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Breast cancer: trends in international incidence in men and women

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Background: The age-standardised incidence of breast cancer varies geographically, with rates in the highest-risk countries more than five times those in the lowest-risk countries.

Methods: We investigated the correlation between male (MBC) and female breast cancer (FBC) incidence stratified by female age-group (<50 years, and $\geqslant 50$ years) and used Poisson regression to examine male incidence rate ratios according to female incidence rates.

Results: Age-adjusted breast cancer incidence rates for males and females share a similar geographic distribution (Spearman's correlation $= 0.51$; $P < 0.0001$). A correlation with male incidence rates was found for the entire female population and for women aged 50 years and over. Breast cancer incidence rates in males aged <50 years were not associated with FBC incidence, whereas those in males aged $\geqslant 50$ years were. MBC incidence displays a small 'hook' similar to the Clemmesen's hook for FBC, but at a later age than the female hook.

Interpretation: Further investigation of possible explanations for these patterns is warranted. Although the incidence of breast cancer is much lower in men than in women, it may be possible to identify a cause common to both men and women.

The age-standardised incidence of breast cancer in men and women varies by country, with rates in the highest-risk countries being more than five times those in the lowest-risk countries (Curado *et al*, 2007). For women, it has been hypothesised that these geographic differences reflect differences in reproductive patterns such as age at menarche, age at first pregnancy, number of births, and duration of breast feeding (Beral *et al*, 2002; Colditz, 2005). It seems likely that reproductive factors cannot completely explain the geographic differences, however, as male breast cancer (MBC) incidence shows similar variation (Ewertz *et al*, 1989; Thomas, 1993; Ly *et al*, 2013). Dietary factors have also been suggested as an explanation for geographical differences in breast cancer incidence (Armstrong and Doll, 1975), but aside from alcohol and obesity, evidence for a role of specific nutrients or diet-related factors in breast cancer is lacking (World Cancer Research Fund, American Institute for Cancer Research, 1997; World Cancer Research Fund, American Institute for Cancer Research, 2007; Hartz and He, 2013; Chajes and Romieu, 2014; Norat *et al*, 2014), It is possible that prenatal factors, including maternal nutrition, may be associated with breast cancer (Park *et al*, 2008; Lillycrop and Burdge, 2014). It is highly likely that some risk factors for breast cancer remain to be identified (MacMahon, 2006; Hoover, 2012). The similar geographic variation for MBC and female breast cancer (FBC) suggests the possibility of a common non-reproductive aetiologic factor (or factors) for breast cancer in men and women.

Previous analyses have found similarities between male and female trends in breast cancer incidence. The incidence of MBC in Scandinavia during 1943–1982 varied over time and by country (Ewertz *et al*, 1989). The variation in incidence between countries was the same for MBC and FBC (with Danish males and females having the highest incidence, followed by Swedish, Norwegian, and

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Finnish males and females), suggesting overlapping aetiology for MBC and FBC. MBC incidence increased monotonically with age in all countries (Ewertz *et al*, 1989). The incidence of breast cancer in US men increased by 26% during 1973–1998, a smaller increase than the 52% increase observed in women during the same time period, but the incidence in women is likely to have been affected by mammographic screening (Giordano *et al*, 2004). A comparison of male and female Surveillance, Epidemiology, and End Results (SEER) breast cancer data from 1976–2005 found similar breast cancer incidence trends for MBC and FBC in the United States (Anderson *et al*, 2010), again suggesting that there may be breast cancer risk factors common to both sexes. Recently, an international comparison showed that MBC and FBC age-adjusted incidence rates are correlated (Ly *et al*, 2013).

A comparison of breast cancer rates in men and women may be helpful in identifying differences and similarities and allowing the identification of common aetiological factor(s). The incidence of breast cancer in males is about 1% than in females. About 20% of men with breast cancer have a first-degree relative with breast cancer, with between 4 and 40% of breast cancers estimated to result from autosomal dominant inheritance (particularly BRCA1 and BRCA2 mutations), compared with 5–10% in women (Fentiman *et al*, 2006). This difference may reflect a similar estimate with greater uncertainty in males because of the much lower incidence. It has been suggested that there may be two types of breast cancer in women: an 'early-onset' type that is dependent on hormonal exposures occurring early in reproductive life, and a 'late-onset' type dependent on accumulated lifetime hormonal and/or environmental exposures. MBC resembles the 'late-onset' type in women (Anderson *et al*, 2004). It is, however, also the case that there are multiple subtypes of FBC, according to receptor status (Potter *et al*, 1995), and also molecular differences (Perou *et al*, 2000). Analyses of MBC reported to the SEER registries (Anderson *et al*, 2004, 2006) found that breast cancer in males occurs later and shows higher stage, lower grade, and more oestrogen-positive (ER+) tumours than in females. The biology of MBC resembles that of postmenopausal FBC, with low-grade and hormone-receptor-positive tumours (Anderson *et al*, 2004, 2006).

Age-distribution patterns of breast cancer in women vary by histologic type (Yasui and Potter, 1999; Anderson *et al*, 2006) and by hormone-receptor status (Yasui and Potter, 1999; Anderson *et al*, 2004). Age-distribution patterns in men also vary by ER status (Anderson *et al*, 2004).

Known positive and inverse associations for MBC and premenopausal and postmenopausal FBC are shown in Table 1. This table provides an indication only; the true picture is further complicated by the fact that, in women, risk factors differ according to receptor status (Potter *et al*, 1995), and some associations found for BC in women have not been investigated in men, particularly in prospective studies, because the incidence of MBC is so much lower (Hankinson *et al*, 2008; Sousa *et al*, 2013).

Risk factors common to MBC and FBC are family history, alcohol, radiation exposure, and (for MBC and postmenopausal FBC) high oestrogen levels and high BMI. Our objective was to further investigate the possibility of shared aetiological factors for MBC and FBC. We undertook a worldwide analysis of patterns in MBC and FBC incidence, and examined whether the correlation between MBC and FBC incidence persists after stratification by age less than 50 years, and 50 years and over. It was important to do this for FBC, because risk factors differ for premenopausal and postmenopausal FBC and because MBC shares many characteristics with postmenopausal FBC. We stratified MBC by age <50 years and $\geqslant 50$ years because, although changes in FBC incidence are consistent with hormonal changes, other factors related to age

Table 1. Positive and inverse associations with premenopausal and postmenopausal female breast cancer and male breast cancer[a]

Associations	Premenopausal female breast cancer	Postmenopausal female breast cancer	Male breast cancer
High risk	Family history of breast cancer Late age at first birth	Family history of breast cancer Late age at first birth High blood oestrogen	Family history of breast cancer Kleinfelter's syndrome Testicular or liver damage Oestrogen intake Radiation exposure
Moderate risk	Height Low BMI Benign breast disease Early menarche Current/recent OC use Cowden syndrome Alcohol Radiation exposure Birth weight	Height High BMI Benign breast disease Early menarche Late menopause Current/recent HRT use Obesity Alcohol Radiation exposure Type II diabetes *In-utero* diethylstilboestrol	Cowden syndrome Occupational exposure (heat) High BMI Obesity
Suspected risk	Low vitamin D intake High blood IGF-1	High blood prolactin Birth order	Occupational exposure (exhaust emissions, magnetic fields) Alcohol Birth order
Inverse associations	Childhood overweight Parity Extended breast feeding Tamoxifen	Childhood overweight Parity Extended breast feeding Tamoxifen Physical activity	Physical activity

Abbreviations: BMI = body mass index; HRT = hormone replacement therapy; IGF-1 = insulin-like growth factor 1; OC = oral contraceptive.
[a]See Michels *et al* (1996); Hankinson *et al* (2008); Ottini *et al* (2010); Ruddy and Winer (2013).

may influence changes in incidence. If so, similar changes may be observed in MBC incidence. We also examined breast cancer incidence rate ratios (IRRs) for males and females, comparing the incidence rate for each male 5-year age group to the incidence rate among 40- to 44-year-old males, and the incidence rate for each female 5-year age group to the incidence rate among females aged 40–44 years.

MATERIALS AND METHODS

We analysed 104 populations where the male population contributed at least 5 million person-years during 1998–2002 (Curado *et al*, 2007). We used the male population size as the inclusion criterion for our analysis to ensure that we obtained stable estimates of MBC rates; estimates of FBC rates are far more stable than those of MBC because FBC is much more common. Some 'geographically defined populations' were stratified by ethnic group. In those cases, each ethnic group of the 'geographically defined population' was regarded as a population (the 104 populations included 98 'geographically defined populations'). Table 2 provides a list of the 104 populations, with the number of male person-years in each population.

We calculated the age-adjusted incidence rates of breast cancer for both males and females (using direct standardisation) and compared them for each population. We used the World Standard Population, using the standard 18 5-year age groups (Ahmad *et al*, 2001). We also investigated the correlation between MBC and FBC stratified by female age group (<50 years and $\geqslant 50$ years).

We performed a Poisson regression of MBC using random effects. We grouped the populations by the age-adjusted female incidence rates: five groups of <40, 40–59, 60–79, 80–99, and $\geqslant 100$ per 100,000 woman-years. We then fitted a Poisson model of the count of breast cancer in each age category for males with an offset of the log person years for males, adjusting for age. We used the 5-group indicator (the female age-adjusted incidence rates) as the only covariate and each population as a random effect (a model without random effects was a poorer fit than the random-effects model). This model yields the MBC IRR for each group of the 5-group indicator, compared with the reference group (<40 per 100 000 woman-years). We removed males <20 years from the analysis, as the incidence rate of breast cancer in those age categories is close to zero.

Last, we examined breast cancer IRRs for males and females, comparing the incidence rate for each male 5-year age group to the incidence rate among 40- to 44-year-old males, and the incidence rate for each female 5-year age group to the incidence rate among females aged 40–44 years.

RESULTS

MBC incidence is correlated with FBC incidence worldwide. In countries where the age-standardised incidence of FBC is high, the age-standardised incidence of MBC is also high (Figure 1).

Because MBC is thought to be similar to postmenopausal FBC, we stratified the female populations into females aged <50 years and females $\geqslant 50$ years, and compared the age-adjusted breast cancer incidence rates for the two stratified populations to the total male age-adjusted breast cancer incidence rate for each population. The correlation between the MBC and FBC incidence rates was the same whether we included the entire female population or restricted the analysis to women aged <50 years (Spearman correlation $= 0.49$; $P<0.0001$) or women $\geqslant 50$ years (0.50; $P<0.0001$).

When we modelled the association between MBC and FBC incidence, the rate ratios for MBC incidence in countries with the highest FBC incidence rates were twice as high (after age adjustment) as in countries with the lowest FBC incidence rates. Calculation of an IRR for males, stratified by male age <50 years and $\geqslant 50$ years showed no correlation between male IRR and female incidence rates for males aged <50 years (Figure 2), but a statistically significant correlation for males aged $\geqslant 50$ years, with the rate ratios for MBC incidence in countries with the highest FBC incidence rates being twice as high as in countries with the lowest FBC incidence rates (Figure 3). Similarly (data not shown), the IRR for males aged <50 years was not correlated with the incidence rates for females aged <50 years, but the IRR for males aged $\geqslant 50$ years was correlated with the incidence rates for females aged $\geqslant 50$ years. Conversely, the IRR for all males was correlated with both the incidence rates for females aged <50 years and for females aged $\geqslant 50$ years (similar to the Spearman correlation results reported above).

We compared IRRs for males and females, comparing the incidence rate for each male 5-year age group to the incidence rate for 40- to 44-year-old males, and the incidence rate for each female 5-year age group to the incidence rate for females aged 40–44 years. Male IRRs are greater than female IRRs, and display a small 'hook' similar to the Clemmesen's hook for FBC (Figure 4). However, the male hook appears to occur at a later age (~ 60 years) than the female hook.

DISCUSSION

Our findings confirm the recent report that MBC incidence is correlated with FBC incidence worldwide (Ly *et al*, 2013). In countries where the age-standardised incidence of FBC is high, the age-standardised incidence of MBC is also high. Although the correlation (Spearman correlation coefficient: 0.51, $P<0.0001$) was moderate, it shows that 25% of the variation in MBC can be explained by variation in FBC. Previously it had been suggested that the geographic variation in breast cancer incidence is due to differences between countries in known risk factors, especially reproductive factors (Beral *et al*, 2002; Colditz, 2005), but the correlation reported here between worldwide MBC and FBC incidence rates supports the hypothesis that known reproductive risk factors cannot completely explain the geographic variation in breast cancer incidence (MacMahon, 2006; Hoover, 2012).

The correlation between MBC and FBC incidence is present for MBC and BC in women aged <50 years, and between MBC and BC in women aged $\geqslant 50$ years. Thus, the correlation did not vary by female age-group (as a proxy for premenopausal and postmenopausal breast cancer). This suggests the possibility of a common aetiologic factor (or factors) for breast cancer in men and women irrespective of menopausal status.

When we modelled the association between MBC and FBC incidence, the rate ratios for MBC incidence in countries with the highest FBC incidence rates were twice as high (after age adjustment) as in countries with the lowest FBC incidence rates. The association between MBC IRRs and FBC incidence rates varied with male age (<50 years and $\geqslant 50$ years); BC rates in males aged <50 years were not associated with FBC incidence, whereas those in males aged $\geqslant 50$ years were associated with FBC incidence.

It is possible that the correlation between BC in males aged $\geqslant 50$ years and FBC (both total FBC and FBC in those aged $\geqslant 50$ years) is related to hormone-receptor status, because older men, as well as women, are more likely to have hormone-receptor-positive cancers. In a US population-based study of breast cancer during 1973–1998, men were statistically significantly more likely to have ER+/progesterone receptor-positive (PR+) BC than women. Over 90% of men had ER+ tumours, and 81% had PR+

Table 2. List of 104 populations included in analysis, showing male person-years 1998–2002

Brazil, Sao Paulo (1998–2002)	24820634
Costa Rica (1998–2002)	9972584
Canada, Alberta (1998–2002)	7597155
Canada, British Columbia (1998–2002)	10081204
Canada, Ontario (1998–2002)	28910687
USA, Alabama: White (1998–2002)	7868931
USA, Arizona (1998–2002)	12884245
USA, California: Asian and Pacific Islander (1998–2002)	10091588
USA, California: Black (1998–2002)	6185706
USA, California: Hispanic White (1998–2002)	26812333
USA, California: non-Hispanic White (1998–2002)	40508432
USA, California, Greater San Francisco Bay Area: non-Hispanic White (1998–2002)	8024193
USA, California, Los Angeles County: Hispanic White (1998–2002)	10262489
USA, California, Los Angeles County: non-Hispanic White (1998–2002)	7682666
USA, Colorado (1998–2002)	10870681
USA, Connecticut: White (1998–2002)	7175648
USA, Florida: Black (1998–2002)	6009715
USA, Florida: White (1998–2002)	32291874
USA, Georgia: Black (1998–2002)	5652359
USA, Georgia: White (1998–2002)	14010547
USA, Georgia, Atlanta (1998–2002)	7185494
USA, Illinois: White (1998–2002)	24662209
USA, Indiana (1998–2002)	14917711
USA, Iowa (1998–2002)	7167835
USA, Kentucky (1998–2002)	9877898
USA, Louisiana: White (1998–2002)	7130305
USA, Massachusetts (1998–2002)	15315553
USA, Michigan: White (1998–2002)	20255042
USA, Michigan, Detroit: White (1998–2002)	7089924
USA, Missouri: White (1998–2002)	11836459
USA, NPCR: Black (1998–2002)	67113198
USA, NPCR: White (1998–2002)	452119975
USA, New Jersey: White (1998–2002)	16169919
USA, New York State: Black (1998–2002)	6769984
USA, New York State: White (1998–2002)	36028895
USA, Ohio: White (1998–2002)	23920372
USA, Oklahoma (1998–2002)	8482218
USA, Oregon (1998–2002)	8514153
USA, Pennsylvania: White (1998–2002)	25963236
USA, SEER (9 Registries): Black (1998–2002)	7731566
USA, SEER (9 Registries): White (1998–2002)	50989670
USA, South Carolina: White (1998–2002)	6784715
USA, Texas: Black (1998–2002)	6025121
USA, Texas: White (1998–2002)	44033895
USA, Utah (1998–2002)	5619190
USA, Washington, Seattle (1998–2002)	10113742
USA, Wisconsin (1998–2002)	13258499
China, Guangzhou City (2000–2002)	5589593
China, Hong Kong (1998–2002)	16352700
China, Shanghai (1998–2002)	15914368
India, Chennai (Madras) (1998–2002)	11017202
India, New Delhi (1998–2002)	34383610
India, Mumbai (Bombay) (1998–2002)	32678581
India, Nagpur (1998–2002)	5222436
India, Poona (1998–2002)	9341935
Israel: Jews (1998–2002)	12121210
Japan, Miyagi Prefecture (1998–2002)	5790926
Japan, Osaka Prefecture (1998–2002)	21520295
Korea, Busan (1998–2002)	9496570
Korea, Daegu (1998–2002)	6367113
Korea, Incheon (1998–2002)	6400210
Korea, Seoul (1998–2002)	24717750
Malaysia, Sarawak (1998–2002)	5265380
Philippines, Manila (1998–2002)	12991010
Singapore: Chinese (1998–2002)	6235690
Turkey, Izmir (1998–2002)	8420512
Austria (1998–2002)	19402182
Belarus (1998–2002)	23503799
Belgium, Flanders (1998–2001)	11718854
Bulgaria (1998–2002)	19676019
Croatia (1998–2002)	10679500
Czech Republic (1998–2002)	24953178
Denmark (1998–2002)	13189753
Finland (1998–2002)	12650851
Germany, Brandenburg (1998–2002)	6391741
Germany, Free State of Saxony (1998–2002)	10749078
Germany, Munich (1998–2002)	5694350
Germany, Northrhine-Westphalia: Munster (1998–2002)	6370497
Ireland (1998–2002)	9439864
Italy, North East Cancer Surveillance Network (1998–2002)	5098417
Latvia (1998–2002)	5495497
Lithuania (1998–2002)	8228924
Norway (1998–2002)	11146041
Portugal, Porto (1998–2002)	7694390
Portugal, South Regional (1999–2001)	6434783
Russia, St Petersburg (1998–2002)	10521466
Serbia (1999–2002)	10682378
Slovak Republic (1998–2002)	13128455
Sweden (1998–2002)	21956316
The Netherlands (1998–2002)	39398982
UK, East of England Region (1998–2002)	6727978
UK, England, Merseyside and Cheshire (1998–2002)	5676126
UK, England, North Western (1998–2002)	10070643
UK, England, Northern and Yorkshire (1998–2002)	15941287
UK, England, Oxford Region (1998–2002)	6733800
UK, England, South and Western Regions (1998–2002)	16297153
UK, England, Thames (1998–2002)	33619900
UK, England, Trent (1998–2002)	11740169
UK, England, West Midlands (1998–2002)	12943866
UK, Scotland (1998–2002)	12172990
Australia, New South Wales (1998–2002)	16105962
Australia, Queensland (1998–2002)	8923441
Australia, Victoria (1998–2002)	11774167
New Zealand (1998–2002)	9476550

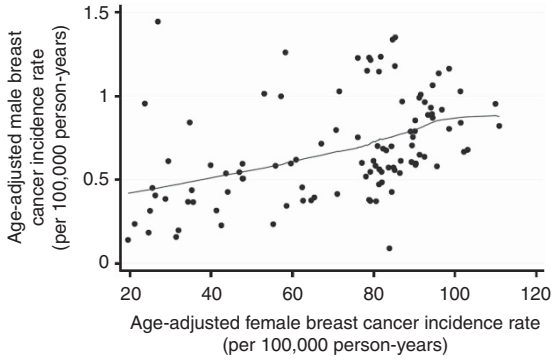

Figure 1. Male and female age-adjusted breast cancer rates by population. Spearman's correlation = 0.51; $P < 0.0001$.

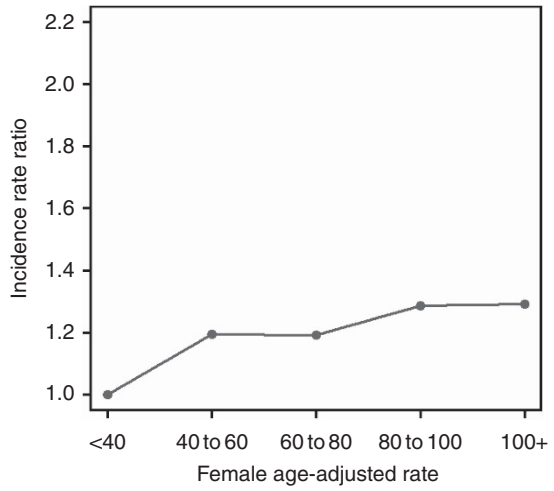

Figure 2. Incidence rate ratios for male breast cancer (under 50 years) in relation to female breast cancer incidence per 100 000 woman-years.

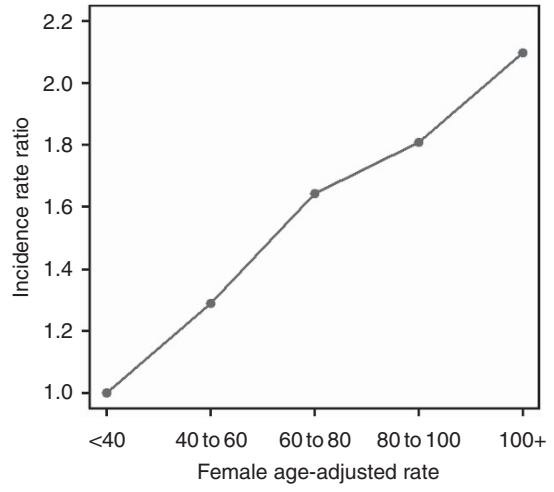

Figure 3. Incidence rate ratios for male breast cancer (50+ years) in relation to female breast cancer incidence per 100 000 woman-years.

tumours, with the proportion of ER+ tumours increasing with increasing age. Whether hormone-receptor status changed over time was not reported (Giordano *et al*, 2004). Male hormone-receptor status more closely resembled that in women aged ⩾50 years than in younger women, but the proportion with receptor-positive tumours (ER+/PR+, ER+/PR−, or ER−/PR+) was even higher among men than among postmenopausal women: in

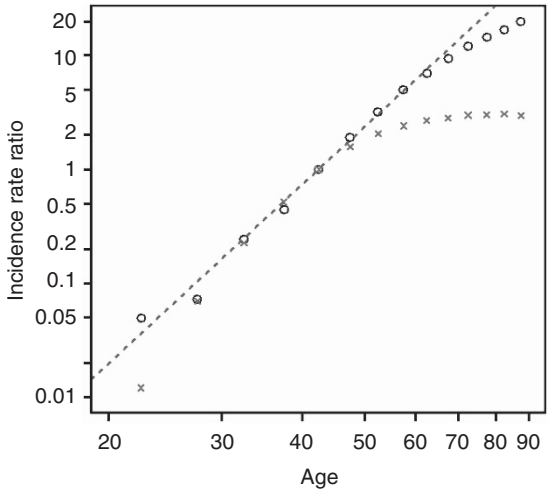

Figure 4. Male and female breast cancer incidence rate ratios by age. Male o o o o, Female x x x x.

men, 78% of tumours were ER+/PR+, whereas in women aged ⩾50 years, 65% were ER+/PR+, and in women under 50 years, 57% were ER+/PR+ (Anderson *et al*, 2004). In a more recent US population-based comparison, 92.4% of breast cancers in men were ER+ compared with 77.5% in women. The incidence of ER+/PR+ and ER+/PR− BC in females continued to rise after age 50 years, in contrast to the incidence of ER−/PR− and ER−/PR+ BC. Patterns in men could not be determined because of small numbers in some groups (Anderson *et al*, 2010).

It is also possible that BC in men <50 years is predominantly the result of genetic predisposition (Ottini *et al*, 2010). This may explain the lack of an association between BC in young males (where a higher proportion will be the result of genetic predisposition) and overall BC in females, whereas BC in older males and females may share a greater proportion of environmental or non-genetic endogenous risk factors. Migrant studies suggest that environmental risk factors contribute to geographic differences in FBC incidence (Hoover, 2012). The patterns we report here may be consistent with an early-stage exposure common to MBC and FBC, with promoter(s) (such as oestrogen) acting later having a greater impact on FBC than on MBC.

A third possibility is that the difference between Figures 2 and 3, showing that BC rates in males aged <50 years were not associated with FBC incidence, whereas those in males aged ⩾50 years were associated, is due to the small number of men aged <50 years diagnosed with BC. However, it is important to note that we restricted our analyses to populations that included a male population contributing at least 5 million person-years during 1998–2002 to obtain stable estimates of MBC incidence rates.

Breast cancer incidence rates increase with age in both males and females. In women, the rate of increase decelerates sharply around age 50 years (a phenomenon known as 'Clemmesen's hook'). An analysis of BC incidence trends in SEER data for men and women from 1976 to 2005 found that age-specific incidence rates among women increased rapidly until age 50 years, paused, and then rose more slowly (Clemmesen's hook; Anderson *et al*, 2010) but this and an earlier study of MBC incidence failed to show a 'Clemmesen's hook' (Ewertz *et al*, 1989; Anderson *et al*, 2010).

In women, the shape of the age-incidence curve may be related to histologic type (Anderson *et al*, 2006) and to hormone receptor status. An analysis of FBC in Denmark (Yasui and Potter, 1999) found that female ER and progesterone receptor (PR)-positive (ER+/PR+) breast cancer increased continuously with age, with a sudden decrease in the rate of increase around age 44 years. The incidence of ER+/PR− increased slightly during the menopausal

period but only slightly thereafter. The incidence of ER − /PR + breast cancer increased to about age 43 years then decreased subsequently. The incidence of ER − /PR − increased with age to about age 50 years, and then remained unchanged.

The shape of the age-incidence curve for BC also varies with the underlying incidence (with different shapes in low-, moderate-, and high-incidence countries) but, in Iceland, rates were seen to transition across these shapes over the period 1911–1972; this was interpreted as a cohort effect (Bjarnason *et al*, 1974). Our finding may be the result of a similar cohort effect in MBC incidence leading to the emergence of a male 'Clemmesen's hook', however, few countries have had a statistically significant increase in recent MBC incidence rates (but the confidence intervals for estimated annual percentage change in MBC incidence were wide, reflecting the small number of MBC cases each year in most countries; Ly *et al*, 2013).

The decline in FBC has been attributed to a decline in oestrogen levels associated with menopause, but Yasui and Potter (1999) previously noted the likelihood that the female decline in incidence is due not exactly to the pre- to post-menopausal breast cancer transition but rather to the way in which the hormone-receptor-defined subtypes change with age. Males do not exhibit a decline in hormone production, but sex hormone-binding globulin rises with age in males whereas in females, it remains flat (Khosla *et al*, 1998), and neither androgen nor ERs are strongly associated with MBC incidence or survival (Pich *et al*, 1999; Kidwai *et al*, 2004). This suggests the possibility of a non-hormonal risk factor that affects both male and female incidence rates and their changes with age similarly.

This was a descriptive study, and therefore limited in its ability to demonstrate causal associations. However, the correlation we found between MBC and FBC incidence rates (Spearman's correlation coefficient 0.51, $P<0.0001$) is strong enough to suggest that there is an association between geographic distribution and BC in both men and women. This association is consistent with regional comparisons in Scandinavia and in the United States, and in a recent international comparison (Ewertz *et al*, 1989; Anderson *et al*, 2010; Ly *et al*, 2013). We have also found a correlation between male and female incidence rates for the entire female population and for women aged 50 years and over. Breast cancer IRRs in males aged <50 years were not associated with FBC incidence, whereas those in males aged $\geqslant 50$ years were associated. Male IRRs are greater than female, and display a small 'hook' similar to the Clemmesen's hook for FBC, but the male hook appears to occur at a later age than the female hook. We have provided biologically plausible explanations for these patterns. The specificity of the association for older males, but not younger males, may support a causal association between geographically distributed environmental risk factors and MBC and FBC.

Further investigation of possible explanations for these patterns is warranted, including further analyses of MBC and FBC incidence by country, taking into account differences between countries in some known risk factors such as BMI and parity. Although the incidence of BC is much lower in men than in women, it may be possible to identify a cause that is common to both men and women, which may be relevant to prevention in both sexes.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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