Chapter 1

Epidemiology of Gynaecological Cancers

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Epidemiological Understanding

Epidemiology is the basic science underpinning public health and clinical medicine. It describes the occurrence of health-related states or events (incidence, prevalence), quantifies the risk of disease (relative risk, attributable risk, odds ratio) and its outcome (prognosis, survival, mortality), and postulates causal mechanisms for disease in populations (aetiology, prevention). The main function of epidemiology is to provide evidence to guide public health policy and clinical practice to protect, restore, and promote health of individuals and populations.

Public health is the collective and organised action by the society to improve the health of populations. This involves collaborative working between doctors, nurses, engineers, environmental scientists, health educators, social workers, nutritionists, administrators, and an effective partnership with non-governmental organisations (NGOs), corporations, and all levels of the government.

The applications of epidemiology in public health and clinical practice can be summarised as follows:

- **To describe the spectrum and extent of disease in the population** – e.g. what is the prevalence of human papilloma virus (HPV) infection among young girls?
- **To identify factors that increase or decrease the risk of disease** – e.g. what factors increase the risk of, or protect against, endometrial cancer?
- **To study the natural history and prognosis of disease** – e.g. does early diagnosis of cervical intraepithelial neoplasia (CIN) through cytological screening prevent future morbidity and improve survival?
- **To monitor and predict disease trends in the population** – e.g. what impact will the increasing prevalence of obesity in women have on future disease trends and healthcare needs?
- **To provide evidence for developing public health policy and making regulatory decisions** – e.g. will a smoking ban in public places promote smoking cessation and reduce the incidence of smoking-related disease?
- **To evaluate the efficacy of preventive and therapeutic interventions** – e.g. does postmenopausal hormone replacement therapy (HRT) do more harm than good?
- **To evaluate public health programmes** – e.g. will vaccination of schoolgirls against oncogenic HPV prevent vulvar/vaginal/cervical cancers and save lives?
- **To evaluate the effectiveness of health services** – e.g. are known contacts of persons with sexually transmitted diseases (STDs) followed up and treated?

Classification of Gynaecological Cancers

The *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) is the global standard diagnostic classification for epidemiological, clinical, and health service data. It is used by hospital records departments, cancer registries, and government agencies responsible for collection of health statistics (e.g. the Office for National Statistics in the United Kingdom) to classify diseases and other health problems recorded on many types of health and vital records. The ICD is essential for compilation of morbidity (e.g. cancer incidence) and mortality statistics (e.g. underlying cause of death) and allows comparison at an international level of health data collected in different countries at different times. In the tenth revision of the ICD (ICD-10, version 2016), malignant neoplasms of female genital organs are coded from C51 to C58. The category C57 (malignant neoplasm of other and unspecified female genital organs) includes neoplasms of the fallopian tube, broad and round ligaments, parametrium, uterine adnexa, and overlapping lesions (e.g. tubo-ovarian, utero-ovarian) (Table 1.1).

Table 1.1 ICD-10 codes and morphological classification of malignant neoplasms of female genital organs

ICD-10 code	Organ	Morphological subtypes
C51	Vulva	Squamous cell carcinoma
		Extramammary Paget's disease
		Malignant melanoma
C52	Vagina	Squamous cell carcinoma
		Adenocarcinoma
		Botryoid rhabdomyosarcoma
C53	Cervix uteri	Squamous cell carcinoma
		Neuroendocrine carcinoma
		Adenocarcinoma
C54	Corpus uteri	Endometrial adenocarcinoma
		Malignant mixed Müllerian tumours
		Leiomyosarcoma
C55		Uterus (part unspecified)
C56	Ovary	Surface epithelial tumours
		Serous adenocarcinoma
		Endometrioid adenocarcinoma
		Mucinous adenocarcinoma
		Clear cell carcinoma
		Germ cell tumours
		Dysgerminoma
		Yolk sac tumour
		Choriocarcinoma
		Mature and immature teratoma
		Sex cord-stromal tumours
		Granulosa cell tumour
		Sertoli–Leydig cell tumour
C57		Other and unspecified female genital organs
C58	Placenta	Hydatidiform mole
		Placental site trophoblastic tumour
		Choriocarcinoma

The *International Classification of Diseases for Oncology* (ICD-O-3) is used principally by cancer registries for coding the site (topography) and the histology (morphology) of the neoplasm, usually obtained from a pathology report.

The *Tumour Node Metastasis Classification of Malignant Tumours* (TNM-8) is an international standard cancer staging system used for describing the anatomical extent and progression of cancer. It is based on the assessment of three components:

T – describes the extent of the primary tumour

N – describes the absence/presence and extent of the regional lymph node involvement/metastasis

M – describes the absence/presence of distant metastasis.

The classification is used to: (i) aid the clinician in the planning and management of treatment; (ii) assist in evaluation of the results of treatment; (iii) provide some indication of individual prognosis;

(iv) facilitate the exchange of information between clinicians/treatment centres; (v) inform and evaluate treatment guidelines, national cancer planning and research; and (vi) evaluate population-based screening and early detection programmes. The TNM system is approved by the International Federation of Gynaecology and Obstetrics (FIGO), and its categories have been defined to correspond to the FIGO classification.

Measuring the Risk or Burden of Gynaecological Cancers

Incidence

Incidence (or *incident cases*) is a count of *new cases* of cancer in the population during a specified time period. The incidence rate is the number of *new cases* of cancer in a defined population within a specified time period (usually a calendar year), divided by total number of persons in that population. Cancer incidence rates in adults are typically expressed as per 100,000 population.

Incidence rate measures the rapidity (or 'speed') of the occurrence of new cases of cancer in the population within a time period. Increase in incidence of a cancer in the population can be due to a variety of factors, which may include: in-migration of susceptible people, a change in diagnostic criteria, improved case ascertainment, introduction of a new screening/diagnostic test, introduction of new, or changes in exposure to existing (e.g. enhanced transmission of HPV), infectious/aetiologic agent(s). Incidence rate is used to:

- predict the average risk (probability) of developing cancer
- research the causes and treatment of cancer
- describe trends of cancer over time
- evaluate the effectiveness of primary prevention and early detection and/or population-based screening (secondary prevention) programmes
- inform and guide health planning, resource allocation and commissioning of clinical and community-based services.

Age-Standardised Incidence (or Mortality) Rate

As the risk of cancer increases exponentially with age, the crude incidence rate (which is influenced by the population age structure) cannot be used to evaluate whether the risk/burden of cancer differs between populations. It is therefore necessary to use age-standardised incidence (or mortality) rates (ASRs) when comparing incidence rates between populations that have different age structures (e.g. the United Kingdom and India). The ASR is obtained by applying the (crude) age-specific rates in the observed population to the age-specific population counts (or weights) of a fixed reference (or standard) population. The most commonly used standard population is the *world* (and also *European*) *standard population* proposed by Sir Richard Doll – the eminent epidemiologist who discovered the main hazards of smoking. Age-standardisation controls for the confounding effect of age on cancer incidence and therefore allows a more direct comparison between different populations.

Cumulative Incidence (or Cumulative Risk)

Cumulative incidence is the probability or risk of developing cancer during a specified period (e.g. lifetime). It measures the number or proportion of people (out of 100 or 1,000) who would be expected to develop a particular cancer by the age of 64 (or 74) if they had the rates (i.e. risk) of cancer currently observed. Like the ASR, cumulative incidence permits comparisons between populations of different age structures. For example, the cumulative incidence of a woman in England developing ovarian cancer by age 74 is about 15/1,000, which can be interpreted as 1.5% (1 in 67) probability or (lifetime) risk of developing ovarian cancer by the time she completes 74 years.

Prevalence

Prevalence is the number of *existing cases* of cancer in a defined population at a notional point in time, divided by the total number of people in the population at that time. It is usually expressed as an absolute number of existing cases or as the proportion of a population with the disease. For example, the prevalence of cervical cancer can be defined as the number of women in a defined population who have been diagnosed with cancer, and who are still alive at a given point in time. Prevalence is a function of both the incidence of the disease and survival.

TIPS

Mathematically prevalence can be defined as follows:

$$\text{Prevalence} = a/a + b$$

where *a* is the number of individuals in the population with the disease at a given time and *b* is the number of individuals in the population without the disease at a given time.

Therefore prevalence is a measure of the burden of cancer in the population, and it is most useful for describing diseases with a gradual onset and long duration. Increase in prevalence of a cancer in the population can be due to a variety of factors, which may include in-migration of cases, increase in incidence, and/or improved prognosis/survival (e.g. due to better treatment). Prevalence data are used for

- health planning, resource allocation and commissioning of clinical and community-based services
- estimation of cancer survivorship
- organisation of prevention programmes.

Partial (or limited duration) prevalence is the estimation of the number of cases of cancer diagnosed within 1, 3, and 5 years to indicate the number of patients undergoing initial treatment (cases within 1 year of diagnosis), clinical follow-up (within 3 years), or not considered cured (before 5 years). Patients alive 5 years after diagnosis are usually considered cured because, for most cancers, the death rates of such patients are similar to those in the general population.

Complete prevalence represents the proportion of patients alive on a certain day who previously had a diagnosis of cancer, regardless of how long ago the diagnosis was, still under treatment, or are considered cured.

Survival

Survival is the proportion (or percentage) of people still alive 1, 3, 5, and 10 years after they have been diagnosed with cancer. This *observed* survival probability is influenced by mortality both from the cancer itself and from other causes. For this reason, relative survival (%) is usually calculated (ratio of the observed survival in a particular group of patients to the survival expected in a group of people in the general population).

Quality-Adjusted Life-Years (Lost)/ Disability-Adjusted Life-Years (Lost)

Quality-adjusted life-years (QALYs) and disability-adjusted life-years (DALYs) quantify the spectrum of morbidity (between the diagnosis and cure/death) due to cancer in terms of its duration and severity. The calculation of these indices requires three elements:

1. the incidence of cancer
2. its mean duration (survival probability) and
3. a measure of life 'quality' between the diagnosis and cure/death.

These indices are used to estimate the impact of cancer on the individual and society and to establish priorities for healthcare programmes.

Mortality

Mortality is the number of deaths occurring, and the mortality rate is the number of deaths in a defined population within a specified time period (usually a calendar year), divided by total number of persons in that population. Cancer mortality rates are typically expressed as per 100,000 persons per year. Mortality is the product of the incidence and the fatality of a given cancer, and measures the average risk to the population dying from a specific cancer within a specified period. Fatality, the complement of per cent survival, is the probability (%) that a cancer patient will die from the disease.

Cancer Screening

Definition

Screening is the presumptive identification (detection) of an unrecognised or hidden disease or defect by the application of tests, examinations or other procedures that can be applied rapidly.

Cancer screening is the testing of apparently healthy volunteers from the general population for the purpose of separating them into high and low probabilities of having a specific cancer. The rationale behind cancer screening is that the disease has a natural history (i.e. phases of pathological progression/cellular transformation) that includes a clearly defined preclinical phase with biological characteristics, which allows for detection of the disease in an early (presumably) treatable stage that, in turn, will reduce the risk of future morbidity and improve survival. For example, cytological screening can detect preinvasive cervical disease, which if followed by treatment can be possibly cured, thereby reducing the risk of invasive cervical cancer. Randomised controlled trials and both case–control and cohort observational study designs are used to evaluate cancer screening programmes.

Screening Test Performance

The performance of a screening test is based on its sensitivity, specificity, and predictive value (Table 1.2).

Table 1.2 Calculation of sensitivity, specificity, and predictive value of a screening test

		Disease according to gold standard		
		Present	**Absent**	**Total**
Screening test result	Positive	A (True +)	B (False +)	A + B
	Negative	C (False –)	D (True –)	C + D
	Total	A + C	B + D	A + B + C + D

Sensitivity = A/(A + C) × 100 (%).
Specificity = D/(B + D) × 100 (%).
Positive predictive value = A/(A + B) × 100 (%).
Negative predictive value = D/(C + D) × 100 (%).
Prevalence of disease = A + C/(A + B + C + D) × 100 (%).

- **Sensitivity** – this is the ability of the test to identify correctly those who *have* the disease (true positives).
- **Specificity** – this is the ability of the test to identify correctly those who *do not have* the disease (true negatives).
- **Predictive value positive (PVP)** – this is the proportion of individuals who test *positive* and actually have the disease. PVP is a function of sensitivity, specificity and prevalence of the detectable preclinical phase. A high PVP is essential for a successful population-based screening programme (e.g. cervical cancer), whereas a low PVP implies that resources are being wasted on diagnostic follow-ups of false-positive individuals.
- **Predictive value negative (PVN)** – this is the proportion of individuals who test *negative* and actually do not have the disease.

Ovarian Cancer

Incidence and Mortality

Ovarian cancer is the seventh most common cancer among women worldwide, with an estimated 239,000 new cases (3.6% of cancer in women) and 152,000 deaths (4.3% of cancer deaths in women) in the year 2012, and a 5-year prevalence of 587,000 cases (3.4% of women with cancer). The incidence rates of ovarian cancer vary from a low of about 2/100,000 women in Tanzania to a high of 14/100,000 in Latvia. In general, incidence rates are relatively higher in developed countries – the highest rates (10–14/100,000 women) are observed in European populations, intermediate rates (7–10/100,000 women) are observed in North America, Australia/New Zealand, and some populations in Asia and the lowest rates (2–7/100,000 women) are observed in Africa, South America, the Caribbean, the Middle East, and parts of Asia. Data from the United Kingdom and the United States suggest that ovarian cancer is relatively more common in White than in Asian or Black women. In the United Kingdom, incidence rates for White women range from 17 to 18/100,000, rates for Asian women range from 9 to 16/100,000 and rates for Black women range from 7 to 12/100,000.

In the United Kingdom, ovarian cancer is the second most common gynaecological cancer (after uterine cancer). It is the sixth most common cancer among women, with about 7,400 new cases in the year 2014 accounting for around 4% of all cancers in women, with a cumulative risk of 1.5% (1 in 67) by age 74 (Figure 1.1). In most European populations, the incidence rates of ovarian cancer generally increase exponentially with age, with a sharp increase after about 40 years of age. It is predominantly a disease of older, postmenopausal women: about 82% of cases occur in women aged over 50 years (Figure 1.2). In 2014, 4,100 women in the United Kingdom died from ovarian cancer, accounting for around 5% of female deaths from cancer. Ovarian cancer has a relatively poor prognosis as the large majority of cases are diagnosed at an advanced stage; overall, about 35% of women diagnosed with ovarian cancer survive their disease for 10 or more years. When diagnosed at its earliest stage (Stage 1), 9 in 10 (90%) women will survive their disease for 5 or more years, compared to 5-year relative survival of 3% for those diagnosed at Stage IV. In the United Kingdom, ovarian cancer survival has been

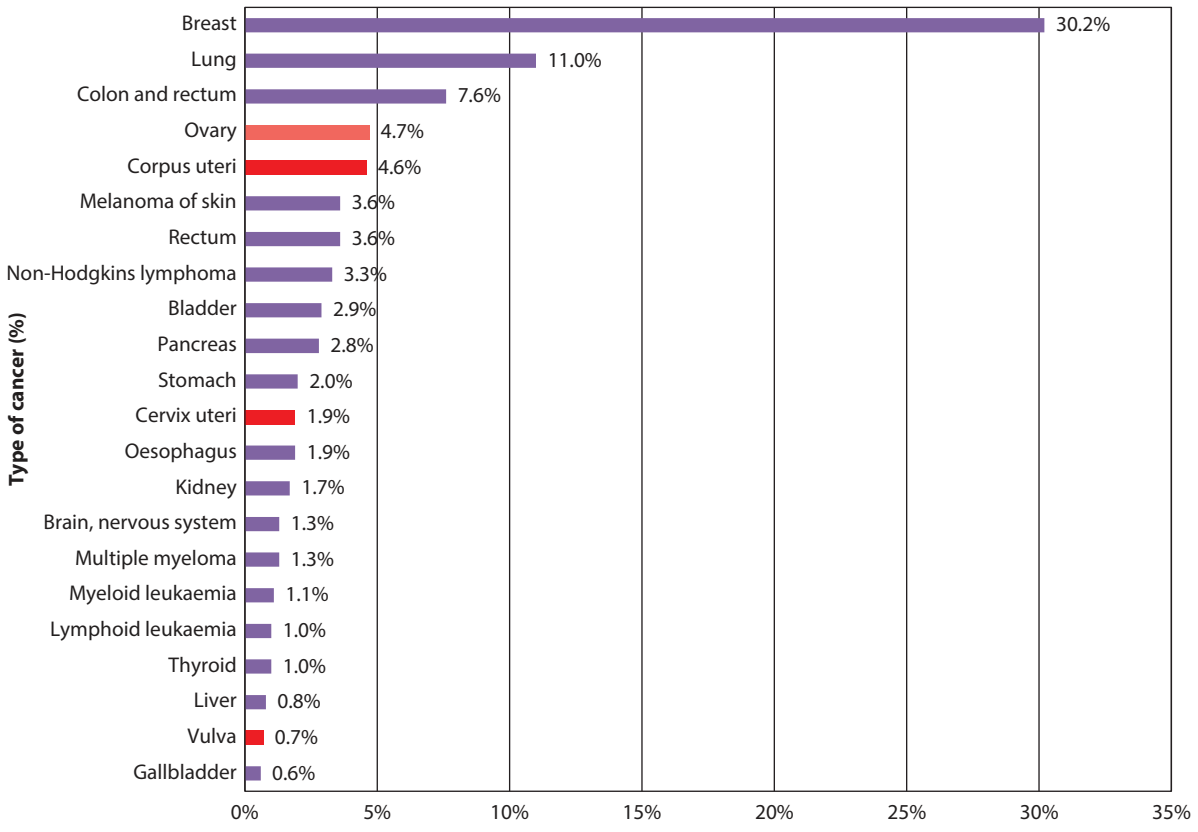

Figure 1.1 Frequency distribution (%) of the 22 most common cancers in women, England 2003–7
Source: *Cancer Incidence in Five Continents* Vol. X, IARC, 2013

steadily improving and has almost doubled in the last 40 years.

Trends in Incidence and Mortality

In most developed countries, there has been little change in the incidence of ovarian cancer over the past 40 or more years. In the United Kingdom, the incidence rates have remained stable since the early 1990s (22.9/100,000 in 1993; 23.3/100,000 in 2014), with a small (4%) decline in the last decade. In most populations, mortality rates have remained fairly stable or declined slightly over the past 40 years. In the United Kingdom, the ASRs (European standard) have decreased by about 20% in women between 2000 and 2014 (from 16 to 13/100,000 women).

Aetiology

Compared with other gynaecological cancers, little is known about the aetiology of ovarian cancer. In most studies, family history of ovarian cancer, smoking, use of HRT, and body fatness have been associated with an increased risk, while states of anovulation (i.e. use of combined oestrogen–progestogen oral contraceptives, pregnancy), breastfeeding, tubal ligation, and hysterectomy have been associated with decreased risk.

Prevention

Apart from prophylactic oophorectomy, oral contraception, and (possibly) tubal ligation or salpingectomy, there are few readily modifiable risk factors for ovarian cancer. There is currently inconsistent evidence for a possible increase in risk with consumption of lactose/galactose-containing foods, saturated or animal fat intake, perineal talcum powder use and postmenopausal HRT and for a decrease in risk with vegetable intake. It is unclear whether obesity, body mass index (BMI) or physical activity influences ovarian cancer risk. It has been estimated that about 21% of ovarian cancer cases

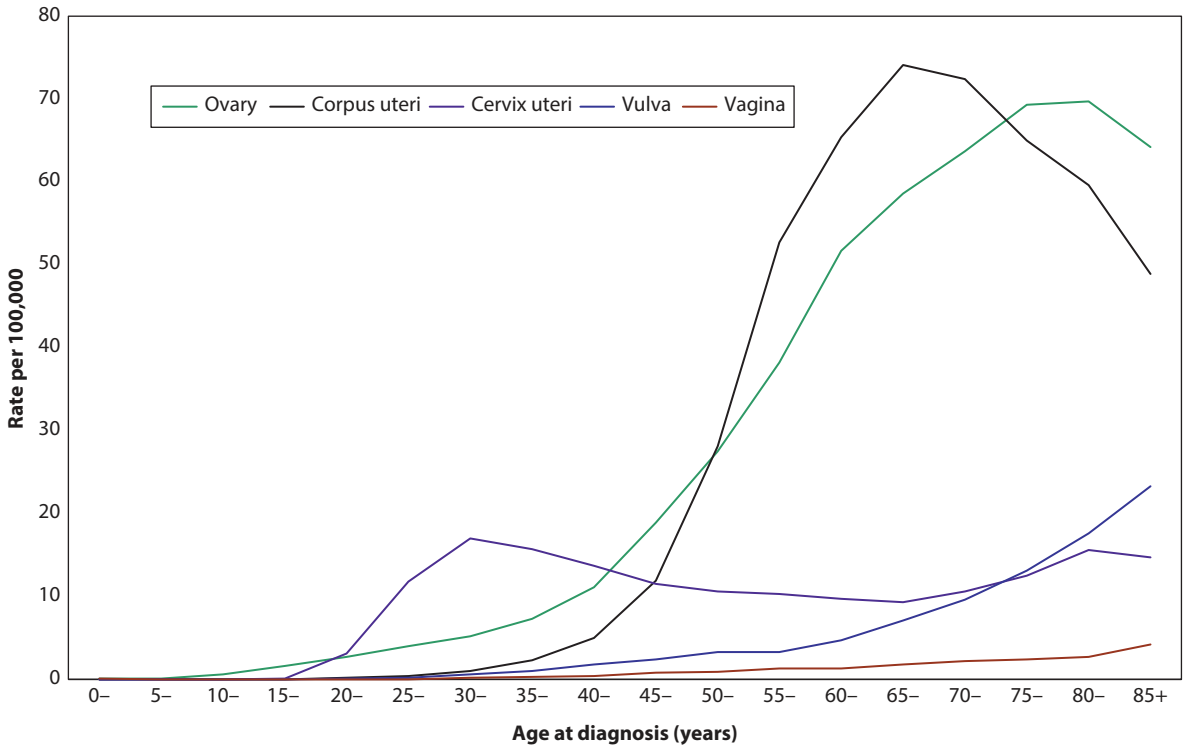

Figure 1.2 Age-specific incidence rates of gynaecological cancers, England 2003–7
Source: Cancer Incidence in Five Continents Vol. X, IARC, 2013

in the United Kingdom can be prevented by changes in lifestyle and risk factor modification.

Endometrial Cancer

Incidence and Mortality

Endometrial cancer is the fifth most common cancer among women worldwide, with an estimated 320,000 new cases (4.8% of cancer in women) and 76,000 deaths (2.1% of cancer deaths in women) in the year 2012, and a 5-year prevalence of 1,217,000 cases (7.1% of women with cancer). In contrast with cervical cancer, endometrial cancer is relatively more common in developed countries with incidence rates more than double those of the less developed countries (14.7/100,000 vs 5.5/100,000). In the United Kingdom, endometrial cancer is the most common gynaecological cancer. It is the fourth most common cancer among women, with about 9,300 new cases in the year 2014 accounting for around 5% of all cancers in women, with a cumulative risk of 1.7% (1 in 59) by age 74 (Figure 1.1). There is no significant variation in the incidence of endometrial cancer by ethnicity in the United Kingdom. About 70% of the cases in the United Kingdom are diagnosed at Stage I. In most European and North American populations, the incidence rates of endometrial cancer begin to rise steadily 5–10 years before the menopause and reach a peak usually around the age of 70 years. It is essentially a cancer of postmenopausal women; over 90% of cases occur in women aged 50 or older, and very few cases are diagnosed under the age of 35 (Figure 1.2). The incidence rates of endometrial cancer vary from a low of 1.5/100,000 women in Algeria to a high of 26.7/100,000 women in Armenia. The highest rates are observed among women in North America, Europe, Australia/New Zealand, and Israel. Incidence rates are generally much lower in most countries in Latin America, Asia, and Africa. In developed countries, the mortality rates of endometrial cancer are substantially lower than the incidence rates (2.3/100,000 vs 14.7/100,000).

In 2014, about 2,200 women in the United Kingdom died from endometrial cancer, accounting for around

3% of female deaths from cancer. Endometrial cancer has a relatively better prognosis than ovarian and cervical cancers. Overall, about 78% (8 in 10) of women diagnosed with endometrial cancer survive their disease for 10 or more years. Five-year relative survival ranges from 95% at Stage I to 14% at Stage IV. In the United Kingdom, endometrial cancer survival has been steadily improving over the past 40 or more years.

Trends in Incidence and Mortality

In the United Kingdom, there has been a steady increase (by 63%) in the incidence of endometrial cancer since the early 1990s; the largest increase (89%) has been observed in women aged 70–9. The ASRs in the United Kingdom declined by 27% between 1971–3 (7.0/100,000) and 1997–9 (5.1/100,000) and then increased by 27% between 1997–9 and 2012–14 (6.5/100,000).

Aetiology

In contrast with cervical cancer, which is a model of viral carcinogenesis, endometrial cancer is a model of hormonal carcinogenesis. The 18-fold variation in ASRs across populations points to the role of modifiable factors in the aetiology of endometrial cancer. Among these, oestrogens and progestins are considered to play an important role in malignant transformation. Exposure to excessive oestrogen of endogenous as well as exogenous origin entailing continued/chronic stimulation of the endometrium is considered to be the main factor in this transformation and this is perhaps a common denominator for most of the established hormonal and reproductive risk factors (Table 1.3). The most compelling evidence has come from studies of HRT following the menopause; exposure to unopposed oestrogen for 10 or more years increases the risk about 10-fold. This excess risk can be counteracted substantially by combined use of oestrogens and progestins.

Prevention

Obesity (which increases peripheral production of oestrogens) and diabetes mellitus are associated with an increased risk of developing endometrial cancer, whereas past oral contraceptive use, childbearing and physical activity (potentially mediated by hormones) are associated with risk reduction. It is therefore possible to substantially reduce the incidence of endometrial cancer through modification of lifestyle, maintenance of normal weight and optimal use of oral contraceptive and postmenopausal HRT. It has been estimated that about 37% of endometrial cancer cases in the United Kingdom can be prevented by changes in lifestyle and risk factor modification.

Table 1.3 Factors associated with the risk of endometrial cancer

Factor	Effect	Strength (RR)
Early menarche	↑	(+) (2.4)
Late menopause	↑	+
Anovulation	↑	++
Nulliparity/low parity	↑	++ (2–3)
Infertility	↑	+ (2–3)
Obesity	↑	++ (2–11)
Metabolic syndrome/diabetes	↑	++ (1.3–2.7)
Alcohol	↑	(+)
Endogenous oestrogen	↑	+
Exogenous unopposed oestrogen-only therapy	↑	+++ (1.6–12)
Tamoxifen	↑	++ (1.7–7.0)
Oestrogen–progestin combined replacement	↑~↓	+
Combination oral contraceptives	↓	+++
High parity/breastfeeding	↓	+
Physical activity	↓	+

RR, Relative risk.
↑ Factor increasing the risk; ↓ factor decreasing the risk; ↑~↓ factor increasing or decreasing the risk.
(+) Inconsistent association; + week association; ++ moderate association; +++ strong association.

Cervical Cancer

Incidence and Mortality

Cervical cancer is the fourth most common cancer among women worldwide, with an estimated 528,000 new cases (7.9% of cancer in women) and 266,000 deaths (7.5% of cancer deaths in women) in the year 2012, and a 5-year prevalence of 1.5 million cases (9% of women with cancer). About 85% of the cases occur in developing countries, where cervical cancer accounts for 12% of all cancers in women. The incidence rates of cervical cancer vary substantially between different regions, from a low of 3.6/100,000 women in Switzerland to a high of 75.9/100,000

in Malawi. The highest rates are observed among populations in sub-Saharan Africa, Melanesia, Latin America and the Caribbean, south-central and south-east Asia. Incidence rates are generally low in developed countries in Europe, North America, Australia/New Zealand, the Middle East, China, and Japan. In the United Kingdom, cervical cancer is the twelfth most common cancer among women, with about 3,200 new cases in the year 2014 accounting for around 1.8% of all cancers in women, with a cumulative risk of 0.62% (1 in 161) by age 74 (Figure 1.1). In most European populations, the incidence rates of cervical cancer begin to increase at 20–4 years and thereafter the risk increases rapidly to reach a peak usually around 35–9 years (Figure 1.2). In the United Kingdom, incidence rates of cervical cancer are similar for White and Black females but significantly lower in Asian females.

Almost nine out of ten (87%) cervical cancer deaths occur in the less developed regions. The mortality rates vary substantially between different regions of the world; from less than 2/100,000 in Western Europe to more than 20/100,000 in Africa. In 2014, 890 women in the United Kingdom died from cervical cancer (2.8/100,000), accounting for around 1% of female deaths from cancer. Cervical cancer generally has an excellent prognosis; overall, in the United Kingdom, about 63% of women diagnosed with cervical cancer survive their disease for 10 or more years. When diagnosed at its earliest stage (Stage I), almost all (96%) of the women will survive their disease for 5 or more years, compared to 5-year relative survival of 5% for those diagnosed at Stage IV. In the United Kingdom, the 5-year net survival has steadily improved from 51.5% in 1971–2 to 67.4% in 2010–11 (an increase of about 31% in the period).

Trends in Incidence and Mortality

Overall, the incidence and mortality from cervical cancer have declined considerably during the past 40 years in Western Europe, North America, Australia/New Zealand, China, and Japan. The decline has been attributed to a combination of factors including improved genital hygiene, increased use of condoms, improved treatment modalities, beneficial effects of organised population-based cytological screening programmes for early diagnosis and introduction of the vaccine against HPV infection. In the United Kingdom, the ASRs (European standard) of cervical cancer have declined by around 28% since the early 1990s, whereas, in the same period, the mortality rates declined by around 62%.

Aetiology

A persistent infection with an oncogenic HPV type is now recognised as a causal factor for preceding precancerous changes and cervical cancer. However, infection with HPV is extremely common compared with the relatively rare development of cervical cancer. There is compelling evidence that HPV is necessary for cervical carcinogenesis, but infection alone is not sufficient for the cancer to develop. A number of cofactors have been identified as possible modifiers of HPV infection during the developmental stages of cervical cancer, including early sexual debut, increasing number of sexual partners, smoking, long-term oral contraceptive use, high parity, dietary factors, certain human leucocyte antigen (HLA) types, and co-infection with other sexually transmitted agents such as *Chlamydia trachomatis*, herpesvirus type 2, and human immunodeficiency virus (HIV).

Prevention

Cervical cancer is one of the most preventable forms of cancer on a global scale. Prevention efforts include increased public awareness about sexually transmitted infections, early detection of precursor lesions by regular cytological screening, HPV testing, and the recently developed vaccine against certain high-risk types of HPV. In the United Kingdom, all girls aged 12–13 are now offered HPV vaccination as part of the childhood immunisation programme. It has been estimated that almost all the cases of cervical cancer in the United Kingdom can be prevented by changes in lifestyle and risk factor modification.

Vulvar and Vaginal Cancers

Incidence and Mortality

Vulvar and vaginal cancers are rare throughout the world and constitute less than 5% of all gynaecological cancers. The ASRs of vulvar cancer vary from a low of 0.3/100,000 women in Republic of Korea to a high of 4.1/100,000 in Saarland, Germany. In general, incidence rates are relatively higher in developed countries; the highest rates are observed in European, North American, and Australia/New Zealand populations and the lowest rates (<1/100,000 women) are observed in parts of Asia, Africa, the Middle East, and South America. In the United Kingdom, there were

about 1,300 new cases of vulvar cancer in the year 2014, accounting for 0.7% of all cancers in women, with a cumulative risk of 0.17 (1 in 588 women) by age 74 (Figure 1.1). Vulvar cancer is predominantly a disease of older women, with a steep rise in incidence after 60–4 years from 6.2/100,000 to 19.7/100,000 women by 85–9 years, and over half of the cases (55%) are diagnosed in women aged over 70 years (Figure 1.2). In 2014, there were about 450 deaths from vulvar cancer in the United Kingdom.

In most world regions, the overall incidence rates of vaginal cancer do not exceed 1/100,000 women. In the United Kingdom, there were about 250 new cases of vaginal cancer in the year 2014, accounting for around 0.1% of all cancers in women, with a cumulative risk of 0.05 (1 in 2,000 women) by age 74 (Figure 1.1). Like vulvar cancer, it is predominantly a disease of older women, with a steep rise in incidence after 60–4 years: from 1.4/100,000 to 3.4/100,000 women by 85–9 years, and about half of the cases (48%) are diagnosed in women aged over 70 years (Figure 1.2). In 2014, there were 110 deaths from vulvar cancer in the United Kingdom. Survival rates for vulvar and vaginal cancers vary significantly by stage of disease and age at diagnosis; overall, about 53% of women diagnosed with vulvar or vaginal cancer survive their disease for 10 or more years.

Trends in Incidence and Mortality

In most developed countries, there has been little change in the overall (i.e. all ages combined) incidence of vulvar and vaginal cancers over the past 40 or more years. In the United Kingdom, the incidence rate of vulvar cancer has remained steady at around 3–4/100,000 women and of vaginal cancer around 0.8–0.9/100,000. However, recently there has been some increase in the rates of vulvar cancer among young women (age <50 years) in some countries, which has been linked to increasing incidence of vulvar intraepithelial neoplasia (VIN) in young women caused by infection with HPV. In most populations, the mortality rates of vulvar and vaginal cancers have declined steadily over the past 40 or more years. In the United Kingdom, the ASRs (European standard) for vulvar and vaginal cancers declined by 44% and 50%, respectively.

Aetiology

A persistent infection with an oncogenic HPV type is now considered to play a central role in the initiation and promotion of the majority of vulvar and vaginal cancers. HPV is more strongly associated with cancers in younger women and about 70% of VIN3 and 20–50% of invasive vulvar cancers contain HPV DNA. About 80% of VaIN3 and 60% of invasive vaginal squamous cell carcinomas contain HPV DNA. A history of cervical intraepithelial neoplasia (CIN) or cervical cancer is considered a strong risk factor for vulvar and vaginal cancers. A number of HPV cofactors have been identified, including a history of genital warts (which are caused most commonly by non-oncogenic HPV types), smoking, and infection with other sexually transmitted agents such as herpes virus type 2 and HIV. Many cases of vulvar cancer are not associated with HPV infection. Chronic vulvar skin conditions, including lichen sclerosus, lichen planus, and Paget's disease, are associated with an increased risk of VIN3 and invasive vulvar cancer. Iatrogenic immune suppression in transplant patients has been associated with a 100-fold increased risk of vulvar cancer.

Prevention

Increased public awareness about sexually transmitted infections, surveillance for precancerous lesions, self-awareness, smoking cessation, HPV testing, and HPV vaccination make vulvar and vaginal cancers one of the most preventable forms of cancer. It has been estimated that about 40% of vulvar cancers and 63% of vaginal cancers in the United Kingdom can be prevented by changes in lifestyle and risk factor modification.

Further Reading

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