EUROPEAN NETWORK OF CANCER REGISTRIES

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

ENCR CANCER FACT SHEETS

VOL. 2, DECEMBER 2002

BREAST CANCER IN EUROPE

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Introduction

Worldwide, breast cancer is the most frequent cancer in women. The highest incidence rates are observed in North America, whereas the lowest risk of breast cancer is observed in Asia and Africa (Parkin et al., 2001).

Breast cancer is also the most common cancer in females in Europe. It is estimated that in the year 2000 there were 350,000 new breast cancer cases in Europe, while the number of deaths from breast cancer was estimated at 130,000. Breast cancer is responsible for 26.5% of all new cancer cases among women in Europe, and 17.5% of cancer deaths.

There are several aetiological factors that are associated with occurrence of breast cancer, such as: age at menarche and menopause, childbearing, breastfeeding, hormonal status, consumption of alcohol and type of diet, obesity, radiation, and genetic susceptibility. Mammographic screening can reduce mortality from breast cancer.

Regional Differences in Breast Cancer

There are substantial differences in breast cancer incidence and mortality across Europe.

The regions of highest incidence are Western and Northern Europe, while Southern and Eastern Europe have lower incidence rates (Fig. 1, 2). The risk of getting breast cancer in Western Europe is 60% greater than in Eastern Europe. The highest mortality rates are also observed in Northern and Western Europe.

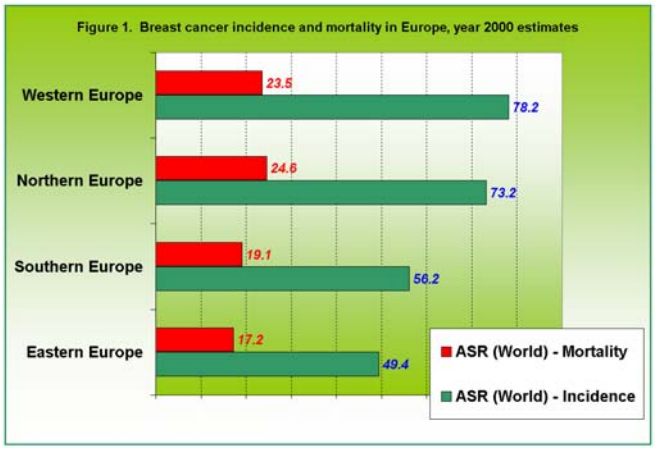
The estimates for individual countries for the year 2000 show the highest incidence rates in the Netherlands ($91.6/10^5$), Denmark ($86.2/10^5$), France ($83.2/10^5$), Belgium ($82.2/10^5$), and Sweden ($81.0/10^5$). The lowest rates in Europe are observed in Macedonia ($38.7/10^5$), Lithuania ($39.8/10^5$), Belarus ($39.8/10^5$), Latvia ($42.2/10^5$), and Estonia ($45.4/10^5$).

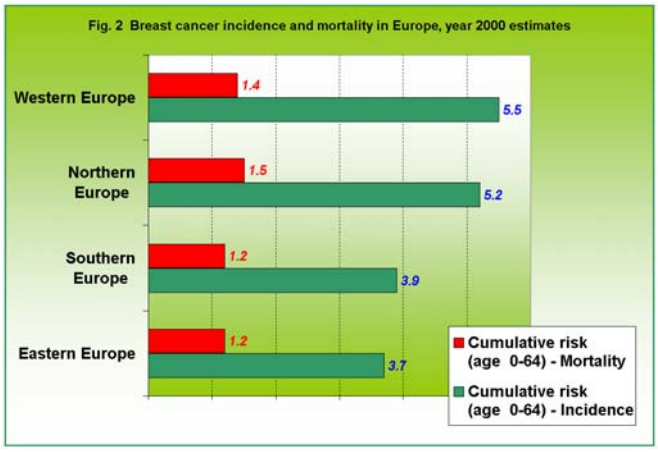
These geographical differences in breast cancer incidence and mortality in Europe in the year 2000 are shown in Figures 3-5.

Temporal Changes in Breast Cancer in Europe

Increasing trends of breast cancer mortality were observed in European countries in the 1950s and 1960s (Fig. 6).

Deceleration of the increase in mortality or the beginning of a decline were observed in the 1970s and 1980s in several Western European countries (Fig. 6) (and also in the United States, Canada, and Australia) (Hermon and Beral, 1996). However, in some countries (mainly in Eastern and Southern Europe) the increase of mortality continued in the 1970s and following decades (Fig. 6).





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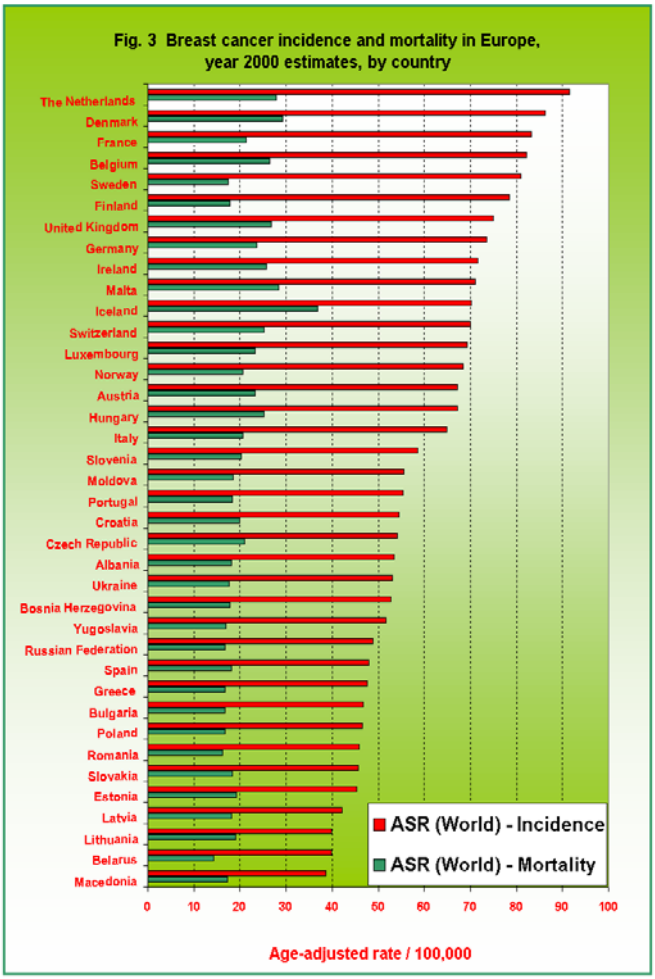
Biology of Breast Cancer

Breast cancers are derived from the epithelial cells that line the terminal duct lobular unit. An invasive breast cancer is one in which there is dissemination of cancer cells outside the basement membrane of the ducts and lobules into surrounding adjacent normal tissue. Breast cancers were previously classified either as ductal or lobular types, since it was believed that ductal carcinomas arose from ducts and lobular carcinomas from lobules. It is now known that both arise from the terminal duct lobular unit (Sainsbury et al., 2000).

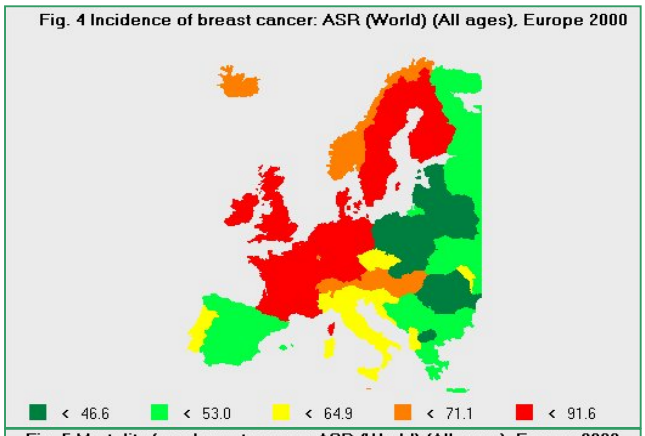


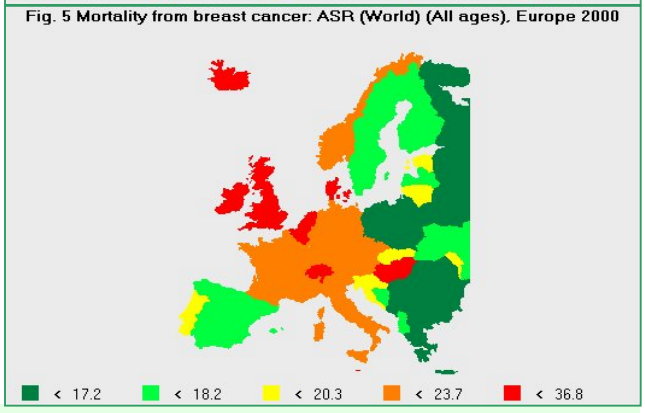
Aetiology of Breast Cancer

There are several factors, both endo- and exogenous, which are known to affect the risk of breast cancer in the population. These include lifestyle factors (i.e. childbearing, breastfeeding, type of diet and obesity, use of alcohol and tobacco), hormonal status (influencing age at menarche and menstrual cycle, and determined by endogenous hormones, oral contraceptives use, and hormone replacement therapy), anthropometric characteristics, radiation, and genetic predisposition (McPherson et al., 2000; Key et al., 2001). Finally, mortality from breast cancer may be influenced by prevention (e.g. chemoprevention using tamoxifen or raloxifene) and screening (Brewster and Helzlsouer, 2001, Vainio and Bianchini, 2002).

Reproductive factors

There have been several studies showing a relationship between reproductive factors and the risk of breast cancer. It has been shown that risk increases with decreasing age at menarche, increasing age at first pregnancy, increasing age at menopause, and low parity (Gao et al., 2000; Clavel-Chapelon et al., 2002).





Tobacco smoking

Although several studies in the past suggested an association (both positive and negative) between exposure to tobacco smoke and breast cancer risk, there is no convincing evidence of such a link (CGHFBC, 2002, Morabia, 2002; Hecht 2002, Terry and Rohan, 2002). Epidemiological data concerning tobacco smoking and breast cancer are inconsistent (IARC, 2002; Kropp and Chang-Claude, 2002).

Breastfeeding

The role of breast-feeding in reducing risk has been suspected for almost a century. The association is not strong, but some minor reduction of risk possibly exists (CGHFBC, 2002).

Anthropometric factors

Several anthropometric factors play a role in breast cancer risk. Increasing height is associated with an increasing risk in both pre- and postmenopausal women. Increased weight (measured by body mass index – BMI) decreases breast cancer risk before menopause, and increases risk after menopause (Friedenreich, 2001).

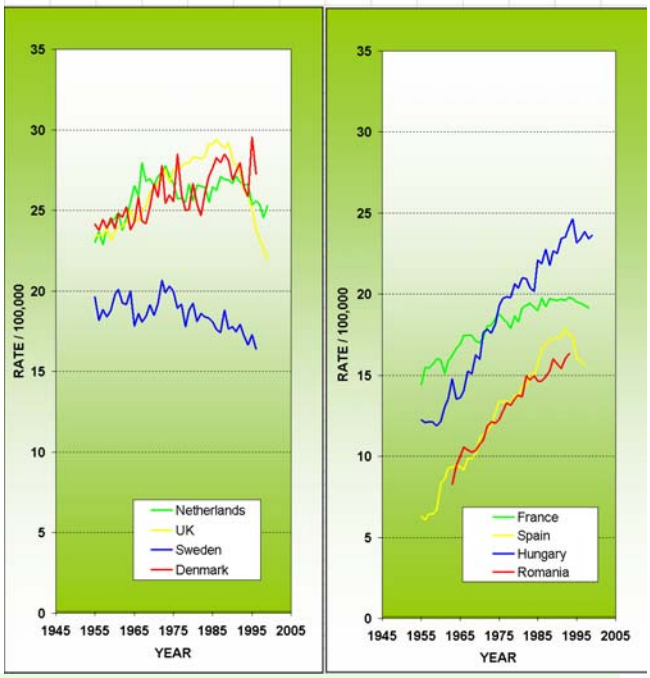
Diet

It has been suggested that consumption of meat (especially red, well-done meat) may increase risk (Dai et al., 2002). However other studies show no significant relationship between breast cancer risk and consumption of meat and dairy products (Missmer et al., 2002). The association with fat consumption, as well as with consumption of fruits and vegetables, is rather weak (Smith-Warner et al., 2001a, 2001b).

Alcohol

Alcohol consumption increases the risk of breast cancer (CGHFBC, 2002). For each additional 10 grams of alcohol

Figure 6. Breast cancer mortality in Europe, 1955-1999



per day, the risk increases by approximately 10% (Smith-Warner et al., 1998).

Oral contraceptives

The role of past oral contraceptive (OC) use in the development of breast cancer is unclear. Some studies suggest that past use of OC may increase risk of breast cancer in postmenopausal women, especially in those with a long history (more than 10 years) of OC use (van Hoften et al, 2000).

Family history and genetic predisposition

Women with a family history of breast cancer are at increased risk of the disease. It was estimated, based on the 52 epidemiological studies, that having one first-degree relative with breast cancer increases risk by about 80%, two first-degree relatives increases risk approximately 3-fold, and in those with 3 or more first-degree relatives the risk is elevated 4 fold (CGHFBC, 2001).

About 10% of breast cancers in developed countries may be due to genetic predisposition (McPherson et al., 2000). The lifetime risks of developing breast cancer for *BRCA1* and *BRCA2* (breast cancer susceptibility genes) mutation carriers is 80-85% (Emery et al., 2001)

Early Diagnosis (Screening)

Screening means the use of tests or examinations on asymptomatic individuals, to identify disease at an early stage (before it becomes clinically apparent) in order to lower the risk of death, or complications of treatment. The only provenly effective method of breast cancer screening is mammography. There is sufficient evidence for the efficacy of screening women aged 50-69 years by mammography (Vainio and Bianchini, 2002). and limited evidence for the efficacy in women aged 40-49 years. There is no benefit for women under 40 or over 69 years of age. There is no evidence that screening by clinical breast examination and/or breast self-examination can reduce mortality from breast cancer (Vainio and Bianchini, 2002).

Breast Cancer Prevention

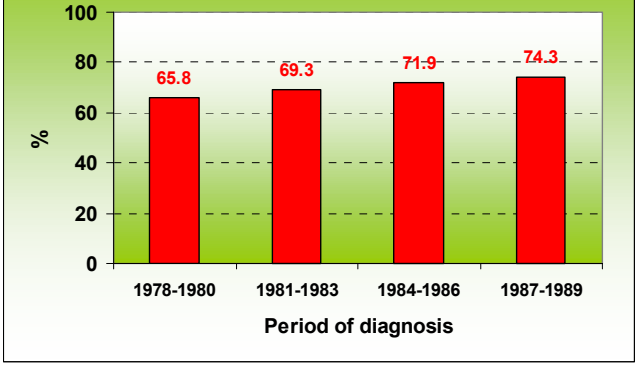
A complementary way of reducing breast cancer mortality is through chemoprevention and treatment procedures. The effectiveness of tamoxifen in reducing mortality from breast cancer has been shown in several randomised clinical trials (Fisher et al., 1998). The best results were observed in oestrogen receptor (ER)-positive breast cancer patients (EBCTCG, 1998). Tamoxifen also prevents invasive breast cancers among women diagnosed with ductal carcinoma in situ (DCIS) (Fisher et al., 1999).

Survival of Breast Cancer Patients

The average 5-year survival of women diagnosed with breast cancer increased in Europe between the end of the 1970s and the end of the 1980s (Fig. 7) (Berrino et al., 1999). However, there were substantial differences in survival among countries in Europe, with survival in cases diagnosed during 1985-1989 ranging from 81% in Swedish women to 58% in Slovakia and Poland (Berrino et al., 1999). The highest survival is in young women aged 40-49 years (Sant et al., 1998).

Survival depends strongly on stage at diagnosis and implemented therapy. In Europe, there are substantial differences in staging of breast cancer at the time of diagnosis.

Fig. 7 Average 5-year relative survivals of breast cancer patients in Europe, 1978-1989



For instance, 34% of cases in France but only 8.5% in Estonia were in stage T1N0M0 at diagnosis. Large differences in methods of treatment are present, e.g. conservative surgery was used in 63% of cases in England and 57% in France, but only in 8% in Estonia and 13% in Spain (Sant et al., 2001).

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Table 1. Estimates of breast cancer incidence in Europe in 2000

Country (region)	Crude rate	ASR (World)	Cumulative risk (age 0-64)	Cases
Eastern Europe	***68.6***	***49.4***	***3.7***	***110,975***
Belarus	54.2	39.8	3.0	2,945
Bulgaria	70.1	46.8	3.5	2,961
Czech Republic	87.5	54.1	3.6	4,598
Hungary	106.5	67.2	4.6	5,579
Moldova	65.3	55.5	4.3	1,490
Poland	63.5	46.6	3.4	12,648
Romania	62.5	45.8	3.5	7,107
Russian Federation	66.7	48.8	3.7	52,185
Slovakia	62.9	45.6	3.2	1,737
Ukraine	73.2	53.0	4.2	19,722
Northern Europe	***113.3***	***73.2***	***5.2***	***54,551***
Denmark	136.4	86.2	6.2	3,648
Estonia	69.8	45.4	3.3	516
Finland	123.3	78.4	5.7	3,272
Iceland	87.4	70.2	5.1	123
Ireland	91.1	71.6	5.2	1,711
Latvia	65.2	42.2	3.0	839
Lithuania	58.0	39.8	2.8	1,123
Norway	103.7	68.5	4.9	2,334
Sweden	133.9	81.0	5.8	6,012
United Kingdom	116.3	74.9	5.3	34,815
Southern Europe	***88.5***	***56.2***	***3.9***	***65,284***
Albania	49.8	53.4	3.7	757
Bosnia Herzegovina	68.4	52.7	3.7	1,373
Croatia	87.6	54.5	3.7	2,024
Greece	78.7	47.6	3.3	4,254
Italy	108.6	64.9	4.5	32,037
Macedonia	49.4	38.7	2.5	500
Malta	102.1	71.1	4.7	200
Portugal	84.4	55.3	3.9	4,324
Slovenia	91.0	58.5	4.1	929
Spain	73.7	47.9	3.5	14,934
Yugoslavia	72.7	51.7	3.7	3,890
Western Europe	***123.3***	***78.2***	***5.5***	***115,308***
Austria	104.8	67.2	4.7	4,359
Belgium	131.4	82.2	5.8	6,813
France	122.8	83.2	6.0	37,193
Germany	123.3	73.6	5.2	51,710
Luxembourg	108.0	69.3	4.8	237
The Netherlands	136.5	91.6	6.4	10,880
Switzerland	109.0	70.1	4.8	4,071

Table 2. Estimates of breast cancer mortality in Europe in 2000

Breast (All ages)	Crude rate	ASR (World)	Cumulative risk (age 0-64)	Deaths
Eastern Europe	***26.6***	***17.2***	***1.2***	***43,058***
Belarus	21.4	14.3	1.0	1,160
Bulgaria	28.3	16.7	1.1	1,194
Czech Republic	37.6	21.0	1.2	1,976
Hungary	45.5	25.3	1.5	2,384
Moldova	22.9	18.5	1.4	523
Poland	25.0	16.8	1.1	4,980
Romania	24.3	16.2	1.1	2,767
Russian Federation	25.4	16.7	1.2	19,843
Slovakia	27.5	18.4	1.1	761
Ukraine	27.7	17.7	1.3	7,472
Northern Europe	***43.6***	***24.6***	***1.5***	***20,992***
Denmark	52.8	29.2	1.8	1,412
Estonia	30.9	19.3	1.4	228
Finland	31.4	17.9	1.1	834
Iceland	49.7	36.8	2.4	70
Ireland	35.4	25.8	1.6	666
Latvia	29.9	18.1	1.2	385
Lithuania	30.0	19.0	1.3	582
Norway	36.1	20.7	1.2	812
Sweden	34.0	17.5	1.0	1,528
United Kingdom	48.1	26.8	1.6	14,415
Southern Europe	***34.2***	***19.1***	***1.2***	***25,205***
Albania	16.9	18.2	1.1	258
Bosnia Herzegovina	24.4	17.9	1.1	490
Croatia	35.7	19.9	1.2	825
Greece	30.7	16.7	1.0	1,660
Italy	40.4	20.7	1.3	11,902
Macedonia	21.6	17.2	1.2	219
Malta	46.4	28.4	1.4	91
Portugal	31.1	18.4	1.2	1,596
Slovenia	35.3	20.3	1.2	360
Spain	31.5	18.1	1.2	6,381
Yugoslavia	26.1	16.9	1.1	1,399
Western Europe	***43.2***	***23.5***	***1.4***	***40,443***
Austria	42.2	23.3	1.3	1,754
Belgium	48.5	26.4	1.6	2,512
France	38.1	21.4	1.3	11,529
Germany	45.6	23.7	1.4	19,149
Luxembourg	40.6	23.2	1.3	89
The Netherlands	46.6	27.8	1.6	3,711
Switzerland	45.0	25.2	1.4	1,682