Incidence of male breast cancer in Scotland over a twenty-five-year period (1992 - 2017)

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Abstract

Male breast cancer (MBC) accounts for around 1% of all breast cancers diagnosed. There are inconsistent reports on the incidence of MBC which some propose may be rising. Here, for the first time, the incidence of MBC in Scotland over 25 years from 1992 to 2017 was examined through interrogating the Information Services Division Scotland database. Results showed MBC incidence rose with age, peaking in the 65-70 and 75-79 age groups. Both the total number and the age-adjusted incidence of MBC increased in Scotland since 1992. This rising trend was most clear in the North of Scotland. Interestingly a higher MBC incidence in some rural areas was also observed. Our findings emphasise the need for a better understanding of MBC risk factors so that improved prevention policies can be applied for patient benefit.

1. Introduction

Breast cancer accounts for <1% of all cancers diagnosed in men and around 1% of all breast cancers (1, 2). Male breast cancer (MBC) fulfils the EU (3) and US (4) classifications of a rare cancer; defined as $\leq$ 6 cases per 100,000 or $\leq$ 15 cases per 100,000 individuals, respectively.

MBC is associated with significant morbidity and mortality; most likely this is due to lack of awareness in the general population, since men generally present with more advanced disease (5) and older age when comorbidities might be confounding (6, 7). Other survival disadvantages in MBC include low income, limited education, black race and receiving treatment outside an academic cancer centre (8). MBC focused research has previously been limited due to the difficulties in obtaining large enough sample numbers to study of the disease, meaning that men are treated in the same way as women, despite consistent emerging evidence that it has unique molecular profiles (9-12), subtleties in prognostic factors and evolution of more bespoke treatment regimens (13) plus encouragement from MBC patient/physician for the disease to recognised as distinct from breast cancer in women (14).

While it is widely reported that the global incidence of female breast cancer is increasing (15, 16), studies on the incidence of MBC are less consistent. Perhaps as a result of the small numbers of cases presenting annually, MBC incidence seems to fluctuate from year to year (15) yet appears more stable when comparisons are made over longer periods of time (7). MBC incidence in the US was reported to have increased from 1 – 1.2 per 100,000 men between the late 1970's to early 2000's (7, 17) with reported annual increase in MBC incidence of 0.86% per year from 1974 to 2005 (7). Similar increasing trends have been reported for Europe (18).

Scotland is a constituent part of the UK, yet has its own devolved healthcare system, operating across 14 regional health boards. Population demographics range from densely populated areas within the Central belt to less populated areas in the Highlands & Islands and Lowland regions. The aim of this study was to interrogate data on age-adjusted incidence of MBC in Scotland from 1992 – 2017 using a national database, testing the hypothesis that regional variations in incidence might be observed.

2. Materials and Methods

All data was collected from the Information Services Division (ISD) Scotland database (date last accessed 29 July 2019). ISD captures national, health service data. These data, including age at diagnosis and incidence, were analysed by region according to the NHS (National Health Service; the publicly funded healthcare system in Scotland and the UK) regions of residence 2014 Health Board configurations. Regions included the North of Scotland, South East of Scotland, and West of Scotland. For some analysis, each region was broken down into constituent health boards. Rurality was calculated using The Scottish Government Urban Rural Classification 2016 (17).

Breast cancer incidence trend was analysed for MBC patients in the whole of Scotland, and each of the constituent NHS regions (North, South East, and West). Data was analysed to evaluate whether trends were present over the 25 years from 1992-2017. Incidence was captured as European Age Standardised Rate (EASR), which gives age-standardised incidence rate per 100,000 person-years at risk, using 2013 European Standard Populations. Graphs were plotted using GraphPad Prism (San Diego, CA). Where appropriate, trend lines were fitted and R^2 was used to determine the fit of the line using in built software.

3. Results

3.1 Age at Diagnosis and Number Diagnosed

MBC was most prevalent in older age groups, with 93.7% of patients being over the age of 49. The number of MBCs diagnosed began to increase gradually after the age of 49, with peak numbers seen between the ages of 65-69, and 75-79; it then sharply decreased in patients over the age of 80 (Figure 1a). As shown in Figure 1b and c, the total number of MBC diagnosed across Scotland showed a gradual rise since the early 1990s ($R^2 = 0.62$). This accounted for 0.36% of all breast cancers diagnosed in 1992, rising to 0.65% in 2017. Cumulatively across the years studied, MBC accounted for 558 diagnoses, 0.52% of all breast cancers in Scotland.

3.2 Male Breast Cancer Incidence Trend

Incidence trends are shown in Figure 2. The overall incidence of MBC across the whole of Scotland appears to have been increasing over the last 25 years (Figure 2a; $R^2 = 0.24$). On a regional basis, similar rising trends were observed in the North of Scotland (Figure 2b; $R^2 = 0.30$) and West of Scotland (Figure 2c; $R^2 = 0.23$). This was less evident in South East Scotland; although the incidence was variable the trend appeared more stable (Figure 2d; $R^2 = 0.05$). Between 1992 and 2017, MBC

EASR rose by 38.5%, 54%, 21.4% and 46.2% in the whole of Scotland, North of Scotland, South East of Scotland and West of Scotland, respectively. Across the whole of Scotland, the incidence was 0.8 in 1992 and 1.3 in 2017.

3.3 Regional Variations

The EASR was taken for each NHS Health Board region and averaged over the 25 years from 1992-2017. The Western Isles, Borders, and Dumfries & Galloway showed highest EASRs; 1.4, 1.33, and 1.33 respectively, indicating that MBC is most prevalent in these regions. Forth Valley had the lowest value (0.73). This is shown in Figure 3. The Western Isles have the highest remote and rural (R&R) population in Scotland (72.4%). Similarly, Dumfries & Galloway and the Scottish Borders have a 20.9% and 10.7% R&R population respectively. Regions within central Scotland had <0.5% R&R population.

4. Discussion

Our study aimed to examine trends in the incidence of MBC in Scotland across a 25-year period, through analysis of publicly available data collated by ISD Scotland. To our knowledge this is the first time Scottish data has been presented.

As with most cancer types, breast cancer risk increases with age. This was reflected in our study where very few cases were reported in the under 50 age group; thereafter this rose steadily with numbers peaking in the 65-70 and 75-79 age brackets, around 5-10 years older than what is seen in females, consistent with other studies (19).

Accounting for age-adjustment, it was clear that rates of MBC have increased across the whole of Scotland over the last 25 years, in line with studies from other geographical areas (1, 7, 17, 18). When trend lines were applied, numbers were clearly increasing, particularly in the North of Scotland ($R^2 = 0.3$). This was not so obvious for South East Scotland ($R^2 = 0.05$) where there was considerable annual variation, with EASRs ranging from <0.5 to >2.0. This has been noted elsewhere (15) and may be explained by the small numbers diagnosed each year. When this was examined at Health Board level, regional trends were observed, with the most striking finding of higher age-standardised MBC incidence in areas of Scotland considered to be remote and rural, notably the Borders, Dumfries & Galloway and the Western Isles.

Within the confines of this observational study, reasons for these regional differences are difficult to reconcile, but potential explanations are offered. Exposure to environmental compounds that mimic oestrogens (so-called Endocrine-Disrupting Chemicals; (EDCs)) might be exacerbated in areas of higher agricultural activity, with potential adverse health consequences. With lifetime exposure to

oestrogen a well-established risk factor for breast cancer, it is reasonable to speculate that EDCs may also contribute to this. Laboratory experiments where non-malignant breast epithelial cells were exposed to mixtures of EDCs showed modulation of total and phosphorylated oestrogen receptor activity, evasion of apoptosis and increased S-phase induction, all characteristics which are associated with carcinogenesis (20). Increased pesticide use associated with the agricultural industry may be a further potential explanation for the rise in incidence of MBC; effects of pesticides on breast cancer incidence in two English counties demonstrated associations in rural Leicestershire but not Lincolnshire (21). A case-control study failed to demonstrate any association in occupational exposure and MBC, instead showing physical activity was associated with reduced disease risk (22). Obesity-associated physical inactivity has been proposed previously as a contributory factor for rises in MBC (23), although one might anticipate this to be associated with urban not rural environments. In support of this, a French study described regional trends in the prevalence of MBC across a shorter timescale (4 years; 2009 - 2013). In contrast to our findings, this reported a higher prevalence of MBC in the more densely populated areas of the Central and Burgundy regions of France (24). In Scotland, regional variations in obesity seem to be driven by lifestyle and socioeconomic factors rather than genetics (25), although genetic predisposition to MBC cannot be ruled out.

In summary, our study clearly demonstrated a rise in MBC incidence in Scotland over the last 25 years, showing significant disparities between regions. Epidemiological studies are required to address these differences and their potential significance.

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Figures

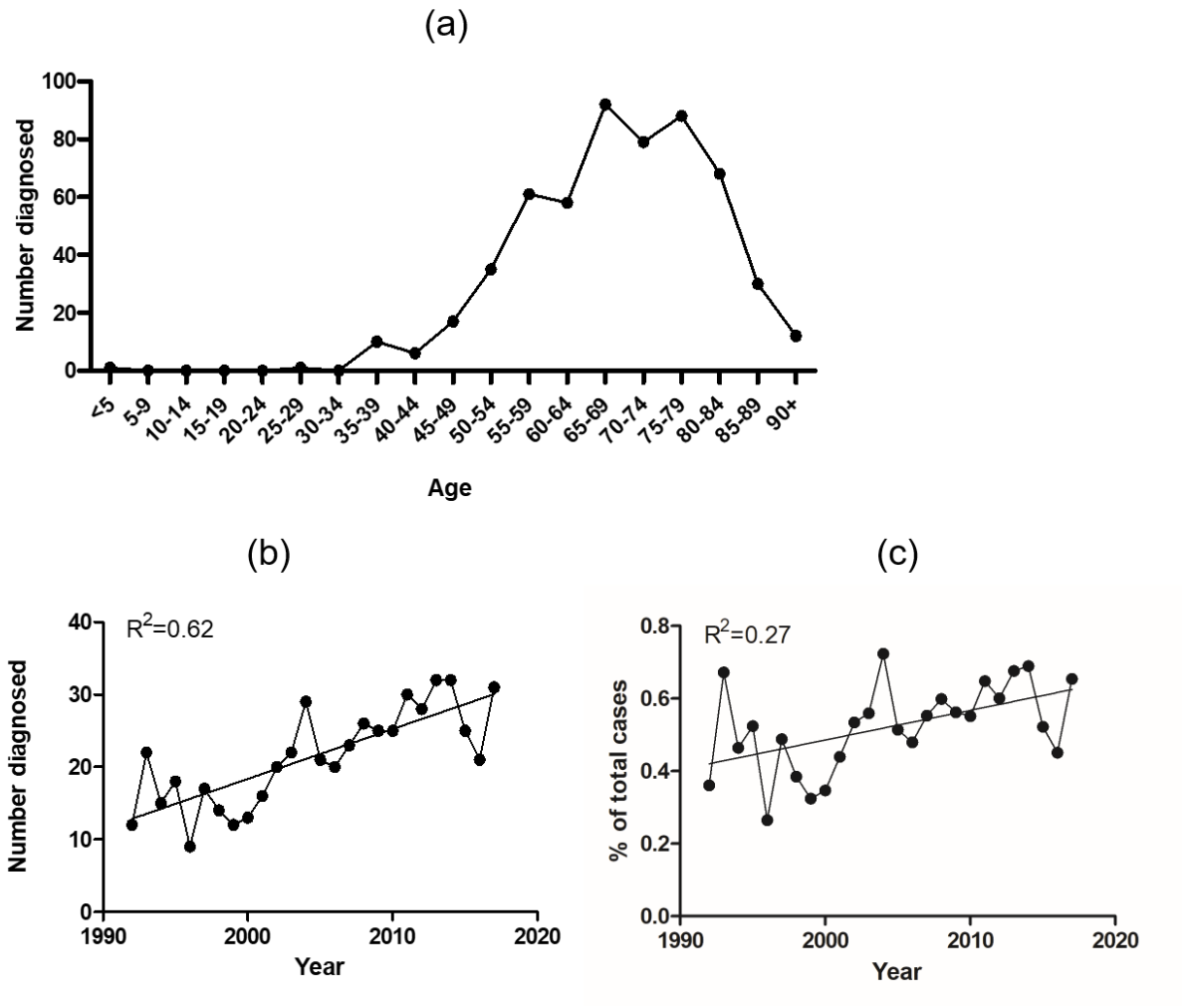

Figure 1. MBC diagnosed in Scotland across a 25-year period. (a) Number of MBCs in different age groups. (b) Total number of MBC diagnosed, and (c) Percentage of MBC diagnosed of all breast cancer.

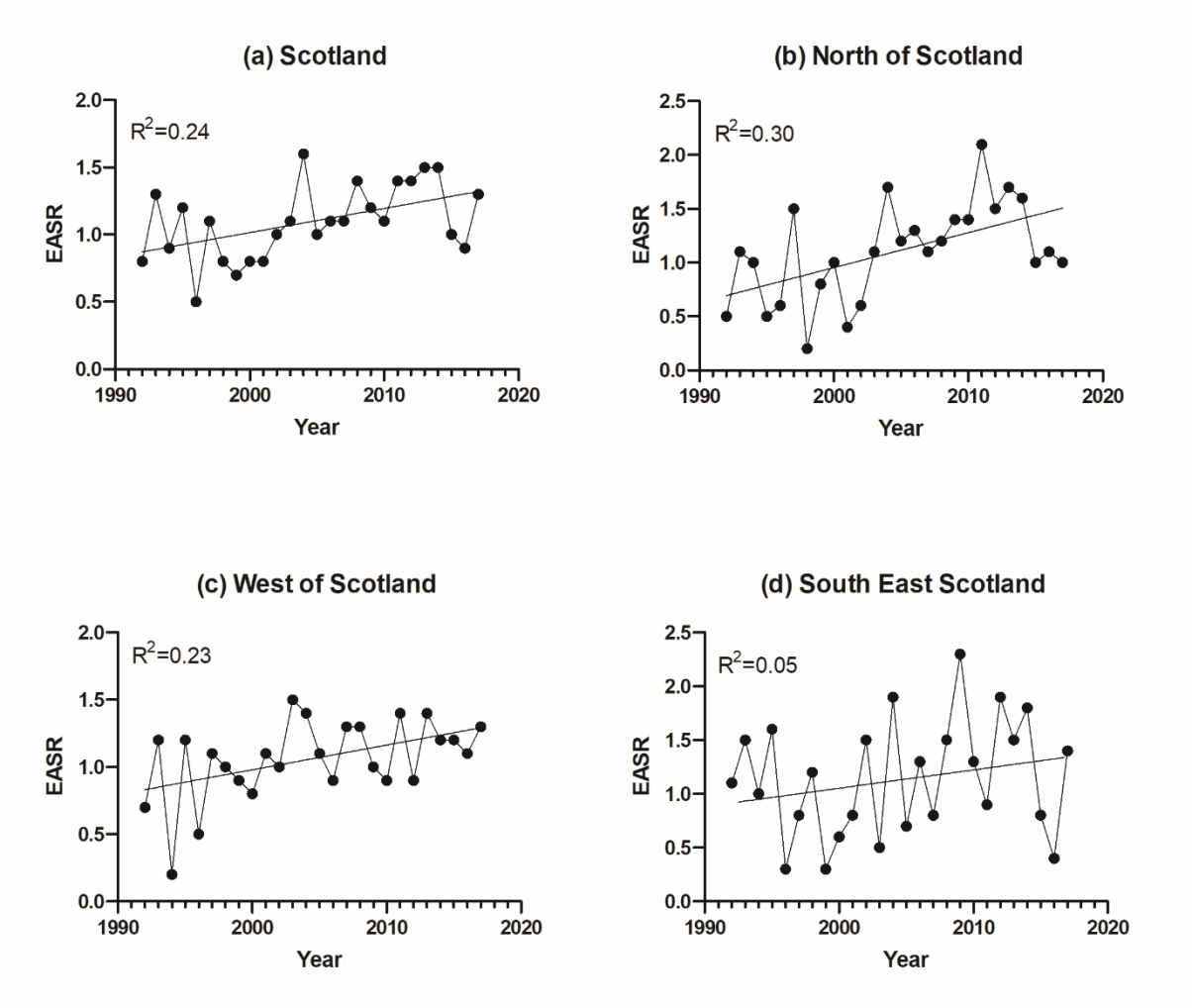

Figure 2. Age-adjusted incidence trends for male breast cancer in Scotland, 1992-2017. Rates were calculated for the whole country (a), the North (b), West (c) and South East (d) of Scotland.

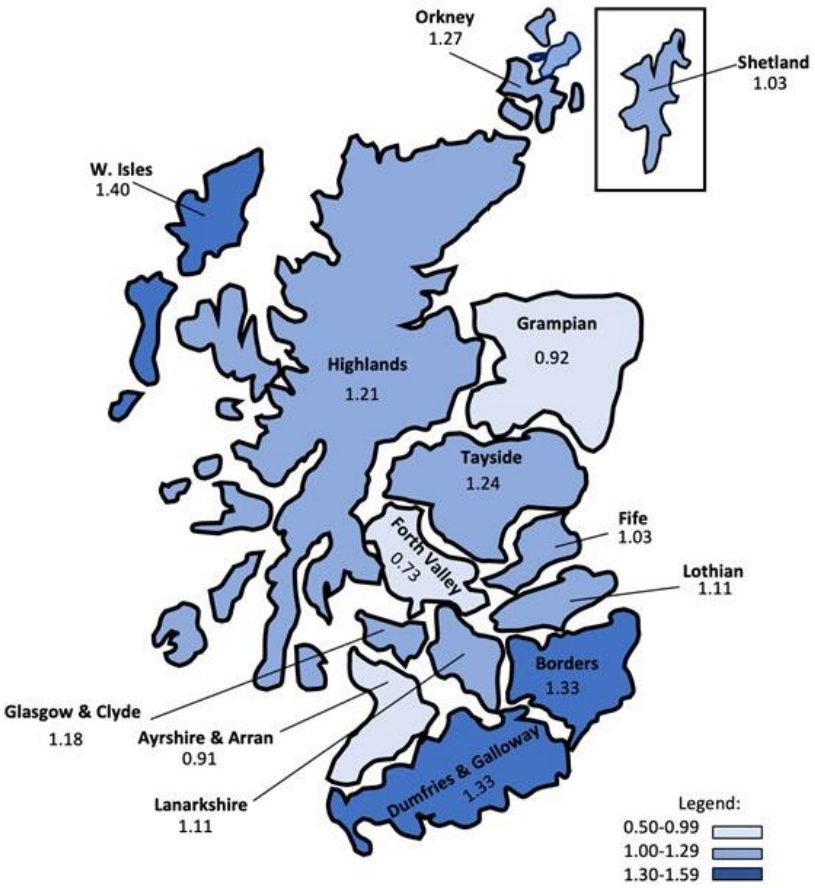

Figure 3. Prevalence of male breast cancer across Scottish Health Boards, 1992 – 2017

Figure 1

MBC diagnosed in Scotland across a 25-year period. (a) MBC occurrence in different age groups. (b) Total number of MBC diagnosed, and (c) the percentage of MBC diagnosed of all breast cancer.

Figure 2

Age-adjusted incidence trends for male breast cancer in Scotland, 1992-2017. Rates were calculated for the whole country (a), the North (b), West (c) and South East (d) of Scotland.

Figure 3

Prevalence of male breast cancer across Scottish health boards, 1992 – 2017. Health boards in the North of Scotland include Grampian, Highland & Argyll, Orkney, Shetland, Tayside and Western Isles; West includes Ayrshire & Arran, Forth Valley, Greater Glasgow & Clyde and Lanarkshire; South East includes Borders, Dumfries & Galloway, Fife and Lothian.