

Special Issue

Long-term cancer survival: patterns and trends in Norway 1965-2007

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Introduction

Alongside statistics on cancer incidence and mortality, cancer survival provides a means to assess the effectiveness of early detection strategies and the quality of clinical care and management. The objective of this Special Issue is to provide descriptions of patterns of long-term cancer survival in Norway today, and illustrate the major trends in cancer survival over the last 40 years. The Cancer Registry of Norway is national and population-based, and therefore this report summarises the overall survival experience of cancer patients nationally, permitting valid comparisons of cancer survival in successive calendar periods.

The report includes detailed site-specific survival analyses of patients diagnosed with 23 common forms of cancer in Norway today. The combined incidence of these cancers represents over 85% of the approximately 26 000 new cancers diagnosed in 2007. The statistics used in this report were selected to reflect a number of diverse methodological developments during the last decade that either improve the validity of the survival estimates, or provide insight into aspects of clinical care and future prospects for cancer patients. For example, the data are analysed using the so-called *period approach*, a method that enables the most recently-diagnosed patients (including those diagnosed in 2007) to be included in the survival calculations. Further, we include methods that attempt to better quantify the lives of cancer patients beyond their initial diagnosis: *conditional survival* is used to estimate the prognosis of patients already surviving a given number of years after diagnosis. Analysis of the *proportion cured* and the *median survival time* of those *uncured* for each cancer is also undertaken, and should aid understanding of the reasons for increasing survival for certain cancers (better therapy, improving palliative care, or possibly, specific biases or artifacts in the data). A description of each method follows in the Data sources and methods section.

While the report is quite comprehensive in terms of methods and analysis, it is appropriately cautious with regards interpretation, and refrains from giving possible explanations for the site-specific survival analyses, pointing only to selected interesting (and possibly key) observations. The rationale is that many of the results are not self-explanatory and require multidisciplinary expertise to be deciphered adequately. This requirement and the inclusion of more sophisticated and informative model-based approaches provides an excellent

opportunity to bring together clinical and other specialists in mutual collaboration, with a view to providing informed conclusions instructive to public health policy and future planning. From 2009, the Registry will make a concerted effort to foster such collaborations among the health research community in Norway, with a view to generating peer-reviewed collaborative research articles focusing on the explanations and implications of these survival results for each of these 23 cancer sites.

This report does not attempt to assess the efficacy of specific therapeutic regimes against other prognostic factors, although many collaborative research studies have been conducted based on clinical registries for cancers of the rectum, ovary, prostate and CNS, and progress is being made towards establishing clinical registries for all common forms of cancer. The ongoing collection of detailed data on diagnostics, therapy, and follow-up of cancer patients in Norway will enable population-based survival research to go beyond its traditional limitations, towards an evaluation of the importance of specific diagnostic, treatment and management-related factors on cancer survival, both regionally and nationally.

We believe the statistics generated in this Special Issue provides key baseline cancer survival statistics in Norway, as well as important specific observations on the survival experience of Norwegian cancer patients that, in collaboration with the health and research community, will yield vital research and further our joint efforts towards the amelioration of cancer control in Norway.

Orientation in reading this report

Long-term cancer survival: patterns and trends in Norway 1965–2007 aims to provide a description of cancer survival in Norway for patients with one of 23 frequently diagnosed cancers today, as well as document the observed trends in the last four decades. The emphasis is on visual descriptions which provide both contemporary and historical perspectives of the survival of cancer patients in Norway. In the first section, Data sources and methods, the sources and quality control checks are documented, each survival method is explained, and an orientation to the layout of the main set of figures is given. The Results section provides a general description of survival variations by cancer site, sex and stage, and a site-by-site commentary of the patterns and trends that accompany the main body of this report, the Figures. A table of 1-, 5-, 10 and 15-year survival by site and sex, with 95% confidence intervals is also provided.

Data sources and methods

Data sources

The survival of cancer patients in clinical trials provides an indicator of the highest survival that may be achieved on the basis of the gold standard intervention. In contrast, population-based studies aim to examine cancer survival with a view to summarising the average survival and the collective impact of a wide range of cancer control activities. Geographical and temporal comparisons of population-based survival from cancer registries will then provide an indication of the average survival attainable in the population under study, as well as the relative success of diagnostic- and clinically-orientated aspects of cancer control over time.

Quality issues

Interpreting such survival estimates in unselected populations requires careful thought, given the variety of putative explanatory factors potentially involved^[1;2]. Black and colleagues^[1] have noted that survival is influenced by factors: 1) related to the health care system (including screening, diagnostic and treatment facilities, follow-up); 2) operating in relation to the host (e.g. age, sex, comorbidity, behaviour); 3) operating in relation to the tumour (e.g. topographic site, morphology, extent of disease), or 4) linked to the registry and its data quality (e.g. completeness of ascertainment and follow-up, accuracy of recorded data, extent of DCO proportion - death certificate only registrations).

Complete ascertainment of cancer cases, ensuring validity of items pertaining to diagnosis, and minimizing the DCO proportion are among the key aspects in ensuring that survival estimation is relatively free of bias and fit for comparisons^[2;3]. Artificial increases in survival can occur if, for example, there is incomplete registration, or if there is an over-reliance on the allocation of non-specific diagnostic categories. The reporting of neoplasms (and certain precancerous lesions) to the Cancer Registry of Norway has been compulsory following a directive from the Ministry of Health and Social Affairs in 1951, further strengthened by the Health Registry Act in 2002 that included statutory regulations and the requirement of appropriate institutions to report new cases to the Registry. This together with multiple source reporting and trace-back has long implied a high overall completeness at the Cancer Registry. This is now supported by the recent comprehensive review of data quality; completeness was estimated at almost 99% for the registration period 2001–5, although under-reporting was higher for haematological malignancies and cancers of the central nervous system^[4].

In terms of validity, the Registry's effective use of reports from pathology laboratories, clinical records and death certificates has been shown to provide reasonable and comparable accuracy, with only a small fraction of cancer registrations obtained solely from death certificate sources^[4]. A review of registrations 2001–5 showed that three-quarters of the main cancer sites had a DCO proportion of less than 1%, although for certain sites, including pancreatic and liver cancer, the percentages were higher, in the 3–4% range. For this report, the data were screened for certain anomalies including instances of negative survival duration, out-of-range dates of diagnosis and/or dates of death, and invalid vital status codes.

Survival data

Incidence data on all cancers recorded at the Registry for diagnoses 1965–2007 were obtained, together with follow-up on matching vital status with the Deaths Registry at Statistics Norway. The last follow-up date was set to 31 December 2007. A total of 23 common cancers were selected for analysis, and grouped according to their respective ICD-10 categories.

Figure S1: Inclusion and exclusion criteria

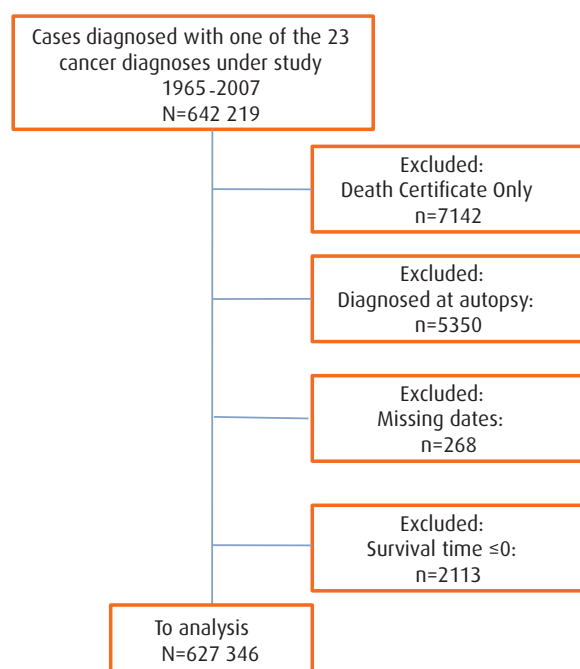


Figure S1 shows the inclusion and exclusion criteria applied for diagnosed cases over the whole study period 1965–2007. Beginning with a total of 642 219 registered diagnoses of the 23 cancers under investigation, we first excluded 7142 DCO cases (1.1%) and 5350 cases diagnosed at autopsy (0.8%). We then removed 268 cases for which a survival time could not be estimated as event dates were missing, and a further 2113 cases (0.3%) with either an erroneous

event date (survival time < 0) and or zero survival time (survival time = 0). Following these eliminations, 627 346 cases were included in the site-specific analyses described below, 97.7% of the number extracted prior to exclusions.

It has been shown that exclusion of patients with a prior cancer diagnosis (usually associated with inferior prognosis) may give higher estimates of survival^[5]. Patients with previous cancer diagnoses were therefore eligible for inclusion in site-specific analyses, thereby avoiding the potential reduction in precision on excluding such cases. Survival times were calculated from the recorded day of diagnosis and the recorded day of death, although it has been shown that less precise units of time (e.g. months) tend to only materially affect very short-term survival for certain sites e.g. within the first few months^[6], which is not a focus of this report.

Statistical methods

Relative survival

The survival time of a cancer patient may be defined as the time that elapsed between a cancer diagnosis and subsequent death. The most basic measure of survival is observed survival, with the 5-year observed survival representing the percentage of patients still alive 5 years after the date of diagnosis. Not all deaths among cancer patients will be due to the primary cancer under study, and deaths from other causes will lower the survival and invalidate comparisons between populations, where the probabilities of death in the general population vary. Relative survival is calculated to circumvent this problem by providing an estimate of *net survival*, and is defined as the observed survival proportion in a patient group divided by the expected survival of a comparable group in the general population with respect to age, sex and calendar period of investigation. At each time t since diagnosis, the relative survival from the cancer, $R(t)$, is defined as follows:

$$R(t) = So(t)/Se(t)$$

where $So(t)$ is the observed survival of cancer patients while the calculation of expected survival $Se(t)$ is based on matching the major demographic characteristics of the patients to the general population. This was achieved using the Norwegian population life tables, available from Statistics Norway by 1-year age group, sex, and 1-year calendar period. While these tables do not exclude patients diagnosed with the specific cancers under investigation in this report, it has been shown that the impact on the estimated survival proportions is, for practical purposes, negligible^[7].

The methods for estimating expected survival depend on the length at which an individual is considered at risk^[8]. The method of Hakulinen^[9] was used

whereby the survival time of the matched individual is censored at the same survival time that the cancer patient is censored. In instances where the cancer patient dies, the matched individual is assumed to be at risk until the closing date of the study. Expected survival proportions are therefore adjusted for potentially heterogeneous follow-up times among patients, are independent of their observed mortality, and are considered more appropriate for estimating longer-term (10 years or more) expected survival than the Ederer I and Ederer II methods^[8;10].

In summary, the major advantages of relative survival is that information on cause of death is not required and it provides a measure of the excess mortality experienced by patients diagnosed with cancer, irrespective of whether the excess mortality is directly or indirectly attributable to the cancer. This estimate of net survival is therefore used throughout this report.

Period analysis

The period approach to survival analysis is now well-established in its application to relative survival, in which it projects the survival obtained from cohorts of cancer patients diagnosed in different years. With traditional cohort-based analyses, the most up-to-date estimates of longer-term survival would have pertained to patients diagnosed in the distant past, with corresponding levels of prognosis. In contrast, period-based analyses consider the survival experience in recent years.

More technically, only person-time at risk and events (death or censoring) occurring during a specified calendar period are considered in the period approach. The estimates of survival proportions are obtained on left truncation of all observations at the beginning of the period and right censoring at the end of the period^[5;11;12].

Cohort estimates represent the survival experience of a defined and followed-up cohort of patients diagnosed during a specified calendar period, whereas period estimates do not represent the survival of a real cohort of patients. Rather, they represent the survival that would have been observed for a hypothetical cohort of patients who experienced the same interval-specific survival as the patients who were actually at risk during a specific calendar period. On the basis of empirical studies comparing the two methods using historical data, Brenner and Hakulinen have concluded that period analysis should be used for routine purposes so as to advance the detection of progress in long-term cancer patient survival^[12]. Both clinicians and patients are primarily interested in up-to-date estimates of survival, and the period method reflects the most recent developments in cancer care.

To allow for sufficient follow-up, traditional estimates of n -year survival have been calculated from patients diagnosed at least n years back in time (the *cohort* approach). For long-term (10- or 15-year) survival estimates, this approach results in outdated cumulative survival estimates where survival in recent intervals has been improving^[12]. Using data from a recent time period (the *period* approach), the cumulative survival can be estimated based on the most recently available data. Thus, for a one-year period window, information from the latest 0, 1, 2, . . . , n years are used in its estimation, as interval-specific survival probabilities are based on contributions from patients diagnosed 0, 1, 2, . . . , n years back in time.

If survival is constant over time, the period and cohort estimates will be equal, while if survival is increasing with time, the period estimates will be more up-to-date and higher than the cohort estimates achievable at the time of analysis. However, period estimates of 15-year survival will, for example, be lower than the equivalent cohort estimates were we to wait and observe the true survival.

In this report, we have used a three-year period window (2005–2007) for the 15-year relative survival analyses, thus accruing sufficient case numbers to ensure the estimates are reasonably up-to-date while retaining an acceptable degree of precision. For the trend analyses, a three-year moving window was used from 1965 to 2007.

Long-term survival

Long-term survival estimates and long-term trends are included in this report, achievable given the lengthy time span of the cancer series at the Registry. Brenner and Hakulinen have provided a convincing rationale for the inclusion of long-term estimates as part of routine cancer survival analyses^[12]. Firstly, 15-year survival will reflect the positive advances seen in cancer care including earlier diagnosis and more effective therapy. Secondly, as rates of other major causes of death have been on the decline, remaining life expectancy at the average age of cancer onset has risen, making long-term survival estimates more meaningful than previously. Finally, the introduction of the period approach to survival analysis, as described above, has opened new perspectives on deriving up-to-date, long-term survival estimates.

Estimating the cure fraction

The point of *statistical cure* is reached when the group of patients have the same mortality as the group of individuals without cancer (for a given age and sex), and the cured proportion is approximated where the cumulative relative survival curve reaches a plateau. In

contrast, *clinical cure* is determined on basis of lack of specific symptoms of the individual, for example, an individual patient may be considered medically cured if all cancerous cells are considered to be eradicated. Specialised survival analysis models have been developed, known as cure models, to predict this cure fraction^[13;14]. In this report the commonly-applied *mixture* model was fitted under the assumption that there exists a cured and an uncured group defined at the time of diagnosis. Estimates of the *proportion cured* and the *median survival time for those uncured*, adjusted for the background (population) mortality were obtained. These mixture cure fraction models are of the form:

$$S(t) = S^*(t)(\pi + (1 - \pi)Su(t))$$

where $S^*(t)$ is the expected survival, π is the proportion cured (*the cure fraction*), $(1 - \pi)$ is the proportion 'uncured' (or those 'bound to die' fatal cases) and $Su(t)$ is the survival function for the uncured individuals. $Su(t)$ is usually the Weibull parametric survival curve function that may vary by age group and period of diagnosis.

The cure model was fitted in this report by applying two different approaches. To estimate trends 1965–2007 in the proportion of cured patients, and the median survival of fatal cases, the *complete* approach was used, whereby all diagnosed cases over the period irrespective of the length of their follow-up were used in the estimations. The main focus here was on estimating changes in trends for patients diagnosed at different five-year time periods, hence period of diagnosis was modeled as a covariate. To provide an up-to-date estimate of the proportion of cured patients and the median survival of uncured cases, the model was fitted using the period method for the window 2005–7.

It was not possible to fit the cure fraction for eight of the 23 cancer sites. For a number of cancer forms, it was reasonable to assume that *statistical cure* could not be estimated as *medical cure* is not established in patients even several decades after diagnosis (melanoma of the skin, female breast cancer, prostate cancer). For the remaining five sites (cervical, endometrial, testicular and thyroid cancer, as well as Hodgkin lymphoma), it is possible that the underlying Weibull distribution may not be sufficiently flexible to capture the shape of the long-term survival curves. Another explanation could relate to the use of general lifetables that insufficiently represent the demographics of the patient groups.

Where estimates could be derived, particular caution must be applied in their interpretation. The existence of a cured and an uncured group of patients is a necessary but strong assumption underlying the mixture model. The absolute estimates of the cured frac-

tions are speculative, particularly for those sites where statistical cure is not clearly indicated e.g. where long-term relative survival fails to reach a plateau.

Conditional survival

The majority of cancer survivors wish to obtain information on their current prognosis, once they have survived a certain period of time after diagnosis. Conditional survival analysis is a key indicator in this respect, estimating survival proportions on the pre-condition that patients have already survived a certain duration of time^[15;16]. Prerequisites for its estimation are long-term and complete follow-up. Analogous to statistical cure, the point at which conditional 5-year relative survival reaches 100% is the point where there is no excess mortality among the cancer patients, and prognosis is equivalent to that experienced in the general population. As with the 15-year relative survival analyses, we have used a three-year period window (2005–2007) for the 10-year conditional survival analyses.

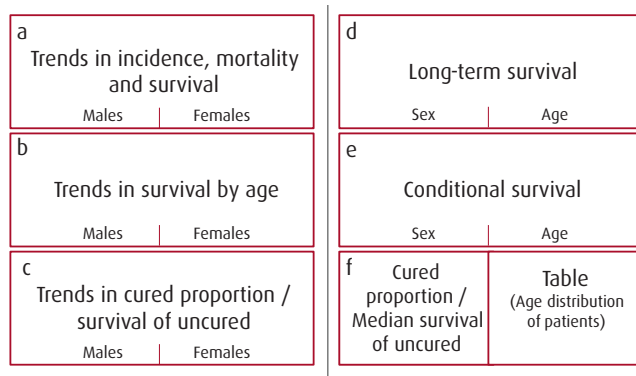
Statistical software

All computations were conducted using the statistical software Stata^[17]. The *strs* (version 1.2.8) command was used for life table estimation of relative survival^[18]. The *strsmix* command (version 1.0.2) was used to fit the mixture cure fraction models^[14].

Survival of cancer patients: a visual description

One of the aims of this report is to provide a comprehensive visual description of contemporary survival and trends for each of 23 frequent cancers in Norway today. Long-term survival and survival trends are conveyed as a series of figures according to the double-page layout in Figure S2 below. Further details of each plot are also provided.

Figure S2: Layout of figures



a Trends in incidence, mortality and survival

Ideally, the evaluation of the complex processes underlying progress in cancer control, trends in incidence, mortality and survival should be examined simultaneously, and we have plotted these in the *top left panel*. All estimates were age-adjusted; incidence and mortality rates were standardised according to the World standard population, while the relative survival probabilities are age-adjusted according to the proposed standard populations of Corazziari *et al*^[19]. The latter consists of three sets of weights that capture the age-incidence patterns for different cancers: (1) those increasing with age (the vast majority of cancers); (2) those broadly constant with age and (3) those mainly affecting young adults. The weights for the age 15–44 were extended in this analysis to include the age group 0–44. Trends were plotted unadjusted for five neoplasms (cancers of the pancreas, lung, testis, central nervous system and Hodgkin lymphoma) as age-specific numbers were sparse in certain years and the standardised estimates could not be calculated. All plotted curves were smoothed using five-year moving averages in an attempt to remove some of the inherent random variation in the estimates.

b Trends in survival by age

The *middle left panel* plots the sex-specific trends in relative survival (three-year period window) 1965–2007 according to five age groups, defined *a priori*, on the basis of clinically relevant groupings. In an attempt to partially account for some of the inherent random variation, the plotted curves were smoothed by applying the *lowess method* (with a bandwidth of 0.8), a locally-weighted regression smoother with useful locality properties and a (desirable) tendency to follow the data, as described in Cleveland^[20].

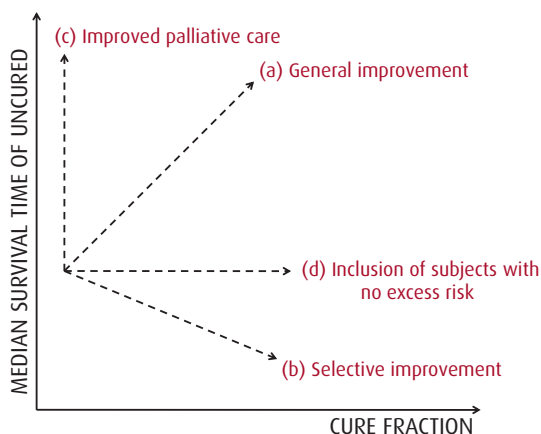
c Trends in the cured proportion and survival of uncured

The *bottom left panel* shows trends in the estimates of proportion of cured patients, as well as the estimated median survival of those who remained uncured (and eventually die of their cancer). The plotted estimates were calculated from successive five-year periods 1965–2007.

The reasons for changes over time in the proportion of cured patients and median time of fatal cases are complex^[13;21;22]. Possible scenarios in terms of trends in the two model-based quantities are depicted in Figure S3, after Verdecchia *et al*^[13]. According to Lambert *et al*^[21], Scenario (a) represents a general improvement, whereby an increasing proportion of patients are cured and those patients we are unable to cure have a longer median survival time. Scenario (b)

suggests selective improvement in that treatment effectiveness is selective, enabling cure of those patients who previously would have had a longer survival time (among the uncured). Scenario (c) might occur following improved palliative care but, alternatively, could arise if new diagnostic techniques were brought into the health care system, advancing the time of diagnosis without affecting the time of death (lead time bias). Lambert *et al*^[21] have noted an appealing property of cure models; the cured fraction cannot be affected by this bias, so other factors must account for observed increases in the proportion cured. Finally, scenario (d) might occur where the introduction of a specific diagnostic procedure resulted in the inclusion of a subset of patients at no excess risk relative to the general population.

Figure S3: Scenarios for trends in proportion cured and median survival of the uncured



d Long-term survival

The *top right panel* plots long-term relative survival for males and females up to 15 years after diagnosis, using the period approach described above. Relative survival curves were not plotted for the oldest age group beyond five years.

e Conditional survival

The *middle right panel* shows survival curves conditional on being alive up to 10 years after diagnosis by sex (left) and age (right). Conditional survival was not plotted where it was considered there were too few cancer survivors. In addition, the estimates were not plotted for the oldest age group, although the 5-year relative survival was denoted by a closed circle. Conditional survival estimates above 100% were not plotted.

f Cured proportion and median survival of uncured

For the majority of cancers, one assumes that a certain fraction of the patients will be cured (in the sense that their mortality will be the same as observed in the general population), while a certain proportion will not

be cured and eventually die of their cancer. In the *bottom right panel* we illustrate this situation for both sexes combined, given a follow-up of fifteen years. The survival of the cured group reaches a plateau (the curve is almost touching a line representing the proportion cured) while the curve for the uncured patients continues its decline to zero indicating, that all these uncured patients died. The oldest age group was excluded from these analyses. For some cancer sites, a clear plateau in the long-term survival estimates is never reached so the proportion cured could not be estimated.

Table (orientation)

A table provides the age and sex distribution of patients diagnosed 2003–7.

Results

We begin with a brief description of certain variations in recent survival by cancer site, sex and stage, followed by a site-by-site commentary outlining the observed patterns and trends in the corresponding figures for each of the 23 sites.

Cancer-specific variations in relative survival

There is substantial variability in short- and long-term patient survival dependant on the form of cancer diagnosed. Figure S4a–c shows the respective distribution of sex-specific survival estimates 1, 5 and 15 year(s) after diagnosis of each of the 23 cancers examined. There is an 80 percentage point survival difference between cancers associated with very poor and very good prognosis (e.g. pancreatic cancer and thyroid cancer, respectively). The survival proportion associated with the latter neoplasm — as well as Hodgkin lymphoma and melanoma of the skin — exceeds 70% both in the short term (one year after diagnosis) and in the long term (15 years after diagnosis). Indeed, one-year survival is above 70%, and five-year survival above 50% for 16 of the 23 cancer types among recently-diagnosed male and female patients in Norway, with five-year survival decreasing to below 50% for cancers of the oral cavity, kidney (in men) and leukemia 15 years after diagnosis.

There is evidently a group of cancers for which survival is comparatively poor, namely cancers of the stomach, gallbladder, lung, liver, oesophagus and pancreas. For cancers affecting either males or females, on the other hand, there is good short- and long-term prognosis, although the high survival one year after a diagnosis of ovarian cancer (about 75%) decreases quite markedly after five years to around 45%.

Cancer-specific variations in conditional survival

A more positive profile with respect to cancer survival in Norway is captured on examining the conditional survival. Figure S5a–c shows the respective distribution of sex-specific five-year relative survival proportions on the pre-condition that patients have already survived one, five and 10 years. The probability of surviving five years for patients alive one year after diagnosis is over 60% for 16 of the 23 sites, and for the remaining sites, with the exception of pancreatic and oesophageal cancer, is around 30% or over. For those surviving five years after diagnosis, 5-year relative survival is almost uniformly above 75% irrespective of cancer site, although caution must be applied in interpreting longer-term conditional survival figures for cancers where few survive five years after diagnosis — those associated with poor prognosis — due to the potential loss of precision in the estimates.

There tends to be little or no excess mortality for cancer patients (compared to the general population) when the conditional 5-year relative survival reaches 90–100%. This phenomenon is already observed after one year for patients diagnosed with thyroid cancer (both sexes), Hodgkin lymphoma (in men), testicular or endometrial cancer. For five-year survivors, there is little excess mortality among female breast and cervix cancer patients. Patients surviving 10 years after diagnosis have high 5-year survival probabilities in general, reaching above 90% for the vast majority of the 23 sites, including patients with previous colorectal or ovarian cancer diagnoses.

Sex-specific variations in relative survival

Figure S6a–c shows the absolute differences in 1-, 5- and 15-year survival for those cancers affecting both sexes. It is evident that there are large differences with respect to short- and long-term survival in men and women following the diagnoses of many cancer forms. Females appear to have consistently higher short-term and long-term survival for cancers of the central nervous system and melanoma of the skin, as well as for colon and lung cancer. Men tend to have comparatively higher survival figures than women one, five and 15 years after diagnoses of bladder and gallbladder cancers. There are also some inconsistent but intriguing differences in long versus short-term sex-specific survival. Male patients, for instance, tend to have a higher survival probability than female patients one year after a diagnosis of rectal cancer, although the observed estimates are higher in women than men five and 15 years after diagnosis.

Cancer-specific variations in the proportion cured and the median survival of those uncured

For the 15 cancer sites for which estimates from the fitted cure models could be attained, the cure fraction and the survival time of the uncured are shown with their corresponding 95% confidence limits (Figure S7). There is considerable variability in the cured proportions according to the cancer diagnosed, from the 5–10% range for pancreas and liver cancer through to cured proportions above 50% for cancers of the bladder, central nervous system, large bowel and leukaemia. There is less variability across cancer diagnoses in the median survival of those who eventually die, and the quantity does not appear highly correlated with the estimates of the proportion cured. Several patterns can however be ascertained. Uncured patients diagnosed with cancers associated with poor prognosis have estimated median survival times in the six to 12 month range, while better prognosis cancers tend to give estimates of median survival time of between 1.5 and 2.5 years. Non-Hodgkin lymphoma patients who eventually die had the longest estimated median survival time of greater than five years, although the associated confidence interval was very wide.

Survival by stage

Figure S8a–f show the stage-specific trends in 5-year relative survival (including unknown stage) alongside relative survival zero to 15 years since diagnosis according to stage for cancers of the colon, female breast and prostate for the diagnostic period 1965–2007. The five-year survival of colon cancer patients diagnosed at localised and regional stages has increased by over 35 percentage points over four decades, with 15-year survival close to 90% for localised disease patients and 65% for patients diagnosed with regional spread. Patients diagnosed with distant metastases have had consistently poor prognosis over time (approximately 5%), although a moderate increase in five-year survival to 10% is observed recently, since around 1995. Survival tends to level off in the long-term regardless of stage. Some caution in the interpretation of trends is advised given the rapidly increasing survival seen among stage-unknown patients.

For breast cancer, the survival of patients diagnosed with stage I–III cancers has generally increased, most evidently in stage II cancers from the mid-1970s. There is a tendency for the survival of breast cancer patients to continue to decline many years after diagnosis, irrespective of the recorded stage at diagnosis. Stage I and II cancers are however associated with good survival one and five years after diagnosis, close to 95% and 85% respectively, although stage II cancers have a

relatively poorer longer-term prognosis. Patients diagnosed with stage III cancers have survival probabilities of around 65% and 40% five and 15 years after diagnosis, respectively. Stage IV trends are rather unchanged over time, but show signs of stabilising or possibly declining after the mid-1990s, with five-year survival around 15%. There are few breast cancers unstaged and therefore they were not included in the trend analyses.

The five-year relative survival patients diagnosed with prostate cancers with either localised disease or regional spread has increased markedly from the early-1990s, partly attributable to the availability and increasing use of the prostate specific antigen (PSA) test as a screening tool since around 1990. In contrast, the trends in distant stage are rather stable between 1990 and 2000, but have increased by a few percentage points for metastatic patients diagnosed up to 2007. Trends are somewhat speculative without knowledge of the stage distribution of the unknown category, for which five-year survival has increased in a manner similar to regional stage cancers. As with breast cancer, prostate cancer survival shows steady declines with each year after diagnosis, regardless of the stage recorded. Patients diagnosed at localised and regional stages had similar survival one year after diagnosis, but thereafter, the localised cancer patients tended to have a 15–20 percentage point survival advantage over those diagnosed with tumours with regional spread. Survival of patients diagnosed with metastatic cancer is 30% after five years, but long-term survival further diminishes to an estimated 5%, 15 years after diagnosis.

Site-by-site description

In Figures S9–S31, trends, long-term survival and cure fraction results are presented together, for each of the 23 cancers. Below is a very brief site-by-site description, which serves to highlight some of the main results.

Mouth and pharynx (Figure S9a–f)

Both incidence rates and survival probabilities have been rather stable over the study period. Five-year relative survival is somewhat superior for females, although current estimates of 15-year survival are quite similar between the sexes at around 40%, with survival highest among patients diagnosed at ages under 50. Patients alive five years after diagnosis have a high relative survival, reaching 90% for males and 80% for females 15 years after diagnosis. The mean proportion of patients cured is estimated to be around 40% and the median survival of those who die around 1.5 years.

Oesophagus (Figure S10a–f)

Minor increases in both incidence and mortality have been observed during the last 20 years, while five-year

relative survival probabilities are poor and unchanging over time for both men and women. For the minority of patients surviving the disease, five-year survival increases to 80% five years after diagnosis. The proportion cured and the median survival of those who die are around 9% and 6 months, respectively.

Stomach (Figure S11a–f)

Incidence and mortality trends have been decreasing for a number of decades in Norway, with 5-year survival increasing in the 1960s and 1970s but more or less stable in the last two decades, at around 20%. The median survival for those uncured of about 6 months (for both sexes) does not appear to have increased measurably in the last 40 years. The estimated proportion cured has, however, doubled over time, from 10% to 20% for both sexes. Male patients surviving 7–8 years have no excess mortality compared to the general population. There are also interesting but unexplained sex-specific differences in longer-term cumulative and conditional survival.

Colon (Figure S12a–f)

Incidence has been increasing quite rapidly over the entire 40-year period, as has 5-year relative survival, for both sexes. Mortality has increased slightly and more notably among men during the mid-1970s through to the 1990s, while five-year relative survival has been steadily increasing for both sexes, reaching 65% for the youngest age group (aged under 50 at diagnosis). The proportion cured has uniformly increased to reach 50%, while the median survival time of those who die has also increased from around one to two years. Those patients surviving eight years after diagnosis have a similar mortality profile to the general population. Long-term differences in relative and conditional survival, with respect to age at diagnosis and sex appear rather minor.

Rectum (Figure S13a–f)

In contrast to the rather stable trends in incidence, mortality rates have steadily declined since 1995. Survival has been increasing from 1965–2007 irrespective of sex and age, from 25% to over 60%. The proportion cured has increased correspondingly, reaching above 50% by 2007 from below 30% circa 1965. The estimated median survival of the uncured has also increased, but mainly from the 1970s through to the mid-1980s. Patients surviving six to eight years after diagnosis have a five-year relative survival probability of over 90%, irrespective of age or sex. The survival of rectal cancer patients is some five percentage points higher in women than men, consistently at 5, 10 and 15 years after diagnosis.

Liver (Figure S14a-f)

Neither incidence nor mortality have changed demonstrably during the study period, and the five-year survival is also stable and quite poor (about 10%) for both sexes. Survival trends by age tend to reflect these patterns, although there is an increasing survival proportion observed among younger women, and indeed, five-year survival is evidently much higher among young patients relative to older patients. The proportion cured among all liver cancer patients has remained low through time, at about 9%.

Gallbladder (Figure S15a-f)

Time trends in gallbladder cancer incidence, mortality and survival are rather stable, with 5-year relative survival around 10–15% and meaningful patterns in the age-specific survival curves are difficult to detect. Neither the proportion cured nor the median survival of those who will eventually die have increased during the period in either sex, with the former estimated at around 13%. In contrast to rectal cancer, the survival of gallbladder cancer patients tends to be higher among men irrespective of year since diagnosis.

Pancreas (Figure S16a-f)

Pancreatic cancer incidence and mortality rates have changed little in 40 years, and their very close proximity reflects the very poor survival of around 5%, with survival slightly higher among men at five and 10 years after diagnosis. As might be anticipated, the estimated proportion cured and the median survival of those who will die are both low and rather stable with time. There is however some suggestion of improving prognosis among patients aged under 50 at diagnosis, with survival reaching above 10% in the last decade.

Lung, trachea (Figure S17a-f)

Incidence and mortality trends closely follow each other and reflect the different phases of the smoking epidemic in men and women currently and over time. Five-year relative survival has not changed substantively during the observation period however, although some increases may be observed among patients younger than 50 year at diagnosis, with their contemporary 5-year relative survival estimated at over 20%. The proportion cured is low at around 10%, while the median survival for those who die is estimated at six months for both sexes. Patients who survive the first five years after diagnosis have a probability of 70% of surviving an additional five years, irrespective of sex. There are some differences apparent in both long-term survival and conditional survival with respect to age.

Melanoma of the skin (Figure S18a-f)

Steady increases in incidence and mortality 1965–1990 have given way to a recent stabilisation of trends in both sexes. While incidence rates are higher in females than males, relative survival — {irrespective of years since diagnosis — {is consistently 15 percentage points higher in women. Five-year relative survival has increased for all age groups and both sexes, although it shows some signs of flattening in the last 20 years. For patients surviving five years after diagnosis, 5-year relative survival is very high, estimated at over 95%. Long-term cumulative survival appears to continue to decrease irrespective of years since diagnosis however, and estimation of the proportion of cured patients was therefore unattainable.

Female breast (Figure S19a-f)

Incidence and survival have been increasing throughout the study period but has increased more rapidly during the 1990s, partially the result of the introduction of mass screening in Norway. Mortality has continually declined since 1990. Relative survival is highest for women aged 45–59 at diagnosis and lowest for the youngest (aged under 30 at diagnosis) and oldest (over 75) age groups. The 15-year survival is slightly over 70% but it is markedly lower for patients aged over 75 at diagnosis. Patients diagnosis have a relative survival of about 85% at diagnosis, and this increases to over 90% given they survive a further five years. As with melanoma, long-term cumulative survival continues to decline many years after diagnosis, and the proportion of cured patients could not be estimated.

Uterine cervix (Figure S20a-f)

There has been a marked decline in both mortality and incidence, especially after 1985, although caution must be applied in interpreting the former as there is a large proportion of unspecified cancers that should have been allocated to cervix or corpus uteri (ICD-10 C55). Survival has increased markedly after 1995 to reach almost 80% one decade later. There are large differences in contemporary 5-year relative survival with respect to age. For women surviving 5 years after diagnosis, expected survival is not very different from the general population; 5-year relative survival reaches 95% within 3–4 years. The proportion of cured patients has increased since 1990 to 70% by 2000, while median survival of those who will eventually die of their cancer has remained rather stable at approximately 18 months.

Uterine corpus (Figure S21a-f)

There has been a slight increase in both incidence and survival, while mortality has remained stable over the study period, though the mortality rates suffer from the

same artefact mentioned above for the cervix trends. Five-year relative survival has increased mainly among patients aged 60 or older at diagnosis. Long-term survival is quite high, about 75% 15 years after diagnosis, although there are large differences between age groups. The 5-year relative survival for women alive five years after diagnosis is over 90%. However, survival 10–15 years after diagnosis continues to decline, and thus the proportion of cured patients was inestimable.

Ovary (Figure S22a–f)

Incidence has declined and survival has increased slightly in the last 20 years, while mortality has modestly declined. The increases in five-year survival appear to be restricted to patients aged under 60 years of age at diagnosis. The estimated proportion of cured patients has not changed much over time (around 30%), however the median survival time of those who will die of this cancer appears to have increased to about two years by 2000. There are very large differences in longer-term survival with respect to age groups, the youngest patients having a 10-year relative survival of over 60% compared with the oldest patients (70–79 years at diagnosis) of less than 20%. However, for patients surviving five years after diagnosis, the expected survival is not that different from the general population.

Prostate (Figure S23a–f)

There has been a marked increase in both incidence and survival from 1990, most likely a result of the commercial availability of the PSA test and an upsurge in its use as a screening test since then (as seen by stage in Figure 8). Mortality has declined slightly since the mid-1990s. Five-year survival has increased for all age groups since 1990, reaching 80–90% for patients diagnosed in 2007 and aged under 80. Survival of patients continues to decrease for every year after diagnosis, reaching about 55% after 15 years, and hence the proportion cured could not be estimated. There are large differences in long-term survival with respect to age at diagnosis. The conditional survival has declined slightly from about 85% at diagnosis, to around 80% for patients surviving 10 years. Although this seems counter-intuitive, it could be explained by the combined effects of rapid increases in prostate cancer survival by year of diagnosis (during the PSA era), and the application of the period approach to conditional survival. To illustrate, given a background of rapid growth in survival, the group of 10-year survivors diagnosed one decade previously will have a lower five-year relative survival than one-year survivors, who were diagnosed recently.

Testis (Figure S24a–f)

There have been rapid increases in incidence and concomitant declines in mortality since the mid- to late-1970s in Norway, while incidence has increased constantly over the last 40 years. Five-year relative survival is very high, except for those older than 70 years at diagnosis. Patients treated in 2005 have a five-year survival of over 90%. Longer-term survival is very high, reaching almost 100% for patients younger than 50 years at diagnosis and about 90% for patients aged above 50 at diagnosis. Patients surviving five years after diagnosis therefore appear to have little or no excess mortality compared to the general population.

Kidney (Figure S25a–f)

Incidence has slightly increased and mortality has slightly decreased since the 1980s, with five-year relative survival most notably increasing in the last decade. Survival has also increased for both sexes across age groups, where there are very wide variations in prognosis. Both the short- and long-term relative survival are higher for females compared to males. The estimated proportion of cured patients has increased after 1985 for both sexes and is now about 47% for both sexes combined; median survival for those uncured has, however, not changed materially over the 40-year period. Five-year relative survival has increased to over 80% for patients alive three years after diagnosis.

Bladder (Figure S26a–f)

Both incidence and survival have increased since 1965 for both sexes, although trends are more stable during the last decade; mortality has been slowly declining for 20 years or so. Five-year survival has increased for all age groups and both sexes, with the youngest patient group having a 30 percentage point advantage in relative survival compared to the oldest group. Long-term relative survival is consistently higher among males relative to females. The estimated proportion of cured patients has increased since 1975 for both sexes, to about 65% in 2000. Five-year relative survival probabilities for those who are alive some time after diagnosis is favourable, and reaches 90% for five-year survivors. Despite the notable differences in long-term survival in men and women, there is little variation in sex-specific conditional survival.

CNS (Figure S27a–f)

Both incidence and mortality rates have generally increased since 1965, while corresponding five-year survival estimates have risen quite rapidly and uniformly in both sexes, and in all age groups over time. Female survival is superior; there is a constant 20% percentage point difference in 5- to 15-year relative (cont. page S15)

Figure S4a: 1-year relative survival by cancer and sex, sorted in descending order of male survival

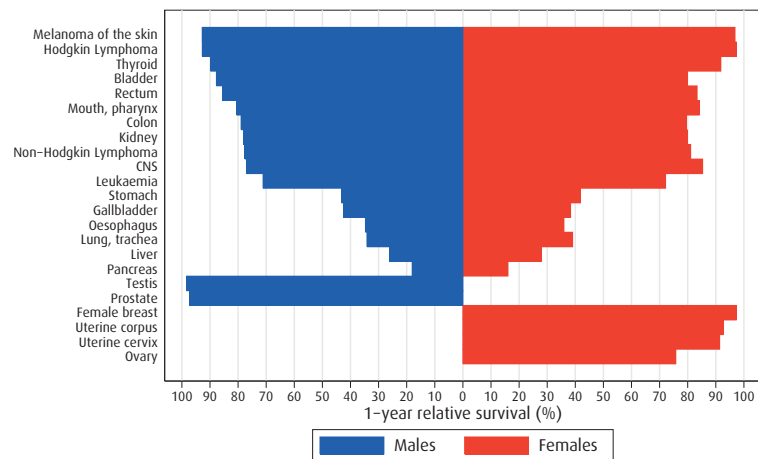


Figure S4b: 5-year relative survival by cancer and sex, sorted in descending order of male survival

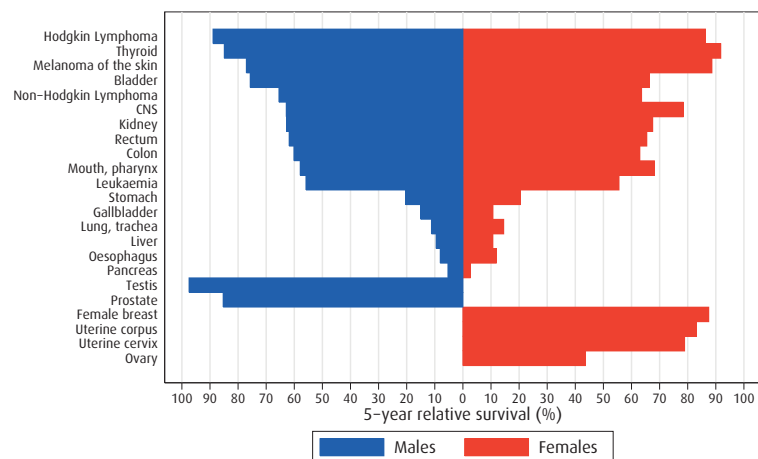


Figure S4c: 15-year relative survival by cancer and sex, sorted in descending order of male survival

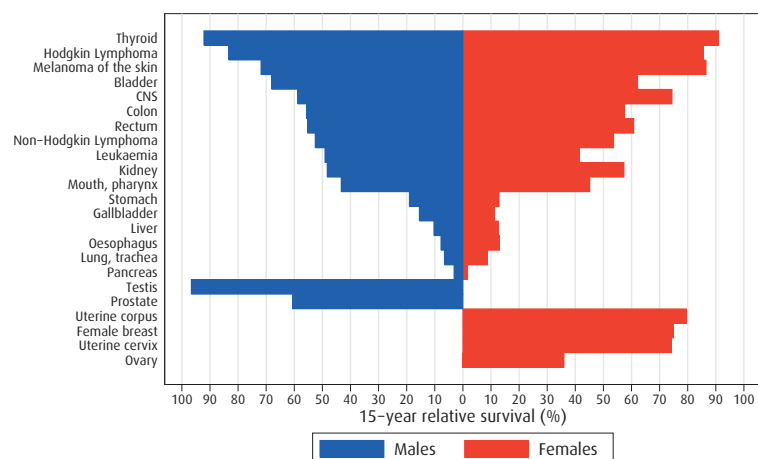


Figure S5a: 5-year relative survival conditional on surviving 1 year by cancer and sex, sorted in descending order of male survival

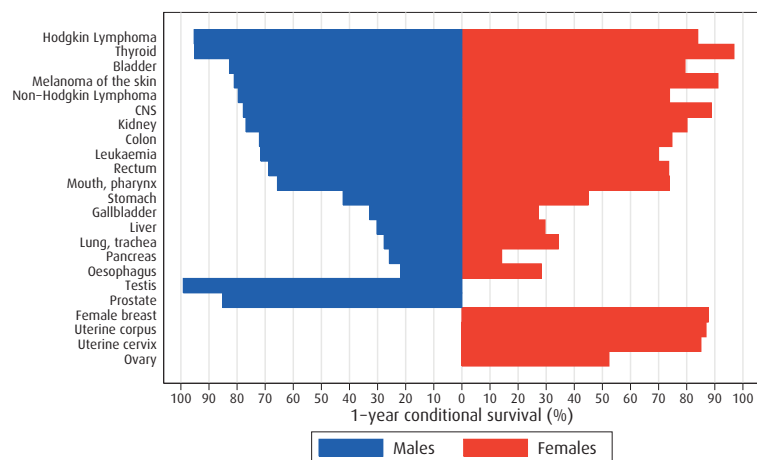


Figure S5b: 5-year relative survival conditional on surviving 5 year by cancer and sex, sorted in descending order of male survival

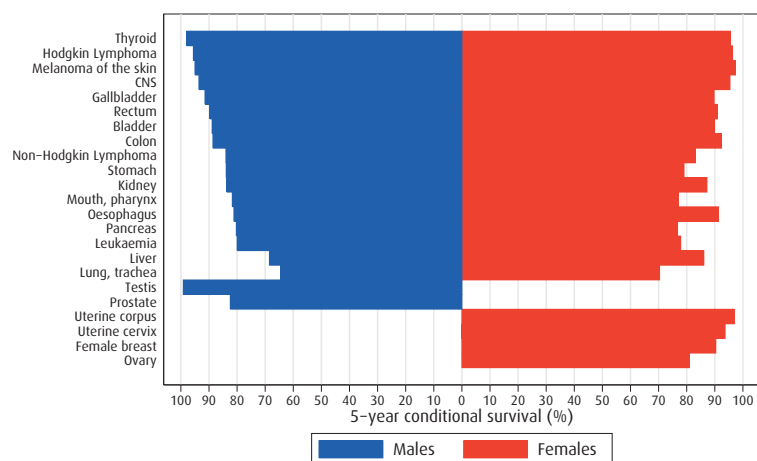


Figure S5c: 5-year relative survival conditional on surviving 10 year by cancer and sex, sorted in descending order of male survival

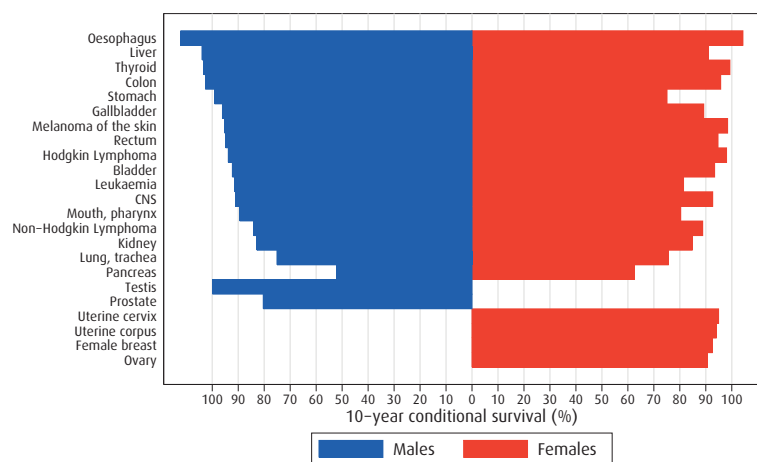


Figure S6a: Sex-specific differences (percentage points) in 1-year relative survival by cancer, sorted according to direction and magnitude of difference

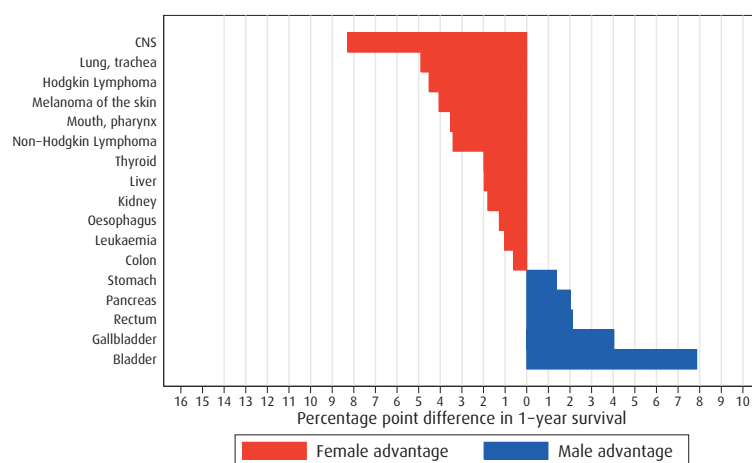


Figure S6b: Sex-specific differences (percentage points) in 5-year relative survival by cancer, sorted according to direction and magnitude of difference

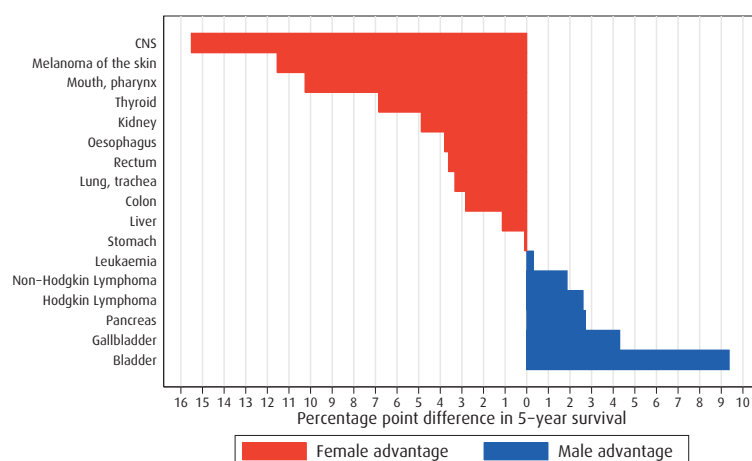
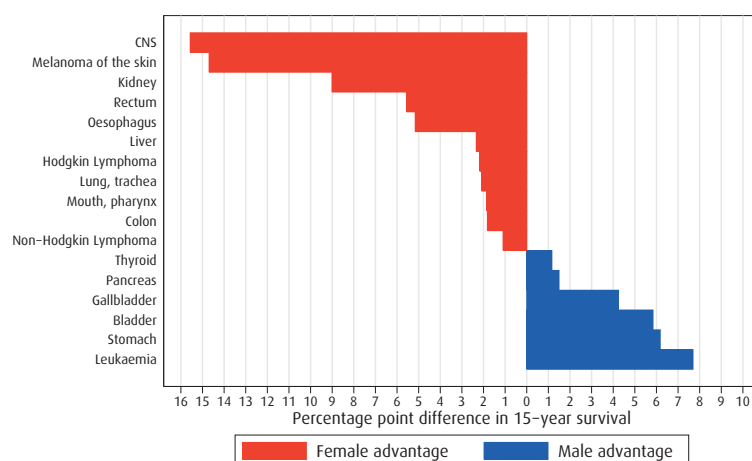


Figure S6c: Sex-specific differences (percentage points) in 15-year relative survival by cancer, sorted according to direction and magnitude of difference



(cont. from page S11) survival estimates between the sexes. The estimated proportion of cured patients appears to have increased markedly since 1980 to over 65%, whereas the median survival of those uncured has remained the same. Estimates of five-year relative survival reach 90% for both sexes in patients alive three years after diagnosis.

Thyroid (Figure S28a-f)

There are suggestions that five-year survival has moderately increased with time, in keeping with the incidence trends, while declining trends in mortality rates are observed during the last two decades. Five-year survival is high in males and female patients, although there are large differences in survival levels and trends with respect to age. Relative survival is highest for patients younger than 60 years at diagnosis, while the greatest increases in five-year survival occur among the oldest patients, irrespective of sex. Five-year relative survival is close to that of the general population in patients who are alive one year after diagnosis. Given the lack of a clear plateau in the long-term survival estimates, the proportion cured could not be estimated for either sex.

Hodgkin Lymphoma (Figure S29a-f)

There have been minor increases in incidence rates during the last two decades in both men and women, accompanied by a larger fall in mortality, particularly from the mid-1970s. Five-year survival has continued to increase over the whole period to over 80% and is higher for young to middle-aged patients (under 60 at diagnosis). Five-year relative survival continues to increase for surviving patients, with those alive three

years or more having little excess mortality relative to the general population. The estimated proportion cured could not be established given the observation of continual declines in long-term survival.

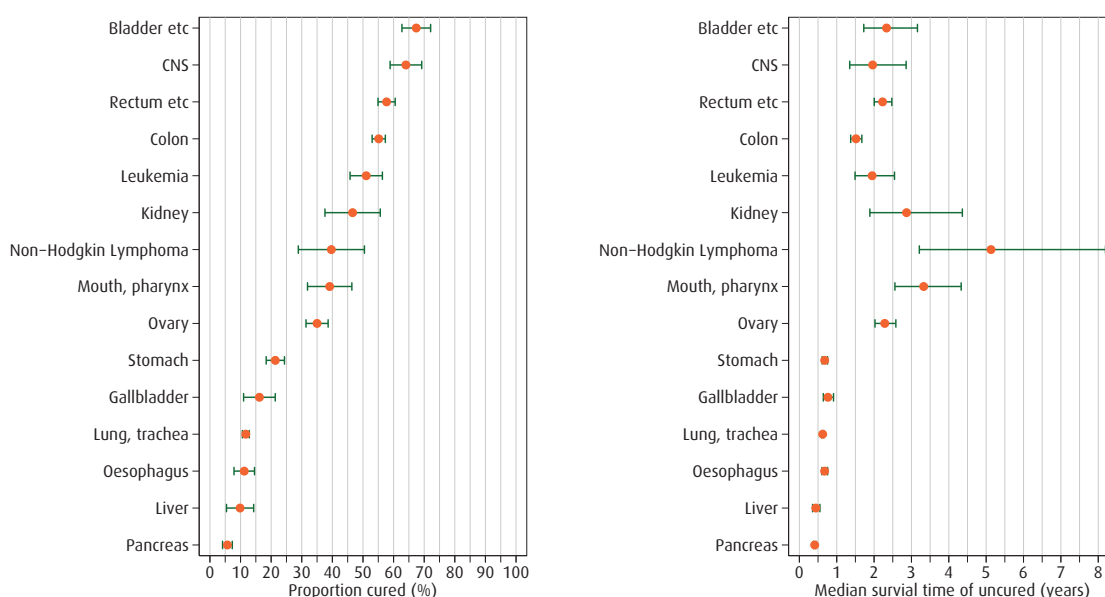
Non-Hodgkin Lymphoma (Figure S30a-f)

Both incidence and survival have been increasing in the last few decades in both sexes, while mortality appears has recently plateaued and declined. Five-year survival is high and has been increasing for all age groups, most notably for patients aged under 30 at diagnosis. The estimated proportion of cured patients has increased after 1985 in both sexes to around 45% by 2000. 15-year survival is estimated at 45% overall, but there is substantive variability in these estimates according to age at diagnosis. For patients surviving the first five years after diagnosis, relative survival reaches 80%.

Leukemia (Figure S31a-f)

Incidence has been stable or slightly increasing over time, while mortality has been declining since at least 1970, mirroring the observation of steady increases in five-year survival for both sexes. These increases are most apparent in patients diagnosed at ages under 30, for which current five-year survival is estimated at about 75%. The estimated proportion of cured patients has increased for both sexes accordingly, reaching over 40% by 2000. There were only slight changes in median survival for those who eventually die of their disease. Five-year relative survival for patients surviving two years reached 75% overall, and for men, continued to increase with each successive year of survival, reaching 90% in male patients alive 10 years after diagnosis.

Figure 7 The estimated proportion cured and median survival of the uncured by cancer, sorted in descending order of proportion cured



Colon cancer by stage

Figure S7a: Trends in 5-year relative survival by stage

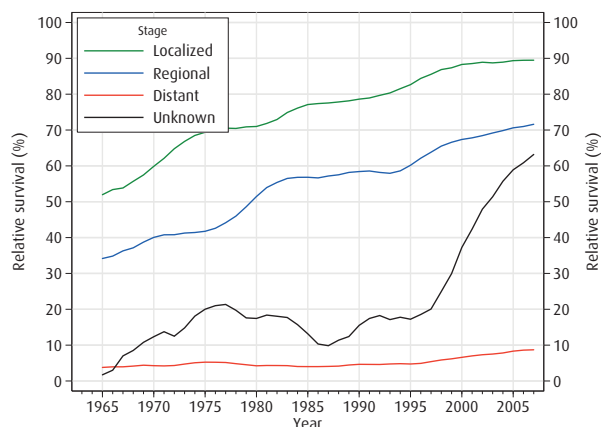
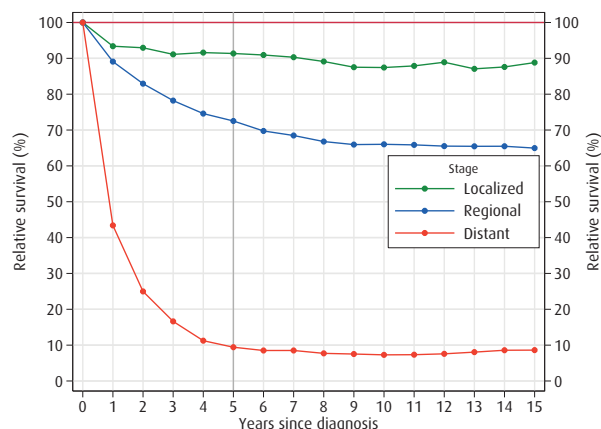


Figure S7b: Long-term relative survival by stage



Breast cancer by stage

Figure S7c: Trends in 5-year relative survival by stage

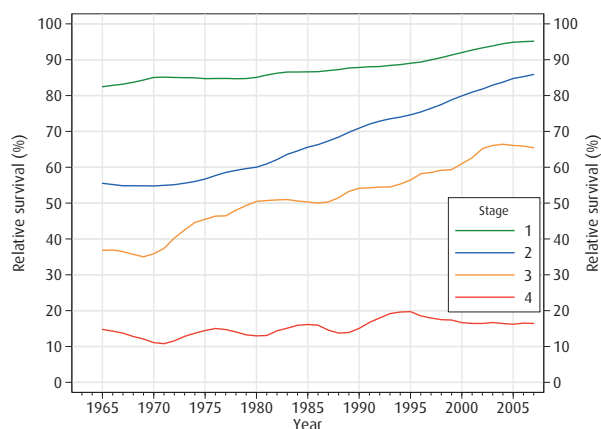
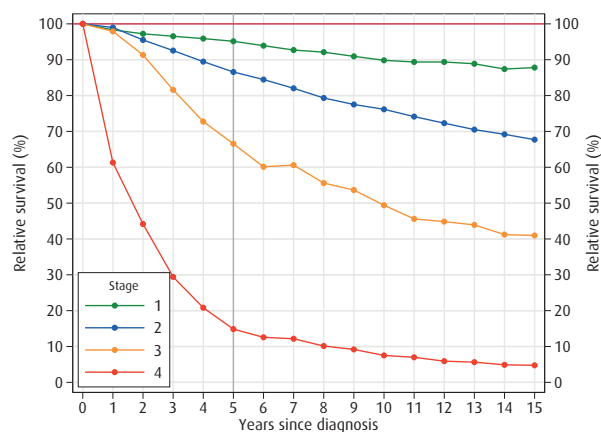


Figure S7d: Long-term relative survival by stage



Prostate cancer by stage

Figure S7e: Trends in 5-year relative survival by stage

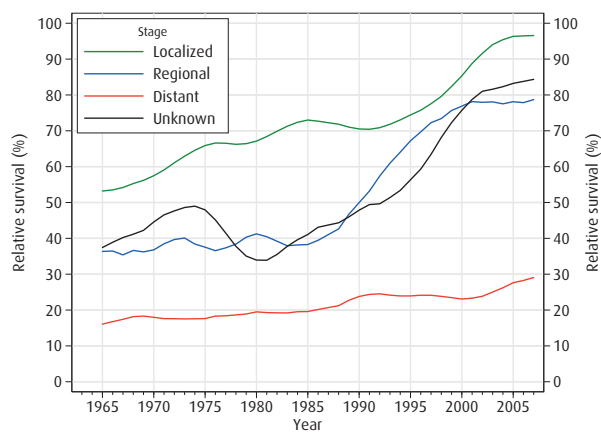


Figure S7f: Long-term relative survival by stage

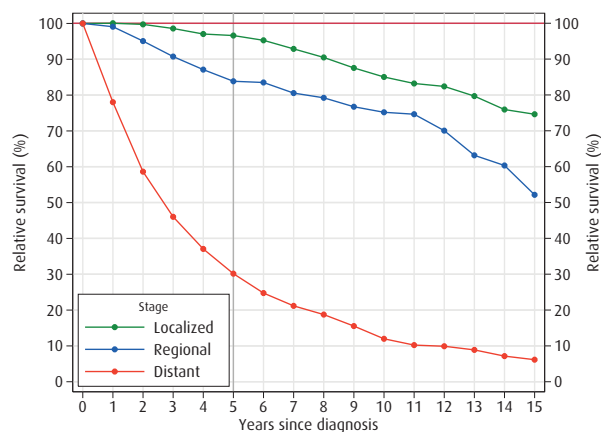


Table S1: 1-, 5-, 10-, and 15-year relative survival by cancer site and sex

Cancer site	Sex	1-year	5-year	10-year	15-year
Mouth, pharynx	Males	80.5 (77.8, 83.1)	57.9 (54.2, 61.4)	47.8 (43.6, 51.9)	43.3 (38.4, 48.4)
	Females	84.1 (80.8, 86.9)	68.1 (63.1, 72.9)	54.2 (48.0, 60.4)	45.2 (38.1, 52.5)
Oesophagus	Males	34.7 (30.6, 38.8)	8.1 (5.7, 11.0)	7.2 (4.6, 10.7)	7.8 (4.5, 12.4)
	Females	35.9 (29.8, 42.2)	11.9 (7.4, 17.6)	10.8 (5.9, 17.8)	13.0 (6.4, 23.0)
Stomach	Males	43.2 (40.5, 45.9)	20.3 (17.8, 22.9)	18.3 (15.6, 21.4)	19.1 (15.6, 23.0)
	Females	41.8 (38.6, 45.0)	20.4 (17.6, 23.4)	17.0 (14.0, 20.2)	12.9 (9.9, 16.4)
Colon	Males	78.9 (77.6, 80.3)	60.1 (58.1, 62.2)	54.0 (51.3, 56.7)	55.6 (51.8, 59.5)
	Females	79.5 (78.3, 80.8)	63.0 (61.1, 64.8)	59.1 (56.7, 61.5)	57.4 (54.2, 60.7)
Rectum etc	Males	85.4 (83.9, 86.9)	61.8 (59.3, 64.3)	56.7 (53.5, 60.0)	55.3 (50.8, 59.8)
	Females	83.3 (81.6, 85.0)	65.4 (62.8, 68.0)	61.7 (58.4, 65.1)	60.8 (56.4, 65.2)
Liver	Males	26.0 (21.4, 30.8)	9.5 (5.8, 14.4)	7.5 (3.7, 13.3)	10.3 (5.1, 18.3)
	Females	28.0 (22.0, 34.3)	10.7 (6.6, 15.9)	11.2 (6.3, 17.9)	12.6 (6.6, 21.4)
Gallbladder	Males	42.3 (36.3, 48.3)	15.0 (10.3, 20.6)	15.8 (10.1, 23.2)	15.5 (7.8, 26.8)
	Females	38.3 (32.6, 44.0)	10.7 (6.8, 15.7)	10.9 (6.5, 16.9)	11.3 (6.0, 18.9)
Pancreas	Males	18.0 (16.1, 20.1)	5.3 (3.9, 7.0)	4.9 (3.3, 7.1)	3.1 (1.0, 7.7)
	Females	16.0 (14.3, 17.9)	2.6 (1.8, 3.6)	2.2 (1.4, 3.4)	1.7 (0.8, 3.0)
Lung, trachea	Males	34.1 (32.9, 35.4)	11.2 (10.3, 12.2)	7.9 (7.0, 9.0)	6.6 (5.5, 7.9)
	Females	39.0 (37.5, 40.5)	14.5 (13.3, 15.8)	10.8 (9.5, 12.2)	8.7 (7.2, 10.3)
Melanoma of the skin	Males	92.8 (91.4, 94.0)	77.1 (74.6, 79.4)	74.2 (71.2, 77.2)	71.8 (68.1, 75.5)
	Females	96.8 (95.8, 97.7)	88.6 (86.7, 90.4)	87.0 (84.5, 89.4)	86.5 (83.5, 89.5)
Female breast	Females	97.3 (96.8, 97.6)	87.5 (86.6, 88.3)	79.8 (78.6, 81.0)	74.9 (73.2, 76.6)
Uterine cervix	Females	91.4 (89.5, 92.9)	78.9 (76.1, 81.4)	75.7 (72.5, 78.7)	74.2 (70.6, 77.7)
Uterine corpus	Females	92.7 (91.5, 93.8)	83.0 (81.0, 84.9)	82.2 (79.4, 84.8)	79.5 (75.8, 83.1)
Ovary	Females	75.8 (73.7, 77.7)	43.5 (41.0, 46.0)	37.3 (34.6, 40.1)	36.0 (32.9, 39.1)
Prostate	Males	97.2 (96.8, 97.6)	85.3 (84.2, 86.4)	72.5 (70.7, 74.3)	60.6 (57.3, 64.0)
Testis	Males	98.4 (97.3, 99.0)	97.4 (96.0, 98.5)	96.7 (94.9, 98.1)	96.6 (94.5, 98.4)
Kidney	Males	78.0 (75.6, 80.2)	62.7 (59.4, 65.8)	54.8 (50.3, 59.3)	48.3 (42.4, 54.4)
	Females	79.8 (76.8, 82.5)	67.5 (63.2, 71.6)	62.7 (57.0, 68.3)	57.3 (49.9, 64.8)
Bladder etc	Males	87.7 (86.4, 88.9)	75.7 (73.5, 77.8)	69.9 (66.7, 73.0)	68.0 (63.8, 72.3)
	Females	79.9 (77.4, 82.1)	66.3 (62.8, 69.7)	62.7 (58.1, 67.4)	62.2 (56.1, 68.4)
CNS	Males	77.0 (74.8, 79.1)	62.9 (60.1, 65.5)	61.2 (57.9, 64.5)	58.8 (54.6, 63.0)
	Females	85.3 (83.7, 86.8)	78.4 (76.2, 80.5)	77.1 (74.2, 79.9)	74.4 (70.4, 78.3)
Thyroid gland	Males	89.8 (84.9, 93.3)	84.9 (78.1, 90.4)	85.2 (76.4, 92.7)	92.2 (81.4, 101.5)
	Females	91.8 (89.2, 93.9)	91.8 (88.4, 94.5)	89.6 (85.0, 93.6)	91.0 (85.4, 96.0)
Hodgkin Lymphoma	Males	92.7 (88.9, 95.4)	88.9 (84.0, 92.7)	86.4 (80.4, 91.3)	83.3 (75.9, 89.6)
	Females	97.3 (93.2, 99.1)	86.3 (79.4, 91.6)	84.9 (77.1, 91.1)	85.5 (76.7, 92.7)
Non-Hodgkin Lymphoma	Males	77.6 (75.5, 79.6)	65.5 (62.5, 68.3)	58.4 (54.5, 62.3)	52.5 (47.7, 57.5)
	Females	81.0 (78.8, 83.1)	63.6 (60.4, 66.7)	56.1 (52.1, 60.0)	53.6 (48.8, 58.6)
Leukemia	Males	71.1 (68.3, 73.7)	55.8 (52.3, 59.3)	47.9 (43.6, 52.3)	49.1 (43.7, 54.6)
	Females	72.1 (69.0, 75.0)	55.5 (51.6, 59.4)	46.0 (41.3, 50.7)	41.4 (35.9, 47.2)

Figure S9a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

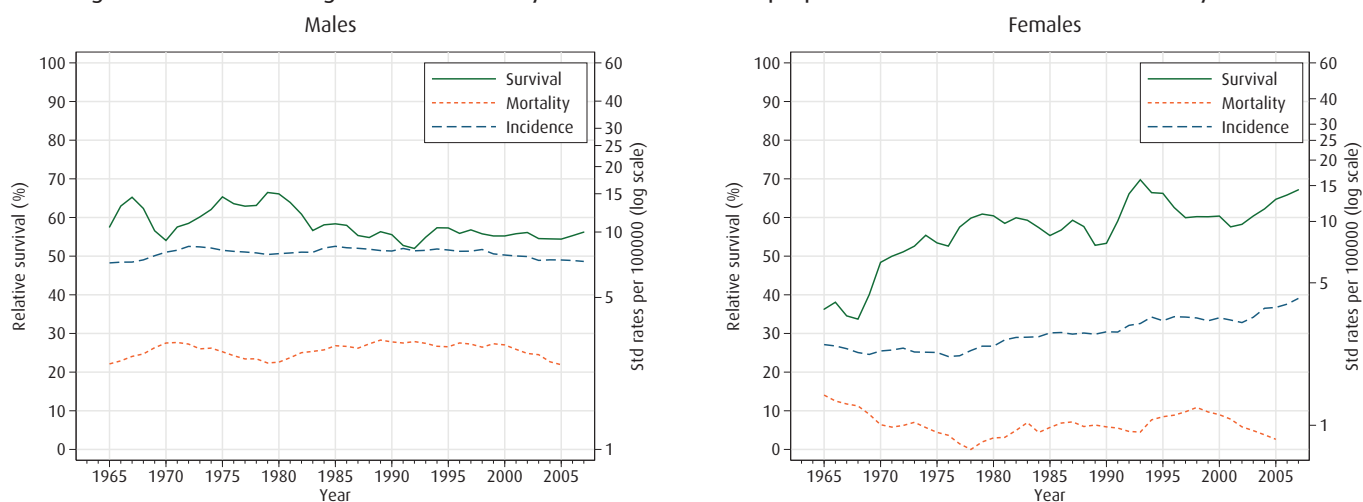


Figure S9b: Trends in 5-year relative survival by age

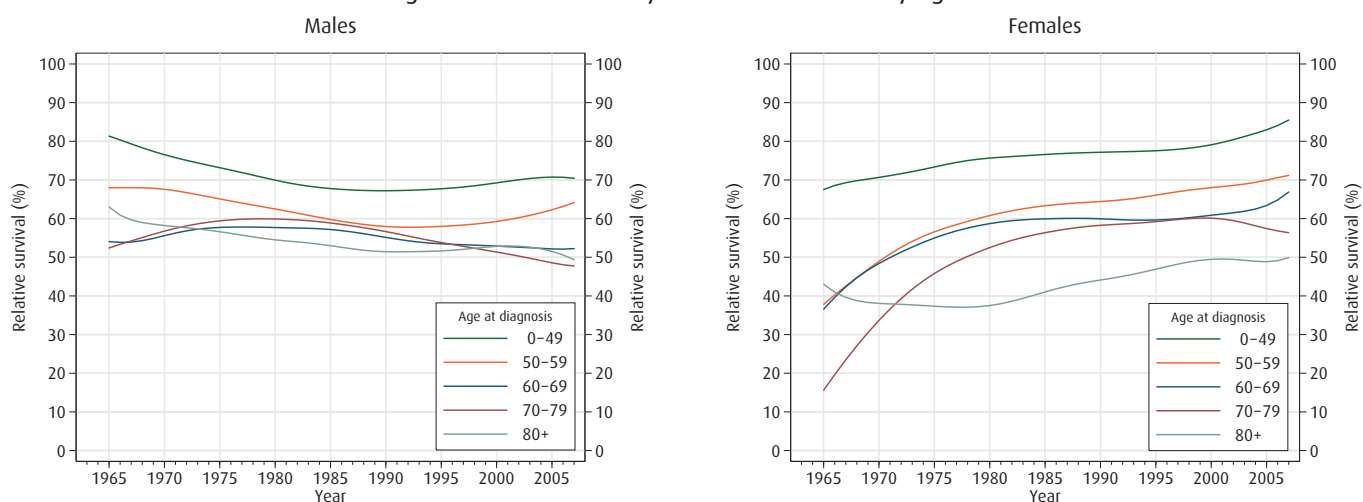


Figure S9c: Estimates of trends in the proportion cured and the median survival time for the uncured

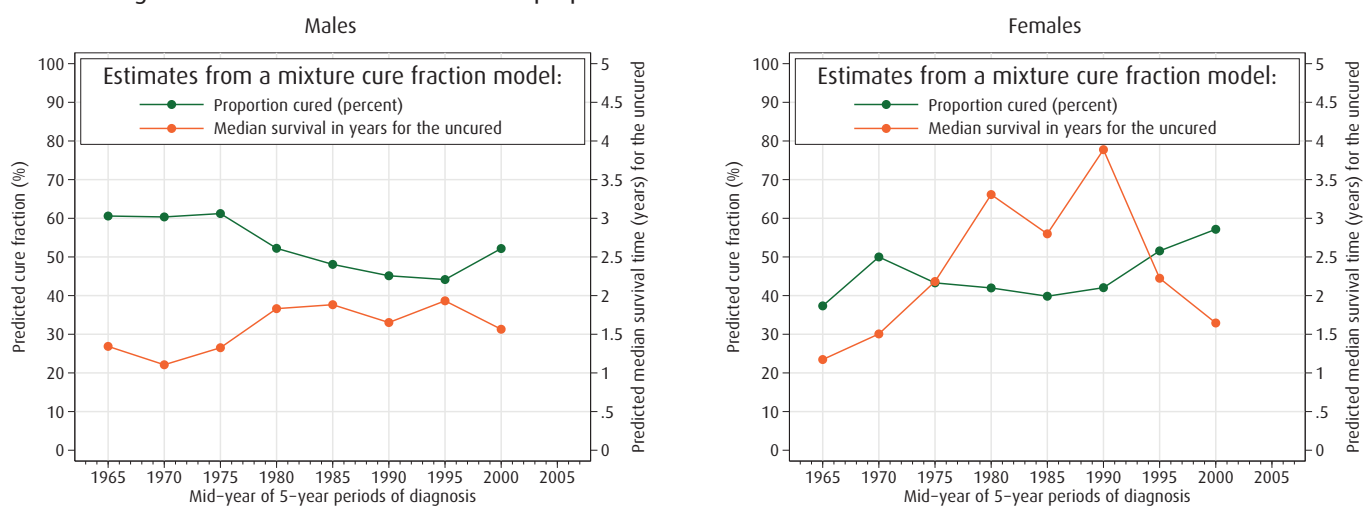


Figure S9d: Relative survival up to 15 years after diagnosis by sex and age

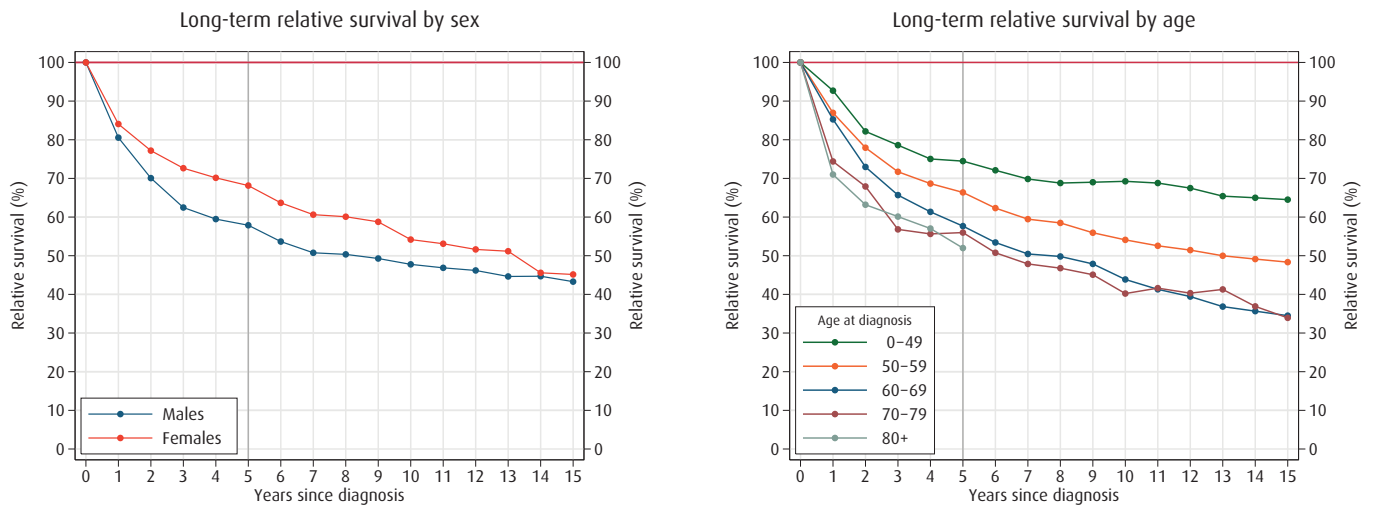


Figure S9e: Conditional 5-year relative survival for every additional year after diagnosis

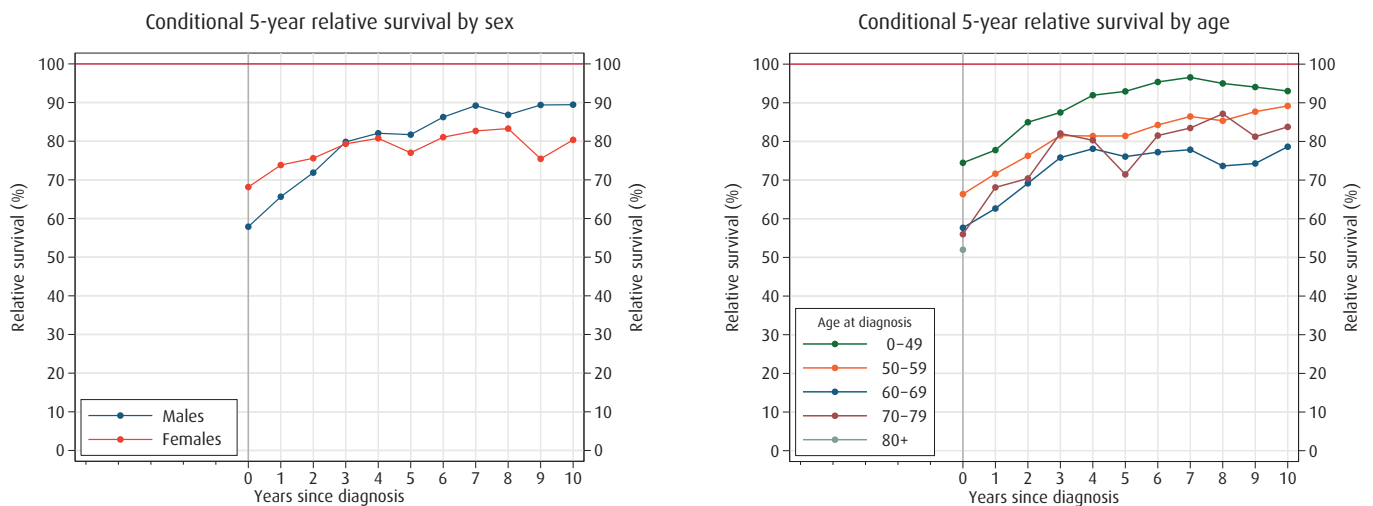
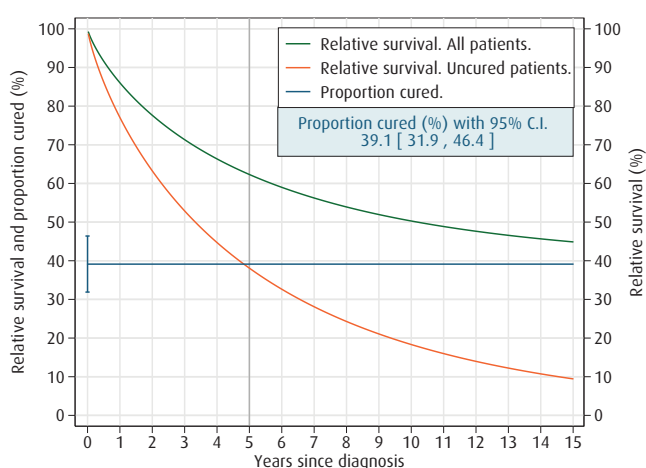


Figure S9f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-49	80	146	226	11.1
50-59	149	313	462	22.8
60-69	184	390	574	28.3
70-79	175	252	427	21.1
80+	187	151	338	16.7
Total	775	1252	2027	100.0

Figure S10a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

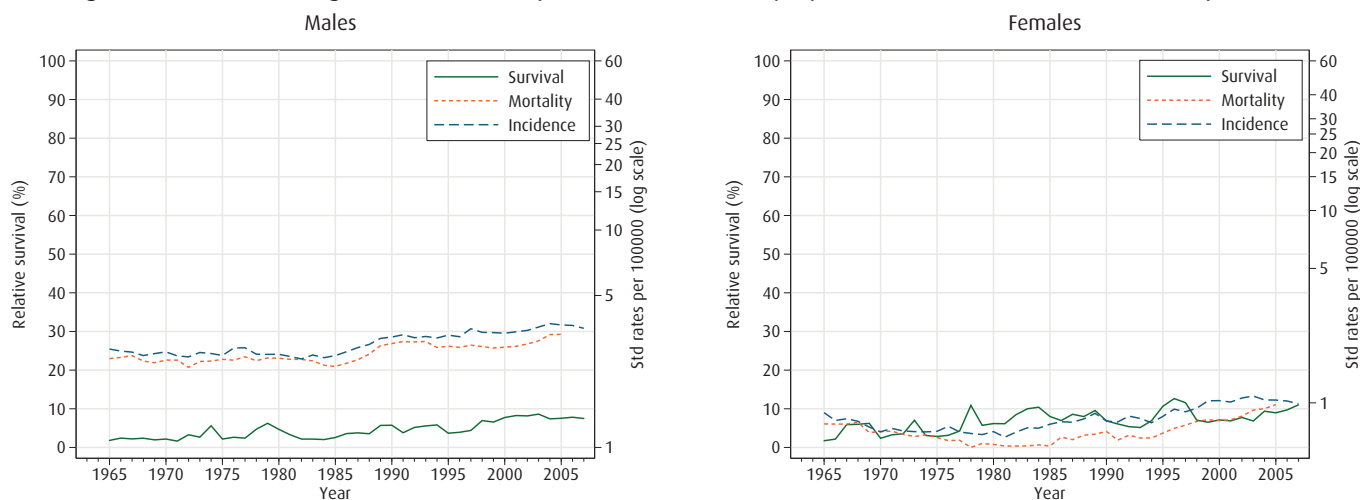


Figure S10b: Trends in 5-year relative survival by age

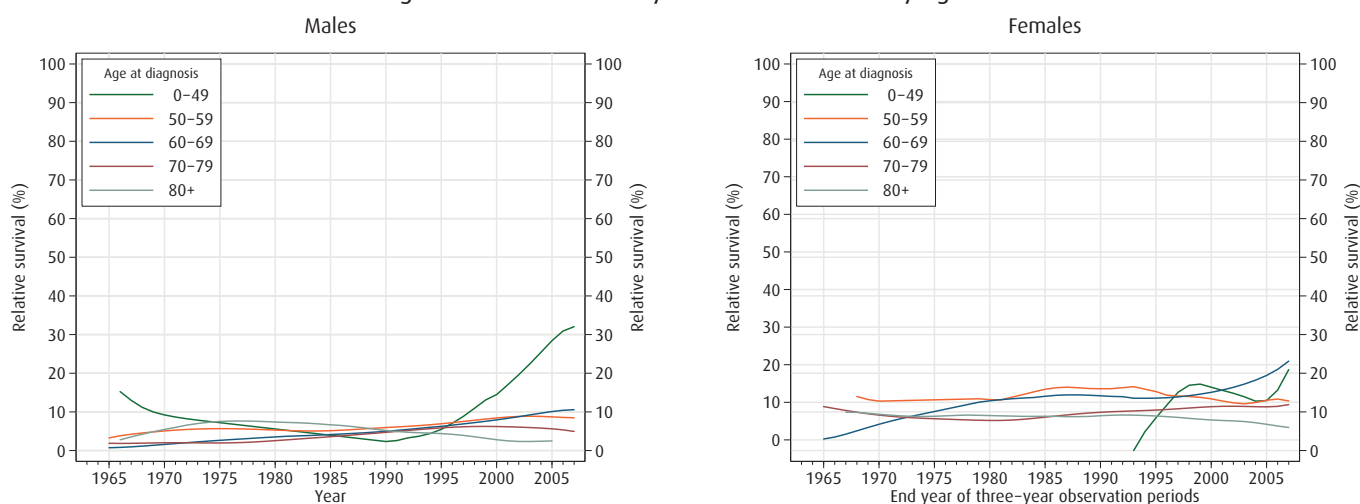


Figure S10c: Estimates of trends in the proportion cured and the median survival time for the uncured

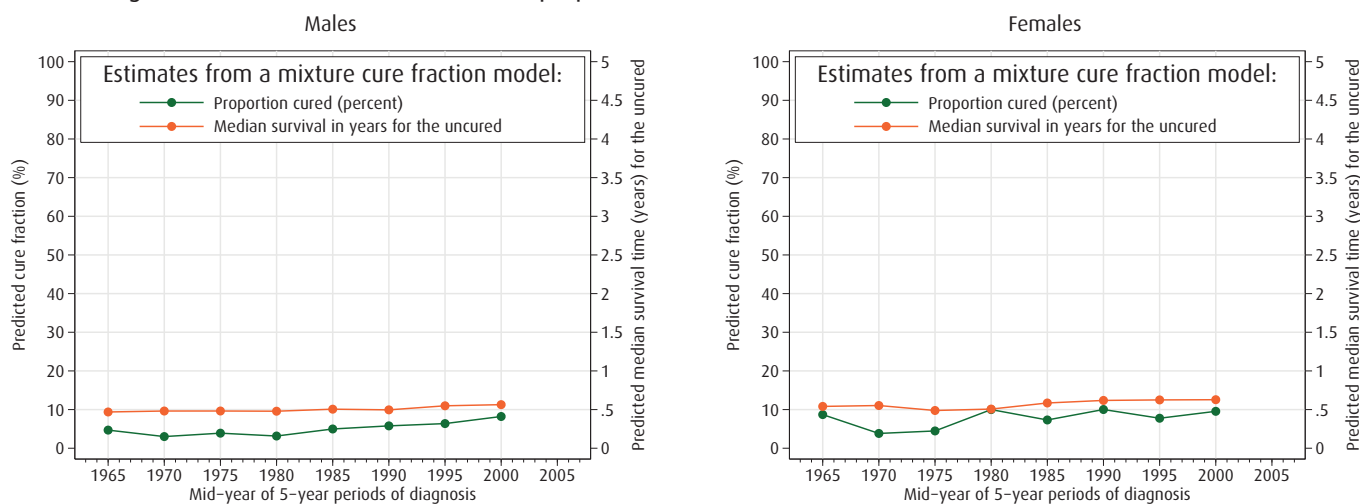


Figure S10d: Relative survival up to 15 years after diagnosis by sex and age

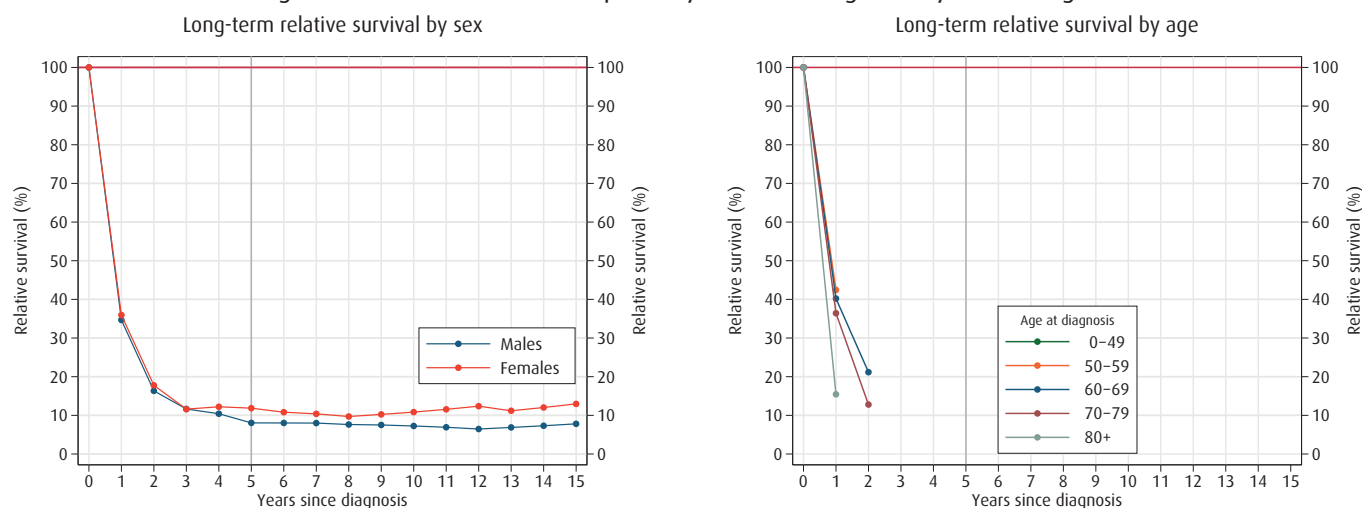


Figure S10e: Conditional 5-year relative survival for every additional year after diagnosis

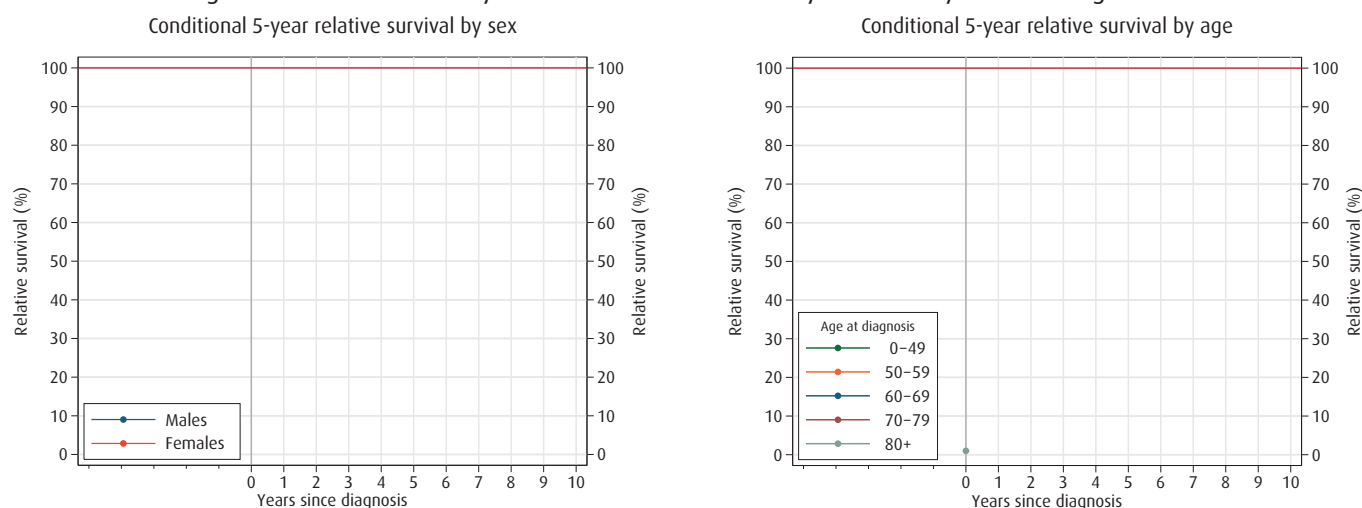
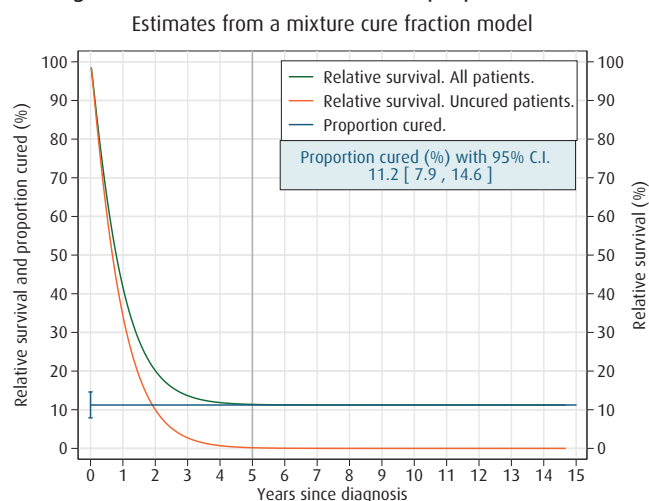


Figure S10f: Relative survival and proportion cured



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-49	10	42	52	5.5
50-59	30	110	140	14.9
60-69	55	197	252	26.8
70-79	75	204	279	29.6
80+	95	124	219	23.2
Total	265	677	942	100.0

Figure S11a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

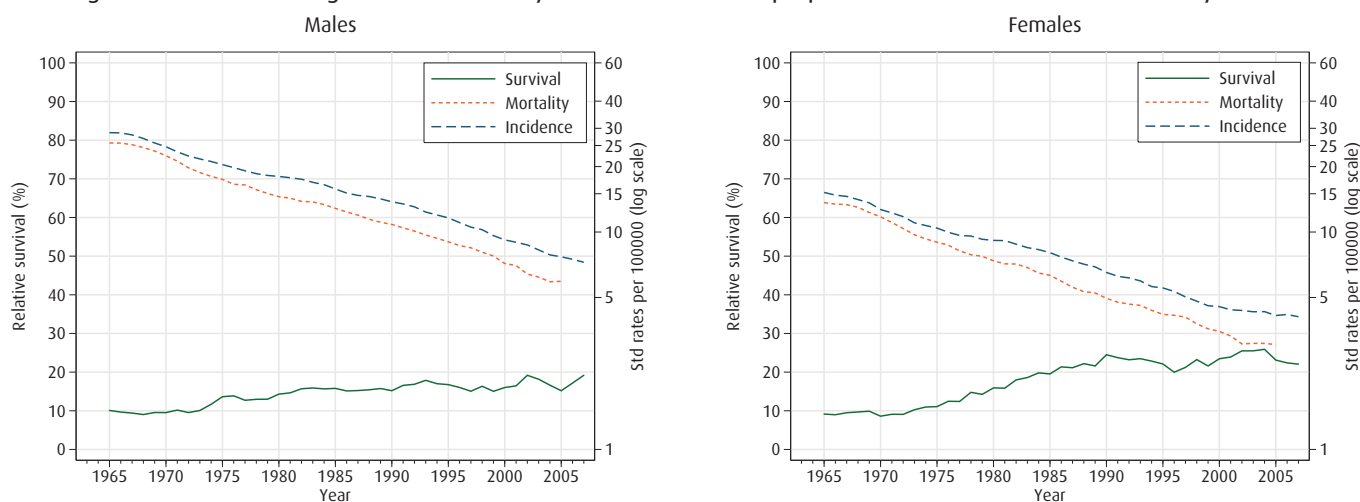


Figure S11b: Trends in 5-year relative survival by age

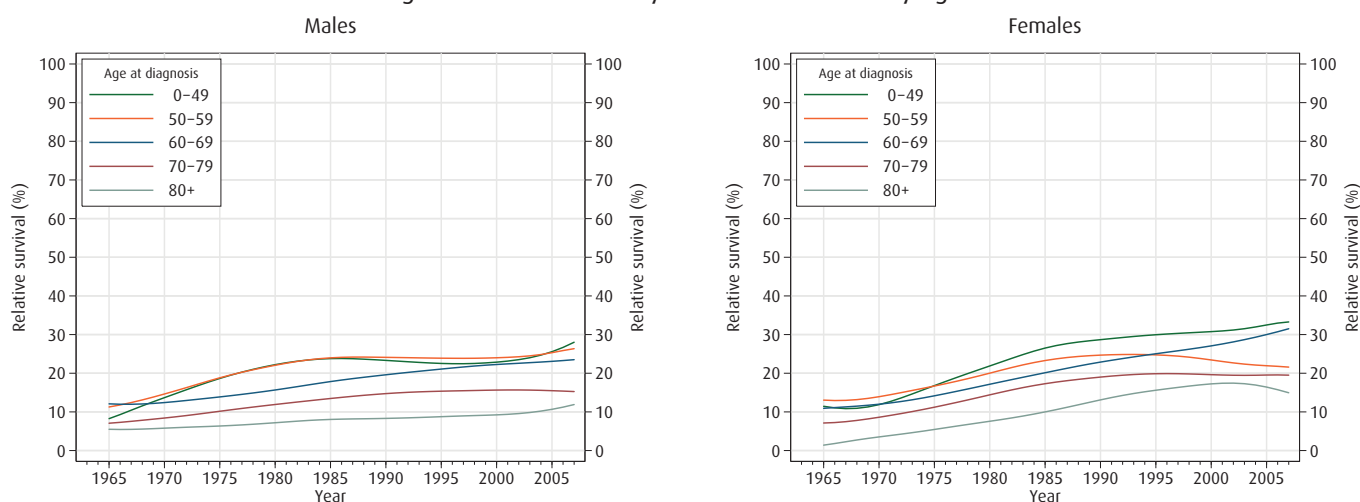


Figure S11c: Estimates of trends in the proportion cured and the median survival time for the uncured

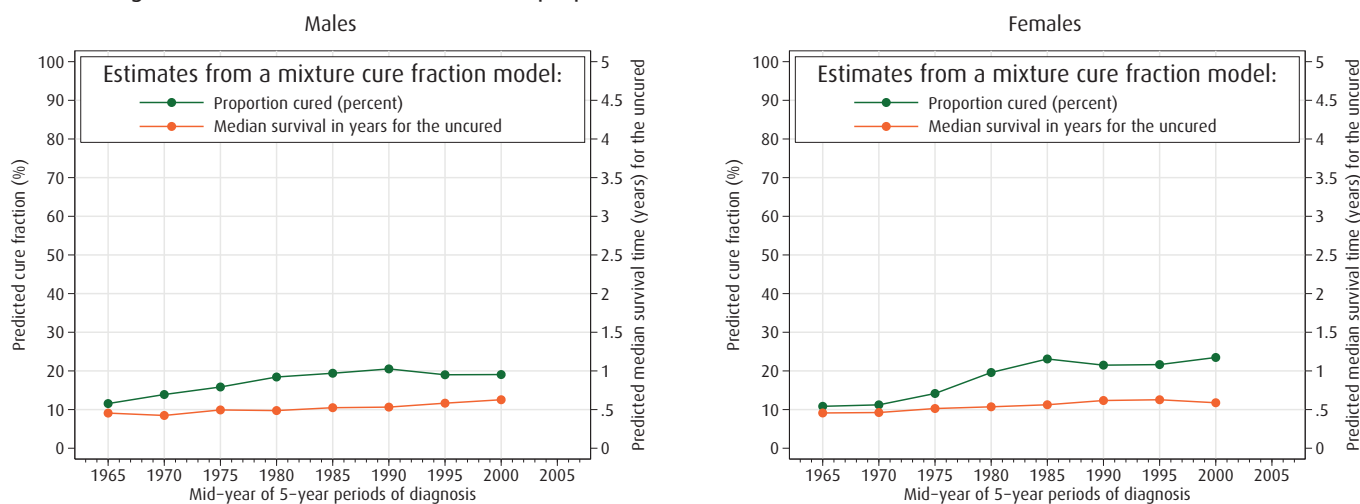


Figure S11d: Relative survival up to 15 years after diagnosis by sex and age

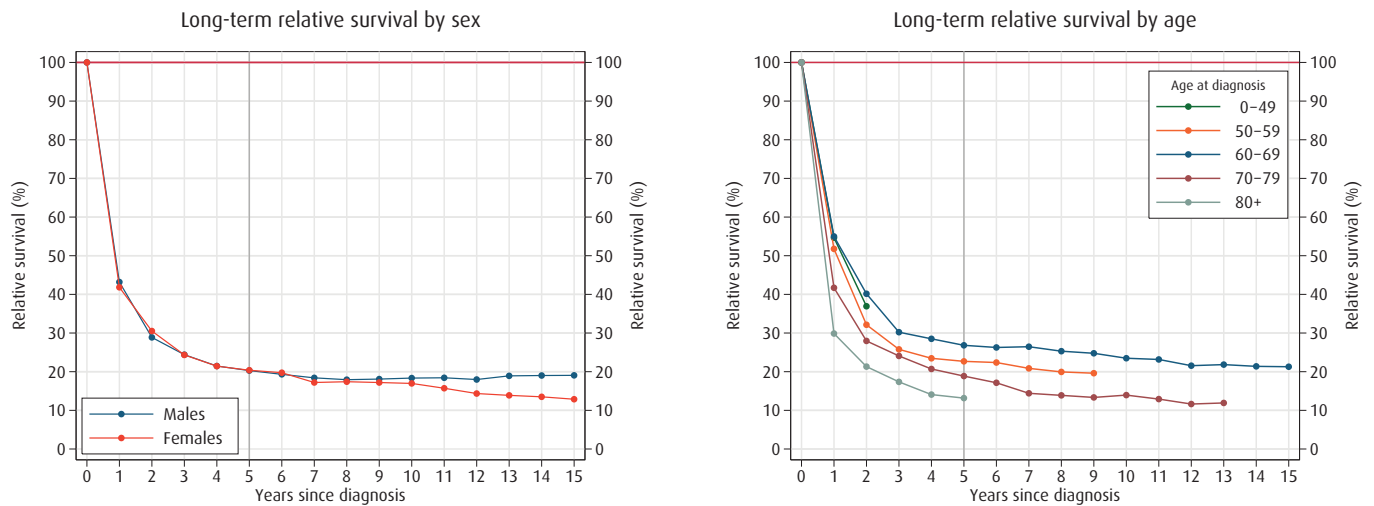


Figure S11e: Conditional 5-year relative survival for every additional year after diagnosis

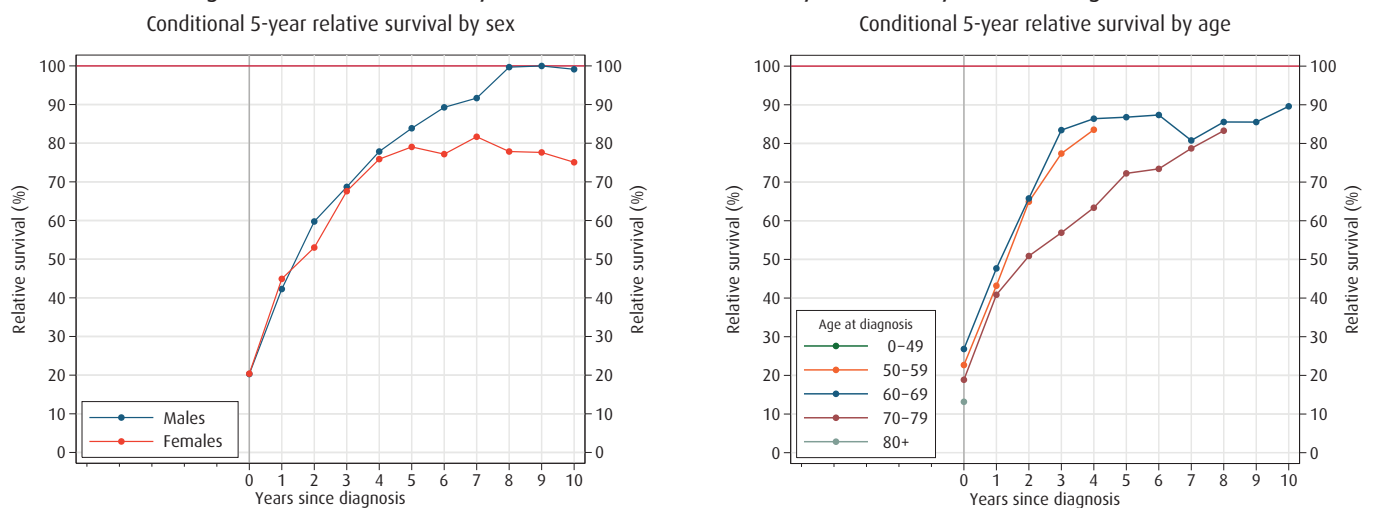
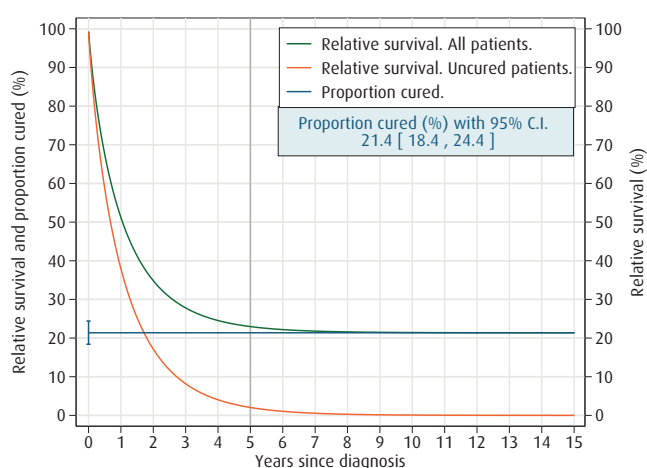


Figure S11f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003–2007)

Age	Males	Females	All	%
0-49	72	73	145	5.5
50-59	114	188	302	11.4
60-69	180	329	509	19.1
70-79	281	542	823	30.9
80+	408	473	881	33.1
Total	1055	1605	2660	100.0

Figure S12a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

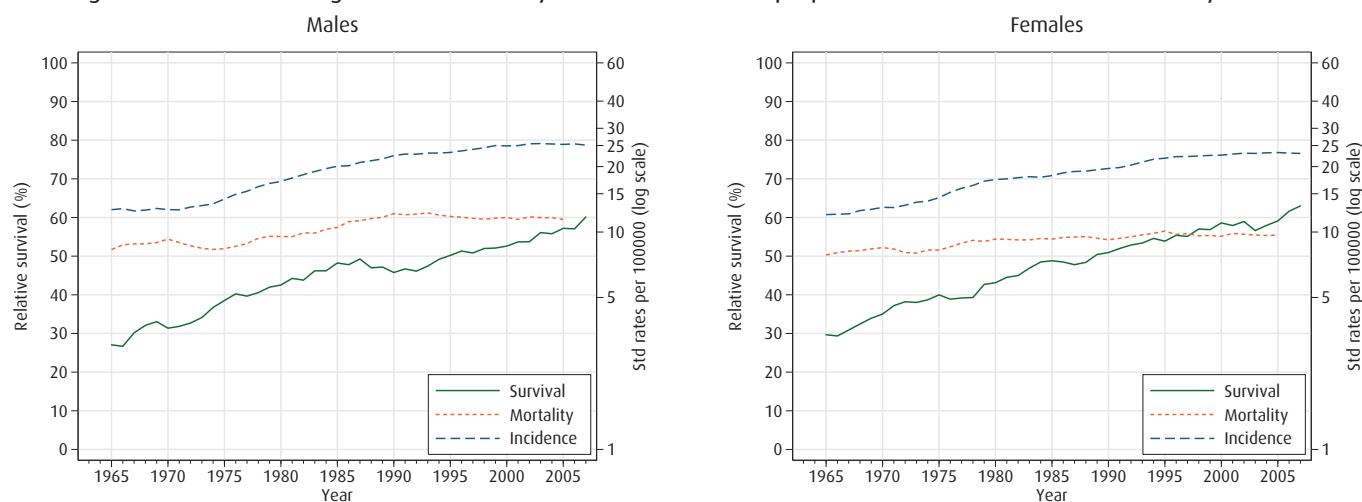


Figure S12b: Trends in 5-year relative survival by age

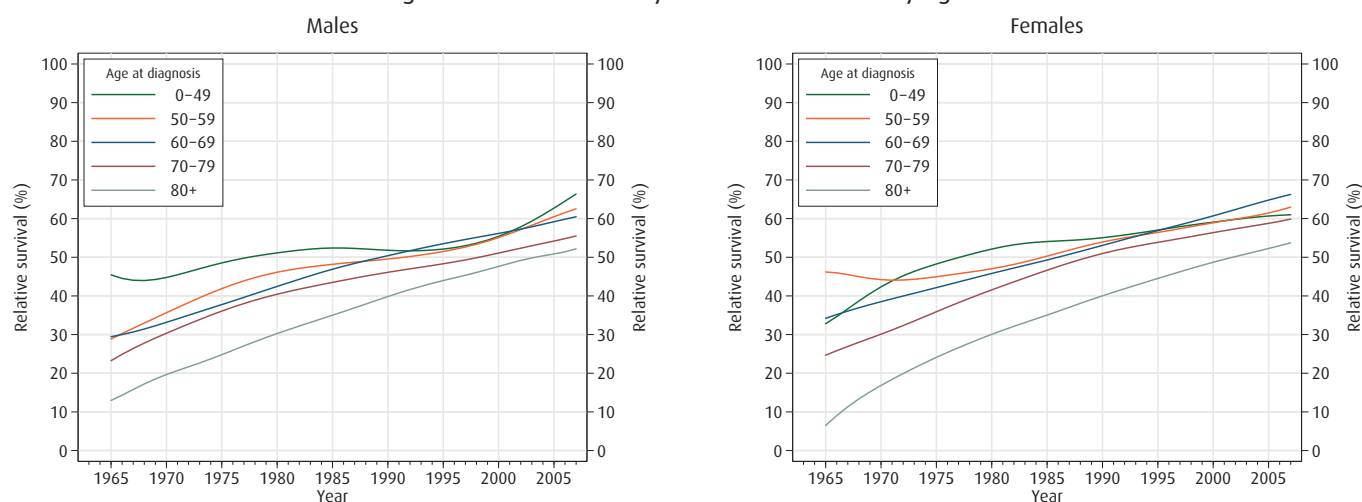


Figure S12c: Estimates of trends in the proportion cured and the median survival time for the uncured

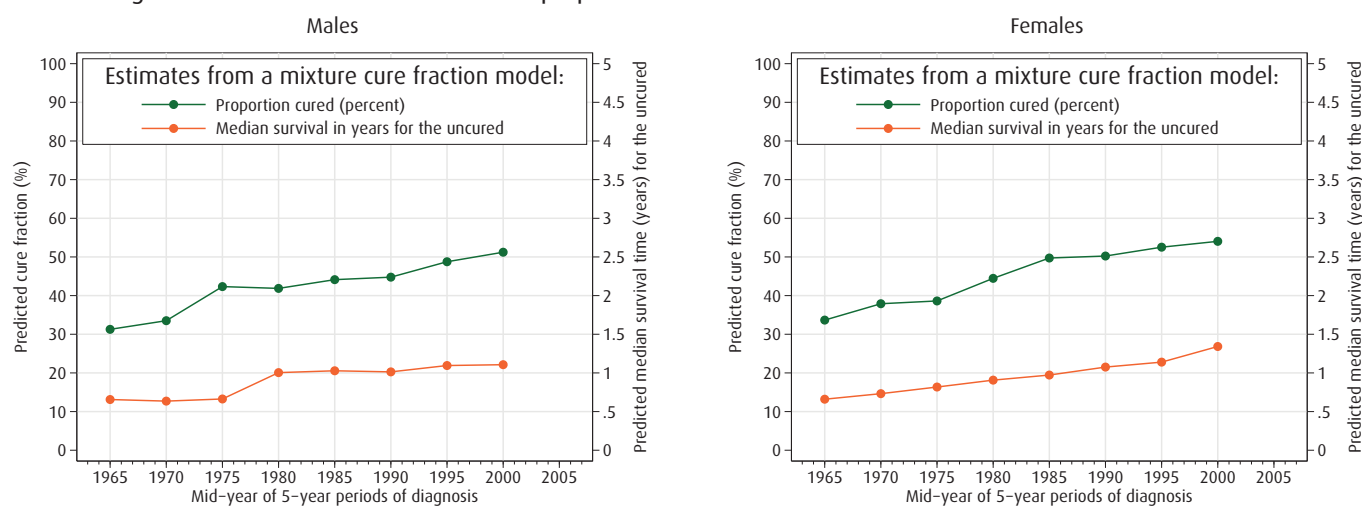


Figure S12d: Relative survival up to 15 years after diagnosis by sex and age

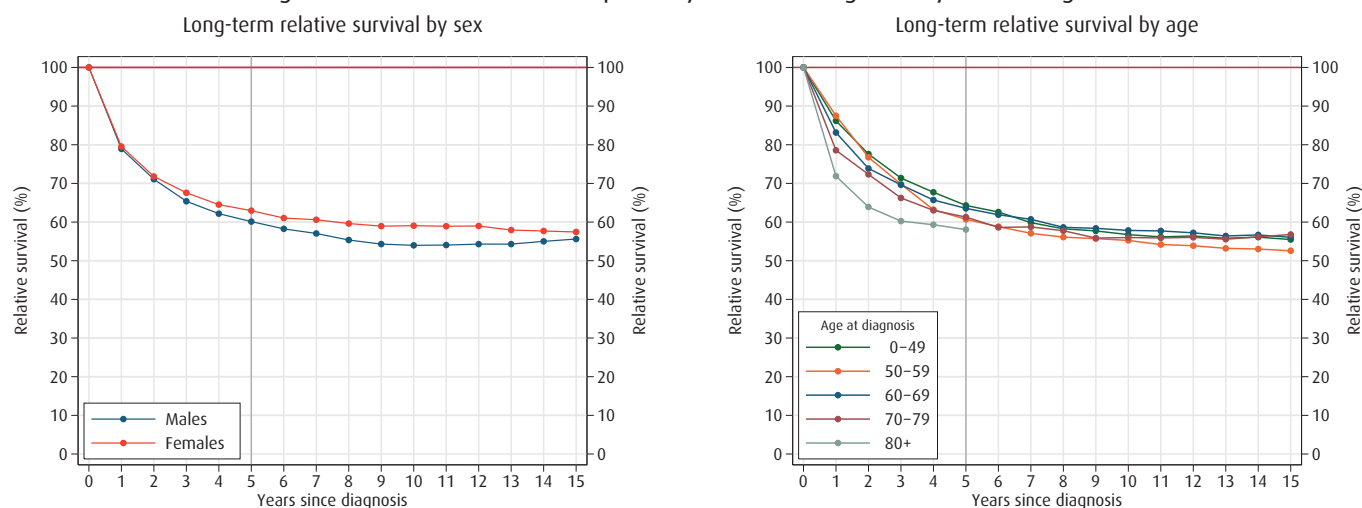


Figure S12e: Conditional 5-year relative survival for every additional year after diagnosis

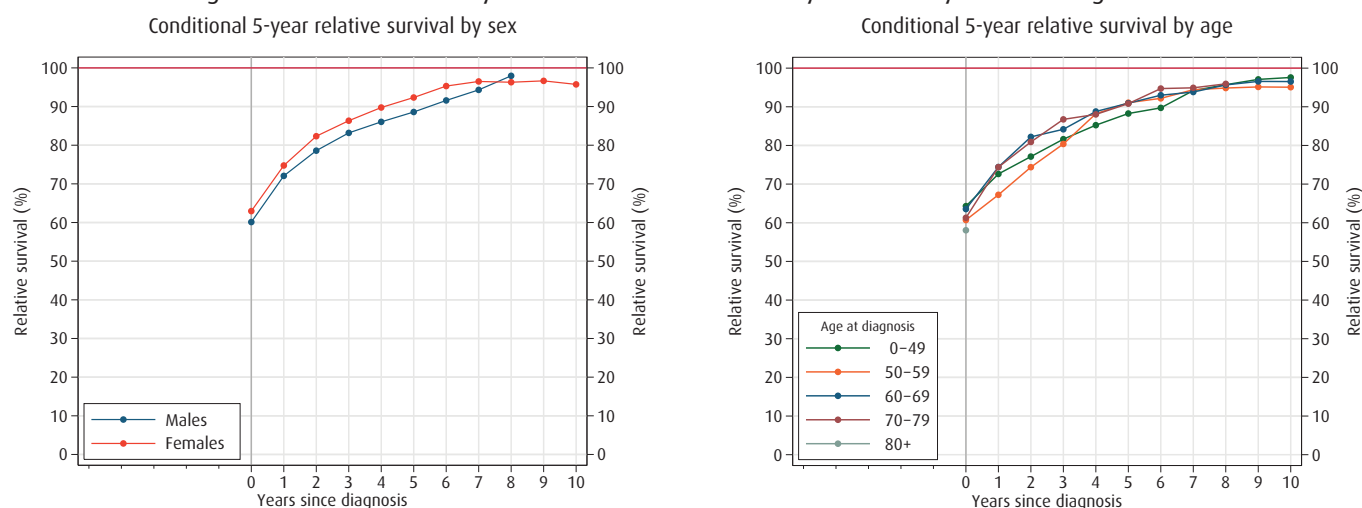
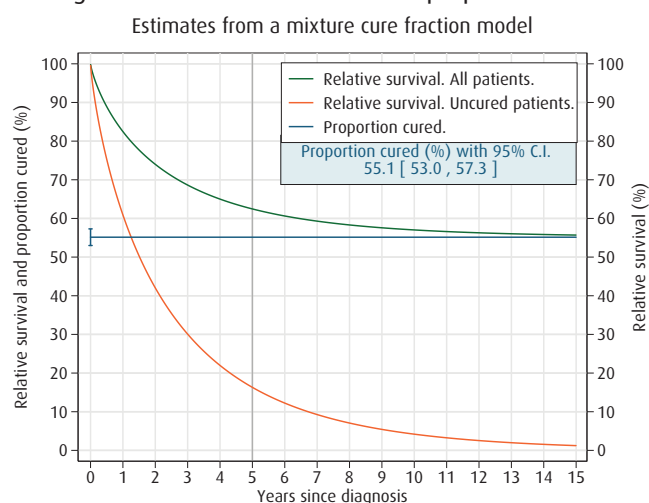


Figure S12f: Relative survival and proportion cured



Age distribution of patients (2003–2007)

Age	Males	Females	All	%
0-49	290	270	560	5.1
50-59	602	607	1209	11.1
60-69	1155	1146	2301	21.0
70-79	1778	1749	3527	32.2
80+	2042	1299	3341	30.5
Total	5867	5071	10938	100.0

Figure S13a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

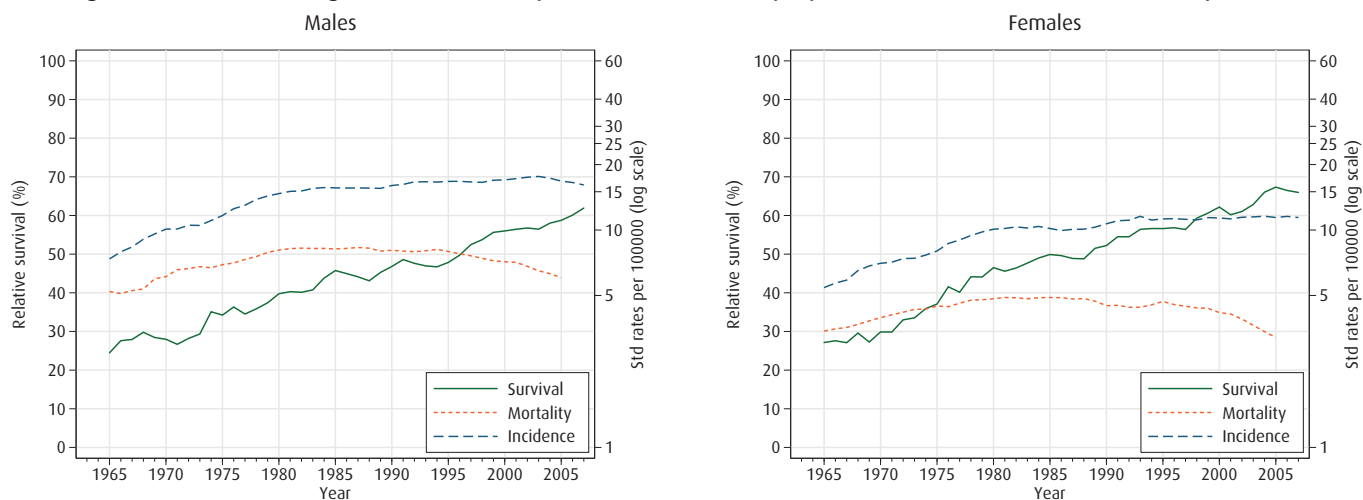


Figure S13b: Trends in 5-year relative survival by age

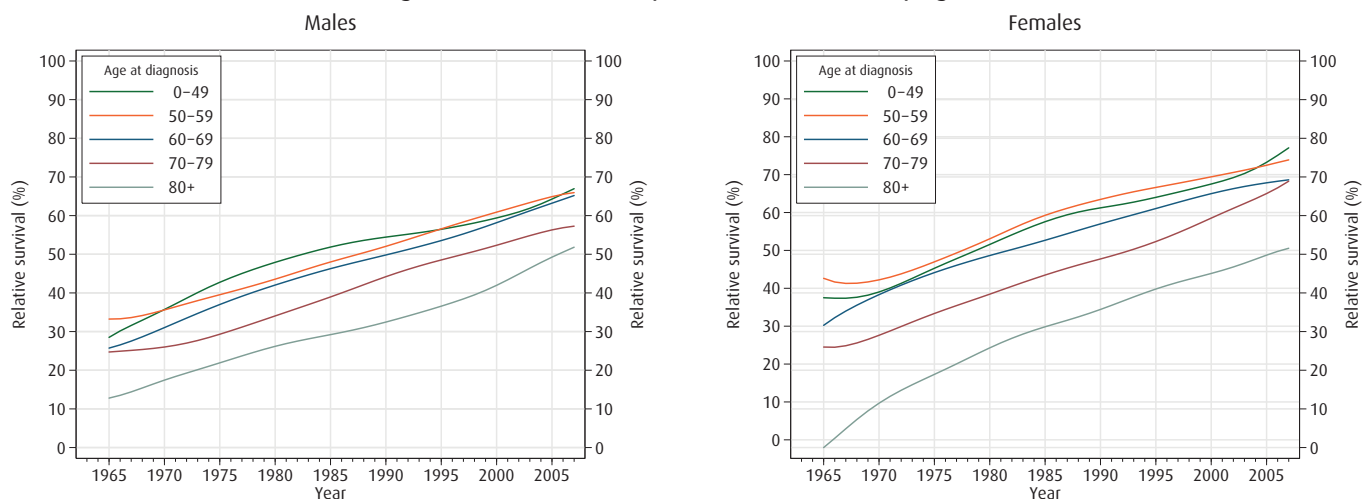


Figure S13c: Estimates of trends in the proportion cured and the median survival time for the uncured

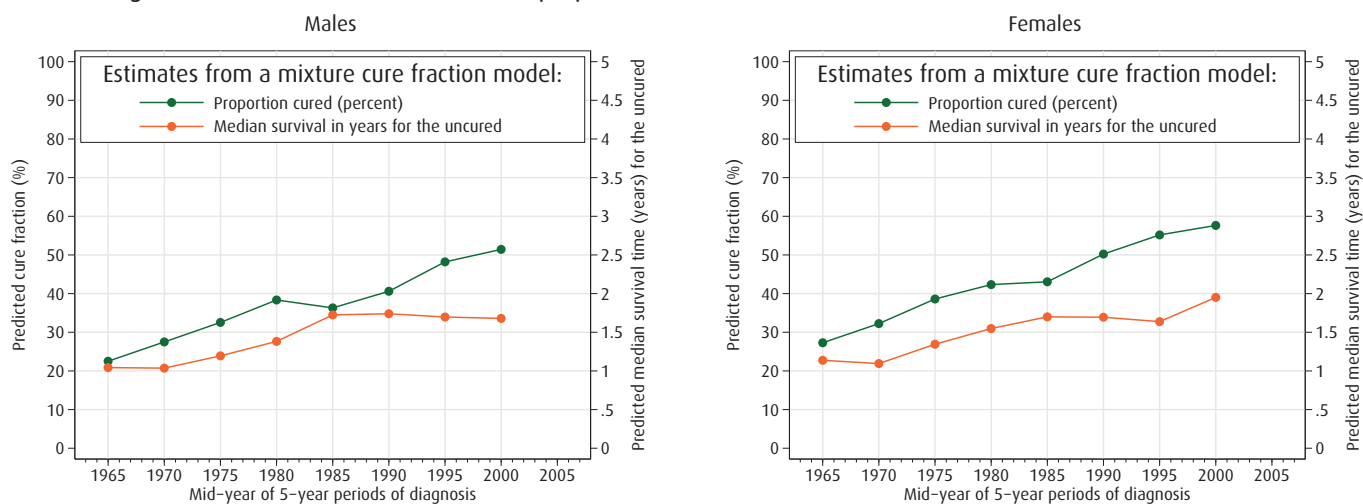


Figure S13d: Relative survival up to 15 years after diagnosis by sex and age

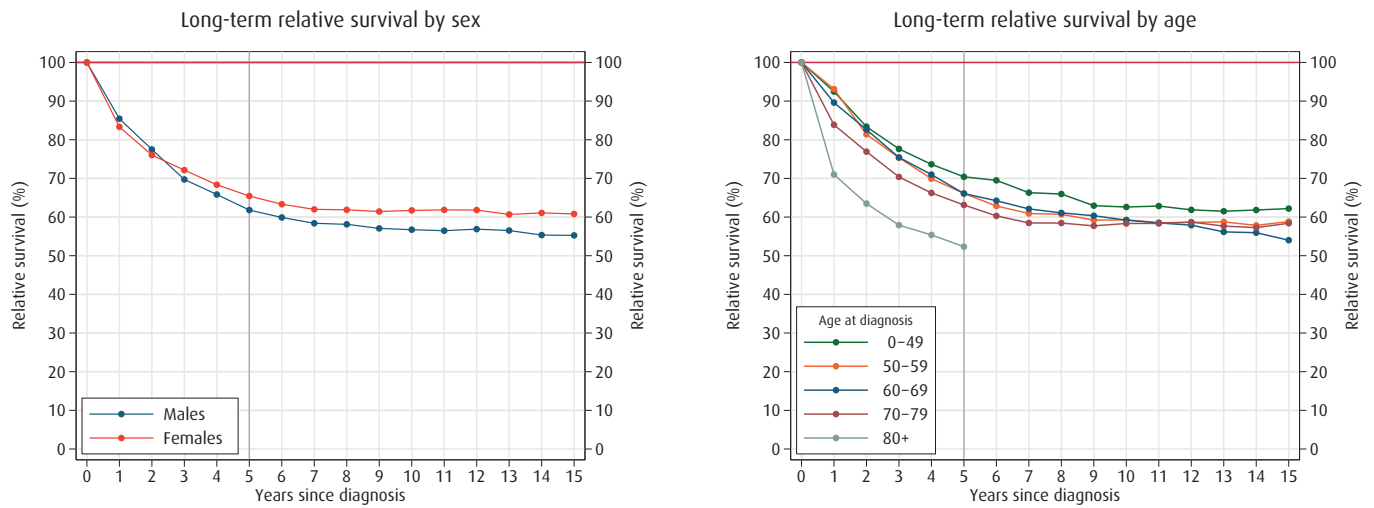


Figure S13e: Conditional 5-year relative survival for every additional year after diagnosis

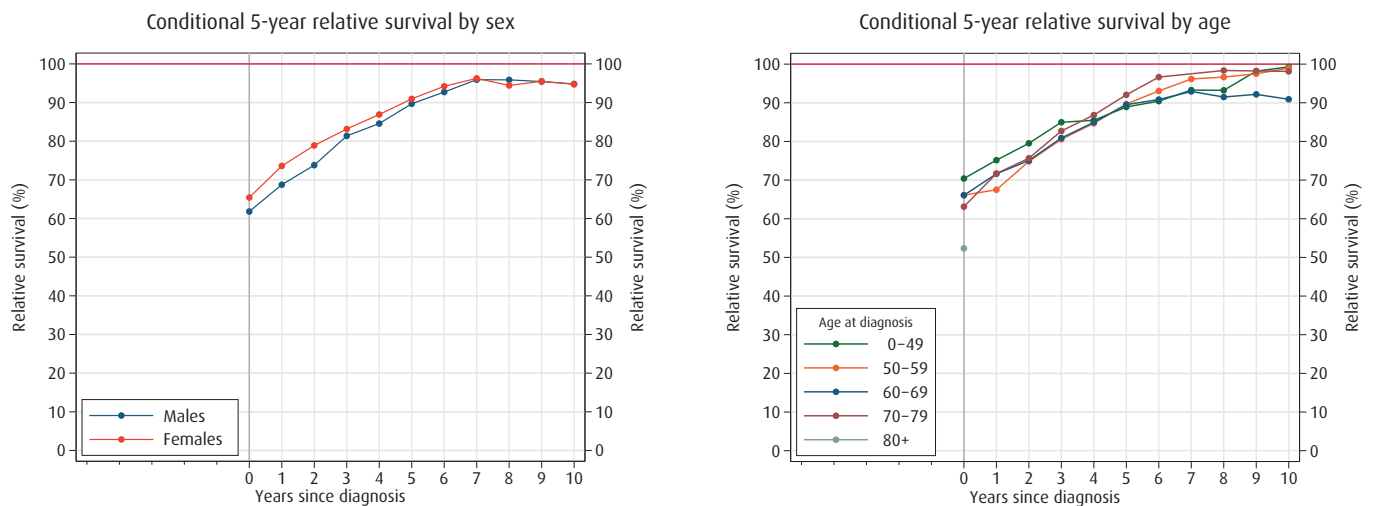
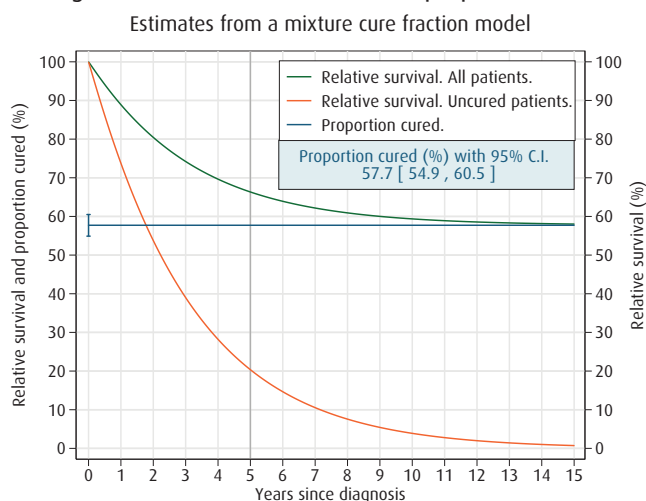


Figure S13f: Relative survival and proportion cured



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-49	188	181	369	6.3
50-59	374	520	894	15.2
60-69	596	869	1465	24.9
70-79	705	976	1681	28.6
80+	767	697	1464	24.9
Total	2630	3243	5873	100.0

Figure S14a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

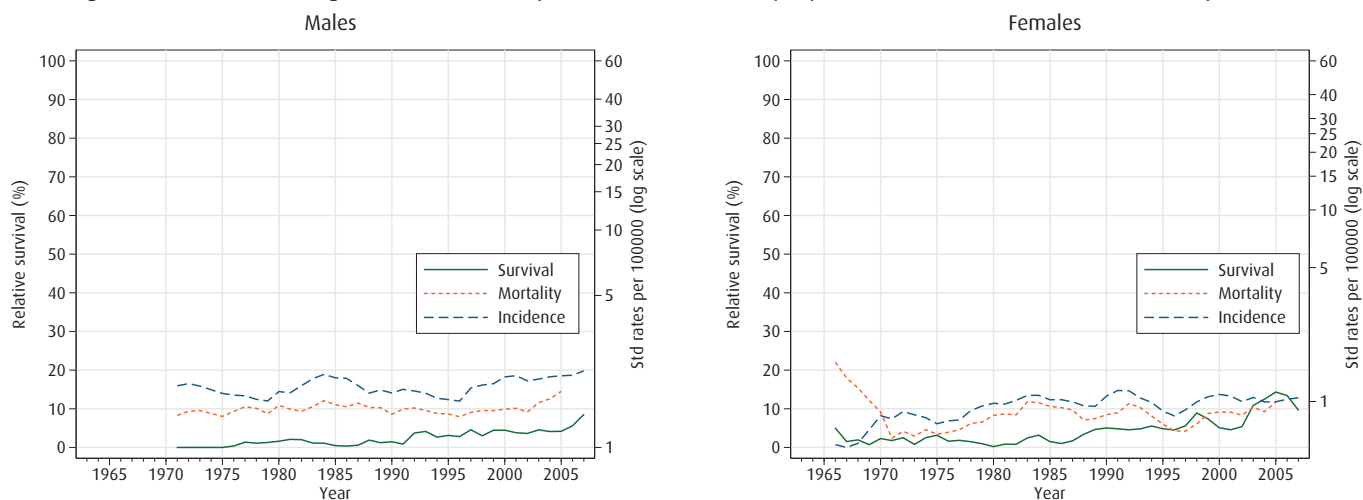


Figure S14b: Trends in 5-year relative survival by age

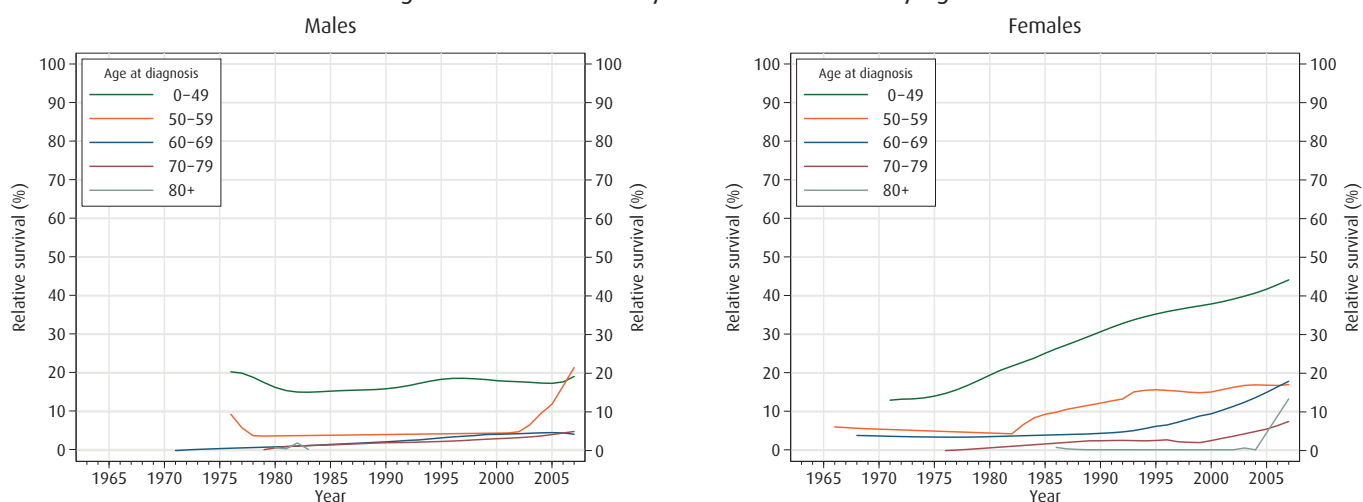


Figure S14c: Estimates of trends in the proportion cured and the median survival time for the uncured

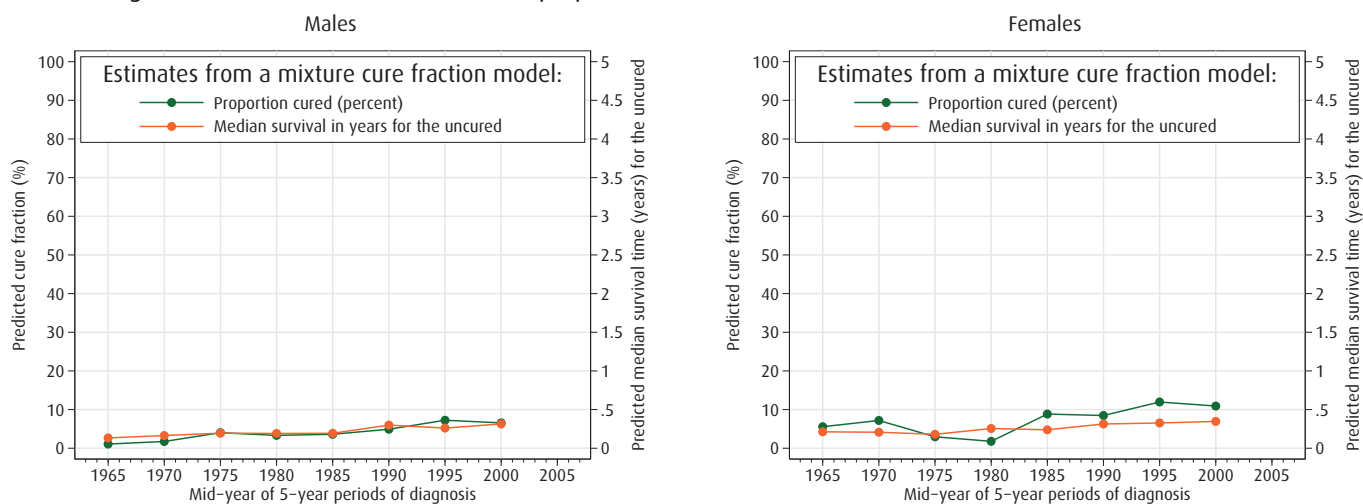


Figure S14d: Relative survival up to 15 years after diagnosis by sex and age

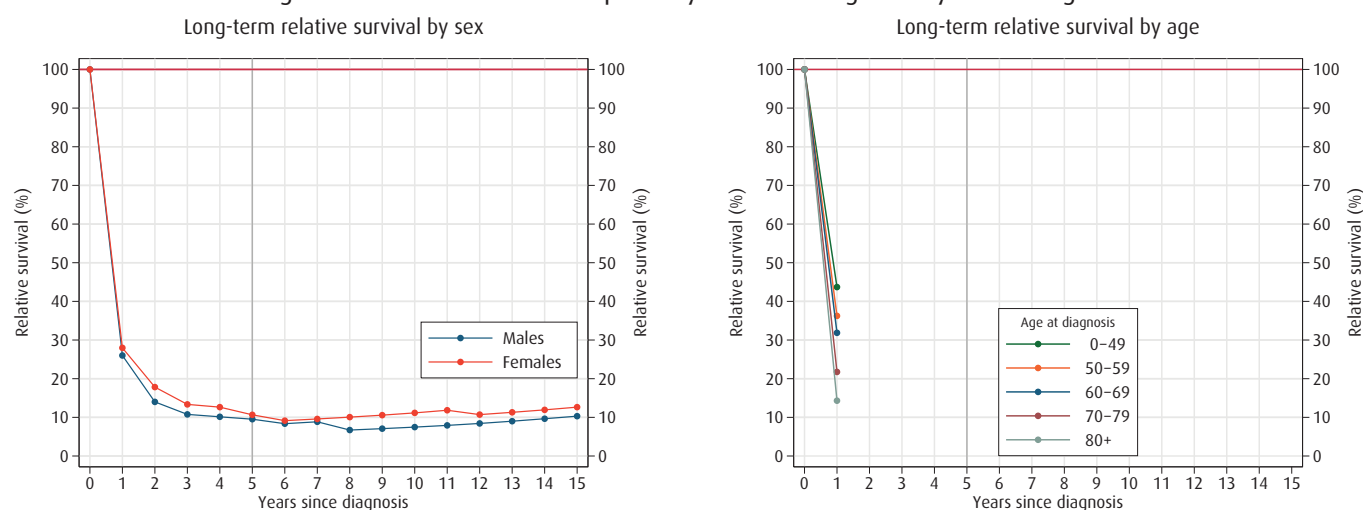


Figure S14e: Conditional 5-year relative survival for every additional year after diagnosis

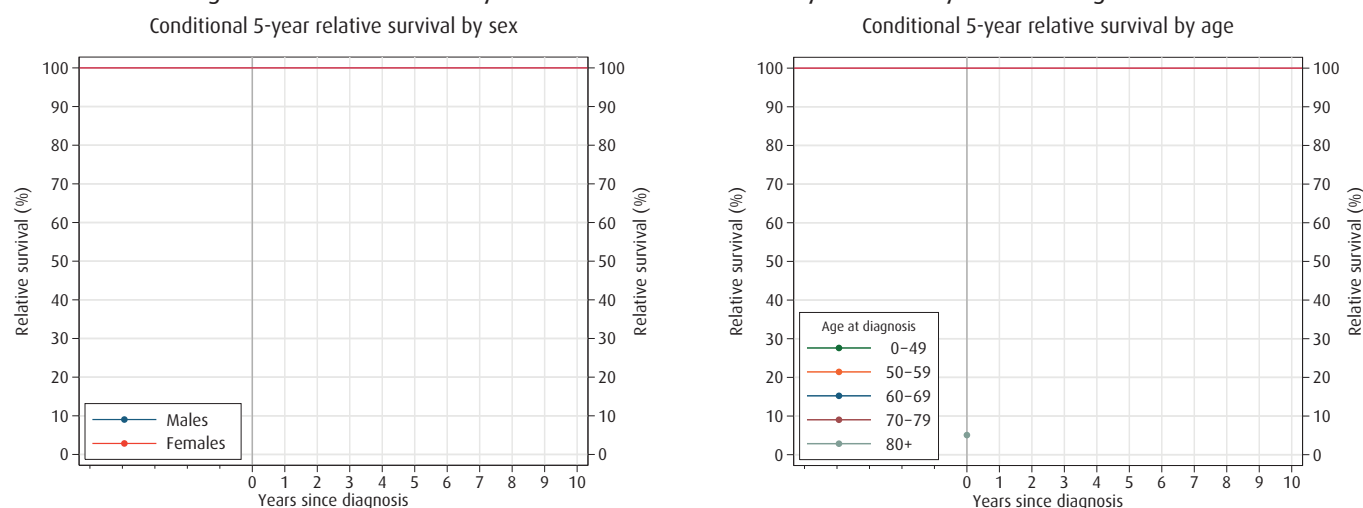
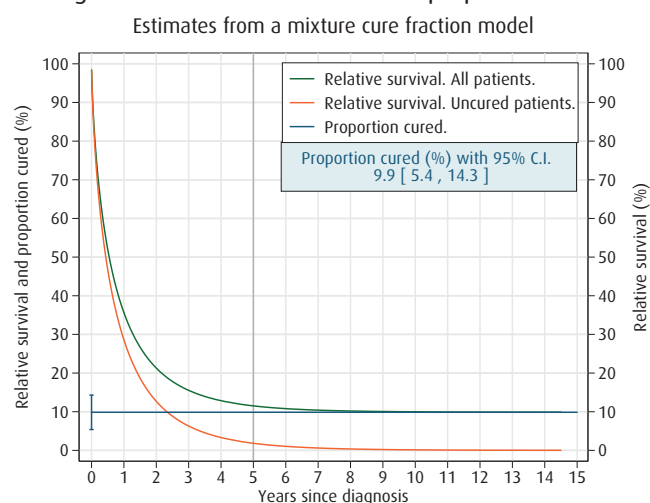


Figure S14f: Relative survival and proportion cured



Age distribution of patients (2003–2007)

Age	Males	Females	All	%
0-49	22	48	70	12.5
50-59	16	59	75	13.3
60-69	41	74	115	20.5
70-79	67	94	161	28.6
80+	63	78	141	25.1
Total	209	353	562	100.0

Figure S15a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

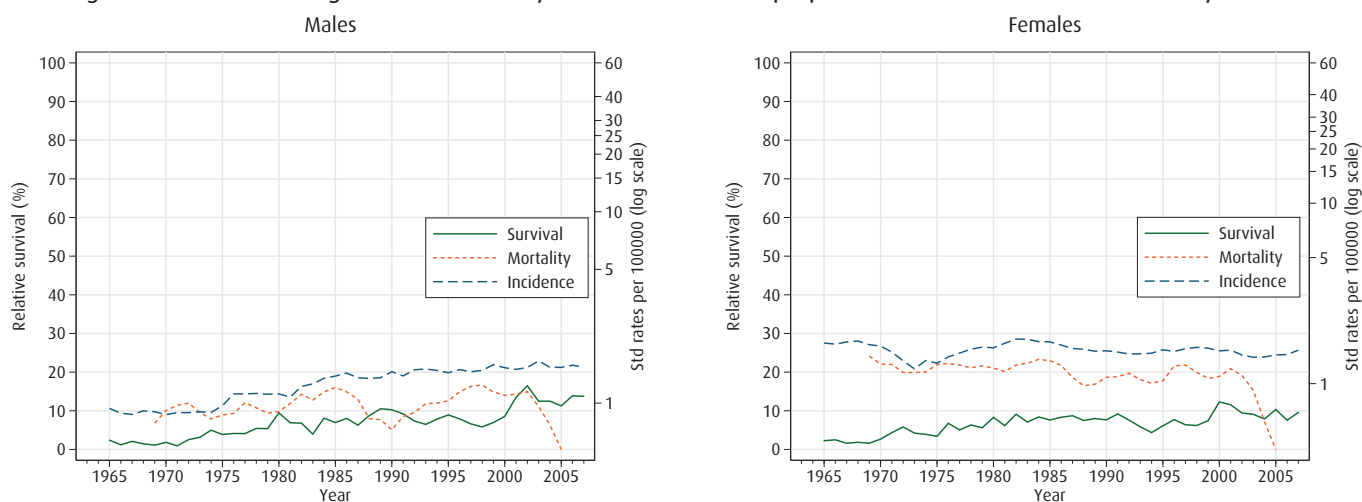


Figure S15b: Trends in 5-year relative survival by age

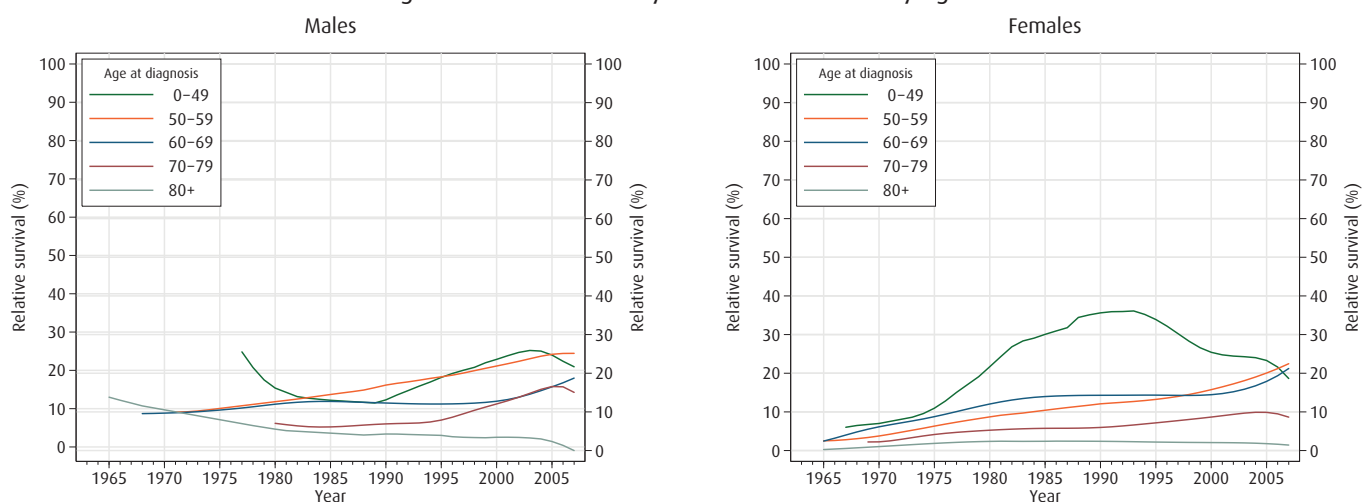


Figure S15c: Estimates of trends in the proportion cured and the median survival time for the uncured

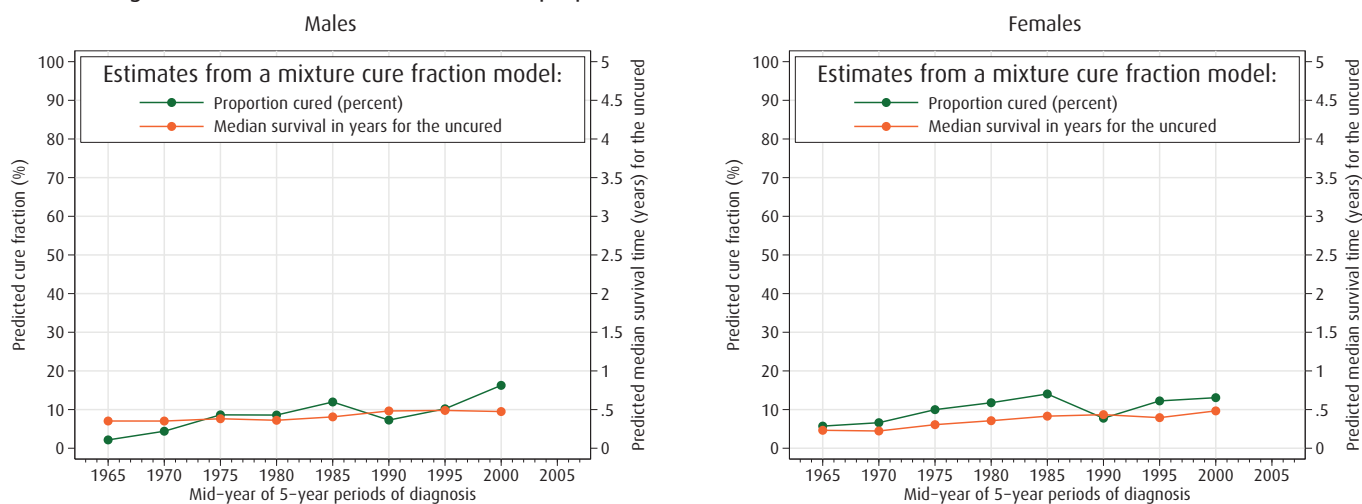


Figure S15d: Relative survival up to 15 years after diagnosis by sex and age

Figure S15e: Conditional 5-year relative survival for every additional year after diagnosis

Figure S15f: Relative survival and proportion cured

Age distribution of patients (2003–2007)

Figure S16a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

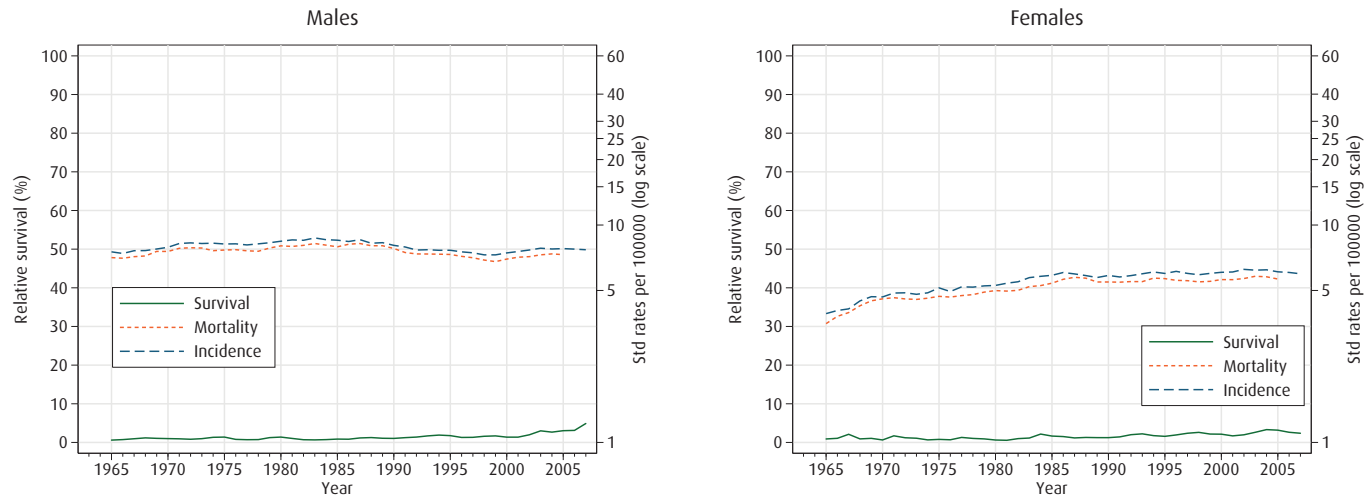


Figure S16b: Trends in 5-year relative survival by age

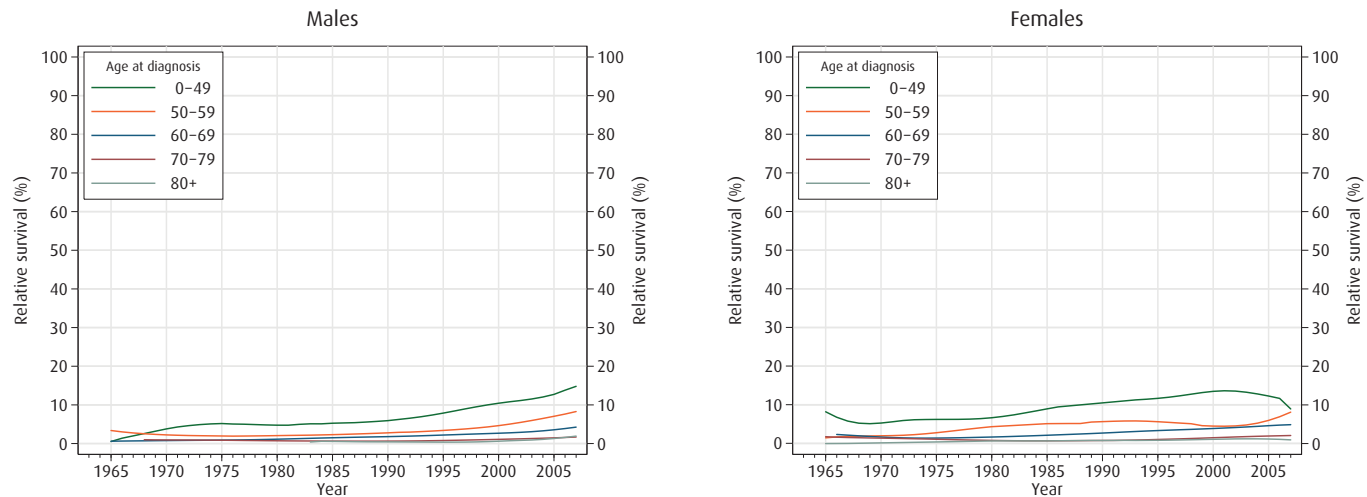


Figure S16c: Estimates of trends in the proportion cured and the median survival time for the uncured

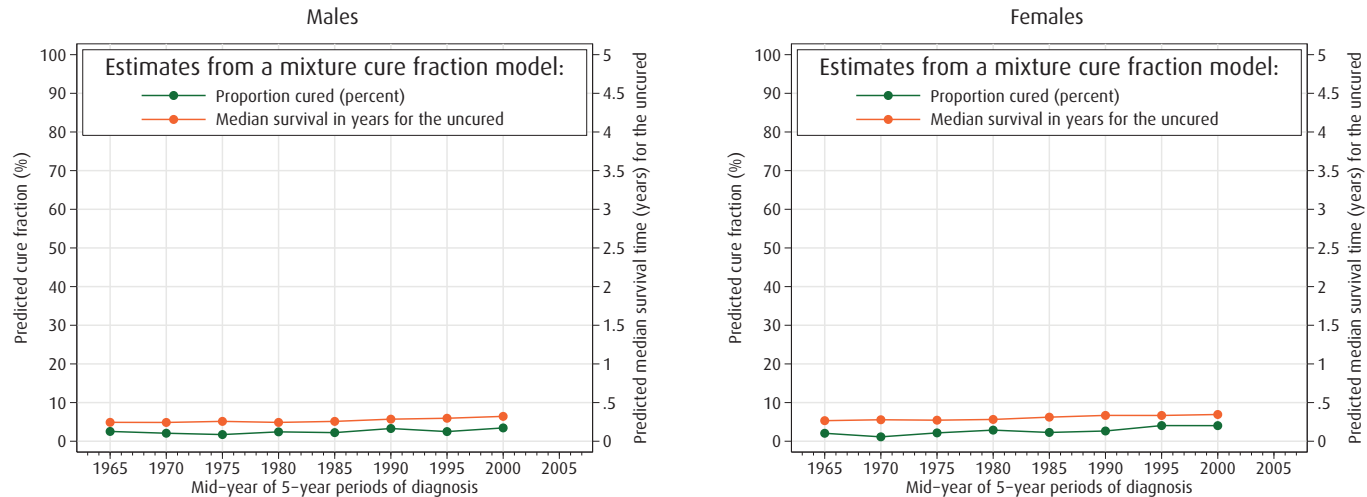


Figure S16d: Relative survival up to 15 years after diagnosis by sex and age

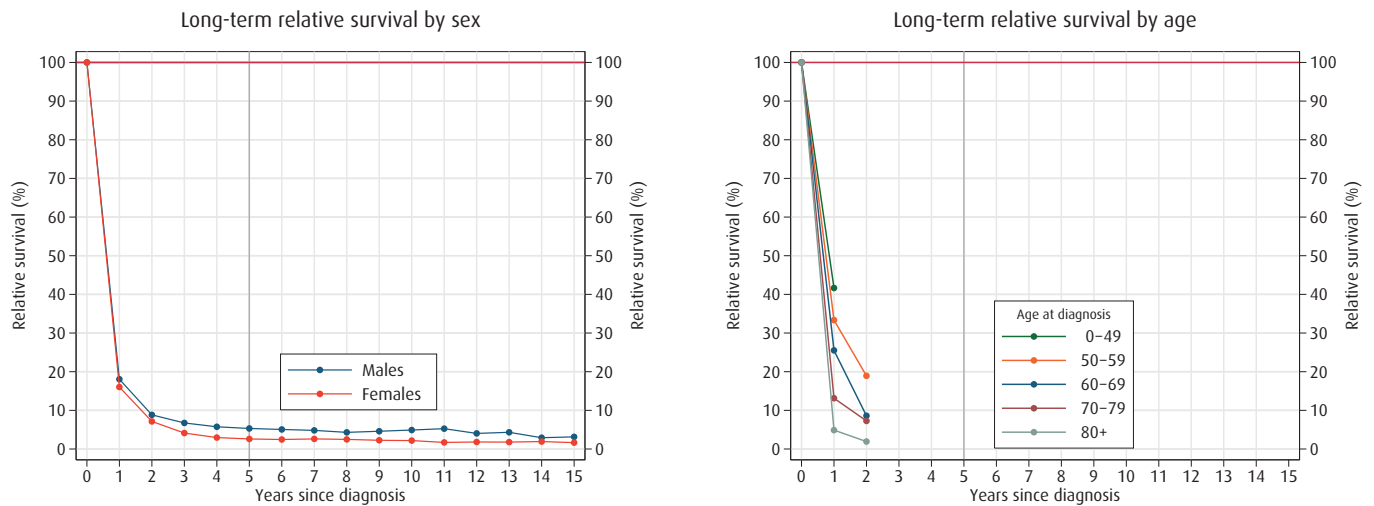


Figure S16e: Conditional 5-year relative survival for every additional year after diagnosis

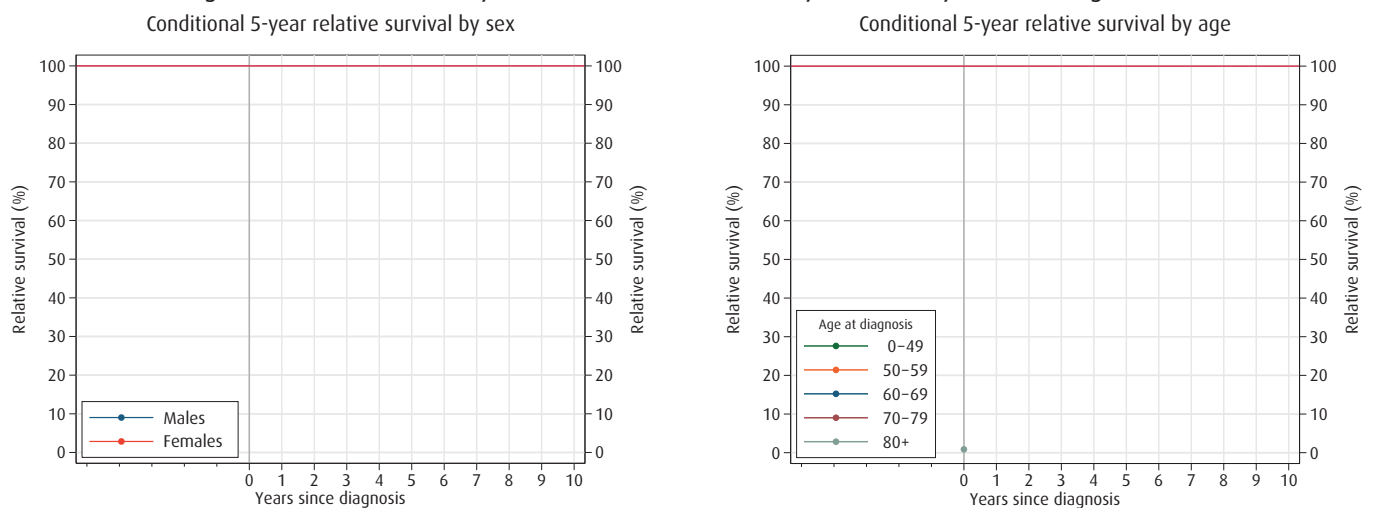
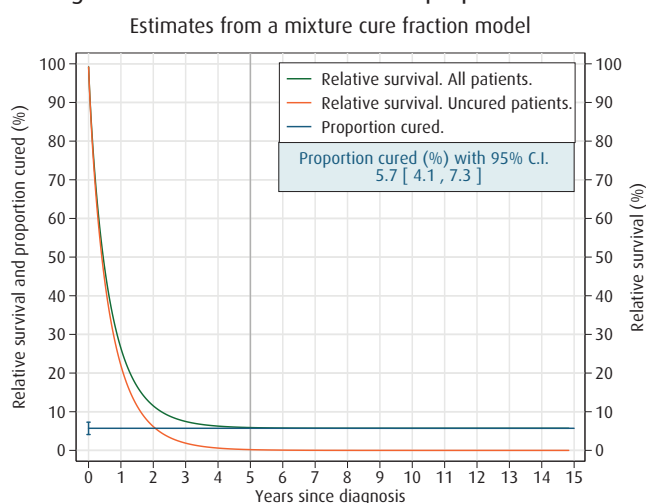


Figure S16f: Relative survival and proportion cured



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-49	67	69	136	4.7
50-59	158	216	374	12.8
60-69	315	412	727	25.0
70-79	420	437	857	29.4
80+	518	301	819	28.1
Total	1478	1435	2913	100.0

Figure S17a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

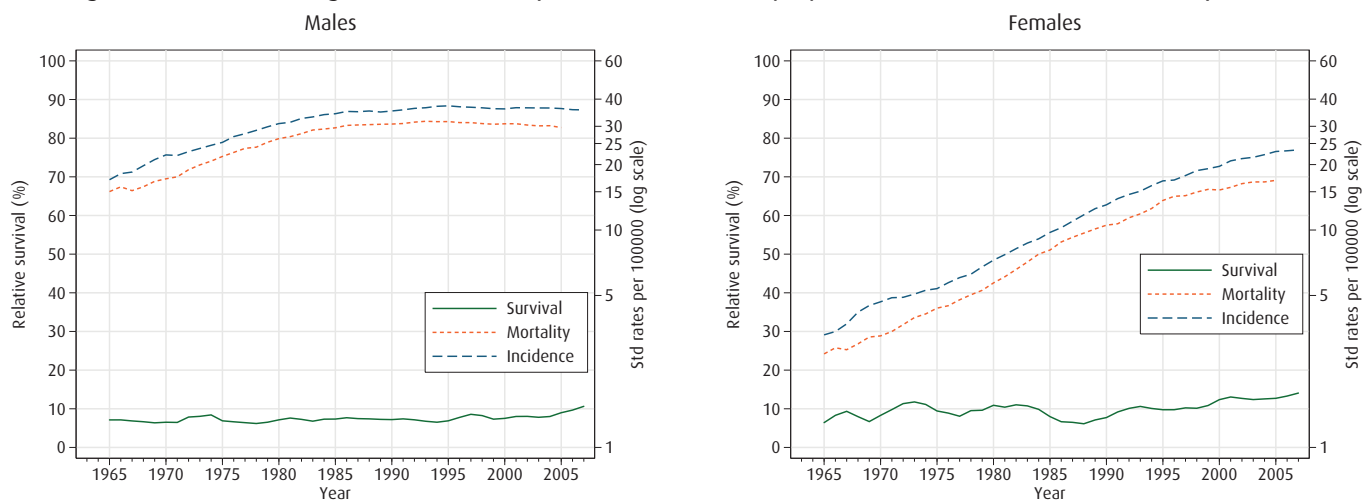


Figure S17b: Trends in 5-year relative survival by age

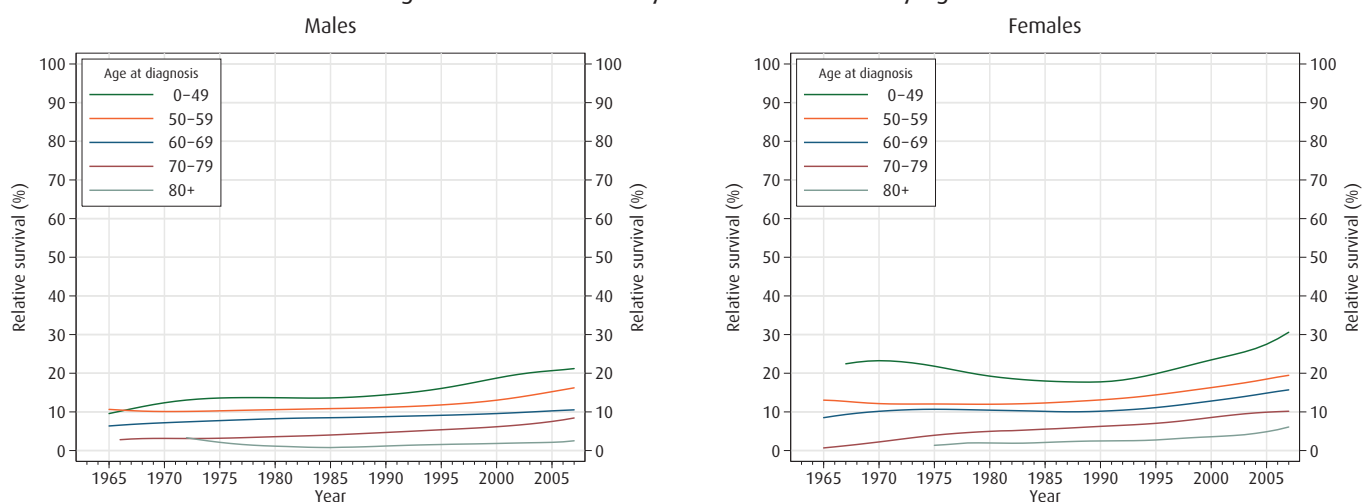


Figure S17c: Estimates of trends in the proportion cured and the median survival time for the uncured

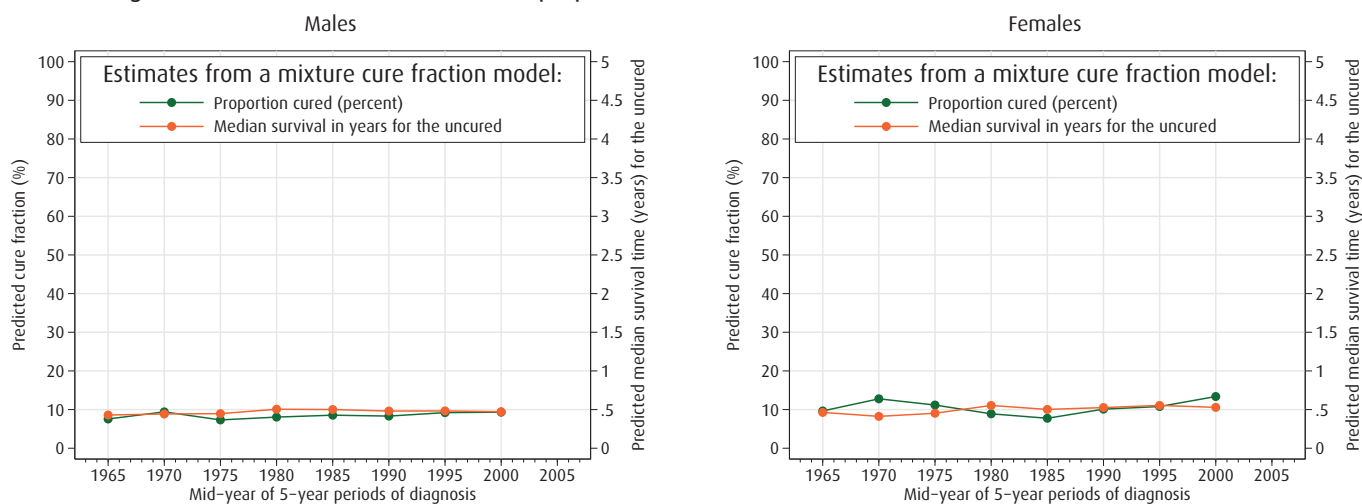


Figure S17d: Relative survival up to 15 years after diagnosis by sex and age

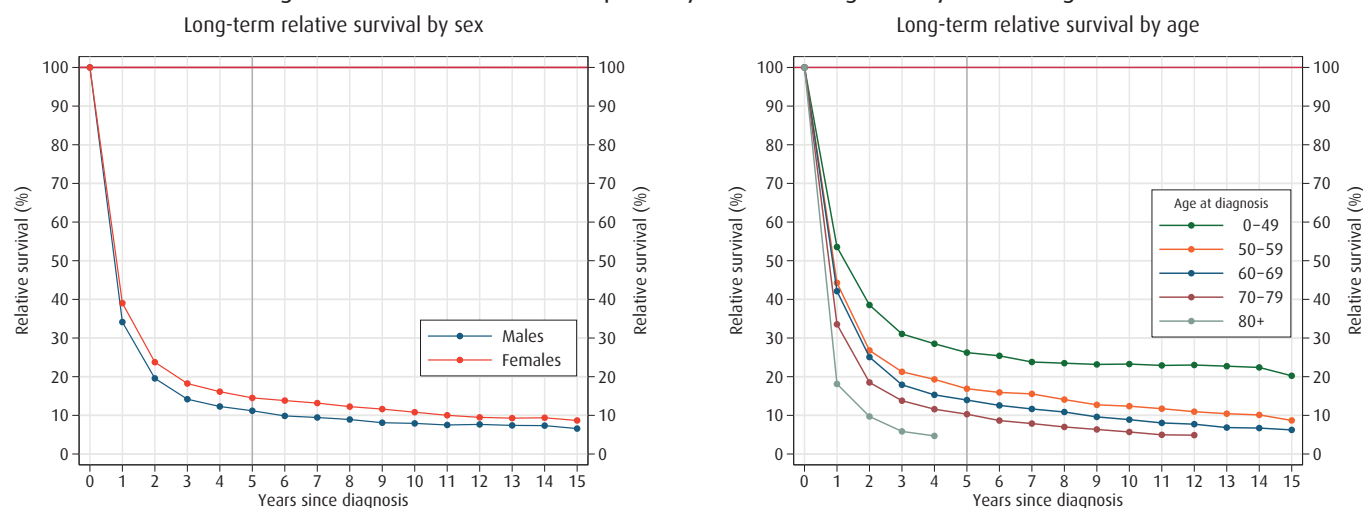


Figure S17e: Conditional 5-year relative survival for every additional year after diagnosis

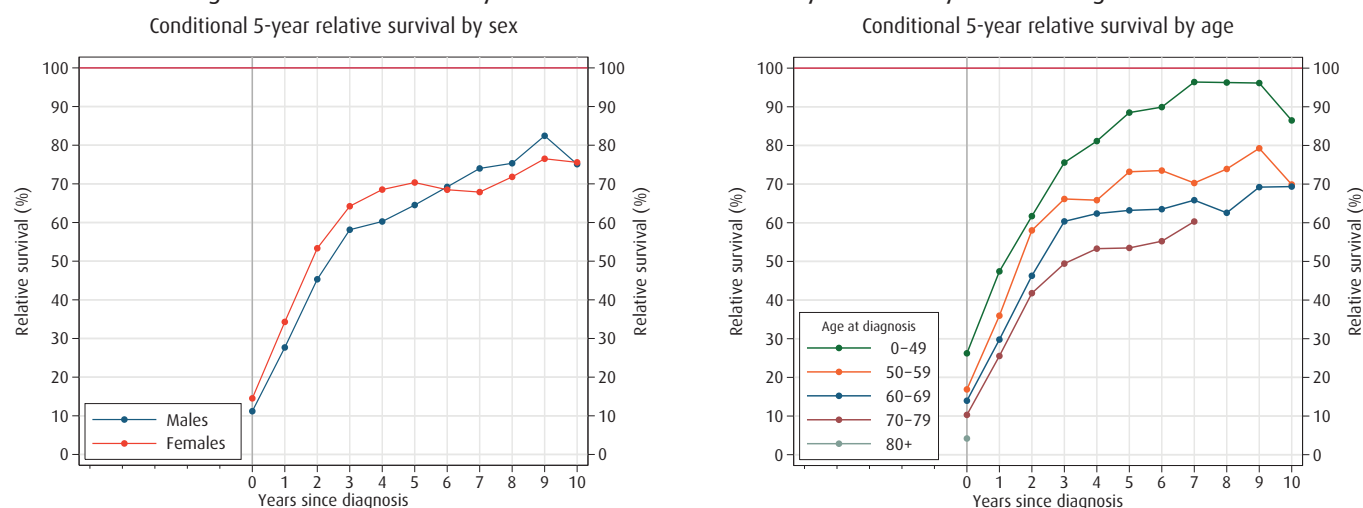
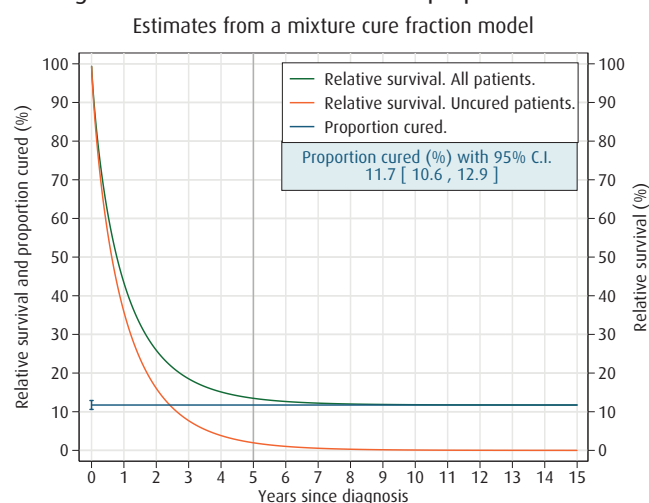


Figure S17f: Relative survival and proportion cured



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-49	228	232	460	4.0
50-59	832	1003	1835	16.1
60-69	1334	1950	3284	28.8
70-79	1533	2399	3932	34.5
80+	674	1210	1884	16.5
Total	4601	6794	11395	100.0

Figure S18a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

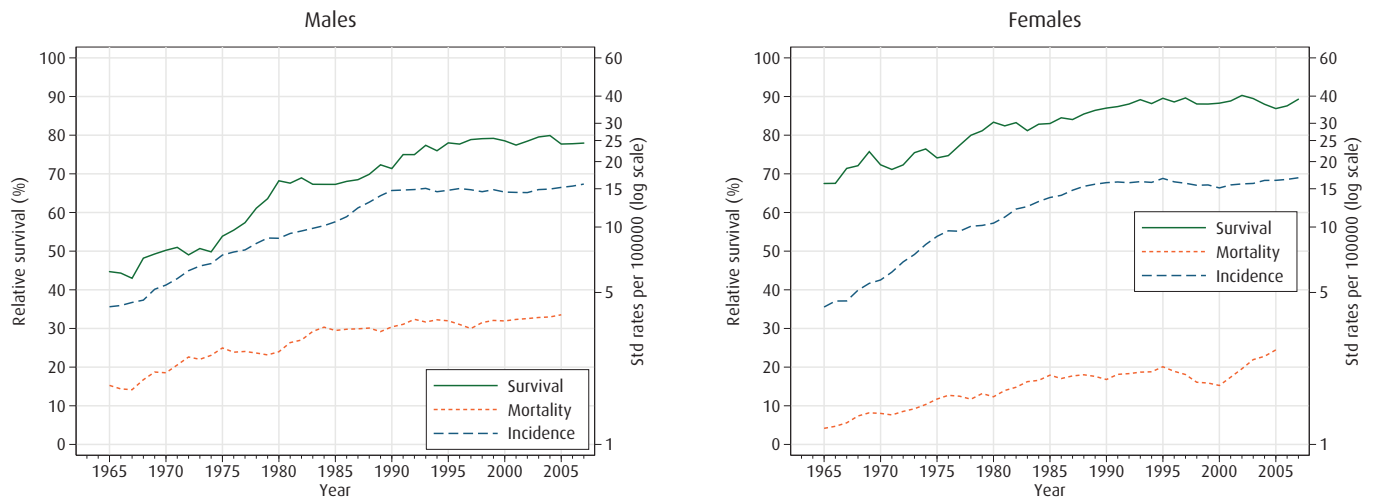


Figure S18b: Trends in 5-year relative survival by age

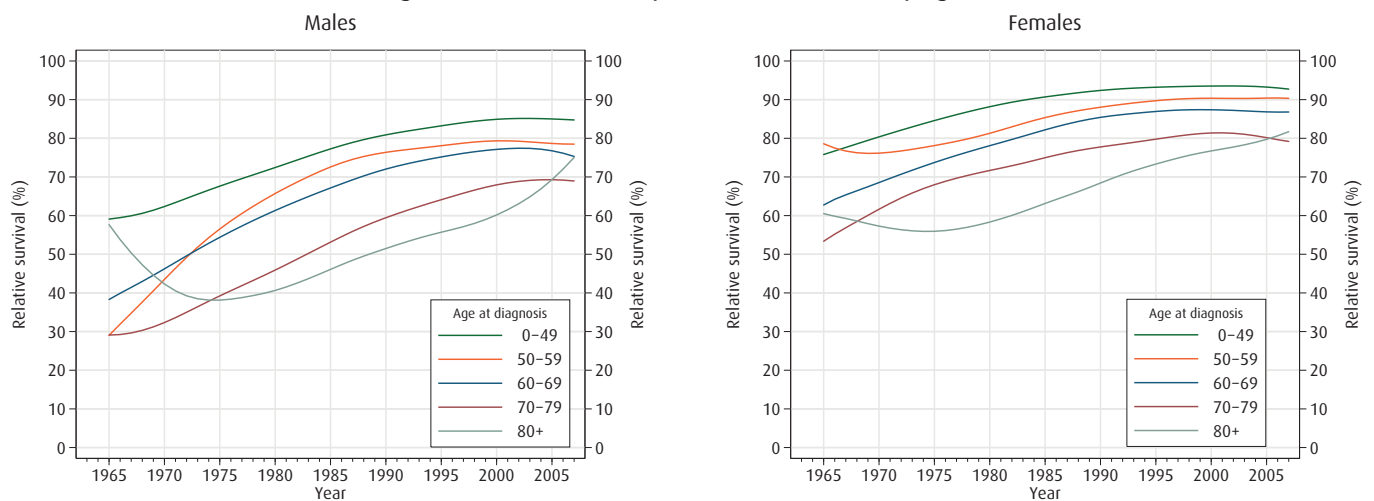


Figure S18c: Estimates of trends in the proportion cured and the median survival time for the uncured

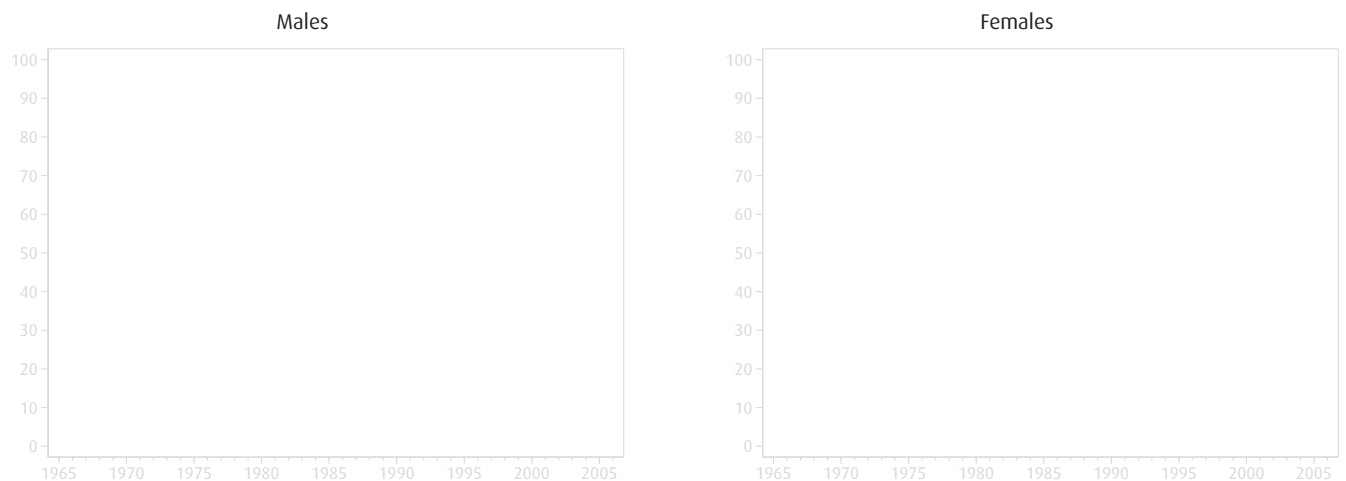


Figure S18d: Relative survival up to 15 years after diagnosis by sex and age

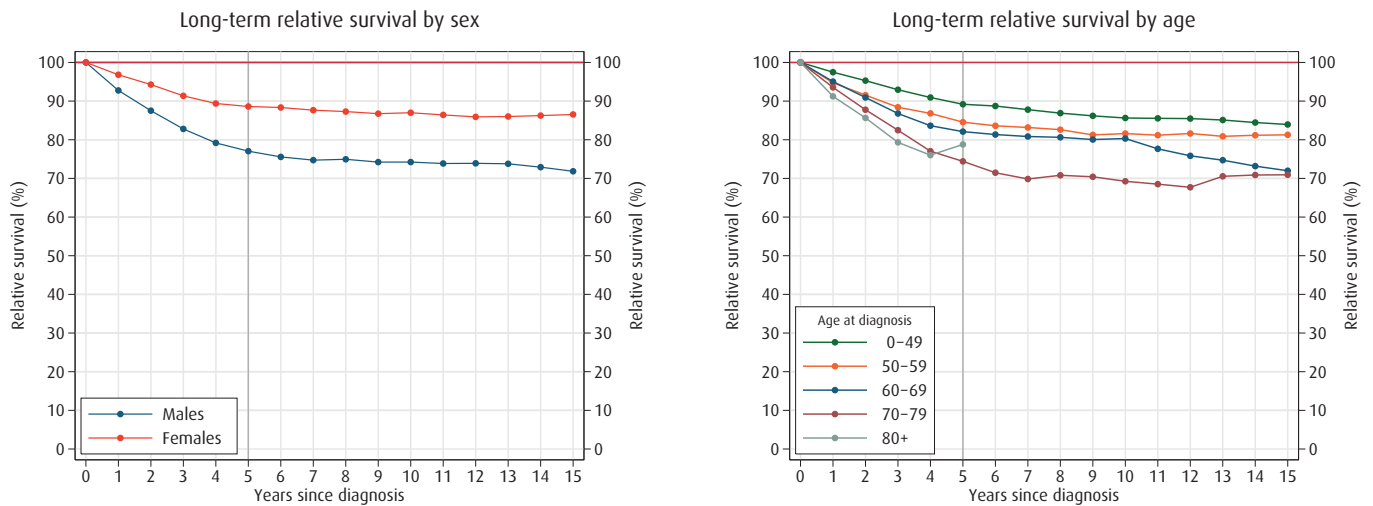


Figure S18e: Conditional 5-year relative survival for every additional year after diagnosis

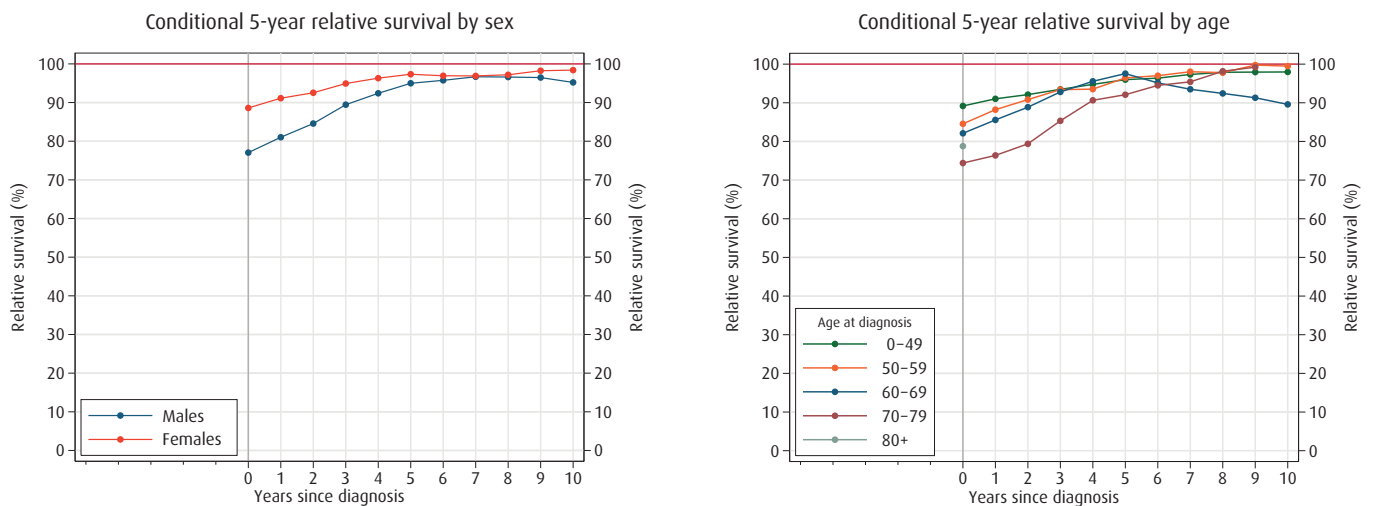
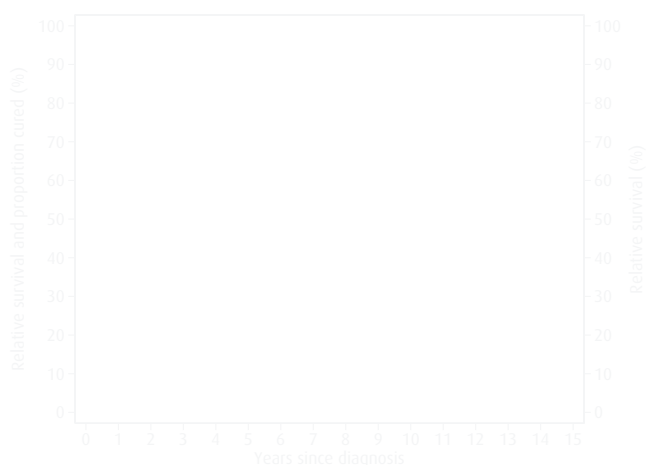


Figure S18f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003–2007)

Age	Males	Females	All	%
0-49	900	529	1429	25.6
50-59	554	545	1099	19.7
60-69	526	620	1146	20.5
70-79	498	588	1086	19.5
80+	447	370	817	14.6
Total	2925	2652	5577	100.0

Figure S19a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

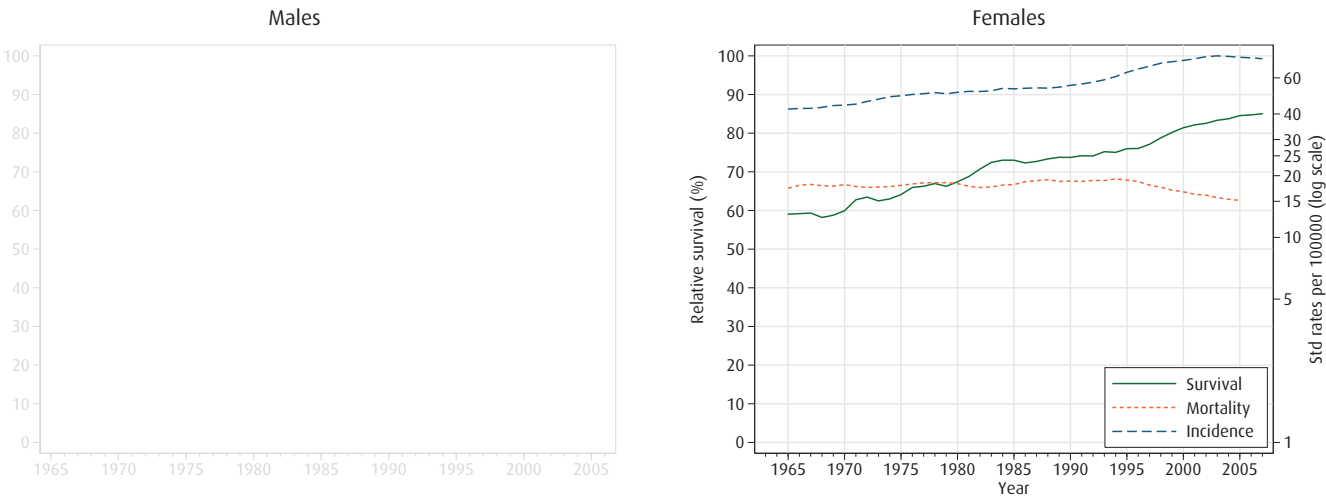


Figure S19b: Trends in 5-year relative survival by age

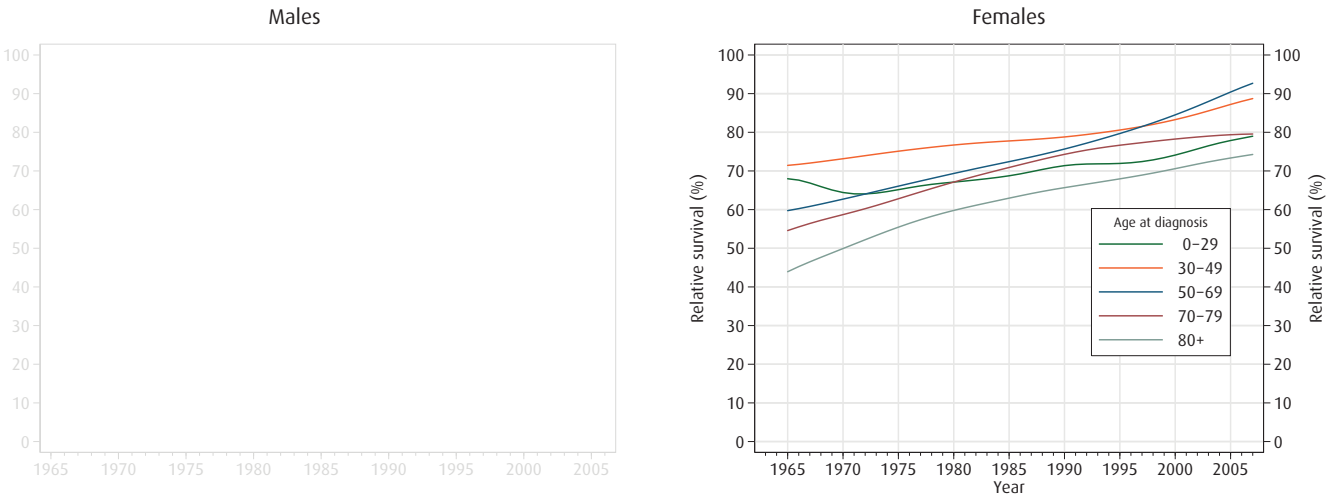


Figure S19c: Estimates of trends in the proportion cured and the median survival time for the uncured

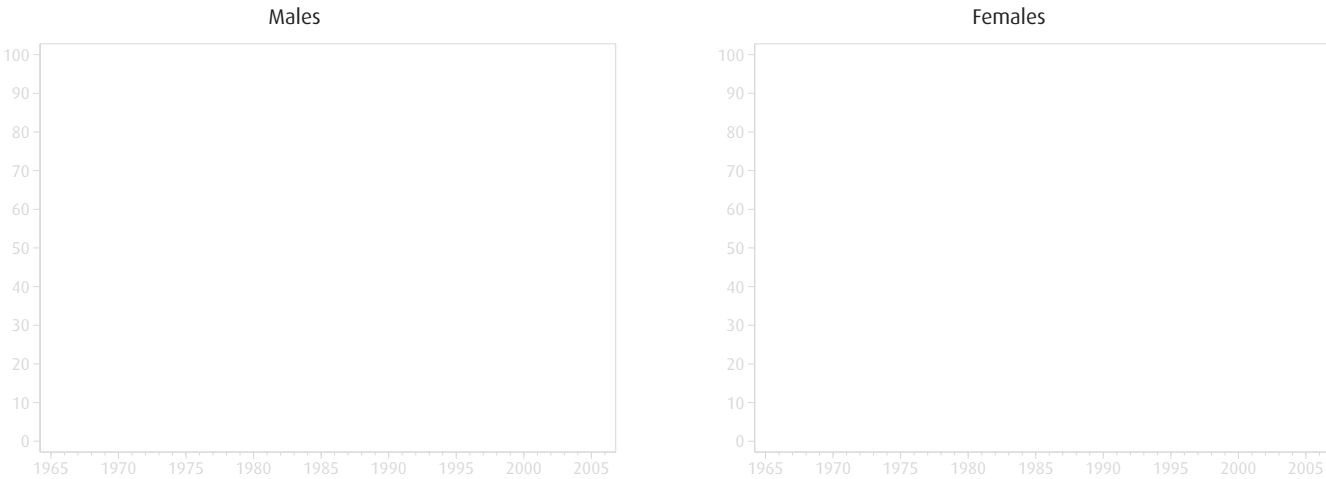


Figure S19d: Relative survival up to 15 years after diagnosis by sex and age

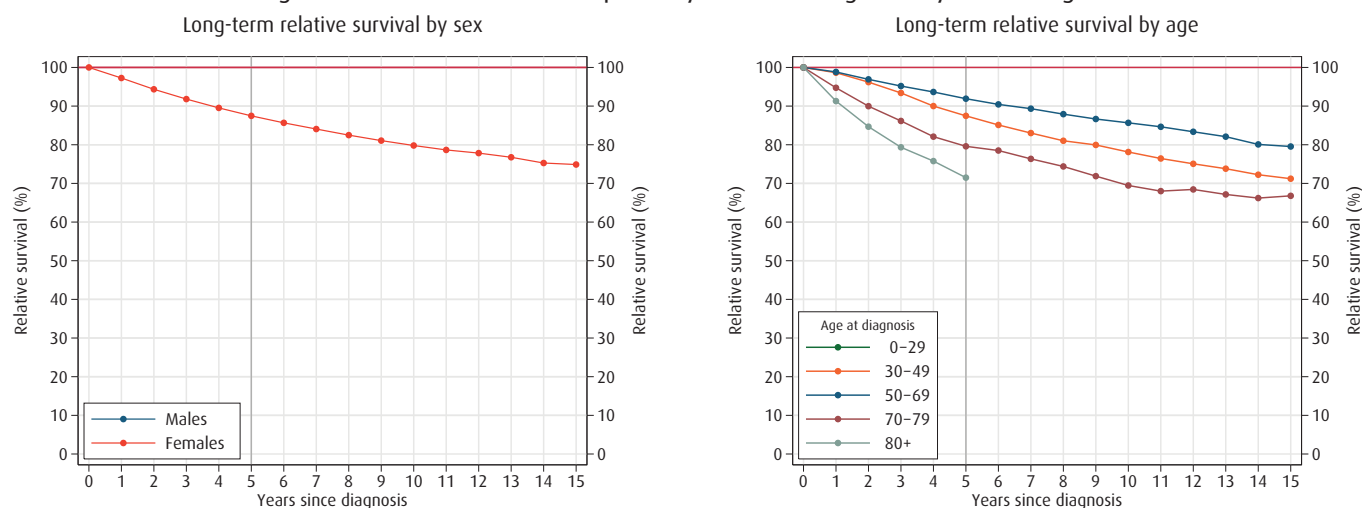


Figure S19e: Conditional 5-year relative survival for every additional year after diagnosis

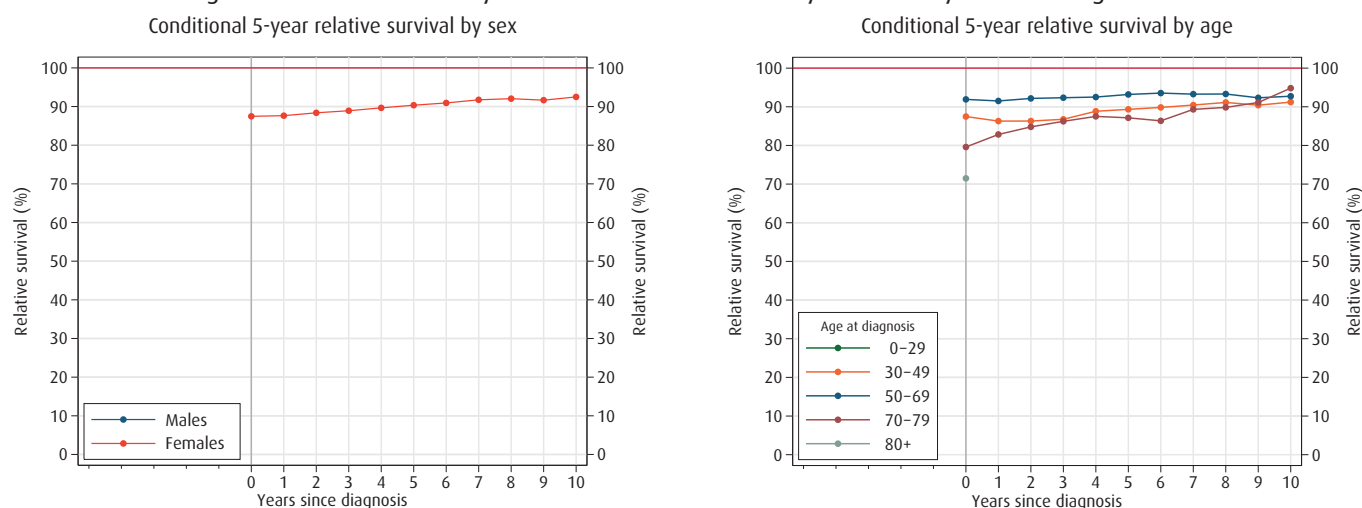
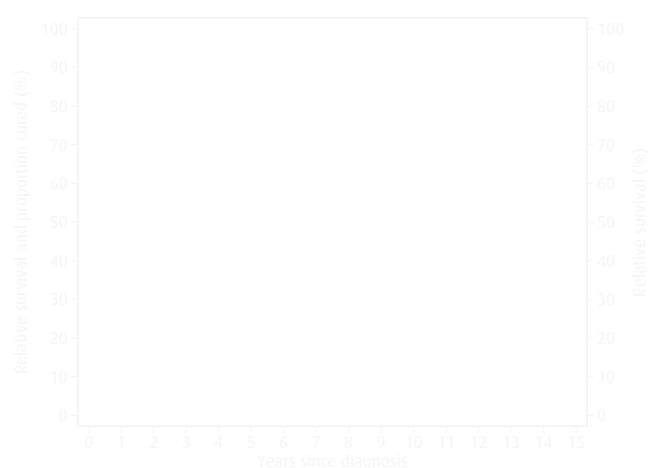


Figure S19f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003–2007)

Age	Males	Females	All	%
0-29		57	57	0.4
30-49		2747	2747	20.1
50-69		7024	7024	51.4
70-79		1836	1836	13.4
80+		1989	1989	14.6
Total		13653	13653	100.0

Figure S20a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

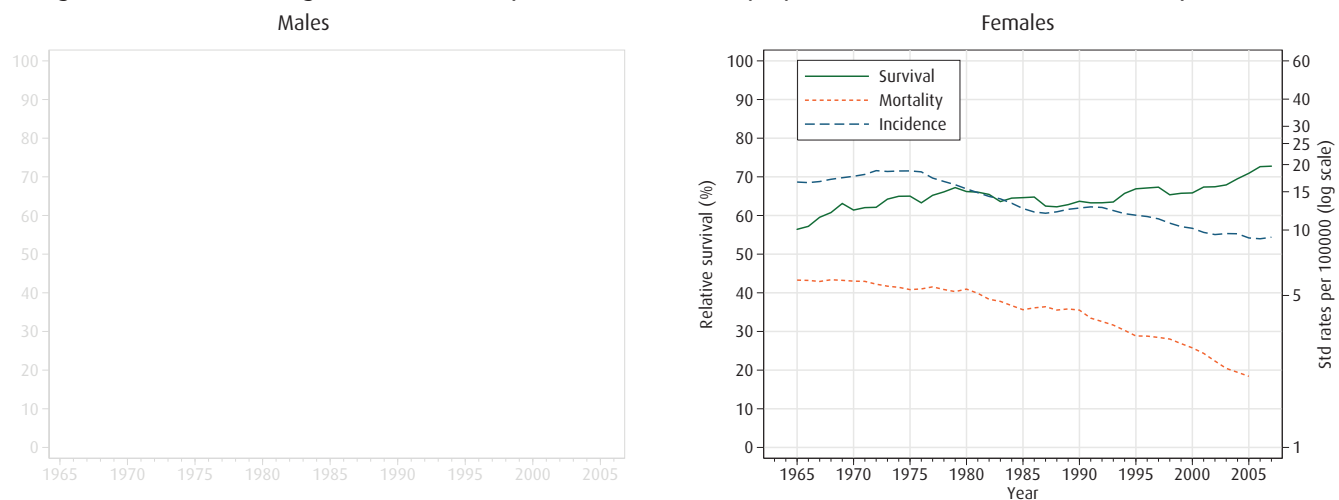


Figure S20b: Trends in 5-year relative survival by age

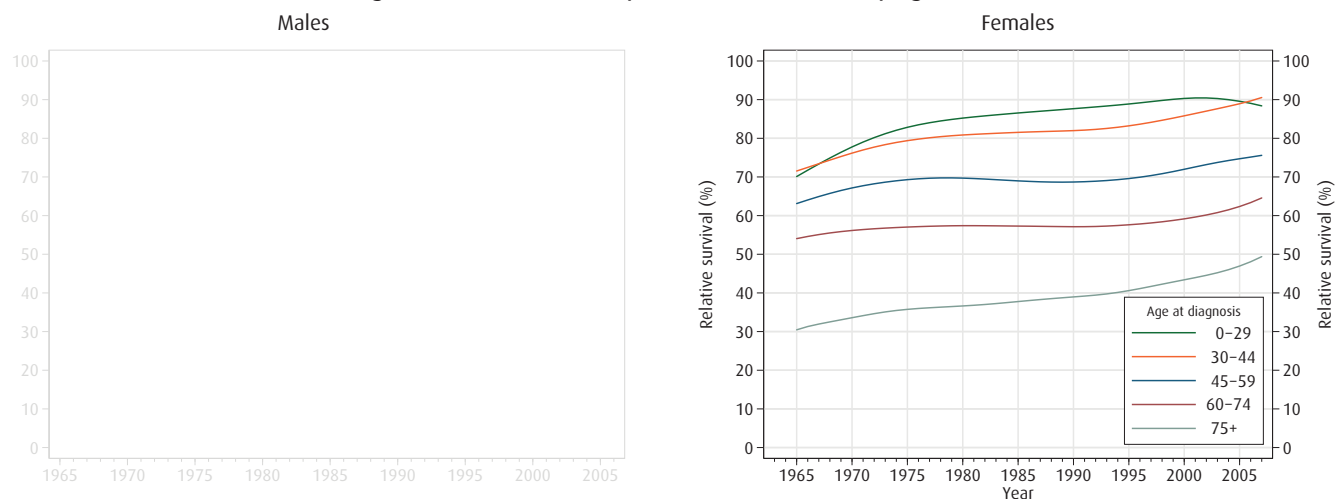


Figure S20c: Estimates of trends in the proportion cured and the median survival time for the uncured

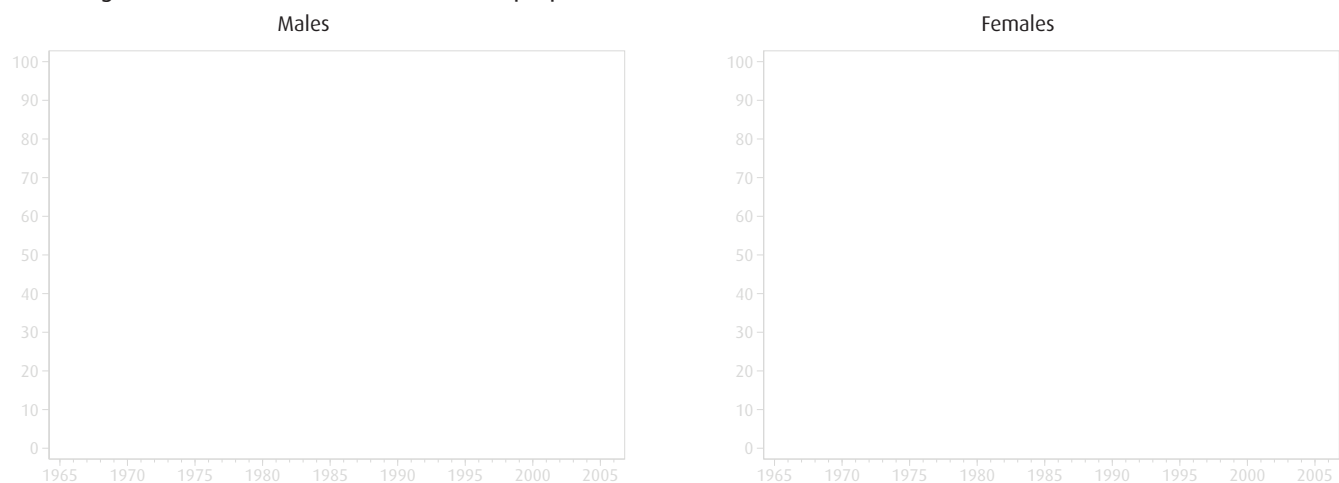


Figure S20d: Relative survival up to 15 years after diagnosis by sex and age

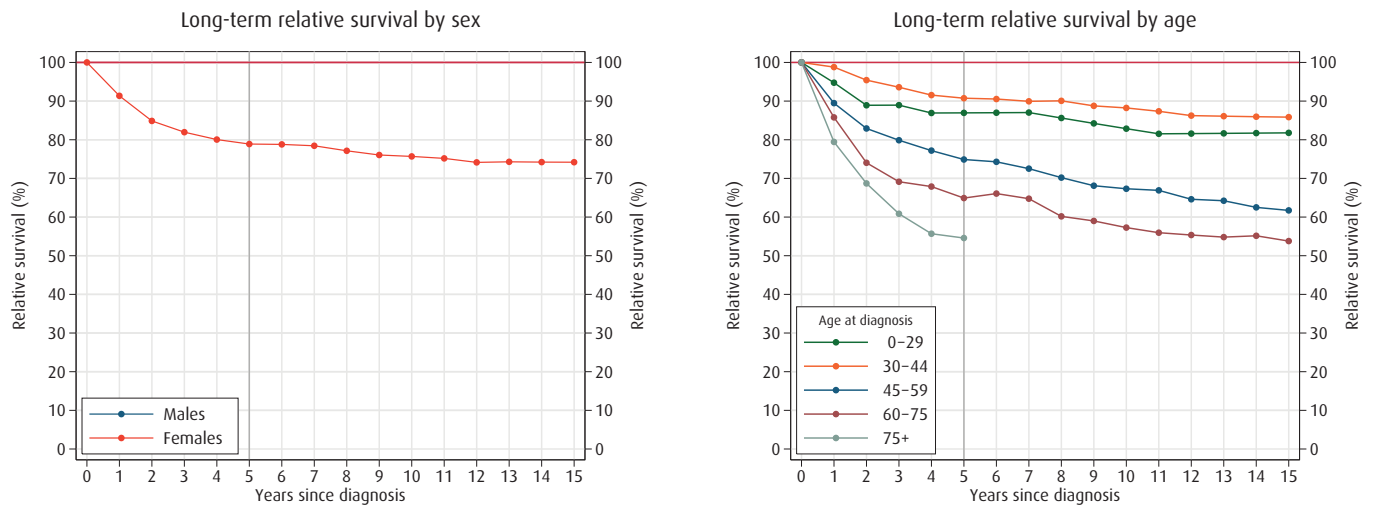


Figure S20e: Conditional 5-year relative survival for every additional year after diagnosis

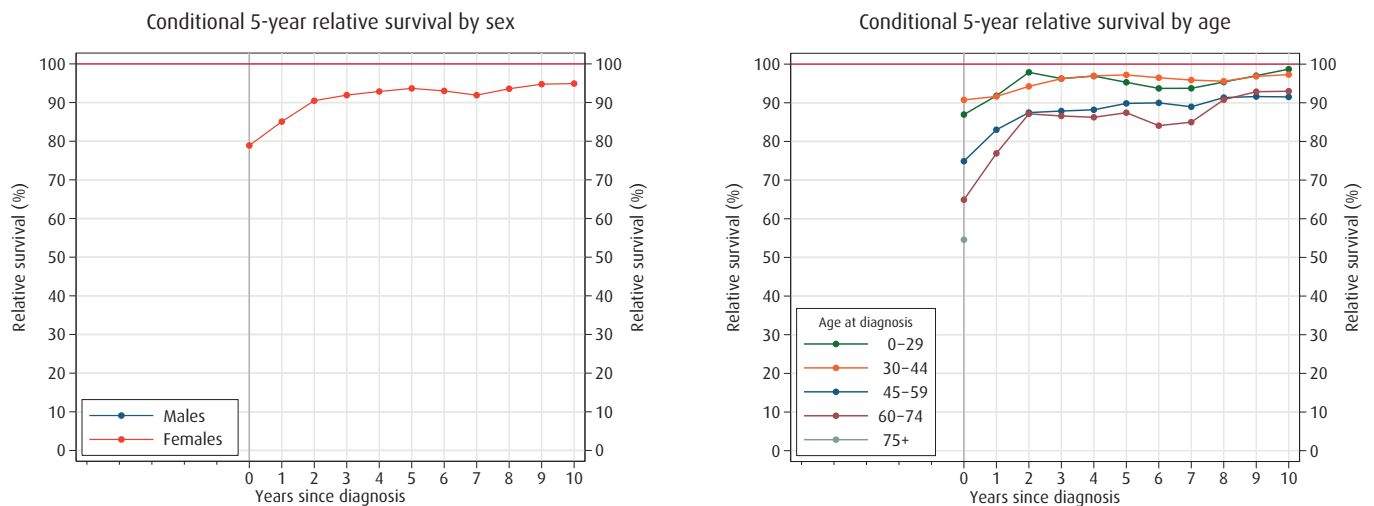
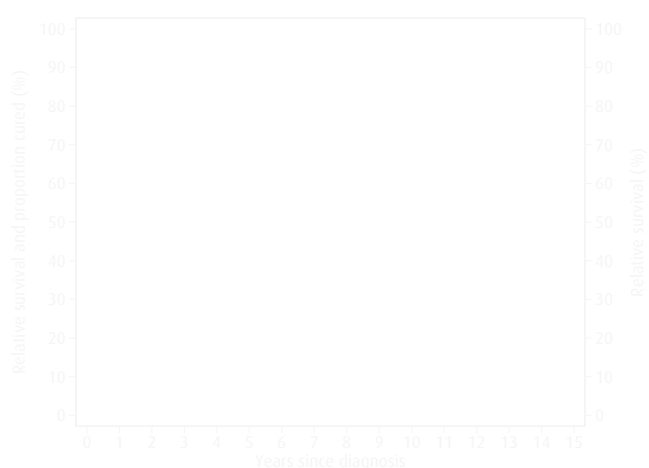


Figure S20f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003–2007)

Age	Males	Females	All	%
0-29		86	86	6.0
30-44		513	513	35.8
45-59		401	401	28.0
60-74		244	244	17.0
75+		188	188	13.1
Total		1432	1432	100.0

Figure S21a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

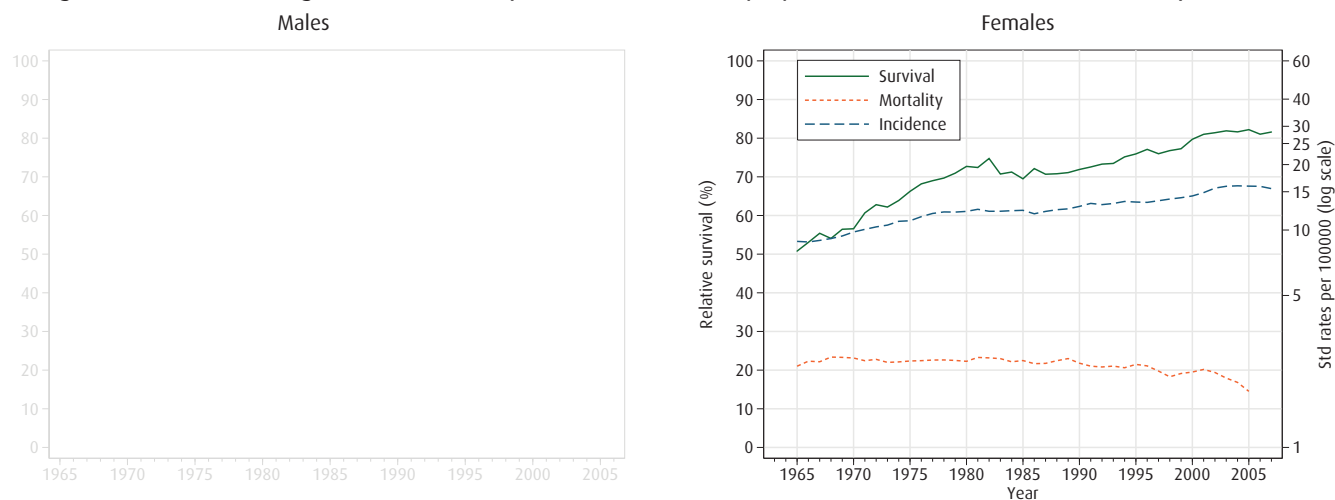


Figure S21b: Trends in 5-year relative survival by age

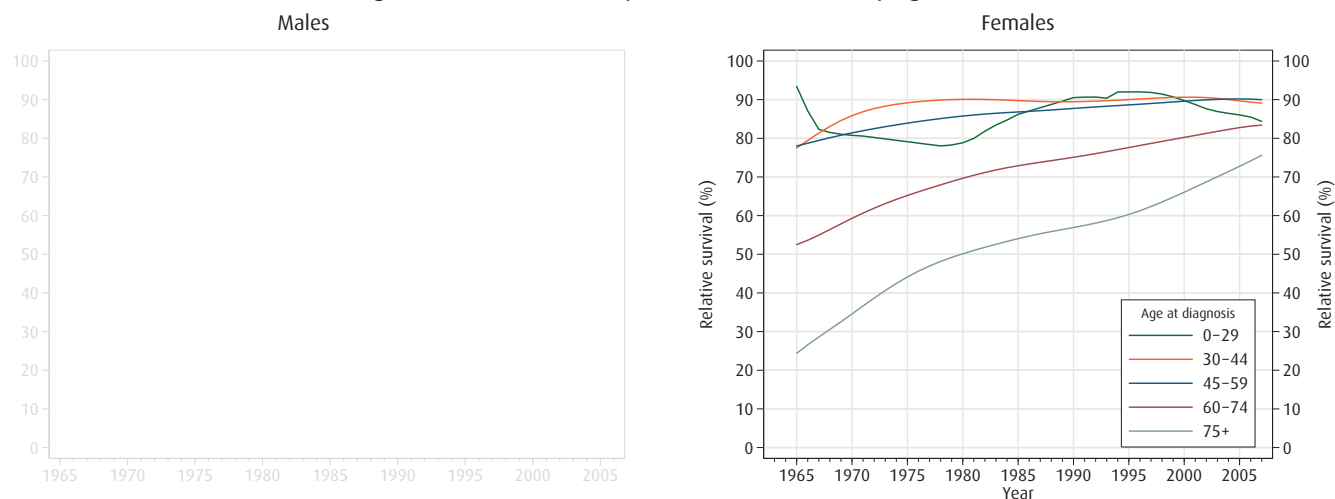


Figure S21c: Estimates of trends in the proportion cured and the median survival time for the uncured

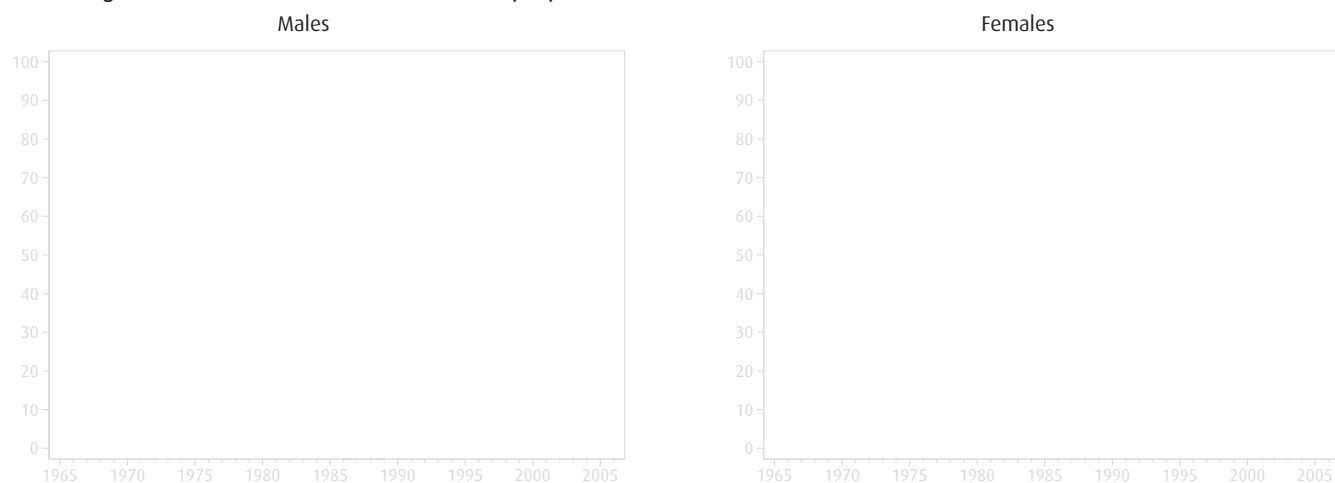


Figure S21d: Relative survival up to 15 years after diagnosis by sex and age

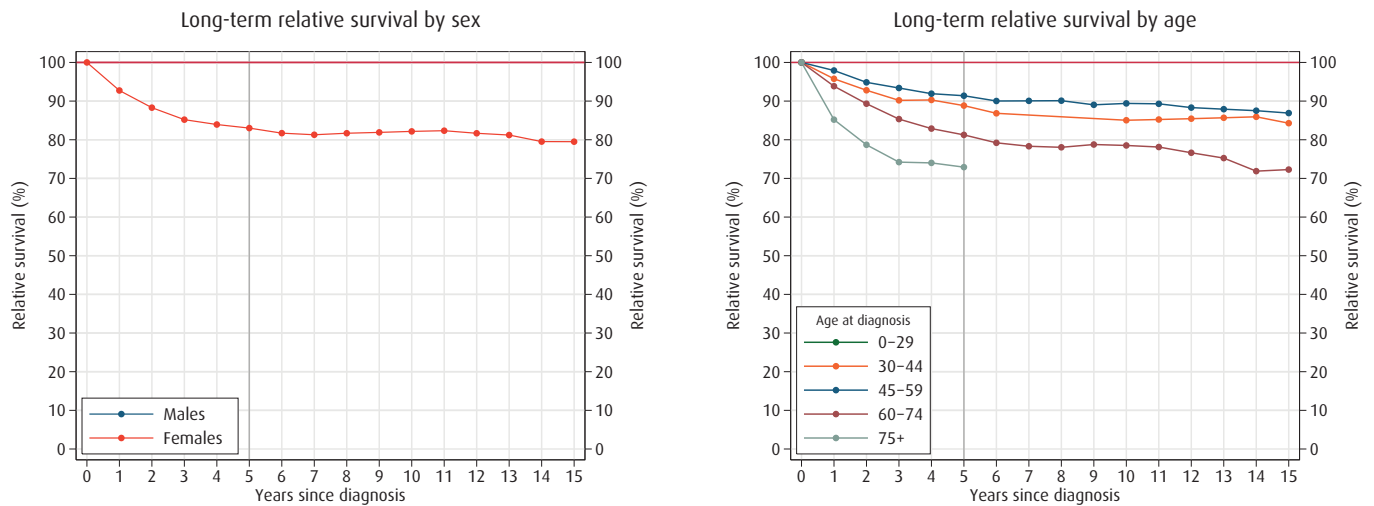


Figure S21e: Conditional 5-year relative survival for every additional year after diagnosis

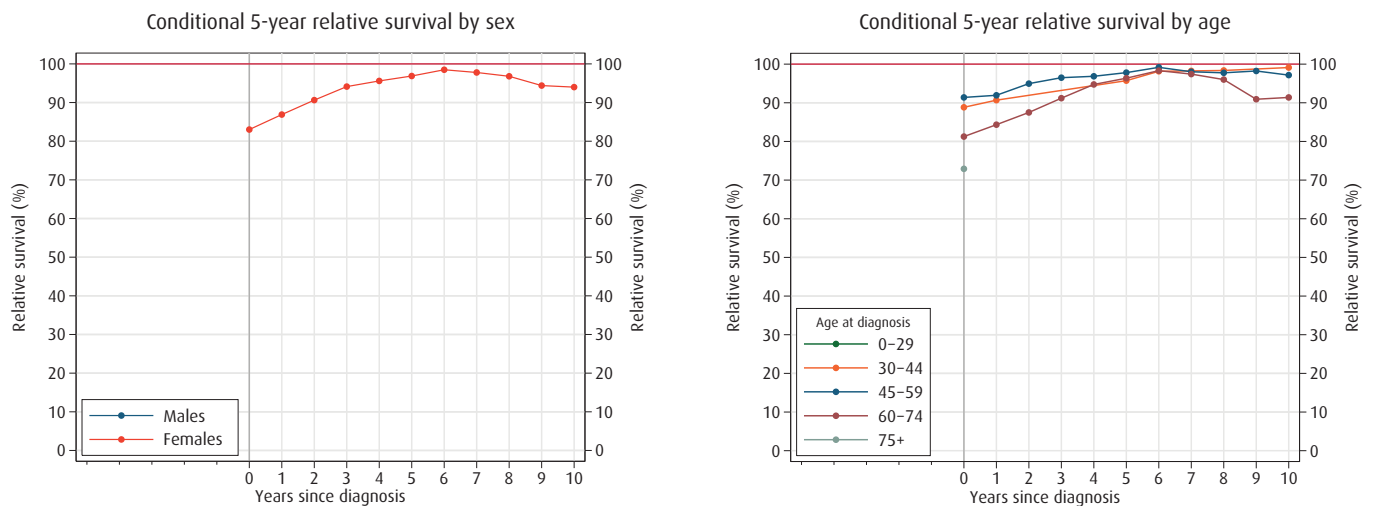
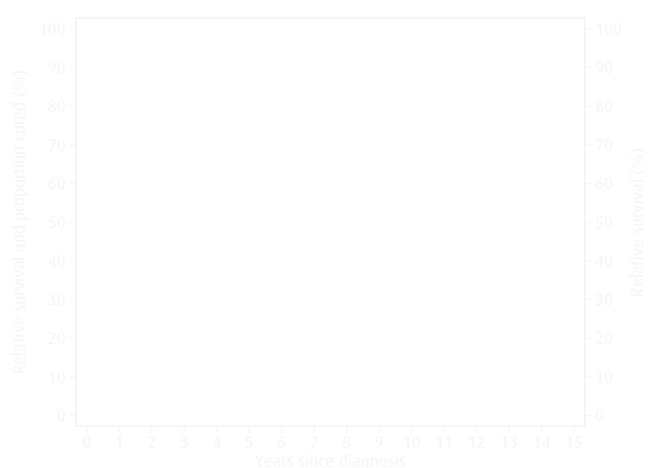


Figure S21f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-29		4	4	0.1
30-44		109	109	3.4
45-59		909	909	28.4
60-74		1257	1257	39.2
75+		924	924	28.9
Total		3203	3203	100.0

Figure S22a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

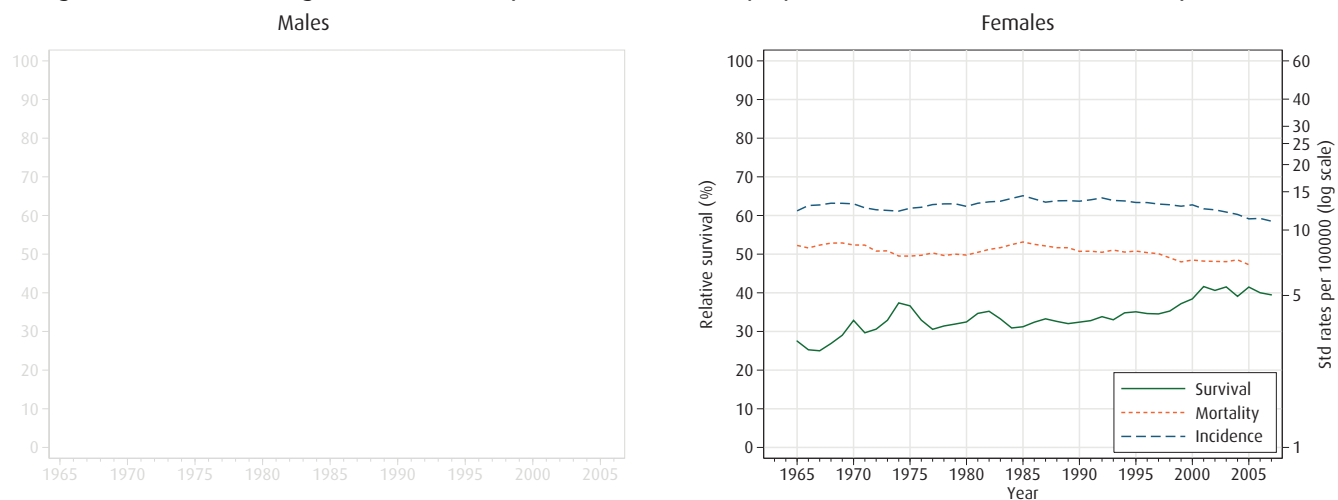


Figure S22b: Trends in 5-year relative survival by age

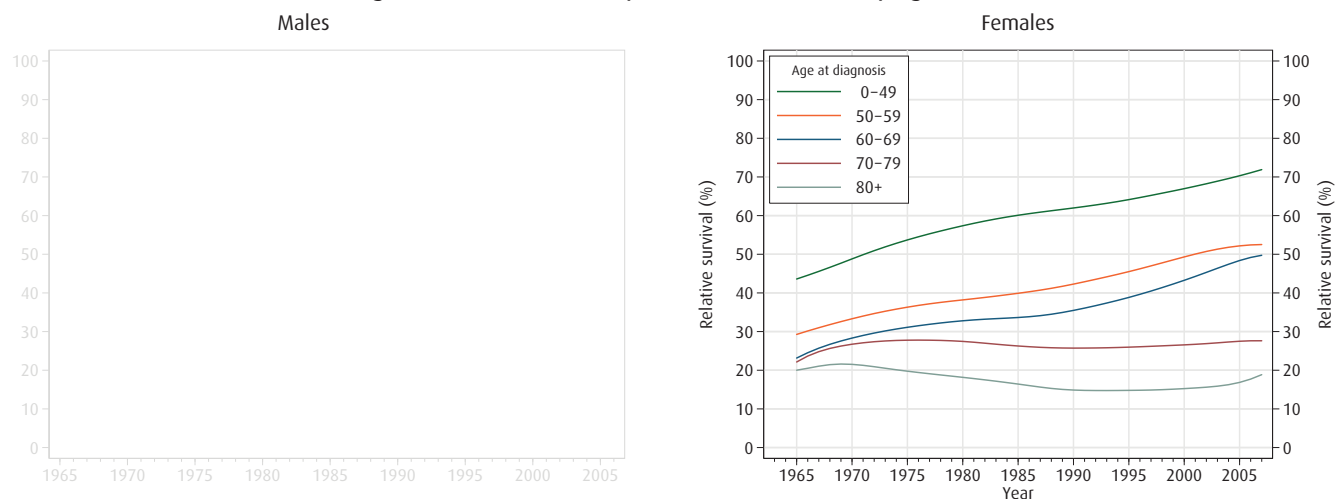


Figure S22c: Estimates of trends in the proportion cured and the median survival time for the uncured

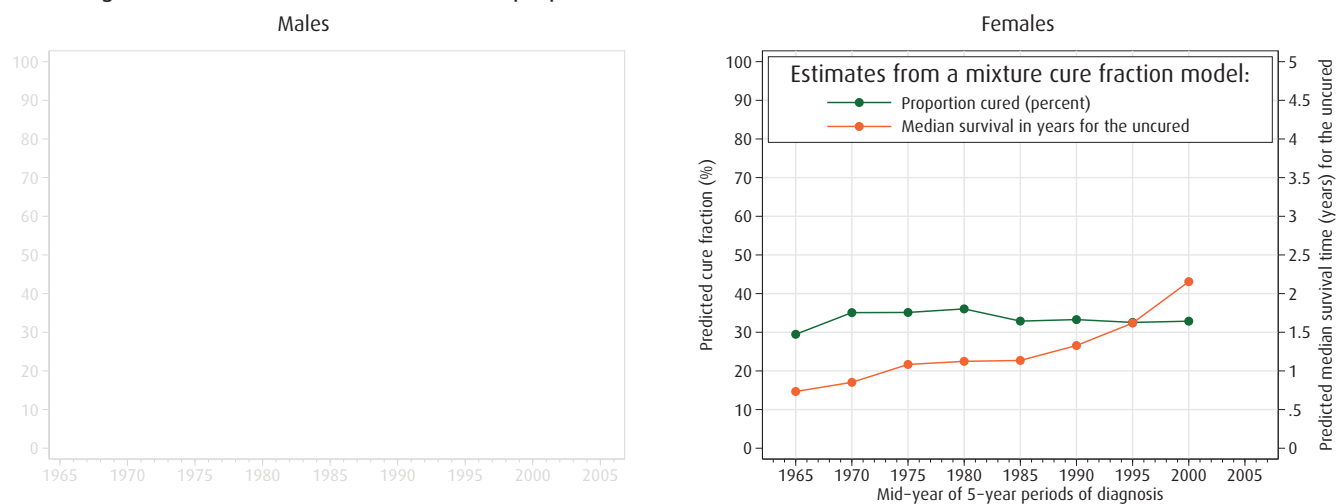


Figure S22d: Relative survival up to 15 years after diagnosis by sex and age

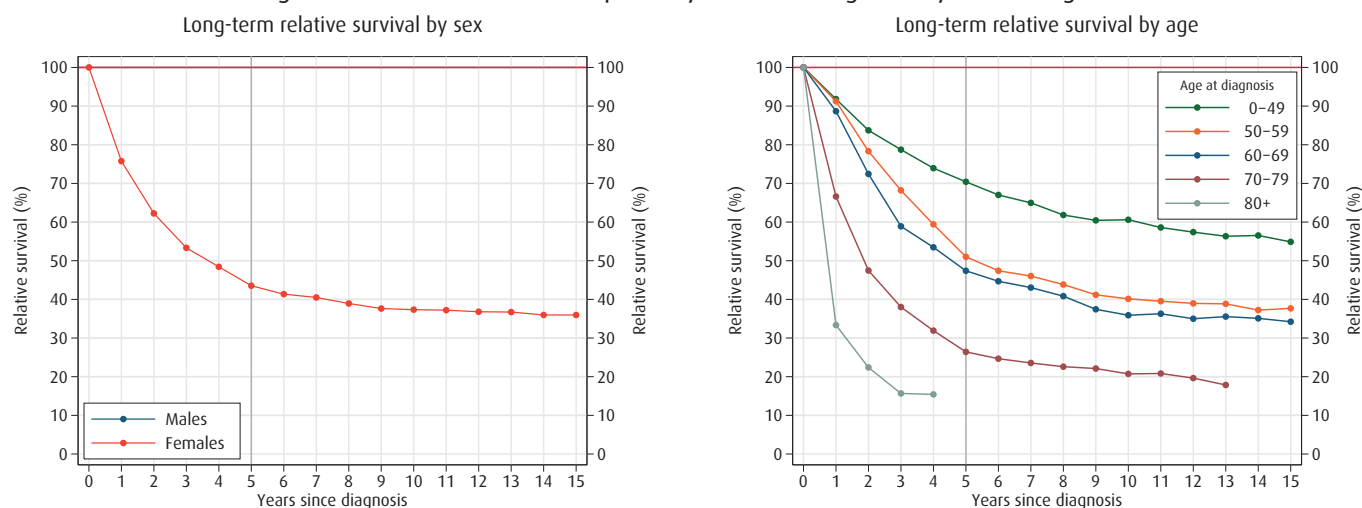


Figure S22e: Conditional 5-year relative survival for every additional year after diagnosis

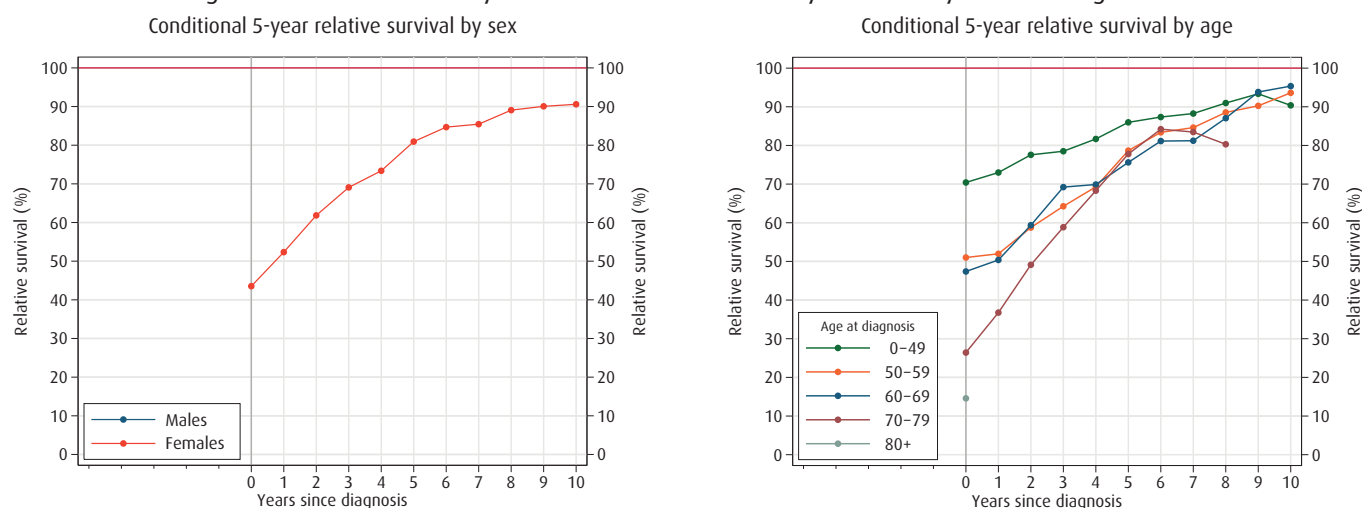
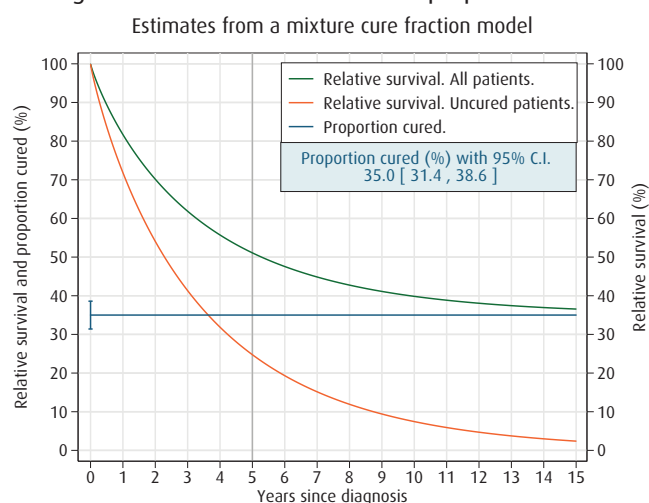


Figure S22f: Relative survival and proportion cured



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-49		334	334	15.5
50-59		473	473	22.0
60-69		499	499	23.2
70-79		455	455	21.1
80+		392	392	18.2
Total		2153	2153	100.0

Figure S23a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

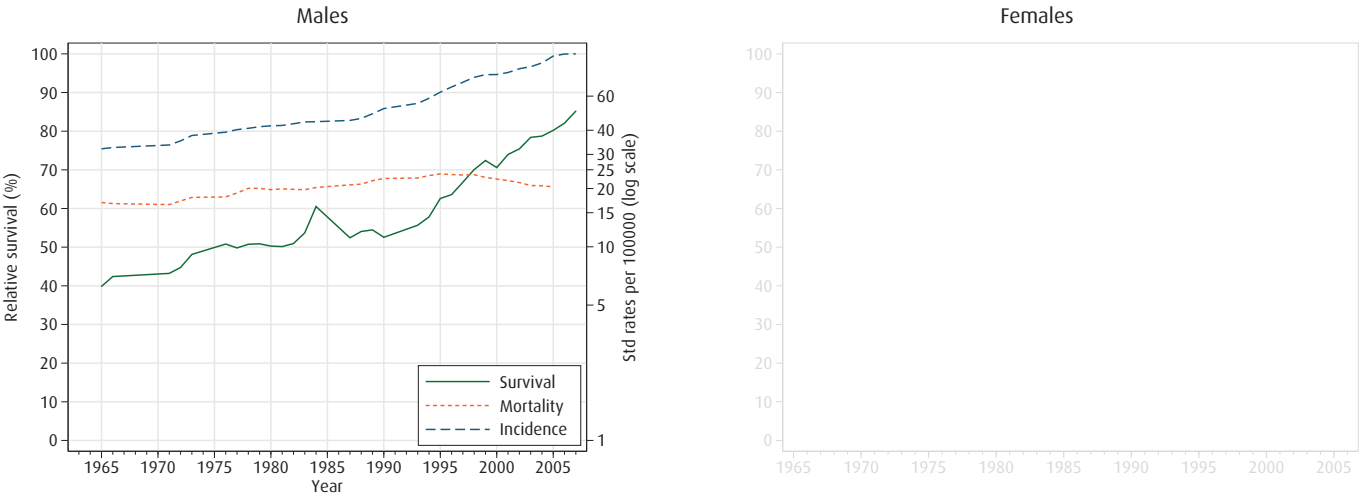


Figure S23b: Trends in 5-year relative survival by age

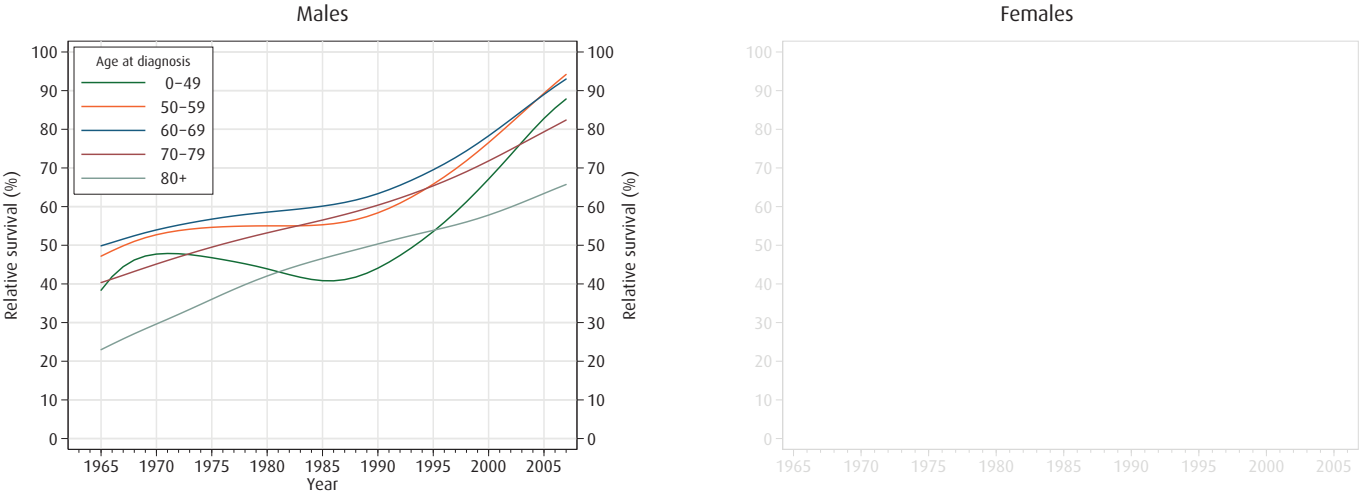


Figure S23c: Estimates of trends in the proportion cured and the median survival time for the uncured

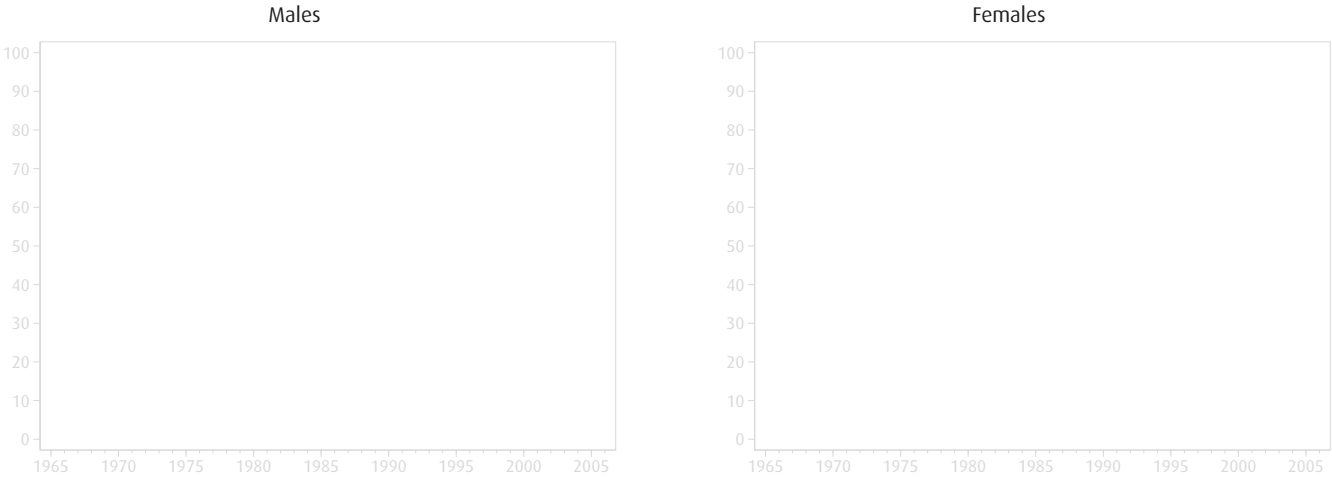


Figure S23d: Relative survival up to 15 years after diagnosis by sex and age

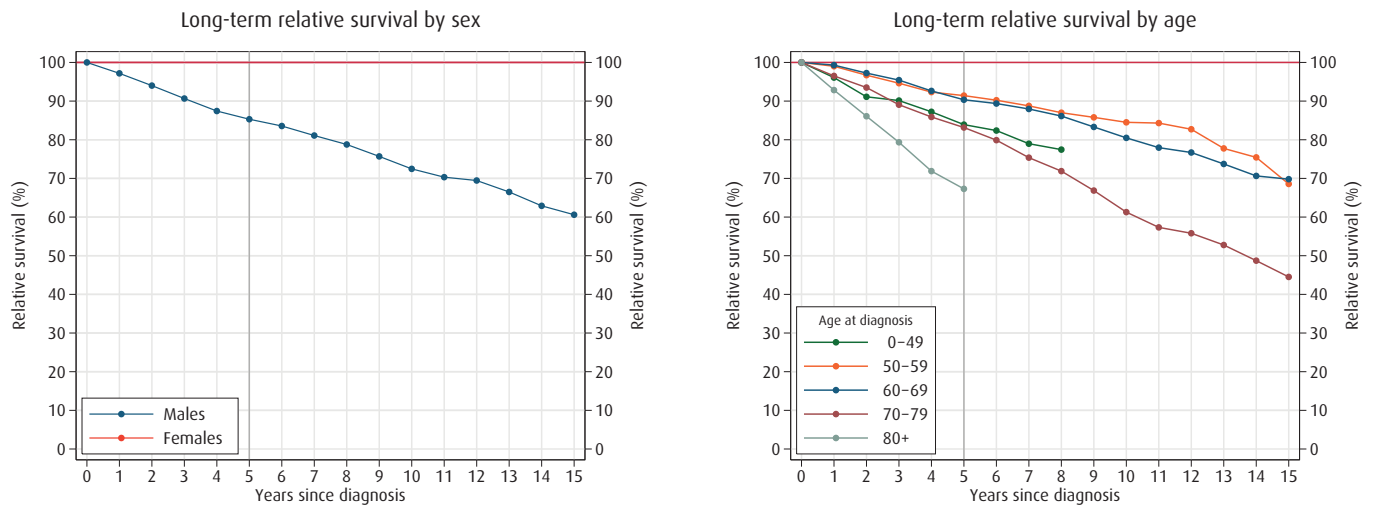


Figure S23e: Conditional 5-year relative survival for every additional year after diagnosis

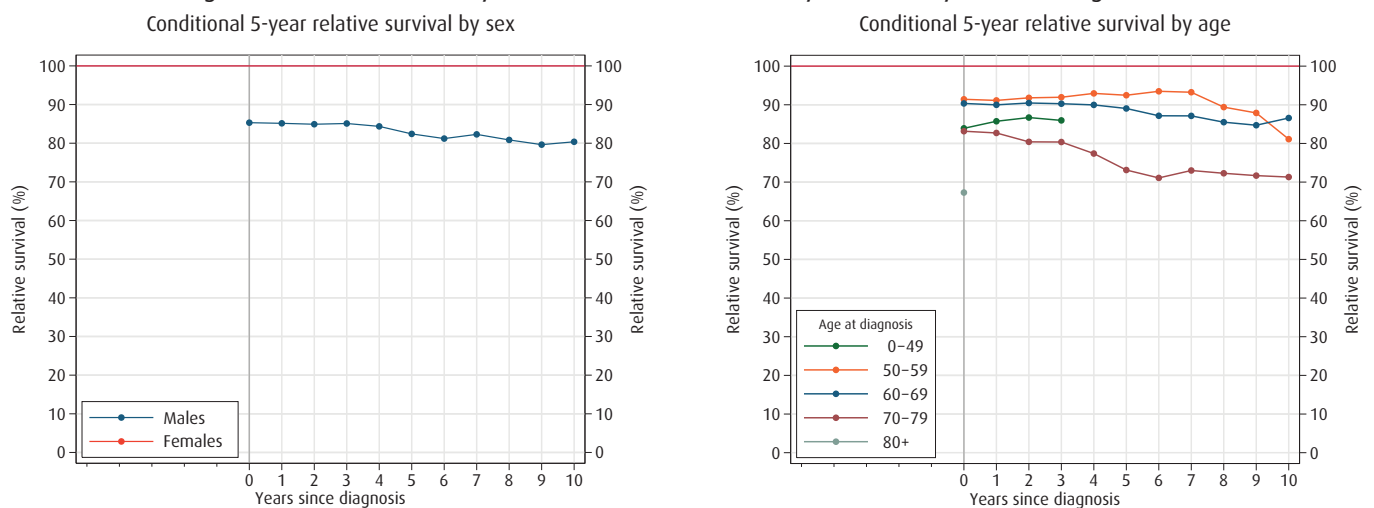
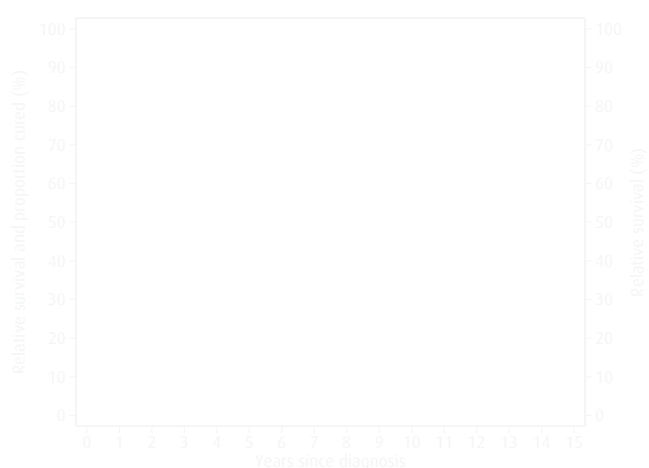


Figure S23f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003–2007)

Age	Males	Females	All	%
0-49	151		151	0.8
50-59	2219		2219	11.9
60-69	6218		6218	33.3
70-79	6346		6346	34.0
80+	3734		3734	20.0
Total	18668		18668	100.0

Figure S24a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

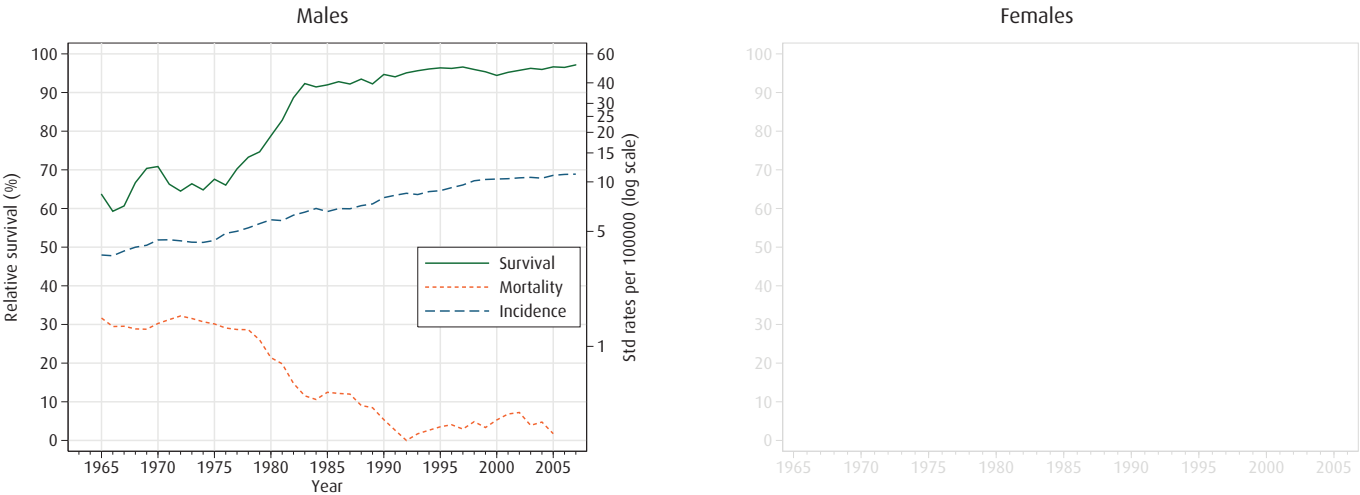


Figure S24b: Trends in 5-year relative survival by age

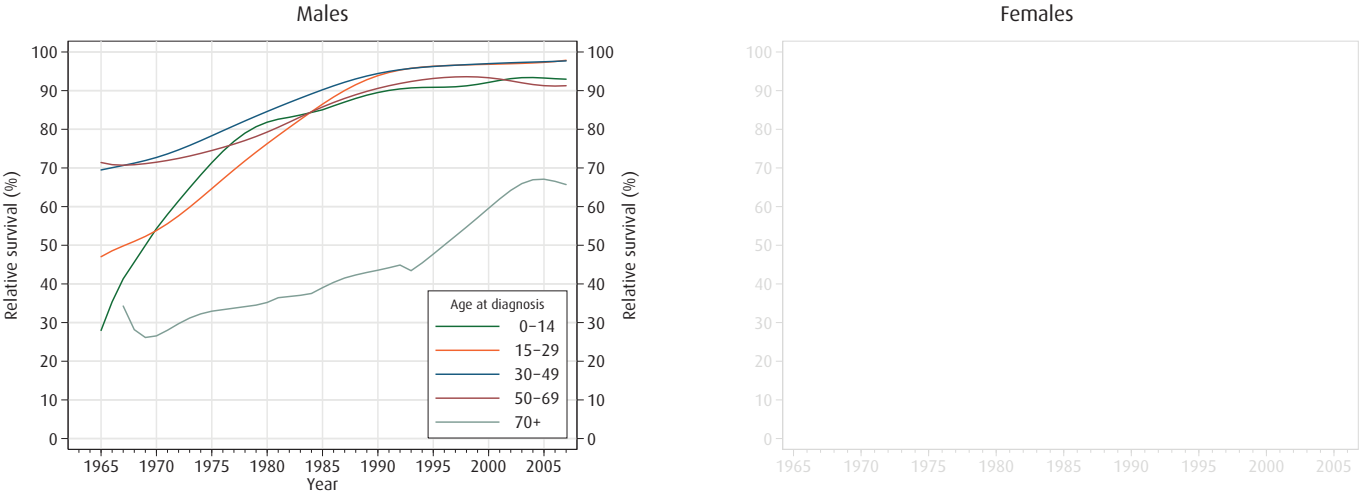


Figure S24c: Estimates of trends in the proportion cured and the median survival time for the uncured

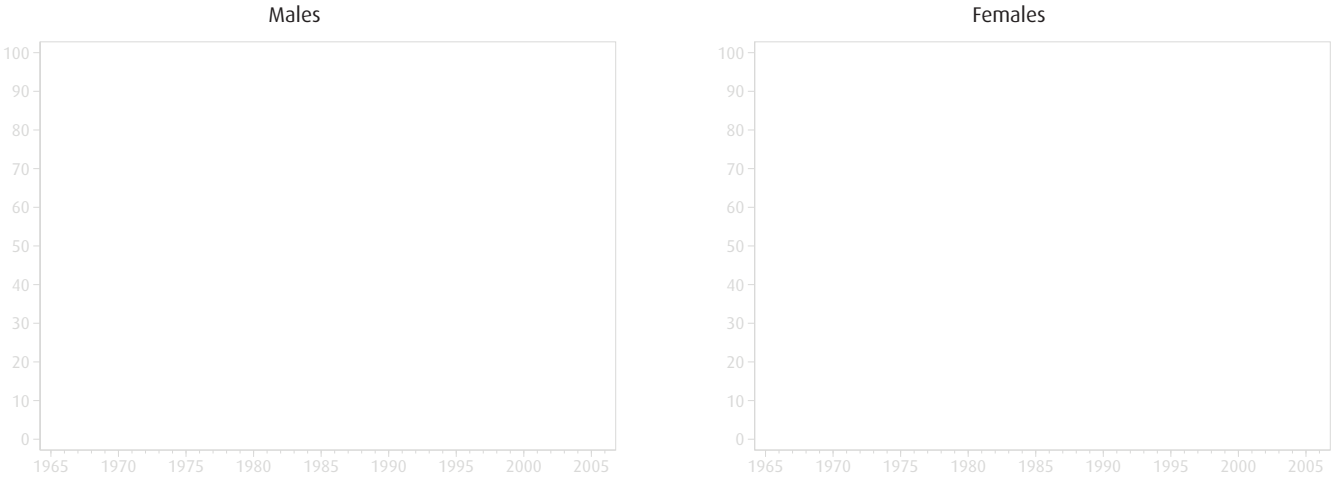


Figure S24d: Relative survival up to 15 years after diagnosis by sex and age

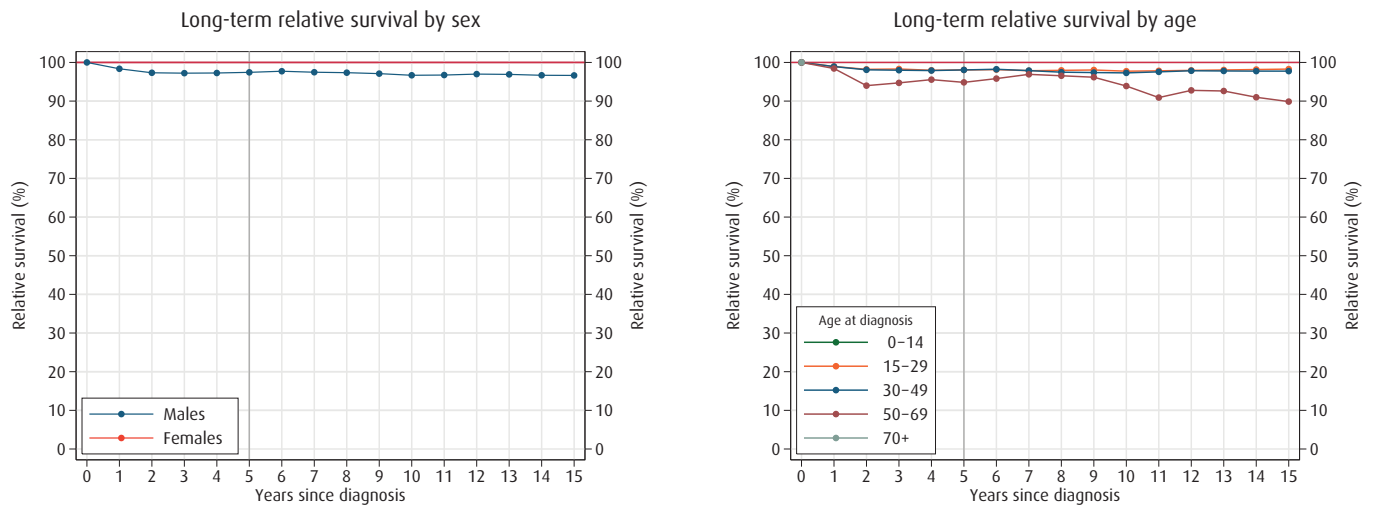


Figure S24e: Conditional 5-year relative survival for every additional year after diagnosis

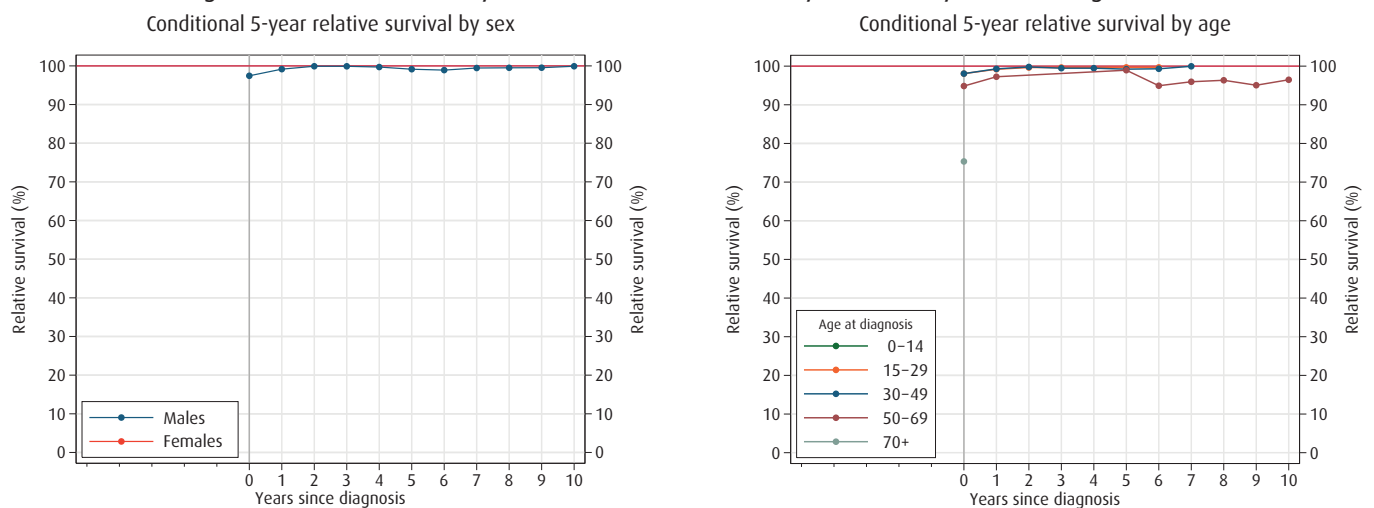
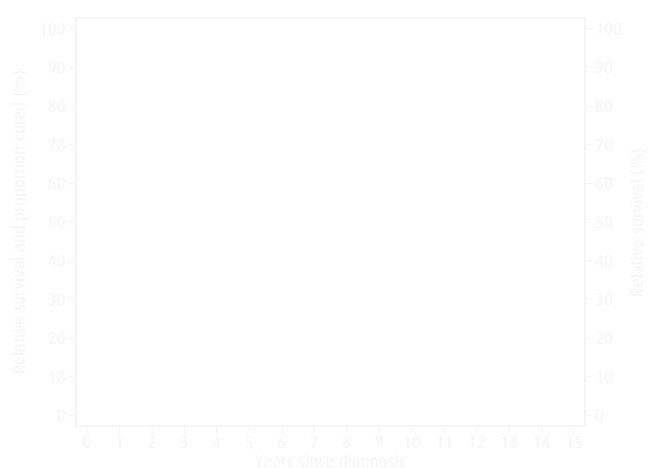


Figure S24f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-14	16		16	1.2
15-29	423		423	32.1
30-49	711		711	54.0
50-69	145		145	11.0
70+	22		22	1.7
Total	1317		1317	100.0

Figure S25a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

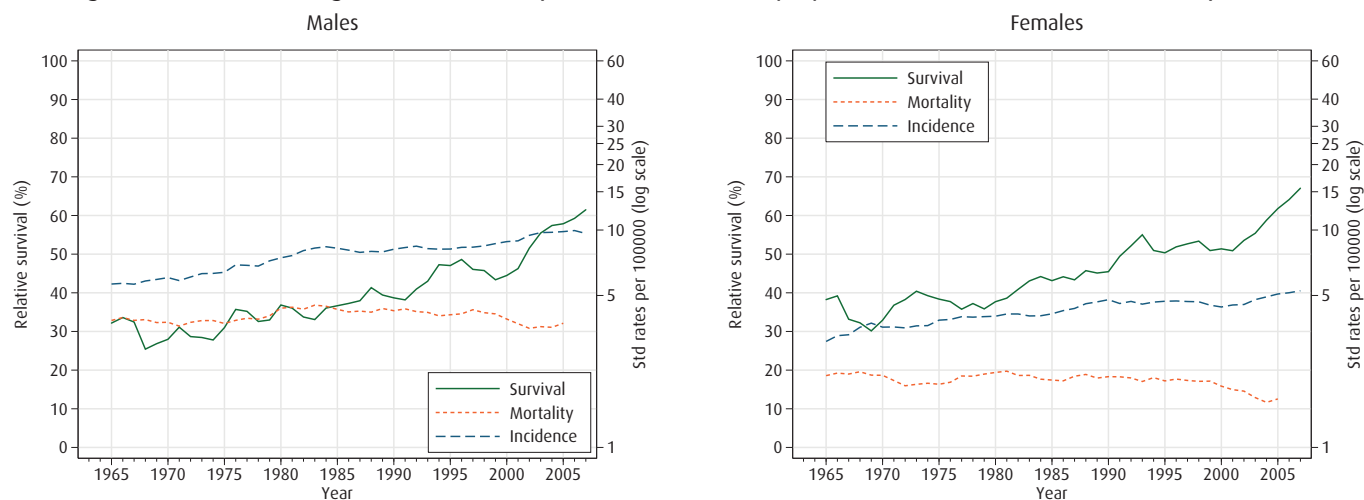


Figure S25b: Trends in 5-year relative survival by age

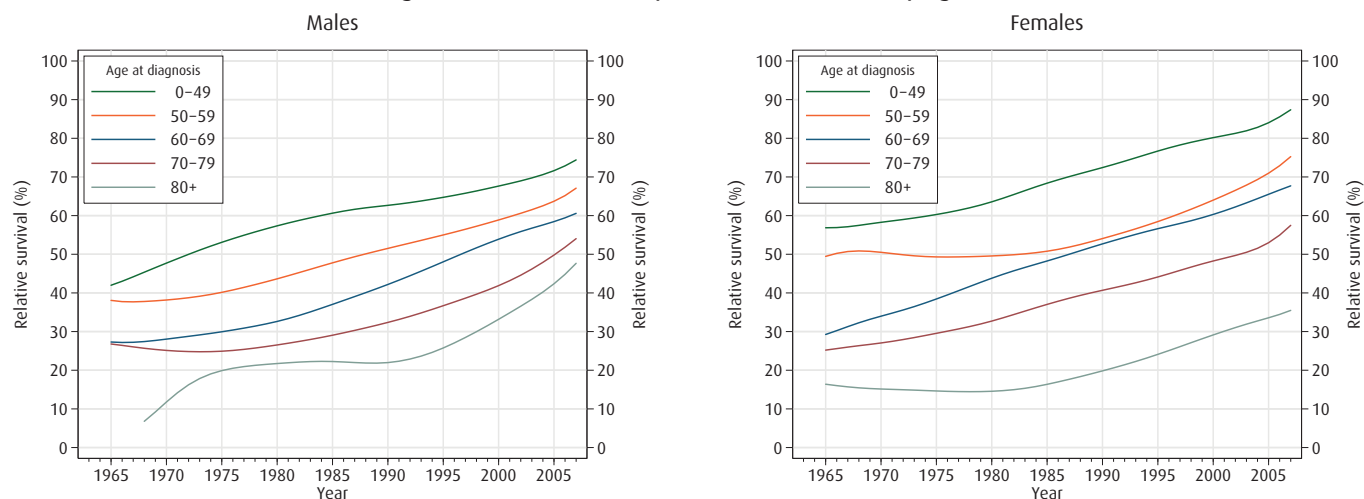


Figure S25c: Estimates of trends in the proportion cured and the median survival time for the uncured

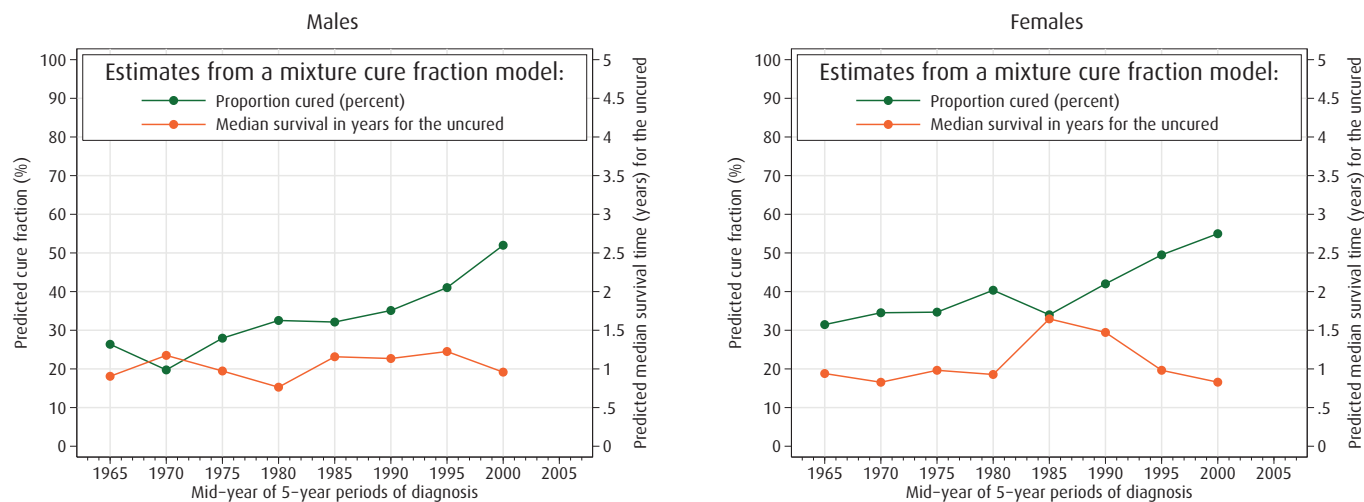


Figure S25d: Relative survival up to 15 years after diagnosis by sex and age

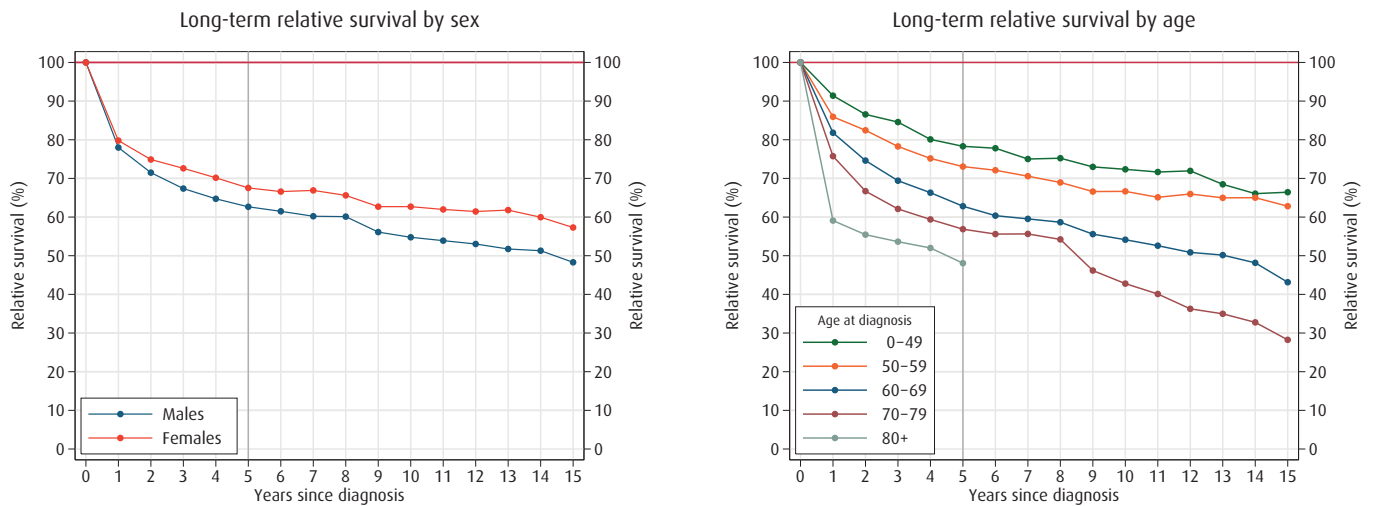


Figure S25e: Conditional 5-year relative survival for every additional year after diagnosis

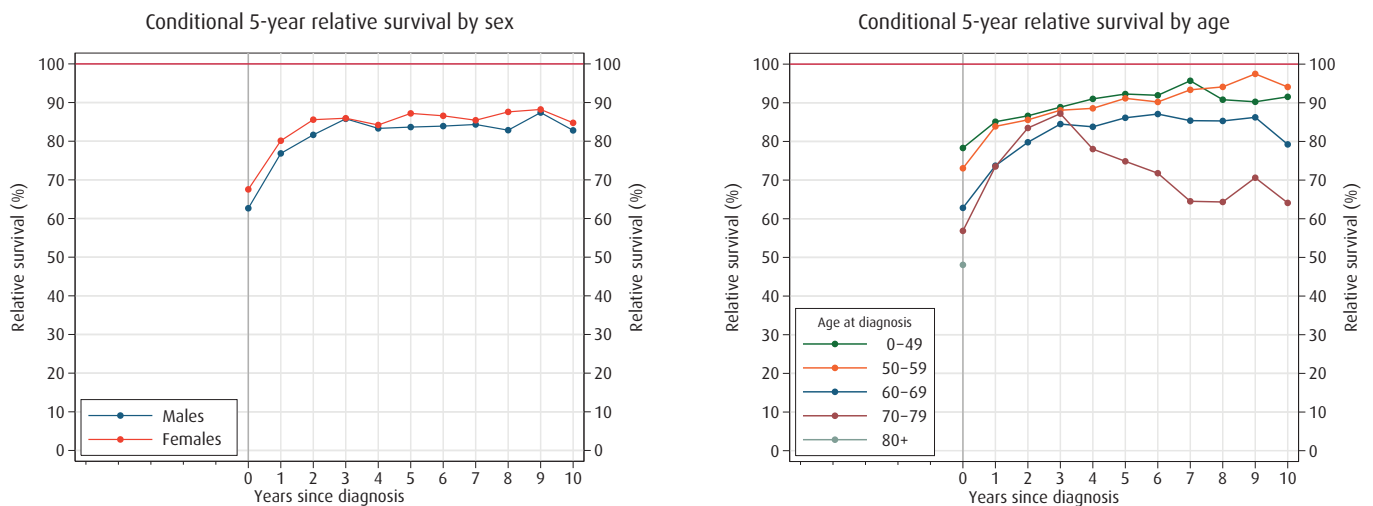
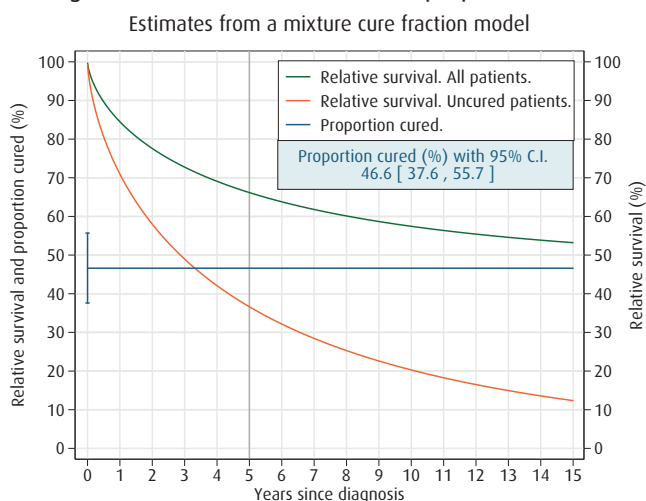


Figure S25f: Relative survival and proportion cured



Age distribution of patients (2003–2007)

Age	Males	Females	All	%
0-49	115	181	296	10.9
50-59	140	356	496	18.3
60-69	243	441	684	25.3
70-79	323	460	783	28.9
80+	200	246	446	16.5
Total	1021	1684	2705	100.0

Figure S26a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

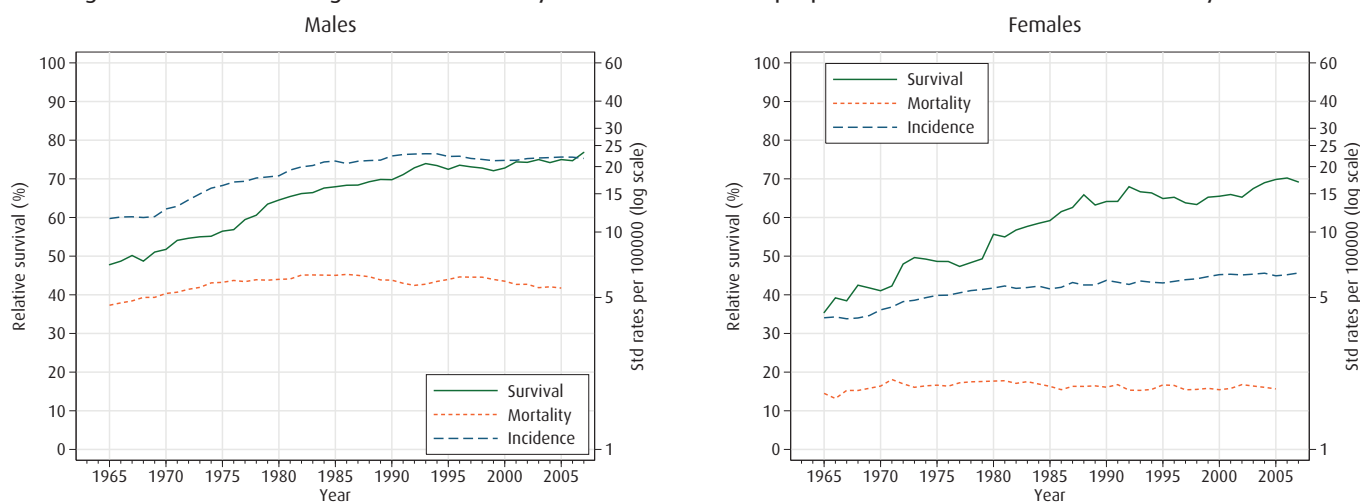


Figure S26b: Trends in 5-year relative survival by age

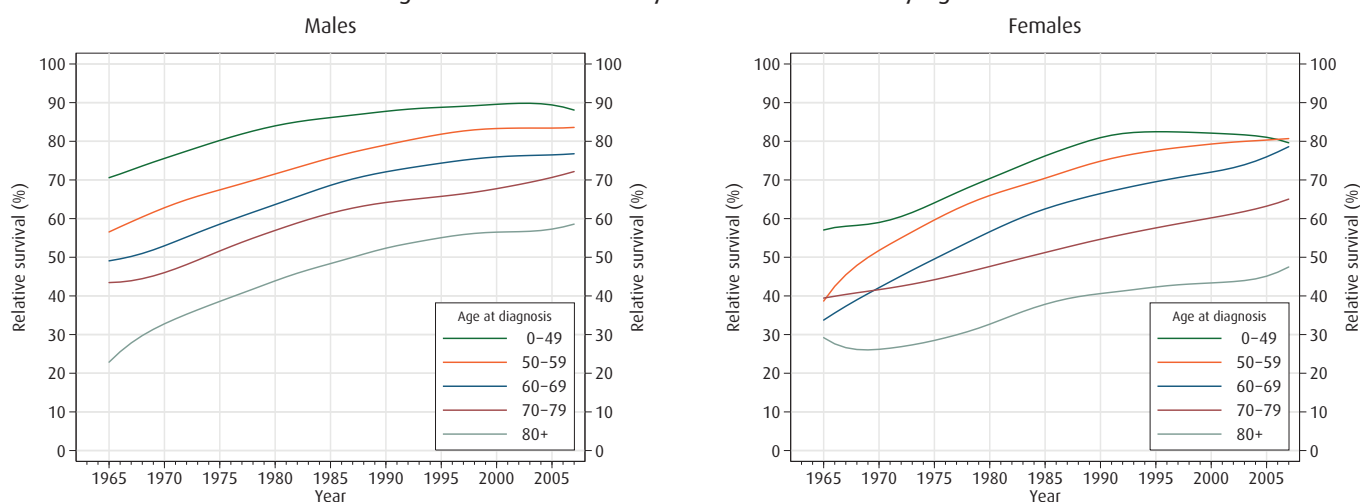


Figure S26c: Estimates of trends in the proportion cured and the median survival time for the uncured

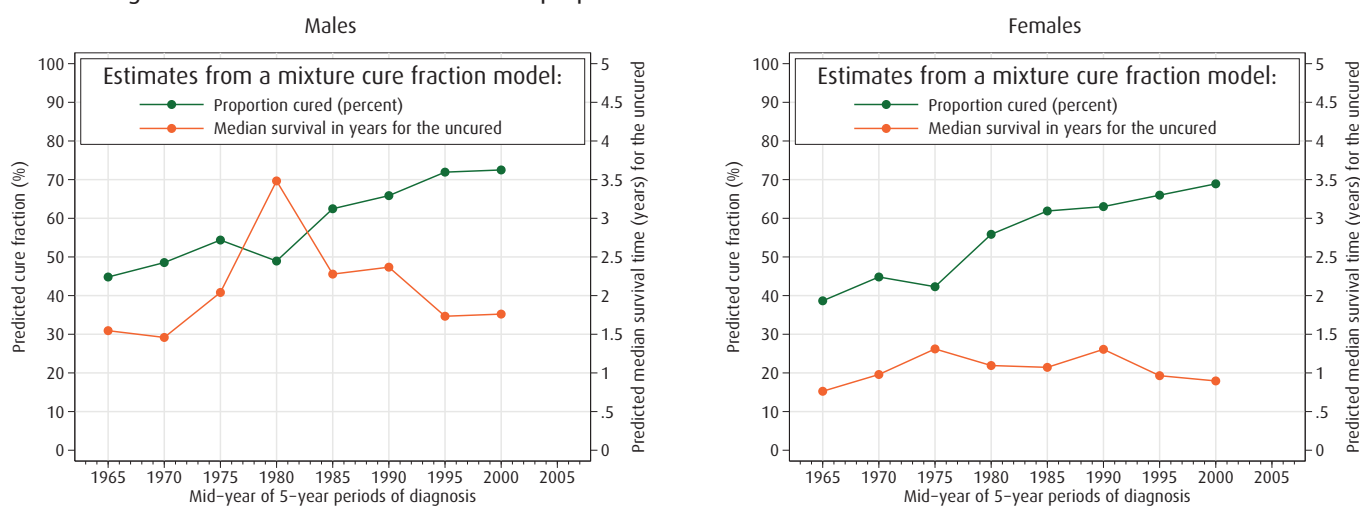


Figure S26d: Relative survival up to 15 years after diagnosis by sex and age

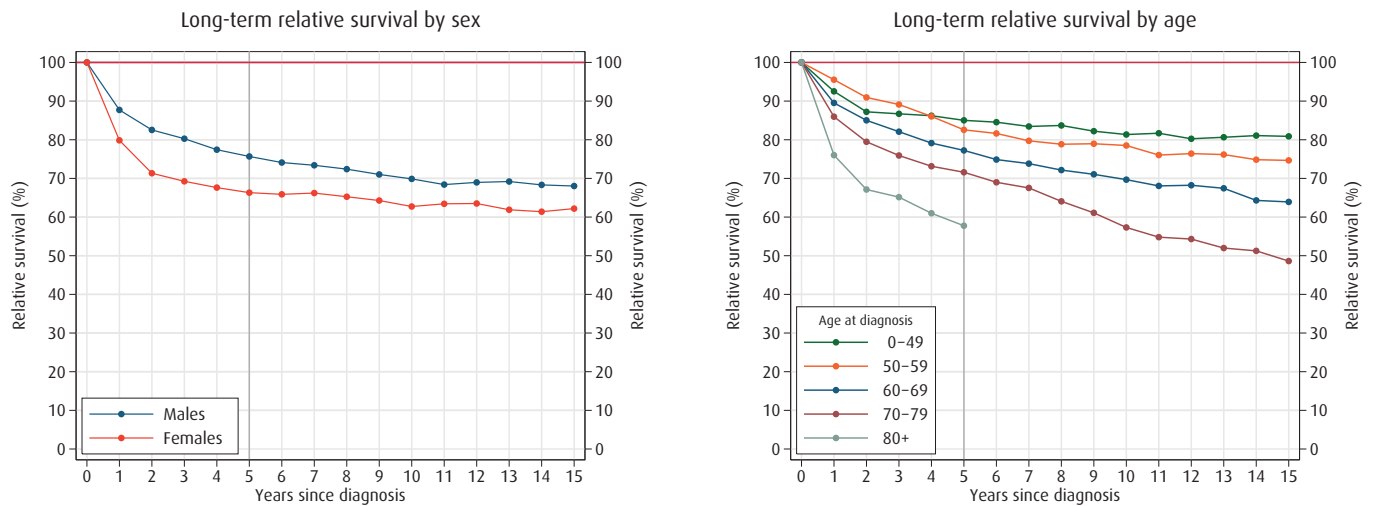


Figure S26e: Conditional 5-year relative survival for every additional year after diagnosis

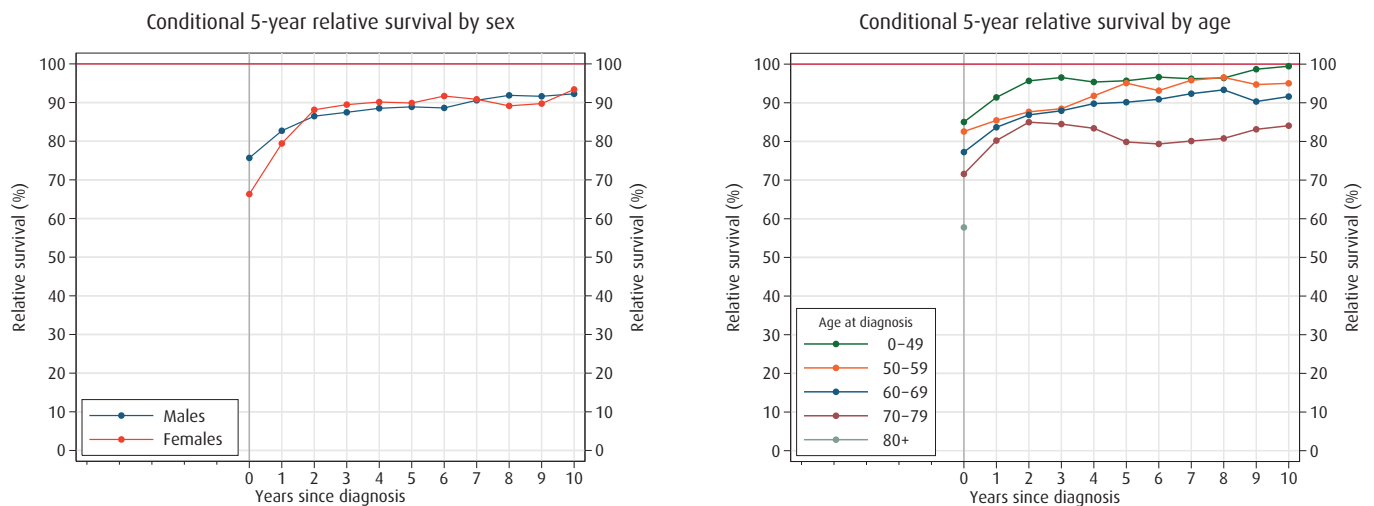
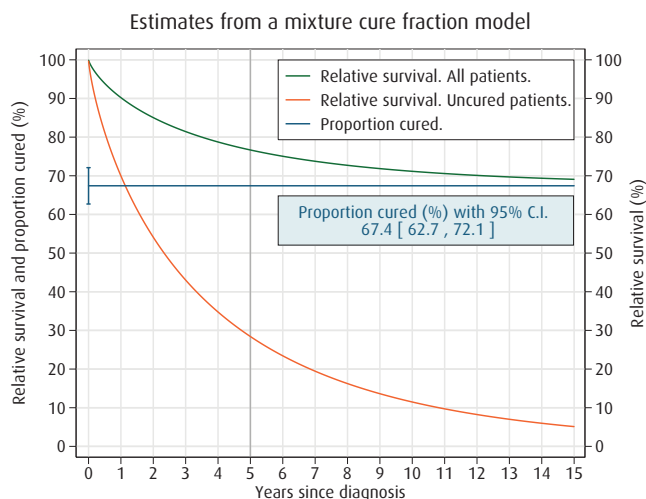


Figure S26f: Relative survival and proportion cured



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-49	60	172	232	3.9
50-59	155	494	649	10.8
60-69	322	993	1315	21.8
70-79	492	1593	2085	34.6
80+	553	1187	1740	28.9
Total	1582	4439	6021	100.0

Figure S27a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

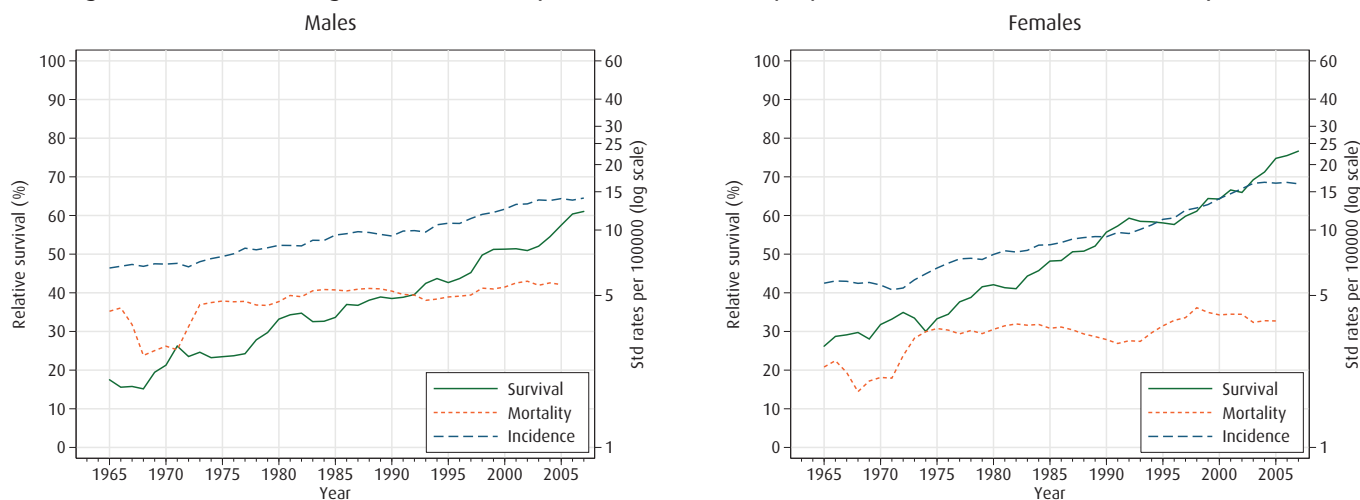


Figure S27b: Trends in 5-year relative survival by age

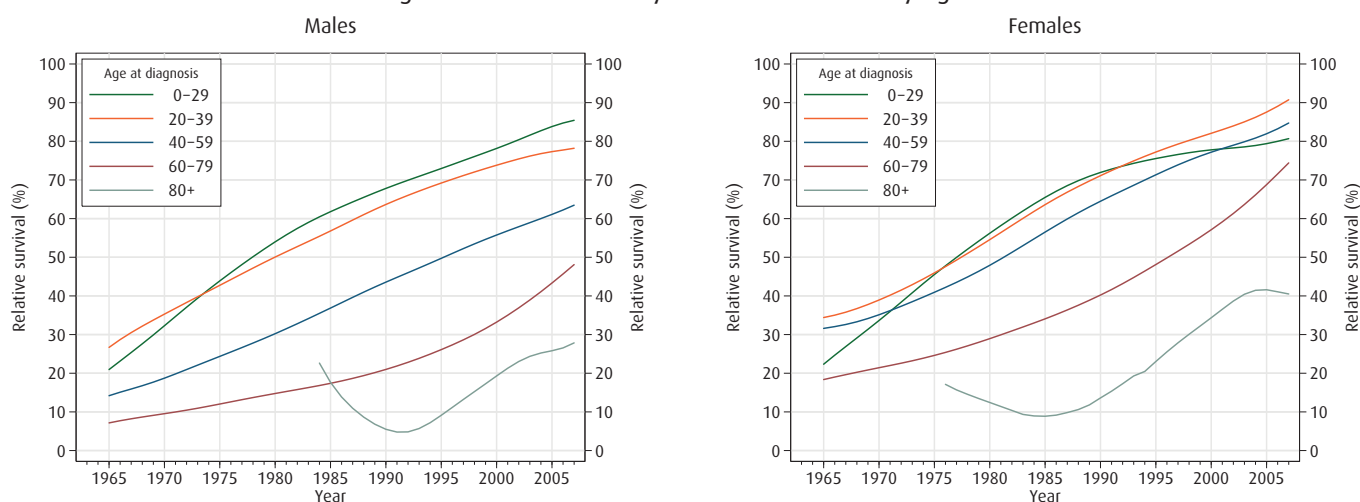


Figure S27c: Estimates of trends in the proportion cured and the median survival time for the uncured

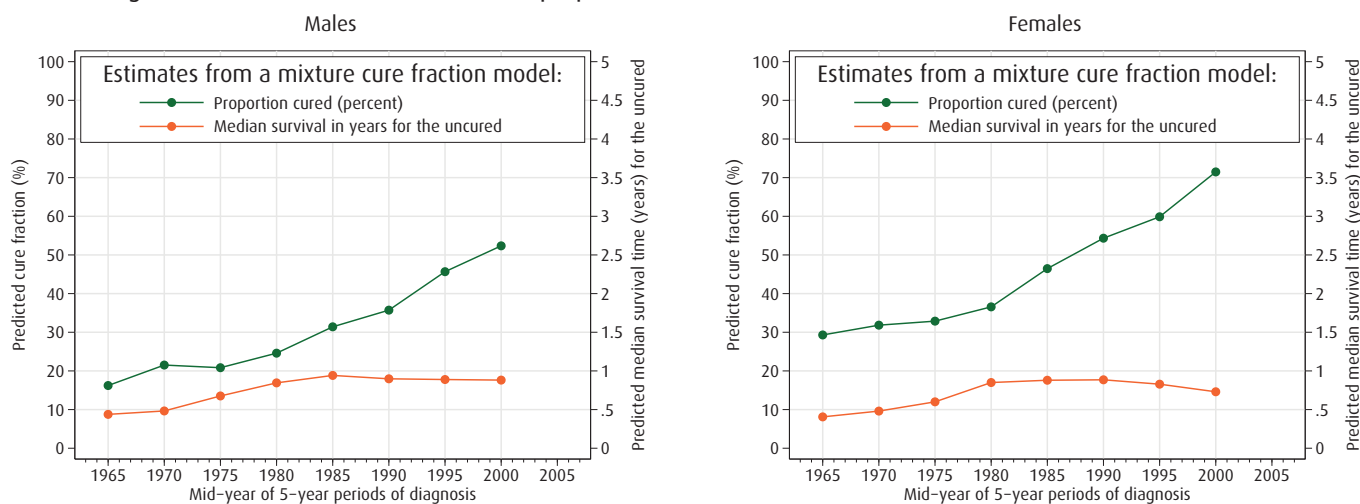


Figure S27d: Relative survival up to 15 years after diagnosis by sex and age

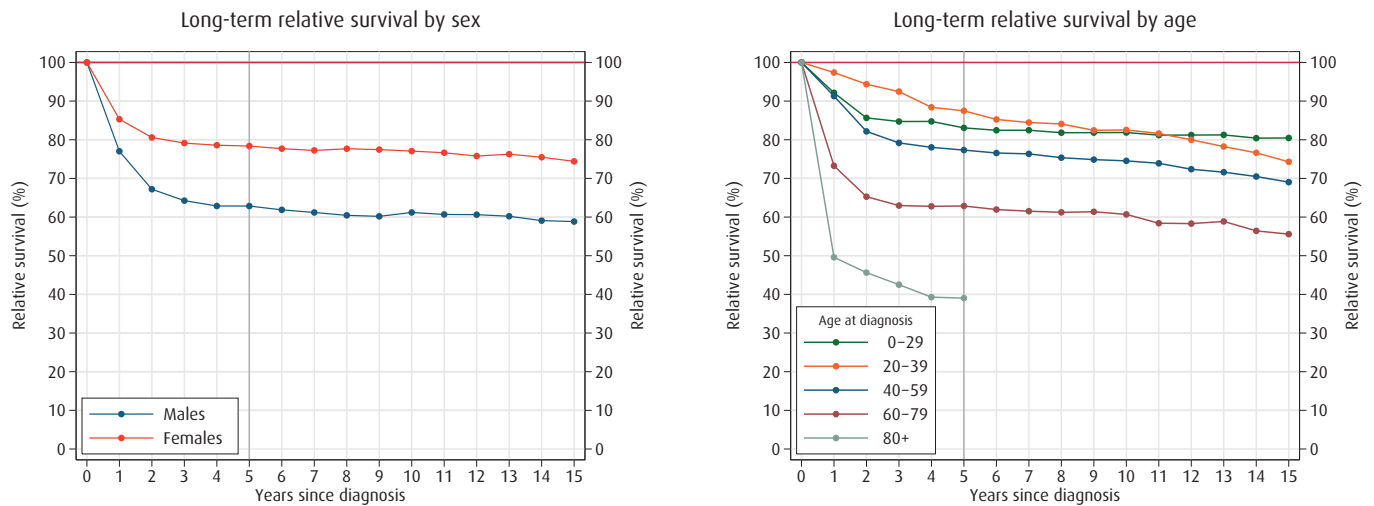


Figure S27e: Conditional 5-year relative survival for every additional year after diagnosis

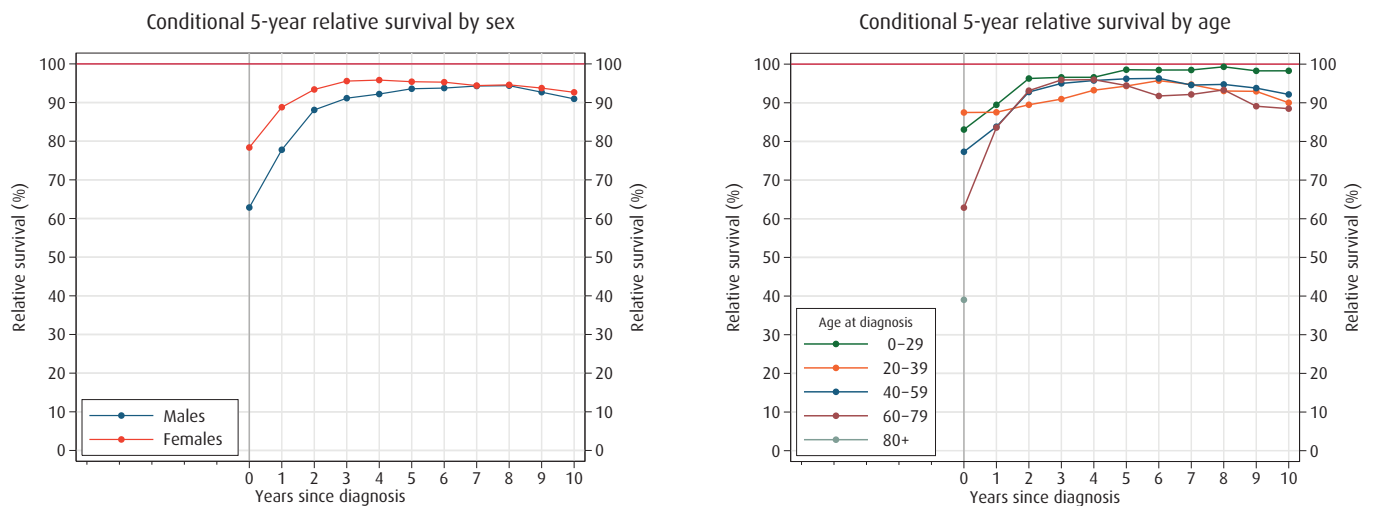
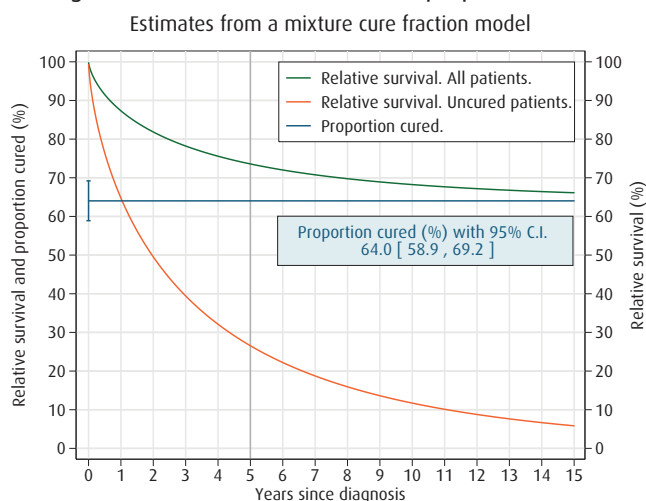


Figure S27f: Relative survival and proportion cured



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-29	148	165	313	6.7
20-39	306	310	616	13.2
40-59	860	671	1531	32.8
60-79	1021	677	1698	36.4
80+	321	184	505	10.8
Total	2656	2007	4663	100.0

Figure S28a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

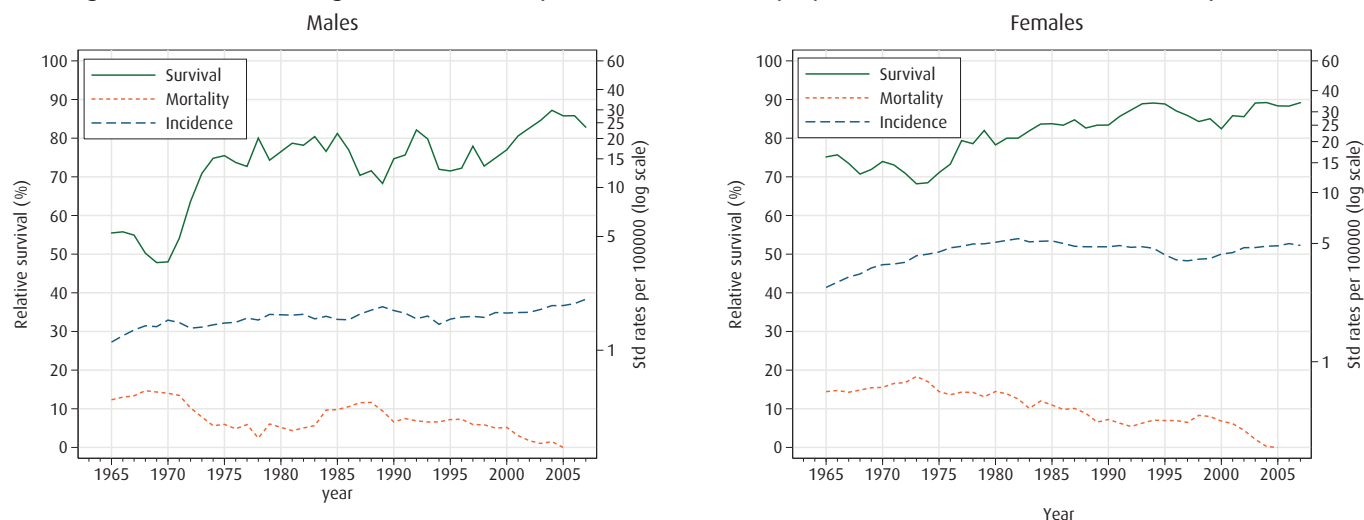


Figure S28b: Trends in 5-year relative survival by age

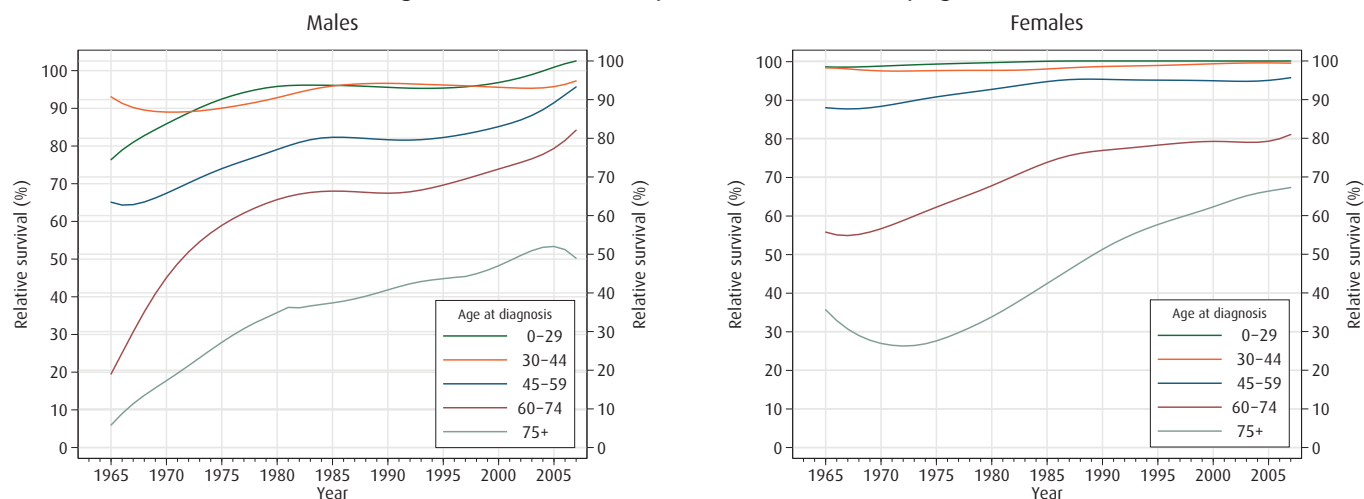


Figure S28c: Estimates of trends in the proportion cured and the median survival time for the uncured

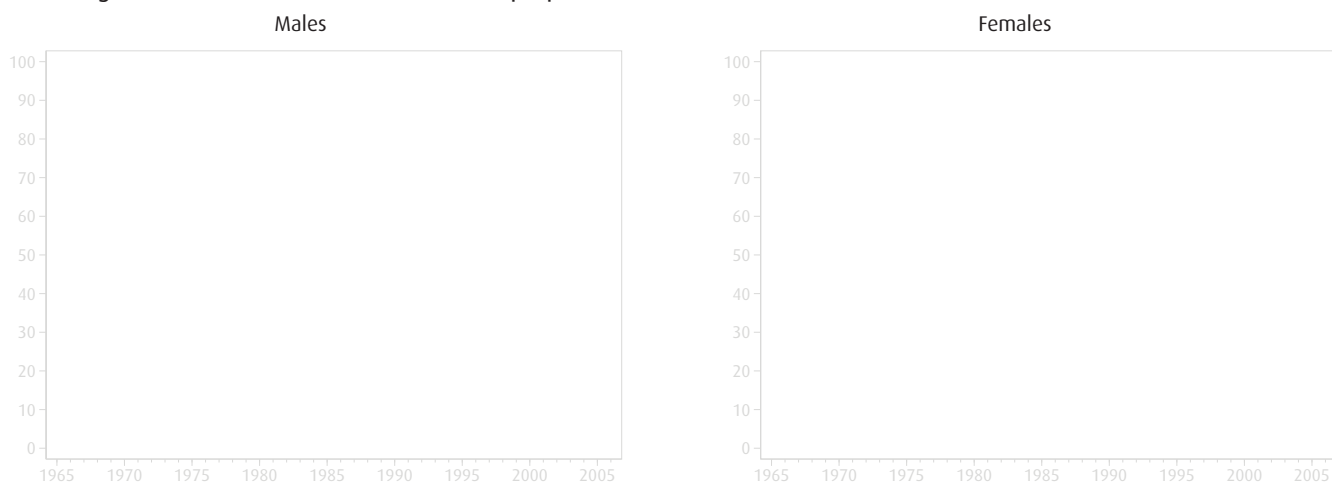


Figure S28d: Relative survival up to 15 years after diagnosis by sex and age

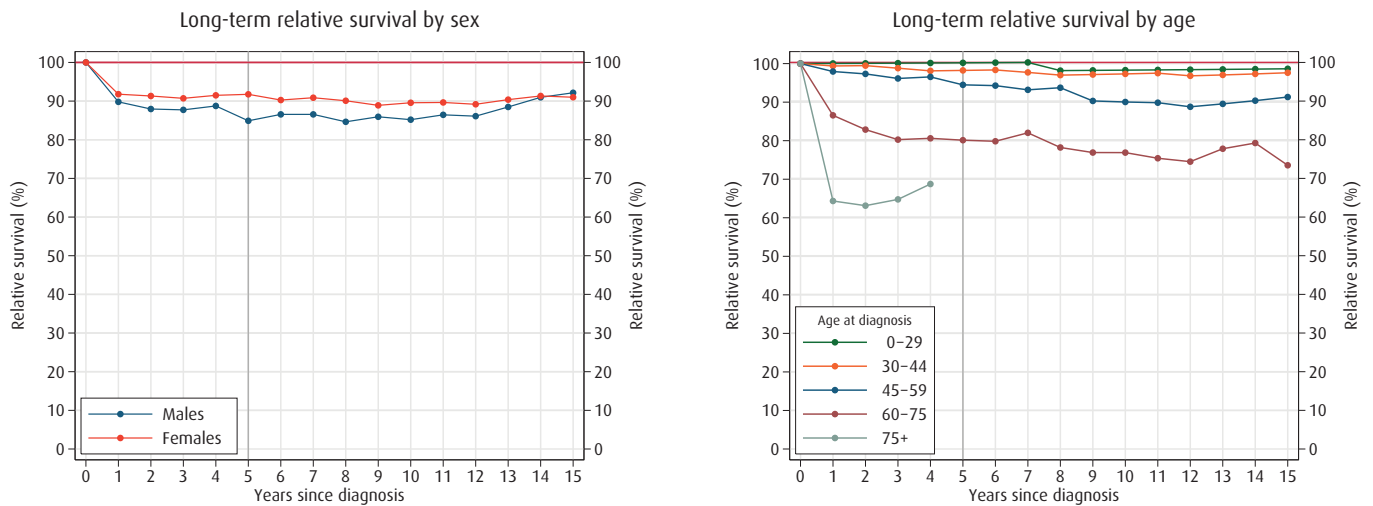


Figure S28e: Conditional 5-year relative survival for every additional year after diagnosis

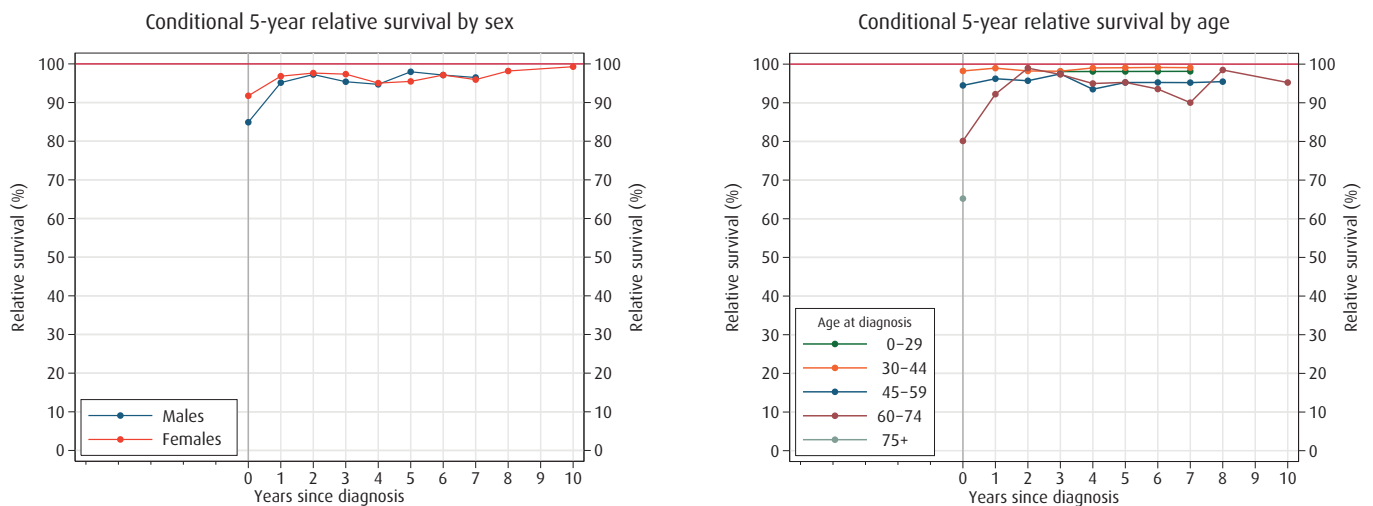
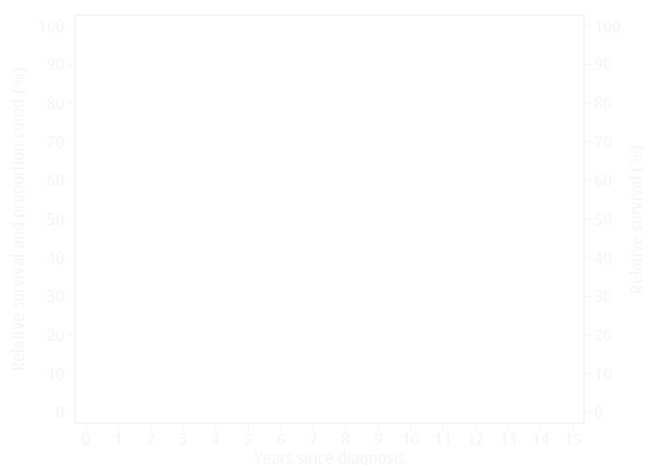


Figure S28f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003–2007)

Age	Males	Females	All	%
0-29	73	9	82	8.0
30-44	177	53	230	22.5
45-59	220	111	331	32.4
60-74	137	74	211	20.6
75+	122	47	169	16.5
Total	729	294	1023	100.0

Figure S29a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

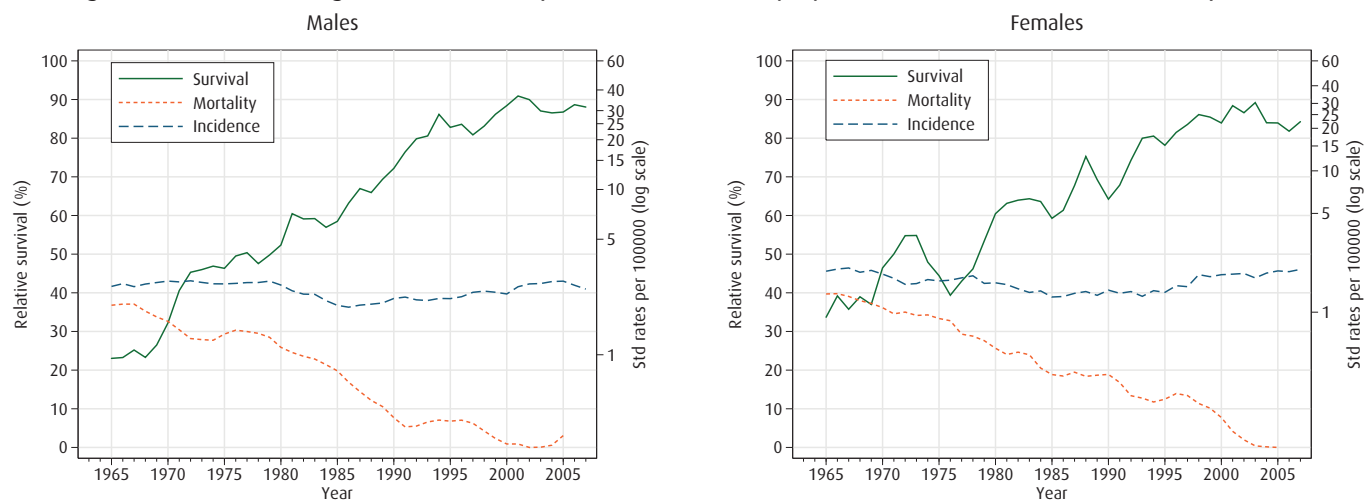


Figure S29b: Trends in 5-year relative survival by age

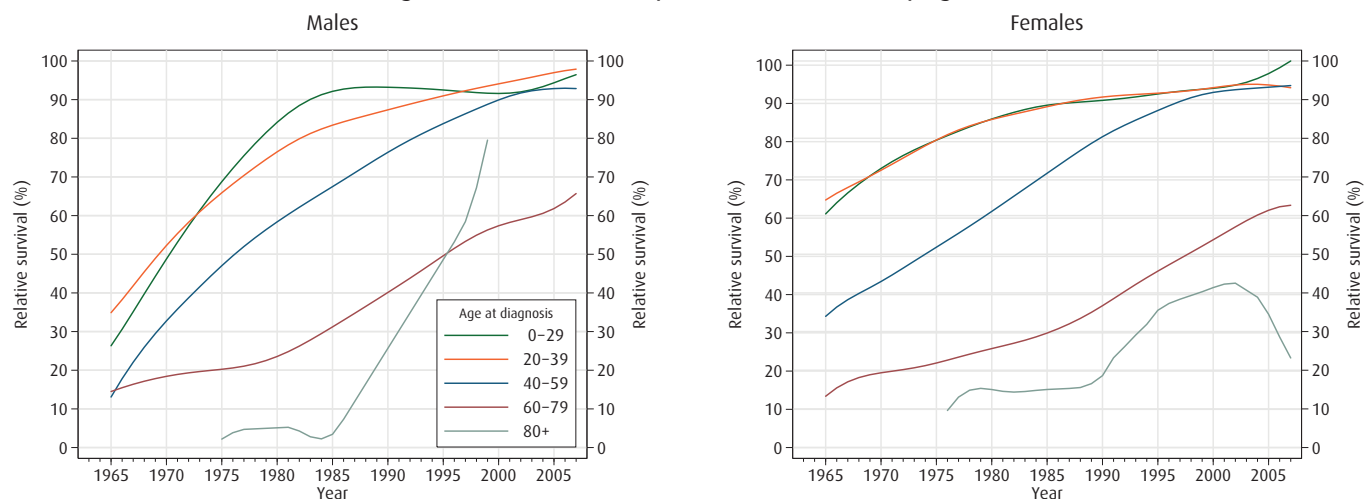


Figure S29c: Estimates of trends in the proportion cured and the median survival time for the uncured

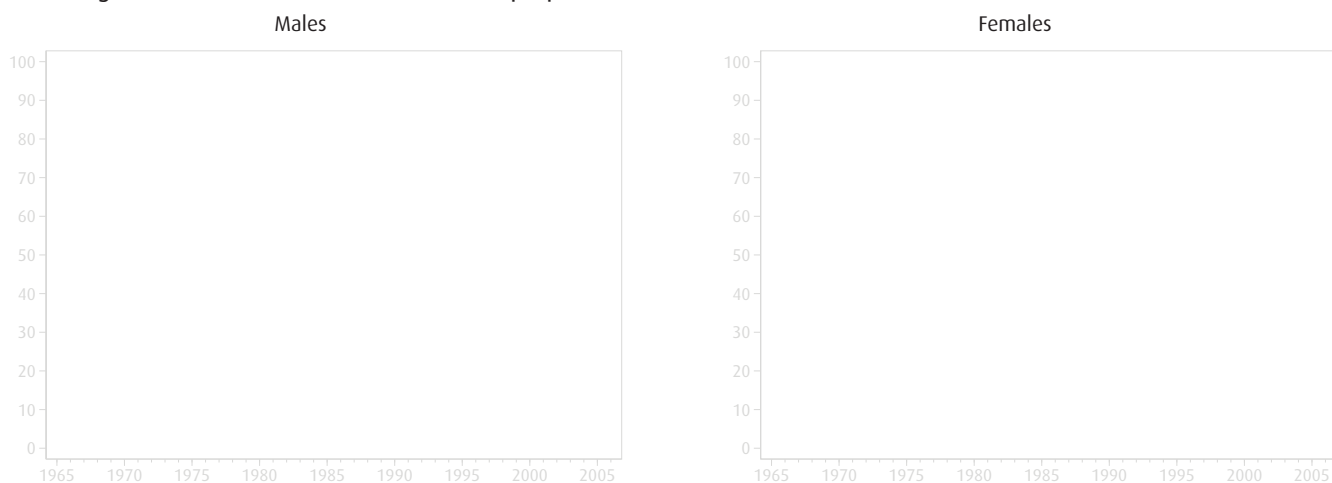


Figure S29d: Relative survival up to 15 years after diagnosis by sex and age

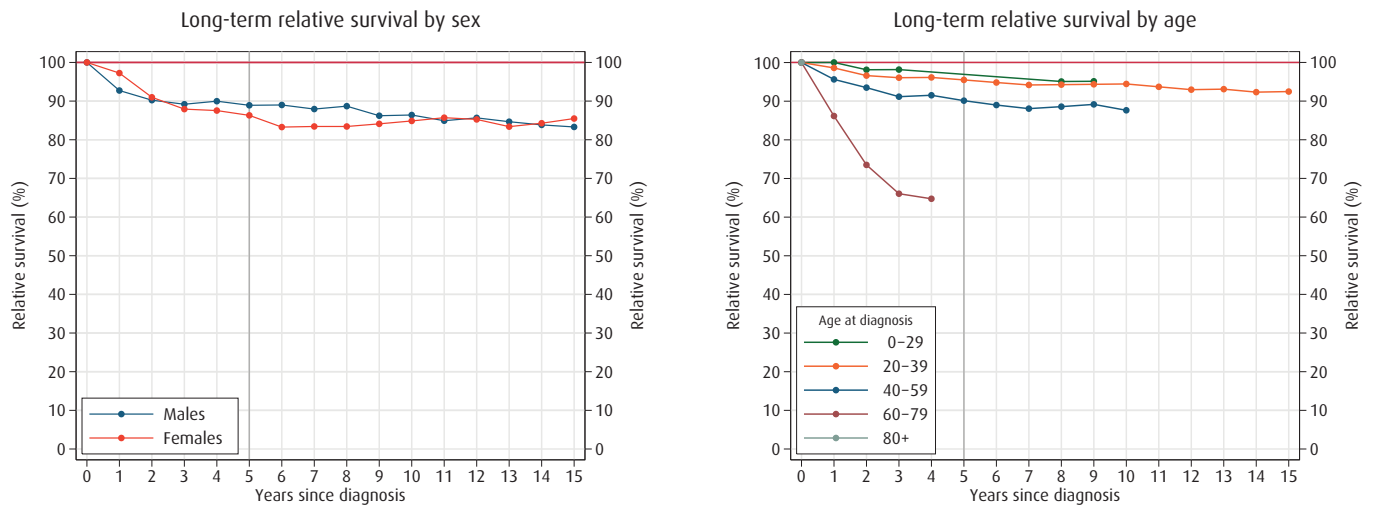


Figure S29e: Conditional 5-year relative survival for every additional year after diagnosis

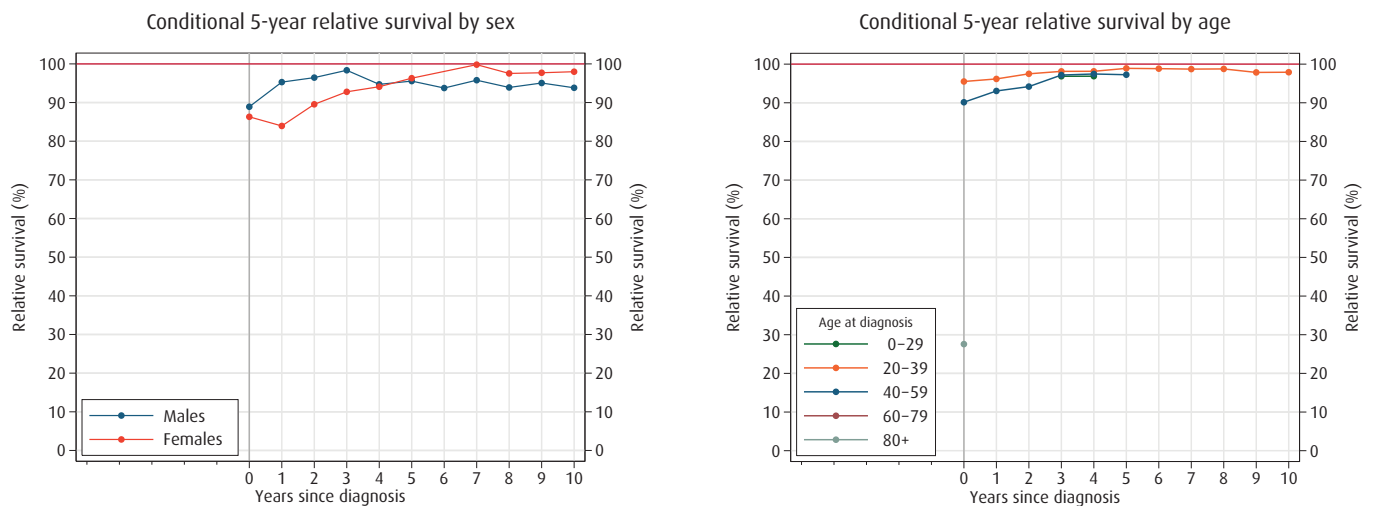
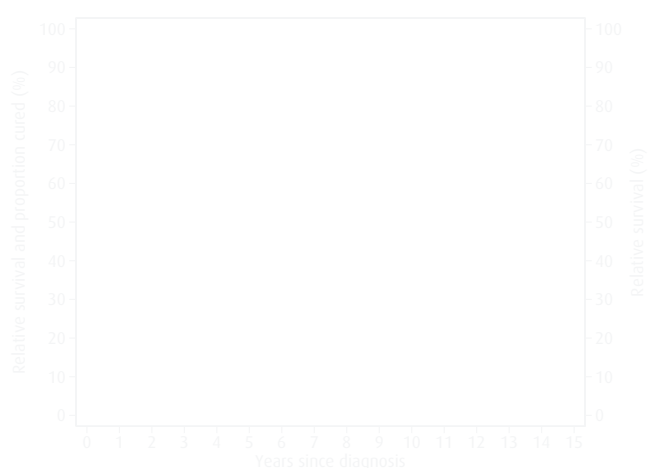


Figure S29f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-29	35	45	80	13.4
20-39	102	139	241	40.5
40-59	49	86	135	22.7
60-79	40	72	112	18.8
80+	17	10	27	4.5
Total	243	352	595	100.0

Figure S30a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

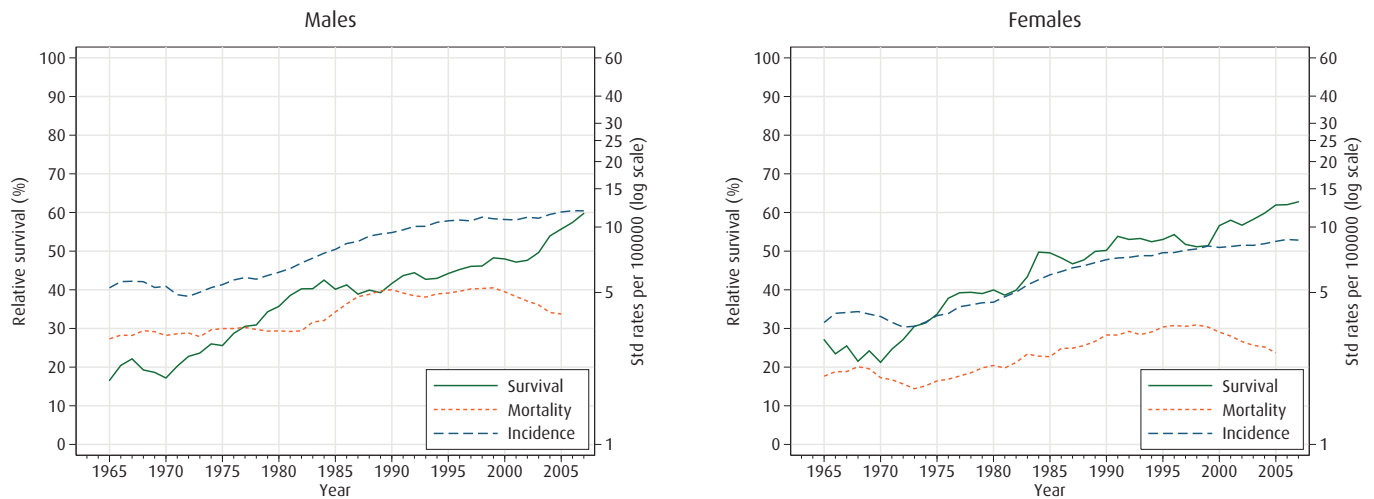


Figure S30b: Trends in 5-year relative survival by age

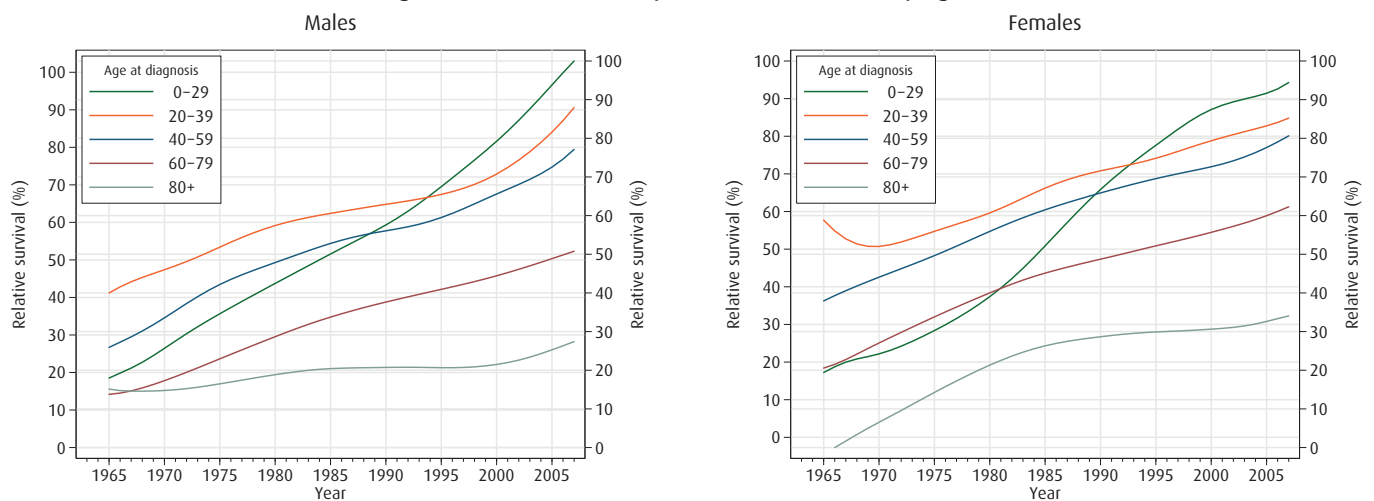


Figure S30c: Estimates of trends in the proportion cured and the median survival time for the uncured

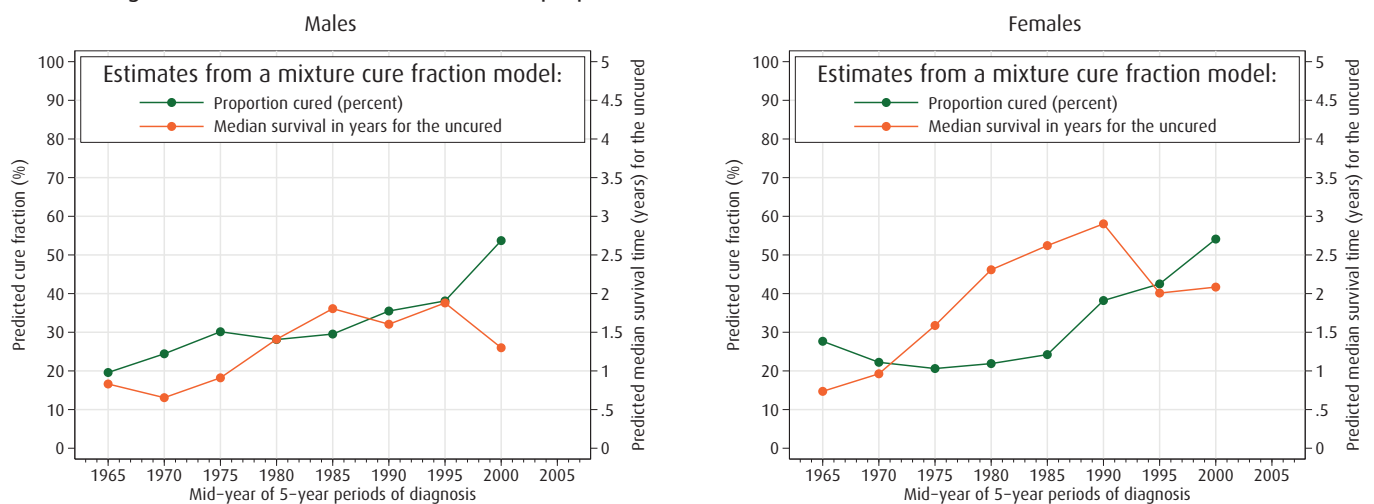


Figure S30d: Relative survival up to 15 years after diagnosis by sex and age

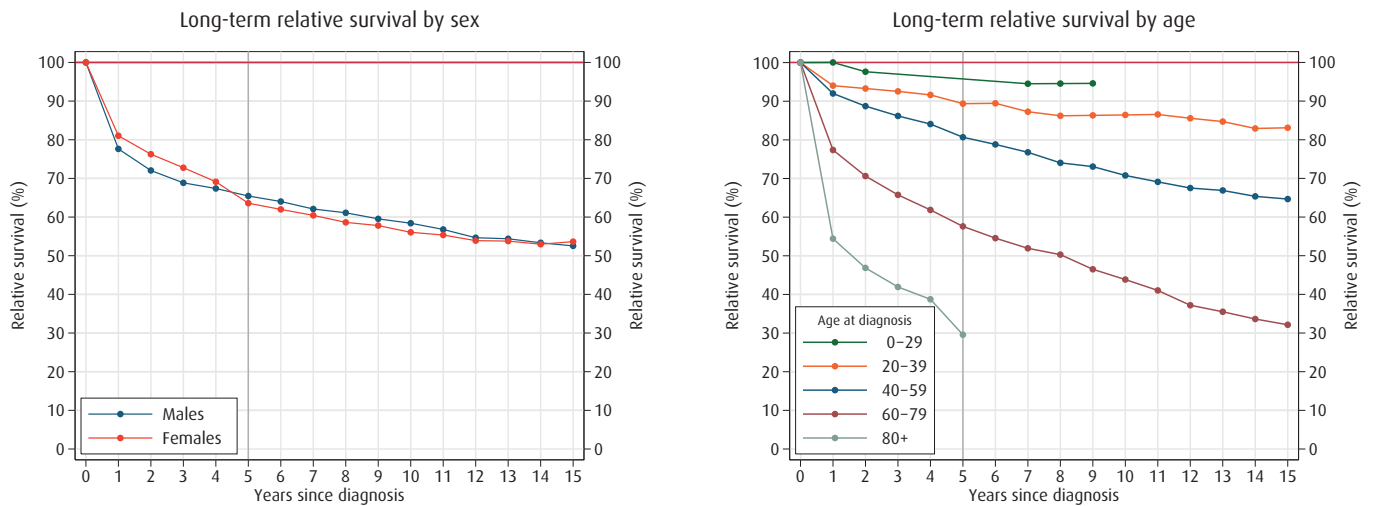


Figure S30e: Conditional 5-year relative survival for every additional year after diagnosis

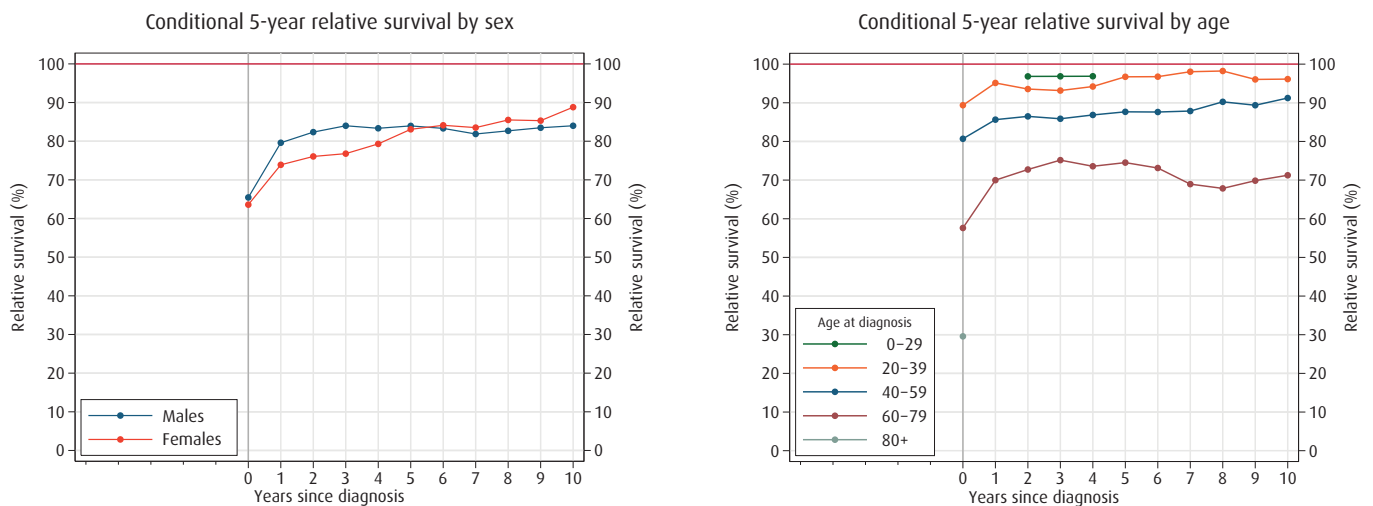
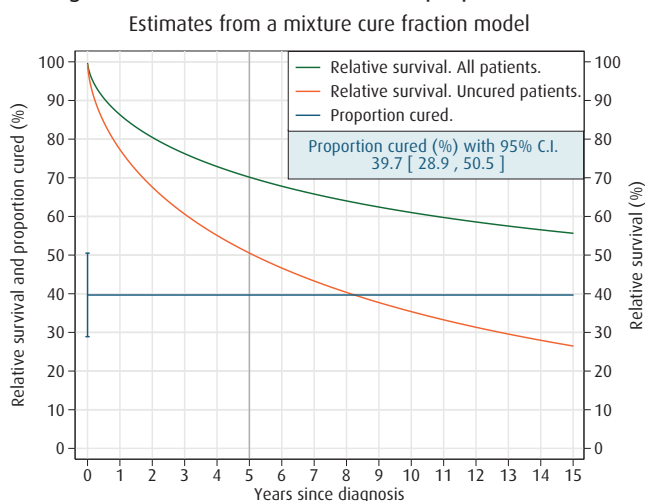


Figure S30f: Relative survival and proportion cured



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-29	24	42	66	1.7
20-39	87	121	208	5.4
40-59	419	597	1016	26.5
60-79	827	999	1826	47.7
80+	405	308	713	18.6
Total	1762	2067	3829	100.0

Figure S31a: Trends in age-standardised 5-year relative survival proportions and incidence and mortality rates

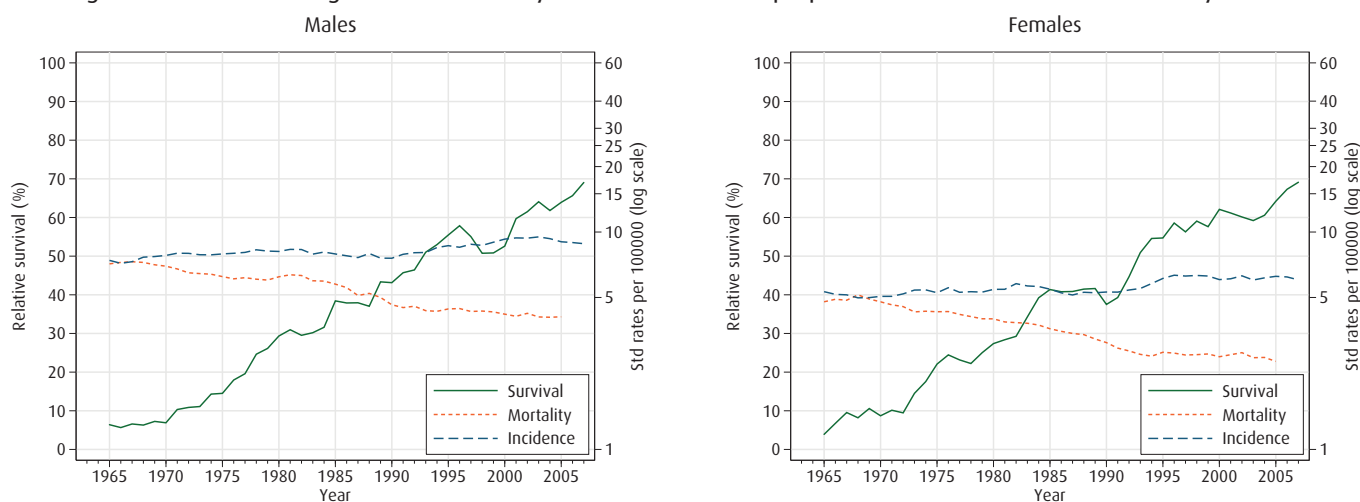


Figure S31b: Trends in 5-year relative survival by age

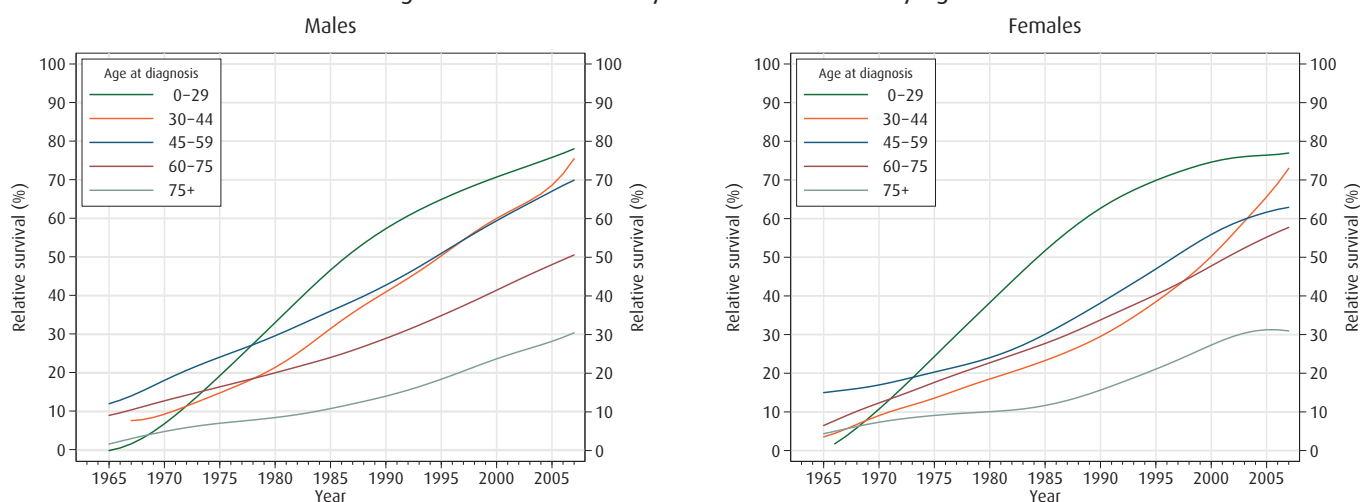


Figure S31c: Estimates of trends in the proportion cured and the median survival time for the uncured

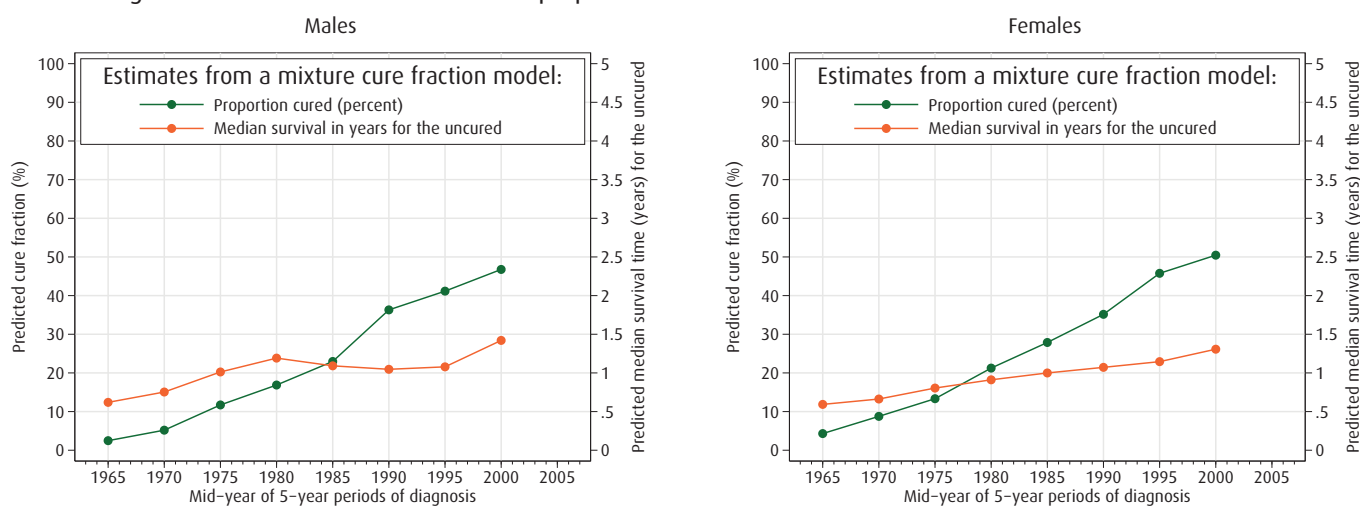


Figure S31d: Relative survival up to 15 years after diagnosis by sex and age

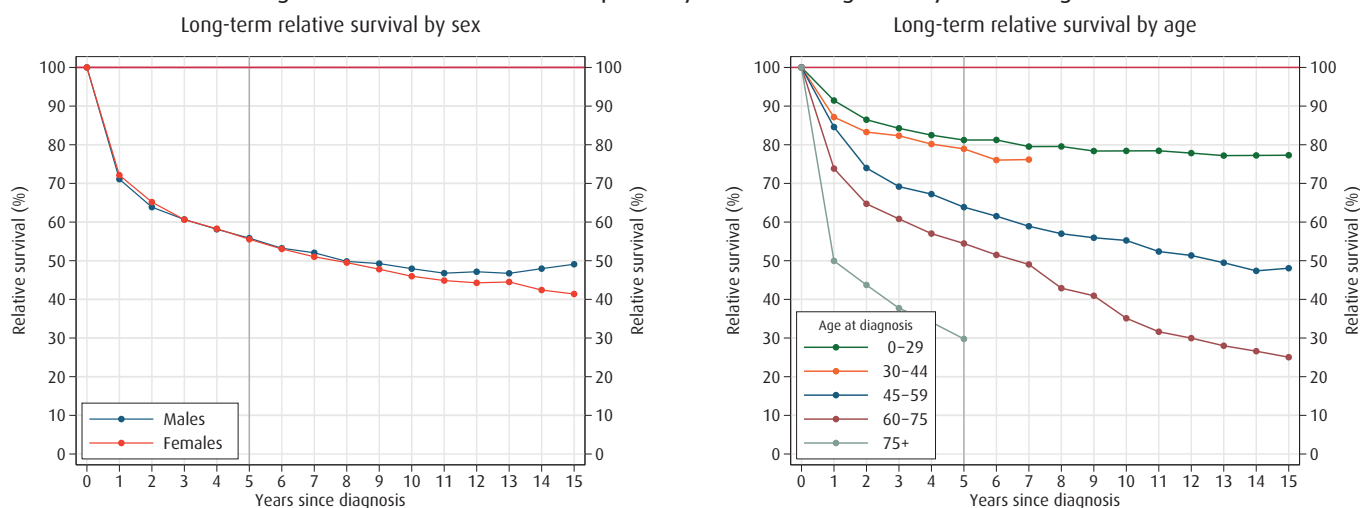


Figure S31e: Conditional 5-year relative survival for every additional year after diagnosis

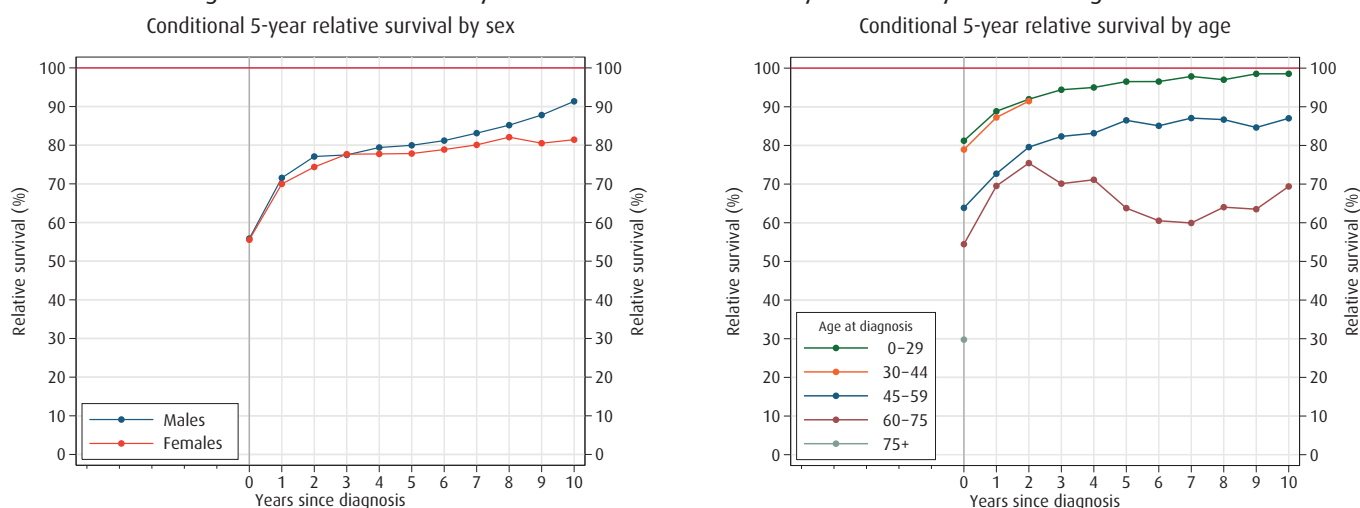
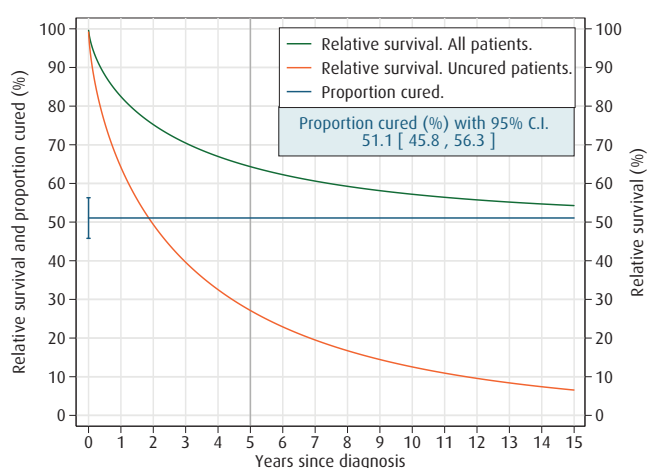


Figure S31f: Relative survival and proportion cured

Estimates from a mixture cure fraction model



Age distribution of patients (2003-2007)

Age	Males	Females	All	%
0-29	139	157	296	11.7
30-44	69	101	170	6.7
45-59	157	258	415	16.5
60-75	326	465	791	31.4
75+	398	450	848	33.7
Total	1089	1431	2520	100.0

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