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Converging patterns of colorectal cancer mortality in Europe

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Abstract

Trends in mortality rates from colorectal cancer during the second half of the 20th century were analysed for 21 European countries and grouped in three broad European regions. For each gender, age-standardised (world standard population) mortality rates were computed by the direct method, and joinpoint analysis was used to identify significant changes in rates. A favourable pattern in colorectal cancer mortality for both genders was observed in most European countries from the 1990s onwards. Colorectal cancer mortality rates were still in the upward direction in some Eastern European countries, as well as in some Mediterranean countries. Mortality rates tended to converge at around 20/100 000 in men and around 11/100 000 in women. This converging pattern is even clearer when colorectal mortality rates are examined in three broad European regions. Similar mortality rates over recent calendar years have been reached by countries where mortality has been decreasing in recent decades and in those countries (mainly Eastern European and Mediterranean countries) which have experienced a recent levelling-off and decrease. If recent trends are maintained, colorectal cancer mortality is likely to decline further in Europe in the current decade.

Keywords: Mortality; Colon; Rectum; Intestines; Cancer; Time trends; Joinpoint regression; Screening; Early detection; Risk factors

1. Introduction

Colorectal cancer is the most common non-tobacco-related cancer in both genders combined in developed countries and the fourth commonest type of cancer worldwide [1,2]. Family history of colorectal cancer in first-degree relatives is the best recognised risk factor, but accounts for less than 5% of cases on the population level [3]. Epidemiological studies have shown that the main environmental correlates of colorectal cancer are dietary factors: high fat and red meat consumption and low vegetable intake have been associated with an increased risk [4]. Physical inactivity, excess body weight, high alcohol consumption, probably in combination with a diet low in some micronutrients, and smoking early in life are likely to increase the risk of colorectal cancer risk [4]. Exogenous female hormones have been inversely associated with colorectal cancer occurrence [5–7].

In the United States of America (USA), colorectal cancer mortality rates peaked in the mid-1940s (35/100 000), were approximately stable for the subsequent three decades, before declining in the 1980s and 1990s (26.1/100 000 among males and 18.6/100 000 among females in 1998) [8]. More recently, a decline in US colorectal cancer incidence has been observed [9]. An

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appreciable fall was also observed in mortality from colorectal cancer in the European Union (from 20.1/100 000 in 1960–1964 to 16.3/100 000 in 1995–1999 in men; from 14.0 to 10.4/100 000 in women) [10].

An updated analysis of colorectal cancer mortality trends within Europe by country and geographical area can offer an interesting picture from an epidemiological and public-health perspective. Thus, we analysed the trends during the second half of the 20th century in colorectal cancer mortality rates in 21 European countries individually and grouped in three broad European regions (Northern and Western countries, Eastern countries, and Mediterranean countries).

2. Patients and methods

Official death certification data for colorectal cancer were abstracted from the World Health Organization (WHO) database (http://www3.who.int/whosis/menu.cfm, last accessed September 2003) over the period of 1950–2001. Estimates of the resident population, generally based on official censuses, were based on the same WHO database.

For the present analysis, we considered trends in mortality from colorectal cancer for 21 individual European countries. We also grouped these countries into three broad regions: Northern and Western Europe (Austria, Belgium, Denmark, Finland, Germany, Ireland, Netherlands, Norway, Sweden, Switzerland and United Kingdom), Eastern Europe (Bulgaria, Czech Republic, Hungary, Poland and Romania), and Mediterranean Europe (France, Greece, Italy, Portugal and Spain).

During the calendar period considered, different revisions of the international classification of diseases (ICD) were used. Classification of cancer deaths was therefore recoded, for all calendar periods and countries, according to the Ninth Revision of the ICD [11]. To improve validity and comparability of data throughout different countries, we pooled together colon and rectum (ICD-9: 153, 154, and 159.0). In a few countries, data were missing for part of one or more calendar years, but no extrapolation was made for missing data.

Mortality rates were computed by the direct method, and standardised by quinquennia of age using the world standard population [12], for comparative purposes to other areas of the world. Joinpoint regression analysis was used to identify points where a significant change in the linear slope of the trend occurred [13]. In joinpoint analysis, the best fitting points (the "joinpoints") are chosen where the rate changes significantly (increases or decreases). The analysis starts with the minimum number of joinpoints (e.g., 0 joinpoints, which is a straight line), and tests whether one or more joinpoints (up to four joinponts) are significant and must be added to the model. In the final model, each joinpoint (if any) informs of a significant change in the slope, and an annual percent of change is computed for each of those trends by means of generalised linear models assuming a Poisson distribution. Significant changes include changes in direction or in the rate of increase or decrease. The computation of mortality rates and their standard errors was implemented in S-PLUS (S-PLUS 2000, MathSoft, Inc. 1999). The joinpoint analyses were performed using the "Joinpoint" software from the Surveillance Research Program of the US National Cancer Institute (http://www-dccps.ims.nci.nih.gov/SRAB).

3. Results

Figs. 1 (men) and 2 (women) present trends in overall age-standardised and truncated (35–64 years) colorectal cancer mortality rates in 21 European countries over the last five decades. A favourable pattern in colorectal cancer mortality for both genders was observed in most European countries (Austria, Finland, Ireland, Netherlands, Norway, Sweden, Switzerland, United Kingdom, France, and Italy) from the 1990s onwards, or even earlier (Belgium, Germany, and Denmark). Colorectal cancer mortality rates were still in the upward direction in Bulgaria, Poland and Romania (Eastern European countries), as well as in some Mediterranean countries (Greece, Portugal, and Spain). Rates were exceedingly high, but tended to level-off in recent years in the Czech Republic, Slovakia (given together in Tables and Figures), and Hungary.

Tables 1 and 2 show calendar years when significant changes in mortality trends occurred in males and females, respectively, and the corresponding annual percent of change (APC). In all countries, the mortality rates in women were lower than in men, and in most countries the levelling-off and decline began earlier in women. For example, in Belgium a steady decline has been present since 1955, with an APC of −1.00% in women (Table 2), while in men the mortality rate started to decline in 1981, with an APC of −1.04% (Table 1). Mortality rates tended to converge around 20/100 000 for men and around 11/100 000 for women in most countries.

This converging pattern is even clearer when colorectal mortality rates are examined in three broad European regions. In the 1960s, death rates from colorectal cancer were only slightly higher for males than for females in the three regions. Trends for females moderately decreased in Northern and Western countries until 1993 (−0.51 APC) and more strongly thereafter (−2.99 APC), while the decline began only in 1987 (−1.02 APC) in Mediterranean countries and in 1986 (−0.72 APC) in Eastern European countries, after

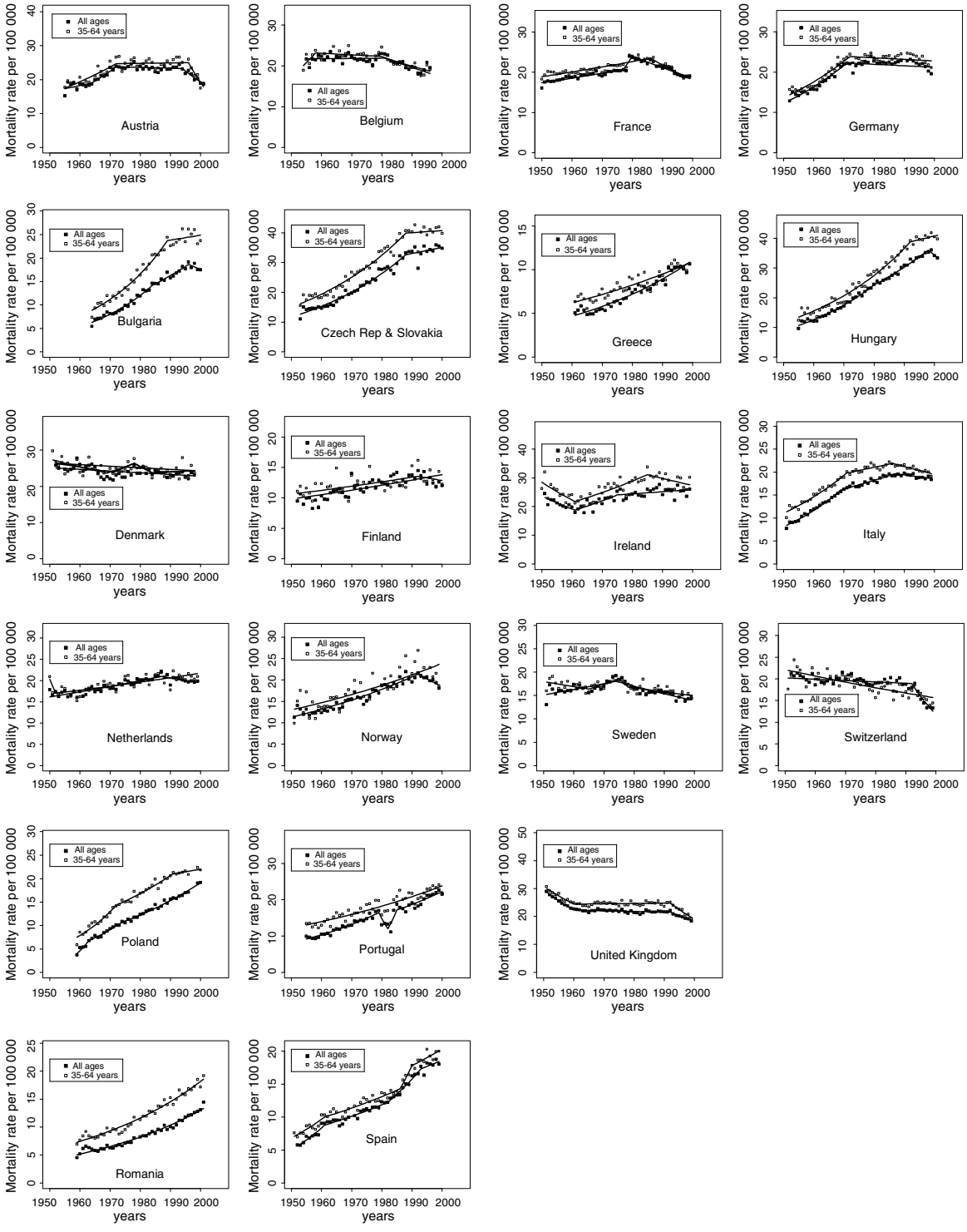

Fig. 1. Joinpoint analysis for colorectal cancer mortality in selected European countries. Males, all ages and 35–64 years old.

previous steady increases (APC of 0.21 between 1959 and 1987 and of 2.15 between 1960 and 1986, respectively). Among males, mortality in the three regions has converged following a similar pattern, starting from higher death rates. In Northern and Western European countries, mortality rates levelled-off around 20/100 000 between the 1960s and the 1990s, with a decline of −2.61 annually since 1995. Colorectal cancer mortality rates in Eastern and Mediterranean European countries have reached similar values after steady increases until the mid-1980s, and a subsequent moderate decline (Table 3 and Fig. 3).

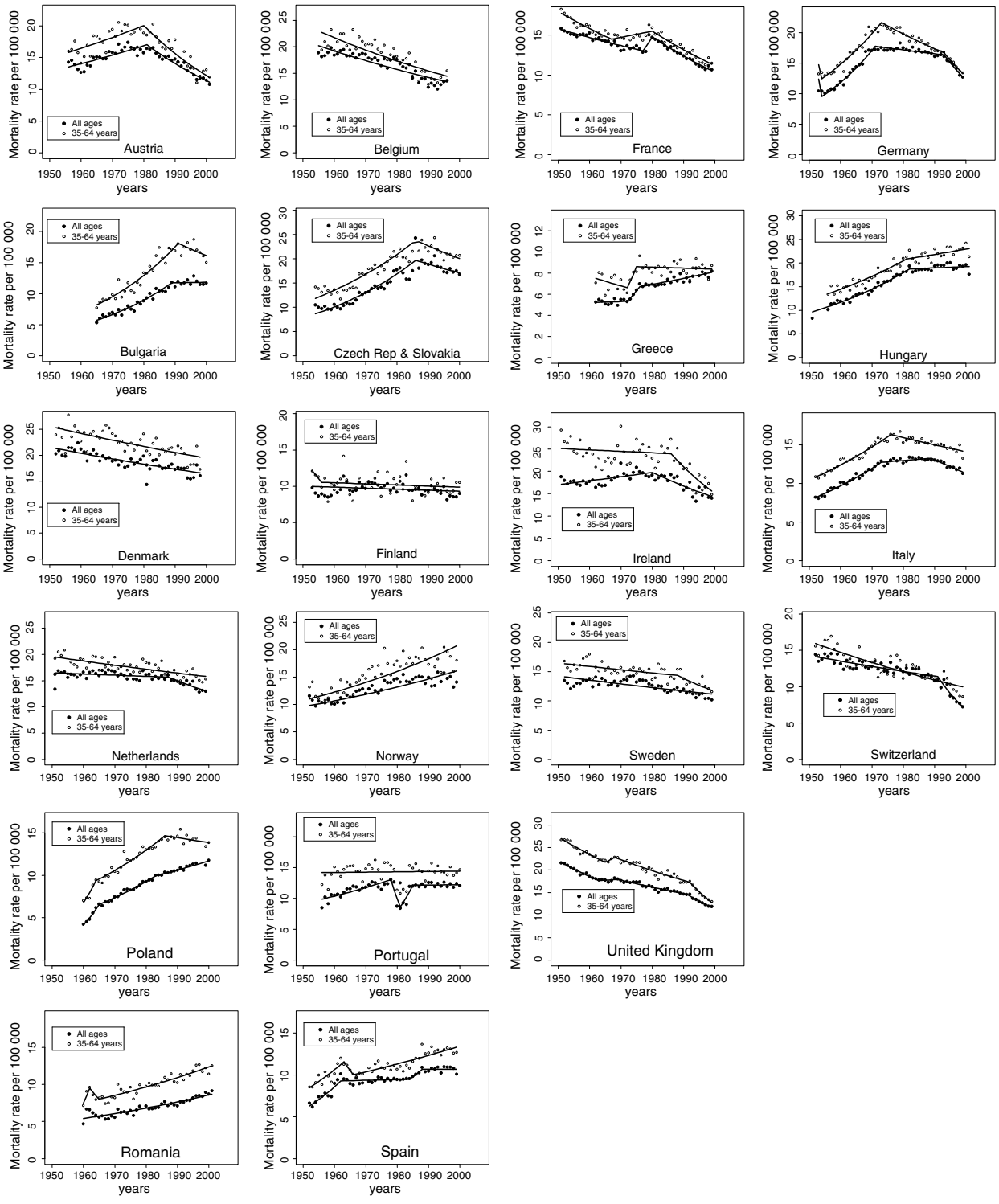

Fig. 2. Joinpoint analysis for colorectal cancer mortality in selected European countries. Females, all ages and 35–64 years old.

4. Discussion

The present updated analysis of colorectal cancer mortality in Europe shows a clear converging pattern between countries and broad geographical areas, with favourable trends in most areas of the continent over recent years not only for females (as already shown in previous analyses [14]), but also for males.

These favourable trends in mortality from colorectal cancer over recent years likely reflect more uniform and favourable changes in dietary and life-style habits [4,15], as well as some potential favourable effects from early

Table 1
Age-standardised (world population) colorectal cancer mortality rates and joinpoint analysis: males, all ages, selected European countries

	Age-standardised mortality rates		Joinpoint analysis							
			Trend 1		Trend 2		Trend 3		Trend 4	
	1955	1999	Years	APC	Years	APC	Years	APC	Years	APC
Austria	15.2	20.3	1955–1964	1.06	1964–1972	2.83[a]	1972–1994	−0.11	1994–2001	−3.09[a]
Belgium	21.7	19.5[c]	1955–1981	0.03	1981–1996	−1.04[a]				
Bulgaria	5.4[b]	17.5	1964–1984	4.15[a]	1984–1996	2.30[a]	1996–2000	−1.46		
Czech Rep. and Slovakia	14.2	35.5	1953–1988	2.74[a]	1988–2000	0.60				
Denmark	24.7	23.1[c]	1952–1998	−0.20[a]						
Finland	9.9	12.6	1952–2000	0.68[a]						
France	18.0	19.1	1950–1977	0.64[a]	1977–1980	5.18[a]	1980–1999	−1.28[a]		
Germany	14.2	19.6	1952–1971	2.23[a]	1971–1999	−1.21[a]				
Greece	5.1[b]	10.6	1961–1999	2.17[a]						
Hungary	9.6	36.1	1955–1980	3.34	1980–1998	2.20[a]	1998–2001	−2.38		
Ireland	21.2	26.0	1951–1961	−2.09[a]	1961–1975	1.79[a]	1975–1999	0.30		
Italy	9.4	18.4	1951–1969	3.67[a]	1969–1987	1.10[a]	1987–1999	−0.46[a]		
Netherlands	17.9	19.8	1950–1987	0.70[a]	1987–1999	−0.57[a]				
Norway	13.2	18.1	1951–1992	1.52[a]	1992–1999	−1.79[a]				
Poland	3.7[b]	19.0	1959–1963	14.03[a]	1963–1974	4.18[a]	1974–2000	2.25[a]		
Portugal	9.9	22.6	1955–1979	2.46[a]	1979–1982	−9.89	1982–1985	12.56	1985–2000	1.74[a]
Romania	4.5[b]	12.8	1959–2001	2.33						
Spain	7.1	18.0	1952–1961	5.03[a]	1961–1982	1.60[a]	1982–1993	3.18[a]	1993–1999	1.04
Sweden	16.1	14.4	1951–1974	0.73[a]	1974–1999	−1.00[a]				
Switzerland	20.7	13.3	1951–1992	−0.16[a]	1992–1999	−5.66[a]				
United Kingdom	25.6	18.4	1951–1960	−2.76[a]	1960–1992	−0.11[a]	1992–1999	−2.10[a]		

APC, annual percent of change.
[a] The APC is significantly different from 0 ($P < 0.05$).
[b] Mortality rate not available for 1955. Rates presented: 1964 for Bulgaria; 1961 for Greece; 1959 for Poland and Romania.
[c] Mortality rate not available for 1999. Rates presented: 1996 for Belgium; 1998 for Denmark.

diagnosis [16,17]. Dietary factors account for a substantial proportion of colorectal cancer, which has been quantified in approximately 25% of incident cases [4,18]. The adoption of a healthier diet, richer in fibre, vegetables, and fruits, has been recommended in Europe over the last two decades, and may have favourably influenced recent trends of digestive tract neoplasms [19–22].

Increased use of aspirin and other anti-inflammatory drugs may also have reduced the incidence of colorectal cancer [23]. Hormone therapy in menopause and other female hormones, including oral contraceptives, may also have played some role in the earlier fall of colorectal cancer in women compared with men [5,6], together with more favourable patterns of exposure for women to dietary factors or to other life-style factors, such as physical activity, obesity or alcohol consumption [24]. Some gender-differences concerning diet have been observed, including a lower consumption of fats and a higher consumption of vegetables, carbohydrates and fibres among women, compared with men, and the beneficial effect of physical activity appears clearer in women than in men [25].

Wider adoption of faecal occult blood testing may also have had a favourable impact on colorectal cancer mortality. Available evidence from observational studies [16] and a meta-analysis of randomised-controlled trials indicate a substantial (23%) reduction in mortality [26]. The issue of effectiveness of various types of faecal occult blood testing in the general population and of comparative cost-effectiveness with other screening tests for colorectal cancer (such as sigmoidoscopy and colonoscopy [17]), however, remain open to discussion [16,27]. Recent progress in survival from colorectal cancer [28] due to higher resection rates associated with improvements in the stage at diagnosis, as well as decreases in operative mortality, have contributed in part to the levelling-off of the mortality rates. Systemic adjuvant chemotherapy is well established and has shown significant benefits for most colorectal cancer patients, mainly with Dukes' C stage (stage III), but also with Dukes' B stage (stage II) [29–34], who are treated in common clinical practice. Moreover, total mesorectal excision and adjuvant radiotherapy [35–38] have provided excellent local tumour control and improved survival for rectal cancer.

There are potential problems of reliability and validity of death certification for colorectal cancer, which may vary across countries, calendar periods and age groups. However, colorectal cancer, is a major neoplasm which is unlikely to pose major diagnosis and certification problems, at least in Europe over the last decades. Although

Table 2
Age-standardised (world population) colorectal cancer mortality rates and joinpoint analysis: females, all ages, selected European countries

	Age-standardised mortality rates		Joinpoint analysis							
			Trend 1		Trend 2		Trend 3		Trend 4	
	1955	1999	Years	APC	Years	APC	Years	APC	Years	APC
Austria	14.3[b]	11.8	1956–1981	0.92[a]	1981–2001	−2.10[a]				
Belgium	18.9	13.6[c]	1955–1996	−1.00[a]						
Bulgaria	5.3[b]	11.5	1965–1989	3.06[a]	1989–2000	0.06				
Czech Rep. and Slovakia	10.0	17.5	1954–1986	2.60[a]	1986–2000	−1.02[a]				
Denmark	19.9	16.0[c]	1952–1998	−0.54[a]						
Finland	8.7	8.6	1953–2000	−0.14						
France	15.1	10.7	1951–1980	4.30	1980–1999	−1.76[a]				
Germany	10.1	12.7	1953–1977	2.23[a]	1977–1999	−1.21[a]				
Greece	10.3	8.2	1962–1972	0.16	1972–1976	5.92	1976–1999	0.81[a]		
Hungary	10.1[b]	19.3	1956–1982	2.16[a]	1982–2001	0.14				
Ireland	17.8	14.0	1951–1980	0.50[a]	1980–1999	−1.66[a]				
Italy	8.3	11.3	1952–1973	2.14[a]	1973–1989	0.24[a]	1989–1999	−1.41[a]		
Netherlands	15.6	13.0	1951–1987	−0.13[a]	1987–1999	−1.52[a]				
Norway	10.6	14.1	1952–1999	1.06[a]						
Poland	9.3	11.2	1960–1965	9.60[a]	1965–1983	2.33[a]	1983–2000	0.95[a]		
Portugal	8.5[b]	12.4	1956–1978	1.27[a]	1978–1981	−12.79	1981–1985	8.92	1985–2000	0.01
Romania	4.7[b]	8.9	1960–2001	1.16[a]						
Spain	7.4	10.1	1952–1961	2.57[a]	1961–1984	0.05[a]	1984–1988	4.48	1988–1999	−0.13
Sweden	12.5	10.2	1952–1999	−0.50[a]						
Switzerland	14.5	7.2	1952–1999	−0.93[a]						
United Kingdom	20.3	11.9	1951–1963	−1.68[a]	1963–1969	0.23	1969–1991	−0.91[a]	1991–1999	

APC, annual percent of change.
[a] The APC is significantly different from 0 ($P < 0.005$).
[b] Mortality rate not available for 1955. Rates presented: 1956 for Austria; 1965 for Bulgaria; 1956 for Hungary and Portugal; 1960 for Romania.
[c] Mortality rate not available for 1999. Rates presented: 1996 for Belgium; 1998 for Denmark.

Table 3
Joinpoint analysis for colorectal cancer mortality in European regions

	Joinpoint analysis					
	Trend 1		Trend 2		Trend 3	
	Years	APC	Years	APC	Years	APC
Males						
Mediterranean	1950–1984	1.31[a]	1984–2001	−0.03		
Northern and Western	1950–1959	−1.48[a]	1959–1995	0.02	1995–2001	−2.61[a]
Eastern	1960–1985	2.80[a]	1985–2001	0.47		
Females						
Mediteranean	1950–1987	0.21[a]	1987–2001	−1.02[a]		
Northern and Western	1950–1993	−0.51[a]	1993–2001	−2.99[a]		
Eastern	1960–1986	2.15[a]	1986–2001	−0.72[a]		

Mediterranean: France, Greece, Italy, Portugal, and Spain. Northern and Western: Austria, Belgium, Denmark, Finland, Germany, Ireland, The Netherlands, Norway, Sweden, Switzerland, and United Kingdom.
Eastern: Bulgaria, Czech Republic and Slovakia, Hungary, Poland, and Romania.
[a] The annual percent of change (APC) is significantly different from 0 ($P < 0.05$).

the distinction between colon and rectum may cause some problems (because a large proportion of cancers arise in the recto-sigmoid junction and a variable proportion of colorectal cancer deaths in different countries is certified as ''intestines, site of origin unspecified''), this cannot have affected our estimates based on all large bowel cancers combined. Changes in diagnosis and certification are therefore unlikely to explain the recent fall in mortality rates across Europe. The use of joinpoint analysis has allowed a detailed description of changes in trends in colorectal cancer mortality over the last decades.

In conclusion, the present analysis of colorectal cancer in Europe shows that similar mortality rates over recent calendar years have been reached by countries in which the mortality has been decreasing for decades, and in those countries (mainly Eastern and Mediterranean countries) which have experienced a more recent levelling-off and incipient decrease. If recent trends are

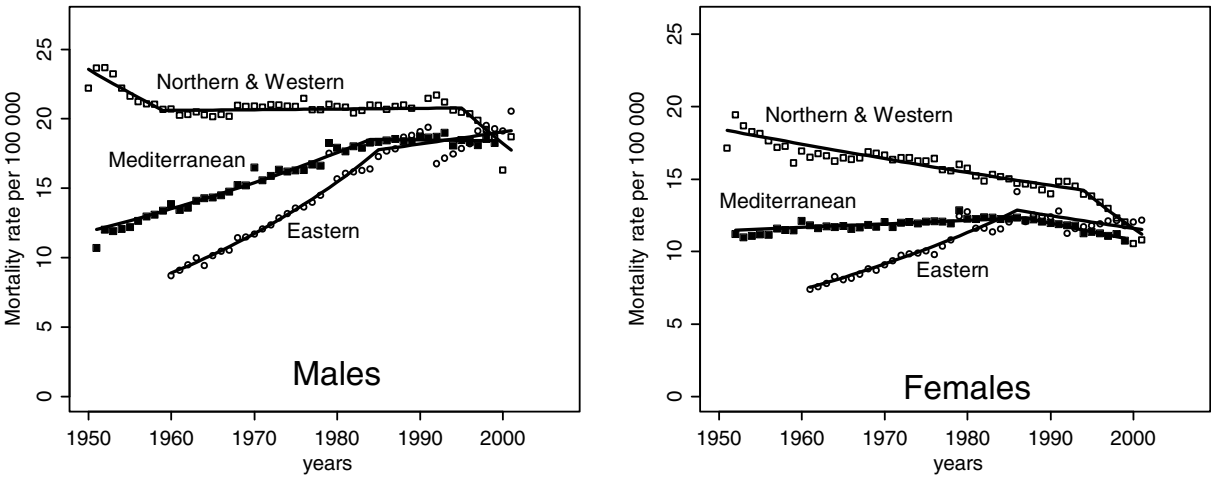

Fig. 3. Joinpoint analysis for colorectal cancer mortality in European regions. Northern and Western: Austria, Belgium, Denmark, Finland, Germany, Ireland, The Netherlands, Norway, Sweden, Switzerland, and United Kingdom. Mediterranean: France, Greece, Italy, Portugal, and Spain. Eastern: Bulgaria, Czech Republic and Slovakia, Hungary, Poland, and Romania.

maintained, colorectal cancer mortality is likely to further decline in Europe in the current decade [39].

Conflict of interest statement

None declared.

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