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Choosing the net survival method for cancer survival estimation

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Abstract ***Background:*** A new net survival method has been introduced by Pohar Perme et al. (2012 [4]) and recommended to substitute the relative survival methods in current use for evaluating population-based cancer survival.
Methods: The new method is based on the use of continuous follow-up time, and is unbiased only under non-informative censoring of the observed survival. However, the population-based cancer survival is often evaluated based on annually or monthly tabulated follow-up intervals. An empirical investigation based on data from the Finnish Cancer Registry was made into the practical importance of the censoring and the level of data tabulation. A systematic comparison was made against the earlier recommended Ederer II method of relative survival using the two currently available computer programs (Pohar Perme (2013) [10] and Dickman et al. (2013) [11]).
Results: With exact or monthly tabulated data, the Pohar-Perme and the Ederer II methods give, on average, results that are at five years of follow-up less than 0.5% units and at 10 and 14 years 1–2% units apart from each other. The Pohar-Perme net survival estimator is prone to random variation and may result in biased estimates when exact follow-up times are not available or follow-up is incomplete. With annually tabulated follow-up times, estimates can deviate substantially from those based on more accurate observations, if the actuarial approach is not used.
Conclusion: At 5 years, both the methods perform well. In longer follow-up, the Pohar-Perme estimates should be interpreted with caution using error margins. The actuarial approach should be preferred, if data are annually tabulated.

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1. Introduction

The population-based cancer registries have used relative survival to give estimates of patients' net survival, i.e. as far as the patients' cancer is concerned when eliminating the effects of the other causes of death [1,2]. In this way, no information on causes of death has been needed as the mortality from the other causes (often called expected mortality) has been estimated from life tables of the underlying general population. Recently, a recommendation of using the Ederer II relative survival method was made based on both theoretical and empirical arguments [3]. This recommendation has been also followed, e.g. by the pan-European EUROCARE-5 study (European cancer registry based study on survival and care of cancer patients).

Even more recently, a new method to estimate net survival has been proposed by Pohar Perme et al. [4] as a substitute of the relative survival approach. This method is not based on a direct comparison of an observed survival proportion of the patients against an expected survival proportion in the comparable general population group as the relative survival methods. It still uses the general population mortality as an estimate of mortality due to the other causes, so that no information on the actual causes of death is needed. This method, unlike the relative survival methods, has been shown to provide an unbiased estimator of the true net survival, if there is no informative censoring of the observed survival (e.g. censoring that would vary by patients' age [5]) and continuous time is used in survival calculations. The international CONCORD-2 (Global surveillance of cancer survival) study will use the Pohar-Perme net survival method.

Also the relative survival methods, including the Ederer II method, aim to estimate net survival. The Ederer II estimator calculates the cumulative product of the interval-specific relative survival ratios, which are based on unweighted observations of patients alive at the beginning of the corresponding intervals. Therefore, patients who have a high probability of dying due to other causes than cancer get too small weights in estimation of net survival, as a patient's contribution to net survival is omitted in subsequent intervals after dying. Because net survival depends almost always on the same demographic variables as the expected hazard due to other causes than cancer, the estimator of the Ederer II method becomes biased. In the classical relative survival methods, stratified analyses and their summarisations, e.g. by (age-)standardisation, have been conducted to reduce this bias.

In the method of Pohar Perme et al., a patient's contribution to net survival is weighted on the basis of the patient's expected survival, i.e. the probability of being alive for a healthy person in the national or other population (comparable with respect to demographic variables e.g. sex, age and calendar year). The method may be viewed also as a generalisation of the gold standard used in an earlier study [3] into a situation where each patient makes her own group defined by sex, age and year of diagnosis. The choice of weights for each group can also be viewed natural, as in a true gold standard, depending on the cancer-related excess hazard of death only.

The present study investigates systematically, using data from the population-based Finnish Cancer Registry and the two publicly available computer programs, how crucial these two assumptions (no informative censoring of the observed survival and use of continuous time) are, particularly the latter one, when a change of method from the traditional relative to the new net survival is done. It is important to know, for national and international population-based cancer survival analyses, how much results obtained by the two methods differ and under which conditions the new method can be recommended in practice.

2. Patients and methods

Patients diagnosed in Finland in 1981–1995 and followed-up until the end of 2010 were included in the analysis with stratification by the most common 26 sites. Table 1 shows the list of the sites and the numbers of

Table 1
The 26 cancer sites included in the analyses and the numbers of patients diagnosed in Finland in 1981–1995 by site and sex.

Cancer site	International Classification of Diseases (ICD)-10 code	Total number of patients	
		Males	Females
Oesophagus	C15	1545	1516
Stomach	C16	8071	7297
Colon	C18	5905	8449
Rectum, rectosigma, anus	C19–20	5006	4991
Liver	C22	1555	1340
Gall bladder, bile ducts	C23–24	1020	2762
Pancreas	C25	4266	5166
Larynx	C32	1672	–
Lung, trachea	C33–34	25,992	5260
Skin, melanoma	C43	3331	3577
Skin, non-melanoma	C44	3538	4236
Soft tissues	C48–49	901	970
Breast	C50	–	35,399
Cervix uteri	C53	–	2420
Corpus uteri	C54	–	7777
Ovary	C56	–	6043
Prostate	C61	21,359	–
Testis	C62	893	–
Kidney	C64–65	4626	3867
Bladder, ureter, urethra	C67–68	7235	2389
Central nervous system	C70–72	3747	5102
Thyroid	C73	783	3128
Hodgkin lymphoma	C81	1007	775
Non-Hodgkin lymphoma	C82–85, C96	4274	4620
Multiple myeloma	C90	1625	2035
Leukaemia	C91–95	3600	3299

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