# Recorded Quadrant Incidence of Female Breast Cancer in Great Britain Suggests a Disproportionate Increase in the Upper Outer Quadrant of the Breast

PHILIPPA D. DARBRE

*Division of Cell and Molecular Biology, School of Animal and Microbial Sciences, The University of Reading, P.O. Box 228, Whiteknights, Reading, RG6 6AJ, U.K.*

**Abstract.** *Background: The upper outer quadrant (UOQ) of the breast is the most frequent site for incidence of breast cancer, but the reported disproportionate incidence in this quadrant appears to rise with year of publication. Materials and Methods: In order to determine whether this increasing incidence in the UOQ is an artifact of different study populations or is chronological, data have been analysed for annual quadrant incidence of female breast cancer recorded nationally in England and Wales between 1979 and 2000 and in Scotland between 1980 and 2001. Results: In England and Wales, the recorded incidence of female breast cancer in the UOQ rose from 47.9% in 1979 to 53.3% in 2000, and has done so linearly over time with a correlation coefficient R of +0.71±SD 0.01 (p<0.001). Analysis of independent data from Scotland showed a similar trend in that recorded female breast cancer had also increased in the UOQ from 38.3% in 1980 to 54.7% in 2001, with a correlation coefficient R for the linear annual increase of +0.80±SD 0.03 (p<0.001). Conclusion: These results are inconsistent with current views that the high level of UOQ breast cancer is due solely to a greater amount of target epithelial tissue in that region. Identification of the reasons for such a disproportionate site-specific increase could provide clues as to causative factors in breast cancer.*

The incidence of breast cancer is rising in Britain (1), and indeed all over the world (2, 3), but the reasons for the rise remain to be identified. Numerous clinical studies, dating back decades, have shown that the upper outer quadrant (UOQ) of the breast is the most frequent site of carcinoma, but an adequate explanation for this asymmetric occurrence of breast cancer within the breast has never been established. This basic observation has become textbook fact (4), and remains true for countries as disparate as India (5), the West Indes (6) and Italy (7), and irrespective of race within any one country (8). Furthermore, the UOQ is not only the most common site of the tumour in cancer, but also in many benign breast conditions including fibroadenoma and breast cysts (9) and phyllodes tumour (10, 11). The UOQ is also the most frequent site of male breast cancer (12, 13).

However, it is interesting to note that the reported incidence of breast cancer in the UOQ of the breast appears to rise disproportionately with year of publication. In 1926, 30.9% of breast cancer was reported to be in the UOQ (14), but reports between the years 1947-1967 suggested that the proportion of breast cancer in the UOQ was 43-48% (15-19). A study in 1994 reported 60.7% of breast cancers in the UOQ (7).

The accepted explanation for the disproportionate incidence of breast cancer in the UOQ of the breast is that this region of the breast contains a greater proportion of the epithelial tissue, which is the target site for breast cancer. However, evidence for this explanation is lacking and seems to be anecdotal in origin (4). If this trend of increasing incidence of breast cancer in the UOQ is a function of time and is not a reflection of different study populations, then this would question the explanation for the high incidence of breast cancer in the UOQ as being due solely to the presence of more epithelial tissue in that region. In order to determine whether there is a chronological increase in breast cancer incidence in the UOQ within a single population, data have been analysed on the quadrant incidence of female breast cancer recorded nationally for England and Wales for the available years of 1979 to 2000. Comparative independent data for Scotland have been analysed for the years 1980 to 2001.

*Correspondence to:* Philippa D. Darbre, Division of Cell and Molecular Biology, School of Animal and Microbial Sciences, The University of Reading, P.O. Box 228, Whiteknights, Reading, RG6 6AJ, U.K. Tel: 0118-9875123 ext 7035 / 7025, Fax: 0118-9310180, e-mail: p.d.darbre@reading.ac.uk

*Key Words:* Breast cancer incidence, epidemiology, upper outer quadrant, underarm cosmetics, cancer prevention.

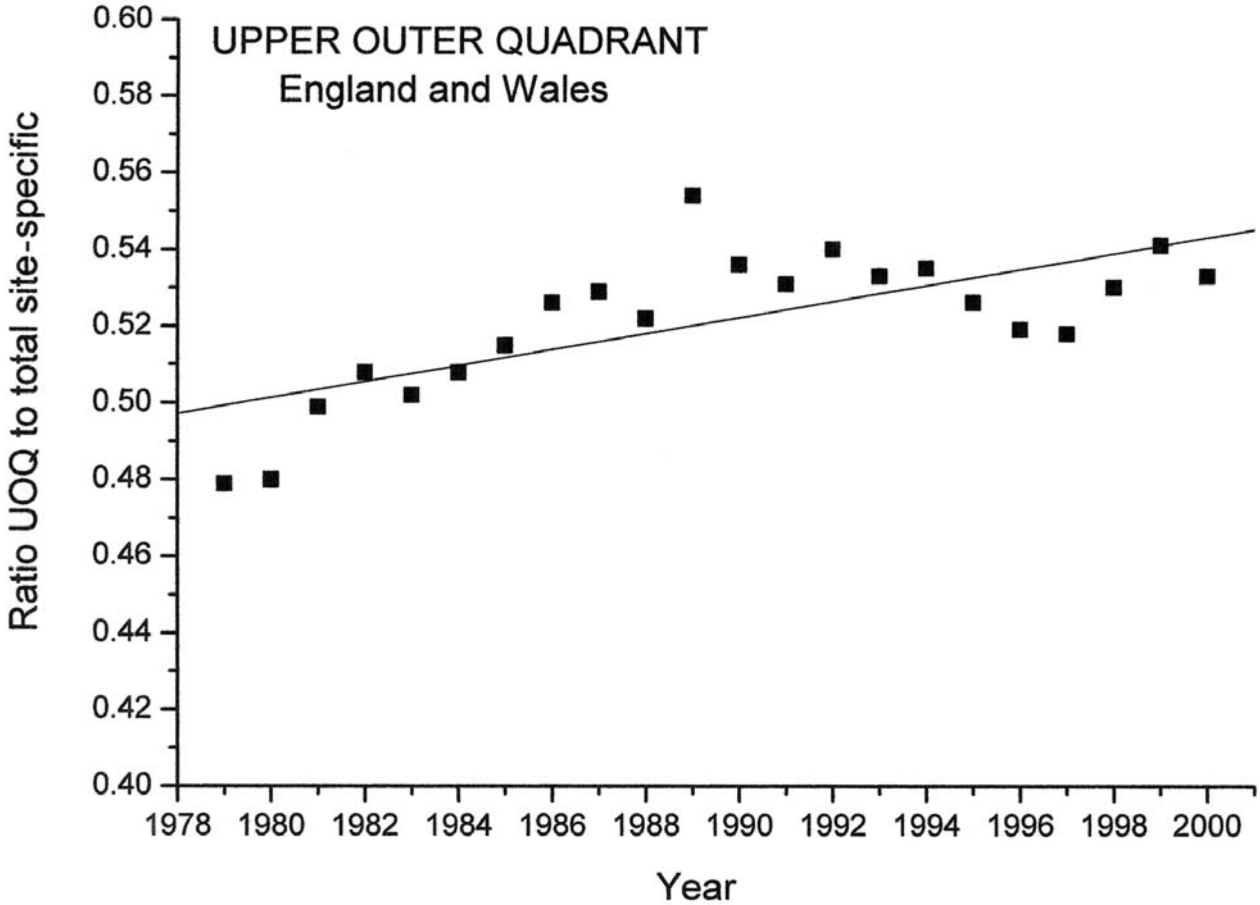


Figure 1. *England and Wales: Trend in proportional annual incidence of female breast cancer in the upper outer quadrant (UOQ) of the breast from 1979 to 2000. Each point represents the ratio of recorded incidence in UOQ to the total incidence recorded in that year with site-specific information. Linear regression analysis was used to calculate a line of best fit. Table I gives the slope of the line, its standard error and the correlation coefficient (R) together with the standard deviation (SD) of the fit; the probability (p value) that R is zero was obtained from the F distribution.*

## Materials and Methods

*Data collection for England and Wales.* The incidence of breast cancer in England and Wales is recorded by the Regional Cancer Registeries and collated on a national basis. From 1979 to 1994, this was recorded collectively by the Office of National Statistics in London, UK. Since 1995, the London Office has continued to record data from England, while the data from Wales has been recorded separately by the Welsh Cancer Intelligence and Surveillance Unit in Cardiff. Since 1979, incidence data has been requested annually according to quadrant under the fourth digit ICD9 codes for 174 (1979-1994) or ICD10 codes for 50 (1995-2000). The information was separated into seven regions of the breast under the following codes: ICD174.0 / 50.0 nipple and areola, ICD174.1 / 50.1 central portion, ICD174.2 / 50.2 upper inner quadrant, ICD174.3 / 50.3 lower inner quadrant, ICD174.4 / 50.4 upper outer quadrant, ICD174.5 / 50.5 lower outer quadrant, ICD174.6 / 50.6 axillary tail. Total incidence data for England and Wales from 1979 to 2000 was returned with quadrant information under the ICD9/10 codes 174.0/50.0 – 174.6/50.6 in 212,677 returns.

*Data collection for Scotland.* The incidence of breast cancer in Scotland is recorded independently by the Cancer Intelligence Group, NHS Scotland in Edinburgh. Incidence data has been requested annually according to quadrant since 1980. Incidence data from 1980 to 2001 was returned with quadrant information in 17,911 returns. The information was recorded using the same coding system of the breast as for the data from the London and Cardiff offices.

Between the years 1980 and 1996, there was an annual lack of compliance with quadrant information in an overall average of 82.5% (± SD 2.53%) of cases. However, as a result of reorganization of cancer registration procedures, the lack of compliance has decreased sharply since 1997 to an overall average between 1997 and 2001 of 47.8% (± SD 2.54%).

*Data analysis.* All data were analysed and statistical parameters calculated using Origin 7 (Microcal Software Inc., Northampton, MA, USA). Linear regression analysis (by the method of least squares) was used to calculate the slope of the line, its standard error and the correlation coefficient (R) together with the standard deviation of the fit (±SD). The probability (*p* value) that R is zero was obtained from the F distribution.

Table I. *Statistical parameters relating to Figures 1-5. Linear regression analysis was used to calculate the slope of the line (slope), its standard error (error) and the correlation coefficient (R) together with the standard deviation of the fit (SD). The probability (p value) that R is zero was obtained from the F distribution. Values are shown for breast cancer in England and Wales in the upper outer quadrant (UOQ) (Figure 1), in other quadrants (Figure 2) and for the UOQ divided into three separate age groupings (Figure 3). Values are shown for breast cancer in Scotland in the UOQ (Figure 4), in other quadrants (graphs not shown) and for the UOQ divided into three separate age groupings (Figure 5).*

| | | England and Wales | | | | | Scotland | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Quadrant of the breast | Ages | Slope | error | R | SD | *p* value | Slope | error | R | SD | *p* value |
| Upper outer quadrant | all ages | +0.0021 | 0.0005 | +0.713 | 0.014 | 0.0002 | +0.0056 | 0.0009 | +0.800 | 0.028 | <0.0001 |
| Nipple and areola | all ages | –0.0015 | 0.0002 | –0.839 | 0.007 | <0.0001 | –0.0023 | 0.0009 | –0.480 | 0.028 | 0.0238 |
| Central portion | all ages | +0.0001 | 0.0003 | +0.048 | 0.009 | 0.8330 | –0.0030 | 0.0009 | –0.604 | 0.027 | 0.0029 |
| Upper inner quadrant | all ages | –0.0005 | 0.0002 | –0.534 | 0.005 | 0.0104 | +0.0007 | 0.0004 | +0.332 | 0.013 | 0.1309 |
| Lower inner quadrant | all ages | +0.0004 | 0.0001 | +0.632 | 0.004 | 0.0016 | +0.0013 | 0.0004 | +0.624 | 0.010 | 0.0019 |
| Lower outer quadrant | all ages | +0.0003 | 0.0002 | +0.368 | 0.005 | 0.0923 | +0.0002 | 0.0005 | +0.087 | 0.014 | 0.7000 |
| Axillary tail | all ages | –0.0009 | 0.0001 | –0.964 | 0.002 | <0.0001 | –0.0024 | 0.0004 | –0.830 | 0.011 | <0.0001 |
| Upper outer quadrant | 0-49 years | +0.0028 | 0.0006 | +0.735 | 0.017 | <0.0001 | +0.0065 | 0.0018 | +0.626 | 0.054 | 0.0018 |
| Upper outer quadrant | 50-69 years | +0.0025 | 0.0005 | +0.753 | 0.144 | <0.0001 | +0.0054 | 0.0010 | +0.762 | 0.030 | <0.0001 |
| Upper outer quadrant | 70+ years | +0.0010 | 0.0005 | +0.400 | 0.015 | 0.0648 | +0.0058 | 0.0015 | +0.663 | 0.043 | 0.0008 |

## Results

*Female breast cancer incidence in England and Wales.* Over the period 1979 to 2000, the incidence of female breast cancer has increased in England and Wales from 74.4 per 100,000 population (European age-standardised rate (EASR)) (21,446 new cases recorded) in the year of 1979 to 113.8 per 100,000 population (EASR) (35,903 new cases recorded) in the year of 2000.

Within the 212,677 returns made with site-specific information between 1979 and 2000, 52.5% of the returns were in the UOQ of the breast (111,583 cases recorded). Other sites in the breast were returned at lower frequencies: 3.9% in the nipple and areola (8,222 cases recorded), 11.2% in the central portion (23,780 cases recorded), 14.6% in the upper inner quadrant (31,064 cases recorded), 6.4% in the lower inner quadrant (13,570 cases recorded), 9.8% in the lower outer quadrant (20,836 cases recorded) and 1.7% in the axillary tail (3,622 cases recorded).

Inspection of the annual incidence rates returned for each of these sites in the breast shows that, as the incidence of breast cancer has risen overall between 1979 and 2000, it is also increasing in all of these sites. However, it does not appear to be increasing in all quadrants relative to one another at the same rate. Figure 1 shows the trend between 1979 and 2000 in breast cancer in the UOQ of the breast, expressed as a ratio of the annual incidence in the UOQ to the total incidence recorded in that year with site-specific information. This shows that within the site-specific returns, the incidence of breast cancer is increasing in the UOQ relative to total site-specific returns. The correlation coefficient (R) for the linear increase in UOQ breast cancer was +0.713 with a standard deviation (SD) of the fit of ±0.014 and a *p*-value obtained from the F distribution of <0.001 (Table I). The rate of increase in the UOQ over and above total breast cancer was calculated from the slope of the line and gave a value of 0.0021±0.0005 per annum (Table I). Over a 21-year time-span from 1979 to 2000, the incidence of breast cancer in the UOQ relative to total site-specific returns has risen disproportionately from 47.9% in 1979 to 53.3% in 2000.

Figure 2 shows the trends in breast cancer for each of the other quadrants of the breast between 1979 and 2000. For each quadrant, the annual incidence was expressed as a ratio of the incidence in that quadrant to the total incidence recorded in that year with site-specific information. Calculation of each correlation coefficient (R) together with the standard deviation of the fit (±SD) confirmed that no other quadrant showed any significant increase in breast cancer incidence relative to total site-specific returns (Table I).

Figure 3 shows the trend in breast cancer in the UOQ relative to total site-specific returns for three separate age groupings: 0-49 years, 50-69 years and 70+ years. Of the 212,677 returns made with site-specific information, there were 48,017 returns in the 0-49 year age grouping, 99,393 returns in the 50-69 year age grouping, and 65,267 returns in the 70+ year age grouping. In both the 0-49 and 50-69 year groups, there was a significant linear increase in UOQ breast cancer with *p*-values obtained from the F distribution of <0.0001 (Table I). It is interesting that the line of best fit suggests the highest proportion of UOQ breast cancer to be in the youngest age group (Figure 3).

*Female breast cancer incidence in Scotland.* In Scotland, the incidence of female breast cancer has risen from 84.9 per 100,000 population (EASR) (2,480 new cases recorded) in

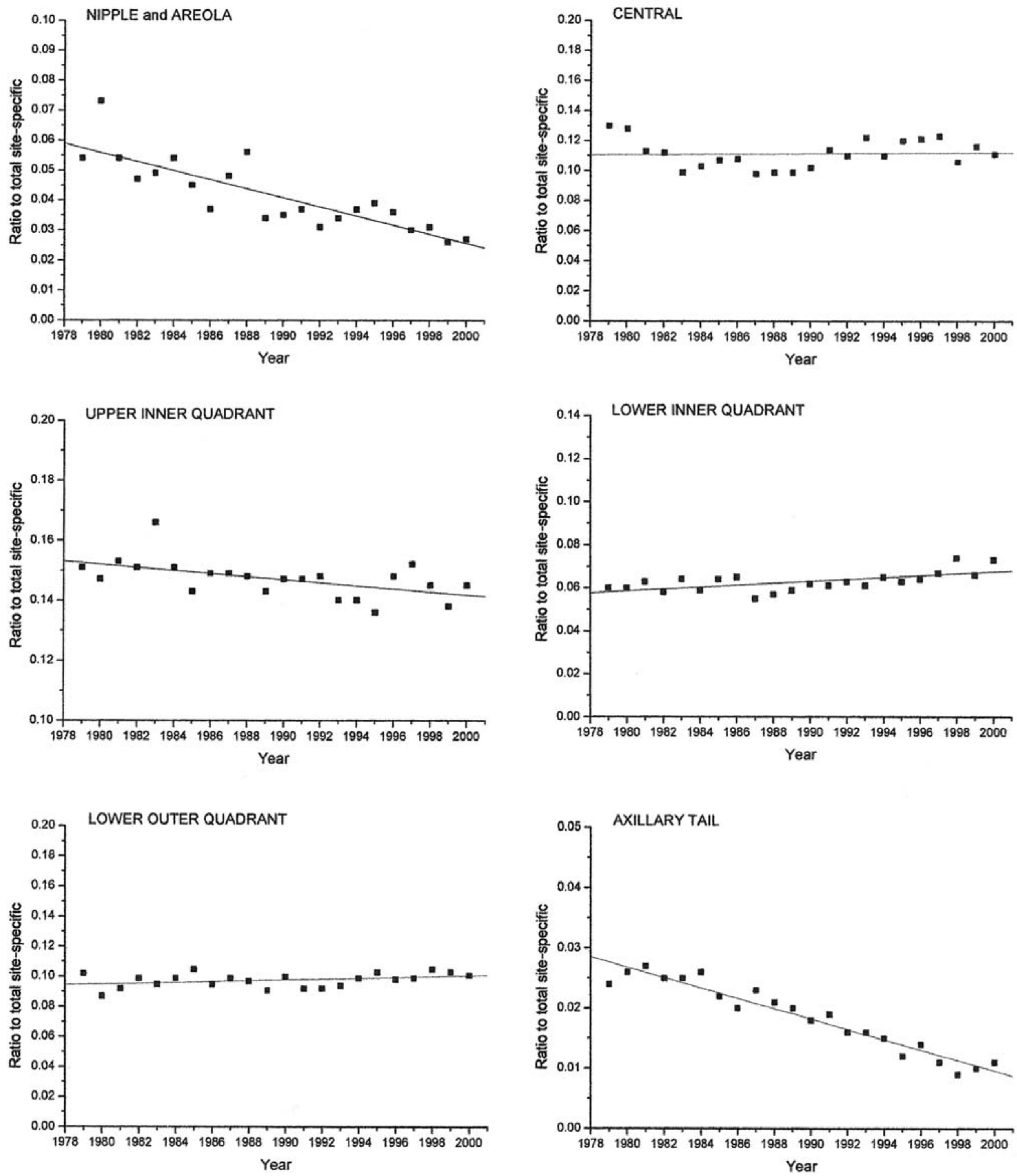


Figure 2. *England and Wales: Trends in proportional annual incidence of female breast cancer in sections of the breast other than the upper outer quadrant from 1979-2000. Each point represents the ratio of recorded incidence in that quadrant of the breast to total incidence recorded in that year with site-specific information. For each graph, linear regression analysis was used to calculate a line of best fit. Table I gives the values for each slope, its standard error and the correlation coefficient (R ) together with the standard deviation (SD) of the fit; the probability (p value) that R is zero was obtained from the F distribution.*

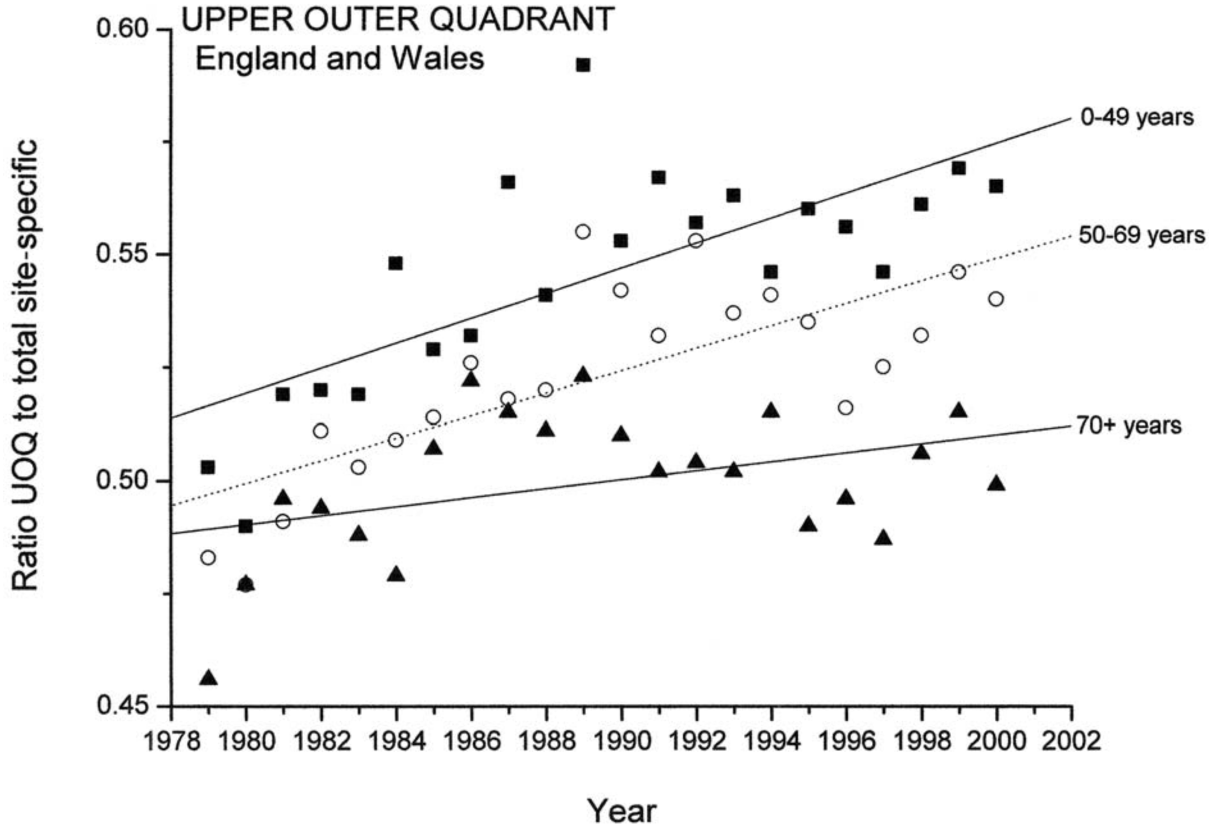


Figure 3. *England and Wales: Trend in proportional annual incidence of female breast cancer in the upper outer quadrant (UOQ) of the breast for three separate age groups 0-49 years, 50-69 years and 70+ years. Presentation of the data is exactly as given in Figure 1 except for the division into the three age groupings. For each age group, linear regression analysis was used to calculate a line of best fit and statistical parameters are given in Table I.*

the year of 1980, to 109.8 per 100,000 population (EASR) (3,485 new cases recorded) in 2001.

Within the 17,911 returns made with site-specific information between 1980 and 2001, the site of greatest incidence within the breast was again the UOQ in 52.6% of the returns (9,418 cases recorded).

Figure 4 shows the increasing trend between 1980 and 2001 of breast cancer in the UOQ, expressed as a ratio of annual incidence rate in the UOQ as a proportion of the total incidence rate recorded in that year with site-specific information. The correlation coefficient for the linear increase observed was +0.800, with a standard deviation of the fit of ±0.028 and a *p*-value obtained from the F distribution of $<0.0001$. As for the data for England and Wales, no other quadrant showed any significant increase over the total (Table I). Over a 21-year time-span, the incidence of breast cancer in the UOQ has risen disproportionately from 38.3% in 1980 to 54.7% in 2001.

As for England and Wales, the trend in breast cancer in the UOQ relative to total site-specific returns has been further analysed for three separate age groupings: 0-49 years, 50-69 years and 70+ years (Figure 5). Of the 17,911 returns made with site specific information, there were 3,909 returns in the 0-49 year age grouping, 8,430 returns in the 50-69 year age grouping, and 5,572 returns in the 70+ year age grouping. In all three age groupings, there was a significant linear increase in UOQ breast cancer (Table I). Furthermore, again the line of best fit suggests the highest proportion of UOQ breast cancer to be in the youngest age group (Figure 5).

## Discussion

Within the overall increase in the rate of breast cancer incidence, this study shows that according to the site-specific information available, female breast cancer in Britain is increasing disproportionately in the UOQ relative to other quadrants of the breast. Furthermore, this disproportionate increase is rising annually in that quadrant in a linear mode. That the UOQ is the most frequent site of breast cancer is in agreement with decades of previous studies (see introduction).

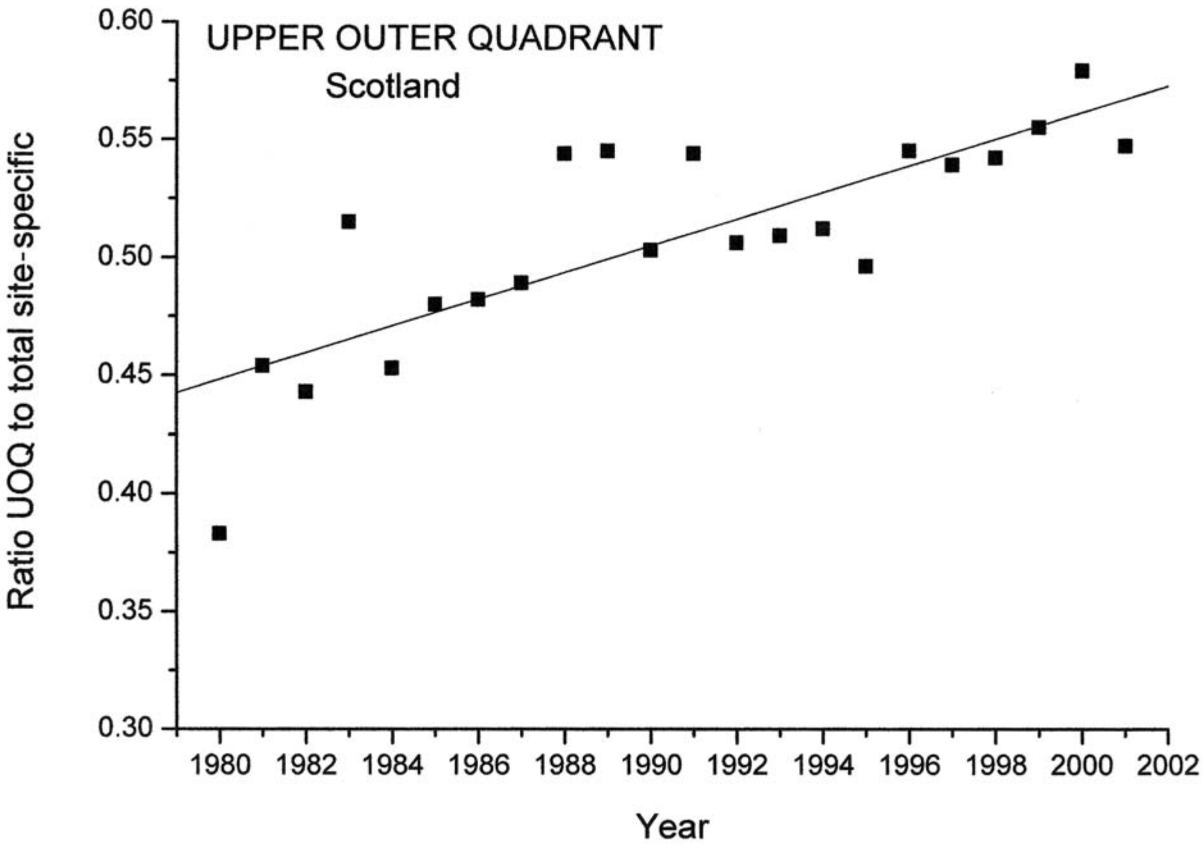


Figure 4. *Scotland: Trend in proportional annual incidence of female breast cancer in the upper outer quadrant (UOQ) of the breast from 1980 to 2001. Each point represents the ratio of recorded incidence in the UOQ to the total incidence recorded in that year with site-specific information. Linear regression analysis was used to calculate a line of best fit. Table I gives the slope of the line, its standard error and the correlation coefficient (R) together with the standard deviation (SD) of the fit; the probability (p value) that R is zero was obtained from the F distribution.*

However, this study describes, for the first time, a disproportionate increase, year by year, in that quadrant within two single populations (England and Wales; Scotland).

The main uncertainty in this study regards the incomplete compliance with returns of quadrant information, which leaves open the possibility of recording bias between the two data sets, one with quadrant information and one lacking site-specific information. Introduction of the breast screening programme in the late 1980s did not influence the overall trends observed, and it is most likely that site-specific recording was related to individual doctor and/or centre compliance. However, although compliance was incomplete, it must be taken into account that the overall numbers of returns made with site-specific information were large, particularly for England and Wales which included 212,677 returns in the study.

An attempt to address the issue of recording bias was made by obtaining incidence data from two independent sources. Breast cancer statistics are recorded for Scotland in Edinburgh independently from those for England and Wales in London and Cardiff. However, a similar disproportionate increase in breast cancer in the UOQ was found within the Scottish data as for data from England and Wales. This makes the results less likely to be due to recording bias since the same bias would have to be operating in the two independent data sets. Furthermore, the sharp increase in Scotland in compliance with return of site-specific information between 1996 and 1997 as a result of reorganization of the cancer registration procedures (see Materials and Methods section) did not influence the overall pattern of increasing UOQ breast cancer. This lack of effect of an increase in site-specific returns from an average of 17.5% (1996 and before) to an average of 52.2% (1997 and after) lends further support to the results not being dependent on a recording bias due to lack of compliance with returns of site-specific information.

Following the introduction in Britain of the breast screening programme in the late 1980s, the recorded

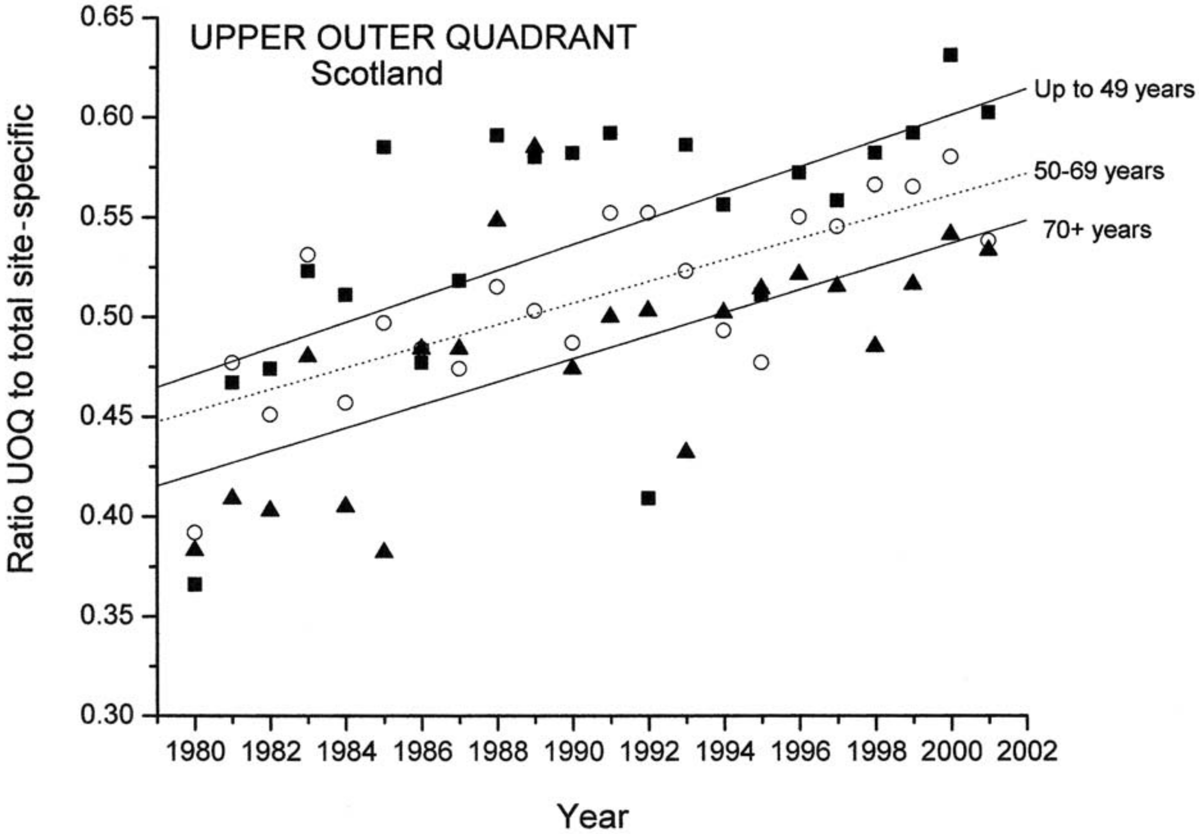


Figure 5. *Scotland: Trend in proportional annual incidence of female breast cancer in the upper outer quadrant (UOQ) of the breast for three separate age groups 0-49 years, 50-69 years and 70+ years. Presentation of the data is exactly as given in Figure 4 except for the division into the three age groupings. For each age group, linear regression analysis was used to calculate a line of best fit and statistical parameters are given in Table I.*

incidence rates of breast cancer rose sharply in immediate subsequent years in the screened age group (50-64 year olds) (1, 20). Further separation of the data used in this study into three age groupings (0-49 years, 50-69 years and 70+ years) demonstrated that the disproportionate increase in UOQ breast cancer was not confined to the screened age group (50-64 years) in either of the two study populations, England and Wales or Scotland. It is noteworthy that, in fact, the proportion of UOQ breast cancer was highest in the youngest age group.

The reasons for the disproportionate annual increase in breast cancer in the UOQ remain unknown at this time. It has long been assumed that more breast cancers occur in the UOQ because there is a larger volume of epithelial breast tissue in that quadrant (4). However, to explain a disproportional annual rise in UOQ breast cancer, as described here, would require an unlikely annual migration of breast tissue into the UOQ. Other workers have also queried the current explanatory dogma through their studies, showing an even distribution of cancer between quadrants in large and small breasts, despite the less marked quadrant distribution of the tissue in the smaller breasts (9). A more recent study of genomic patterns of loss of heterozygosity and allelic imbalance in breast quadrants from 21 breast cancer patients showed increased levels of genomic instability in the outer breast quadrants, suggesting that increased levels of breast cancer in the UOQ might result from the development of genetic alterations in that region of the breast rather than from only a greater tissue volume (21). The results presented here add to the uncertainty of the explanation of the large incidence of breast cancer in the UOQ being due solely to a greater amount of breast tissue in that region. Whilst more breast cancers will occur at the site of greatest target tissue, other reasons must also exist to explain the site-specific increase. One possible explanation could relate to the increasing use of cosmetics applied to the adjacent underarm and upper breast area. Risk factors for breast cancer include genetic and hormonal components (3) and these underarm cosmetics are known to contain both DNA-damaging chemicals and chemicals which can mimic oestrogen action (22-25), and recent epidemiological research shows that greater use of these cosmetics can reduce the age of breast cancer diagnosis (26). However, it is possible that other aetiologies also exist. Alterations to the proportion of breast cancers in each quadrant are important clinically in view of reported differences in survival of patients with inner *versus* outer quadrant breast cancers (27). Of greater importance, however, is the possibility that this disproportional site-specific increase in UOQ breast cancer could provide clues to causative factors in breast cancer, the identification of which are essential if a strategy for breast cancer prevention is ever to become a realistic goal.

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## References

1 Quinn M and Allen E: Changes in incidence of and mortality from breast cancer in England and Wales since introduction of screening. Br Medical J *311*: 1391-1395, 1995.
2 Ursin G, Bernstein L and Pike MC: Breast cancer. Cancer Surveys *19/20*: 241-264, 1994.
3 Lipworth L: Epidemiology of breast cancer. Eur J Cancer Prevent *4*: 7-30, 1995.
4 Haagensen CD: Diseases of the Breast, 2nd edn. Philadelphia: WB Saunders, 1971.
5 Hussain MA, Sawkat A, Tyagi SP and Reza H: Incidence of cancer breast at Aligarh. J Indian Med Assoc *92*: 296-297, 1994.
6 Raju GC and Naraynsingh V: Breast cancer in West Indian women in Trinidad. Trop Geogr Med *41*: 257-260, 1989.
7 Azzena A, Zen T, Ferrara A, Brunetti V, Vasile C and Marchetti M: Risk factors for breast cancer. Eur J Gynaecol Oncol *15*: 386-392, 1994.
8 Patterson SK, Helvie MA, Joynt LK, Roubidoux MA and Strawderman M: Mammographic appearance of breast cancer in African-American women: report of 100 consecutive cases. Acad Radiol *5*: 2-8, 1998.
9 Rimsten A: Symptoms and signs in benign and malignant tumours of the breast. Upsala J Med Sci *81*: 54-60, 1976.
10 Stebbing JF and Nash AG: Diagnosis and management of phyllodes tumour of the breast: experience of 33 cases at a specialist centre. Ann R Coll Surg Engl *77*: 181-184, 1995.
11 Alam I, Awad ZT and Given HF: Cystosarcoma phyllodes of the breast: a clinicopathological study of 11 cases. Ir Med J *96*: 179-180, 2003.
12 Jaiyesimi IA, Buzdar AU, Sahin AA and Ross MA: Carcinoma of the male breast. Ann Intern Med *117*: 771-777, 1992.
13 Rizk SN, Assimacopoulos CA and Ryan JJ: Male breast cancer: three case reports and review of the literature. SDJ Med *47*: 343-346, 1994.
14 Lane-Claypon JE: A further report on cancer of the breast with special reference to its associated antecedent conditions. Reports on Public Health and Medical Subjects no 32, London: Ministry of Health, 1926.
15 Truscott BM Carcinoma of the breast. Br J Cancer *1*: 129, 1947.
16 Harnett WL: A statistical report on 2529 cases of cancer of the breast. Br J Cancer *2*: 212, 1948.
17 Nohrman BA: Cancer of the breast. Acta Radiol, Suppl 77, 1949.
18 Smithers DW, Rigby-Jones P, Galton DAG and Payne PM: Cancer of the breast. Br J Radiol, Suppl 4, 1952.
19 Donegan WL and Spratt JS: Cancer of the second breast. *In:* Spratt JS, Donegan WL (eds.). Cancer of the Breast, Philadelphia: WB Saunders, pp. 179, 1967.
20 Quinn M, Babb P, Brock A, Kirby E and Jones J: Cancer trends in England and Wales 1950-1999. Studies on Medical and Population Subjects No 66. Crown copyright, London: The Stationery Office, 2001 (available on line through http://www.statistics.gov.uk).
21 Ellsworth DL, Ellsworth RE, Love B, Deyarmin B, Lubert SM, Mittal V, Hooke JA and Shriver CD: Outer breast quadrants demonstrate increased levels of genomic instability. Ann Surg Oncol *11*: 861-868, 2004.
22 Darbre PD: Underarm cosmetics are a cause of breast cancer. Eur J Cancer Prevent *10*: 389-393, 2001.
23 Darbre PD: Underarm cosmetics and breast cancer. J Appl Toxicol *23*: 89-95, 2003.
24 Harvey PW: Parabens, oestrogenicity, underarm cosmetics and breast cancer: a perspective on a hypothesis. J Appl Toxicol *23*: 285-288, 2003.
25 Harvey PW and Darbre P: Endocrine disrupters and human health: Could oestrogenic chemicals in body care cosmetics adversely affect breast cancer incidence in women? A review of evidence and call for further research. J Appl Toxicol *24*: 167-176, 2004.
26 McGrath KG: An earlier age of breast cancer diagnosis related to more frequent use of antiperspirants/deodorants and underarm shaving. Eur J Cancer Prevent *12*: 479-485, 2003.
27 Gaffney DK, Tsodikov A and Wiggins, CL: Diminished survival in patients with inner *versus* outer quadrant breast cancers. J Clin Oncol *21*: 467-472, 2003.

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