

# Chapter 18

## Ovary

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### Summary

- In the UK and Ireland in the 1990s, ovarian cancer accounted for 1 in 20 cases of cancer and 1 in 17 deaths from cancer in females.
- There was little geographical variation in incidence and less for mortality.
- Incidence was higher than average in a few areas in the West Midlands, Wales, South East England, and in Scotland, and lower in a few areas in north east England and around London. There was a similar pattern for mortality.
- Some of the observed variations in incidence may be explained by differences in registration practices across cancer registries.
- There was no clear relationship between the geographical variations in ovarian cancer and socio-economic deprivation, or any known or suspected risk factors for the disease.
- The geographical distribution of ovarian cancer was broadly similar to that for cancers of the breast and uterus. These cancers have several risk factors in common.

### Introduction

Geographic variations in ovarian cancer incidence may have arisen because of differences in diagnostic criteria or in cancer registration practice. True geographic variation in underlying risk is therefore difficult to establish. In particular, a proportion of ovarian cancers are so-called 'borderline' malignancies, of low malignant potential. Cancers of borderline malignancy are classified as malignant, according to the International Classification of Disease for Oncology, second edition (ICDO2) rules. The ICDO2 rules were introduced with the change to the International Classification of Disease, tenth revision (ICD10). Cancers of borderline malignancy were not classified as malignant prior to the introduction of ICDO2 rules. Ireland has used ICDO2 coding rules since collection of data for the entire country began in 1994. The ICDO2 classification was introduced by the cancer registries of England and Wales in 1995, Scotland in 1997 and Northern Ireland in 1996. Between

the introduction of ICDO2 and 1999, borderline cases accounted for 10 per cent of ovarian malignancies in Northern Ireland and Ireland, 14 per cent in Scotland, 8 per cent in England and 4 per cent in Wales. (For the entire period of the analysis, this might approximate to around 6 per cent of all registered invasive cases in Northern Ireland, five per cent in Scotland, 4 per cent in England and 2 per cent in Wales – compared to 10 per cent in Ireland.) The proportions of borderline malignancies in the regions of England varied from 11 per cent in the North West to 4 per cent in London. Inclusion of borderline malignancies increases the recorded incidence. Borderline malignancies are rarely fatal, and have much better prognosis than other malignant tumours arising in the ovary, thus their registration also increases the apparent survival rates for ovarian cancer.

### Incidence and mortality

Ovarian cancer was the fourth commonest cancer in women, after breast, colorectal and lung and accounted for 5 per cent of all newly diagnosed cancers. About 6,700 cases of ovarian cancer were diagnosed annually in the UK and Ireland during the 1990s; the overall age-standardised rate was 18 per 100,000. Few cases occurred in pre-menopausal women; over 90 per cent of cases were in women aged 45 or over, with age-specific rates peaking in the range 70-84 years. The lifetime risk<sup>1,2</sup> of being diagnosed with ovarian cancer, based on data from England and Wales for 1997, was 2.1 per cent (1 in 48).<sup>3</sup>

During the 1990s, about 4,600 women died annually from ovarian cancer in the UK and Ireland – 6 per cent of all cancer deaths in women. Ovarian cancer was the fourth commonest cause of cancer death in women, and accounted for more deaths than all the other gynaecological cancers together. The overall age-standardised mortality rate was 11.5 per 100,000. The pattern of age-specific mortality broadly followed that of incidence, peaking in women aged 75-84.

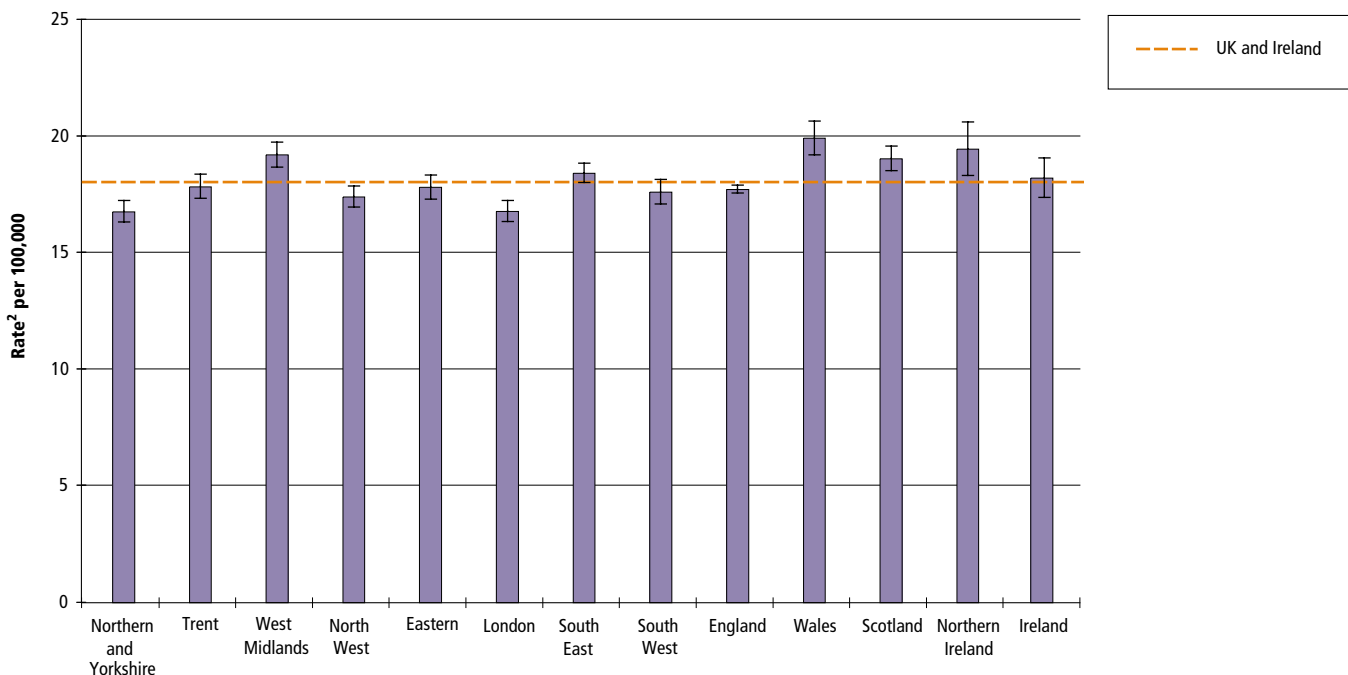
### Incidence and mortality trends

Since the early 1970s, the age-standardised incidence rate for ovarian cancer in England and Wales has gradually increased; age-specific rates increased markedly in older women,<sup>4</sup> whereas in women aged under 65 they were relatively stable. In Scotland, the increase in the incidence of ovarian cancer from the early 1960s to the late 1980s was attributed mainly to the increase in registered cases among women over 60 years, with no upward trend for younger women.<sup>5</sup> The pattern in the risk of ovarian cancer by birth cohort is similar to that for breast cancer, with rates increasing up to the cohorts born around 1930 and then declining, but appearing to increase again for women born from the early 1960s onwards.<sup>4</sup>

(continued on page 198)

**Figure 18.1**

**Ovary: incidence by country, and region of England  
UK and Ireland 1991-99<sup>1</sup>**

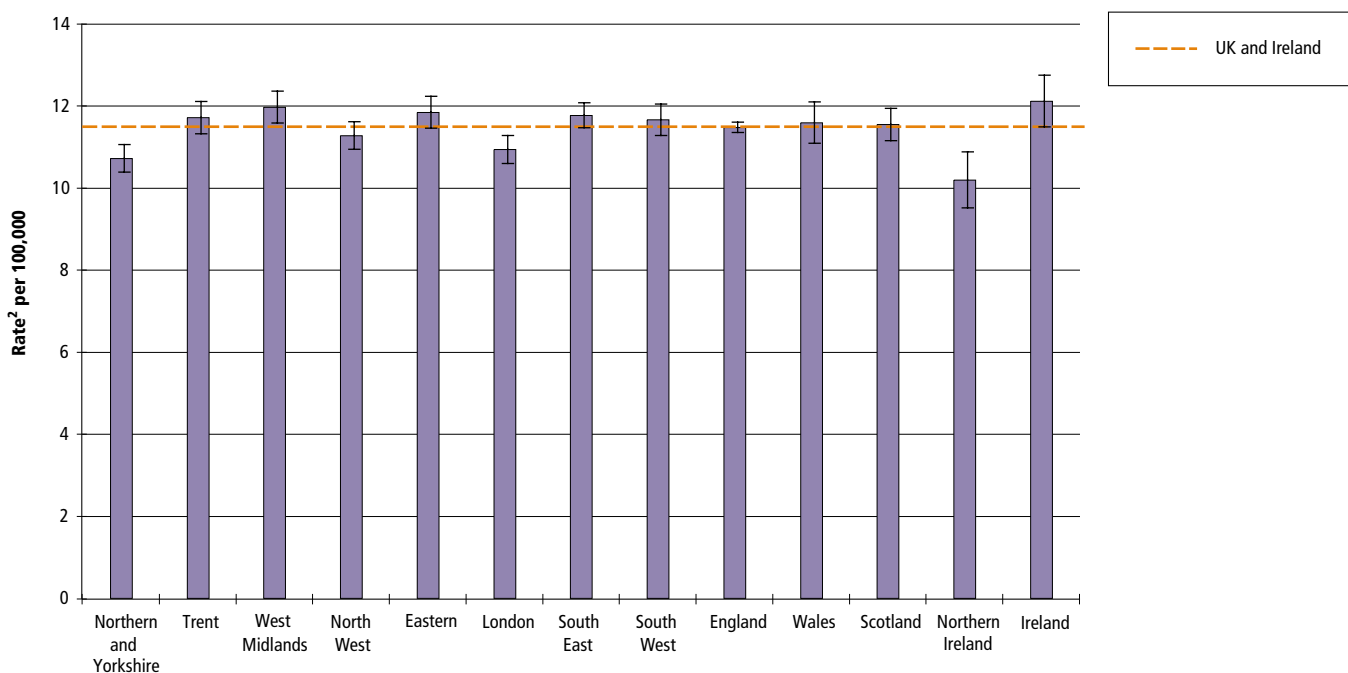


<sup>1</sup> Northern Ireland 1993-99, Ireland 1994-99

<sup>2</sup> Age standardised using the European standard population, with 95% confidence interval

**Figure 18.2**

**Ovary: mortality by country, and region of England  
UK and Ireland 1991-2000<sup>1</sup>**

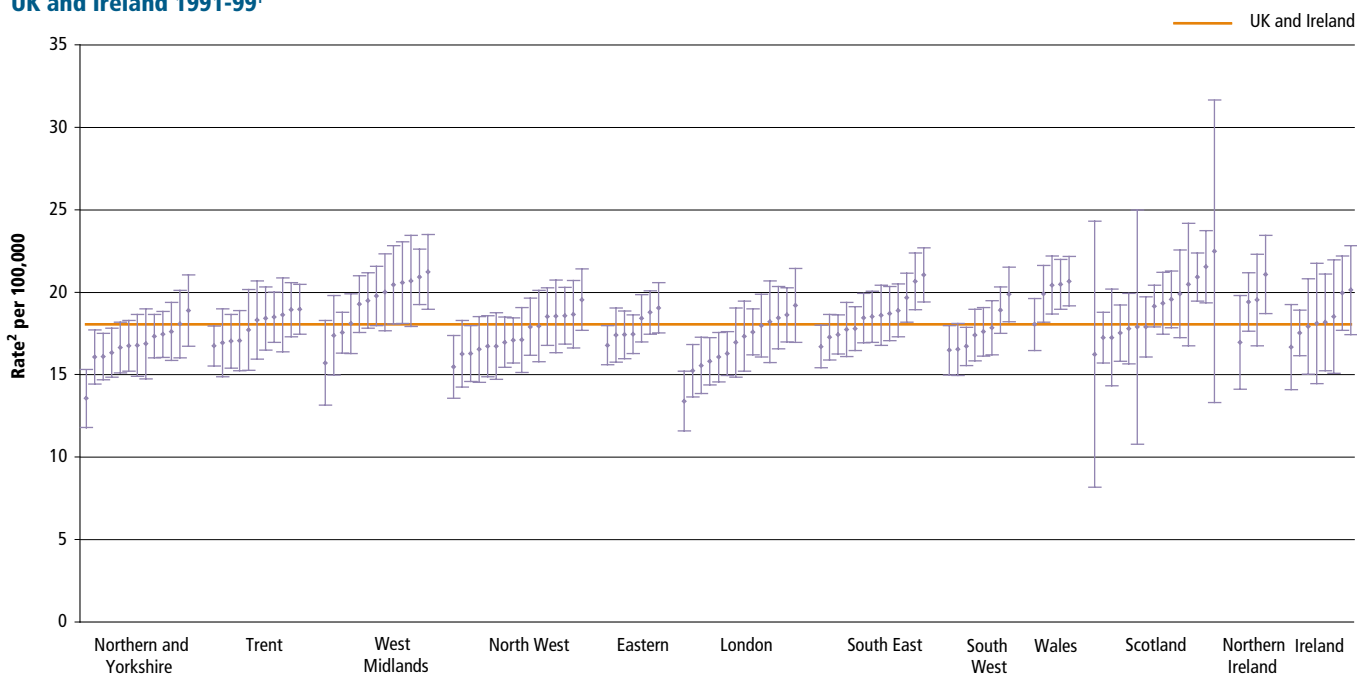


<sup>1</sup> Scotland 1991-99, Ireland 1994-2000

<sup>2</sup> Age standardised using the European standard population, with 95% confidence interval

**Figure 18.3**

**Ovary: incidence by health authority within country, and region of England UK and Ireland 1991-99<sup>1</sup>**

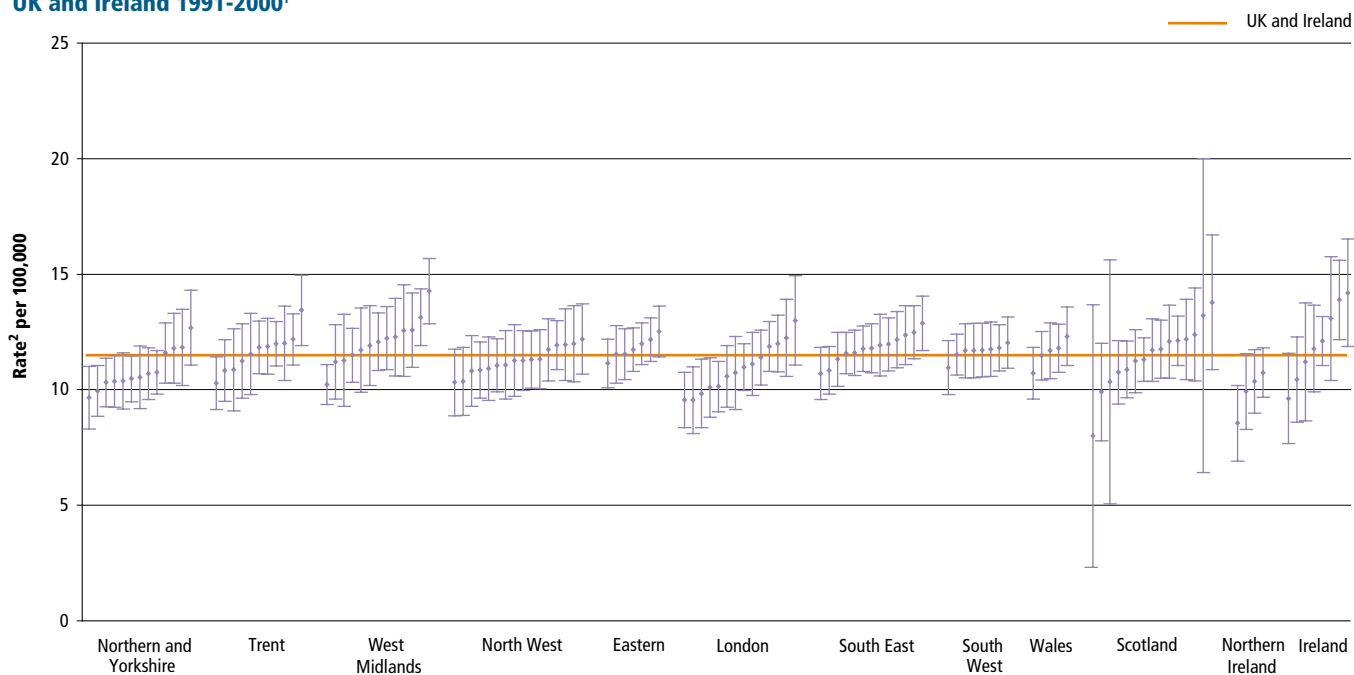


1 Northern Ireland 1993-99, Ireland 1994-99

2 Age standardised using the European standard population, with 95% confidence interval

**Figure 18.4**

**Ovary: mortality by health authority within country, and region of England UK and Ireland 1991-2000<sup>1</sup>**

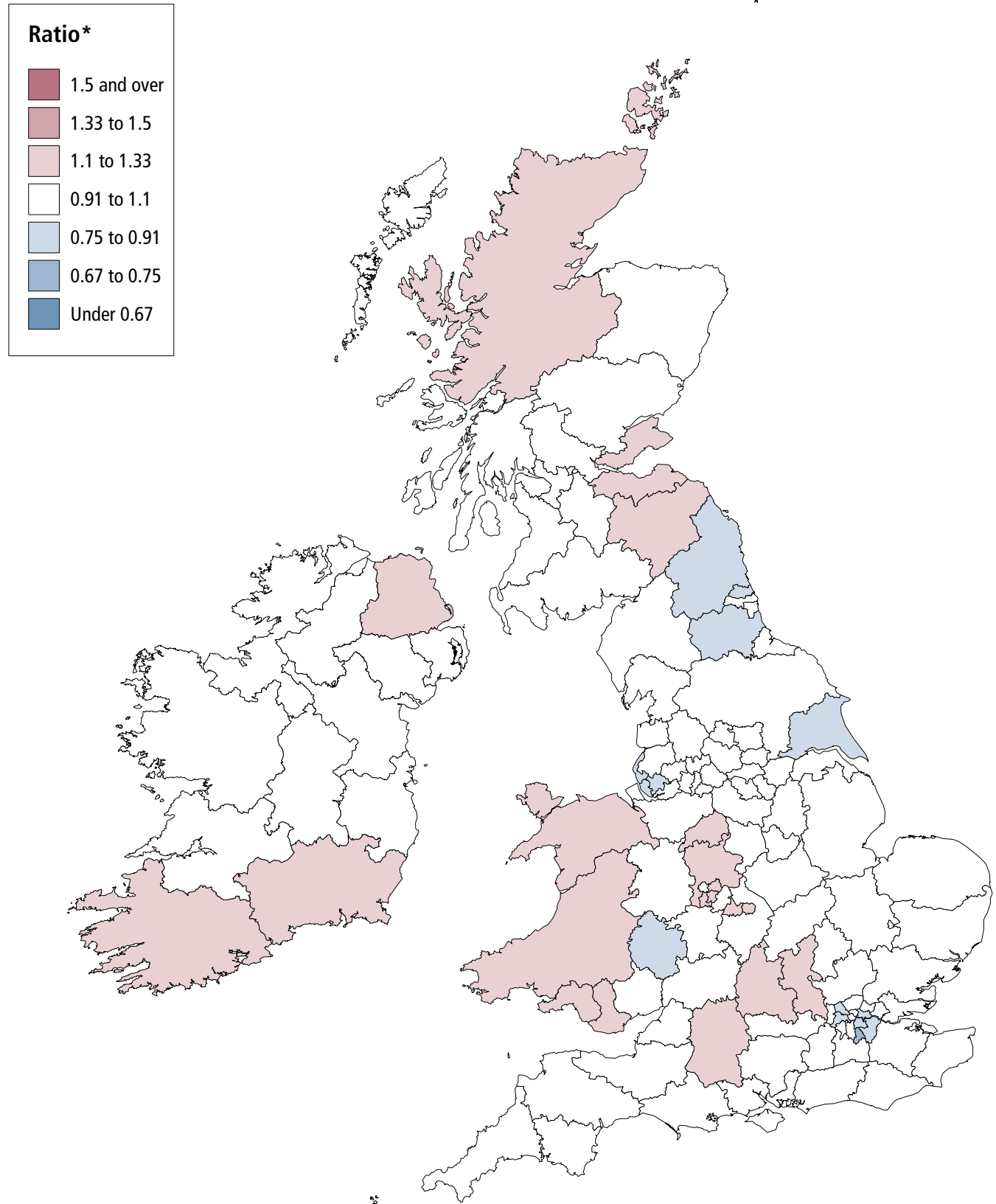


1 Scotland 1991-99, Ireland 1994-2000

2 Age standardised using the European standard population, with 95% confidence interval

## Map 18.1

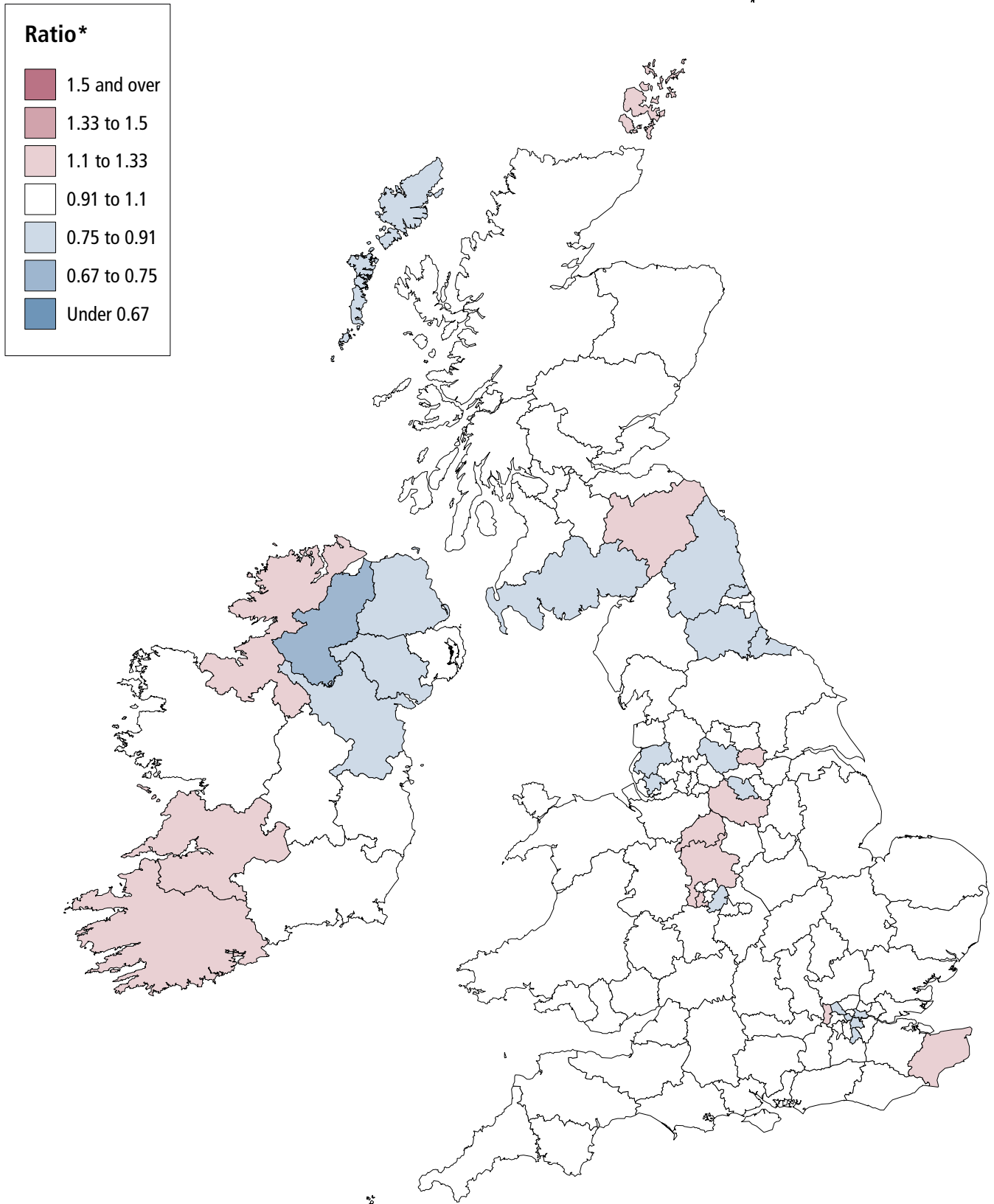
Ovary: incidence\* by health authority  
UK and Ireland 1991-99



\*Ratio of directly age-standardised rate in health authority to UK and Ireland average

## Map 18.2

### Ovary: mortality\* by health authority UK and Ireland 1991-2000



\*Ratio of directly age-standardised rate in health authority to UK and Ireland average

In England and Wales, age-standardised mortality rates for ovarian cancer showed continuous, marked increases from early in the twentieth century until the 1980s.<sup>4</sup> This was attributed to a combination of more accurate diagnosis and an increase in underlying incidence. Over the period 1950-99, increases in mortality rates were greatest for older women – a doubling of rates for those aged 75 and over and a 50 per cent increase for those aged 65-74. In the age group 55-64, there was a less steep increase up to the late 1970s, then rates stabilised, and in those aged 45-54, mortality rates were stable up to the late 1970s, then declined. Mortality rates in Scotland showed no overall trend up to 1995,<sup>5,6</sup> but some reduction in mortality was seen among younger women.<sup>5</sup> In Northern Ireland, the mortality rate increased from 10.2 to 12.0 per 100,000 over the period 1993-2001.<sup>7</sup> In Ireland, mortality rates showed a sustained increase during the period 1956-2000, especially in older women (over 65), with no evidence for any recent downturn in rates (National Cancer Registry, in preparation).

## Survival

Ovarian cancer has the lowest survival of the gynaecological cancers, largely because it is often at an advanced stage when diagnosed. Symptoms of ovarian cancer are frequently vague and are difficult to distinguish from other conditions. In England and Wales, relative survival for women diagnosed during 1996-99 was 65 per cent at one year and 36 per cent at five years after diagnosis.<sup>8</sup> In the early 1990s, five-year relative survival rates from ovarian cancer in England, Scotland and Wales were 5.2, 6.6 and 7.6 percentage points, respectively, below the European average.<sup>9</sup> Differences in the mix of histological sub-types could explain some of the variation in survival across Europe. It is difficult to compare the survival rates between the countries of the UK and Ireland because of the differences in inclusion criteria and the case mix for histological sub-types of malignant ovarian cancer.

## Geographical patterns in incidence

The incidence rates for ovarian cancer show no extreme variability among the countries of the UK and Ireland (Figure 18.1). The highest incidence rates occurred in Wales, Scotland, and Northern Ireland, with incidence rates 10, 6 and 8 per cent higher, respectively, than the average. The rate for Ireland was close to the average. Within England, incidence was higher than average in the West Midlands and below in Northern and Yorkshire, and London, but the rates for all English regions were within 7 per cent of the UK and Ireland average.

There was inevitably more variation among health authorities than within countries and regions of England, but rates were all within 25 per cent of the UK and Ireland average (Figure 18.3). The map (Map 18.1) shows that the incidence of ovarian cancer was notably higher in the Highlands and also on the east coast of Scotland in Fife (19 per cent higher than average), Lothian, and Borders. There was a band of high incidence of ovarian cancer in the West Midlands covering the area from North and South Staffordshire, to the urban area surrounding Birmingham (Walsall, Dudley [18 per cent higher than average], Sandwell) and Solihull, and Coventry. A further band of high incidence is apparent in the south of England, in Buckinghamshire, Oxfordshire, and Wiltshire. In Wales, all areas with the exception of one (Gwent) had rates above the average for the UK and Ireland. The Southern and South Eastern areas in Ireland both had higher than average incidence rates, as did the Northern area in Northern Ireland.

Incidence for ovarian cancer was generally lower than average in the Northern and Yorkshire region of England, especially along the east coast with notably low rates in Northumberland; Newcastle and North Tyneside; County Durham; and East Riding (which includes Hull). In the North West region, Liverpool and its surrounding areas of St Helen's and Knowsley, and Sefton all had distinctly lower than average incidence of ovarian cancer. The north west and south east areas of London also had lower incidence of ovarian cancer, with Croydon in south London having a rate that was 25 per cent lower than the average.

As mentioned above, some of the apparent geographic variation in ovarian cancer incidence may have arisen due to differences in the classification of borderline malignancies. These differences may arise from diagnostic criteria or cancer registration practice, or both.

## Geographical patterns in mortality

As for incidence, mortality rates for ovarian cancer showed relatively little variation among countries (Figure 18.2). The overall mortality rates were 5 per cent above the UK and Ireland average in Ireland, close to the overall average in England, Wales and Scotland, and relatively low in Northern Ireland (11 per cent below average). All regions in England were within 7 per cent of the average, with rates for Northern and Yorkshire, and London markedly lower than average.

The map of mortality for ovarian cancer (Map 18.2), as for that of incidence, shows markedly higher rates in Borders in Scotland, North and South Staffordshire, and Dudley in the

West Midlands, and the Southern area in Ireland. There also appeared to be isolated higher areas of ovarian cancer mortality in Wakefield, North Derbyshire, Hillingdon, and East Kent in England, and in the Mid Western and North Western areas in Ireland, although none of these areas had notably higher incidence rates.

The ovarian mortality rate in Dumfries and Galloway in Scotland was below average. Areas with low incidence rates in the Northern and Yorkshire region along the east coast (from Northumberland southwards) also tended to have lower mortality rates. South Lancashire; St Helen's and Knowsley; Calderdale and Kirklees; Sheffield; and Birmingham all had lower than average ovarian mortality. In London, three out of the six health authorities that had markedly low ovarian cancer incidence also had lower than average mortality.

Mortality rates were low, relative to incidence rates, in Scotland, Wales and, especially, Northern Ireland, but high in Ireland. These countries showed perhaps less agreement than England between the geographical patterns of mortality and incidence. It is not clear to what extent these differences reflect variations in diagnostic or registration criteria, random variation in rate estimates, or other factors.

### Risk factors and aetiology

A woman's history of ovulation appears to play a role in the development of the disease. Higher rates of ovarian cancer occur among women who do not have children, and the risk decreases with the number of pregnancies (parity). The incidence is strongly correlated with breast (Chapter 5) and uterine cancer (Chapter 23); all are related to hormone levels and share many of the same risk factors. It is well established that a reduction in ovarian cancer risk is associated with an increased duration of oral contraceptive use.<sup>10</sup> The widespread use of the contraceptive pill is one possible explanation for the stability of rates in younger women.

Tubal ligation (a form of female sterilisation) has a protective effect on ovarian cancer with an estimated reduced risk of 39-70 per cent.<sup>11,12</sup> There is also evidence, although it is less conclusive, that risk is increased by hormone replacement therapy in post-menopausal women<sup>13,14</sup> and in women treated for infertility.<sup>10</sup> A small proportion of ovarian cancers are attributable to specific inherited mutations, notably those of the BRCA-1 and BRCA-2 genes.<sup>15,16</sup> There is limited, and inconclusive, evidence to suggest that greater height or body weight, dietary fat consumption, and talcum powder use might be associated with increased risk.<sup>10</sup>

It is difficult to discern any geographic patterns within the UK and Ireland that might be confidently attributed to variations in reproductive or hormonal factors. Maps of total fertility rates and live birth rates by mother's age in the United Kingdom for 1991-97<sup>17</sup> show no clear correlation between areas of higher fertility and those with low ovarian cancer incidence and mortality rates. In 2002-03, a quarter of women aged 16-49 in Great Britain used oral contraceptives. Women aged 18-29 were those most likely to use the contraceptive pill, with 48 per cent of women aged 20-24 using oral contraceptives.<sup>18</sup> However, this information is not available at a regional or lower geographical level. This makes it difficult to disentangle the influences of parity and oral contraceptive use in a given population, and it may be that their separate protective effects predominate in different regions.

### Socio-economic deprivation

In England and Wales, based on data from 1993,<sup>4</sup> both incidence and mortality rates for ovarian cancer were marginally higher in women from more affluent areas than those from deprived areas.<sup>4</sup> This was similar to, but less defined than, the trend for breast cancer incidence.<sup>4</sup> For both breast and ovarian cancer, the trend is consistent with the known protective effect of higher parity, with total fertility rates being higher in more deprived areas.<sup>17</sup> However, there is no available information on oral contraceptive use by area or social class. Thus, it is not clear if the protective effect of oral contraceptive use plays any role in the relationship between ovarian cancer and deprivation. In Scottish data for 1986-95, there was no obvious relationship between ovarian cancer incidence and deprivation.<sup>6</sup>

For women diagnosed with ovarian cancer in 1996-99 in England and Wales, there was no difference in five-year survival between those living in the most affluent and the most deprived areas. Ovarian cancer was one of only five cancer-sex combinations in which this was the case.<sup>19</sup> The key issue around ovarian cancer is that diagnosis often occurs when the disease is at an advanced stage, which limits the potential for treatment to improve survival. Population screening for ovarian cancer, which has the potential to detect the disease at an earlier stage, is currently being evaluated in the United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS).<sup>20</sup>

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