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Conditional relative survival: A different perspective to measuring cancer outcomes

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Survival estimates for individuals who have survived a specified time since diagnosis, known as conditional survival, are not often reported despite their relevance to patients and clinicians. Relative survival from diagnosis is most commonly used to estimate net cancer survival from diagnosis [1], or the likelihood of surviving five years in the absence of other competing causes of death. Life tables are used to estimate the background risk of death which is defined at least by age, sex and calendar period. Although life tables include deaths due to cancer this has little or no impact on the estimated background risks of death [1]. Relative survival is useful because it removes the requirement for information on cause of death, therefore enabling comparisons between countries or patient groups with different underlying mortality (e.g. between regions, age or ethnic groups). However, conditional relative survival, an estimate that expresses the likelihood of surviving into the future at various points since diagnosis relative to the expected survival of similar people in the general population, can provide a more relevant estimate of survival for those who have already survived a time period when the risk of mortality is high [2]. Conditional relative survival is the probability of living an additional number of years (y) given that the person has already survived a fixed number of years (x) since diagnosis. This measure can be obtained by dividing the cumulative survival at $x + y$ years by the cumulative survival at x years. While relative survival is useful to researchers and upon initial diagnosis, conditional relative survival is a practical approach to assess improvements in prognosis since diagnosis.

The proposal to use conditional relative survival as a method to assess improvements and explore variations in survival is not new. While the reporting of conditional relative survival is increasing, it is still relatively uncommon. A search of PubMed and MEDLINE was conducted using the combined terms conditional, relative survival and cancer without a limitation on the publication years. As of writing, there were just over 20 peer reviewed studies that report conditional relative survival. Most used data from Europe or the USA, and were published since 2007 [2–19]. The majority of these studies focused on a detailed assessment of variations for one cancer type—most commonly by age—and reported conditional relative survival increases with time since diagnosis with the magnitude of the improvement differing by cancer type, age, stage or ethnicity. Larger improvements in conditional relative survival were seen for patients diagnosed at an advanced stage [5–7], older age groups [8] and for some ethnic groups [7,9]. Regional- and age-specific variations in conditional relative survival have been attributed to health system variations [10,11].

1. Conditional relative survival: methods and use

Conditional relative survival focuses on the period of time since diagnosis when the impact of late effects, complications and reoccurrence have the greatest influence on prognosis. Conditional relative survival is usually measured as either (i) survival at five years after diagnosis conditional on surviving the first year after diagnosis or (ii) 5-year relative survival after surviving 1, 2, 3, 4 or 5 years after diagnosis. The distinction between the first year after diagnosis and subsequent years in conditional relative survival is important because the relative influences on mortality vary over time. High mortality in the first year after diagnosis has been attributed to late stage at diagnosis [2], perioperative mortality or comorbid conditions [4]. Mortality after the first year has been attributed to late reoccurrences, late effects of treatment or higher

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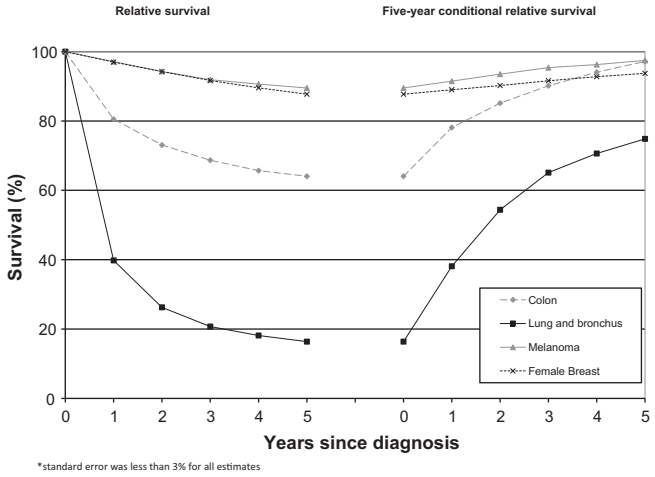

Fig. 1. Five-year cumulative relative survival and five-year conditional relative survival (conditional on number of years already survived since diagnosis), for colon, lung and bronchus, melanoma and female breast cancer, Canada (excluding Quebec), 2005–2007*.

mortality due to comorbid conditions [2]. The rate of improvement in conditional survival over time, and the specific time interval since diagnosis where the greatest improvement in survival occurs, will vary depending on the cancer type and associated prognosis. The sample size will also decrease with the time since diagnosis due to mortality, and the confidence intervals for conditional relative survival will increase. For the purposes of this discussion, examples of cancers with a poor (lung and bronchus), fair (colon) and good (breast and melanoma) survival will be used to highlight the interplay of these factors and the utility of conditional relative survival using Canadian survival analysis (Fig. 1). For this discussion we defined cancer prognosis as poor, fair and good based on a 5-year relative survival of <50%, 50–70% and over 70%, respectively. The decrease in relative survival and the increase in five-year conditional relative survival at yearly intervals up to 5 years demonstrates a more rapid decrease in relative survival for cancers with a poorer prognosis (e.g. lung and bronchus) and a more rapid increase in conditional survival compared to cancers with a fair and good prognosis (e.g. breast, melanoma and colon) (Fig. 1). The standard error for all the example cancers did not exceed 3%.

2. Examples of conditional survival

Generally, conditional relative survival most rapidly increases with time since diagnosis for cancers with a poor prognosis, such as lung and bronchus cancer. Most lung cancer patients are diagnosed at an advanced stage when curative treatment options are limited. For the minority of lung cancer patients who are diagnosed at an early stage and survive the first year after diagnosis, the chances of surviving subsequent years is substantially improved. For lung cancer patients diagnosed between 2005 and 2007 in Canada relative survival was 40% at one year after diagnosis decreasing to 16% at five years. The generally late stage at diagnosis and poor survival results in a small minority of patients surviving long enough to experience latent effects thus conditional relative survival for the first year to five years after diagnosis is the period of greatest improvement. Conditional relative survival was 38% for those who survived the first year after diagnosis and increased to 75% at five years after diagnosis.

For cancers with a good prognosis, such as breast cancer and melanoma, relative survival from diagnosis to five years is over 80% and increases further with each year survived since diagnosis. Conditional relative survival at one year for melanoma was 92% and was 89% for breast cancer. Among cancer types with a good prognosis some cancer types are associated with few latent effects or re-occurrences following treatment, such as melanoma, while other cancer types are associated with latent effects and re-occurrences which may occur for years or even decades after a diagnosis, such as breast cancer. These stark variations in longer term prognosis suggest differences in the time period since diagnosis for which conditional relative survival is most useful. For cancers, such as melanoma, with a good prognosis and few late effects conditional relative survival continues to increase up to five years after diagnosis and may approach or reach that of the general population, or a 'statistical cure' [20]. Five years after diagnosis conditional survival was 98% for patients diagnosed with melanoma and 94% for breast cancer patients.

For cancers with a fair prognosis there is a mix of factors that play a role in survival soon after diagnosis and years after diagnosis including advanced post-operative mortality, stage at diagnosis, complications due to comorbid conditions, late effects of treatment and reoccurrence. Colon cancer patients had an intermediate 5-year relative survival of 64% but the conditional relative survival improved rapidly from 78% at one year increasing to 97% at five years. The advantages of conditional relative survival for this group are a hybrid of those previously described for cancers with a good and poor prognosis. Colon cancer is an example of a cancer with a fair prognosis for which there is a mix of influences on mortality. Post-operative mortality and complications play a major role in mortality soon after diagnosis for colon cancer. In the longer term reoccurrence also plays a major role in prognosis. Increases in conditional relative survival since diagnosis for cancer types with a fair prognosis are in between that of cancers with a poor or good prognosis. However, at five years after diagnosis five-year conditional relative survival for most cancers with a poor or fair prognosis will approach that of cancers with a good prognosis. The conditional relative survival at five years after diagnosis for cancers with a fair prognosis is generally over 80% and frequently in the mid-90% thereby approaching or the same as that of cancer types with a good prognosis at diagnosis.

International comparisons have shown a narrowing of the survival differences in conditional survival compared to relative survival. An international comparison of cancer survival by Coleman et al. found that (period) relative survival at five years after diagnosis for colorectal cancer patients diagnosed 2005–2007 varied from 53.6% for the UK to 65.9% for Australia (a range of 12.3%). However, the range for conditional survival (at five years after diagnosis for those who survived one year) narrowed to 6% (71.8% in the UK compared to 77.7% in Australia). A lower conditional survival points towards factors influencing late mortality, such as advanced stage and later effects such as treatment. Assessing relative survival and conditional relative survival up to five years after diagnosis captures the majority of the improvement in survival for cancers with a fair prognosis.

As survival outcomes improve for cancer patients' conditional relative survival can be used to provide information specifically relevant to late effects and investigate regional and health system specific issues. Conditional relative survival is being increasingly used in national and international studies, but still remains under utilized. We recommend that when possible conditional relative survival is estimated in addition to relative survival. Conditional relative survival up to five years after diagnosis may be the most relevant period to capture improvement for cancer types with a poor and fair prognosis or cancers with a good prognosis that have few late effects.

Conflicts of interest

None declared.

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