The Characteristics of Breast Cancer Patients in "Dharmais" Hospital National Cancer Center Jakarta Based on Occupational and Environmental Status

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ABSTRACT

Occupations related to breast cancer vary between countries. This study's goal is to identify the different risk factors for breast cancer in Indonesia with occupation and environment factors in emphasis. This descriptive study lasted 1 month involving 103 breast cancer patients in "Dharmais" hospital National Cancer Center. Breast cancer patients in "Dharmais" hospital are mostly of the old age 51-60 years old (35%), have family history of cancer (61.2%), have a history of pregnancy and delivery of 3-4 (42,7%), and consume high fat diet (76.7%). As for cancer-related exposures, most patients are exposed to smoke (76%) and interestingly are less exposed to estrogen (43%), industrial substances (41%), and radiation (21%). The occupation factor for breast cancer in Indonesia does not play a major part as seen from the exposures to industrial substances. However, environmental and individual aspect does have a high influence in Indonesia.

***Keyword**: breast cancer, occupation, environment.*

ABSTRAK

Hubungan jenis pekerjaan (okupasi) dengan kanker payudara bervariasi di tiap negara. Tujuan dari studi ini adalah untuk mengetahui faktor risiko kanker payudara di Indonesia berupa faktor pekerjaan dan lingkungan. Studi deskriptif ini mengambil 103 sampel pasien kanker payudara di RS "Dharmais". Hasilnya adalah karakteristik mayoritas pasien kanker payudara adalah berumur 51-60 tahun (35%), memiliki riwayat keluarga (61,2%); melahirkan 3 hingga 4 kali (42,7%); dan konsumsi tinggi lemak(76,7%). Faktor pajanan yang berhubungan dengan kanker payudara adalah rokok (76%); estrogen (43%); bahan industry (41%); dan radiasi (21%). Faktor okupasi tidak berperan penting, tetapi factor lingkungan memiliki peran yang tinggi dalam terjadinya kanker payudara di Indonesia.

Kata kunci: kanker payudara, okupasi, lingkungan

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INTRODUCTION

Breast cancer has high prevalence in the world. According to data of WHO in 2008, prevalence of breast cancer had reached 1.38 million cases. This data shows that breast cancer dominate 23% from prevalence of all cancers worldwide. WHO also reported that there are 209.000 new cases in Asia, especially South-east Asia.[1] Incidence of breast cancer at "Dharmais" Hospital National Cancer Center is 437 new cases in 2007. This number has increased since 2004 with 279 new cases.[2] Not only the prevalence of breast cancer is big, but also the effect

of it is big enough, especially in increasing mortality rate. At present, breast cancer is the fifth highest cancer that causes death among other kinds of cancer. In 2008, 458 patients that suffered from breast cancer died. This number competes the mortality number of lung cancer.[1,2]

There are many risk factors believed as risk factor for breast cancer, such as demographic variety, age, genetic and inherited, estrogen replacement post-menopause, oral contraceptive, carcinogen exposure, and other risk factor, such as alcohol consumption, fat consumption, and smoking. The incidence of breast cancer differs in every country. North America and West Europe have higher incidence than Asia. This fact shows that, not only breast cancer has varying incidence in every country, but it also shows that genetic factor influence the incidence of breast cancer. Mutation in BRCA-1 and BRCA-2 will make women susceptible to breast cancer. Breast cancer often occurred in female over 30 years old and increases until post-menopause. Post-menopausal woman who uses estrogen therapy for osteoporosis has risk to get breast cancer. The use of oral contraceptive is also suspected to be a risk factor of breast cancer. Another risk factor is from carcinogenic materials, such as plastic, pesticide, food canning, smoking, etc.[3,4]

Occupation is an activity that produces income to support sufficient basic necessities of life. Occupations also correlate with daily activities of people which represent their environment as well. Some chemicals or carcinogenic agents often found in the environment of some occupation actually could increase the risk of breast cancer. A study in Canada showed that there is relation between risk factors of breast cancer and some kinds of occupation, such as agricultural, automotive plastic manufactory, bars gambling, food canning, or some occupation use metal processing. Data of that study showed the increase of breast cancer (42%) in women who have high exposure of PVC (polyvinyl chloride), plastic, acrylonitrile, formaldehyde and styrene in their occupation during 10 years or more.[5,6] Therefore, in this study, we will show the relation between breast cancer and occupational risk factors, especially in Indonesia based on our descriptive study in "Dharmais" Hospital National Cancer Center in Indonesia, which represent the characteristic of breast cancer in Indonesia.

MATERIAL AND METHODS

This cross-sectional study to determine the characteristics of breast cancer patients was done in one-month period February - April of 2013 in "Dharmais" Hospital National Cancer Center. The respondents were Breast Cancer Patients of all criteria that are presently diagnosed or are currently still being treated in the hospital. A total of 103 respondents were chosen based on consecutive sampling and were studied with questionnaire. The questionnaire comprised questions regarding basic personal information, history of diseases, family history of diseases, radiation and pollution level in their houses, work history including the exposure rate to estrogen and radiation, and other risk factors to breast cancer such as the use of hormonal contraceptive, smoking and alcohol history, high-fat diet, and all types of long-term drug consumption. The Institutional Review Board approved this study with the respondents first asked for informed consent. The collected data is analyzed using SPSS 13.0 for Windows descriptively. Through SPSS, the data is presented descriptively without any interaction, sensitivity, or correlation test. All confounding factors are disposed. This research utilized the Per-Protocol convention; therefore all missing data is excluded.

RESULTS

From 103 subjects that we collected, the result of our descriptive analysis shows that the most common breast cancer patient are women who are 51-60 years old (35%), followed by women in age group 41-50 years (29.1%). They also on average have high education level (bachelor and senior high school) and no history of breast cancer or any other cancer in their family. The patients mostly are housewife (39.8%) and come from Java (82.5%), with the comparison between Jakarta and outer is almost equal. (Table 1)

This study shows patients who are classified as obese are more common (39.6%) than underweight BMI patient (13.6%). Most breast cancer patients had experienced pregnancy and delivery 3-4 times, but the frequency decreases, which mean some of them, may get abortive during pregnancy. They also commonly don't use any contraceptive (oral or inject), however 56% breast cancer patients who has used contraceptive used it in long term (1-5 years). (Table 2)

From the survey result, it was found that 14.6% of positively diagnosed patients of breast cancer was an active smoker in the past time. In addition, we also collect the data about subjects who are secondhand smoker, which is also exposed to smoke and have the same risk as active smokers. The data of secondhand smokers showed that 52.4% of subject gets high smoke exposure in their environment and 16.5% of subjects get low smoke exposure, with the criteria of high exposure being a family member has a habit of smoking and it is inside the house, while low exposure refers to outside of the house. That result is similar with the data fat diet of subjects. Most of them confessed that they have high fat diet before diagnosed as breast cancer patient (61.2%). However, only a few of them have consumed alcoholic substance (6.8%). (Table 2)

Tabel 1: The general charateristics of breast cancer patients

Variable	Category	Frequency (%)
Age	≤ 18 years old (%)	0 (0)
	19-30 years old (%)	8 (7,8)
	31-40 years old (%)	13 (12,6)
	41-50 years old (%)	30 (29,1)
	50-60 years old (%)	36 (35,0)
	> 60 years old (%)	16 (15,5)
Gender	Male (%)	0 (0)
	Female (%)	103 (100)
Educational level	Bachelor degree (%)	32 (31,1)
	Senior high school (%)	33 (32,0)
	Junior high school (%)	20 (19,4)
	Elementary school (%)	16 (15,5)
	No education (%)	2 (1,9)
Area of residence	Jakarta (%)	48 (46,6)
	Java island (%)	37 (35,9)
	Outside Java island (%)	18 (17,5)
Family history of cancer	Yes (%)	41 (39,8)
	No (%)	62 (60,2)
Family history of breast cancer	Yes (%)	22 (21,4)
	No (%)	81 (78,6)
Occupation	Enterpreneur (%)	14 (13,6)
	Civil servants (%)	23 (22,3)
	Housewife (%)	41 (39,8)
	Employee (%)	25 (24,3)
Total		103

For environment and occupational exposure that can influence the incidence of breast cancer, we analyzed it in 4 factors: radiation, estrogen, industrial, and smoke. From the result of 103 respondents, they commonly are unexposed by radiation, estrogen, or industry, but most of them are exposed by smoke (76%), which matches the number of active and passive smokers. (Diagram 1)

Table 2: The health characteristics of breast cancer patients

Variable	Category	Frequency (%)
BMI (Body Mass Index)	< 18,5 / Underweight (%)	14 (13,6)
	18,5 - 22,9 / Normal (%)	33 (32,0)
	23 - 24,9 / Overweight (%)	18 (17,5)
	≥ 25 / Obese (%)	38 (36,9)
Number of pregnancy	0 (%)	15 (14,6)
	1-2 (%)	33 (32,0)
	3-4 (%)	46 (44,7)
	5 (%)	9 (8,7)
Number of delivery	0 (%)	16 (15,5)
	1-2 (%)	36 (35,0)
	3-4 (%)	44 (42,7)
	5 (%)	7 (6,8)
Oral contraceptive	Yes (%)	23 (22,3)
	No (%)	80 (77,7)
Inject contraceptive	Yes (%)	35 (34,0)
	No (%)	68 (68,0)
Duration usage of oral and inject contraceptive	< 1 year	1 (1,0)
	1-5 years	23 (22,3)
	> 5 years	17 (16,5)
	Never use	62 (60,2)
Active smoker	Yes (%)	15 (14,6)
	No (%)	88 (85,4)
Passive smoker	Yes, high exposure (%)	54 (52,4)
	Yes, low exposure (%)	17 (16,5)
	No (%)	32 (31,1)
High fat diet	Yes, high exposure (%)	63 (61,2)
	Yes, low exposure (%)	16 (15,5)
	No (%)	24 (23,3)
Alchohol consumption	Yes (%)	7 (6,8)
	No (%)	96 (93,2)
Total		103

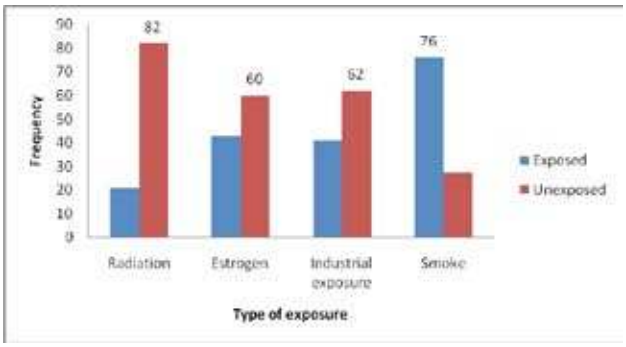

Diagram 1: Estrogen, radiation, smoke and industrial exposure of breast cancer patients

DISCUSSION

Educational Factor

This study shows that educational level is not related with incidence of breast cancer. A recent study in Turkey said that education influences women to do breast self-examination (BSE). This study has opposite result with our study. Our study shows that the higher incidence of breast cancer occurred in woman who has higher educational level. We think that this result indicates the bad introduction of BSE from government to Indonesian people. We hope that the government can educate more Indonesian women about BSE. With more education about BSE, early stage for breast cancer can be recognized.[7] We also see this result is related with the patient's income. Patients who have higher educational level usually have higher income. The high cost for cancer treatment cause patients rarely come to hospital for treatment.

Family History of Breast Cancer

Most of positive diagnosed patients of breast cancer have family history of cancer (61.2%) and >20% have specific breast cancer family history. This is supported with previous study, which shows that 5-10% of breast cancers incidence are inherited from the parents through mutation in specific genes. This is called familial breast cancer. The risk of familial breast cancer in first generation is 3.6 times greater than second generation.[8]

Body Mass Index

Previous studies has shown the relation between body mass index (BMI) and breast cancer incidence.[9,10,11] For postmenopausal women, previous study has shown a greater risk for developing breast cancer in association with increasing adiposity. It is believed that adipose tissue is the major source of estrogen after menopause, the greater their adiposity, as shown by body mass index, the greater the concentrations of circulating estrogens in obese postmenopausal women.[13,14] On the other hand,among premenopausal women, increased BMI is associated with a reduced risk for developing breast cancer. However, the relationship between BMI and breast cancer risk in premenopausal women has remained unclear.[15] From those previous studies, we could conclude that BMI is not associated directly with the incidence of breast cancer. However, the status of menopausal and BMI collaborate as the factor of developing breast cancer. In our study shows no significance BMI among the patients.

Pregnancy and Delivery

From the result we found, an increased number of both pregnancy and delivery is more likely to be found in breast cancer patients (more than 2 times). This is in line with the previous research data concerning pregnancy experience with breast cancer. Nausea and vomiting in pregnancy, which are associated with elevated serum estradiol levels during pregnancy, may increase risk. The treatment for nausea and vomiting was also associated with an increased risk, especially women experiencing recent pregnancies. This may be induced by hormonally induced differentiation and proliferation of breast stem cells, which some may have undergone malignant transformation. Breast stem cells differentiate during the first full-term pregnancy and first lactation rendering them less susceptible to carcinogenesis. While being pregnant and breastfeed may induce a protective effect (reducing the cyclic hormonal stimulation of breast cells), those who have experienced severe nausea and vomiting of pregnancy may have excessively elevated estradiol levels, therefore irreversibly promoting premalignant breast cells.[12,13]

High Fat Diet

The relationship between dietary fat and the risk of breast cancer has been controversial, yet unknown. Some studies suggested that high dietary fat intake was associated with a higher incidence of breast cancer. The association was found especially between saturated fat intake and breast cancer risk. And also, a cohort study shows that dietary fat intake was directly associated with the risk of postmenopausal invasive breast cancer.[14,15] On the other hand, a different cohort study conclude that there is no evidence of a positive association between total dietary fat intake and the risk of breast cancer.[16] Controversial results existed because there are differences among how dietary fat intake was measured, and the difficulty to investigate dietary factor as single factor influencing breast cancer. As for our study, the epidemiology result shows that 76.7% of breast cancer patients in Indonesia were likely to consume high fat diet, where 61.2% of them were highly exposed by high fat diet. The effect of a high fat diet on the risk of breast cancer may not be as important as the effect other factor influencing breast cancer. But the high

number of high fat diet of breast cancer patients in Indonesia means there is an association between high dietary fat intake and breast cancer.

Alcohol

In our study, data of alcohol exposure do not have a significant number as a risk factor of breast cancer, which 6.8% of respondents have a habit of consuming alcohol. This result is different with the result of recent meta-analysis that said incidences of breast cancer have a linear increase with alcohol consumption.[17] Many recent studies also discussed about the relationship of breast cancer and alcohol consumption. Another study shows that alcohol consumption is related with the incidence of breast cancer. That author also suggests that although Asians do not have a habit of consuming alcohol, risk factor still needs to be considered.[18] We see that a not significant number is caused by Indonesian's habit. Indonesian people who have majority religion of Moslem are prohibited to consume alcohol. But now, Indonesian people have different lifestyle. Many people, both teenager and adult and both male and female, have a habit of consuming alcohol. Data from a study shows that alcohol consumption in Indonesia increases from year to year. This can be an alert for Indonesian people to change their habit of alcohol consumption.

Radiation Exposure

The result of radiation exposure is not significant. Only 21% of respondents live and work at the location that is exposed with radiation. Most respondents said that they are exposed with radiation when they work with computer. Recent study said that radiation, especially electromagnetic radiation, is believed to be a risk factor of breast cancer. A study in America has the conclusion that radiation is a risk factor for breast cancer.[19] In the same study, characteristic of breast cancer patient who has been exposed by radiation is that their age is approximately 20 years old and seldom occurred in postmenopausal women.[20]

Estrogen Exposure

From the results above, it is shown that nearly half of the breast cancer patients have had an exposure of estrogen from either oral contraceptive (22,3%), or inject contraceptive (34%). And also, most of the breast cancer patients (97,6%) had used oral or inject estrogen for more than 1 year, some of them used it for 1-5 years period (56,1%), and some of them for more than 5 years period (41,5%). A number of studies suggest that current use of oral and inject contraceptives which content is estrogen appears to slightly increase the risk of breast cancer. It is said that some factors contributing to development of breast cancer includes hormones, which is estrogen itself.[21] The use of oral and inject contraceptive which contain estrogen allow breast tissue to be exposed to high levels of hormones for longer periods of time. Nevertheless, the pathogenesis of estrogen exposure towards breast cancer is yet unknown, but it is believed that estrogen stimulates growth factors that exist in breast cancer cells resulting in tumor progression.[3]

Industrial Exposure and Occupational Status

Based on our results, industrial exposure was not a major risk factor for breast cancer patients in "Dharmais" Hospital, because the number of those unexposed exceeds those who are exposed. This result is different with a study done in Canada, where females who work in industrial factories (especially involving PVC) have a 42% risk of breast cancer. The effect of carcinogenic substances is the cause of this risk. Carcinogenic substances can disrupt the endocrine system of human body, which can then be the cause of several diseases, including breast cancer. In some industrial factories, these carcinogenic substances can be found. Another important factor is Estrogen-like Industrial Chemicals. Xenoestrogens, which are chemicals with estrogen-like effect, have been suspected to be a risk factor. Several particular concerns are pesticides containing organochlorines (DDT and its metabolites, such as dieldrin) and pyrethroids (permethrin), however their causal link has not yet been fully proven.[6]

A study in the UK comparing different work fields to the risk of cancer showed that the highest number of cancer registrations occurred because of shifts work and in metal workers (exposure to mineral oils), in personal and household services sector (repair trades, laundries and dry cleaning, domestic services, hairdressing and beauty), land transport and mining (diesel engine exhaust from vehicles and machinery), the printing industry (lung cancer), and public administration and defense (non-melanoma skin cancer in outdoor workers). Nearly 2 million female night-shift workers associated with health care, transport, communication, leisure, and hospitality sectors as well as air transport were

exposed to a possible risk of breast cancer, and breast cancer registration from these sectors were the most out of all other types of cancer (93% - 1957 registrations). From their research it can be concluded that construction and service sector also has large contributions to occupational cancer, other than the primary industrial exposure. As for breast cancer, the service sector was one with the most number of breast cancer patients.[22]

One reason for this difference in result compared to the previous literatures is that the risk factor for patients in "Dharmais" hospital are more exposed to other risk factors than those in the UK and Canada, considering the occupational factor is not a direct cause of the disease. Work fields in Canada and in the UK that have high risk to breast cancer are also different, even though the suspected main risk factor was the carcinogens found mostly in industrial factories involving metal and PVC. The location of their work might also be related, since in a research done by a Denmark researcher those who lived in rural areas have a higher number in breast cancer patients.[23] One other reason is that Indonesian females are mostly housewives; therefore the exposure is not limited to occupations, but also to their industrial exposure at home. We conclude that the risk factor of industrial pollution in patients in "Dharmais" hospital does exist, however the gravity of the risk is overwhelmed by other factors that is related to breast cancer.

Smoking Exposure

This study shows that environment exposure; such as cigarette smoke may be a breast cancer risk factor because most of them, 86.58%, get exposure from cigarette smoke, as active or secondhand smokers. Although secondhand smokers are in higher amount than active smoker, more than 50% secondhand smokers are highly exposed so the risk that can be caused by smoke is also relatively high. Smoking exposure is one of the breast cancer risk factor because the variable hazard contents of a cigarette and its smoke are potentially carcinogenic. Right now, cigarette's content is considered as xenoestrogen, which is a foreign substance like estrogen in the body and has ability to bind estrogen receptors. Polonium is one of metalloestrogen which is found in cigarette. Metalloestrogen and its variable species can be found in human mammary tissue and induce cancer. In addition, cigarettes also contain methylnitosamino-pyridyl-butanone which is a strong carcinogen agent and related to beta estrogen receptor. An increase in the amount of estrogen in the body induces more active mammary gland cells and increases the chance of cells to be uncontrollably actively proliferating.[24]

CONCLUSION

The major general characteristic of breast cancer patients in Indonesia is the age of patients and family history. In terms of occupational and industrial exposure characteristic, they do not play a major role in inducing breast cancer, as the occupation of women in Indonesia is mostly housewife. Major health characteristics include high-fat diet, number of pregnancy, and estrogen exposure especially by the long-term usage of oral and injection contraceptives. Passive smokers are also at higher risk to breast cancer, and it is of prevalence in Indonesia. In conclusion, occupational factors of breast cancer patient have less effect in Indonesia compared to the environmental factors, such as age, family history, high-fat diet, number of pregnancy, estrogen exposure, and smoke exposure.

REFERENCES

1. IARC. GLOBOCAN 2008 Breast Cancer Incidence and Mortality Worldwide in 2008 Summary[internet]. 2010 [cited 2013 January 22]. Available in: http://globocan.iarc.fr/factsheets/cancers/breast.asp
2. Bidang Rekam Medis RSKD. 10 Besar Kanker Tersering di RS Kanker "Dharmais" Rawat Jalan (KasusBaru) Tahun 2007 [internet].2009[cited 2013 January 22]. Available in: http://www.dharmais.co.id/index.php/statistic-center.html
3. Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Cotran Pathologic Basis of Disease. 8th edition. Philadelphia: Saunders Elseiver;2010. Page 1073-96.
4. Longo DL, Kasper DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo J. Harrison's Principles of Internal Medicine. 16th edition. United States of America: The McGraw-Hill Companies;2012. Chapter 90, Breast Cancer. [Ebook]
5. Brophy JT, Keith MM, Watterson A, et al. Breast cancer risk in relation to occupations with exposure to carcinogens and endocrine disruptors: A canadian case-control study. *Environmental Health* 2012;11:87.
6. Blanchard K. Canadian Study Suggest Occupational Risks for Breast Cancer[internet]. 2012 [cited 2013 December 23]. Available in: http://digitaljournal.com/article/337318.
7. Gurdal SO, Saracoglu GV, Oran SE, Yankol Y, Soybir GR. The effect of educational level on breast cancer awareness: a cross-sectional study in turkey. *Asia Pacific Journal of Cancer Prevention* 2012;13:295-301.

8. American Cancer Society. Breast cancer[internet]. 2011 [cited 2012 March 7]. Available in: http://www.cancer.org/Cancer/BreastCancer/index.
9. Cecchini RS, Costantino JP, Cauley JA, et al. Body mass index and the risk for developing invasive breast cancer among high-risk women in NSABP P-1 and STAR breast cancer prevention trials. *Cancer Prev Res* 2012;5(4):583-92.
10. Siiteri PK. Adipose Tissue as a Source of Hormones. *American Journal of Clinical Nutrition* 1987;45(1):277-82.
11. Cheraghi Z, Poorolajal J, Hashem T, Esmailnasab N, Irani AD. Effect of Body Mass Index on Breast Cancer during Premenopausal and Postmenopausal Periods: A Meta-Analysis. Thesis. 2012
12. Chedin P. Pregnancy-associated breast cancer and metastasis. *Nature Reviews Cancer* 2006;6:281-291.
13. Enger SM, Ross RK, Henderson B, Bernstein L. Breastfeeding history, pregnancy experience and risk of breast cancer. *British Journal of Cancer* 1997;76(1):118-123
14. Sieri S, Krogh V, Ferrari P, Berrino F, Pala V. Dietary Fat and Breast Cancer Risk in the European Prospective investigation into Cancer and Nutrition. *American Society for Clinical Nutrition* 2008;88(5):1304-12.
15. Thiebaut ACM, Kipnis V, Chang S, et al. Dietary fat and postmenopausal invasive breast cancer in the National Institutes of Health-AARP Diet and Health Study Cohort. *J Natl Cancer Inst* 2007; 99: 451-62.
16. Hunter DJ, Spiegelman D, Adami HO, et al. Cohort studies of fat intake and the risk of breast cancer–a pooled analysis. *N Engl J Med* 1996;334(6):356-61.
17. Smith-Warner SA, Spiegelman D, Yaun SS, et al. Alcohol and breast cancer in woman a polled analysis of cohort studies. *JAMA* 1998;279:535-541.
18. Wu AH, Vigen C, Razavi P, Tseng CC, Stancyzk FZ. Alcohol and breast cancer risk among Asian-American women in Los Angeles country. *Breast Cancer Research* 2012;14:1-11.
19. Samet J, Armstrong B, Degrave E, et al. Carcinogenicity of radiofrequency electromagnetic fields. *The Lancet Oncology* 2011;11:524-625.
20. Ronckers CM, Erdmann CA, Land CE. Radiation and breast cancer: a review of current evidence. *Breast Cancer Research* 2005;7:21-32.
21. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996;347(9017):1713–27.
22. Hutchings SJ, Rushton L. Occupational cancer in Britain. *British Journal of Cancer* 2012;107:S92–S103.
23. Dalton SO, During M, Ross L, et al. The relation between socioeconomic and demographic factors and tumor stage in women diagnosed with breast cancer in Denmark, 1983-1999. *British Journal of Cancer* 2006;95:653–659
24. Fucic A, Gamulin M, Ferencic Z, Katic J, Krauss MKV, Bartonova A, Merlo DF. Environmental exposure to xenoestrogens and estrogen related cancers: reproductive system, breast, lung, kidney, pancreas, and brain. *Environmental Health* 2012; 11(Suppl 1):S8