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Time trends in ovarian cancer mortality in Europe (1955–1993): effect of age, birth cohort and period of death

P. González-Diego *, G. López-Abente, M. Pollán, M. Ruiz

Cancer Epidemiology Department, National Centre for Epidemiology, Carlos III Institute of Health, Sinesio Delgado 6, 28029 Madrid, Spain

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Abstract

The time trend in ovarian cancer mortality in the European Union over the period 1955–1993, and the age, period-of-death and birth cohort components underlying the trend's evolution were analysed using log–linear Poisson models to quantify risk of dying from ovarian cancer in the different countries and regions of Europe, and ascertain the relative annual trend for each country. Furthermore, age–period–cohort models were fitted for each country in order to ascertain the effect on time trend exerted by the respective age, period-of-death and birth cohort components. Ovarian cancer mortality proved 2.77-fold (95% confidence interval (CI) 2.60–2.95) higher in northern versus southern Europe over the period 1955–1993. Denmark registered the highest adjusted rates, namely, 14.3 per 100 000 person-years for the 1989–1993 5-year period, the last studied, with Portugal (4.5 per 100 000) and Greece (4.5 per 100 000) being the countries with the lowest rates. Spain and Greece, with annual rises of 5.8% (95% CI 5.3–6.3) and 5.1% (95% CI 4.2–6.0) respectively, were the countries that displayed the greatest increase in ovarian cancer mortality. Risk of death associated with the birth cohort effect declined in all northern countries from 1920 to 1930. In the south, Italy and France recorded a decline in risk from 1930. Women in Spain and Greece registered an increase in birth cohort-associated mortality, which became less pronounced after 1930. Ovarian cancer mortality in Europe evinces a south–north distribution pattern. The mortality risk for women cohorts born in northern Europe witnessed a gradual decline from 1920 to 1930. In the southern region: (1) Italy and France display a cohort effect of decreased risk from 1930; and (2) Greece and Spain show a cohort effect of increased risk among the different generations of women, though this became less pronounced from 1930 onwards.

Keywords: Ovarian cancer; Mortality; Time trend; Poisson regression; Age–period–cohort

1. Introduction

Ovarian cancer is the fifth leading cause of death due to malignant tumours among women in the European Union [1]. A total of 1–2% of all European women present with ovarian cancer at some point in their lives [1]. The 5-year relative survival rate does not exceed 35% [2], without any appreciable improvement in recent years despite the introduction of new forms of treatment [3].

In a recently published study [4], in which age, period-of-death and birth cohort components were analysed as determinants of the mortality time trend for the most frequent cancer sites in 16 European countries, the results obtained for ovarian cancer revealed very heterogeneous patterns for countries in the northern and southern regions of Europe.

Using log–linear Poisson, age, period and birth cohort models, the present study sought to carry out an in-depth analysis of the trend over time in ovarian cancer mortality, characterise any differences existing between neighbouring countries, and outline the possible causes underlying such findings.

2. Patients and methods

2.1. Mortality and population data

Ovarian cancer mortality data distributed by 5-year age group intervals (from 0 to 4 to 85 and over) for each

* Corresponding author. Tel.: +34-91-387-7802; fax: +34-91-387-7815.

E-mail address: pgdiego@isciii.es (P. González-Diego).

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of the countries examined were drawn from the World Health Organisation (WHO) database for the period, 1955–1993. Populations estimated on the basis of official censuses for each year of the time framework studied, and distributed by age group and sex, were likewise obtained from the WHO database. Cancer of the ovary corresponds to the International Classification of Diseases (ICD) 6th and 7th revisions, Code 175, and ICD 8th and 9th revisions, Code 183. In the following countries, ovarian cancer mortality data proved to be unavailable for certain parts of the study period, namely: Austria, 1955–1968; Germany, 1955–1968; Finland, 1989–1993; the UK, 1955–1968; Portugal, 1955–1983; and Greece, 1955–1963.

2.2. Specific and adjusted rates

Age-specific mortality rates were calculated for the 5-year age groups, except for the initial period of the time series (1955–1958). In order to compute age-adjusted rates for all ages and the truncated rate for ages 35–64 years, the European population was used as standard. The rates shown were calculated separately for each country, for the northern European region (Austria, Denmark, Germany, Finland, Sweden, Switzerland, Norway, The Netherlands, Ireland and the UK), and for the southern or Mediterranean region (France, Greece, Italy, Portugal and Spain).

2.3. Poisson models

Assuming that deaths from ovarian cancer for each age group and period were distributed as a Poisson variable, log–linear models were used to calculate the rates ratio between countries and the relative annual trend for each country. For modelling, account was taken of cases occurring in the age ranges 30–84 and 35–64 years, with the 30-year age group being established as the lower limit to reduce random variability due to the low numbers of deaths at younger ages.

These indicators were calculated for the whole period analysed and for the last three quinquennia, with the aim of ascertaining the most recent time trend. France was chosen as the reference level, since its age-adjusted rate figured midway in the range and it possessed complete population and mortality data for the entire period under review.

2.4. Age–period–cohort models

Based on the matrix of ovarian cancer deaths and populations broken down by age group and 5-year calendar periods, log–linear Poisson models were used to estimate the effect exerted by age, birth cohort and period of death, respectively, on the evolution of the time trend in each country. The 30-year age group was chosen as the lower limit. The age, period and birth cohort variables are arithmetically interrelated (age of death = year of death − year of birth), thus implying the existence of multiple solutions for any model including these three factors, a problem known as 'non-identifiability of parameters'. In order to obtain a single model, certain constraints have therefore to be imposed, which amount to distributing the total time trend (net drift) between the period and cohort factors [5–7]. The solution adopted was that proposed by Osmond and Gardner [8], a solution that is based on statistical criteria and entails minimising the Euclidean distance between the estimators of the final three-factor model and the three partial two-factor models, weighted by the goodness-of-fit of the latter. Two extreme solutions are also presented, which resulted from alternatively attributing the slope of the time trend to the cohort and period effects, respectively, thereby creating a bound of confidence around the chosen solution.

2.5. Extra-Poisson variability

Taking each model, we evaluated whether the random variability observed in respect of the specific rates for each of the strata was greater than that forecast by the Poisson distribution (overdispersion) [9]. The confidence intervals of the estimators of the rates ratio and relative annual trend were calculated using robust methods [10].

3. Results

Tables 1 and 2 show adjusted mortality rates for ovarian cancer for all age groups and for the truncated 35–64 year age group, respectively. Fig. 1 plots the age-adjusted mortality rates for the period, 1955–1993, taking the European population as a standard. A heterogeneous geographical distribution of the mortality rates was observed for countries in northern versus southern regions of Europe. Over the period, 1989–1993, the last period analysed, countries in the north registered higher rates, e.g. Denmark (14.3 per 100 000 person-years) and Ireland (12.4 per 100 000 person-years), whilst Mediterranean Basin countries such as Italy (6.3 per 100 000), Spain (5.3 per 100 000), Portugal (4.5 per 100 000) and Greece (4.5 per 100 000), all recorded lower mortality rates. Although this south–north pattern was in evidence throughout the study period (1955–1993), there was an overall reduction in the prevailing range of variability, with maxima/minima of 14.6 per 100 000 in Denmark and 0.7 per 100 000 in Spain (ratio 20:1) in the first period studied, 1955–1958, narrowing to 14.3 per 100 000 in Denmark and 4.5 per 100 000 in Greece (ratio 3:1) in the last period, 1989–1993. Furthermore, the latter decades saw mortality rates stabilising or declining in the countries of the north as opposed to a gradual

Table 1
Ovarian cancer mortality in Europe (1955–1993). Adjusted mortality rates per 100 000 person-years. (Standard European population). All age groups. Rates ratio and relative annual trend for the periods, 1955–1993 and 1979–1993.

	Adjusted rates								RT[a] (95% CI)	RAT[b] (95% CI)	RT[a] (95% CI)	RAT[b] (95% CI)
	1955–1958	1959–1963	1964–1968	1969–1973	1974–1978	1979–1983	1984–1988	1989–1993	1955–1993		1979–1993	
Denmark	14.6	15.0	16.0	16.5	15.1	15.2	14.0	14.3	2.30 (2.16–2.45)	−0.3 (−0.6, −0.1)	1.77 (1.68–1.86)	−0.8 (−1.6, −0.1)
Norway	11.1	11.0	11.1	12.2	11.9	11.5	12.1	11.3	1.80 (1.69–1.92)	0.1 (−0.2, 0.4)	1.43 (1.35–1.50)	−0.3 (−1.1, 0.6)
Austria	–	–	–	12.7	12.6	12.1	11.7	11.2	1.60 (1.49–1.71)	−0.8 (−1.5, −0.1)	1.43 (1.36–1.49)	0.8 (−1.5, −0.1)
Germany	–	–	–	10.8	11.2	11.0	11.1	10.8	1.45 (1.36–1.55)	−0.5 (−1.3, 0.2)	1.33 (1.28–1.39)	−0.6 (−1.3, −0.1)
Finland	7.0	8.0	8.6	9.1	9.7	9.0	8.7	–	1.39 (1.31–1.47)	0.5 (0.1, 1.0)	1.09 (1.03–1.15)	−1.1 (−2.5, 0.3)
Sweden	11.8	12.4	13.0	13.4	13.4	12.7	11.2	10.6	1.87 (1.75–1.99)	−0.5 (−0.8, −0.1)	1.40 (1.32–1.48)	−2.0 (−2.8, −1.1)
Switzerland	10.9	11.1	11.8	11.6	12.1	11.1	10.3	9.9	1.64 (1.53–1.76)	−0.5 (−0.9, −0.1)	1.23 (1.16–1.31)	−1.3 (−2.4, −0.1)
Ireland	5.8	6.6	7.7	8.2	10.3	9.5	11.7	12.4	1.38 (1.25–1.46)	2.1 (1.6, 2.5)	1.36 (1.27–1.45)	2.7 (1.5, 3.9)
The Netherlands	10.6	11.0	11.8	13.2	12.9	11.3	11.4	11.2	1.81 (1.70–1.93)	−0.3 (−0.6, 0.1)	1.37 (1.31–1.43)	−0.4 (−1.1, −0.4)
UK	–	–	–	12.2	12.2	11.7	12.0	11.8	1.58 (1.48–1.68)	−0.6 (−1.1, −0.1)	1.45 (1.38–1.53)	−0.6 (−1.4, 0.3)
France	4.2	4.7	5.4	6.0	7.0	7.7	8.3	8.3	1	1.8 (1.4, 2.3)	1	0.3 (−0.9, 1.4)
Greece	–	–	1.3	1.8	2.6	3.4	4.0	4.5	0.41 (0.37–0.45)	5.1 (4.2, 6.0)	0.51 (0.47–0.56)	2.9 (1.0, 4.8)
Italy	3.5	4.1	4.5	4.9	5.3	5.8	6.8	6.3	0.83 (0.78–0.88)	1.6 (1.1, 2.0)	0.81 (0.77–0.85)	0.2 (−1.0, 1.4)
Portugal	–	–	–	–	–	–	4.2	4.5	–	1.7 (−0.6, 4.0)	0.54 (0.49–0.59)	1.7 (−1.0, 4.6)
Spain	0.7	0.9	1.2	1.6	2.5	3.3	4.3	5.3	0.35 (0.32–0.38)	5.8 (5.3, 6.3)	0.55 (0.51–0.60)	4.1 (2.5, 5.8)
Northern Europe	6.9	7.5	8.2	10.4	10.8	10.6	10.8	10.5	2.77 (2.60–2.95)	0.1 (−0.1, 0.3)	2.10 (2.00–2.21)	−0.4 (−1.0, 0.1)
Southern Europe	2.5	2.9	3.2	3.8	4.1	4.7	5.6	5.7	1	2.4 (1.7, 3.0)	1	1.4 (−0.1, 2.8)

[a] RT, rates ratio for each country and region, 95% confidence interval, derived from Poisson models after adjustment for age and period. France, country of reference because of its central position in the range of mortality rates. Southern Europe, region of reference.

[b] RAT, relative annual trend for each country and region is expressed as a percentage, 95% confidence interval.

Table 2
Ovarian cancer mortality in Europe (1955–1993). Adjusted mortality rates per 100 000 person-years (Standard European population). Women aged 35–64 years. Rates ratio and relative annual trend for the periods, 1955–1993 and 1979–1993.

	Adjusted rates								RT[a] (95% CI)	RAT[b] (95% CI)	RT[a] (95% CI)	RAT[b] (95% CI)
	1955–1958	1959–1963	1964–1968	1969–1973	1974–1978	1979–1983	1984–1988	1989–1993	1955–1993		1979–1993	
Denmark	22.6	23.2	23.3	25.1	21.9	21.4	19.7	19.6	2.30 (2.17–2.44)	−0.8 (−1.1, −0.4)	1.87 (1.77–1.98)	−1.0 (−2.1, 0.1)
Norway	18.6	18.0	17.2	19.3	17.9	17.0	17.3	15.5	1.86 (1.76–1.97)	−0.6 (−0.9, −0.2)	1.54 (1.45–1.64)	−1.1 (−2.3, 0.2)
Austria	–	–	–	18.1	17.9	16.1	14.9	13.5	1.54 (1.45–1.64)	−1.8 (−2.3, −1.2)	1.38 (1.31–1.45)	−1.9 (−2.8, −1.0)
Germany	–	–	–	16.5	16.3	15.2	14.2	13.1	1.43 (1.35–1.52)	−1.8 (−2.5, −1.1)	1.32 (1.26–1.38)	−1.8 (−2.5, −1.2)
Finland	10.7	12.1	12.5	13.4	13.7	12.1	11.2	–	1.32 (1.25–1.40)	−0.1 (−0.6, 0.4)	1.06 (1.00–1.12)	−1.6 (−3.4, 0.1)
Sweden	19.0	19.1	19.4	19.7	18.9	18.2	15.5	13.9	1.85 (1.74–1.98)	−1.0 (−1.4, −0.7)	1.46 (1.38–1.55)	−2.8 (−3.5, −2.1)
Switzerland	16.2	16.9	16.5	15.7	16.3	13.9	12.5	10.7	1.49 (1.39–1.59)	−1.3 (−1.7, −1.0)	1.13 (1.06–1.20)	−2.7 (−3.6, −1.7)
Ireland	10.4	11.1	12.4	13.1	16.3	14.2	17.4	17.4	1.49 (1.41–1.59)	1.3 (0.9, 1.7)	1.52 (1.42–1.62)	1.9 (0.5, 3.3)
The Netherlands	16.4	16.7	17.0	19.0	18.5	15.3	13.9	13.4	1.70 (1.60–1.81)	−1.0 (−1.4, −0.6)	1.31 (1.25–1.37)	−1.5 (−2.2, −0.8)
UK	–	–	–	19.0	18.9	17.7	17.3	16.4	1.71 (1.61–1.81)	−1.4 (−2.0, −0.7)	1.59 (1.52–1.66)	−1.4 (−2.2, −0.6)
France	7.0	7.7	8.5	9.4	10.2	10.8	10.9	10.2	1	0.9 (0.5, 1.2)	1	−1.0 (−1.9, 0.1)
Greece	–	–	2.4	3.2	4.7	5.6	6.3	6.6	0.50 (0.45–0.55)	3.6 (2.6, 4.6)	0.60 (0.55–0.65)	1.4 (−0.2, 3.0)
Italy	6.1	6.7	7.3	7.8	8.3	8.6	9.4	8.3	0.86 (0.82–0.90)	0.7 (0.3, 1.1)	0.85 (0.80–0.90)	−0.9 (−1.8, 0.1)
Portugal	–	–	–	–	–	–	4.2	4.5	0.61 (0.55–0.69)	1.2 (−0.2, 4.1)	0.59 (0.54–0.66)	1.1 (−0.3, 4.9)
Spain	1.2	1.6	2.2	2.7	4.3	5.3	6.7	7.7	0.39 (0.36–0.43)	5.1 (4.5, 5.6)	0.64 (0.59–0.69)	3.4 (2.1, 4.7)
Northern Europe	15.2	15.6	16.1	18.8	18.8	17.1	16.7	15.8	2.51 (2.33–2.70)	−0.6 (−0.8, −0.4)	1.92 (1.79–2.06)	−1.4 (−2.1, −0.7)
Southern Europe	5.4	6.0	6.4	7.2	7.8	8.4	8.9	8.5	1	1.7 (0.9, 2.4)	1	0.5 (−1.0, 1.9)

[a] RT, rates ratio for each country and region, 95% confidence interval, derived from Poisson models after adjustment for age and period. France, country of reference because of its central position in the range of mortality rates. Southern Europe, region of reference.

[b] RAT, relative annual trend for each country and region is expressed as a percentage, 95% confidence interval.

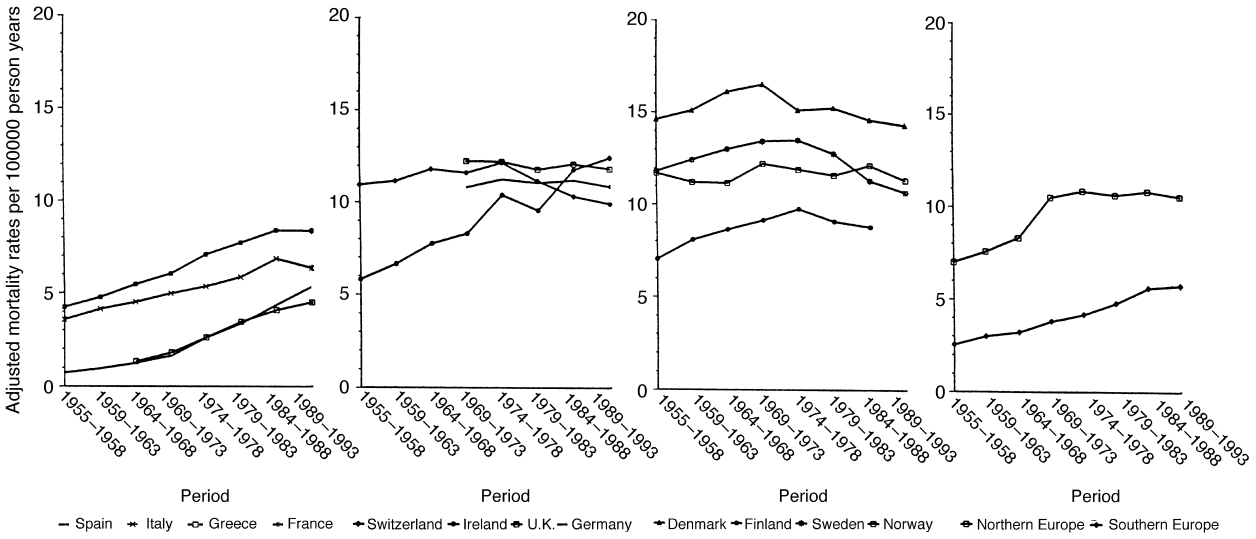

Fig. 1. Adjusted mortality rates for ovarian cancer. Per 100 000 person-years. Standard European population. All ages. Period: 1955–1993.

rise in rates registered for Mediterranean countries as a whole. Ireland was the lone exception to this pattern, evincing a trend similar to that of the southern countries, albeit starting from higher mortality rates.

Tables 1 and 2 set out the mortality rates ratio for women, all age groups and 35–64 years, both for the entire period, 1955–1993, and for the last 15 years, 1979–1993. Risk of dying from ovarian cancer among women born in northern Europe over the last 39 years proved 2.77-fold higher than their contemporaries in the Mediterranean area, with the figure dropping slightly to 2.10-fold in the last three quinquennia. This decrease in risk was similar in women aged 35–64 years, among whom excess risk was 2.51 for the period, 1955–1993, and 1.92 for the last 15 years. Women, particularly those in the 35–64 year age range, in Spain and Greece in the south, and in Ireland in the north witnessed a rise in the risk of death due to ovarian cancer in the last three quinquennia.

Spain and Greece, with annual increases of 5.8% and 5.1%, respectively, were the countries that experienced the greatest increase in ovarian cancer mortality in the European Union over the period, 1955–1993 (Tables 1 and 2). Ireland, with an annual growth of 2.1% proved the exception to the pattern of evolution among the northern-European countries (Tables 1 and 2).

3.1. Age–period–cohort effect

Table 3 shows the goodness-of-fit for the age–period–cohort models for each of the countries studied. We observed that the time trend in ovarian cancer mortality was best explained by the cohort effect. Those models that contained the birth cohort variable had the best goodness-

Table 3
Goodness-of-fit for the different age, age + drift, age + period, age + cohort, age + period + cohort models for each country

	Age		Age + drift		Age + period		Age + cohort		Age + period + cohort	
	Deviance	DF	Deviance	DF	Deviance	DF	Deviance	DF	Deviance	DF
Denmark	179	77	175	76	148	70	67	60	53	54
Norway	181	77	173	76	164	70	56	60	49	54
Austria	129	44	119	43	119	40	21	30	27	20
Germany	1085	44	1036	43	1014	40	60	30	46	27
Finland	172	66	146	65	122	60	52	50	43	45
Sweden	340	77	320	76	230	70	77	60	50	54
Switzerland	305	77	294	76	263	70	64	60	55	54
Ireland	487	77	170	76	156	70	62	60	47	54
The Netherlands	576	77	575	76	467	70	102	60	50	54
UK	631	44	630	43	615	40	69	30	23	27
France	6205	77	1832	76	1691	70	185	60	124	54
Greece	814	55	196	54	170	50	59	40	48	36
Italy	3579	77	1233	76	1105	70	234	60	103	54
Spain	6922	77	497	76	440	70	91	60	52	54

DF, Degrees of freedom.

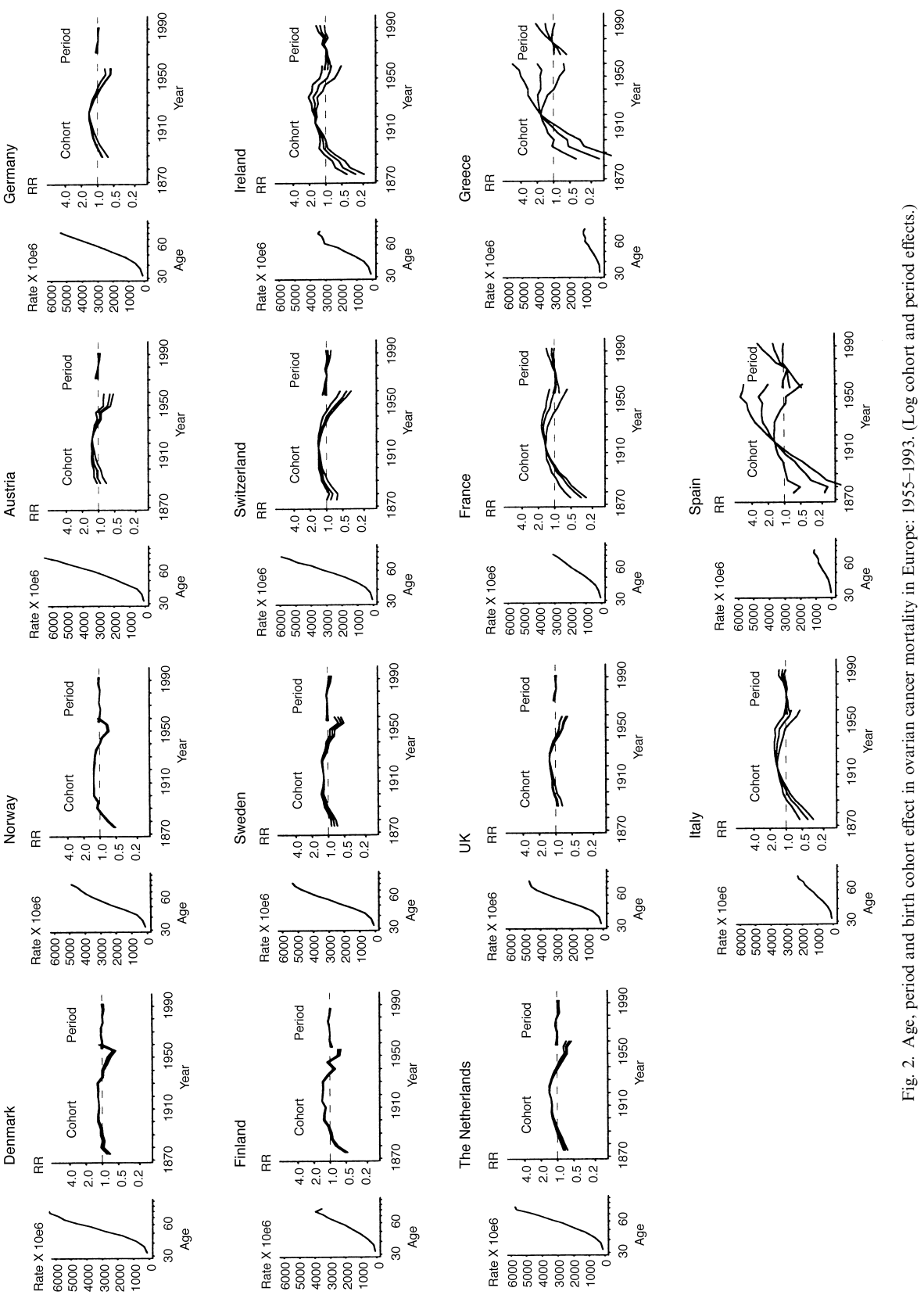

Fig. 2. Age, period and birth cohort effect in ovarian cancer mortality in Europe: 1955–1993. (Log cohort and period effects.)

of-fit. Fig. 2 depicts the graphs for the age, period and cohort effects. The cohort and period effect graph in a logarithmic scale shows Osmond and Gardner's solution (the intermediate line) and the two extreme solutions.

The graphs revealed a well-defined pattern of steadily declining risk among generations of women in northern Europe born after the decade, 1920–1930. Two patterns of behaviour were observed for the Mediterranean Basin: (1) a continuous increase in risk of death among all young generations of women born in Greece and Spain, with the trend becoming less pronounced from 1930 onwards; and (2) a decrease in risk in France and Italy from 1930. The period effect displayed a behaviour pattern similar to that of the cohort effect for all countries studied.

4. Discussion

The results obtained reveal differences between northern and southern European countries in the respective time trends for ovarian cancer mortality. The countries in the north showed higher adjusted rates throughout the entire time series analysed, with a process of stabilisation or continuous decline in evidence from approximately the 1970s onwards. In contrast, the countries in the south experienced a gradual rise in mortality rates, albeit with very low rates at the outset (1955–1958). On examination of the age, period-of-death and birth cohort components of the time trend, the cohort component was shown to have a predominant effect in both northern and southern regions of Europe. Within the context of time-trend studies on mortality or incidence, the relevance of such an analysis of the birth cohort effect is based on the assumption that generation of birth constitutes the natural grouping of the population *vis-à-vis* possible exposures to the most relevant risk factors. In northern Europe a decline in risk was observed among women born after the decade, 1920–1930. Young generations of women in the Mediterranean Basin exhibited two patterns of evolution: (1) gradually decreasing risks in Italy and France from 1930; and (2) a continuously rising risk of death among all young generations of women born in Greece and Spain, becoming less pronounced from 1930 onwards.

In all likelihood, the variability observed in the time trend and the differences in mortality between countries and regions reflect a series of changes in exposure to various factors (environmental, occupational, lifestyle) over the course of the period analysed, in tandem with diagnostic and therapeutic improvements, bilateral ovariectomy, and changes in verification and certification of cause of death [11].

Accuracy of death certificates and correct coding may limit the validity of the data analysed, yet in the case of malignant tumours, European countries register a high degree of concordance where these indicators are concerned [12,13].

Lack of information meant that the mortality rates calculated for ovarian cancer failed to take into account the respective proportions of women in the countries studied who had undergone a bilateral ovariectomy in each of the periods analysed and who, as a result, were thus not at risk of suffering cancer. Despite this, any underestimation of mortality rates thus obtained would probably be small.

Risk factors for ovarian cancer are, as yet, only partly known [14–16]. The role of oral contraceptives as a protective factor against ovarian cancer has been well defined and quantified by numerous epidemiological studies [17–22]. The protective effect increases in direct proportion to the time of use [19,21]. Hankinson and colleagues quantified a reduction in the risk of ovarian cancer of 11% per year of use [19]. Dating from the introduction of oral contraceptives in the early 1960s, expansion in the use of these drugs among northern European women was different to that observed in the south. It is estimated that in the 1970s, the percentage of women of fertile age taking oral contraceptives in northern Europe was 20–30% versus 5–10% for women of comparable age in Italy, Spain and Greece [11,23,24]. By the late 1980s and early 1990s, 30–40% of women in northern Europe aged 15–45 years were in the habit of using oral contraceptives [11,24,25]. Recent studies point to a moderate rise in the use of oral contraceptives on the part of women of fertile age in Spain and Greece, with approximately 15–20% reporting consumption of oral contraceptives at some time [26–28]. Percentages of use recorded for France and Italy approach those of countries in the north of Europe [29,30]. These differences in oral contraceptive use may explain, in part, the different pattern in ovarian cancer mortality trends plotted for generations born from 1920 to 1930 in southern and northern Europe.

There is consistent evidence of the protective effect afforded by fertility against ovarian cancer [31–35]. Whittemore and colleagues observed a negative linear correlation between the number of full-term pregnancies and the risk of suffering ovarian cancer [20]. Hankinson and associates quantified a reduction of 16% for each new full-term pregnancy [34]. Similarly, changes in the fertility rates of the different cohorts of European women may serve to explain part of the variability in the mortality rates. In a time-trend study into ovarian cancer incidence and mortality in England and Wales, dos Santos Silva and Swerdlow observed an increased risk in successive cohorts of women born prior to 1920 [35]. This rise in the mortality risk was accompanied by a decline in the fertility rate. However, rather than coinciding with a rise in the fertility rate, the decline in risk observed from 1920 coincided instead with the introduction of oral contraceptives. A similar pattern

was observed in studies conducted in The Netherlands and Denmark [24,31]. Another pregnancy-related process, such as lactation, was independently associated with the decline in risk of ovarian cancer [36–38]. Analysis of the WHO Collaborative Study, which included women in seven countries, revealed a significant reduction in risk associated with maternal lactation [38]. In the case of the Cancer and Steroid Hormone Study, analysis showed that a month of pregnancy was more protective than a month of lactation [37].

Aside from hormonal factors, gynaecological surgical procedures, such as tubal ligation or hysterectomy, also provide protection against the appearance of ovarian cancer [39–42]. The hypothesis that underlies this finding postulates that the disrupture of the natural route of transit from the vagina to the ovary via the uterus prevents or hinders exposure to exogenous carcinogenic agents [20].

Genetic factors play a significant role in the aetiology of ovarian cancer. A family history of ovarian cancer is a strong and consistent risk factor for ovarian cancer [43–49]. The Cancer and Steroid Hormone Study reported 3.6-fold and 2.9-fold higher risks among first- and second-degree relatives, respectively, of patients with primary ovarian cancer [45].

Evidence associating diet and the intake of nutrients with ovarian cancer is scant and rather inconsistent. In some studies, a positive association was observed with the consumption of meat, whole milk, eggs, cholesterol and saturated fats [50–52]. Ingestion of green vegetables has shown itself to be a protective factor [52]. Differences in eating habits between northern and southern Europe and changes in these habits over the course of the study period can very probably explain part of the geographical variability observed.

Few epidemiological studies have been undertaken to evaluate and quantify the association between occupational factors and ovarian cancer [16]. In particular, there is a dearth of studies on chemical agents to which women are exposed in their work environment, while those studies that do exist are generally found wanting with regard to information on confounding factors, such as reproductive history, use of contraceptives and ovulation-inducing drugs. Exposure to talc, mainly for cosmetic use, has been assessed by different authors and an association with ovarian cancer observed [53–57].

Thanks to the use of combinations of the most effective chemotherapies as well as diagnosis at earlier stages of the disease, improvements in medical treatment in recent years have, albeit slightly, enhanced overall ovarian cancer survival in Europe [2]. Risk of death (RR = Relative survival rate at 5 years) due to ovarian cancer from 1987–1989 compared with 1978–1980 was 0.9 [2]. The improvement in survival proved greater in women aged 15–64 years (RR = 0.8) [2]. This improved survival was likewise reflected in the mortality indicators observed in our study for women in the above age range.

In brief, the results show a different time sequence in the evolution of ovarian cancer mortality for northern versus southern regions of Europe. Examination of the trend in mortality rates and age–period–cohort effects leads to the deduction that countries in southern Europe are destined to follow a similar course to that traced by countries in the north, though possibly without ever attaining the high mortality rates experienced by their northern neighbours.

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