



Cervical cancer mortality in young women in Europe: patterns and trends

F. Levi^{a,*}, F. Lucchini^a, E. Negri^b, S. Franceschi^c, C. la Vecchia^{b,d}

^a*Registre Vaudois des Tumeurs and Unité d'Épidémiologie du Cancer, Institut Universitaire de Médecine Sociale et Préventive, CHUV-Falaises 1, 1011 Lausanne, Switzerland*

^b*Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62, 20157 Milan, Italy*

^c*Unit of Field and Intervention Studies, International Agency for Research on Cancer, 150 Cours Albert-Thomas, 69372 Lyon, France*

^d*Istituto di Statistica Medica e Biometria, Università degli Studi di Milano, Via Venezian 1, 20133 Milan, Italy*

Abstract

On the basis of overall national death certification data, it is not possible to analyse mortality from cervical cancer in Europe, since 20–65% of deaths from uterine cancer in largest countries are still certified as uterus, unspecified. We analysed, therefore, age-standardised death certification rates from uterine cancer between 1960 and 1998 in women aged 20–44 years, since most deaths from uterine cancer below the age of 45 years arise from the cervix. In all Western European countries, except Ireland, substantial declines in cervical cancer mortality in younger women were observed, although the falls were larger and earlier for some Nordic countries. The trends were irregular in the UK, with earlier declines between 1960 and 1970, followed by a rise between 1970 and 1985, and a subsequent fall. In Ireland, mortality from uterine cancer at age 20 to 44 years has been rising since the early 1980s, to reach 3.4/100 000 in 1995–1996. In Eastern Europe, some fall in mortality was observed in Hungary and Poland, while trends were upwards in Romania since 1980, and in Bulgaria. In all these countries, moreover, absolute rates remained appreciably higher than in most of Western Europe, and in the late 1990s there was over a 10-fold variation between the highest rates in Romania (10.6/100 000 women aged 20–44 years) and the lowest ones in Finland (0.5/100 000) or Sweden (0.9/100 000). Within the European Union, the variation was over 6-fold, the highest rates being registered in Ireland (3.4/100 000) and Portugal (3.2/100 000). The declines registered in cervical cancer mortality in young women were largely due to screening, and the persisting variations in mortality across Europe underline the importance of the adoption of organised screening programmes, with specific urgency in Eastern Europe. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Uterus; Cervix uteri; Neoplasms; Mortality; Epidemiology; Time trends; Europe

Incidence of cervical cancer has been declining in several (developed) areas of the world over the last few decades, mainly following the adoption of screening programmes, or high levels of opportunistic screening [1,2]. There are, however, contrasting trends, including recent rises in incidence for younger women in the UK, Ireland and a few other European countries, and generalised increases in adenocarcinoma of the cervix, which accounts for 10–15% of all cervical cancers [3–5]. Major geographical variation in incidence is observed not only between developed and developing countries, but also within developed areas of the world. Thus,

within Europe, in the early 1990s, cervical cancer incidence varied by over a factor of 3, between the highest rates registered in Poland and Eastern states of Germany (over 20/100 000, world standard), and the lowest ones in Italy, Switzerland, Spain and The Netherlands (below 7/100 000 [6].

Valid inference on cervical cancer mortality is much more difficult, since in several countries it is not possible, on the basis of death certification, to distinguish between cervix, corpus and unspecified uterine cancer deaths. Within Europe, the highest overall death certification rates from all uterine cancers combined were in Romania, Poland, Hungary and other eastern countries, indicating that the excess is largely attributable to cervical cancer [6]. Furthermore, recent trends in uterine cancer mortality have been less

* Corresponding author. Tel.: +41-21-314-7311; fax: +41-21-323-0303.

E-mail address: fabio.levi@inst.hospvd.ch (F. Levi).

favourable in these countries than in Western Europe [7,8].

To provide a comprehensive picture of cervical cancer mortality in Europe, we have systematically considered death certification data from the World Health Organisation (WHO) mortality database for cancer of the cervix, corpus, and uterus unspecified, and analysed trends in age-standardised rates between 1960 and 1998 below the age of 45 years, when most deaths from uterine cancer are due to cervical neoplasms.

1. Material and methods

Official death certification numbers for 24 European countries (including the Russian Federation, but excluding a few small countries such as Andorra and Liechtenstein) were derived from the World Health Organisation (WHO) database as available on electronic support [8]. During the calendar period considered (1960–1998), five different revisions of the International Classification of Diseases (ICD) were used [9–13]. Classification of cancer deaths were thus re-coded, for all calendar periods and countries, according to the ninth revision [12].

Estimates of the resident population, generally based on official censuses, were obtained from the same WHO

databank. From the matrices of certified deaths and resident populations, age-specific rates for each 5-year age group within the 20–44 years age span considered (i.e. 20–24, 25–29, 30–34, 35–39, 40–44 years) and the calendar period were computed. Age-standardised rates were based on the world standard population [14].

In a few countries, data were missing for part of one or more calendar years [8]. No extrapolation was made for missing data.

2. Results

Table 1 gives the average annual number of certified deaths from cervix, corpus uteri and unspecified uterus for selected European countries around 1960 and 1995. In 1960, the proportion of unspecified uterine cancers ranged between 6.0 in England and Wales, 10.6–12.5% in Switzerland and Norway, and 18.2–26.4% in the other Scandinavian countries to over 70% in France, Greece, Italy and Spain, with several countries showing proportions of unspecified uterine cancers of 35–50%. These figures tended to decline over the most recent calendar period. However, the proportions of unspecified uterine cancers around 1995 were still 59.4% in France, 32.1% in Germany, 65.4% in Italy, 32.1% in Spain and 21.2% in England and Wales, to mention the

Table 1

Average annual numbers of certified deaths from cervix, corpus and unspecified uterine cancers and per cent of unspecified cancers on all uterine cancers in selected European countries, 1960 and 1995

	Average annual number of certified deaths around 1960			Average annual number of certified deaths around 1995		
	Cervix	Corpus	Uterus unspecified (%)	Cervix	Corpus	Uterus unspecified (%)
Austria ^a	308	59	684 (65.1)	181	125	233 (43.2)
Belgium	298	278	425 (42.5)	187	163	229 (39.6)
Bulgaria	127	64	188 (49.6)	324	159	229 (32.2)
Denmark	337	105	145 (24.7)	173	133	67 (18.0)
Finland	153	73	81 (26.4)	51	141	16 (7.7)
France	964	273	3175 (72.0)	720	489	1771 (59.4)
Germany ^a	3366	848	2278 (35.1)	2144	1385	1667 (32.1)
Greece ^a	59	6	305 (82.4)	86	44	198 (60.4)
Hungary ^a	509	290	564 (41.4)	449	269	145 (16.8)
Iceland	6	3	2 (18.2)	4	5	2 (18.2)
Ireland	45	7	92 (63.9)	77	47	15 (10.8)
Italy	596	123	3840 (84.2)	459	528	186 (65.4)
The Netherlands	414	154	176 (23.7)	233	293	79 (13.1)
Norway	147	46	23 (10.6)	124	115	12 (4.8)
Portugal ^b	170	56	395 (63.6)	199	124	294 (47.6)
Spain	118	22	1828 (92.9)	596	653	591 (32.1)
Sweden	307	173	128 (21.1)	156	132	148 (33.9)
Switzerland ^a	253	223	68 (12.5)	154	226	44 (10.4)
UK, England and Wales	2531	1208	238 (6.0)	1293	756	552 (21.2)
UK, N. Ireland	44	8	35 (40.2)	30	12	19 (31.1)
UK, Scotland	250	43	141 (32.5)	143	81	22 (8.9)

^a First available period was 1970.

^b 1980 for Portugal.

largest European countries only. Given these figures, as well as some potential degree of misclassification between cervix and corpus uteri, it is clearly not possible to use overall (all-age) national mortality data to investigate patterns and trends in cervical cancer rates in Europe.

It is known, however, that below the age of 45 years most deaths from uterine cancer arise from the cervix. We, therefore, restricted our analyses to women aged 20 to 44 years. Fig. 1 gives trends in age-standardised death certification rates from uterine (including cervix, corpus and uterus unspecified) cancer between 1960 and 1998 in 22 European countries. In all Western European countries — except Ireland — substantial declines over time were observed, although the falls were earlier for some Nordic countries (Denmark, Finland, Iceland, Sweden), and somewhat later and more steady in most other countries, including some of the largest ones such as France, Germany, Italy and Spain. The trends were irregular in UK, with earlier declines between 1960 and 1970, followed by a rise between 1970 and 1985 (to 4.1/100 000 in England and Wales), and a subsequent fall (to 2.6/100 000 in 1995–1998). In Ireland, uterine cancer mortality in young women declined from 3.1/100 000 in 1960–1964 to 1.6 in 1980–1984, but rose thereafter to reach 3.4 in 1995–1996. Only 47 deaths from all uterine cancers at age 20–44 years, however, were registered in Ireland in 1995–1996, and hence the lowest confidence limit of this estimate is 2.4/100 000. Of the four Eastern European countries providing data, some fall in mortality was observed in Hungary and Poland, while the trends were upwards in Romania after 1980, and in Bulgaria. In all these countries, moreover, absolute rates remained appreciably higher than in most of Western Europe. In the European Union (EU) death rates steady declined from 5.6 in 1960–1964 to 2.0 in 1995–1998, and the falls appeared steeper in the first and last decade. In the four Eastern European countries considered, in contrast, after a fall from 9.3 to 5.6/100 000 between 1960–1964 and 1975–1979, death rates from all uterine cancers rose to 7.3 in 1995–1998.

Fig. 2 gives the histogram of age-standardised uterine cancer mortality at age 20–44 years in the most recent calendar period available in 35 European countries. There was an over 10-fold variation between the highest rate in Romania (10.6/100 000) and the lowest ones in Finland (0.5/100 000), Sweden (0.9/100 000), Luxembourg (1.1/100 000) or The Netherlands (1.2/100 000). Most Eastern European countries were in the upper part of the distribution, with rates over 3/100 000, whereas most western European countries had rates between 1 and 2.5/100 000, except Ireland (3.4/100 000), Portugal (3.2/100 000) and England and Wales (2.6/100 000).

Within the EU, the variation was over 6-fold, the highest rates (over 3/100 000) being registered in Ireland

and Portugal. A striking difference was also observed between Denmark (2.5/100 000) and Sweden (0.9/100 000) and Finland (0.5/100 000).

3. Discussion

Two main messages can be derived from the present systematic analysis of uterine cancer mortality in Europe: first, overall national death certification rates can not be used to obtain meaningful measures of patterns of trends in uterine cancer mortality, due to a substantial and variable proportion of deaths from unspecified uterine neoplasms and, second, death certification rates from uterine cancer in younger women (20–44 years) declined substantially in most Western European countries, but not in Eastern Europe [15].

The interpretation of these trends has essentially to be related to the adoption and utilisation of cervical screening programmes in various European countries. Organised screening programmes were first adopted in the 1960s in selected Nordic countries, which generally showed earlier and greater declines in cervical cancer mortality [16–18]. However, also opportunistic screening — as adopted in France, Germany or Italy — seems to have had a relevant impact on cervical cancer rates, at least in young women, although in the 1980s it was still estimated that inadequate screening could account for over 80% of all cervical cancers in Italy [19]. The gross excess cervical cancer mortality still observed in Eastern Europe is, therefore, largely attributable to inadequate screening implementation in these countries, and underlines the importance of rational and organised screening programmes in these areas of the continent.

Other factors may, however, also have a role in cervical cancer mortality across Europe. The rises observed in the UK and, mostly, Ireland since the earlier 1980s, are likely to be due to changed sexual habits in younger generations, with increased exposure to the main risk factors for cervical cancer, human papilloma virus (HPV) [20–22]. Further, a minor role of other risk factors for cervical cancer, including tobacco smoking [23,24] and oral contraceptives [25] is also conceivable. Screening may have counterbalanced more unfavourable underlying trends in these countries over recent calendar periods, since it was estimated that screening had reduced mortality from cervical cancer by over 60% in women aged under 55 years in England and Wales [26,27]. In Finland, where a nationwide screening programme for cervical cancer started from 1963 onwards, mortality rates were still downwards in the early 1990s, while incidence increased by 60% [28].

Finally, it must be borne in mind that the trends analysed and described in this paper refer to women below the age of 45 years only, i.e. to a small proportion of all cervical cancer deaths, and are not, therefore,

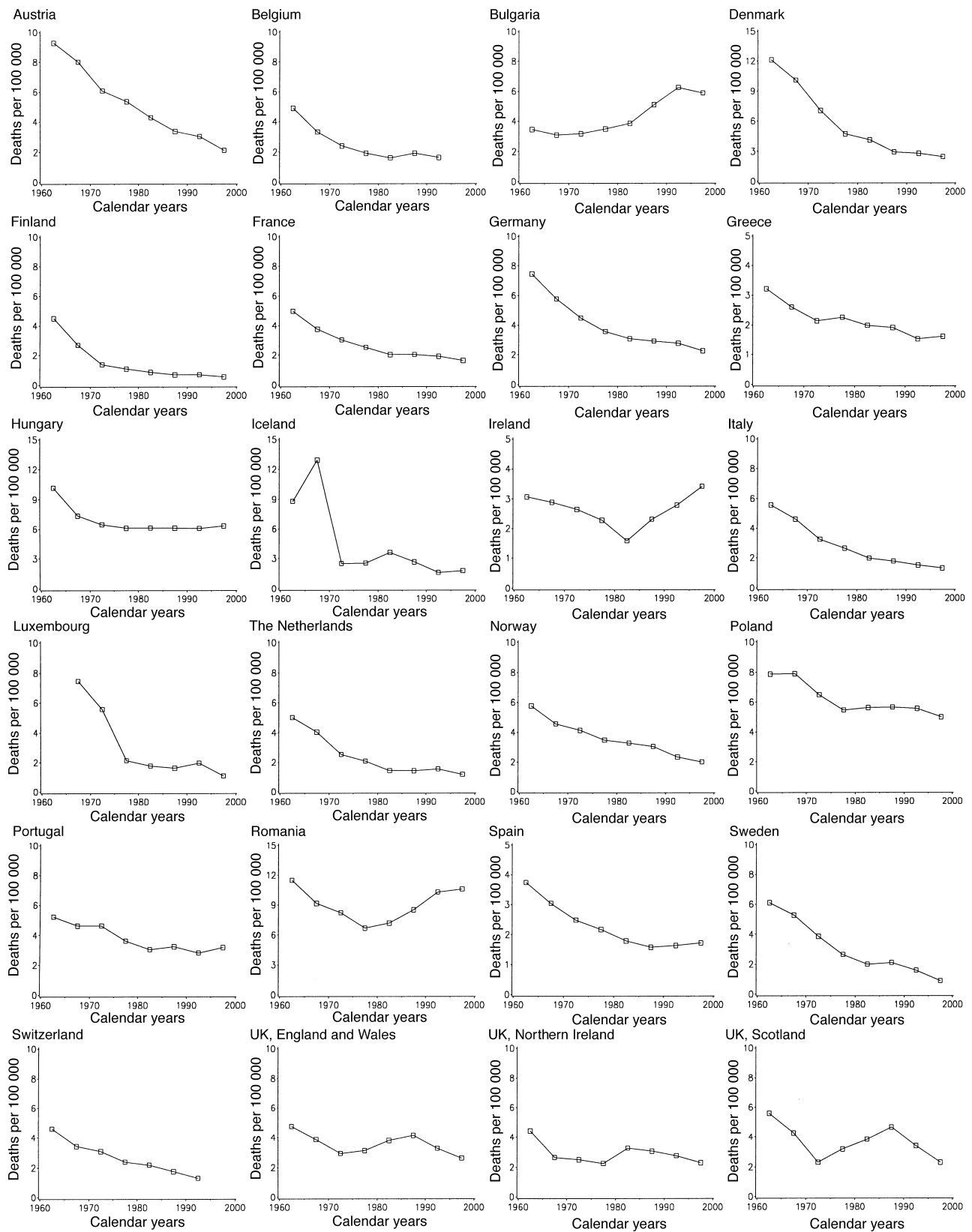


Fig. 1. Trends in age-standardised (world) death certification rates from all uterine cancers per 100 000 women aged 20–44 years in 22 European countries, from 1960–1964 to 1995–1998.

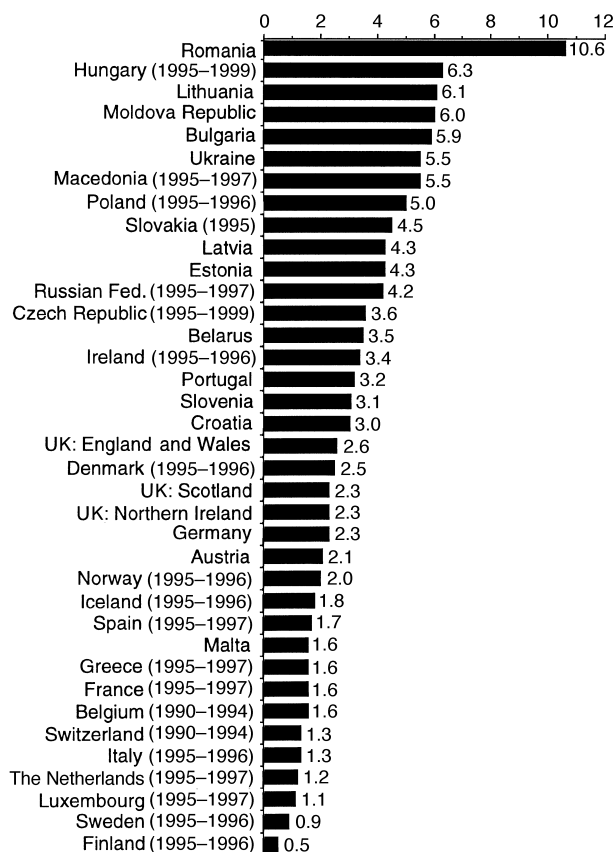


Fig. 2. Age-standardised (world population) death certification rates from all uterine cancers per 100 000 women aged 20–44 years in various European countries, in 1995–1998 (unless specified in parentheses). Source WHO.

directly applicable to rates in the elderly population and subsequent generations, since the efficiency of screening may be lower in older women [29], and there are complex age and cohort effects in cervical cancer rates [3,26,30]. Trends in mortality from all uterine cancers in Europe at all ages and truncated for 35–64 years have been reported elsewhere [8], but the impact of cervical cancer mortality alone remains difficult to quantify in these age groups.

Acknowledgements

Supported by the Swiss League against Cancer and the Italian Association for Cancer Research. The project received financial support from the European Commission (Contract grant sponsor: European Union, Commission of the European Communities, Directorate-General for Employment, Industrial Relations and Social Affairs; Contract grant number: SOC 97 201143).

Neither the European Commission nor any person acting on its behalf is liable for any use made of this information.

References

- Bergström R, Sparén P, Adami H-O. Trends in cancer of the cervix uteri in Sweden following cytological screening. *Br J Cancer* 1999, **81**, 159–166.
- Levi F, La Vecchia C, Te VC, Gutzwiller F. Incidence of invasive cervical cancer in the Swiss canton of Vaud, and a note on screening. *J Epidemiol Comm Health* 1989, **49**, 121–124.
- Zheng T, Holford TH, Zheng MA, et al. The continuing increase in adenocarcinoma of the uterine cervix: a birth cohort phenomenon. *Int J Epidemiol* 1996, **25**, 252–258.
- Vizcaino AP, Moreno V, Bosch FX, Munoz N, Barros-Dios XM, Parkin DM. International trends in the incidence of cervical cancer: I Adenocarcinoma and adenosquamous cell carcinoma. *Int J Cancer* 1998, **75**, 536–545.
- Vizcaino AP, Moreno V, Bosch FX, et al. International trends in incidence of cervical cancer: II Squamous-cell carcinoma. *Int J Cancer* 2000, **86**, 429–435.
- Levi F, Lucchini F, Boyle P, Negri E, La Vecchia C. Cancer incidence and mortality in Europe, 1988–92. *J Epidemiol Biostat* 1998, **3**, 295–373.
- Cuzick J, Boyle P. Trends in cervix cancer mortality. *Cancer Surv* 1988, **7**, 417–439.
- Levi F, Lucchini F, Negri E, Boyle P, La Vecchia C. Cancer mortality in Europe, 1990–1994, and an overview of trends from 1955 to 1994. *Eur J Cancer* 1999, **35**, 1477–1516.
- WHO. *International Classification of Diseases: 6th Revision*. Geneva, World Health Organisation, 1950.
- WHO. *International Classification of Diseases: 7th Revision*. Geneva, World Health Organisation, 1957.
- WHO. *International Classification of Diseases: 8th Revision*. Geneva, World Health Organisation, 1967.
- WHO. *International Classification of Diseases: 9th Revision*. Geneva, World Health Organisation, 1977.
- WHO. *International Statistical Classification of Diseases and Related Health Problems: 10th Revision*. Geneva, World Health Organisation, 1992.
- Doll R, Smith PG. Comparison between registries: age-standardised rates. In Waterhouse JAH, Muir CS, Shanmugaratnam K, et al., eds. *Cancer Incidence in Five Continents Vol. 4*. IARC Scientific Publications No. 42. Lyon, International Agency for Research on Cancer, 1982, 671–675.
- Franceschi S, Levi F, Lucchini F, Negri E, Boyle P, La Vecchia C. Trends in cancer mortality in young adults in Europe, 1955–1989. *Eur J Cancer* 1994, **30A**, 2096–2118.
- Cuzick J. Screening for cancer: future potential. *Eur J Cancer* 1999, **35**, 1925–1932.
- Franceschi S, Herrero R, La Vecchia C. Cervical cancer screening in Europe: what next? *Eur J Cancer* 2000, **36**, 2272–2275.
- Coebergh JW. Challenges and pitfalls of mass-screening in the European Union. *Eur J Cancer* 2000, **36**, 1469–1472.
- Parazzini F, Hildesheim A, Ferraroni M, La Vecchia C, Brinton L. Relative and attributable risk for cervical cancer: a comparative study in the United States and Italy. *Int J Epidemiol* 1990, **19**, 539–545.
- IARC. Human Immunodeficiency Viruses and Human T-Cell Lymphotropic Viruses. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 67, Lyon, International Agency for Research on Cancer, 1996.
- Cuzick J. Viruses and cancer. *J Epidemiol Biostat* 2000, **5**, 143–152.
- Walboomers JMM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol* 1999, **189**, 12–19.
- Winkelstein Jr W. Smoking and cervical cancer-current status. A review. *Am J Epidemiol* 1990, **131**, 945–957.
- Ylitalo N, Sorensen P, Josefsson A, et al. Smoking and oral

- contraceptives as risk factors for cervical carcinoma *in situ*. *Int J Cancer* 1999, **81**, 357–365.
25. IARC. *Hormonal Contraception and Post-Menopausal Hormonal Therapy. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 72*. Lyon, International Agency for Research on Cancer, 1999.
26. Sasieni P, Adams J. Effect of screening on cervical cancer mortality in England and Wales: analysis of trends with age period cohort models. *Br Med J* 1999, **318**, 1244–1245.
27. Quinn M, Babb P, Jones J, Allen E. Effect of screening on incidence of and mortality from cancer of cervix in England: evaluation based on routinely collected statistics. *Br Med J* 1999, **318**, 904–908.
28. Anttila A, Pukkala E, Söderman B, Kallio M, Nieminen P, Hakama M. Effects of organised screening on cervical cancer incidence and mortality in Finland, 1963–1995: recent increase in cervical cancer incidence. *Int J Cancer* 1999, **83**, 59–65.
29. Gustafsson L, Sparén P, Gustafsson M, et al. Low efficiency of cytologic screening for cancer in situ of the cervix in older women. *Int J Cancer* 1995, **63**, 804–809.
30. La Vecchia C, Negri E, Levi F, Decarli A, Boyle P. Cancer mortality in Europe: effects of age, cohort of birth and period of death. *Eur J Cancer* 1998, **34**, 118–141.