Cancer Survival Corrected for Heterogeneity in Patient Withdrawal

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SUMMARY

Survival from cancer over a certain time period is often measured by the 'relative survival rate'. This is the ratio of the observed survival rate in the group of patients to the survival rate expected in a group of people in the general population, who are similar to the patients with respect to all of the possible factors affecting survival at the beginning of the period, except for the disease under study. When patterns of patient withdrawal differ for a number of subgroups of patients with equal relative survival rates, the current method of derivation of the relative survival rate is biased. A method based on the concept of an 'expected life table' is proposed for removal of the bias. Examples based on material from the Finnish Cancer Registry suggest that the practical performance of the proposed method is better than that of other alternatives, even when the relative survival rates in the subgroups are not equal.

1. Introduction

In medical follow-up studies, patient survival is usually evaluated by calculation of the survival rate, i.e. the number of patients alive at the point of observation expressed as a proportion of the patients alive at the beginning of the follow-up. When a specific disease such as cancer is of primary interest, deaths due to other causes reduce this proportion unduly. Berkson and Gage (1950) have suggested that this proportion should be compared with an expected proportion of survivors, i.e. with an 'expected survival rate' derived for similar people from the general population, most of whom do not have the cancer in question. The ratio between the observed and expected survival rates has been used as a measure of survival from cancer and called the 'relative survival rate'.

For many cancers, the relative survival rate over a given time is approximately constant for a number of patient subgroups, for instance for many age groups (Cancer Registry of Norway, 1975; Axtell, Asire and Myers, 1976; Hakulinen et al., 1981). It can be considered a biological property of the cancer in question, reflecting the malignancy of the tumour. On the other hand, the relative survival rate for very old patients (over 75 years of age at diagnosis) tends to be lower than that for other patients. Also, the relative survival rates for many prognostic factors, such as clinical stages, in general differ.

Both the incidence of cancer and the size of the population subgroups may change with time, both changes exerting an effect upon the admission rate of cancer patients in these subpopulations. A common closing date for the follow-up study (Chiang, 1968) in turn causes the potential withdrawal patterns of the patients in the subgroups to vary with time. When the number of old people in the population increases and that of young people decreases, as happens in many industrialized countries, the potential follow-up times of young cancer patients are, on average, longer than those of old patients.

Key words: Relative survival rate; Heterogeneous censoring; Competing risks; Cancer.

It is demonstrated below that the current method for the derivation of the relative survival rate (Ederer, Axtell and Cutler, 1961) gives biased results in a situation where the potential withdrawal patterns of patients from different subgroups are heterogeneous. An alternative method, which removes the bias, is proposed.

2. Methods for Derivation of the Relative Survival Rate

Let $_xp_0$ be the observed survival rate in the group of patients from the beginning of follow-up to time x, $_xp_0^*$ the corresponding expected survival rate, and $_xr_0 = {_xp_0}/{_xp_0^*}$ the relative survival rate. Let the patients be divided into m homogeneous subgroups with quantities (in a similar notation to that for the whole group) $_xp_0(a)$, $_xp_0^*(a)$, and $_xr_0(a) = {_xr_0}$, $a = 1, \ldots, m$. Further, suppose that cancer and other causes of death act independently of each other (Gail, 1975) in each subgroup. In this case, $_xr_0$ may be interpreted as the probability of escaping death prior to x if the cancer in question were the only cause of death (Berkson and Gage, 1950). Let $\mu_t(a)$ be the force of mortality, $-(d/dt)\{{_tp_0(a)}\}/{_tp_0(a)}$, and let $\mu_t^*(a)$ and $\mu_t^c(a) = \mu_t^c$ be the cause-specific forces of mortality defined by $_tp_0^*(a)$ and $_tr_0(a) = {_tr_0}$, respectively.

Now let $_tc_0(a)$ be the proportion of patients in Stratum a with a potential follow-up time $\geq t$, and let the potential withdrawal be independent of survival in each stratum. The proportion of patients alive and under observation at time t with respect to patients alive at the beginning of the follow-up is then

$$\sum_{a=1}^{m} w_a\{{_tp_0(a)}\}\{{_tc_0(a)}\},$$

where w_a is the proportion of patients belonging to Stratum a at the beginning of follow-up. The probability that an individual alive at t will die in a short interval $[t, t+\Delta)$ is thus equal to

$$\left[\sum_{a=1}^{m} W_a(t)\{\mu_t(a)\Delta + o(\Delta)\}\right]\bigg/ \sum_{a=1}^{m} W_a(t),$$

where $W_a(t) = w_a\{{_tp_0(a)}\}\{{_tc_0(a)}\}$. The use of one life table (with infinitesimal time intervals) for all patients then implies that

$$\begin{aligned}
_xp_0 &= \exp \int_0^x \left[-\left\{\sum_{a=1}^{m} W_a(t)\mu_t(a)\right\}\bigg/\left\{\sum_{a=1}^{m} W_a(t)\right\}\right] dt \\
&= {_xr_0} \exp \int_0^x \left[-\left\{\sum_{a=1}^{m} W_a^*(t)\mu_t^*(a)\right\}\bigg/\left\{\sum_{a=1}^{m} W_a^*(t)\right\}\right] dt,
\end{aligned} \tag{2.1}$$

where $W_a^*(t) = w_a\{{_tp_0^*(a)}\}\{{_tc_0(a)}\}$.

Ederer *et al.* (1961) suggested that the expected survival rate should be calculated as

$$_xp_0^* = \sum_{a=1}^{m} w_a\{{_tp_0^*(a)}\}. \tag{2.2}$$

It is easily verified that $_xp_0/_xp_0^* = {_xr_0}$ only if $_tc_0(a) = {_tc_0}$, $a = 1, \ldots, m$. This method is henceforth called Ederer I.

Another method suggested as a practical simplification of (2.2) by Ederer and Heise

(1959) (see Rothman and Boice, 1979) is to choose

$$_xp_0^* = \exp \int_0^x \left[-\left\{ \sum_{a=1}^m W_a(t)\mu_t^*(a) \right\} \Big/ \left\{ \sum_{a=1}^m W_a(t) \right\} \right] dt, \tag{2.3}$$

by which $_xp_0/_xp_0^* = _xr_0$ even when the potential withdrawal patterns, $_tc_0(a)$, differ between strata. This advantage was not discovered by the authors, and Ederer I was adopted as the preferred method (Ederer *et al.*, 1961). Let us call (2.3) Ederer II.

A third formula for $_xp_0^*$ can be derived directly from (2.1):

$$_xp_0^* = \exp \int_0^x \left[-\left\{ \sum_{a=1}^m W_a^*(t)\mu_t^*(a) \right\} \Big/ \left\{ \sum_{a=1}^m W_a^*(t) \right\} \right] dt. \tag{2.4}$$

This is exactly the same as (2.3) when the assumption $_tr_0(a) = _tr_0$, $a = 1, \ldots, m$, holds and thus also gives $_tp_0/_tp_0^* = _tr_0$ when the stratum-specific withdrawal patterns differ.

3. Derivation of the Expected Survival Rate in Practice

In this section we consider only the derivation of (2.4) in practice. For the other two alternatives, see the literature cited in §2. The observed survival rate, $_xp_0$, is obtained in the same way (see, for example, Berkson and Gage, 1950; Chiang, 1968) in all the methods considered. The relative survival rate is derived as $_xp_0/_xp_0^*$.

The first equation for $_xp_0$ in (2.1) is formally identical with expression (2.4) for $_xp_0^*$. Thus, actuarial methods of estimating $_xp_0$ (Berkson and Gage, 1950; Chiang, 1968) may be applied to derive $_xp_0^*$. Let the time of follow-up be divided into w intervals $[x_j, x_{j+1})$, $j = 0, \ldots, w-1$, with $x_0 = 0$, and let k_j be the number of patients with potential follow-up time $\geq x_j$. Further, let $p_j^*(h)$ be the expected survival probability from x_j to x_{j+1} for a person in the general population alive at x_j and having the same relevant demographic factors as the hth patient with potential follow-up time $\geq x_j$. Let

$$_ip_0^*(h) = \prod_{j=0}^{i-1} p_j^*(h)$$

be the expected probability for the hth person at time 0 to survive from 0 to x_i. Let us order the k_j persons so that the first k_{j+1} are patients with potential follow-up time $\geq x_{j+1}$, and the remaining $k_j - k_{j+1}$ are potential withdrawals during $[x_j, x_{j+1})$. Assuming that the distribution of the potential times of withdrawal is approximately uniform and that the distribution of the times of expected deaths is approximately exponential in $[x_j, x_{j+1})$, the expected probability for a potential withdrawal, h, to withdraw alive is approximately equal to $\{p_j^*(h)\}^{\frac{1}{2}}$ (cf. Chiang, 1968, p. 272).

An expected life table can now be constructed with quantities analogous to those of the ordinary life table (Chiang, 1968) as follows. Let

$$l_j^* = \sum_{h=0}^{k_j} {}_jp_0^*(h)$$

be the expected number of patients alive and under observation at x_j: let

$$w_j^* = \sum_{h=k_{j+1}+1}^{k_j} {}_jp_0^*(h)\{p_j^*(h)\}^{\frac{1}{2}}$$

be the expected number of patients withdrawing alive during $[x_j, x_{j+1})$; let

$$\delta_j^* = \sum_{h=k_{j+1}+1}^{k_j} ({}_jp_0^*(h)[1 - \{p_j^*(h)\}^{\frac{1}{2}}])$$

be the expected number of patients dying during $[x_j, x_{j+1})$ with potential follow-up time ending during the same interval; and let

$$d_j^* = \sum_{h=1}^{k_{j+1}} [_j p_0^*(h)\{1 - p_j^*(h)\}] + \delta_j^*$$

be the expected number of patients dying during $[x_j, x_{j+1})$. An expected survival rate for the $(j+1)$th subinterval may now be derived, for example from the formula of Chiang (1968, p. 274), as follows:

$$p_j^* = \tfrac{1}{4}(l_j^* - \tfrac{1}{2}n_j^*)^{-2}[-\tfrac{1}{2}\delta_j^* + \{\tfrac{1}{4}(\delta_j^*)^2 + 4(l_j^* - \tfrac{1}{2}n_j^*)(l_{j+1}^* + \tfrac{1}{2}w_j^*)\}^{\frac{1}{2}}]^2,$$

where $n_j^* = w_j^* + \delta_j^*$. Finally,

$$_i p_0^* = \prod_{j=0}^{i-1} p_j^*.$$

4. Discussion

If an expected survival rate alone were needed, the Ederer I method, (2.2), would be the best as the rate derived by this method is independent of the potential withdrawal patterns, $_t c_0(a)$, of the population subgroups. The problem of dependence arises since the observed survival rate is not calculated in a corresponding way. A separate life-table calculation for each subgroup, or at least for each set of subgroups with the same potential withdrawal pattern, would be required to make the observed survival rate independent of the potential withdrawal pattern. The resulting observed survival rates should then be weighted in proportion to the corresponding totals at the beginning of follow-up. However, the use of several life tables complicates the analysis and also yields less reliable estimates, since these are based on stratum-specific, and perhaps rather small, numbers of patients. It is even possible that long-term survival estimates are unavailable for some subgroups, e.g. the oldest patients (Hakulinen, 1977). Moreover, decisions about the homogeneity of the stratum-specific withdrawal patterns would be needed in order that the strata might be pooled.

Furthermore, the use of the Ederer I method often requires information on life tables of the general population in the future, e.g. when an expected 10-year survival probability is needed for a patient diagnosed two years ago. One possibility is to replace the future probabilities which are required with those from the most recent life table (Hakama and Hakulinen, 1977); another is to use predicted life tables. However, it seems unfair to compare the observed survival, based on past experience of the patients, with expected survival, based on future experiences of the general population. The other methods presented here do not require any life-table projections.

The expressions (2.3) and (2.4) make use of the bias in $_x p_0$ by biasing $_x p_0^*$ in a corresponding way. An unbiased ratio $_x r_0 = {_x p_0}/{_x p_0^*}$ is obtained. In addition to the nonoptimal situation $_x r_0(a) \neq {_x r_0}$, $a = 1, \ldots, m$, these two methods differ in one basic respect, even when the potential withdrawal patterns in the subgroups are homogeneous. In the Ederer II method, the structure of the patient population at the beginning of follow-up is not sufficient for determination of the expected survival rate for the patients; observed (in fact, *relative*) survival is also needed for the quantities $W_a(t)$, $a = 1, \ldots, m$. When $_x r_0(a) \neq {_x r_0}$, the relative survival also affects that expected, and the expected survival rate becomes dependent on the cancer in question. In practice, the expected survival rate for a subinterval is derived by averaging the expected survival probabilities of patients

observed alive at the beginning of that interval (Ederer and Heise, 1959; Rothman and Boice, 1979).

No information about observed events is needed in the calculation based on (2.4). The expected survival rates for subintervals are thus only appropriate in the derivation of $_x p_0^*$, and should not be used as such. Relative survival rates for individual subintervals, e.g. for decision-making about the cure of cancer patients (Cutler and Axtell, 1963), are best derived by means of the Ederer II method.

In reality the relative survival rates in different subgroups are not exactly equal. However, the relative survival rate for a pooled group always lies within the range of the relative survival rates of the subgroups unless the potential withdrawal patterns in the subgroups differ (Hakulinen, 1977). The longer the follow-up time in question, the closer is the relative survival rate for the pooled group to that of the subgroup with the highest expected survival rate. Unequal withdrawal patterns in the subgroups may put the relative survival rate for a pooled group outside the range of the stratum-specific relative survival rates.

In principle, the use of (2.4) requires a complete follow-up of the patients. This is almost totally achievable in countries with a centralized population registration system. Of the slightly more than 200 000 cancer patients diagnosed in Finland in 1953–1974 and followed up from 0 to 22 years (with a common closing date of 31 December 1974) only 22 were lost from follow-up (Hakulinen *et al.*, 1981). For lost patients the potential follow-up may, in general, be considered as terminated at the date of last contact. This assumption does not introduce any error if the risk of being lost and the expected risk of dying act independently.

All these methods may be replaced by the methodology of competing risks of death (Chiang, 1968), if information on the causes of death of the patients exists. However, replacement of the relative survival rate by the theory of competing risks of death is greatly restricted by the vagueness of this information (Hakulinen, 1977).

5. Examples

5.1. *Equal Relative Survival Rates in Subgroups*

Three cancer sites in males are considered as an example: cancer of the skin (melanomas and basal cell carcinomas excluded) with favourable survival, cancer of the colon with intermediate survival, and cancer of the lung with poor survival. It is assumed that the patient population at each site consists of two age groups with equal numbers of patients: those aged 35 years at the beginning of follow-up, and those aged 55 years. For comparison, an alternative with one group aged 55 years and the other aged 70 years is also considered. It is assumed that the patients are admitted over a period of 20 years, with the following possible annual patterns:

W_0: 5% of the patients are admitted each year.

W_1: 4.05% of the patients are admitted during the first year, and in each succeeding year this figure is increased by 0.1% units $(4.15\%, 4.25\%, \ldots, 5.95\%)$.

W_2: 3.1% of the patients are admitted during the first year, and each year this figure is increased by 0.2% units $(3.3\%, 3.5\%, \ldots, 6.9\%)$.

The common closing date is at the end of the 20th year. It is assumed for simplicity that the life tables for the general population remain unchanged, being the same as for 1971–1975 in Finland (Central Statistical Office of Finland, 1980), during the 20-year

Table 1

Long-term relative survival rate (%) *for cancer at three sites derived by the method of Ederer et al.* (1961) *when the age-specific relative survival rates are homogeneous and potential withdrawal patterns heterogeneous. Hypothetical example* (*see text*)

Primary site and years of follow-up	Refer-ence*	Ages and potential withdrawal pattern							
		35/55 yr				55/70 yr			
		W_2/W_0	W_1/W_0	W_0/W_1	W_0/W_2	W_2/W_0	W_1/W_0	W_0/W_1	W_0/W_2
Skin									
5	85.1	85.0	85.0	85.1	85.2	84.9	85.0	85.2	85.3
10	81.5	81.0	81.2	81.7	82.0	80.2	80.9	82.2	82.8
15	81.4	79.8	80.6	82.1	82.9	77.4	79.5	83.2	85.2
20	84.7	80.7	82.9	86.4	88.5	75.6	80.6	88.6	92.9
Colon									
5	30.8	30.8	30.8	30.8	30.8	30.7	30.8	30.9	30.9
10	27.0	26.8	26.9	27.1	27.1	26.5	26.8	27.2	27.4
15	26.2	25.7	25.9	26.4	26.7	24.9	25.6	26.8	27.4
20	19.7	18.8	19.3	20.1	20.6	17.6	18.8	20.6	21.6
Lung									
5	7.1	7.1	7.1	7.1	7.1	7.1	7.1	7.1	7.1
10	4.9	4.9	4.9	4.9	4.9	4.8	4.9	4.9	5.0
15	4.1	4.0	4.1	4.2	4.2	3.9	4.0	4.2	4.3
20	4.7	4.5	4.6	4.8	4.9	4.2	4.5	4.9	5.2

* Any ages, with homogeneous potential withdrawal patterns.

period, and that the annual relative survival rates in each age group for each cancer are equal to those calculated for all ages combined in Finland in 1953–1974 (Hakulinen *et al.*, 1981).

The reference values in Table 1 are those assumed to be valid for each age group separately and also those derived for the combined material by the Ederer II method (2.3) and by the proposed method (2.4). These values are also derived by the Ederer I method when the potential withdrawal patterns are equal in both age groups. When the potential withdrawal patterns are unequal the results yielded by Ederer I become dependent on them. The dependence is almost negligible for five years but larger for longer follow-up periods, and quite marked for 20 years. The absolute range of the results is largest for higher relative survival rates, but the relative ranges (i.e. ranges expressed as proportions of reference values) are, from (2.1), (2.2) and (2.4), exactly equal for all the sites considered: e.g. for ages 55 and 70, 0.5% (five years), 3.3% (10 years), 9.6% (15 years) and 20.4% (20 years). The range of the results when the 35 and 55 year age groups are combined is narrower, due to less heterogeneity in the expected survival: relative range 0.2% (five years), 1.2% (10 years), 3.7% (15 years) and 9.2% (20 years).

5.2. *Unequal Relative Survival Rates in Subgroups*

Again, three cancer sites in males are considered. Patients with melanoma of the skin have an intermediate relative survival rate which is only slightly higher for younger ages. The relative survival for thyroid cancer is rather high but depends strongly on patient's

age at diagnosis. Cancer of the lung is associated with a poor relative survival which also is strongly age-dependent. It is assumed that the patient population consists of two age groups: patients aged 35 and 55 years at the beginning of follow-up. The admission alternatives and the expected survival rates are the same as in the previous example. The annual relative survival rates of patients aged 35 and 55 years are assumed to be equal to those calculated for ages 0–44 and 45–64 years, respectively, in Finland in 1953–1974 (Hakulinen *et al.*, 1981).

The reference values in Table 2 are the ratios between the observed and the expected survival rates when no withdrawals take place. When the withdrawal patterns in the subgroups are homogeneous these values are obtained by the Ederer I method and by the proposed method. How much the values given by the Ederer II method in such a situation ('Homog.' in Table 2) differ from these reference values depends on the cancer in question. If the relative survival rates in the subgroups are equal, there is no difference, but the difference becomes larger when the discrepancy between the age-specific relative survival rates increases. For melanoma of the skin the relative differences (differences expressed as proportions of reference values) are 0.1% (five years), 0.7% (10 years) and 1.0% (15 and 20 years), whereas for thyroid cancer they are 0.6% (five years), 2.1% (10 years), 5.3% (15 years) and 10.4% (20 years). The figures for lung cancer are close to those for cancer of the thyroid.

The results given by the Ederer II method tend to be below the reference values since the relative survival for the cancers in this example is poorer for older patients and these

Table 2

Long-term relative survival rate (%) for cancer at three sites as assumed for patients aged 35 and 55 years, and as derived for the pooled group with three alternative methods, when the age-specific potential withdrawal patterns are heterogeneous. Hypothetical example (see text)

Primary site and years of follow-up	Age (yr)		Refer-ence*	Method and potential withdrawal pattern for ages 35/55						
				Ederer II (2.3)			Ederer I (2.2)		Proposed method (2.4)	
	35	55		Homog. W_2/W_0	W_0/W_2		W_2/W_0	W_0/W_2	W_2/W_0	W_0/W_2
Melanoma										
5	47.2	42.3	44.9	44.8	44.8	44.8	44.8	44.9	44.8	44.9
10	40.5	33.2	37.2	37.0	36.9	37.1	36.9	37.6	37.1	37.4
15	36.1	35.0	35.6	35.3	35.5	35.0	35.2	36.1	35.9	35.4
20	37.3	35.9	36.8	36.5	36.6	36.3	35.3	38.3	37.0	36.7
Thyroid										
5	78.5	50.2	64.9	64.9	64.4	64.7	64.7	65.1	64.8	65.1
10	77.7	44.1	62.7	61.3	61.0	61.7	62.0	63.3	62.4	63.0
15	71.3	25.1	52.8	50.0	48.5	51.4	50.3	55.0	51.3	54.0
20	59.8	19.6	46.3	41.5	40.0	42.8	43.1	49.1	45.2	47.0
Lung										
5	14.5	8.6	11.7	11.6	11.6	11.7	11.6	11.8	11.6	11.7
10	12.4	5.9	9.5	9.3	9.1	9.4	9.3	9.6	9.3	9.6
15	11.6	4.9	8.9	8.4	8.3	8.6	8.6	9.2	8.8	9.0
20	12.7	5.8	10.4	9.4	9.2	9.5	9.9	10.9	10.4	10.4

* Homogeneous withdrawal patterns, Ederer I and the proposed method.

are thus more frequently withdrawn from the calculation of the expected survival rate than the younger patients. This results in an unduly high expected rate and hence in a low relative survival rate.

The results derived by all the methods are now dependent on the potential withdrawal patterns. This dependence is much larger for the Ederer I method than for the other methods, and is substantial in the 15- and 20-year relative survival rates. The absolute ranges of the results derived by the two other methods are almost equal. For the Ederer II method, the bias due to heterogeneity in the relative survival is larger than that due to heterogeneity in the potential withdrawal patterns.

6. Applications

In §4 it was stated that unequal withdrawal patterns in patient subgroups may cause the relative survival rate for a pooled group to lie outside the range of the stratum-specific relative survival rates. This property of convexity in pooling (here called 'consistency') was used as a crude indicator in studying the relative merits of the three methods for calculation of the relative survival rate. The work was conducted in connection with the estimation of survival for all major cancer sites in Finland [21 sites in males and 23 sites in females (Hakulinen *et al.*, 1981)]. Five-, 10-, 15- and 20-year relative survival rates were calculated for patients with cancer diagnosed between 1953 and 1974 inclusive, by each of the methods. The rates were derived for all age groups within the range 0–74 years, and for all combinations resulting from pooling two adjacent age groups. The most common age division employed was 0–44, 45–64 and 65–74 years with possible combinations of 0–64 and 45–74 years, although other divisions were also used for a few sites, (see Hakulinen *et al.*, 1981). Annual follow-up intervals were used. Rates were rounded to the closest 0.1% before decisions about convexity were made. The observed survival rates were obtained by the method of Berkson and Gage (1950).

All combinations were convex among the five-year relative survival rates. For 10-year relative survival rates the Ederer I method gave a rate for the pooled group in one instance that exceeded the rates for the subgroups (see Table 3). In one instance the Ederer II method gave a rate for the pooled group that was smaller than the rate for the subgroups. No excesses or deficits were observed for the proposed method (2.4). The

Table 3

Number of excesses and deficits in pooling convexity, tabulated by follow-up time and method of calculation of the relative survival rate, for cancer at 21 sites in males and at 23 sites in females in Finland, 1953–1974*

Method	Formula	Follow-up (yr)						Total	
		10		15		20			
		+	−	+	−	+	−	+	−
Ederer I	(2.2)	1	—	5	1	12	1	18	2
Ederer II	(2.3)	—	1	—	6	1	7	1	14
Proposed	(2.4)	—	—	—	1	2	2	2	3

* +(excess): the relative survival rate for the pooled age group is larger than those for the subgroups.

−(deficit): the relative survival rate for the pooled age group is smaller than those for the subgroups.

numbers of excesses and deficits increased when the follow-up time was lengthened and showed a general tendency toward excess for the Ederer I method and deficit for Ederer II. All of the methods were inconsistent on two occasions, the Ederer I method was the only inconsistent method on 15 occasions, the Ederer II method on 10 occasions and the proposed method on one occasion. The methods were the only consistent ones on one, one and two occasions (for the Ederer I, Ederer II and the proposed method, respectively). Of the 44 sex-specific sites, the Ederer I method produced inconsistencies at 15 sites, the Ederer II method at 11 sites and the proposed method at four sites.

The number of old cancer patients in Finland increased more rapidly than that of young patients, because of aging of the population. For example, in males the number of annual cancer registrations in the 45–64 age group increased by 45% from 1953–1954 to 1973–1974. In the 65–74 age group this increase was much larger: 144%. There were several sites in which the trend in the ratio between the age-specific annual numbers of registrations was similar to those of W_0/W_1 and W_0/W_2 of the examples in §5, e.g. cancer of the stomach, lung, colon, breast, cervix and corpus uteri, ovary and skin.

Thus, the potential follow-up times of young patients tend on average to be longer than those of old patients. When one life table is used in the calculation of the observed survival rates the more favourable survival of young patients will to a great extent be assumed for the withdrawn old patients. As a result, the observed survival rate will be too high. On the other hand, the Ederer I method, although giving an unbiased expected survival rate, also results in an unduly high relative survival rate.

By contrast, the example in §5.2 shows that the Ederer II method gave biased relative survival rates when the relative survival rates in the subgroups differed, in spite of the possible homogeneity of the potential withdrawal patterns. The rates are generally biased downwards as the relative survival rate tends more often to be lower for old than for young patients, and this bias is more important than the bias caused by a possible hererogeneity in the potential withdrawal in the subgroups.

Nonconvexity in pooling is a very crude property for indicating the biases which may exist even when the pooling is convex. The actuarial methods of estimation may also produce some numerical inconsistency, but the differences were in general of the order of those in the examples in §5.

7. Conclusions

The results suggest that if 10-year relative survival rates, at most, are needed, any of the methods will give roughly unbiased results. For longer follow-up periods the method of Ederer *et al.* (1961) should be avoided when the admission rates in patient subgroups are heterogeneous. Also the method of Ederer and Heise (1959) should be avoided for longer periods of follow-up when the relative survival rates in the subgroups differ. The method proposed in this paper has theoretical advantages and seems to work better with pooled data than do the other two alternatives.

RÉSUMÉ

On mesure souvent la survie au cancer sur une période de temps par le 'taux de survie relatif'. On entend par là le quotient du taux de survie observé dans le groupe des malades par l'espérance du taux de survie d'un groupe issu de la même population, similaire au groupe des malades pour tous les facteurs possibles qui peuvent influer sur la survie au début de la période d'observation excepté pour la maladie étudiée. Lorsque la façon dont les malades se retirent diffère d'un sous groupe de malades à l'autre, même s'ils ont le même taux de survie relatif, la méthode courante d'estimation du taux de survie relatif est biaisée. Une méthode.fondée sur le concept de 'table de survie espérée' est proposée pour supprimer le biais. Des exemples fondés sur des données du Registre finlandais du cancer suggèrent que les performances practiques de la méthode proposée sont meilleures que celles des méthodes alternatives, même lorsque les taux de survie relatifs dans les sous groupes de malades sont inégaux.

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