European Journal of Cancer (2015) 51, 1164–1187

Available at www.sciencedirect.com

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Recent trends in incidence of five common cancers in 26 European countries since 1988: Analysis of the European Cancer Observatory

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Available online 8 October 2013

KEYWORDS
Europe/epidemiology
Trends
Cancer registry
Neoplasms
Public health surveillance

Abstract ***Background:*** Individual country- and cancer site-specific studies suggest that the age-adjusted incidence of many common cancers has increased in European populations over the past two decades. To quantify the extent of these trends and the recent burden of cancer, here we present a comprehensive overview of trends in population-based incidence of the five common cancers across Europe derived from a new web-based portal of the European cancer registries.

Methods: Data on incidence for cancers of the colon and rectum, prostate, breast, corpus uteri and stomach diagnosed from 1988 to 2008 were obtained from the European Cancer Observatory for cancer registries from 26 countries. Annual age-standardised incidence rates and average annual percentage changes were calculated.

Results: Incidence of four common cancers in eastern and central European countries (prostate, postmenopausal breast, corpus uteri and colorectum) started to approach levels in northern and western Europe, where rates were already high in the past but levelled off in some countries in recent years. Decreases in stomach cancer incidence were seen in all countries.

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http://dx.doi.org/10.1016/j.ejca.2013.09.002

Discussion: Increasing trends in incidence of the most common cancers, except stomach cancer, are bad news to public health but can largely be explained by well-known changes in society in the past decades. Thus, current and future efforts in primary cancer prevention should not only remain focussed on the further reduction of smoking but engage in the long-term efforts to retain healthy lifestyles, especially avoiding excess weight through balanced diets and regular physical exercise.

1. Introduction

Cancer has emerged as a leading cause of morbidity and mortality in European populations [1]. This development has made population-based, accurate and near-term information on cancer occurrence extremely valuable in order to identify trends, and risk factors driving those trends. Such data are also the foundation for adequate and purposeful cancer prevention, which needs to be continuously adapted according to the best available scientific evidence and knowledge [2]. Several initiatives at the European level have led to the formation of a network of cancer registries, allowing for comparisons across countries that provide insights into the

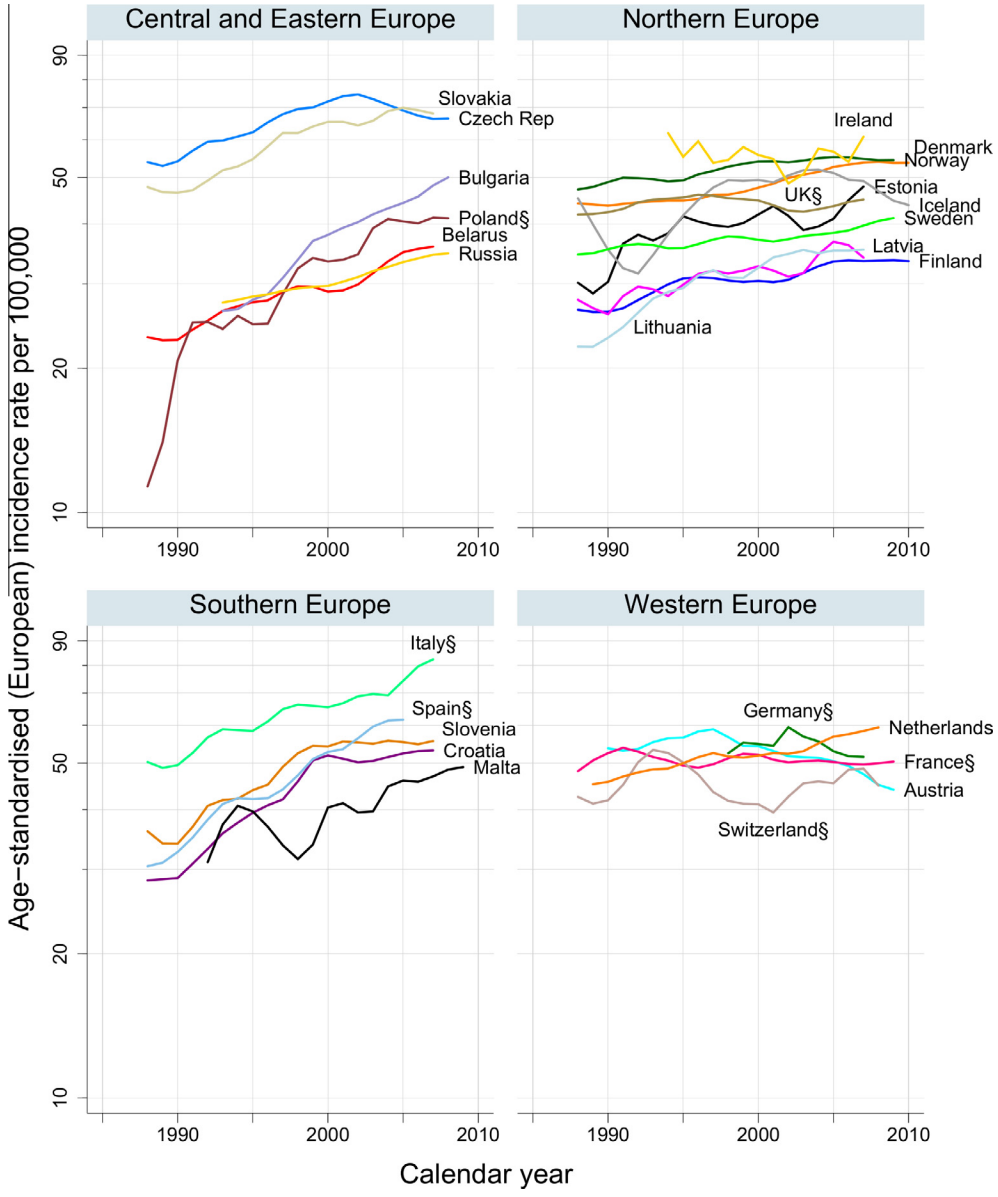

Fig. 1. Trends in colon cancer incidence in *males* by country and region, 1988–2008. §Regional registries.

impact of different risk factors, detection methods and treatment practices on the variation in cancer incidence and survival [3,74].

Smoking, dietary habits and reproductive factors have been identified as the main (modifiable) risk factors for cancer in populations in industrialised countries, with different magnitudes and implications across countries and regions [4,5]. Parallels between changes in the prevalence of those risk factors in the past and cancer incidence today highlight and confirm associations known for years. While smoking prevalence is still increasing in women in some countries in southern and central Europe [6,7], it has decreased in men in Europe since the 1960s, leading to declines in lung cancer incidence since the 1980s or 1990s, first in northern and western Europe and later in eastern and southern Europe [8,74]. At least 3–6% of all cancers in Europe have been related to high body mass index (BMI) and currently observed increases in BMI across all European countries [9,10]. Although the impact of these recent changes in risk factor prevalence will only be fully reflected in cancer burden in the next 20–30 years [11], monitoring current trends may enable us to anticipate future increases in cancer burden.

Progress in cancer control has recently been measured using trends in incidence, mortality and survival based on data from 21 European cancer registries [12]. While improvements in early detection as well as treatment options have translated into an ongoing increase in survival and decrease in mortality, cancer prevention

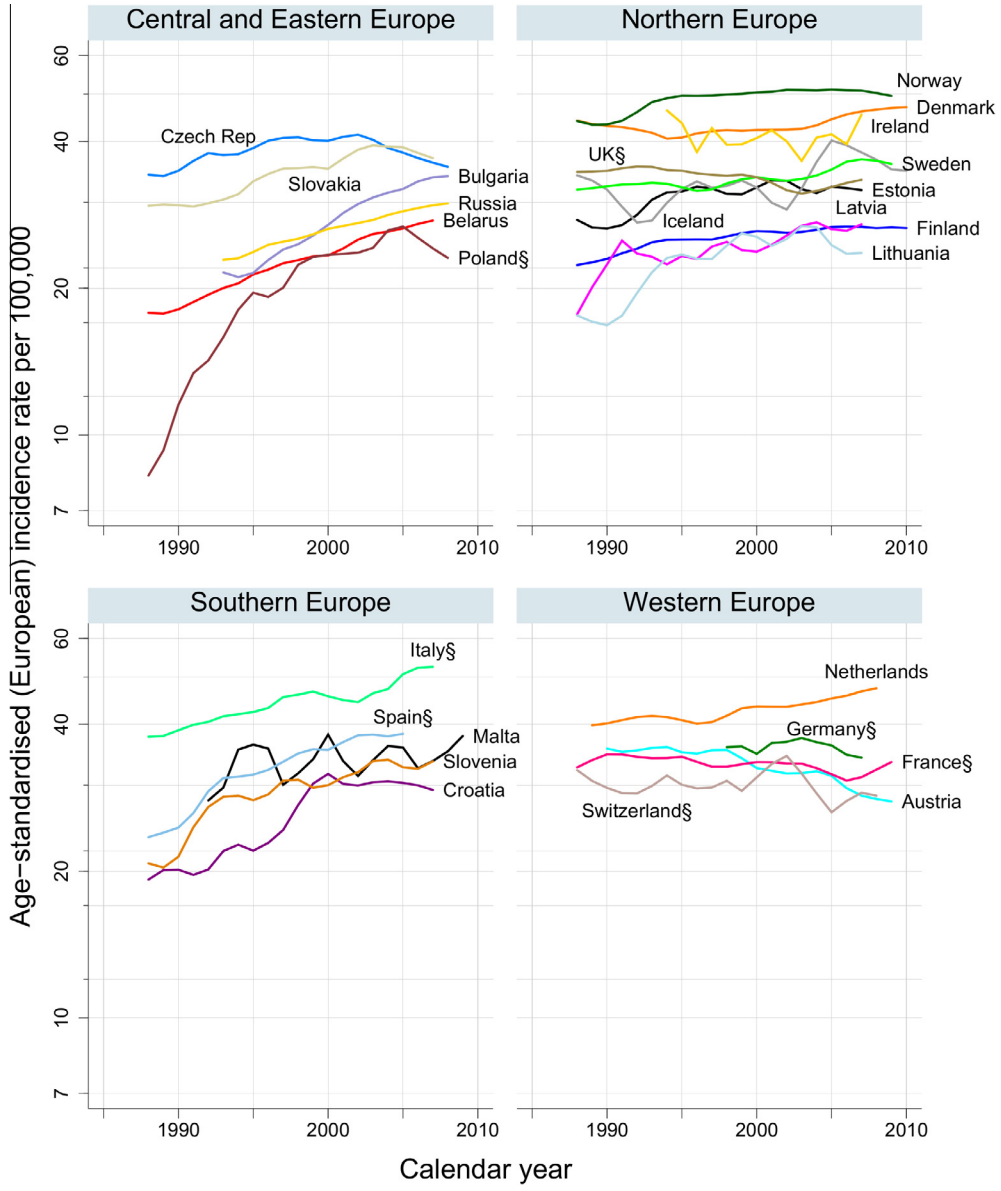

Fig. 2. Trends in colon cancer incidence in *females* by country and region, 1988–2008. §Regional registries.

efforts have so far yielded only moderate successes. In this study, we aim to describe recent trends in incidence of the most common cancers in Europe in the past two decades, complementing the study of [74] on trends in incidence of smoking-related cancers. Population-based incidence data from cancer registries in 26 countries from the European Cancer Observatory [13] and *Cancer Incidence in Five Continents* (CI5) [14] were used to assess trends across European regions, age groups and sex. Where possible, incidence trends were assessed in the light of the changing prevalence of several known risk factors in European populations. This approach will shed light on the potential for improvement in cancer prevention.

2. Methods

Cancer incidence data by age and sex and corresponding population figures were obtained from the EUREG database (http://eu-cancer.iarc.fr/EUREG/Default.aspx), which has been developed in the framework of the EUROCOURSE project and is part of the European Cancer Observatory (ECO) website [13]. Annual country- and sex-specific age-standardised

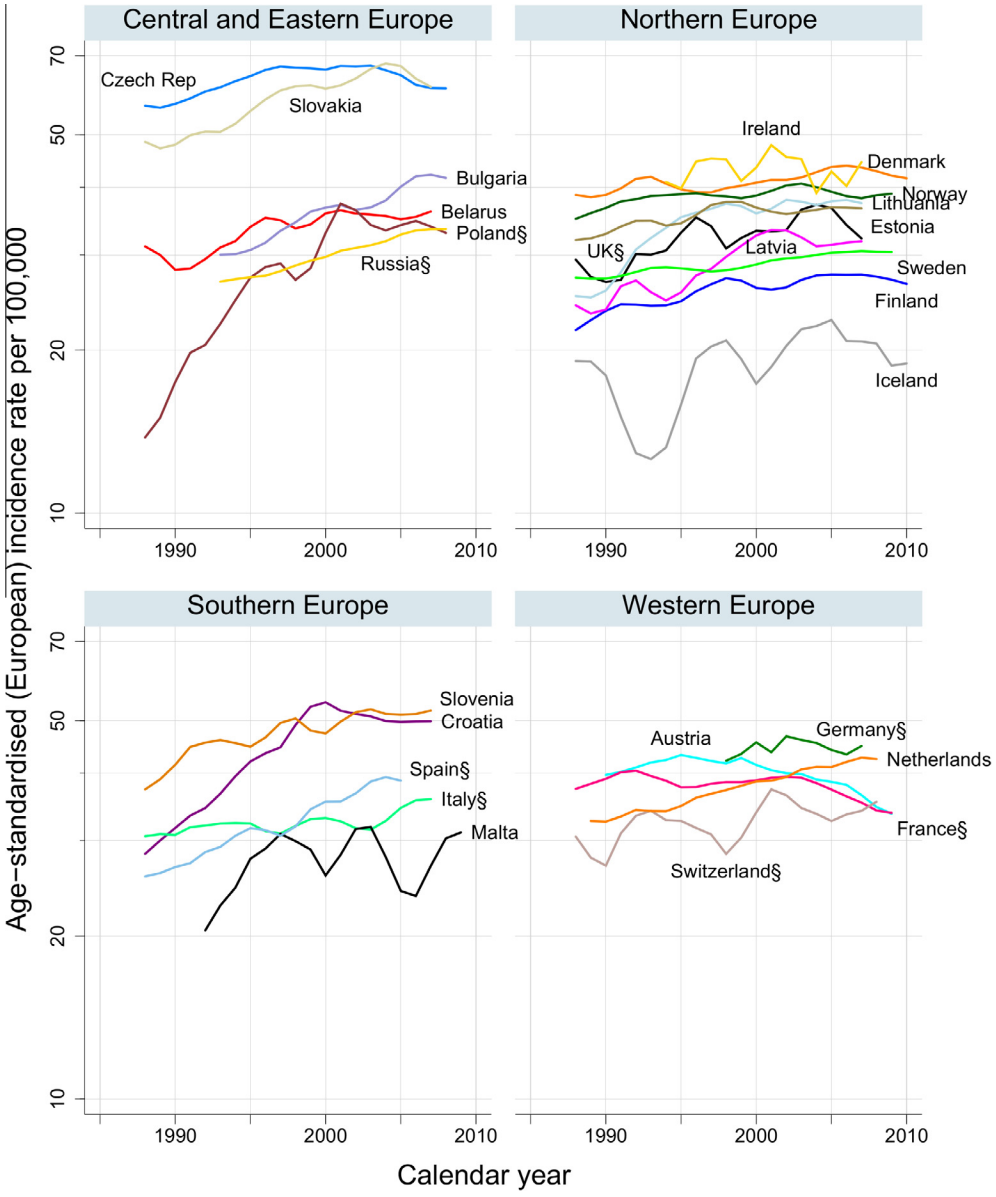

Fig. 3. Trends in rectal cancer incidence in *males* by country and region, 1988–2008. §Regional registries.

incidence rates (ASR), using the European Standard population, were calculated for 26 European countries between 1988 and 2008. Average annual percentage change (AAPC) was calculated for the last 10-year period (1998–2007) for all age groups (35–74 years) and by age group (35–64, 65–74 years) to assess the most up-to-date trends. A more detailed description of the data sources and analysis methods is provided in [74], which also lists the countries included and summarises the population coverage of their cancer registries.

The following cancer sites (and corresponding International Classification of Diseases-10 codes) were selected based on the most recent estimates of cancer incidence in Europe in 2012 [15]: stomach (C16), colon and rectum (C18–21), breast (C50) (divided into pre- and postmenopausal, defined as age <50 years and ⩾50 years at diagnosis, complying with scientific evidence in women in developed countries [16] and corresponding to the lower age threshold of mammography screening eligibility in most countries [17]), corpus uteri (C54) and prostate (C61). Colorectal cancer was subdivided into cancer of the colon (C18) and cancers of the rectum and anus (C19–21). Incidence trends of smoking-related cancers, including lung cancer, which ranks fourth among the most common cancers, are presented elsewhere [74]. Cancer of the urinary bladder ranked sixth, but due to changing registration practices between countries, we excluded this cancer and present data for stomach cancer, which ranked seventh, instead.

3. Results and discussion

Trends in incidence of five major cancers in Europe since 1988 are presented by sex and region in

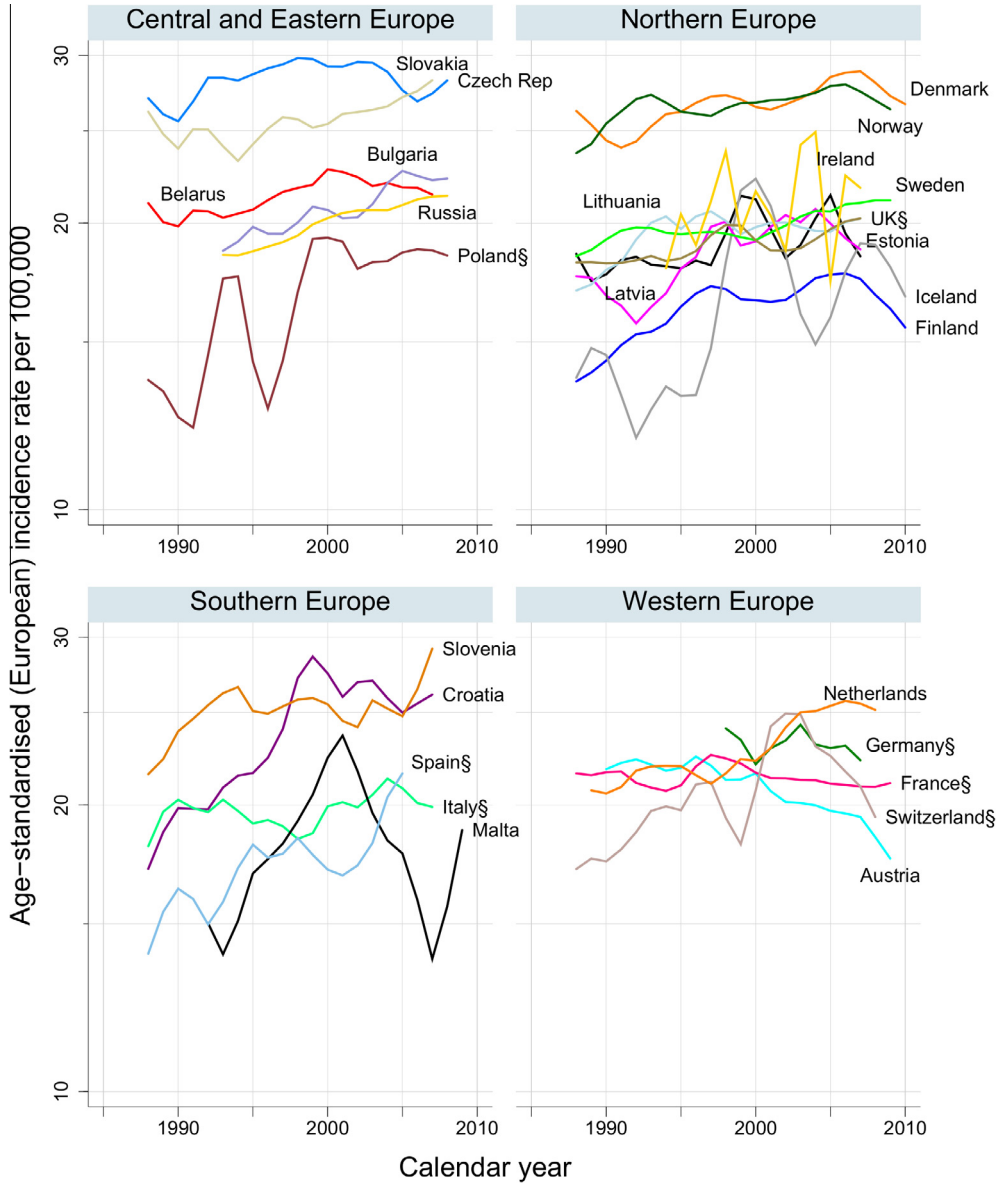

Fig. 4. Trends in rectal cancer incidence in *females* by country and region, 1988–2008. §Regional registries.

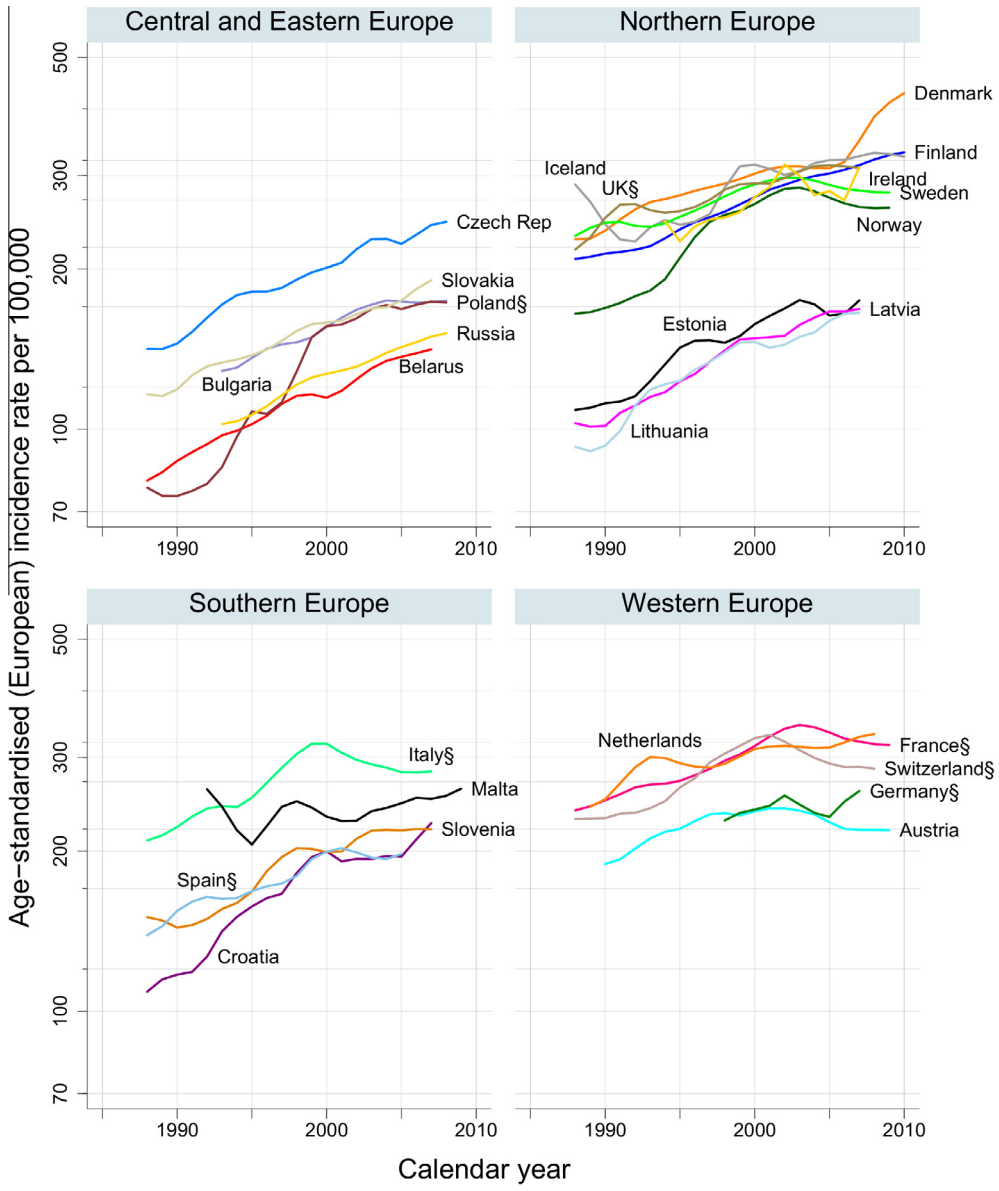

Fig. 5. Trends in postmenopausal breast cancer incidence by country and region, 1988–2008. §Regional registries.

Figs. 1–10. Table 1 lists the corresponding absolute numbers of cancer cases at the beginning and at the end of the study period. The AAPC plotted against the incidence in the most recent year are displayed by cancer site and sex in Figs. 11–20 and by sex and age in Tables 1–4 of the Appendix. For comparability, incidence rates and male–female ratios are reported as 3-year moving averages of the most recent data, unless otherwise mentioned. Table 2 summarises the potential effects of modifiable risk factors and secondary prevention measures on the incidence of the cancer sites under study.

3.1. Colorectal cancer

For *colon cancer*, incidence rates were almost equal in males and females (male–female ratio: 1.1 (Sweden and Norway) to 1.8 (Croatia, Slovakia and the Czech Republic)). In males, the highest rates were observed in Italy, Slovakia and the Czech Republic (>66 per 100,000), whereas the lowest rates were reported in Finland and Russia (<35 per 100,000). Increasing trends in colon cancer in males were seen in countries in central, eastern and southern Europe (Figs. 1 and 11). Different patterns across age groups were observed, with strong increases in the older age group in central and eastern European countries, e.g. a 4.2% annual increase in Bulgaria, while in northern and southern European countries such as Denmark, Finland and Italy the increase was strongest in the younger age group (Appendix Table 1). In females, the highest incidence rates of colon cancer were also observed in Italy (79 per 100,000) and the lowest in Lithuania (35 per 100,000). The increase in incidence during the study period was, however, smaller

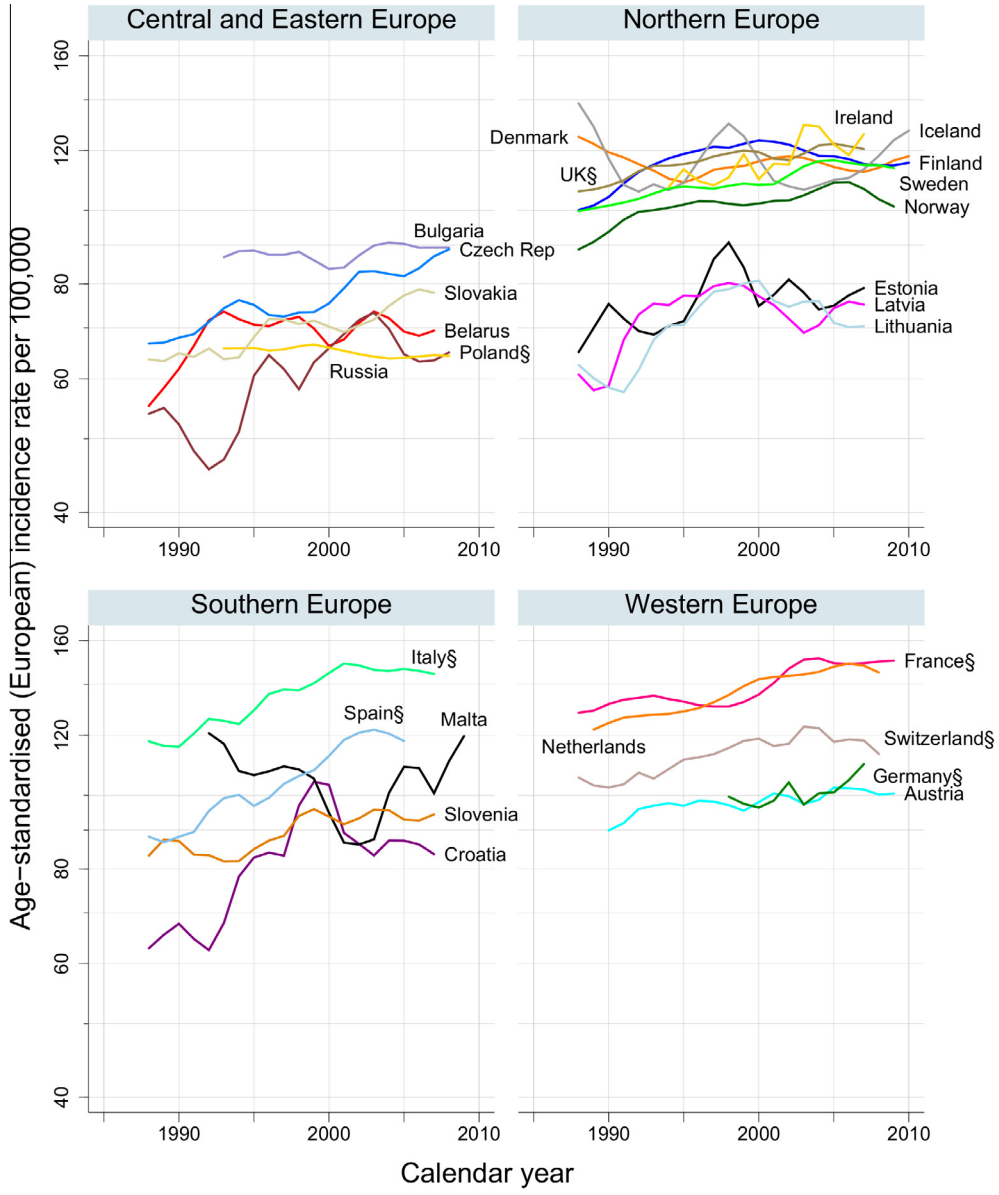

Fig. 6. Trends in premenopausal breast cancer incidence by country and region, 1988–2008. §Regional registries.

in women than in men (Figs. 2 and 12). While significant decreases in incidence occurred in the older age group in Austria (AAPC: −4.7; 95% confidence interval (CI): −6.9, −2.5) and Germany (AAPC: −2.0; 95% CI: −2.9, −1.0), incidence increased in most other countries (Appendix Table 1).

Similarly to colon cancer, *rectal cancer* was more common among males (male–female ratio: 1.1 (Iceland) to 2.3 (Slovakia)) and rates were highest in the Czech Republic and Slovakia (>60 per 100,000 during the most recent 3 years). The lowest rates were seen in Iceland, Malta and Finland (<30 per 100,000) (Figs. 3 and 13). Incidence increased in younger males in central and eastern Europe but also in several northern European countries, while it decreased or stabilised in western and southern Europe (except in males in the Netherlands and Italy). Similar, but less pronounced, patterns were seen in females (Fig. 4; Appendix Table 2).

Differences in the prevalence of risk factors for colon and rectal cancer (Table 2) across European countries a few decades ago are likely to be reflected in the geographical variation seen in incidence in recent years, i.e. higher rates in northern and western Europe than in south-eastern Europe. For instance, the high prevalence of obesity, alcohol consumption and smoking in the Czech Republic potentially explains the high colorectal cancer rates there. The implementation of colorectal cancer screening, during which precancerous polyps and early-stage cancers can be detected and removed [18], is unlikely to have affected the current trends. Primary prevention measures aiming to reduce the burden of colorectal cancer should mainly focus on maintaining

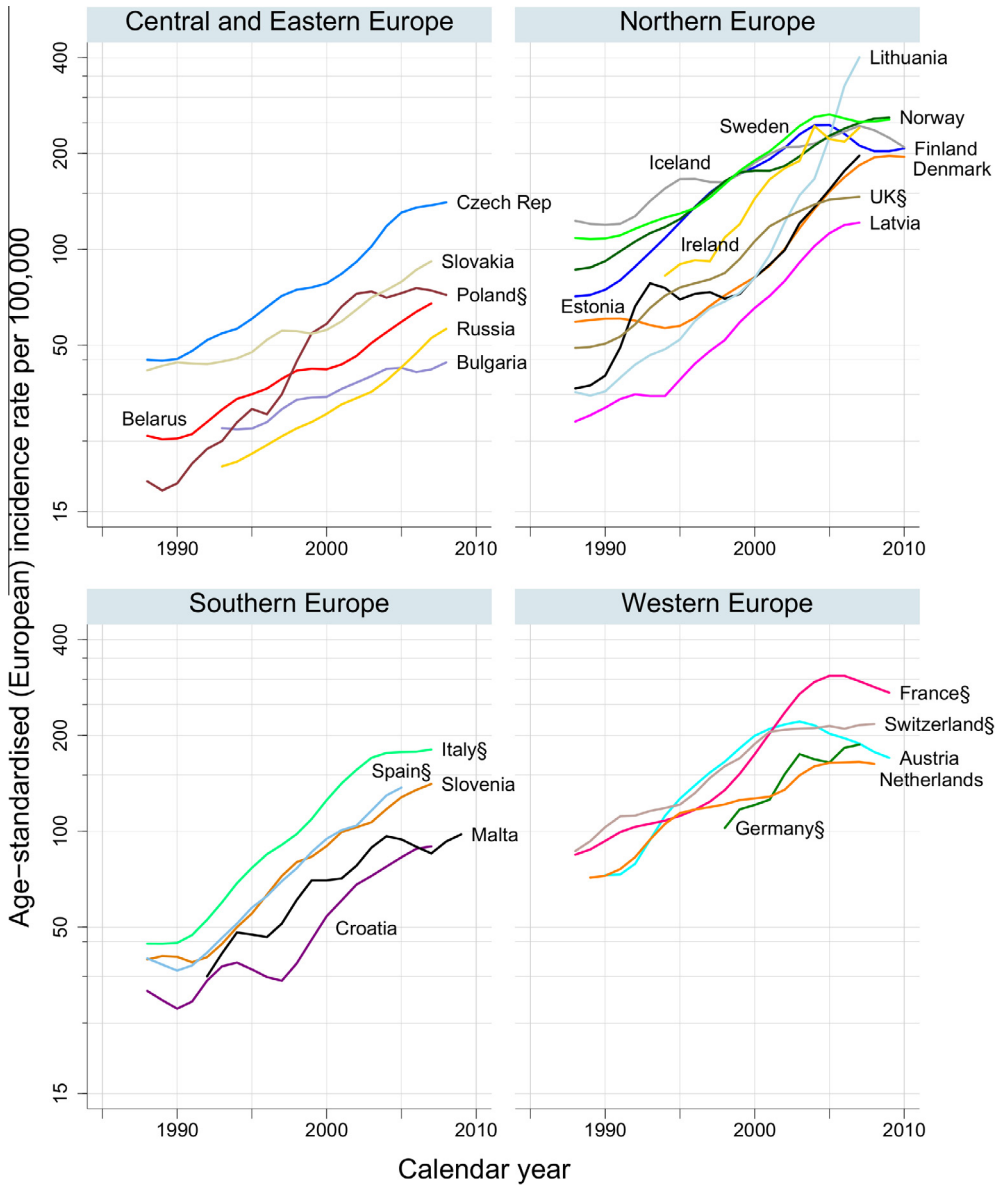

Fig. 7. Trends in prostate cancer incidence by country and region, 1988–2008. §Regional registries.

a healthy body weight and a balanced diet as well as smoking and alcohol cessation [19].

3.2. Breast cancer

In the most recent years, the highest rates of *postmenopausal* breast cancer were found among northern European women, with the exception of the three Baltic countries, where the rates were the lowest in Europe and similar to those observed in eastern and central Europe (Fig. 5). In southern, western and northern Europe (except for the Baltic countries), where rates were already relatively high in 1998, incidence rates have stabilised, with small increases such as in Slovenia, Germany and the Netherlands. In some of these countries, breast cancer rates were observed to decrease in the mid-2000s, in particular in Italy and France. In contrast to these trends, in eastern European and the Baltic countries, where rates had been relatively low, rates were observed to increase markedly (Fig. 15). The incidence of *premenopausal* breast cancer was highest in southern and western Europe, with the highest rates observed in Italy, France and the Netherlands (>140 per 100,000). The lowest rates were seen in central and eastern Europe as well as the Baltic countries (<90 per 100,000; Fig. 6). Rates seem to have stabilised since 1998, even in countries where rates had increased substantially in the earlier period of this study, e.g. in Slovakia, Ireland, Spain, France and the Netherlands.

Societal changes have greatly affected the main risk factors for breast cancer, contributing to an increase in incidence (Table 2). However, these changes have been

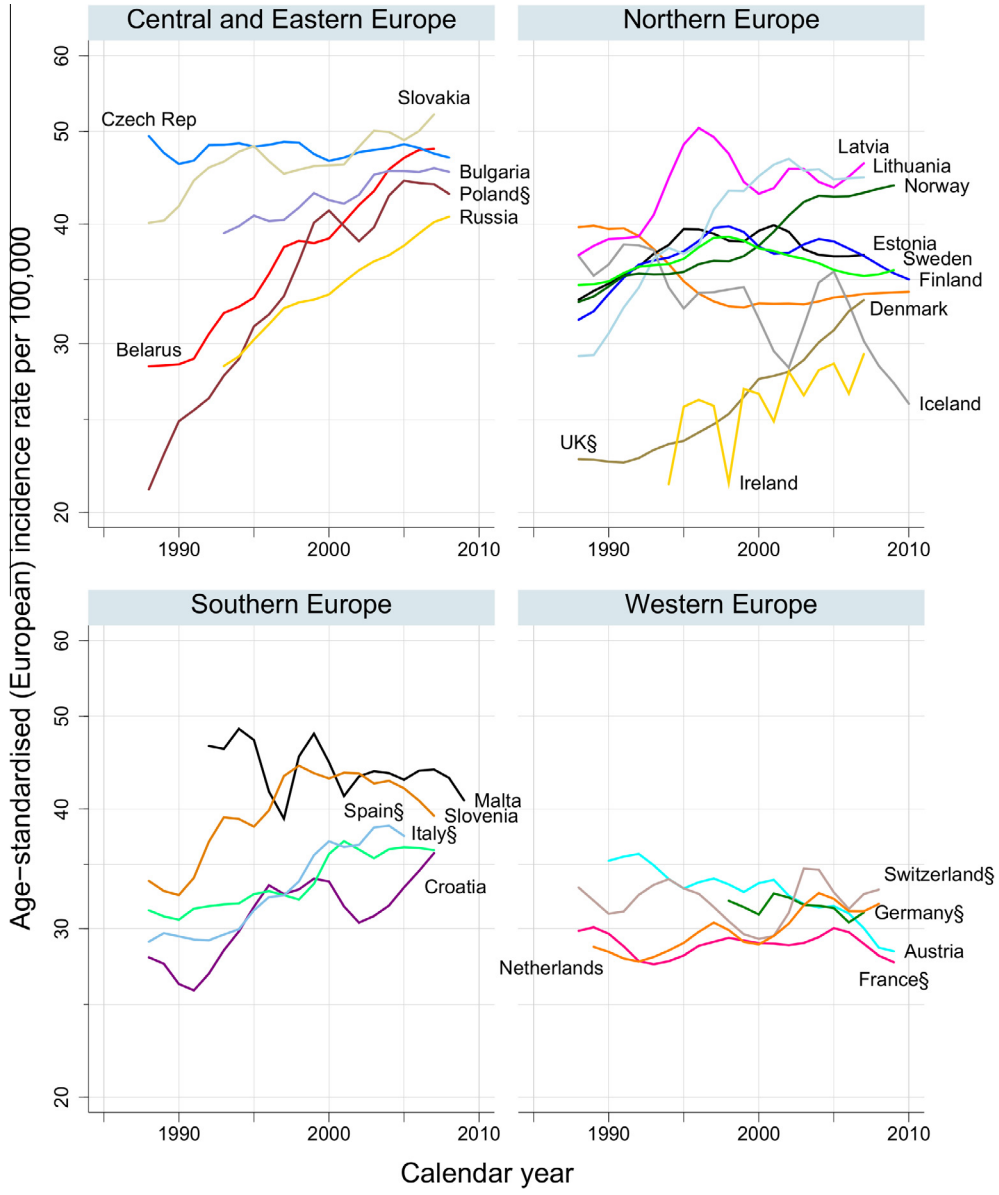

Fig. 8. Trends in corpus uteri cancer incidence by country and region, 1988–2008. §Regional registries.

beneficial for women and therefore modifying these factors may not be desirable. Another key factor behind the rising incidence of postmenopausal breast cancer is the implementation of organised or opportunistic breast cancer screening in many European countries [17]. Modifiable risk factors such as excess weight [10,20,21], alcohol consumption [22,23], physical inactivity [24] and the promotion of breastfeeding [25,26] should be the main focus of primary prevention interventions to reduce breast cancer burden.

3.3. Prostate cancer

Prostate cancer is the most frequent cancer among males in Europe. It is highest in northern and western Europe (>200 per 100,000), but rates in eastern and southern Europe have increased continuously (AAPC range, 2.1–28.0; Fig. 7; Appendix Table 4) and appear to be reaching the levels seen in northern and western Europe. The incidence of prostate cancer increased in all parts of Europe (Fig. 17), most notably in northern Europe and in the younger age group (35–64 years), with annual increases of up to 28% seen in Lithuania in this age group. In some northern and western European countries, incidence rates seem to have stabilised or dropped in the most recent years (Fig. 7).

The risk factors for prostate cancer are still largely unclear (Table 2). The strong increase in prostate cancer incidence is mainly due to the introduction of prostate-specific antigen (PSA) testing and consequent biopsy in asymptomatic men and in men with lower urinary tract symptoms [27]. However, the benefit of population

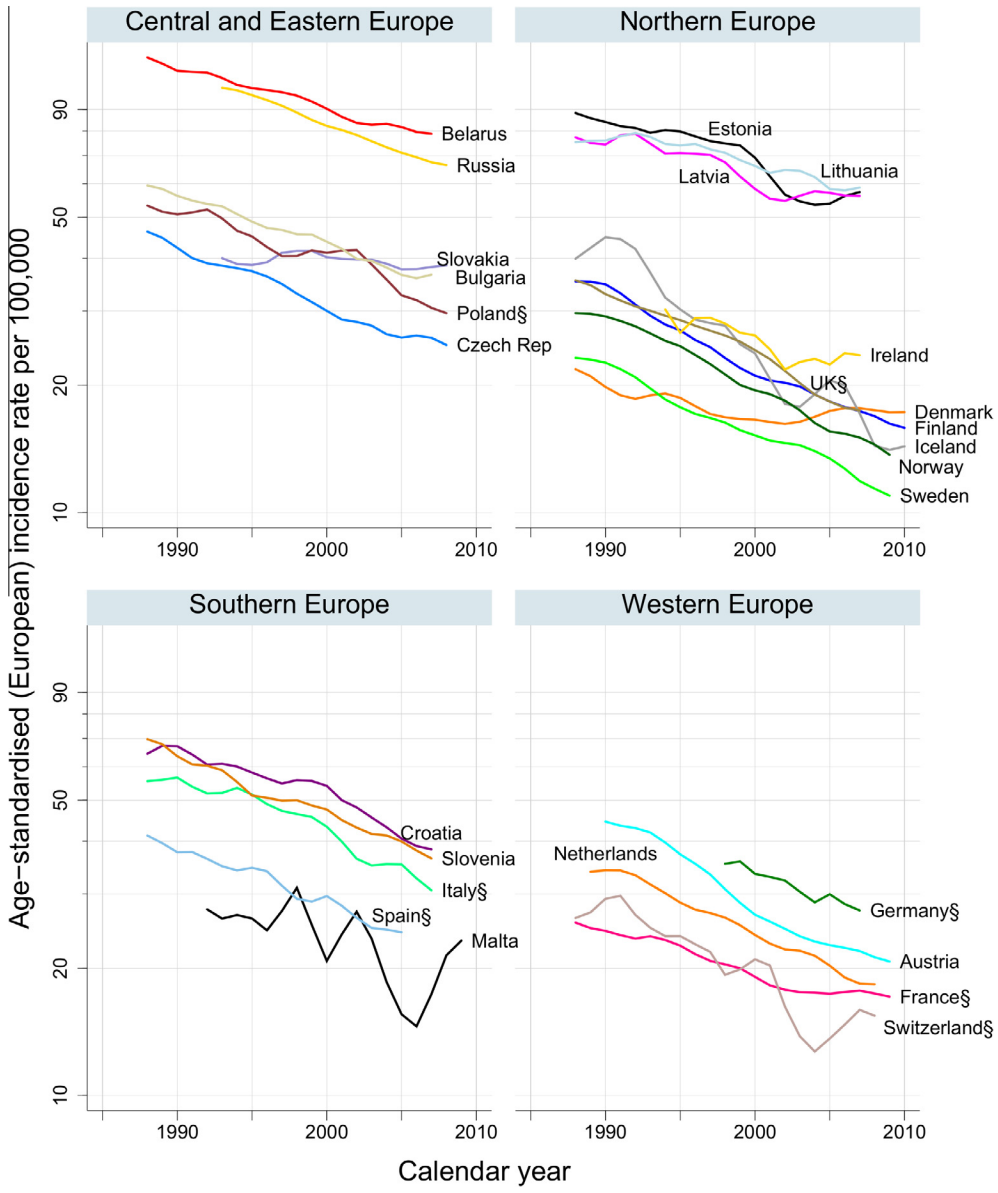

Fig. 9. Trends in stomach cancer incidence in *males* by country and region, 1988–2008. [§]Regional registries.

screening using PSA testing remains controversial. A clinical trial in Europe showed a 29% reduction in mortality after 11 years of follow-up in the screened arm [28], in contrast to a finding from a United States (U.S.) trial, where no significant reduction in mortality was found [29,30]. Similarly, recent findings from Finland showed no significant differences in mortality between the control and the screening arm after 12 years of follow-up, at the cost of moderate overdiagnosis [31]. In the European trial [28], the number needed to invite for screening in order to prevent one prostate cancer death was 1055 (number needed to detect: 37). Clearly, a more sensitive screening test is needed.

In the last 3-year period of our study, the incidence of cancer of the corpus uteri, of which 80% were cancers of the endometrium, was highest in Slovakia and Belarus (>48 per 100,000; Fig. 8). The lowest rates were observed in Iceland and France (<29 per 100,000). In general, the incidence of corpus uteri cancer increased in central and eastern Europe since 1988 (Figs. 8 and 18), most remarkably in Belarus (AAPC, 1998–2007: 3.3; 95% CI: 2.2, 4.5; Appendix Table 4). Among the northern and western European countries, significantly increasing trends were found in Norway, the United Kingdom, Ireland and the Netherlands (Fig. 18) and were more pronounced in the older age group (Appendix Table 4). Decreasing trends were observed in Austria (−1.3; 95% CI: −2.4, −0.1), particularly among the younger age group (−1.5; 95% CI: −2.8, −0.2), and also in the younger age group in Sweden (−1.9; 95% CI: −3.0, −0.9) and Germany (−1.5; 95% CI: −2.3, −0.8).

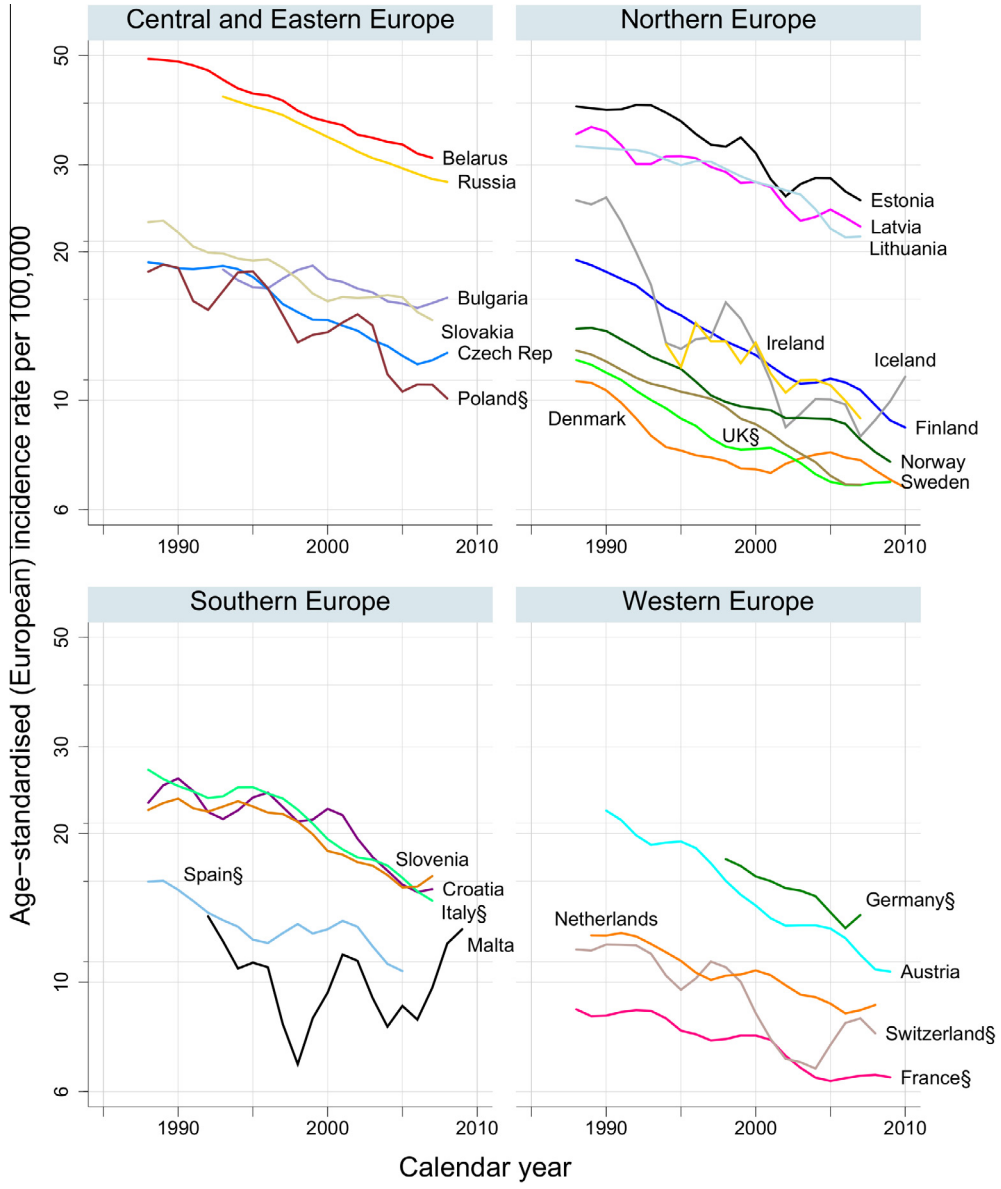

Fig. 10. Trends in stomach cancer incidence in *females* by country and region, 1988–2008. §Regional registries.

Similarly to breast cancer, for cancer of the corpus uteri varying reproductive risk factors mostly explain the difference in risk (Table 2), and hence rates and trends across Europe. Studies have observed that increases were confined to (oestrogen-dependent) type 1 cancers or endometrioid endometrial cancers [32,33], endorsing the role of excess weight as a significant driver for this cancer, in addition to the varying reproductive risk factors [33]. Increasing hysterectomy rates can also affect the incidence of uterine cancers and lead to underestimation of the risk if hysterectomised women are not excluded from the population at risk. Studies in Germany and Finland have shown that the incidence of cervical and uterine cancer increased by 67% in elderly women ($\geqslant$65 years) [34] and by 29% of endometrial cancer in women of all ages after correcting for hysterectomised women [35].

3.4. Stomach cancer

Stomach cancer incidence was in general higher in central and eastern Europe as well as in the Baltic countries (rate ratio, highest versus lowest risk: 7.0 in males and 4.9 in females) and was considerably higher in males than in females (male–female ratio: 1.4 (Iceland) to 2.9 (Poland)). In terms of trends, consistent decreases were seen across countries and regions (Figs. 9 and 10); the strongest decreases were in southern and western Europe, where rates have historically been higher (Figs. 19 and 20), with annual decreases of up to 6% in Italy and Switzerland. Due to this consistent decrease in incidence across Europe, the gap in incidence between northwestern and eastern Europe has persisted over the past decades.

Table 1
Absolute number of cases (males and females combined, age 35–74) at the beginning and end of the study period, by cancer site and country.

Country	Study period		Breast		Colon		Corpus uteri		Prostate		Rectum		Stomach	
	Begin	End	Begin	End	Begin	End	Begin	End	Begin	End	Begin	End	Begin	End
Central and eastern Europe														
Belarus	1988	2007	1571	2890	802	1465	681	1284	350	1318	1044	1309	3159	2378
Bulgaria	1993	2008	2412	2962	1137	1843	880	1033	656	959	1105	1377	1383	1163
Czech Republic	1988	2008	2553	4822	1956	2833	1207	1405	865	3732	1823	2458	1407	1021
Poland[§]	1988	2008	165	664	47	322	54	245	36	323	70	246	158	189
Russian Federation	1993	2008	30972	43924	16305	22071	10568	16229	5010	15435	14324	17991	44031	29506
Slovakia	1988	2007	964	1896	728	1233	417	735	345	979	737	1049	797	611
Northern Europe														
Denmark	1988	2010	2200	3979	1157	1583	514	508	726	2867	824	1025	419	360
Estonia	1988	2007	327	517	206	289	132	154	94	591	162	161	401	277
Finland	1988	2010	1830	3539	556	939	356	557	676	3237	378	612	606	352
Iceland	1988	2010	108	155	36	49	18	11	53	132	12	19	24	21
Ireland	1994	2007	1252	2017	754	930	145	256	574	2072	403	579	304	287
Latvia	1988	2007	600	827	265	376	261	331	113	618	253	296	621	434
Lithuania	1988	2007	687	1086	306	486	268	437	210	3044	295	467	759	644
Norway	1988	2009	1270	2129	915	1182	290	497	912	3034	572	777	448	222
Sweden	1988	2009	3480	4862	1491	1980	765	962	2639	7382	991	1320	812	466
United Kingdom[§]	1988	2007	20012	31175	9909	11447	2914	4982	6309	20695	6351	8035	6232	3485
Southern Europe														
Croatia	1988	2007	1003	2168	522	1047	351	481	286	1076	466	952	882	684
Italy[§]	1988	2007	1593	2675	849	1645	326	476	404	2394	453	720	781	569
Malta	1992	2009	156	233	41	97	40	46	19	116	28	61	34	38
Slovenia	1988	2007	545	888	225	507	156	222	110	774	236	444	346	288
Spain[§]	1988	2005	696	1286	336	845	183	290	238	1106	229	485	363	285
Western Europe														
Austria	1990	2009	2651	3709	1573	1602	698	662	1105	3683	1054	1094	1138	693
France[§]	1988	2009	1473	2572	594	954	244	330	588	2756	459	590	264	245
Germany[§]	1998	2007	6587	7915	3512	3816	1349	1376	3800	8248	2571	2901	2057	1772
Switzerland[§]	1988	2008	333	531	150	164	68	86	154	537	97	125	73	57
The Netherlands	1989	2008	5987	10447	2748	4731	967	1399	2161	6901	1730	2833	1462	1195

[§] Regional registries: France (Doubs, Herault, Isere, Haut-Rhin, Somme, Tarn); Germany (Brandenburg, Hamburg, Saxony, Mecklenburg, North Rhine-Westphalia, Saarland); Poland (Kielce, Cracow); Italy (Modena, Parma, Ragusa, Romagna, Torino, Varese); Spain (Granada, Murcia, Navarra, Tarragona); Switzerland (Geneva, St. Gall-Appenzell); United Kingdom (England and Scotland).

A decrease in the rate of infection with *Helicobacter pylori* (*H. pylori*) is the most important factor contributing to the declining trends in incidence of stomach cancer (Table 2) [36]. The eradication of *H. pylori*, which has been postulated to have a large role in determining the risk of stomach cancer in central, southern and eastern European countries, might help to reduce the observed gap in incidence between northern and western Europe [37]. In addition, preventive measures in Europe should tackle other risk factors for stomach cancer including the reduction of consumption of salted and preserved foods, smoking cessation and increasing consumption of fresh fruits and vegetables [36,38].

The results presented here are based on both national or (combined) regional data and different population sizes. With the inclusion of a cancer registry in *CI5* IX as a criterion for inclusion in this study, we ensure a minimum data quality [74]. Regional data may not be representative of national data because of regional differences in risk factor prevalence and access to early detection services, and thus may not be generalisable to the whole country. Some registries cover only relatively small national populations (e.g. Malta and Iceland), which can cause random fluctuations in the number of cases (Table 1) and in incidence rates. Interpretation of and comparison with such data should be done with caution. Moreover, some registries seem to have faced temporary problems with the completeness of the registry; e.g. in Bulgaria there seemed to be under-registration before 1998 compared with later years. In addition, high percentages of death-certificate-only cases and a low proportion of morphologically verified cases in central and eastern Europe might have reduced data quality [3]. Differences in tumour classification practices in the past and across countries might have influenced incidence rates of cancers of the colon/rectum and the corpus uteri/cervix.

4. Conclusion

Increasing trends in incidence of the most common cancers in Europe are of concern, in particular those

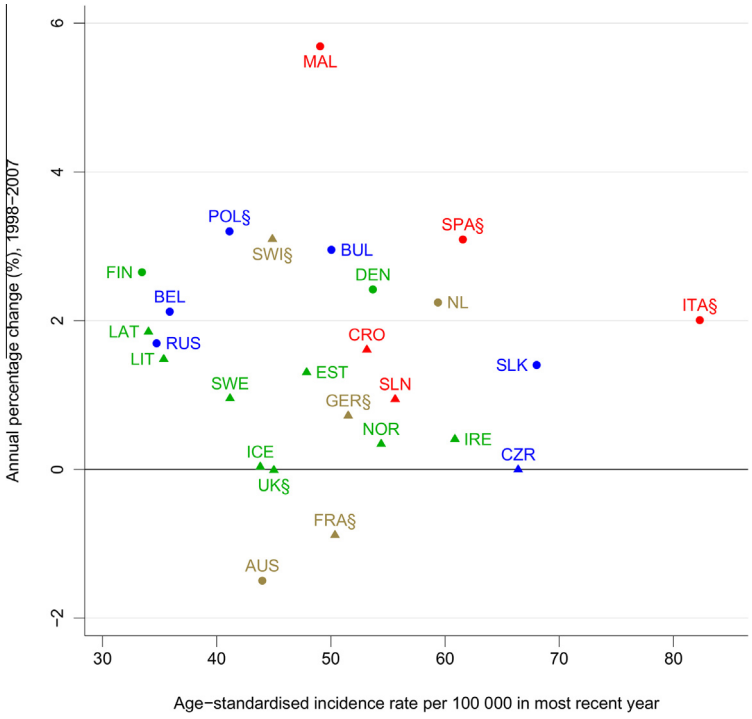

Fig. 11. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of colon cancer in *males*. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

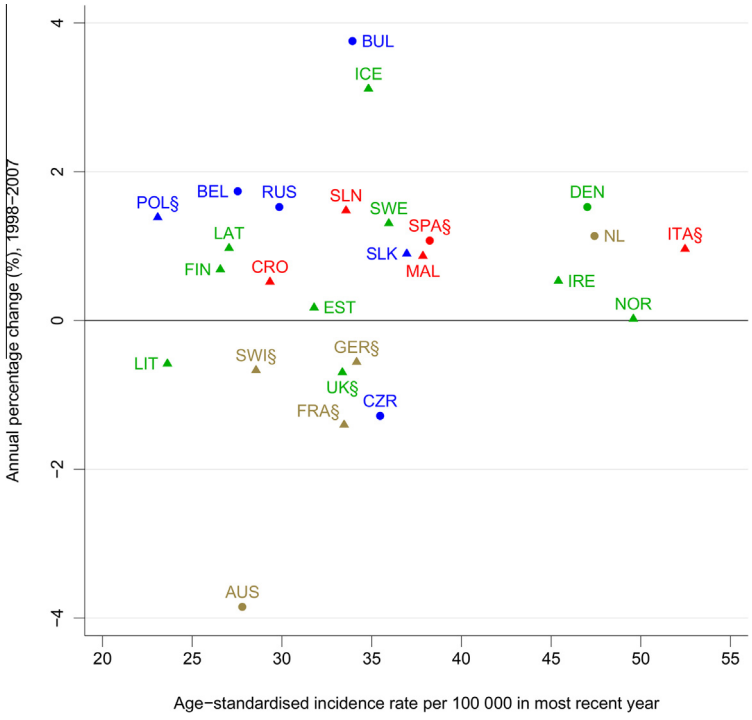

Fig. 12. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of colon cancer in *females*. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

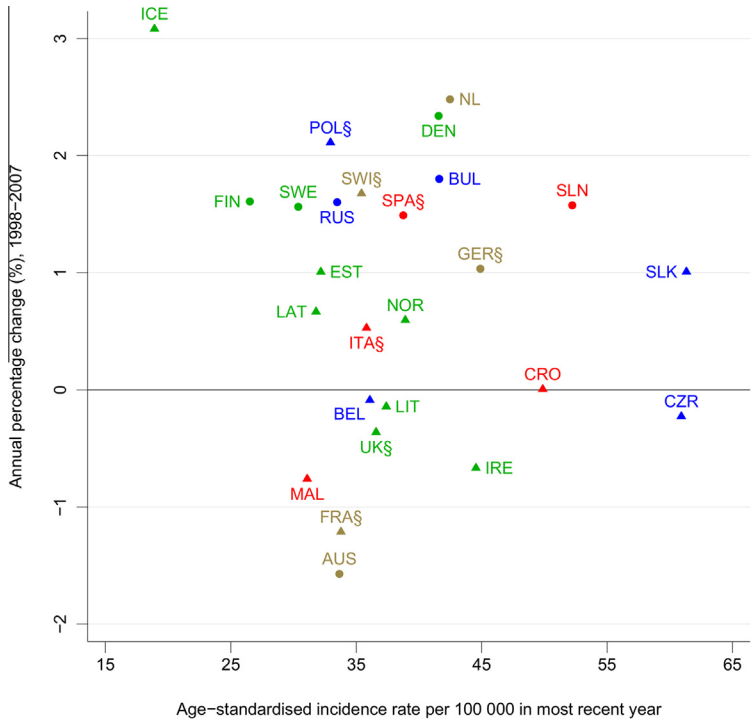

Fig. 13. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of rectal cancer in *males*. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

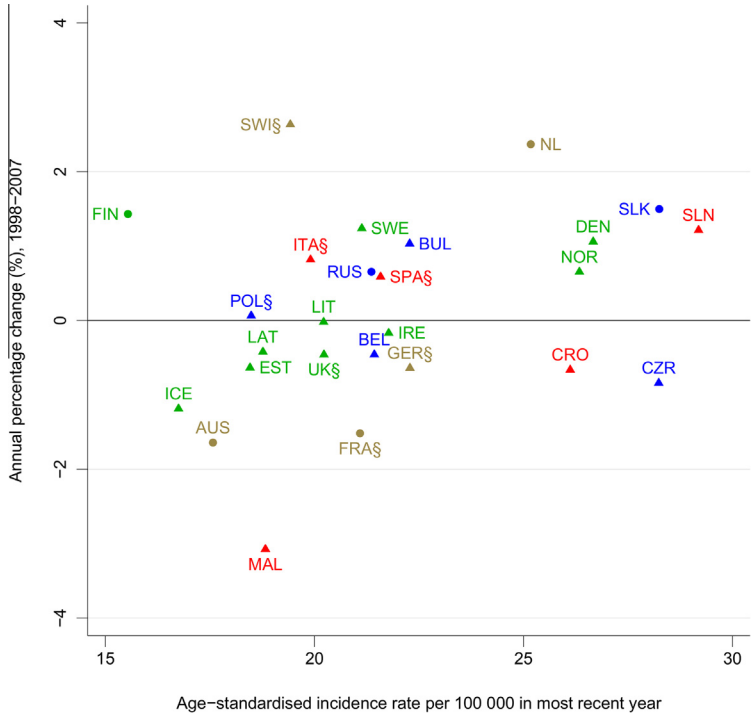

Fig. 14. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of rectal cancer in *females*. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

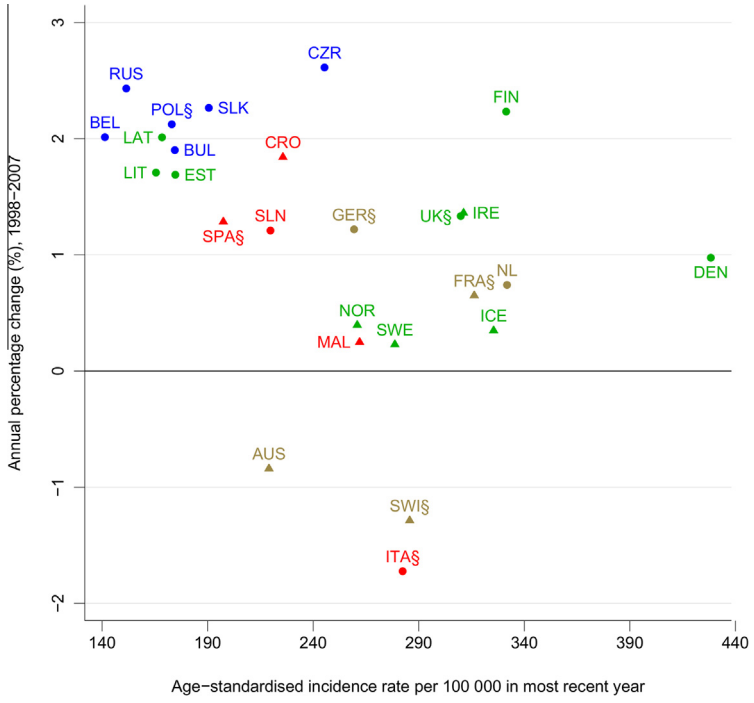

Fig. 15. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of postmenopausal breast cancer. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

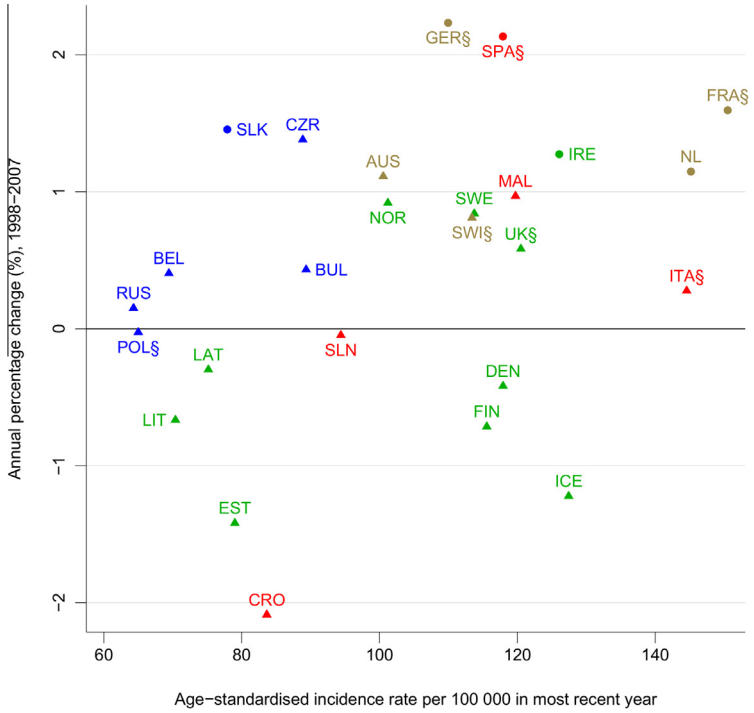

Fig. 16. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of premenopausal breast cancer. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

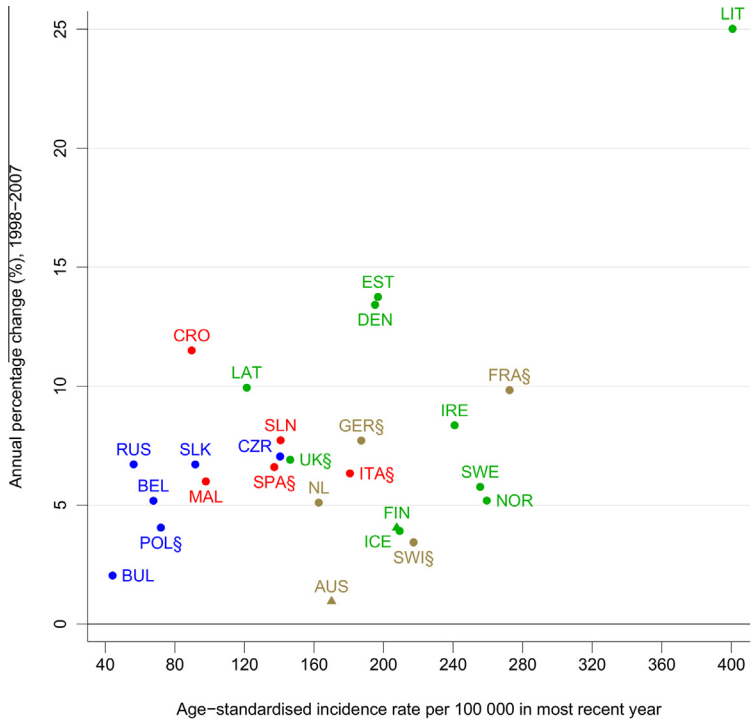

Fig. 17. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of prostate cancer. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

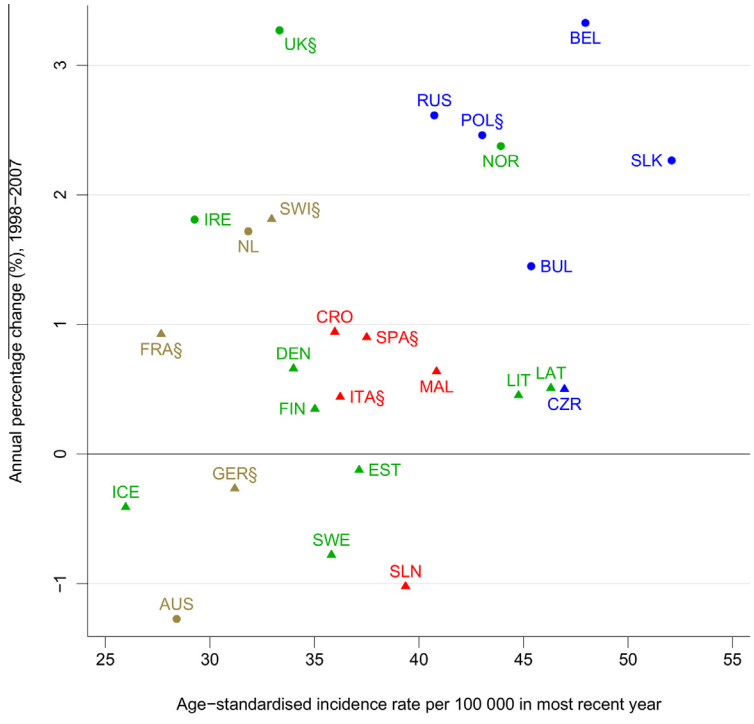

Fig. 18. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of corpus uteri cancer. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

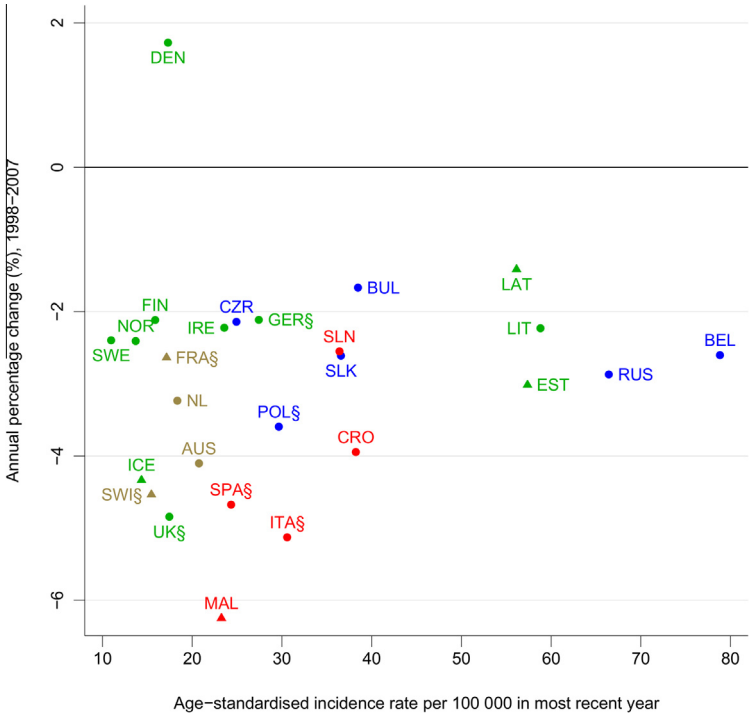

Fig. 19. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of stomach cancer in *males*. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

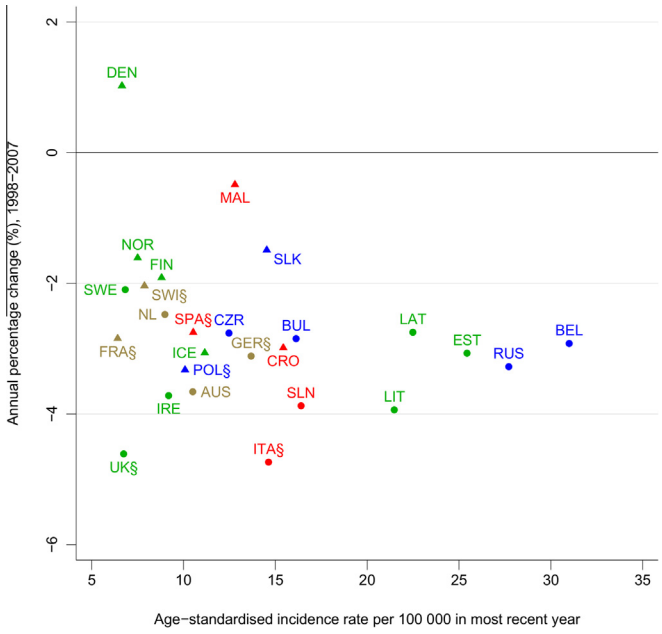

Fig. 20. Average annual percentage change (AAPC) between 1998 and 2007 and age-standardised incidence rates (ASIR) of the most recent year of stomach cancer in *females*. §Regional registries. Dots indicate statistically significant AAPC ($p \leqslant 0.05$); triangles indicate non-significant AAPC; green: northern Europe; red: southern Europe; blue: central–eastern Europe; brown: western Europe.

Table 2
Trends and prevalence of lifestyle-related and reproductive risk factors and the use of secondary prevention measures in Europe and their impact on cancer incidence of the cancer sites included in this study.

Risk factors	Cancer sites associated with risk factor and direction of association/ incidence (+ increasing; − decreasing)*	Trends and prevalence (of use) of risk factors in Europe
Alcohol	*Colorectum* (+) [49,50], *breast* (++) [22,23]	Alcohol consumption has gradually decreased in many European countries, but risen in some northern European countries [51]
Smoking	*Colorectum* (+) [52], *breast* (+) [53], *stomach* (*cardia*) (++) [36]	Prevalence of daily smokers amongst adults decreased, except in females in southern and eastern Europe [4]
Diet	*Colorectum* (+): high consumption of red and processed meat [49,50], low fibre intake [49,50] *Colorectum* (−): diet high in fibre (− −), high intake of fresh fruits and vegetables (−) [49,50] *Stomach* (++): high salt intake [36] *Stomach* (−): high fruit and vegetable consumption (−) [36], high vitamin C intake (−) [36]	Fruit and vegetable consumption and availability varied greatly between countries and is highest (but decreasing) in southern Europe [4,51] Salt intake in Europe is dominated by sodium added in manufactured foods [54]; consumption seems to decrease in most parts of Europe [54,55]
Physical inactivity	*Colorectum* (++) [49,50] *Colorectum* (−): leisure time physical exercise (− −) [19] *Breast* (−): physical activity (− −) [24]	Levels of physical activity vary greatly across Europe and have been highest in the Netherlands and lowest in Sweden [4]; based on several available datasets, generally the trend is stable [56] or increasing [57,58] There is evidence that physical activity decreased among children in recent years [51]
Obesity	*Colorectum* (++) [49,50], *breast* (*postmenopausal*) (++) [10,20,21], *corpus uteri* (+++) [49]	Prevalence of overweight and obesity continued to increase across all European countries [1,4]
Reproductive risk factors	*Breast* (++): later age at first childbirth, fewer children, higher proportion of nulliparous women [21,59]; hormone replacement therapy (HRT) [60–62] *Breast* (−): breastfeeding (− −) [25,26] *Corpus uteri* (++): use of HRT, sequential oral contraceptives, nulliparity [63]	Age at first birth continued to increase [64] Breastfeeding increased in some parts of Europe [65] HRT use decreased [61,62,66]
Infections	*Stomach* (*non-cardia*) (++): *Helicobacter pylori* (*H. pylori*) infection [36,37]	Decreasing *H. pylori* infection rate in general and in upcoming generations [38,67]
Other exogenous factors	*Stomach* (+): poor sanitary conditions [37] *Stomach* (−): better methods of preserving food [36]	
Secondary prevention measures	*Colorectum:* During colorectal cancer screening (faecal occult blood test, flexible sigmoidoscopy and colonoscopy), usually done at ages 45–74 years at both 1- and 2-year intervals, precancerous polyps (−) and early-stage cancers (+) can be detected and removed is [18] *Breast:* mammography screening in women aged 50–69 years (detection of slow-growing and early-stage tumours) (+) [17,42,43] *Prostate:* prostate-specific antigen (PSA) testing and consequent biopsy in asymptomatic men and in men with lower urinary tract symptoms (++) [27,41]	Colorectum: Screening is unlikely to have affected the current trends in incidence much yet (low screening coverage; organised population-based screening often only regionally; opportunistic screening) [68]; different screening methods may have different test sensitivities [69,70] Breast: organised or opportunistic screening performed in many European countries [17]; overdiagnosis constitutes a major concern in terms of harms of screening [42,43] Prostate: Few population-based screening programmes; opportunistic screening (case finding) much more common [18,71]; estimates of overdiagnosis up to 42% [41]
Other diagnostic and therapeutic measures	*Breast:* diagnostic activities outside of screening (+), e.g. increasing availability and awareness of genetic counselling in women below age 50 [72] *Corpus uteri:* hysterectomy (−)	Corpus uteri: Possible underestimation of incidence due to increasing hysterectomy rates [35,73]

* risk factors were rated according to probable (+/−) or convincing (++/− −) evidence of the association with the (incidence of) corresponding cancer sites.

at younger ages, as observed for colorectal cancer in some central and eastern European countries, where incidence is high and still continues to increase. Although incidence rates have decreased for some cancers in some countries, e.g. corpus uteri cancer in western Europe, the absolute number of cases remained relatively stable (or even increased) during the study period due to ageing of the population (Table 1). In the past 20 years, the combined effect of increasing risks and ageing has led to a strong increase in the absolute numbers of cases of the most common cancer sites. But there is also good news. The rise in incidence of prostate and colorectal cancer seems to have come to a halt in some countries like Finland, France and Austria, possibly indicating that a plateau has been reached or, in the case of prostate cancer, reductions in the use of the PSA test. Furthermore, stomach cancer incidence continues to decrease, also in countries with a historically low incidence.

A large proportion of the studied cancers are potentially avoidable [39], and primary cancer prevention has achieved some important successes in the past. Today it is more important than ever before, with smoking being the most important modifiable cause of cancer and target for preventive measures [4]. Increasing tobacco prices through taxation and increasing awareness seemed to be highly effective in reducing the smoking prevalence, which has declined in most European countries in the past decades. As, subsequently, smoking-related cancer rates have started to decrease [74], alcohol consumption, excess weight and physical inactivity have become the next important candidates for future prevention efforts. Long-term preventive strategies and policies should be directed into promoting

Appendix Table 1
Average annual percentage change (AAPC) and 95% confidence interval (CI) for colon cancer incidence by sex and age group during 1998–2007.

Country	AAPC (95% CI) for colon cancer incidence					
	Males			Females		
	35–74 years	35–64 years	65–74 years	35–74 years	35–64 years	65–74 years
Central and eastern Europe						
Belarus	2.1* (1.0, 3.3)	0.9 (−0.1, 1.8)	4.1* (2.4, 5.9)	1.7* (1.2, 2.3)	0.9* (0.2, 1.7)	2.3* (1.4, 3.3)
Bulgaria	3.0* (2.4, 3.5)	2.8* (1.9, 3.7)	4.2* (2.8, 5.6)	3.8* (3.0, 4.5)	4.3* (3.5, 5.0)	3.8* (2.6, 4.9)
Czech Republic	−0.0 (−0.8, 0.8)	0.5 (−1.5, 2.6)	−0.2 (−1.6, 1.3)	−1.3* (−2.4, −0.1)	−0.2 (−1.6, 1.2)	−1.1 (−2.7, 0.6)
Poland§	3.2* (0.4, 6.1)	3.4* (1.2, 5.7)	3.7 (−0.2, 7.7)	1.4 (−1.5, 4.3)	1.3 (−2.4, 5.2)	2.1 (−1.8, 6.2)
Russian Federation	1.7* (1.3, 2.1)	0.7* (0.2, 1.1)	2.2* (1.7, 2.7)	1.5* (1.3, 1.8)	0.7* (0.1, 1.3)	2.2* (1.9, 2.6)
Slovakia	1.4* (0.4, 2.5)	1.6* (0.2, 2.9)	2.4* (0.5, 4.4)	0.9 (−0.5, 2.3)	0.9 (−0.4, 2.2)	1.8 (−0.3, 4.0)
Northern Europe						
Denmark	2.4* (1.2, 3.6)	2.5* (0.4, 4.6)	1.9* (0.9, 2.9)	1.5* (0.5, 2.6)	2.0* (0.1, 3.9)	1.2* (0.3, 2.1)
Estonia	1.3 (−1.4, 4.1)	1.2 (−2.7, 5.3)	0.8 (−2.1, 3.8)	0.2 (−1.6, 2.0)	0.2 (−2.1, 2.6)	−0.1 (−3.2, 3.2)
Finland	2.7* (1.4, 3.9)	3.2* (1.4, 5.0)	1.6 (−0.5, 3.6)	0.7 (−0.2, 1.6)	2.4* (0.9, 3.9)	−0.9 (−2.3, 0.6)
Iceland	0.0 (−4.2, 4.5)	4.8 (−2.2, 12.4)	−2.4 (−8.7, 4.3)	3.1 (−3.1, 9.7)	5.7 (−1.1, 13.0)	1.7 (−7.2, 11.4)
Ireland	0.4 (−1.3, 2.1)	1.0 (−1.6, 3.6)	0.6 (−0.8, 2.1)	0.5 (−0.8, 1.9)	0.8 (−1.2, 2.8)	1.4 (−0.7, 3.6)
Latvia	1.9 (−0.1, 3.8)	−0.4 (−3.1, 2.4)	2.6* (0.2, 5.2)	1.0 (−0.9, 2.8)	1.1 (−2.4, 4.8)	−0.4 (−3.2, 2.6)
Lithuania	1.5 (−0.6, 3.6)	−0.3 (−2.8, 2.2)	3.1* (1.0, 5.3)	−0.6 (−2.4, 1.3)	−1.6 (−4.1, 1.0)	0.6 (−2.2, 3.5)
Norway	0.3 (−0.6, 1.3)	1.3 (−0.4, 3.0)	0.9 (−0.5, 2.3)	0.0 (−0.7, 0.8)	−0.1 (−1.2, 1.0)	1.7* (0.5, 3.0)
Sweden	1.0 (−0.0, 2.0)	0.4 (−0.8, 1.7)	1.4* (0.4, 2.5)	1.3 (−0.2, 2.8)	1.6 (−0.5, 3.8)	1.7* (0.7, 2.7)
United Kingdom§	−0.0 (−1.0, 1.0)	0.1 (−0.6, 0.9)	0.2 (−0.9, 1.4)	−0.7 (−1.4, 0.0)	−0.1 (−1.2, 1.0)	−0.4 (−1.1, 0.3)
Southern Europe						
Croatia	1.6 (−0.3, 3.5)	1.6 (−0.5, 3.7)	0.7 (−1.3, 2.7)	0.5 (−1.7, 2.8)	0.4 (−2.5, 3.4)	0.2 (−1.5, 2.0)
Italy§	2.0* (0.2, 3.8)	2.0* (0.2, 4.0)	1.9 (−0.3, 4.2)	1.0 (−1.1, 3.1)	0.8 (−1.7, 3.2)	1.4 (−0.8, 3.6)
Malta	5.7* (1.8, 9.7)	8.5* (0.1, 17.6)	3.0 (−5.1, 11.7)	0.9 (−5.1, 7.2)	1.4 (−7.6, 11.4)	0.7 (−7.3, 9.4)
Slovenia	0.9 (−0.3, 2.2)	−0.5 (−2.5, 1.5)	1.6 (−0.1, 3.2)	1.5 (−0.3, 3.3)	0.3 (−2.5, 3.2)	3.2* (0.8, 5.7)
Spain§	3.1* (2.0, 4.2)	2.6* (0.4, 4.9)	5.3* (3.4, 7.2)	1.1* (0.1, 2.1)	0.3 (−1.3, 1.9)	3.1* (1.4, 4.9)
Western Europe						
Austria	−1.5* (−2.3, −0.7)	−1.1 (−3.0, 0.7)	−2.6* (−3.7, −1.4)	−3.8* (−6.7, −0.9)	−1.4* (−2.5, −0.2)	−4.7* (−6.9, −2.5)
France§	−0.9 (−1.8, 0.0)	0.3 (−1.5, 2.2)	−1.1* (−1.9, −0.4)	−1.4 (−3.1, 0.3)	−0.4 (−2.6, 1.8)	−1.2 (−3.2, 0.9)
Germany§	0.7 (−0.3, 1.7)	−1.3 (−2.7, 0.2)	−0.7 (−2.0, 0.6)	−0.6 (−1.7, 0.6)	−0.1 (−1.0, 0.7)	−2.0* (−2.9, −1.0)
Switzerland§	3.1 (−0.4, 6.7)	2.5 (−2.5, 7.7)	3.3 (−0.3, 7.0)	−0.7 (−4.4, 3.3)	2.0 (−2.1, 6.3)	−3.2 (−8.3, 2.2)
The Netherlands	2.2* (1.5, 3.0)	2.6* (1.8, 3.3)	1.7* (1.0, 2.4)	1.1* (0.8, 1.5)	1.4* (0.4, 2.4)	1.5* (0.7, 2.3)

§ Regional registries: France (Doubs, Herault, Isere, Haut-Rhin, Somme, Tarn); Germany (Brandenburg, Hamburg, Saxony, Mecklenburg, North Rhine-Westphalia, Saarland); Poland (Kielce, Cracow); Italy (Modena, Parma, Ragusa, Romagna, Torino, Varese); Spain (Granada, Murcia, Navarra, Tarragona); Switzerland (Geneva, St. Gall-Appenzell); United Kingdom (England and Scotland).
* $p \leqslant 0.05$.

healthy habits, e.g. by reducing the price of fruits and vegetables or by increasing incentives for physical activity [40]. Cancer registries will contribute to monitoring the impact of cancer prevention programmes, by providing early signs of changes in risk factors and hence cancer incidence through birth cohort analysis in particular at middle age.

Secondary prevention through earlier diagnosis has improved survival, but it has also increased the diagnosis of slow-growing tumours that may not necessarily need treatment [41–43]. In order to reach an appropriate balance between harms (including overdiagnosis of cancers or pre-cancers) and intended benefits (such as mortality reductions) of screening programmes, they should be implemented following best practices and up-to-date scientific evidence [18]. The same principles of evidence-based working models and careful evaluation should be adopted also in other forms of early diagnosis in the health services.

Real progress against cancer, including successes of primary and secondary prevention, should, however, be assessed in the light of both incidence and mortality trends and wherever possible, including information on cancer survival [44]. While cancer mortality in Europe has continued to decline since decades, survival has increased for most cancer sites due to better diagnoses and treatment [12,45,46]. But at the same time, as found in this study, the (largely avoidable) burden of cancer in Europe is still rising [5]. Cancer diagnosis is related with significant morbidity and quality of life lost for the patient and society [47], hence preventing occurrence of disease should remain the main strategy in the war against cancer. Delays between the change or emergence of risk factors and their identification and subsequent counteraction with preventive measures are some of the most challenging aspects of cancer surveillance and control. Current trends in major cancers in Europe represent steps backwards on the road towards successful cancer control [48].

Appendix Table 2
Average annual percentage change (AAPC) and 95% confidence interval (CI) for rectal cancer incidence by sex and age group during 1998–2007.

Country	AAPC (95% CI) for rectal cancer incidence					
	Males			Females		
	35–74 years	35–64 years	65–74 years	35–74 years	35–64 years	65–74 years
Central and eastern Europe						
Belarus	−0.1 (−1.3, 1.2)	1.8 (−1.9, 5.6)	−0.7 (−3.9, 2.7)	−0.5 (−1.5, 0.6)	0.3 (−0.7, 1.4)	1.1 (−0.4, 2.6)
Bulgaria	1.8* (0.6, 3.0)	3.0* (1.3, 4.7)	1.7* (0.4, 3.0)	1.0 (−0.2, 2.2)	1.6 (−0.2, 3.4)	0.8 (−1.5, 3.1)
Czech Republic	−0.2 (−1.2, 0.8)	1.0 (−0.0, 2.0)	−0.2 (−1.1, 0.7)	−0.8 (−1.8, 0.2)	−1.1 (−2.6, 0.4)	−0.5 (−2.2, 1.2)
Poland§	2.1 (−0.7, 5.0)	3.9* (0.2, 7.7)	0.6 (−2.3, 3.6)	0.1 (−2.5, 2.7)	0.9 (−2.4, 4.3)	0.3 (−2.9, 3.7)
Russian Federation	1.6* (1.3, 1.9)	1.2* (0.6, 1.8)	0.3 (−0.3, 1.0)	0.7* (0.3, 1.0)	1.5* (0.9, 2.0)	1.0* (0.5, 1.4)
Slovakia	1.0 (−0.5, 2.5)	1.2 (−0.5, 3.0)	1.8* (0.2, 3.4)	1.5* (0.2, 2.8)	1.3 (−1.4, 4.0)	2.0* (0.4, 3.6)
Northern Europe						
Denmark	2.3* (1.4, 3.3)	2.7* (1.4, 4.0)	2.7* (0.6, 4.9)	1.1 (−0.8, 2.9)	1.5* (0.4, 2.6)	−0.8 (−2.9, 1.3)
Estonia	1.0 (−1.9, 4.0)	0.7 (−3.5, 5.1)	−1.2 (−6.7, 4.6)	−0.6 (−4.2, 3.0)	0.8 (−2.0, 3.7)	−0.3 (−5.9, 5.7)
Finland	1.6* (0.3, 2.9)	2.5* (0.5, 4.6)	2.4* (0.6, 4.2)	1.4* (0.2, 2.7)	0.1 (−1.6, 1.8)	0.5 (−1.2, 2.2)
Iceland	3.1 (−5.8, 12.8)	6.7 (−6.7, 22.1)	0.1 (−13.8, 16.1)	−1.2 (−9.4, 7.7)	−0.2 (−6.6, 6.5)	−2.2 (−10.4, 6.8)
Ireland	−0.7 (−2.2, 0.9)	0.3 (−0.9, 1.5)	1.2 (−2.1, 4.5)	−0.2 (−3.2, 2.9)	−1.1 (−3.3, 1.2)	−0.8 (−4.2, 2.7)
Latvia	0.7 (−2.0, 3.4)	−1.7 (−3.4, 0.1)	−0.3 (−3.3, 2.9)	−0.4 (−2.8, 2.0)	1.1 (−1.3, 3.5)	−1.1 (−4.3, 2.2)
Lithuania	−0.1 (−1.2, 0.9)	0.0 (−2.4, 2.5)	−0.2 (−2.5, 2.2)	−0.0 (−0.9, 0.9)	−0.3 (−1.5, 1.0)	0.3 (−1.8, 2.4)
Norway	0.6 (−0.5, 1.7)	1.3* (0.3, 2.4)	0.7 (−0.4, 1.8)	0.7 (−0.0, 1.3)	1.1 (−0.9, 3.1)	2.0* (0.5, 3.6)
Sweden	1.6* (0.9, 2.2)	2.9* (1.6, 4.2)	3.6* (1.2, 6.0)	1.2 (−0.2, 2.7)	0.4 (−0.5, 1.3)	−0.6 (−2.4, 1.2)
United Kingdom§	−0.4 (−1.2, 0.5)	−0.0 (−0.6, 0.5)	1.1 (−0.3, 2.6)	−0.5 (−1.4, 0.5)	−0.2 (−1.6, 1.2)	−1.2 (−2.7, 0.3)
Southern Europe						
Croatia	0.0 (−1.6, 1.6)	−0.2 (−2.4, 1.9)	−1.5 (−4.4, 1.4)	−0.7 (−3.0, 1.7)	−0.7 (−2.0, 0.6)	−0.3 (−2.6, 2.2)
Italy§	0.5 (−0.7, 1.8)	1.1* (0.0, 2.3)	0.3 (−1.5, 2.1)	0.8 (−0.9, 2.6)	0.0 (−1.6, 1.7)	1.5 (−1.6, 4.7)
Malta	−0.8 (−4.7, 3.4)	−1.9 (−6.2, 2.5)	−1.1 (−8.6, 7.1)	−3.1 (−7.0, 1.0)	−0.2 (−6.4, 6.4)	−2.7 (−9.9, 5.1)
Slovenia	1.6* (0.1, 3.0)	1.0 (−0.5, 2.5)	1.7 (−2.4, 6.0)	1.2 (−1.3, 3.8)	1.7 (−2.0, 5.4)	1.3 (−1.3, 4.0)
Spain§	1.5* (0.4, 2.6)	1.7 (−0.5, 3.9)	1.1 (−2.3, 4.6)	0.6 (−2.2, 3.5)	2.9* (1.2, 4.7)	1.3 (−1.8, 4.5)
Western Europe						
Austria	−1.6* (−2.4, −0.7)	−1.4* (−2.6, −0.1)	−0.6 (−2.6, 1.4)	−1.6* (−2.9, −0.4)	−2.1* (−3.1, −1.0)	−2.2* (−4.0, −0.4)
France§	−1.2 (−2.9, 0.5)	−0.3 (−2.0, 1.4)	0.4 (−2.0, 2.8)	−1.5* (−2.8, −0.2)	−1.3 (−3.5, 1.0)	−2.8* (−4.8, −0.7)
Germany§	1.0* (0.1, 1.9)	−0.7 (−1.5, 0.2)	−0.7 (−1.9, 0.6)	−0.6 (−2.4, 1.1)	0.3 (−0.9, 1.4)	−1.0* (−1.9, −0.1)
Switzerland§	1.7 (−2.1, 5.6)	0.9 (−4.1, 6.2)	2.6 (−1.9, 7.4)	2.6 (−2.3, 7.8)	2.6 (−2.0, 7.3)	2.3 (−1.7, 6.4)
The Netherlands	2.5* (1.8, 3.2)	2.8* (2.3, 3.2)	3.5* (2.3, 4.6)	2.4* (1.4, 3.3)	1.9* (0.9, 3.0)	1.6* (0.2, 3.0)

§ Regional registries: France (Doubs, Herault, Isere, Haut-Rhin, Somme, Tarn); Germany (Brandenburg, Hamburg, Saxony, Mecklenburg, North Rhine-Westphalia, Saarland); Poland (Kielce, Cracow); Italy (Modena, Parma, Ragusa, Romagna, Torino, Varese); Spain (Granada, Murcia, Navarra, Tarragona); Switzerland (Geneva, St. Gall-Appenzell); United Kingdom (England and Scotland).
* $p \leqslant 0.05$.

Authors' contributions

M.A. contributed to study design, data analysis, data interpretation and wrote the first draft of the manuscript. H.K.K., J.W.C., G.B., A.A., J.F., A.R., D.F. and I.S. contributed to data interpretation, writing and reviewing the manuscript. I.S. additionally contributed to study design and supervised the study.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Conflict of interest statement

None declared.

Acknowledgements

M.A. is supported by the World Cancer Research Fund, Grant number SG 2012/619. I.S. is funded through the Marie Curie Action Intra-European Fellowship, contract number 302050. EUROCOURSE (EUROpe against Cancer: Optimisation of the Use of Registries for Scientific Excellence in research), an EC 7th Framework Programme of DG Research and Innovation under Grant agreement number LSSH-CT-2008-219453 provided logistic support and time of J.W.C. through Workpackage 8. We thank Joannie Lortet-Tieulent and Elisenda Renteria for their assistance with the data analysis and the graphs.

Appendix A.

Appendix Table 3
Average annual percentage change (AAPC) and 95% confidence interval (CI) for stomach cancer incidence by sex and age group during 1998–2007.

Country	AAPC (95% CI) for stomach cancer incidence					
	Males			Females		
	35–74 years	35–64 years	65–74 years	35–74 years	35–64 years	65–74 years
Central and eastern Europe						
Belarus	−2.6* (−3.2, −2.0)	−2.4* (−3.2, −1.7)	−2.9* (−4.0, −1.7)	−2.9* (−3.8, −2.0)	−2.3* (−3.2, −1.4)	−2.4* (−3.7, −1.1)
Bulgaria	−1.7* (−2.5, −0.8)	−0.9 (−2.2, 0.5)	−2.1* (−3.8, −0.4)	−2.8* (−4.1, −1.6)	−1.5* (−2.2, −0.8)	−3.0* (−4.8, −1.1)
Czech Republic	−2.1* (−3.4, −0.9)	−0.9 (−2.5, 0.7)	−0.7 (−2.6, 1.2)	−2.8* (−4.1, −1.4)	−2.7* (−4.7, −0.7)	−3.8* (−6.6, −0.9)
Poland§	−3.6* (−5.5, −1.6)	−3.1 (−6.7, 0.6)	−1.2 (−7.2, 5.3)	−3.3 (−7.4, 0.9)	−3.5* (−5.5, −1.4)	−4.4* (−8.1, −0.6)
Russian Federation	−2.9* (−3.1, −2.6)	−3.3* (−3.7, −2.9)	−3.5* (−3.9, −3.0)	−3.3* (−3.6, −2.9)	−2.8* (−3.2, −2.4)	−3.1* (−3.7, −2.5)
Slovakia	−2.6* (−4.1, −1.1)	−1.6 (−3.4, 0.2)	1.6 (−0.5, 3.8)	−1.5 (−3.1, 0.1)	−2.7* (−4.2, −1.2)	−3.6* (−5.8, −1.3)
Northern Europe						
Denmark	1.7* (0.4, 3.0)	2.2* (0.7, 3.6)	1.3 (−3.0, 5.8)	1.0 (−2.5, 4.6)	0.7 (−1.1, 2.7)	0.7 (−3.2, 4.8)
Estonia	−3.0 (−6.6, 0.7)	−3.8* (−6.1, −1.4)	−3.7* (−6.5, −0.7)	−3.1* (−5.5, −0.5)	−3.7* (−7.2, −0.0)	−2.8 (−5.5, 0.1)
Finland	−2.1* (−3.7, −0.5)	−0.6 (−2.6, 1.3)	0.4 (−1.7, 2.6)	−1.9 (−3.9, 0.1)	−4.2* (−6.6, −1.8)	−4.3* (−6.3, −2.1)
Iceland	−4.3 (−12.3, 4.3)	0.7 (−8.1, 10.3)	−3.2 (−15.7, 11.1)	−3.1 (−14.3, 9.7)	−6.7 (−17.0, 5.0)	2.0 (−11.9, 18.0)
Ireland	−2.2* (−3.3, −1.1)	−2.5* (−4.5, −0.6)	−4.5* (−7.6, −1.4)	−3.7* (−5.1, −2.3)	−0.9 (−3.6, 1.8)	−2.9* (−5.2, −0.6)
Latvia	−1.4 (−3.0, 0.2)	−2.5 (−5.1, 0.1)	−3.6 (−7.5, 0.3)	−2.8* (−4.3, −1.1)	−0.8 (−2.3, 0.8)	−2.2 (−4.5, 0.0)
Lithuania	−2.2* (−3.6, −0.8)	−1.7* (−3.4, −0.1)	−3.6* (−6.1, −1.1)	−3.9* (−5.0, −2.9)	−2.8* (−4.8, −0.7)	−4.1* (−5.9, −2.3)
Norway	−2.4* (−3.4, −1.4)	−0.3 (−1.7, 1.0)	1.0 (−1.9, 4.1)	−1.6 (−3.8, 0.7)	−4.1* (−6.3, −1.9)	−2.4 (−6.5, 1.9)
Sweden	−2.4* (−3.5, −1.3)	−1.2 (−3.1, 0.8)	−1.5 (−3.5, 0.6)	−2.1* (−3.9, −0.3)	−3.4* (−5.6, −1.2)	−0.6 (−3.8, 2.6)
United Kingdom§	−4.8* (−5.6, −4.0)	−4.6* (−5.7, −3.4)	−3.3* (−4.5, −2.2)	−4.6* (−5.4, −3.8)	−4.8* (−5.6, −4.0)	−4.7* (−5.4, −4.0)
Southern Europe						
Croatia	−3.9* (−5.7, −2.1)	−3.7* (−6.3, −1.1)	−4.7* (−8.3, −1.0)	−3.0 (−7.0, 1.2)	−5.1* (−6.5, −3.6)	−3.8* (−5.6, −1.9)
Italy§	−5.1* (−6.7, −3.5)	−5.4* (−6.6, −4.3)	−5.9* (−7.4, −4.3)	−4.7* (−5.8, −3.7)	−4.9* (−7.4, −2.4)	−3.7* (−4.8, −2.5)
Malta	−6.2 (−12.6, 0.6)	−8.3 (−16.3, 0.5)	3.6 (−9.2, 18.1)	−0.5 (−9.2, 9.1)	−6.1 (−15.2, 4.0)	−2.6 (−14.1, 10.5)
Slovenia	−2.6* (−3.5, −1.5)	−2.4* (−4.7, −0.1)	−2.1 (−5.9, 1.9)	−3.9* (−5.9, −1.8)	−3.3* (−5.3, −1.3)	−4.6* (−7.1, −2.1)
Spain§	−4.7* (−6.1, −3.2)	−4.4* (−6.8, −1.9)	0.6 (−3.3, 4.6)	−2.8 (−6.1, 0.7)	−3.6* (−5.1, −2.0)	−4.5 (−9.3, 0.6)
Western Europe						
Austria	−4.1* (−5.9, −2.2)	−2.5* (−3.3, −1.6)	−1.8* (−3.2, −0.4)	−3.7* (−4.9, −2.4)	−5.1* (−6.2, −3.9)	−4.5* (−6.1, −2.9)
France§	−2.6 (−5.5, 0.3)	−1.0 (−3.7, 1.7)	−1.2 (−5.2, 3.0)	−2.8 (−5.7, 0.1)	−3.7 (−7.5, 0.3)	−2.9 (−8.0, 2.4)
Germany§	−2.1* (−2.7, −1.5)	−2.3* (−2.8, −1.8)	−2.9* (−4.1, −1.6)	−3.1* (−3.7, −2.5)	−4.5* (−5.3, −3.7)	−4.7* (−5.6, −3.8)
Switzerland§	−4.5 (−9.5, 0.7)	−4.4 (−11.9, 3.8)	4.3 (−6.1, 15.9)	−2.0 (−8.0, 4.3)	−5.9* (−11.0, −0.4)	−6.1 (−13.5, 1.8)
The Netherlands	−3.2* (−4.0, −2.5)	−3.0* (−4.0, −2.0)	−1.4 (−3.3, 0.4)	−2.5* (−4.0, −0.9)	−3.6* (−4.3, −3.0)	−3.0* (−4.5, −1.4)

§ Regional registries: France (Doubs, Herault, Isere, Haut-Rhin, Somme, Tarn); Germany (Brandenburg, Hamburg, Saxony, Mecklenburg, North Rhine-Westphalia, Saarland); Poland (Kielce, Cracow); Italy (Modena, Parma, Ragusa, Romagna, Torino, Varese); Spain (Granada, Murcia, Navarra, Tarragona); Switzerland (Geneva, St. Gall-Appenzell); United Kingdom (England and Scotland).
* $p \leqslant 0.05$.

Appendix Table 4
Average annual percentage change (AAPC) and 95% confidence interval (CI) for corpus uteri, breast and prostate cancer incidence by age group during 1998–2007.

Country	AAPC (95% CI) for incidence							
	Corpus uteri cancer			Breast cancer		Prostate cancer		
	35–74 years	35–64 years	65–74 years	35–49 years	50–74 years	35–74 years	35–64 years	65–74 years
Central and eastern Europe								
Belarus	3.3* (2.2, 4.5)	3.3* (2.4, 4.2)	3.7* (1.6, 6.0)	0.4 (−1.4, 2.2)	2.0* (0.8, 3.3)	5.2* (3.8, 6.5)	4.0* (2.5, 5.6)	6.5* (4.6, 8.5)
Bulgaria	1.4* (0.5, 2.4)	0.8 (−0.5, 2.2)	3.0* (2.2, 3.9)	0.4 (−0.5, 1.4)	1.9* (0.6, 3.2)	2.0* (0.4, 3.8)	2.1 (−2.3, 6.6)	2.5* (0.6, 4.4)
Czech Republic	0.5 (−0.2, 1.3)	1.6* (0.7, 2.5)	−0.3 (−1.3, 0.6)	1.4 (−0.0, 2.8)	2.6* (1.1, 4.2)	7.0* (2.8, 11.5)	15.3* (12.8, 17.8)	4.5* (1.9, 7.3)
Poland§	2.5* (0.2, 4.8)	2.9* (0.8, 5.1)	2.1 (−1.3, 5.6)	−0.0 (−3.1, 3.2)	2.1* (1.1, 3.2)	4.1* (1.3, 6.9)	7.3* (3.9, 10.9)	3.3* (0.5, 6.2)
Russian Federation	2.6* (2.2, 3.0)	2.7* (1.9, 3.4)	2.7* (2.1, 3.4)	0.2 (−0.3, 0.6)	2.4* (2.0, 2.9)	6.7* (5.3, 8.1)	5.5* (3.8, 7.3)	6.7* (5.3, 8.0)
Slovakia	2.3* (1.2, 3.4)	2.8* (1.6, 4.1)	2.1* (0.4, 3.8)	1.5* (0.4, 2.5)	2.3* (1.4, 3.1)	6.7* (5.3, 8.2)	9.0* (3.7, 14.5)	6.1* (4.6, 7.7)
Northern Europe								
Denmark	0.7 (−0.4, 1.7)	1.0 (−0.5, 2.5)	0.3 (−0.7, 1.2)	−0.4 (−1.3, 0.5)	1.0* (0.4, 1.6)	13.4* (11.3, 15.6)	16.5* (14.4, 18.7)	11.1* (9.2, 13.0)
Estonia	−0.1 (−1.3, 1.1)	−1.4 (−2.9, 0.1)	1.9 (−1.2, 5.0)	−1.4 (−4.1, 1.4)	1.7* (0.0, 3.4)	13.7* (10.6, 17.0)	16.8* (13.6, 20.1)	11.7* (8.0, 15.5)
Finland	0.3 (−1.1, 1.8)	−0.4 (−3.0, 2.3)	0.9 (−1.1, 2.9)	−0.7 (−1.6, 0.2)	2.2* (1.6, 2.9)	4.1 (−0.0, 8.3)	7.9* (3.1, 13.0)	0.7 (−2.9, 4.5)
Iceland	−0.4 (−7.5, 7.2)	−0.8 (−9.8, 9.0)	1.0 (−6.0, 8.4)	−1.2 (−3.7, 1.3)	0.3 (−2.2, 2.9)	3.9* (1.5, 6.4)	6.6* (1.0, 12.6)	4.5* (2.0, 7.1)
Ireland	1.8* (0.3, 3.4)	2.3 (−0.4, 4.9)	1.7* (0.2, 3.3)	1.3* (0.1, 2.5)	1.4 (−0.4, 3.1)	8.4* (6.1, 10.7)	13.3* (10.4, 16.2)	5.7* (2.9, 8.6)
Latvia	0.5 (−0.8, 1.9)	−0.3 (−1.7, 1.1)	1.5 (−0.1, 3.2)	−0.3 (−2.1, 1.6)	2.0* (1.1, 3.0)	9.9* (7.5, 12.5)	11.6* (9.1, 14.0)	8.4* (7.3, 9.5)
Lithuania	0.5 (−1.0, 1.9)	−0.9 (−3.0, 1.3)	2.9* (0.8, 5.1)	−0.7 (−2.4, 1.1)	1.7* (0.2, 3.3)	25.0* (19.5, 30.8)	28.0* (19.3, 37.3)	22.2* (17.3, 27.4)
Norway	2.4* (1.1, 3.7)	2.1* (0.7, 3.5)	3.8* (2.1, 5.6)	0.9 (−0.1, 1.9)	0.4 (−0.9, 1.7)	5.2* (2.7, 7.7)	8.2* (5.5, 11.1)	4.5* (2.4, 6.7)
Sweden	−0.8 (−1.6, 0.1)	−1.9* (−3.0, −0.9)	1.2 (−0.0, 2.4)	0.8 (−0.2, 1.9)	0.2 (−0.8, 1.2)	5.8* (3.7, 7.9)	10.2* (8.3, 12.2)	2.8* (0.5, 5.2)
United Kingdom§	3.3* (2.4, 4.1)	3.1* (2.1, 4.2)	4.2* (3.4, 4.9)	0.6 (−0.1, 1.2)	1.3* (0.7, 2.0)	6.9* (4.8, 9.1)	10.0* (8.7, 11.4)	5.3* (3.7, 7.0)
Southern Europe								
Croatia	0.9 (−1.2, 3.1)	1.2 (−0.9, 3.3)	0.4 (−2.0, 2.8)	−2.1 (−6.0, 2.0)	1.8 (−0.7, 4.4)	11.5* (7.1, 16.1)	13.3* (7.4, 19.6)	8.2* (6.0, 10.4)
Italy§	0.4 (−0.7, 1.6)	0.8 (−2.1, 3.8)	1.1 (−1.2, 3.4)	0.3 (−0.4, 0.9)	−1.7* (−2.5, −0.9)	6.3* (4.6, 8.1)	7.9* (5.0, 11.0)	6.1* (1.1, 11.5)
Malta	0.6 (−1.9, 3.3)	0.9 (−2.5, 4.4)	−3.5 (−13.3, 7.3)	1.0 (−3.2, 5.3)	0.2 (−2.2, 2.8)	6.0* (2.3, 9.8)	10.8* (4.7, 17.3)	2.3 (−1.4, 6.2)
Slovenia	−1.0 (−2.4, 0.4)	−0.4 (−1.9, 1.1)	−1.5 (−3.3, 0.3)	−0.0 (−1.0, 0.9)	1.2* (0.3, 2.2)	7.7* (5.6, 9.9)	10.5* (7.7, 13.4)	5.5* (3.2, 7.8)
Spain§	0.9 (−0.4, 2.2)	0.9 (−0.9, 2.7)	1.9* (0.1, 3.7)	2.1* (0.9, 3.4)	1.3 (−0.2, 2.8)	6.6* (5.0, 8.2)	8.8* (6.5, 11.2)	7.8* (6.1, 9.4)
Western Europe								
Austria	−1.3* (−2.4, −0.1)	−1.5* (−2.8, −0.2)	−0.3 (−2.0, 1.4)	1.1 (−0.0, 2.3)	−0.8 (−2.4, 0.7)	1.0 (−1.6, 3.5)	2.6 (−0.7, 6.0)	−0.7 (−3.1, 1.6)
France§	0.9 (−0.5, 2.3)	0.1 (−2.1, 2.4)	3.1* (0.6, 5.7)	1.6* (0.2, 3.0)	0.7 (−0.1, 1.4)	9.8* (8.7, 10.9)	15.9* (13.9, 17.9)	7.5* (5.5, 9.5)
Germany§	−0.3 (−0.7, 0.1)	−1.5* (−2.3, −0.8)	−0.1 (−1.0, 0.8)	2.2* (0.1, 4.4)	1.2* (0.5, 2.0)	7.7* (5.6, 9.9)	6.1* (3.5, 8.8)	5.7* (3.7, 7.7)
Switzerland§	1.8 (−0.6, 4.3)	1.2 (−1.9, 4.4)	3.3 (−1.0, 7.8)	0.8 (−0.9, 2.5)	−1.3 (−2.8, 0.3)	3.4* (1.0, 5.9)	6.4* (3.8, 9.2)	0.9 (−1.7, 3.6)
The Netherlands	1.7* (0.6, 2.8)	1.4* (0.0, 2.7)	2.8* (1.5, 4.1)	1.1* (0.4, 1.9)	0.7* (0.1, 1.4)	5.1* (3.6, 6.6)	8.4* (6.8, 9.9)	2.9* (1.4, 4.4)

§ Regional registries: France (Doubs, Herault, Isere, Haut-Rhin, Somme, Tarn); Germany (Brandenburg, Hamburg, Saxony, Mecklenburg, North Rhine-Westphalia, Saarland); Poland (Kielce, Cracow); Italy (Modena, Parma, Ragusa, Romagna, Torino, Varese); Spain (Granada, Murcia, Navarra, Tarragona); Switzerland (Geneva, St. Gall-Appenzell); United Kingdom (England and Scotland).

* $p \leqslant 0.05$.

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