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On crude and age-adjusted relative survival rates

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Abstract

Relative survival rates, such as 5- or 10-year relative survival rates, which quantify "net survival" of cancer patients, are the most commonly reported measures of cancer outcome by cancer registries. Because relative survival rates vary with age for many forms of cancer, and because the age distribution of cancer patients varies between different populations or within one population over time, age adjustment of relative survival rates is often employed in international comparisons or in time series analyses of cancer patient survival. In this article, we show that derivation of crude and of age-adjusted relative survival rates in the traditional way is conceptually inconsistent, and that this inconsistency has important practical implications. We show ways to overcome this inconsistency in the derivation and interpretation of crude and age-adjusted relative survival rates.

Keywords: Age adjustment; Biostatistics; Cancer registries; Epidemiologic methods; Survival; Time trends

1. Introduction

Relative survival rates, such as 5- or 10-year relative survival rates, are commonly reported by cancer registries to quantify "net survival" of cancer patients. Relative survival rates are calculated as ratios of observed survival of groups of cancer patients divided by the expected survival of groups of persons from the general population with the same age and sex (and possibly race) distribution [1–3]. Under the assumption that the mortality from the cancer of interest in the general population is small (which is mostly the case, at least for limited intervals of follow-up), the relative survival rates are commonly interpreted as survival rates cancer patients would be expected to have in the absence of competing causes of death.

Although less so than the absolute (observed) survival rates, relative survival rates often vary by age of cancer patients. In particular, they tend to be lower among older patients than among younger patients for many forms of cancer. As the age distribution of cancer patients often varies between different populations or within one population over time, age-adjusted relative survival rates are often presented rather than or along with crude relative survival rates in international comparisons (e.g., [4–6]) or in time series analyses (e.g., [7]) of cancer patient survival. In this context, age adjustment of relative survival rates to some standard population is typically performed by the so-called direct method, which provides a weighted average of relative survival rates within defined age groups with weights equal to the proportions of cancer patients within those age groups in the standard population [8,9].

We will show in this article that derivation and interpretation of crude and of age-adjusted relative survival rates in this way is conceptually inconsistent, and that this inconsistency has important practical implications. We discuss an alternative option to derive and interpret crude and age-adjusted relative survival rates in a consistent way, and we illustrate our findings with empirical examples using data from the nationwide Finnish Cancer Registry.

2. A simple example

To introduce our point, we start with a simple hypothetical example, which is shown in Table 1. In this example, relative 10-year survival and 20-year survival is estimated for a sample of 200 patients, with 100 patients in each of two age groups. We assume that follow-up is complete for all patients. We further assume that both observed and expected survival as well as relative survival are lower for the older patients than for the younger patients, a pattern that is found for many forms of cancer.

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Table 1
Hypothetical example of observed, expected and relative 10- and 20-year survival rates

		10-year survival (%)			20-year survival (%)		
Age group	Number of patients	Observed	Expected	Relative	Observed	Expected	Relative
Young	100	60	80	75	28	40	70
Old	100	20	40	50	3	10	30
total (crude)	200	40	60	66.7	15.5	25	62

Now let us consider what would happen if we derived crude and age-adjusted 10- and 20-year relative survival rates in the traditional manner. The crude relative survival rates would be obtained as the ratios of the crude observed survival rates and the crude expected survival rates. Of course, the age-adjusted relative survival rates depend on the age structure of the standard population used. With the study population itself as the standard, the age-adjusted relative survival rates, which are commonly interpreted as the survival rates the cancer patients would be expected to have if they had the same age distribution as the standard population, would be expected to equal the crude relative survival rates in case there is no loss to follow-up (as was assumed here).

In our simple example, the 10-year relative survival rate adjusted to the study population's own age distribution in the traditional manner equals the arithmetic mean of the two age-specific relative survival rates, (75% + 50%)/2 = 62.5%, that is, it is more than 4% units lower than the crude relative survival rate. The discrepancy is even larger for the 20-year relative survival rate: the crude 20-year relative survival rate is 62%, whereas the adjusted 20-year relative survival rate is only 50%. By contrast, the adjusted observed (absolute) 10- and 20-year survival rates (40 and 15.5%, respectively) equal the crude observed survival rates as expected.

3. A more formal approach

The example given above points to an inconsistency in crude and adjusted relative survival rates derived in the traditional manner. To illustrate the origin of this inconsistency, we will now introduce some minimum formal notation: Let o_i and e_i be the observed and expected survival rate within age group i, respectively. Let p_i and s_i be the proportions of the patients in age group i in the study population of interest and in the standard population, respectively.

Then, assuming there is no loss to follow-up (or that potential loss to follow-up is unrelated to risk of death and to age), the crude relative survival rate is given as

$$\sum_i p_i * o_i \Big/ \sum_i p_i * e_i = \sum_i (p_i * e_i) * (o_i / e_i) \Big/ \sum_i p_i * e_i,$$

that is, the crude relative survival rate can be interpreted as a weighted average of age specific relative survival rates (o_i/e_i), with weights equal to the proportion of patients not expected to die from other causes in the study population ($p_i * e_i$).

By contrast, the age-adjusted relative survival rate derived in the traditional way is given as

$$\sum_i s_i * (o_i / e_i) \Big/ \sum_i s_i,$$

that is, it also can be interpreted as a weighted average of age-specific relative survival rates (o_i/e_i), but with weights equal to the proportion of all patients (including those expected to die from other causes) in the standard population (s_i). Unless relative survival (o_i/e_i) or expected survival (e_i) is the same for all age groups i, this measure will usually not be equivalent with the crude relative survival rate even if the study population itself is used as standard, that is, if s_i equals p_i for all age groups i, as illustrated in the example given in Table 1.

In summary, there is a conceptual difference in the interpretation of the crude and the adjusted relative survival rate: whereas the crude relative survival rate quantifies relative survival among those patients expected not to die from other causes, the adjusted relative survival rate derived in the traditional way quantifies relative survival among all patients, assuming a certain age structure of the initial cancer patient population, that is, it neglects the fact that the age distribution of patients at risk of dying from cancer may change with increasing length of follow-up.

To be consistent with the crude relative survival rate, the age-adjusted relative survival rate would have to be obtained as

$$\sum_i (s_i * s_{ei}) * (o_i / e_i) \Big/ \sum_i (s_i * s_{ei})$$

$$\text{rather than } \sum_i s_i * (o_i / e_i) \Big/ \sum_i s_i,$$

where s_i, o_i, and e_i are defined as previously outlined, and s_{ei} equals the expected survival rate in age group i in the standard population. The latter can, in principle, be obtained from population life tables for the standard population in the same way as the e_i can be obtained from population life tables for the study population. This approach should, in fact, ensure that the crude and the age-adjusted survival rates are the same in situations in which age standardization is made using the study population itself as the standard, provided that there is no loss to follow-up or that potential loss to follow-up is unrelated to risk of death and to age.

The latter condition deserves some further discussion in the context of expected survival rates, and hence, of relative survival rates. The two most commonly used methods for calculating expected survival rates are the so-called Ederer II method [10] and Hakulinen's method [11]. Both methods yield similar results for short-term survival rates, but results may differ substantially for longer term (such as 10-, 15-, or 20-year) survival rates for which use of Hakulinen's method is generally recommended. In fact, the essential feature of Hakulinen's method is that it corrects for potentially heterogeneous follow-up times in calculating expected survival rates, whereas such heterogeneity is the rule rather than the exception if the Ederer II method is used (at least for the crude relative survival rates). This suggests that consistent results for the crude and the age-adjusted relative survival rates (using the study population itself as the standard) should be obtained if the alternative method of age adjustment is applied, and expected survival rates are calculated according to Hakulinen's method rather than the Ederer II method.

4. Empirical examples

To evaluate the relevance of the inconsistency of crude and traditionally derived age-adjusted relative survival rates in practice, and to evaluate the possibilities to overcome this inconsistency by the alternative method outlined above, we applied age adjustment to 5-, 10-, 15-, and 20-year relative survival rates of patients diagnosed with 10 common forms in Finland in 1975–1979, respectively (the most recent cohort of patients for whom 20-year follow-up was complete at the time of this analysis). Our analysis is based on data from the nationwide Finnish Cancer Registry, which is among the highest quality cancer registries in the world with respect to both completeness of registration and completeness of follow-up of cancer patients [12,13]. Because childhood cancers differ from adulthood cancers in many respects, patients whose cancer was detected below age 15 were excluded from the analyses. Relative survival rates were obtained as ratios of observed and expected survival rates, where observed survival rates were derived by standard life table methodology [14] with 1-year intervals of follow-up, and expected survival rates were estimated from sex and calendar year specific life tables for the general Finnish population according to either the Ederer II method [10] or Hakulinen's method [11].

Survival rates were adjusted to the age structure of the study populations' own age distribution in the same way as in the example introduced above, but with stratification of the cancer populations by five age groups (15–44, 45–54, 55–64, 65–74 and ⩾75), as applied in the EUROCARE-2 study [5]. Tables 2–4 show the results that would be obtained if 5-, 10-, 15-, and 20-year absolute and relative survival rates were adjusted to the study populations' own age distributions in the traditional manner. In addition, the crude absolute and relative survival rates and the differences between the adjusted and the crude rates are shown.

As expected, the adjusted absolute (observed) survival rates were essentially identical to the crude absolute survival rates for all forms of cancer, regardless of the length of follow-up (see Table 2). By contrast, the adjusted relative survival rates often differed substantially from the crude relative survival rates (see Tables 2, 3). In most cases, the former were lower than the latter. The discrepancy was modest for 5-year relative survival rates, but it became quite substantial for longer term survival rates, and in most cases it was more pronounced if relative survival rates were calculated according to Hakulinenn's method (Table 3) rather than according to the Ederer II method (see Table 2). The differences between adjusted and crude relative survival rates calculated according to Hakulinen's method ranged from ±0% to −1.6% for 5-year relative survival, from +0.7% to −4.9% for 10-year relative survival, from +1.4% to −5.7% for 15-year relative survival, and from +2.9% to −14.1% for 20-year relative survival. The corresponding ranges for relative survival rates calculated according to the Ederer II method were +0.4% to −0.7%, +0.3% to −2.0%, +1.6% to −2.0%, and +1.4% to −7.1%, respectively. Whereas the crude 10-, 15-, and 20-year relative survival rates calculated according to the Ederer II method were often much lower than the crude relative survival rates calculated according to Hakulinen's method, the adjusted relative survival rates calculated by both methods were quite close in most cases.

Tables 5 and 6 show the results obtained if the alternative method of age adjustment introduced above was applied to relative survival rates calculated according to the Ederer II method (Table 5) or according to Hakulinen's method (Table 6). The age-adjusted relative survival rates, in particular long-term relative survival rates, were quite different from (mostly higher than) the crude relative survival rates in case of use of the Ederer II method, and the discrepancy again increased with increasing length of follow-up (ranges of differences: +1.2% to +0.1%, +3.5% to ±0%, +5.7% to −0.1%, and +8.2% to −0.2%, for 5-, 10-, 15-, and 20-year relative survival rates, respectively). However, as expected from theory, application of the alternative method of age adjustment yielded very similar results for the crude and the age-adjusted relative survival rates calculated according to Hakulinen's method, even for the very long-term survival rates (ranges of differences: +0.3% to ±0%, +0.6% to ±0%, +1.0% to ±0%, and +1.5% to ±0% for 5-, 10-, 15-, and 20-year relative survival rates, respectively). Again, in contrast to the crude relative survival rates, the adjusted relative survival rates calculated according to the Ederer II method and Hakulinen's method were quite close in all cases.

5. Discussion

This article illustrates both formally and by hypothetical and empirical examples that derivation and interpretation of

Table 2
Crude and age-adjusted 5-, 10-, 15-, and 20-year absolute survival rates (%) of patients who were reported to the Finnish Cancer Registry with a diagnosis of one of 10 common forms of cancer in 1975–1979

	Crude				Adjusted[a]				Difference[b]			
	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years
Stomach	11.2	7.3	4.9	3.1	11.2	7.3	4.9	3.1	±0.0	±0.0	±0.0	±0.0
Colon	32.5	22.3	17.0	12.0	32.5	22.4	17.0	12.0	±0.0	±0.0	±0.0	±0.0
Rectum	33.4	23.0	15.9	11.1	33.4	23.1	15.9	11.1	±0.0	±0.0	±0.0	±0.0
Pancreas	1.0	0.6	0.4	0.3	1.0	0.6	0.4	0.3	±0.0	±0.0	±0.0	±0.0
Lung	7.5	3.9	2.3	1.2	7.5	3.9	2.3	1.2	±0.0	±0.0	±0.0	±0.0
Breast	62.6	43.2	31.9	24.5	62.6	43.2	31.9	24.5	±0.0	±0.0	±0.0	±0.0
Corpus uteri	68.4	58.4	47.6	36.8	68.4	58.4	47.6	36.8	±0.0	±0.0	±0.0	±0.0
Prostate	37.4	15.9	6.4	2.2	37.4	15.9	6.4	2.2	±0.0	±0.0	±0.0	±0.0
Bladder	43.5	27.6	17.5	11.2	43.5	27.6	17.5	11.2	±0.0	±0.0	±0.0	±0.0
Leukemia	23.1	9.4	4.6	1.8	23.1	9.4	4.6	1.8	±0.0	±0.0	±0.0	±0.0

Age adjustment was made in the traditional manner to the study populations' own age distribution.
[a] Adjusted to the cancer populations' own age structure using the following age categories: 15–44, 45–54, 55–64, 65–74, ⩾75 (prostate: 15–54, 55–64, 65–74, ⩾75).
[b] Difference between age-adjusted and crude absolute survival rate.

crude and adjusted relative survival rates in the traditional way is inconsistent, as it is based on different concepts of what the relative survival rate is intended to measure. Whereas the crude relative survival rate quantifies relative survival among those patients expected not to die from other causes, the adjusted relative survival rate derived in the traditional way quantifies relative survival among all patients, assuming a certain initial age structure of the cancer patient population (i.e., it neglects the fact that the age distribution of patients at risk of dying from cancer may change with increasing length of follow-up). Our empirical examples illustrate that this inconsistency is quite relevant in practice, at least for longer term relative survival rates, such as 10-, 15-, and 20-year relative survival rates, and that it may affect both descriptive and comparative analyses of cancer patient survival. No such inconsistency applies to crude and age-adjusted absolute (observed) survival rates.

In principle, there are two ways to overcome the conceptual inconsistency between crude and adjusted relative survival rates. One way would be to modify derivation of crude relative survival rates to make them conceptually consistent with age-adjusted relative survival rates, and the other way would be to modify derivation of adjusted relative survival rates to make them consistent with crude relative survival rates. An option for the first way would be, for example, to replace the crude relative survival rates by relative survival rates adjusted to the study population's own age distribution as in the analyses presented in this article. An advantage of this option would be that, like in traditional age adjustment, comparability of relative survival rates over different intervals of follow-up is ensured by assuming a fixed age structure of the cancer population for each interval. We, therefore, recommend this option along with traditional age adjustment whenever comparability of relative survival rates within various intervals of follow-up (or over follow-up periods of different lengths) is of primary concern.

However, the majority of cancer patients are in an age where competing causes of death are of concern and clearly have to be taken into account in both clinical and public health

Table 3
Crude and age-adjusted 5-, 10-, 15-, and 20-year relative survival rates (%) of patients who were reported to the Finnish Cancer Registry with a diagnosis of one of 10 common forms of cancer in 1975–1979

	Crude				Adjusted[a]				Difference[b]			
	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years
Stomach	14.0	11.9	10.8	9.5	13.9	11.8	11.5	8.0	−0.1	−0.1	+0.7	−1.5
Colon	40.7	35.9	36.2	34.9	40.3	35.9	37.5	36.3	−0.4	±0.0	+1.3	+1.4
Rectum	42.4	37.9	35.5	34.3	41.7	37.4	33.8	32.7	−0.7	−0.5	−1.7	−1.6
Pancreas	1.2	1.1	1.0	1.1	1.3	1.2	1.6	0.7	+0.1	+0.1	+0.6	−0.4
Lung	9.3	5.9	4.4	3.2	8.9	5.6	4.1	3.1	−0.4	−0.3	−0.3	−0.1
Breast	70.6	56.1	48.3	43.9	70.5	54.9	46.3	41.5	−0.1	−1.2	−2.0	−2.4
Corpus uteri	76.1	73.8	71.0	67.4	75.8	73.1	69.2	61.4	−0.3	−0.7	−1.8	−6.0
Prostate	56.6	38.9	27.9	19.1	57.0	38.9	28.1	14.9	+0.4	±0.0	+0.2	−4.2
Bladder	57.1	47.6	41.0	36.5	56.4	45.6	42.6	29.4	−0.7	−2.0	+1.6	−7.1
Leukemia	28.2	14.4	9.2	4.8	28.2	14.7	9.6	6.0	±0.0	+0.3	+0.4	+1.2

Relative survival rates were calculated according to the Ederer II method. Age adjustment was made in the traditional manner to the study populations' own age distribution.
[a] Adjusted to the cancer populations' own age structure using the following age categories: 15–44, 45–54, 55–64, 65–74, ⩾75 (prostate: 15–54, 55–64, 65–74, ⩾75).
[b] Difference between age-adjusted and crude relative survival rate.

Table 4
Crude and age-adjusted 5-, 10-, 15-, and 20-year relative survival rates of patients who were reported to the Finnish Cancer Registry with a diagnosis of one of 10 common forms of cancer in 1975–1979

	Crude				Adjusted[a]				Difference[b]			
	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years
Stomach	14.7	13.3	12.8	11.9	14.0	12.0	11.8	8.4	−0.8	−1.2	−1.0	−3.5
Colon	41.9	38.3	40.0	39.5	40.7	36.6	38.9	38.8	−1.2	−1.7	−1.1	−0.7
Rectum	43.4	40.4	39.2	39.9	42.1	38.0	34.4	33.3	−1.3	−2.4	−4.9	−6.6
Pancreas	1.3	1.1	1.1	1.1	1.3	1.2	1.7	0.9	±0.0	+0.1	+0.6	−0.2
Lung	9.6	6.7	5.6	4.5	8.9	5.8	4.3	3.5	−0.7	−1.0	−1.3	−1.1
Breast	70.6	56.2	49.2	45.7	70.4	54.8	46.2	41.5	−0.1	−1.4	−2.9	−4.3
Corpus uteri	77.0	76.6	75.5	74.0	75.9	73.5	69.8	62.2	−1.2	−3.0	−5.7	−11.8
Prostate	57.0	39.7	28.7	19.5	57.0	38.9	28.1	14.9	−0.1	−0.7	−0.6	−4.6
Bladder	58.2	51.1	46.6	44.6	56.5	46.2	43.5	30.5	−1.6	−4.9	−3.1	−14.1
Leukemia	28.6	14.7	9.2	4.6	28.5	15.4	10.6	7.4	−0.1	+0.7	+1.4	+2.9

Relative survival rates were calculated according to the Hakulinen method. Age adjustment was made in the traditional manner to the study populations' own age distribution.

[a] Adjusted to the cancer populations' own age structure using the following age categories: 15–44, 45–54, 55–64, 65–74, ⩾75 (prostate: 15–54, 55–64, 65–74, ⩾75).

[b] Difference between age-adjusted and crude relative survival rate.

decisions. From this point of view, one might question the use of outcome measures that can only be interpreted in an entirely hypothetical context (assuming the absence of competing causes of death and a constant age distribution of cancer patients within various intervals of follow-up) that has little to do with real-life conditions. In more formal terms, one might argue that only those patients who do not die from other causes of death are actually at risk of dying from cancer, and, as for other epidemiologic measures, it may be prudent to include only subjects at risk into pertinent calculations of relative survival rates (as it is implicitly done in calculations of the crude relative survival rates).

It may therefore also be worthwhile to consider the second way to overcome the inconsistency between crude and age-adjusted relative survival rates, that is, to modify derivation of age-adjusted relative survival rates. In this article, we have outlined an option how this may be achieved, and we have illustrated successful application of this method by empirical examples. The principle of this method lies in choosing modified weights for the various age groups, in that the proportions of cancer patients within age groups (which are used as the weights in traditional age adjustment) are multiplied by the expected survival of patients in these age groups. At the same time, care has to be taken that expected survival rates are calculated according to Hakulinen's method, because the crude long-term relative survival rates may be much too low if expected survival is calculated according to the Ederer II method. Application of the alternative method of age adjustment outlined in this article has the additional advantage that it gives less weight to the often very

Table 5
Crude and age-adjusted 5-, 10-, 15-, and 20-year relative survival rates (%) of patients who were reported to the Finnish Cancer Registry with a diagnosis of one of 10 common forms of cancer in 1975–1979

	Crude				Adjusted[a]				Difference[b]			
	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years
Stomach	14.0	11.9	10.8	9.5	14.7	13.2	12.8	12.0	+0.7	+1.3	+2.0	+2.5
Colon	40.7	35.9	36.2	34.9	41.8	38.2	40.0	39.8	+1.1	+2.3	+3.8	+4.9
Rectum	42.4	37.9	35.5	34.3	43.2	40.3	39.5	40.3	+0.8	+2.4	+4.0	+6.0
Pancreas	1.2	1.1	1.0	1.1	1.3	1.1	1.0	[c]	+0.1	±0.0	±0.0	[c]
Lung	9.3	5.9	4.4	3.2	9.6	6.5	5.4	4.2	+0.3	+0.6	+1.0	+1.0
Breast	70.6	56.1	48.3	43.9	70.8	56.7	49.7	46.4	+0.2	+0.6	+1.4	+2.5
Corpus uteri	76.1	73.8	71.0	67.4	77.1	76.6	75.7	74.5	+1.0	+2.8	+4.7	+7.1
Prostate	56.6	38.9	27.9	19.1	57.3	40.2	29.3	20.2	+0.7	+1.3	+1.4	+1.1
Bladder	57.1	47.6	41.0	36.5	58.3	51.1	46.7	44.7	+1.2	+3.5	+5.7	+8.2
Leukemia	28.2	14.4	9.2	4.8	28.4	14.6	9.1	4.6	+0.2	+0.2	−0.1	−0.2

Relative survival rates were calculated according to the Ederer II method. Age adjustment was made in the alternative manner outlined in this article to the study populations' own age distribution.

[a] Adjusted to the cancer populations' own age structure using the following age categories: 15–44, 45–54, 55–64, 65–74, ⩾75 (prostate: 15–54, 55–64, 65–74, ⩾75).

[b] Difference between age-adjusted and crude relative survival rate.

[c] Not estimable due to sparseness of data in the oldest age group.

Table 6
Crude and age-adjusted 5-, 10-, 15-, and 20-year relative survival rates of patients who were reported to the Finnish Cancer Registry with a diagnosis of one of 10 common forms of cancer in 1975–1979

	Crude				Adjusted[a]				Difference[b]			
	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years	5 years	10 years	15 years	20 years
Stomach	14.7	13.3	12.8	11.9	14.8	13.4	13.1	12.3	+0.1	+0.1	+0.3	+0.4
Colon	41.9	38.3	40.0	39.5	42.1	38.8	41.0	41.0	+0.2	+0.5	+1.0	+1.5
Rectum	43.4	40.4	39.2	39.9	43.6	40.8	40.0	41.2	+0.2	+0.4	+0.8	+1.3
Pancreas	1.3	1.1	1.1	1.1	1.3	1.1	1.1	1.1	±0.0	±0.0	±0.0	±0.0
Lung	9.6	6.7	5.6	4.5	9.6	6.8	5.7	4.6	±0.0	±0.0	+0.1	+0.1
Breast	70.6	56.2	49.2	45.7	70.8	56.6	49.7	46.6	+0.2	+0.4	+0.6	+0.8
Corpus uteri	77.0	76.6	75.5	74.0	77.2	76.9	76.3	75.2	+0.1	+0.4	+0.7	+1.2
Prostate	57.0	39.7	28.7	19.5	57.3	40.2	29.3	20.2	+0.3	+0.5	+0.7	+0.7
Bladder	58.2	51.1	46.6	44.6	58.4	51.7	47.6	46.0	+0.3	+0.6	+1.0	+1.5
Leukemia	28.6	14.7	9.2	4.6	28.7	14.9	9.3	4.7	+0.1	+0.2	+0.2	+0.1

Relative survival rates were calculated according to the Hakulinen method. Age adjustment was made in the alternative manner outlined in this article to the study populations' own age distribution.

[a] Adjusted to the cancer populations' own age structure using the following age categories: 15–44, 45–54, 55–64, 65–74, ⩾75 (prostate: 15–54, 55–64, 65–74, ⩾75).

[b] Difference between age-adjusted and crude relative survival rate.

unstable estimates of relative survival rates in the highest age groups, which are often based on very small numbers (even if initial numbers of patients are high), and which often render relative survival rates derived in the traditional way very shaky [15].

Application of the alternative method of age adjustment outlined in this article is straightforward in any analyses in which some internal standard population is used. Such situations are commonly encountered in practice. For example, in a comparative analysis of cancer patient survival between various countries, such as the EUROCARE project, one typically uses the pooled population of cancer patients as the standard. In comparisons between two specific cancer populations, one also may consider one of them (usually the larger one) as the standard to which the relative survival rate in the other population (usually the smaller one) is adjusted (e.g., [6]). Another important application of age adjustment of relative survival rates is in time series analysis for disclosing unbiased trends in cancer patient survival, because cancer populations, on average, have become older in many countries during the past decades (e.g., [7,16]). In such applications, use of an internal standard is also common practice. For example, relative survival rates of patients diagnosed in various calendar periods are often adjusted to either the age distribution of the pooled sample of all patients or to the age distribution of patients diagnosed within one (e.g., the first or the last) calendar period. In all these situations, age adjustment of relative survival rates by the traditional method does not achieve comparability with the crude relative survival rates in the standard population. By contrast, using the age distribution of patients not expected to die from other causes (which is obtained by further weighting of the numbers of patients within age groups in the standard population by their expected survival in the absence of cancer), rather than taking the initial age distribution of all patients in the standard population for weighting, will ensure comparability of adjusted relative survival rates among each other as well as comparability with the (crude, overall) relative survival rate in the standard population (provided that bias due to differential loss to follow-up of patients is negligible and Hakulinen's method is used to derive expected survival rates).

In other situations, adjustment is made to some external standard, such as the world standard cancer patient population [17]. This strategy can be particularly useful to allow for comparisons of relative survival rates between different studies. In such situations, modification of weights for age adjustment using appropriate life tables for the standard population may be considered. One might also argue, however, that, in some way, the choice of an external standard population is arbitrary anyway, and that there is nothing wrong with using any standard population with a reasonable age distribution and not too narrow age intervals, as long as the age distribution of the standard population is interpreted as reflecting the age distribution of patients not expected to die from other causes within the follow-up period (rather than the age distribution of all patients).

Finally, although the alternative way of age adjustment proposed in this article was illustrated in the context of traditional "cohort-wise" survival analyses only, it is equally applicable to the more recently introduced period analysis methodology, which allows for more up-to-date monitoring of cancer patient survival [1,11,18–22].

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