ELSEVIER

European Journal of Cancer 41 (2005) 2321–2330

European Journal of Cancer

www.ejconline.com

Stage-specific survival of epithelial cancers in North-Holland/Flevoland, The Netherlands

O. Visser [a,*], F.E. van Leeuwen [b]

[a] *Comprehensive Cancer Centre Amsterdam, P.O. Box 9236, 1006 AE, Amsterdam, The Netherlands*
[b] *Netherlands Cancer Institute, Department of Epidemiology, Plesmanlaan 121, 1066 CX, Amsterdam, The Netherlands*

Received 20 January 2005; received in revised form 23 February 2005; accepted 1 March 2005
Available online 26 August 2005

Abstract

While stage is the most important factor for determining cancer survival, population-based survival data according to stage are rarely presented. We present such data for a large population diagnosed with cancer in the area covered by the Amsterdam Cancer Registry for the period 1989–2001 ($n = 108{,}251$). Cases were grouped according to the TNM-classification. For all sites, a close correlation between stage at diagnosis and survival was observed. The stage-specific 5-year relative survival rate (RSR) ranged from close to 100% for stage I carcinoma of the salivary glands, thyroid, colon/rectum, skin, breast, female genitals, prostate and urethra to $\leqslant 1\%$ for stage IV carcinoma of the oesophagus, stomach, liver, gallbladder, pancreas and lung. Between 1989–1991 and 1999–2001, we observed an increase in the stage-specific RSR for carcinoma of colon/rectum (stages II–IV), lung (stages I–II), breast (stages I–III) and prostate (stages II–IV). Changes in diagnostic (breast, prostate) and staging procedures (lung), surgery (rectum, prostate) and adjuvant treatment (breast, colon) are likely to have contributed to this increase.

Keywords: Stage-specific; Survival; Cancer; Stage; Epidemiology

1. Introduction

Information on the prognosis of cancer patients is important for both patients and their clinicians. The EUROCARE-3 study provides age- and site-specific survival rates for many European countries [1]. However, the prognosis of a cancer patient is also influenced by many other factors, such as morphological type, treatment and co-morbidity [2,3]. For epithelial cancers, stage is the most important factor, and most survival differences between populations can be explained by differences in stage distribution [4,5]. Moreover, stage-specific survival rates are essential for the interpretation of differences in survival rates between sexes or changes in the overall survival rates over time, as the overall survival will change as a result of changes in stage distribution. Unfortunately, data on stage-specific survival is unavailable in the majority of the European cancer registries, and this hampers the comparison of survival rates between registries and the explanation of survival changes over time.

The nationwide Netherlands Cancer Registry collects stage information for all relevant cancer sites and, consequently, is uniquely positioned to examine population-based survival according to stage. In this paper, we present stage-specific survival rates for all major epithelial cancers as well as melanoma skin cancer, based on a

* Corresponding author. Tel.: +31 20 346 2531; fax: +31 20 346 2525.
E-mail address: o.visser@ikca.nl (O. Visser).

0959-8049/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ejca.2005.03.037

very large population-based cohort of cancer patients in the north-western part of The Netherlands.

2. Patients and methods

2.1. Amsterdam cancer registry

The Amsterdam Cancer Registry (ACR) is a regional, population-based cancer registry with complete regional coverage since 1st January 1988. The region of the ACR covers the major part of 2 out of 12 provinces of The Netherlands: North-Holland and Flevoland. Its population was 2.84 million on 31st December 2001, approximately 17% of the total population of The Netherlands. The ACR is part of the nationwide Netherlands Cancer Registry, whose data are included in *Cancer Incidence in Five Continents* as of volume VII [6,7]. Cases diagnosed in a hospital outside the ACR region, but with residence in the ACR region, are routinely obtained from the national registry and included in the regional registry.

The information for the registry is extracted from the medical records by registration clerks. Apart from demographic data, data are collected on tumour site and morphological classification (according to the International Classification of Diseases for Oncology), stage of the tumour and primary treatment of the patients. For the stage of the tumour, tumour-node-metastasis (TNM) is registered whenever applicable. We used the 4th edition for cases diagnosed in 1989–1992, the 2nd revision of the 4th edition in 1993–1998 and the 5th edition in 1999–2001 [8,9].

2.2. Study population

For this study, we selected cancer sites included in the 5th edition of the TNM-classification [9]. Cancer sites with mainly non-epithelial cancers (bone, soft tissue, eye) were excluded. Skin melanoma was included.

Stage grouping was according to the 5th edition of the TNM-classification, based on a combination of cTNM and pTNM. If pTNM was available (61% of the cases) we used pTNM-data, otherwise cTNM-data were used. In case of small numbers, stages were grouped together.

The TNM-classification for carcinoma of the small intestines was not available until the 2nd revision of the 4th edition. We converted the extent of disease as registered in 1989–1992 to TNM-stage as follows: localised = stage I, direct extension = stage II, regional lymph node metastasis = stage III, distant metastasis = stage IV.

Between 1st January 1989 and 31st December 2001 a total of 130,619 first invasive cancers were registered. After exclusion of sites with mainly non-epithelial cancers and sites for which TNM was not applicable, 108,251 cancers remained (Table 1).

2.3. Follow-up

For patients with residence in the ACR region and diagnosed in 1989–1997, the vital status was updated by linking electronic files with deceased persons to the cancer registry. These files were made available in 1999/2000 by 54 municipal population registers (covering 90% of the population of the region) out of a total of 74 registers in the region. The files included all deceased residents (irrespective of cause of death) of those municipalities, generally covering the period 1989–1999. Active follow-up was performed in the hospitals for all patients with residence in the remaining 20 municipalities and in case the data-file made available by the municipal population register covered only a part of the period 1989–1999. In case of missing data in the hospital, the municipal population registers were asked for the date of death of individual patients.

In September 2003, the vital status of all patients (diagnosed 1989–2001) still alive at last follow-up was updated by linkage to the electronic death register of the Central Bureau for Genealogy (CBG), which contains all deceased residents of The Netherlands as of 1st October 1994. This electronic register is updated on a daily basis with data from all municipal population registers in The Netherlands. Patients who probably died before 1st October 1994 according to hospital information, but with unknown date of death, were checked in the personal record card register of the CBG, which contains all Dutch residents who died before 1st October 1994. Finally, all patients not known by CBG were assumed to be alive at 1st September 2003, 1 week before record linkage with the electronic death register was performed.

Checks on the vital status of patients assumed to be alive at 1st September 2003 were performed in the hospitals for all patients with metastatic disease at diagnosis, patients over 95 years of age in 2003 and patients with cancer of the oesophagus, stomach, liver, gallbladder, bile ducts, pancreas and lung. This procedure revealed that the number of patients assumed to be alive after record-linkage but who turned out to have died according to hospital information was negligible. Overall, missing dates of death are estimated to be well below 0.5%.

2.4. Statistical analysis

Because the cause of death is not available in the population registers and consequently not complete in our data set, and because linkage with the cause of death registration of Statistics Netherlands is not possible because of privacy regulations, we were unable

Table 1
Invasive cancers according to TNM-stage, North-Holland/Flevoland, The Netherlands, 1989–2001 (second and subsequent cancers excluded)

	Number of cases	TNM-stage (%)					Non-epithelial cancers[a] (%)	No microscopic confirmation (%)
		I	II	III	IV	Unknown		
Lip/oral cavity	1654	40	16	10	29	3	1	0
Pharynx	889	5	10	21	63	1	1	0
Larynx	1353	39	25	11	23	1	1	0
Maxillary sinus	66	3	6	26	58	0	5	3
Salivary glands	232	38	11	6	22	11	12	0
Thyroid gland	665	43	19	19	17	2	0	0
Oesophagus	2014	4	12	19	28	36	0	1
Stomach	4472	15	11	17	36	16	2	2
Small intestine	305	5	16	12	17	4	43	4
Colon/rectum	15,685	17	31	25	20	3	1	2
Anal canal	238	13	40	25	5	14	3	1
Liver	581	1	12	14	39	16	5	13
Gallbladder	452	7	11	15	47	9	0	12
Extrahepatic bile ducts	834	5	5	7	29	18	1	35
Pancreas	3185	10	6	7	38	5	1	33
Lung	17,448	17	4	35	32	4	1	5
Skin[b], non-melanoma	4987	63	11	2	0	20	3	0
Skin, melanoma[c]	4718	53	28	13	1	4		
Breast	21,121	34	50	8	6	2	0	1
Vulva[d]	439	30	31	20	12	6	1	0
Vagina	99	25	18	16	21	7	12	0
Cervix uteri	1835	51	17	22	7	2	0	0
Corpus uteri	2649	70	8	7	4	2	8	0
Ovary	2438	20	7	44	17	2	8	2
Penis[d]	177	47	21	13	3	15	0	1
Prostate	12,131	4	49	15	26	4	0	2
Kidney	2638	9	32	18	23	1	3	13
Renal pelvis/ureter	434	28	13	23	26	7	0	3
Bladder	4471	45	24	12	14	3	1	1
Urethra	41	22	29	12	20	15	2	0
Total	108,251	26	27	18	19	5	1	3

[a] Mainly carcinoid tumours of the lung and gastrointestinal tract (appendix, small intestines), mixed tumours of the female genital organs and salivary glands, leiomyosarcoma of the corpus uteri, as well as germ cell and stromal tumours of the ovaries.
[b] Including scrotum.
[c] Including melanoma of vulva ($n = 25$), penis ($n = 1$) and scrotum ($n = 2$).
[d] Excluding melanoma.

to calculate disease specific survival. As an alternative, we calculated relative survival and 95% confidence intervals (CI) using STATA 7.0 (StataCorp, Stata Statistical Software: Release 7.0. College Station, TX, United States of America (USA): Stata Corporation) with software written by Dickman *et al.* [10], based on a computer package developed by Hakulinen and Abeywickrama [11]. This method corrects observed survival for expected mortality according to annual life tables of the general population. We used national age-, sex- and calendar year-specific life tables from Statistics Netherlands [12].

3. Results

Out of a total of 108,251 patients with a primary cancer of one of the selected tumour sites (Table 1), TNM-stage was available for 95% of the cases (98,210 epithelial cancers as well as 4718 skin melanomas). A total of 1554 non-epithelial cancers (other than skin melanoma) of the selected tumour sites were registered (1% of the cases). A total of 3769 cancers (3%) were not microscopically confirmed, mostly cancers of the pancreas (1043 cases) and the lung (925 cases). The highest percentage of non-microscopically confirmed tumours was observed for cancers of the extrahepatic bile ducts (35%, 293 cases).

Stage I was the most registered stage for carcinoma of the lip/oral cavity, larynx, salivary glands, thyroid, skin, uterus, penis and bladder (Table 1). For carcinoma of the pharynx, maxillary sinus and the digestive organs (small intestines, colon/rectum and anal canal excluded) stage IV was the most registered stage. The proportion of unknown stage was particularly high for oesophageal (36%) and skin (20%) carcinoma, mostly due to an unknown T-category.

Figs. 1 and 2 show a clear correlation between stage at diagnosis and the RSR for all cancer sites: a relatively high RSR in early stages and low RSRs in advanced or

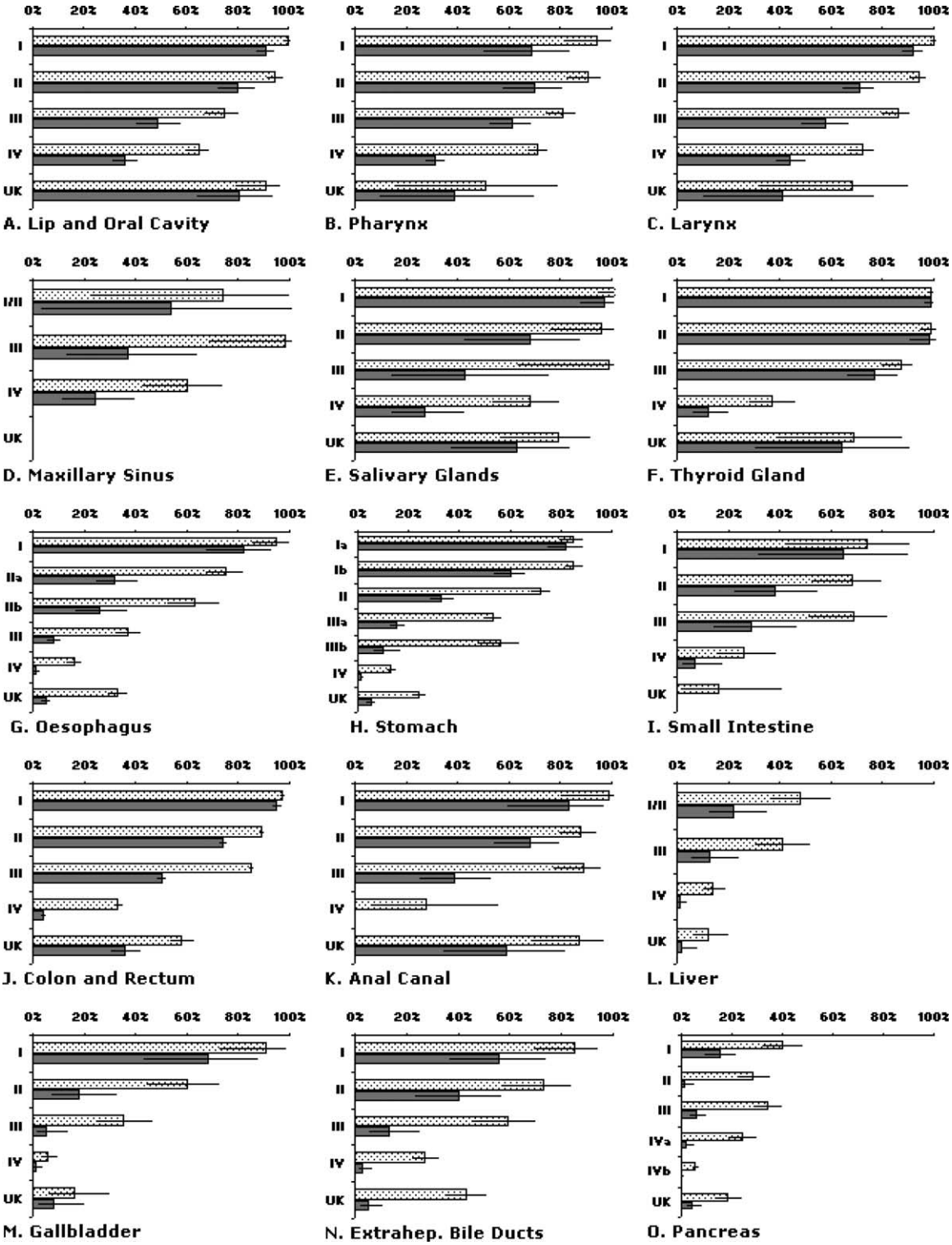

Fig. 1. One-year (□) and 5-year (■) relative survival of patients in North-Holland/Flevoland, The Netherlands, diagnosed with cancer of head and neck or the gastrointestinal organs in 1989–2001, according to tumour-node-metastasis (TNM)-stage (UK = unknown). Lines represent 95% confidence intervals (CI).

metastatic disease. The 5-year RSRs were almost equal for stages I and II pharyngeal carcinoma (69% and 70%, respectively), stages I and II thyroid carcinoma (99% and 98%, respectively) and stages II and III prostate carcinoma (91% and 88%, respectively). For carcinoma of the vagina and the penis the 5-year RSR was slightly higher in stage II than in stage I, but the 95% CIs largely overlapped.

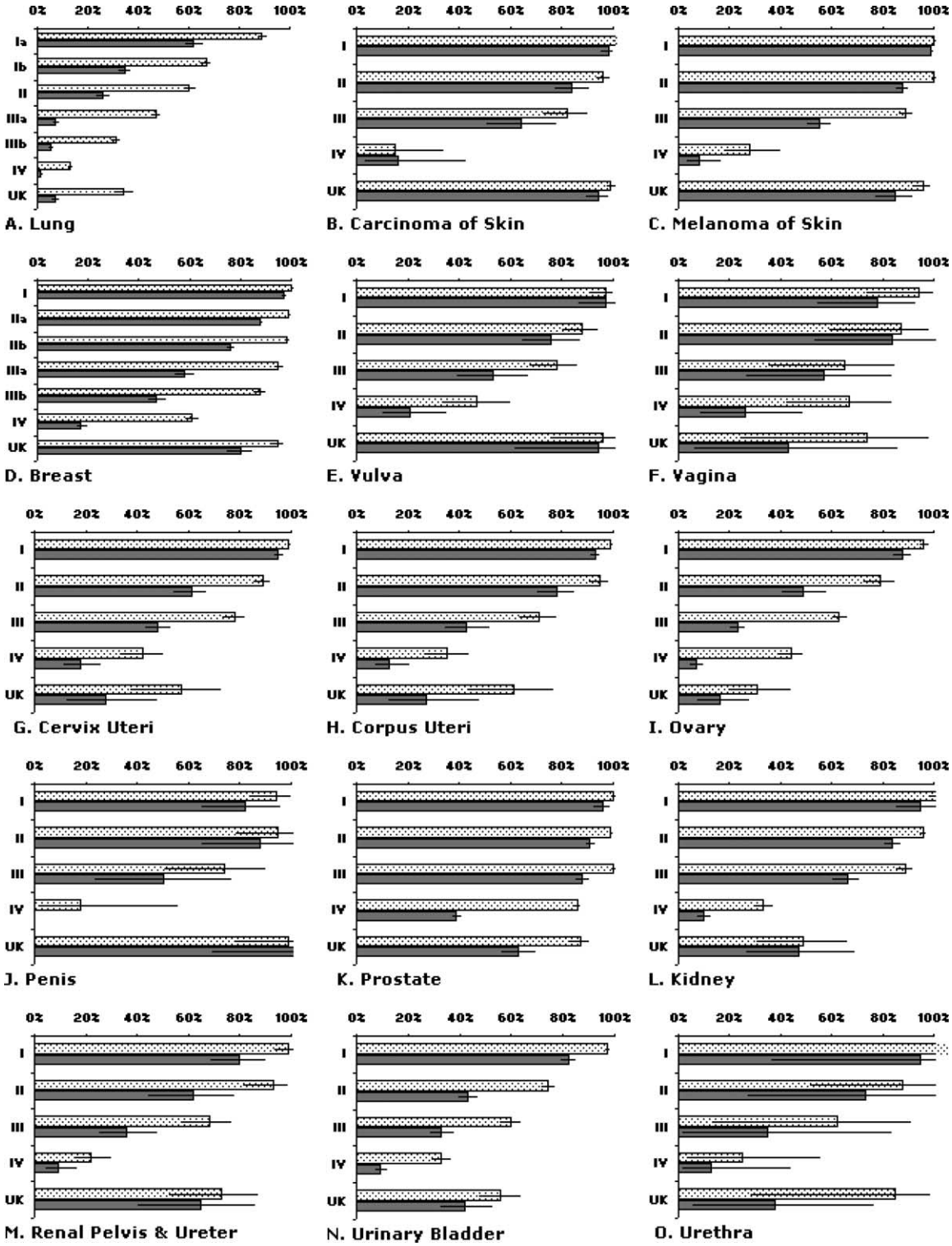

Fig. 2. One-year (⊡) and 5-year (■) relative survival of patients in North-Holland/Flevoland, The Netherlands, diagnosed with cancer of the lung, skin, breast, genital or urological organs in 1989–2001, according to tumour-node-metastasis (TNM)-stage (UK = unknown). Lines represent 95% confidence intervals (CI).

For stage I carcinomas, the 5-year RSR was generally between 80% and 100%. The risk of dying was almost equal to the general population risk for patients with stage I carcinoma of the salivary glands, thyroid, colon/rectum, skin, breast, female genital organs and urethra. For prostate carcinoma this figure was even above 100%. The 5-year RSR was relatively low for stage I lung carcinoma (62% and 35% for stages Ia and Ib,

respectively). The lowest RSR of stage I carcinoma was observed for pancreas (15%).

For the most frequent cancer sites (breast, lung, colon/rectum, prostate), 1-year RSRs for stage IV disease were observed of 61%, 13%, 33% and 86%, respectively. For many sites, the 5-year RSR for stage IV disease was ⩽1% (oesophagus, stomach, liver, gallbladder, pancreas, lung), but relatively high rates were observed for carcinoma of the lip/oral cavity (36%), pharynx (31%), larynx (44%) and prostate (31%). The 5-year RSR for stage IV breast carcinoma was also relatively high (17%).

Survival of cases with an unknown stage was close to stage I or stage II disease for cancers of the lip/oral cavity, skin, breast, vulva and penis, because these cases were mostly localised with an unknown T-category. For most other sites, survival of cases with unknown stage was intermediate to stages III and IV, because of the absence of apparent distant metastases.

In general, the variation in the stage-specific RSRs 5 years after diagnosis exceeded the variation in stage-specific RSRs 1 year after diagnosis. For example, the absolute differences in RSRs between stage I and stage IV breast cancer were 38% 1 year after diagnosis and 80% 5 years after diagnosis. For stages I and IV prostate carcinoma these figures are 17% and 68%, respectively.

No gender differences in stage-specific survival of lung or colorectal carcinoma were observed (Table 2). However, stage-specific survival of melanoma was more favourable in females, while stage-specific survival of bladder carcinoma was more favourable in males. Gender differences in survival for all stages combined were also observed for carcinoma of the larynx (higher survival in males), pharynx and thyroid (higher survival in females). This was mainly due to differences in stage distribution according to gender and no significant differences in stage-specific survival were observed (results not shown).

The 3-year RSR for all stages combined increased significantly between 1989–1991 and 1999–2001 for carcinomas of the breast, colon/rectum and prostate, but not for lung carcinoma (Table 3). Nevertheless, we ob-

Table 2
Percentage 5-year relative survival for selected sites according to stage and gender, North-Holland/Flevoland, The Netherlands, 1989–2001

Stage at diagnosis	Gender					
	Males			Females		
	Cases		% Survival (95% confidence interval)	Cases		% Survival (95% confidence interval)
	n	%		*n*	%	
Colon/rectum						
Stage I	1393	18	95 (92–98)	1346	18	96 (93–99)
Stage II	2410	32	74 (71–76)	2507	33	74 (72–77)
Stage III	1900	25	51 (48–54)	2020	26	48 (45–51)
Stage IV	1631	22	4 (3–5)	1504	20	4 (3–5)
Unknown	241	3	36 (28–45)	273	4	36 (28–44)
All stages	7575		55 (54–57)	7650		56 (55–57)
Lung						
Stage Ia	722	6	59 (55–64)	272	6	68 (61–74)
Stage Ib	1620	13	34 (31–37)	414	10	38 (33–43)
Stage II	956	8	26 (22–29)	233	6	28 (22–35)
Stage IIIa	1680	14	8 (7–10)	585	14	9 (6–11)
Stage IIIb	2570	21	4 (4–5)	915	22	5 (4–7)
Stage IV	3999	33	1 (1–1)	1597	38	1 (1–2)
Unknown	561	5	5 (3–7)	173	4	13 (8–19)[a]
All stages	12,108		13 (12–13)	4189		13 (12–14)
Melanoma						
Stage I	931	48	98 (95–100)	1561	56	100 (98–101)
Stage II	574	30	83 (79–87)	761	27	91 (88–94)[a]
Stage III	324	17	49 (42–56)	134	5	61 (54–68)
Stage IV	39	2	11 (4–24)	26	1	0
Unknown	69	4	79 (63–92)	132	5	88 (78–95)
All stages	1937		83 (81–86)	2781		92 (90–93)[a]
Bladder						
Stage I	1644	48	83 (80–86)	356	37	78 (72–85)
Stage II	855	25	45 (41–50)	240	25	37 (29–45)
Stage III	402	12	38 (32–44)	137	14	20 (13–29)[a]
Stage IV	428	12	8 (5–12)	185	19	9 (5–14)
Unknown	108	3	47 (34–60)	42	4	29 (14–46)
All stages	3437		58 (56–60)	960		45 (41–48)[a]

[a] Survival in males differs from survival in females ($P < 0.05$).

Table 3
Percentage 3-year relative survival according to stage and period of diagnosis, North-Holland/Flevoland, The Netherlands

Stage at diagnosis	Period of diagnosis					
	1989–1991			1999–2001		
	Cases		% Survival (95% confidence interval)	Cases		% Survival (95% confidence interval)
	n	%		*n*	%	
Colon/rectum						
Stage I	612	19	96 (92–99)	624	17	96 (93–99)
Stage II	999	31	76 (73–80)	1246	33	81 (78–84)
Stage III	798	25	57 (54–61)	1018	27	65 (61–69)
Stage IV	659	21	5 (4–7)	771	20	13 (11–16)[a]
Unknown	105	3	38 (27–50)	112	3	36 (25–49)
All stages	3173		59 (57–61)	3771		64 (62–66)[a]
Lung, small cell carcinoma						
Stage I and II	96	12	15 (9–24)	39	6	24 (11–40)
Stage IIIa	121	15	12 (7–18)	105	15	12 (6–20)
Stage IIIb	125	15	7 (3–13)	150	22	9 (5–15)
Stage IV	394	49	1 (1–3)	382	55	2 (1–4)
Unknown	72	9	8 (3–16)	18	3	6 (0–25)
All stages	808		9 (4–8)	694		6 (5–9)
Lung, non-small cell carcinoma						
Stage Ia	229	8	66 (59–73)	195	7	86 (79–92)[a]
Stage Ib	481	16	39 (35–44)	326	11	54 (48–60)[a]
Stage II	288	10	29 (24–35)	214	7	42 (34–50)
Stage IIIa	434	14	13 (10–17)	354	12	18 (13–22)
Stage IIIb	602	20	6 (6–9)	664	23	9 (6–11)
Stage IV	769	26	2 (1–3)	1074	37	3 (2–4)
Unknown	210	7	11 (7–17)	62	2	16 (8–28)
All stages	3013		19 (17–20)	2889		20 (19–22)
Breast						
Stage I	1166	29	97 (96–99)	2023	36	100 (99–101)
Stage IIa	1296	32	91 (89–93)	1724	31	97 (95–98)[a]
Stage IIb	817	20	84 (81–87)	1032	19	89 (87–92)
Stage IIIa	157	4	62 (54–70)	184	3	69 (60–76)
Stage IIIb	189	5	58 (50–66)	261	5	60 (52–67)
Stage IV	268	7	32 (26–38)	296	5	28 (23–34)
Unknown	128	3	89 (80–95)	58	1	76 (61–88)
All stages	4021		85 (83–86)	5578		90 (89–91)[a]
Prostate						
Stage I	91	4	104 (91–114)	75	2	99 (86–107)
Stage II	887	43	92 (86–95)	1716	54	99 (96–101)
Stage III	216	10	92 (79–95)	667	21	97 (94–101)
Stage IV	670	32	47 (32–41)	685	22	60 (55–64)[a]
Unknown	215	10	72 (54–72)	40	1	64 (40–85)
All stages	2079		76 (68–74)	3183		90 (88–92)[a]

[a] Survival in 1999–2001 differs from survival in 1989–1991 ($P < 0.05$).

served an increase in the 3-year RSR for the lower stages of non-small cell lung carcinoma (NSCLC). The 3-year RSR for stage Ia increased from 66% to 86%, for stage Ib from 39% to 54% and for stage II from 29% to 42%. This increase in RSR for the lower stages of NSCLC coincided with a decrease in the proportion of early stages of NSCLC. The proportion of stage I decreased from 24% in 1989–1991 to 18% in 1999–2001, stage II decreased from 10% to 7% and stage IIIa from 14% to 12%. The proportions of stages IIIb and IV increased.

The 3-year RSR increased for all stages of colorectal carcinoma, except for stage I. The largest increase was observed for stages III and IV (7% and 8%, respectively). The increase for stage II was 5%. The stage distribution of colorectal cancer hardly changed between 1989–1991 and 1999–2001.

For breast carcinoma, the largest increases in 3-year RSR were observed for stages II and IIIa (5–7%). The increase was statistically significant for stage IIa only. The 3-year RSR of stage I breast carcinoma increased by 3% to reach 100% in 1999–2001, while no increase was observed for stage IV breast carcinoma.

For stages I–III prostate carcinoma, the 3-year observed survival in 1999–2001 almost equalled expected

survival (RSR 97–99%), but the largest increase was observed for stage IV (47% in 1989–1991, 60% in 1999–2001).

4. Discussion

The Amsterdam Cancer Registry is one of few population-based cancer registries worldwide collecting data on stage and follow-up. The excellent population registers in The Netherlands enabled us to obtain near complete data on the vital status of 108,000 cancer patients diagnosed in 1989–2001. Stage-specific 5-year RSRs ranged from close to 100% for stage I carcinoma of the salivary glands, thyroid, colon/rectum, skin, breast, female genital organs, prostate and urethra to 1% or less for stage IV carcinoma of the oesophagus, stomach, liver, gallbladder, pancreas and lung. Although the poor survival for metastatic disease may be somewhat disappointing, it reflects common knowledge and is an indication for a high level of completeness of follow-up in our data.

Comparison with other registries is hampered by a variety of factors. The observed RSRs were generally equal to the rates from another Dutch registry with similar methods as our registry, the Eindhoven Cancer Registry [13], but Table 4 shows that our rates are generally lower than in the USA according to SEER Program data [14,15]. This difference might be real, but could also be caused by a lower level of completeness of follow-up in SEER-data, as suggested by relatively high RSRs for stage IV disease in the USA. Differences in staging procedures also might influence stage-specific RSRs. For example, in endometrial carcinoma the stage-specific RSRs are lower in our data than in SEER-data, but the difference for all stages combined is only 1%. As survival of cases with unknown stage is rather high according to SEER, these cases also comprise many cases with localised disease, while in our data the cases with unknown stage are mostly cases with advanced disease. This implies that the level of certainty of the reported TNM-stage differs considerably between our data and the SEER-data. Screening procedures may also influence stage-specific survival. Although screening for prostate-specific antigen (PSA) also occurred in our region to some extent, prostate cancer incidence in the USA is twice as high [16] and the vast majority of localised prostate cancers in the USA is detected by PSA-screening. These cases have a survival which equals or even exceeds the survival of the general population, which was also observed for stage I prostate carcinoma in our region. A higher socio-economic status of patients with prostate carcinoma detected by PSA-screening might contribute to this observation. Finally, more aggressive treatment regimens in the USA may have caused a

Table 4
Five-year relative survival rates for selected cancer sites according to stage in The Netherlands (1989–2001) and the United States of America (USA) (1990–1999)

Cancer site/stage	Cancer registry		Cancer site/stage	Cancer registry	
	ACR, % survival[a]	SEER, % survival[b]		ACR, % survival[a]	SEER, % survival[b]
Colon and rectum			Breast		
Stage I	95	95	Stage I	97	100
Stage II	74	82	Stage II	83	85
Stage III	50	57	Stage III	52	58
Stage IV	4	7	Stage IV	17	19
Unknown	36	61	Unknown	80	80
All stages	56	62	All stages	82	86
Lung			Corpus uteri		
Stage I	44	56	Stage I	93	98
Stage II	26	32	Stage II	78	82
Stage III	6	9	Stage III	43	62
Stage IV	1	2	Stage IV	13	28
Unknown	7	16	Unknown	27	71
All stages	13	15	All stages	83	84
Prostate			Ovary		
Stage I	96	100	Stage I	88	94
Stage II	91	100	Stage II	49	78
Stage III	88	100	Stage III	23	45
Stage IV	39	53	Stage IV	7	19
Unknown	63	100	Unknown	16	49
All stages	76	96	All stages	37	53

[a] The ACR (Amsterdam Cancer Registry) covers 17% of the population of The Netherlands.
[b] Based on 9 SEER (Surveillance, Epidemiology, and End Results) registries which cover approximately 9.5% of the population of the USA.

better survival in the USA than in The Netherlands [17,18].

Gender differences in stage-specific survival were confined to melanoma and bladder carcinoma, probably caused by differences in distribution according to subsite (melanoma) and anatomical dissimilarities (bladder).

Although the overall survival of patients with lung cancer was poor and no significant increase in overall survival was observed over time, the increase in survival of the lower stages of NSCLC was remarkable. As this increase in survival coincided with a decrease in the proportion of lower and unknown stages, while the proportion of the higher stages increased, this phenomenon (stage migration) is probably caused by improved staging procedures for lung cancer, as described earlier by Feinstein *et al.* [19]. In 1999, imaging with positron emission tomography (PET) was introduced in our region for pre-operative staging of NSCLC patients. Consequently, the total number of thoracotomies and the number of futile thoracotomies decreased [20], while the patients without lymph node metastasis who remained eligible for a thoracotomy, experienced an improved survival.

Stage-specific survival of breast cancer patients increased for stages I–IIIb. Although the stage distribution of patients with breast cancer changed between 1989–1991 and 1999–2001, improved staging procedures are less likely to have caused the improved survival. Axillary lymph node dissections were routinely performed throughout the study period and no stage migration towards higher stages was observed. To the contrary, the proportion of lower stages increased between 1989–1991 and 1999–2001, due to the start of the breast cancer screening in 1990. Because the overall incidence of breast cancer increased by 25% between 1990 and 2000 and even by 40% for women between 50 and 70 years of age [21], overdiagnosis of screen-detected breast cancers may have occurred. This phenomenon may have contributed to improved survival in early stage breast cancer. It is likely that adjuvant treatment of breast cancer with hormones and/or chemotherapy also has contributed to improved survival [22], as its application gradually increased between 1989–1991 and 1999–2001 in our region, from 11% to 24% in stage I, from 35% to 75% in stage IIa and from 70% to 90% in stage IIb. In a study by Vervoort *et al.* [23], the increased adjuvant treatment in The Netherlands is predicted to reduce breast cancer mortality in women aged 55–74 years by 7% in the year 2007. Finally, stage migration within stages may have contributed to improved survival. For example, in stage I the proportion of tumours with a diameter of 10 mm or less (T1a/b) increased from 23% in 1989–1991 to 32% in 1999–2001 and in stage IIa the proportion of tumours with a diameter of 20 mm or less (T1) increased from 38% in 1989–1991 to 55% in 1999–2001.

Overdiagnosis of previously unnoticed cases may have contributed to improved survival of localised prostate cancer. Between 1989–1991 and 1999–2001, the number of localised carcinomas doubled (mostly due to PSA screening), while the number of stage IV carcinomas hardly increased. However, the increase in the RSR for stage IV prostate carcinoma cannot be attributed to effects of early detection and a more likely explanation relates to changes in the hormonal treatment of stage IV carcinoma. In localised prostate carcinoma, treatment may also have improved survival, as the percentage of patients with wait-and-see policy decreased in favour of the percentage of patients who underwent a prostatectomy or curative radiotherapy.

The stage distribution of colorectal cancer hardly changed in the 1990s. Thus, the increase in survival of colorectal cancer cannot be attributed to improved staging procedures or early detection. Most likely, changes in treatment practices have contributed to an improved stage-specific survival of colorectal cancer. Between 1989–1991 and 1999–2001, the proportion of patients with stage III colon carcinoma who received adjuvant chemotherapy increased from 5% to 49% and the application of radiotherapy for stage II/III rectal carcinoma changed from post-operative to pre-operative. Also, the surgical procedures for rectal surgery improved by the introduction of the total mesorectal excision in 1996/97. As the survival of colorectal carcinoma mainly increased in stages II and III, and the largest increase was observed for rectal carcinoma (results not shown), the above changes in the treatment of colorectal cancer are likely to have caused the improvement in survival [24]. In stage IV colorectal carcinoma, the increased application of metastasectomy (in 3% and 6% of patients in 1989–1991 and 1999–2001, respectively) and increased treatment with chemotherapy (15% and 42% in 1989–1991 and 1999–2001, respectively) may have contributed to an increased survival.

In conclusion, in comparison with 1989–1991 improved stage-specific RSRs were observed for the most common cancers diagnosed in 1999–2001, probably related to screening (breast, prostate), treatment (breast, colon/rectum, prostate) and staging procedures (lung). Improved stage-specific RSRs may contribute to an overall improvement in the survival of specific cancers and, in the end, a decreased mortality due to these cancers, but, as the results for lung cancer show, this is not necessarily so.

Conflict of interest statement

None declared.

Acknowledgements

We thank the registration clerks of the Amsterdam Cancer Registry for collecting and checking the data.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ejca.2005.03.037.

References

1. Coleman MP, Gatta G, Verdecchia A, *et al.* EUROCARE-3 summary: cancer survival in Europe at the end of the 20th century. *Ann Oncol* 2003, **14**(Suppl. 5), v128–v149.
2. Piccirillo JF, Tierney RM, Costas I, *et al.* Prognostic importance of comorbidity in a hospital-based cancer registry. *JAMA* 2004, **291**, 2441–2447.
3. Houterman S, Janssen-Heijnen ML, Verheij CD, *et al.* Comorbidity has negligible impact on treatment and complications but influences survival in breast cancer patients. *Br J Cancer* 2004, **90**, 2332–2337.
4. Sant M, Allemani C, Capocaccia R, *et al.* Stage at diagnosis is a key explanation of differences in breast cancer survival across Europe. *Int J Cancer* 2003, **106**, 416–422.
5. Monnet E, Faivre J, Raymond L, *et al.* Influence of stage at diagnosis on survival differences for rectal cancer in three European populations. *Br J Cancer* 1999, **81**, 463–468.
6. Van der Sanden GA, Coebergh JWW, Schouten LJ, *et al.* Cancer incidence in the Netherlands in 1989 and 1990. First results of the nationwide Netherlands Cancer Registry. *Eur J Cancer* 1995, **31**, 1822–1829.
7. Parkin DM, Whelan SL, Ferlay J, *et al.*, editors. Cancer incidence in five continents volume VII. Lyon: IARC Scientific Publication No. 143; 1997.
8. International Union Against Cancer (UICC) Hermanek P, Sobin LH, eds. *TNM classification of malignant tumours*. 4th ed. Berlin, Springer, 1987. revised 1992.
9. International Union Against Cancer (UICC) Sobin LH, Wittekind C, eds. *TNM classification of malignant tumours*. 5th ed. New York, Wiley, 1997.
10. Dickman P, Sloggett A, Hills M. Life table estimates of relative survival, July; 2002. Available from: www.pauldickman.com/index.php.
11. Hakulinen T, Abeywickrama KH. A computer package for relative survival analysis. *Comp Biomed* 1985, **19**, 197–207.
12. Statistics Netherlands. Statline. March 2003. Available from: http://statline.cbs.nl/StatWeb/start.asp?LA=nl&lp=Search/Search.
13. Voogd AC, Coebergh JWW, Janssen-Heijnen MLG, et al., eds. *Cancer incidence, care and survival in the South of the Netherlands, 1955–1999*. Eindhoven, Integraal Kankercentrum Zuid, 2001.
14. Gloeckler Ries LA, Reichman ME, Lewis DR, *et al.* Cancer survival and incidence from the Surveillance, Epidemiology, and End Results (SEER) program. *Oncologist* 2003, **8**, 541–552.
15. SEER Cancer Statistics Review, 1975–2001. 5-Year Survival Rates, August; 2004. Available from: http://seer.cancer.gov/csr/1975_2001/results_merged/topic_survival. pdf.
16. Ferlay J, Bray F, Pisani P, *et al. GLOBOCAN 2002: Cancer incidence, mortality and prevalence worldwide. ARC CancerBase No. 5. Version 2.0*. Lyon, IARC Press, 2004.
17. Stanford JL, Stephenson RA, Coyle LM, *et al. Prostate Cancer Trends 1973–1995, SEER Program, National Cancer Institute*. NIH Publication No. 99-4543, Bethesda, MD: NIH; 1999.
18. Visser O, Horenblas S. Incidentie en behandeling van prostaatkanker in de regio van het Integraal Kankercentrum Amsterdam Incidence and treatment of prostatic carcinoma in the region of the Comprehensive Cancer Center Amsterdam, 1989–1994. *Ned Tijdschr Geneeskd* 1996, **140**, 2627–2631.
19. Feinstein AR, Sosin DM, Wells CK. The Will Rogers phenomenon. Stage migration and new diagnostic techniques as a source of misleading statistics for survival in cancer. *N Engl J Med* 1985, **312**, 1604–1608.
20. Van Tinteren H, Hoekstra OS, Smit EF, *et al.* Effectiveness of positron emission tomography in the preoperative assessment of patients with suspected non-small-cell lung cancer: the PLUS multicentre randomised trial. *Lancet* 2002, **359**, 1388–1393.
21. Visser O, Siesling S, Van Dijck JAAM, eds. *Incidence of cancer in the Netherlands 1999/2000*. Utrecht, Vereniging van Integrale Kankercentra, 2003.
22. Gray R, Clarke M, Collins R, *et al.* The EBCTCG overview of adjuvant therapy of breast cancer. What are the implications for future studies? Early Breast Cancer Trialists' Collaborative Group. *Ann NY Acad Sci* 1993, **698**, 339–448.
23. Vervoort MM, Draisma G, Fracheboud J, *et al.* Trends in the usage of adjuvant systemic therapy for breast cancer in the Netherlands and its effect on mortality. *Br J Cancer* 2004, **91**, 242–247.
24. Taal BG, VanTinteren H, Zoetmulder FANACCP group. Adjuvant 5FU plus levamisole in colonic or rectal cancer: improved survival in stage II and III. *Br J Cancer* 2001, **85**, 1437–1443.