Trends in Irish cancer mortality rates 1950-2002 with predictions to 2015

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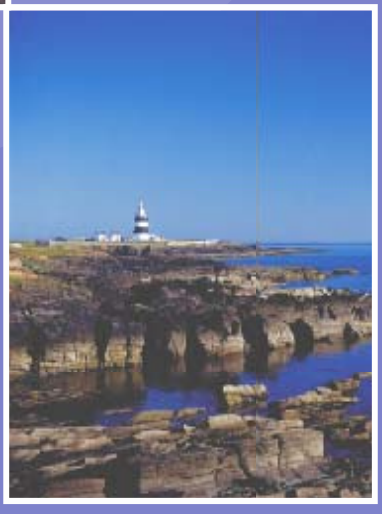

National Cancer Registry Ireland

TRENDS IN IRISH CANCER MORTALITY RATES 1950-2002, WITH PREDICTIONS TO 2015

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Glossary of terms and methods

Aetiology, aetiological factors

Aetiology describes the cause of a disease, and aetiological factors are those which are implicated in causing a disease, or making it more likely.

Age-period-cohort (APC) models

Statistical models of health events (e.g. disease incidence, or death), taking into account and describing variation by age, calendar period in which event occurs, and birth cohort (period of birth).

Age-specific baseline rate

For each cancer for which predictions are made here, a "baseline rate" or a baseline trend in rates, was chosen; that is a rate or trend which was considered sufficiently stable that future predictions could be made from it.

Age-specific (mortality) rate

The number of deaths per person at risk in a specific age-class, usually for five-year age-classes (0-4 years to 85+ years), generally expressed per 100,000 persons per year.

Age-standardised (mortality) rate

The incidence rate that would have been found if the population being studied had the same age-composition (proportion of total population in each five-year age-class) as a hypothetical European or World population. The rates are calculated by applying the age-specific rates for Ireland (or any subdivision thereof) to a theoretical European or World standard population; usually expressed per 100,000 persons per year:

$$ASR = \frac{\sum_{i=1}^{15} a_i . w_i}{\sum_{i=1}^{15} w_i}$$

where: a_i = age-specific rate for the i^{th} age group; w_i = standard "World" or "European" weights

(Estimated) annual percentage rate of change

The average annual rate of change, derived here from linear percentage increase or log-linear regression of annual decrease in rates or numbers. This was calculated by a linear regression of the log of the rate or number on the year of death. Given 100 deaths in year 1, and an annual percentage increase of x%, the estimated number in year 2 would be 100+x, in year 3, $(100+x)^2$, and in year n $(100+x)^{n-1}$.

Artefacts

An artefact, in the context of epidemiology, is a result created by an unwanted effect of the methods used.

Birth cohort

A group of persons born in the same year or group of years. See Chapter 2 for method of constructing 'synthetic' birth cohorts using data on age and calendar year of death.

Central Statistics Office

The body in Ireland with responsibility for compiling statistics on births, deaths and marriages. It also carries out the quinquennial censuses and provides population estimates for intercensal years.

Coding

Two related systems of coding of neoplasms (cancers) are in common use: the International Classification of Diseases (ICD; WHO 1977, 1992) and the International Classification of Diseases for Oncology (ICD-O). ICD-O is routinely used by the National Cancer Registry (Ireland) for recording incident cancers in Ireland. The "site" coding axis of ICD-O corresponds to the malignant neoplasms section of ICD, which is used for registration of deaths in Ireland (currently ICD version 9).

Cohort trends

A "cohort trend" or "cohort effect" is a shared tendency to some characteristic (e.g. higher mortality from a particular cancer) among a group of people who were born during the same period (in the context of this report, usually a five-year period).

Confidence intervals

A range of values within which we believe that the true value we are attempting to measure (or predict) lies. The degree of confidence is usally expressed as a percentage (e.g. 95% confidence interval)

Crude mortality rate

The number of deaths divided by the population at risk; usually expressed per 100,000 persons per year.

Cumulative risk of dying from cancer

The risk to an "average" individual, given cancer mortality rates in a given year, of dying from cancer (or a specific cancer-type) by a given age – in this report, by age 64 (i.e. before 65th birthday) – if death from another cause does not occur; usually expressed as a percentage. Cumulative risk is derived from cumulative rate as follows:

$$cumulative\ risk = 1\text{-}\ (1 - e^{-cumulative\ rate})$$

where cumulative rate is the total accumulated cancer mortality rate up to a given age. Cumulative rate to age 64 is calculated as:

$$cumulative\ rate = \sum_{i=1}^{13} a_i * 5$$

where: ai. = age-specific mortality rate for the ith age-class; 5 = number of years included in each of the 13 age-classes included (0-4 to 60-64 years).

Demographic factors

The number of deaths (or cases) due to cancer is dependent of the size of the population studied, and also its age and sex composition. These three factors are described as "demographic".

Five-year relative survival

The ratio between the survival of cancer cases to five years post-diagnosis and the expected survival of persons of the same age and sex in the general population, For example, if observed (crude) five-year survival is 60%, compared with expected survival of 80% in the general population, five-year relative survival is estimated as (60/80)% = 75%.

Histology

Microscopic study of tissue structure using special staining techniques; for cancers, used to confirm presence of neoplastic cells, cell-type, grade, and occurrence of tissue-invasion

Likelihood ratio test

A test based on the ratio of the likelihood (the probability or density of the data given the parameters) under a general model, to the likelihood when another, specified hypothesis is true. See http://life.bio.sunysb.edu/morph/glossary/gloss2.html

Incidence

A measure of the occurrence of new cases of illness or other morbidity in a population over time; for cancer, typically expressed as a incidence rate per 100 000 persons per year, expressed as either a *crude* or an *age-standardised* rate.

Inflection point

A point in time (particular year) at which a significant change in trend occurs, e.g. from an increase to a decrease,or from an increase to a 'flat' trend (see *Joinpoint*).

International Statistical Classification of Diseases

The World Health Organisation has published a series of detailed classifications of cause of death which are recommended for use by all countries in coding certificates of death. The classification is also widely used for classification of disease in the living. The classification is revised at approximately 10-year intervals, the most recent (10^{th}) version having appeared in 2002.

Joinpoint, Joinpoint regression

The joinpoint program was developed by the Statistical Research Applications Brach (SRAB) of the National Cancer Institute and models disease incidence and mortality by fitting a series of line segments (either linear or exponential) to the age-standardised rates. The program gives (a) slopes and (b) inflection points for the fitted lines, and tests for best fit between lines having from zero up to a user-defined maximum of inflection points.

Life expectancy

The number of further years an average person, of a given age and sex in a given population and year, can expect to live, based on cross-sectional estimates of age-specific death rates in that population. Typically quoted as life expectancy at birth.

Metastatic

Refers to distant (as opposed to localized or regional) spread of a cancer from its original (primary) location in the body, almost always reflected in markedly reduced survival.

Mortality rate

The rate of death in the general population typically expressed per 100 000 persons per year, either for a specific cause of death or (total mortality) for all causes. May be expressed as either *crude* or *age-standardised* rate.

Not otherwise specified (NOS)

For cancer types or sites, refers to non-specific diagnoses, for example "cancer of uterus, NOS" (cervix or corpus uteri not specified), "leukaemia, NOS" (cell-type not specified).

Poisson distribution

In probability theory and statistics, the Poisson distribution is a discrete probability distribution. It expresses the probability of a number of events occurring in a fixed time if these events occur with a known average rate, and are independent of the time since the last event.

Population projections

Estimates of likely future populations, based on pre-defined assumptions about rates of birth, death, immigration and emigration.

Population-based studies

Studies using data applicable to and representative of a defined resident population, e.g. all persons in Ireland or all cancer patients in Ireland, rather than based on selected or potentially non-representative subgroups (e.g. patients in a particular hospital).

Survival

Typically, an estimate of the probability (or percentage) of patients diagnosed with a specific condition surviving to various times after diagnosis, e.g. one-year survival, five-year survival. Because patients may die of unrelated causes, 'net' survival (excluding unrelated deaths) is generally of interest. For population-based studies of cancer patients, this is typically calculated as *relative survival* –survival observed in a particular group of patients as a percentage of to the survival expected among persons of the same age and sex in the general population.

Years of potential life lost (YPLL)

A measure of "premature" mortality which attempts to summarize the number of person-years lost to a given cause of death, e.g. cancer. The most meaningful estimate is obtained by multiplying the number of persons dying at particular age by the average life expectancy for persons of that age. For practical purposes, a simpler measure is typically used, based on an arbitrary age. For this report, YPLL by age 64 is calculated, i.e. the number of person-years lost before age 65: for example, if 10 persons die of a particular cancer at ages 50-54, YPLL = 10*(65-52.5) = 125 years 'lost'. (Note that the midpoint of age-range 50-54 is taken to be 52.5 years, on the assumption that the average person dying at age 52 will be 52.5 years old.)

Abbreviations used

APC.....age-period-cohort

CSO .....Central Statistics Office

EAPC .....estimated annual percentage rate of change

HL.....Hodgkin lymphoma

HPV ..... human papilloma virus

IARC.....International Agency for Research on Cancer

ICD.....International Classification of Diseases

NHL .....non-Hodgkin lymphoma

NOS.....not otherwise specified

PI ..... prediction interval

WASMR .....world [population] age-standardised mortality rate

Chapter 1. Introduction

Public health importance of cancer

Cancer is a major cause of morbidity and mortality throughout the world, reducing quality of life, causing premature death and requiring the allocation of significant resources, both human and financial, to provide diagnostic and treatment facilities. The World Health Organisation estimates (World Health Organisation, 2005) that 11 million new cancer cases are diagnosed and 7 million persons die from cancer annually. In Ireland, the burden of cancer is 20,000 new cancers and over 7,500 deaths annually (National Cancer Registry 2005). More than a quarter of all deaths in Ireland are due to cancer.

As the Irish population continues to grow, and as life expectancy increases, the cancer burden will increase significantly in the next few decades. Estimating the magnitude of this increase is essential for the assessment of the future burden of cancer, its personal, social and economic impact and the implications for health services and for resource allocation.

Aim of report

This report brings together for the first time a significant amount of data on cancer mortality in Ireland, derived from the annual Reports on Vital Statistics of the Central Statistics Office (CSO) and the earlier Annual Reports of the Registrar General (Office of the Registrar General, 1950-1952. Central Statistics Office, 1953-2005). Its main purpose is to provide detailed information on current, past and estimated future mortality from the commonest cancers, by age and sex. The cancers included are responsible for over 75% of all cancer deaths in Ireland at present. We hope that these data will stimulate new research and assist decision-making and priority setting at national level.

The aims of the report are

1. To describe cancer mortality trends in Ireland over an approximately fifty-year period, up to 2002.

2. To identify significant trends in mortality, and significant changes in these trends.

3. To use recent trends in mortality to predict numbers of deaths from cancer up to 2015.

Report contents and layout

One chapter is devoted to each of the major cancer sites. Each begins with a brief description of the epidemiology of the cancer, including a summary of known risk factors. As the emphasis in this report is on factors which might cause changes in cancer mortality, genetic factors, which are unlikely to have changed substantially over the period discussed, are not included in this discussion. This is followed by a closer examination of mortality from 1950 to 2002. All major cancers, accounting for 75% of all cancer mortality, are described in this report (Table 1.1), with the exception of bladder and kidney cancers, for which variation in coding practice over time prevented useful analysis. Predictions were not attempted for less common cancer types, as the accuracy of these would be substantially lower (given the uncertainties involved in predictions even for the major cancers).

For each cancer we provide general descriptions of trends (graphs and long-term average rates of change) in numbers, in crude and age-standardised mortality rates and, for the under-65 population, cumulative risks of dying and number of years of potential life lost, between 1950 and 2002. For a number of cancers, data consistent with later years was not available for the years 1950-1954 and this is indicated where applicable. Recent trends in mortality rate for a number of European countries

and the USA are given for comparison purposes. Joinpoint models of the age-standardised rates, giving inflection points and annual percentage rates of change, are used to provide a more objective description of trends and their changes. More detailed information on age, period and cohort trends is also provided. Finally, details of the prediction models fitted and prediction of age-standardised mortality and number of deaths are given for the years 2005, 2010 and 2015.

Table 1.1. Cancer deaths 1994-2001: specified malignant cancers as a proportion of all cancer deaths

	female		*male*		*both sexes*	
cancer site	*number of deaths*	*% of all cancer deaths*	*number of deaths*	*% of all cancer deaths*	*number of deaths*	*% of all cancer deaths*
trachea, bronchus and lung	4277	15%	7723	24%	12000	20%
colorectal	3233	11%	4206	13%	7439	12%
female breast	5156	18%	—	—	5156	8%
prostate		—	4154	13%	4154	7%
stomach	1213	4%	1788	5%	3001	5%
pancreas	1407	5%	1475	5%	2882	5%
oesophagus	942	3%	1526	5%	2468	4%
lymphoma	914	3%	1079	3%	1993	3%
ovary	1813	6%	—	—	1813	3%
leukaemia	780	3%	1023	3%	1803	3%
corpus uteri	380	1%	—	—	380	1%
cervix uteri	586	2%	—	—	586	1%
brain and CNS	754	3%	990	3%	1744	3%
other	6733	24%	8583	26%	15352	25%
all cancers	28194	—	32524	—	60718	—

Why mortality?

Cancer mortality depends on two main factors—incidence and survival. Trends in these may frequently be in opposition, so mortality trends, in the absence of matching data on incidence and survival, may be difficult to interpret. However, for Ireland, no information on cancer incidence or survival is available for the years before 1994, so the study of time trends in incidence and survival is currently limited to cancers diagnosed in the period 1994-2002. Apart from this purely practical reason, there are a number of more general reasons for studying mortality, as opposed to incidence and survival. Death is the outcome of almost half of all malignant cancers (or over half of those excluding non-melanoma skin cancers), and is one of the most important measures of the impact of cancer on the community and of the effectiveness of cancer control strategies. Cancer incidence and survival are subject to artefacts, the best known being the apparent increases in both incidence and survival (Prorok 1992) associated with screening programmes even in the absence of an impact on life expectancy or mortality. Thus cancer mortality remains the "gold standard" against which most population-based interventions must be measured. However, it is important to remember that cancer control programmes may take some time to affect cancer mortality. Improvements in treatment should have an almost immediate impact, the effects of screening and early diagnosis should be manifest somewhat later, while success in prevention may not become apparent for 15 or more years. It must also be acknowledged that cancer mortality statistics, themselves, are potentially subject to artefacts, if the accuracy of death certification, the specificity of the codes used, or the rules used to attribute deaths to specific underlying causes change substantially over time.

Aims of modelling

The study of cancer mortality trends has a number of applications:

- measuring the impact of past interventions e.g. cancer strategies, treatment improvements, screening programmes;
- identifying new risk factors;
- identifying emerging problems;
- predicting future mortality for needs assessment.

This report is focussed on the last two of these applications, as being of the most immediate value. We have, in any case, only very limited information on past risk factors and interventions, and it is too early to look for the effect of some recent interventions such as the breast and cervical screening programmes (Department of Health, and Children, 1996).

Measures of cancer mortality can be considered to consist of three elements:

1. the underlying population risk of dying of cancer (reflecting incidence and survival);
2. the effects of population size and age composition (demographic factors);
3. random variation.

Interpretation of trends and their extrapolation into the future is usually based on the assumption that the underlying risk changes in a relatively smooth and predictable way but that this may be obscured by random year-to-year variation in numbers or rates. The aim of statistical modelling is to distinguish the underlying trend from the random variation.

As with the study of trends in general, models have two broad purposes—to understand the past or to predict the future. These purposes are not always compatible and the choice of modelling technique may depend on the main aims of the study.

Models which attempt to help understanding of the past are focussed on the effect of independent variables (risk factors) on cancer mortality trends. The model attempts to fit the trends as closely as possible over a long period, during which, ideally, variation in risk factors can also be measured and incorporated into the model. Predictions of future trends may be made, but perhaps more usefully to test the hypotheses of causation rather than to make practical predictions.

Models which attempt to predict future trends (which are the focus of this report) tend to be simpler, with few independent variables, and to cover a relatively short recent period during which it is hoped that all major factors are changing in a predictable way. As these models attempt to provide data for practical application, each prediction is accompanied by a range within which the actual value is likely to fall (prediction interval).

Chapter 2. Methodology

Data Sources

Four main data sources were used in the preparation of this report. These were:

- Official statistics on cancer mortality from 1950 to 2002 (Central Statistics Office, 1953 -2004).
- Population data for the censuses held in 1951, 1956, 1961, 1966, 1971, 1979, 1981, 1986, 1991, 1996 and 2002 (Central Statistics Office, 1952-2003).
- Population projections for the years 2005-2036 (Central Statistics Office, unpublished & 2004).
- World Health Organization databank of international cancer mortality statistics (WHO, 2005).

Data Quality, Coverage and Completion

Census and Population Projections

Censuses, covering the entire resident population, are carried out in Ireland every five years. Eleven five-yearly censuses cover the period 1951 and 2002 (the census due to be held in 2001 census having been deferred to 2002 as a result of the foot-and-mouth disease outbreak). For intercensal years up to 1990, population numbers were calculated by simple linear interpolation by sex and in eighteen five-year age groups from 0 to 85. For 1992-95 and 1996-2001, official intercensal estimates provided by the Central Statistics Office were used.

For future periods, projected population figures for 2005, 2010 and 2015 were used (Central Statistics Office, unpublished and 2004). These published projections offer a number of alternatives, based on differing assumptions about fertility and migration rates. The projection giving the highest overall projected population for each year (labelled projection M1F1 in the publication cited) was used. Although the highest of the available projections was used in these predictions, most of the difference between projections was in the younger age groups, and the population projection chosen had very little impact on projected cancer mortality rates (Table 2.1).

Table 2.1. Projected annual average number (with 95% prediction intervals) of cancer deaths in 2015, using different population projections.

projection	*lung; males*	*lung; females*	*breast; females*	*prostate*
M1F1	1077 (982, 1171)	844 (755, 933)	695 (607, 784)	787 (654, 919)
M1F2	1077 (982, 1171)	844 (755, 933)	695 (607, 784)	787(654, 919)
M1F3	1077 (982, 1171)	844 (755, 933)	694 (606, 783)	786 (654, 919)
M2F1	1069 (975, 1163)	839 (750, 928)	689 (601, 777)	782 (651, 914)
M2F2	1069 (975, 1163)	839 (750, 928)	689 (601, 776)	782 (651, 914)
M2F3	1068 (974, 1162)	839 (750, 927)	688 (600, 776)	782 (651, 914)

Mortality Statistics

For each death occurring in Ireland a death registration is completed by the Registrar of Births, Deaths and Marriages from details supplied by an "informant", usually a family member, and from the medical certificate of cause of death (or coroner's certificate). A death must be registered, by law, within a year of its occurrence. A copy of the death certificate is forwarded to the Central Statistics Office (CSO) where the underlying cause of death and other conditions present at death are coded using standard WHO procedures. Inadequate, unclear or apparently incorrect certificates are referred back to the registrar or coroner, or to the medical certifier. It is estimated that this occurs for approximately 30% of all certificates (Balanda and Wilde, 2001). The CSO produces an annual statistical report on all deaths occurring in the year. These reports were the primary source of data for this report, but data from 1994 onwards was provided electronically to the Registry (and cross-checked against published CSO figures).

Four revisions of the International Classification of Diseases were used by the Registrar General and CSO between 1950 and 2002 (Table 2.2). In this report, all causes of death were re-coded, following WHO guidelines (WHO, 2005), to the ninth edition of the International Classification of Diseases (ICD-9) (WHO, 1972).

Table 2.2. Versions of ICD (International Classification of Disease) used in coding death certificates in Ireland 1950-2001

ICD version	*years covered*
ICD-6	1950–1957*
ICD-7	1958–1967
ICD-8	1968–1978
ICD-9	1979–2004

** A non-standard version of ICD-6 was used in 1952 and 1953*

Data Limitations and Restrictions

Completeness

Deaths which have not been registered within one year of their occurrence can be registered only if an inquest has been held or on the authority of the Registrar General, and are otherwise excluded from official death statistics. Deaths of residents which occur outside the country are not included in the mortality data. Deaths of non-residents are normally included.

Accuracy and precision

Many studies have shown wide variability in certification and coding, particularly between countries (Heasman and Lipworth 1966; Alderson and Meade 1967; Percy and Dolman 1978; Percy et al. 1981; Percy and Muir 1989; Percy et al. 1990; Ashworth 1991; Hoel et al. 1993; Lindlahl and Johannsson 1994; Grulich 1995; Garne, Aspergren and Balldin 1996; Coleman and Aylin 2000). In 2002, for instance, 6% of cancer deaths in Ireland were coded to "site unspecified" (ICD-9 199) whereas only 3.5% of incident cancer cases were so classified (National Cancer Registry 2005). Even this comparison over-estimates the precision and accuracy of death certification, as some deaths attributed to specific primary cancer sites may in fact have involve cancer spread from a different primary site. The National Cancer Registry has matched registrations of cancer to all cancer death certificates for the years 1994–2002, and this matching has shown some inconsistencies between the cancer registration and the officially registered cause of death. In most cases, the cancer registration, which is based on a detailed assessment of the medical record, can be taken to be the more reliable source of information for cancer incidence purposes, but the "official" cause of death, as coded by the CSO, has always been used for purposes of the analyses in this report, in line with international reporting practice for mortality statistics.

Some advantages and disadvantages of mortality data are summarised in Table 2.3. Detailed recommendations for changes in the data collection protocols and procedures in Ireland have been made elsewhere (Balanda and Wilde, 2001).

Table 2.3. Some advantages and disadvantages of mortality data

Disadvantages	*Advantages*
Diagnostic accuracy less certain than for incidence	Virtually 100% complete
Site or broad cancer type only, no detailed histology	Timely (within months of the end of a data year)
Higher proportion of site unspecified than for incidence	Very long time series (if not affected by ICD or other coding changes)
Deaths in any one year result from cases diagnosed over a long previous period	

In 1952 and 1953 a non-standard variant of ICD-6 was used to classify cause of death and it has not been possible to assign deaths from lung cancer, lymphoma or uterine cancer to an equivalent ICD-9 code. Data for those cancers for those years have been excluded. Changes in classification of cancers of the urinary tract in different versions of ICD have made it impractical to provide a consistent picture of historical trends, and no data for bladder or kidney cancer are presented here.

As mentioned above, many changes have occurred in diagnostic methods, in the recognition of new cancers and the re-classification of known diseases over a period of more than 50 years. In some cases these changes have been captured in changes in classification and coding. In others, such as the case of uterine cancer described above, it is almost impossible to differentiate long-term trends in cancer mortality from changes in disease nomenclature. Older versions of ICD allowed for the coding of metastatic disease to the organ of metastasis, and for categories such as "lung cancer, not known whether primary or secondary". These categories are not strictly compatible with those in ICD-9, and in some cases a "best guess" has had to be made. However, there appear to have been few shifts in diagnostic labelling from 1970 onwards, and as the period from 1979 onwards (and usually much later) is that on which all our extrapolations have been based, the difficulties in interpretation of data for the 1950s and 1960 have not had any implications for the projections.

Data analysis

Descriptive Analysis

This report uses the direct method of standardisation (Jensen et al. 1991), which uses the observed age-specific rates to calculate an overall rate based on a hypothetical "world" standard population. These are referred to in the text as "world age-standardised mortality rates" (WASMRs) and are expressed as deaths per 100,000 person-years. (Details of the methods are given in the Glossary). The report also describes trends in cumulative risk of dying of cancer before age 65 and potential years of life lost, as measures of "premature" cancer mortality (O'Lorcain et al, in press).

Modelling techniques

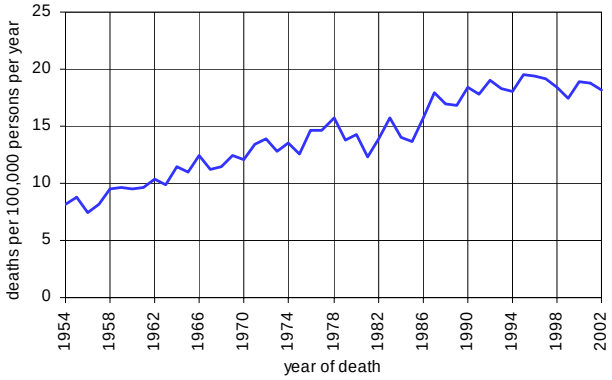
In theory, at least, the estimation of cancer mortality trends could be based on knowledge of the factors determining incidence and survival and an extrapolation of these into the future. The events determining cancer incidence usually take place many years before the cancer becomes clinically apparent and, in theory, it should be possible to predict cancer trends by observation of the changes in the prevalence of risk factors. For instance, lung cancer mortality could be predicted from current and past patterns in smoking, and an estimate of likely changes in survival. For the cancers caused by tobacco, the temporal links between consumption and cancer are clear, with a lag of about fifteen years between tobacco trends and the corresponding mortality (and, by inference, incidence) trends. For the majority of cancers, however, our understanding of important risk factors,

their proportion of cancer risk contributed by each of these factors and their distribution in the population is limited, and not sufficient to allow any accurate prediction of future trends.

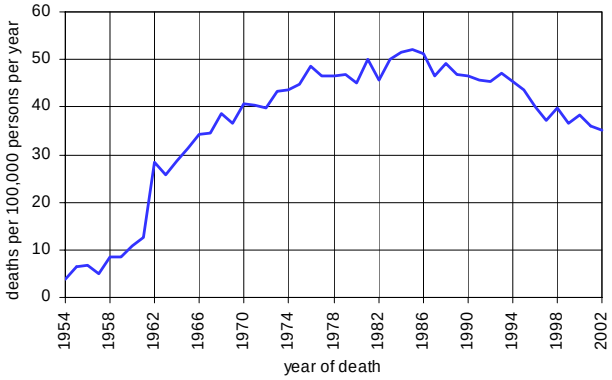
Consequently, the general approach to predictions of mortality has been to use past trends as a guide to future rates, making few, if any, assumptions about the underlying processes. This "black box" approach has led to a number of quite different methodologies, with more pragmatic than theoretical foundation. As trends in any cancer may be influenced by different trends in a large number of risk factors, as well as trends in survival, there is no *a priori* reason to expect the trend curve to follow any particular pattern. The annual number of deaths is also subject to Poisson uncertainty and so the trend line will not be an exact reflection of the trends in underlying risk.

Figure 2.1. Time trends in age-standardised mortality rate—prostate and lung cancer in males, 1954-2002

prostate cancer



lung cancer



The simplest approach to assessing a mortality trend is to fit a simple linear or log-linear regression line (with year of death as the independent variable) to either the number of deaths or the mortality rate (crude or age-standardised). In certain cases the linear nature of the trend is clear, as shown for prostate cancer in Figure 2.1, but in others (as shown for lung cancer) the trend is obviously non-linear. An elaboration of this method is to divide the trend-line into a number of linear or log-linear segments, either by eye or by identifying inflection points using software designed for the purpose (Joinpoint regression program: Kim, Fay et al. 2000). A further development of this approach has been to assume that the trends for different age groups or birth cohorts are independent of each other, and to fit Poisson models to the number of deaths for each age group or cohort, with correction for the population in each group/cohort. Linear, log-linear and non-linear models have all been fitted by this method, the main criterion being the goodness of fit of the model. The choice between linear and log-linear assumptions is somewhat arbitrary, as both often fit the data equally well. However, as with the simpler models, this approach depends on the assumption that the trends in mortality are approximately (log) linear over the period studied. Quadratic and higher-order terms can be

incorporated into the models, but these are somewhat arbitrary and have no justification external to the model. These models may fit the data accurately while having limited predictive power.

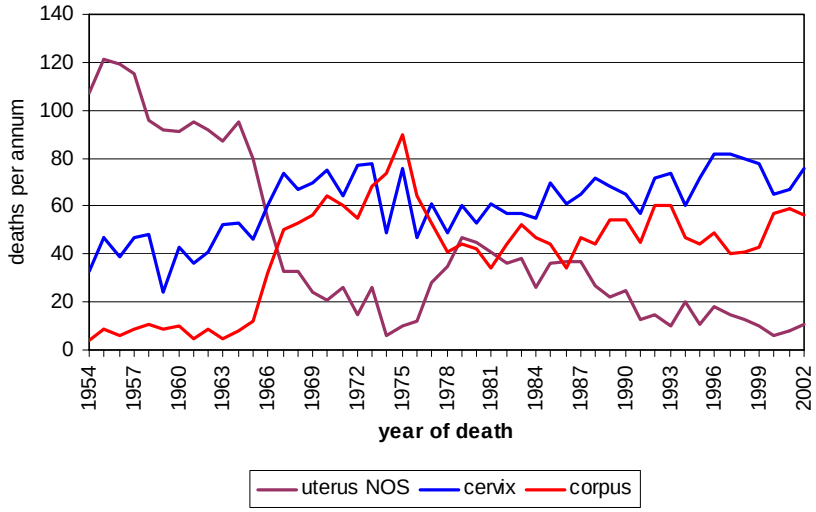
The third approach, not widely used, has been to use curve-fitting software to fit a curve or spline of quadratic or higher order to the data (Boyle, Golia et al. 2003). This allows a close fit to historical data, but future predictions are very sensitive to the order of the curve chosen.

The methods used in this report to model observed trends were a combination of the first two approaches (see "Methods"). Inflection points were first identified (producing a description of any major changes in trends over time), and a linear/log-linear model, incorporating age variables, was fitted to the most recent linear trend in the data.

Using models in prediction

Making a cancer mortality prediction has inherent difficulties and uncertainties. The usual method is to construct a model which fits the historical data, and to assume stability (or, at least, consistent or gradual change) in cancer causes and survival, and consistency in data collection methods and definitions, within the period on which the model is based. This model is then used to extrapolate past trends to make future predictions. Models used for prediction tend to use time variables as surrogates for unknown exposures. A good fit of the model to past data does not guarantee a good prediction, and model assumptions that held true with historical data do not necessarily hold true in the future (Hakulinen 1996). This is especially true of more complicated models containing several parameters. Simpler models make fewer assumptions, and although the fit to past data may not be perfect the model is less likely to be falsified by recent changes in trends. In practice, aetiological factors are often represented only by simple proxy variables such as age, sex and year of death. These variables can be interpreted as surrogates of exposure and changes in diagnostic and treatment practices (Hakulinen 1996).

Figure 2.2. Deaths in Ireland from uterine cancer, 1954-2002



Changes in cancer definitions, or the diagnostic labels used by doctors when certifying deaths, are inevitable when studying trends over long time spans, and data from different periods may not be strictly comparable. Where several diseases or conditions are noted on a death certificate, the rules used to decide which is the "underlying cause" can also change over time, notably between revisions of the International Statistical Classification of Diseases (e.g. World Health Organization, 1992, 177). A number of studies have concluded that the accuracy of death certification diagnosis is quite low, especially in countries with a low post-mortem rate. The precision with which causes of death are described can also change. Figure 2.2 shows, for example,

how the use of the term “uterus, part not otherwise specified” has declined in Ireland, while the more specific attribution of uterine cancer deaths to “cervix uteri” and “corpus uteri” has increased. This makes the interpretation of trends in cancer of either cervix or corpus uteri difficult.

Changes may take place in diagnostic methods, making the diagnosis of certain types of cancer more likely. For example, the availability of computerized tomography (CT) scanning has probably contributed to the increased diagnosis of brain cancer in the elderly.

Prediction of future cancer rates based solely on the factors which have determined the historical rates cannot take into account all potential improvements in diagnosis or treatment or in the way health services are delivered. Major new health developments such as the recent ban on smoking in public places in Ireland, the introduction of cancer screening programmes and the development of new techniques in surgery and oncology cannot be fully anticipated in any model. For models based on observed trends to date the best that can be hoped for is that the model can illustrate what is likely to happen in the absence of new initiatives. Nevertheless, as shown by a recent “Cancer Scenarios” study in Scotland, expert opinion may provide useful guidance on plausible further improvements in prevention, screening and treatment, allowing a more informed estimate of likely future mortality than if recent trends continue unchanged (Black & Stockton 2001). This approach also allows the effects of different interventions to be modelled, giving guidance as to the likely impact and relative effectiveness of various strategies for cancer control. This type of modelling, carefully used, is a natural extension of the work described in this report and could, for instance, inform decisions as to the likely effects of dietary change, screening or treatment improvements on colorectal cancer mortality.

Cancer mortality trends are an imperfect indicator of current cancer control. Trends in mortality give may give a fairly up-to-date indication of improvements in survival, but a delayed (or unpredictable) and somewhat inaccurate indication of trends in incidence. However, if incidence rates increase because of ‘over-diagnosis’ e.g. prostate cancer screening, this may never be seen in mortality trends unless it translates into a true survival benefit. As has been noted earlier, for many common cancers recorded incidence is currently increasing, as is survival, but the combination of these important, but opposing, trends may lead to unchanged cancer mortality.

Trends and modelling

For descriptive analyses of mortality trends up to 2002, rates were described using a number of age-period-cohort (APC) plots and modelled using Joinpoint regression. Predictions for the years 2005, 2010 and 2015 were made using either log-linear or linear modelling of age-specific rates. Expected numbers of deaths were calculated by combining these modelled rates with population projections.

Analyses were based on data collapsed by age and (for APC analysis) period and cohort. For calculation of observed rates and trends, age data were grouped by five-year categories from 0-4 to 85+ years. For predictions, age data were grouped into the categories 0-44, 45-54, 55-64, 65-74, 75-84 and 85+. The latter age groups generally provided a good ‘fit’ to the data and provided a compromise between having too many groups, which introduces more random variation into the prediction model, and having too few, which may lose information on differences in age-specific trends. Separate predictions are given for all ages combined and for the age-band 0-64. Further details of the models used are given in each chapter.

Trends were modelled in two stages:

- The Joinpoint program was used to identify points of inflection in the time-trend data on the age-standardised rate. Using the best fit from this program, the most recent continuous period of linear change (or lack of change) in rate was identified.

- The period from, or after, the most recent point of inflection to the present was used as the starting point from which to search for an appropriate "prediction baseline" for age-period modelling of the trend, using a Poisson assumption. This model provided predictions of rates and prediction intervals (similar to confidence intervals) for the predictions.

These two stages are described in more detail below (pages 14-15).

Joinpoint Analysis

Joinpoint (version 2.5, http://srab.cancer.gov/joinpoint/) is statistical software used to analyse joinpoint models, that is, models where the trends are considered to consist of a series of straight lines joined at a number of points of inflection or "joinpoints". The software fits the simplest joinpoint model to trend data (in this cases age-adjusted cancer mortality rates), using regression models and permutation tests to identify changes in trends over time (Kim, Fay et al. 2000). In joinpoint analysis, points where the rate changes significantly (increase or decrease) are identified. The analysis starts with the no joinpoints, and tests whether one or more joinpoints are statistically significant and should be added to the model (up to a user-defined maximum; in this case, three). In the final model, each joinpoint indicates a statistically significant change in trend, and an estimated annual percentage change (EAPC) is computed for each trend by means of generalised linear models assuming a Poisson distribution. Significant changes include changes in direction or in the rate of increase or decrease.

Age-period-cohort profiling

For each cancer site, the data were tabulated into 5-year periods between 1953 and 2002, 5-year age classes, typically from 30-34 to 80-84 years (i.e. excluding younger age groups with too few deaths), and also into "synthetic" cohorts, derived by subtracting the age-class mid-point from the 5-year period mid-point, thereby producing birth-cohorts from 1869 to 1968. A change in rate across all age groups at the same time is best described by an age-period profile. This may be the result in advances in treatment, greater use of screening or new diagnostic techniques, as long as such advances are not age-specific. On the other hand, the effects of changes in population exposure based on lifestyle may be most apparent in persons born at around the same time, and the age-cohort profile can provide a better description of such influences (Clayton and Schifflers 1987a; Clayton and Schifflers 1987b).

Predictions

Predictions of age-standardised mortality and the number of cancer deaths are given for the years 2005, 2010 and 2015. The models and the predictions of age-standardised rates are based on age-specific rates (for age-bands 0-44 to 85+ as previously described) and make no assumptions about future population growth. However, the predicted number of deaths uses projected population sizes, adding further uncertainty to the predictions, due to the approximations inherent in the population projections. A change in the number of cancer deaths therefore can be broken down into a component attributable to population change and a component dependent on change in mortality rates. These components may have opposite effects (Hakulinen 1996).

The impact of population change on mortality

All official predictions of the population for the years 2005-2015 show both an increase in the population and in the proportion of older persons. The population projection used here (M1F1) gives a predicted overall increase of 26% in population, but 52% for men and 37% for women over 65 (Table 2.4). As the majority of cancer deaths occur in those over 65, this increase in the older population is an important determinant of the number of cancer deaths.

We can calculate the expected increase in the number of cancer deaths due to this change in population size and age composition alone (usually referred to as demographic change), in the absence of any change in cancer rate for individual age

groups. This gives an estimate of how cancer mortality would change if the risk to the individual remained the same as "current" or recent estimates of risk.

Table 2.4. Increase in population, by age group, between 1998-2002 and 2015

		males			*females*	
age	*1998-2002*	*2015*	*% increase*	*1998-2002*	*2015*	*% increase*
0-4	136839	184646	35%	129158	173764	35%
5-9	137318	180609	32%	130361	170437	31%
10-14	151642	163992	8%	144278	156730	9%
15-19	169083	146746	-13%	160875	140748	-13%
20-24	158849	131106	-17%	155489	133565	-14%
25-29	147261	158558	8%	145939	164369	13%
30-34	139276	196058	41%	141359	198861	41%
35-39	137346	198284	44%	140495	195510	39%
40-44	129659	181231	40%	130997	177237	35%
45-49	120236	161318	34%	119725	157494	32%
50-54	112317	149133	33%	109332	149181	36%
55-59	89826	132478	47%	87693	133093	52%
60-64	74172	119119	61%	74298	119558	61%
65-69	63417	103934	64%	66497	106766	61%
70-74	50523	74207	47%	61042	78934	29%
75-79	37035	51063	38%	52008	60141	16%
80-84	21177	30980	46%	35075	43061	23%
85+	12097	19276	59%	27708	42446	53%
0-64	1703824	2103278	23%	1669999	2070547	24%
65+	184249	279460	52%	242330	331348	37%
all ages	1888073	2382738	26%	1912329	2401895	26%

The numbers are calculated by multiplying recent age- and sex-specific rates (in five year age groups from 0-4 to 85 and over) by the numbers in the corresponding groups in the projected M1F1 populations for 2005, 2010 and 2015. The numbers for each age/sex group are summed to give predicted numbers of deaths for males and females for each of the years (Table 2.5). For leukaemia in males, the projected number of deaths in 2015, assuming no change from the 1998-2002 incidence rates, is 212.

Table 2.5. Calculation of expected increase in male leukaemia deaths due to population change, 1998-2002 to 2015

age	*1998-2002 deaths*	*1998-2002 population*	*age-specific mortality rate (per 100,000)*	*2015 population*	*projected 2015 deaths*	*variance of projected 2015 deaths*
0-4	6	684194	8.77	184646	1.6	0.4
5-9	5	686592	7.28	180609	1.3	0.3
10-14	1	758208	1.32	163992	0.2	0.0
15-19	7	845416	8.28	146746	1.2	0.2
20-24	8	794245	10.07	131106	1.3	0.2
25-29	7	736303	9.51	158558	1.5	0.3
30-34	12	696378	17.23	196058	3.4	1.0
35-39	11	686728	16.02	198284	3.2	0.9
40-44	17	648293	26.22	181231	4.8	1.3
45-49	24	601179	39.92	161318	6.4	1.7
50-54	23	561583	40.96	149133	6.1	1.6
55-59	42	449128	93.51	132478	12.4	3.7
60-64	47	370862	126.73	119119	15.1	4.8
65-69	95	317087	299.60	103934	31.1	10.2
70-74	124	252615	490.87	74207	36.4	10.7
75-79	127	185173	685.85	51063	35.0	9.7
80-84	86	105885	812.20	30980	25.2	7.4
85+	82	60487	1355.66	19276	26.1	8.3
all ages (annual average)	145				212	62.9

Standard deviations and 95% confidence intervals were derived for these numbers by treating them as age-standardised rates, with the projected populations functioning as weights. A variance (standard error squared) was calculated for the projected deaths in each age group. The total of these variances gave the variance for the total of projected deaths (Table 2.6). A variance due to Poisson error was added to this, to allow for random variation in the projected number. The square root of this total variance gave the standard error, and the 95% confidence limits were calculated from the standard error multiplied by 1.96. An example of the calculation is given in Table 2.6 for leukaemia in men. Demography alone, in this case, is predicted to increase mortality (numbers of deaths) by 47% in 2015, compared to the 1998-2002 average. Similar predictions are given for each cancer in the corresponding chapter.

Table 2.6. Calculation of 95% prediction limits for projected number of deaths, based on demographic change

Projected number of deaths		212
Variance		63
Poisson variance	(number of deaths)	212
Total variance	(212+63)	278
Total standard error	(square root of variance)	17
95% prediction interval	(standard error * 1.96)	±33
Prediction with 95% prediction intervals		212 (180, 245)

Where the risk or rates of a cancer are changing over time, more realistic predictions of future numbers of cancer deaths take these changes into account. For such predictions, the least uncertainty in prediction is associated with simple linear or log-linear models of rate with respect to time (Hakulinen, Teppo et al. 1986) which assume a Poisson, rather than a normal, distribution with regard to rates or numbers (Dyba and Hakulinen 2000). Models with complex mathematical forms or many parameters produce even wider prediction intervals (see below), which greatly reduces their value. Simple linear and log-linear Poisson models have proved valuable in making short-term predictions, up to 10-15 years into the future (Hakulinen, Teppo et al. 1986; Dyba and Hakulinen 2000). A prediction horizon exceeding 10-15 years into the future is not particularly useful in planning resources or evaluation of interventions as risk (or populations) may change unpredictably over such a period of time.

The use of a relatively short prediction base stresses the importance of recent developments in determining mortality rates in the near future. The use of the Joinpoint program allowed us to identify the most recent significant change, if any, in rates, and to base our predictions only on the most recent trends. In some cases, trends in age-standardised rates have remained stable over the last 20 years, and this stability has allowed for more precise predictions.

The fit of the models was measured using a deviance or likelihood-ratio criterion, assuming Poisson variability. If any model gives a true description of the underlying rates, the corresponding deviance should be distributed as chi-squared with the appropriate degrees of freedom.

Selecting the base of the prediction for these models is critical. In most cases, linear and log-linear models give almost equally good fit to the data, and the choice between them has to be based on other criteria. If the fit of both models (assessed by the deviance value generated) was similar, linear models were applied to rates which were increasing with time, because log-linear models, in this context, can give rise to unrealistic exponential rates of increase in mortality. On the other hand, linear models can give rise to predictions of negative rates and numbers if applied to rates which are decreasing, and so, log-linear models are preferred in this situation. Two models were used in the trend analysis and are described in Table 2.7. All modelling was performed using the Stata 6.0 package for Windows (Stata Corporation, 2003) using the methodology of Dyba & Hakulinen (2000). The Stata programs used were based on samples provided by Dr. Tadeusz Dyba.

Table 2.7. Details of the models used in the trend analysis

Log-linear model	$\ln R_{it} = a_i + b_i t$
Linear model	$R_{it} = a_i + b_i t$
where	
R=	age-specific mortality rate
i=	age group
t=	period (year of death)
a_i =	underlying base rate
b =	increment rate for all age groups
b_i =	increment rate for individual age groups

Prediction intervals

The reliability of any incidence or mortality prediction should always be expressed as a "prediction interval" based on the model that has been chosen, but many published predictions lack any statement of confidence (Hakulinen, 1992). The prediction intervals given here are 95% prediction intervals; that is, the model predicts that there is a 95% probability that the true value will fall within this interval. Both the prediction and the prediction interval, of course, are only as valid as the model on which

they are based, as discussed earlier. Confidence intervals take into account the inherent uncertainty in the modelling process but assume that variation in the number of predicted cases is solely due to uncertainty in the model parameters. However, a second source of error in the predicted figures is random variation in future observations (Hakulinen 1996). Prediction intervals allow for the fact that the predicted number of cases will be subject to Poisson variation around the modelled value (Hakulinen, 2000) and so are wider than the corresponding confidence intervals.

The use of population projections introduces a third source of error into the projections of number of deaths (but not of age-standardised rates), although this is not formally quantified in the prediction model. As shown above, the current range of projections gives quite similar projections with regard to the number of deaths. However, the projections are based on a number of assumptions, any of which may prove to be incorrect, and the extent of the possible error is unquantifiable. In all cases, therefore, the projected incidence rates can be taken as more reliable than the projections of numbers of deaths.

In addition to the three sources of error noted above, the model used for prediction involves the assumption that current trends will continue (or, for predictions based only demographic change, that current rates will continue to apply). Only direct comparison with actual mortality rates and numbers of deaths (when they occur) allows any quantitative measure of this source of error.

Selection of prediction baseline

Choosing a long set of historical mortality data as the prediction baseline carries with it the danger of giving too much weight to past trends that may no longer be applicable. In contrast, selecting a short i.e. recent set of mortality data carries the risk of giving too much emphasis to data that may not have within it any significant upward or downward trend. Thus, some predictions can involve a choice between producing a relatively precise, but possibly invalid, result based on a long series of observations or a less precise, but probably more valid, one based on more recent data.

The approach that was adopted was a step-wise one, and was necessarily somewhat complex:

1. Identification of the most recent inflection point: Using the Joinpoint program the year in which the last statistically significant change in the mortality trend (for the relevant population, either all ages or ages 0-64), was identified.

2. Identification of the most recent linear trend: Again, using the Joinpoint application it was established whether or not the estimated annual percentage change (EAPC) was statistically significant.

3. Where both 1 and 2 above occurred, a potential prediction baseline starting at the inflection point was identified.

4. A likelihood ratio test was performed on this potential identified prediction baseline to observe whether or not the linearity (i.e. either an upward or downward trend) within it was statistically significant, i.e. did inclusion of year (as a continuous variable) improve the statistical fit of the model.

5. If the prediction baseline identified in (4) above yielded a statistically significant likelihood ratio test result then it was chosen. If not, then a more recent (i.e. shorter) prediction baseline was tested, going forward one year at a time until a statistically significant trend was produced, or to 1994 at the latest. A prediction baseline based on the period between 1995 (or more recent years) and 2002 was considered too short to give acceptable predictions intervals.

6. If a prediction baseline was identified in (5) above then it was chosen for modelling. If not (or if the most recent linear trend identified in (1) was not statistically significant in (2)) then a search for a 'suitable' prediction baseline was

made. To avoid using very long prediction baselines in the analysis, no mortality data prior to 1972 were ever used in this selection process.

7. The search for this 'suitable' prediction baseline in the absence of an inflection point (1972 or later) was begun by choosing a 15-year prediction baseline (i.e. 1988-2002) and checking, using the likelihood ratio, if it produced a statistically significant result. If so, then this baseline prediction was chosen for modelling. If not, then the period 1989-2002 was tested. This process proceeded one year at a time up to 1994.

8. If a prediction baseline was not identified by (7) above, then the process was repeated, beginning with 1987-2002 and going backwards one year at a time until 1979[¶], checking each period by likelihood-ratio testing.

9. If no period between 1979-2002 and 1994-2002 produced a statistically significant likelihood ratio test result then a prediction baseline based on the years 1979-2002 was chosen.

10. Having selected the prediction baseline, the choice of model (linear or log-linear) was based on the general direction of the predicted trend. Generally, log-linear models were applied to decreasing trends while linear models were used for increasing trends[*]. The difference in the goodness of fit values (deviance and Pearson chi square between the models was often very small, even slight, but the model chosen could generate quite different predictions and prediction intervals. Only in the absence of a clearly defined trend direction was the goodness of fit/deviance value generated by both models above noted when deciding between them. In some cases, the direction of the trend was clearly opposite in direction from that predicted by the applied model with the lower deviance value. In this case, the model with the slightly higher deviance value was chosen.

11. The model chosen was then used to generate predictions for 2005, 2010 and 2015.

[¶] 1979 was the year in which the 9th edition of the International Classification of Diseases (ICD-9) was introduced in Ireland and was thus considered an appropriate "earliest possible start of baseline".

[*] This was to avoid models which predicted unrealistic rates of growth or negative values for mortality rates.

Chapter 3. Summary

Trends 1993-2002

Table 3.1 and Figure 3.1 summarise recent time trends for the cancers described in this report, for the last decade (1993-2002). The current time trends for many cancers began in the 1970s or 1980s, and many of the predictions made later in the report are based on these longer-term trends, as described in "Methods". The data given below are shown merely to illustrate more recent trends. Because of the shorter time period chosen, some of the trends shown are not statistically significant, although those on which the corresponding prediction is based may be. For most of the cancers described here, the most recent trends in age-standardised mortality rate have been downwards. The largest decrease has been in cancer of the stomach, over almost 5% per year in men and 4% in women. The downward trend in lung cancer is much greater for men than for women. Leukaemia is the only cancer for which an upward trend is seen for both sexes, but this is not statistically significant. All of the significant trends in mortality rate are downwards.

Table 3.1. Trends in age-standardised mortality rates 1993-2002; annual percentage change (95% confidence limits)

cancer	*males*	*females*
oesophagus	-0.8% (-2.5%, 0.9%)	-2.3% (-4.8%, 0.2%)
stomach	**-4.7% (-5.8%, -3.7%)**	**-3.8% (-5.2%, -2.4%)**
colorectal	**-1.5% (-2.6%, -0.4%)**	**-2.3% (-3.9%, -0.7%)**
colon	**-2.5% (-3.5%, -1.4%)**	**-2.9% (-4.7%, -1.2%)**
rectum	0.3% (-2.3%, 2.8%)	-0.5% (-3.3%, 2.4%)
pancreas	**-1.6% (-3.2%, -0.0%)**	0.0% (-1.2%, 1.2%)
lung	**-3.0% (-3.9%, -2.2%)**	-0.6% (-1.9%, 0.7%)
breast	—	**-1.8% (-3.0%, -0.7%)**
cervix	—	-1.6% (-4.0%, 0.9%)
corpus	—	-1.4% (-5.6%, 2.8%)
ovary	—	-0.6% (-2.5%, 1.3%)
prostate	-0.2% (-1.0%, 0.6%)	—
brain	**-1.7% (-3.4%, -0.1%)**	**-3.6% (-6.7%, -0.5%)**
lymphoma	-0.3% (-2.5%, 1.9%)	1.5% (-1.7%, 4.8%)
leukaemia	1.6% (-0.5%, 3.7%)	1.3% (-0.8%, 3.5%)

Statistically significant trends are shown in bold

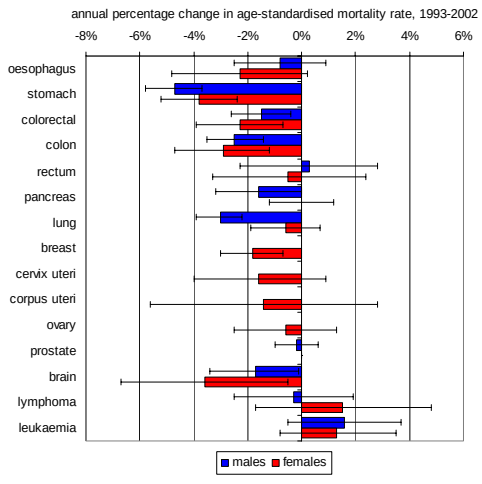


Figure 3.1. Changes in world age-standardised mortality rate, 1993-2002

The age-standardised mortality rate for most cancers is predicted to fall between 1998-2002¶ and 2015 (Table 3.2; Figure 3.2). In absolute terms, the largest projected fall is in lung cancer in men, which is predicted to fall by almost 9 deaths per 100,000 person-years, or 25% of the 1998-2002 rate. The largest fall in women is predicted to be in breast cancer, by 5 deaths per 100,000 person-years, a fall of 21%.

Table 3.2. Predicted change in world age-standardised mortality rate (deaths per 100,000 person-years), 1998-2002 to 2015

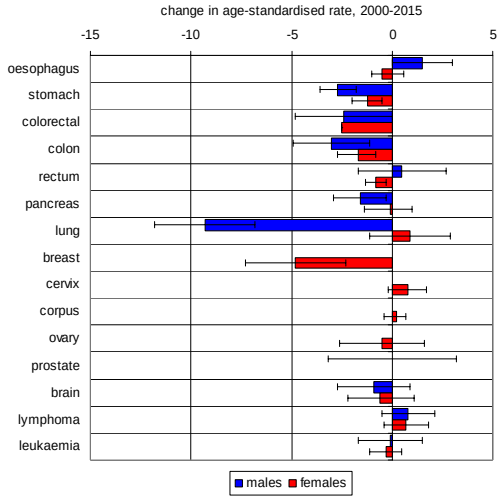
	males			*females*		
	1998-2002 (observed)	*2015 (predicted)*	*predicted change*	*1998-2002 (observed)*	*2015 (predicted)*	*predicted change*
oesophagus	7.6	9.1 (7.6, 10.6)	1.5 (-0.1, 3.0)	3.2	2.7 (1.7, 3.8)	-0.5 (-1.0, 0.6)
stomach	8.0	5.3 (4.5, 6.2)	-2.7 (-3.5, -1.8)	4.1	2.9 (2.1, 3.6)	-1.2 (-2, -0.5)
***colorectal**	20.5	18.1	-2.4	11.3	8.7	-3.5
colon	14.1	11.2 (9.3, 13.1)	-3 0 (-4.8, -1.1)	8.5	6.8 (5.8, 7.7)	-1.7 (-2.7, -0.8)
rectum	6.4	7.0 (4.7, 9.2)	0.5 (-1.7, 2.7)	2.7	1.9 (1.4, 2.5)	-0.8 (-1.3, -0.3)
pancreas	7.4	5.9 (4.6, 7.1)	-1.6 (-2.8, -0.3)	5.2	5.1 (3.8, 6.2)	-0.1 (-1.4, 1.0)
lung	37.2	27.9 (25.5, 30.4)	-9.3 (-11.8, -6.8)	17.5	18.5 (16.4, 20.5)	0.9 (-1.1, 2.9)
breast	—			23.2	18.4 (16.0, 20.9)	-4.8 (-7.3, -2.3)
cervix	—			3.0	3.8 (2.8, 4.7)	0.8 (-0.2, 1.7)
corpus	—			1.6	1.8 (1.2, 2.3)	0.2 (-0.4, 0.7)
ovary	—			8.2	7.7 (5.6, 9.8)	-0.5 (-2.6, 1.6)
prostate	18.4	18.4 (15.2, 21.6)	0 .0 (-3.2, 3.2)	—		
brain	5.3	4.5 (2.7, 6.2)	-0.9 (-2.6, 0.9)	3.4	2.8 (1.2, 4.4)	-0.6 (-2.2, 1.1)
lymphoma	6.0	6.8 (5.5, 8.1)	0.8 (-0.5, 2.1)	4.3	5.0 (3.9, 6.1)	0.7 (-0.4, 1.8)
leukaemia	5.8	5.7 (4.1, 7.3)	-0.1 (-1.7, 1.5)	3.4	3.1 (2.3, 3.9)	-0.3 (-1.1, 0.5)
***all cancers described**	116.4	97.6	-18.8	88.3	80.5	-7.8

**Data for colorectal cancer and for "all cancers described" have no prediction intervals, as they were not modelled but have been calculated from the sum of the predictions for their constituent cancers.*

A number of other cancers, although not predicted to fall by as much in absolute terms, are expected to fall by similarly large proportions of their 1998-2002 rates. The biggest proportionate falls are predicted for cancer of the stomach (predicted to fall by 33% of the 1998-2002 rate in men, by 30% in women); cancer of the colon (a 21% fall in men and 20% fall in women); and cancer of the rectum in women (a 29% fall).

¶ The period 1998-2002 was chosen for comparison purposes, as the five-year average gives an estimate of current mortality which is less affected by random year-to-year variation than a figure for a single year.

Figure 3.2. Predicted change in world age-standardised mortality rate, 1998-2002 to 2015



Predicted number of deaths

Although death rates are predicted to fall for most of the major cancers, the increase in population size, and, in particular, the increase in the older population, in whom most cancers arise, will oppose the overall tendency to a fall in cancer mortality. With only minor exceptions, the number of deaths is predicted to increase for all of the cancers described in this report (Table 3.3; Figure 3.3)

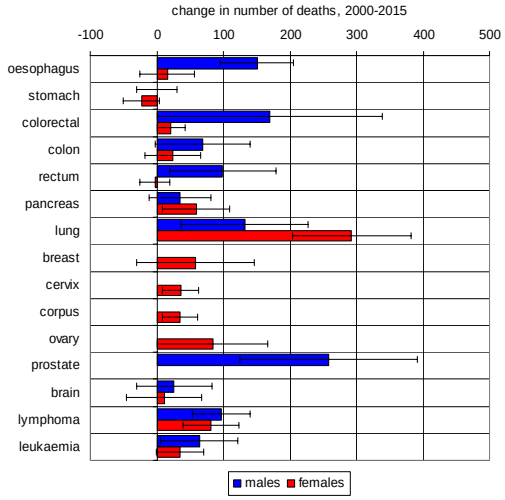
Table 3.3. Predicted change in average annual number of deaths, 2000 (1998-2002 average) to 2015

	males			*females*		
cancer	*1998-2002*	*2015*	*predicted change*	*1998-2002*	*2015*	*predicted change*
oesophagus	193	344 (289, 399)	151 (96, 206)	114	130 (89, 172)	16(-25, 58)
stomach	204	204 (173, 236)	0 (-31, 32)	142	119 (92, 146)	-23 (-50, 4)
***colorectal**	527	696	169	387	408	21
colon	364	433 (362, 505)	69 (-2, 141)	294	318 (276, 361)	24 (-18, 67)
rectum	164	263 (183, 343)	99 (19, 179)	93	90 (68, 113)	-3 (-25, 20)
pancreas	191	226 (179, 273)	35 (-12, 82)	180	239 (188, 290)	59 (8, 110)
lung	946	1077 (982, 1171)	132 (37, 226)	551	844 (755, 933)	293 (204, 382)
breast	—			638	695 (607, 784)	58 (-30, 147)
cervix	—			73	109 (82, 136)	36 (9, 63)
corpus	—			51	86 (59, 113)	35 (8, 62)
ovary	—			231	315 (232, 399)	84 (1, 168)
prostate	528	787 (654, 919)	258 (125, 390)	—		
brain	122	145 (88, 203)	26 (-31, 84)	88	98 (41, 156)	11 (-46, 69)
lymphoma	143	240 (197, 283)	97 (54, 140)	128	209 (167, 250)	81 (39, 122)
leukaemia	148	209 (151, 266)	64 (6, 121)	109	144 (108, 180)	35 (-1, 71)
all cancers described	3003	3928	925	2692	3396	704

**Data for colorectal cancer and for "all cancers described" have no prediction intervals, as they were not modelled but have been calculated from the sum of the predictions for their constituent cancers.*

However, in many cases the 95% prediction intervals for many cancers are quite wide, and increases can be predicted with confidence only for deaths from oesophageal cancer in men (midpoint estimate 151 extra deaths), rectal cancer in men (99 extra deaths), lung cancer in both sexes (132 extra deaths in men and 293 in women), cervical cancer in women (36 extra deaths), ovarian cancer in women (84 extra deaths), prostate cancer in men (258 extra deaths), lymphoma and leukaemia in both sexes (97 extra deaths in men and 81 in women) males (64 extra deaths) The overall predicted increase in number of deaths for the 14 cancers studied is 925 for men and 704 for women.

Figure 3.3. Predicted change in average annual number of deaths between 2000 (1998-2002 average) and 2015



The age-standardised mortality rate for most cancers is predicted to fall between 1998-2002¶ and 2015 in persons under 65 years of age (Table 3.4). In absolute terms, the largest projected fall is in lung cancer in men, which is predicted to fall by 5.6 deaths per 100,000 person-years, or 41% of the 1998-2002 rate. The largest fall in women is predicted to be in breast cancer, by 2.7 deaths per 100,000 person-years, a fall of 18%.

Table 3.4. Predicted change in world age-standardised mortality rate in persons under 65 (deaths per 100,000 person-years), 1998-2002 to 2015

	males			*females*		
cancer	*1998-2002 (observed)*	*2015 (predicted)*	*predicted change*	*1998-2002 (observed)*	*2015 (predicted)*	*predicted change*
oesophagus	3.1	3.6 (2.6, 4.6)	0.5 (-0.6, 1.5)	1.1	0.8 (0.4, 1.2)	-0.3 (-0.8, 0.1)
stomach	2.9	1.67 (1.1, 2.2)	-1.3 (-1.8, -0.7)	1.4	1.0 (0.2, 1.7)	-0.5 (-1.2, 0.3)
***colorectal**	7.5	5.4	-2.1	4.3	2.5	-1.8
colon	5.0	3.1 (2.1, 4.2)	-1.9 (-3.0, -0.8)	3.3	1.9 (1.1, 2.6)	-1.5 (-2.2, -0.7)
rectum	2.5	2.2 (1.4, 3.0)	-0.2 (-1.0, 0.6)	1.0	0.6 (0.3, 1.0)	-0.4 (-0.7, -0.0)
pancreas	2.8	1.7 (0.9, 2.5)	-1.2 (-2.0, -0.4)	1.7	1.2 (0.7, 1.7)	-0.5 (-1.0, 0.0)
lung	13.6	8.0 (6.6, 9.3)	-5.6 (-6.9, -4.2)	6.7	5.2 (3.9, 6.4)	-1.5 (-2.8, -0.3)
breast	—			15.4	12.7 (10.6, 14.8)	-2.7 (-4.8, -0.7)
cervix	—			2.5	3.4 (2.4, 4.3)	0.9 (-0.1, 1.8)
corpus	—			0.7	0.4 (0.0, 0.7)	-0.3 (-0.6, 0.1)
ovary	—			4.9	3.7 (2.1, 5.3)	-1.2 (-2.8, 0.4)
prostate	2.3	2.5 (1.7, 3.2)	0.2 (-0.6, 1.0)	—		
brain	4.0	2.8 (1.6, 4.0)	-1.2 (-2.4, 0.0)	2.3	1.3 (0.4, 2.3)	-1.0 (-1.9, -0.0)
lymphoma	2.9	3.6 (2.6, 4.6)	0.6 (-0.4, 1.6)	2.0	1.6 (0.6, 2.6)	-0.4 (-1.3, 0.6)
leukaemia	2.3	1.9 (1.2, 2.8)	-0.4 (-1.1, 0.3)	1.7	1.2 (0.6, 1.7)	-0.5 (-1.0, 0.1)
***all cancers described**	48.9	31.0	-17.9	48.9	34.8	-14.1

**Data for colorectal cancer and for "all cancers described" have no prediction intervals, as they were not modelled but have been calculated from the sum of the predictions for their constituent cancers.*

¶ The period 1998-2002 was chosen for comparison purposes, as the five-year average gives an estimate of current mortality which is less affected by random year-to-year variation than a figure for a single year.

Predicted number of deaths

In contrast to the population as a whole, the number of deaths in the under 65s is predicted to fall, or remain stable, for many cancers (Table 3.5). The main exceptions to this are cancers of the oesophagus, colorectum, prostate, lymphoma and leukaemia in men, and cancer of the cervix in women.

Table 3.5. Predicted change in average annual number of deaths in persons under 65, 2000 (1998-2002 average) to 2015

	males			*females*		
cancer	*1998-2002 (observed)*	*2015 (predicted)*	*predicted change*	*1998-2002 (observed)*	*2015 (predicted)*	*predicted change*
oesophagus	60	96 (69, 124)	36 (9, 63)	21	21 (10, 33)	0 (-11, 11)
stomach	56	46 (31, 61)	-10 (-25, 5)	27	24 (7, 40)	-3 (-20, 14)
***colorectal**	142	148	6	82	66	-16
colon	95	87 (57, 116)	-8 (-38, 22)	63	49 (30, 67)	-14 (-33, 5)
rectum	47	61 (39, 83)	14 (-8, 36)	19	17 (8, 27)	-2 (-11, 7)
pancreas	54	47 (24, 69)	-7(-30, 16)	31	34 (20, 48)	3 (-11, 17)
lung	258	223 (186, 261)	-35 (-72, 2)	127	136 (104, 168)	9 (-23, 41)
breast	–	–	–	296	335 (280, 389)	39 (-16, 94)
cervix	–	–	–	48	76 (54, 98)	28 (6, 50)
corpus	–	–	–	12	10 (1, 18)	-2 (-11, 7)
ovary	–	–	–	94	94 (54, 133)	0 (-40, 40)
prostate	42	71 (49, 93)	29 (7, 51)		–	–
brain	75	72 (41, 103)	-3 (-34, 28)	43	31 (9, 52)	-12 (-34, 10)
lymphoma	56	91 (66, 116)	35 (10, 60)	37	43 (17, 69)	6 (-20, 32)
leukaemia	42	47 (30, 65)	5 (-12, 22)	30	28 (15, 42)	-2 (-15, 11)
all cancers described	927	841	-86	930	898	-32

**Data for colorectal cancer and for "all cancers described" have no prediction intervals, as they were not modelled but have been calculated from the sum of the predictions for their constituent cancers.*

Chapter 4. Oesophageal cancer (ICD-9 150)

Epidemiology

Oesophageal carcinoma was the ninth most common cancer and the seventh commonest cause of cancer death in the period 1994-2001, with an annual average of 305 cases and 309 deaths during this period. Female cases made up 39% of the total and female deaths 38%.

Oesophageal cancer is mainly a disease of older populations (Table 4.1). 56% of cases and 60% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined.

Table 4.1. Age distribution of oesophageal cancer deaths and cases, 1994-2001

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	<1%	<1%	<1%	<1%	<1%	<1%
30-39	<1%	1%	1%	1%	1%	1%
40-49	3%	3%	5%	6%	4%	5%
50-59	8%	10%	14%	16%	12%	14%
60-69	18%	19%	27%	28%	23%	25%
70-79	34%	33%	34%	32%	34%	32%
80+	37%	33%	19%	16%	26%	23%

Survival from oesophageal cancer is poor. Data from EUROCARE 3 (Sant et al, 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 10% for both men and women, while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 5% (Berrino et al. 1995).

Five-year survival for patients diagnosed in Ireland in 1994-1996 was 10.9% (95% CI 7.5-14.3%) for men and 14.8% (10.9-19.3%) for women; in 1997-1999, 11.4% (7.6-15.2%) for men, 12.2% (7.4-18.3%) for women (National Cancer Registry 2003).

Non-genetic risk factors

Oesophageal cancer has two main sub-types—squamous cell carcinoma and adenocarcinoma. These are not distinguished in coding death certificates, but incidence data for Ireland (National Cancer Registry, unpublished data) shows that the proportion of adenocarcinoma is increasing for both men and women (Table 4.2). In the 1960s, squamous cell cancers comprised over 90% of all oesophageal tumours in the US, but the incidence of adenocarcinoma has risen so that it is now more frequent than squamous cell cancer (Blot and McLaughlin 1999).

These two types of oesophageal carcinoma differ in their aetiology. While risk factors for squamous cell carcinoma of the oesophagus have been identified (such as tobacco use, alcoholism, malnutrition and infection with human papilloma virus) (Chow, Blot et al. 1998) the risk factors associated with adenocarcinoma are less well defined. The most important epidemiological difference between squamous cell cancer and adenocarcinoma is the association between gastro-oesophageal reflux and adenocarcinoma. The frequency, severity, and duration of reflux symptoms are positively associated with increased risk of oesophageal adenocarcinoma (Lagergren, Bergstrom et al. 1999).

Table 4.2. Percentage of adenocarcinoma in newly incident cases of oesophageal cancer, Ireland 1994-2001

	female	*male*
1994	17%	37%
1995	17%	45%
1996	26%	47%
1997	25%	39%
1998	19%	49%
1999	27%	52%
2000	21%	53%
2001	25%	51%

The main risk factor for adenocarcinoma of the oesophagus is obesity, which may act by increasing gastro-oesophageal reflux. Squamous cell carcinoma, on the other hand, is associated with poor nutrition; increased consumption of fresh fruit and vegetables is protective against both types (Devesa, Blot et al. 1998).

The risk of squamous cell carcinoma is greatly increased by tobacco smoking and by excessive alcohol consumption, which between them account for the majority of cases in developed countries. For cigarettes, heavy smoking is associated with a 5- to 10-fold risk (with the risk particularly high for high-tar cigarettes, pipes and cigars) (Siemiatycki, Krewski et al. 1995). Strong links have also been demonstrated with alcohol abuse, with possibly up to a 20-fold risk in the heaviest drinkers. In individuals who both smoke and drink heavily the two risk factors exhibit a synergistic relationship (World Cancer Research Fund, 1997). The risk of adenocarcinoma also appears to be higher in smokers (Brown, Silverman et al. 1994).

Squamous carcinoma is associated with human papilloma virus (HPV) infection (Farhadi, Tahmasebi et al. 2005), although possibly only in high-incidence areas (Kamath, Wu et al. 2000; Awerkiew, Bollschweiler et al. 2003; Weston and Prolla 2003). The rise in the incidence of oesophageal adenocarcinoma may be linked to the declining prevalence of *Helicobacter pylori* infection. Gastric infection with *H. pylori* may protect the oesophagus from reflux and its complications by causing a decrease in gastric acid production (Graham and Yamaoka 1998).

A systematic review and meta-analysis of the association of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) with oesophageal cancer showed a protective association between aspirin/NSAID use and oesophageal cancer (Corley, Kerlikowske et al. 2003). Medications which reduce the tone of the lower gastro-oesophageal sphincter predispose to gastro-oesophageal reflux, Barrett's oesophagus and, probably, adenocarcinoma of the oesophagus (O'Connor 1999).

Trends

Between 1950 and 2002, the annual number of oesophageal cancer deaths rose from 73 to 190 in men and from 70 to 100 in women, corresponding to an average increase of 1.8% per year for men and 1.3% for women over the whole period (Figure 4.1). Crude mortality rates also increased, by 1.2% annually for men and by 0.6% for women (Figure 4.2). However, the trends in age-standardised rates (Figures 4.3, 4.4) show different patterns of change for men and women. For men there has been a steady increase in rate since 1950, while for women, the mortality rate and increase were similar to that for men up to around 1970, but have fallen slightly since then. Similar trends were seen in cumulative risk of death from oesophageal cancer before age 65 (Figure 4.5). This increased from 0.18% in 1950 to 0.35% in 2002 for men, but, for women, fell from 0.28% in 1966 to 0.09% in 2002. The number of years of potential life lost to oesophageal cancer has followed a pattern almost identical to that for cumulative risk (Figure 4.6). Trends since 1992 indicate a non-significant annual increase in total age-standardised mortality rates for males and a non-significant annual decrease for females (see Figures 4.11, 4.12).

Figure 4.1. Number of deaths per year, 1950-2002

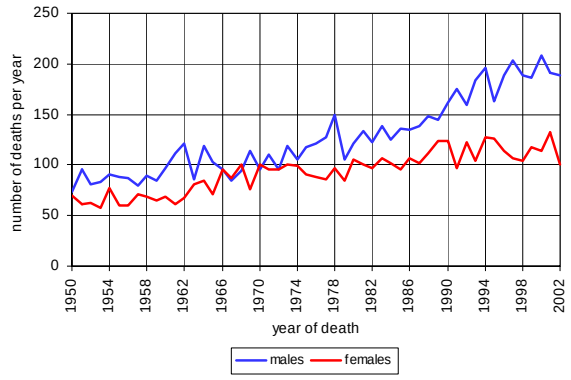


Figure 4.2. Crude mortality rate, 1950-2002

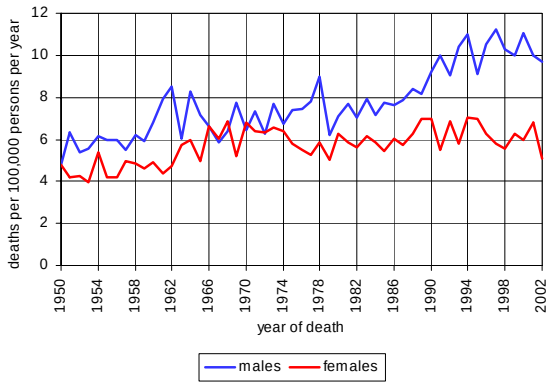


Figure 4.3. World age-standardised mortality rate, all ages, 1950-2002

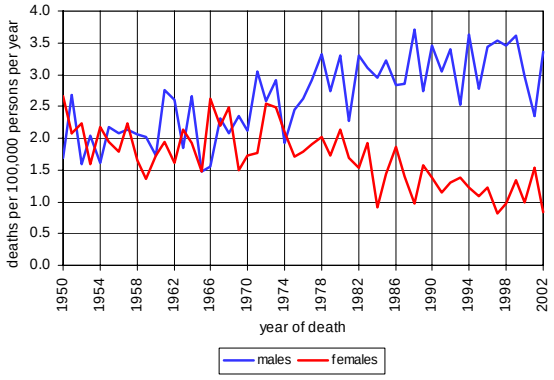


Figure 4.4. World age-standardised mortality rate, 0-64 years, 1950-2002

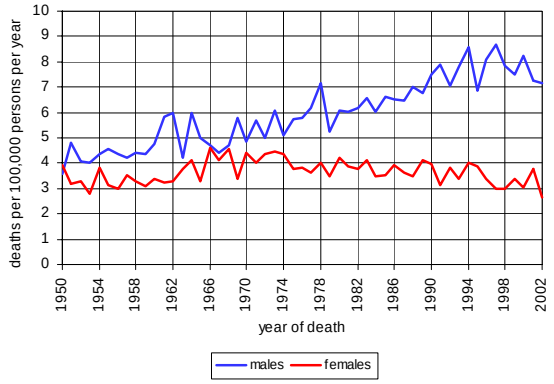


Figure 4.5. Cumulative risk of dying of cancer before age 65, 1950-2002

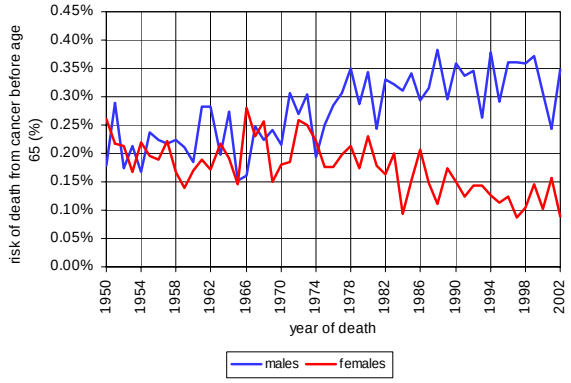
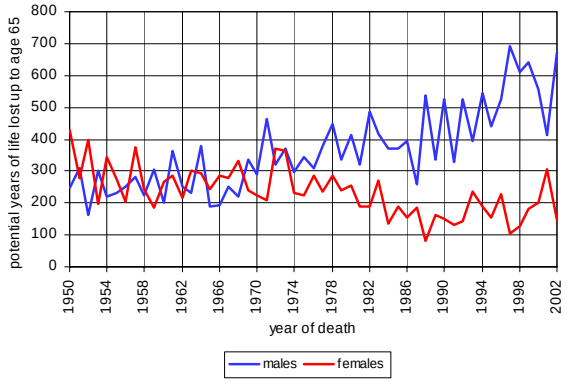


Figure 4.6. Years of potential life lost up to age 65, 1950-2002



Joinpoint regression analysis

Table 4.3. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1950		1950		1950		1950	
↓	1.3% (1.2%, 1.5%)	↓	1.4% (0.6%, 2.2%)	↓	1.1% (0.8%, 1.4%)	↓	0.2% (-0.9%, 1.3%)
2002		1972 (1966, 1977)		2002		1973 (1966, 1983)	
		↓	-0.9% (-1.3%, -0.4%)			↓	-2.4% (-3.2%, -1.5%)
		2002				2002	

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised mortality rate for men showed a constant increase of 1.3% per annum from 1950 to 2002 (Table 4.3, Figure 4.7). For women, the rate increased by 1.4% annually between 1950 and 1972 but decreased by 0.9% per annum between 1972 and 2002.

For men under 65 years of age the mortality rate increased by 1.1% annually from 1950 to 2002, while for women there was little change between 1950 and 1973 followed by a 2.4% decrease annually from 1973 to 2002 (Figure 4.8).

Figure 4.7. Joinpoint models (line) and actual (points) World age-standardised mortality rate, all ages, 1950-2002

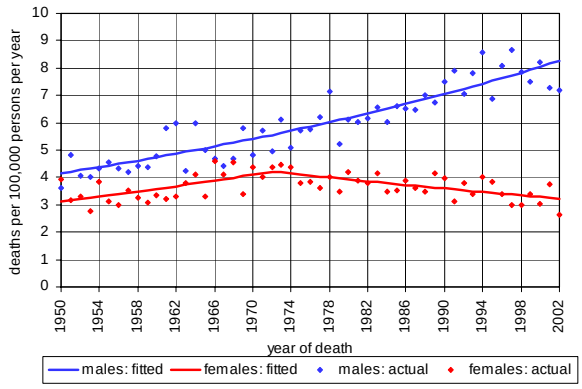
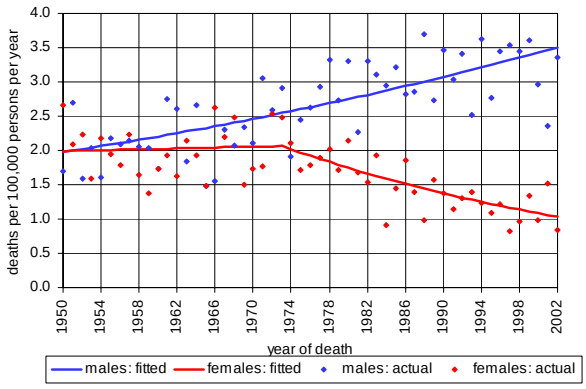


Figure 4.8. Joinpoint models (line) and actual (points) World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

The age-period analyses (Figures 4.9, 4.10) show an increasing mortality rate for males of 70 and over from 1972 onwards and for women of 75 and over from 1953. A particularly large increase in mortality occurred in men aged 75-79 after 1987. There has been a fall in mortality for women under 60 since the 1970s and for women of all ages since 1997. The fall in mortality in men has been slight and in only a few age groups.

There is some slight evidence of increased mortality for the cohort of men born around 1923-1927 (Figure 4.11), and for women born in 1918-1922 (Figure 4.12), but apart from this, there is very little evidence that year of birth had any effect on mortality independent of age, or period of death.

Figure 4.9. Age-specific mortality by period of death, males, 1950-2002

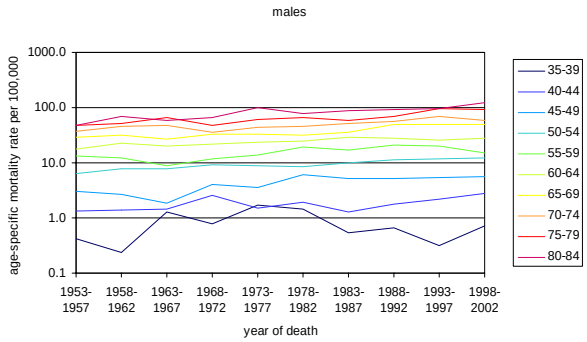


Figure 4.10. Age-specific mortality by period of death, females, 1950-2002

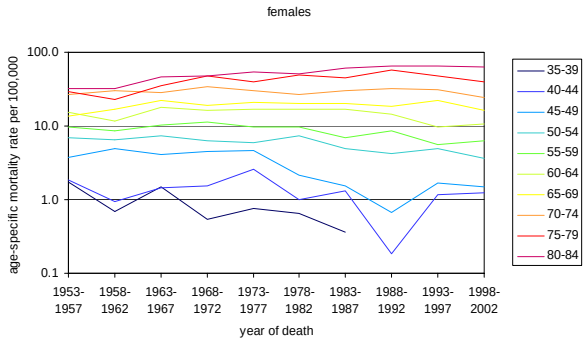


Figure 4.11. Age-specific mortality by birth cohort, males, 1950-2002

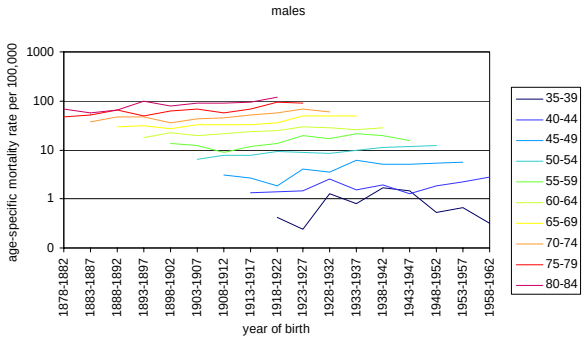
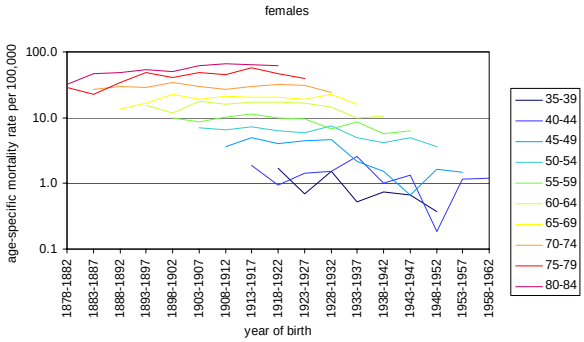


Figure 4.12. Age-specific mortality by birth cohort, females, 1950-2002



International trends

With the exception of France, where mortality rates for males were much higher than elsewhere during most of the period 1950-2002 (Figures 4.13, 4.15), most countries in north-western Europe and the USA had age-standardised mortality rates for oesophageal cancer in men ranging from 2 to 6 per 100,000 in the early 1950s. Rates have increased steadily since the 1950s in many countries, but have fallen sharply in France since the 1960s to values close to those for neighbouring countries. The rates in Sweden and the USA have remained much the same as the 1950 values. Mortality rates for women were generally lower, in the region of 1 to 2 per 100,000 (Figures 4.14, 4.16). The UK and Ireland were an exception, with rates almost double this in the 1950s. Mortality rates have increased in England, Wales and Scotland, but have remained unchanged in Ireland. Many other countries seem to have a pattern of decrease from 1950 to the 1970s, followed by a gradual increase to levels higher than in earlier years. Although information is not available on the type of cancer causing death, this may reflect a change from predominantly squamous cell carcinoma to adenocarcinoma.

Figure 4.13 Rolling 5-year average World age standardised mortality rates in Europe and USA, males, all ages, 1950 to 2002

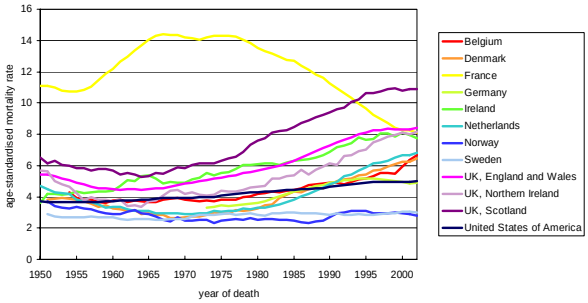
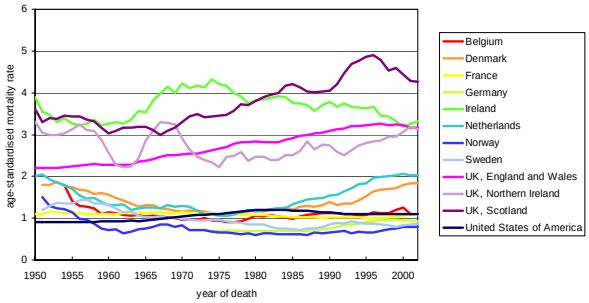


Figure 4.14. Rolling 5-year average World age standardised mortality rates in Europe and USA, females, all ages, 1950 to 2002



More recent estimates of change (Figures 4.15, 4.16) indicate significant increases in age-standardised mortality since 1992 for men in Belgium, Denmark and the Netherlands, and for women in Denmark and the Netherlands. Significant decreases have been seen in male mortality in France and Germany and in female mortality in Scotland. The trends in Ireland are not significant for either sex.

Figure 4.15. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

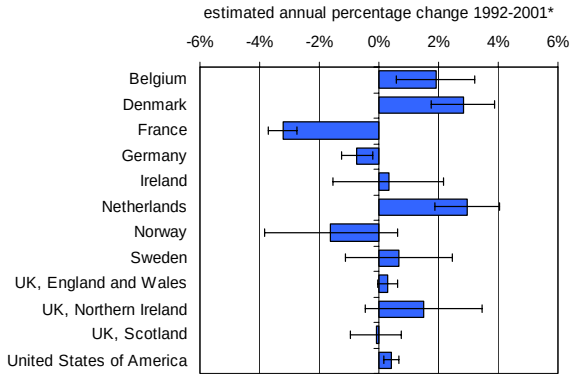
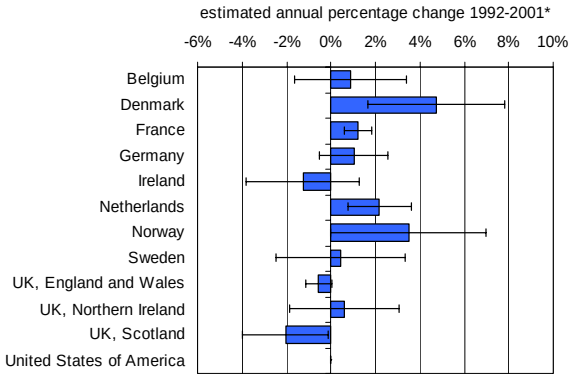


Figure 4.16. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



**or nearest available period*

Predictions for the period 2005-2015

Oesophageal cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to increase from 7.61 in 1998-2002 to 9.06 (95% prediction interval 7.55, 10.58) in 2015 (Figure 4.17, Table 4.5). The number of deaths in men is predicted to rise from 193 per year in 1998-2002 to 244 (289, 399) in 2015. In men under 65 the mortality rate is predicted to increase from 3.15 in 1998-2002 to 3.61 (2.56, 4.65) in 2015, with an accompanying increase in the number of deaths from 60 per year in 1998-2002 to 96 (69, 124) in 2015.

Table 4.4. Models chosen for predictions

model	*sex*	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	males	1984-2002	108	linear	0.0029
	females	1989-2002	84	log-linear	0.0648
0-64	males	1979-2002	72	log linear	0.5434
	females	1973-2002	69	log linear	0.0493

Mortality rates in women are predicted to fall from 3.17 in 1998-2002 to 2.74 (1.65, 3.84) in 2015. The number of deaths is also predicted to increase—from 114 per year in 1998-2002 to 130 (89, 172) in 2015. In women under 65 mortality rates are also expected to fall, from 1.13 in 1998-2002 to 0.79 (0.35, 1.23) in 2015. The number of deaths in this age group is expected to show little change–21 per year in 1998-2002 and 21 (10, 33) in 2015.

Table 4.5. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	7.61	8.33 (7.06, 9.60)	8.70 (7.32,10.07)	9.06 (7.55,10.58)
No. of deaths (95% PI)	193	234 (200, 269)	281 (238, 324)	344 (289, 399)
females, all ages				
WASMR (95% PI)	3.17	3.01 (2.27, 3.76)	2.84 (2.00, 3.69)	2.74 (1.65, 3.84)
No. of deaths (95% PI)	114	116 (90, 141)	121 (89, 153)	130 (89, 172)
males, 0-64				
WASMR (95% PI)	3.15	3.36 (2.48, 4.23)	3.47 (2.54, 4.40)	3.61 (2.56, 4.65)
No. of deaths (95% PI)	60	74 (55, 93)	86 (63, 109)	96 (69, 124)
females, 0-64				
WASMR (95% PI)	1.13	0.97 (0.51, 1.43)	0.87 (0.43, 1.32)	0.79 (0.35, 1.23)
No. of deaths (95% PI)	21	21 (11, 31)	22 (11, 32)	21 (10, 33)

The numbers of deaths presented in Table 4.5 and in Figures 4.19 and 4.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 4.6, which shows the effect of population change in the absence of any trend in rates.

For males, demographic change accounts for over half of the increase in the projected number of deaths, while for females it can be seen that, in the absence of a downward trend in rates, demographic change alone would result in an additional 42 deaths per year in 2015.

Table 4.6. Predictions of number of deaths at all ages, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths (95% PI)	193	214 (182, 246)	245 (211, 279)	286 (248, 324)	114	124 (100, 148)	138 (112, 164)	156 (128, 184)

Figure 4.17. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

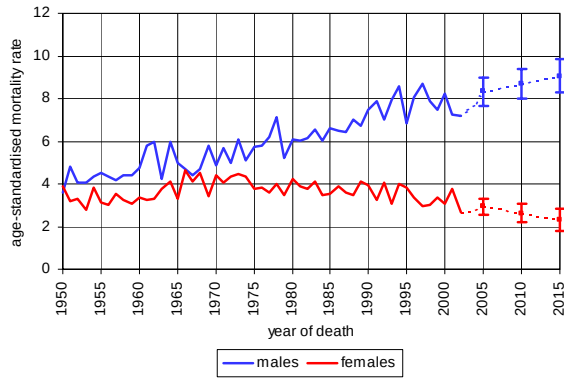


Figure 4.18. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

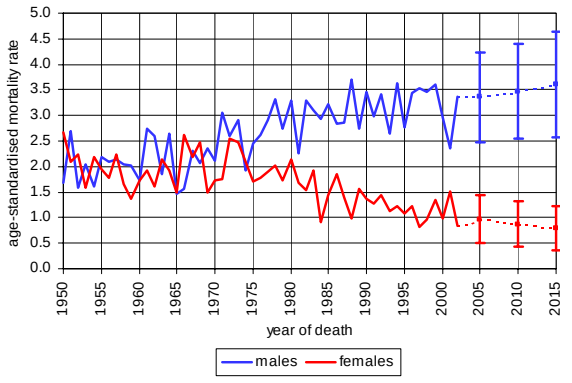


Figure 4.19. Actual and predicted number of deaths, all ages, 1950-2015

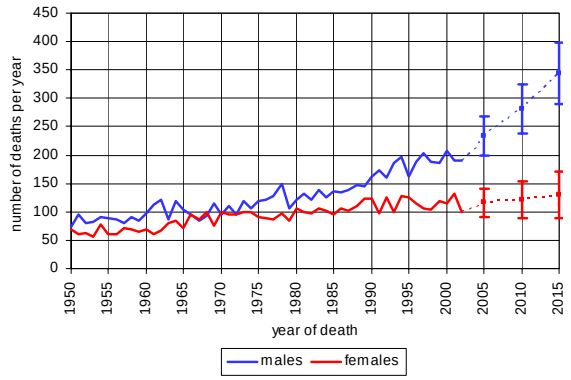
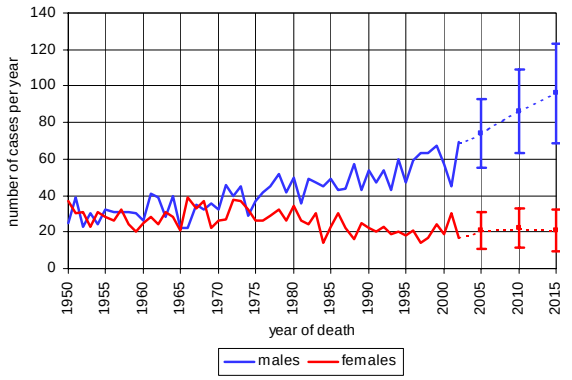


Figure 4.20. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Trends to 2002

As with most cancers, the number of deaths from oesophageal cancer increased for both sexes between 1950 and 2002. However, there was no overall increase in the age-standardised mortality rate for women, with a suggestion of a fall in recent years. For men, the mortality rate has continued to increase.

Joinpoint analysis indicated a long-term annual percentage rate of increase of 1.3% in the mortality rate for men, and a recent fall (since around 1972) of 0.9% per annum in women. For men under 65 the annual rate of increase was 1.1% and for women the rate of fall (since around 1973) was 2.4%.

The increase in rate in men seemed to be strongest in the 75-79 year age group. There was some evidence of dependence of year of birth, as mortality was highest in men born between 1918 and 1927.

Predictions

Mortality rates are predicted to rise in men by 19% over the 15-year period between 1998-2002 and 2015 and to fall in women by 14% in the same period. In men under 65 the mortality rate in this period is predicted to rise by 15% and to fall in women by 30%. The number of deaths is expected to increase in men from an average of 193 per annum in 1998-2002 to 344 in 2015 (a 78% increase) but show little change in women, from 114 to 116. The annual number of deaths in those under 65 is predicted to increase from 60 to 96 in men, a 60% increase, but to show no change, from 21 deaths, in women.

Conclusions

The long-term rise in mortality rates from oesophageal cancer in men appears set to continue over the next decade. In contrast, rates are expected to fall in women although numbers will show little change. Although a decrease in smoking in males might be expected to lead to reductions in oesophageal cancer mortality, this is possibly countered by increasing alcohol consumption in Ireland (EHFA 2003). Interpretation of patterns is further complicated by changes in the relative frequency of the two main types of oesophageal carcinoma, with adenocarcinoma now more common than squamous cell carcinoma in men and also increasing in women. As the aetiology of adenocarcinoma is quite different from that of squamous carcinoma, past trends in squamous carcinoma will not predict future rates of adenocarcinoma, thus predictions for oesophageal cancer as a whole should (as applies to all such predictions to some extent) be taken as little more than best guesses.

Poor survival from oesophageal carcinoma and the absence of any proven method of screening emphasise the importance and potential effectiveness of preventive measures for this cancer, including smoking cessation, moderation in alcohol intake and (for adenocarcinoma) weight reduction.

Chapter 5. Stomach cancer (ICD-9 151)

Epidemiology

Stomach (gastric) carcinoma was the fourth most common cancer and the fifth commonest cause of cancer death in the period 1994-2001, with an annual average of 482 cases and 375 deaths during this period. Female cases made up 38% of the total and female deaths 40%.

Stomach cancer is mainly a disease of older populations (Table 5.1). 56% of cases and 62% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined.

Table 5.1. Age distribution of stomach cancer deaths and cases, 1994-2001

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	0%	0%	0%	0%	0%	0%
30-39	2%	2%	1%	2%	1%	2%
40-49	4%	5%	4%	5%	4%	5%
50-59	7%	9%	12%	14%	10%	12%
60-69	17%	21%	27%	28%	23%	25%
70-79	37%	36%	37%	37%	37%	37%
80+	32%	27%	19%	15%	24%	19%

Survival from stomach cancer is poor. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 22% for men and 26% for women, while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 14% for men and 18% for women (Berrino et al. 1995).

Five-year relative survival estimates for patients diagnosed in Ireland in 1994-1996 were 15.6% for men and 19.2% (15.0-23.4%) for women; in 1997-1999, 16.9% (13.2-20.6%) for men and 22.2% (17.6-26.8%) for women (National Cancer Registry 2003).

Non-genetic risk factors

Decreases in mortality rates from stomach cancer in western countries have been associated (at least in part) with improvements in food-preservation (in particular, availability of refrigeration as an alternative to salting) (Issenberg 1976; Weisburger 1985). Grilling or barbecuing of meat and fish possibly increase risk (Ward, Sinha et al. 1997).

Cigarette smoking is considered a further likely risk factor for stomach cancer (Lindblad, Rodriguez et al. 2005).

Alcohol consumption increases the risk of cancer of, specifically, the gastric cardia (gastro-oesophageal junction) (Kikuchi, Nakajima et al. 2002; Sasazuki, Sasaki et al. 2002).

Mortality from stomach cancer seems to be more strongly associated with general socio-economic conditions at the time of birth than at the time of death (Leon and Davey Smith 2000). *Helicobacter pylori* infection, most common where socio-economic conditions are poor, is a prime candidate for an early life influence on risk of stomach cancer, given that persistent infections are often acquired in childhood (Forman and Goodman 2000). The decline in stomach cancer death rates

internationally is closely correlated with the prevalence of *H. pylori* infections (Goodman and Correa 1995). The evidence for the role of *H. pylori* infection in the aetiology of stomach cancer does not negate the potential relevance of salt or other factors (Tsugane 2005).

Chronic atrophic gastritis (which often progresses to a gastric ulcer) increases the risk of stomach cancer (Whiting, Sigurdsson et al. 2002), and can arise as a result of *H. pylori* infection or excessive salt intake.

Trends

Between 1950 and 2002, the annual number of stomach cancer deaths fell from 545 to 202 in men and from 448 to 133 in women, corresponding to an average increase, over the whole period, of 2.1% per year for men and 2.4% for women (Figure 5.1). Crude mortality rates also decreased, by 2.6% annually for men and 3.0% for women (Figure 5.2). Trends in age-standardised rates (Figures 5.3, 5.4), cumulative risks of dying before age 65 (Figure 5.5) and years of potential life lost (Figure 5.6) showed similar patterns of change with annual rates of decrease ranging from 2.6% to 4.1%. Trends since 1992 indicate a significant annual decrease in total age-standardised mortality rates for both males (Figure 5.16) and females (Figure 5.17).

Although the absolute difference in rate between men and women has decreased, the ratio of male to female mortality has increased from 1.2 in 1950 to 1.5 (number of deaths) and 2.1 (age-standardised rates) in 2002 (Figure 5.8).

Figure 5.1. Number of deaths per year, 1950-2002

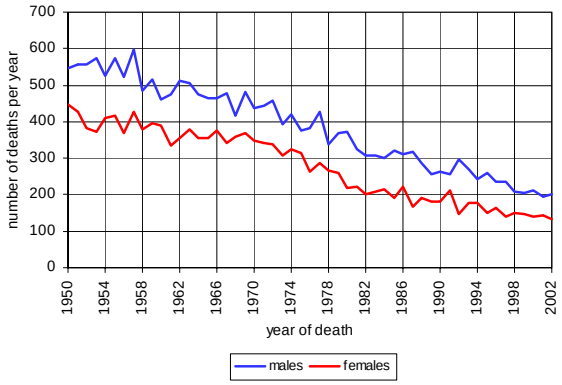


Figure 5.2. Crude mortality rate, 1950-2002

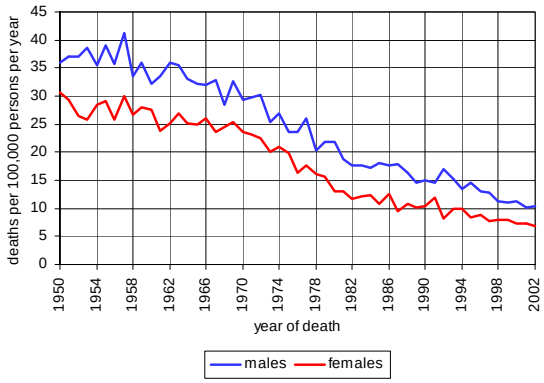


Figure 5.3. World age-standardised mortality rate, all ages, 1950-2002

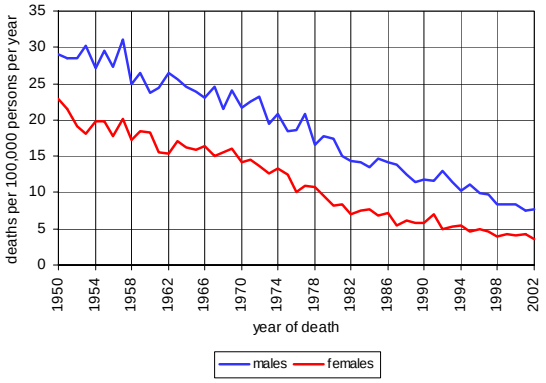


Figure 5.4. World age-standardised mortality rate, 0-64 years, 1950-2002

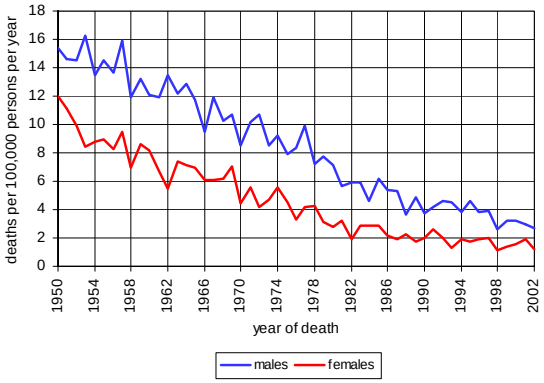


Figure 5.5. Cumulative risk of dying of cancer before age 65, 1950-2002

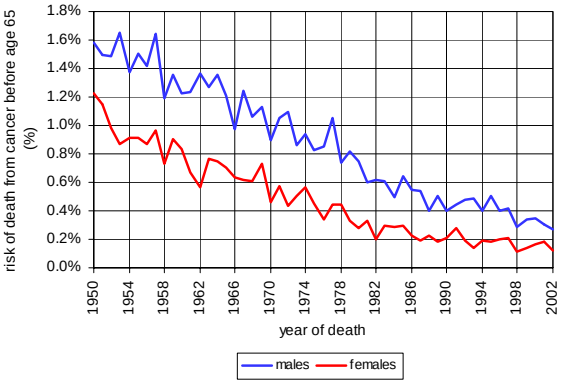


Figure 5.6. Years of potential life lost up to age 65, 1950-2002

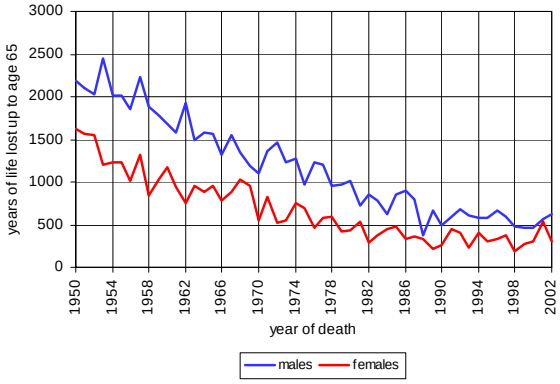
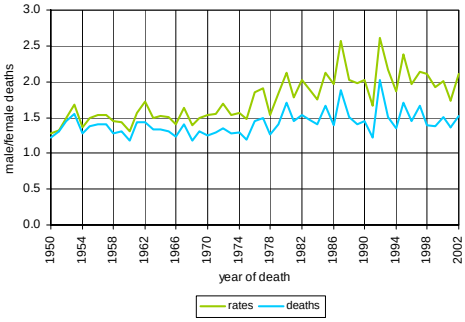


Figure 5.7. Ratio of male to female deaths and age-standardised rate,1950-2002



Joinpoint regression analysis

Table 5.2 Joinpoint models: points of inflection and estimated annual percentage change (EAPC) in age-standardised rate, 1950-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1950		1950		1950		1950	
↓	-1.4% (-1.7%, -1.1%)	↓	-1.8% (-2.2%, -1.4%)	↓	-2.2% (-2.8%, -1.6%)	↓	-4.0% (-4.3%, -3.7%)
1972 (1968, 1976)		1972 (1968, 1977)		1972 (1961, 1978)		2002	
↓	-3.3% (-3.6%, -3.0%)	↓	-5.8% (-7.5%, -4.0%)	↓	-4.1% (-4.6%, -3.6%)		
2002		1982 (1975, 1991)		2002			
		↓	-3.5% (-4.2%, -2.8%)				
		2002					

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate for men showed a decrease of 1.4% per annum from 1950 to 1972 (Table 5.2, Figure 5.8) and a decrease of 3.3% annually from 1972 to 2002. For women, the rate decreased by 1.8% annually up to 1972, by 5.8% between 1972 and 1982 and by 3.5% after 1982.

For men under 65, the rate of decrease was greater—2.2% annually from 1950 to 1972 and 4.1% from 1972 to 2002. For women the rate decreased steadily by 4.0% annually from 1950 to 2002 (Figure 5.9).

Figure 5.8. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

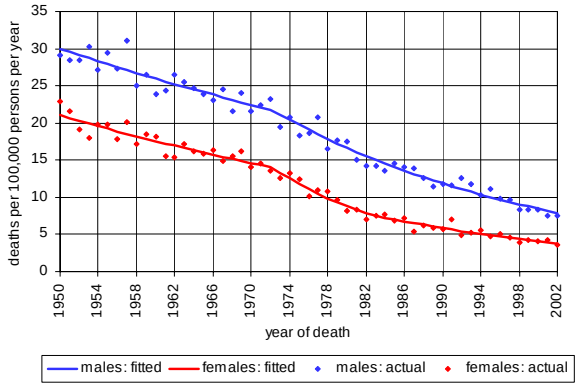
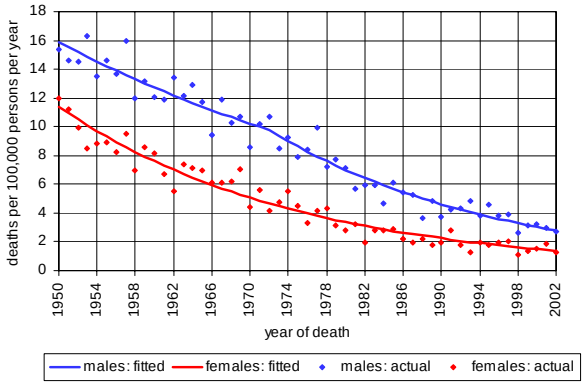


Figure 5.9. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

The age-period analyses (Figures 5.10, 5.11) show a falling mortality rate for both men and women throughout the period 1950-2002, for all age groups.

Figure 5.10 Age-specific mortality by period of death, males, 1950-2002

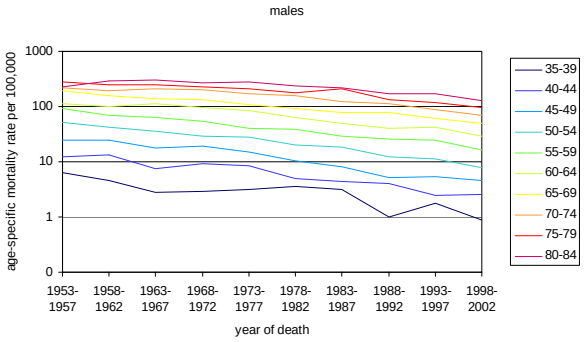
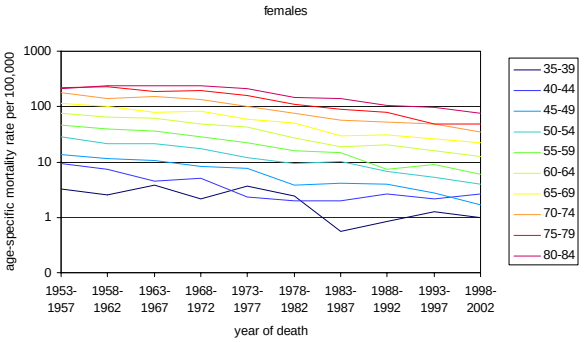


Figure 5.11 Age-specific mortality by period of death, females, 1950-2002



Age-cohort plots (Figure 5.12-5.15) provide little evidence that year of birth had any effect on mortality, independent of age or period of death.

Figure 5.12. Age-specific mortality by birth cohort, males, 1950-2002

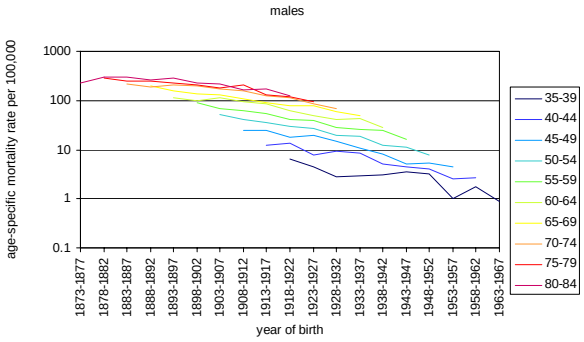
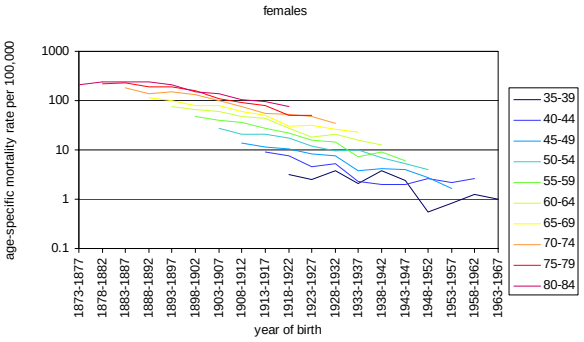


Figure 5.13. Age-specific mortality by birth cohort, females, 1950-2002



International trends

All western countries included below showed a major fall in stomach cancer mortality with very similar patterns for men (Figure 5.14) and women (Figure 5.15). Rates of decrease varied little between European countries. By far the lowest rates and smallest decreases in rate were seen in the United States.

Figure 5.14. Rolling 5-year average World age standardised mortality rates in Europe and USA, males, all ages, 1950 to 2002

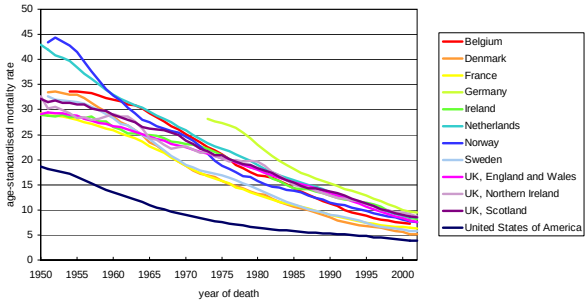
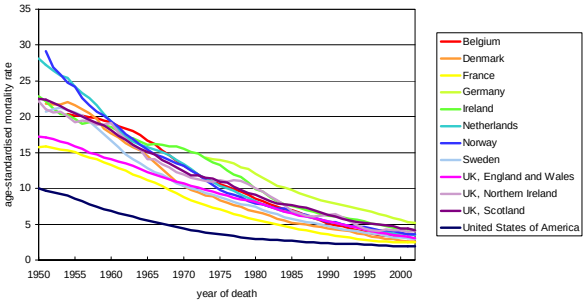


Figure 5.15. Rolling 5-year average World age standardised mortality rates in Europe and USA, females, all ages, 1950 to 2002



Recent estimates of change (Figures 5.16, 5.17) indicate significant falls in age-standardised mortality since 1992 for both sexes for all the countries shown, with those in Ireland, England and Wales being the largest (although the differences from most other countries were not statistically significant).

Figure 5.16. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

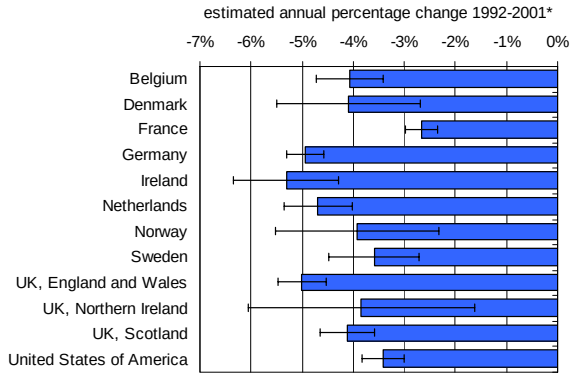
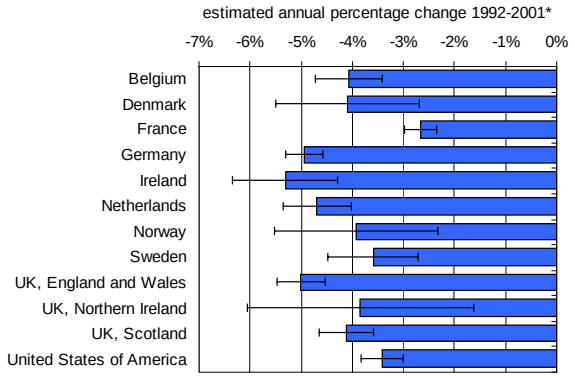


Figure 5.17. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



** or nearest available period*

Predictions for the period 2005-2015

Stomach cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to fall from 8.01 in 1998-2002 to 5.34 (95% prediction interval 4.49, 6.19) in 2015 (Figure 5.18, Table 5.4). However, the number of deaths in men is predicted to show no change—204 per year in 1998-2002 and 204 (173,236) in 2015 (Figure 5.20). In men under 65 the mortality rate is predicted to fall from 2.94 in 1998-2002 to 1.67 (1.13, 2.21) in 2015 (Figure 5.19), with an accompanying fall in the number of deaths from 56 per year in 1998-2002 to 46 (31, 61) in 2015 (Figure 5.21).

Table 5.3. Models chosen for predictions

model	*sex*	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	males	1972-2002	186	log linear	0.0000
	females	1982-2002	126	log linear	0.0000
0-64	males	1972-2002	93	log linear	0.0000
	females	1991-2002	36	log linear	0.0375

Mortality rates in women are predicted to fall from 4.06 in 1998-2002 to 2.85 (2.09, 3.61) in 2015. The number of deaths is also predicted to fall, from 142 per year in 1998-2002 to 119 (92, 146) in 2015. In women under 65 mortality rates are also expected to fall, from 1.43 in 1998-2002 to 0.96 (0.24, 1.68) in 2015. The number of deaths in this age group is also expected to fall, from 27 per year in 1998-2002 to 24 (7, 40) in 2015.

Table 5.5. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	8.01	7.33 (6.24, 8.42)	6.25 (5.29, 7.22)	5.34 (4.49, 6.19)
No. of deaths (95% PI)	204	207 (177, 237)	203 (173, 234)	204 (173, 236)
females, all ages				
WASMR (95% PI)	4.06	3.72 (2.94, 4.50)	3.24 (2.48, 4.00)	2.85 (2.09, 3.61)
No. of deaths (95% PI)	142	131 (106, 156)	123 (97, 148)	119 (92, 146)
males, 0-64				
WASMR (95% PI)	2.94	2.49 (1.79, 3.20)	2.04 (1.43, 2.65)	1.67 (1.13, 2.21)
No. of deaths (95% PI)	56	55 (40, 71)	52 (36, 67)	46 (31, 61)
females, 0-64				
WASMR (95% PI)	1.43	1.32 (0.70, 1.94)	1.12 (0.46, 1.78)	0.96 (0.24, 1.68)
No. of deaths (95% PI)	27	27 (15, 40)	26 (11, 41)	24 (7, 40)

The numbers of deaths presented in Table 5.4 and in Figures 5.20 and 5.21 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 5.5, which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would result in an additional 101 deaths per year in men (a 49% increase) and 76 in women (a 37% increase) by 2015.

Table 5.5. Predictions of number of deaths, at all ages based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths (95% PI)	204	227 (194, 260)	261 (225, 296)	305 (266, 344)	142	155 (128, 182)	172 (143, 201)	195 (164, 226)

Figure 5.18. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

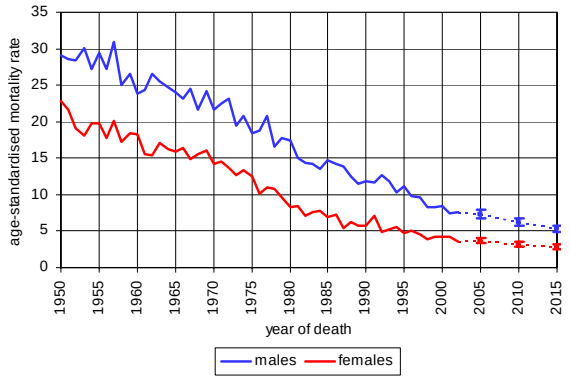


Figure 5.19. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

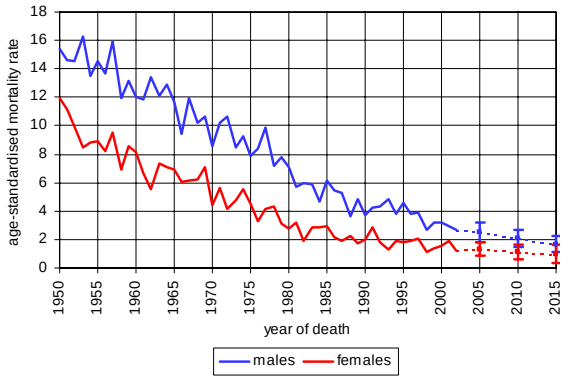


Figure 5.20. Actual and predicted number of deaths, all ages, 1950-2015

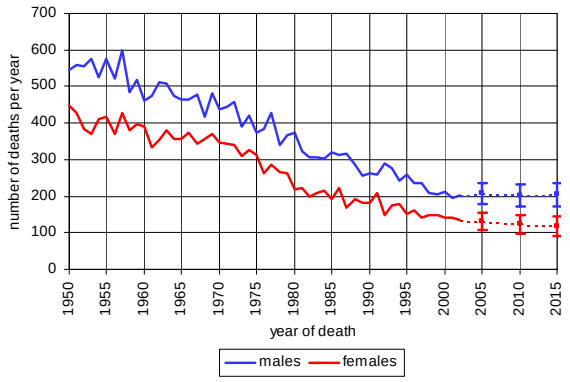
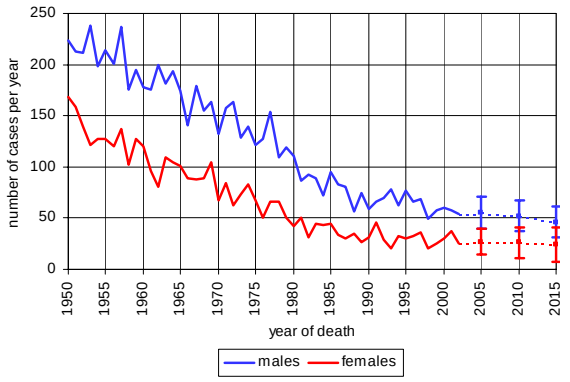


Figure 5.21. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Trends to 2002

Unlike the majority of cancers, there has been an ongoing fall since 1950 in stomach cancer mortality rates for both men and women. This has become more marked since the early 1970s, with decreases since then of 3.3% per annum for males and at least 3.5% for females. The annual number of deaths fell by 658 between 1950 and 2002, the largest absolute fall in mortality for any cancer. Similar trends were seen for those under 65.

The fall in rate was seen in most age groups, and there was very little evidence that year of birth had any effect on mortality, independent of age or period of death.

This fall in stomach cancer has been seen in most other European countries and in the USA.

Predictions

Mortality rates are predicted to fall in men by 33% over the 15-year period between c.2000 and 2015 and in women by 30% in the same period. In men under 65 men the mortality rate in this period is predicted to fall by 43% and in women under 65 by 33%. The number of deaths in men is expected to show no change (from an average of 204 per annum in 1998-2002) by 2015 and to decrease in women from 142 to 119, a 16% decrease. The annual numbers of deaths in those under 65 are predicted to decrease by 18% in men and by 11% in women.

Conclusions

It seems likely that the long-term decrease in stomach cancer mortality will continue. This fall in mortality has not been completely explained, but seems likely to be attributable to a combination of improving diet and decreasing *H. pylori* infection. Despite the probable role of *H. pylori*, there is insufficient evidence at present that its eradication reduces stomach cancer risk in the individual (Malfertheiner et al. 2005) and a more effective preventive strategy, based on current knowledge, may be to promote a diet rich in fresh produce. Early detection through regular gastroscopy appears to have been effective in reducing mortality in the high-risk population of Japan (Tsubono et al. 2000), but is not recommended on a population basis in Europe (Everett and Axon 1997).

Chapter 6. Colorectal cancer (ICD-9 153-154)

Epidemiology

Colorectal cancer was the commonest cancer and the second commonest cause of cancer death in the period 1994-2001, with an annual average of 1821 cases and 930 deaths during this period. Female cases and female deaths both made up 43% of the total.

As with most cancers, the majority of cases and deaths were in older patients (Table 6.1). 53% of cases and 62% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined.

Table 6.1. Age distribution of colorectal cancer deaths and cases

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	0%	0%	0%	0%	0%	0%
30-39	1%	1%	1%	1%	1%	1%
40-49	4%	6%	4%	5%	4%	6%
50-59	9%	13%	12%	14%	11%	14%
60-69	18%	22%	26%	29%	23%	26%
70-79	32%	33%	35%	34%	34%	33%
80+	35%	24%	22%	16%	28%	19%

Roughly half of all colorectal cancer patients survive their disease. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 49% for men and 51% for women.

Five-year relative survival for patients diagnosed in Ireland in 1994-1996 was 47.4% (95% CI 44.6-50.2%) for men and 50.8% (48.0-53.5%) for women; in 1997-1999, 55.1% (51.7-58.6%) for men and 55.4% (52.0-58.7%) for women (National Cancer Registry 2003).

Non-genetic risk factors

Colorectal cancer, as is the case with most cancers, results from complex interactions between inherited susceptibility and environmental factors and although its aetiology is understood in general terms, the contributions of individual risk factors to the overall burden of disease and to trends over time is difficult to quantify.

Diet and energy balance

Diet appears to be an important risk factor in many cases, either directly (Doll and Peto 1981) or by increasing the incidence of adenomas which are a well-recognized potential precursor to adenocarcinoma (Winawer, Zauber et al. 1993).

Fat consumption tends to be high in western countries with a high incidence of colorectal cancer, but forms a much lower percentage of dietary calories in low-risk countries. However, this ecological correlation has been difficult to prove in population-based studies, possibly because of the much smaller variation in fat and meat intake within a specific population. Dietary components are often highly correlated, so that individuals with high fat intake tend to have low fibre intake. But studies have shown lower rates of colon cancer in populations with a high intake of fat if fibre intake is also high (Reddy, Hedges et al. 1978).

Colorectal cancer risk may therefore be associated with some interaction of dietary fat, fibre and caloric intake. Increased secretion of bile acids has been suggested as one method of carcinogenesis by dietary fat, and fibre may provide some protection against this (Cheah 1990).

The evidence of a protective effect dietary fibre on bowel cancer is suggestive but not definitive. A meta-analysis of 13 case-control studies from nine countries concluded that intake of fibre-rich foods is inversely related to cancers of both colon and rectum for left-sided and right-sided colon and rectal cancers, men and women, and different age groups (Howe, Benito et al. 1992). Results of the EPIC prospective study also support a protective effect of fibre, greatest for left-sided colon cancer (Bingham et al. 2003). However, as mentioned above with regard to fat, there are some inconsistencies across studies with regard to the effects of fibre. This may be due to the fact that fibre intake is highly corrected with other dietary components such as vegetables, fruits, legumes, nuts, and grains and it may be that these, rather than fibre, are the protective agents. However, adjustment for folate intake did not substantially alter the association with fibre found by the EPIC study (Bingham et al. 2005).

A number of studies have suggested that high calcium intake may be protective; however this is not a consistent finding and is difficult to interpret (Kune, Kune et al. 1987; Slattery, Sorenson et al. 1988; Kampman, Giovannucci et al. 1994; Yang and Chiu 1998; Zheng, Anderson et al. 1998).

In summary, diets high in total fat, protein, calories, alcohol, and meat (both red and white) and low in calcium and folate, appear to be associated with an increased incidence of colorectal cancer. Cereal fibre supplementation and diets low in fat and high in fibre, fruits, and vegetables, however, do not reduce the rate of adenoma recurrence over a 3-year to 4-year period (Schatzkin et al. 2000).

Physical activity

Most studies have shown a relationship between sedentary lifestyle or level of physical activity and colon cancer incidence. Some of this association may be due to diet, and, less probably, to genetic predisposition to colorectal cancer. Obesity is associated with a two-fold increase in the risk of colorectal cancer in premenopausal women (Friedenreich 2001).

Alcohol Consumption

There is evidence of a weak association between colorectal cancer risk and alcohol intake (Longnecker, Orza et al. 1990; Kune and Vitetta 1992; Meyer and White 1993; Newcomb, Storer et al. 1993). The evidence is strongest with respect to beer consumption and rectal cancer in males. Subsequently published case-control studies suggest a modest-to-strong positive relationship between alcohol consumption and large bowel cancers. A case-control study of diet, genetic factors and the adenoma-carcinoma sequence suggests that alcohol intake could increase the rate of transformation of adenomas to carcinoma (Newcomb, Storer et al. 1993).

Hormonal and reproductive factors

Women taking postmenopausal hormone replacement therapy (HRT) have been found to have a decreased risk (by about 50%) of developing colon cancer (Calle, Miracle-McMahill et al. 1995; Newcomb and Storer 1995; Grodstein, Newcomb et al. 1999; Terry, Neugut et al. 2002), but the risk of rectal cancer is unaffected (Gerhardsson de Verdier and London 1992; Risch and Howe 1995).

Other risk factors

Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) may prevent the formation of adenomas, or cause them to regress (Reddy and Rao 2002). Many, but not all, epidemiological studies have reported a reduction in colon cancer incidence associated with the use of aspirin (Chan, Giovannucci et al. 2004). Non-aspirin NSAID use among individuals is also associated with lower risk, particularly for longer durations of use. NSAIDs are being studied for their potential in primary prevention; however, the proper dose and duration is not known, nor is it certain if the benefits would outweigh the risks of gastric ulcers and haemorrhagic stroke for the average-risk individual (Keller and Giardiello 2003; Tuynman, Peppelenbosch et al. 2004).

Inverse associations have been found between the risk of colon cancer and vitamin D, vitamin E and folate intake. However meta-analysis has shown no evidence of prevention of colorectal cancer from the use of supplemental antioxidant vitamins (Bostick, Potter et al. 1993; Giovannucci, Stampfer et al. 1998).

One study has shown that colorectal cancer mortality rates are highest among current smokers, intermediate among former smokers, and lowest in never smokers (Boutron, Faivre et al. 1995). Cigarette smoking is associated with an increased tendency to form adenomas (Neugut, Jacobson et al. 1993).

Trends

Between 1950 and 2002, the annual number of colorectal cancer deaths rose from 407 to 510 in men and from 319 to 388 in women, corresponding to an average increase, over the whole period, of 0.6% per year for men and 0.3% for women (Figure 6.1). Most of this increase took place between 1965 and 1980. Crude mortality rates remained unchanged overall for men, but fell by 0.3% annually for women (Figure 6.2). Age-standardised rates (Figures 6.3, 6.4), cumulative risk of dying before age 65 (Figure 6.5) and years of potential life lost (Figure 6.6) all showed similar patterns of small, or no increase (0% to 0.2% annually) for men and decreases of 0.8% to 1.3% annually in women. Almost all of the decrease in women has happened since the mid-1970s. While the age-standardised mortality rate was almost (82%) as high in women as in men in 1950, by 2002 the rate in women was only 56% that in men. Trends since 1992 indicate a non-significant annual decrease in total age-standardised mortality rates for males (Figure 6.15) and a significant annual decrease for females (Figure 6.16).

Figure 6.1. Number of deaths per year, 1950-2002

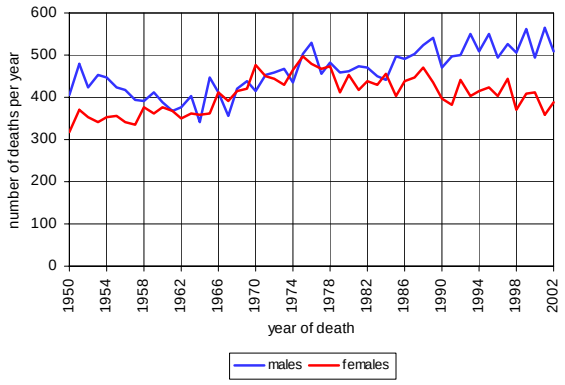


Figure 6.2. Crude mortality rate, 1950-2002

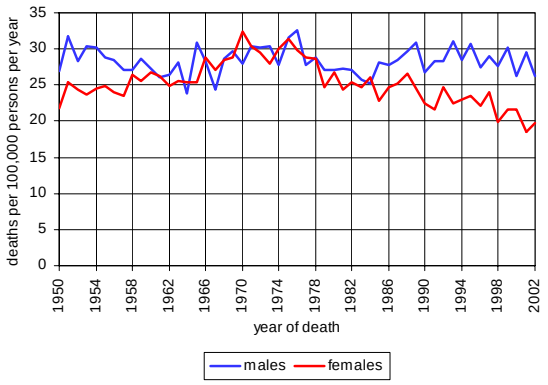


Figure 6.3. World age-standardised mortality rate, all ages, 1950-2002

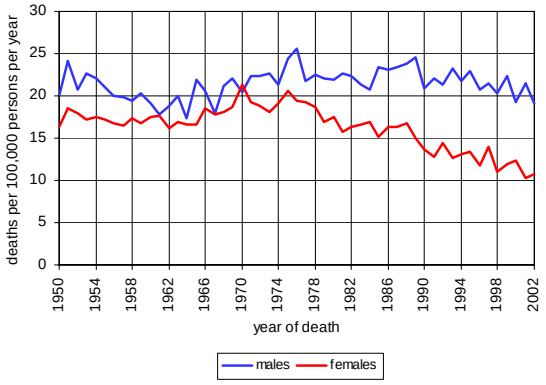


Figure 6.4. World age-standardised mortality rate, 0-64 years, 1950-2002

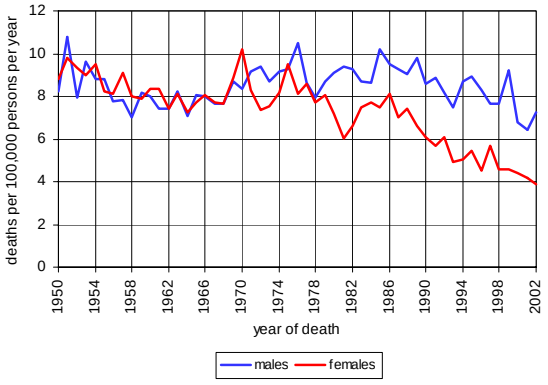


Figure 6.5. Cumulative risk of dying of cancer before age 65, 1950-2002

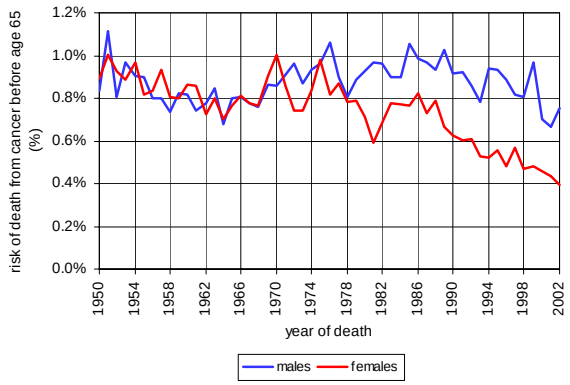


Figure 6.6. Years of potential life lost up to age 65, 1950-2002

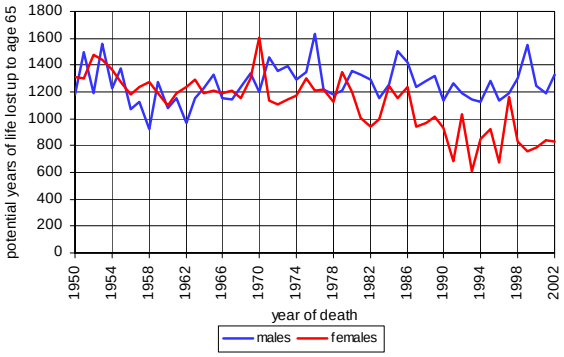


Table 6.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1950		1950		1950		1950	
↓	-1.8% (-2.9%, -0.5%)	↓	0.6% (0.2%, 0.9%)	↓	-2.9% (-5.5%, -0.1%)	↓	-0.5% (-0.8%, -0.2%)
1961 (1957, 1968)		1976 (1973, 1979)		1958 (1954, 1966)		1986 (1983, 1989)	
↓	1.6% (0.7%, 2.6%)	↓	-2.1% (-2.4%, -1.8%)	↓	0.8% (0.4%, 1.3%)	↓	-3.9% (-4.9%, -2.8%)
1975 (1970, 1982)		2002		1986 (1972, 1992)		2002	
↓	-0.4% (-0.7%, -0.1%)			↓	-1.8% (-2.6%, -0.9%)		
2002				2002			

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate for men showed a complex pattern, with an initial decrease in rate of 1.8% per annum from 1950 to 1961 (Table 6.2, Figure 6.7) followed by an increase of 1.6% annually until 1975 and then a decrease of 0.4% per annum up to 2002. For women, the rate increased by 0.6% annually from 1950 to 1976, but fell by 2.1% per annum between 1976 and 2002, four times faster than the fall in rate in men over the same period.

For men under 65, the pattern of decrease was similar to that for men of all ages, although the rates of decrease were greater (Table 6.2, Figure 6.8). The initial fall in rate of 2.9% per annum between 1950 and 1958 was followed by an increase in rate of 0.8% between 1958 and 1986, and a more recent fall of 1.8% per year. The rate in women under 65 fell initially by 0.5% between1950 and 1986 and more rapidly, by 3.9% annually, from 1986 to 2002.

Figure 6.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

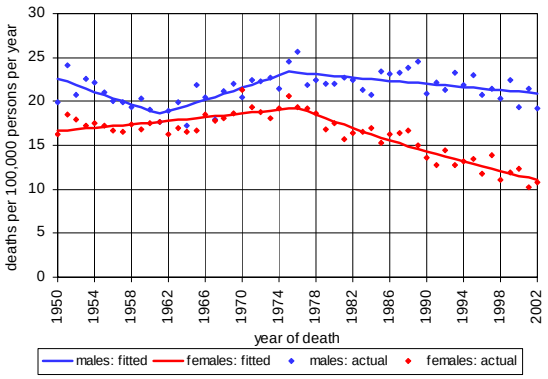
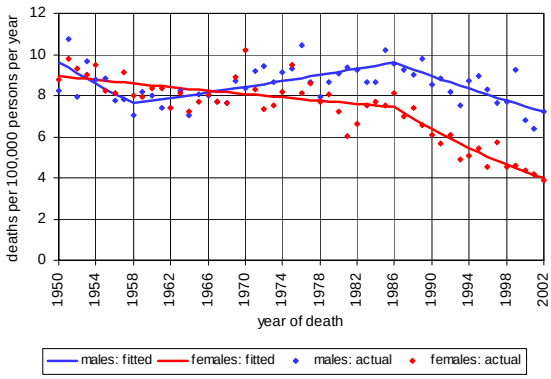


Figure 6.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

The age-period plots for men (Figure 6.9) show similar patterns for all age groups under 65—an initial fall in mortality, followed by a gradual increase, and then a fall in the last decade (with the exception of those aged 45-49). Men aged 65 and over have shown very little change in mortality. For women most age groups showed a pattern of decreasing mortality since the 1970s (Figure 6.10).

There was no strong evidence of any effect of birth cohort on mortality rates (Figures 6.11, 6.12)

Figure 6.9. Age-specific mortality by period of death, males, 1950-2002

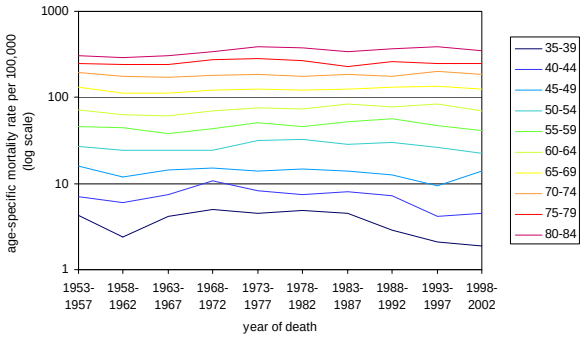


Figure 6.10. Age-specific mortality by period of death, females, 1950-2002

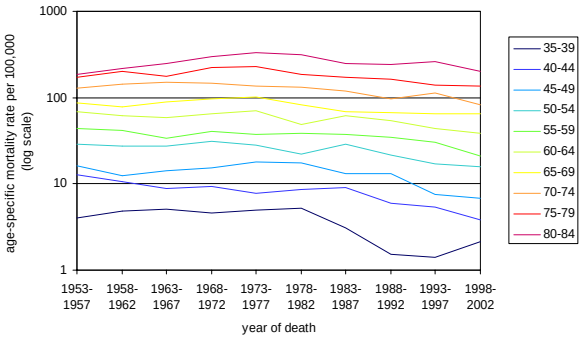


Figure 6.11. Age-specific mortality by birth cohort, males, 1950-2002

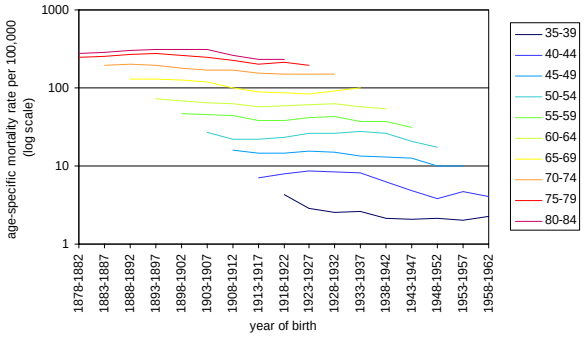
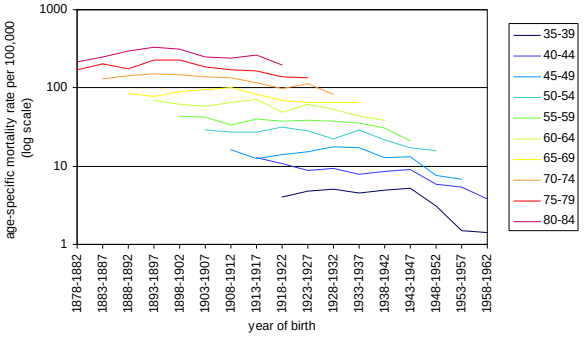


Figure 6.12. Age-specific mortality by birth cohort, females, 1950-2002



International trends

The mortality rate from colorectal cancer in males in Ireland in 1950 was close to the average for the countries shown, but by 2002 had risen relative to most other countries, to be second only to that in Denmark (Figure 6.13). There was no consistent pattern in male colorectal cancer trends internationally. Some countries (UK, USA) had a marked decrease, others (Ireland, Norway) an increase, while the majority showed no major change, although quite a few countries had a peak of mortality in the 1970s. For females, there was a more consistent decrease, most rapid since the 1960s, and the relative position of Ireland was much the same throughout the period studied (Figure 6.14). In general the countries with the largest decrease in rate for women were also those which had had a fall in mortality in men, and Norway, which had the largest increase in rate in men, was the only country to have an increase in mortality in women also.

Figure 6.13. Rolling 5-year average World age standardised mortality rates in Europe and USA, males, all ages, 1950 to 2002

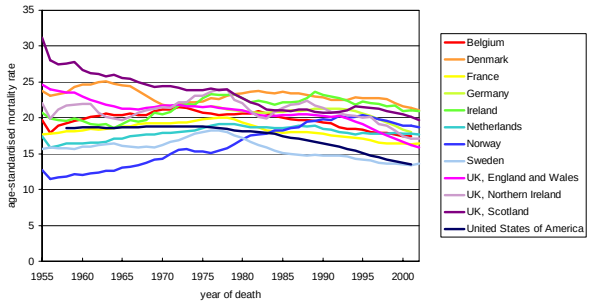
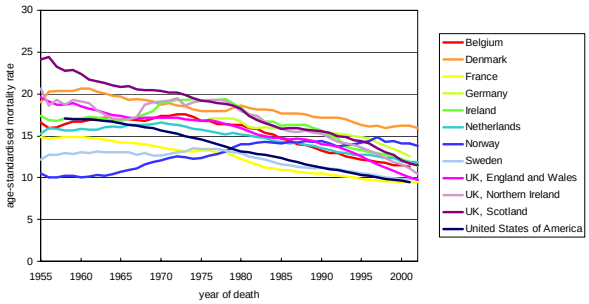


Figure 6.14. Rolling 5-year average World age standardised mortality rates in Europe and USA, females, all ages, 1950 to 2002



Recent estimates of change (Figures 6.15, 6.16) indicate significant falls in age-standardised mortality since 1992 for men in Belgium, Denmark, France, Germany, Norway, the UK and the USA and for women in Belgium, France, Germany, Ireland, the Netherlands, Sweden, the UK and the USA. No increases were seen in any of the countries described here.

Figure 6.15. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

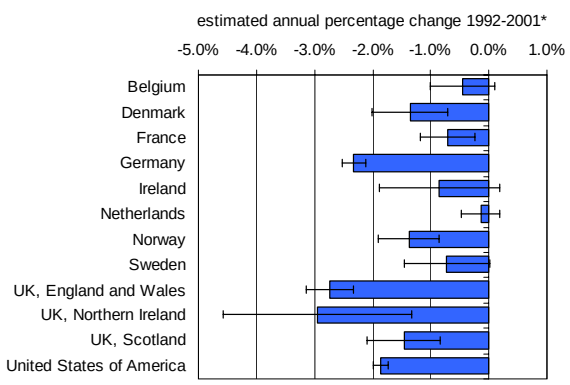
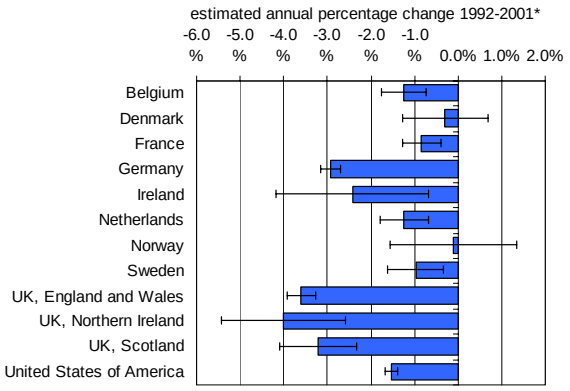


Figure 6.16. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



** or nearest available data period*

Predictions

The models used are described in the subsequent chapters on colon and anorectal cancer.

Colorectal cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to fall from 20.54 in 1998-2002 to 18.13 in 2015 (Figure 6.17, Table 6.3). The number of deaths in men is predicted to increase, from 527 per year in 1998-2002 to 696 in 2015 (Figure 6.19). In men under 65 the mortality rate is predicted to fall, from 7.47 in 1998-2002 to 5.35 in 2015 (Figure 6.18), with an accompanying slight increase in the number of deaths from 142 per year in 1998-2002 to 148 in 2015 (Figure 6.20).

Table 6.3. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	20.54	19.80	18.91	18.13
No. of deaths (95% PI)	527	561	616	696
females, all ages				
WASMR (95% PI)	11.26	10.66	9.63	8.71
No. of deaths (95% PI)	387	393	397	408
males, 0-64				
WASMR (95% PI)	7.47	6.61	5.95	5.35
No. of deaths (95% PI)	142	147	151	148
females, 0-64				
WASMR (95% PI)	4.32	3.60	2.99	2.49
No. of deaths (95% PI)	82	77	73	66

Note: The rates and numbers for colorectal cancer have been calculated from the sum of colon and anorectal cancer data, and consequently have no prediction intervals attached.

Mortality rates in women are predicted to fall from 11.26 in 1998-2002 to 8.71 in 2015. The number of deaths is also predicted to fall, from 387 per year in 1998-2002 to 408 in 2015. In women under 65, mortality rates are also expected to fall, from 4.32 in 1998-2002 to 2.49 in 2015. The number of deaths in this age group is also expected to fall, from 82 per year in 1998-2002 to 66 in 2015.

The numbers of deaths presented in Table 6.3 and in Figures 6.19 and 6.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 6.4 which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would result in an additional 89 deaths per year in men (a 49% increase from the 1998-2002 figure) and 124 in women (a 38% increase) by 2015.

Table 6.4. Predictions of number of deaths at all ages, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths (95% PI)	527	586 (534, 638)	672 (615, 728)	785 (723, 848)	387	423 (378, 468)	471 (423, 518)	532 (481, 584)

Figure 6.17. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

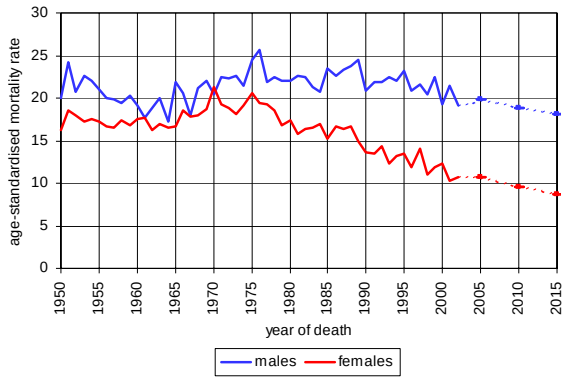


Figure 6.18. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

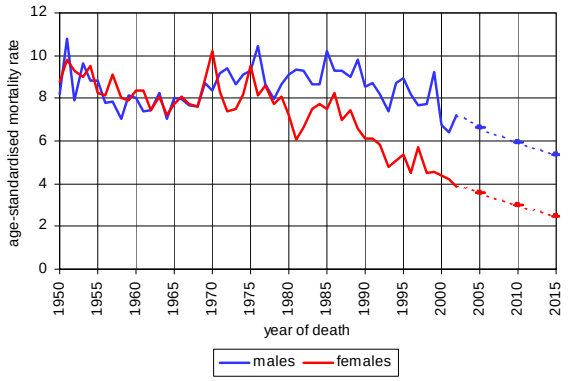


Figure 6.19. Actual and predicted number of deaths, all ages, 1950-2015

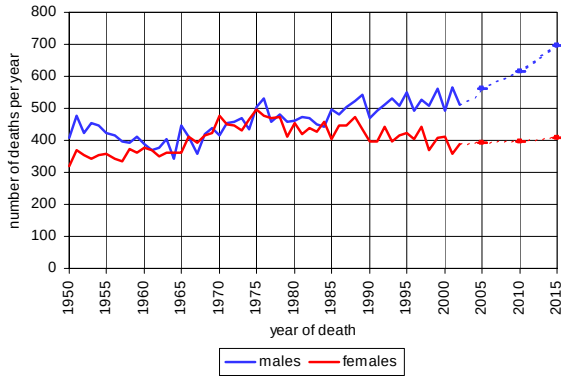
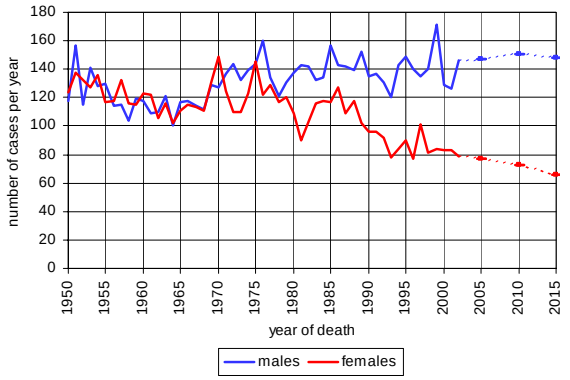


Figure 6.20. Actual and predicted number of deaths, 0-64 years, 1950-2015



Note:
Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values..

Historical trends

The number of deaths, and the mortality rate, for colorectal cancer were similar for men and women from about 1960 to 1980, since when deaths in males have increased, and those in females have decreased. The age-standardised rate for men is falling slowly, while that for women is falling quite rapidly. The trends for men and women under 65 are quite similar. Joinpoint analysis suggests a fall in male mortality rates by1.8% annually from 1950 to 1961, an increase by 1.6% annually to 1975 and a non-significant fall by 0.4% annually since then. Rates in females increased by 0.6% annually to 1976 and have been falling by 2.1% annually since then. The pattern in those under 65 is similar but with greater rates of decrease in rate in recent years. International trends in colorectal cancer mortality have been inconsistent over the past 50 years, but the rates in Ireland have risen relative to most other western countries.

Predictions

A 12% fall in age-standardised mortality for men is predicted over 15-year period from approximately 2000 to 2015, while a 23% fall by 2015 is expected for women. For those under 65, larger falls are expected—28% for men and 42% for women.

However, due to demographic change, the number of deaths due to colorectal cancer is expected to increase by 32% for men and by 5% for women over the same period. In populations below age 65, the number of deaths is predicted to rise by 4% and to fall by 20% for women.

Conclusions

The more rapid (and longer-term) fall in colorectal cancer mortality in women than in men is presumably attributable to differences in incidence, as survival does not differ appreciably between the sexes. A fall in incidence is most likely to be attributable to dietary factors, although, as already noted, NSAID and hormone replacement therapy use may have played a part. There is insufficient information available on possible differences in diet between men and women in Ireland in the 1960s, when major differences in rates first became evident. The SLÁN survey (Kelleher et al. 2003) shows higher levels of obesity in Irish men than women and a higher consumption of saturated fat, and it seems reasonable to assume that these differences are of long standing. However the fall in mortality rates in women began in the mid 1970s and we have no detailed information on dietary changes in the 1950 and 1960s.

The predictions suggest that the long-term trends in mortality rates for both sexes will be maintained but that, unless some changes occur in the risk profile of men, the gap in numbers of deaths between men and women will widen. In 1998-2002 there were 140 more deaths in men than in women, and this excess mortality is predicted to double, to 288 deaths, by 2015. It is obviously important to attempt to identify the reasons for the different risk profiles of men and women and to address this. The continuing fall in mortality rates will also need to be included in any consideration of the cost-effectiveness of screening for colorectal cancer.

Chapter 7. Colon cancer (ICD-9 153)

Epidemiology

Colon cancer made up 63% of colorectal cancer cases and 74% of colorectal cancer deaths in the period 1994-2001, with an annual average of 1,145 cases and 686 deaths during this period. Female cases made up 48% of this total and female deaths made up 46%.

55% of cases and 63% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined (Table 7.1).

Table 7.1. Age distribution of colon cancer deaths and cases

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	0%	0%	0%	0%	0%	0%
30-39	1%	1%	1%	1%	1%	1%
40-49	4%	6%	4%	5%	4%	5%
50-59	9%	13%	11%	13%	10%	13%
60-69	18%	22%	26%	28%	22%	25%
70-79	32%	33%	36%	37%	34%	34%
80+	36%	25%	23%	17%	29%	21%

Survival for colon cancer alone is slightly better than for all colorectal cancer. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 51% for men and 52% for women, while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 41% for men and 40% for women (Berrino et al. 1995). (See Chapter 6 for Irish survival rates from colorectal cancer as a whole).

Non-genetic risk factors

These are described in Chapter 6: Colorectal cancer.

Trends

Between 1950 and 2002, the annual number of colon cancer deaths rose from 258 to 334 in men and from 217 to 283 in women, corresponding to an average increase, over the whole period, of 1.0% per year for men and 0.4% for women (Figure 7.1). Most of this increase took place between about 1965 and 1980. Crude mortality rates increased by 0.4% annually for men, but fell by 0.2% annually for women (Figure 7.2). Age-standardised rates (Figures 7.3, 7.4), cumulative risk of dying before age 65 (Figure 7.5) and years of potential life lost (Figure 7.6) all showed similar patterns of small increases (0.3% to 0.5% annually) for men and decreases of 0.2% to 1.1% annually for women. Almost all of the decrease in rate for women has happened since the mid-1970s. While the age-standardised mortality rate was almost (85%) as high in women as in men in 1950, by 2002 the rate in women was only 65% that in men. Trends since 1992 indicate a significant annual decrease in total age-standardised mortality rates for both males (Figure 7.15) and females (Figure 7.16).

Figure 7.1. Number of deaths per year, 1950-2002

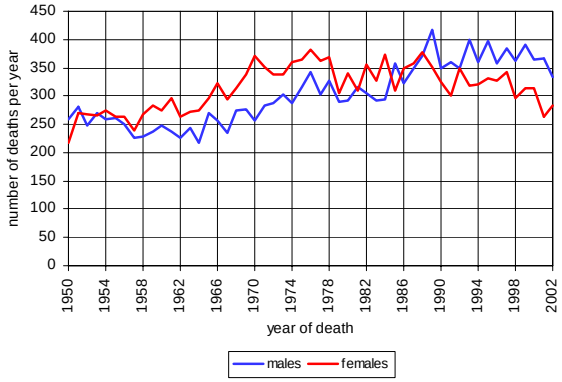


Figure 7.2. Crude mortality rate, 1950-2002

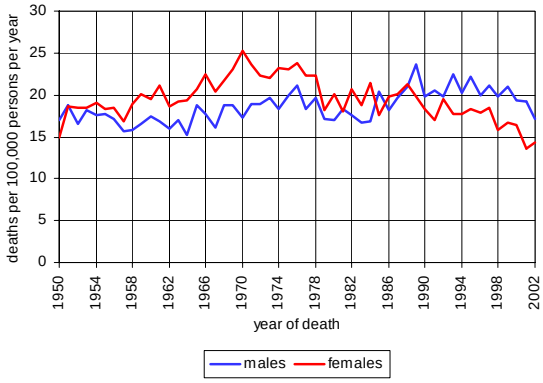


Figure 7.3. World age-standardised mortality rate, all ages, 1950-2002

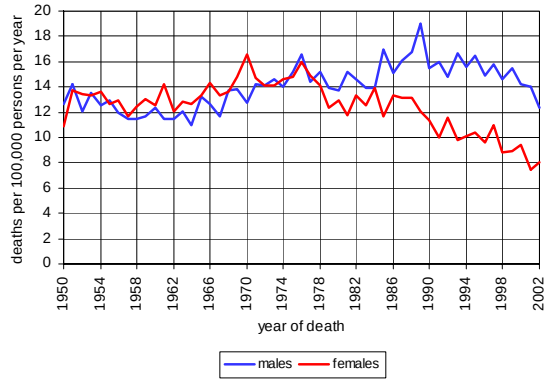


Figure 7.4. World age-standardised mortality rate, 0-64, 1950-2002

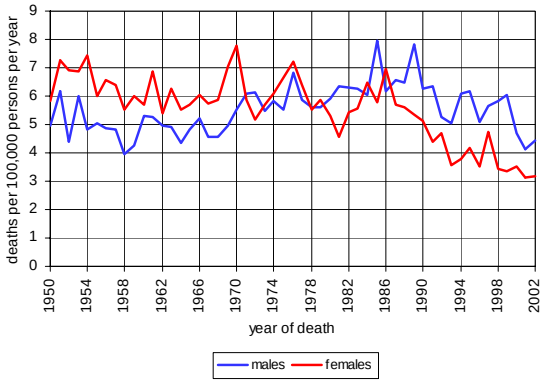


Figure 7.5. Cumulative risk of dying of cancer before 65, 1950-2002

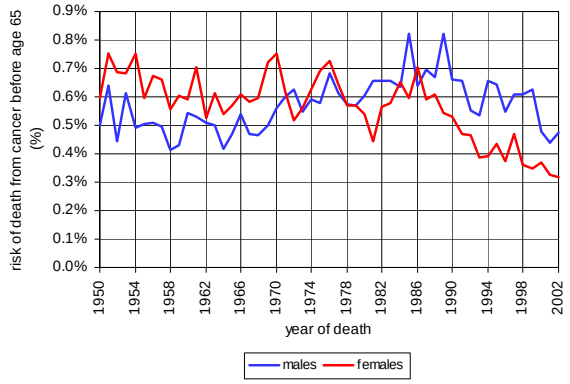


Figure 7.6. Years of potential life lost up to age 65, 1950-2002

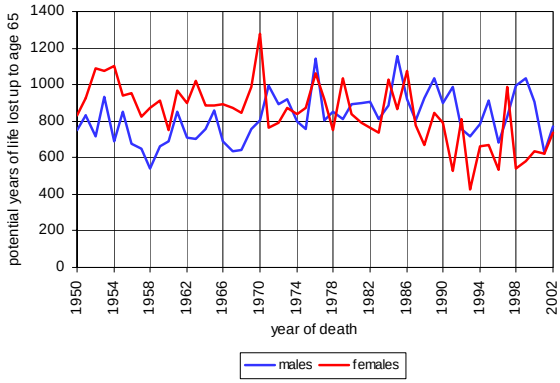


Table 7.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1950		1950		1950		1950	
↓	-1.9% (-4.1%, 0.3%)	↓	0.8% (0.4%, 1.2%)	↓	-2.4% (-5.7%, 1.0%)	↓	-0.3% (-0.6%, 0.0%)
1958 (1954, 1966)		1976 (1973, 1979)		1958 (1953, 1970)		1986 (1983, 1990)	
↓	1.2% (0.9%, 1.5%)	↓	-2.1% (-2.5%, -1.7%)	↓	1.3% (0.9%, 1.8%)	↓	-3.9% (-5.1%, -2.7%)
1989 (1986, 1996)		2002		1989 (1983, 1992)		2002	
↓	-1.4% (-2.3%, -0.6%)			↓	-3.0% (-4.4%, -1.6%)		
2002				2002			

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate for men showed an initial decrease in rate of 1.9% per annum from 1950 to 1958 (Table 7.2, Figure 7.7) followed by an increase in rate of 1.2% annually until 1989, then a decrease of 1.4% per annum up to 2002. For women, the rate increased by 0.8% annually from 1950 to 1976, but fell by 2.1% per annum between 1977 and 2002. The pattern of change for colon cancer for women can be seen to be close to that observed for colorectal cancer, while the male pattern is slightly different.

For men under 65 the pattern was similar to that for men of all ages (Figure 7.8). Rates decreased by 2.4% annually from 1950 to 1958 and then increased by 1.3% annually from 1958 to 1989, followed by a more recent fall, by 3.0% per annum, between 1989 and 2002. Mortality rates for women decreased over the entire period—by only 0.3% per annum between 1950 and 1986, but by 3.9% per annum since then.

Figure 7.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

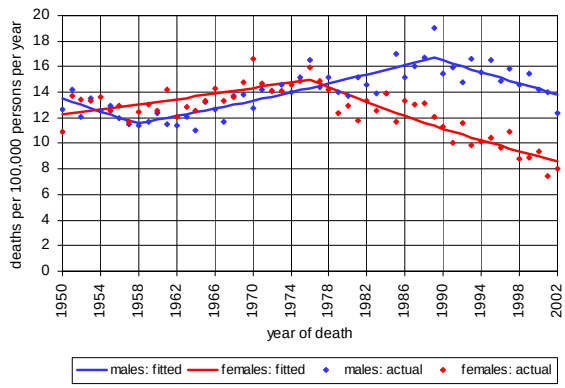
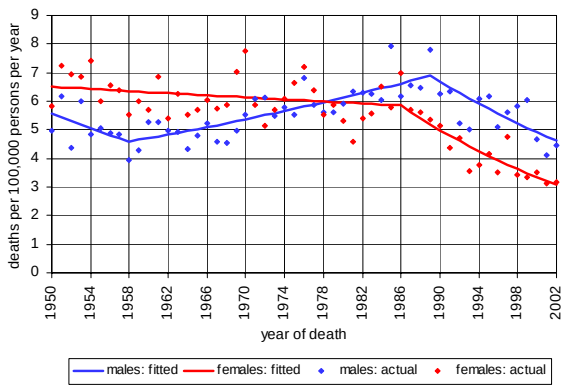


Figure 7.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

The age-period plots show an increase in mortality for all men of 60 and over since 1953, although with some variation (Figure 7.9). However, the mortality rate has fallen since 1992 for almost all age groups. A similar pattern is seen in women (Figure 7.10), but with the major difference that the decline in mortality in women began around 1973-1977 for most age groups and in the following five-year period for the oldest women.

There was little evidence that year of birth (Figures 7.11, 7.12) had any strong effect on mortality, independent of age or period of death.

Figure 7.9. Age-specific mortality by period of death, males, 1950-2002

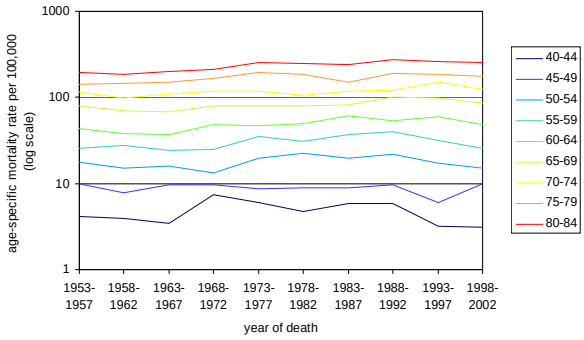


Figure 7.10. Age-specific mortality by period of death, females, 1950-2002

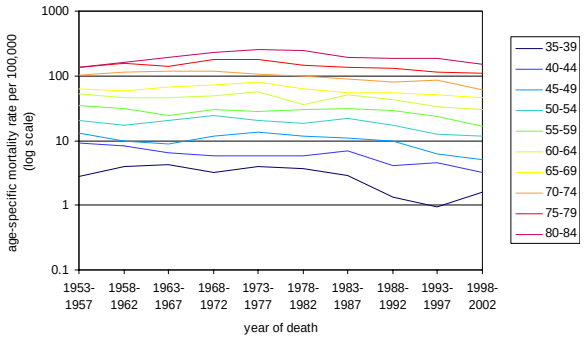


Figure 7.11. Age-specific mortality by birth cohort, males, 1950-2002

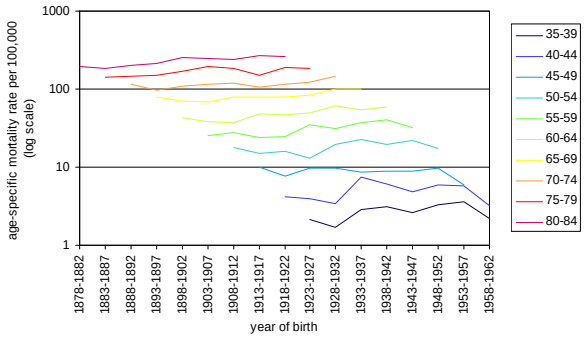
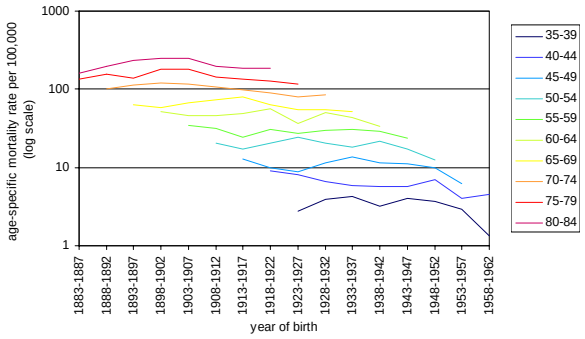


Figure 7.12. Age-specific mortality by birth cohort, females, 1950-2002



International trends

The mortality rate from colon cancer in males in Ireland in 1950 was close to the average for the countries shown, but, by the late 1980s onwards, had risen to be the highest of all the countries shown (Figure 7.13). As would be expected, trends for colon cancer closely resembled those for colorectal. There was no consistent pattern in male trends, with some countries (UK, USA) showing a decrease, others (Ireland, Norway) an increase, and the majority showing no major change, although quite a few countries had a peak of mortality in the 1970s. The trend in Ireland peaked in the early 1990s; although it has since fallen steadily it is still the highest for the countries shown

For females, there was a more consistent decrease, most rapid since the 1960s (Figure 7.14). Mortality for women in Ireland was relatively high between 1970 and 1990, but is now more typical.

Figure 7.13. Rolling 5-year average World age standardised mortality rates in Europe and USA, males, all ages, 1950 to 2002

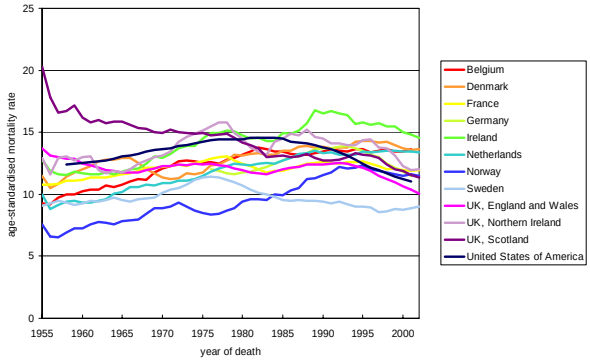
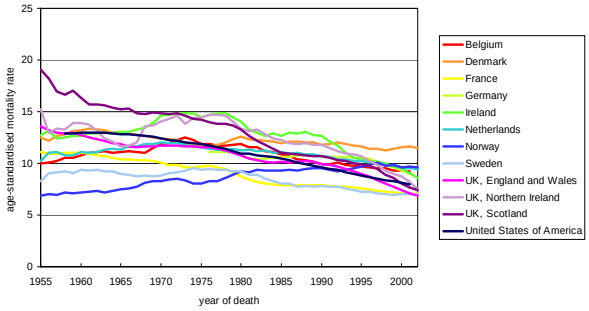


Figure 7.14. Rolling 5-year average World age standardised mortality rates in Europe and USA, females, all ages, 1950 to 2002



Recent estimates of change (Figures 7.15, 7.16) indicate significant increases in age-standardised mortality since 1992 for men in Denmark, France, Germany, Ireland, the UK and the USA and for women in France, Germany, Ireland, the Netherlands, the UK and the USA.

Figure 7.15. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

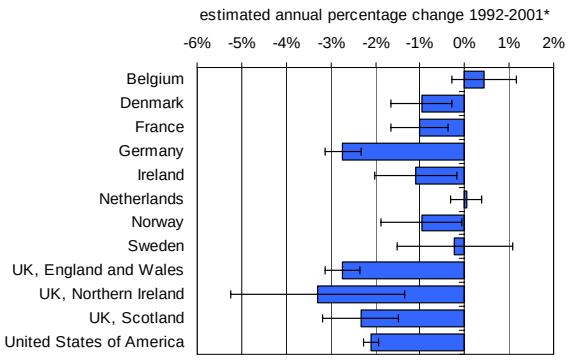
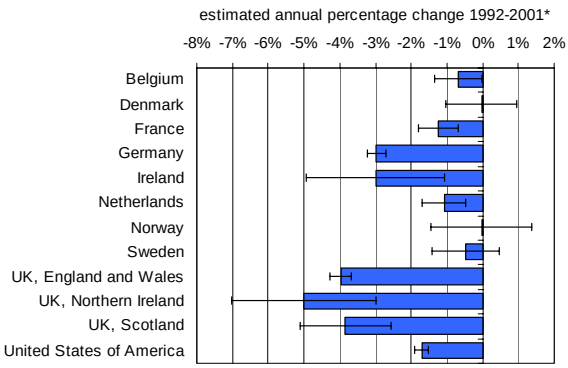


Figure 7.16. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



** or nearest available period*

Predictions for the period 2005-2015

Colon cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to fall from 14.13 in 1998-2002 to 11.17 (95% prediction interval 9.29, 13.05) in 2015 (Table 7.3, Figure 7.17). The number of deaths in men is predicted to rise, from 364 per year in 1998-2002 to 433 (362, 505) in 2015 (Figure 7.19). In men under 65 the mortality rate is predicted to fall, from 5.03 in 1998-2002 to 3.13 (2.07, 4.19) in 2015 (Figure 7.18), with an accompanying fall in the number of deaths from 95 per year in 1998-2002 to 87 (57, 116) in 2015 (Figure 7.20).

Table 7.3. Models chosen for predictions

model	*sex*	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	males	1989-2002	84	log linear	0.0001
	females	1976-2002	162	linear	0.0000
0-64	males	1989-2002	42	log linear	0.0005
	females	1986-2002	51	log linear	0.0000

Mortality rates in women are predicted to fall from 8.51 in 1998-2002 to 6.77 (5.80, 7.74) in 2015 (Table 7.4, Figures 7.17-7.20). The number of deaths is predicted to rise from 294 per year in 1998-2002 to 318 (276, 361) in 2015. In women under 65 mortality rates are also expected to fall, from 3.33 in 1998-2002 to 1.87 (1.14, 2.60) in 2015. The number of deaths in this age group is expected to fall, from 63 per year in 1998-2002 to 49 (30, 67) in 2015.

Table 7.4. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	14.13	13.13 11.48, 14.79)	12.10 (10.34, 13.85)	11.17 (9.29, 13.05)
No. of deaths (95% PI)	364	374 (328, 421)	397 (340, 453)	433 (362, 505)
females, all ages				
WASMR (95% PI)	8.51	8.30 (7.19, 9.41)	7.50 (6.46, 8.53)	6.77 (5.80, 7.74)
No. of deaths (95% PI)	294	307 (270, 344)	3.10 (270, 349)	318 (276, 361)
males, 0-64				
WASMR (95% PI)	5.03	4.22 (3.18, 5.25)	3.63 (2.59, 4.67)	3.13 (2.07, 4.19)
No. of deaths (95% PI)	95	94 (71, 117)	92 (66, 118)	87 (57, 116)
females, 0-64				
WASMR (95% PI)	3.33	2.76 (1.95, 3.58)	2.27 (1.51, 3.03)	1.87 (1.14, 2.60)
No. of deaths (95% PI)	63	59 (42, 77)	55 (37, 73)	49 (30, 67)

The numbers of deaths presented in Table 7.4 and in Figures 7.19 and 7.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 7.5 which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would result in an additional 109 deaths per year in men (a 49% increase over the 1998-2002 numbers) and 86 in women (a % 37% increase) by 2015.

Table 7.5. Predictions of number of deaths at all ages based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths (95% PI)	364	404 (361, 448)	463 (416, 511)	542 (490, 594)	294	321 (282, 360)	357 (316, 398)	404 (359, 448)

Figure 7.17. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

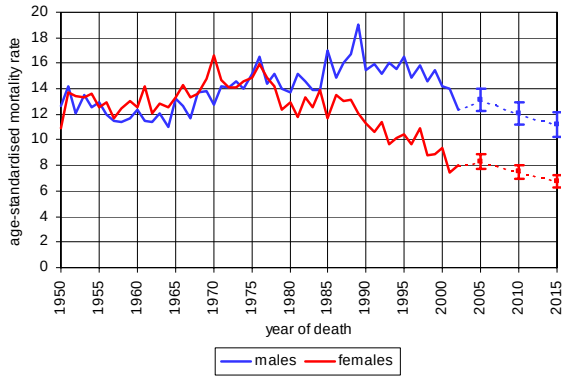


Figure 7.18. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

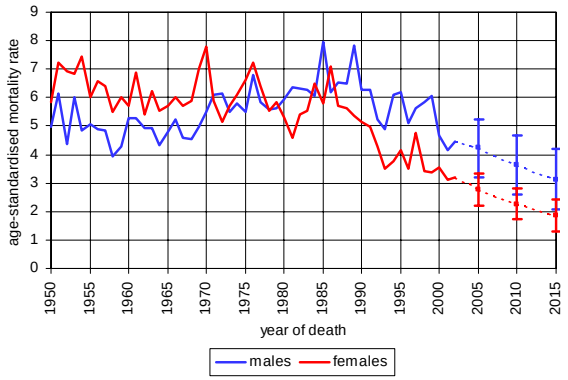


Figure 7.19. Actual and predicted number of deaths, all ages, 1950-2015

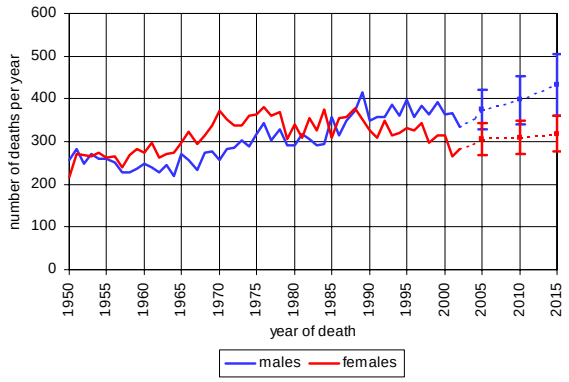
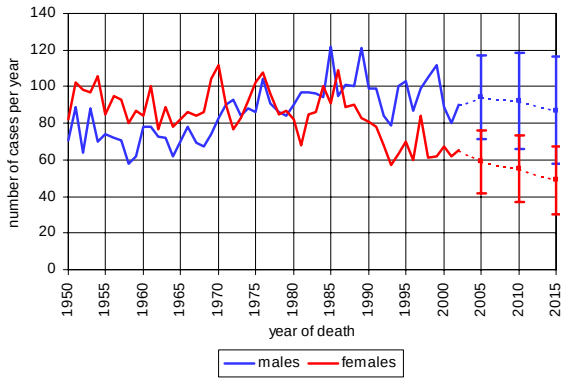


Figure 7.20. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

As would be expected, the findings for colon cancer were similar to those for all colorectal cancer, with fall in rate seen for both sexes, greater for women than men. The decrease in rate for men seems to have begun more recently than that for women. Joinpoint analysis shows an annual fall in rate of 1.4% in men since 1989 and 2.1% in women since 1976. The decrease in rate for women under 65 has averaged 3.9% per annum since 1986, and for men under 65 3.0% since 1989. As with colorectal cancer, recent trends in mortality internationally have been inconsistent, but mostly involve declines.

Predictions

A fall in age-standardised rate is predicted for both sexes, by 21% between approximately 2000 and 2015 for men and by 20% for women. In the same period, the number of deaths is expected to increase by 19% for men and by 8% for women. For men under 65, the rate is expected to fall by 38% and the number of deaths by 8% between 1998-2002 and 2015, while for women the rate is expected to fall by 45% and the number of deaths by 24%.

Conclusions

The patterns of past and predicted future mortality are quite similar to those already discussed for all colorectal cancer combined, and the conclusions to be drawn are identical.

Chapter 8. Anorectal cancer (ICD-9 154)

Epidemiology

Anorectal cancer made up 37% of colorectal cancer cases and 26% of colorectal cancer deaths in the period 1994-2001, with an annual average of 677 cases and 243 deaths during this period. Female cases made up 39% of this total and female deaths made up 37%.

50% of cases and 60% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined (Table 8.1).

Table 8.1. Age distribution of anorectal cancer deaths and cases

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	0%	0%	0%	0%	0%	0%
30-39	1%	2%	1%	1%	1%	1%
40-49	3%	7%	3%	6%	3%	6%
50-59	10%	14%	14%	16%	12%	15%
60-69	19%	23%	25%	31%	23%	28%
70-79	31%	33%	34%	31%	33%	31%
80+	35%	21%	22%	15%	27%	17%

Survival from rectal cancer is poorer than for colon cancer. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 47% for men and 50% for women, while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 34% for men and 38% for women (Berrino et al. 1995). (See Chapter 6 for Irish survival rates from colorectal cancer as a whole.)

Non-genetic risk factors

These are described in Chapter 5: Colorectal cancer.

While the aetiology of anal cancers is different from that of rectal cancers, with most cases of anal carcinoma resulting from human papilloma virus infection (Ryan et al. 2000), they make up only about 3% of anorectal cancer cases and deaths in Ireland (based on 1994-2001 data).

Trends

Between 1950 and 2002, the annual number of rectal cancer deaths rose from 149 to 176 in men and from 102 to 105 in women. However, the number of deaths in men in 1950 was low relative to the rest of the early 1950s, and there was an average decrease, over the whole period, of 0.2% in the number of deaths per year for men between 1950 and 2002, while the number of deaths in women remained unchanged, on average (Figure 8.1). Crude mortality rates fell by 0.8% annually for men and by 0.6% annually for women (Figure 8.2). Age-standardised rates (Figures 8.3, 8.4), cumulative risk of dying before age 65 (Figure 8.5) and years of potential life lost (Figure 8.6) all showed similar patterns of small falls (0.5% to 0.7% annually) for men and somewhat larger decreases (1.1% to 1.8% annually) for women. Almost all of the decrease in women, and to a lesser extent that in men, has happened since the mid-1970s. The age-standardised mortality rate for women was 74% that for men in 1950, but by 2002 had fallen to only 40% that of the male rate. Trends since 1992 indicate a non-significant annual decrease in total age-standardised mortality rates for both males (Figure 8.15) and females (Figure 8.16).

Figure 8.1. Number of deaths per year, 1950-2002

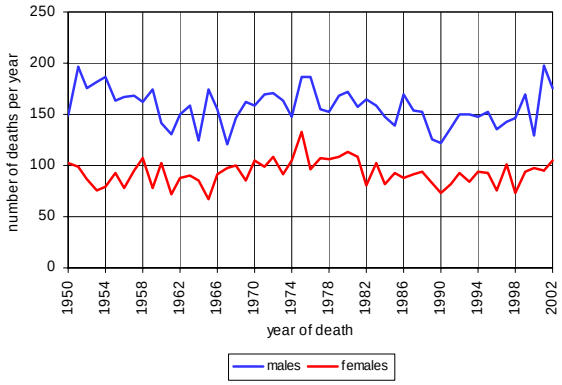


Figure 8.2. Crude mortality rate, 1950-2002

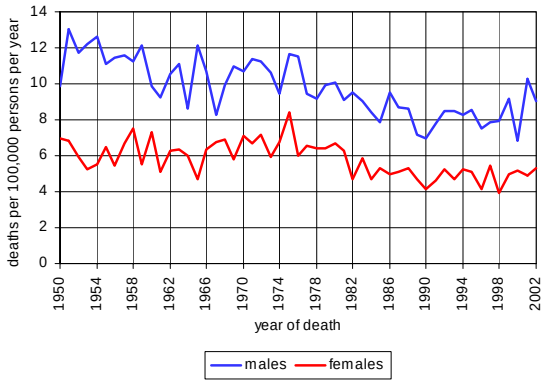


Figure 8.3. World age-standardised mortality rate, all ages, 1950-2002

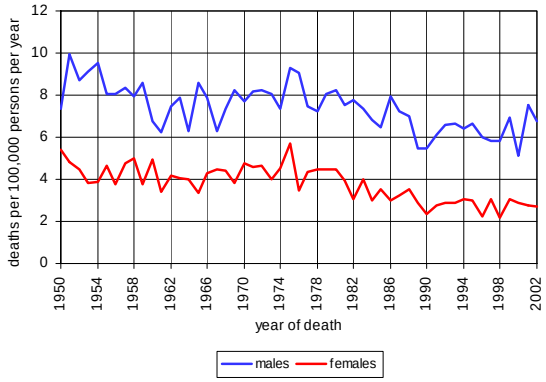


Figure 8.4. World age-standardised mortality rate, 0-64 years, 1950-2002

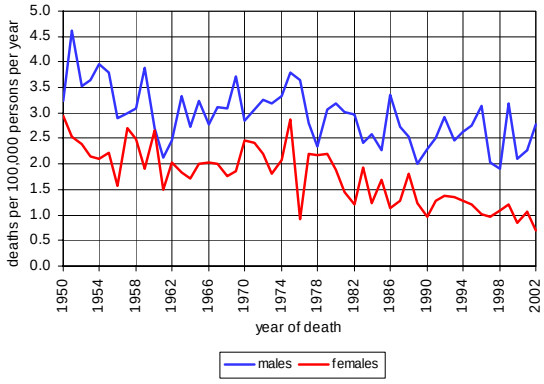


Figure 8.5. Cumulative risk of dying of cancer before age 65, 195-2002

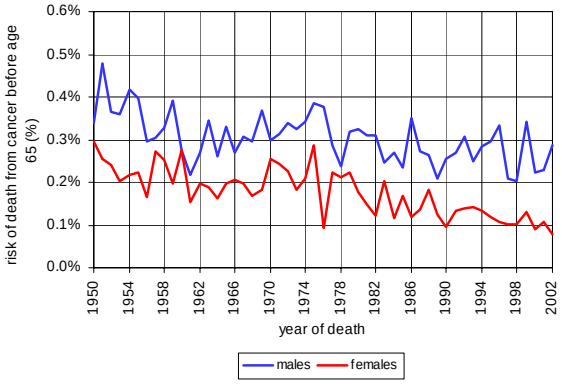
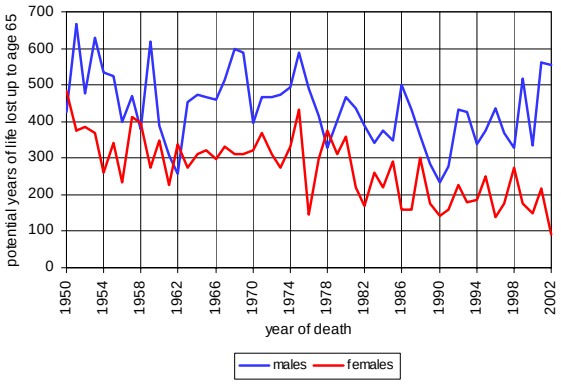


Figure 8.6. Years of potential life lost up to age 65, 1950-2002



Joinpoint regression analysis

Table 8.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1950		1950		1950		1950	
↓	-0.6% (-0.8%, -0.4%)	↓	-0.1% (-0.7%, 0.6%)	↓	-0.7% (-1.0%, -0.5%)	↓	-0.6% (-1.5%, 0.3%)
2002		1975 (1969, 1981)		2002		1977 (1969, 1986)	
		↓	-2.0% (-2.7%, -1.4%)			↓	-3.1% (-4.3%, -1.9%)
		2002				2002	

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate for men showed a steady fall of 0.6% per annum from 1950 to 2002 (Table 8.2, Figure 8.7). For women, the rate decreased very slightly (the trend was not statistically significant), by 0.1% annually, from 1950 to 1975, but has fallen by 2.0% per annum since then.

For men under 65, the pattern was very similar, with an ongoing decrease of 0.7% per annum over the entire period 1950-2002, while for women under 65 there was again an initial slow fall in rate of 0.6% per annum (not statistically significant), followed by a more rapid fall of 3.1% per annum from 1977 to 2002 (Figure 8.8).

Figure 8.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

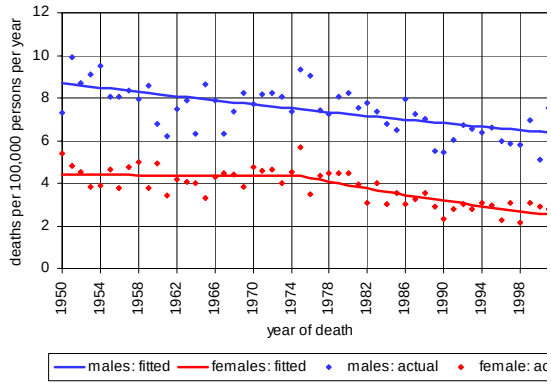
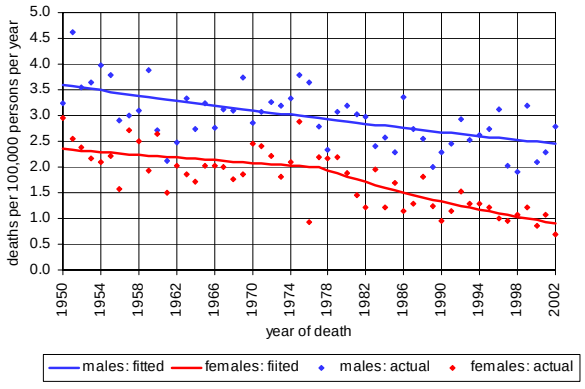


Figure 8.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

The age-period plots for men and women show a tendency for higher mortality rates from the late 1960s to mid 1980s, mainly in the oldest age groups (Figures 8.9, 8.10). For almost all age groups, there has been a decrease in mortality since the 1970s. This fall has been much more marked in women than men, particularly those under 50. There was no evidence for any cohort effect on mortality, i.e. no obvious association with period of birth (Figures 8.11, 8.12).

Figure 8.9. Age-specific mortality by period of death, males, 1950-2002

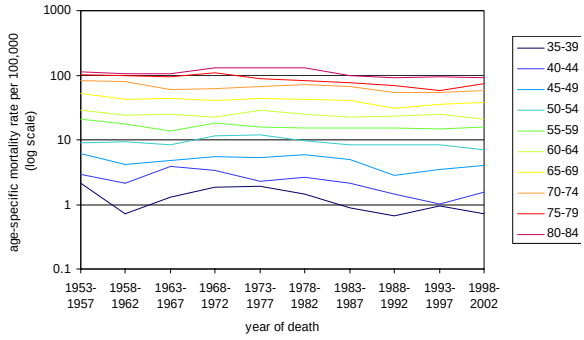


Figure 8.10. Age-specific mortality by period of death, females, 1950-2002

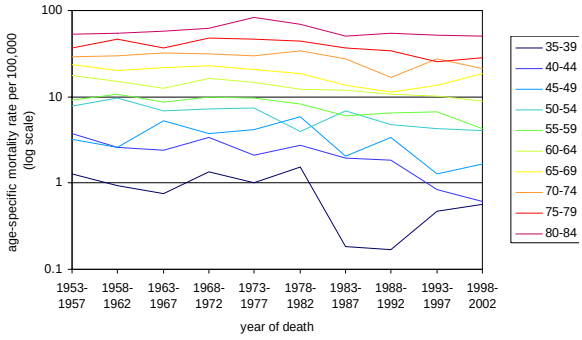


Figure 8.11. Age-specific mortality by birth cohort, males, 1950-2002

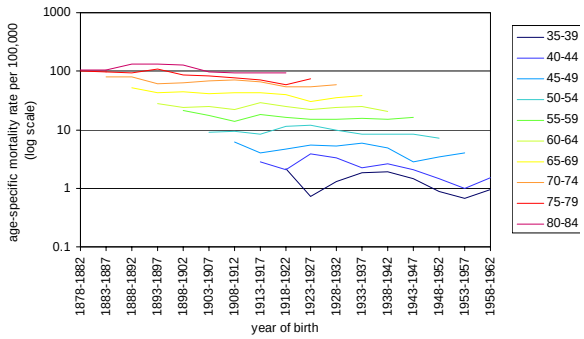
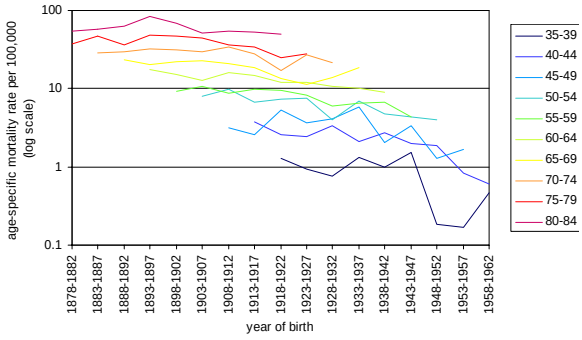


Figure 8.12. Age-specific mortality by birth cohort, females, 1950-2002



International trends

All countries studied, with the exception of Norway, have had a decrease in male anorectal cancer mortality over most of the period 1950-2002 (Figure 8.13). Recent trends (1992-2002) also show fairly consistent decreases (Figure 8.15), with the possible exception of Scotland. The rate of decrease in Ireland has been less than average, and, among the countries shown, we have gone from the sixth highest (in 1951) to the fourth highest (2002) age-standardised rate for males. Very similar international trends can be seen for females (Figures 8.14).

Figure 8.13. Rolling 5-year average World age standardized mortality rates in Europe and USA, males, all ages, 1950 to 2002

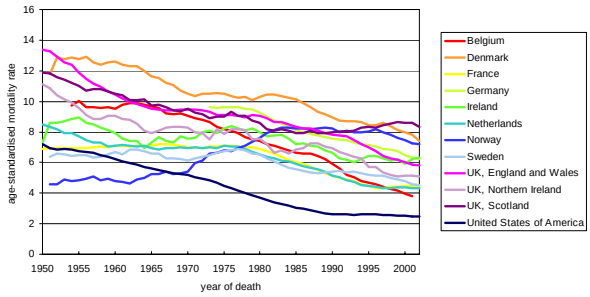
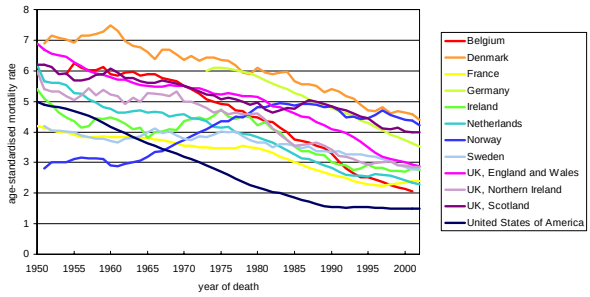


Figure 8.14. Rolling 5-year average World age standardized mortality rates in Europe and USA, females, all ages, 1950 to 2002



Recent estimates of change (Figures 8.15, 8.16) indicate significant increases in age-standardised mortality since 1992 for men in Belgium, Denmark, Germany, Norway, Sweden, England/Wales and the USA and for women in Belgium, Germany, the Netherlands, Sweden, England/Wales and Scotland.

Figure 8.15. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

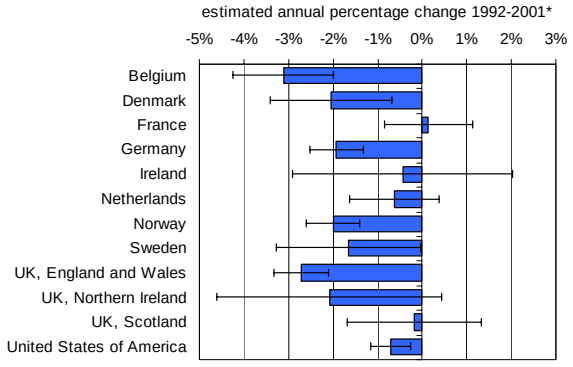
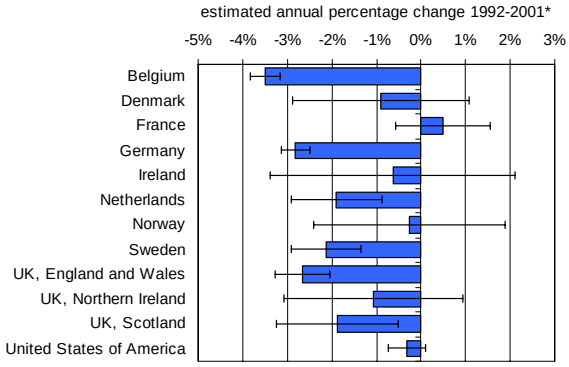


Figure 8.16. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



** or nearest available data period*

Predictions for the period 2005-2015

Anorectal cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to increase from 6.43 in 1998-2002 to 6.96 (95% prediction interval 4.75, 9.16) in 2015 (Figure 8.17, Table 8.4). The number of deaths in men is predicted to rise from 164 per year in 1998-2002 to 263 (183, 343) in 2015 (Figure 8.19). In men under 65 the mortality rate is predicted to fall, from 2.45 in 1998-2002 to 2.22 (1.43, 3.02) in 2015 (Figure 8.18), but again with a rise in the number of deaths, from 47 per year in 1998-2002 to 61 (39, 83) in 2015 (Figure 8.20).

Table 8.3. Models chosen for predictions

model	*sex*	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	males	1993-2002	60	linear	0.0424
	females	1975-2002	168	log linear	0.0000
0-64	males	1979-2002	72	log linear	0.4011
	females	1975-2002	78	log linear	0.0062

Mortality rates in women are predicted to fall from 2.73 in 1998-2002 to 1.94 (1.42, 2.45) in 2015 (Table 8.4, Figures 8.17-8.20). The number of deaths is also predicted to fall slightly, from 93 per year in 1998-2002 to 90 (68, 113) in 2015. In women under 65 mortality rates are also expected to fall, from 0.98 in 1998-2002 to 0.62 (0.27, 0.98) in 2015. The number of deaths in this age group is also expected to fall slightly, from 19 per year in 1998-2002 to 17 (8, 27) in 2015.

Table 4.5. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	6.43	6.67 (5.33, 8.00)	6.81 (5.08, 8.54)	6.96 (4.75, 9.16)
No. of deaths (95% PI)	164	187 (150, 223)	219 (165, 273)	263 (183, 343)
females, all ages				
WASMR (95% PI)	2.73	2.36 (1.77, 2.95)	2.13 (1.58, 2.68)	1.94 (1.42, 2.45)
No. of deaths (95% PI)	93	86 (66, 106)	87 (66, 108)	90 (68, 113)
males, 0-64				
WASMR (95% PI)	2.45	2.39 (1.67, 3.12)	2.32 (1.59, .05)	2.22 (1.43, 3.02)
No. of deaths (95% PI)	47	53 (37, 69)	59 (40, 77)	61 (39, 83)
females, 0-64				
WASMR (95% PI)	0.98	0.84 (0.42, 1.26)	0.72 0.34, 1.10)	0.62 (0.27, 0.98)
No. of deaths (95% PI)	19	18 (9, 27)	18 (9, 28)	17 (8, 27)

The numbers of deaths presented in Table 8.4 and in Figures 8.19 and 8.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 8.5 which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would result in an additional 35 deaths per year in women (a 38% increase). Of the projected increase of 99 deaths per annum in men between 1998-2002 and 2015, 80 (80%) would be due to demographic change.

Table 8.5. Predictions of number of deaths at all ages, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths (95% PI)	164	182 (153, 212)	209 (177, 240)	244 (209, 279)	93	102 (80, 123)	113 (90, 136)	128 (103, 154)

Figure 8.17. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

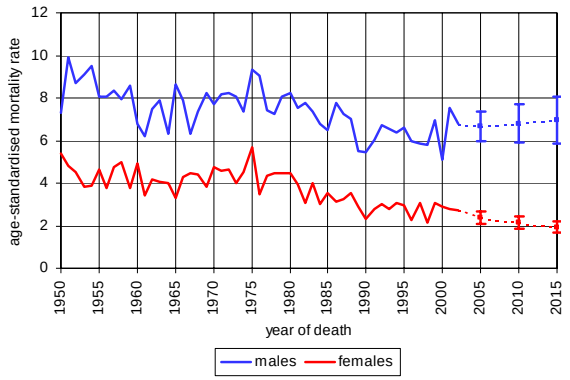


Figure 8.18. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

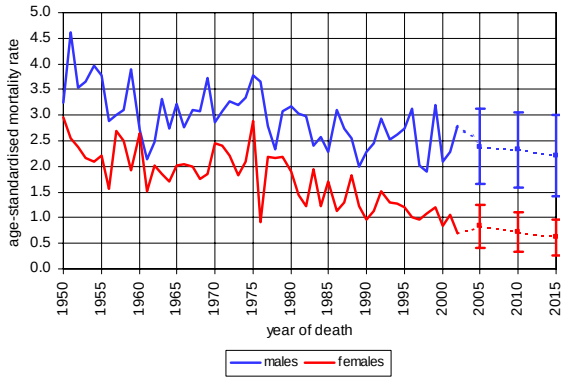


Figure 8.19. Actual and predicted number of deaths, all ages, 1950-2015

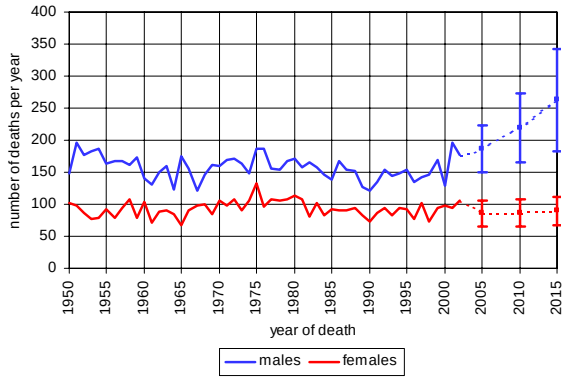
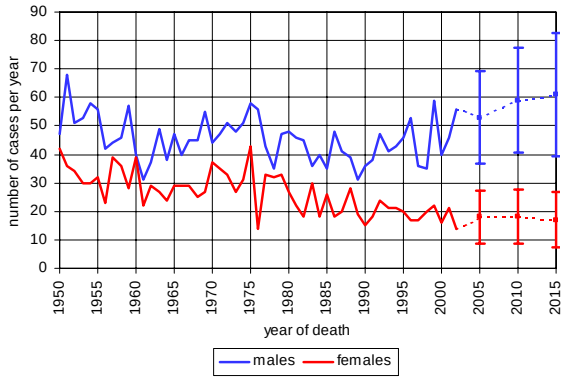


Figure 8.20. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

Although the number of deaths from anorectal cancer had changed very little between the 1970s and 1990s, there has been a steady increase in the last few years—by about 2% per year for men and 1.6% per year for women since 1993. Age-standardised rates are still falling, but the rate of decrease appears to have lessened. However, joinpoint analysis suggests a 0.6% annual fall in rate for men since 1950 and 2.0% for women since 1975 and does not show any more recent point of inflection, so the recent changes may be due to random variation and may not be sustained in the longer term. Over those periods, rates in men under 65 have been falling by 0.7% per year and those in women by 3.1%. Compared with colon cancer, there is less evidence of an effect of year of birth on mortality, independent of age or of period of death, and trends for different cohorts and age groups are similar for men and women. Internationally there has been quite a consistent fall in anorectal cancer rates. This fall has been less marked in Ireland than in most other countries.

Predictions

A fall in mortality rates is predicted for females (by 29%) between 2000 and 2015, but an 8% increase in overall rates for men, although rates are predicted to fall by 9% in men under 65. Numbers of deaths are predicted to increase in men, but to fall slightly in women. The expected overall increase in rates among men contrasts with the decline predicted for colon cancer in both sexes.

Conclusions

Although there are similarities between colon and anorectal cancer in their current and predicted mortality patterns (for females and for younger males), the historical trends have been quite different, perhaps reflecting some differences in aetiology. However, assignment of cancers to colon and rectum on death certificates is not always reliable, and we cannot rule out an effect on the trends from increasing availability of endoscopy and more accurate certification. Similar considerations with regard to diet and screening must apply, as for colon cancer. The ratio of male to female deaths in 1998-2002 was 1.8 and is predicted to rise to 2.9 by 2015, as compared with a change in ratio from 1.2 to 1.4 for colon cancer, so preventive efforts may need to be more strongly focused on men for rectal cancer. Rectal cancers are also more accessible to screening, and although they have made up only 28% of colorectal cancers in recent years, screening for them may be more cost-effective.

Chapter 9. Pancreatic cancer (ICD-9 157)

Epidemiology

Pancreatic cancer was the eighth most common cancer and the sixth commonest cause of cancer death in the period 1994-2001, with an annual average of 349 cases and 360 deaths during this period. Female cases made up 50% of this total and female deaths made up 49%.

Pancreatic cancer is mainly a disease of older populations (Table 9.1). 61% of cases and 62% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined.

Table 9.1. Age distribution of pancreatic cancer deaths and cases

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	0%	0%	0%	0%	0%	0%
30-39	0%	1%	1%	1%	1%	1%
40-49	2%	3%	4%	4%	3%	4%
50-59	8%	9%	13%	13%	10%	11%
60-69	20%	22%	25%	25%	22%	23%
70-79	36%	35%	36%	37%	36%	36%
80+	34%	31%	20%	19%	27%	25%

Survival from pancreatic cancer is very poor. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 4% for men and 5% for women while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 3% for men and 5% for women (Berrino et al. 1995).

Five-year survival for patients diagnosed in Ireland in 1994-1996 was 4.8% (95% CI 2.8-7.6%) for men and 6.6% (4.3-9.5%) for women; in 1997-1999, 5.9% (3.6-9.1%) for men and 5.6% (2.8-9.7%) for women (National Cancer Registry 2003).

Non-genetic risk factors

Diet and energy balance

A diet high in saturated fat and meat appears to increase the risk of pancreatic cancer (Stolzenberg-Solomon, Pietinen et al. 2002), while increased consumption of fish, fruits and vegetables seems to reduce the risk (Soler, Chatenoud et al. 1998). Pancreatic cancer has been shown to be associated, although not strongly, with obesity (Berrington de Gonzalez, Sweetland et al. 2003; Fryzek, Schenk et al. 2005), while a link with exercise (Patel, Rodriguez et al. 2005; Sinner, Schmitz et al. 2005) or total caloric intake (Stolzenberg-Solomon, Pietinen et al. 2002) has not been confirmed in recent studies.

Cigarette smoking

Smoking is the strongest known environmental risk factor for pancreatic cancer (Simon and Printz 2001; Potter 2002). Carcinogens probably reach the pancreas via the bloodstream after being absorbed from the lungs, but ingested tobacco products may also reach the pancreas through reflux from the duodenum. Smoking increases the risk of pancreatic cancer by

about two-fold compared to non-smokers, and it has been estimated that about 30% of pancreatic cancer is attributable to smoking (Wang and Wang 2005).

Alcohol Consumption

Although alcohol is a major risk factor for pancreatitis, few studies have shown an association between alcohol intake and pancreatic cancer (Velema, Walker et al. 1986).

Other risk factors

Chronic pancreatitis is associated with an increased risk of pancreatic cancer (Cavestro, Comparato et al. 2003) although in some cases this may be due to shared genetic or environmental risk factors.

As diabetes may be an early manifestation of pancreatic cancer, it has been difficult to establish the direction of causation unambiguously, but it is now generally accepted that diabetics have about a two-fold increased risk of pancreatic cancer (Huxley, Ansary-Moghaddam et al. 2005; Senior 2005).

Trends

Between 1950 and 2002, the number of pancreatic cancer deaths rose from 63 to 199 in men and from 54 to 191 in women, corresponding to an average increase, over the whole period, of 1.6% per year for men and 1.9% for women (Figure 9.1). Crude mortality rates increased by 1.0% annually for men and by 1.2% annually for women (Figure 9.2). Most of this increase took place between 1950 and 1970. Age-standardised rates (Figures 9.3, 9.4), cumulative risk of dying before age 65 (Figure 9.5) and years of potential life lost (Figure 9.6) all showed similar patterns of increase (0.3% to.1.2% annually) for men. However for women, while the overall age-standardised rate increased by 0.6%, trends for women under 65 (age-standardised rate, cumulative risk to age 65 and person-years of life lost) showed annual decreases by 0.1-0.3%. These decreases among younger women have happened recently, since the mid 1970s. Trends since 1992 indicate a significant annual decrease in total age-standardised mortality rates for males (Figure 9.15) and a non-significant annual decrease for females (Figure 9.16).

Figure 9.1. Number of deaths per year, 1950-2002

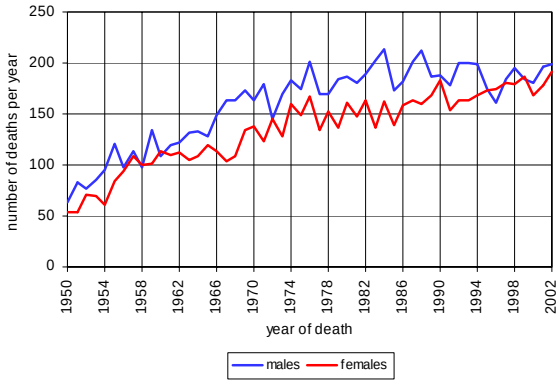


Figure 9.2. Crude mortality rate, 1950-2002

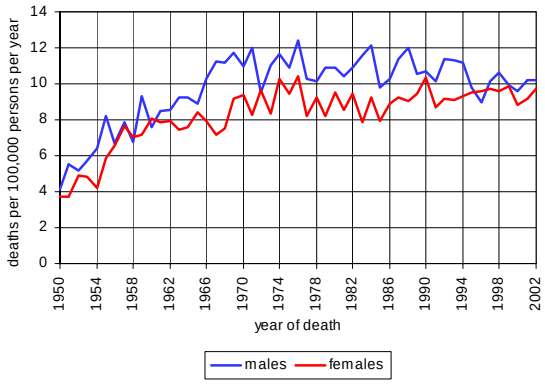


Figure 9.3. World age-standardised mortality rate, all ages, 1950-2002

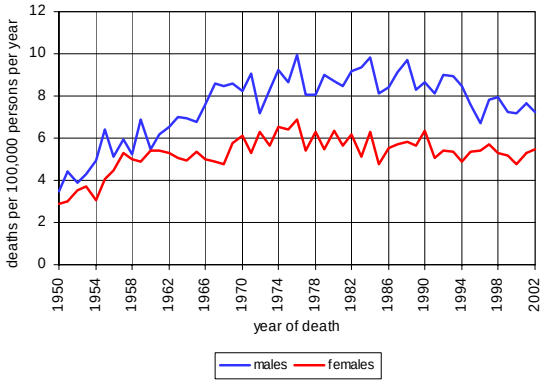


Figure 9.4. World age-standardised mortality rate, 0-64 years, 1950-2002

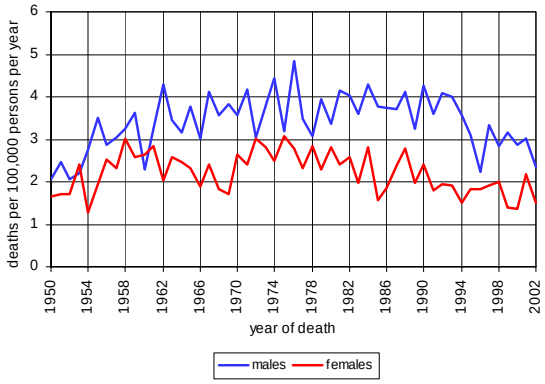


Figure 9.5. Cumulative risk of dying of cancer before age 65, 1950-2002

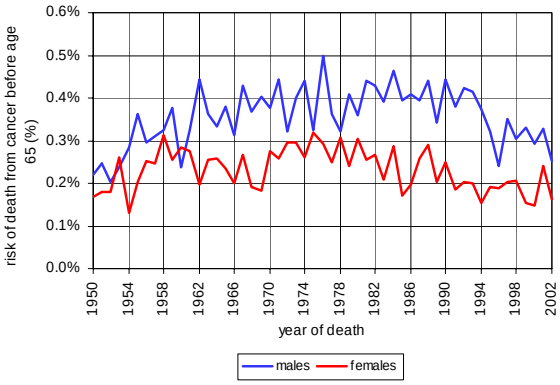


Figure 9.6. Years of potential life lost up to age 65, 1950-2002

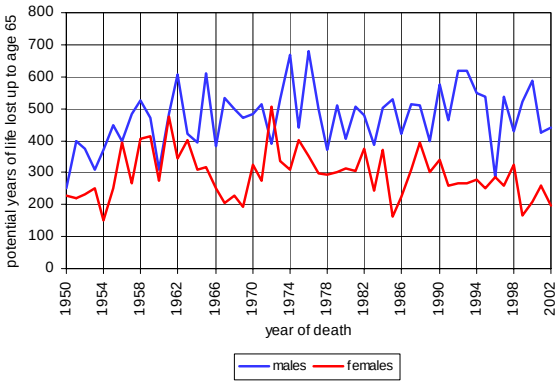


Table 9.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1950		1950		1950		1950	
↓	4.0% (3.1%, 5.0%)	↓	8.0% (3.5%, 12.7%)	↓	4.1% (1.3%, 6.9%)	↓	1.3% (0.2%, 2.3%)
1968 (1954, 1972)		1957 (1954, 1961)		1962 (1952, 1976)		1975 (1970, 1984)	
↓	0.4% (-0.2%, 1.1%)	↓	1.3% (0.5%, 2.2%)	↓	0.2% (-0.4%, 0.9%)	↓	-1.8% (-2.7%, -1.0%)
1987 (1973, 1995)		1975 (1970, 1982)		1990 (1974, 1996)		2002	
↓	-1.6% (-2.5%, -0.7%)	↓	-0.6% (-1.0%, -0.2%)	↓	-3.3% (-5.4%, -1.1%)		
2002		2002		2002			

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate for men showed a complex pattern, with an initial rapid increase in rate of 4.0% per annum from 1950 to 1968 (Table 9.2, Figure 9.7) followed by a much smaller increase (not statistically significant) of 0.4% annually until 1987, and finally a decrease in rate of 1.6% per annum up to 2002. For women, the pattern was equally complex, with an initial, very rapid, increase in rate of 8.0% per year between 1950 and 1957, a more gradual increase of 1.3% annually up to 1975, and a fall of 0.6% annually since then.

For men under 65 the pattern was similar to that for men of all ages, with an initial increase of 4.1% annually, followed by a period of 28 years from 1962 to 1990 with no significant change in rate, and a fall of 3.3% annually from 1990 to 2002 (Figure 9.8). The fitted model for women under 65 was less complex, with an initial period of increase from 1950 to 1975 (1.3% per annum) followed by a decrease, from 1975 to 2002 (1.8% per annum).

Figure 9.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

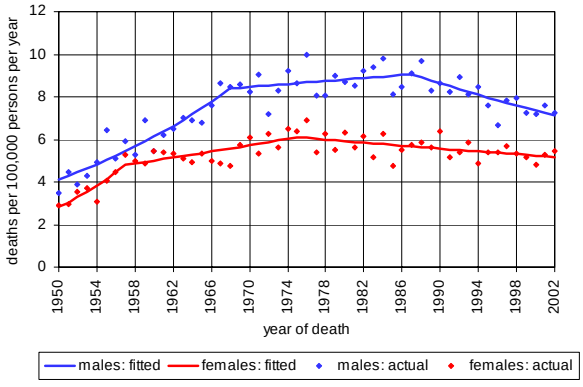
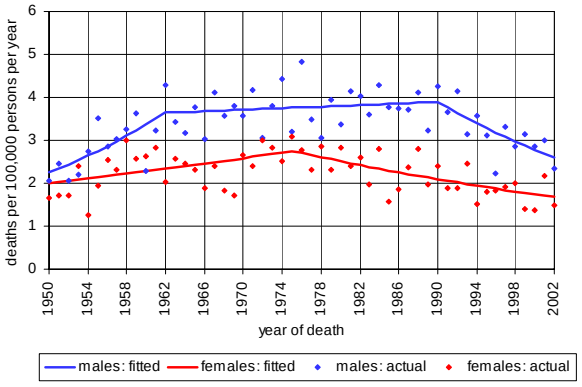


Figure 9.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

The age-period plots for men show an increase throughout the entire period for men aged 75+; for men younger than this, the increase in mortality rate ended around 1983 and was followed by a decrease (Figure 9.9). This pattern was seen for all but the youngest men. The pattern of mortality for women was almost identical (Figure 9.10).

There was no strong evidence for an effect of year of birth on mortality rates (Figures 9.11, 9.12).

Figure 9.9. Age-specific mortality by period of death, males, 1950-2002

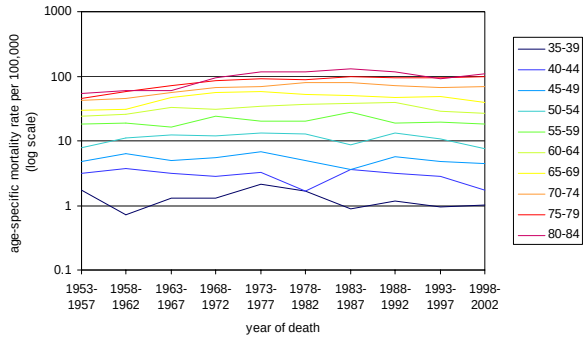


Figure 9.10. Age-specific mortality by period of death, females, 1950-2002

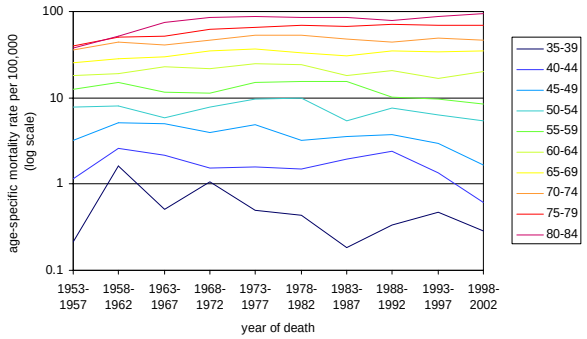


Figure 9.11. Age-specific mortality by birth cohort, males, 1950-2002

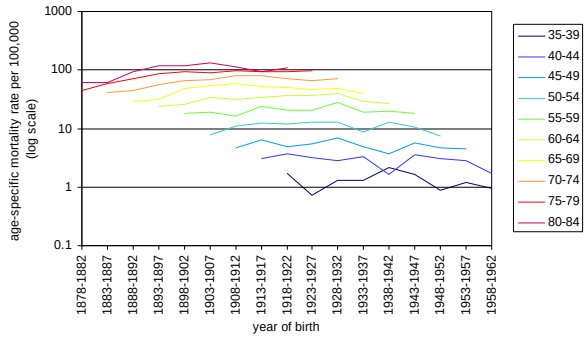
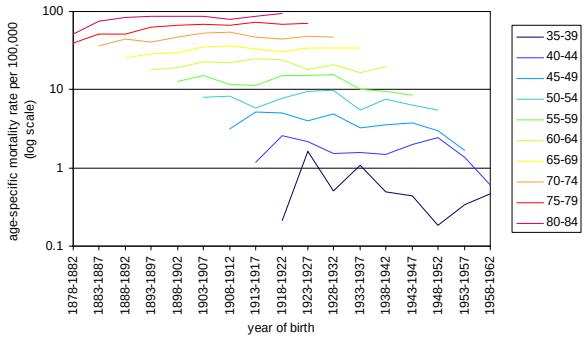


Figure 9.12. Age-specific mortality by birth cohort, females, 1950-2002



International trends

Almost all countries show the same pattern in male pancreatic mortality, with an increase in rate up to the 1980s, followed by a fall (Figure 9.13). In some countries (Scotland, USA) this fall in mortality began in the 1970s, while in France, which had the second lowest mortality in the 1950s, there is no evidence yet of a decrease (Figure 9.13). Mortality trends in males in Ireland are similar to the overall pattern although the peak in mortality occurred relatively late.

For females, the same pattern of increase up to the 1980s can be observed (Figure 9.14). However, while there have been significant falls in mortality in the UK and Denmark since then, mortality has continued to rise in France and Belgium (which had the lowest initial rates) and have not changed significantly in other countries. The position of Ireland relative to other countries was much the same throughout the period studied.

Figure 9.13. Rolling 5-year average World age standardized mortality rates in Europe and USA, males, all ages, 1950 to 2002

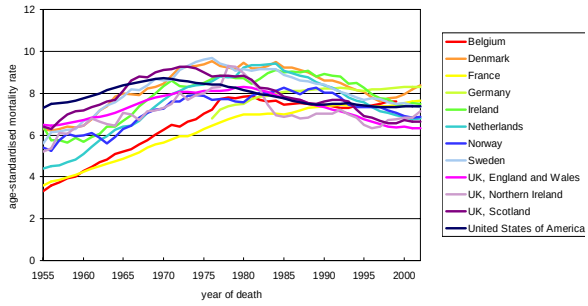
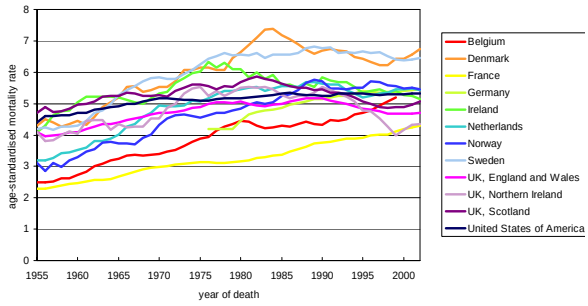


Figure 9.14. Rolling 5-year average World age standardized mortality rates in Europe and USA, females, all ages, 1950 to 2002



Recent estimates of change (Figures 9.15, 9.16) indicate significant increases in age-standardised mortality since 1992 for men in Belgium and falls in Ireland and England/Wales, while for women increases were seen in Belgium and France.

Figure 9.15. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

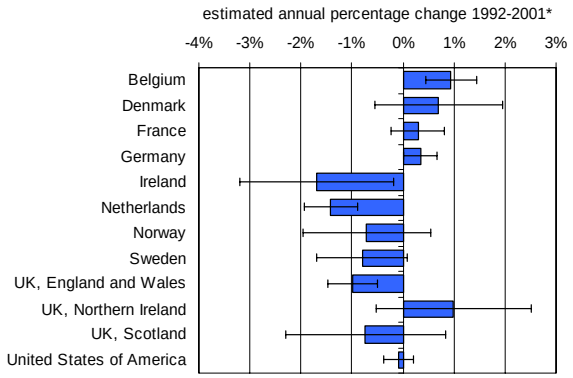
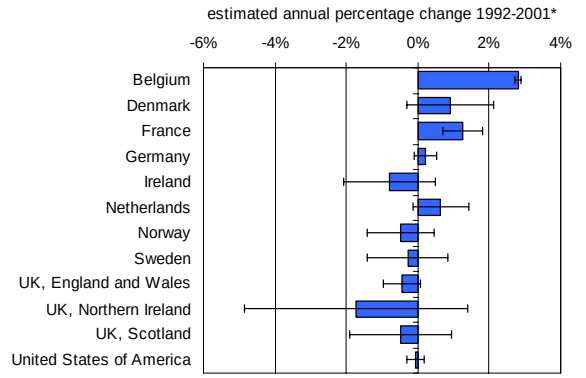


Figure 9.16. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



**or nearest available data period*

Predictions for the period 2005-2015

Pancreatic cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to fall from 7.44 in 1998-2002 to 5.88 (95% prediction interval 4.63, 7.12) in 2015 (Figure 9.17, Table 9.4). However, the number of deaths in men is predicted to increase, from 191 per year in 1998-2002 to 226 (179, 273) in 2015 (Figure 9.19). In men under 65 the mortality rate is predicted to fall from 2.84 in 1998-2002 to 1.68 (0.87, 2.50) in 2015 (Figure 9.18) while the number of deaths will fall slightly, from 54 per year in 1998-2002 to 47 (24, 69) in 2015 (Figure 9.20).

Table 9.3. Models chosen for predictions

model	*sex*	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	males	1987-2002	96	log-linear	0.0504
	females	1987-2002	96	log-linear	0.9772
0-64	males	1990-2002	39	log-linear	0.0190
	females	1975-2002	84	log-linear	0.0051

Mortality rates in women are predicted to fall from 5.21 in 1998-2002 to 5.05 (3.89, 6.21) in 2015 (Table 9.4, Figures 9.17-9.20). As with men, the number of deaths is predicted to increase, from 180 per year in 1998-2002 to 239 (188, 290) in 2015. In women under 65 mortality rates are also expected to fall, from 1.68 in 1998-2002 to 1.22 (0.73, 1.72) in 2015. The number of deaths in this age group is expected to increase slightly, from 31 per year in 1998-2002 to 34 (20, 48) in 2015.

Table 9.4. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	7.44	6.87 (5.70, 8.04)	6.35 (5.15, 7.55)	5.88 (4.63, 7.12)
No. of deaths (95% PI)	191	194 (162, 226)	207 (168, 245)	226 (179, 273)
females, all ages				
WASMR (95% PI)	5.21	5.18 (4.23, 6.12)	5.10 (4.07, 6.13)	5.05 (3.89, 6.21)
No. of deaths (95% PI)	180	192 (160, 225)	210 (171, 250)	239 (188, 290)
males, 0-64				
WASMR (95% PI)	2.84	2.35 (1.57, 3.13)	1.98 (1.19, 2.77)	1.68 (0.87, 2.50)
No. of deaths (95% PI)	54	52 (35, 70)	50 (30, 71)	47 (24, 69)
females, 0-64				
WASMR (95% PI)	1.68	1.50 (0.94, 2.06)	1.36 (0.84, 1.88)	1.22 (0.73, 1.72)
No. of deaths (95% PI)	31	33 (21, 45)	34 (21, 47)	34 (20, 48)

The numbers of deaths presented in Table 9.4 and in Figures 9.19 and 9.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 9.5 which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would result in an additional 93 deaths per year in men (a 49% increase on the 1998-2002 average) and 67 in women (a 37% increase) by 2015.

Table 9.5. Predictions of number of deaths at all ages, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths (95% PI)	191	213 (181, 244)	244 (209, 278)	284 (247, 322)	180	196 (166, 226)	218 (185, 250)	247 (212, 282)

Figure 9.17. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

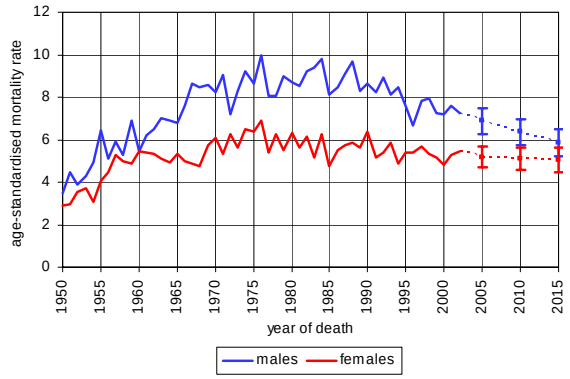


Figure 9.18. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

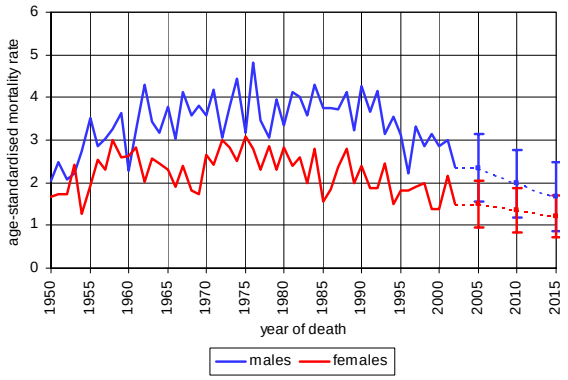


Figure 9.19. Actual and predicted number of deaths, all ages, 1950-2015

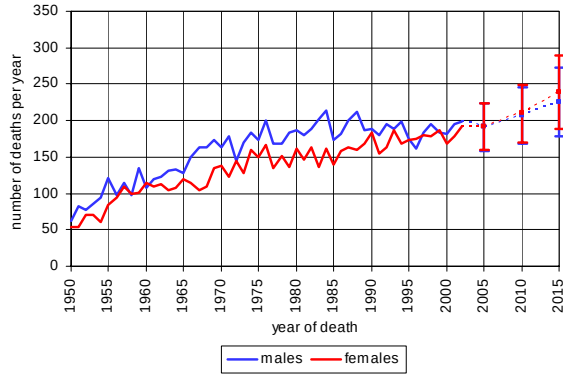
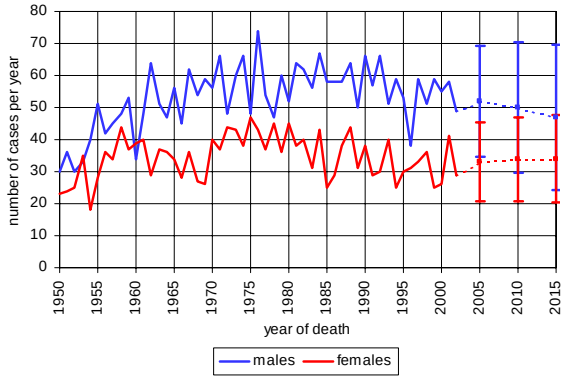


Figure 9.20. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

Pancreatic cancer mortality increased rapidly, both numbers and age-standardised rate, up to the late 1960s or early 1970s, but has stabilised since then, with a decline in the rate in recent years, especially in males. Some of the initial increase in mortality may have been due to changes in certification. Even at present, pancreatic cancer appears to be over-diagnosed on death certificates. In 1994-2001 an average of 360 deaths each year was certified as being due to pancreatic cancer, while in the same period only 349 new cases of the cancer were registered annually by the National Cancer Registry. Mortality rates fell by 1.6% per annum during 1992-2001 for men but did not fall significantly for women. Although rates remain slightly lower in women than in men, the number of deaths in women exceeded that in men for the first time in 1996.

Joinpoint analysis shows an annual fall of 1.6% in age-standardised mortality rate annually for men since 1987 and 0.6% for women since 1975. For those under 65 there have been annual falls of 3.3% for men and 1.8% for women over similar periods.

Most countries in Europe have shown a rise and fall in mortality similar to that seen in Ireland, although mortality has not begun to fall in some countries.

Predictions

A fall in age-standardised mortality rate is predicted for both sexes and for both age groups, but, for demographic reasons, this will not be accompanied by any fall in number of deaths, except among men under 65. The biggest fall in rate (by 40% between c.2000 and 2015) is expected in men under 65, and the smallest (by 10%) in women of all ages combined. The largest increase in number of deaths is expected in women, by 27%. By 2015 the annual number of deaths in women is expected to exceed that in men, but the age-standardised mortality rate for women is predicted to remain below that for men.

Conclusions

The continuing fall in mortality from pancreatic cancer is welcome, although the reasons for this are not very clear. The greater fall in rates in men compared to women points to a decrease in smoking as a likely explanation. Survival remains extremely low, and improvements in survival are unlikely to have made any significant contribution to the decrease. It may, unfortunately, be the case that some of the apparent improvement in mortality is attributable to more accurate death certification. Data from the National Cancer Registry since 1994 (National Cancer Registry 2005) show no equivalent fall in pancreatic cancer incidence over the period 1994-2001, but in fact a slight increase in incidence in men.

Most pancreatic cancer is advanced at diagnosis, and no useful screening method has been developed. Prevention is difficult as the aetiology of the condition, apart from the link with smoking, is poorly understood in many cases, and much more information is needed on the genetic background and risk factors for this cancer.

Chapter 10. Cancer of trachea, bronchus and lung (ICD-9 162)

Epidemiology

Cancer of the trachea, bronchus and lung was the third most common cancer and the commonest cause of cancer death in the period 1994-2001, with an annual average of 1,580 cases and 1,499 deaths during this period. Female cases made up 36% of the total, as did female deaths.

54% of cases and 57% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined (Table 10.1).

Table 10.1. Age distribution of lung cancer deaths and cases (including cancer of trachea)

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	0%	0%	0%	0%	0%	0%
30-39	0%	1%	0%	1%	0%	1%
40-49	4%	4%	3%	3%	3%	3%
50-59	10%	11%	12%	14%	12%	13%
60-69	24%	26%	29%	31%	27%	29%
70-79	40%	41%	38%	37%	39%	38%
80+	21%	18%	17%	15%	19%	16%

Survival from lung cancer is poor. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 11% for men and 10% for women while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 7% for men and 9% for women (Berrino et al. 1995). Five-year survival for patients diagnosed in Ireland in 1994-1996 was 8.5% (95% CI 7.3-9.7%) for men and 10.0% (8.2-11.7%) for women; in 1997-1999, 8.0% (6.3-9.7%) for men and 11.2% (9.3-13.1%) for women (National Cancer Registry 2003).

Non-genetic risk factors

Cigarette smoking

Cigarette smoking is accepted to be the primary cause of lung cancer (Gazdar and Minna 1997; Proctor 2004). The percentages of lung cancers estimated to be caused by tobacco smoking in males and females are 90% and 78%, respectively. Cigar and pipe smoking also have been associated independently with increased lung cancer risk (Boffetta, Pershagen et al. 1999; Iribarren, Tekawa et al. 1999). Environmental, or second-hand, tobacco smoke is also implicated in causing lung cancer (Hackshaw, Law et al. 1997).

Other risk factors

In miners, radon, independently and in combination with smoking, is an established lung cancer risk factor. Lung cancer risk, for both smokers and non-smokers, has been estimated to increase by about 16% for every 100 Bq/m^2 of domestic radon exposure (Darby, Hill et al. 2005). On this basis, about 10% of all lung cancer deaths in Ireland are attributable to indoor radon (Radiological Protection Institute of Ireland/National Cancer Registry 2005). The validity of extrapolation from higher levels of radon to the average exposures in Irish homes of <100 Bq/m^2 is not, however, definitively proven.

There is a dose-response relationship between asbestos exposure and lung cancer risk, and asbestos exposure is synergistic with smoking in increasing this risk (Hessel, Gamble et al. 2005).

Trends

Cancer of the trachea, lung and bronchus are classified together and have similar aetiology, and are described here as a single condition. For simplicity, they will be referred to as "lung" cancer. ICD-7 allowed a category of "lung cancer, not specified whether primary or secondary" and mortality data on lung cancer for Ireland in the early 1950s are thus not reliable. All data below refers to the period 1954 to 2002.

Between 1954 and 2002, the number of lung cancer deaths rose from 68 to 925 in men and from 20 to 544 in women, corresponding to an average increase, over the whole period, of 4.2% per year for men and 6.6% for women (Figure 10.1). Most of the increase in men took place between 1960 and 1970, with a fall in numbers after 1986, but the increase in women has been more consistent. Crude mortality rates increased by 3.2% annually for men and by 5.5% annually for women (Figure 10.2). Age-standardised rates (Figure 10.3) have increased by about 3% annually for men and 5% annually for women, while rates of increase in younger age groups—age-standardised rate (Figure 10.4), cumulative risk before age 65 (Figure 10.5) and years of potential life lost (Figure 10.6)—have been lower (1.2%-1.5% for men and 3.2%-3.5% in women) but still higher for women. Age-standardised mortality rates for women, which were 25% those for men in 1955, are now 48% of the male value. Trends since 1992 indicate a significant annual decrease in total age-standardised mortality rates for males (Figure 10.15) and a non-significant annual decrease for females (Figure 10.16).

Figure 10.1. Number of deaths per year, 1954-2002

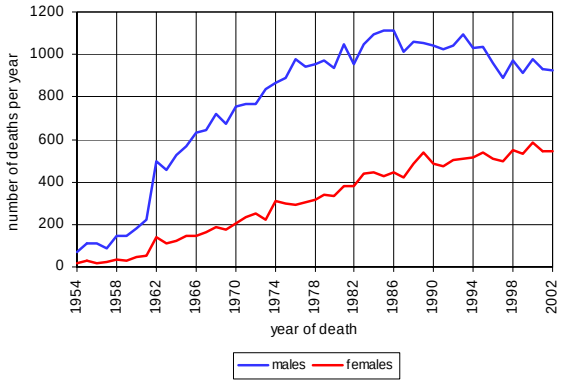


Figure 10.2. Crude mortality rate, 1954-2002

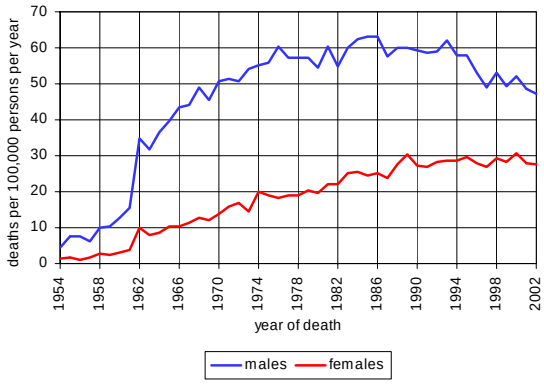


Figure 10.3. World age-standardised mortality rate, all ages, 1954-2002

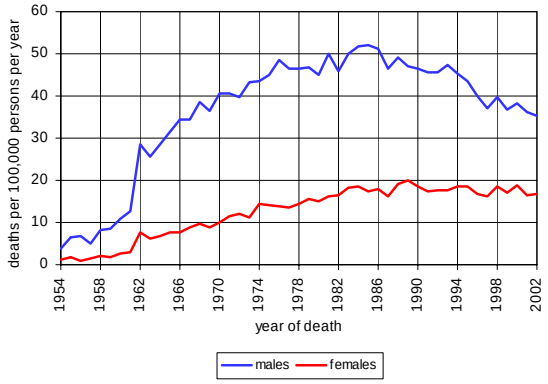


Figure 10.4. World age-standardised mortality rate, 0-64 years, 1954-2002

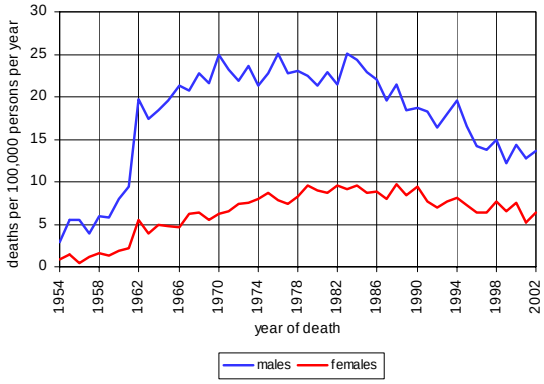


Figure 10.5. Cumulative risk of dying of cancer before age 65, 1954-2002

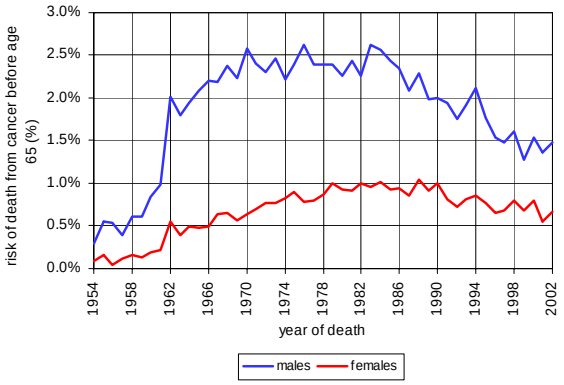
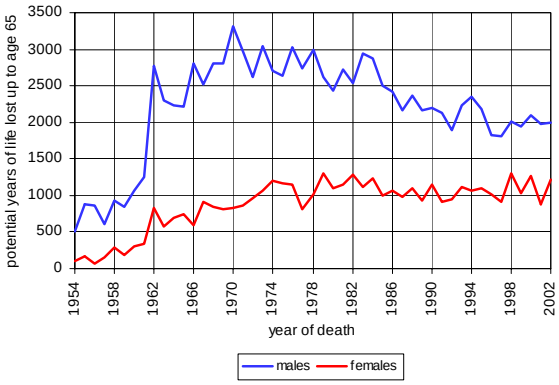


Figure 10.6. Years of potential life lost up to age 65, 1954-2002



Joinpoint regression analysis

Table 10.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1954-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1954		1954		1954		1954	
↓	21.8% (18.3%, 25.5%)	↓	6.7% (-9.7%, 26.0%)	↓	4.6% (-7.1%, 17.8%)	↓	21.5% (14.8%,28.6%)
1965 (1963, 1967)		1959 (1956, 1964)		1959 (1956, 1961)		1964 (1961, 1967)	
↓	1.9% (1.3%, 2.6%)	↓	60.4% (-8.3%, 180%)	↓	54.3% (5.8%, 125%)	↓	3.5% (2.2%, 4.9%)
1985 (1980, 1988)		1962 (1961, 1977)		1962 (1961, 1964)		1982 (1976, 1986)	
↓	-2.2% (-2.8%, -1.6%)	↓	4.8% (4.0%, 5.5%)	↓	1.0% (0.3%, 1.6%)	↓	-2.2% (-3.0%, -1.3%)
2002		1983 (1978, 1991)		1983 (1975, 1987)		2002	
		↓	-0.4% (-0.9%, 0.2%)	↓	-3.4% (-4.1%, -2.6%)		
		2002		2002			

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate for men showed a rapid increase in rate from 1954 to 1965 of 21.8% annually for men, a more gradual increase of 1.9% annually from 1965 to 1985 and a fall in rate of 2.2% annually from 1985 to 2002 (Table 10.2, Figure 10.7). For women, the initial rate of increase, from 1954 to 1959, was less (6.7% annually), followed by a brief very rapid increase of 60% annually from 1959 to 1962, and a slower increase (4.8% annually), from 1962 to 1983. Since 1983 there has been no significant upward or downward trend.

For men and women under 65, the patterns up to the 1980s again show increasing mortality rates, although the detailed patterns (as modelled by Joinpoint) differed somewhat from those for all ages (Table 10.2, Figure 10.8). Recent decreases were greater for men under 65 (3.4%) than for all ages, while for women under 65 there has been a significant decrease in mortality rate, by 2.2% per annum since 1982, compared with the non-significant decrease for women of all ages since 1983.

Figure 10.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1954-2002

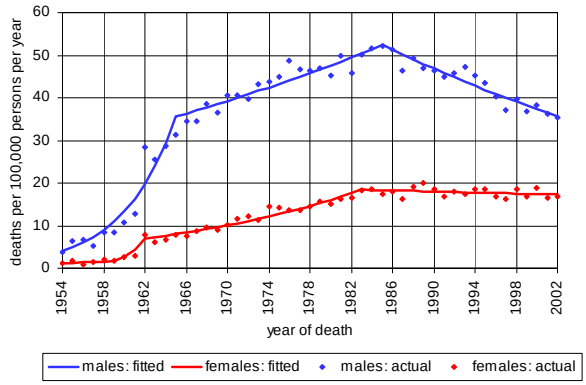
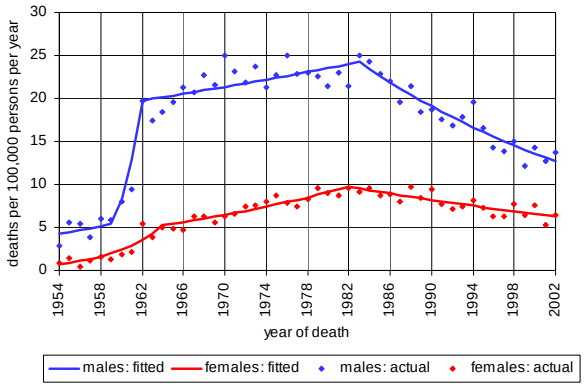


Figure 10.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1954-2002



Age-period-cohort trends

The age-period plots for men show a rapid increase in mortality between 1954* and 1968 (Figure 10.9). This trend then began to flatten out—earliest for the younger age groups, for whom a decline in mortality was seen in 1968-72, and latest for the oldest men for whom a decrease in mortality was not observed until 1998-2002. The decline in mortality in women, where it occurred, was later (Figure 10.10). Definite falls in mortality can be seen in women aged 55-64 from 1998 onwards, but mortality in other age groups is constant, and in the case of women aged 40-44, increasing.

Figure 10.9. Age-specific mortality by period of death, males, 1954-2002

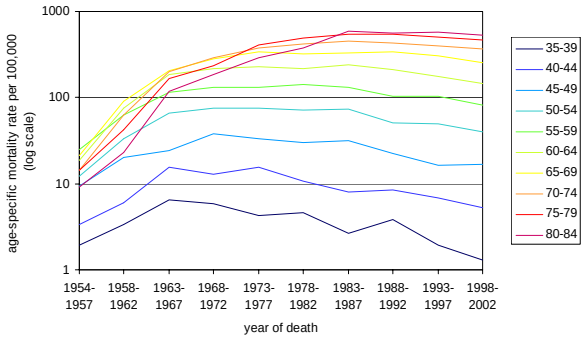
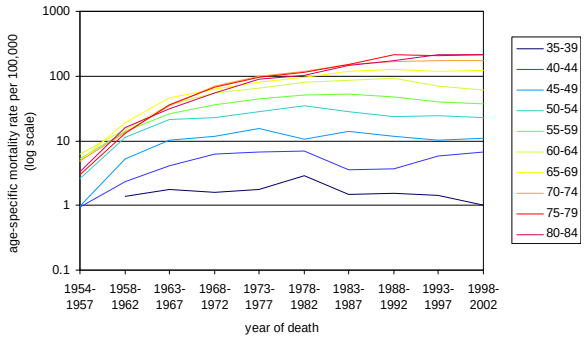


Figure 10.10. Age-specific mortality by period of death, females, 1954-2002



Lung cancer mortality in men was generally highest for cohorts born between about 1903 and 1927, or during 1923-27 for men under 65 (Figures 10.11), and in women, in those born between about 1913 and 1932, or during 1928-32 for women under 65 (Figures 10.12).

Figure 10.11. Age-specific mortality by birth cohort, males, 1954-2002

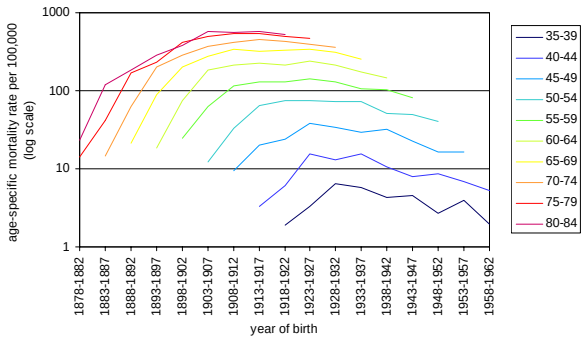
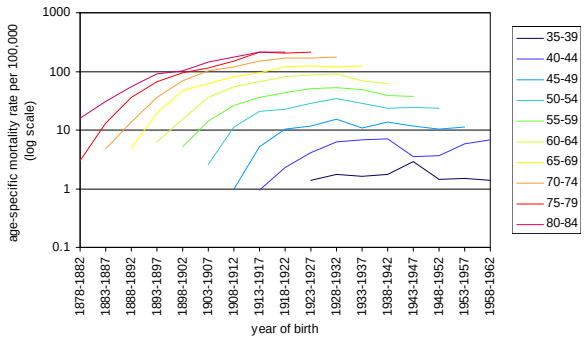


Figure 10.12. Age-specific mortality by birth cohort, females, 1954-2002



* As data for 1953 were not available, the first cohort covers only the four years 1954-1957.

International trends

Almost all countries, with the exception of France and Norway, show a pattern of mortality in males similar to that in Ireland, with a rapid increase in the 1950s and 1960s, followed by a decrease (Figure 10.13). This decrease in mortality began earliest in England and Wales, and latest in the US and France. Male lung cancer mortality in Ireland has remained consistently third or fourth lowest of the countries studied.

Figure 10.13. Rolling 5-year average World age standardized mortality rates in Europe and USA, males, all ages, 1950 to 2002

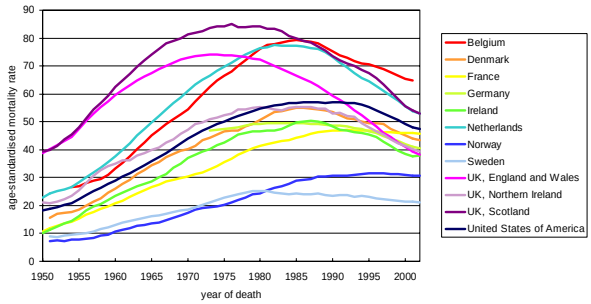
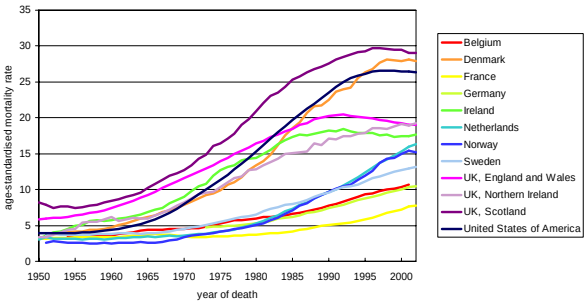


Figure 10.14. Rolling 5-year average World age standardized mortality rates in Europe and USA, females, all ages, 1950 to 2002



Lung cancer mortality in women was slower to increase in most countries, but by contrast with males, many countries have not experienced a decrease in mortality in recent years (Figure 10.14). Rates have fallen in England and Wales, and levelled off in Ireland, the US, Denmark and Scotland. Mortality rates among women in Ireland, which were the third highest during the 1960 and 1970s, are now sixth highest of those studied.

Recent estimates of change (Figures 10.15, 10.16) indicate significant falls in age-standardised mortality since 1992 for men in all countries shown, By contrast, the mortality rate for women has increased recently in many countries—Belgium, Denmark, France, Germany, the Netherlands, Norway and Sweden.

Figure 10.15. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

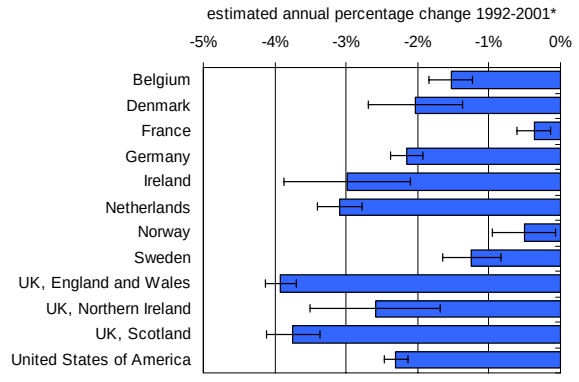
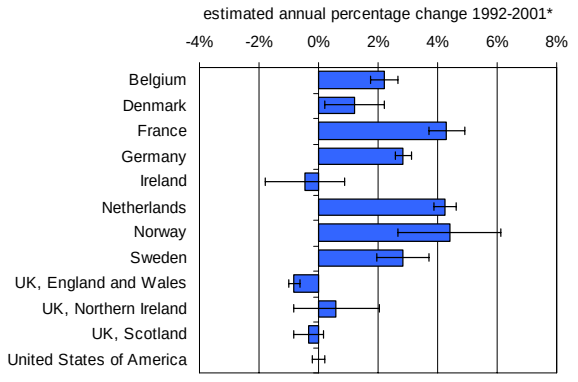


Figure 10.16. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



** or nearest available data period*

Predictions for the period 2005-2015

Lung cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to fall from 37.27 in 1998-2002 to 27.94 (95% prediction interval 25.46, 30.43) in 2015 (Figure 10.17, Table 10.4). The number of deaths in men is, however, predicted to rise, from 946 per year in 1998-2002 to 1077 (982, 1171) in 2015 (Figure 10.19). In men under 65 the mortality rate is also predicted to fall, from 13.57 in 1998-2002 to 7.98 (6.63, 9.32) in 2015 (Figure 10.18), with an accompanying fall in the number of deaths from 258 per year in 1998-2002 to 223 (186, 261) in 2015 (Figure 10.20).

Table 10.3. Models chosen for predictions

model	*sex*	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	males	1985-2002	108	log linear	0.0000
	females	1983-2002	120	log linear	0.0934
0-64	males	1983-2002	60	log linear	0.0000
	females	1983-2002	60	log linear	0.0000

Mortality rates in women are predicted to increase from 17.54 in 1998-2002 to 18.46 (16.44, 20.47) in 2015 (Table 10.4, Figures 10.17-10.20). The number of deaths is also predicted to rise, from 551 per year in 1998-2002 to 844 (755, 933) in 2015. In women under 65 mortality rates are expected to fall, from 6.70 in 1998-2002 to 5.16 (3.90, 6.42) in 2015. The number of deaths in this age group is expected to rise slightly, from 127 per year in 1998-2002 to 136 (104, 168) in 2015.

Table 10.4. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	37.27	34.03 (31.50, 36.56)	30.79 (28.30, 33.28)	27.94 (25.46, 30.43)
No. of deaths (95% PI)	946	962 (892, 1032)	1003 (923, 1082)	1077 (982, 1171)
females, all ages				
WASMR (95% PI)	17.54	17.84 (16.10, 19.59)	18.07 (16.23, 19.92)	18.46 (16.44, 20.47)
No. of deaths (95% PI)	551	620 (563, 676)	709 (640, 778)	844 (755, 933)
males, 0-64				
WASMR (95% PI)	13.57	11.27 (9.71, 12.84)	9.48 (8.04, 10.92)	7.98 (6.63, 9.32)
No. of deaths (95% PI)	258	253 (218, 288)	243 (207, 280)	223 (186, 261)
females, 0-64				
WASMR (95% PI)	6.70	6.05 (4.86, 7.23)	5.56 (4.36, 6.75)	5.16 (3.90, 6.42)
No. of deaths (95% PI)	127	131 (106, 157)	136 (108, 165)	136 (104, 168)

The numbers of deaths presented in Table 10.4 and in Figures 10.19 and 10.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 10.5 which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would have result in an additional 466 deaths per year in men (a 49% increase over the 1998-2002 average). Of the projected increase of 293 deaths per annum in women between 1998-2002 and 2015, 202 (69%) would occur as a result of demographic change alone.

Table 10.5. Predictions of number of deaths at all ages based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths (95% PI)	945	1051 (980, 1121)	1206 (1130,1282)	1412 (1328,1496)	551	595 (543, 648)	660 (604, 716)	753 (692, 814)

Figure 10.17. Actual and predicted World age-standardised mortality rates, all ages, 1955-2015

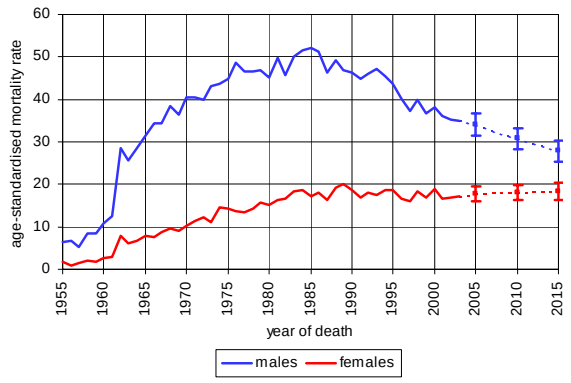


Figure 10.18. Actual and predicted World age-standardised mortality rates, 0-64 years, 1955-2015

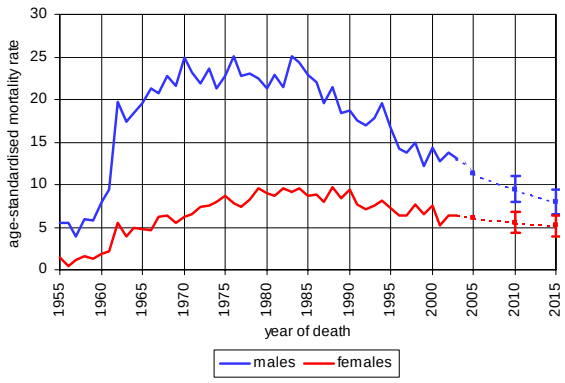


Figure 10.19. Actual and predicted number of deaths, all ages, 1955-2015

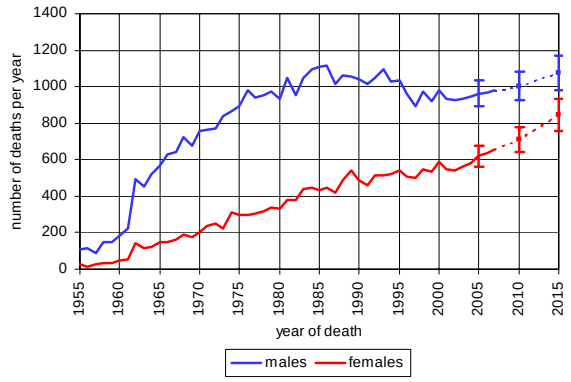
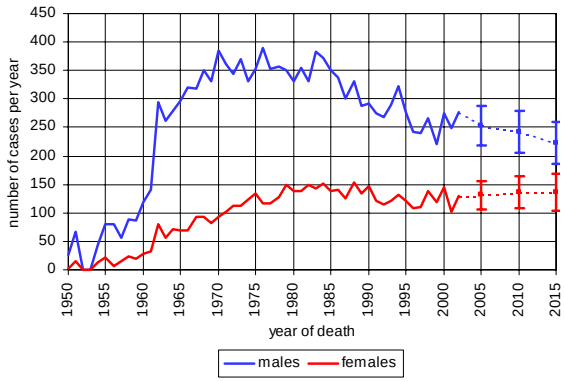


Figure 10.20. Actual and predicted number of deaths, 0-64 years, 1955-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

The number of cases and the mortality rate from lung and bronchus cancer has fallen for men since the late 1980s or early 1990s, but there has been no fall in overall rate or in numbers of deaths for women. However, for women under 65, the age-standardised mortality rate has fallen.

Joinpoint analysis shows an annual fall in rate of 2.2% for men since 1985, with no significant overall trend for women over a similar period. For men under 65 the rate has been falling by 3.4% per annum since 1983 and for women under 65 by 2.2% since 1982.

Cohort analysis shows increasing mortality with each successive cohort born from the 1880s up to early in the 20th century, with a rapid increase in male mortality for cohorts born up to about 1927. A similar pattern is seen for women, though slightly later and with a smaller increase, suggesting that the increase in smoking happened for both sexes at roughly the same time, but for a smaller percentage of women. Mortality rates subsequently fell in successive cohorts, decreasing for all age groups in men, but not for women, where little or no decrease has been seen. Encouragingly, however, mortality seems to have passed its peak in most all age groups for men and for younger age groups in women.

Most countries show the same pattern of rise and fall in men, but only a few countries show a fall in mortality in women by 2001.

Predictions

The decrease in mortality rates for men is predicted to continue, with a 25% fall in rates expected between approximately 2000 and 2015, although the number of deaths is expected to increase by 14%. Both mortality rates and numbers are predicted to increase in women, rates by 5% over the 15-year period, and numbers by 53%. However mortality rates under 65 are predicted to fall, by 41% for men and 23% for women between approximately 2000 and 2015, with a 14% decrease in the number of male deaths but a 6% increase in female deaths.

Conclusions

More is known of the causes and prevention of lung cancer than of any other malignancy. A fall in smoking in men in Ireland over the last 30 years is the most likely explanation of the continuing fall in lung cancer at all ages (Statistics Sweden 1997, Bray et al 2004). For women the picture is more complex, but suggests that the absence of a fall in mortality rates is mainly attributable to the delayed effects of smoking in older women, and that mortality in younger women is decreasing. These projections, however, are limited in their predictive value, as changes in smoking habits will take a minimum of 15 years to have an effect on mortality rates, thus changes in smoking habits in the last 15 years are not taken account of by these predictions.

Chapter 11. Female breast cancer (ICD-9 174)

Epidemiology

Female breast cancer was by far the commonest cancer and the commonest cause of cancer death in women in the period 1994-2001, with an annual average of 1726 cases and 644 deaths during this period. During the same period there was an annual average of 14 male breast cancer cases and 5 deaths. Male breast cancer is not discussed further in this chapter.

Breast cancer tends to affect younger women (under 70) disproportionately. Only 28% of cases and 42% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined (Table 11.1).

Table 11.1. Age distribution of female breast cancer deaths and cases

age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*
<30	0%	1%
30-39	3%	6%
40-49	12%	19%
50-59	20%	25%
60-69	22%	21%
70-79	23%	18%
80+	19%	10%

Survival from female breast cancer is relatively good. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 77%, while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 67% (Berrino et al. 1995).

Five-year relative survival for female patients diagnosed in Ireland in 1994-1996 was 72.8% (95% CI 71.1-74.5%.); in 1997-1999, 78.9% (76.6-81.2%) (National Cancer Registry 2003).

Non-genetic risk factors

Diet and energy balance

A low-fat diet might influence breast cancer risk through hormonal mechanisms but studies so far have been inconclusive. Fruit and vegetable consumption (or specific fruits or vegetables) may be associated with reduced breast cancer risk, but again pooled analyses of large studies shows no strong relationship (Hunter, Spiegelman et al. 1996; Smith-Warner, Spiegelman et al. 2001). Some studies have shown an inverse association between dietary beta-carotene intake and breast cancer risk (Zhang, Hunter et al. 1999a), and foods containing folate (Zhang, Hunter et al. 1999b), beta-carotene, and vitamins A and C may also reverse the increased risk associated with alcohol use (see below). However, intervention studies with these vitamins have shown no significant effect (Bohlke, Spiegelman et al. 1999; Lee, Cook et al. 1999).

A protective effect of exercise early in life has been suggested (Lagerros, Hsieh et al. 2004) although there are many potential confounders. Some observational studies have suggested an increased risk of breast cancer in women with high levels of occupational activity (Moradi, Adami et al. 1999), although not at all age groups. The evidence for a protective effect of non-occupational physical activity is less strong (Margolis, Mucci et al. 2005).

Obesity is associated with increased breast cancer risk, especially among postmenopausal women who do not use hormone replacement therapy (Morimoto, White et al. 2002). Increased breast cancer risk is associated with higher weight, body mass

index (BMI) (Petrelli, Calle et al. 2002), maximum BMI, adult and postmenopausal weight change, and waist and hip circumference (Morimoto, White et al. 2002).

Rapid growth during childhood and greater adult height (or maximum height reached at an earlier age) have been associated with increased risk of breast cancer, particularly post-menopausally (Li et al. 2000, van den Brandt 2000).

Alcohol Consumption

Many studies have shown an increased risk of breast cancer associated with alcohol consumption (Hamajima, Hirose et al. 2002). The relative risk of breast cancer increases by about 7% for each 10 g (1 drink) per day. This effect is independent of race, education, family history, age of menarche, height, weight, BMI, breastfeeding, oral contraceptive use, menopausal hormone use, and type and age of menopause.

Hormonal and reproductive factors

Events associated with hormonal changes have been found to influence breast cancer risk. Childbirth brings about a long-term reduction in risk, dependent on age (Pike, Krailo et al. 1983; Kampert, Whittemore et al. 1988; Lambe, Hsieh et al. 1994). Age at menarche (first menstrual period) has been linked to breast cancer risk; women who experienced menarche at 11 years or younger have about a 20% greater chance of developing breast cancer than women who experienced menarche at 14 years or older (Brinton, Schairer et al. 1988). However, these associations between age at first birth, menarche, and menopause and the development of breast cancer may not hold in women with breast cancer in a first-degree relative (Colditz, Rosner et al. 1996).

Breastfeeding is also associated with a decreased risk of breast cancer (Furberg, Newman et al. 1999). Endogenous oestrogen may be reduced by lower body weight (Prentice, Thompson et al. 1990), a low-fat diet in postmenopausal women, and moderate exercise in adolescent girls (Bernstein, Ross et al. 1987) but it is not clear if these factors decrease breast cancer risk.

Post-menopausal hormone replacement therapy is associated with an increased risk of breast cancer (Collaborative Group on Hormonal Factors in Breast Cancer 1997; Chlebowski, Hendrix et al. 2003). The evidence concerning the association between oestrogen-only therapy and breast cancer incidence is mixed.

Other risk factors

Exposure of the breast to ionizing radiation is associated with an increased risk of developing breast cancer, especially when the exposure occurs at a young age (John and Kelsey 1993). An estimate of the risk of breast cancer associated with medical radiology puts the figure at less than 1% of the total (Evans, Wennberg et al. 1986). However, women treated for Hodgkin lymphoma by age 16 may have a risk of up to 35% of developing breast cancer by age 40 (Bhatia, Robison et al. 1996; Sankila, Garwicz et al. 1996).

Trends

Between 1950 and 2002, the annual number of female breast cancer deaths rose from to 312 to 604, corresponding to an average increase, over the whole period, of 1.6% per year (Figure 11.1). All of this increase took place before 1987. Crude mortality rates increased by 0.9% annually (Figure 11.2). Age-standardised rates (Figures 11.3, 11.4), cumulative risk of dying before age 65 (Figure 11.5) and years of potential life lost (Figure 11.6) all showed similar patterns of small increases (0.4% to 0.7% annually). Both the age-standardised rate and cumulative risk seem to have decreased in recent years, with trends since 1992 indicating a significant annual decrease in the overall age-standardised rate (Figure 11.12).

Figure 11.1. Number of deaths per year, 1950-2002

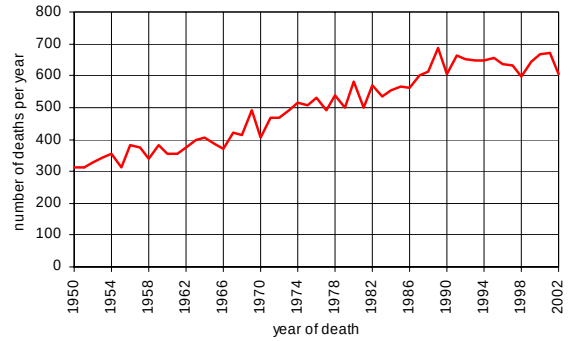


Figure 11.2. Crude mortality rate, 1950-2002

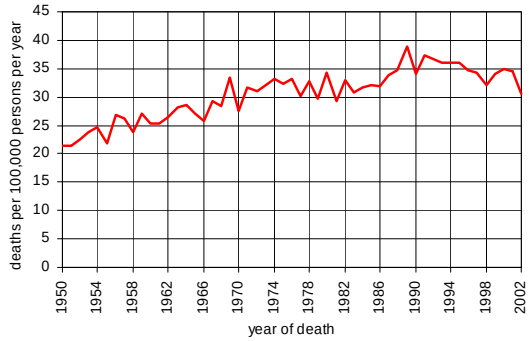


Figure 11.3. World age-standardised mortality rate, all ages, 1950-2002

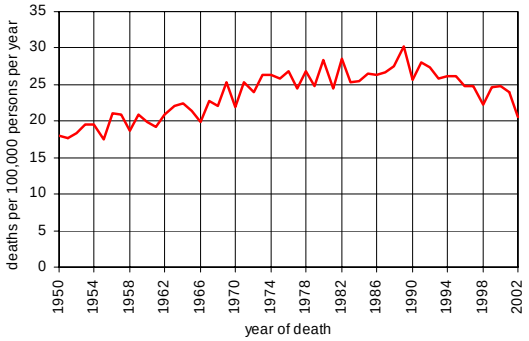


Figure 11.4. World age-standardised mortality rate, 0-64 years, 1950-2002

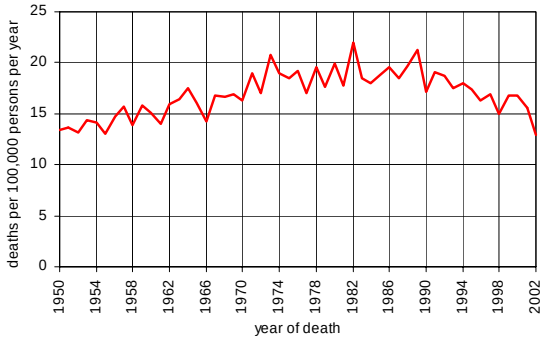


Figure 11.5. Cumulative risk of dying of cancer before age 65, 1950-2002

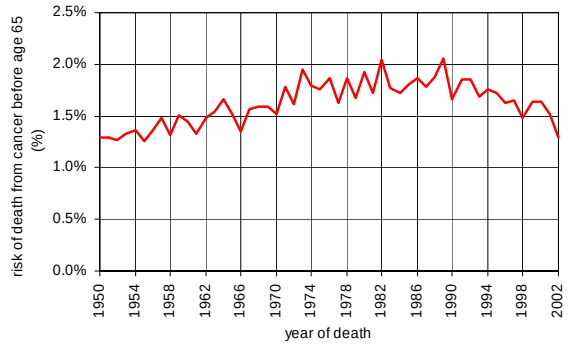
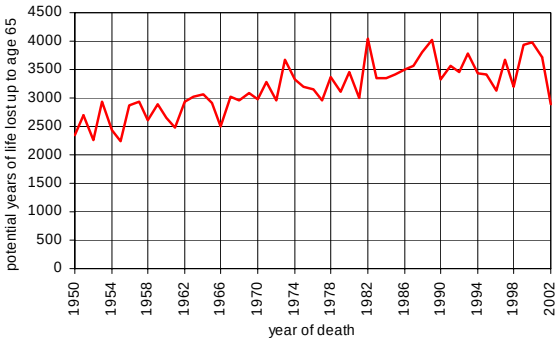


Figure 11.6. Years of potential life lost up to age 65, 1950-2002



Joinpoint regression analysis

Table 11.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

all ages		*0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*
1950		1950	
	1.1% (0.9%, 1.3%)		1.1% (0.9%, 1.4%)
1989 (1984, 1991)		1986 (1979, 1990)	
↓	-1.9% (-2.6%, -1.1%)		-1.9% (-2.6%, -1.2%)
2002		2002	

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate showed an initial increase in rate of 1.1% per annum from 1950 to 1989 (Table 11.2, Figure 11.7), followed by a decrease of 1.9% annually up to the present. The trends were almost identical for women under 65 (Figure 11.8), although the fall in mortality in this age group may have begun a little earlier.

Figure 11.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

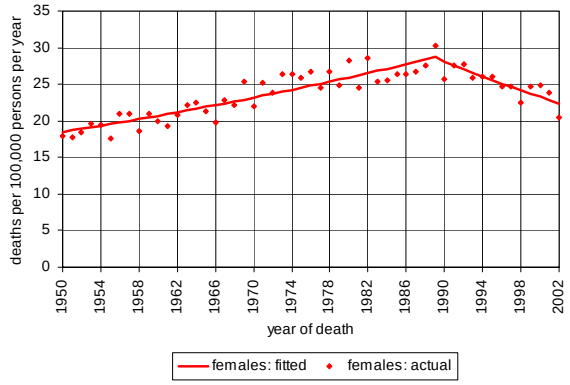
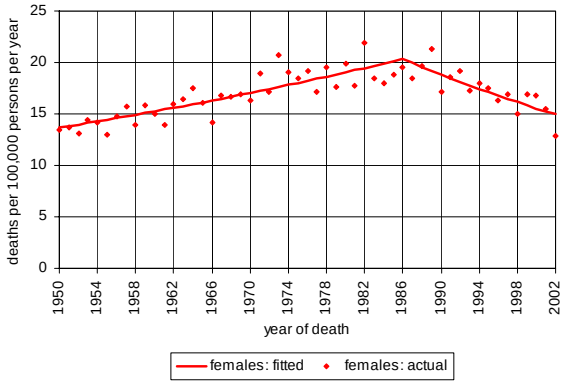


Figure 11.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

Breast cancer mortality increased for all age groups up to 1968-72 (Figure 11.9). For women aged under 45 mortality decreased from 1968-72 while for women aged 45 to 54 the decrease began five years later. For women over 54, a decrease in mortality has occurred only since 1993-1997. While age at diagnosis affected the mortality rate, mortality did not appear to be otherwise related to year of birth (Figure 11.10).

Figure 11.9. Age-specific mortality by period of death, 1953-2002

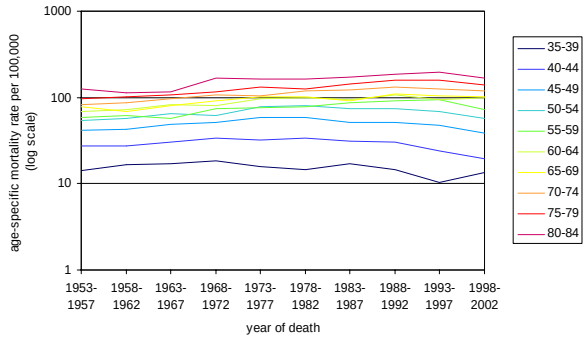
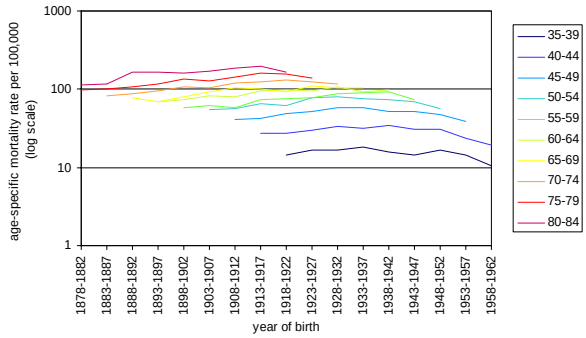


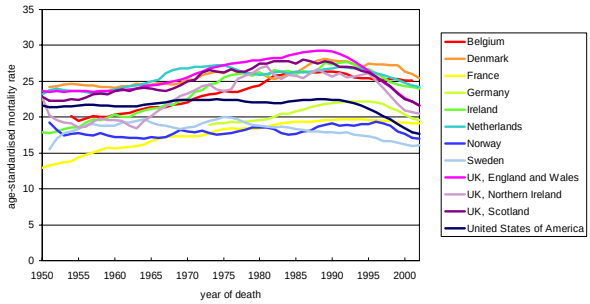
Figure 11.10. Age-specific mortality by birth cohort, 1953-2002



International trends

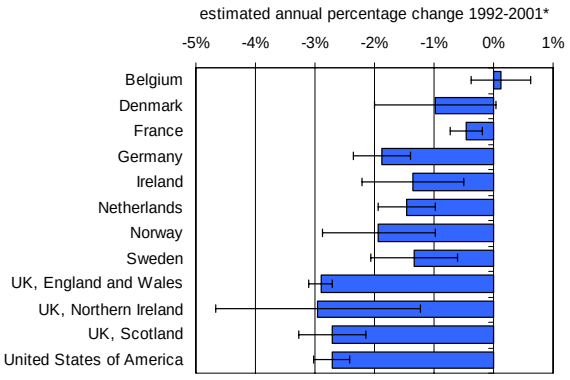
Many countries experienced an increase in age-standardised breast cancer mortality in the 1950s and 1960s, with the most rapid increases in the UK, Ireland and France, and much smaller, or no, increase in the Scandinavian countries and the US (Figure 11.11). In more recent years, and particularly since 1990, there has been a fall in breast cancer mortality in all countries shown, with the exception of France (Figure 11.12). This fall has been largest in the UK, US and Ireland, but despite the fall in mortality in Ireland, the relative position of Ireland with regard to the countries studied has gone from sixth to third highest.

Figure 11.11. Rolling 5-year average World age standardized mortality rates in Europe and USA, all ages, 1950 to 2002



Recent estimates of change (Figure 11.12) indicate significant falls in age-standardised mortality since 1992 for women in all countries shown, with the exception of Belgium. The largest falls have been in the UK.

Figure 11.12. Annual percentage change in mortality rate in Europe and USA, 1992-2001*



** or nearest available data period*

Predictions for the period 2005-2015

Female breast cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) are predicted to fall from 23.27 in 1998-2002 to 18.43 (95% prediction interval 15.95, 20.91) in 2015 (Figure 11.13, Table 11.4). The number of deaths, however, is predicted to increase, from 638 per year in 1998-2002 to 695 (607,784) in 2015 (Figure 11.14).

Table 11.3. Models chosen for predictions

model	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	1989-2002	84	log linear	0.0000
0-64	1986-2002	51	linear	0.0000

In women under 65 the mortality rate is predicted to fall, from 15.41 in 1998-2002 to 12.69 (10.62, 14.75) in 2015 (Figure 11.14), with an increase in the number of deaths from 296 per year in 1998-2002 to 335 (280, 389) in 2015 (Figure 11.16).

Table 11.4. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
all ages				
WASMR (95% PI)	23.27	21.89 (19.71, 24.07)	20.07 (17.76, 22.39)	18.43 (15.95, 20.91)
No. of deaths (95% PI)	638	649 (588, 710)	669 (596, 741)	695 (607, 784)
0-64 years				
WASMR (95% PI)	15.41	14.88 (12.95, 16.81)	13.73 (11.75, 15.71)	12.69 (10.62, 14.75)
No. of deaths (95% PI)	296	316 (275, 357)	332 (284, 379)	335 (280, 389)

The numbers of deaths presented in Table 11.4 and in Figure 11.16 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 11.5, which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would result in 257 additional deaths per year in women (a 40% increase over the 1998-2002 average) by 2015, compared with only 57 extra deaths if current trends continue.

Table 11.5. Predictions of number of deaths at all ages based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	1998-2002	*2005*	*2010*	*2015*
No. of deaths (95% PI)	637	705 (648, 763)	793 (731, 855)	895 (829, 962)

Figure 11.13. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

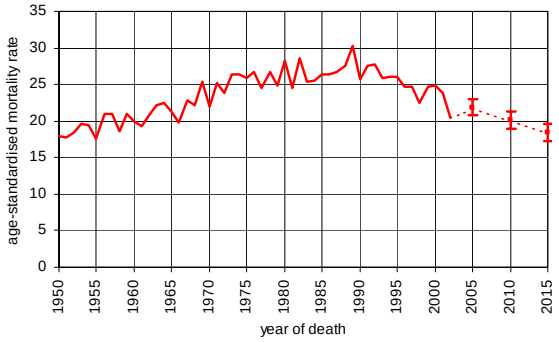


Figure 11.14. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

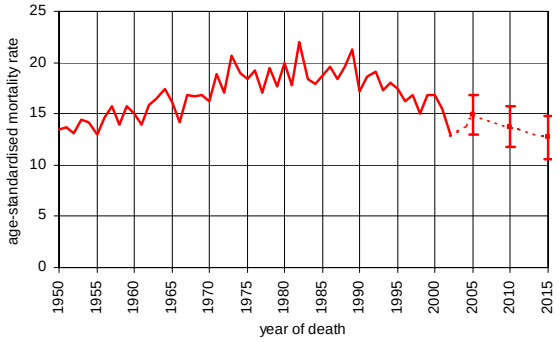


Figure 11.15. Actual and predicted number of deaths, all ages, 1950-2015

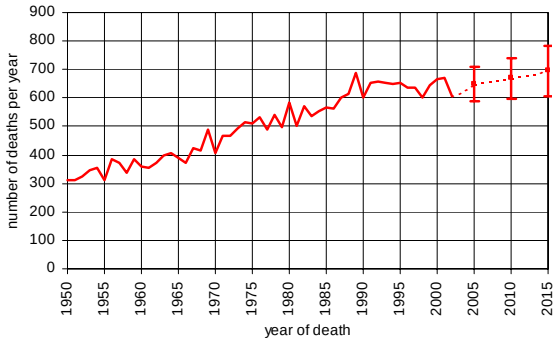
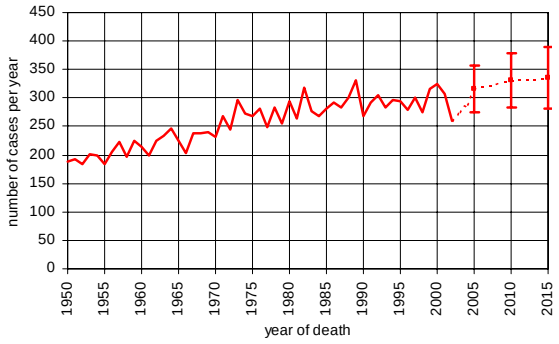


Figure 11.16. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

The number of deaths from female breast cancer increased steadily from 1950 to about 1989, but since then has remained fairly steady at around 640 per year. The crude and age-standardised mortality rates seem to have levelled off earlier, in about the mid 1970s, and show a definite decline from about 1990. The picture is almost identical for women under 65.

Joinpoint analysis does not suggest any change in the overall rate of increase between 1950 and 1989, which averaged 1.1% per annum. The rate of increase was the same for women under 65 but with an earlier inflection point, at 1986. For women of all ages, and for those under 65, mortality has fallen by 1.9% per year since then.

International experience has been similar to that in Ireland, with a long-term increase in all countries, followed by a more recent decrease. The decrease began in Sweden in the 1970s, and in most other countries in the 1980s or early 1990s.The rate of decrease has been greatest in the past 10 years in Sweden, the USA and the UK.

Predictions

The death rate from female breast cancer is predicted to fall by 21% for all women, and by 18% for women under 65, between approximately 2000 and 2015. In the same period, the number of deaths is predicted to increase, from 638 a year to 695 (a 9% increase) in women of all ages, and from 296 to 335 (a 13% increase) in women under 65. Successful implementation of population-based screening (http://www.breastcheck.ie) may further reduce future observed rates below predicted rates, but it should be noted that, as at the time of writing, national screening is not yet in place.

Conclusions

The historical increase in breast cancer which has been seen throughout the developed world has been attributed to changes in reproductive patterns, diet, body weight and oral contraceptive use (Veronesi et al, 2005; Key et al. 2004; International Agency for Research on Cancer 2002b), and it seems likely that all of these have played a part. As incidence seems to be rising steadily, improvements in survival must be largely responsible for the recent fall in mortality. Explanations for this recent increase in survival have been controversial, with roles being claimed for screening and better treatment, although evidence to date suggests that treatment improvements have been more important (Blanks et al. 2000, Botha et al. 2003).

While it is true that the greatest falls in mortality have occurred where breast screening is most active, whether population-based as in Sweden and the UK, or opportunistic, as in the US (International Agency for Research on Cancer 2002a) falls in mortality have pre-dated, or occurred in the absence of, widespread screening (Botha et al. 2003). The introduction of tamoxifen, greater use of chemotherapy (where appropriate) and a general improvement in the quality of care of breast cancer patients, have also been suggested as explanations. Breast screening was not widely available in Ireland in the late 1980s, when the decline in mortality was first seen, and even now (2000-2005) population-based screening is available to only about half the women in the target age group. Data from the National Cancer Registry show a continuing increase in breast cancer incidence (National Cancer Registry 2005) but improvement in survival (National Cancer Registry 2003) since 1994. The reasons for this improvement in survival are unclear, but are likely to include more effective treatment and, possibly, detection of more cancers at a treatable stage. As breast cancer incidence is continuing to increase, it is clear that more effort needs to be expended on identifying and changing key modifiable risk factors in the Irish population.

Chapter 12. Cancer of cervix uteri (ICD-9 180)

Epidemiology

ICD-9 has three separate categories for cancers of the uterus—cancer of the cervix uteri, cancer of corpus uteri and cancer of uterus, not otherwise specified. In general, cancer of the cervix and corpus can be readily distinguished, and "cancer of uterus, not otherwise specified" is now rarely given as a cause of death (see page 8). This was not true, however, in the 1950s, when cancer of the cervix was relatively rare, and time trends for the earlier periods need to be interpreted with caution. Methods for "reallocation" of non-specific and misclassified uterine deaths have been discussed in detail by Loos et al. (2004), but we have restricted detailed analysis here to deaths coded to cancer of the cervix uteri only, with the proviso that only the more recent trends may be meaningful. For simplicity, cancer of cervix uteri will be referred to in the text as "cancer of the cervix", or "cervical cancer", as is normal usage.

The majority of cervical cancers (80%) are squamous cell carcinomas, but another 15% are adenocarcinoma (National Cancer Registry, unpublished data). Recent incidence data for Ireland (1994-2001) does not suggest any significant change in the proportion of adenocarcinoma, although a number of countries have reported recent increases in adenocarcinoma (Bray et al, 2005). Mortality data from Ireland does not allow us to distinguish between the morphological types.

Cervical cancer was the twelfth most common cancer and the thirteenth most common cause of cancer death in women in the period 1994-2001, with an annual average of 180 cases and 73 deaths during this period. Its significance, for a relatively uncommon cancer, lies in the fact that, with effective screening, detects almost all cervical cancer in the premalignant phase, when treatment will prevent invasive cancer.

Cervical cancer tends to affect younger women disproportionately. Only 13% of cases and 26% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined.

Table 12.1. Age distribution of cervical cancer deaths and cases

age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*
<30	2%	4%
30-39	11%	24%
40-49	24%	31%
50-59	18%	16%
60-69	19%	11%
70-79	17%	9%
80+	9%	4%

Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 63%. while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 58% (Berrino et al. 1995). Five-year survival for patients diagnosed in Ireland in 1994-1996 was 58.6% (53.3-63.8%); in 1997-1999, 66.7% (60.8-72.6%) (National Cancer Registry 2003).

Non-genetic risk factors

Infection

It is now widely accepted that infection with "high-risk" types of human papilloma virus (HPV) is the most important risk factor for cervical carcinoma, although other sexually transmitted factors, including herpes simplex virus 2, may play a role (Schiffman, Bauer et al. 1993). HPV types 16 and 18 are most often associated with invasive disease (Clifford, Smith et al. 2003).

Diet and energy balance

Some studies show an association between intake of micronutrients and risk of cervical cancer, but the results are not completely controlled for other risk factors (Key 1994).

Cigarette smoking

Cigarette smoking or exposure to environmental smoke is also associated with increased risk, among HPV-infected women (Brock, MacLennan et al. 1989; Ho, Kadish et al. 1998).

Hormonal and reproductive factors

High parity has long been recognized as a risk factor for cervical cancer. Studies of cervical cancer in women who were positive for HPV showed the odds ratio for women with 7 or more full-term pregnancies to be 3.8 (95% CI 2.7- 5.5) compared with nulliparous women and 2.3 compared with women with 1 or 2 full-term pregnancies (Munoz, Franceschi et al. 2002).

Long-term use of oral contraceptives (OC) is associated with cervical cancer, but this may be confounded with HPV infection (Moreno, Bosch et al. 2002). HPV positive women using OCs for more than 5 years have an increased risk of cervical cancer.

Trends

Between 1950 and 2002, the annual number of deaths from cancer of the uterine cervix rose from 26 to 76 (Figure 12.1). Most of this increase took place in a relatively short period, between 1960 and 1970 and, as described above, may have been partly due to changes in certification and/or coding practices. Crude mortality rates increased by 0.6% annually (Figure 12.2), while age-standardised rates (Figures 12.3 and 12.4) increased by 0.5%, cumulative risk of dying before age 65 by 0.4% (Figure 12.5) and years of potential life lost by 1.5% annually (Figure 12.6). Although these long-term trends are not strictly reliable, trends since 1976 show broadly the same patterns of increase (see also Joinpoint results below), though with a more marked increase in years of potential life lost (by 3.2% annually) in part reflecting a decrease in average age at death. Trends since 1992 indicate a non-significant decrease in total age-standardised mortality rates (Figure 12.12).

Figure 12.1. Number of deaths per year, 1950-2002

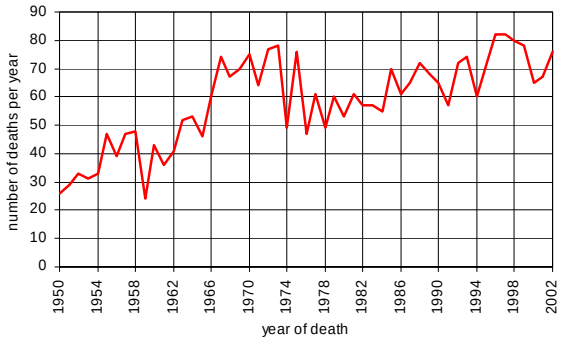


Figure 12.2. Crude mortality rate, 1950-2002

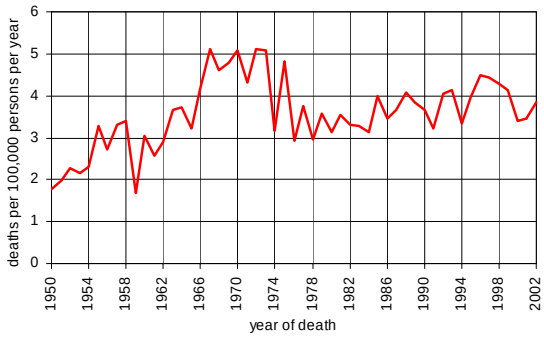


Figure 12.3. World age-standardised mortality rate, all ages, 1950-2002

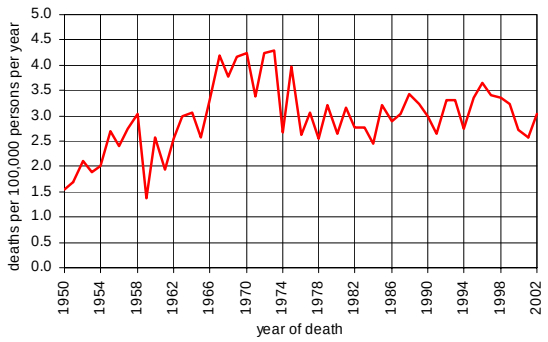


Figure 12.4. World age-standardised mortality rate, 0-64 years, 1950-2002

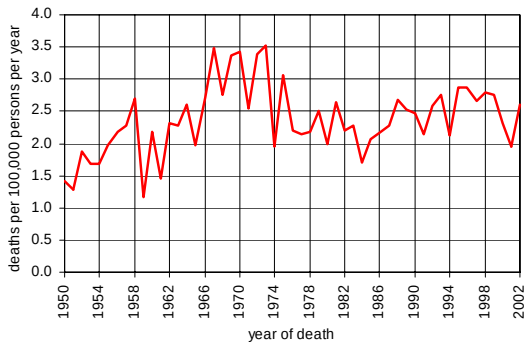


Figure 12.5. Cumulative risk of dying of cancer before age 65, 1950-2002

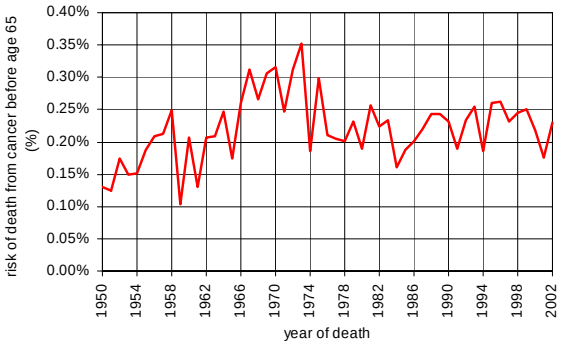
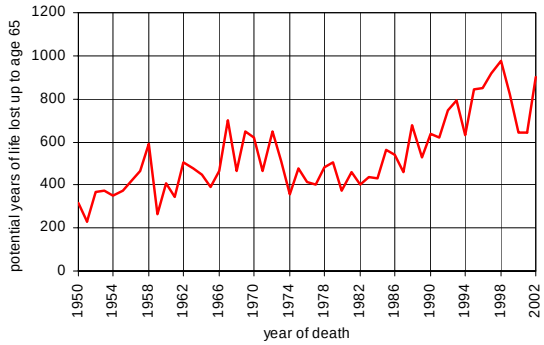


Figure 12.6. Years of potential life lost up to age 65, 1950-2002



Joinpoint regression analysis

Table 12.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

all ages		*0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*
1950		1950	
↓	4.1% (2.9%, 5.2%)	↓	3.6% (2.3%, 4.9%)
1972 (1967, 1975)		1972 (1966, 1975)	
↓	-9.2% (-24.3%, 9.0%)	↓	-8.2% (-20.4%, 5.9%)
1976 (1973, 1986)		1977 (1973, 1987)	
↓	0.3% (-0.4%, 1.1%)	↓	0.7% (-0.2%, 1.6%)
2002		2002	

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate showed a complex pattern, with an increase in rate, of 4.1% per annum, from 1950 to 1972 (Table 12.2, Figure 12.7), followed by a very rapid (but not statistically significant) fall of 9.1% per annum between 1972 and 1976. Since 1976, there has been no significant upward or downward trend. The pattern for women under 65 was almost identical (Figure 12.8).

Figure 12.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

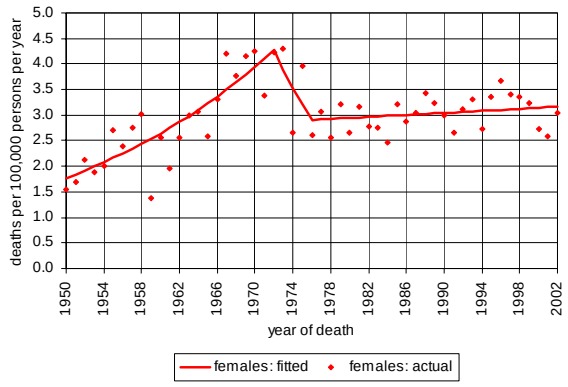
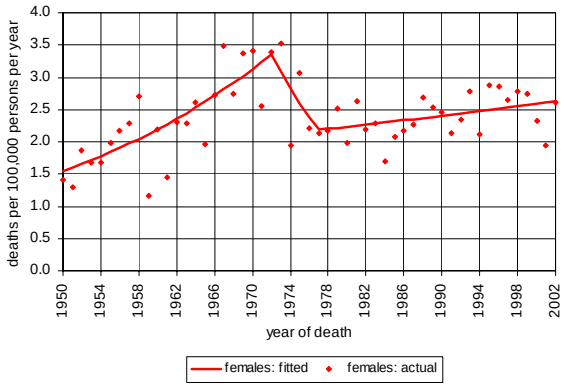


Figure 12.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age period cohort trends

As discussed above, mortality patterns for cervical cancer before 1978 are not very informative. The pattern of change in mortality has been quite different for women over and under 55 years of age. For women under 55, the overall trend since 1978 has been upward, although with a fall in mortality for those aged 35-44 years in 1998-2002 (Figure 12.9). For women of 55 and over, the overall trend has been downwards since 1983-1987. There is no evidence that year of birth had any effect on mortality, independent of age or period of death (Figure 12.10).

Figure 12.9. Age-specific mortality by period of death, 1978-2002

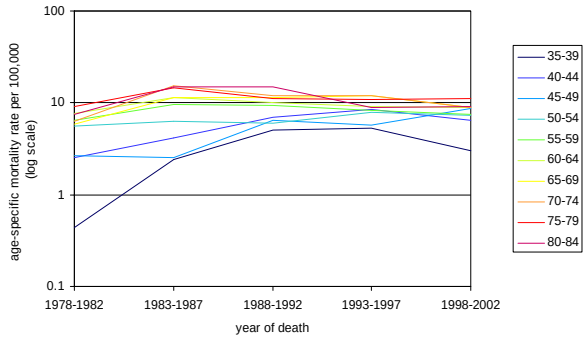
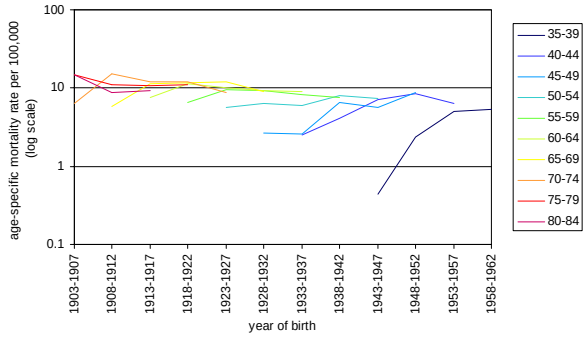


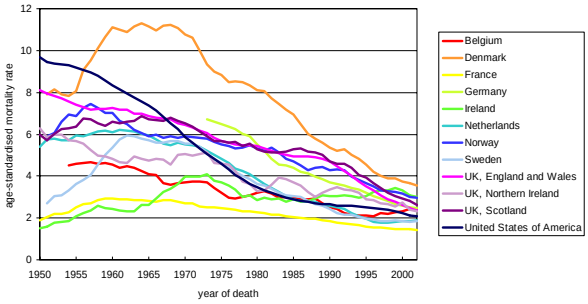
Figure 12.10. Age-specific mortality by birth cohort, 1978-2002



International trends

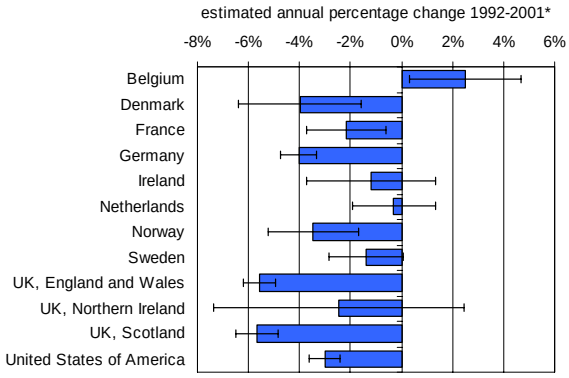
Mortality from cervical cancer has been falling in almost all of the countries studied since the 1960s, the exceptions being Denmark, in which mortality did not begin to fall until about 1970, and Ireland, in which there has been no significant fall (Figures 12.11). As a result, mortality from cervical cancer in Ireland, which was the lowest of all the countries studied in the 1950s and most of the 1960s, is now second only to that in Denmark.

Figure 12.11. Rolling 5-year average World age standardized mortality rates in Europe and USA, all ages, 1950 to 2002



Recent estimates of change (Figure 12.12) indicate significant falls in age-standardised mortality since 1992 in Denmark, France, Germany, Norway, England/Wales, Scotland and the USA, with a significant increase in mortality in Belgium.

Figure 12.12. Annual percentage change in mortality rate in Europe and USA, 1992-2001*



** or nearest available data period*

Table 12.3. Models chosen for predictions

	prediction baseline	*observations*	*model type*	*p (trend)*
all ages	1979-2002	144	linear	0.8674
0-64	1979-2002	72	log linear	0.5903

Cervical cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) are predicted to increase from 2.99 in 1998-2002 to 3.77 (95% prediction interval 2.81, 4.72) in 2015 (Table 12.4, Figure 12.13). The number of deaths is also predicted to rise, from 73 per year in 1998-2002 to 109 (82, 136) in 2015 (Figure 12.15). In women under 65 the mortality rate is also predicted to rise, from 2.48 in 1998-2002 to 3.36 (2.40, 4.32) in 2015 (Figure 12.14), with an accompanying increase in the number of deaths, from 48 per year in 1998-2002 to 76 (54, 98) in 2015 (Figure 12.16).

Table 12.4. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
all ages				
WASMR (95% PI)	2.99	3.52 (2.66, 4.38)	3.64 (2.75, 4.54)	3.77 (2.81, 4.72)
No. of deaths (95% PI)	73	86 (66, 107)	97 (74, 121)	109(82, 136)
0-64 years				
WASMR (95% PI)	2.48	3.02 (2.16, 3.88)	3.19 (2.29, 4.09)	3.36 (2.40, 4.32)
No. of deaths (95% PI)	48	59 (42, 76)	68 (49, 87)	76 (54, 98)

The numbers of deaths presented in Table 12.4 and in Figures 12.15 and 12.16 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 12.5 which shows the effect of population change in the absence of any trend in rates.

Of the 36 additional deaths projected in 2015 compared to 1998-2002, 29 (80%) would be expected as a result of demographic change alone.

Table 12.5. Predictions of number of deaths at all ages, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	1998-2002	*2005*	*2010*	*2015*
No. of deaths (95% PI)	73	81 (62, 101)	91 (70, 112)	102 (80, 124)

Figure 12.13. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

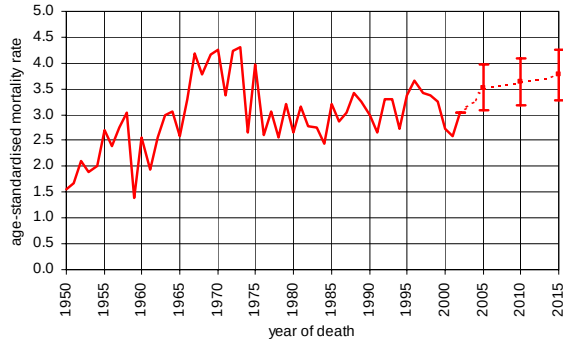


Figure 12.14. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

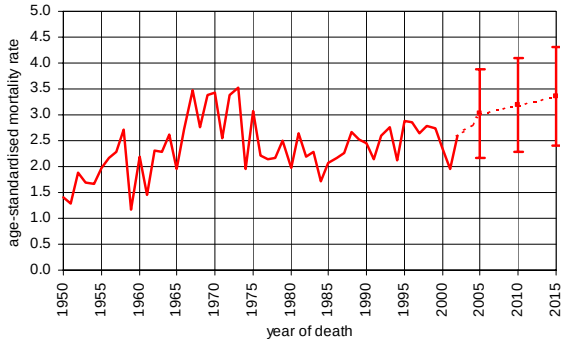


Figure 12.15. Actual and predicted number of deaths, all ages, 1950-2015

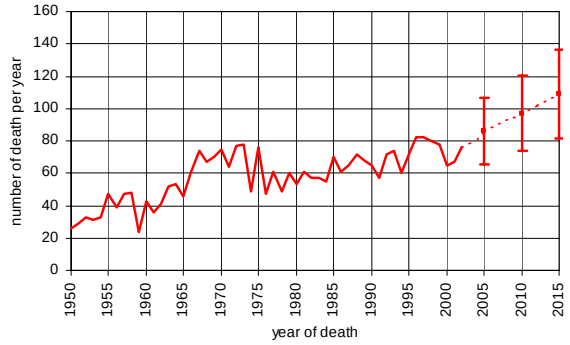
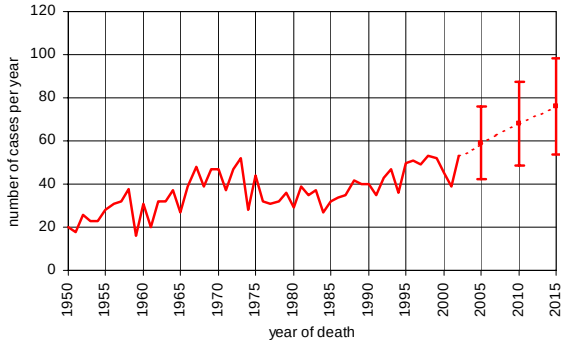


Figure 12.16. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

Unfortunately, long-term trends in cervical cancer mortality are difficult to interpret, as practices in certification have changed dramatically before the mid 1970s. Since then, however, it is clear that the number of deaths, and to a lesser extent the age-standardised mortality rate, have been increasing, although slowly. The same has been true of women under 65, and there has been a particularly striking increase in the number of years of potential life lost, from 415 in 1976 to 978 in 1998, in part because the average age of women dying of cervical cancer fell from 61 to 58.

Joinpoint analysis shows that there has been a 0.3% (not statistically significant) annual increase in cervical cancer mortality in women of all ages since 1976, and a 0.7% annual increase (again not statistically significant) in women under 65.

Age-period-cohort analysis shows a rapid increase in mortality for the younger age groups, but the short period for which reliable data are available makes interpretation difficult.

Most western countries for which trends are summarized here have had a fall in cervical cancer mortality in the past 20 years. The decrease has been greatest in Denmark and the UK and least in the US, which has had the lowest mortality over most of the past 50 years. Although it has been noted that practices in certification of cancer of the uterus may have affected mortality rates in Ireland, it is unlikely that such a widespread, consistent and ongoing fall in mortality across so many countries could be an artefact.

Predictions

Although the Joinpoint analysis suggested that the current trends were not statistically significant, age-period modelling, projecting from those trends predicts an overall increase in the age-standardised mortality rate of 26% between approximately 2000 and 2015, and of 35% in women under 65. However, it should be noted that the 95% prediction intervals for the 2015 period include the rates for 1998-2002, and so the predictions include the possibility that there will be no increase. The number of deaths is predicted to increase by 49%, from 73 to 109 over the same period, and the number of deaths in women under 65 by 58%, from 48 to 76, which is significantly above the 1998-2002 average. Of the 36 additional deaths in women of all ages projected for 2015 compared to 1998-2002, 29 (80%) would be expected as a result of demographic change alone.

As for breast cancer, successful implementation of population-based screening may reduce future observed rates below predicted rates, but it should be noted that, as of the time of writing, national screening is not yet in place.

Conclusions

It is generally accepted that the fall in cervical cancer mortality that has been seen in Europe and the USA is largely attributable to screening. At present, population-based screening for cervical cancer is available to only a small proportion of Irish women in the target age groups (Irish Cervical Screening Programme 2006), and this has been suggested as the major factor in the differences in mortality trends between Ireland and its neighbours (Comber and Gavin 2004).

Chapter 13. Cancer of corpus uteri (ICD-9 182)

Epidemiology

ICD-9 has three separate categories for cancer of the uterus—cancer of the cervix uteri (code 180), cancer of corpus uteri or body of uterus (182) and cancer of uterus, part unspecified (179). In general, cancer of the cervix and corpus can be readily distinguished, and "cancer of uterus, part unspecified" is now rarely given as a cause of death. This was not true, however, in the 1950s, when cancer of the cervix was relatively rare, and time trends for the earlier periods need to be interpreted with caution (See Chapter 12). Methods for "reallocation" of non-specific and misclassified uterine deaths have been discussed in detail by Loos et al. (2004), but we have restricted detailed analysis here to deaths coded to cancer of the corpus uteri only, with the proviso that only the more recent trends are likely to be meaningful.

Cancer of the corpus uteri (referred to as "uterine cancer" hereafter) was the seventh commonest cancer and the seventeenth commonest cause of cancer death in women in the period 1994-2001, with an annual average of 223 cases and 48 deaths during this period.

33% of cases and 60% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined (Table 13.1).

Table 13.1. Age distribution of uterine cancer deaths and cases

age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*
<30	0%	0%
30-39	1%	2%
40-49	4%	9%
50-59	10%	27%
60-69	25%	29%
70-79	38%	23%
80+	22%	10%

Survival from uterine cancer is relatively good. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 78% while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 70% (Berrino et al. 1995).

Five-year relative survival for patients diagnosed in Ireland in 1994-1996 was 74.6% (95% CI 69.9-79.4%); in 1997-1999, 80.6% (74.7-86.6%) (National Cancer Registry 2003).

Non-genetic risk factors

Diet and energy balance

A diet low in saturated fats and high in fruit and vegetable intake (Levi, Franceschi et al. 1993; Terry, Vainio et al. 2002) has been suggested as being associated with reduced risk of developing uterine cancer, but energy intake is not consistently related to risk (Levi, Franceschi et al. 1993; Jain, Howe et al. 2000; McCann, Freudenheim et al. 2000).

Elevated body mass index (BMI) (Jain, Howe et al. 2000) and obesity (Kaaks, Lukanova et al. 2002) have been associated in many studies with increased risk of uterine cancer. Analysis has suggested that 39% of uterine cancers in Europe are attributable to obesity (Bergstrom, Pisani et al. 2001). Several studies have observed a stronger association between uterine

cancer and obesity close to the time of diagnosis compared to obesity earlier in life (Olson, Trevisan et al. 1995; Weiderpass, Persson et al. 2000). Several studies have demonstrated a weak to moderate inverse relationship to physical activity; however, it is difficult to make comparisons between studies due to the varying methods of assessing physical activity levels (Goodman, Hankin et al. 1997; Moradi, Nyren et al. 1998). Obesity, diet and physical activity are closely inter-related, and confounding in these studies cannot be completely ruled out.

Hormonal and reproductive factors

A number of studies have shown a decrease in risk with increasing duration of combined oral contraceptive use (Vessey and Painter 1995; Weiderpass, Adami et al. 1999; Deligeoroglou, Michailidis et al. 2003).

Tamoxifen is widely used for the treatment and prevention of breast cancer. An association between tamoxifen use and increased risk of uterine cancer has been confirmed from randomized clinical trials using tamoxifen for breast cancer treatment and prevention (Rutqvist, Johansson et al. 1995; Cuzick 2000; Swerdlow and Jones 2005).

A number of studies have indicated that the risk of developing uterine cancer increases with duration of use of post-menopausal oestrogen replacement therapy, and the risk may persist for more than 10 years after discontinuation (Van Gorp and Neven 2002; Newcomb and Trentham-Dietz 2003). However, combination oestrogen-progesterone replacement therapy is not associated with increased risk of uterine carcinoma (Beral, Bull et al. 2005).

Trends

Between 1953 and 2002, the annual number of deaths attributed to cancer of the corpus uteri rose from 8 to 56, an overall increase of 4.3% per year (Figure 13.1). Crude mortality rates increased by 3.6% annually (Figure 13.2) and age-standardised rates by 2.8% (Figure 13.3). The measures for younger women increased less rapidly—age-standardised rates by 1.5% annually (Figure 13.4), cumulative risk of dying before age 65 (Figure 13.5) by 1.6% and potential years of life lost (Figure 13.6) by 1.7% annually. However, these long-term trends are misleading, as it is clear that changes in coding of uterine cancers over time account for much of the changes seen before 1976. Since then, age-standardised mortality rates have fallen by about 1.6% annually overall and by 3.6% annually among the under-65 population. Trends since 1992 indicate a significant annual decrease in total age-standardised mortality rates (Figure 13.12).

Figure 13.1. Number of deaths per year, 1953-2002

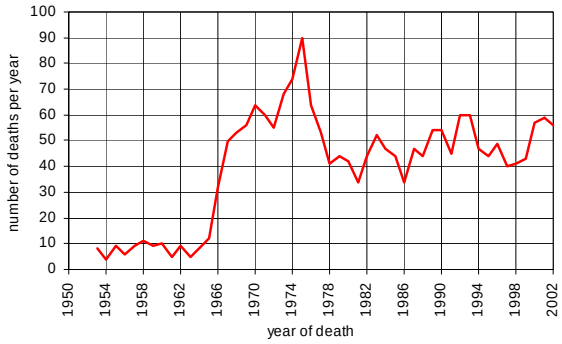


Figure 13.2. Crude mortality rate, 1953-2002

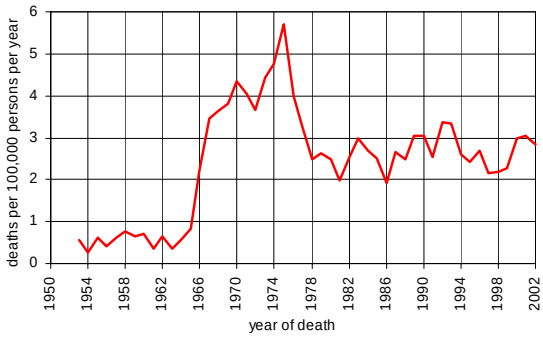


Figure 13.3. World age-standardised mortality rate, all ages, 1953-2002

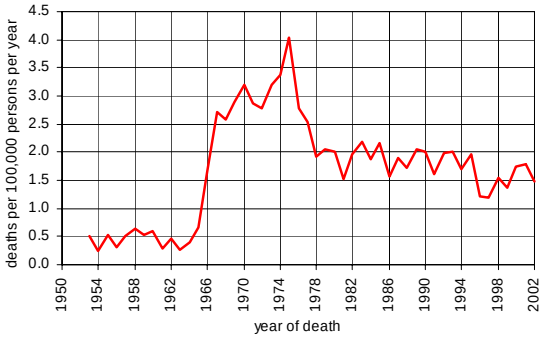


Figure 13.4. World age-standardised mortality rate, 0-64 years, 1953-2002

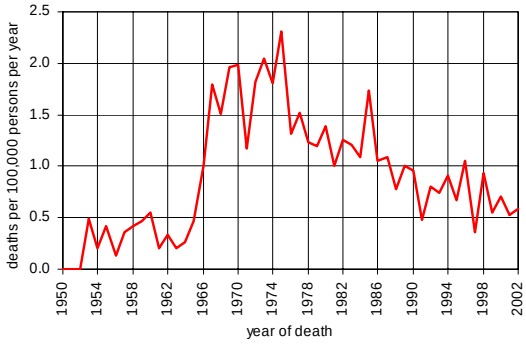


Figure 13.5. Cumulative risk of dying of cancer before age 65, 1953-2002

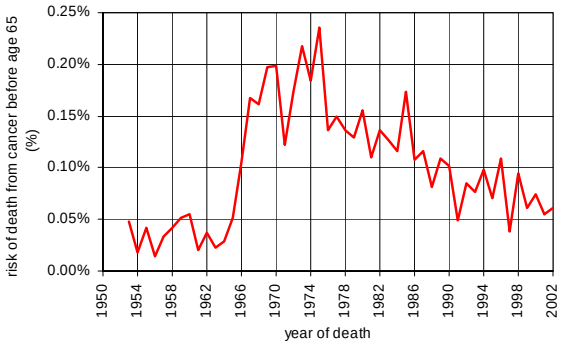
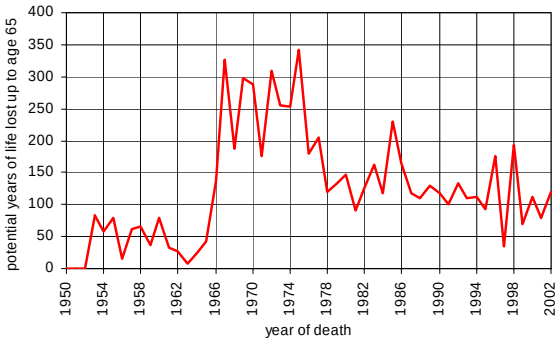


Figure 13.6. Years of potential life lost up to age 65, 1953-2002



Joinpoint regression analysis

Table 13.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1953-2002

all ages		*0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*
1953		1953	
↓	-2.2% (-10.3%, 6.6%)	↓	-3.7% -11.8%, 5.1%)
1964 (1962, 1965)		1964 (1961, 1966)	
↓	99.4% (-9.4%, 338.8%)	↓	92.7% (-23.0%, 382.2%)
1967 (1966, 1969)		1967 (1966, 1970)	
↓	-2.2% (-2.7%, -1.7%)	↓	-3.4% (-4.1%, -2.6%)
2002		2002	

95% confidence intervals for the inflection points and annual percentage change are given in brackets

As noted earlier, trends before the 1970s are unreliable, as the large changes in rate are almost certainly due to changes in death certification practice. Joinpoint analysis indicates that, since 1967, there has been an ongoing annual decrease of 2.2% in the mortality rate for women of all ages (Table 13.2, Figure 13.7) and of 3.4% for women under 65 (Figure 13.8). These trends would essentially be the same if restricted to the years 1976 onwards.

Figure 13.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1953-2002

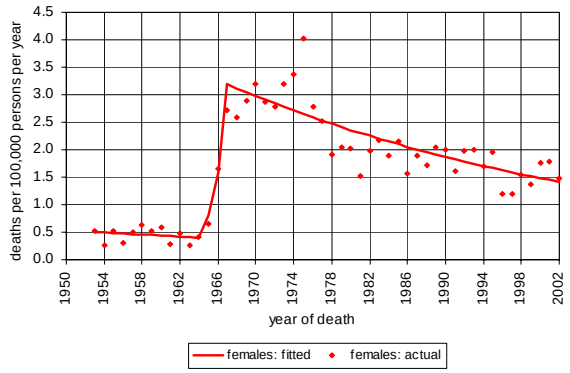
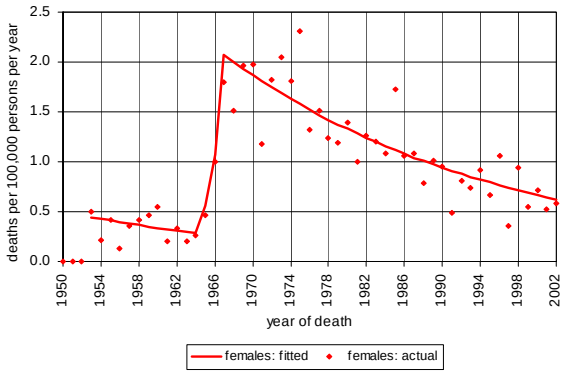


Figure 13.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1953-2002



Age-period-cohort trends

The age-period plot shows an increase in mortality since 1978-82 for women over 70, with a fall in rate, or no definite trend, in younger women (Figure 13.9). While age at diagnosis affected the mortality rate, mortality did not appear to be otherwise related to year of birth (Figure 13.10).

Figure 13.9. Age-specific mortality by period of death, 1976-2002

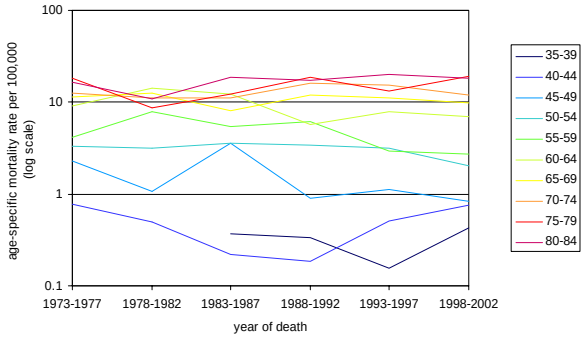
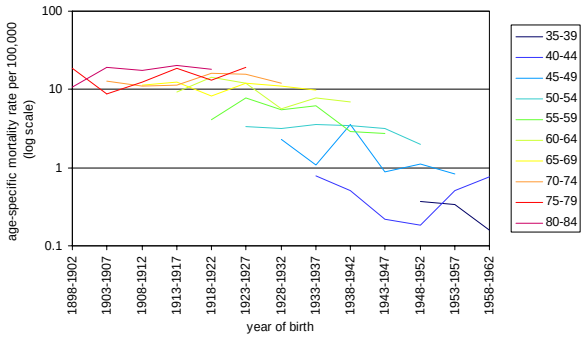


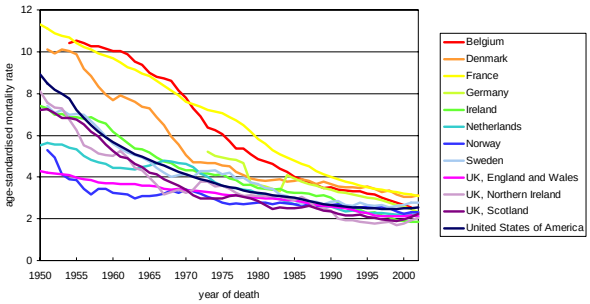
Figure 13.10. Age-specific mortality by birth cohort, 1976-2002



International trends

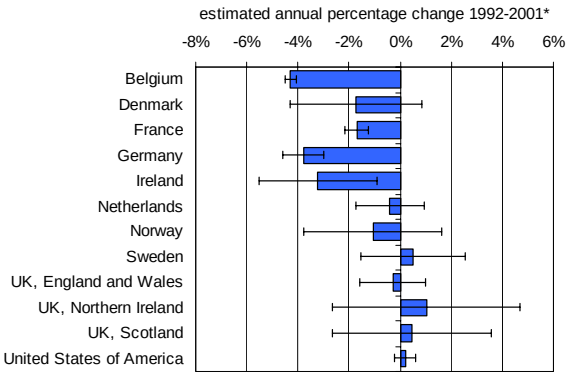
All countries studied experienced a fall in mortality from cancer of the corpus uteri# between 1950 and 2002, with a convergence on quite a narrow range of values by 2000 (Figure 13.11).

Figure 13.11. Rolling 5-year average World age standardized mortality rates in Europe and USA, all ages, 1950 to 2002



Recent estimates of change (Figures 13.12) indicate significant falls in age-standardised mortality since 1992 in Belgium, France, Germany and Ireland. No country had a significant increase in mortality.

Figure 13.12. Annual percentage change in mortality rate in Europe and USA, 1992-2001*



**or nearest available data period*

This data, from the WHO Mortality databank, includes the ICD10 categories C54 (corpus uteri), C55 (uterus not otherwise specified) and C58 (placenta) and figures are higher than for C54 alone, which is the subject of the rest of this chapter.

Table 13.3. Models chosen for predictions

	prediction baseline	*observations*	*model type*	*p (trend)*
all ages	1979-2002	144	log-linear	0.4913
0-64	1985-2002	54	log linear	0.0245

Mortality rates from cancer of the corpus uteri (all rates are World age-standardised mortality rates per 100,000 person-years) are predicted to increase from 1.59 in 1998-2002 to 1.75 (1.17, 2.34) in 2015 (Figure 13.13, Table 13.3). The number of deaths is also predicted to rise, from 51 per year in 1998-2002 to 86 (59, 113) in 2015 (Figure 13.15). In women under 65 the mortality rate is also predicted to fall, from 0.66 in 1998-2002 to 0.37 (0.02, 0.73) in 2015 (Figure 13.14), with a small decrease in the number of deaths from 12 per year in 1998-2002 to 10 (1, 18) in 2015 (Figure 13.16).

Table 13.4. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
all ages				
WASMR (95% PI)	1.59	1.66 (1.15, 2.17)	1.69 (1.16, 2.22)	1.75 (1.17, 2.34)
No. of deaths (95% PI)	51	60 (43, 78)	71 (50, 92)	86 (59, 113)
0-65 years				
WASMR (95% PI)	0.66	0.51 (0.16, 0.85)	0.43 (0.09, 0.77)	0.37 (0.02, 0.73)
No. of deaths (95% PI)	12	11 (3, 18)	10 (2, 18)	10 (1, 18)

The numbers of deaths presented in Table 13.4 and in Figures 13.19 and 13.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 13.6, which shows the effect of population change in the absence of any trend in rates.

Of the 35 additional deaths per annum projected for 2015 compared to 1998-2002, 20 (57%) are attributable to demographic change.

Table 13.5 Predictions of number of deaths, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	1998-2002	*2005*	*2010*	*2015*
No. of deaths (95% PI)	51	56 (40, 72)	62 (45, 80)	71 (52, 90)

Figure 13.13. Actual and predicted World age-standardised mortality rates, all ages, 1953-2015

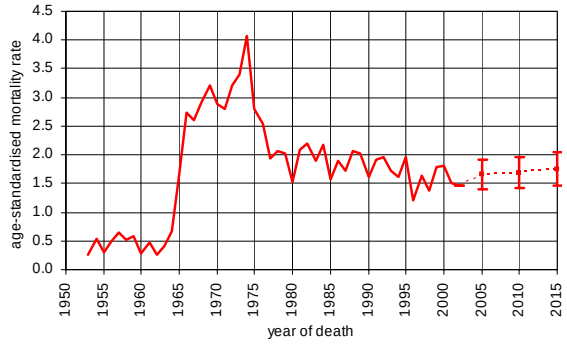


Figure 13.14. Actual and predicted World age-standardised mortality rates, 0-64 years, 1953-2015

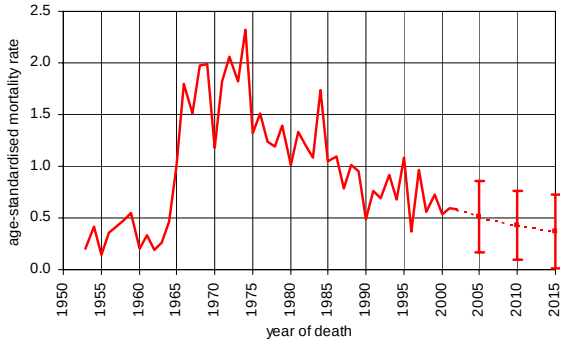


Figure 13.15. Actual and predicted number of deaths, all ages, 1953-2015

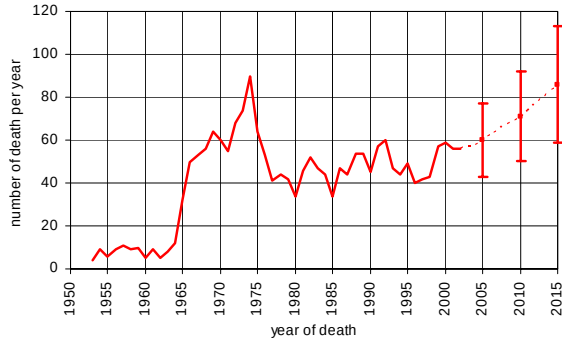
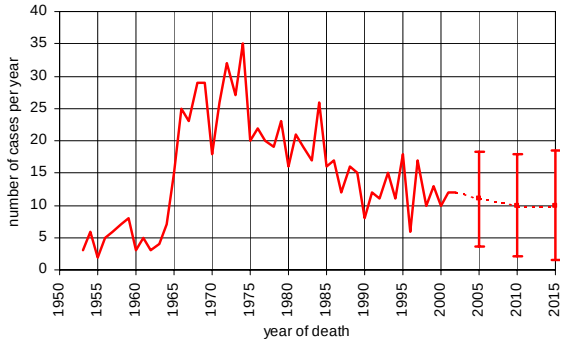


Figure 13.16. Actual and predicted number of deaths, 0-64 years, 1953-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

As noted above, changes in certification and coding make the data inconsistent across the period described here, and only trends since the mid 1970s are likely to be informative. Since 1976, the trend in rates has been downwards, especially for women under 65. International data show a fall in mortality rates in almost all countries.

Predictions

The age-standardised rate for all ages combined is predicted to fall by 13% between approximately 2000 and 2015, while the number of deaths is expected to increase by 41%. For women under 65, the age-standardised rate is also expected to fall, by 44% over the same period, with a 17% decrease in deaths.

Conclusions

Despite the uncertainties caused by coding and classification problems, recent experience in Ireland is consistent with the general downward international trend in mortality from cancer of the corpus uteri. However, recent reports of an increase in incidence in Ireland (National Cancer Registry 2005), and the known association of this cancer with obesity (International Agency for Research on Cancer 2002b) which is increasing in both men and women (SLÁN 2003) suggest that the fairly modest downward trends shown here may reverse in the future.

Chapter 14. Ovarian cancer (ICD-9 183)

Epidemiology

Ovarian cancer was the seventh most common cancer and fourth the commonest cause of cancer death in women in the period 1994-2001, with an annual average of 334 cases and 227 deaths during this period.

Cancer of the ovary affected a relatively young group of women; 34% of cases and 46% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined (Table 14.1).

Table 14.1. Age distribution of ovarian cancer deaths and cases

age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*
<30	1%	4%
30-39	2%	6%
40-49	7%	13%
50-59	19%	21%
60-69	25%	22%
70-79	28%	23%
80+	18%	11%

Survival from ovarian cancer is poor. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 38% while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 30% (Berrino et al. 1995).

Five-year relative survival for patients diagnosed in Ireland in 1994-1996 was 40.0% (95% CI 36.4-43.5%); in 1997-1999, 38.1% (33.9-42.2%) (National Cancer Registry 2003).

Non-genetic risk factors

Diet and energy balance

Obesity, and measures of obesity including high body mass index, (Engeland, Tretli et al. 2003; Schouten, Goldbohm et al. 2003) are associated with an increased incidence of ovarian cancer. The risk also appears to be greater in taller women (Rodriguez, Calle et al. 2002; Engeland, Tretli et al. 2003; Schouten, Goldbohm et al. 2003). Associations with specific dietary factors and ovarian cancer are not consistent. Studies have shown an increased risk with higher consumption of milk or of fat and decreased risk with consumption of fruit and vegetables (La Vecchia, Decarli et al. 1987; Larsson, Holmberg et al. 2004) although a recent meta-analysis found no significant link to milk or milk products (Qin, Xu et al. 2005).

Hormonal and reproductive factors

Repeated ovulation is a risk factor for ovarian cancer (Tung, Wilkens et al. 2005). The decreased risk of ovarian cancer associated with parity (Riman, Dickman et al. 2002; Vachon, Mink et al. 2002), lactation (Siskind, Green et al. 1997) and the oral contraceptive pill (Whittemore 1993; Ness, Grisso et al. 2001) suggest that preventing ovulation can protect against ovarian cancer.

Oral contraceptives have a protective effect which increases with the duration of use and persists for 10 to 15 years after discontinuation (Ness, Grisso et al. 2001). This reduced risk is present among both nulliparous and parous women.

Longer duration of breast feeding appears to reduce risk from ovarian cancer (Zhang, Xie et al. 2004)

Ovarian cancer risk is reduced among women who underwent tubal sterilization, independently of oral contraceptive use, parity, and other ovarian cancer risk factors (Miracle-McMahill, Calle et al. 1997; Narod, Sun et al. 2001). There appears to be a small decrease in risk associated with simple hysterectomy.

Postmenopausal use of hormone replacement therapy (HRT) is associated with an increased risk of developing ovarian cancer. Meta-analysis of nine studies concluded that the relative risk of ovarian carcinoma in users of HRT was 1.15 (1.05-1.27) and that use for more than 10 years was associated with the greatest risk.

The use of fertility drugs may be associated with an increased risk of ovarian cancer, but the evidence is inconclusive (Ness, Cramer et al. 2002; Ayhan, Salman et al. 2004; Rossing, Tang et al. 2004).

Other risk factors

Some studies have suggested a link between the use of perineal talc and ovarian cancer (Cramer, Liberman et al. 1999; Ness, Grisso et al. 2000; Mills, Riordan et al. 2004).

Trends

Between 1950 and 2002, the number of ovarian cancer deaths rose from 74 to 222, corresponding to an average increase, over the whole period, of 2.8% per year (Figure 14.1). This increase was relatively constant throughout the whole period. Crude mortality rates increased by 2.1% annually (Figure 14.2), while age-standardised rates increased by 1.7% (Figures 14.3). The rates for younger women increased to a lesser extent—the age-standardised rate by 1.0%, (Figure 14.4), the cumulative risk of dying before age 65 (Figure 14.5) by 1.2% and years of potential life lost (Figure 14.6) by 0.9% annually. Trends since 1992 indicate a non-significant annual decrease in total age-standardised mortality rates (Figure 14.12).

Figure 14.1. Number of deaths per year, 1950-2002

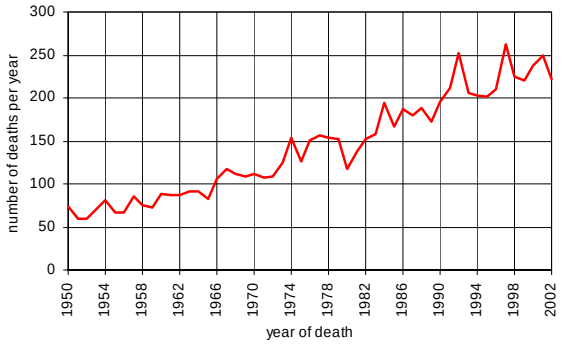


Figure 14.2. Crude mortality rate, 1950-2002

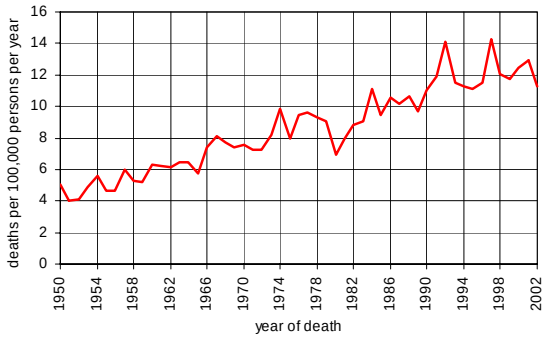


Figure 14.3. World age-standardised mortality rate, all ages, 1950-2002

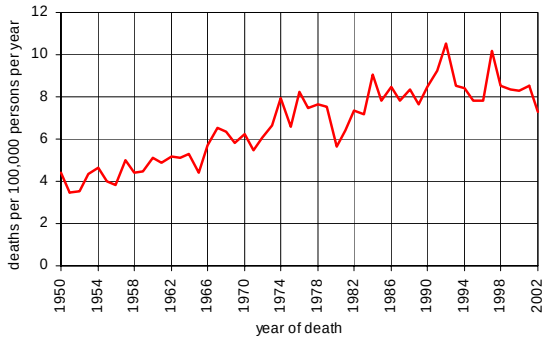


Figure 14.4. World age-standardised mortality rate, 0-64 years, 1950-2002

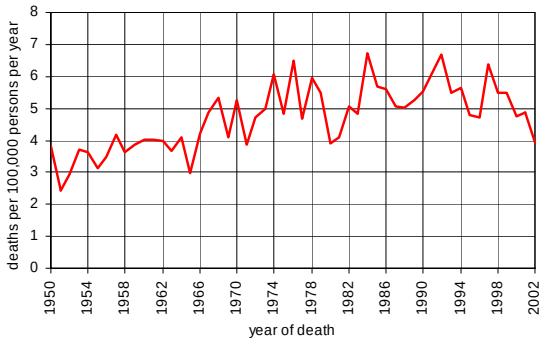


Figure 14.5. Cumulative risk of dying of cancer before age 65, 1950-2002

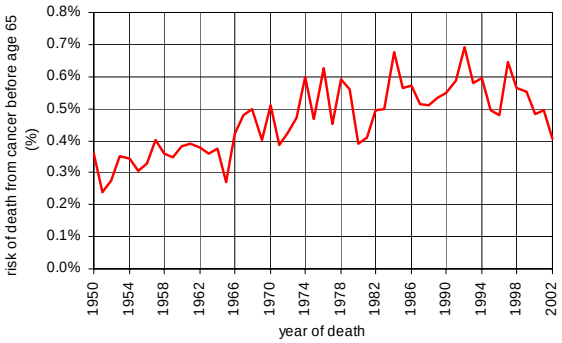
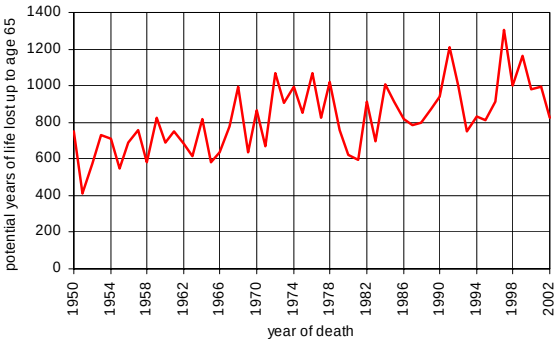


Figure 14.6. Years of potential life lost up to age 65, 1950-2002



Joinpoint regression analysis

Table 14.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

all ages		*0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*
1950		1950	
↓	2.0% (1.7%, 2.3%)	↓	1.4% (1.0%, 1.8%)
1992 (1983, 1995)		1992 (1971, 1999)	
↓	-1.5% (-3.3%, 0.4%)	↓	-2.8%(-5.5%, -0.1%)
2002		2002	

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate shows an initial period of increase in mortality, by 2.0% annually, up to 1992, and a decrease (which was not statistically significant) by 1.5% annually since 1992 (Table 14.2, Figure 14.7). The pattern was similar for women under 65, but with a lower initial rate of increase and a more rapid fall, by 2.8% annually (Figure 14.8).

Figure 14.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

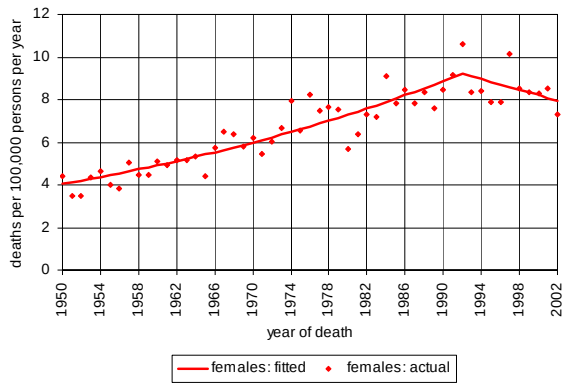
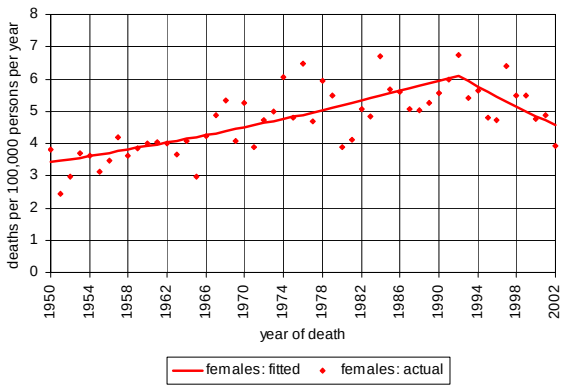


Figure 14.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

Mortality from ovarian cancer has been increasing since 1953 for all women over 50, with the rate of increase being greatest in the older age groups (Figure 14.9). By contrast, mortality has been falling since about 1973 for women under 50. There is some indication that risk was highest for women born between 1928 and 1942 (Figure 14.10).

Figure 14.9. Age-specific mortality by period of death, 1950-2002

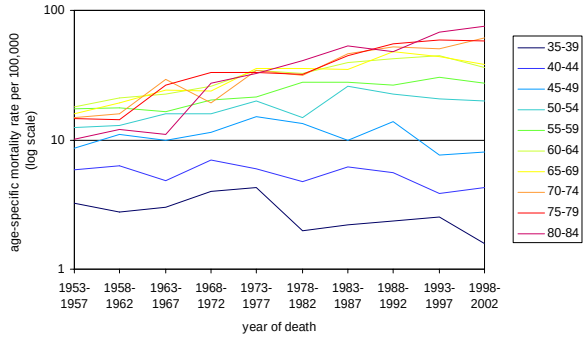
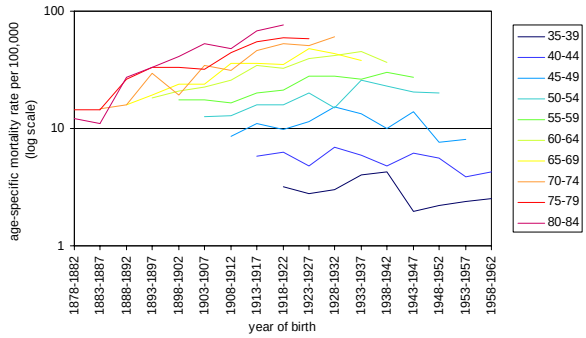


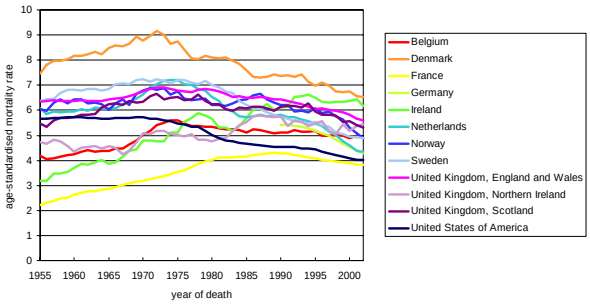
Figure 14.10. Age-specific mortality by birth cohort, 1950-2002



International trends

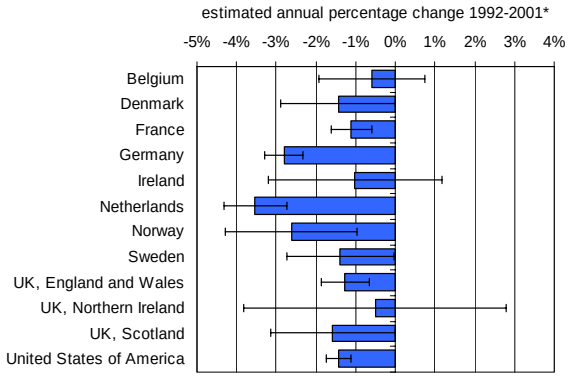
For most countries there was a similar pattern to that seen in Ireland—an increase in mortality to the 1980s and then a fall, (Figure 14.11).

Figure 14.11. Rolling 5-year average World age standardized mortality rates in Europe and USA, all ages, 1950 to 2002



Recent estimates of change (Figure 14.12) indicate significant falls in age-standardised mortality since 1992 in Denmark, France, Germany, the Netherlands, Norway, England/Wales and the USA, with no increases shown in any country.

Figure 14.12. Annual percentage change in mortality rate in Europe and USA, 1992-2001*



**or nearest available data period*

Predictions for the period 2005-2015

Table 14.3. Models chosen for predictions

	prediction baseline	*observations*	*model type*	*p (trend)*
all ages	1992-2002	66	log linear	0.0323
0-64	1992-2002	33	log linear	0.0230

Table 14.4. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
all ages				
WASMR (95% PI)	8.21	8.08 (6.67, 9.48)	7.85 (6.15, 9.55)	7.73 (5.63, 9.83)
No. of deaths (95% PI)	231	250 (209, 291)	276 (219, 333)	315 (232, 399)
under 65				
WASMR (95% PI)	4.90	4.44 (3.27, 5.61)	4.02 (2.6, 5.38)	3.69 (2.06, 5.31)
No. of deaths (95% PI)	94	95 (70, 119)	96 (64, 127)	94 (54, 133)

Ovarian cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) are predicted to fall from 8.21 in 1998-2002 to 7.73 (95% prediction interval 5.63, 9.83) in 2015 (Figure 14.13, Table 14.4). The number of deaths, however, is predicted to rise, from 231 per year in 1998-2002 to 315 (232, 399) in 2015 (Figure 14.15). In women under 65 the mortality rate is also predicted to fall, from 4.90 in 1998-2002 to 3.69 (2.06, 5.31) in 2015 (Figure 14.14), with no change in the number of deaths (Figure 14.16).

The numbers of deaths presented in Table 14.4 and in Figures 14.15 and 14.16 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 14.5, which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would result in an additional 321 deaths per year (a 39% increase from the 1998-2002 average), compared with only 84 extra deaths if current trends continue.

Table 14.5. Predictions of number of deaths, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	1998-2002	*2005*	*2010*	*2015*
No. of deaths (95% PI)	231	254 (220, 289)	284 (247, 321)	321 (282, 361)

Figure 14.13. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

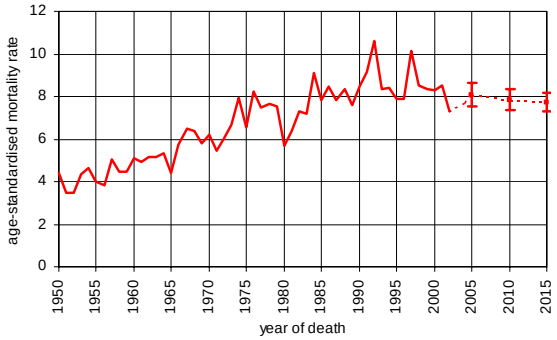


Figure 14.14. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

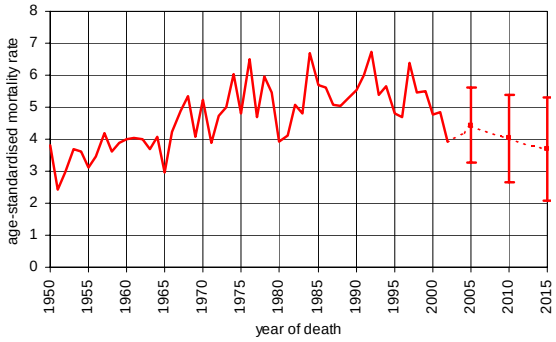


Figure 14.15. Actual and predicted number of deaths, all ages, 1950-2015

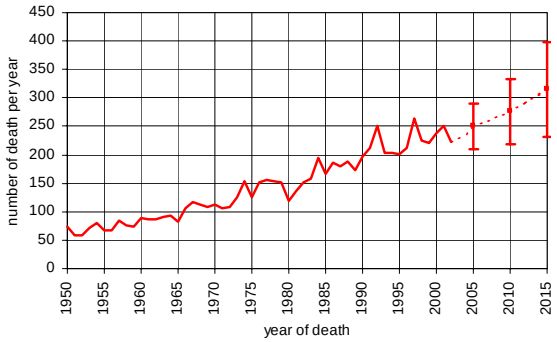
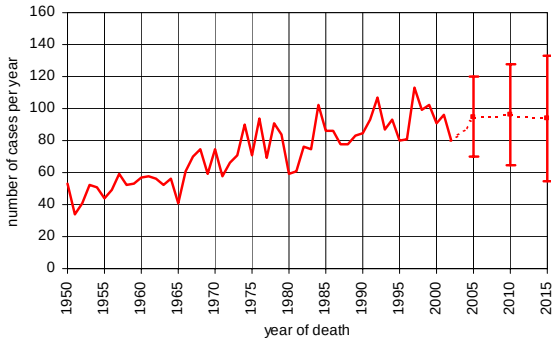


Figure 14.16. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

The number of deaths from ovarian cancer increased steadily from 1950 onwards, while the age-standardised mortality rates increased up to the 1980s or early 1990s, then declined. The overall pattern of mortality with time was quite similar to that for breast cancer. Both are associated with increasing obesity and falling parity, but other risk factors differ between the two cancers. Women born between 1928 and 1942 appeared to be the group at highest risk.

International trends have been generally downwards.

Predictions

The death rate from ovarian cancer is predicted to fall by 6% for all women and by 25% for women under 65, between approximately 2000 and 2015. In the same period, the number of deaths is predicted to increase by 36% for all women but to show no change for women under 65.

Conclusions

The small overall rate of decrease in mortality from ovarian cancer, and the predicted increase in numbers of deaths (at least for women over 65), are worrying. Survival from this cancer is poor, largely because of late presentation, but available screening tests are unsatisfactory. Not enough is known of the aetiology of the disease for a preventive programme to be dependable in reducing either incidence or mortality. Screening, although having some promise, does not yet appear to be an option (Garner, 2005).

Chapter 15. Prostate cancer (ICD-9 185)

Epidemiology

Prostate cancer was the commonest cancer overall in men, and the second commonest cause of cancer death, in men in the period 1994-2001, with an annual average of 1,371 cases and 519 deaths during this period.

Prostate cancer is predominantly a disease of older men. 64% of cases and 83% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined (Table 15.1).

Table 15.1. Age distribution of prostate cancer deaths and cases

age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*
<30	<1%	0%
30-39	<1%	<1%
40-49	<1%	1%
50-59	3%	8%
60-69	14%	27%
70-79	45%	41%
80+	38%	23%

Survival from prostate cancer is reasonably good. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 67%.

Five-year survival for patients diagnosed in Ireland in 1994-1996 was 64.1% (95% CI 61.2-67.0%); in 1997-1999, 75.9% (71.7-80.2%).

Non-genetic risk factors

Diet and energy balance

Ecological studies have demonstrated a direct relationship between a country's prostate cancer-specific mortality rate and average total calories from fat consumed by the country's population (Armstrong and Doll 1975; Rose and Connolly 1992) Some case-control studies have found an association between dietary fat and prostate cancer (Ross, Shimizu et al. 1987; Kolonel, Yoshizawa et al. 1988), but not consistently so (Mettlin, Selenskas et al. 1989; Severson, Nomura et al. 1989). Overall about half the descriptive and case-control studies found an increased risk with increased dietary fat and half found no association (Zhou and Blackburn 1997).

Hormonal and reproductive factors

The development of the prostate gland is dependent on androgen secretion. At an ecological level, risks for prostate cancer in different ethnic groups parallel androgen levels. A number of studies have demonstrated that levels of testosterone, and especially dihydrotestosterone, are highest in black males, of intermediate levels in white males, and lowest in native Japanese males (Ellis and Nyborg 1992; Ross, Bernstein et al. 1992). Androgen deprivation is also effective in reducing the size of most prostate cancers (Miyamoto, Messing et al. 2004). However, the epidemiological evidence linking prostate cancer to hormone levels is still unclear (Parnes, Thompson et al. 2005).

Other risk factors

There is some evidence of association between smoking and prostate cancer, but this is not consistent or strong (Giles, Severi et al. 2001; Hickey, Do et al. 2001; Plaskon, Penson et al. 2003).

Trends

Between 1950 and 2002, the number of prostate cancer deaths rose from 165 to 543, an overall increase of 2.4% per year (Figure 15.1). There seem to have been two phases of increase—before 1978 and a more rapid increase after 1986. Crude mortality rates increased by 1.8% annually (Figure 15.2) and age-standardised rates (Figure 15.3) by 1.9%. The rates for the under 65s—age-standardised rate (Figure 15.4), cumulative risk (Figure 15.5) and years of potential life lost (Figure 15.6)—seem to have increased much less, by about 0.6-0.7% annually, but the numbers were quite small and an overall trend is difficult to see. Trends since 1992 indicate a non-significant annual decrease in total age-standardised mortality rates (Figure 15.12).

Figure 15.1. Number of deaths per year, 1950-2002

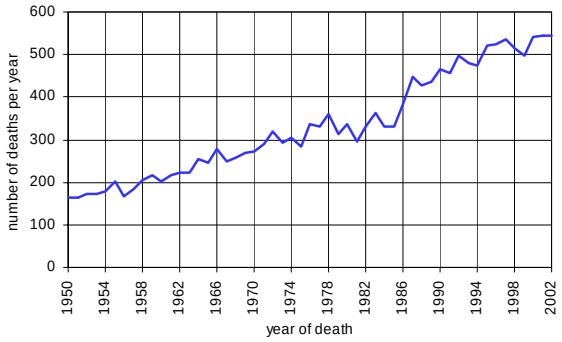


Figure 15.2. Crude mortality rate, 1950-2002

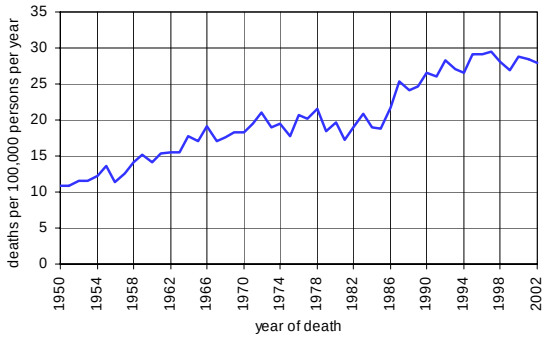


Figure 15.3. World age-standardised mortality rate, all ages, 1950-2002

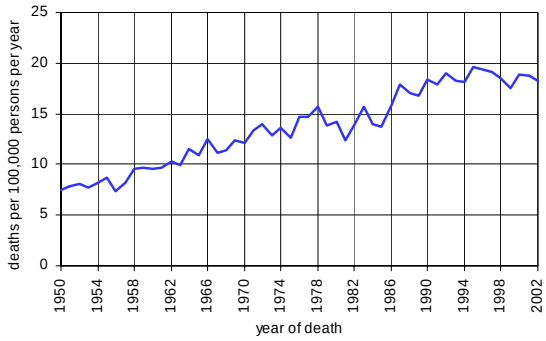


Figure 15.4. World age-standardised mortality rate, 0-64 years, 1950-2002

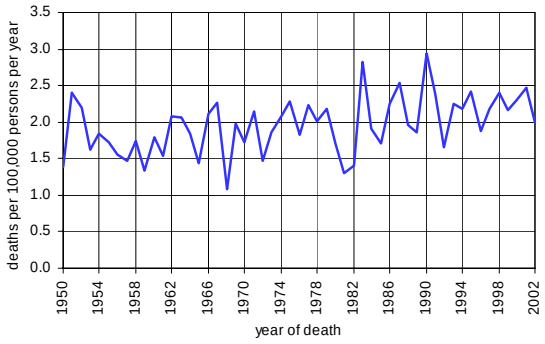


Figure 15.5. Cumulative risk of dying of cancer before age 65, 1950-2002

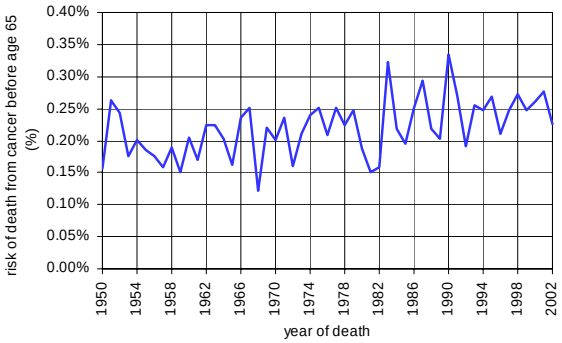
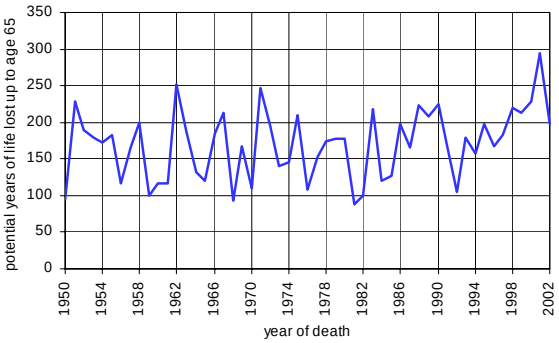


Figure 15.6. Years of potential life lost up to age 65, 1950-2002



Joinpoint regression analysis

Table 15.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

all ages		*0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*
1950		1950	
↓	2.6% (2.3%, 2.9%)	↓	0.6% (0.2%, 0.9%)
1978 (1970, 1979)		2002	
↓	-4.3% (-18.1%, 11.7%)		
1981 (1979, 1986)			
↓	3.3% (2.2%, 4.5%)		
1992 (1986, 1997)			
↓	-0.4% (-1.3%, 0.6%)		
2002			

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate showed an increase in rate from 1950 to 1978 of 2.6% annually then a brief fall in rate, of 4.3% annually, from 1978 to 1981 (Table 15.2, Figure 15.7). The mortality rate increased by 3.3% per annum from 1981 to 1992, and since then there has been no significant trend. Although the pattern shown is quite complex, analysis showed that it was a much better fit to the data than a model with fewer inflection points. This short-term fluctuation in numbers may be related to the move from ICD-8 to ICD-9 in 1978.

For men under 65, the patterns were much simpler, probably due to the small number of deaths, showing an annual rate of increase of 0.6% over the period 1950-2002 (Figure 15.8).

Figure 15.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

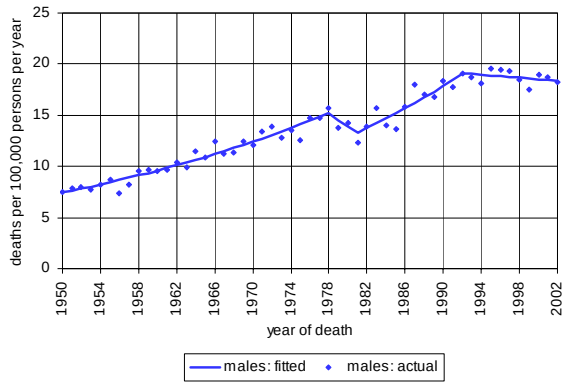
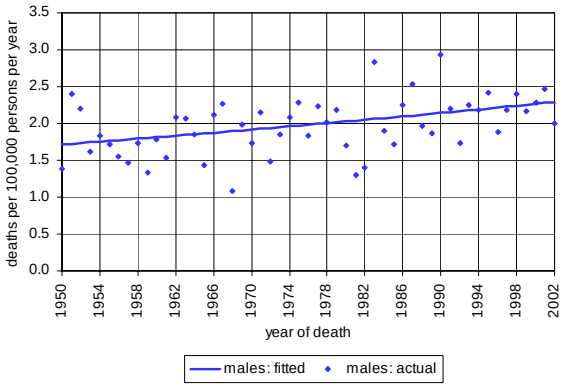


Figure 15.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

Prostate cancer mortality has been increasing since 1953 for all men aged 60 and over (Figure 15.9); the rate of increase in mortality was greatest for the older age groups. For men aged under 60, there was little increase, but mortality rates are very low in this age group. There is no evidence that year of birth had any effect on mortality, independent of age or period of death (Figure 15.10).

Figure 15.9. Age-specific mortality by period of death, 1950-2002

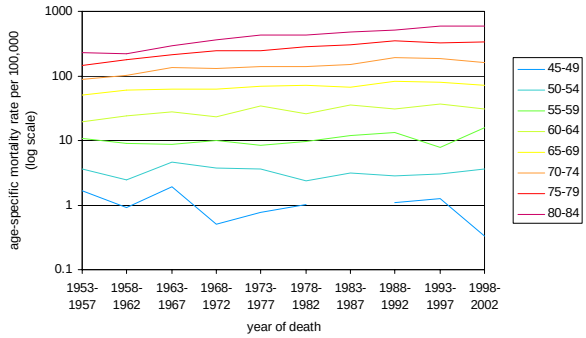
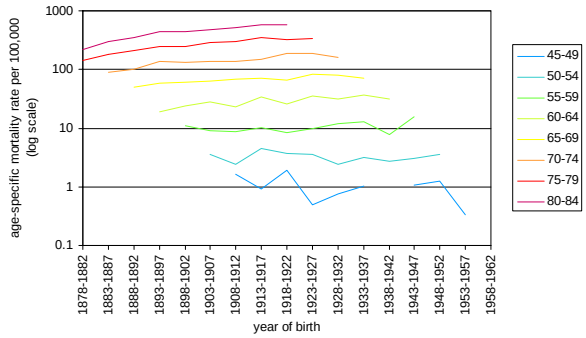


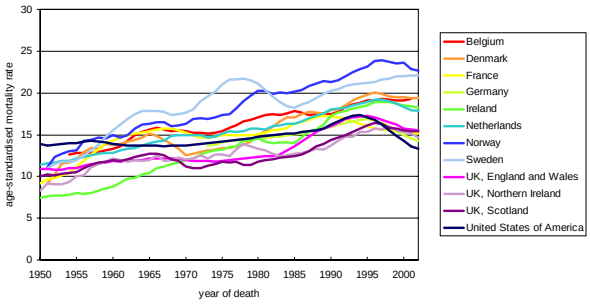
Figure 15.10. Age-specific mortality by birth cohort, 1950-2002



International trends

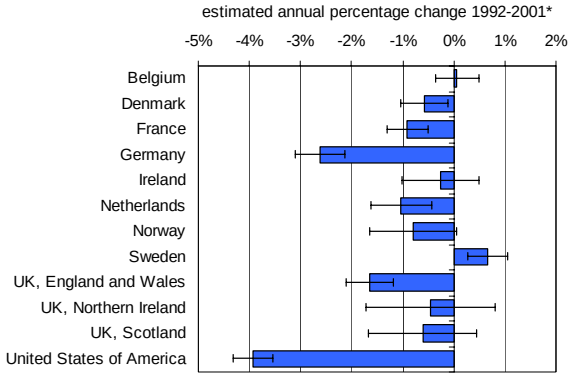
Many European countries show a trend in mortality rates similar to that seen in Ireland, with a dip, or levelling off, of mortality in the 1970s or 1980s, followed by an increase, and a more recent fall (Figures 15.11, 15.12). However, for most countries there has been a net increase in mortality rate over the past 20 years. Mortality rates in the US, like those in Europe, are now falling, and began to fall earlier. Mortality rates in Ireland were the lowest of the countries shown until 1969, but are now near the European median.

Figure 15.11. Rolling 5-year average World age standardized mortality rates in Europe and USA, all ages, 1950 to 2002



Recent estimates of change (Figure 15.12) indicate significant falls in age-standardised mortality since 1992 for men in Denmark, France, Germany, the Netherlands, England/Wales and the USA, with the largest fall in the USA.

Figure 15.12. Annual percentage change in mortality rate in Europe and USA, 1992-2001*



** or nearest available period*

Table 15.3. Models chosen for predictions

model	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	1992-2002	66	log linear	0.8111
0-64	1979-2002	72	linear	0.179

Prostate cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to show no change from 18.36 in 1998-2002 to 18.40 (95% prediction interval 15.21, 21.59) in 2015 (Figure 15.13, Table 15.4). The number of deaths in men is, however, predicted to rise, from 528 per year in 1998-2002 to 787 (654, 919) in 2015, reflecting demographic changes (Figure 15.15). In men under 65 the mortality rate is predicted to increase, from 2.26 in 1998-2002 to 2.47 (1.70, 3.23) in 2015 (Figure 15.14), with an accompanying increase in the number of deaths from 42 per year in 1998-2002 to 71 (49, 93) in 2015 (Figure 15.16). It should be noted, however, that predictions for age group 0-64 are from a longer-term prediction baseline than for all ages, reflecting the difficulty of identifying recent trends in younger age groups for this cancer, which is rare in young men.

Table 15.4. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
all ages				
WASMR (95% PI)	18.36	18.60 (16.55, 20.65)	18.46 (15.92, 21.01)	18.40 (15.21, 21.59)
No. of deaths (95% PI)	528	583 (521, 646)	669 (579, 759)	787 (654, 919)
0-64 years				
WASMR (95% PI)	2.26	2.31 (1.61, 3.01)	2.39 (1.67, 3.11)	2.47 (1.70, 3.23)
No. of deaths (95% PI)	42	53 (37, 69)	63 (44, 82)	71 (49, 93)

The numbers of deaths presented in Table 15.5 and in Figures 15.19 and 15.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 8.6, which shows the effect of population change in the absence of any trend in rates.

As rates are not predicted to change, the projected increase of 259 deaths per annum in men between 1998-2002 and 2015 is almost identical to that predicted on demographic grounds alone (261 deaths per annum).

Table 15.5. Predictions of number of deaths, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	1998-2002	*2005*	*2010*	*2015*
No. of deaths (95% PI)	529	583 (531, 636)	668 (612, 725)	789 (726, 851)

Figure 15.13. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

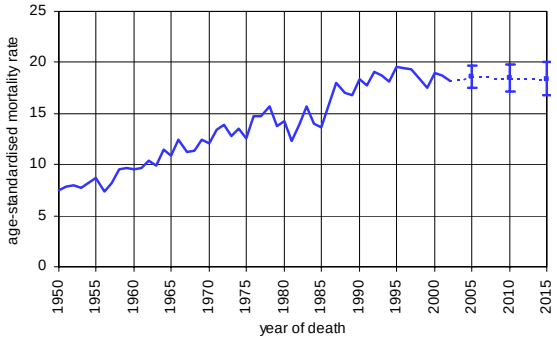


Figure 15.14. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

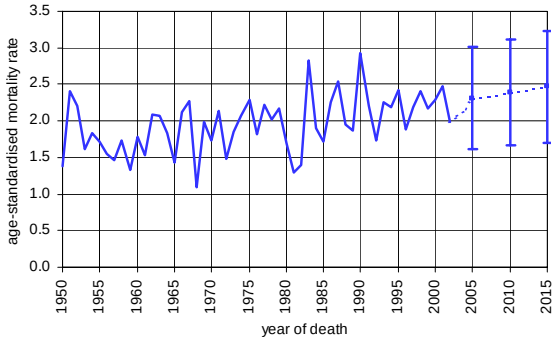


Figure 15.15. Actual and predicted number of deaths, all ages, 1950-2015

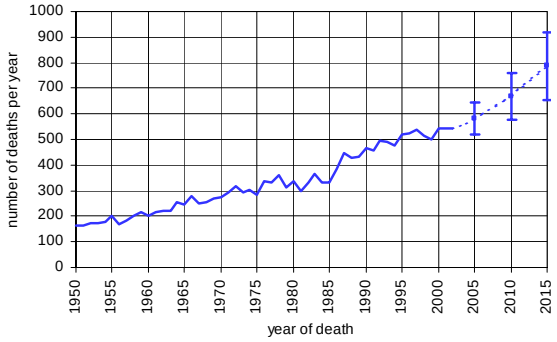
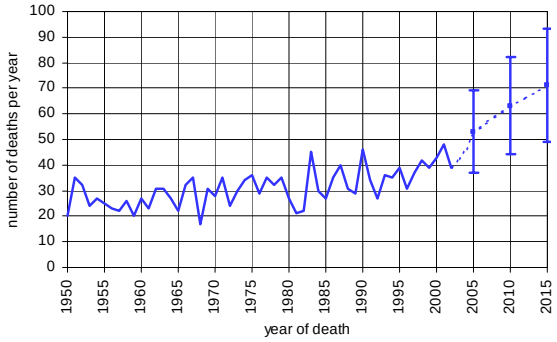


Figure 15.16. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

Despite recent rapid increases in incidence in Ireland (National Cancer Registry 2005), mortality rates for prostate cancer have been falling in the recent past. While there is a long-term slight upward trend in men under 65, mortality in this age group makes up only about 10% of the total, and, even if a small downward trend existed, the number of deaths is too few to show this.

International trends are very similar to those seen in Ireland, with a steady increase in rate up to the early 1980s, with a decrease thereafter.

Predictions

Overall rates are not predicted to change between approximately 2000 and 2015, although, because of population aging, the number of deaths is predicted to increase by 49%. Mortality rates and numbers in men under 65 are predicted to increase over the same period—rates by 9% and numbers by 69%. However the prediction intervals on the rate estimates for younger men are quite large and include no change; or a possible decrease; also, the predictions for younger men are less influenced by recent trends than is the case for all ages (because of greater instability in prediction models derived from low rates in the under-65s).

Conclusions

The aetiology and natural history of prostate cancer are poorly understood. The widespread availability, in the past ten years, of the prostate-specific antigen (PSA) test facilitating early diagnosis of prostate cancer has introduced a new factor into time trends in both mortality and incidence. It is difficult to tell, at this stage, if the falls in prostate cancer mortality, seen first in the USA in the 1980 and now widespread across Europe, are due to survival benefits (if any) of early detection by PSA testing (or other means), or to more effective treatment by hormones and radiotherapy; or to a combination of these.

There is still no consensus on the benefits of prevention or screening in the control of prostate cancer (Roemeling and Schröder, 2006).

Chapter 16. Brain and central nervous system cancer (ICD-9 191 & 192)

Epidemiology

Cancer of the brain and central nervous system (CNS) is relatively uncommon. It was the 14th most common cancer and the 12th commonest cause of cancer death in the period 1994-2001, with an annual average of 280 cases and 218 deaths during this period. Female cases made up 42% of cases and 43% of deaths. Almost all cases (94%) were cancers of the brain, with 4% being cancers of spinal cord and 2% tumours of the meninges. 98% of deaths were due to cancers of brain (ICD-9 191) and only 2% to cancers of other parts of the nervous system (including meninges). Benign tumours of the brain and central nervous system (which caused approximately 10 deaths per years between 1994 and 2001) are not included in this chapter.

Brain and CNS cancer tends to affect younger individuals disproportionately. Only 26% of cases and 31% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined (Table 16.1). Although deaths from brain cancers in the patients under 15 make up only 3% of the total mortality for these cancers, they are (with leukaemia) the commonest cause of cancer death in that age group.

Table 16.1. Age distribution of brain and central nervous system cases and deaths 1994-2001

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	7%	19%	8%	19%	8%	19%
30-39	6%	8%	5%	8%	6%	8%
40-49	8%	8%	13%	12%	11%	10%
50-59	15%	13%	22%	19%	19%	17%
60-69	24%	19%	26%	21%	25%	20%
70-79	29%	23%	20%	17%	24%	19%
80+	10%	9%	6%	5%	8%	6%

Survival prospects are generally poor. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 18% for both men and women (ICD-9 code 191 only). However, five-year relative survival for patients aged 15-44 was 47%, while for those aged over 65 it was only 5%. Patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 14% for men and 15% for women (Berrino et al. 1995).

Five-year relative survival for patients diagnosed in Ireland in 1994-1996 was 16.3% (95% CI 12.9-19.7%) for men and 20.7% (16.8-24.7%) for women; in 1997-1999, 21.6% (17.2-26.0%) for men and 16.3% (12.4-22.2%) for women (National Cancer Registry 2003).

Non-genetic risk factors

Brain cancers are a heterogeneous group (Table 16.2) and little is known of their aetiology. Risk factors probably vary by histological type, and by age group. Although childhood CNS tumours are rare compared to those in adults, their aetiology has been more thoroughly studied (Preston-Martin 1996; Baldwin and Preston-Martin 2004). Suggested risk factors for childhood cancers have included magnetic or electromagnetic fields (Preston-Martin, Navidi et al. 1996; Kheifets, Sussman et al. 1999) dietary nitrates, nitrites and nitrosamines (Pogoda and Preston-Martin 2001; McKean-Cowdin, Pogoda et al. 2003; Mueller, Nielsen et al. 2004), hair dyes (Holly, Bracci et al. 2002) and parental occupation (Cordier, Mandereau et al. 2001). Among the factors which have been suggested to predispose to CNS tumours in adults are trauma (Preston-Martin, Pogoda et al. 1998), and epilepsy (Schlehofer, Blettner et al. 1999), but the associations are weak and account for only a small number of cancers. Also important in understanding trends in brain cancer mortality is the consistent finding that recent trends are more likely to be due to improvements in diagnostic imaging than in an increase in the underlying incidence rate of brain cancer (Preston-Martin 1996).

Table 16.2. Percentage distribution of incident malignant brain and CNS tumours in Ireland 1994-2002 by histological type

tumour type	*% of all malignant brain and CNS tumours, 1994-2002*
glioblastoma	39%
astrocytoma	29%
glioma	6%
oligodendroglioma	5%
medulloblastoma	2%
other	19%

Source: National Cancer Registry

Trends

Between 1950 and 2002, the number of deaths from cancer of the brain and central nervous system rose from 23 to 123 in men and from 10 to 95 in women, corresponding to an average increase, over the whole period, of 2.9% per year for men and 3.5% for women (Figure 16.1). Crude mortality rates increased by 2.3% annually for men, and by 2.8% annually for women (Figure 16.2). Age-standardised rates (Figures 16.3, 16.4) increased by a similar amount, 2.5% annually for men and 2.6% for women. The cumulative risk of dying before age 65 increased a little less, by 1.7% annually for men and 1.6% for women (Figure 16.5), while years of potential life lost (Figure 16.6) had the smallest increases (1.3% for men and 1.4% for women). The female/male ratio in age-standardised rate, although varying from year to year, has remained close to the average value of 0.67 since 1950. Trends since 1992 indicate a non-significant annual decrease in total age-standardised mortality rates for both males (Figure 16.15) and females (Figure 16.16).

Figure 16.1. Number of deaths per year, 1950-2002

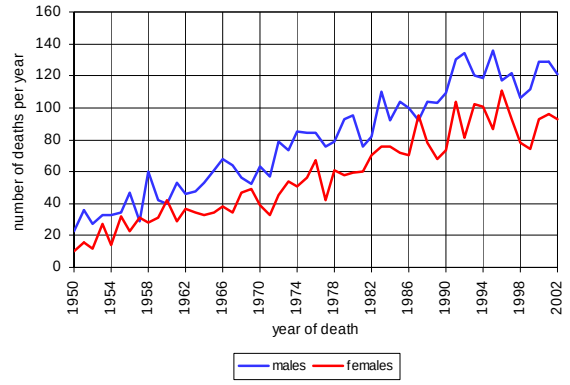


Figure 16.2. Crude mortality rate, 1950-2002

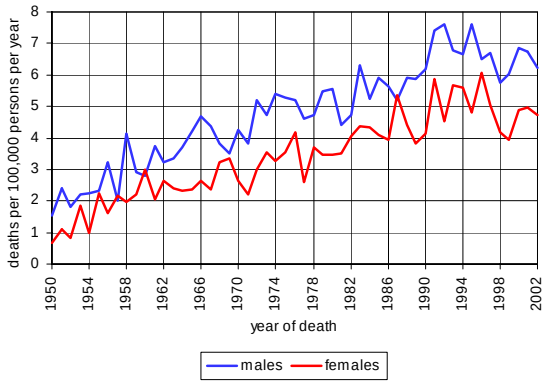


Figure 16.3. World age-standardised mortality rate, all ages, 1950-2002

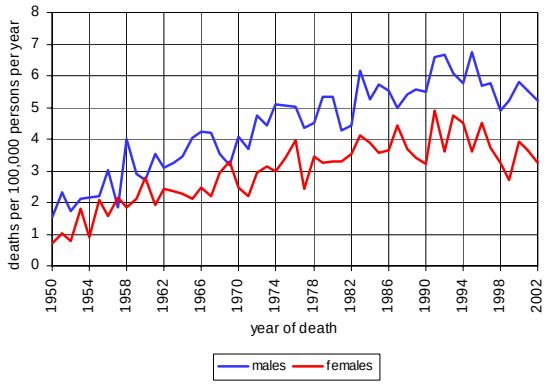


Figure 16.4. World age-standardised mortality rate, 0-64 years, 1950-2002

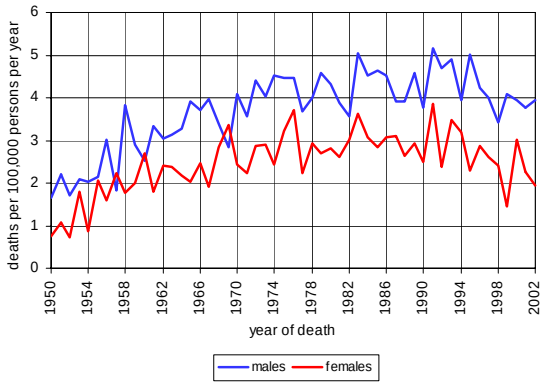


Figure 16.5. Cumulative risk of dying of cancer before age 65, 1950-2002

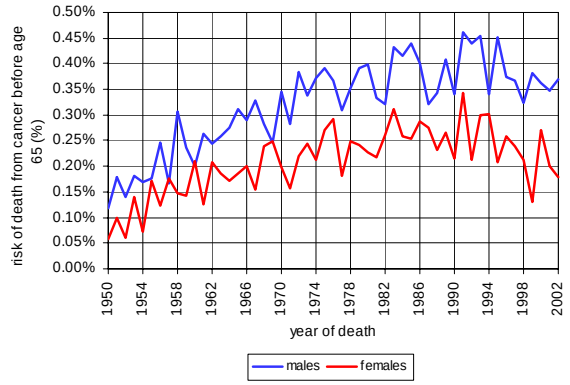
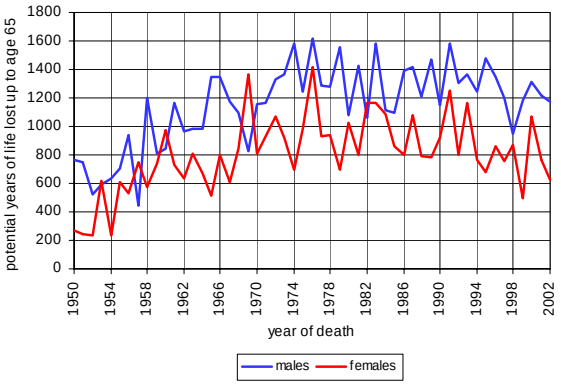


Figure 16.6. Years of potential life lost up to age 65, 1950-2002



Joinpoint regression analysis

Table 16.3. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1950		1950		1950		1950	
↓	8.5% (2.8%, 14.6%)	↓	14.1% (2.6%, 26.8%)	↓	3.4% (2.4%, 4.4%)	↓	14.9% (2.9%, 28.2%)
1958 (1954, 1978)		1957 (1952, 1967)		1973 (1964, 1979)		1957 (1952, 1974)	
↓	2.0% (1.6%, 2.4%)	↓	2.0% (1.5%, 2.5%)	↓	-0.1% (-0.6%, 0.4%)	↓	1.1% (0.4%, 1.7%)
1993 (1982, 1998)		1994 (1983, 1997)		2002		1993 (1971, 1998)	
↓	-1.9% (-4.2%, 0.3%)	↓	-3.8% (-7.4%, 0.0%)			↓	-4.8% (-8.9%, -0.5%)
2002		2002				2002	

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate showed a rapid rate of increase in the 1950s (8.5% annually for men and 14% for women), followed by more gradual rises (2.0% per annum for both sexes) until 1993/1994 (Table 16.3; Figure 16.7). Since then, mortality has decreased by 1.9% per annum for men and 3.8% for women, although only the trend for women is statistically significant.

For men under 65, there was an increase in mortality rate of 3.4% per annum from 1950 to 1973, and no significant trend after 1973 (Figure 16.8). For women under 65, the pattern of change was very similar to that for women of all ages combined, with a recent annual decrease of 4.8% since 1993.

Figure 16.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

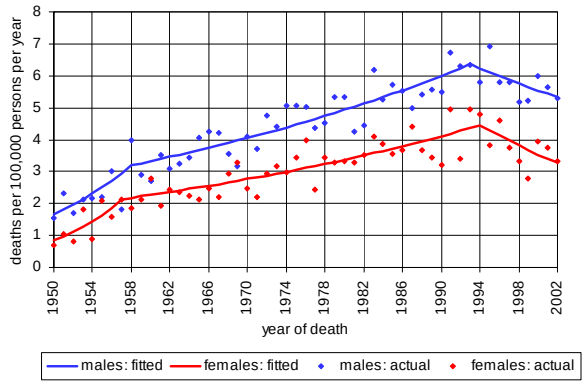
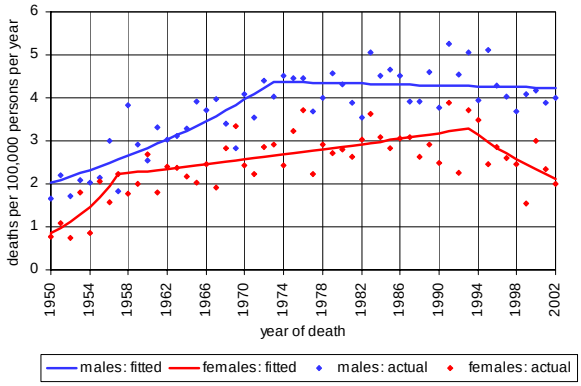


Figure 16.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

The age-period plots for both sexes show a very rapid increase in brain cancer mortality for the oldest age groups, from 55 years of age upwards, but no real change for men or women under 55 (Figures 16.9, 16.10). Although this increase seems to have begun around 1973 for those aged 80 and over, for the other age groups the upward trend goes back to 1953. There is some suggestion that mortality was higher in those born between 1918 and 1932 (Figures 16.11, 16.12).

Figure 16.9. Age-specific mortality by period of death, males, 1950-2002

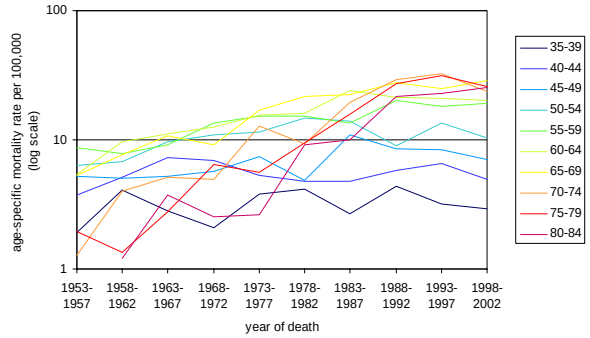


Figure 16.10. Age-specific mortality by period of death, females, 1950-2002

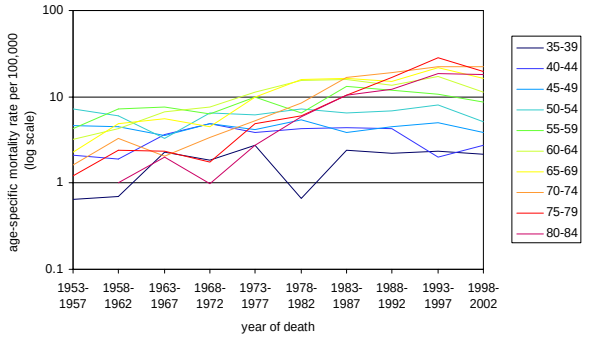


Figure 16.11. Age-specific mortality by birth cohort, males, 1950-2002

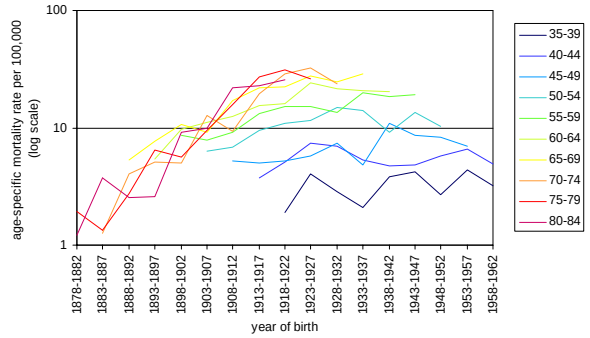
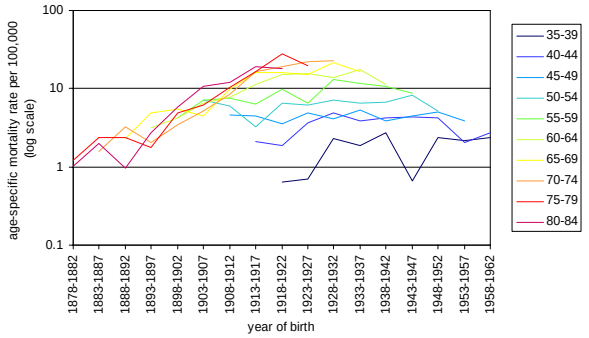


Figure 16.12. Age-specific mortality by birth cohort, females, 1950-2002



International trends

The mortality rate from cancer of brain and CNS has been increasing in all of the countries studied since 1955 (Figures 16.13, 16.14). The most rapid rate of increase in both men and women has been in France, where the rate was exceptionally low until the 1990s. In most countries there has been a fall in mortality since the mid-1990s; this trend is clearer for men than for women. There has been a recent significant increase in mortality for both men and women in the Netherlands. In the case of the Netherlands and many other countries it can be seen that the upwards and downwards trends for both men and women are synchronous; this seems more likely to be related to trends in diagnosis than in incidence or survival.

Figure 16.13. Rolling 5-year average World age standardized mortality rates in Europe and USA, males, all ages, 1950 to 2002

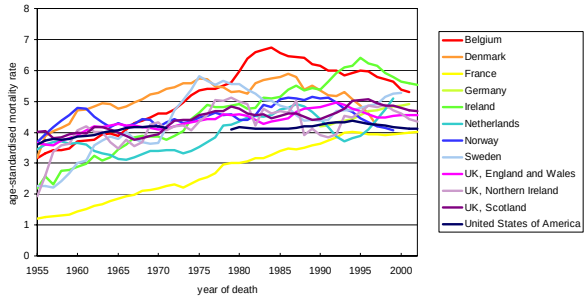
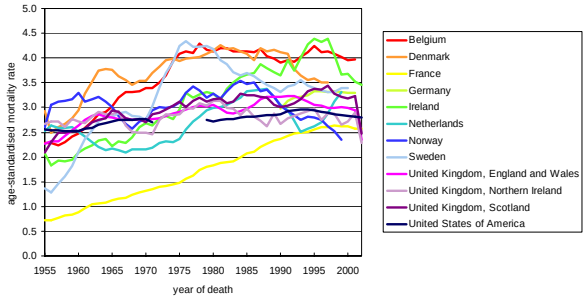


Figure 16.14. Rolling 5-year average World age standardized mortality rates in Europe and USA, females, all ages, 1950 to 2002



Recent estimates of change (Figures 16.15, 16.16) indicate significant falls in age-standardised mortality since 1992 for men in Belgium, Norway and the USA and for women in Norway and the USA.

Figure 16.15. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

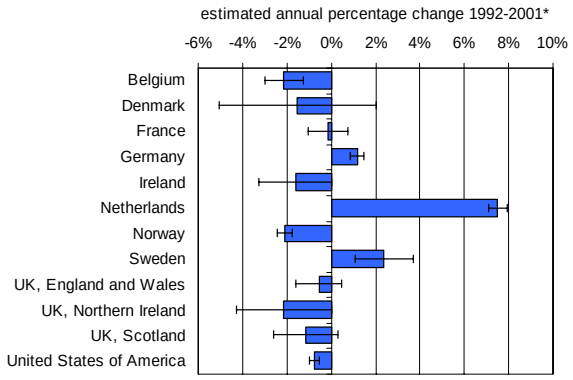
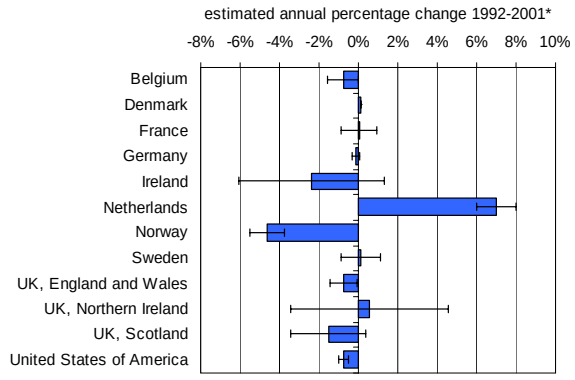


Figure 16.16. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



** or nearest available data period*

Predictions for the period 2005-2015

Table 16.4 Models chosen for predictions

model	*sex*	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	males	1993-2002	60	log linear	0.5822
	females	1994-2002	54	log linear	0.1082
0-64	males	1991-2002	36	log linear	0.3234
	females	1993-2002	30	log linear	0.0124

Table 4.5. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	5.47	5.13 (3.91, 6.35)	4.78 (3.31, 6.25)	4.47 (2.72, 6.22)
No. of deaths (95% PI)	122	127 (97, 157)	135 (94, 176)	145 (88, 203)
females, all ages				
WASMR (95% PI)	3.43	3.21 (2.22, 4.20)	2.97 (1.70, 4.23)	2.80 (1.17, 4.43)
No. of deaths (95% PI)	88	63 (89, 114)	91 (54, 128)	98 (41, 156)
males, 0-64				
WASMR (95% PI)	3.96	3.54 (2.52, 4.56)	3.14 (2.04, 4.25)	2.79 (1.60, 3.99)
No. of deaths (95% PI)	75	74 (53, 95)	74 (48, 100)	72 (41, 103)
females, 0-64				
WASMR (95% PI)	2.28	1.91 (1.11, 2.71)	1.58 (0.70, 2.46)	1.32 (0.37, 2.28)
No. of deaths (95% PI)	43	38 (22, 54)	35 (16, 53)	31 (9, 52)

Brain and central nervous system cancer mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to decrease from 5.47 in 1998-2002 to 4.47 (95% prediction interval 2.72, 6.22) in 2015 (Table 16.5, Figure 16.17). The annual number of deaths in men is predicted to increase, from 122 per year in 1998-2002 to 145 (88, 203) in 2015 (Figure 16.19). In men under 65 the mortality rate is predicted to fall, from 3.96 in 1998-2002 to 2.79 (1.60, 3.99) in 2015 (Figure 16.18), with a smaller decrease in the annual number of deaths from 75 per year in 1998-2002 to 72 (41, 103) in 2015 (Figure 16.20).

Mortality rates in women are predicted to fall from 3.43 in 1998-2002 to 2.80 (1.17, 4.43) in 2015 (Table 16.5, Figures 16.17-16.20). The annual number of deaths is, however, predicted to increase, from 88 per year in 1998-2002 to 98 (41, 156) in 2015. In women under 65 mortality rates are also expected to fall, from 2.28 in 1998-2002 to 1.32 (0.37, 2.28) in 2015. The annual number of deaths in this age group is also expected to fall, from 43 per year in 1998-2002 to 31 (9, 52) in 2015.

The numbers of deaths presented in Table 16.5 and in Figures 16.19 and 16.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 16.6, which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would result in an additional 51 deaths per year in men (a 42% increase from the 1998-2002 average) and 31 in women (a 35% increase) by 2015.

Table 16.6. Predictions of number of deaths at all ages, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths (95% PI)	119	134 (109, 159)	152 (125, 179)	173 (144, 203)	87	95 (74, 116)	105 (83, 128)	119 (95, 143)

Figure 16.17. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

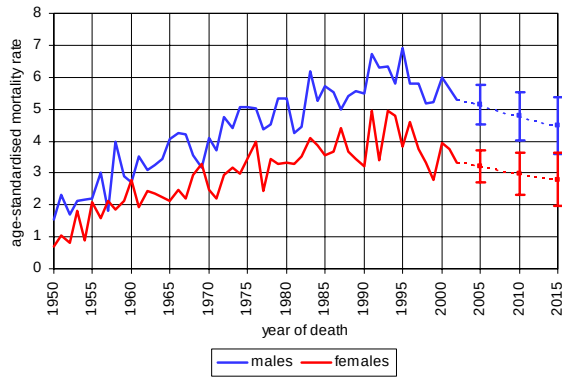


Figure 16.18. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

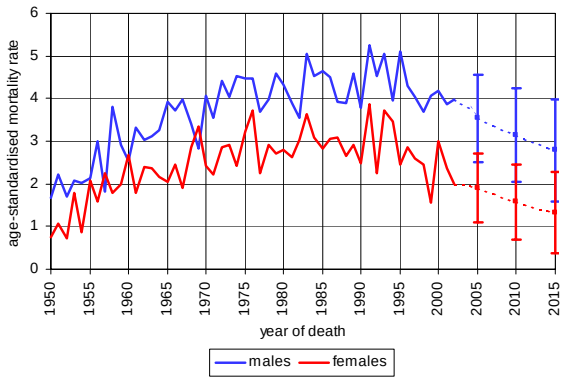


Figure 16.19. Actual and predicted number of deaths, all ages, 1950-2015

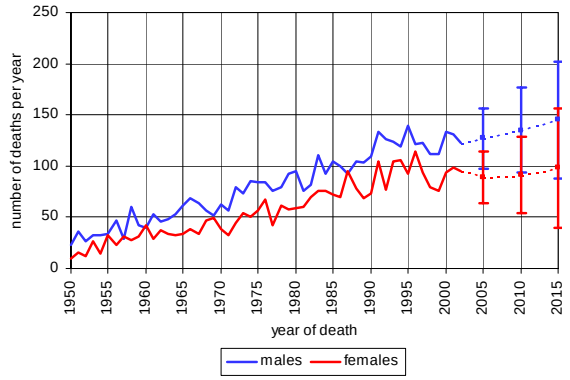
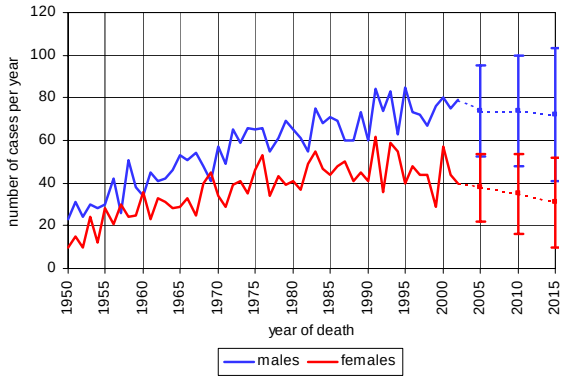


Figure 16.20. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

The long-term increase in brain and CNS cancer mortality seen since 1950 seemed to reach a plateau in the early s1990. For women, and possibly for men, age-standardised rates have decreased since then. Much of the increase seen before 1990 was in the oldest patients, and may be in part attributable to more accurate diagnosis. International trends are obscured by changes in coding and classification in many countries since the late 1960s, and by relatively small numbers.

Predictions

The overall mortality rate is predicted to decrease in both men and women by 18% between approximately 2000 and 2015. The number of deaths is expected to increase from 122 to 145 (+19%) in men and from 88 to 98 (+11%) for women over the same period. More marked falls in mortality rate are expected for men and women under 65, by 30% and 42% respectively, with slight decrease in deaths, from 75 to 72 for men and from 43 to 31 for women, from 43 to 36, between c.2000 and 2015.

Conclusions

Overall mortality from cancers of the brain and central nervous system is currently fairly stable, and historical increases may have been artefactual rather than real. Little is known of the aetiology of this group of cancers, and prospects for prevention seem remote. Screening has not been proposed as a realistic intervention, and a significant fall in mortality in the near future is likely to come about only through therapeutic advances.

Chapter 17. Lymphoma (ICD-9 200-202)

Epidemiology

Lymphoma describes a range of lymphoid malignancies with different behaviours and, possibly, different aetiologies. A number of classifications have been suggested (World Health Organisation, 2002), but the main sub-divisions available consistently from death certificate data have been Hodgkin and non-Hodgkin lymphoma.

Hodgkin lymphoma (HL) is an uncommon condition, averaging 84 cases and 24 deaths annually in Ireland during 1994-2001. Non-Hodgkin lymphoma (NHL) averages 429 cases per year and is the 10th most common cancer. It accounts for 225 deaths annually, 3.0% of the total, and is the 11th commonest cause of death. Female cases made up 45% of HL and 47% of NHL and females accounted for 40% of deaths due to HL and 47% of deaths due to NHL (Table 17.1).

Table 17.1. Age distribution of lymphoma deaths and cases

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	2%	10%	4%	12%	3%	11%
30-39	3%	8%	5%	9%	4%	9%
40-49	6%	9%	10%	13%	8%	11%
50-59	12%	16%	16%	18%	14%	17%
60-69	21%	21%	24%	21%	22%	21%
70-79	33%	23%	28%	19%	31%	21%
80+	23%	13%	13%	8%	18%	10%

Both HL and NHL affect younger patients disproportionately. For HL, only 11% of cases and 34% of deaths were in patients of 70 and older, while for NHL the percentages were 35% of cases and 50% of deaths, as compared to 46% of cases and 58% of deaths for all cancers combined.

Survival prospects are generally good for lymphoma, especially Hodgkin lymphoma. Data from EUROCARE 3 (Sant et al, 2003) for patients diagnosed in 1990-1994 with Hodgkin lymphoma showed mean five-year relative survival to be 78% for men and 82% for women, and for non-Hodgkin lymphoma 51% for men and 54% for women.

Five-year survival for patients diagnosed with non-Hodgkin lymphoma in 1994-1996 was 43.7% (95% CI 38.4-49.0%) for men and 53.6% (48.7-58.5%) for women; in 1997-1999, 54.3% (46.9-91.7%) for men and 54.7% (48.6-60.8%) for women (National Cancer Registry 2003).

Non-genetic risk factors

Diet and energy balance

A high intake of fruit and vegetables has been shown to be associated with a lower risk of NHL (Ward, Zahm et al. 1994; Zhang, Hunter et al. 2000), while a diet high in meat is associated with a higher risk (Chiu, Cerhan et al. 1996; De Stefani, Fierro et al. 1998). Obesity does not appear to be a risk factor (Bosetti, Dal Maso et al. 2005; Chang, Hjalgrim et al. 2005).

Infection

Epstein-Barr virus (EBV) seroconversion is estimated at 80-90% in most countries. While implicated in the aetiology of Burkitt's lymphoma in Africa, infection with *Plasmodium falciparum*, and possibly other factors, is also necessary for lymphoma development, and it does not appear to have any aetiological role in NHL in western countries (Young and Rickinson 2004). A role of EBV in the aetiology of HL is more likely (McCunney 1999).

Gastric NHL has been shown to be associated with *Helicobacter pylori* infection in a number of studies (Farinha and Gascoyne 2005; Marshall and Windsor 2005).

Other risk factors

Increased risk has been found in persons occupationally exposed to electromagnetic fields (Cano and Pollan 2001) insecticides, pesticides (Fritschi and Siemiatycki 1996) and wood (McCunney 1999), and a range of occupations where no obvious aetiological link exists (Figgs, Dosemeci et al. 1995).

Although the risk of skin cancer and of NHL are linked, and there is some ecological correlation between sun exposure and NHL incidence (Langford, Bentham et al. 1998), recent studies have shown that there is no direct link between UV exposure and NHL (Hu, Federman et al. 2005; Smedby, Hjalgrim et al. 2005).

Some studies have shown an increased risk from use of hair dyes, but this has not been confirmed by recent work (Zhang, Holford et al. 2004; Tavani, Negri et al. 2005) and an earlier review had concluded that the evidence was inconclusive (Correa, Jackson et al. 2000).

NHL incidence and mortality increases in conditions leading to suppression of the immune response (Levine 1994). These include congenital immunodeficiency (Cunningham-Rundles, Cooper et al. 2002), AIDS (Scadden 2003), immunosuppressive medication (e.g. in organ transplant recipients) (Swinnen 2000) and in autoimmune disease, such as rheumatoid arthritis (Ehrenfeld, Abu-Shakra et al. 2001).

NHL incidence is increased up to nine-fold in patients with coeliac disease (Catassi, Bearzi et al. 2005; Smedby, Akerman et al. 2005), and the relative risk is even higher for NHL of the small intestine. A number of different pathways of carcinogenesis appear to be involved.

Trends

Between 1950 and 2002, the number of deaths from all lymphomas (HL and NHL combined) rose from 37 to 135 in men and from 20 to 121 in women, with an overall increase over this period averaging 2.3% per year for men and 3.8% for women (Figure 17.1). Most of this increase took place since 1980. Crude mortality rates increased by 1.7% annually for men and by 3.1% annually for women (Figure 17.2). Age-standardised rates (Figure 17.3, 17.4) increased by 1.4% annually for men and 2.3% for women. The cumulative risk of dying before age 65 showed smaller increases (Figure 17.5) with a 0.6% increase for men and a 1.5% increase for women; years of potential life lost (Figure 17.6) showed no average change for men and a 0.5% increase for women. Trends since 1992 indicate a non-significant annual increase in total age-standardised mortality rates for both males (Figure 17.15) and females (Figure 17.16).

Figure 17.1. Number of deaths per year, 1950-2002

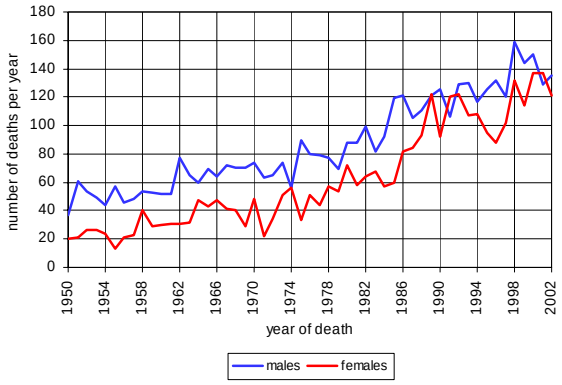


Figure 17.2. Crude mortality rate, 1950-2002

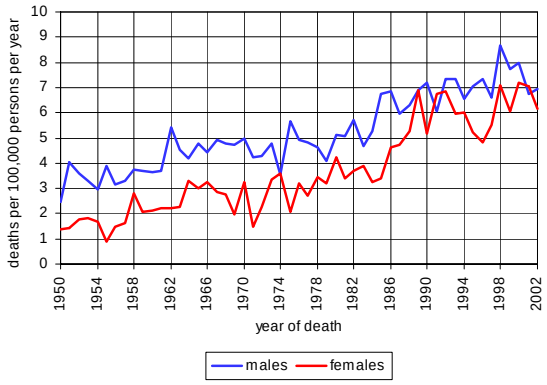


Figure 17.3. World age-standardised mortality rate, all ages, 1950-2002

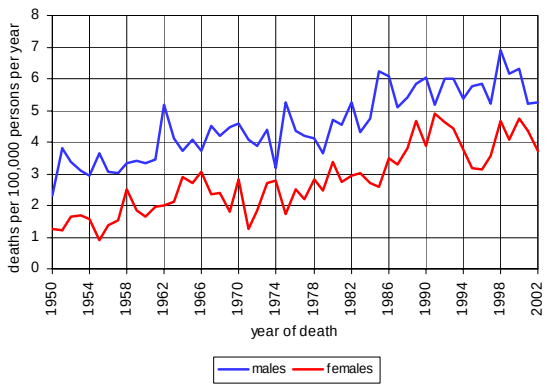


Figure 17.4. World age-standardised mortality rate, 0-64 years, 1950-2002

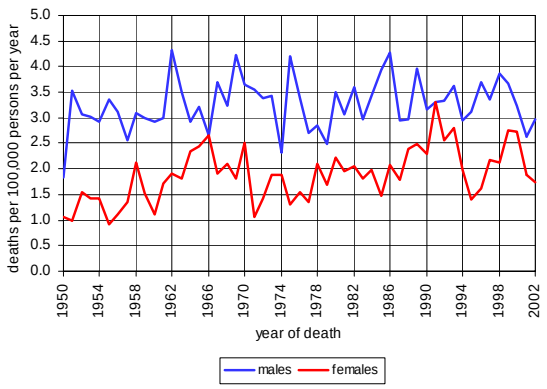


Figure 17.5. Cumulative risk of dying of cancer before age 65, 1950-2002

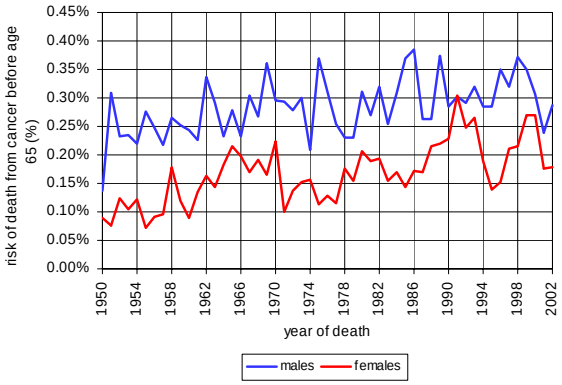
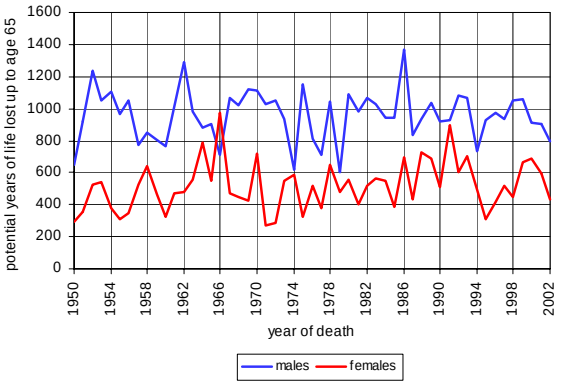


Figure 17.6. Years of potential life lost up to age 65, 1950-2002



Joinpoint regression analysis

Table 17.2. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1950		1950		1950		1950	
↓	1.3% (1.1%, 1.5%)	↓	2.1% (1.7%, 2.5%)	↓	0.2% (-0.1%, 0.4%)	↓	3.8% (-0.1%, 7.8%)
2002		2002		2002		1964 (1952, 2000)	
						↓	0.4% (-0.2%, 1.1%)
						2002	

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate for men showed a steady increase in rates of 1.3% per annum from 1950 to 2002 (Table 17.2, Figure 17.7), with no significant trend for men under 65 (Figure 17.8). For women, the rate increased by 2.1% annually from 1950 to 2002, while for women under 65 after an initial increase of 3.8% annually from 1950 there was no significant trend after 1964.

Figure 17.7. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

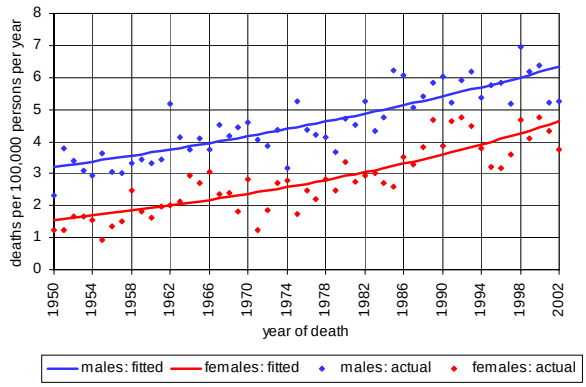
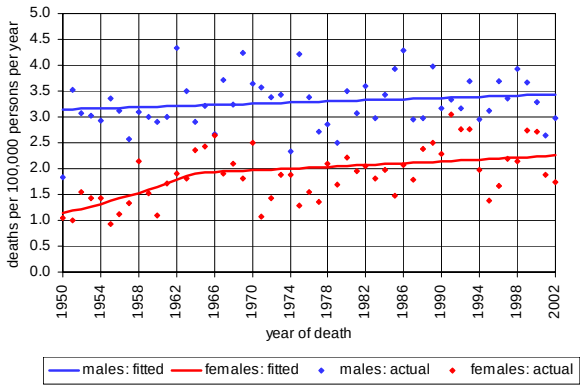


Figure 17.8. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

The age-period analyses (for all lymphoma combined) show a steady increase in mortality for all age groups older than 50 for both women and men (Figures 17.9, 17.10). There is evidence of a flattening of the trend in the past decade, but no decrease. There is no evidence that year of birth had any effect on mortality, independent of age or period of death (Figures 17.11-17.12).

Figure 17.9. Age-specific mortality by period of death, males, 1950-2002

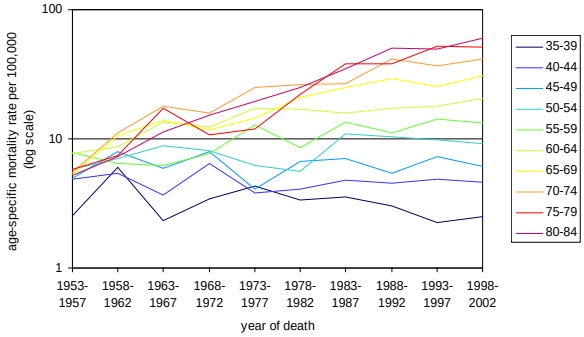


Figure 17.10. Age-specific mortality by period of death, females, 1950-2002

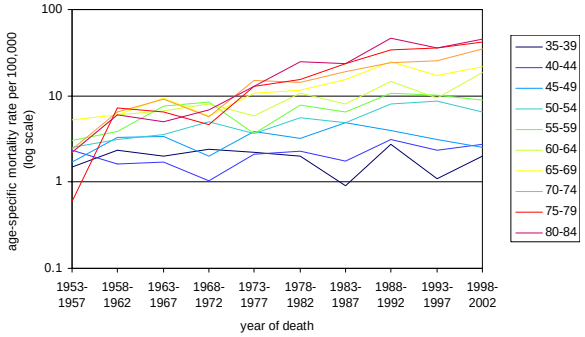


Figure 17.11. Age-specific mortality by birth cohort, males, 1950-2002

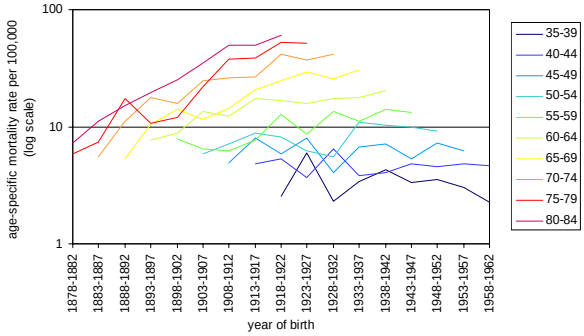
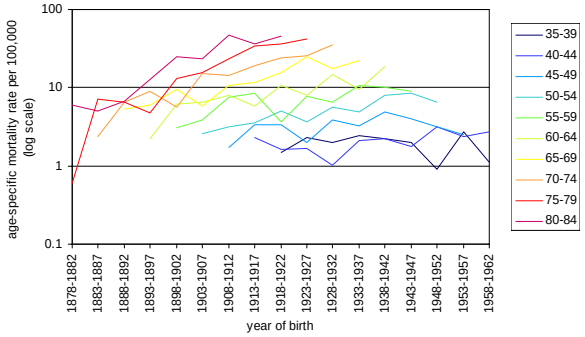


Figure 17.12 Age-specific mortality by birth cohort, females, 1950-2002



International trends

All countries studied show a similar increase in mortality from non-Hodgkin lymphoma in men since 1950, but in many cases (US, UK, Sweden, Germany, Netherlands) the rate has decreased since 1995 (Figure 17.13). The US, with the highest rate, has also shown the largest recent decrease. Ireland, which had one of the lowest mortality rates in the 1950s, now has the second highest mortality rate. Very similar trends were seen for women (Figure 17.14).

Figure 17.13. Rolling 5-year average World age standardized mortality rates in Europe and USA, males, all ages, 1950 to 2002

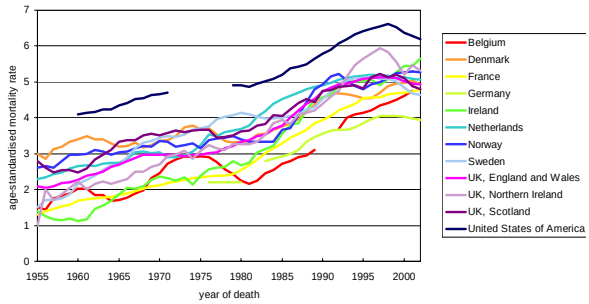
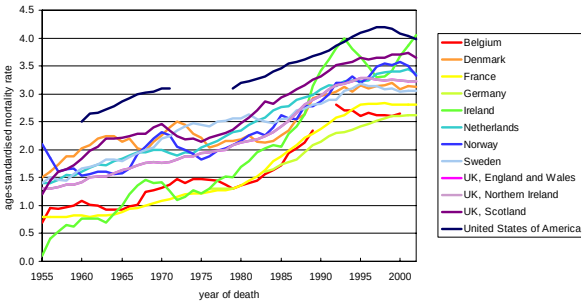


Figure 17.14. Rolling 5-year average World age standardized mortality rates in Europe and USA, females, all ages, 1950 to 2002



Recent estimates of change (Figures 17.15, 17.16) indicate significant falls in age-standardised mortality since 1992 for men in Sweden and England/Wales and increases for men in Belgium and France. The mortality rate for women increased in Germany, but did not fall significantly in any of the countries shown.

Figure 17.15. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

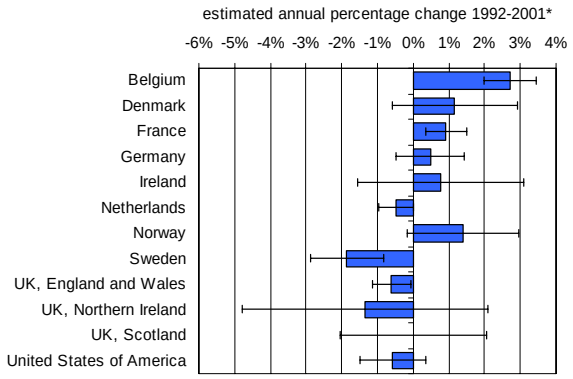
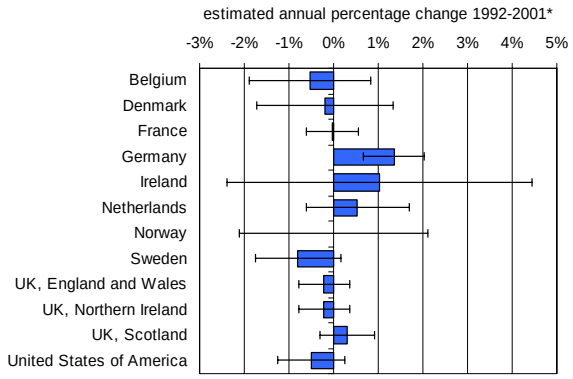


Figure 17.16. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



** or nearest available data period*

Table 17.3. Models chosen for predictions

model	*sex*	*prediction baseline*	*observations*	*model type*	*p (trend)*
all ages	males	1983-2002	72	log linear	0.0334
	females	1985-2002	78	log linear	0.0000
0-64	males	1979-2002	45	log linear	0.4499
	females	1991-2002	54	log linear	0.0069

Mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) for lymphoma in men are predicted to increase from 5.46 in 1998-2002 to 6.76 (95% prediction interval 5.48, 8.05) in 2015 (Table 17.4, Figure 17.17). The number of deaths in men is also predicted to increase, from 132 per year in 1998-2002 to 240 (197, 283) in 2015 (Figure 17.19). In men under 65 the mortality rate is predicted to increase, from 2.92 in 1998-2002 to 3.56 (2.57, 4.55) in 2015 (Figure 17.18), with an accompanying increase in the number of deaths, from 56 per year in 1998-2002 to 91 (66,116) in 2015 (Figure 17.19).

Table 4.5. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	5.46	5.75 (4.66, 6.84)	6.06 (4.88, 7.24)	6.36 (5.70, 7.02)
No. of deaths (95% PI)	144	167 (138, 196)	198 (163, 233)	240 (197, 283)
females, all ages				
WASMR (95% PI)	3.93	4.20 (3.32, 5.08)	4.46 (3.51, 5.41)	4.72 (4.19, 5.25)
No. of deaths (95% PI)	128	147 (120, 174)	173 (140, 206)	209 (168, 250)
males, 0-64				
WASMR (95% PI)	3.30	3.49 (2.58, 4.40)	3.52 (2.59, 4.45)	3.56 (2.57, 4.55)
No. of deaths (95% PI)	63	73 (54, 92)	83 (61, 105)	91 (66, 116)
females, 0-64				
WASMR (95% PI)	2.25	1.92 (1.17, 2.67)	1.74 (0.90, 2.58)	1.60 (0.65, 2.55)
No. of deaths (95% PI)	42	41 (25, 57)	42 (21, 63)	43 (17, 69)

Mortality rates for lymphoma in women are predicted to increase from 3.93 in 2002 to 4.98 (3.88, 6.08) in 2015. The number of deaths is also predicted to increase, from 118 per year in 1998-2002 to 209 (167, 250) in 2015. In women under 65 mortality rates are expected to decrease, from 1.97 in 1998-2002 to 1.60 (0.64 2.55) in 2015. The number of deaths in this age group is expected to rise, from 37 per year in 1998-2002 to 43 (17, 69) in 2015.

The numbers of deaths presented in Table 17.4 and in Figures 17.19 and 17.20 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 17.5 which shows the effect of population change in the absence of any trend in rates.

Of the projected increase of 108 deaths per annum in men between 1998-2002 and 2015, 77 (72%) are attributable to demographic change alone, while for women 58 deaths (63%) of the projected increase of 91 deaths per annum are attributable to demographic change.

Table 17.5. Predictions of number of deaths at all ages, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths	143	160	182	209	128	139	155	176
(95% PI)		(132, 187)	(152, 211)	(177, 242)		(114, 165)	(128, 182)	(146, 205)

Figure 17.17. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

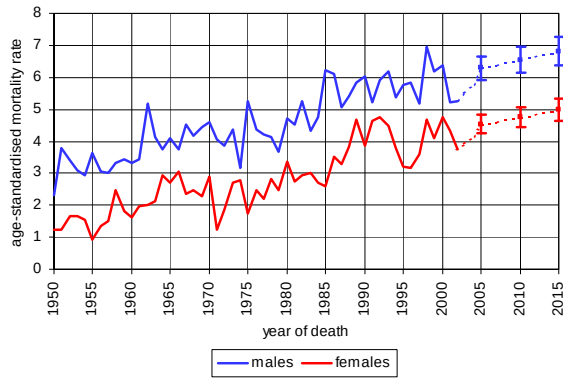


Figure 17.18. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

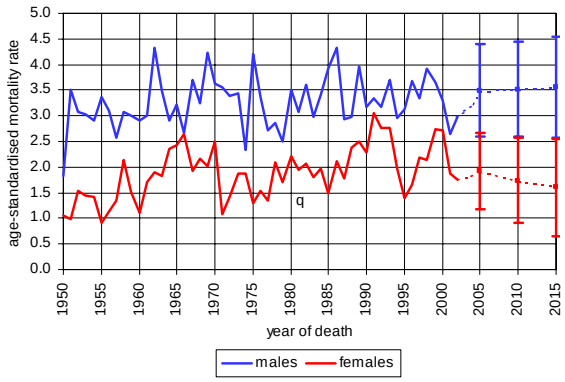


Figure 17.19. Actual and predicted number of deaths, all ages, 1950-2015

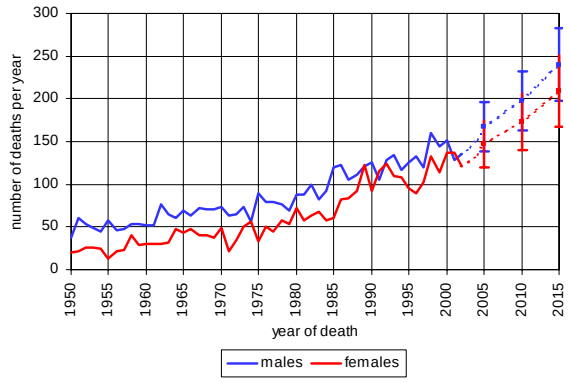
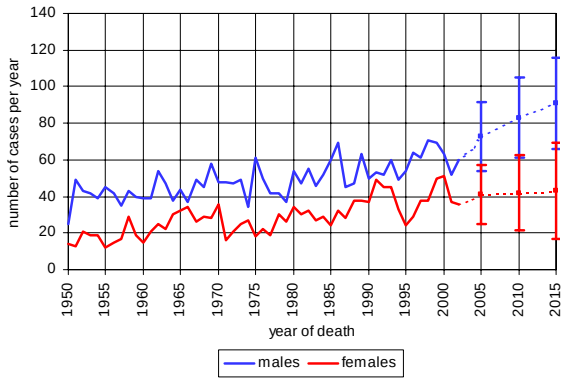


Figure 17.20. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

The number of lymphoma deaths increased from 37 to 135 in men between 1950 and 2002, and in women from 20 to 121. Most of this increase took place after 1980. Over the period 1950-2002 the age-standardised mortality rate appeared to increase steadily by about 1.3% annually for men and by 2.1% annually for women. For those under 65 any increase has been slight and not statistically significant. Age-period analysis shows that the increases in mortality have mainly occurred in those aged over 50.

International trends show an increase in mortality in all countries, but with a levelling-off since the mid 1990. The relative position of Ireland with regard to NHL mortality has worsened considerably since 1950.

Predictions

The age-standardised mortality rate is expected to increase by 24% for men between approximately 2000 and 2015, and for women by 27%. The numbers of deaths are expected to increase by 82% and 77%, respectively, over the same period. For those under 65, the rate is expected to increase by 22% between c.2000 and 2015 for men but to decrease by 19% for women, while the number of deaths is predicted to increase by 62% for men and show no change for women.

Conclusions

Non-Hodgkin lymphoma, which accounts for the great majority of lymphoma deaths, is a heterogeneous condition, possibly with multiple aetiologies. No useful prevention or screening strategies exist for it at present. Although mortality from the condition is falling in most countries, the incidence is generally reported to be increasing, (Clarke and Glaser, 2002; Bhurgri et al, 2005; Broccia et al, 2001) suggesting that most, if not all, of the fall in mortality is due to better survival. Whether this is due to earlier diagnosis or better treatment, the failure of Irish rates to fall, unlike those in most of Europe and the US, is troubling.

Chapter 18. Leukaemia (ICD-9 204-208)

Epidemiology

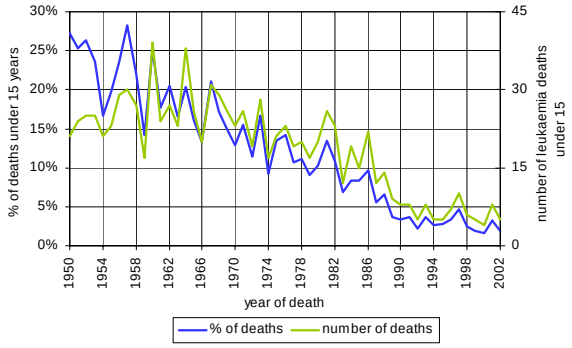
Leukaemia is not a single condition, but consists of two main types—lymphoid and myeloid—and three less frequent types. Each type is further subclassified as acute, subacute and chronic (Table 18.1). The predominant leukaemia in children is acute lymphoid, and, in adults, chronic lymphoid and chronic myeloid are the commonest types. Leukaemia and brain cancer are the two commonest causes of cancer mortality in children, causing 30% of all cancer deaths in the under-15s. In 1950 deaths of children under 15 made up 27% of all leukaemia deaths (Figure 18.1), but they now (because of substantial improvements in survival) make up only 3%, and contribute very little to overall trends. Predictions of future leukaemia trends, are therefore, largely dependent on trends in chronic lymphoid and myeloid leukaemia in adults.

Leukaemia was the 12th commonest cancer and the 11th commonest cause of cancer death in the period 1994-2002, with an annual average of 373 cases and 225 deaths during this period. Females accounted for 42% of both cases and deaths.

Table 18.1.Types of leukaemia causing death, 1994-2002

		number of deaths 1994-2002			*% of all leukaemia deaths*	
	age at death	*0-14*	*15 and over*	*all*	*0-14*	*15 and over*
lymphoid leukaemia	acute	37	169	206	61%	8%
	chronic	1	459	460	2%	23%
	unspecified	7	59	66	11%	3%
all lymphoid		45	687	732	74%	34%
myeloid leukaemia	acute	10	561	571	16%	28%
	chronic	1	248	249	2%	12%
	myeloid sarcoma	0	1	1	0%	0%
	unspecified	1	43	44	2%	2%
all myeloid		12	853	865	20%	43%
monocytic leukaemia	acute	0	12	12	0%	1%
	chronic	0	3	3	0%	0%
	other	0	1	1	0%	0%
other specified leukaemia	unspecified	0	1	1	0%	0%
	erythroleukaemia	0	2	2	0%	0%
	megakaryocytic	1	0	1	2%	0%
other leukaemia	acute	1	48	49	2%	2%
	chronic	0	8	8	0%	0%
	other	0	2	2	0%	0%
all other leukaemia	unspecified	2	385	387	3%	19%
		4	462	466	7%	23%
all leukaemias	acute	48	790	838	79%	39%
	chronic	2	718	720	3%	36%
	other	11	494	505	18%	25%
	total	61	2002	2063		

Figure 18.1. Number and percentage of leukaemia deaths in children under 15, 1950-2002



Death from leukaemia occurs predominantly in the older population: 44% of cases and 61% of deaths were in patients of 70 and older, as compared to 46% of cases and 58% of deaths for all cancers combined (Table 18.2).

Table 18.2. Age distribution of leukaemia deaths and cases 1994-2002

	female		*male*		*both*	
age at death or diagnosis	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*	*% of deaths at all ages*	*% of cases at all ages*
<30	11%	16%	12%	13%	12%	15%
30-39	3%	4%	3%	4%	3%	4%
40-49	2%	7%	3%	6%	3%	6%
50-59	5%	11%	7%	12%	6%	11%
60-69	8%	17%	20%	22%	15%	20%
70-79	29%	25%	32%	27%	31%	26%
80+	41%	20%	23%	16%	30%	18%

Survival from leukaemia is relatively poor. Data from EUROCARE 3 (Sant et al. 2003) for patients diagnosed in 1990-1994 showed mean five-year relative survival to be 39% for men and 38% for women, while patients diagnosed in 1978-1985 were shown in a similar study to have a survival of 26% for both men and for women (Berrino et al. 1995).

Five-year relative survival for patients diagnosed in Ireland in 1994-1996 was 39.0% (95% CI 33.3-44.6%) for men and 48.8% (42.5-55.1%) for women and, in 1997-1999, 42.8% (35.4-50.2%) for men and 45.3% (36.3-54.2%) for women (National Cancer Registry 2003).

Non-genetic risk factors

Chronic lymphoid leukaemia

Chronic lymphoid leukaemia (CLL) rarely occurs before the age of 40 and is thought to be a spontaneously occurring disorder of lymphocytes. There are no firmly established risk factors. The role of radiation is controversial (Richardson, Wing et al. 2005) but it seems unlikely that it has a significant part in the aetiology of the disease.

Chronic myeloid leukaemia

Some studies have reported chronic myeloid leukaemia following irradiation (Walgraeve, Verhoef et al. 1991; Corso, Lazzarino et al. 1995; Richardson, Wing et al. 2005) and an increased incidence has been reported in atom-bomb survivors. No other aetiological factors have been established.

Acute leukaemia

Acute leukaemia in adults is usually the end-stage of a chronic leukaemia. A number of aetiological factors have been suggested for acute lymphoid leukaemia (the predominant form) in children, among them being infection, ionizing and non-ionizing radiation and chemicals (Lightfoot T 2005).

Trends

Between 1950 and 2002, the annual number of deaths from leukaemia rose from 45 to 157 in men and from 32 to 110 in women, corresponding to an average increase, over the whole period, of 1.6% per year for men and 1.8% for women (Figure 18.2). Crude mortality rates increased by, on average, 1.0% annually for men and 1.2% annually for women (Figure 18.3). Total age-standardised rates (Figure 18.4) increased to a lesser extent—by 0.6% annually for men and 0.2% for women—but fell for those under 65 (Figure 18.5). For the population under 65, the cumulative risk of dying before age 65 fell by 0.7% annually in men and 0.9% in women (Figure 18.6), while years of potential life lost also fell, by 1.6% annually in men and 1.2% in women (Figure 18.7). Trends since 1992 indicate a non-significant annual decrease in total age-standardised mortality rates for males (Figure 18.16) and a non-significant annual increase for females (Figure 18.17).

Figure 18.2. Number of deaths per year, 1950-2002

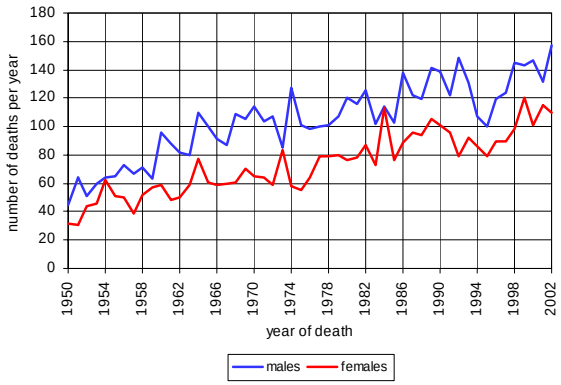


Figure 18.3. Crude mortality rate, 1950-2002

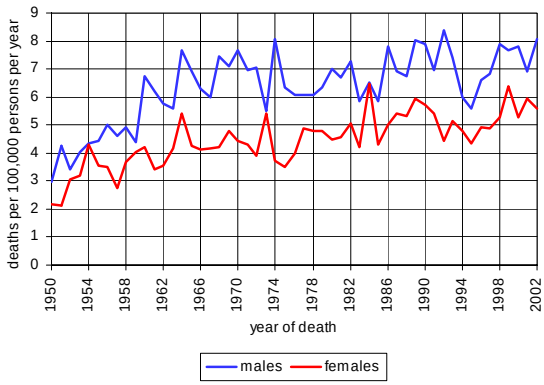


Figure 18.4. World age-standardised mortality rate, all ages, 1950-2002

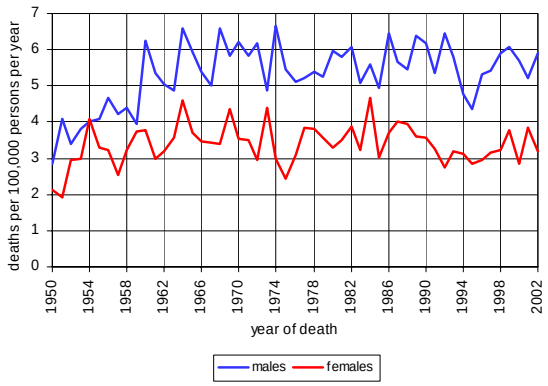


Figure 18.5. World age-standardised mortality rate, 0-64 years, 1950-2002

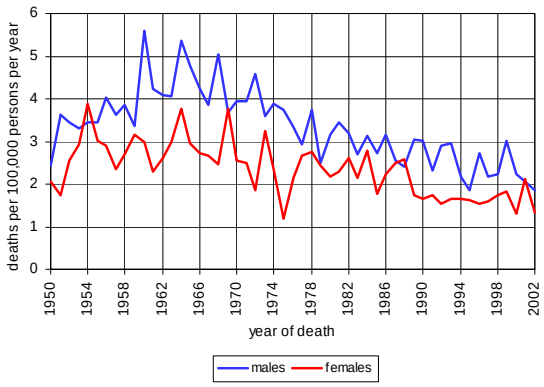


Figure 18.6. Cumulative risk of dying of cancer before age 65, 1950-2002

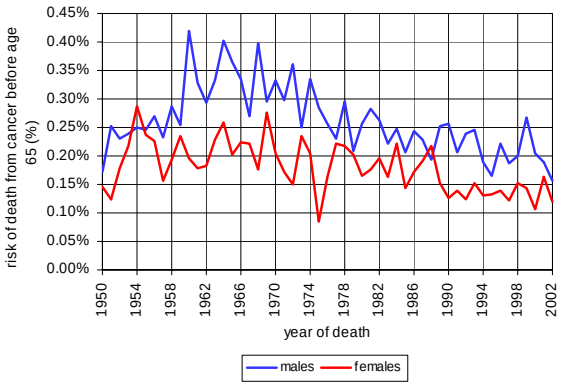
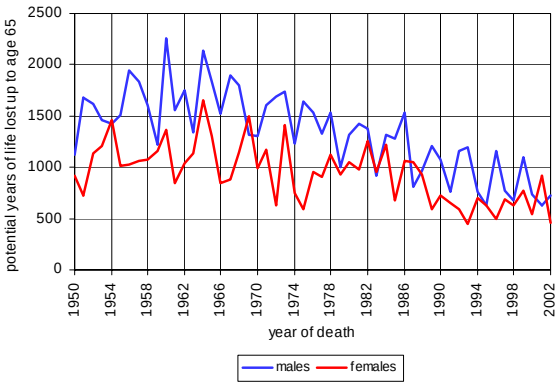


Figure 18.7. Years of potential life lost up to age 65, 1950-2002



Joinpoint regression analysis

Table 18.3. Joinpoint models: points of inflection and estimated annual percentage change in age-standardised rate (EAPC), 1950-2002

males, all ages		*females, all ages*		*males, 0-64*		*females, 0-64*	
joinpoint	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*	*joinpoint*	*EAPC*
1950		1950		1950		1950	
↓	3.9% (2.1%, 5.8%)	↓	16.2% (-2.0%, 37.8%)	↓	2.9% (1.1%, 4.7%)	↓	16.1% (-2.3%, 38.0%)
1964 (1959, 1968)		1954 (1952, 1966)		1964 (1959, 1966)		1954 (1952, 1956)	
↓	-0.1% (-0.4%, 0.2%)	↓	-0.2% (-0.5%, 0.1%)	↓	-2.0% (-2.4%, -1.7%)	↓	-1.5% (-1.9%, -1.1%)
2002		2002		2002		2002	

95% confidence intervals for the inflection points and annual percentage change are given in brackets

The Joinpoint model of age-standardised rate for men showed an initial increase in rate of 3.9% per annum from 1950 to 1964 (Table 18.3, Figure 18.8) with no significant trend thereafter. For women, the rate increased rapidly, by 16.2% annually, up to 1954, but since then, as with men, there has been no significant trend.

For men and women under 65, after early increases in mortality rate, there has been a steady decrease, by 2.0% annually for men and 1.5% for women (Figure 18.9).

Figure 18.8. Joinpoint models and actual World age-standardised mortality rate, all ages, 1950-2002

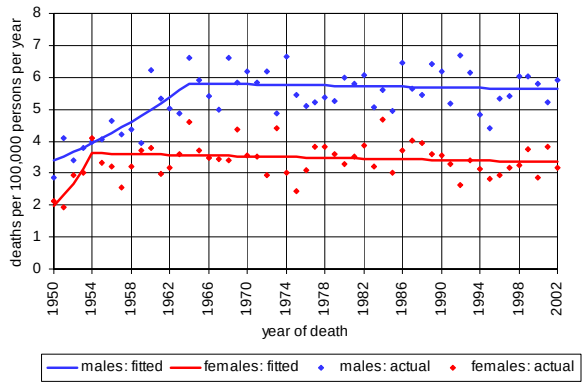
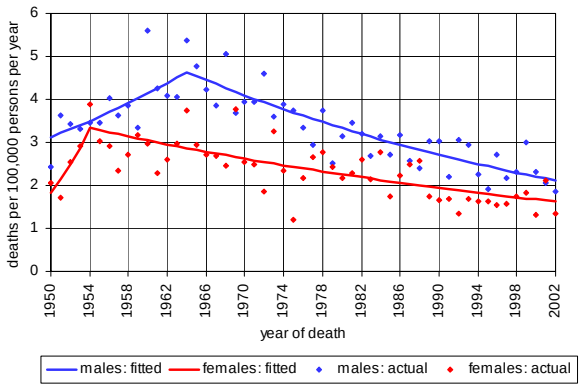


Figure 18.9. Joinpoint models and actual World age-standardised mortality rate, 0-64, 1950-2002



Age-period-cohort trends

The age-period analyses show an increase in mortality for all age groups above 65, for both men and women (Figures 18.10, 18.11). The rate of increase is small, but has been consistent since 1953. For younger age groups there is no evidence of any significant trend. There was little evidence that year of birth had any effect on mortality, independent of age or period of death for either men or women (Figures 18.12, 18.13).

Figure 18.10. Age-specific mortality by period of death, males, 1950-2002

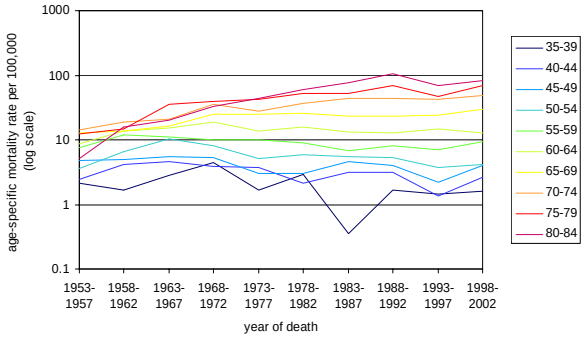


Figure 18.11. Age-specific mortality by period of death, females, 1950-2002

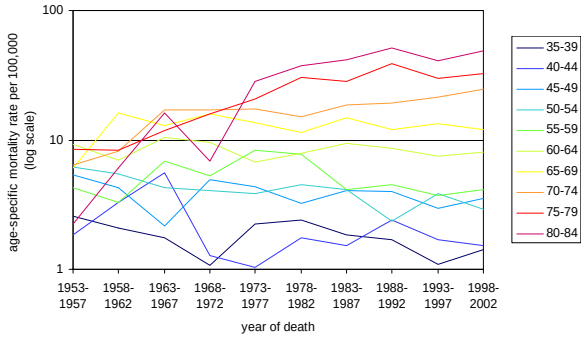


Figure 18.12. Age-specific mortality by birth cohort, males, 1950-2002

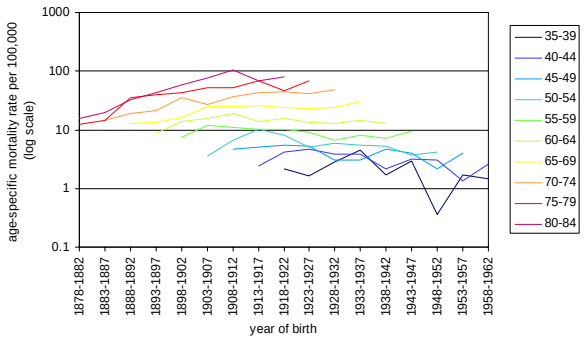
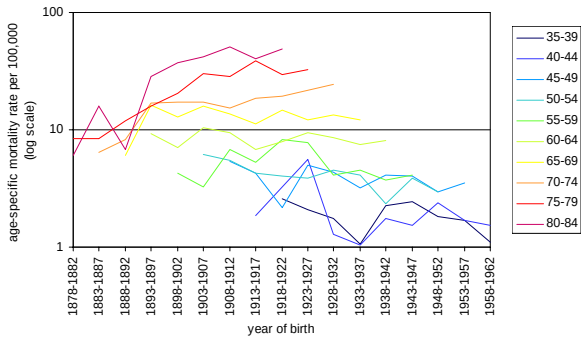


Figure 18.13. Age-specific mortality by birth cohort, females, 1950-2002



International trends

All countries studied (with the exception of Ireland for women) have similar time trends in leukaemia mortality, at least until the mid 1990s (Figures 18.14, 18.15). For both men and women, mortality increased in the 1950s and 1960s, and began to decrease around 1970. A recent increase in mortality in men can be seen in the UK, Ireland and Denmark. Ireland appears to be the only country with an apparent recent increase in mortality in females; however, the number of deaths in Ireland is small compared to most other countries and the trend may be due to random year-to-year variation (Figures 18.16, 18.17).

Figure 18.14. Rolling 5-year average World age standardized mortality rates in Europe and USA, males, all ages, 1950 to 2002

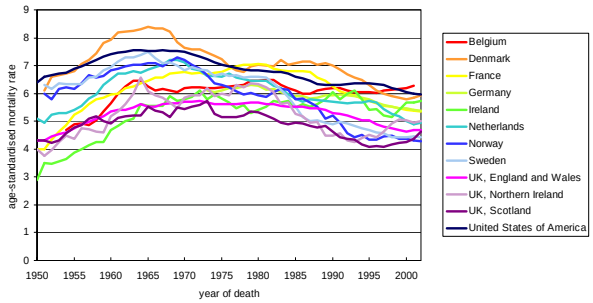
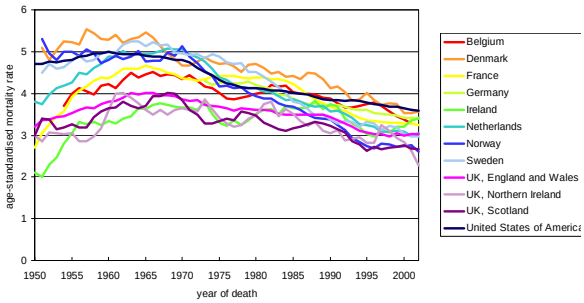


Figure 18.15. Rolling 5-year average World age standardized mortality rates in Europe and USA, females, all ages, 1950 to 2002



Recent estimates of change (Figures 18.16, 18.17) indicate significant falls in age-standardised mortality since 1992 for men in France, Germany, the Netherlands and the USA and for women in France, Germany and the USA. There were no significant increases in mortality.

Figure 18.16. Annual percentage change in mortality rate in Europe and USA, males, 1992-2001*

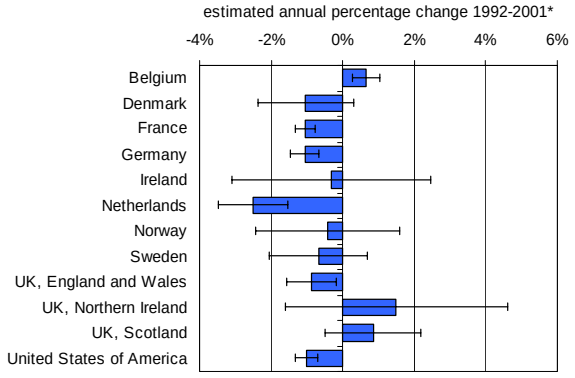
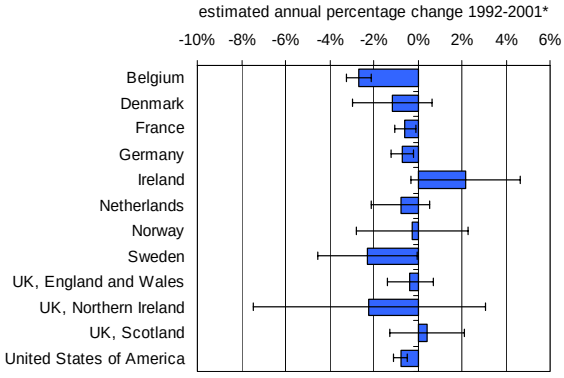


Figure 18.17. Annual percentage change in mortality rate in Europe and USA, females, 1992-2001*



**or nearest available data period*

Table 18.4. Models chosen for predictions

model	*sex*	*prediction baseline*	*observations*	*model type*	*p (trend)*
All ages	males	1989-2002	129	log-linear	0.0361
	females	1983-2002	159	log-linear	0.0854
0-64	males	1979-2002	234	log-linear	0.1283
	females	1979-2002	234	log-linear	0.1108

Table 4.5. Predictions of mortality rates and number of deaths to 2015

	1998-2002	*2005*	*2010*	*2015*
males, all ages				
WASMR (95% PI)	5.80	5.56 (4.44, 6.69)	5.59 (4.28, 6.89)	5.67 (4.09, 7.25)
No. of deaths (95% PI)	148	151 (122, 181)	174 (134, 214)	209 (151, 266)
females, all ages				
WASMR (95% PI)	3.37	3.19 (2.44, 3.93)	3.13 (2.36, 3.90)	3.09 (2.28, 3.90)
No. of deaths (95% PI)	109	112 (88, 36)	125 (97, 154)	144 (108, 180)
males, 0-64				
WASMR (95% PI)	2.30	2.14 (1.43, 2.85)	2.00 (1.31, 2.69)	1.87 (1.18, 2.57)
No. of deaths (95% PI)	42	44 (29, 58)	46 (30, 62)	47 (30, 65)
females, 0-64				
WASMR (95% PI)	1.66	1.43 (0.84, 2.01)	1.29 (0.73, .85)	1.18 (0.63, 1.72)
No. of deaths (95% PI)	30	28 (17, 40)	29 (16, 41)	28 (15, 42)

Leukaemia mortality rates (all rates are World age-standardised mortality rates per 100,000 person-years) in men are predicted to remain fairly steady, from 5.80 in 1998-2002 to 5.67 (95% prediction interval 4.09, 7.25) in 2015 (Table 18.5, Figure 18.18,). The number of deaths in men is predicted to increase, from 148 per year in 1998-2002 to 209 (151, 266) in 2015 (Figure 18.20). In men under 65 the mortality rate is predicted to fall, from 2.30 in 1998-2002 to 1.87 (1.18, 2.57) in 2015 (Figure 18.19), with the number of deaths increasing slightly from 42 per year in 1998-2002 and 47 (30, 65) in 2015 (Figure 18.21).

Mortality rates in women are predicted to fall from 3.37 in 1998-2002 to 3.09 (2.28, 3.90) in 2015. The number of deaths is predicted to rise, from 109 per year in 1998-2002 to 144 (108, 180) in 2015. In women under 65 mortality rates are expected to fall more markedly, from 1.66 in 1998-2002 to 1.18 (0.63, 1.72) in 2015. The number of deaths in this age group is expected to show little change, from 30 per year in 1998-2002 to 28 (15, 42) in 2015.

The numbers of deaths presented in Table 18.4 and in Figures 18.20 and 18.21 are based on two factors—an underlying trend in the mortality rate and changes in the age composition and size of the population. The latter has a major impact on cancer mortality, as can be seen from Table 18.6, which shows the effect of population change in the absence of any trend in rates.

In the absence of the downward trend in rate, demographic change would result in an additional 64 deaths per year in men (a 44% increase over the 1998-2002 average) and 37 in women (a 34% increase) by 2015.

Table 18.6. Predictions of number of deaths at all ages, based on population changes only, 2005-2015 (assuming that 1998-2002 average rates continue to apply)

	males				*females*			
	1998-2002	*2005*	*2010*	*2015*	*1998-2002*	*2005*	*2010*	*2015*
No. of deaths	145	160	183	212	109	118	131	146
(95% PI)		(133, 188)	(153, 212)	(180, 245)		(95, 142)	(106, 156)	(120, 173)

Figure 18.18. Actual and predicted World age-standardised mortality rates, all ages, 1950-2015

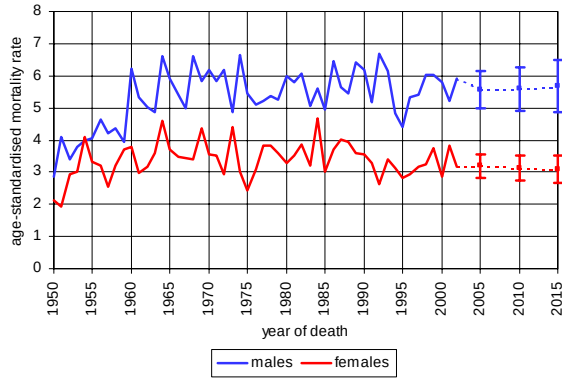


Figure 18.19. Actual and predicted World age-standardised mortality rates, 0-64 years, 1950-2015

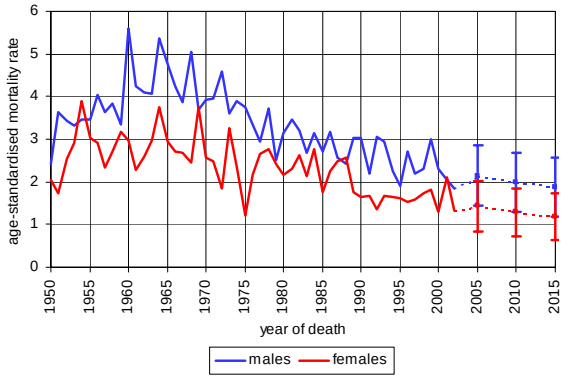


Figure 18.20. Actual and predicted number of deaths, all ages, 1950-2015

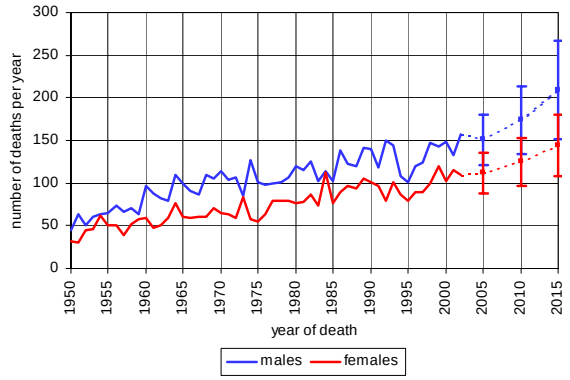
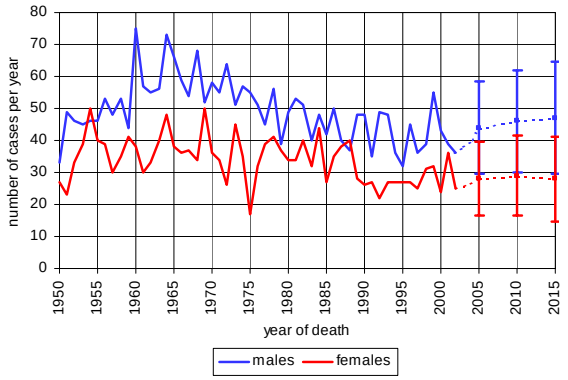


Figure 18.21. Actual and predicted number of deaths, 0-64 years, 1950-2015



Notes:
1. Data to 2002 are actual values. The points at 2005, 2010 and 2015 represent predicted values.
2. The vertical bars at each predicted point give the 95% prediction interval.

Historical trends

The number of deaths from leukaemia increased from 45 to 157 in men and from 32 to 110 in women between 1950 and 2002. Over the same period the age-standardised mortality rate rose by, on average, 1.4% annually for men and 0.8% for women. Joinpoint analysis showed that most of this increase took place in the in the 1950s and early 1960s, and that more recently there has been no significant overall trend for both either men or women. For those under 65, the same increase in mortality was seen in the 1950s and 1960s, but since then the mortality trend has been significantly downwards, by 2.0% annually for men and 1.5% annually for women.

International trends are similar, with an increase in mortality in most countries to the mid 1960s and a fall since then.

Predictions

Age-standardised rates are predicted to fall slightly for both men and women, by <8% between c.2000 and 2015, while the number of deaths is expected to increase by 41% and 32%, respectively. In those under 65, the rates are predicted to fall more markedly, by 19% in men and by 29% in women, while the number of deaths is expected to increase by 12% in men and fall slightly in women.

Conclusions

The increase in leukaemia deaths in the 1950s and 1960s is likely to have been due to improved diagnosis, particularly in the elderly. The overall gradual fall in mortality since then, taken with increasing incidence, is likely to be due to improvements in treatment—particularly in those aged under 65. At least part of the increasing incidence can be attributed to greater awareness and pickup of chronic lymphocytic leukaemia in the elderly.

As the aetiology of the great majority of cases is unknown and no useful screening tests exist, future falls in mortality are likely to depend on continuing improvements in treatment.

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