



**Karolinska
Institutet**

Department of Medical Epidemiology and Biostatistics

Development and application of statistical methods for population-based cancer patient survival

AKADEMISK AVHANDLING

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ABSTRACT

The overarching aim of this work has been to develop and apply statistical methods for estimating cancer patient survival from population-based register data. Particular focus has been on statistical methods that can be used for presenting cancer survival statistics from administrative health data registers in a manner that is relevant for physicians and patients.

Study 1: In this study we clarify and discuss the relative merits of estimates of crude and net cancer patient survival, respectively. In addition, we demonstrate how period analysis, applied in a competing risks setting, can be utilised to predict crude survival probabilities applicable to newly diagnosed cancer patients. As a motivating clinical example, we use data from the National Prostate Cancer Register to assess the impact of prognostic factors on the risk of prostate cancer death in relation to death from other causes than prostate cancer, and event-free survival, among recently diagnosed patients. We conclude that the period estimates of crude survival offer a useful basis for risk communication between physicians and clinicians and advocate their use as means to answer prognostic questions.

Study 2: Late adverse health effects in cancer patients are a growing problem given the longer survival seen for most cancers. Deaths that occur as a consequence of treatment toxicity can be regarded as indirect deaths due to cancer. In this methodological study we extend flexible parametric survival models for relative survival by partitioning the overall excess mortality from cancer into two component parts; excess mortality from diseases of the circulatory system, DCS, (assumed caused by the treatment), and remaining excess cancer mortality. We present summary measures for quantifying the risk for death from late effects of treatment relative to the overall risk of dying of breast cancer, or causes unrelated to the cancer. The method is illustrated using data obtained from the Swedish Cancer Register on women diagnosed with breast cancer in Sweden between 1973 and 1992.

Study 3: Survival after Hodgkin lymphoma has increased substantially in the past four decades, following the development of effective multi-agent chemotherapy, introduction of combined-modality therapy with reductions in radiation field size and dose, and more apt evaluation of treatment response. The aim of this study was to present clinically interpretable estimates of temporal trends in the burden of fatal excess DCS mortality among Hodgkin lymphoma survivors who were treated in the 1970's through 1990's, and to predict the future clinical burden among patients diagnosed more recently. Using data from the Swedish Cancer Registry we showed how the excess DCS mortality, within 20 years after diagnosis, has decreased continually since the mid-1980s and is expected to further decrease among patients diagnosed in the modern era. However, when accounting for competing causes of death, we found that excess DCS mortality constitutes a relatively small proportion of the overall mortality among Hodgkin lymphoma patients in Sweden.

Study 4: In this study we show how recently developed flexible parametric cure models, combined with competing risks theory, can be used to estimate crude probabilities that cancer patients who are alive will eventually die from their cancer, or from other causes, respectively. Moreover, we show how to 'update' the prognosis for patients who have survived some time after their diagnosis via the use of conditional probabilities. The method is discussed and demonstrated using data from the Swedish Cancer Register on patients diagnosed with melanoma, colon cancer and acute myeloid leukemia between 1973 and 2007.