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Reduction of population-based cancer survival estimates by trace back of death certificate notifications: An empirical illustration ☆

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ABSTRACT

Background: Survival studies using data from population-based cancer registries allow assessing effectiveness of cancer care on a population level. However, population-based cancer registries differ in the proportion of cases first notified by death certificate, as well as in the efforts to trace back such death certificate notifications (DCN). We aimed to assess the impact of such trace back on population-based cancer survival estimates.

Materials and methods: In this study from the population-based Saarland Cancer Registry (Germany) we investigated the survival experience of successfully traced back DCN cases from 1994 to 2003. Five-year relative survival of patients with DCN cancers and the effect of trace back on population-based 5-year relative survival estimates were analysed by age and tumour site.

Results: Twelve percent of all cancers were DCN and such cases occurred most often amongst sites with poor prognosis and amongst elderly patients. Approximately half of DCN cases could be successfully traced back. Five-year relative survival of patients with DCN cancers with trace back was 2%. The inclusion of DCN cancers with additional registrations reduced the 5-year relative survival estimate for all cancers combined by 4% points. Reductions were stronger for older patients and highly fatal cancers.

Conclusions: Trace back results in increased inclusion of patients with very poor prognosis. Varying extent of trace back across registries may compromise comparability of cancer survival estimates and should be taken into account in comparative cancer survival studies.

1. Introduction

Survival studies using data from population-based cancer registries are a means to assess the effectiveness of cancer care in the respective target populations and allow comparisons over time or with other populations. A major issue in cancer survival studies is how to deal with cancers that first come to the attention of a registry from a death certificate (denoted as death certificate notified (DCN) cases). In some cancer registries they are simply excluded from survival analyses. In other registries, major efforts of 'trace back' are made to achieve additional notifications for DCN cases, and only those cases are excluded from survival analyses for which such trace back is unsuccessful and for which notifications

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remain restricted to death certificates only.[1,2] However, little is known about how much survival estimates are influenced by such differential registry practices.

In this study from the population-based Saarland Cancer Registry (Germany) we investigated cancer patients first notified by death certificate in the period 1994–2003. We analysed cumulative 5-year relative survival of patients with DCN cancers with additional registrations after trace back and the change in survival estimates by including such patients in population-based cancer survival analyses.

2. Materials and methods

This study used data from the population-based Saarland Cancer Registry, which covers the federal state of Saarland in South-West Germany with about 1.03 million inhabitants. The registry is operating since 1968. The completeness of the case ascertainment is estimated to exceed 95%[3,4] and the registry regularly contributes to descriptive and analytic studies in national or international collaborations.[5–9]

The registry obtains notifications from general practitioners, hospitals, pathology laboratories, radiotherapy departments and outpatient clinics. Cancer registration in Saarland is based on state legislation and reporting of cancers is mandatory for any physician. Up to now, the registry obtains completed notification forms (or copies of histology reports from pathology departments) which contain personal identifiers and socio demographic items, tumour information (e.g. site, date of diagnosis, morphology, stage, treatment, basis of diagnosis) and information about the provider of the notification. The registry not only includes incident cases but also follow-up information on local recurrence or distant metastasis and eventual death of the patient. Mortality follow-up is based on death certificates including the cause of death, cancers as secondary disorders and the physician certifying death from the local health authorities and the state statistical office.

If a cancer first comes to the attention of the registry from a death certificate, trace back is initiated to request further information. Then a prepared notification form is sent to the hospital or physician certifying death to obtain a notification or appoint the patient's general practitioner for a further request. However, if follow back is unsuccessful, no other information except cause and date of death, sex and age at diagnosis are available. These cases are denoted as death certificate only (DCO) cases. Cancers first notified from death certificates but with subsequent notifications from other sources are treated as cases notified during lifetime.

The registry started follow back of DCN cases in the late 1980s. For this study, data from patients diagnosed with invasive cancer except non-melanoma skin cancer (ICD-9: 140–208 except 173) in 1994–2003 and aged 15 years or older were used. Mortality follow-up was available until the end of 2008. Whereas DCO cancers are flagged and their database records may easily be accessed, the identification of DCN cancers with trace back and additional registrations required an inspection of all archived notification forms.

Numbers of DCN cancers reported to the registry in the calendar period 1994–2003 were tabulated by age category (15–54, 55–74 and 75 years or older), sex and tumour site according to the outcome of trace back. For DCN cancers with successful trace back, observed mean survival time was calculated. Mean age at diagnosis and numbers and proportions of patients aged 75 years or older were tabulated by sex and cancer site according to the type of notification (registration at lifetime, DCN with additional registration from trace back and DCO notified, respectively). Time trends of proportions of death certificate notifications and DCO cases were computed over the 1994–2003 period.

Cancer sites were presented individually if there were at least 100 DCN cases with additional registrations after follow back. This criterion was met by cancers of the stomach, colon and rectum, liver and gallbladder, pancreas, lung, female breast and prostate and leukaemia.

Relative survival was derived as the ratio of the patients' observed survival to the survival expected for age- and sex-matched persons from the general population (thus reflecting excess mortality of cancer patients compared to the general population). Although knowledge about the cause of death is not required, relative survival may be interpreted as disease specific survival, i.e. survival that would be expected if the cancer under study was the only cause of death.[10] Expected survival was calculated according to the Ederer II method.[11] Life tables including age specific survival probabilities for successive calendar periods of 5 years since 1990 were derived from counts of deaths and populations up to the age of 89 years. Survival probabilities for patients aged from 90 to 99 years were projected using the Coale–Kisker model for mortality rates at high ages.[12,13]

Population-based 5-year relative survival estimates were derived according to trace back: firstly, assuming no follow back was initiated and all DCN cases were excluded from estimation (approach 1; also denoted as 'DCN excluded') and secondly, using data from trace back and including DCN cases with additional registrations but excluding remaining DCO cases, which is common practice in population-based survival studies (approach 2; also denoted as 'DCO excluded'). To evaluate survival trends over time, cumulative 5-year relative survival for all cancer sites combined were also derived over the 1994–2003 period according to trace back. Additionally, site specific 5-year relative survival curves were estimated for patients with DCN cancers.

The reported cumulative 5-year relative survival estimates are classical cohort based estimates for cancer patients diagnosed in 1994–2003 and followed up until the end of 2008 using standard actuarial methodology.[14,15] Patients, for whom trace back provided a date of diagnosis prior to 1994 were excluded from the analysis.

For both the 'DCN excluded' and the 'DCO excluded' approaches, age adjusted cumulative 5-year relative survival (derived from age specific survival using weights from the International Cancer Survival Standards (ICSS; age categories: 15–44, 45–54, 55–64, 65–74 and 75 years or older)[16]) and age group specific survival (age categories 15–54, 55–74 and 75 years and older) were estimated.[17] Standard errors of the survival estimates were calculated by Greenwood's formula.[14,18] The ICSS weights were also used when adjusting site specific survival of DCN cancers.

For data preparation and analysis, the freely available R Language and Environment for Statistical Computing (release

2.8.0; R Foundation for Statistical Computing, Vienna, 2009) and the add-on package 'periodR' (release 1.0–5) were used.[19]

3. Results

Table 1 shows overall numbers of cancer cases as well as numbers of DCN cancers reported to the Saarland Cancer Registry in 1994–2003, along with results of trace back by age category, sex and tumour site. In total 58,506 invasive cancers except non-melanoma skin cancer (ICD-9: 140–208 except 173) were included, whereof 17%, 55% and 28% were amongst patients aged 15–54, 55–74 and 75 years or older. The overall proportion of DCN cancers was 12%. This proportion varied substantially by age and cancer site. 24% of the cancers amongst elderly patients aged 75 years or older were first notified from a death certificate, whereas the corresponding proportions were only 8% and 3% amongst patients aged 55–74 and 15–54 years, respectively. The proportions of DCN cancers were similar amongst both sexes. Notifications from death certificates were highest for cancer sites with very poor prognosis (pancreas: 47%; liver and gallbladder: 37%), intermediate for lung cancer, leukaemia and stomach cancer (23%, 19% and 12%, respectively) and lowest for cancers with above average prognosis (colon and rectum: 7%; prostate: 5%; female breast: 4%).

Additional notifications were received for about 50% of the DCN cancers irrespective of age and cancer site. Trace back resulted in an overall proportion of DCO cases of 6% with highest proportions observed for sites with poor prognosis (pancreas: 22%; liver and gallbladder: 18%) and lowest proportions amongst cancers with above average prognosis (breast cancer: 2%; prostate: 2%). For 12% of the cancers of patients aged 75 years or over, a death certificate remained the only source of information, whereas the proportions of DCO cancers were only 4% and 1% amongst patients aged 55–74 and 15–54 years, respectively. Mean observed survival time of patients with DCN cancers with trace back was 5 months. There was only little variation in the observed mean survival across age groups. Observed mean survival was highest (but still rather short) for prostate cancer, leukaemia and female breast cancer (13, 9 and 7 months, respectively), and below 6 months for the remaining sites.

Table 2 presents mean age and proportions of patients aged 75 years or older according to the type of notification (either notified during lifetime, DCN with additional registration or DCO notified) by sex and tumour site. Overall, mean age was 74.2 years for patients with DCN cancers with additional registrations, 76.5 years for patients with DCO notified cancers and 65.0 years for patients with cancers notified during lifetime. More than half of the patients with DCN cases with trace back (53%) and DCO cases (61%) were 75 years or older compared to only 24% of patients with cancers notified during lifetime. Similar age gradients between the three groups were seen for all individually assessed cancer sites. Site specific age distributions of DCN cases and of all cases combined (irrespective of type of notification) were more similar amongst cancers of poor prognosis (particularly for lung cancer; data not shown). The proportions of elderly patients were substantially higher amongst female than amongst male cancer patients for all three types of notification.

Age adjusted and age group specific 5-year relative survival of patients with DCN cancers with additional registrations from trace back diagnosed in 1994–2003 are plotted in Fig. 1. Overall 5-year relative survival was 2%. Survival was essentially the same across age categories (3%, 2% and 2%, respectively). Age adjusted 5-year relative survival was 3% or less for all sites except female breast, prostate and leukaemia (5%, 10% and 4%, respectively).

Table 3 presents age adjusted and age group specific cumulative 5-year relative survival of cancer patients by tumour

Table 1 – Numbers of DCN cancers from Saarland diagnosed 1994–2003 with results of trace back by age category, sex and tumour site.

Category	Subgroup	All cancers	DCN cases		Additional registration from trace back				
					Yes			No (DCO notified)	
		n	*n*	%	*n*	%	$\bar{S}$	*n*	%
All cases		58,506	6843	11.7	3654	6.2	5.1	3189	5.5
Age	15–54 years	10,168	317	3.1	194	1.9	7.4	123	1.2
	55–74 years	32,264	2662	8.3	1539	4.8	5.2	1123	3.5
	⩾75 years	16,074	3864	24.0	1921	12.0	4.8	1943	12.1
Sex	Male	30,371	3500	11.5	1893	6.2	5.5	1607	5.3
	Female	28,135	3343	11.9	1761	6.3	4.7	1582	5.6
Cancer site (ICD-9 code)	Stomach (151)	2432	292	12.0	148	6.1	4.1	144	5.9
	Colon and rectum (153 + 154)	9619	699	7.3	385	4.0	5.7	314	3.3
	Liver and gallbladder (155 + 156)	1683	623	37.0	322	19.1	4.2	301	17.9
	Pancreas (157)	1540	722	46.9	379	24.6	4.0	343	22.3
	Lung (162)	7623	1755	23.0	991	13.0	3.6	764	10.0
	Female breast (174)	7901	281	3.6	148	1.9	6.8	133	1.7
	Prostate (185)	6226	300	4.8	164	2.6	12.6	136	2.2
	Leukaemia (204–208)	1325	253	19.1	122	9.2	8.9	131	9.9

Abbreviations: ICD-9: International Classification of Diseases (9th revision); DCN: death certificate notified; $\bar{S}$: observed mean survival in months; DCO: death certificate only.

Table 2 – Age distribution of cancer patients from Saarland diagnosed 1994–2003 according to type of notification by sex and cancer site.

Category	Subgroup	Notified during lifetime				DCN with additional registration from trace back				DCO notified			
		n	Mean age	⩾75 years	%	*n*	Mean age	⩾75 years	%	*n*	Mean age	⩾75 years	%
All cases		51,663	65.0	12,210	23.6	3654	74.2	1921	52.6	3189	76.5	1943	60.9
Sex	Males	26,871	65.0	5425	20.2	1893	71.5	777	41.0	1607	73.8	803	50.0
	Females	24,792	65.0	6785	27.4	1761	77.1	1144	65.0	1582	79.3	1140	72.1
Cancer site (ICD-9 code)	Stomach (151)	2140	69.2	746	34.9	148	77.3	99	66.9	144	78.6	98	68.1
	Colon and rectum (153+154)	8920	69.0	2921	32.7	385	77.6	255	66.2	314	79.1	218	69.4
	Liver and gallbladder (155+156)	1060	68.3	301	28.4	322	72.4	151	46.9	301	76.0	174	57.8
	Pancreas (157)	818	66.3	188	23.0	379	74.6	208	54.9	343	75.8	207	60.3
	Lung (162)	5868	64.7	916	15.6	991	71.0	376	37.9	764	73.6	364	47.6
	Female breast (174)	7620	62.4	1584	20.8	148	77.0	100	67.6	133	79.5	98	73.7
	Prostate (185)	5926	69.3	1583	26.7	164	78.5	113	68.9	136	80.5	105	77.2
	Leukaemia (204–208)	1072	63.2	230	21.5	122	75.5	73	59.8	131	77.6	92	70.2

Abbreviations: ICD-9: International Classification of Diseases (9th revision); DCN: death certificate notified; DCO: death certificate only.

site according to trace back. Five-year relative survival for all cancer sites combined (ICD-9: 140–208 except 173) was 59% if all DCN cases were excluded from survival estimation (approach 1). Trace back and exclusion of remaining DCO cases only (approach 2) decreased survival by 4% units to 55%. Age adjusted survival estimates were almost identical to crude estimates (absolute difference for all cancer sites combined: 0.3% units; individual sites: ⩽1.8% units) and are presented as overall survival estimates in the text and Table 3.

The effect of trace back and inclusion of tumours with additional notifications (approach 2) was highest for cancers of the liver and gallbladder and leukaemia (4% units, respectively) and lowest for cancer of the female breast and stomach (2% units, respectively). The relatively high effect for all cancer sites combined partly reflects a change in 'case mix', as adding DCN cases leads to higher proportions of cases with poor prognosis in the total sample.

The effect of the inclusion of additional registrations was highest amongst patients aged 75 years or older. Trace back reduced 5-year relative survival of elderly cancer patients by 7% units for all cancers combined, whereas trace back resulted in decreases of only 3% units and 1% unit amongst patients aged 55–74 and 15–54 years, respectively. Increasing effects of trace back with age could be observed for all individually analysed cancer sites except for cancer of liver and gallbladder.

Fig. 2 shows time trends of death certificate notifications, DCO cases and age adjusted 5-year relative survival for all cancer sites combined in the calendar period 1994–2003. The overall proportion of death certificate notifications steadily decreased from 12% to 8%, whereas the proportion of DCO cases was rather stable (it slightly decreased from 5.4% to 3.8%). At the same time, 5-year relative survival estimates increased from 62% to 70% in case no trace back would have been initiated and from 58% to 67% in case of trace back.

4. Discussion

In this population-based study from Saarland (Germany) we investigated cancer patients first notified by death certificate in the calendar period 1994–2003. We analysed cumulative 5-year relative survival of patients with DCN cancers with additional registrations and the effect of the inclusion of such cancer patients on survival estimates by age category and tumour site. Overall, 12% of all included cancers were notified by death certificates. The majority of DCN cancers were amongst patients aged 75 years or older. Trace back of DCN cancers reduced the proportions of DCO notified cancers by about 50%. Cumulative 5-year relative survival of DCN cancers with follow back was 2%. The inclusion of DCN cancers with additional registrations in survival estimation reduced overall 5-year relative survival by 4% units to 55%. Effects of trace back on survival estimates were highest for cancers of the liver and gallbladder and leukaemia (4% units, respectively), and a particularly strong decrease of 5-year relative survival estimates was observed amongst patients aged 75 years or older (7% units).

To our knowledge no comprehensive empirical evaluation of the effect of trace back of DCN cancers on population-based

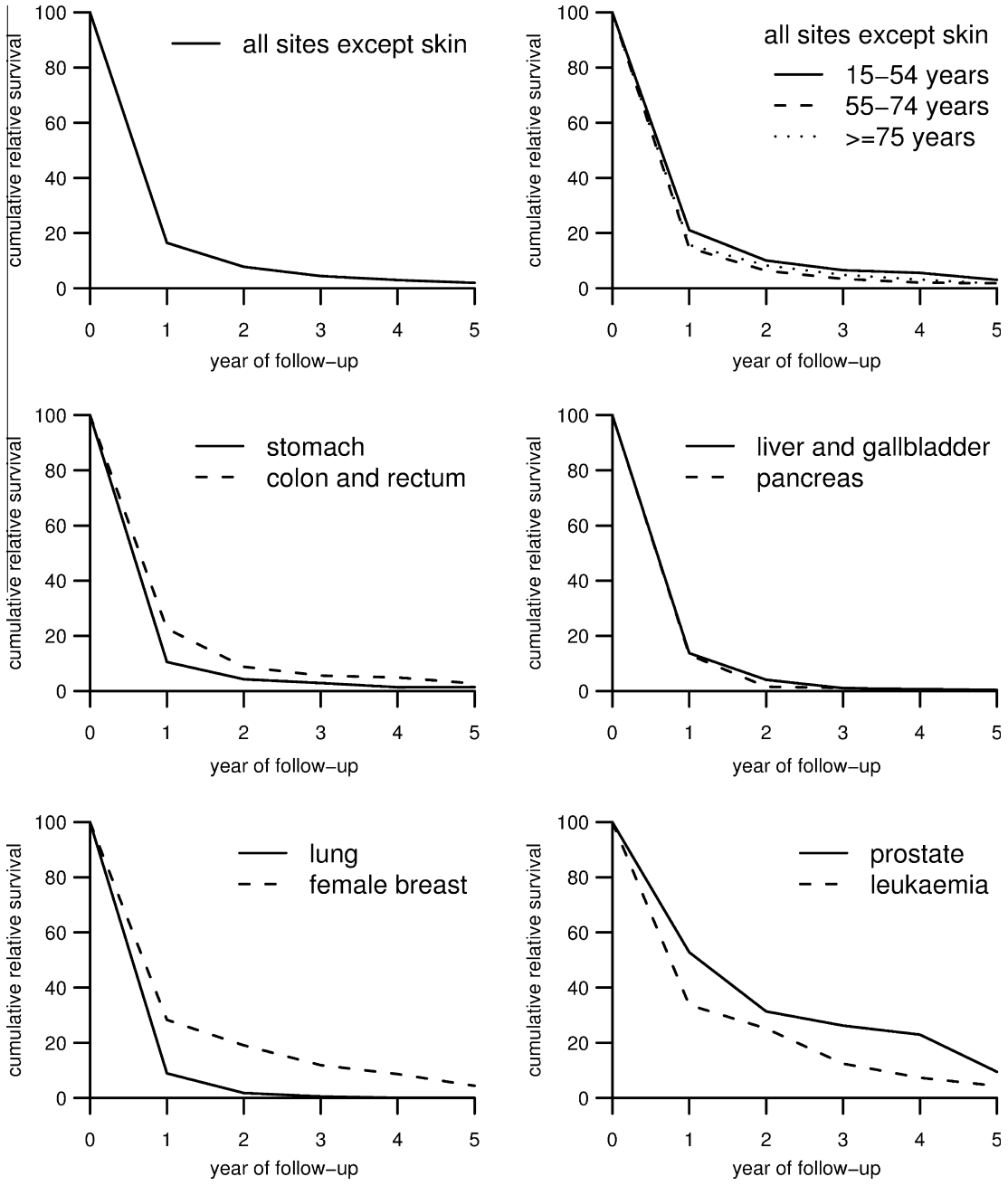

Fig. 1 – Age adjusted overall and age group specific 5-year relative survival of patients from Saarland diagnosed 1994–2003 with death certificate notified cancers with successful trace back according to cancer site.

cancer survival estimates has been provided. Recent publications reported higher mortality and selection bias as reasons for worse prognosis of death certificate notifications[20] or suggested an adjustment of survival estimates for remaining DCO cases.[21]

Substantial proportions of DCN cancers may indicate underreporting of cancers during lifetime. Missed registrations include both patients who die from the cancer (then, the registry may receive a notification from a death certificate) and cured patients who eventually will die from other causes. Generally, the longer a patient survives with a cancer, the more likely it is that the tumour will sometime be reported, but cancer patients with poor prognosis or geriatric patients often have fewer treatment options and are more likely to escape cancer registration. Therefore, just excluding cases not registered at lifetime (including all DCN cases) from survival analyses most likely leads to overestimation of survival.[22] On the other hand, selective inclusion of all missed patients who died whilst excluding all of the missed survivors (which might be achieved if trace back was 100% successful) would be expected to result in underestimation of survival.[17,22] In our study, the additional inclusion of remaining DCO cases (assuming '0' survival) would have led to a further reduction of 5-year relative survival of approximately same amount as trace back (e.g. all sites combined: –2.9% units; patients aged 15–54, 55–74 and 75 years or older: –0.8% units,

Table 3 – Age adjusted overall and age group specific cumulative 5-year relative survival of cancer patients from Saarland diagnosed 1994–2003 with regard to trace back.

Cancer site (ICD-9 code)	Category	Exclusion of any DCN cancer (1)		Trace back and exclusion of remaining DCO cases only (2)		Difference between (2) and (1)
		RS	SE	RS	SE	
All sites[a]	Age adjusted[b]	58.5	0.3	54.7	0.3	−3.8
	15–54 years	67.2	0.5	65.9	0.5	−1.3
	55–74 years	57.1	0.3	54.3	0.3	−2.8
	⩾75 years	55.7	0.7	48.4	0.6	−7.3
Stomach (151)	Age adjusted[b]	32.4	1.2	30.8	1.1	−1.6
	15–54 years	36.5	3.2	35.3	3.1	−1.2
	55–74 years	32.3	1.5	31.3	1.5	−1.0
	⩾75 years	29.3	2.4	26.0	2.1	−3.3
Colon and rectum (153 + 154)	Age adjusted[b]	61.9	0.7	59.7	0.6	−2.2
	15–54 years	65.6	1.6	64.8	1.6	−0.8
	55–74 years	62.3	0.8	60.9	0.8	−1.4
	⩾75 years	58.4	1.5	53.8	1.4	−4.6
Liver and gallbladder (155 + 156)	Age adjusted[b]	20.4	1.5	16.2	1.2	−4.3
	15–54 years	29.8	4.4	24.5	3.8	−5.3
	55–74 years	18.0	1.6	14.7	1.3	−3.2
	⩾75 years	17.0	2.8	11.2	1.9	−5.8
Pancreas (157)	Age adjusted[b]	10.0	1.2	7.6	0.9	−2.4
	15–54 years	12.8	3.2	11.4	2.9	−1.3
	55–74 years	9.5	1.4	7.2	1.1	−2.2
	⩾75 years	7.8	2.4	4.1	1.2	−3.7
Lung (162)	Age adjusted[b]	16.8	0.6	14.3	0.5	−2.5
	15–54 years	19.8	1.3	18.5	1.2	−1.3
	55–74 years	16.6	0.6	14.6	0.6	−2.0
	⩾75 years	14.6	1.5	10.4	1.1	−4.2
Female breast (174)	Age adjusted[b]	82.1	0.7	80.2	0.7	−1.9
	15–54 years	84.6	0.8	84.1	0.8	−0.5
	55–74 years	81.9	0.7	81.2	0.7	−0.8
	⩾75 years	81.3	1.9	76.5	1.9	−4.8
Prostate (185)	Age adjusted[b]	89.4	1.4	87.3	1.4	−2.1
	15–54 years	87.9	2.7	87.4	2.7	−0.4
	55–74 years	91.4	0.8	90.3	0.8	−1.0
	⩾75 years	91.2	2.2	86.0	2.1	−5.1
Leukaemia (204–208)	Age adjusted[b]	46.1	1.9	42.2	1.7	−3.9
	15–54 years	56.5	3.3	54.8	3.2	−1.6
	55–74 years	47.5	2.3	44.7	2.2	−2.8
	⩾75 years	36.1	4.4	28.6	3.5	−7.5

Abbreviations/annotations: ICD-9: International Classification of Diseases (9th revision); DCN: death certificate notified; DCO: death certificate only; RS: cumulative 5-year relative survival; SE: standard error.

[a] Except non-melanoma skin cancer (ICD-9: 140–208 excl 173).

[b] Weights from the International Cancer Survival Standards were used for standardization.[16]

−1.9% units and −5.7% units, respectively; pancreas: −1.2% units; lung: −1.3% units; female breast: −1.5% units; leukaemia: −3.2% units).

Trace back of DCN cases which is 'partially successful' (as in our examples where it was achieved for about 50% of the patients) is expected to lead to survival estimates that are in between those extremes. As illustrated in our examples, trace back may have a substantial impact on survival estimates for DCN and DCO proportions which are commonly encountered in population-based cancer registries: during 1998–2002 at least 11 out of 99 other population-based cancer registries from Europe included in 'Cancer Incidence in Five Continents' reported similar or higher proportions of DCN cancers than the Saarland Cancer Registry for all cancer sites combined and twice as many reported similar or higher DCO proportions, whereas only 15 registries reported DCN percentages of 2% or less.[8]

According to the considerations made above, the inclusion of patients with DCN cases with additional registrations but exclusion of DCO cases (which is common practice in population-based cancer survival studies.[1,2]) may provide reasonable estimates for the unknown 'true' survival of all patients even in the case of non-negligible proportions of DCN registrations, as the derived estimate should be located between the

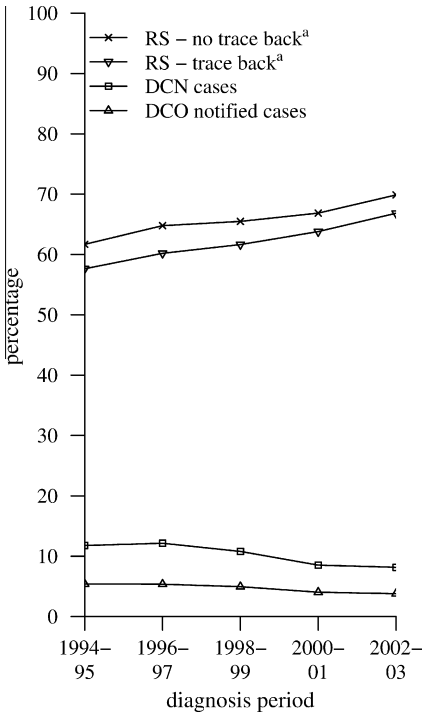

Fig. 2 – Time trends of death certificate notifications, DCO cases and cumulative 5-year relative survival according to trace back. RS: cumulative 5-year relative survival; DCN: death certificate notified; DCO: death certificate only; a) weights from the International Cancer Survival Standards were used for standardization.[16]

'optimistic' estimate obtained in the absence of trace back and the 'pessimistic' estimate obtained in the case of 'fully successful' trace back. However, the extent of trace back that would give the least biased survival estimates remains unknown, and heterogeneity in the extent of trace back may account for non-negligible proportions of the variation of survival estimates between cancer registries.[17,22] Nevertheless, for cancer sites or age categories with low proportions of DCN cancers (e.g. younger patients or tumours with favourable prognosis) the observed effects of trace back may often be rather small and reasonable estimates may be obtained regardless of the extent of trace back.

This study has several limitations. As the Saarland Cancer Registry covers a small population of about 1.03 million inhabitants, only the most frequent cancer sites (including prostate, female breast, colon and rectum) and cancer sites with poor prognosis (such as lung, pancreas or liver and gallbladder) for which at least 100 DCN cases were observed in 1994–2003 were included. Nevertheless, the analysis included both cancers with poor, intermediate and favourable prognosis and thus allowed to disclose the extent of death certificate notification and effects of trace back on survival estimation for different tumour sites and age categories.

Whereas cancers which were missed during lifetime but notified from a death certificate were known and addressed in our analyses, nothing was known about cured cancers or those with favourable prognosis that had been missed during lifetime.

Our analyses pertain to a cancer registry with comprehensive access to death certificates. Magnitude and meaning of DCO and DCN proportions may be different in registries in which such access is restricted (e.g. to death certificates listing cancer as the main cause of death only). Furthermore, our analyses pertain to a situation with long standing cancer registration. In 'younger' cancer registries, high DCN and DCO proportions may to a non-negligible extent be due to cancer diagnoses made before initiation of registration.

Time trend analysis revealed a rather stable difference of survival estimates according to trace back. However, the start or modification of trace back activities may distort survival trends. Additional simultaneous analyses of DCN and DCO registrations may help to disclose such artefacts.

Despite its limitations, our analysis clearly demonstrates the strong impact trace back of DCN cases can have on survival estimates from population-based cancer registries. These results underline the need to consider the extent of notifications from death certificates and the effect of trace back on survival estimates in comparative studies of population-based survival. At the same time, population-based cancer registries should first and foremost take action to improve their coverage and case ascertainment in case of incomplete registration.

Conflict of interest statement

None declared.

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