Best Practice & Research Clinical Obstetrics and Gynaecology
Vol. 20, No. 2, pp. 207–225, 2006
doi:10.1016/j.bpobgyn.2005.10.007
available online at http://www.sciencedirect.com

1

Worldwide burden of gynaecological cancer: The size of the problem

R. Sankaranarayanan* MD
Head, Screening Group

J.Ferlay ME
Informatics Officer, Descriptive Epidemiology Group
International Agency for Research on Cancer, 150 Cours Albert Thomas, Lyon 69008, France

The estimation of cancer burden is valuable to set up priorities for disease control. The comprehensive global cancer statistics from the International Agency for Research on Cancer indicate that gynaecological cancers accounted for 19% of the 5.1 million estimated new cancer cases, 2.9 million cancer deaths and 13 million 5-year prevalent cancer cases among women in the world in 2002. Cervical cancer accounted for 493 000 new cases and 273 000 deaths; uterine body cancer for 199 000 new cases and 50 000 deaths; ovarian cancer for 204 000 new cases and 125 000 deaths; cancers of the vagina, vulva and choriocarcinoma together constituted 45 900 cases. More than 80% of the cervical cancer cases occurred in developing countries and two-thirds of corpus uteri cases occurred in the developed world. Political will and advocacy to invest in healthcare infrastructure and human resources to improve service delivery and accessibility are vital to reduce the current burden in low- and medium-resource countries.

Key words: burden; cervical cancer; control; early detection; gynaecological cancer; ovarian cancer; prevention; screening; uterine body cancer.

The most commonly used indicators of cancer burden are incidence, mortality and prevalence. Cancer incidence is expressed as the absolute number of new cases occurring in a defined population in 1 year, or as a rate in terms of number of new cases per 100 000 people per year. Cancer mortality is also expressed as the absolute number of people who die from a specific cancer during a given year or as a rate in terms of cancer deaths per 100 000 people per year. Prevalence pertains to the absolute number, and relative proportion, of individuals affected by the disease during a defined period in a population. Other more complex indices of disease burden used

* Corresponding author. Tel.: +33 472 73 8599; Fax: +33 472 73 8518.
E-mail address: sankar@iarc.fr (R. Sankaranarayanan).

include 'person-years of life lost', which is defined as how many years of normal life are lost due to deaths from a given disease; and 'disability-adjusted life-years lost', which attempts to give a numerical score to the years lived with a reduced quality of life between diagnosis and death.

The estimation of cancer burden in terms of incidence, mortality and prevalence is necessary when formulating cancer control policies and planning health services. It enables an assessment of the demands of care and the implementation of strategies to provide healthcare services to reduce disease burden and relieve suffering. It helps to define priorities for preventive, diagnostic, therapeutic and palliative care services and to evaluate the outcomes of targeted interventions in relation to costs and resource inputs. The comparison of disease burden between different populations over time enables the causal definition of hypotheses and the critical evaluation of the underlying risk factors, thereby providing potential opportunities for prevention.

In order to present the global gynaecological cancer burden in the year 2002, this chapter describes the incidence, mortality and prevalence of cancers of the uterine cervix (International Classification of Disease [ICD]-10 code C53), uterine body (corpus uteri, ICD-10 C54), ovary and other uterine adnexa (ICD-10 C56, C57.0-4), together with the incidence of vagina (ICD-10 C51), vulva (ICD-10 C52) and choriocarcinoma (ICD-10 C58) for 18 world regions. It briefly discusses the sources and methods of estimation and data validity and the implications for health services worldwide in general, and those of the developing countries in particular.

INDICES OF CANCER BURDEN

'Incidence' provides an indication of the average risk of developing a cancer in a population.[1,2] When expressed as an absolute number of cases per year, it reflects the load of new patients diagnosed in a given region. The risk of disease in different populations within countries, regions, ethnicities or over different time periods can be compared using incidence. The impact of prevention strategies based on reducing or eliminating exposure of populations to disease-causing risk factors (e.g. tobacco use or infection with human papillomavirus (HPV), etc.) or early detection and treatment of precancerous lesions (e.g. cervical cancer screening) is measured in terms of reduction in incidence.

'Mortality' is the product and fatality of incidence, and provides an unambiguous measure of the outcome of disease.[1,2] 'Fatality' refers to the proportion of incident cancer cases that die. Mortality rates measure the average risk of dying from a given cancer in a given population, whereas fatality reflects the probability of an individual with cancer dying from it. Mortality rates are influenced by the trends in incidence rates as well as by the natural history of the disease, the efficacy of treatment interventions and of health services delivery. It is inappropriate to use mortality rate as a proxy measure of cancer incidence when comparing different populations, assuming equal survival/fatality in the populations compared, which is rarely true. The survival time of a cancer patient refers to the time duration between the diagnosis and death.

'Prevalence' refers to the number of persons who have had cancer diagnosed at some time in the past in a defined population, during a given period of time.[1,2] The prevalence of cancer cases diagnosed with in 1, 3 and 5 years is likely to be relevant to the different phases of cancer management, such as initial treatment (1-year

prevalence) and treatment of residual/recurrent disease and clinical follow-up (3- or 5-year prevalence).

Sources and methods of estimation of data

The data discussed in this chapter are essentially derived from the comprehensive global cancer statistics published by the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO).[1] The database is available on internet at the CANCER mondial website (http://www-dep.iarc.fr) and provide the best possible estimates of the global cancer burden in 2002.

A brief description of how the cancer statistics have been compiled is useful to understand the validity, limitations and applications of the data in national, regional and global contexts. The methods of assembling these data have been described elsewhere.[1–4] The building-blocks of the global data are the best and most up-to-date information on incidence, mortality and survival in a given country, and are available from the Descriptive Epidemiology Group of the IARC.

Population-based cancer registries produce cancer incidence data by systematically collecting information on a continuing basis on all new cancer cases diagnosed by all means (histological or clinical) in a defined resident population in a given geographical region.[5] However, many countries do not have cancer registries and many populations, particularly in sub-Saharan Africa, certain regions of Asia (e.g. Central Asia) and Latin America (e.g. Central America) are not covered. Where available, cancer registries might cover the entire geographical regions of a country (national registries; e.g. Singapore, Oman, Finland, Costa Rica) or populations living in some regions in a country (e.g. Shanghai municipal area in China, Kyadondo county in Uganda, Bas-Rhin department in France, Lima city in Peru). It is estimated that 16% of the world population (comprising 64% of developed and 5% of developing country populations) were covered by population-based cancer registries in 1995. The latest volume of Cancer Incidence in Five Continents (CI5) contains comprehensive and comparable incidence data from 186 population-based cancer registries in 57 countries for the period 1993–1997.[6]

For this chapter, incidence rates were estimated, in order of priority, from:

- national incidence data
- national mortality data, with an estimation of incidence using sets of regression models that are specific for site, sex and age, derived from local cancer registry data (incidence plus mortality)
- local incidence from one or more regional cancer registries within a country
- frequency data from hospital registries or pathology registers.

If there are no data, the country-specific rates are calculated from neighbouring countries for which estimates could be made.

For cancers of the vagina, vulva and placenta, estimates for 18 world regions, as defined by the UNO population division, were calculated by the population weighting average of the age-specific incidence rates observed in local cancer registries in the area.

We derived the mortality data from the different countries' death registration systems. The data are produced according to the underlying cause of death, which are available through the World Health Organization (WHO). However, the completeness, quality, accuracy and validity of mortality data available from different countries are

highly variable. For instance, in 1995, only 29% of the world population was covered by death registration. In most developing countries, particularly in sub-Saharan Africa and certain areas of Asia and Latin America, the coverage of populations by death registration is grossly incomplete, and the mortality rates reported from these regions are low and unreliable. For countries where mortality data were of poor quality or unavailable, they were estimated from incidence, using survival data specific to a country or region.

We estimated the prevalence data from incidence and population-based cancer survival data produced by cancer registries by following-up all the incident cancer cases. Population-based survival rates indicate the average prognosis from a given cancer in a given region and reflect the efficiency of the local health services. Such survival data are widely available for developed countries, but for only limited regions in a few developing countries. The sources of population survival data include the population-based cancer registries under the Surveillance, Epidemiology and End Results (SEER) programme, which covers 13% of the US population[7]; the EUROCARE-3 project, which provides survival data for registries in several European countries[8]; and the 'Cancer Survival in Developing Countries monograph', which provides survival data for selected populations in China, Cuba, India, the Philippines and Thailand[9,10], Singapore[11] and first results from Uganda[12] and Zimbabwe.[13]

From the above description, it is evident that the estimates of cancer burden for different countries vary in accuracy, depending on the extent and validity of the data available for each country. For several developing countries from where no data are available (e.g. Cambodia, Democratic Republic of Congo) our estimate was derived from neighbouring countries.

2002 ESTIMATES OF GYNAECOLOGICAL CANCER BURDEN

It has been estimated that there were 10.9 million new cancer cases (all cancers excluding non-melanoma skin cancer) in both sexes in the world around the year 2002: 5.8 million cases in men and 5.1 million cases in women.[1,2] There were 6.7 million cancer deaths, 3.8 million in men and 2.9 million in women. There were 24.6 million persons with a diagnosis of cancer within 5 years from the initial diagnosis, of which 13.0 million were women.

The burden of uterine body, uterine cervix and ovarian cancer worldwide, in developing and developed countries and for 18 world regions is given in Table 1. The incidence rates and number of incident cases in 2002 of vaginal cancer, vulva cancer and choriocarcinoma are given in Table 2. Developed countries include North America, Europe (including all of Russia), Australia, New Zealand and Japan. Those in the remaining regions constitute 'developing countries'.

New cases of uterine body, cervix, ovary, vagina, vulva, and choriocarcinoma cancers together constituted 942 000 cases, accounting for 18.6% of all incident cancers in women in the world. They accounted for 22.1% of all new cancer cases among women in developing countries compared to 14.5% of all new cases among women in developed nations. Of the total 2.9 million cancer deaths worldwide among women, gynaecological cancer (excluding vagina, vulva and placental malignancies) accounted for 15.3% deaths; of the total 5-year prevalent cases, gynaecological cancer accounted for 20.9% cases.

Table 1. Cancers of the uterine cervix, uterine body, ovary, etc. Incident cases, deaths and 5-year prevalence in 18 world regions in 2002.

	Cervix			Uterine body			Ovary			All		
	Cases	Deaths	5-year prev.	Cases	Deaths	5-year prev.	Cases	Deaths	5-year prev.	Cases	Deaths	5-year prev.
World	492 800	273 200	1 409 200	198 600	50 200	775 400	204 200	124 700	538 400	895 600	448 100	2 723 000
More developed countries	83 400	39 500	309 900	136 300	29 100	557 400	96 700	62 200	262 300	316 400	130 800	1 129 600
Less developed countries	409 400	233 700	1 099 300	62 300	21 100	218 000	107 500	62 500	276 100	579 200	317 300	1 593 400
Eastern Africa	33 900	27 100	57 200	2400	800	8600	4700	3300	10 400	41 000	31 200	76 200
Middle Africa	8200	6600	13 900	700	200	3000	1100	800	2600	10 000	7600	19 500
Northern Africa	8100	6500	14 000	1500	600	5200	1800	1300	4200	11 400	8400	23 400
Southern Africa	7600	4400	13 100	600	200	2100	1000	600	2200	9200	5200	17 400
Western Africa	20 900	16 700	35 700	1400	500	5100	3600	2500	7900	25 900	19 700	48 700
Caribbean	6300	3100	18 400	1600	800	5400	800	400	2000	8700	4300	25 800
Central America	17 100	8100	49 300	2400	1000	8600	4000	1900	10 100	23 500	11 000	68 000
South America	48 300	21 400	139 200	10 600	3200	34 900	12 700	6100	31 500	71 600	30 700	205 600
Northern America	14 600	5700	58 200	51 500	6300	223 200	25 100	16 000	74 400	91 200	28 000	355 800
Eastern Asia	61 100	31 300	191 900	20 200	4700	80 000	30 600	15 000	88 000	111 900	51 000	359 900
South-eastern Asia	42 500	22 500	132 500	9100	3200	32 400	16 800	9200	44 300	68 400	34 900	209 200
South central Asia	157 700	86 700	446 100	13 100	5400	45 600	32 500	22 800	83 500	203 300	114 900	575 200
Western Asia	4400	2100	13 700	4100	1900	13 800	4000	2400	10 200	12 500	6400	37 700
Eastern Europe	30 800	17 100	107 700	29 600	10 100	111 500	23 600	15 200	56 700	84 000	42 400	275 900
Northern Europe	5600	2800	21 100	10 500	2200	39 500	10 500	7100	24 700	26 600	12 100	85 300
Southern Europe	10 600	4100	40 900	15 800	3600	61 600	11 600	6400	32 000	38 000	14 100	134 500
Western Europe	12 700	5600	49 200	21 000	4500	86 700	17 600	12 100	48 400	51 300	22 200	184 300
Oceania	2000	800	6500	2000	400	7500	1700	1000	4500	5700	2200	18 500

Cancer of the uterine cervix

Cancer of the cervix is the second most common cancer among women worldwide, with an estimated 493 000 new cases and 273 000 deaths (Table 1) in the year 2002. Eighty-three percent of new cases and 85% of deaths from cervical cancer occur in developing countries, where it is the most common cancer among women in many regions. Being the most common gynaecological cancer in the developing world, it accounts for two-thirds of cases and continues to be a serious health problem. Of cervical cancers worldwide, 80–95% are squamous cell carcinomas.[6]

There is an 8-fold variation in the incidence rates of cervical cancer worldwide. The highest incidence rates are observed in sub-Saharan Africa, Melanesia, Latin America and the Caribbean, South-Central Asia, and South-East Asia (Figures 1 and 2). One-third of the cervical cancer burden in the world is experienced in South-Central Asia (Table 1). The incidence is generally low in developed countries, with age-standardised rates less than 14 per 100 000 women (Figures 1 and 2). The low risk in such countries is due to effective screening programmes. Before the introduction of screening programmes, the incidence rates in most of developed countries were similar to those found in developing countries today.[14] Rates lower than 7 per 100,00 women are also observed in the middle eastern countries and China.

Age-adjusted cervical cancer mortality rates exceed 15 per 100 000 women in most developing regions of the world, with rates as high as 35 per 100 000 in Eastern Africa (Figure 2). The high mortality rates are due to advanced clinical stage at presentation and to the fact a significant proportion of patients do not receive or complete prescribed courses of treatment, due to deficiencies in treatment availability, accessibility and affordability in many developing countries. Mortality rates seldom exceed 5 per 100 000 women in developed countries with successful screening programmes (Figure 2).

Higher survival is observed in populations in developed countries as compared to selected populations in developing countries from where survival data are available (Table 3). Five-year survival in the SEER registries, Europe and Singapore are considerably higher than those reported from sub-Saharan Africa, whereas survival rates are fair in India, China and Thailand. The 5-year prevalence exceeds 1.4 million in the world, with 1 million of these cases being in the developing world (Table 1).

Cancer of the uterine body

Cancer of the uterine body, a cancer of the postmenopausal women, has a similar geographic distribution to ovarian cancer and accounted for 199 000 new cases (3.9% of cancers in women) and 50 000 deaths (1.7% of all cancer deaths in women) worldwide in 2002 (Table 1). It is the most common gynaecological cancer in developed countries, which account for two-thirds of the global burden. Around 90% of the uterine body cancers are endometrial adenocarcinomas; papillary serous carcinoma, clear cell carcinomas, papillary endometrial carcinoma and mucinous carcinoma account for the remaining cases. The highest incidences are observed in North America, with rates exceeding 20 per 100 000 women, whereas in Europe it varies between 11 and 14 per 100 000 women (Figures 3 and 4). Incidence rates in South America are intermediate, whereas rates are low in Southern and Eastern Asia (including Japan) and most of Africa (less than 4 per 100 000). More than 90% of cases occur in women aged 50 years and over. Cancer of uterine body has a

Table 2. Cancer of the vulva, vagina and choriocarcinoma: estimated incident cases and age-standardised incidence rates (world) per 100 000 (all ages) in 18 world regions (2002).

Estimated number of cases and ASR (World) per 100 000—2002							
	Vulva (C51)		Vagina (C52)		Choriocarcinoma (C58)		All
Area	Cases	Rate	Cases	Rate	Cases	Rate	Cases
Eastern Africa	0.5	0.80	0.3	0.34	0.5	0.46	1.3
Middle Africa	0.2	0.56	0.1	0.31	0.1	0.18	0.3
Northern Africa	0.2	0.35	0.2	0.30	0.0	0.04	0.5
Southern Africa	0.2	0.78	0.1	0.25	0.1	0.40	0.3
Western Africa	0.4	0.57	0.4	0.50	0.3	0.33	1.1
Caribbean	0.2	1.09	0.1	0.75	0.0	0.03	0.4
Central America	0.4	0.87	0.3	0.53	0.1	0.13	0.8
South America	2.4	1.46	1.1	0.68	0.5	0.26	4.0
Northern America	4.0	1.63	1.2	0.47	0.1	0.08	5.4
Eastern Asia	2.3	0.26	1.7	0.20	1.3	0.15	5.2
South-Eastern Asia	1.2	0.55	0.6	0.26	1.2	0.43	3.0
Southern Asia	2.6	0.46	4.1	0.70	1.0	0.13	7.7
Western Asia	0.4	0.61	0.2	0.24	0.2	0.16	0.8
Eastern Europe	4.8	1.61	1.3	0.47	0.2	0.10	6.2
Northern Europe	1.5	1.58	0.4	0.43	0.0	0.04	1.9
Southern Europe	2.4	1.45	0.5	0.36	0.0	0.05	2.9
Western Europe	2.7	1.33	0.8	0.45	0.0	0.05	3.5
Oceania	0.3	1.51	0.1	0.45	0.0	0.07	0.4
World	26.9		13.2		5.8		45.9

much more favourable prognosis than ovarian and cervical cancer, with 5-year survival rates around 80% in developed countries and 70% in the developing countries (Table 2). The 5-year prevalence is around 775 000 cases worldwide.

Ovarian cancer

Fallopian tube cancers and extraovarian primary peritoneal cancers are considered along with ovarian cancers because their biology and clinical characteristics are

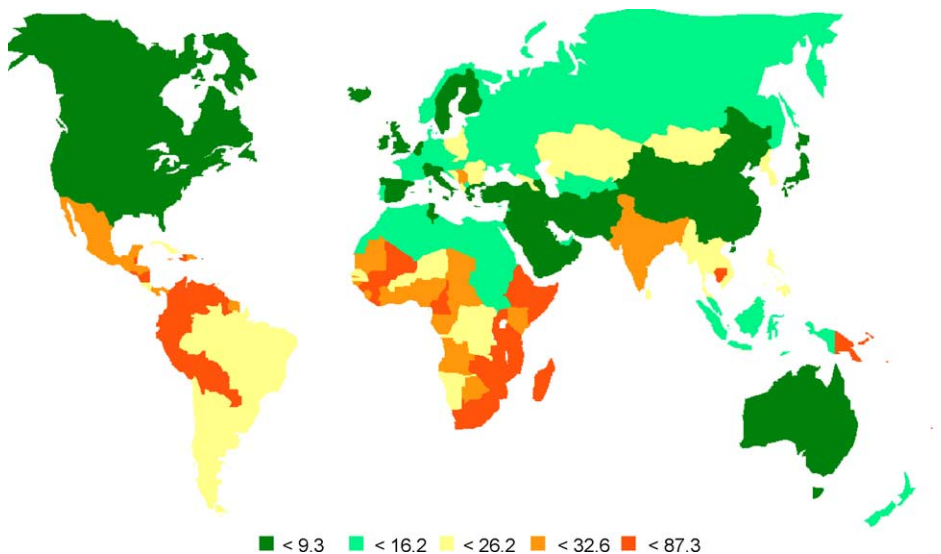

Figure 1. Incidence of cancer of the uterine cervix: age-standardised rates (world) per 100 000 (all ages).

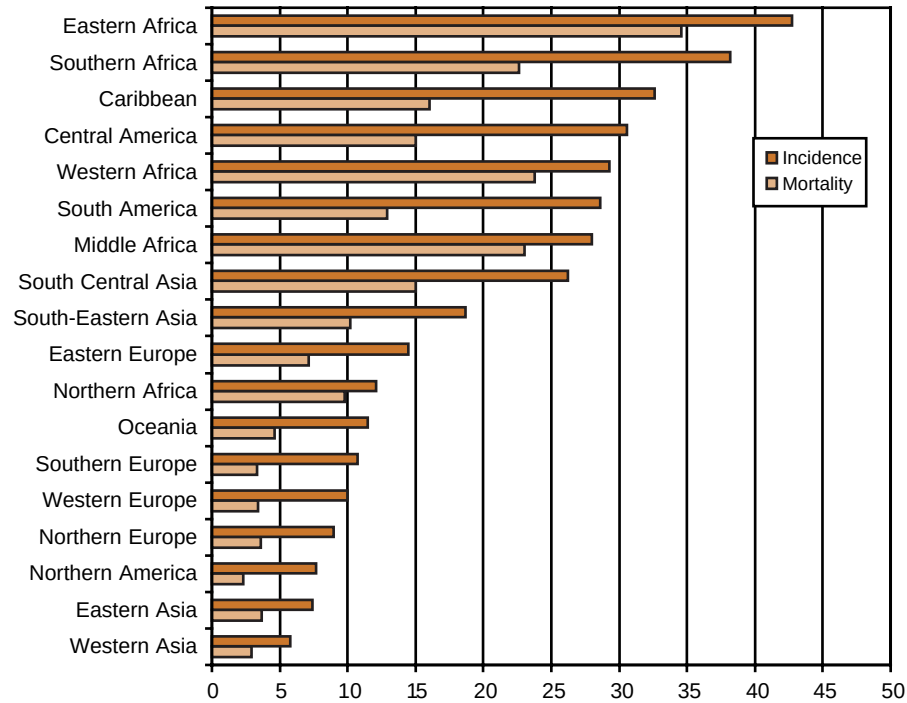

Figure 2. Cancer of the uterine cervix: age-standardised (world) incidence and mortality rates per 100 000 (all ages) in 18 world regions.

similar to ovarian cancer, although they are much less common. Ovarian cancer ranks as the sixth most common cancer in women and accounted for 204 000 cases and 125 000 deaths worldwide around 2002 (Table 1). It constitutes 4.0% of all female cancers and 4.2% of cancer deaths in women. It is the second most common gynaecological cancer, accounting for 18.8% of all gynaecological cancers in developing countries and 28.7% in developed countries. Developed countries account for half the worldwide burden of ovarian cancer. In the developed countries, more than 90% of ovarian cancers are epithelial in origin, the remaining constituted by germ cell tumours (2–3%) and sex cord-stromal tumours (5–6%). Germ cell tumours account for 10–15% of ovarian cancers in Asian and African populations. Dysgerminoma accounts for more than 70% of germ cell tumours, whereas granulosa tumours constitute the most common sex cord-stromal tumour. The vast majority of epithelial ovarian cancers are diagnosed in postmenopausal women, whereas germ cell tumours occur in young women of child-bearing potential, who are often in their twenties.

Incidence rates are highest in developed countries (Figure 5), with rates in these areas exceeding 10 per 100 000 (Figure 6), except for Japan (6.4 per 100 000). The incidence in South America (7.7 per 100 000) is relatively high compared to many regions in Asia and Africa. The incidence rate of ovarian cancer has been slowly increasing in many developed countries over the last two decades.

Table 3. Five-year relative survival (1990).

Region/country	Uterine body	Cervix uteri	Ovary
USA, SEER	83	72	42
English registries	74	64	31
French registries	73	68	38
Italian registries	76	67	37
Finland	81	66	35
Singapore	68	57	51
India, Mumbai		51	
India, Chennai		60	
China, Shanghai	77	52	44
Thailand, Chiang Mai	69	68	45
Thailand, Khon Kaen	79	57	36
Philippines, Rizal		29	
Uganda, Kampala		18	16
Harare, Zimbabwe: black		30	38

SEER, Surveillance, Epidemiology and End Results program.

The high proportion of deaths in relation to new cases reflects the much less favourable prognosis of ovarian cancer compared to uterine body and cervical (Table 3). Ovarian cancer mortality rates exceed 5 per 100 000 women in developed countries (Figure 6). The 5-year survival from ovarian cancer is mostly less than 50% (Table 2) and the 5-year prevalence is 538 000 cases worldwide.

Other gynaecological cancers

Cancer of the vagina is rare, constituting less than 2% of gynaecological cancers. It accounted for 13 200 cases worldwide around 2002 (Table 3); of these, 9000 occurred in developing countries. The incidence rates do not exceed 0.8 per 100 000 women in any world region. More than three-quarters of cases occur in women older than 60 years. Except for clear cell carcinomas associated with maternal diethyl stilboestrol (DES) exposure, vaginal cancer is rare in women younger than 40 years. Half of the tumours occur in the upper third of vagina.

Cancer of the vulva constitutes 3% of gynaecological cancers. It accounted for 26 800 cases, of which 15 700 occurred in developed countries. The incidence rates exceed 1.5 per 100 000 women in North America, South America and Europe, whereas the rates are less than 1.0 per 100 000 in developing countries (Table 3). More than 50% of the cases are diagnosed in women over the age of 70; incidence rates peak in women aged 75 and above. Two-thirds or more of the vulva cancers occur in the labia majora.

Choriocarcinoma is a rare cancer constituting 0.6% of all gynaecological cancers. It accounted for 5800 cases worldwide, of which 5400 occurred in developing countries. Incidence rates in different regions vary 10-fold: age-standardised incidence rates of choriocarcinoma ranged from 0.04 in Southern Africa and Northern Europe to 0.43 per 100 000 women in South East Asia. An incidence rate of 1.7 per 100 000 women has been reported from Vietnam.[15]

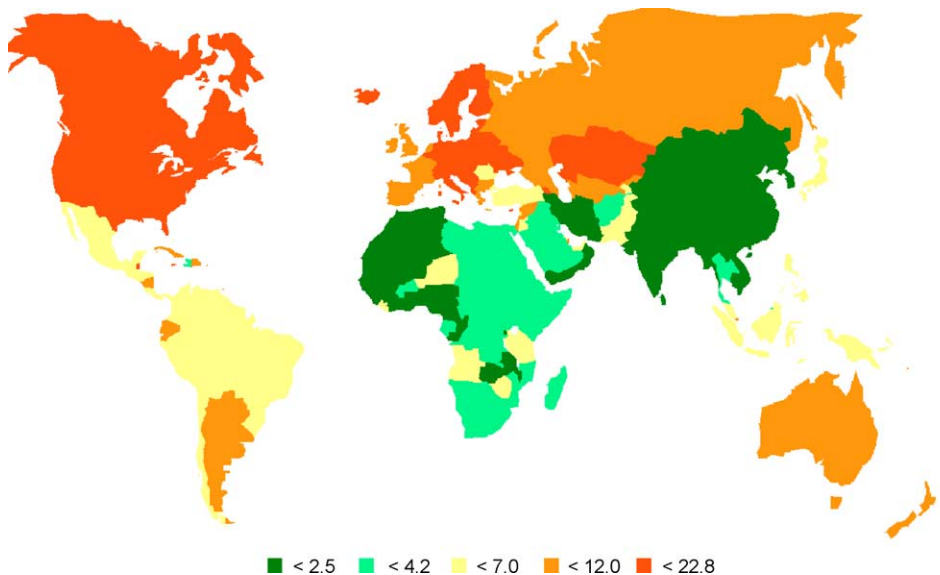

Figure 3. Incidence of cancer of the uterine body: age-standardised rates (world) per 100 000 (all ages).

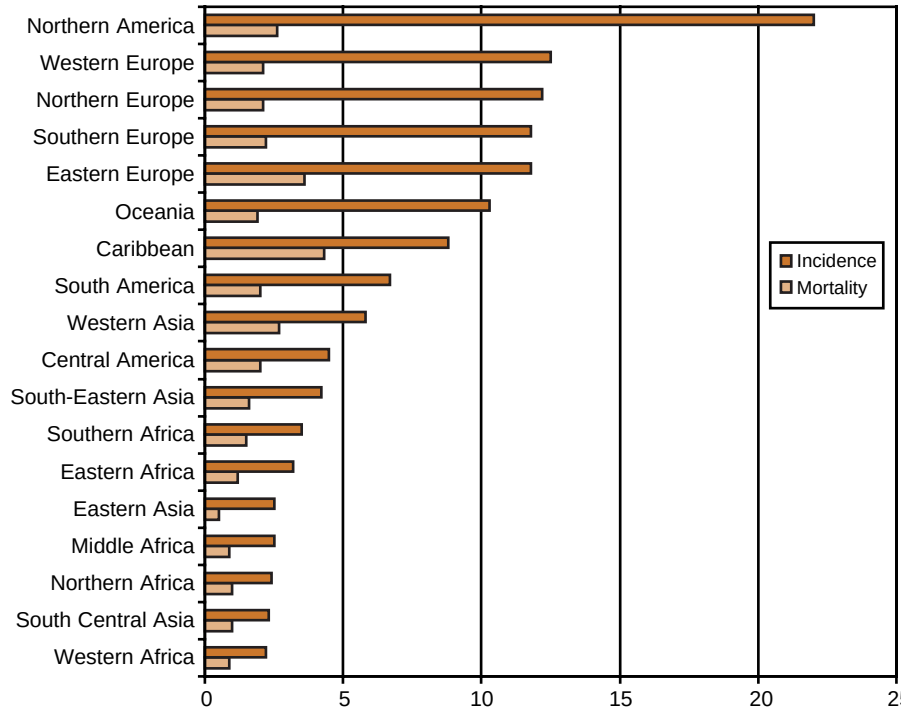

Figure 4. Cancer of the uterine body: age-standardised (world) incidence and mortality rates per 100 000 (all ages) in 18 world regions.

DISCUSSION

The estimates—the best possible information on global cancer burden—are more or less accurate for the different regions, depending on the extent and validity of the data available from those regions. The data indicate striking variations in the burden of different cancers, due to variations in exposure to suspected and established risk factors and wide disparity and inequality in healthcare infrastructure and accessibility between developed countries and the medically underserved less developed countries across the world.

Among the gynaecological cancers, cervical cancer offers a great potential for prevention, early detection and cure. Yet despite the slowly declining incidence rates, it remains the leading cause of cancer death for women in many developing countries due to lack of or inefficient existing screening programmes combined with a high background prevalence of HPV infection and high parity.[16–18] A low burden of disease is experienced in developed countries with screening programmes and in countries with strict religious regulation of sexual behaviour and a high prevalence of male circumcision (e.g. countries of the Middle East).

Persistent infection with one or more of the high-risk types of HPV types is now accepted as a necessary cause of cervical cancer and HPV DNA can be identified in

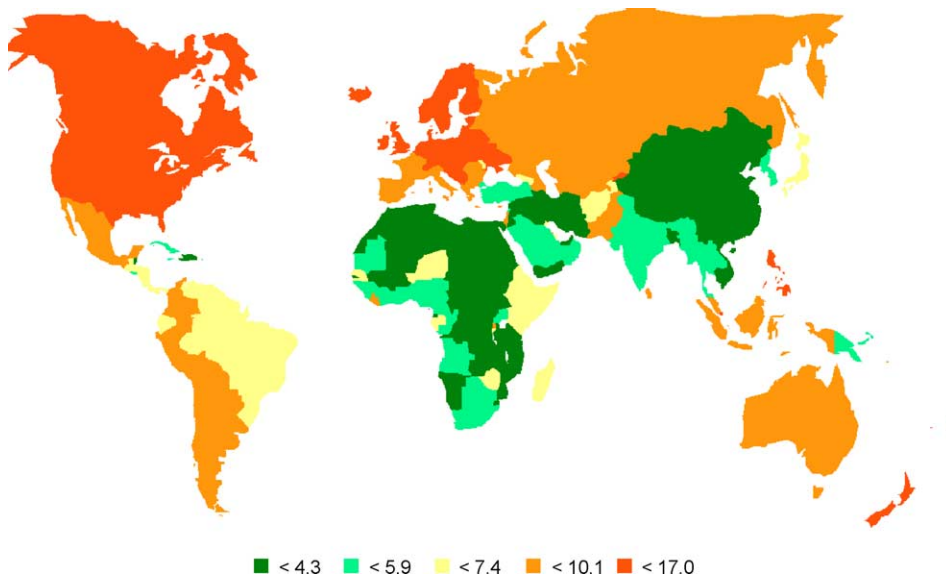

Figure 5. Incidence of ovarian cancer: age-standardised rates (world) per 100 000 (all ages).

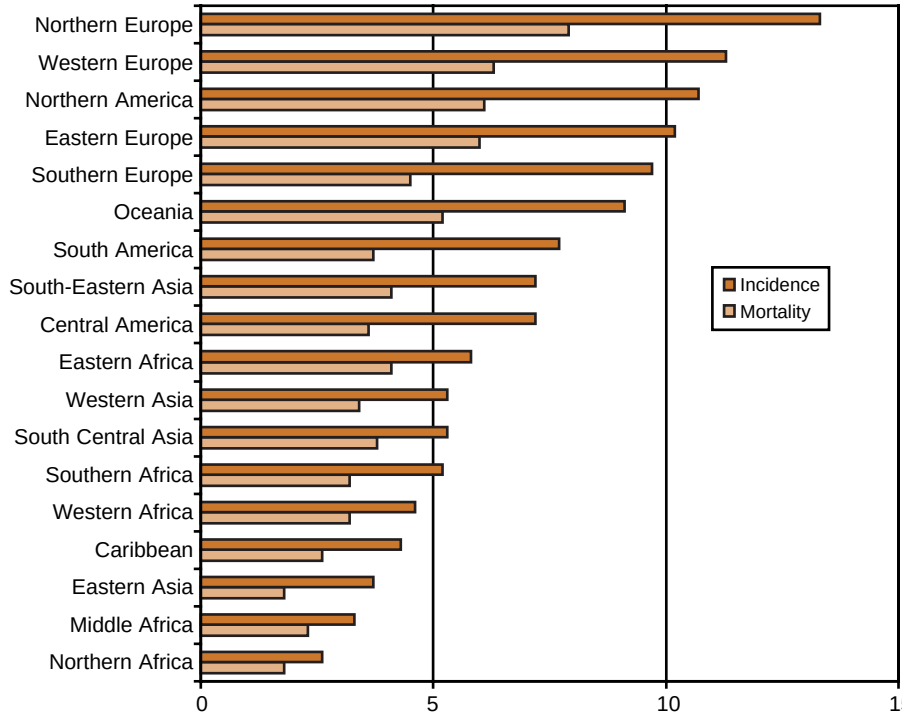

Figure 6. Cancer of the ovary: age-standardised (world) incidence and mortality rates per 100 000 (all ages) in 18 world regions.

more than 95% of cervical cancers.[18,19] The high risk associated with high parity and oral contraceptive use seem to be due to the hormonal influences that maintain the transformation zone on the ectocervix, facilitating exposure to HPV and other cofactors. A lower risk of HPV infection in circumcised than in uncircumcised males, with a corresponding lower incidence of cervical cancer in their female partners, has been reported.[20]

The central role of HPV infection in the causation of cervical neoplasia has led to efforts to evaluate prophylactic vaccination in preventing infection and cervical intraepithelial neoplasia (CIN) and evaluating HPV detection and typing in cervical screening. Large-scale HPV vaccine efficacy trials are now in progress with protection from the development of high-grade CIN as the primary endpoint.[21] The early results of trials indicate that vaccinated women were protected against persistent infection with HPV 16 and 18 and CIN induced by these viral types.[22–24] There is widespread optimism that a licensed HPV vaccine will be available within the next few years.[21]

Most HPV infections are transient but some women with persistent infections have an increased risk of developing high-grade CIN, one-third to a half of which will progress to cervical cancer over a period of 10–15 years. Prevention of cervical cancer by early detection and treatment of CIN currently offers the most cost-effective, long-term strategy for cervical cancer control.[16,17] Cytology screening is a viable option for medium-resourced countries only if they have the ability to meet the requirements for testing such as trained human resources, supplies, mechanisms for delivery of samples

and results, laboratory infrastructure, and the needed financial resources. A critical appraisal of reasons for the failure or suboptimal performance of cytology screening has led to the evaluation of alternative testing approaches such as visual inspection with acetic acid (VIA), visual inspection with Lugol's iodine (VILI) and HPV testing. Currently, several studies are addressing the prospects of introducing HPV testing in mass screening programmes in developed countries,[25] whereas recent studies in developing countries indicate that VIA and VILI are accurate screening tests to detect CIN and early invasive cancer.[26] Results from a randomised intervention trial in India comparing VIA, cytology and HPV testing indicate that all tests had similar detection rates of CIN 2–3 lesions.[27] Findings from the ongoing trials on the impact on disease burden are important for further conclusive evaluation of the HPV and visual screening tests in reducing disease burden.[27,28] A commendable global effort in the context of reducing disease burden in recent years has been the studies of the Alliance for Cervical Cancer Prevention (ACCP) supported by the Bill & Melinda Gates Foundation.[29]

A number of studies in developed countries indicate that the incidence of cervical adenocarcinoma is increasing while the overall incidence of cervical cancer is declining.[30,31] Although the impact of human immunodeficiency virus (HIV) infection on the risk of progression of CIN to invasive cancer is not clear, the high risk of HPV infection and CIN in HIV-positive women demands active surveillance of these women with pelvic examination and screening.

Oestrogenic stimulation produces cellular growth and glandular proliferation in the endometrial epithelium of the uterine body, which is balanced by the cyclical maturational effects of progesterone. Increased risk of endometrial cancer, associated with factors such as oral intake of oestrogens (without progestins), early menarche, late menopause, low parity, extended periods of anovulation and obesity can be related to chronic unopposed oestrogenic stimulation, leading to abnormal proliferation and neoplastic transformation of endometrial tissue. The association between long-term use of tamoxifen and endometrial cancer has been attributed to its oestrogen agonist properties, and women receiving tamoxifen should be monitored carefully. Diabetes mellitus and hypertension have also been associated with increased risk. High parity, late age at last birth, long-term use of combined oral contraceptives and physical activity have a protective effect. Increasing trends among postmenopausal women have been observed in developed countries; in premenopausal and perimenopausal women, endometrial cancer is relatively rare, and where long-term data are available, incidence is decreasing.[32] The continuing increases in obesity and decreases in fertility, however, forewarn that endometrial cancer, as a postmenopausal disease, will become a more important public health problem in future years.

Most ovarian cancers are diagnosed in advanced clinical stages with poor prospects of long-term survival, particularly in developing countries. Early detection and treatment should decrease mortality from this disease. Screening methods currently undergoing evaluation include transvaginal ultrasound scanning of the ovaries and measurement of the tumour-marker cancer antigen 125 (CA 125).[33,34] Routine screening for asymptomatic ovarian cancer is not currently recommended.[35] There has been a significant improvement in the 5-year survival rates over the last decades in developed countries due to a better definition of patterns of spread of the disease, improvements in surgical techniques and supportive care and more effective chemotherapy regimes.[36]

The relatively stable incidence of vulva cancer, despite a steady increase in the diagnosis of vulva intraepithelial neoplasia (VIN), suggests that effective treatment of VIN has prevented a significant increase in the incidence of invasive cancer in developed

countries. An association between HPV infection and vaginal cancer has been reported.[37] Rapid growth, a high frequency of metastases in the lungs, vagina, pelvis, liver and brain, as well as haemorrhage, make choriocarcinoma a medical emergency for which chemotherapy is highly effective. Treatment has dramatically improved the outcome for this disease that had previously resulted in the death of 60% of patients with localised and 90% with disseminated disease.

Early clinical diagnosis and multidisciplinary treatment involving surgery, radiotherapy and chemotherapy are important in reducing mortality from gynaecological cancers. Early clinical diagnosis and prompt treatment improves outcome from gynaecological cancers. The death rates from cervical cancer had began to decline before the implementation of cytology screening programmes, possibly due to improved awareness, early clinical recognition of disease and prompt treatment, among other factors.[38,39] Survival rates suggest that early gynaecological cancers have an excellent prognosis even in low- and medium-resource settings.[9–11] Day-to-day translation of cancer management plans require adequate healthcare infrastructure for diagnosis and treatment as well as adequate trained human and financial resources. The health services infrastructure for diagnosis and management of cancers is poorly developed in many developing countries, and particularly in sub-Saharan Africa.[40] For instance, histopathology services are not available or are very limited in more than 20 African countries where cancer surgery facilities are also extremely limited.[40] In 32 countries in Africa with populations of >157 million, no radiotherapy services are available.[41] There are only 155 radiotherapy machines in the entire African continent, which is less than the number of radiotherapy machines in Italy alone.[41] The availability of radiotherapy services in many Asian countries also seems to be suboptimal.[42] Trained human resources in cancer diagnosis and management are distinctly inadequate in many regions. Training programmes to generate such resources either do not exist or are strikingly limited in many countries.

Hospital cancer registry data from five premier cancer hospitals in different regions of India indicated that 12–37% of cervical cancer patients were not prescribed, or did not complete, the prescribed treatment.[43]

SUMMARY

Approximately one out of six cancer cases among women in the world is a gynaecological cancer. Whereas cervical cancer is the most common gynaecological cancer in developing countries, endometrial cancer is the most common in developed countries. Although mortality from cervical cancer is potentially entirely avoidable by current technologies, it still accounts for half of the global gynaecological cancer burden due to lack of effective screening in low- and medium-resource countries. Implementation of current developments in screening has the potential to dramatically reduce the burden of this cancer. Prophylactic vaccination holds promise for cervical cancer prevention in the future. The treatment outcomes in gynaecological cancer can be improved by early clinical detection and appropriate treatment. The differences in the outcome of cancer treatment across the world are due to vast disparities in health service infrastructures, human resources, service delivery and accessibility to services. A significant proportion of patients, in many countries, are unable to access and avail themselves of (or complete) preventive, diagnostic and therapy services because of

inadequate healthcare services and financing. Creating awareness among the public and professionals is conducive for early detection. Advocacy and the political will to invest in the development of human resources and healthcare infrastructure hold the key for effective gynaecological cancer control and reducing the burden of disease in several regions of the world. A National Cancer Control Programme (NCCP), as advocated by the WHO, provides a suitable and realistic framework to improve cancer preventive and management services in general.[44]

Practice points

- documenting the primary site of cancer, accurate clinical staging and treatment in medical records helps to quantify cancer burden and progress in cancer control
- documenting the underlying cause of death accurately in the death certificates helps to evaluate the outcome of cancer treatment and cancer control
- regular auditing of medical records and facilitating data collection by cancer registries can improve accuracy and validity of cancer statistics

Research points

- establishing population-based cancer registries in countries/regions with no or inadequate coverage will improve the accuracy and validity of data on global cancer burden
- estimating population-based cancer survival data will help to evaluate and improve the efficiency of cancer health services in medically underserved countries/regions

ACKNOWLEDGEMENTS

The authors thank Mrs Evelyn Bayle for her help in preparing this manuscript.

REFERENCES

*1. Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2002. Cancer Incidence, Mortality and Prevalence Worldwide. IARC Cancer Base No. 5 Version 2.0. Lyon: IARC Press; 2004.
*2. Parkin DM, Bray F, Ferlay J & Pisani P. Global cancer statistics, 2002. *CA:A Cancer Journal for Clinicians* 2005; **55:** 74–108.
3. Parkin DM, Bray FI & Devessa SS. Cancer burden in the year 2000. The global picture. *European Journal of Cancer* 2001; **37:** S4–S66.
4. Pisani P, Bray F & Parkin DM. Estimates of the worldwide prevalence of cancer for 25 sites in the adult population. *International Journal of Cancer* 2002; **97:** 72–81.
*5. Armstrong BK. The role of the cancer registry in cancer control. *Cancer Causes Control* 1992; **3:** 569–579.
*6. Parkin DM, Whelan SL & Ferlay J et al (eds.) *Cancer Incidence in Five Continents*, vol. VIII. Lyon: IARCPress, 2002 [IARC Scientific Publication No.155].

7. Ries LAG, Eisner MP, Kosary CL, et al. (eds). SEER Cancer Statistics Review, 1975–2001. Bethesda, MD: National Cancer Institute; 2004. Available at: http://seer.cancer.gov/csr/1975_2001/. Accessed December 22, 2004.
8. The EUROCARE working group. EUROCARE-3: survival of cancer patients diagnosed 1990-94 — results and commentary. *Annals of Oncology* 2003; **14:** v61–v118.
9. Sankaranarayanan R, Black RJ & Parkin DM (eds.) *Cancer Survival in Developing Countries, IARC Scientific Publications No.15*. Lyon: IARCPress, 1988.
10. Sankaranarayanan R, Swaminathan R & Black RJ. Global variations in cancer survival. *Cancer* 1996; **78:** 2461–2464.
11. Chia KS, Du WB, Sankaranarayanan R et al. Population-based cancer survival in Singapore, 1968 to 1992: an overview. *International Journal of Cancer* 2001; **93:** 142–147.
12. Gondos A, Chokunonga E, Brenner H et al. Cancer survival in a Southern African urban population. *International Journal of Cancer* 2004; **112:** 860–864.
13. Gondos A, Brenner H, Wabinga H et al. Cancer survival in kampala, Uganda. *British Journal of Cancer* 2005; **92:** 1808–1812.
14. Gustafsson L, Ponten J, Bergstrom R & Adami HO. International incidence rates of invasive cervical cancer before cytological screening. *International Journal of Cancer* 1997; **71:** 159–165.
*15. Altieri A, Franceschi S, Ferlay J et al. Epidemiology and aetiology of gestational trophoblastic diseases. *The Lancet Oncology* 2003; **4:** 670–678.
16. Sankaranarayanan R, Budukh A & Rajkumar R. Effective screening programs for cervical cancer in low- and middle-income developing countries. *Bulletin of the World Health Organization* 2001; **79:** 954–962.
*17. IARC Handbooks of Cancer Prevention, vol. 10. Cervix Cancer Screening. Lyon: IARCPress; 2005.
18. Bosch FX & de Sanjose S. Human papillomavirus and cervical cancer burden and assessment of causality. *Journal of the National Cancer Institute Monographs* 2003; **31:** 3–13.
19. Munoz N, Bosch FX, de Sanjose S et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *The New England Journal of Medicine* 2003; **348:** 518–527.
20. Castellsague X, Bosch FX, Munoz N et al. Male circumcision, penile human papillomavirus infection, and cervical cancer in female partners. *The New England Journal of Medicine* 2002; **346:** 1105–1112.
*21. Schiller JT & Davies P. Delivering on the promise: HPV vaccines and cervical cancer. *Nature Reviews Microbiology* 2004; **2:** 343–347.
22. Koutski LA, Ault KA & Wheeler CM. A controlled trial of a human papillomavirus type 16 vaccine. *The New England Journal of Medicine* 2002; **347:** 1645–1651.
23. Harper DM, Franco EL & Wheeler CM. Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomized controlled trial. *Lancet* 2004; **364:** 1757–1765.
24. Villa LL, Costa RR & Petta CA. Prophylactic quadrivalent human papillomavirus (types 6,11,16 and 18) L1 virus-like particle vaccine in young women: a randomized double-blind placebo-controlled multicentre phase II efficacy trial. *The Lancet Oncology* 2005; **6:** 271–278.
25. Franco EL. Primary screening of cervical cancer with human papillomavirus tests. *Journal of the National Cancer Institute Monographs* 2003; **31:** 89–96.
26. Sankaranarayanan R, Gaffikin L, Jacob M et al. A critical assessment of screening methods for cervical neoplasia. *International Journal of Gynaecology and Obstetrics* 2005; **89:** S4–S12.
27. Sankaranarayanan R, Nene BN, Dinshaw KA et al. A cluster randomised controlled trial of visual, cytology and HPV screening for cancer of the cervix in rural India. *International Journal of Cancer* 2005; [Epub ahead of print].
28. Sankaranarayanan R, Rajkumar R, Theresa R et al. Initial results from a randomized trial of cervical visual screening in rural south India. *International Journal of Cancer* 2004; **109:** 461–467.
*29. Alliance for cervical cancer prevention (ACCP). Planning and implementing cervical cancer prevention and control programs: a manual for managers. Seattle: ACCP; 2004.
30. Vizcaino AP, Moreno V, Bosch FX et al. International trends in the incidence of adenocarcinoma and adenosquamous carcinoma. *International Journal of Cancer* 1998; **75:** 536–545.
31. Smith HO, Tiffany MF, Qualis CR et al. The rising incidence of adenocarcinoma relative to squamous cell carcinoma in the United States-a 24-year population-based study. *Gynecologic Oncology* 2000; **78:** 97–105.

*32. Bray F, Dos Santos Silva I, Moller H & Weiderpass E. Endometrial cancer incidence trends in Europe: underlying determinants and prospects for prevention. *Cancer Epidemiology, Biomarkers and Prevention* 2005; **14:** 1132–1142.
33. Kramer BS, Gohagen J, Prorok PC & Smart C. A national cancer institute sponsored screening trial for prostatic, lung, colorectal, and ovarian cancers. *Cancer* 1993; **71:** 589–593.
34. Jacobs IJ, Skates SJ, Mac Donald N et al. Screening for ovarian cancer: a pilot randomized controlled trial. *Lancet* 1999; **353:** 1207–1210.
35. U.S. preventive services task force. screening for ovarian cancer: brief evidence update; May 2004. agency for healthcare research and quality, rockville, MD. http://www.ahrq.gov/clinic/3rduspstf/ovariancan/ovcanup.htm.
36. Jemal A, Murray T, Samuels A et al. Cancer Statistics 2003. *CA: A Cancer Journal for Clinicians* 2003; **50:** 5–26.
37. IARC monographs on the evaluation of carcinogenic risks to humans. Human papillomaviruses. IARC Monographs Lyon: IARCPress; 1995. vol. 64.
38. Wingo PA, Tong T & Bolden S. Cancer Statististics 1995. *CA:A Cancer Journal for Clinicians* 1995; **45:** 8–30.
39. Ponten J, Adami HO & Bergstrom R. Strategies for global control of cervical cancer. *International Journal of Cancer* 1995; **60:** 1–26.
*40. Stewart BW & Kleihues P. *World Cancer Report*. Lyon: IARC Press; 2003.
41. Levin CV, El Gueddari B & Meghzifene A. Radiation therapy in Africa: distribution and equipment. *Radiotherapy and Oncology* 1999; **52:** 79–84.
42. Tatsuzaki H & Levin CV. Quantitative status of resources for radiation therapy in Asia and Pacific region. *Radiotherapy and Oncology* 2001; **60:** 81–89.
43. National Cancer Registry Programme. *Five-Year consolidated report of the hospital cancer registries 1994–1998 An Assessment of the Burden and Care of Cancer Patients*. New Delhi: Indian council of medical research; 2002 p. 90–95.
44. World Health Organization. National cancer control programmes: policies and managerial guidelines, 2nd edn, Geneva; 2002.