MODELLING BREAST CANCER RISK FACTORS WITH FUZZY COGNITIVE MAP

(GÖĞÜS KANSERİNE ETKİ EDEN FAKTÖRLERİN BULANIK BİLİŞSEL HARİTALAMA İLE MODELLENMESİ)

by

Ayşegül BÜYÜKAVCU, B.S.

Thesis

Submitted in Partial Fulfillment

of the Requirements

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Ayşegül Büyükavcu,
2013

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LIST OF SYMBOLS

AMS	:	Aggregated Matrix of Supporting Factors
BBD	:	Benign Breast Disease
BC	:	Breast Cancer
BMI	:	Body Mass Index
CMs	:	Cognitive Maps
COG	:	Centre of Gravity
ER	:	Oestrogen Receproor
FCM	:	Fuzzy Cognitive Map
HRT	:	Hormone Replacement Therapy
IMS	:	Initial Matrix of Supporting Factors
LMC	:	Low-middle income countries
MWS	:	MillonWomenStudy
NM	:	Negatively Medium
NS	:	Negatively Strong
NVS	:	Negatively Very Strong
NW	:	Negatively Weak
OCs	:	Oral Contraceptive Usage
PM	:	Positively Medium

PR	:	Progestrogene Receptor
PS	:	Positively Strong
PVS	:	Positively Very Strong
PW	:	Positively Weak
WHI	:	Women's Health Initiative
WMS	:	Weight Matrix of Supporting Factors
Z	:	Zero

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ABSTRACT

Cancer is the most important health problems nowadays. Due to the frequent occurrence and high level of fatality, it was ranked four among known cause of death in 1970's but now it is ranked second after the cardiovascular disease.

Overall breast cancer mortality declined 2.3% annually between 1990 and 2001 because of advances in awareness, detection, protection and treatment. However it is well known that breast cancer has expensive treatment also needs to use of limited resources. All of these bring burden on not only patients but also government. Thus originating strategies against breast cancer prevention, protection and treatment have crucial value.

In this study, we propose Fuzzy Cognitive Map (FCM) model that can help breast cancer oncologists to better identify and evaluate the weights of modifiable and non-modifiable factors that are contributing to the occurrence of breast cancer in their patients. In that paper we will focus on preventive and protective actions. The results of the FCM will allow better understanding several root causes, thus oncologists can improve their prevention and protection recommendation. There is no comprehensive model is available to serve this purpose yet.

Medical decision systems are complex systems that can be decomposed to non-related and related subsystems and elements, where many factors have to be taken into consideration that may be complementary, contradictory, and competitive; these factors influence each other and determine the overall clinical decision with a different degree. Thus, FCMs are suitable for medical decision support systems. In this paper we combined the opinions of the breast cancer experts with the help of FCM and main risk factors are put in order then relation among these factors are brought out. Then preventive and protective actions against Breast cancer will be proposed.

This thesis is organized as follows: The next chapter presents an overwiev to breast cancer and reviews the modifiable and non modifiable risk factors for breast cancer. In chapter 3, the base concepts of FCM are defined. In the study, for the construction of Fuzzy Cognitive Map (FCM), experts based method is used. Chapter 4 presents the construction process of FCM. The basic definitions of FCM, such as three main steps to create FCM, the construction of Initial Matrix of Supporting, Aggregated Matrix of Supporting Factors and lastly Weight Matrix of Supporting Factors, are described. In chapter 5, the application of FCM to breast cancer risk factors is done to indicate casual relatonship and generate the weights of factors. To construct casual relationship, the mapping of linguistic terms to numerical values is used. Centre of Gravity method and experts approach is determined in Weigth Matrix of Breast Cancer Risk Factors. Chapter 6 presents a scenario analysis to propose the preventive and protective actions against breast cancer. The study is concluded in Chapter7.

Keywords: *Medical Decision System, Breast Cancer, Fuzzy Cognitive Map*

RESUME

Le cancer est l'un des problèmes de santé le plus important de nos jours. En raison de l'apparition fréquente et le niveau élevé de la fatalité, il a été classé parmi les quatre causes connues de décès en 1970, mais maintenant il est classé deuxième après la maladie cardio-vasculaire.

La mortalité globale, par cancer du sein, a diminué de 2,3% par an entre 1990 et 2001 en raison des progrès de la connaissance, la détection, la protection et le traitement, Toutefois, il est bien connu que le cancer du sein a un traitement coûteux et comme il doit utiliser des ressources limitées, le traitement du cancer du sein amène un fardeau supplémentaire sur les individus, les patients et le gouvernement. Grace a ceux-ci, la lutte contre la prévention du cancer du sein, la protection et le traitement ont une valeur cruciale.

Dans cette étude, nous proposons un modèle de la carte cognitive flou (CCF) qui peuvent aider les oncologues du cancer du sein à mieux identifier et évaluer le poids des facteurs modifiables et non modifiables qui contribuent à l'apparition du cancer du sein chez leurs patients. Ici, nous divisons les patients en trois catégories différentes: en bonne santé, risqué et malades. Dans cet étude nous allons concentrer sur les mesures de prévention et de protection. Les résultats du modèle permettra de mieux comprendre plusieurs causes profondes, ainsi oncologues peuvent améliorer leur prévention et à la recommandation de protection. Il n'ya pas un modèle complet qui est disponible pour servir cet objectif encore.

Les systèmes de décision médicales sont des systèmes complexes qui peuvent être décomposés en sous-systèmes avec des éléments non liés et connexes, où de nombreux facteurs doivent être pris en considération que peuvent être complémentaires, contradictoires, et concurrentiels; ces facteurs influencent et déterminent les décisions

cliniques globales avec un degré différent. Ainsi, la méthode CCF est adaptée pour les systèmes d'aide à la décision médicale. Dans cette étude, nous avons utilisé les jugements des experts du cancer du sein pour déterminer des facteurs du risque et nous avons trouvé des poids des relations parmi ceux-ci. Ensuite les actions de prévention et de protection contre le cancer du sein sont proposées.

Cette thèse est organisé comme suivant: Le chapitre suivant présente un aperçu au cancer du sein et examine les modifiables et les facteurs de risque non modifiables pour le cancer du sein. Dans le chapitre 3, les concepts de base de la CCF sont définis. Dans cette étude, on a utilisé la carte cognitive floue (CCF), une méthode basée sur les jugements des experts. Le chapitre 4 présente le processus de construction de CCF. Les définitions de base de CCF, matrice initiale de soutien, la matrice agrégé des facteurs de soutien et enfin matrice de poids de soutien des facteurs sont définis. Dans le chapitre 5, l'application de la CCF pour des facteurs de risque du cancer du sein est faite pour indiquer des relations causales et générer les poids des facteurs. Pour construire des relations causales, la transformation des termes linguistiques à des valeurs numériques sont utilisé. La méthode du centre de gravité et de l'approche des experts est utilisée pour construire la matrice des poids des facteurs de risque du cancer du sein. Le chapitre 6 présente une analyse de scénario pour proposer des actions de prévention et de protection contre le cancer du sein. L'étude est conclue dans le chapitre 7.

Mots-clés: *Décision Médicale, le Cancer du Sein, Carte Cognitive Floue*

ÖZET

Kanser günümüzün en önemli sağlık sorunlarından biridir. Sık görülmesi ve yüksek ölüm oranı nedeniyle, 1970 yılında ölüm nedeni bilinen hastalıklar arasında dördüncü sırada yer alırken şimdi kalp hastalıklarından sonra ikinci sırada yer almaktadır.

Meme kanseri sebebiyle ölen kişilerin oranı 1990 yılından 2001 yılına kadar %2,3 gerilemiştir; bunun sebepleri arasında hastalık hakkındaki farkındalık, erken teşhis ve tedavi yöntemleri, toplumun bilinçlendirilmesi olarak sıralayabiliriz. Fakat meme kanseri tedavisi pahalı bir tedavidir ve uzman doktor, özel bakım gibi kısıtlı kaynakların kullanılmasını gerektirir bu da sadece bireylere değil; devlet yönetimine de ekstra yük getirmektedir. Tüm bu sebeplerden ötürü meme kanserinin erken teşhis ve tedavisi toplum için büyük önem arz etmektedir.

Bu çalışmada Bulanık Bilişsel Haritalama (BBH) ile onkologlara meme kanserine sebep olan değiştirilebilir ve değiştirilemeyen risk faktörlerinin hastalığa olan katkısının numerik değerlerle ortaya konması ve aksiyon alması gereken alanını belirlemeye yardımcı olması hedeflenmiştir.

Bu araştırmada koruyucu ve önleyici tedbirler üzerinde durulacaktır. BBH sonucunda onkologların öncelikle bakacağı risk faktörlerinin bulunması ile meme kanserinden korunma ve önlemeye yönelik tavsiyelerinin kalitesi artacaktır.

Tıbbi karar sistemleri kompleks sistemlerdir ve birbiri ile alakalı alakasız bir çok alt sistem barındırır. Üstelik bu alt sistemler klinik karar vermeyi zorlaştırarak hastalık hakkında doğru teşhis ve tedavi yönteminin bulunmasını zorlaştırır. BBH yöntemi alt sistemlerin birbiri ile olan ilişkisini incelediğinden tıbbi karar verme sistemlerine oldukça uygundur.

Bu çalışmada meme kanseri uzmanlarının görüşleri alınarak temel meme kanseri risk faktörleri belirlendi ve bunlar arasındaki ilişkiler BBH ile ağırlıklandırıldı. Daha sonra önleyici ve koruyucu aksiyonlar sunuldu.

Bir sonraki kısımda meme kanserine etki eden ve değiştirilebilir ve değiştirilemez diye ayırdığımız risk faktörleri açıklanacak. Üçüncü kısımda ise BBH'nın temel konseptleri açıklanacak. BBH yapılandırılırken uzman görüşüne dayanan bir yol izlenmiştir. Dördüncü kısımda BBH yapılandırılması ve üç farklı uzmanın görüşlerin kombinlenmesi açıklanmıştır. Beşinci kısımda ise meme kanserine etki eden risk faktörlerinin kendi içinde ve birbirleri ile olan ağırlıkları bulunmuştur. Altıncı kısımda senaryo analizleri ile değiştirilebilir ve değiştirilemeyen risk faktörlerinin ağırlıkları değiştirilerek önem kazanan risk faktörleri hesaplanmıştır ve yedinci kısımda bu sonuçlar göz önünde bulundurularak önleyici ve koruyucu yöntemler önerilmiştir.

Anahtar Kelimeler: *Tıbbi Karar Verme Sistemleri, Meme Kanser, Bulanık Bilişsel Haritalama*

1. INTRODUCTION

Cancer is the most important health problems nowadays. Due to the frequent occurrence and high level of fatality, it was ranked four among known cause of death in 1970's but now it is ranked second after the cardiovascular disease. It may be regarded as a single disease; actually cancer is often a complex group of diseases that affect the cell tissues and organs.

Breast cancer has the highest second incidence rate in the world after the lung cancer and it is the leading cause of death from cancer in women (Scwartz et al., 1999; Parkin et al., 2002). Breast cancer incidence and mortality may have conversion in different geographical areas. Though developed countries report higher rates of breast cancer incidence and mortality, changes in the incidence of breast cancer are most dramatic in low-middle income countries (LMC) including Turkey (Kim et al., 2007).

Breast cancer incidence has increased in Turkey and the estimated number of breast cancer cases was 44,253 in 2007 (Tuncer, 2008). The distribution of breast cancer incidence varies significantly among different regions of Turkey due to geographical, economic, social, and cultural factors. The breast cancer incidence in Western Turkey (50/100,000 in 2000) is more than two times that of Eastern Turkey (20/100,000) (Ozmen V., 2008).

Overall breast cancer mortality declined 2.3% annually between 1990 and 2001 because of advances in awareness, detection, protection and treatment (American Cancer Society, 2006). However it is well known that breast cancer has expensive treatment also needs to use of limited resources. All of these bring burden on not only patients but also government. Thus originating strategies against breast cancer prevention, protection and treatment have crucial value.

In this study, we propose Fuzzy Cognitive Map(FCM) model that can help breast cancer oncologists to better identify and evaluate the weights of modifiable and non-modifiable factors that are contributing to the occurrence of breast cancer in their patients. Here we divide the patients into three different categories; healthy, risky and sick. In that paper we will focus on preventive and protective actions. The results of the FCM will allow better understanding of several root causes, so oncologists can improve their prevention and protection recommendation. There is no comprehensive model is available to serve this purpose yet.

Building a mathematical model to identify the illness has previously been advocated using statistical model (Yong Xu, et al., 2011), generalized linear models (Zilin Li, et al., 2012) and so on. However the model need to be specified by a set of differential equations derived from quantitative datasets and this builds several issues. Firstly, quantitative data has been reported in very different units by cancer researchers and the lack of consistency in units makes it challenging to combine these reports in a dataset from which equations could be derived, regardless of whether these equations would specify a rate of change or the strength of interactions (Giabbanelli et al., 2012).

Fuzzy Cognitive Map is relatively new soft computing approach that uses existing experience in the operation of a complex system and compound fuzzy logic and neural networks. Another very useful property of FCM is to enable to use several expert opinions, giving the opportunity to predict the degradation of a product. FCMs can successfully represent knowledge and human experience, introducing concepts to represent the “essential elements and the cause and effect relationships among the concepts to model the behaviour of any system.

Medical decision systems are complex systems that can be decomposed to non-related and related subsystems and elements, where many factors have to be taken into consideration that may be complementary, contradictory, and competitive; these factors influence each other and determine the overall clinical decision with a different degree. Thus, FCMs are suitable for medical decision support systems. In this paper we combined the opinions of the breast cancer experts with the help of FCM and main risk

factors are put in order then relation among these factors are brought out. Then propose preventive and protective actions against Breast Cancer.

This thesis is organized as follows: The next chapter presents an overview to breast cancer and reviews the modifiable and non modifiable risk factors for breast cancer. In chapter 3, the base concepts of FCM are defined. In the study, for the construction of Fuzzy Cognitive Map (FGM), experts based method is used. Chapter 4 presents the construction process of FCM. The basic definitions of FCM, such as three main steps to create FCM, the construction of Initial Matrix of Supporting, Aggregated Matrix of Supporting Factors and lastly Weight Matrix of Supporting Factors, are described. In chapter 5, the application of FCM to breast cancer risk factors is done to indicate casual relatonship and generate the weights of factors. To construct casual relationship, the mapping of linguistic terms to numerical values is used. Centre of Gravity method and experts approach is determined in Weigth Matrix of Breast Cancer Risk Factors. Chapter 6 presents a scenario analysis to propose the preventive and protective actions against breast cancer. The study is concluded in Chapter7.

2. AN OVERVIEW TO BREAST CANCER

Breast cancer forms in tissues of the breast, usually the ducts (tubes that carry milk to the nipple) and lobules (glands that make milk). It occurs in both men and women, although male breast cancer is rare (www.cancer.gov, 2013). Breast cancer is ranked third among all cancer types.

Breast cancer is the most common form of cancer diagnosed among women in the United States, with approximately 270,000 new cases forecast for the year 2005 (American Cancer Society, 2005). Estimated new cases and deaths from breast cancer in the United States in 2013 for new cases are 232,340 and deaths 39,620 (www.cancer.gov, 2013). Similar results are valid for Turkey. Breast cancer is the deadliest cancer types among women (Turkish Health Ministry, 1996).

Breast cancer is the most common female cancer and the second most common cause of cancer death in women. The etiology of breast cancer has great number of factors. Most breast cancer risk factors relate to gynaecological or endocrine events in a women's life (McPherson et al., 2000). The risk factors for breast cancer can be divided into "factors that cannot be modified" and "Life style related factors that can be modified".

Non modifiable factors can be counted as breast density, benign breast disease, menarche age, menopause, BRCA1/2 genes, TP53, family history, height, nullparity, sporadic. Modifiable factors also can be counted as oral contraceptive usage, body mass index, social class, meat intake, alcohol consumption, time interval in pregnancy, abortion, early maternal age, late maternal age, hormone replacement therapy, breastfeeding, age at first birth, radiation, taking aspirin, underarm cosmetics, smoking.

2.1 Factors That Can Not Be Modified

2.1.1 Breast Density

Mammography is the widely used cancer detection device for the breast cancer. On the other hand breast density causes complexity in detection breast cancer. When the breast density increases, the correction detection rate in other words mammography sensitivity decreases (Kerlikowske et al., 1996). As it can be understood, when the breast is getting denser, it will be more difficult to see breast tumours due to the reduced radiolucency of dense parenchymal tissue (Crest et al., 2006). According to Boyd et al. (2007) women who have mammographic breast density are 4-5 times riskier than others. Moreover Crest et al., (2006) claimed that having a family history of breast cancer was associated with an increase in the odds of having dense breasts. They revealed stronger association when the affected relatives were more genetically similar and/or were diagnosed with breast cancer at an earlier age.

2.1.2 Benign Breast Disease

It is assumed that benign breast disease (BBD) is a very important risk factor for the subsequent breast cancer (Schnitt et al., 2004). BBD may itself have a heritable component, with deficient DNA repair genes exerting influence before BBD; the association between BBD and variant alleles in DNA repair genes was significantly stronger among women with a family history of breast cancer.

2.1.3 Menarche Age

The time period between menarche and first full term pregnancy had the highest rate of breast tissue aging thus this time interval was the time when the breast tissue was most vulnerable to mutagenesis (Colditz and Frazier, 1995). Based on this, early menarche cause earlier exposure to cycling endogenous hormone and leads to increase the risk of breast cancer (Kopans,1998). Buttler et al., 2000 claim that early breast cancer risk

increases with earlier ages at menarche, although subjects with very early ages (<12) were at an attenuated risks.

2.1.4 Menopause

Age specific occurrence rates for female breast cancer rise rapidly until age 50 years and goes on escalating at a slower rate (Anderson et al., 2006). On the other hand Dixon and Sainsbury, (1998) claimed that women who have a natural menopause after the age of 55 years have twice the risk of developing breast cancer compared to women whose menopause occurs before the age of 45, but those women who undergo a bilateral oophorectomy before the age of 35 have a 40% higher risk than those who have a natural menopause

2.1.5 BRCA 1/2 Genes

BRCA1 and BRCA2 genes are classified as tumour suppressor genes and they have capability to disrupt the function of BRCA protein product thus they can affect the risk for malignant disease (Brankovic et al., 2012). BRCA1 and BRCA2 mutation carriers have high lifetime risk of breast cancer (Scott et al., 2003). Intensive screening of breast is recommended to mutation carriers and first degree relatives (Struikmans et al., 2008). However some studies proved that rare but high-penetrance germline mutations in BRCA1 and BRCA2 explained only about 2-4% of breast cancer incidence in the general female population (Easton, 1999).

2.1.6 TP 53

Extensive studies have revealed genetic polymorphisms in genes involved in the repair of DNA damage and cell cycle control played an important role in the development of breast cancer. TP 53 is counted as tumour suppression gene that responsible from maintenance of genomic stability, DNA repair, cell cycle regulation and apoptosis (Naidu et al., 2011). Schmidt et al., 2009 claim that although combination of MDM2

SNP309 and TP53 R72P does not have contribution to the breast cancer this combination affects onset age and survival of breast cancer.

2.1.7 Family History

The risk of developing breast cancer is higher among women whose close blood relatives have breast cancer. The term “hereditary cancer” refers to cancer associated with specific germ-line mutations in highly penetrant genes which are inherited as a Mendelian trait, whether through an oncogene, a tumour suppressor gene or a DNA repair gene (Barankovic et al., 2012). It is estimated that 22% of individuals have a family history that suggests familial or hereditary predisposition to cancer (Scheuner MT, et al., 2010). Family history is counted as strong breast cancer risk since 1970’s (Anderson, 1972). According to Swanson (1998) younger women with both a mother and sister with breast cancer had a ten times increased risk of developing the breast cancer themselves. In this group the risk elevates up to 50% by the age of 65. Family history is an important risk factor for breast cancer. Having one relative who has breast cancer increases breast cancer risk 1,8 times, if person has two relatives who have breast cancer this risk upgrade 2,9 times (Lancet, 2001).

2.1.8 Height

Epidemiological studies have revealed that taller people are at increased risk of cancer, but it is ambiguous if height –associated risk vary by cancer site (Green et al., 2011). Height, menarche age, breast tissue maturation are affected by the endocrinological modifications during prepubertal and adolescent life, that can be critical for the development of breast cancer in life (Hunter and Willett, 1993). This concept is also controversial. Swanson et al., (1996) conduct a direct relationship between height and breast cancer. According to this study the woman who is higher height than 167cm 46% riskier than a woman who is smaller than 159 cm. On the other hand, another important research presented no association with height, overall or in specific risk factor subgroups (Zhang et al., 1996).

2.1.9 Nullparity

Several cohort studies of infertile women have reported an incidence of breast cancer similar to that of the general population (Cetin et al., 2008). Nulliparous women have declined breast cancer risk prior to age 35 years and then increased risk thereafter (Pathak, 2002). According to Terry et al. (2006), infertility due to ovulatory disorders and incidence of breast cancer found a significantly lower breast cancer risk in women who have infertility than who did not have infertility.

2.1.10 Sporadic

Breast cancer can appear as sporadic, familial and hereditary. The big parts of breast cancer are accepted as sporadic in patients with no cancer history in the family. The incidence of sporadic breast cancer rises in women over 50 years old (Brankovic et al., 2012). Moreover nearly 80% of breast cancer cases are thought to be sporadic with no associated family history (Pruthi et al., 2010).

2.2 FACTORS THAT CAN BE MODIFIED

2.2.1 Body Mass Index (BMI)

Heavier body size is measured by body mass index (BMI). Overweight and obesity are clearly associated with increased risk for developing many cancers, including cancers of the breast in postmenopausal women, although knowledge about the relationship between weight loss and cancer risk is incomplete, recent studies suggest that losing weight may reduce the risk of (post-menopausal) breast cancer (American Cancer Society, 2013). The reason of this can be explained because of high levels of adiposity that leads to the production of excess levels of circulating endogenous estrogens that in turn raise mammary carcinogenesis (Paffenbarger et al., 1980, Ballard-Barbash, 1994). Also according to Torio et al., (2010) BMI change is a valid prognosticator of breast cancer incidence after altering with age, individual and contextual social class indicators, and rural residence. On the other hand surprisingly, premenopausal

overweight and obese women have reduced levels of estradiol during the anovulatory cycles, conferring decreased breast cancer risk.

2.2.2 Social Class

It is widely accepted that women who belong to high social class are more likely to be older at first give birth, intend to have very few children and to be older at menopause (WHO, 1997; Kelsey et al., 1993; Krieger, 1989). On the other hand the study of Torio et al. could not completely respond even if the effect of social class on breast cancer risk works exclusively through reproductive behaviours. Thus, although reproductive factors important, this cannot simplify the current relationship between social class and breast cancer.

2.2.3 Meat Intake

Meat is unavoidable nutrition source for human. According to the study of Ferrucci et al. (2009), among 1205 invasive breast cancer incidences, women in the highest quintile of red meat intake were slightly younger, less educated, less likely to have family history of breast cancer. Also it is not surprising that women who are consuming more red meat, have higher BMI, energy and fat intakes. The importance of this study is that they found positive relation between red meat and postmenopausal breast cancer, while there is no association between processed meat, white meat or individual meat items. On the other hand, another prospective study of Larsson et al. (2009) examined the association of meat intake with incidence of breast cancer defined by oestrogen receptor(ER) and progestrogene receptor (PR) status. They concluded that there is no relation between total red meat, fresh red meat or processed meat intake with breast cancer risk. On the other hand taking pan-fried meat was positively associated with a risk of ER+/PR- breast cancer.

2.2.4 Alcohol Consumption

Alcohol consumption is known one of the few modifiable factors that increasing breast cancer risk. Alcohol consumption raises level of ostradiol serum and it is shown that taking one or two glass of alcohol increases the breast cancer incidence 30-50% (Terry et al., 2006). Also, according to Berkey and her colleagues work is parallel to the Schnitt et al.'s study, suggest that regardless of the exact nature of family history (BC in her mother, aunt, or grandmother, or biopsy-confirmed BBD in her mother), that avoiding alcohol intake during adolescence may reduce her risk of BBD as a young woman, which likely reflects reduced risk of BC.

2.2.5 Oral Contraceptive Usage (OCs)

Oral contraceptive is highly common birth control method among women. It is demanded because of highly effective, safe, cheap so advantageous for great amount of women. In earlier studies showed that there was a relation between OCs and breast cancer due to high level of estrogen dose and older progestin OC formulation (Kahlenborn et al., 2006). However Wingo et al. (2007) revealed no association between breast cancer mortality and OC use when duration of OC us, time since first use, and use of specific formulations were examined among 4200 breast cancer patients.

2.2.6 Abortion

The maternal hormonal milieu and its potential effect on breast cell proliferationand differentiation are likely to differ by type of abortion. In a viable pregnancy, human chronic gonadotropin, serum estrogen, and serum progesterone levels rise to predictable levels early in pregnancy (Lichtman et al., 1990, Deutchman, 1991). Thus, induced abortion usually interrupts the increasing hormone levels present in a viable pregnancy. Spontaneous abortion occurs when the embryo is nonliving or the pregnancy is abnormal occurs when the embryo is nonliving or the pregnancy is abnormal. Women who have spontaneous abortions and women who undergo induced abortions appear to have different demographic and reproductive characteristics that are independent risk

factors for breast cancer (Daling et al., 1994, Calle et al., 1995). According to Carroll, 2002 induced abortion was the most important risk factor breast cancer not only British but also Swedish women older than 45 years. Moreover Ymeri et al., 2010 support this idea also they offer that the time month when the pregnancy was interrupted is important factor. On the other hand Collaborate Group on Hormonal Factors in Breast Cancer claims that the totality of the worldwide epidemiological evidence points out that pregnancies ending as either spontaneous or induced abortion does not have negative effects on women's current risk of developing breast cancer.

2.2.7 Time Interval in Pregnancy

Pregnancy has a vital importance for women not only for emotional feelings but also physical returns. The first pregnancy had a significant role in the maturation of the breast resistance against carcinogenic influences (Russo et al, 1994a, 2005). According to Kauppila et al,(2009) short birth interval between first and second birth was significantly associated with increased risk of advanced ductal cancer in young grand multiparous mothers. In the beginning of second pregnancy, abnormal cellular changes owing to the potential for breast cancer development. Alternatively, the long-term joint stimulatory actions of placental hormones (estrogens and progesterone) and prolactin during two closely consecutive pregnancies may serve as initiators for malignant transformation of epithelial breast cells.

2.2.8 Early Maternal Age

It is well established that childbirth affects a woman's breast cancer risk (Wohlfahrt and Melbye, 2000). It is assumed that breast cells tend to carcinogenic stimuli before a first pregnancy and that growth and protection of breast cells occur during the time of a first pregnancy, early age childbearing reduces the risk of breast cancer, because it shortens the nulliparous period (Kelsey et al., 1993). According to Wohlfahrt and Melbye, (2000) all childbirths result in a long term reduction in maternal breast cancer risk if the woman delivers at an early age. Another prospective research examined breast cancer risk based on median age at first birth revealed a 3,5 times higher relative risk in women

with a median age of 41 at first birth when compared with a median age of 23 at first birth (Lagiou et al., 2003).

2.2.9 Late Maternal Age

First full term births to women 35 years of age and older age generally considered to reflect older age at first birth (Merril et al., 2005). Research indicates late age childbearing is directly related to raise breast cancer risk. It is assumed that nearly 30% of breast cancers in the U.S. women were attributed to later age at first birth and/or nullparity (Merril et al., 2005). According to Newcomb et al., 2011 women with later childbirth were more likely to develop ductal, lobular and mixed ductal-lobular breast cancer than women who had children at early ages.

2.2.10 Age at First Birth

Large case-control study of Newcomb et al, 2010, women with earlier childbirth were less likely to develop ductal, lobular, and mixed ductal-lobular breast cancer than women who had children at later ages or remained nulliparous.

2.2.11 Hormone Replacement Therapy (HRT)

The main aim of prescribing HRT is to increase not only quality but also duration of life in post-menopausal women (Fenton A., 1996). Women's Health Initiative (WHI) and MillionWomenStudy (MWS) announce that the increase of breast cancer cases begins immediately after the initiation of the HRT. If HRT would really cause breast cancers, the rise in incidences would be expected to come out much later (Dietel, 2009). As a result there has been enough exploration to create a consensus that that short-term HRT use, i.e. below 5 years, does not increase breast cancer risk (Grady et al., 1992, Colditz et al., 1995). The risk appears to increase with long-term use in 'older' women (>30 years) (Colditz et al., 1995).

2.2.12 Breastfeeding

Many important studies proved that there is a direct relationship between decreased developing breast cancer and breast feeding (Morris GJ, 2009). In other words the risks of breast cancer are higher in women who do not breastfeed, and these risks are inversely associated with the duration of breastfeeding (Eglash et al., 2008). According to a review of 47 epidemiological studies from 30 countries (Lancet , 2002) concluded that an average fewer pregnancies and that the relative risk of breast cancer was independently shown to decrease by 4.3% for every 12 month of breastfeeding.

2.2.13 Radiation

Exposure to radiation is controversial issue for breast cancer. It is claimed that if she was exposed to radiation between age 10-14, breast cancer risk increased (John, 1993). Also premenopausal mammography with early and repeated exposure is a contested breast cancer risk factor. It is known that repeated x-rays promote DNA damage in breast tissue and breast compression from the mammography plates has been found to create breast trauma thus breast thermography and MRI can be counted as safer alternative to x-rays (Vanderhaeghe, 2004).

2.2.14 Taking Aspirin

Bosco, 2011 claimed that regular usage of aspirin more than 5 years reduce the breast cancer risk moreover The Women‘s Health Initiative Observational Study observed decreased risk of breast cancer for regular aspirin use for more than 5 years of duration.

2.2.15 Underarm Cosmetics

Modern social life force the people being presentable and because of this requirement women are exposed to use underarm antiperspirants, deodorants, body lotions, breast

firming, cellulite cream etc. Unfortunately the effects of long term low dose exposure to these creams that contain multiple chemical are unknown.

2.2.16 Smoking

Bennicke et al, 1995 supported that the smoking increase the risk of breast cancer. Moreover limited but accumulating evidence suggests that long-term, heavy smoking increases the risk of breast cancer, particularly among women who began smoking at an early age (Reynolds, 2012). On the other hand Baron et al., 1996 claimed that smoking does not have any effect on breast cancer.

All the counted non modifiable and modifiable concepts of breast cancer are shown in Figure 2.1.

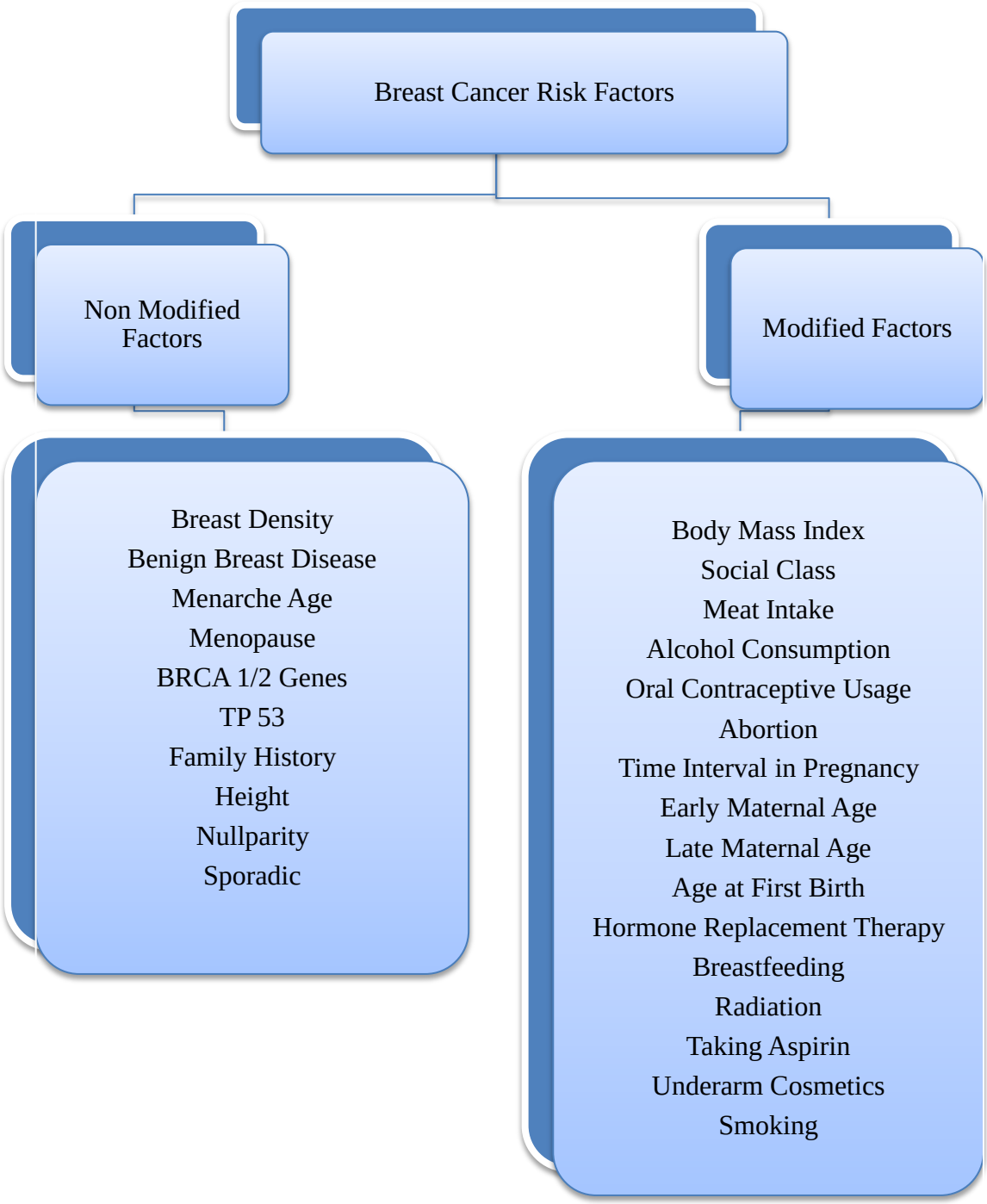

Figure 2.1 Non modifiable and modifiable concepts of breast cancer

3. OVERVIEW OF FUZZY COGNITIVE MAP

3.1 Cognitive Map

3.1.1 Definition of Cognitive Map

Cognitive Maps (CMs) were introduced by Tolman (1948) in his cognitive psychology research but as a modelling tool for decision making, first practical application was done by Axelrod (1976) in politics.

CMs are a type of directed graph that offers a means to model interrelationships or causalities among concepts; there are various forms of CMs, such as signed digraphs, weighted graphs, and functional graphs. The differences amongst these various forms can be found in Kardaras and Karakostas (1999).

The use of simple binary relationships (i.e., increase and decrease) is done in a *conventional* (crisp) CM. CMs have a clear way to visually represent causal relationships, they expand the range of complexity that can be managed, they allow users to rapidly compare their mental models with reality, they make evaluations easier, and they promote new ways of thinking about the issue being evaluated (Ross, 2010)

3.1.2 Concept Variables and Causal Relations of Cognitive Map

CMs graphically describe a system in terms of two basic types of elements: concept variables and causal relations. Nodes represent concept variables, Ci, where i = 1, . . .,N. A concept variable at the origin of an arrow is a cause variable, whereas a concept variable at the endpoint of an arrow is an effect variable. For example, for $Cj \rightarrow Ci$, Cj is the cause variable that impacts Ci , which is the effect variable. Arrows represent the causal relations between concept variables, which can be positive or negative.

Although they are easy to use, CMs have trouble while quantifying casual relationships among variables. CMs have lack of capability to differentiate the strength of relationships, it just express the relation positively or negatively. Also every node just makes its decision according to the number of positive impacts and the number of negative impacts; thus, a CM is an oversimplified model for many applications.

If one were to emphasize that the simple binary relationship of a CM needed to be extended to include various degrees of increase or decrease (small decrease, large increase, almost no increase, etc.), then an FCM is more appropriate.

3.2 Fuzzy Cognitive Map

3.2.1 Definition of Fuzzy Cognitive Map

An FCM extends the idea of conventional CMs, that are using fuzzy weights by using linguistic representation with an associated fuzzy set, instead of binary variables. Extensions by Taber (1994) and Kosko (1992) allow fuzzy numbers or linguistic terms to be used to describe the degree of the relationship between concepts in the FCM.

FCMs can display successfully the knowledge and experience of the experts by defining important elements as concepts and cause and effect relationship among these concepts to understand the behaviour of the system.

3.2.2 Fuzzy Cognitive Map Applications

FCM has been widely used in modelling and preparing decision supportive systems tool in different scientific and managerial problems. FCMs allow focusing on many areas such as earth and environmental sciences (Fons et al., 2004; Ozesmi and Ozesmi, 2003), engineering (Pelaez and Bowles, 1996; Subramanian and Dagli, 2003), economics, business and management (Kardaras and Karakostas, 1999; Carvalho and Tome, 2004), entertainment (Parenthoen et al., 2002).

The medical decision process is complex because data collection is hard and combination of this data vogue, conflicting or tough to interpret. In that stage FCM helps to overcome these difficulties and it has been used many different research areas in medicine. the Table 3.1. shows the authors and objective of their study in medical decision.

Table 3.1 The authors and objective of their study in medical decision

Authors	**Objective of the Study**
Papageorgiou et al., 2002	Estimate the radiation dose
Innocent & John, 2004	Estimation of the stage of a disease
Papageorgiou et al., 2007	Brain tumor characterization
Stylios and Georgopoulos, 2008	Support the speech therapist in the diagnosis process
Froelich et al., 2012	The long-term prediction of prostate cancer

3.2.3 Properties of Fuzzy Cognitive Map

Fuzzy Cognitive Maps (FCMs) include concept nodes and weighted arcs that are graphically showed as a signed weighted graph with feedback. Signed weighed arcs, connecting the concept nodes, display the causal relationship that exists among concepts. Generally, concepts of a FCM, represent key-factors and characteristics of the modeled complex system and stand for: events, goals, inputs, outputs, states, variables and trends of the complex system been modeled (Glykas, 2010).

Fuzzy cognitive map is a causal knowledge-driven methodology for modeling complex decision systems, come out from the combination of fuzzy logic and neural networks (Kosko, 1986). A FCM describes the behavior of a knowledge based system in terms of concepts; each concept represents an entity, a state, a variable, or a characteristic of the system (Kosko, 1992).

Concepts variables are represented by nodes and this set can be shown like C = {C1,C2, . . . ,Cn}. Arcs (Cj,Ci) are used to define causal links between concepts; that is how concept Cj causes concept Ci. Causality between concepts allows degrees of causality and not the usual binary logic, so the weights of the interconnections can range in the interval [-1,1] or linguistic terms, such as "negatively very strong", "zero", "positively weak" etc. **Figure 3.1** illustrates the graphical representation of a simple FCM. Relationships between concepts have three possible types; if $w_{ij} > 0$, positive causality between concepts Ci and Cj, if $w_{ij} < 0$, negative causality between concepts Ci and Cj, if $w_{ij} = 0$, no relationship between concepts Ci and Cj.

The sign of w_{ij} indicates whether the relationship between concepts C_i and C_j is direct or inverse. The direction of causality indicates whether concept C_i causes concept C_j , or vice versa. These parameters have to be considered when a value is assigned to weight w_{ij}.

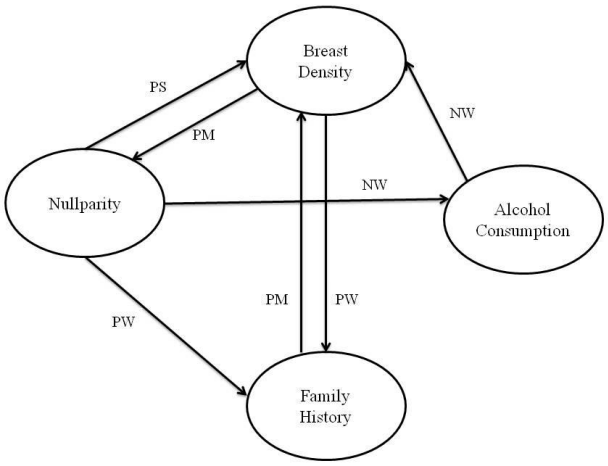

Fig. 3.1 The graphical representation of a simple FCM

The value of each concept is calculated, computing the influence of other concepts to the specific concept, by applying the following calculation rule:

$$A_i^{(k+1)} = f\left(\sum_{\substack{J=1 \\ J\neq i}}^{N} A_j^{(k)} w_{ji} \right) \quad (3.1)$$

where Ai(k) being the value of concept Ci at iteration step k, Aj(k-1) the value of the interconnected concept Cj at iteration k-1, wij the weighted arc from Ci and Cj and f a threshold function.

Two threshold functions are usually used. The unipolar sigmoid function where $\lambda > 0$ determines the steepness of the continuous function $f(x)=1/(1+e-\lambda x)$. When concepts can be negative and their values belong to the interval [-1, 1] like in our case, function $f(x)= tanh(x)$ is used. This method accepts negative values for one concept i.e. there is a concept named "decision" that can take negative values to describe the wrong decision and positive values to describe the right decision. In the latter the values of concept belong to the interval [-1,1] (Stylios and Groumpos, 2004). The system is free to interact. This transaction continues until the model:

- Reaches equilibrium at a fixed point, with the output values, being decimals in the interval, stabilizing at fixed numerical values.
- Exhibits limit cycle behavior, with the output values falling in a loop of numerical values under a specific time period.
- Exhibit a chaotic behavior, with each output value reaching a variety of numerical values in a nondeterministic, random way. **Figure 3.2** visualize transaction behaviour (Yaman, 2010).

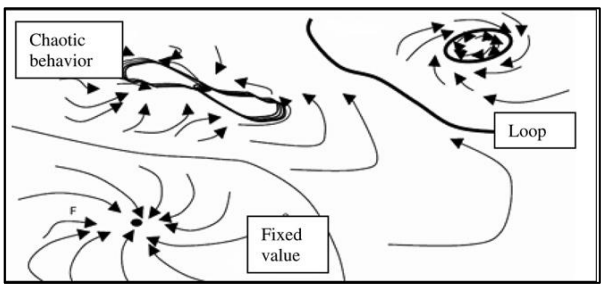

Figure 3.2 Transaction behaviour

4. CONSTRUCTION OF FUZZY COGNITIVE MAP

4.1. Overview

FCM is powerful machinery for modelling of dynamic systems. It defines a system as a collection of interconnected concepts where connections reflect cause-effect relationships between the concepts. It has a convenient graph representation, which consists of nodes (concepts) and weighted casual edges (relationships) representing knowledge that is easy to visualize and manipulate (Aguilar, 2005).

Following that, this thesis will focus on following chapters by designing of FCMs models, including deciding on the concepts relevant to a given system and defining relationships (weights) between the selected concepts, according to expert based method.

According to Stylios and Groumpos (2004), three main steps are required for creating FCM. First one is Initial Matrix of Supporting Factors (IMS), second one is Aggregated Matrix of Supporting Factors (AMS), and lastly Weight Matrix of Supporting Factors (WMS). Detailed representation can be found in **Figure 4.1**.

4.2. Creating Fuzzy Cognitive Map

4.2.1 Initial Matrix of Supporting Factors (IMS)

In this chapter expert-based methods and explanation of the steps that are performed by an expert to create an FCM model will be explained.

Experts based development of FCM depends on human expertise and domain knowledge (Stach et al., 2010). The experts are also required to have a solid knowledge of the FCM theory to understand the meaning of the weights and the direction of the

causal effects. In order to increase credibility of the model, a group of experts instead of a single person may be involved in the development process.

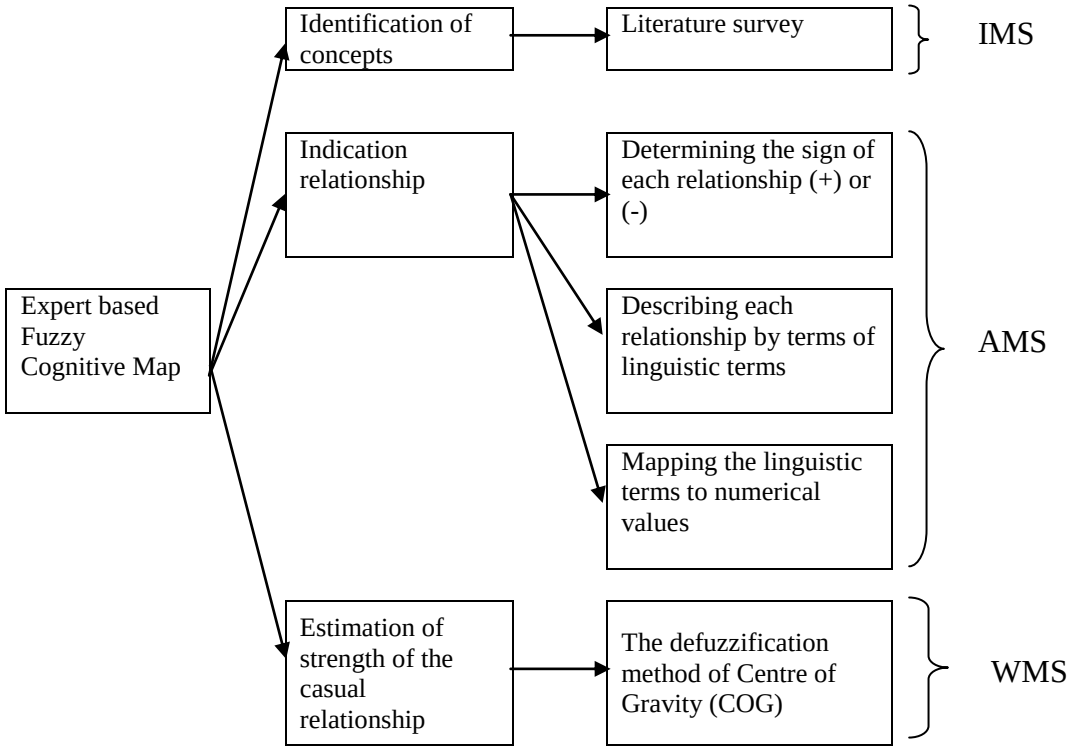

Figure 4.1 Flow chats of creating FCM

Experts can work together or design individual maps that represent their own understanding of a given system. In the latter case the individual maps can be combined into a single model (Glykas, 2010). In our case we combined 3 experts viewand will be presented section 5.

While creating Initial Matrix of Supporting Factors, concepts can be written by experts or created with literature survey. In that thesis concepts are written by literature survey.

4.2.2 Aggregated Matrix of Supporting Factors (AMS)

In that step relations between concepts are defined. As we stated before, important concepts were identified by making deep and long literature survey. Then indication of casual relationship among defined concepts can be divided into three steps. (Kosko 1986, Khan and Quaddus 2004). **Figure 4.2** shows the steps of Aggregated Matrix of Supporting Factors.

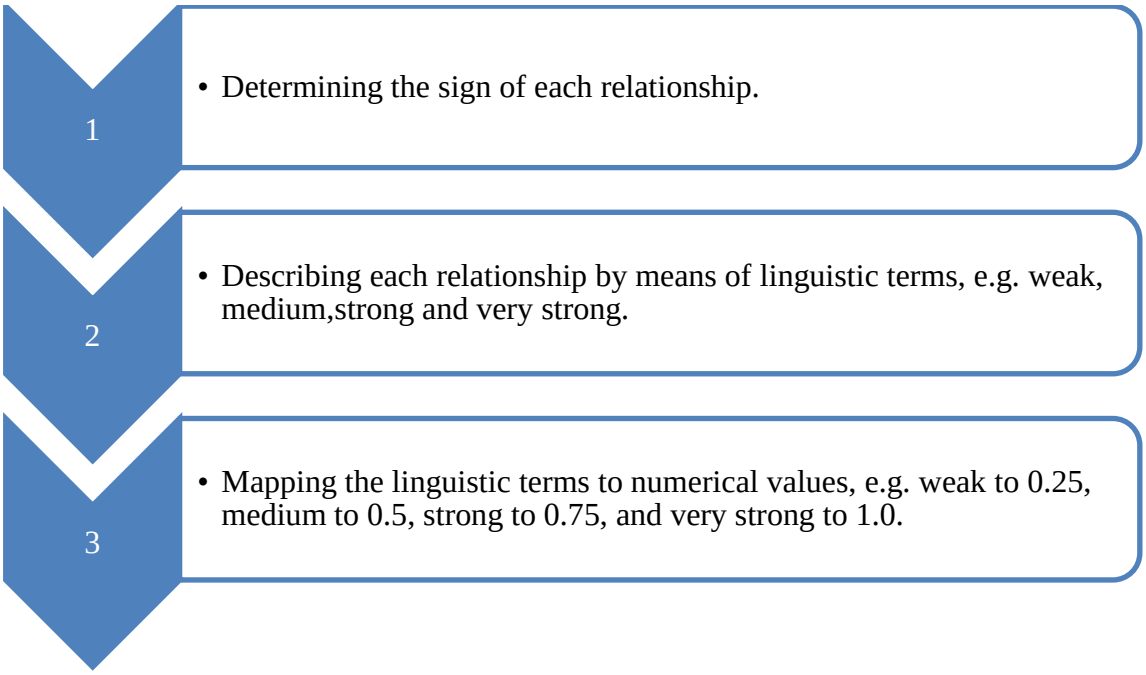

Figure 4.2 shows the steps of Aggregated Matrix of Supporting Factors

4.2.3 Weight Matrix of Supporting Factors (WMS)

When the estimation of strength of the casual relationship is finished, all the linguistic variables are considered and an overall linguistic weight is obtained, which transformed to a numerical weight with the defuzzification method of Centre of Gravity (COG) (Jang, 1997).

5. APPLICATION OF FUZZY COGNITIVE MAP TO BREAST CANCER RISK FACTORS

Decision making in medicine is hard and complex due to the vast amount of medical interrelated data and different source of information. Therefore knowledge processing systems are used in medicine for the task of diagnosis, prognosis, treatment planning and decision support (Fayyad and Uthurusamy, 1996; Fayyad et al., 1996). In our study, for the construction of Fuzzy Cognitive Map, experts based method is used.

In this chapter expert-based methods and explanation of the steps that are performed by an expert to create an FCM model will be explained and it is also described how to combine multiple maps that are created by different experts for the same underlying system.

5.1 Initial Matrix of Breast Cancer Risk Factors

Breast cancer risk factors are determined based on deep literature survey. We decided to use 26 risk factors among various concepts; As a result, the dimension of the IMS will be 26x26. Initial Matrix of Breast Cancer Risk Factors is shown **Table 5.1** for one expert.

5.2 Aggregated Matrix of Breast Cancer Risk Factors

The negative or positive relationship among concepts will be determined in Aggregated Matrix of Breast Cancer Risk Factors. Thus each expert be able to determine the influence of one concept on another.

The indication of casual relationship among defined concepts can be divided into three steps. (Kosko 1986, Khan and Quaddus 2004). First one is determining the sign of each relationship. Our experts are highly specialized on medical oncology and they have

deep knowledge which elements of the systems have an effect on other elements; for the corresponding concepts they determine the negative or positive effect of one concept on

Table 5.1 Breast Cancer Risk Factors

#	Breast Cancer Risk Factors
1	Breast Density
2	Benign Breast Disease
3	Menarche Age
4	Menopause
5	BRCA 1/2 Genes
6	TP 53
7	Family History
8	Height
9	Nullparity
10	Oral Contraceptive Usage
11	Body Mass Index
12	Social Class
13	Meat Intake
14	Alcohol Consumption
15	Time Interval in Pregnancy
16	Abortion
17	Early Maternal Age
18	Late Maternal Age
19	Hormone Replacement Therapy
20	Sporadic
21	Breastfeeding
22	Age at First Birth
23	Radiation
24	Taking Aspirin
25	Underarm Cosmetics
26	Smoking

the others, with a fuzzy degree of causation. In this way, they turned their knowledge on a dynamic weighted graph, the FCM. Thus each expert determined the influence of one concept on another as ‘‘negative’’ or ‘‘positive’’.

While indicating casual relationship second step is evaluating the degree of influence using a linguistic variable for example “very”, “some”, “few”, etc. In our study, the causal interrelationships among concepts are explained using the variable *Influence* which is interpreted as a linguistic variable taking values in the universe U=[-1,1]. Its term set *T(influence)* is suggested to contain nine variables. Employing nine linguistic variables, our expert defined in detail the influence of one concept on another and could distinguish between different degrees of influence. The nine variables used like : *T(influence)* = { Negatively very strong (NVS), Negatively strong (NS), Negatively medium (NM), Negatively weak (NW), Zero (Z), Positively weak (PW), Positively medium (PM), Positively strong (PS), Positively very strong (PVS). The corresponding memberships functions for these terms are shown in **Figure 5.1** and they are: μ_{NVS}, μ_{NS}, μ_{NM}, μ_{NW}, μ_{Z}, μ_{PW} μ_{PM} μ_{PS} μ_{PWS}.

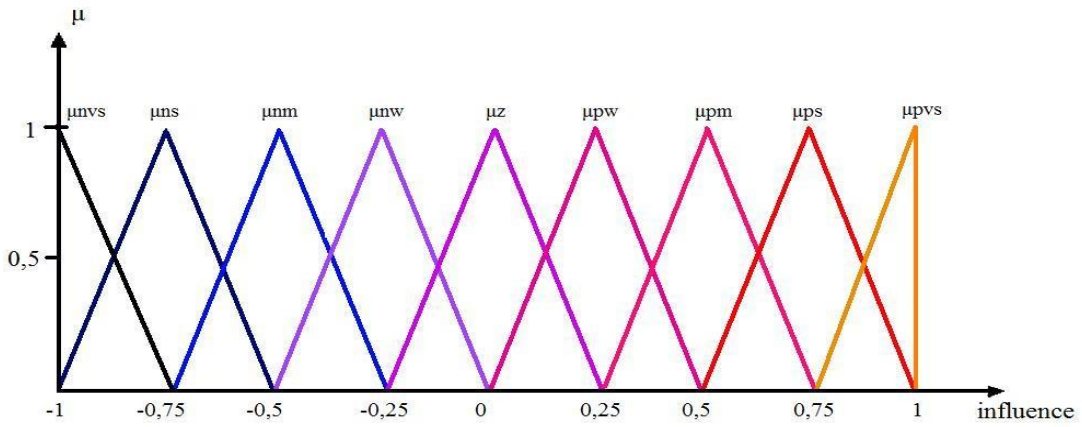

Figure 5.1 Membership functions for the linguistic variable influence (Stylios and Groumpos, 2004).

The sign of each relationship, relationship by means of linguistic terms and conversion from linguistic terms to numerical values according to first expert is shown **Table 5.2**, **Table 5.3**, **Table 5.4** respectively.

Third step of indicating casual relationship can be defined as mapping the linguistic terms to numerical values. In a simple FCM, all fuzzy variables are mapped into interval [-1, 1]. For example, positively weak is mapped to 0.25, negatively medium to -0.5, positively strong to 0.75 (Stylios and Groumpos, 2004).

Then, all the suggested by experts linguistic variables, are considered and an overall linguistic weight is obtained, which transformed to a numerical weight with the defuzzification method of Centre of Gravity (COG) (Jang, 1997). This approach has the advantage that experts do not have to assign numerical causality weights but to describe the degree of causality among concepts. Centre of Gravity method and experts approach will be determined in Weight Matrix of Breast Cancer Risk Factors.

5.3 Weight Matrix of Breast Cancer Risk Factors

Our experts have deep knowledge about cancer. One of them is working as a professor in Acıbadem Maslak Hospital, the other associate professor is working in Italian Hospital and the assistant professor is working in Edirne Government Hospital. All of them have solid background and great clinical experience in medical oncology, especially breast cancer. As we stated before, the concepts are prepared by making deep literature survey and they were given to the experts to evaluate the relation. The experts explained the degree of influence between the concepts and they determined the relationship among concepts by using if-then rule to reveal a linguistic weight representing the cause and effect relationship between each pair of concepts.

The three oncologist offered that the degree of influence between concepts was described by a linguistic variable taking value in [-1, 1] and its fuzzy set defined in Section 5.2, corresponds to a membership function shown in **Figure 5.1**. It is important that these membership functions have a finer distinction between grades in the lowest and highest end of the influence scale.

Table 5.2 The sign of each relationship in Breast Cancer Risk Factors according to Expert 1

	1	2	3	4	5	6	7	8	9	1	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
1		+	+	-			+	-	+		+	-	+	-	-	-	+	+	+		+	+	+			-
2	+		+	+	+	+	+	-	+		+		+	+		-	+	+	+		-	-	+			+
3	+			+	+		+	-	+		-	+	+	+	+	+	+	+			-	+				-
4	-	+	+				+	-	+		-	-	-	+	-	-	+	-	-		+	-	+			-
5		+				+			-						-			-								+
6		+			+				-		+							-					+			
7	+	+	+	+	+	+		+	+		+	+	+	+	+	+	+	+		+	-	+				+
8			-	+			+		-		-	+	+	-	+						+					-
9	+	+	+	+			+				-	+		-		-			-		+	+				-
1		+														-	-	+	+			-				+
11	+	+	+	-		+	+	+	+			+	-	+	+	-	+	-			-	+	+			-
12				+	+	+	+	+	+		-		+	+	+	+	-	+	+		-	-	+	+	+	+
13	+	+	+	+	+	+	+	+	-		+	+		-	+	+	-	+	-		+	-	+			-
14	-	+	-	-	-		+	-	-		+	+	-		-	+	+	+	-		-	+	+	+	+	+
15	+	-		+			-				+	+	+	-		+	-	-	-		-	+	+	-		+
16									-		-	+	-	+	-		-	+	-		-	+	+	-		+
17	-	+	+	+	+	+	-				+	-	-	+	+	+		+	-		-	+	-			+
18	+	+	+	-	-	-	-				+	+	+	-	-	-	-		+		+	-	+			-
19	+	+		+					-		+	+	+	-	-	-	-	-			-	-	+		+	-
2					-	-	-																			
21	-			+	-	-	-				-	-	-	-	-	-	-	-	-			+	-	-	-	-
22	-		+	+	-	-	-	-			-	+	+		+	+	+	-	-		-		-		-	+
23	+	+	+	-	+	+		-	+		-	+			-	+		-			-	-			-	-
24												+			-						-					+
25						+															-		-			
26	-	+	-	-		+	+	-	+		-	+	-	+	-	+	+	+	+		-	+	+	+	+	

Table 5.3 Relationship by means of linguistic terms in Breast Cancer Risk Factors according to Expert 1

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
1		pw	pw	nvs	z	z	ps	nw	pw	z	ps	nw	pw	nw	nw	nw	ps	ps	pvs	z	pw	pw	ps	z	z	nw
2	pm		pw	pm	pw	pw	ps	nw	pw	z	ps	z	pw	pw	z	nw	ps	ps	ps	z	nw	nw	ps	z	z	pw
3	pw	z		pw	pw	z	ps	nw	pw	z	ns	pw	ps	pw	pw	ps	pw	pw	z	z	nw	pw	z	z	z	nw
4	ns	pw	pw		z	z	ps	nw	pw	z	ns	nw	ns	pw	nw	nw	pw	nw	nw	z	pw	nw	ps	z	z	nw
5	z	pw	z	z		pw	z	z	nw	z	z	z	z	z	nw	z	z	nw	z	z	z	z	z	z	z	pw
6	z	ps	z	z	pw		z	z	nw	z	pw	z	z	z	z	z	z	nw	z	z	z	z	ps	z	z	z
7	pm	ps	pw	pw	ps	pw		ps	ps	z	ps	ps	pw	pw	pw	ps	ps	ps	z	pw	nw	ps	z	z	z	ps
8	z	z	nw	pw	z	z	pw		ns	z	ns	pw	pw	nw	pw	z	z	z	z	z	pw	z	z	z	z	nw
9	ps	pw	pw	pw	z	z	pw	z		z	ns	pw	z	nw	z	ns	z	z	nw	z	pw	ps	z	z	z	ns
1	z	pw	z	z	z	z	z	z	z	z	z	z	z	z	z	nw	nm	pm	pw	z	z	nw	z	z	z	pm
11	ps	pw	pw	nw	z	pw	pw	pw	pw	z		pw	nw	pw	pvs	nw	pw	nw	z	z	nw	pw	pw	z	z	ns
12	z	z	z	pw	pw	pw	pw	pw	pw	z	ns		pw	pw	pvs	pw	nvs	pvs	pw	z	nw	nvs	pw	pw	pvs	pw
13	pw	pw	pw	pw	pw	pw	pw	pw	nw	z	pw	pw		nw	pw	pw	nw	pw	nw	z	pw	nw	pw	z	z	nw
14	nw	pw	nw	nw	nw	z	pw	nw	nw	z	ps	pw	nw		nw	pvs	ps	pvs	nw	z	nw	pvs	pw	pw	ps	pvs
15	pw	nw	z	pw	z	z	nw	z	z	z	pw	pw	pw	nw		pvs	nw	nw	nw	z	nw	ps	pw	nw	z	pvs
16	z	z	z	z	z	z	z	z	nw	z	nw	pw	nw	ps	ns		nvs	pvs	nw	z	nw	pvs	pvs	nw	z	pvs
17	nw	pw	pw	pw	pw	pw	nw	z	z	z	pw	nw	nw	ps	ps	pvs		pvs	nw	z	nw	pvs	nw	z	z	ps
18	pw	pw	pw	nw	nw	nw	nw	z	z	z	pw	ps	pw	nw	ns	nw	nvs		pw	z	pw	ns	pw	z	z	nw
19	ps	ps	z	pw	z	z	z	z	nw	z	pw	ps	pw	nw	ns	nw	nw	nw		z	nw	nw	pw	z	pw	nw
2	z	z	z	z	ns	nm	nv	z	z	z	z	z	z	z	z	z	z	z	z		z	z	z	z	z	z
21	nw	z	z	pw	nw	nw	nw	z	z	z	nw	nm	nw	nm	nvs	nvs	nw	ns	nw	z		pw	nw	nvs	nw	ns
22	ns	z	pw	pw	nw	nw	nw	nw	z	z	nw	ps	pw	z	ps	pvs	pvs	ns	nw	z	nw		nw	z	nw	pvs
23	pw	ps	ps	ns	pw	ps	z	nw	ps	z	nw	ps	z	z	nw	pvs	z	ns	z	z	nw	ns		z	nw	nw
24	z	z	z	z	z	z	z	z	z	z	z	pw	z	z	nw	z	z	z	z	z	nw	z	z		z	pw
25	z	z	z	z	z	pw	z	z	z	z	z	z	z	z	z	z	z	z	z	z	nw	z	nw	z		z
26	nw	pw	nw	nw	z	ps	pw	nw	ps	z	ns	pw	nw	pvs	nw	ps	pvs	pvs	pw	z	ns	pvs	pvs	ps	ps	

Table 5.4 Conversion from linguistic terms to numerical values in Breast Cancer Risk Factors according to Expert 1

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
1		0,25	0,25	-1	0	0	0,75	-0,25	0,25	0	0,75	-0,25	0,25	-0,25	-0,25	-0,25	0,75	0,75	1	0	0,25	0,25	0,75	0	0	-0,25
2	0,5		0,25	0,5	0,25	0,25	0,75	-0,25	0,25	0	0,75	0	0,25	0,25	0	-0,25	0,75	0,75	0,75	0	-0,25	-0,25	0,75	0	0	0,25
3	0,25	0		0,25	0,25	0	0,75	-0,25	0,25	0	-0,75	0,25	0,75	0,25	0,25	0,75	0,25	0,25	0	0	-0,25	0,25	0	0	0	-0,25
4	-0,75	0,25	0,25		0	0	0,75	-0,25	0,25	0	-0,75	-0,25	-0,75	0,25	-0,25	-0,25	0,25	-0,25	-0,25	0	0,25	-0,25	0,75	0	0	-0,25
5	0	0,25	0	0		0,25	0	0	-0,25	0	0	0	0	0	-0,25	0	0	-0,25	0	0	0	0	0	0	0	0,25
6	0	0,75	0	0	0,25		0	0	-0,25	0	0,25	0	0	0	0	0	0	-0,25	0	0	0	0	0,75	0	0	0
7	0,5	0,75	0,25	0,25	0,75	0,25		0,75	0,75	0	0,75	0,75	0,25	0,25	0,25	0,75	0,75	0,75	0	0,25	-0,25	0,75	0	0	0	0,75
8	0	0	-0,25	0,25	0	0	0,25		-0,75	0	-0,75	0,25	0,25	-0,25	0,25	0	0	0	0	0	0,25	0	0	0	0	-0,25
9	0,75	0,25	0,25	0,25	0	0	0,25	0		0	-0,75	0,25	0	-0,25	0	-0,75	0	0	-0,25	0	0,25	0,75	0	0	0	-0,75
1	0	0,25	0	0	0	0	0	0	0	0	0	0	0	0	0	-0,25	-0,5	0,5	0,25	0	0	-0,25	0	0	0	0,5
11	0,75	0,25	0,25	-0,25	0	0,25	0,25	0,25	0,25	0		0,25	-0,25	0,25	1	-0,25	0,25	-0,25	0	0	-0,25	0,25	0,25	0	0	-0,75
12	0	0	0	0,25	0,25	0,25	0,25	0,25	0,25	0	-0,75		0,25	0,25	1	0,25	-1	1	0,25	0	-0,25	-1	0,25	0,25	1	0,25
13	0,25	0,25	0,25	0,25	0,25	0,25	0,25	0,25	-0,25	0	0,25	0,25		-0,25	0,25	0,25	-0,25	0,25	-0,25	0	0,25	-0,25	0,25	0	0	-0,25
14	-0,25	0,25	-0,25	-0,25	-0,25	0	0,25	-0,25	-0,25	0	0,75	0,25	-0,25		-0,25	1	0,75	1	-0,25	0	-0,25	1	0,25	0,25	0,75	1
15	0,25	-0,25	0	0,25	0	0	-0,25	0	0	0	0,25	0,25	0,25	-0,25		1	-0,25	-0,25	-0,25	0	-0,25	0,75	0,25	-0,25	0	1
16	0	0	0	0	0	0	0	0	-0,25	0	-0,25	0,25	-0,25	0,75	-0,75		-1	1	-0,25	0	-0,25	1	1	-0,25	0	1
17	-0,25	0,25	0,25	0,25	0,25	0,25	-0,25	0	0	0	0,25	-0,25	-0,25	0,75	0,75	1		1	-0,25	0	-0,25	1	-0,25	0	0	0,75
18	0,25	0,25	0,25	-0,25	-0,25	-0,25	-0,25	0	0	0	0,25	0,75	0,25	-0,25	-0,75	-0,25	-1		0,25	0	0,25	-0,75	0,25	0	0	-0,25
19	0,75	0,75	0	0,25	0	0	0	0	-0,25	0	0,25	0,75	0,25	-0,25	-0,75	-0,25	-0,25	-0,25		0	-0,25	-0,25	0,25	0	0,25	-0,25
2	0	0	0	0	-0,75	-0,5	-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
21	-0,25	0	0	0,25	-0,25	-0,25	-0,25	0	0	0	-0,25	-0,5	-0,25	-0,5	-1	-1	-0,25	-0,75	-0,25	0		0,25	-0,25	-1	-0,25	-0,75
22	-0,75	0	0,25	0,25	-0,25	-0,25	-0,25	-0,25	0	0	-0,25	0,75	0,25	0	0,75	1	1	-0,75	-0,25	0	-0,25		-0,25	0	-0,25	1
23	0,25	0,75	0,75	-0,75	0,25	0,75	0	-0,25	0,75	0	-0,25	0,75	0	0	-0,25	1	0	-0,75	0	0	-0,25	-0,75		0	-0,25	-0,25
24	0	0	0	0	0	0	0	0	0	0	0	0,25	0	0	-0,25	0	0	0	0	0	-0,25	0	0		0	0,25
25	0	0	0	0	0	0,25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-0,25	0	-0,25	0		0
26	-0,25	0,25	-0,25	-0,25	0	0,75	0,25	-0,25	0,75	0	-0,75	0,25	-0,25	1	-0,25	0,75	1	1	0,25	0	-0,75	1	1	0,75	0,75	

One example of the if-then rule for the 3 experts explained in below

1st Expert

IF a positive small change happens in the value of concept “Family History” THEN positive small change in the value “Benign Breast Disease” is occurred.

Infer: The influence from Family History to Benign Breast Disease is positively weak

2nd Expert

IF a positive small change happens in the value of concept “Family History” THEN positive small change in the value “Benign Breast Disease” is occurred.

Infer: The influence from Family History to Benign Breast Disease is positively strong.

3rd Expert

IF a positive high change happens in the value of concept “Family History” THEN positive very high change in the value “Benign Breast Disease” is occurred.

Infer: The influence from Family History to Benign Breast Disease is positively very strong.

Figure 5.2 illustrates the three suggested linguistic variables, for this particular example. These linguistic variables (positively strong, positively weak, positively very strong) are summed and an overall linguistic weight is produced (also in **Figure. 5.2**), with which the defuzzification method of Center of Gravity is transformed into the numerical value of $e_{72} = 0.56$.

In that thesis, Center of Gravity of the matrix is found by using MATLAB. MATLAB (matrix laboratory) is a numerical computing environment and fourth-generation

programming language. It allows matrix manipulations, plotting of functions and data, implementation of algorithms. COG values are found by using fuzzy trim functions and defuzzy centroid functions. The result of Weight Matrix of Breast Cancer Risk Factors is located in **Table 5.5**

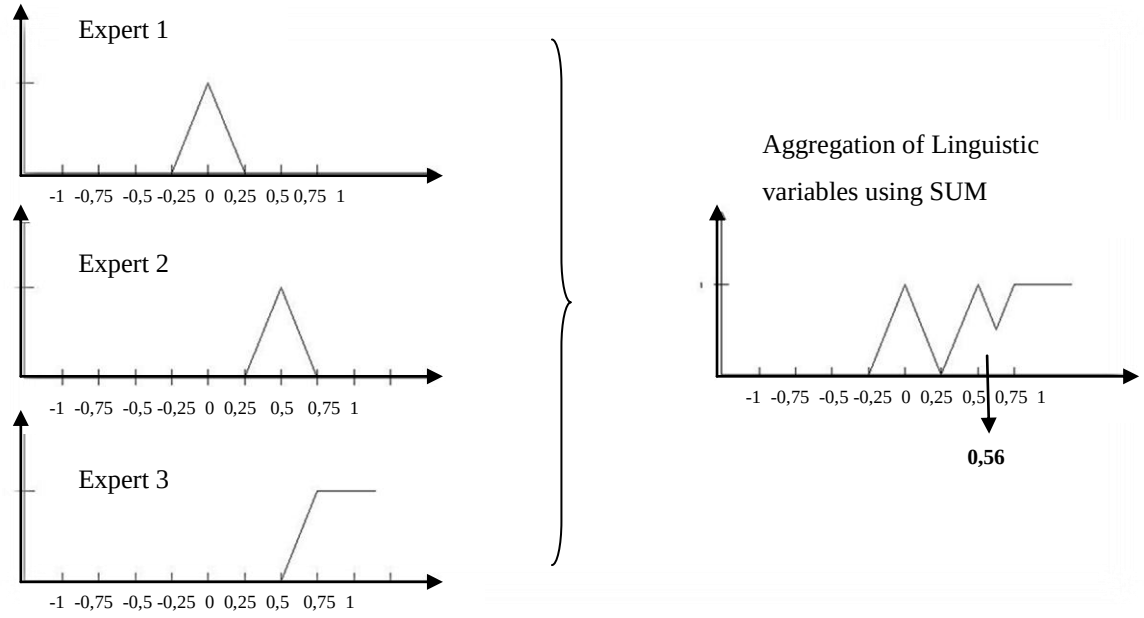

Figure 5.2 Aggregation of three linguistic variables using the SUM technique. 0,56 is the numerical weight after defuzzification using the Center of Gravity method.

Table 5.5 The result of Weight Matrix of Breast Cancer Risk Factors according to 3 Expert

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
1	0,00	0,25	0,13	-0,46	0,00	0,00	0,50	-0,13	0,25	0,00	0,38	-0,13	0,13	-0,13	-0,13	-0,13	0,38	0,38	0,31	0,00	0,00	0,13	0,38	0,00	0,00	-0,13
2	0,13	0,00	0,13	0,13	0,13	0,13	0,50	-0,13	0,13	0,13	0,50	0,00	0,13	0,13	0,00	-0,13	0,38	0,38	0,50	0,00	-0,13	-0,13	0,38	0,00	0,00	0,13
3	0,13	0,00	0,00	0,13	0,13	0,00	0,75	0,25	0,25	0,00	-0,25	0,25	0,50	0,13	0,13	0,38	0,13	0,13	0,00	0,00	-0,13	0,13	0,00	0,00	0,00	-0,13
4	-0,38	0,13	0,13	0,00	0,00	0,00	0,75	-0,13	0,25	0,00	-0,25	-0,13	-0,38	0,13	-0,13	-0,13	0,13	-0,13	-0,13	0,00	0,13	-0,13	0,38	0,00	0,00	-0,13
5	0,00	0,13	0,00	0,00	0,00	0,13	0,44	0,00	-0,13	0,00	0,00	0,00	0,00	0,00	-0,13	0,00	0,00	-0,13	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,13
6	0,00	0,38	0,00	0,00	0,13	0,00	0,13	0,00	-0,13	0,00	0,13	0,00	0,00	0,00	0,00	0,00	0,00	-0,13	0,00	0,00	0,00	0,00	0,38	0,00	0,00	0,00
7	0,25	0,56	0,25	0,25	0,75	0,25	0,00	0,38	0,35	0,00	0,38	0,38	0,13	0,13	0,13	0,38	0,35	0,35	0,00	0,13	-0,13	0,38	0,00	0,00	0,00	0,38
8	0,00	0,00	0,25	0,13	0,00	0,00	0,50	0,00	-0,38	0,00	-0,38	0,13	0,13	-0,13	0,13	0,00	0,00	0,00	0,00	0,00	0,13	0,00	0,00	0,00	0,00	-0,13
9	0,50	0,13	0,13	0,13	0,00	0,00	0,13	0,00	0,00	0,00	-0,38	0,25	0,00	-0,13	0,00	-0,38	0,00	0,00	-0,13	0,00	0,13	0,38	0,00	0,00	0,00	-0,38
10	0,00	0,25	0,00	0,00	0,00	0,00	0,00	0,00	0,13	0,00	0,00	0,13	0,00	0,00	0,00	-0,13	-0,25	0,13	0,13	0,00	0,00	-0,13	0,00	0,00	0,00	0,13
11	0,35	0,25	0,25	0,00	0,00	0,13	0,13	0,13	0,13	0,00	0,00	0,13	-0,13	0,13	0,31	-0,13	0,13	-0,13	0,00	0,00	-0,13	0,13	0,13	0,00	0,00	-0,38
12	0,00	0,00	0,13	0,13	0,13	0,13	0,13	0,13	0,25	0,00	-0,38	0,00	0,13	0,13	0,44	0,13	-0,46	0,44	0,13	0,00	-0,13	-0,46	0,13	0,13	0,44	0,13
13	0,13	0,13	0,13	0,13	0,13	0,13	0,13	0,13	-0,13	0,00	0,25	0,13	0,00	-0,13	0,13	0,13	-0,13	0,13	-0,13	0,00	0,13	-0,13	0,13	0,00	0,00	-0,13
14	-0,13	0,13	-0,13	-0,13	-0,13	0,00	0,13	-0,13	-0,13	0,00	0,50	0,25	-0,13	0,00	-0,13	0,44	0,38	0,44	-0,13	0,00	0,00	0,31	0,13	0,13	0,38	0,31
15	0,13	-0,13	0,00	0,13	0,00	0,00	-0,13	0,00	0,00	0,00	0,13	0,13	0,13	-0,13	0,00	0,31	-0,13	-0,13	-0,13	0,00	-0,13	0,38	0,13	-0,13	0,00	0,31
16	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	-0,13	0,13	-0,13	0,35	-0,38	0,00	-0,46	0,31	-0,13	0,00	-0,13	0,31	0,31	-0,13	0,00	0,31
17	-0,13	0,13	0,13	0,13	0,13	0,13	-0,13	0,00	0,00	0,00	0,13	-0,13	-0,13	0,35	0,38	0,44	0,00	0,44	-0,13	0,00	-0,13	0,31	-0,13	0,00	0,00	0,35
18	0,13	0,13	0,13	-0,13	-0,13	-0,13	-0,13	0,00	0,00	0,00	0,13	0,38	0,13	-0,13	-0,38	-0,13	-0,46	0,00	0,13	0,00	0,13	-0,38	0,13	0,00	0,00	-0,13
19	0,38	0,50	0,00	0,13	0,00	0,00	0,00	0,00	-0,13	0,00	0,13	0,38	0,13	-0,13	-0,38	-0,13	-0,13	-0,13	0,00	0,00	-0,13	-0,13	0,13	0,00	0,13	-0,13
2	0,00	0,00	0,00	0,00	-0,67	-0,63	-0,25	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
21	-0,25	0,00	0,00	0,13	-0,13	-0,13	-0,13	0,00	0,00	0,00	-0,13	-0,25	-0,13	-0,25	-0,37	-0,46	-0,13	-0,38	-0,13	0,00	0,00	0,13	-0,13	-0,46	-0,13	-0,38
22	-0,38	0,00	0,13	0,13	-0,13	-0,13	-0,13	-0,13	0,00	0,00	-0,13	0,38	0,13	0,00	0,38	0,44	0,44	-0,38	-0,13	0,00	-0,13	0,00	-0,13	0,00	-0,13	0,44
23	0,13	0,38	0,38	-0,38	0,13	0,38	0,00	-0,13	0,38	0,00	-0,13	0,38	0,00	0,00	-0,13	0,31	0,00	-0,38	0,00	0,00	-0,13	-0,38	0,00	0,00	-0,13	-0,13
24	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,13	0,00	0,00	-0,13	0,00	0,00	0,00	0,00	0,00	-0,13	0,00	0,00	0,00	0,00	0,13
25	0,00	0,00	0,00	0,00	0,00	0,13	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	-0,13	0,00	-0,13	0,00	0,00	0,00
26	-0,13	0,13	-0,13	-0,13	0,00	0,38	0,13	-0,13	0,38	0,00	-0,38	0,13	-0,13	0,31	-0,13	0,38	0,44	0,44	0,13	0,00	-0,38	0,44	0,31	0,38	0,38	0,00

6. SCENARIO ANALYSES

In order to present scenario analyses to propose the preventive and protective actions against breast cancer, we need to change the factors weight and try to understand the behaviour of the system. To do so FCMapper software is used.

6.1 FCMapper Software

FCM has the capability to incorporate feedback processes. It can be used to simulate the changes of a system over time and address "what if" questions. In regards of modelling FCM combines aspects of qualitative methods with the advantages of quantitative methods. FCMapper allows to dynamically simulate the resulting system and to test the influence of experts' scenarios on system components.

FCMapper has one user interface that shows the steps and from here we can track the all the process. First step begins with importing a matrix. In our study firstly experts defined the relationship among concepts by using linguistic variables and then they were transformed to numbers by using SUM method that was coded in MATLAB.

Secondly we check the matrix if the range of numbers lay between [-1,1] or not, then we get standardized matrices. After standardized matrices the scenario analysis begins.

In scenario analysis, first you choose scene, threshold function (we used tanh(x)) then iteration number. We realized that after 125 iterations our system is stabilized thus while chancing factors iteration number is not changed

After calculating the weights, we started to change the weights of the factors and tried to understand the changes other factors weights. The changes can be positive or

negative. Moreover the strength of the change can be tracked. Strength value of concepts and explanation is located **Table 6.1**

Table 6.1 Strength value of concepts and explanation

Strength Value	Explanation
1	Strong Change
2	Medium Change
3	Weak Change
4	Very Weak Change

Different case analyses are located in section 6.2

6.2 Case Analyses

While doing case analysis, first we ranked the most important concepts according to their weights, then we used them as an input to our cases. The rank of the concepts is shown in **Table 6.2**

Table 6.2 The rank of the concepts of Breast Cancer

Non Modified Factors	W_i	Modified Factors	W_i
Benign Breast Disease	0,98863553	Social Class	0,98947027
Family History	0,98820417	Late Maternal Age	0,97772468
Breast Density	0,91902238	Radiation	0,96244081
Menarche Age	0,89371293	Abortion	0,93377112
TP 53	0,87849744	Meat Intake	0,74555894
BRCA 1/2 Genes	0,84542735	Underarm Cosmetics	0,73881126
Nullparity	0,84370037	Alcohol Consumption	0,69344926
Height	0,32139326	Smoking	0,63572163
Sporadic	0,12290106	HRT	0,62071620
Menopause	-0,13942472	BMI	0,60284633
		Taking Aspirin	0,59476445
		Early Maternal Age	0,44840942
		Age at First Birth	0,36446827
		OCs	0,12295416
		Time Interval in Pregnancy	0,07466840
		Breastfeeding	-0,77981231

When we interpret the **Table 6.2** we conclude that the most important five non modified factors can be counted as Benign Breast Disease, Family History, Breast Density, Menarche Age, TP 53. This rank is not confusing because Benign Breast Disease has potential for the patients who are seen not only people who have family history but also sporadic factors. Second rank belongs to Family History, as expected due to the proven investigations and interpretations. Third one is belongs to Breast Density. This point can be a contribution to the literature. Because it is generally associated with genetic factors on the other hand it also affects mammography results and influence the early detection and treatment so while examining patients who have higher breast density, doctors should be more attentive towards them. Fourth one is Menarche age, which is highly related with breast tissue aging and becoming sensitive to the mutation. Last one is related with TP53 gene which can be counted as a subset of family history as genetic heredity.

6.2.1 Changing Social Class

When we change Social Class value from 0,9894703 to 0,9 and 0,8 the others changed as **Table 6.3**

Table 6.3 Changing values when Social Class value has changed

Concepts	**Results - No Changes (Scene 1)**	**Results - Scene 2**	**Results - Scene 3**
Breast Density	0,91902238	0,91062991	0,90386179
Benign Breast Disease	0,98863553	0,98876520	0,98880632
Menarche Age	0,89371293	0,89313569	0,89220436
Menopause	-0,13942472	-0,13917095	-0,14250035
BRCA 1/2 Genes	0,84542735	0,84077580	0,83579700
TP 53	0,87849744	0,87997309	0,87912937
Family History	0,98820417	0,98708946	0,98590810
Height	0,32139326	0,29309543	0,27010949

Nullparity	0,84370037	0,84604583	0,84497439
OCs	0,12295416	0,12297013	0,12297519
BMI	0,60284633	0,62180221	0,64399123
Social Class	**0,98947027**	**0,90000000**	**0,80000000**
Meat Intake	0,74555894	0,73404643	0,72289608
Alcohol Consumption	0,69344926	0,71828391	0,73345876
Time Interval in Pregnancy	0,07466840	0,10380952	0,11784037
Abortion	0,93377112	0,94689886	0,95398464
Early Maternal Age	0,44840942	0,53308358	0,59884338
Late Maternal Age	0,97772468	0,97759077	0,97656033
HRT	0,62071620	0,59833324	0,57866947
Sporadic	0,12290106	0,12276382	0,12261838
Breastfeeding	-0,77981231	-0,79470655	-0,80226750
Age at First Birth	0,36446827	0,46150840	0,53420456
Radiation	0,96244081	0,96182709	0,96054268
Taking Aspirin	0,59476445	0,60271434	0,60340487
Underarm Cosmetics	0,73881126	0,72741295	0,70880959
Smoking	0,63572163	0,68595086	0,71479116

Table 6.4 When Social Class change 0,98947 to 0,9, strength of other concepts

Social Class 0,98947 to 0,9			
Positive Changes	Strength (positive)	Negative Changes	Strength (negative)
Benign Breast Disease	3	Breast Density	2
Menopause	3	Menarche Age	3
TP 53	2	BRCA 1/2 Genes	2
Nullparity	2	Family History	2
OCs	4	Height	1
BMI	1	Meat Intake	1
Alcohol Consumption	1	Late Maternal Age	3
Time Interval in Pregnancy	1	HRT	1
Abortion	1	Sporadic	3
Early Maternal Age	1	Breastfeeding	1
Age at First Birth	1	Radiation	3
Taking Aspirin	2	Underarm Cosmetics	1
Smoking	1		

Table 6.5 When Social Class change 0,9 to 0,8, strength of other concepts

Social Class 0,9 to 0,8			
Positive Changes	Strength (positive)	Negative Changes	Strength (negative)
Benign Breast Disease	3	Breast Density	1
TP 53	3	Menarche Age	2
Nullparity	2	Menopause	2
OCs	4	BRCA 1/2 Genes	2
BMI	1	Family History	2
Alcohol Consumption	1	Height	1
Time Interval in Pregnancy	1	Meat Intake	1
Abortion	1	Late Maternal Age	2
Early Maternal Age	1	HRT	1
Age at First Birth	1	Sporadic	3
Taking Aspirin	2	Breastfeeding	1
Smoking	1	Radiation	2
		Underarm Cosmetics	1

We conclude that if we decrease the weight of social class, Alcohol consumption, time interval in pregnancy, age at first birth and smoking weight increase and gain importance to the contribution of occurrence of breast cancer.

Thus we can come up with that people who belong to low social class should be careful while consuming alcohol and smoking also for women time interval in pregnancy have importance.

6.2.2 Changing Meat Intake

When we change Meat Intake value from 0,74555894 to 0,8 and 0,9 and the others changed as **Table 6.6**

Table 6.6 Changing values when Meat Intake value has changed

Concepts	**Results - No Changes (Scene 1)**	**Results - Scene 2**	**Results - Scene 3**
Breast Density	0,91902238	0,92269155	0,95425107
Benign Breast Disease	0,98863553	0,98865896	0,96503356
Menarche Age	0,89371293	0,89594045	0,90774924
Menopause	-0,13942472	-0,13413014	0,20973817
BRCA 1/2 Genes	0,84542735	0,84785768	0,87114731
TP 53	0,87849744	0,87715571	0,59717730
Family History	0,98820417	0,98877684	0,99237673
Height	0,32139326	0,33743735	0,64078568
Nullparity	0,84370037	0,83804687	0,61473259
OCs	0,12295416	0,12295705	0,12005910
BMI	0,60284633	0,61044126	0,60793324
Social Class	0,98947027	0,98911385	0,78829819
Meat Intake	**0,74555894**	**0,80000000**	**0,90000000**
Alcohol Consumption	0,69344926	0,67661994	-0,43121875
Time Interval in Pregnancy	0,07466840	0,06571674	0,17736817
Abortion	0,93377112	0,92708941	-0,39526744
Early Maternal Age	0,44840942	0,41837735	-0,17657361
Late Maternal Age	0,97772468	0,97676647	0,41005949
HRT	0,62071620	0,62119745	0,67070633
Sporadic	0,12290106	0,12297156	0,12341429
Breastfeeding	-0,77981231	-0,76686915	0,10396873
Age at First Birth	0,36446827	0,32884927	-0,69685639
Radiation	0,96244081	0,96261431	0,81423588
Taking Aspirin	0,59476445	0,58266197	-0,26780386
Underarm Cosmetics	0,73881126	0,73149930	-0,05310174
Smoking	0,63572163	0,60288012	-0,79407122

Table 6.7 When Meat Intake change 0,74555894 to 0,8 strength of other concepts

Meat Intake 0,74555894 to 0,8			
Positive Changes	Strength (positive)	Negative Changes	Strength (negative)
Breast Density	2	TP 53	2
Benign Breast Disease	4	Nullparity	2
Menarche Age	2	Social Class	3
Menopause	2	Alcohol Consumption	1
BRCA 1/2 Genes	2	Time Interval in Pregnancy	2

Family History	3	Abortion	2
Height	1	Early Maternal Age	1
OCs	4	Late Maternal Age	3
BMI	2	Age at First Birth	1
HRT	3	Taking Aspirin	1
Sporadic	4	Underarm Cosmetics	2
Breastfeeding	1	Smoking	1
Radiation	3		

Table 6.8 When Meat Intake change 0,8 to 0,9 strength of other concepts

Meat Intake 0,8 to 0,9			
Positive Changes	strength (pos)	Negative Changes	strength (neg)
Breast Density	1	Benign Breast Disease	1
Menarche Age	1	TP 53	1
Menopause	1	Nullparity	1
BRCA 1/2 Genes	1	OCs	2
Family History	2	Social Class	1
Height	1	Alcohol Consumption	1
BMI	2	Abortion	1
Time Interval in Pregnancy	1	Early Maternal Age	1
HRT	1	Late Maternal Age	1
Sporadic	3	Age at First Birth	1
Breastfeeding	1	Radiation	1
		Taking Aspirin	1
		Underarm Cosmetics	1
		Smoking	1

6.2.3 Changing Meat Intake and Alcohol Consumption

FCMapper allows changing more than one concepts so we combined meat intake and alcohol consumption. When we change Meat Intake value from 0,74555894 to 0,8, 0,9, 0,99 and alcohol consumption value from 0,69344926 to 0,8, 0,9, 0,99 and the remains changed as **Table 6.9**

Table 6.9 Changing values when Meat Intake, Alcohol Consumption value have changed

Concepts	Results - No Changes (Scene 1)	Results - Scene 2	Results - Scene 3	Results - Scene 4
Breast Density	0,91902238	0,91206248	0,90811863	0,90499519
Benign Breast Disease	0,98863553	0,98925039	0,98984033	0,99030929
Menarche Age	0,89371293	0,89566644	0,89914703	0,90195504
Menopause	-0,13942472	-0,13241887	-0,12217255	-0,11418455
BRCA 1/2 Genes	0,84542735	0,84404661	0,84446627	0,84480497
TP 53	0,87849744	0,88695184	0,89374862	0,89898564
Family History	0,98820417	0,98824733	0,98876151	0,98922079
Height	0,32139326	0,30164477	0,29524111	0,29109961
Nullparity	0,84370037	0,84920982	0,84961408	0,84897729
OCs	0,12295416	0,12302986	0,12310248	0,12316022
BMI	0,60284633	0,63115150	0,66647070	0,69721458
Social Class	0,98947027	0,99100358	0,99209008	0,99288075
Meat Intake	**0,74555894**	**0,80000000**	**0,90000000**	**0,99000000**
Alcohol Consumption	**0,69344926**	**0,80000000**	**0,90000000**	**0,99000000**
Time Interval in Pregnancy	0,07466840	0,13206483	0,18132362	0,22096075
Abortion	0,93377112	0,95290449	0,96383655	0,97089760
Early Maternal Age	0,44840942	0,51828778	0,56259879	0,59663114
Late Maternal Age	0,97772468	0,98109094	0,98345992	0,98525159
HRT	0,62071620	0,59439617	0,56693109	0,54244841
Sporadic	0,12290106	0,12290637	0,12296967	0,12302621
Breastfeeding	-0,77981231	-0,80018987	-0,80928233	-0,81523771
Age at First Birth	0,36446827	0,45328458	0,50987908	0,55235534
Radiation	0,96244081	0,96512495	0,96767480	0,96965357
Taking Aspirin	0,59476445	0,61853935	0,63223992	0,64271595
Underarm Cosmetics	0,73881126	0,76181787	0,77867402	0,79230465
Smoking	0,63572163	0,70030225	0,73541352	0,76040084

Table 6.10 When Meat Intake change 0,74555894 to 0,8 and Alcohol Consumption change from 0,69344926 to 0,8, the strength of other concepts

Meat Intake 0,74555894 to 0,8 Alcohol Consumption 0,69344926 to 0,8			
Positive Changes	strength (pos)	Negative Changes	strength (neg)
Benign Breast Disease	3	Breast Density	2
Menarche Age	2	BRCA 1/2 Genes	2
Menopause	2	Height	1
TP 53	2	HRT	1
Family History	4	Breastfeeding	1
Nullparity	2		
OCs	4		
BMI	1		
Social Class	2		
Time Interval in Pregnancy	1		
Abortion	1		
Early Maternal Age	1		
Late Maternal Age	2		
Sporadic	4		
Age at First Birth	1		
Radiation	2		
Taking Aspirin	1		
Underarm Cosmetics	1		
Smoking	1		

Table 6.11 When Meat Intake change 0,8 to 0,9 and Alcohol Consumption change from 0,8 to 0,9, the strength of other concepts

Meat Intake 0,8 to 0,9 Alcohol Consumption 0,8 to 0,9			
Positive Changes	strength (pos)	Negative Changes	strength (neg)
Benign Breast Disease	3	Breast Density	2
Menarche Age	2	BRCA 1/2 Genes	2
Menopause	2	Height	1
TP 53	2	HRT	1
Family History	4	Breastfeeding	1
Nullparity	2		
OCs	4		
BMI	1		
Social Class	2		
Time Interval in Pregnancy	1		
Abortion	1		
Early Maternal Age	1		
Late Maternal Age	2		
Sporadic	4		
Age at First Birth	1		
Radiation	2		
Taking Aspirin	1		
Underarm Cosmetics	1		
Smoking	1		

Table 6.12 When Meat Intake change 0,9 to 0,99 and Alcohol Consumption change from 0,9 to 0,99, the strength of other concepts

Meat Intake 0,9 to 0,99 Alcohol Consumption 0,9 to 0,99			
Positive Changes	strength (pos)	Negative Changes	strength (neg)
Benign Breast Disease	2	Breast Density	1
Menarche Age	2	BRCA 1/2 Genes	3
Menopause	1	Height	1
TP 53	1	HRT	1
Family History	3	Breastfeeding	1
Nullparity	2		
OCs	3		
BMI	1		
Social Class	2		
Time Interval in Pregnancy	1		
Abortion	1		
Early Maternal Age	1		
Late Maternal Age	2		
Sporadic	4		
Age at First Birth	1		
Radiation	2		
Taking Aspirin	1		
Underarm Cosmetics	1		
Smoking	1		

We can see that when the weight of meat intake and alcohol consumption increases, they have impact on not only on modifiable but also non modifiable factors like Menopause, TP 53, and Breast Density.

6.2.4 Changing Alcohol Consumption and Smoking

These two concepts are thought strictly related and to explore this assumption Alcohol Consumption changed from 0,69344926 to 0,8, 0,9. Like Alcohol Consumption, Smoking values changed from 0,63572163 to 0,8, 0,9.

Table 6.13 Changing values when Alcohol Consumption and Smoking value have changed

Concepts	Results - No Changes (Scene 1)	Results - Scene 2	Results - Scene 3
Breast Density	0,91902238	0,90534346	0,89598824
Benign Breast Disease	0,98863553	0,98936213	0,98987112
Menarche Age	0,89371293	0,89104363	0,88857905
Menopause	-0,13942472	-0,14242191	-0,14943816
BRCA 1/2 Genes	0,84542735	0,84201358	0,83841926
TP 53	0,87849744	0,89294111	0,90115504
Family History	0,98820417	0,98736046	0,98677390
Height	0,32139326	0,27376383	0,24193282
Nullparity	0,84370037	0,86167025	0,87100343
OCs	0,12295416	0,12304362	0,12310628
BMI	0,60284633	0,60345718	0,61623036
Social Class	0,98947027	0,99148527	0,99260892
Meat Intake	0,74555894	0,73162044	0,72019003
Alcohol Consumption	**0,69344926**	**0,80000000**	**0,90000000**
Time Interval in Pregnancy	0,07466840	0,13681789	0,17403107
Abortion	0,93377112	0,95990937	0,97122366
Early Maternal Age	0,44840942	0,56441905	0,63476283
Late Maternal Age	0,97772468	0,98276947	0,98563991
HRT	0,62071620	0,59949595	0,58429605
Sporadic	0,12290106	0,12279719	0,12272497
Breastfeeding	-0,77981231	-0,82222249	-0,84482158
Age at First Birth	0,36446827	0,50536715	0,58793989
Radiation	0,96244081	0,96565603	0,96753937
Taking Aspirin	0,59476445	0,64625985	0,67692885
Underarm Cosmetics	0,73881126	0,77588551	0,80079212
Smoking	**0,63572163**	**0,80000000**	**0,90000000**

Table 6.14 When Alcohol Consumption change 0,69344926 to 0,8 and Smoking change from 0,63572163 to 0,8, the strength of other concepts

Alcohol Consumption 69344926 to 0,80 Smoking 0,63572163 to 0,80			
Positive Changes	strength (pos)	Negative Changes	strength (neg)
Benign Breast Disease	3	Breast Density	1
TP 53	1	Menarche Age	2
Nullparity	1	Menopause	2
OCs	4	BRCA 1/2 Genes	2
BMI	3	Family History	3
Social Class	2	Height	1
Time Interval in Pregnancy	1	Meat Intake	1
Abortion	1	HRT	1
Early Maternal Age	1	Sporadic	3
Late Maternal Age	2	Breastfeeding	1
Age at First Birth	1		
Radiation	2		
Taking Aspirin	1		
Underarm Cosmetics	1		

Table 6.15 When Alcohol Consumption change 0,8 to 0,9 and Smoking change from 0,8 to 0,9 the strength of other concepts

Alcohol Consumption 0,80 to 0,9 Smoking 0,8 to 0,9			
Positive Changes	strength (pos)	Negative Changes	strength (neg)
Benign Breast Disease	2	Breast Density	1
TP 53	1	Menarche Age	2
Nullparity	1	Menopause	1
OCs	3	BRCA 1/2 Genes	1
BMI	1	Family History	2
Social Class	2	Height	1
Time Interval in Pregnancy	1	Meat Intake	1
Abortion	1	HRT	1
Early Maternal Age	1	Sporadic	3
Late Maternal Age	1	Breastfeeding	1

Age at First Birth	1		
Radiation	2		
Taking Aspirin	1		
Underarm Cosmetics	1		

Nullparity and abortion weight gain importance and women who are used to use alcohol and smoking, should be careful if they are nullparious or aborte a child.

6.2.5 Changing Family History

Before that we made scenario analysis about modified risk factors but many people do not have any family history or genetic heritage so with FCMapper we could also try what is the important factor if one does not have any clear risk factor. To understand taht family history changed from 0,98820417 to 0.

Table 6.16 Changing values when Family History value has changed

Concepts	Results - No Changes (Scene 1)	Results - Scene 2
Breast Density	0,91902238	0,92794697
Benign Breast Disease	0,98863553	0,85604481
Menarche Age	0,89371293	0,69025040
Menopause	-0,13942472	-0,36345602
BRCA 1/2 Genes	0,84542735	0,46359292
TP 53	0,87849744	0,43626661
Family History	**0,98820417**	**0,00000000**
Height	0,32139326	0,29851607
Nullparity	0,84370037	0,36143076
OCs	0,12295416	0,10307437
BMI	0,60284633	0,57899342
Social Class	0,98947027	0,66572358
Meat Intake	0,74555894	0,73906468

Alcohol Consumption	0,69344926	-0,46577158
Time Interval in Pregnancy	0,07466840	-0,26779139
Abortion	0,93377112	-0,66009468
Early Maternal Age	0,44840942	-0,52178887
Late Maternal Age	0,97772468	0,39611765
HRT	0,62071620	0,75423778
Sporadic	0,12290106	0,00000000
Breastfeeding	-0,77981231	0,06145745
Age at First Birth	0,36446827	-0,88350359
Radiation	0,96244081	0,69293360
Taking Aspirin	0,59476445	0,00950975
Underarm Cosmetics	0,73881126	0,16411363
Smoking	0,63572163	-0,84379122

Table 6.17 When Family History changes 0,98820417 to 0, the strength of other concepts

Family History 0,98820417 to 0			
Positive Changes	strength (pos)	Negative Changes	strength (neg)
Breast Density	2	Benign Breast Disease	1
HRT	1	Menarche Age	1
Breastfeeding	1	Menopause	1
		BRCA 1/2 Genes	1
		TP 53	1
		Height	1
		Nullparity	1
		OCs	1
		BMI	1
		Social Class	1
		Meat Intake	2
		Alcohol Consumption	1
		Time Interval in	1

		Pregnancy	
		Abortion	1
		Early Maternal Age	1
		Late Maternal Age	1
		Sporadic	1
		Age at First Birth	1
		Radiation	1
		Taking Aspirin	1
		Underarm Cosmetics	1
		Smoking	1

When Family History weight change, apart from 3 concepts (Breast Density, HRT, Breast Feeding) all the concepts'' weights dropped dramatically. The most decreased ones are BRCA1/2 Gene, TP53, Nullparity and Early Maternal Age. Surprisingly Sporadic weight also dropped to 0

7. CONCLUSION

The goal of FCM analysis is detecting and interpreting relations between entities found in a map and understanding its structural properties and dynamics. The structured way of collecting and coding data enables a comparison between different case studies and even aggregation of data.

FCM has the capability to incorporate feedback processes. It can be used to simulate the changes of a system over time and address "what if" questions. In regards of modelling FCM combines aspects of qualitative methods with the advantages of quantitative methods. FCMapper allows to dynamically simulate the resulting system and to test the influence of experts' scenarios on system components.

We select 26 breast cancer risk factors that divide two as non modifiable and modifiable factors. We determine their weight with the combination of the expert views and FCMapper computation.

After analysing the results of the FCMapper, the results showed that Social Class and Late Maternal Age can be seen as important modifiable factors; on the other hand Benign Breast Disease, Family History and Breast Density can be considered as important factors as non modifiable risk factors.

When we sort the non modifiable factors the first one is Social Class. At first sight it can be confusing but Social Class consist of many sub factors like income level, education level moreover maternal age, oral contraceptive usage abortion etc. Although early detection possibility could be higher than when we compare the low income level, they are exposed to more sub factors so that they should focus on more protective factors instead of preventive factors.

Also when we consider alcohol consumption, meat intake and smoking; different results come out. Menopause, TP 53, Breast Density weights which are the contributor to the breast cancer are affected from modifiable factors and gain importance. Moreover nullparity and abortion become serious threat if women consume alcohol and smoking.

In this study we used expert based FCM and we did not consider Breast Cancer as a concept, next step could be assuming disease as a concept and making Neural Network Analysis to predict the probabilty of the occurance of the breast cancer.

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BIOGRAPHICAL SKETCH

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