO 5) OCIJENITE VAŠE MIŠLJENJE O POSTAVLJENOJ TVRDNJI | | | | | |
|---|---|---|---|---|---|
| MOJ RIZIK OBOLIJEVANJA OD RAKA DOJKE | | | | | |
| u sljedećih pet godina je | 1 – jako malen | 2 – malen | 3 – prosječan | 4 – velik | 5 – jako velik |
| u cijelom životu je | 1 – jako malen | 2 – malen | 3 – prosječan | 4 – velik | 5 – jako velik |

| ZAOKRUŽIVANJEM JEDNOG BROJA (OD 1 DO 5) OCIJENITE VAŠE MIŠLJENJE O POSTAVLJENOJ TVRDNJI | | | | | |
|---|---|---|---|---|---|
| MOJ RIZIK OBOLIJEVANJA OD RAKA DOJKE U USPOREDBI SA ŽENAMA ISTE DOBI | | | | | |
| u sljedećih pet godina je | 1 – jako malen | 2 – malen | 3 – prosječan | 4 – velik | 5 – jako velik |
| u cijelom životu je | 1 – jako malen | 2 – malen | 3 – prosječan | 4 – velik | 5 – jako velik |

| ZAOKRUŽIVANJEM JEDNOG BROJA (OD 1 DO 5) OCIJENITE VAŠ STAV O POSTAVLJENOJ TVRDNJI | | | | | |
|---|---|---|---|---|---|
| ZABRINUTA SAM DA ĆU OBOLJETI OD RAKA DOJKE | | | | | |
| u sljedećih pet godina | 1 –nisam niti malo zabrinuta | 2 – niti jesam niti nisam zabrinuta | 3 – malo sam zabrinuta | 4 – zabrinuta sam | 5 – jako sam zabrinuta |
| u cijelom životu | 1 –nisam niti malo zabrinuta | 2 – niti jesam niti nisam zabrinuta | 3 – malo sam zabrinuta | 4 – zabrinuta sam | 5 – jako sam zabrinuta |

| ŠTO OD NAVEDENOG PREMA VAŠEM SAZNANJU POVEĆAVA, A ŠTO SMANJUJE MOGUĆNOST OBOLIJEVANJA OD RAKA DOJKE? | | | | |
|---|---|---|---|---|
| Rastuća životna dob<br>(žene starije životne dobi obolijevaju češće nego mlađe žene) | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Rana dob prve mjesečnice | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Kasni ulazak u menopauzu | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Neradanje djeteta | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Rađanje prvog djeteta prije 30. godine života | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Blisko srodstvo s osobom koja je imala rak dojke (majka, sestra, kći, baka) | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Biopsijom dokazan brzi rast promjenjenih stanica (atipična hiperplazija, neinvazivni rak-DCIS,LCIS) | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Nasljedna mutacija gena *BRCA1/BRCA2* gen | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Uzimanje hormonske nadomjesne terapije nakon menopauze | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Prekomjerno konzumiranje alkohola | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Prekomjerna tjelesna težina u postmenopauzi | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Dojenje svakog djeteta dugačko vremensko razdoblje ( ukupno 12 mjeseci i dulje) | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Redovita fizička aktivnost i aktivan život, hodanje, vožnja biciklom | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Korištenje antiperspiranata | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |

| | | | | |
|---|---|---|---|---|
| Estetska operacija dojke i implantati u dojci | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |
| Povećana gustoća dojki | Smanjuje rizik od raka dojke | Nema utjecaja na rizik | Povećava rizik od raka dojke | Ne znam |

**Procjena rizika uz pomoć BCRAT modela i ostali podaci o ispitanici**

1. Prethodno mi je dijagnosticiran invazivni karcinom dojke, LCIS – lobularni karcinom in situ ili DCIS – duktalni karcinom in situ
   - □ Da
   - □ Ne

2. Prethodno sam bila liječenja radioterapijom (zračenjem) zbog zloćudne bolesti na području prsa (toraksa)
   - □ Da
   - □ Ne

3. Genetičkim testiranjem dokazana mi je mutacija BRCA1 ili BRCA 2 gena ili dijagnoza nasljednog sindroma povezanog s karcinomima
   - □ Da
   - □ Ne

4. Koliko godina imate? _____

5. Moja dob kada sam dobila prvu mjesečnicu
   - □ 7 do 11
   - □ 12 do 13
   - □ 14 i više

6. Moja dob kada sam kada sam rodila prvo dijete
   - □ Nisam rodila dijete
   - □ <20
   - □ 20-24
   - □ 25-29
   - □ 30 i više

7. U bliskom srodstvu sam s osobom koja je imala rak dojke. Molim upišite pored tko vam je osoba koja je oboljela od karcinoma dojke (majka, sestra, kći)?
   - □ Da, u bliskom srodstvu sam s 1 osobom koja je imala rak dojke _____
   - □ Da, u bliskom srodstvu sam s više od 1 osobe koja je imala rak dojke _____
   - □ Ne

8. Prethodno sam bila na biopsiji tkiva dojke
   - □ Da, prethodno sam bila na jednoj biopsiji tkiva dojke
   - □ Da, prethodno sam bila na više od jedne biopsije tkiva dojke

□ Ne

9. Nalaz biopsije bio je pozitivan na staničnu atipiju
   □ Da
   □ Ne
   □ Nikada nisam bila na biopsiji tkiva dojke

**Podaci o ispitanici**

10. Koliko djece imate? _____

11. Najviša postignuta razina obrazovanja
   □ NK, PK, NSS (niža stručna sprema)
   □ KV, SSS (srednja stručna sprema, 3-godišnja ili 4 –godišnja srednja škola)
   □ VŠS ( viša stručna sprema); bacc. (sveučilišni prvostupnik)
   □ VSS (visoka stručna sprema); mag. (magistar struke)
   □ mr.sc. (magistar znanosti)
   □ dr.sc. (doktor znanosti)

12. Radni status
   □ Učenica
   □ Studentica
   □ Zaposlena u privatnom sektoru
   □ Zaposlena u državnom sektoru
   □ Slobodna profesija
   □ Nezaposlena
   □ Umirovljenica

13. Osoba iz moje najbliže obitelji imala je bilo koju vrstu raka?
   □ Da
   □ Ne

14. Osoba iz moje obitelji, uključujući i druge osobe osim najbližih srodnike (majku, sestru, kći) imala je rak dojke?
   □ Da
   □ Ne

15. U bliskom srodstvu sam s osobom koja je imala rak jajnika (majka, sestra, kći, teta). Molim upišite pored tko vam je osoba koja je oboljela od karcinoma dojke (majka, sestra, kći, teta) ?

   □ Da

□ Ne

16. Imam aktivan menstrualni ciklus i mjesečnice
    □ Da
    □ Ne, u postmenopauzi sam i nemam više mjesečnice niti aktivan menstrualni ciklus

17. Bolujete li od neke kronične bolesti za koju svakodnevno uzimate terapiju ( primjericepovišeni krvni tlak, šećerna bolest, bolest štitnjače...), i ako DA, navedite o kojoj se bolesti radi
    □ Da
    □ Ne

18. Pušite li?
    □ Da
    □ Ne

19. Konzumirate li redovito alkoholna pića (2dcl alkoholnog pića na dan)?
    □ Da
    □ Ne

| KOLIKO LIJEKOVA UZIMATE REDOVITO ( NPR. SVAKI DAN/SVAKA DVA DANA/SVAKI TJEDAN) | | | | | |
|---|---|---|---|---|---|
| Lijekova koje mi je propisao liječnik | Niti jedan | 1 lijek | 2 lijeka | 3 lijeka | 4 lijeka ili više |
| Lijekova koji su dostupni u ljekarni bez recepta | Niti jedan | 1 lijek | 2 lijeka | 3 lijeka | 4 lijeka ili više |

**Znanje o kemoprevenciji raka dojke**

| MOLIM VAS OCIJENITE VAŠ STAV U ODNOSU NA POSTAVLJENE TVRDNJE | | | | | |
|---|---|---|---|---|---|
| Čula za mogućnost sprječavanja nastanka raka uzimanjem lijekova | 1 - UOPĆE SE NE SLAŽEM | 2 - NE SLAŽEM SE | 3 - NITI SE SLAŽEM NITI SE NE SLAŽEM | 4 – SLAŽEM SE | 5 - U POTPUNOSTI SE SLAŽEM |

| MOLIM VAS OCIJENITE VAŠ STAV U ODNOSU NA POSTAVLJENE TVRDNJE | | | | | |
|---|---|---|---|---|---|
| Jeste li ikada čuli za lijek tamoksifen (Nolvadex) ? | ne, nikada nisam čula | možda sam čula, nisam sigurna | prepoznajem samo naziv lijeka | prepoznajem naziv i namjenu lijeka | DA, prepoznajem naziv, namjenu i nuspojave lijeka |
| Jeste li ikada čuli za lijek raloksifen (Evista)? | ne, nikada nisam čula | možda sam čula, nisam sigurna | prepoznajem samo naziv lijeka | prepoznajem naziv i namjenu lijeka | DA, prepoznajem naziv, namjenu i nuspojave lijeka |
| Jeste li ikada čuli za lijek eksemestan (Aromasin, Etadron, Exedral, Peramit)? | ne, nikada nisam čula | možda sam čula, nisam sigurna | prepoznajem samo naziv lijeka | prepoznajem naziv i namjenu lijeka | DA, prepoznajem naziv, namjenu i nuspojave lijeka |
| Jeste li ikada čuli za lijek anastrozol (Anastris, Astralis, Strazolan, Arimidex)? | ne, nikada nisam čula | možda sam čula, nisam sigurna | prepoznajem samo naziv lijeka | prepoznajem naziv i namjenu lijeka | DA, prepoznajem naziv, namjenu i nuspojave lijeka |
| Jeste li ikada čuli za lijek letrozol (Siletris, Femara, Avomit, Letrilan)? | ne, nikada nisam čula | možda sam čula, nisam sigurna | prepoznajem samo naziv lijeka | prepoznajem naziv i namjenu lijeka | DA, prepoznajem naziv, namjenu i nuspojave lijeka |

**Stavovi o kemoprevenciji raka dojke lijekovima**

Lijekovi **RALOKSIFEN I TAMOKSIFEN** u nekim zemljama odobreni su u svrhu prevencije razvoja karcinoma dojke. Lijekovi raloksifen i tamoksifen pripadaju grupi lijekova pod nazivom SERM - selektivni modulatori estrogenskih receptora. Ovi lijekovi mogu izazvati brojne neželjene nuspojave i ne smiju se primjenjivati tijekom trudnoće i dojenja.

Lijekovi raloksifen i tamoksifen imaju dio neželjenih učinaka koji su nužno vezni uz njihov terapijski učinak i pojavljuju se vrlo često ( kod ≥ 10% žena koja uzimaju lijek). Neke od ovih nuspojava veoma nalikuju simptomima menopauze: naleti crvenila uz osjećaj vrućina, vaginalno krvarenje, iscjedak iz rodnice, umor. Druge vrlo česte (kod ≥ 10% žena koja uzimaju lijek) nuspojave uključuju mučninu, zadržavanje tekućine, osip kože, povišen krvni tlak.

Lijekovi **EKSEMESTAN, ANASTROZOL I LETROZOL** pripadaju grupi lijekova pod nazivom inhibitori aromataze. Ova grupa lijekova može uzrokovati sljedeće neželjene učinke: nesanica, glavobolja, naleti crvenila uz osjećaj vrućina, mučnina, pojačano znojenje, umor, mišićno-koštana bol (kod ≥ 10% žena koja uzimaju lijek); depresija, anoreksija, omaglice, bol u abdomenu, povraćanje, osip, osteoporoza ( kod 1 ≥ 10% žena koja uzimaju lijek). Lijekovi iz ove grupe ne smiju se primjenjivati tijekom trudnoće i dojenja.

Trenutno postoje samo pripravci ovih ili srodnih lijekova u formi tableta, ali se istražuje mogućnost primjene ovih lijekova direktno na kožu dojke čime bi se maksimalno pokušao smanjiti utjecaj lijeka na sva ostala tkiva izuzev tkiva dojke. Molimo Vas da odgovorite o svojoj spremnosti na uzimanje takvih lijekova kao preventivne terapije koja bi značajno umanjila Vaš rizik za pojavu karcinoma dojke u slučaju da Vas Vaš liječnik prepozna kao pacijenticu s vrlo visokim rizikom pojave bolesti.

**STAVOVI O KEMOPREVENCIJI RAKA DOJKE LIJEKOVIMA**

| LIJEK ZA SPRJEČAVANJE NASTANKA RAKA DOJKE: | | | | | |
|---|---|---|---|---|---|
| Na preporuku liječnika uzimala bih lijek | UOPĆE SE NE SLAŽEM | NE SLAŽEM SE | NITI SE SLAŽEM NITI SE NE SLAŽEM | SLAŽEM SE | U POTPUNOSTI SE SLAŽEM |
| Uzimala bih lijek bez obzira na moguće nuspojave | UOPĆE SE NE SLAŽEM | NE SLAŽEM SE | NITI SE SLAŽEM NITI SE NE SLAŽEM | SLAŽEM SE | U POTPUNOSTI SE SLAŽEM |
| Uzimala bih lijek ako mi liječnik predoči jasne dokaze o smanjenju mogućnosti obolijevanja od raka | UOPĆE SE NE SLAŽEM | NE SLAŽEM SE | NITI SE SLAŽEM NITI SE NE SLAŽEM | SLAŽEM SE | U POTPUNOSTI SE SLAŽEM |

| | | | | | |
|---|---|---|---|---|---|
| Uzimala bih lijek u slučaju da liječnik moj rizik od raka procjeni kao izrazito visok | UOPĆE SE NE SLAŽEM | NE SLAŽEM SE | NITI SE SLAŽEM NITI SE NE SLAŽEM | SLAŽEM SE | U POTPUNOSTI SE SLAŽEM |
| Ne bih nikada uzimala lijek za prevenciju raka | UOPĆE SE NE SLAŽEM | NE SLAŽEM SE | NITI SE SLAŽEM NITI SE NE SLAŽEM | SLAŽEM SE | U POTPUNOSTI SE SLAŽEM |

| U UZIMANJU LIJEKOVA ZA SPRJEČAVANJE NASTANKA RAKA DOJKE OGRANIČAVALO BI ME: | | | | | |
|---|---|---|---|---|---|
| Problem mi je izdvajati dodatne novce za lijek, ako cijena lijeka ne bi bila u potpunosti pokrivena osnovnim osiguranjem | UOPĆE SE NE SLAŽEM | NE SLAŽEM SE | NITI SE SLAŽEM NITI SE NE SLAŽEM | SLAŽEM SE | U POTPUNOSTI SE SLAŽEM |
| Brinule bi me moguće nuspojave lijeka | UOPĆE SE NE SLAŽEM | NE SLAŽEM SE | NITI SE SLAŽEM NITI SE NE SLAŽEM | SLAŽEM SE | U POTPUNOSTI SE SLAŽEM |
| Brinula bi me mogućnost neplanirane trudnoće i mogući učinak lijeka na dijete | UOPĆE SE NE SLAŽEM | NE SLAŽEM SE | NITI SE SLAŽEM NITI SE NE SLAŽEM | SLAŽEM SE | U POTPUNOSTI SE SLAŽEM |
| Teško mi je paziti da svakodnevno koristim lijek u isto vrijeme | UOPĆE SE NE SLAŽEM | NE SLAŽEM SE | NITI SE SLAŽEM NITI SE NE SLAŽEM | SLAŽEM SE | U POTPUNOSTI SE SLAŽEM |

## 5. Information leaflet



**1 od 11** žena u RH tijekom života će oboljeti od karcinoma dojke

## Rizični faktori

- Rastuća životna dob (u RH najčešće u dobi 60-65 god)
- Izloženost estrogenu
  - Rana 1.mjesečnica
  - Kasna menopauza
  - Izostanak dojenja
  - Kontracepcijske tablete i hormonsko nadomjesno liječenje
- Nerađanje djece
- Obiteljska anamneza karcinoma dojke
- Atipična hiperplazija
- Povećana gustoća dojki
- Prekomjerni unos alkohola
- Povećana tjelesna težina (u postmenopauzi)
- Nasljedni oblik: *BRCA1 i BRCA2 geni*

## Zaštitni faktori



Tjelesna aktivnost
Zdrava prehrana



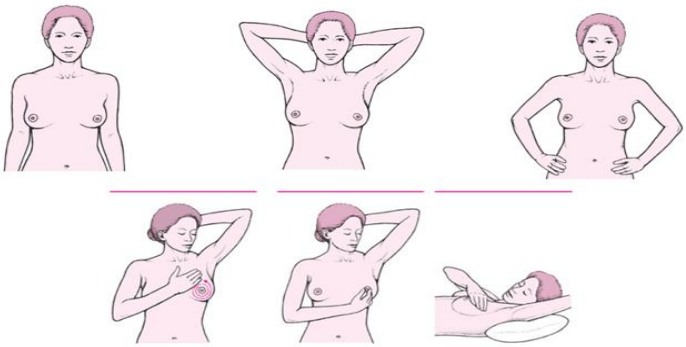


Trudnoća prije 30.godine

Dojenje



## Samopregled dojki-jednom mjesečno



**Mogući znaci raka**

