Chapter 10
Surface Plots for Cancer Survival

10.1 Introduction and Overview: The Impact of Cancer on Mortality in the United States

With 23.4% or 614,348 out of 2,626,418 deaths in the United States, heart diseases remained the leading cause of the death in the United States in 2014 (CDC/NCHS 2015). Hence, heart diseases contributed most to the age-standardized crude death rate in that year. The absolute level of mortality from heart diseases and other circulatory diseases diminished remarkably during recent decades as we show in Fig. 10.1. To avoid spurious results from the changing age composition of the population, we used the population of the year 2000 to age-standardize the rates. During the observed 60 years, mortality—as measured by the age-standardized crude death rate—dropped steadily for women as well as for men. This trend of declining mortality from circulatory diseases and rather stagnant cancer mortality may result in a reversal of the leading group of causes of death in the near future when more people might die of malignant neoplasms than of heart diseases or stroke.

The converging trajectories of these two major causes of death can be also presented from the perspective of cause-elimination life tables (results not shown here; see, for instance Preston et al. (2001) or Kintner (2004) for the methodology): If circulatory diseases had been non-existent, life expectancy at birth would have been 11 years higher in the 1960s. This gap decreased to about 4 years during the most recent years (3.62 for women, 4.16 for men), whereas the impact of eradicating cancer remained relatively stationary over time for malignant neoplasms.

The proportion of deaths from cancer in relation to all causes varies considerably by age as well as over time as we show in Fig. 10.2. The marginal distribution over age is bimodal. A local peak is reached at childhood ages with the main contributing cancers being leukemia and lymphoma as pointed out in Moore and Hurvitz (2009).

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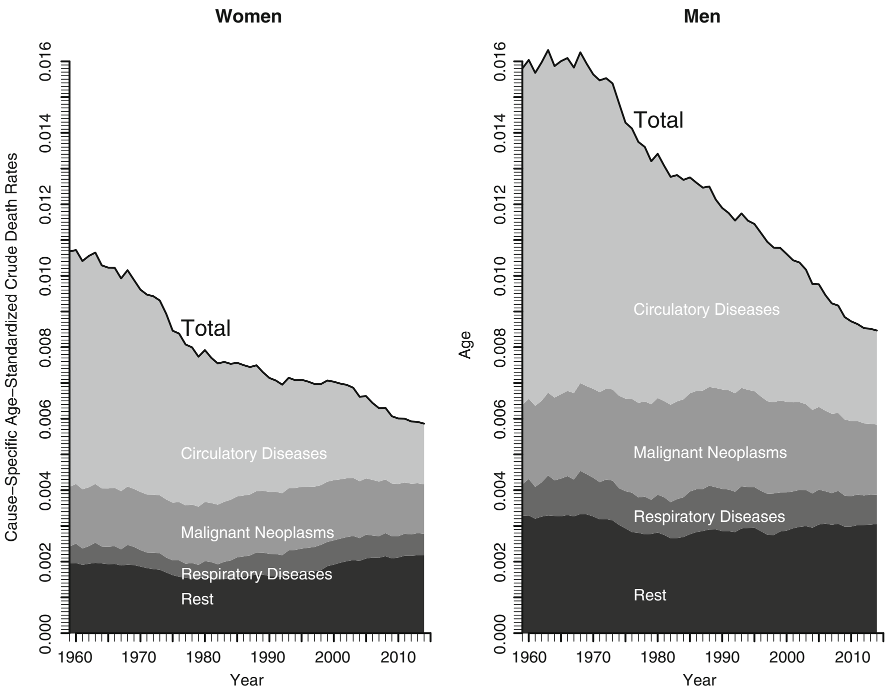

Fig. 10.1 Age-standardized crude death rates by cause and sex (*left panel*: women; *right panel*: men) in the United States from 1959–2014 (Data source: Own estimation based on data from the Human Mortality Database and the National Center for Health Statistics. The population of the year 2000 was used as the standardization population)

The age when the global peak is reached depends on the sex. 40% or more of all deaths of women around age 50 can be attributed to cancers whereas the largest proportion among men is reached between ages 60 and 70.

10.2 Dynamics of Cancer Survival by Cancer Site

People are usually not healthy and then die suddenly of a chronic, non-communicable disease such as cancer. In a very simplified manner, we can regard this as a two-step process: (1) People are healthy and then are diagnosed with a certain chronic disease x. (2) People who are diagnosed with disease x die of x or of another disease. The SEER data allow us to investigate developments for both steps. We can look at incidence data for the first step and see how incidence has changed over time by age. This might allow us to make inferences about the successes and failures of cancer *prevention*. We focus, however, on the second step: Analyzing survival from the moment of diagnosis to death. Thus, our focus is rather on the successes and failures of cancer *treatment*.

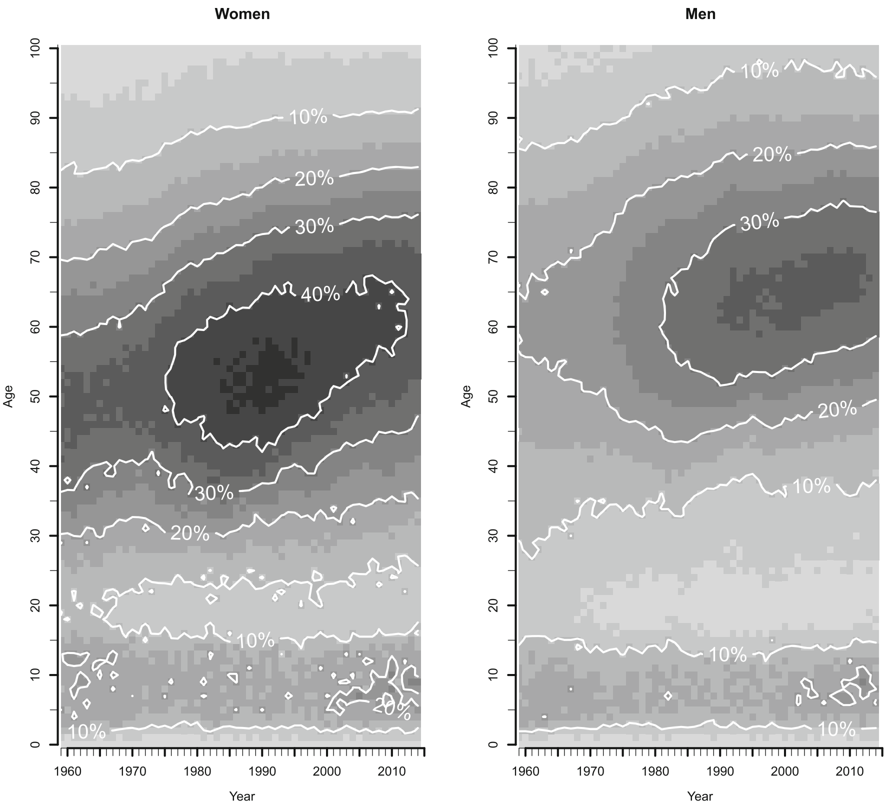

Fig. 10.2 Proportion of deaths from cancer in relation to all causes (*left panel*: women; *right panel*: men) in the United States at ages 0–100 from 1959–2010 (Data source: National Center for Health Statistics)

We decided to base our analysis on the five year survival rate. According to the National Cancer Institute (2017) it is the "percentage of people in a study or treatment group who are alive 5 years after they were diagnosed with or started treatment for a disease, such as cancer."[1] We use three different operationalizations of five-year survival:

1. For each cancer site and sex we estimate by single calendar year and single age how many persons are still alive 60 months after diagnosis. Thus, the first approach measures the survival chances *in general* of someone who was diagnosed with a specific cancer.
2. Obviously, the first operationalization is highly dependent on age: someone aged 95 years has much lower survival chances in general than someone aged 45 years with the same diagnosis. The interest is often not on survival/mortality in general but on mortality due to the diagnosed disease. We therefore estimated also the

[1]Since it is a percentage/proportion, we wonder why the term "rate" has become so commonly used.

probability that someone will not die of the diagnosed cancer within 5 years. This second operationalization is sometimes called “corrected survival rate”, “net survival” or “disease-specific survival” (Parkin and Hakulinen 1991, p. 167). We use the last term.

3. While the first two approaches describe the risk of dying of any cause (1) or of the diagnosed cancer (2), the third approach compares the survival chances of the diagnosed individuals with the general population. The ratio of observed survival to expected survival is called “relative survival” and can be traced back to Berkson and Gage (1952). Relative survival is “defined as the observed survival of the cancer patients divided by the expected survival of a comparable group from the general population, free from the cancer under study” (Talbäck and Dickman 2011, p. 2626). The observed survival rate for relative survival corresponds to our first approach, i.e., the probability of surviving from all causes of death. The most common methods to estimate relative survival (e.g., Ederer I, Ederer II, Hakulinen) differ with regard to the estimation of expected survival, though (Cho et al. 2011). As shown by Rutherford et al. (2012, p. 20), “[t]aking age into account [. . .] removes most of the differences between the methods.” Since we analyze by single ages and single calendar years, the choice of method to estimate expected survival is less of a problem. We estimated expected survival with life table data from the Human Mortality Database (2017): Expected five year survival for 55 year old women in the year 2000 was the probability to survive age 55 in the year 2000 multiplied by the probability to survive age 56 in the year 2001, . . . multiplied by the probability to survive age 59 in the year 2004. Using the general population instead of the general population free from cancer violates the definition of relative survival. It has been done and justified, however, since the inception of the method (please see Appendix Note 2 of Berkson and Gage (1952) or Ederer et al. (1961)). Also recent papers such as Talbäck and Dickman (2011, p. 2626 and Table 2) argue “that the bias is sufficiently small to be ignorable for most applications.” Not accounting for the inclusion of cancer patient mortality becomes a problem only for the oldest subjects and follow-up times of 10 years or more. We would also argue that our estimates for five-year survival are sufficiently close to the official estimates. For example, SEER estimates relative survival of women diagnosed with breast cancer aged 50–64 years to be 90.1% during the period 2007–2013.[2] Our results for the most recent 3 years of our analysis varied between 90.05% and 91.08%.

The three approaches are featured in a panel each of Fig. 10.3 for breast cancer. We restricted our analysis of breast cancer to women although men can die from it as well. Our estimates for single year and age for breast cancer as well as for all other cancer sites have been smoothed, again using *P*-Splines as outlined in Chap. 5 Eilers and Marx (1996); Camarda (2012, 2015).

[2]See https://seer.cancer.gov/explorer/application.php?site=55&data_type=4&stat_type=5&compareBy=sex&series=race&chk_sex_3=3&chk_race_1=1&chk_age_range_141=141&chk_age_range_160=160&chk_stage_101=101&advopt_precision=1&showDataFor=age_range_160_and_stage_101.

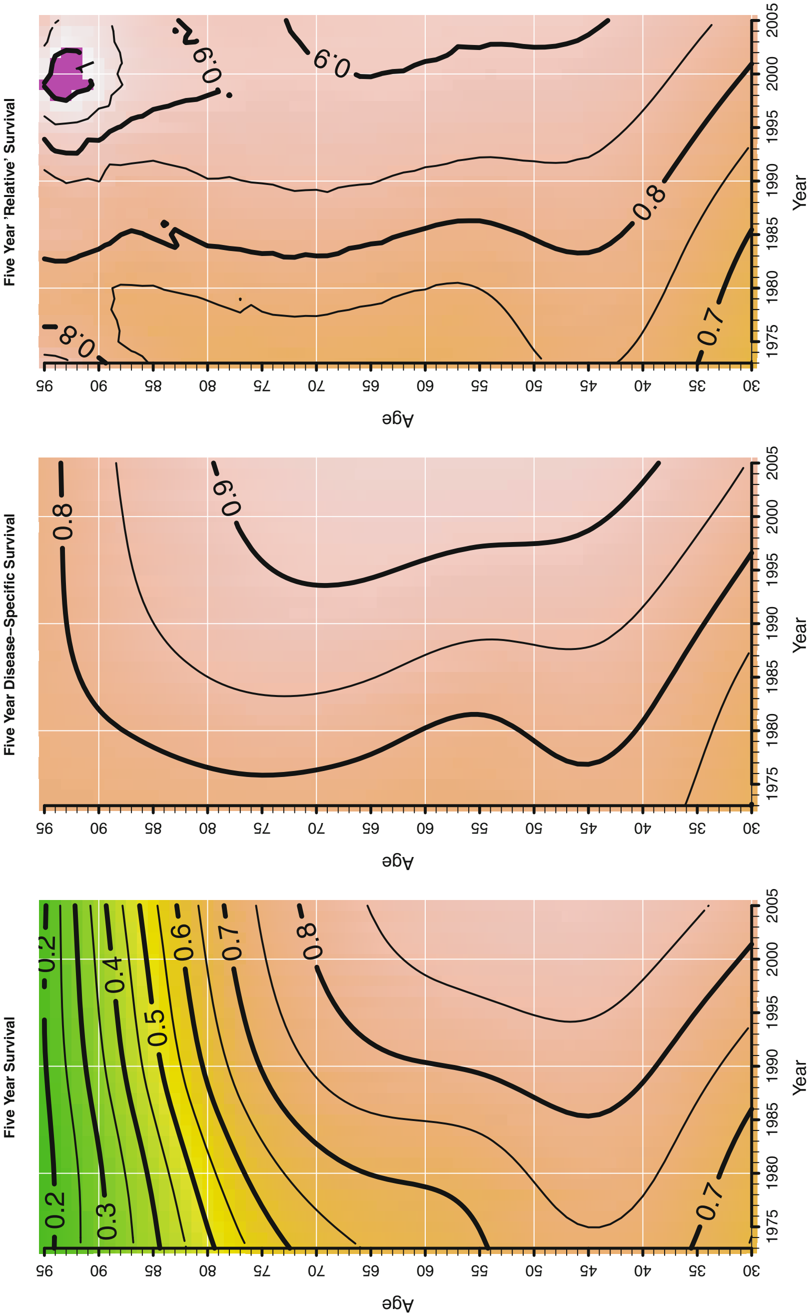

Fig. 10.3 Five year survival for breast cancer at ages 30–95 from 1973–2005. *Left panel*: Probability to survive for 5 years after diagnosed with breast cancer (any cause). *Middle panel*: Probability of not dying from breast cancer within 5 years after diagnosis. *Right panel*: Five year survival of women diagnosed with breast cancer in relation to five year survival of women in the general population (Data Source: SEER and Human Mortality Database)

The panel on the left denotes the probability to survive for another 5 years after being diagnosed with breast cancer, regardless of the actual cause of death. The figure exhibits an obvious age gradient: Values of 30% or less at ages above 90 are the consequence that the women are not only at an elevated risk of dying from breast cancer. Other causes, most notably circulatory diseases, further reduce the chances to survive for five more years. Consequently, the upward trend of the contour lines can not be interpreted as progress made against the lethality of breast cancer. Still it provides the answer to the question "How likely is it that I survive for another five years?" for someone who got diagnosed with breast cancer.

While the left panel takes all "exit" possibilities into account, the panel in the middle looks only at death from breast cancer. As a consequence, one minus the depicted value equals the probability to die from breast cancer within 5 years after diagnosis. The rather vertical lines from about age 40 to about age 80 indicate that the chance of surviving breast cancer for at least 5 years has increased over time. For instance, the probability for 60-year-old women who got diagnosed with breast cancer in 1980 to survive 5 years was 80%; the equivalent value in 2000 was higher than 90%. To express it even more positively: The risk of dying was cut in half within less than 20 years (1980: $1 - 0.8 = 20\%$; $\sim 1995 : 1 - 0.9 = 10\%$)!

The panel on the right of Fig. 10.3 shows "relative survival", i.e., it illustrates the relative survival disadvantage of those diagnosed with breast cancer in relation to the general population. A level of one would indicate that there was no difference in the chance to survive for five more years between someone with a cancer diagnosis and the general population. Unfortunately—but also not surprisingly—women with breast cancer have lower survival chances than the general population. We can detect, however, progress over time. The excess risk is less than 10% in recent years for women with breast cancer in comparison to the general population (contour line of 0.9) whereas it was about 30% just 25 years earlier. It is important to point out that the increasing values of the vertical lines suggest a clear period effect: Progress against breast cancer was faster than progress in survival in general, regardless of the age when the woman was diagnosed.

It is theoretically possible to observe relative survival estimates that are higher than one. For instance, it could be the outcome of a selection effect: Persons that take advantage of screening programs and other early preventive measures are possibly leading rather healthy lifestyles. If those persons are diagnosed with a cancer that is virtually non-lethal, their survival advantage of their health behavior might be stronger than the additional mortality risk of the malignant neoplasm. Hence, it can not be concluded that getting diagnosed with a certain cancer could actually improve survival chances. We would argue, though, that the small area at ages 90–95 in 2000 is not the outcome of such a selection effect. Instead, we assume that it is the outcome of random data fluctuations due to small numbers of persons getting diagnosed. For example, 46 women at age 93 were diagnosed with breast cancer in 2000.

The corresponding estimates for colorectal cancer are depicted in Figs. 10.4 and 10.5 for women and men, respectively (pages 129 & 130). Both sexes feature comparable estimates. The dynamics are somehow reminiscent of breast cancer

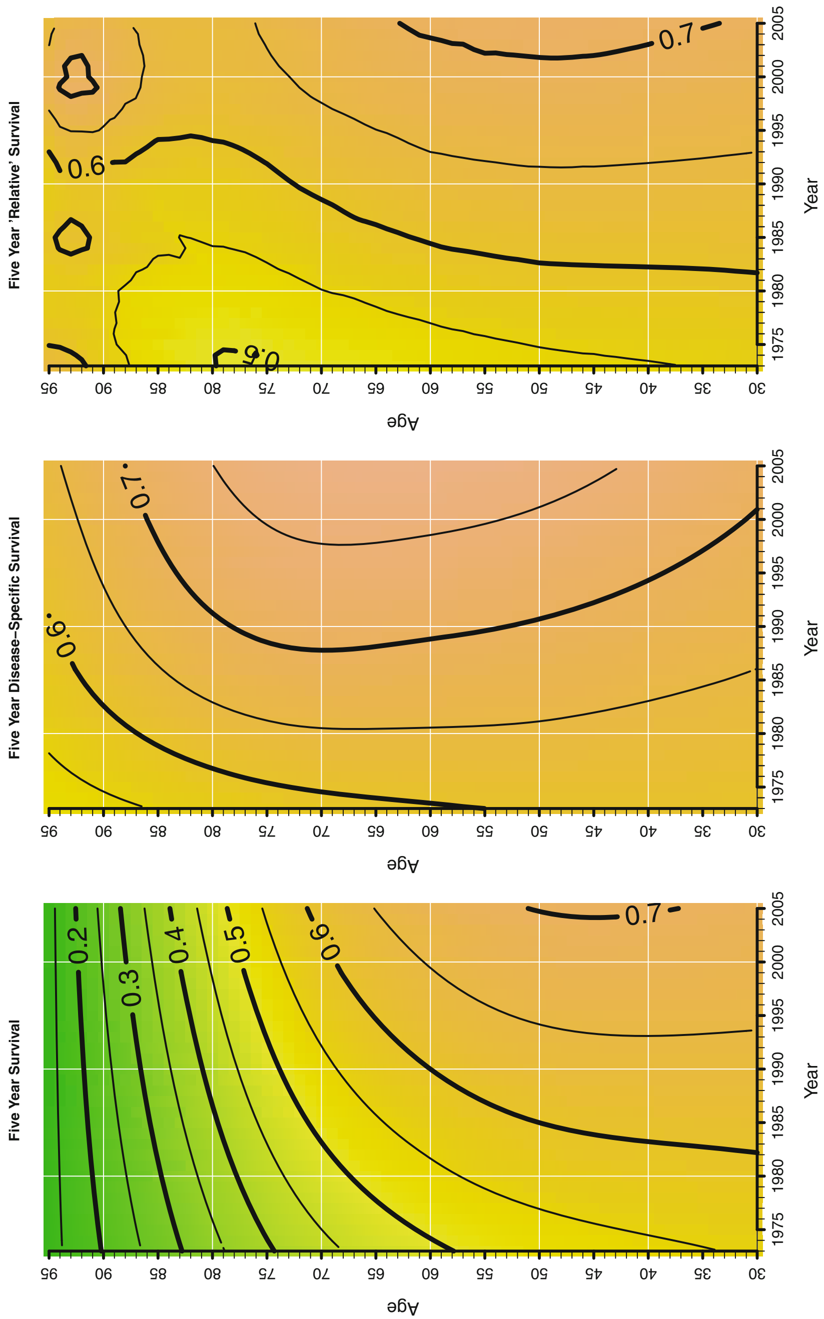

Fig. 10.4 Five year survival for colorectal cancer at ages 30–95 from 1973–2005. *Left panel*: Probability to survive for 5 years after diagnosed with colorectal cancer (any cause). *Middle panel*: Probability of not dying from colorectal cancer within 5 years after diagnosis. *Right panel*: Five year survival of women diagnosed with colorectal cancer in relation to five year survival of women in the general population (Data Source: SEER and Human Mortality Database)

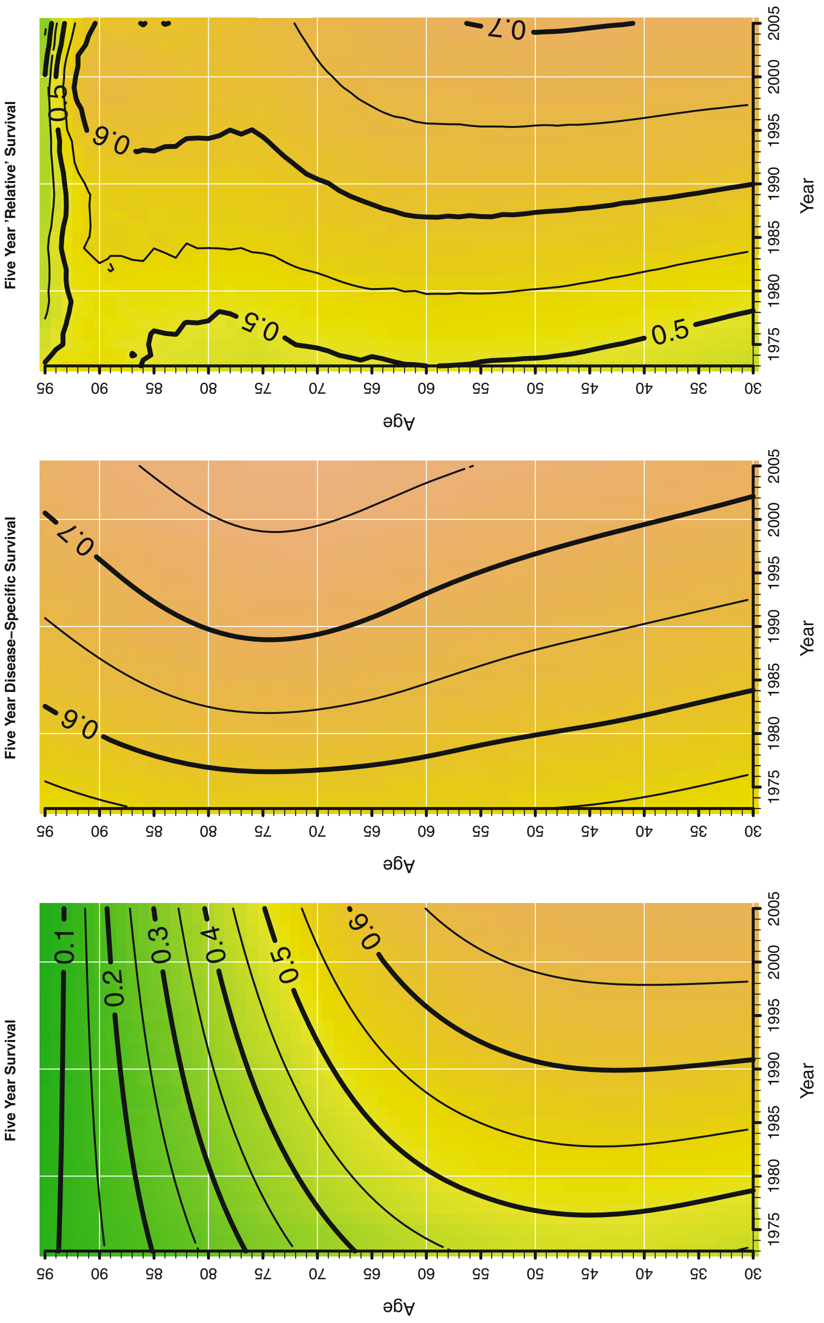

Fig. 10.5 Five year survival for colorectal cancer at ages 30–95 from 1973–2005. *Left panel*: Probability to survive for 5 years after diagnosed with colorectal cancer (any cause). *Middle panel*: Probability of not dying from colorectal cancer within 5 years after diagnosis. *Right panel*: Five year survival of men diagnosed with colorectal cancer in relation to five year survival of men in the general population (Data Source: SEER and Human Mortality Database)

albeit on a lower survival level: The chances to survive for another 5 years (left panels) above age 80 tend to follow a horizontal trend over time. This could be caused by at least two factors: Either there was no progress over time or that competing causes at those advanced ages are more important. There was, indeed, progress over time as shown by the panels in the middle of both figures. But despite all this progress, relative survival is still at least 30% lower than in the general population (right panels).

The dominance of shades of green in Figs. 10.6 and 10.7 illustrate that survival chances are much worse for lung cancer than for breast or colorectal cancer. The chances to survive for another 5 years after being diagnosed with cancer are less than 30%. Even at very advanced ages, relative survival is very low. On average it is about 80% lower in comparison to the general population.

Pancreatic cancer, as shown in Fig. 10.8 for women and men, belongs to the cancer sites with the worst survival chances. Living for another 5 years after diagnosis is extremely unlikely with a proportion of survivors of less than 10%. It is therefore not surprising that relative survival is also very low.

The last cancer site we investigated was prostate cancer (see Fig. 10.9). In terms of survival it can be found at the other side of the spectrum of pancreatic cancer. The vertical, numerically increasing, contour lines in the panel for relative survival provide evidence for a clear period effect: Relative survival became more common at all ages at a pace that was faster than improvements in survival in the general population. The most recent estimates show values of relative survival of more than 95%.

Differences in survival do not only exist between cancer sites. An important factor is also the stage when the cancer is diagnosed first. The data used in this study provide stage information for[3]

- "in situ"—a noninvasive neoplasm
- "localized"—an invasive neoplasm confined entirely to the organ of origin
- "regional"—a neoplasm that can not only be found in the organ of origin
- "distant"—a neoplasm that has spread to parts of the body remote from the primary tumor site.

We only present an example for colorectal cancer, contrasting the survival chances of persons where a localized tumor was detected with those with a distant malignant neoplasm. Figure 10.10 present the results for women; the corresponding plots for males are contained in Fig. 10.11. Both six-panel plots provide clear evidence that early detection of colorectal cancer is, literally, a matter of life

[3]Further details can be found in the field description of variable "SEER Historic Stage A" in the SEER research data record description.

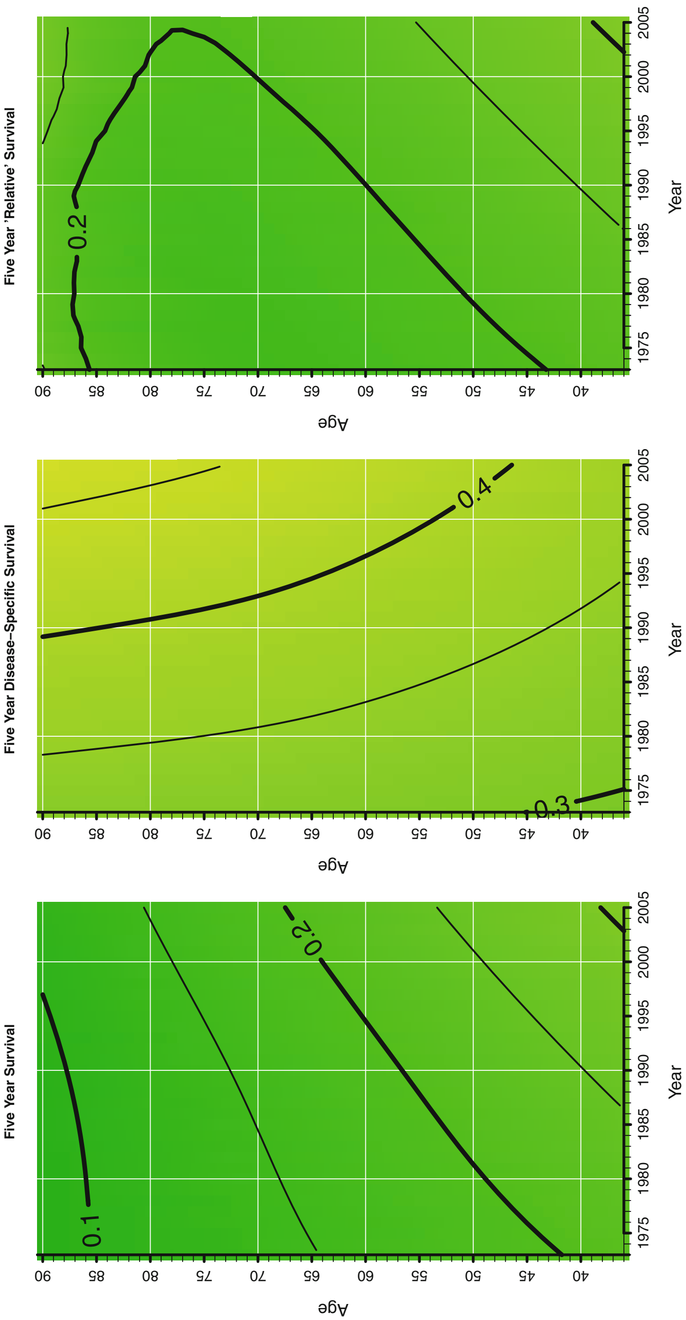

Fig. 10.6 Five year survival for lung cancer at ages 36–95 from 1973–2005. *Left panel*: Probability to survive for 5 years after diagnosed with lung cancer (any cause). *Middle panel*: Probability of not dying from lung cancer within 5 years after diagnosis. *Right panel*: Five year survival of women diagnosed with lung cancer in relation to five year survival of women in the general population (Data Source: SEER and Human Mortality Database)

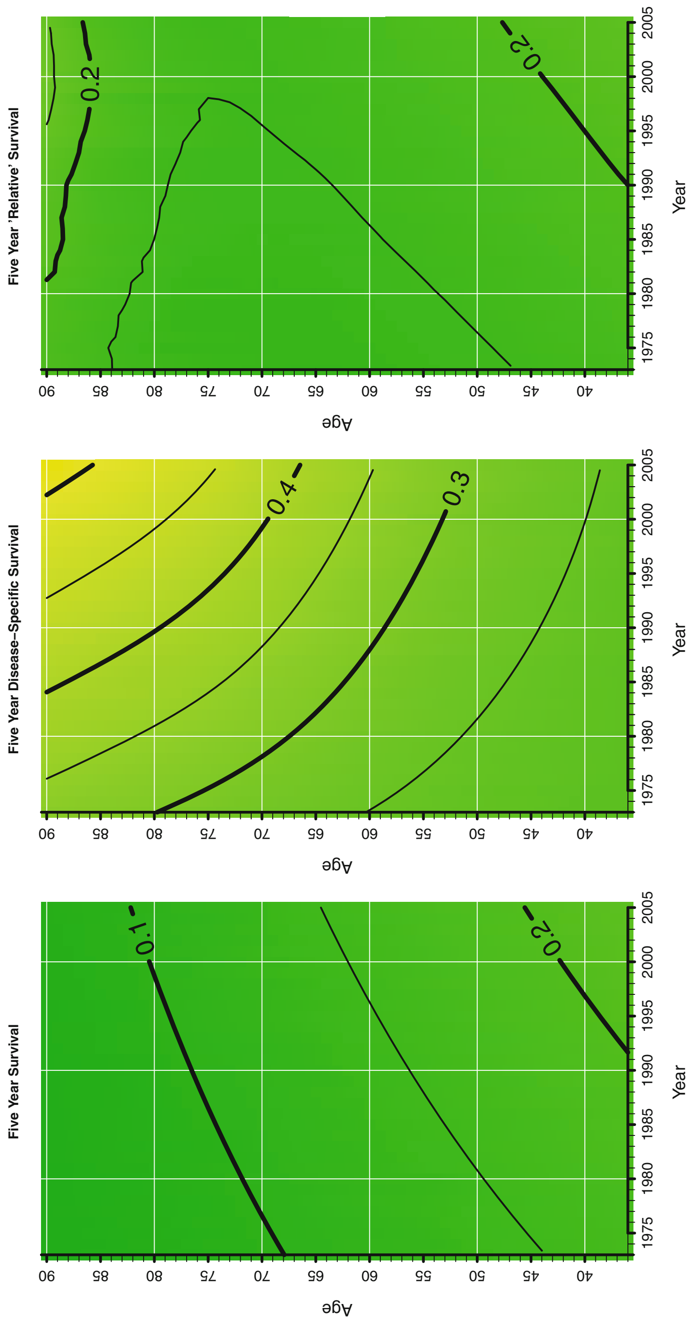

Fig. 10.7 Five year survival for lung cancer at ages 36–95 from 1973–2005. *Left panel*: Probability to survive for 5 years after diagnosed with lung cancer (any cause). *Middle panel*: Probability of not dying from lung cancer within 5 years after diagnosis. *Right panel*: Five year survival of men diagnosed with lung cancer in relation to five year survival of men in the general population (Data Source: SEER and Human Mortality Database)

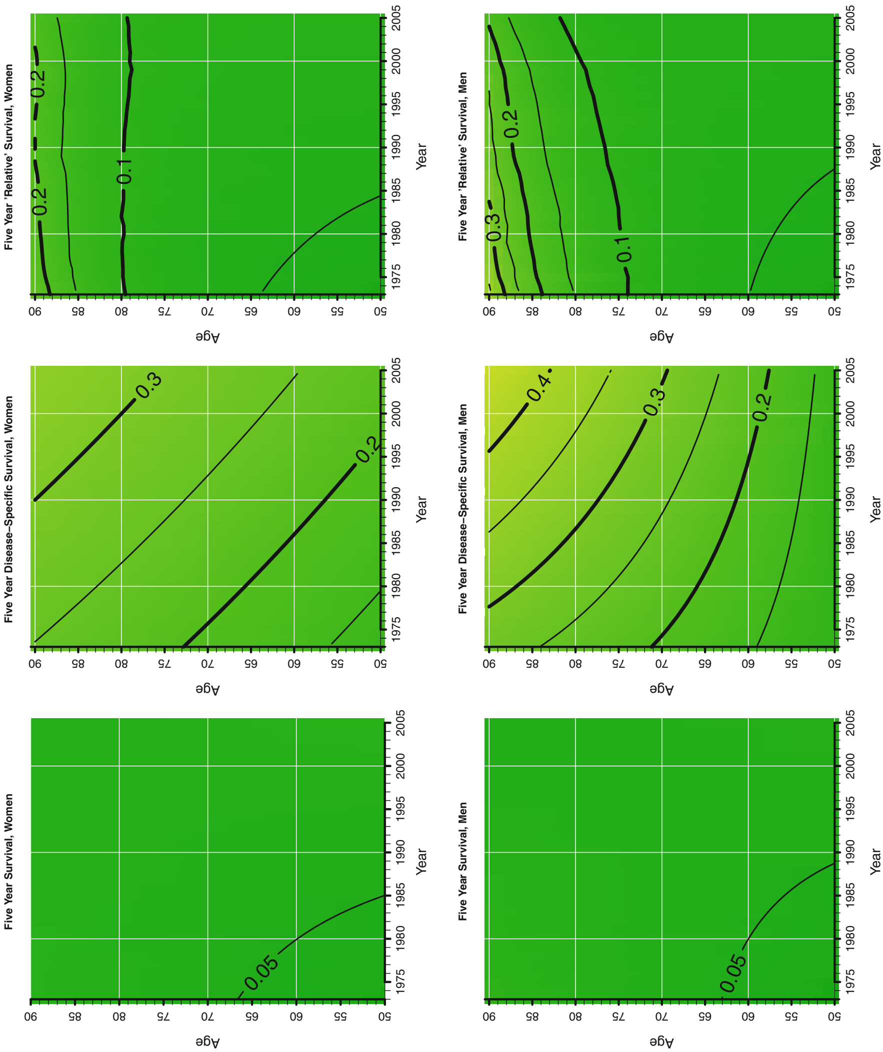

Fig. 10.8 Five year survival for pancreatic cancer at ages 50–90 from 1973–2005. *Left column*: women; *right panel*: men. *Upper panels*: Probability to survive for 5 years after diagnosed with pancreatic cancer (any cause). *Middle panels:* Probability of not dying from pancreatic cancer within 5 years after diagnosis. *Lower panels*: Five year survival of women or men diagnosed with pancreatic cancer in relation to five year survival of women or men in the general population (Data Source: SEER and Human Mortality Database)

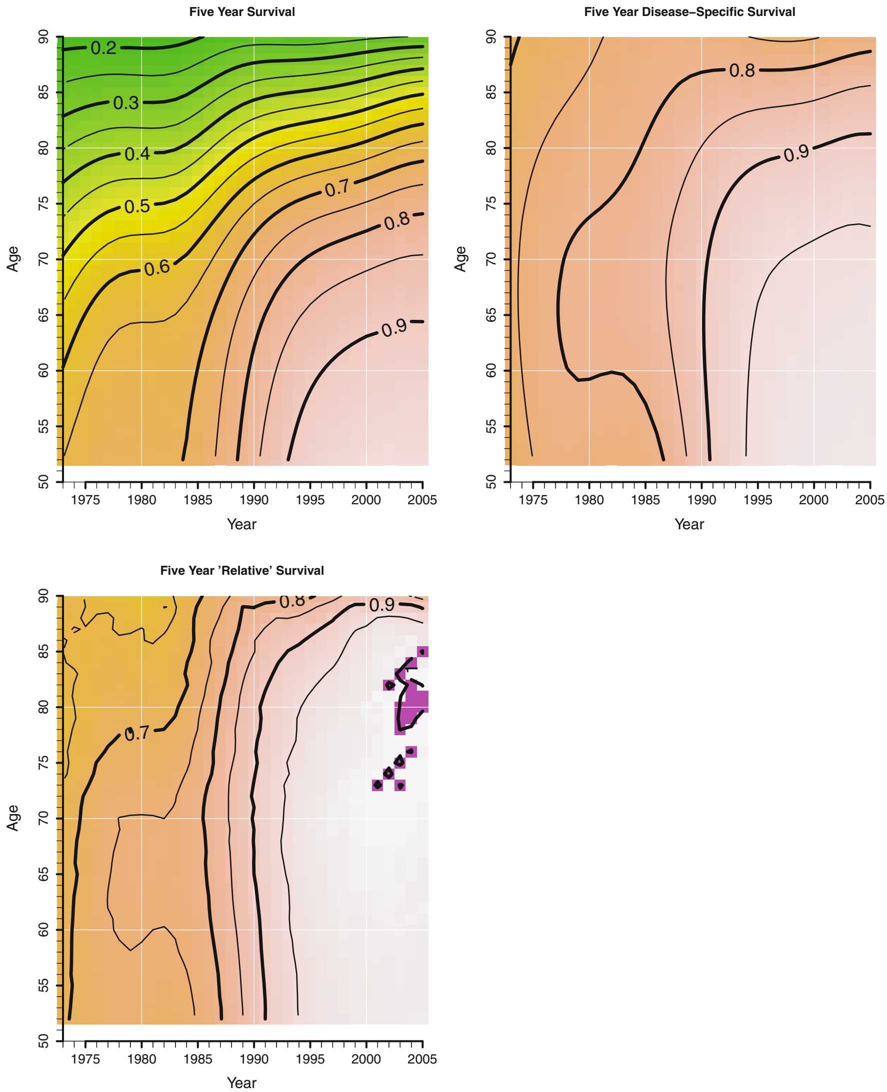

Fig. 10.9 Five year survival for prostate cancer at ages 52–90 from 1973–2005. *Upper left panel*: Probability to survive for 5 years after diagnosed with prostate cancer (any cause). *Upper right panel*: Probability of not dying from prostate cancer within 5 years after diagnosis. *Lower left panel*: Five year survival of men diagnosed with prostate cancer in relation to five year survival of men in the general population (Data Source: SEER and Human Mortality Database)

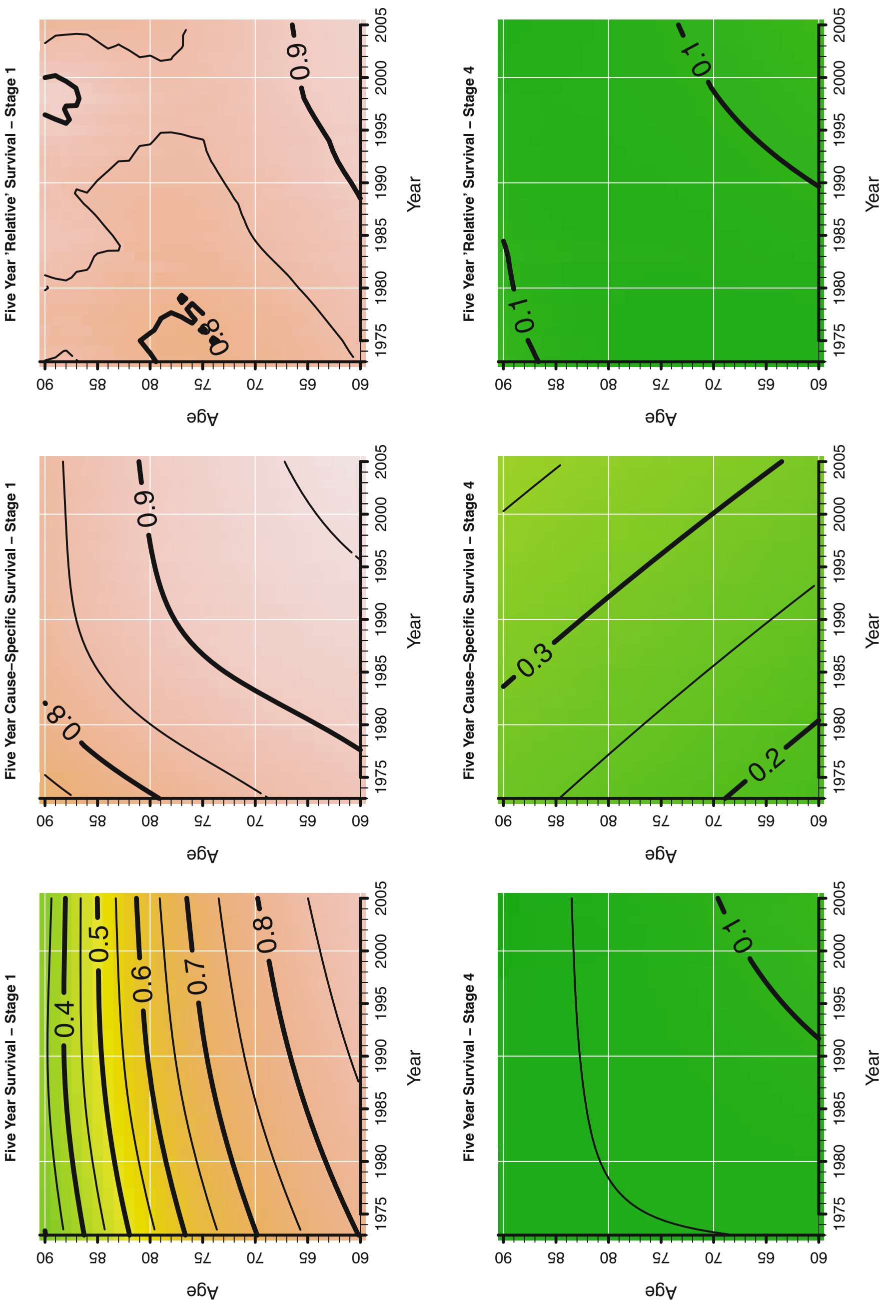

Fig. 10.10 Five year survival for colorectal cancer at ages 60–95 from 1973–2005 by stage. *Upper row*: Stage 1, localized cancer. *Lower row*: Stage 4, distant cancer. *Left panels*: Probability to survive for 5 years after diagnosed with colorectal cancer (any cause). *Middle panels*: Probability of not dying from colorectal cancer within 5 years after diagnosis. *Right panels*: Five year survival of women diagnosed with colorectal cancer in relation to five year survival of women in the general population (Data Source: SEER and Human Mortality Database)

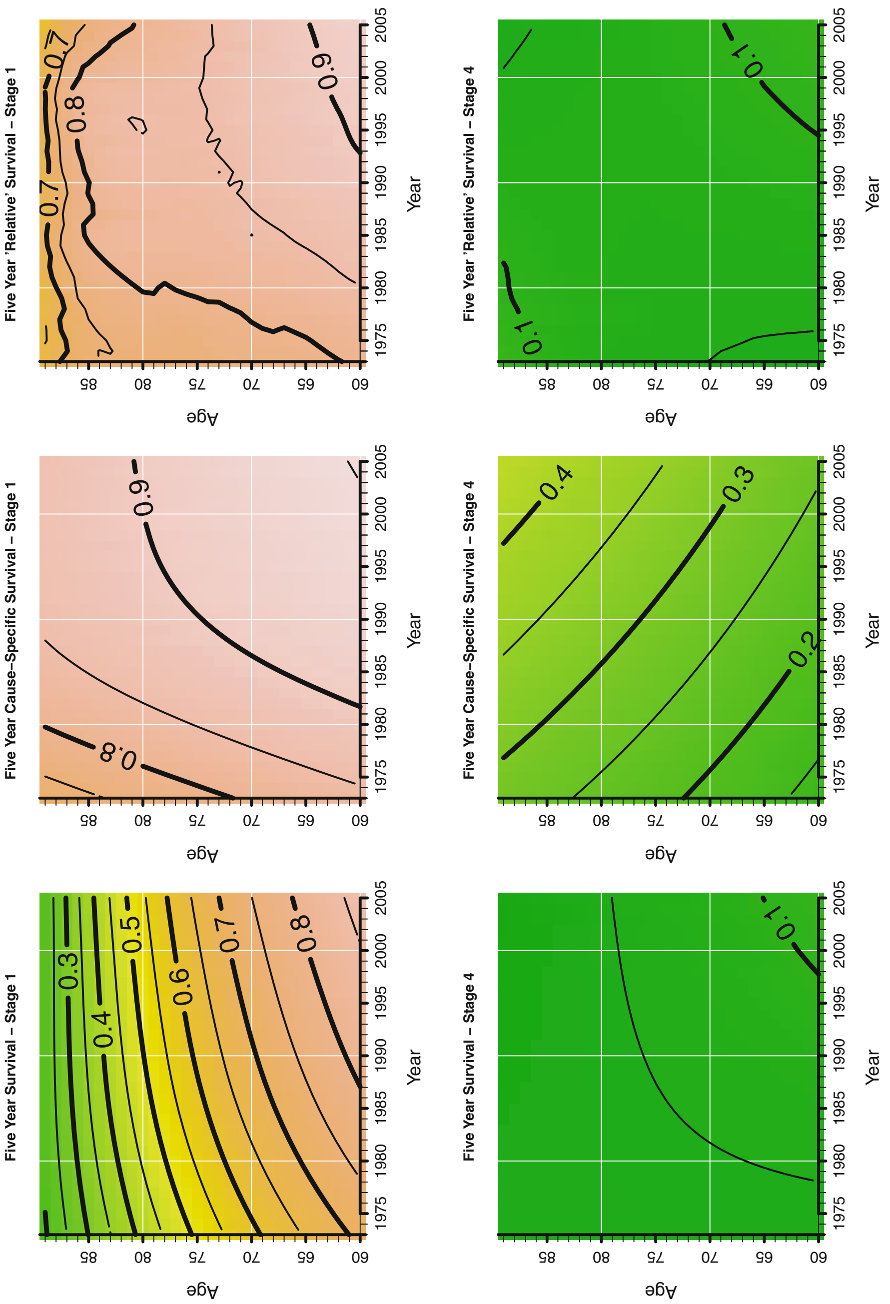

Fig. 10.11 Five year survival for colorectal cancer at ages 60–89 from 1973–2005 by stage. *Upper row*: Stage 1, localized cancer. *Lower row*: Stage 4, distant cancer. *Left panels*: Probability to survive for 5 years after diagnosed with colorectal cancer (any cause). *Middle panels*: Probability of not dying from colorectal cancer within 5 years after diagnosis. *Right panels*: Five year survival of men diagnosed with colorectal cancer in relation to five year survival of men in the general population (Data Source: SEER and Human Mortality Database)

and death: Relative survival is about ten to 20% lower than in the general population when being diagnosed at an early stage (upper three panels in each figure). This excess mortality is pale beside cancer that has already metastasized when being diagnosed (lower three panels in each figure): Only 10% as many people survive the next 10 years as in the general population.