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Increasing incidence and improved survival of cancer in children and young adults in Southern Netherlands, 1973–1999

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Abstract

The aim of this study was to describe time trends in incidence, treatment and survival of children (0–14 years) and young adults (15–24 years) with cancer in an area in the Netherlands with a long registration period. Between 1973 and 1999, the population-based Eindhoven Cancer Registry (ECR) recorded 852 children and 1162 young adults with a malignancy and they were actively followed up until 1 July, 2003. The world standardised incidence rates for both children and young adults showed an increasing trend until 1997 and this flattened off afterwards (estimated annual percentage change [EAPC] = 3.1%, $P = 0.66$ for children and EAPC = 3.6%, $P = 0.06$ for young adults). Lymphomas in children and testicular malignancies and melanomas in young adults seemed to increase in particular. Better detection probably led to higher completeness for gliomas. Initial treatment for leukaemias and lymphomas in children has changed, protocols prescribe more chemotherapy and less radiotherapy. For all cancers combined, the 10-year survival rate for children significantly improved from 53% (95% confidence interval [95% CI] 45–61%) in 1973–1982 to 75% (95% CI 69–81%) in 1993–1999 (P-value < 0.05). The 10-year survival rate for young adults significantly improved from 57% (95% CI 49–65%) to 81% (95% CI 77–85%) (P-value < 0.05). We demonstrated significantly higher five-year survival rates for children with Hodgkin's disease (HD) and young adults with HD, non-seminoma or melanoma diagnosed in 1993–1999.

Keywords: Cancer; Childhood; Young adults; Incidence; Survival; Trends; Treatment

1. Introduction

Childhood malignancies are rare. In the 1990's, the cumulative risk for children 0–14 years of age was approximately 2 per 1000 children. They comprise 0.7% of all cancer diagnoses [1]. The incidence of childhood cancer shows great similarities in industrialised countries. Still, in Western countries, cancer is the second cause of death among children and adolescents [2].

In Europe, recently, a number of reports have been published on temporal variations in the incidence of childhood malignancies since the 1970's [3–6]. These studies exhibit an increasing trend in incidence for malignancies that commonly affect children: acute lymphoblastic leukaemia (ALL), Hodgkin's disease (HD) and malignant tumours of the central nervous system (CNS). Increases were also found for other tumours like germ cell tumours and hepatic tumours.

The survival of children (<15 years) with a malignancy in Western countries has improved considerably during the past 30 years due to improvements in therapy

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[7–10]. A clear decrease in mortality from all malignancies, by almost 50% since the late 1960's, has been observed for European children [2].

Cancer is also uncommon in young adults (15–24 years), with an annual incidence of approximately 2 per 1000 [11]. Until now, only a few studies have been published on cancer incidence and survival among young adults, particularly in the age group of 20–24 years. Indications for an increasing incidence of malignancies among 15–19 year-olds have been found in Europe [11–13] and the United States [7,14]. Over the last three decades mortality has decreased by more than 40% for patients aged 15–24 years in Europe, but by slightly less for male Dutch patients [15]. Compared with children younger than 15 years of age, the prognosis for all malignancies in 15–24 year-olds was worse [16].

We report here on the long-term trends in incidence, treatment and survival for different malignancies in children (0–14 years) and young adults (15–24 years) using data collected from the long-standing population-based Eindhoven Cancer Registry (ECR) in Southern Netherlands, during the period 1973–1999. Children and young adults were considered separately because of the different spectrums of cancers. In addition, in the Netherlands, children are treated in 5–7 specialised paediatric oncology centres and young adults, especially those 18 years and older, are treated in general and university hospitals.

Besides leukaemia, which was registered nationally since 1970 (the Dutch Childhood Leukemia Study Group (DCLSG)), this would be the only area in the Netherlands reporting such data for a period of more than 25 years.

2. Patients and methods

Data were collected from the ECR, which is part of one of nine Comprehensive Cancer Centres in the Netherlands. The ECR has collected data on all patients with cancer within a population living in a circumscribed area including the Dutch province of North Brabant and the northern part of the adjacent province of Limburg since the late 1950's [17]. Until 1988, only patients diagnosed in the south-eastern part of the area were registered, but since that year patients diagnosed in the middle and western part of North Brabant have also been registered. Nowadays, the registry serves a population of 2.3 million inhabitants. Since 1973, the registry is checked regularly for completeness [18], and is also compared with data from the DCLSG (renamed in 2003 as the Dutch Children Oncology Group (DCOG)) [19] and the adjacent paediatric oncology centres in Nijmegen, Amsterdam and Rotterdam. Since 1989, data on patients living in the registration area, but diagnosed and treated outside of the registration area, are obtained from adjacent registries through the Netherlands Cancer Registry.

The cancer registry receives lists of newly diagnosed cases on a regular basis, initially from 3, but now from 6 Pathology Departments in the region. In addition, lists of hospitalised cancer patients are provided from the Medical Records Departments of the hospitals. Following this notification, trained personnel from the registry actively collect data on patient and tumour characteristics from the medical records. Since children diagnosed with a malignancy in a regional hospital are usually referred to a paediatric oncology centre outside of the registration area, mostly Rotterdam and Nijmegen, supplementary information about their treatment and recent vital-status was also obtained from these centres. Active follow-up of all patients was performed through municipal population registries (until 1994) and through linkage with the national Central Bureau of Genealogy (CBG). The CBG automatically registers every death in the Netherlands since October 1994. The latest vital-status check was on 1 July, 2003.

Malignancies are classified according to histological origin, as described in the third revision of the International Classification of Diseases for Oncology (ICD-O) and further grouped according the International Classification for Childhood Cancer (ICCC) criteria [20] (Table 1).

For our statistical analyses, year of diagnosis was divided into three periods: 1973–1982, 1983–1992 and 1993–1999. These time periods were determined by the availability of data as the original area grew with the extension of the cancer registry and the neurosurgical centre allowing for complete data collection in 1983. Analyses were performed for all malignancies combined and for the most common malignancies separately: leukaemias, lymphomas, gliomas and other CNS tumours, testicular carcinomas and melanomas. Since recording of CNS tumours may have been incomplete before the 1980's, only patients diagnosed from 1983 onwards were included in these analyses.

The population-at-risk for each year was determined by using data from Statistics Netherlands. For each tumour type, age-specific (<1 year, 1–4 years, 5–9 years, 10–14 years, 15–19 years and 20–24 years of age) incidence rates were calculated per 1,000,000 person-years, according to gender and period of diagnosis. For the three above-mentioned time intervals, age-standardised incidence rates were calculated using the World Standard Population as a reference group [21]. In addition, three-year moving world standardised incidence and mortality rates were calculated for children as well as for young adults for the period of 1983–1999. Trends were estimated by calculating the Estimated Annual Percentage Change (EAPC). A regression line was fitted to the natural logarithm of the rates using calendar year as a regressor variable, i.e., $y = mx + b$, where $y = \ln(\text{rate})$

Table 1
Classification and numbers of patients in the different and most frequent disease subgroups, diagnosed in 1973–1999 in Southern Netherlands

ICCC-code	Diagnostic group[a]	Morphology (ICD-O-3)	Children (0–14 years)				Young adults (15–24 years)			
			Male		Female		Male		Female	
			N	(%)[c]	N	(%)[c]	N	(%)[c]	N	(%)[c]
I	**Leukaemia**		**154**	**(32.2)**	**119**	**(31.8)**	**66**	**(11.1)**	**40**	**(7.1)**
(a)	Acute lymphoblastic	9820–9827, 9832–9837, 9850	115	(24.1)	93	(24.9)	34	(5.7)	18	(3.2)
(b)	Acute non-lymphoblastic	9840, 9841, 9861, 9864, 9866, 9867, 9871–9874, 9891, 9894–9897, 9910, 9920	28	(5.9)	16	(4.3)	22	(3.7)	17	(3.0)
(c + d + e)	Other specified and unspecified	9800–9804, 9830, 9835–9837, 9842, 9860, 9862, 9863, 9868, 9870–9890, 9892, 9893, 9900, 9930–9946	11	(2.3)	10	(2.7)	10	(1.7)	5	(0.9)
II	**Lymphomas and reticuloendothelial neoplasms**		**74**	**(15.5)**	**44**	**(11.8)**	**145**	**(24.3)**	**112**	**(19.8)**
(a)	Hodgkin's disease	9650–9667	24	(5.0)	17	(4.5)	82	(13.8)	84	(14.8)
(b + c)	Non-Hodgkin's lymphoma and Burkitt's lymphoma	9591–9595, 9670–9719, 9723, 9727–9729, 9755	40	(8.4)	21	(5.6)	60	(10.1)	25	(4.4)
(d + e)	Other specified neoplasms and unspecified lymphomas	9590, 9596, 9720, 9722, 9730–9754, 9756–9764	10	(2.1)	6	(1.6)	3	(0.5)	3	(0.5)
III	**CNS and miscellaneous intracranial and intraspinal neoplasms[d]**		**65**	**(13.6)**	**64**	**(17.1)**	**42**	**(7.0)**	**42**	**(7.4)**
(a + b + d)	Astrocytoma, ependymoma and other gliomas	9380–9384, 9390–9394, 9400–9460, 9481	46	(9.6)	43	(11.5)	37	(6.2)	35	(6.2)
(c + e + f)	Primitive neuroectodermal tumours, other specified and unspecified intracranial and intraspinal neoplasms	8000–8005, 8270–8281, 8300, 9350–9362, 9470–9474, 9480, 9493, 9505, 9530–9539, 9990	19	(4.0)	21	(5.6)	5	(0.8)	7	(1.2)
X	**Germ cell, trophoblastic and other gonadal neoplasms**		**14**	**(2.9)**	**15**	**(4.0)**	**169**	**(28.4)**	**58**	**(10.2)**
(c)	Gonadal germ cell tumours	9060-9102[b]	7	(1.5)	5	(1.3)	151	(25.3)	14	(2.5)
XI	**Carcinomas and other malignant epithelial neoplasms**		**13**	**(2.7)**	**20**	**(5.3)**	**95**	**(15.9)**	**238**	**(42.0)**
32(d)	Malignant melanoma	8720–8780	5	(1.0)	7	(1.9)	29	(4.9)	103	(18.2)
	Other		158	(33.1)	112	(29.9)	79	(13.3)	76	(13.4)
	All malignancies		478	(100%)	374	(100%)	596	(100%)	566	(100%)

CNS, central nervous system; ICCC, International Classification for Childhood Cancer; ICD, International Classification of Diseases.

[a] Used in this study.

[b] Subclassified as seminoma (codes 9060–9064) and non-seminoma (other codes) for males.

[c] % of all registered malignancies, coded according to the ICD-O-3 codes and diagnosed between 1973 and 1999.

[d] Diagnosed since 1983.

and x = calendar year [22]. This calculation assumes that the rates have changed at a constant rate over the entire period. Disease-specific mortality rates were derived from Statistics Netherlands.

For primary treatment, three or four major subgroups were considered for each malignancy; chemotherapy alone, chemotherapy in combination with radiotherapy, radiotherapy alone, surgery alone and surgery in combination with chemotherapy or radiotherapy. In 1993–1999, therapy 'other' was composed of chemotherapy in combination with bone marrow or stem cell transplantation. For both children (0–14 years) and young adults (15–24 years), plausible changes in primary treatment over time were considered. Treatment of melanomas and testicular carcinomas was only considered for young adults.

Crude survival rates were computed (LIFETEST procedure) as the time between diagnosis and death or the end of study (1 July, 2003). 1-, 3-, 5-, 10-, 15- and 20-year survival rates were computed according to age group (child or young adult), period of diagnosis and tumour type. Confidence Intervals (CIs) of crude and tumour-specific proportions were computed using the same procedure. CNS tumours were considered as one tumour type.

A total number of 2014 patients younger than 25 years of age were included in our study. For the treatment and survival analyses, second malignancies ($N = 35$, 2%) were excluded. Patients who survived less than one day ($N = 20$, 1%) were also excluded in the survival analyses. For these analyses, 6% ($N = 113$) of the patients were lost to follow-up; 39 children and 74 young adults.

3. Results

3.1. Incidence and mortality

852 children (<15 years) and 1162 young adults (15–24 years) were diagnosed with a malignancy between 1973 and 1999. The histological distribution of tumours is shown in Table 1. For all malignancies combined, the male-female ratio was 1.3 for children and 1.1 for young adults.

The most frequent malignancies in children were ALL and gliomas (24% and 11%, respectively). Young adults suffered mainly from HD, testicular carcinomas and melanomas (14%, 13% and 11%, respectively). Melanomas were almost four times more common among young women than young men.

The age-specific incidence rates for all tumour types together appeared to increase over time for all age groups, except for infants (Tables 2A and 2B). Among boys, incidence rates of HD showed a marked increase, especially in age groups 10–14 and 20–24 years and incidence rates of gliomas have also increased considerably in these two age groups. Incidence rates of testicular carcinomas and melanomas (both young adults) more than doubled in 25 years. Among girls, incidence rates have increased remarkably for gliomas in the age group 15–19 years, for melanomas (young adults) and for ALL and NHL among 20–24-year-old females. Among boys, increased incidence rates of ALL were found for 10–14-year-olds and increased incidence rates of NHL at age 15–19 years. But, the low numbers of patients in certain age groups refrain us from designating the increases as unequivocal trends.

The world standardised incidence rates for both children and young adults increased until 1997, but flattened after that year (Fig. 1) and was not significant for children (EAPC = 3.1%, $P = 0.66$), in contrast to young adults (EAPC = 3.6%, $P = 0.06$).

The world standardised mortality rate for children exhibited a decreasing trend, but was not significant (EAPC = −3.1%, $P = 0.71$) (Fig. 1(a)). The regression line of the mortality rate for young adults showed a slight, but insignificant increase (EAPC = 12.6%, $P = 0.88$) (Fig. 1(b)).

3.2. Treatment

Figs. 2(a)–(e) show the observed changes in initial treatment over time for children and young adults. In the period 1993–1999, most children with ALL received chemotherapy alone, whereas many children received radiotherapy alone or in combination with chemotherapy in the first period. Young adults also received more chemotherapy over time, though this was often given in combination with radiotherapy.

For patients with HD, treatment with chemotherapy alone has increased dramatically, from 20% of the children receiving chemotherapy in 1973–1982 to >95% in 1993–1999. Since the beginning of the 1980's, children with NHL were more often given chemotherapy alone, whereas young adults were more frequently given radiotherapy.

Children and young adults with a glioma increasingly appeared to undergo surgery without radiotherapy.

Testicular tumours were analysed as seminoma and non-seminoma ($N = 151$). No 15–19 year old patients and only 20 of these patients aged 20–24 were diagnosed with seminoma. In the period from 1983 to 1992, patients with non-seminoma received surgery alone more often compared with patients treated in 1970's. In the older age group, a continuing increase in surgery alone was seen in the 1990's. In the last time period, treatment seemed to change for patients aged 15–19 years, they received more surgery in combination with chemotherapy.

All patients with melanoma underwent surgery.

Table 2A
Age-specific and age-adjusted (WSR) incidence rates per 1,000,000 for children and young adults (males) diagnosed in Southern Netherlands

Males		Children (groups in years)						Young adults (groups in years)		
Tumour	Period of diagnosis	No.	0	1–4	5–9	10–14	WSR	No.	15–19	20–24
ALL	1973–82	33	–	48.9	26.3	10.8	30.5	7	11.0	4.9
	1983–92	33	4.6	43.5	20.8	6.2	27.1	18	19.1	11.1
	1993–99	49	2.1	51.2	32.6	20.6	37.1	9	11.1	7.6
ANLL	1973–82	10	2.9	20.1	4.8	–	10.4	3	4.4	2.4
	1983–92	4	2.3	4.6	–	2.1	3.3	9	5.2	9.5
	1993–99	14	4.3	8.5	6.5	11.4	10.4	10	13.3	7.6
Other leukaemias	1973–82	4	5.8	5.8	–	–	4.5	4	4.4	4.9
	1983–92	3	–	4.6	–	2.1	2.4	1	–	1.6
	1993–99	4	4.3	4.3	–	–	3.3	5	6.7	3.8
HD	1973–82	3	–	2.9	2.4	2.2	2.5	21	22.0	26.7
	1983–92	9	–	2.3	–	16.6	5.7	25	19.1	22.2
	1993–99	12	–	–	4.2	22.9	8.0	36	22.2	49.7
NHL	1973–82	13	–	2.9	19.1	8.6	9.8	10	11	12.1
	1983–92	13	–	4.6	16.1	8.3	9.4	28	20.9	25.4
	1993–99	14	–	6.4	13.0	11.4	10.0	22	24.4	21.0
Other lymphomas	1973–82	7	5.8	8.6	2.4	2.2	7.0	1	–	2.4
	1983–92	2	–	–	4.6	–	1.5	1	–	1.6
	1993–99	1	–	2.1	–	–	0.8	1	–	1.9
Glioma	1983–92	24	4.6	16.0	18.5	14.5	18.1	19	15.6	15.9
	1993–99	22	2.1	12.8	10.9	22.9	15.9	18	13.3	22.9
Other CNS	1983–92	10	–	–	11.5	6.2	5.5	–	1.7	6.4
	1993–99	9	–	8.5	8.7	2.3	6.8	5	–	–
Melanoma	1973–82	–	–	–	–	–	–	5	2.2	9.7
	1983–92	2	–	–	–	4.1	1.2	9	1.7	12.7
	1993–99	3	–	–	–	6.9	2.0	15	6.7	22.9
Testicular carcinoma	1973–82	4	2.9	8.6	–	–	4.5	20	11.0	36.4
	1983–92	2	–	4.6	–	–	1.8	63	24.3	77.8
	1993–99	1	2.1	–	–	–	0.8	68	37.7	97.5
Total male	1973–82[a]	102	25.9[a]	132.3[a]	67.0[a]	40.9[a]	94.7[a]	111	103.4[a]	155.2[a]
	1983–92	170	38.9	139.6	92.3	107.8	130.1	245	151.2	251.0
	1993–99	206	36.3	164.3	117.4	132.5	154.0	240	188.7	296.3

ALL, acute lymphoblastic leukaemia; ANLL, acute non-lymphoblastic leukaemia; HD, Hodgkin's disease; NHL, Non-Hodgkin's lymphoma.
[a] Partial incompleteness during 1973–1982, since brain tumours are not considered in this time interval in this study.

3.3. Survival

Since patients with second malignancies and those who survived less than one day were excluded from the survival analysis, data from 1959 patients were analysed. Of these, 603 (31%) had died and 113 (6%) were lost to follow-up.

For all cancers combined, the 10-year survival rate for children significantly improved from 53% (95% CI [95% CI] 45–61%) in 1973–1982 to 75% (69–81%) in 1993–1999 (P-value < 0.05) (Table 3A). Children with ALL or NHL exhibited the most marked improvement in survival, both 3-year survival rates significantly increased (ALL: 1973–1982; 67% (95% CI 55–79%) and 1993–1999; 88% (95% CI 80–96%). NHL: 1973–1982; 50% (95% CI 25–75%) and 1993–1999; 90% (95% CI 76–100%)). Five-year survival for children with ALL in 1993–1999 (85% (95% CI 77–93%)) was also significantly higher compared with the first period (61% (95% CI 47–75%)). Children with HD still have the best prognosis, 5-year survival 94% (95% CI 82–100%).

Ten-year overall survival rate for young adults significantly improved from 57% (95% CI 49–65%) to 81% (95% CI 77–85%) (P-value < 0.05) (Table 3B).

Five-year survival for young adult patients with non-seminoma and melanoma was high; in 1983–1992; 90% (95% CI 82–98%) and 87% (95% CI 77–97%), respectively, and in 1993–1999; 100% and 94% (95% CI 88–100%). It was significantly higher than the five-year

Table 2B
Age-specific and age-adjusted (WSR) incidence rates per 1,000,000 for children and young adults (females) in Southern Netherlands

Females		Children (groups in years)						Young adults (groups in years)		
Tumour	Period of diagnosis	No.	0	1–4	5–9	10–14	WSR	No.	15–19	20–24
ALL	1973–82	23	–	39.2	15.0	9.0	22.6	2	4.7	–
	1983–92	34	–	35.9	28.8	15.2	27.6	8	9.1	5.2
	1993–99	36	–	37.9	27.3	16.6	28.3	8	7.0	10.2
ANLL	1973–82	3	–	6.0	–	2.2	3.0	4	2.3	7.9
	1983–92	7	2.4	7.2	–	6.5	5.6	9	5.5	10.4
	1993–99	6	–	4.5	4.6	4.8	4.6	4	4.6	4.1
Other leukaemias	1973–82	4	–	6.0	–	4.5	3.6	1	2.3	–
	1983–92	5	–	9.6	2.4	–	4.5	2	1.8	1.7
	1993–99	1	–	–	2.3	–	0.7	2	–	4.1
HD	1973–82	5	–	–	2.5	9.0	3.4	23	18.6	39.7
	1983–92	6	–	–	2.4	10.9	3.9	29	14.6	36.4
	1993–99	6	–	–	2.3	11.9	4.2	32	32.5	36.7
NHL	1973–82	4	–	6.0	2.5	2.2	3.8	5	9.3	2.6
	1983–92	10	–	7.2	2.4	13.0	7.3	9	7.3	8.7
	1993–99	7	–	–	9.1	7.1	5.0	11	7.0	16.3
Other lymphomas	1973–82	–	–	–	–	–	–	1	2.3	–
	1983–92	4	4.8	2.4	2.4	–	3.6	1	–	1.7
	1993–99	2	2.2	–	–	2.4	1.6	1	–	2.0
Glioma	1983–92	20	–	12.0	19.2	15.2	15.2	19	9.1	24.2
	1993–99	23	6.7	15.6	15.9	14.3	17.9	16	20.9	14.3
Other CNS	1983–92	9	–	7.2	7.2	6.5	7.0	4	1.8	5.2
	1993–99	12	–	15.6	4.6	7.1	9.6	3	4.6	2.0
Melanoma	1973–82	1	–	–	–	2.2	0.7	11	7.0	21.2
	1983–92	2	–	2.4	–	2.2	1.6	41	16.4	55.4
	1993–99	4	–	2.2	–	7.1	2.9	51	25.5	81.6
Total female	1973–82[a]	85	30.2	93.5[a]	40.0[a]	62.9[a]	79.0[a]	97	88.6[a]	156.2[a]
	1983–92	144	43.1	117.2	69.7	104.2	114.8	230	137.0	268.5
	1993–99	145	22.3	120.5	84.3	104.5	112.8	239	188.0	322.4

[a] Partial incompleteness during 1973–1982, since brain tumours are not considered in this time interval in this study.

overall survival rate in 1983–1992; 70% (95% CI 66–74%) and in 1993–1999 82% (95% CI 78–86%). Patients with HD, diagnosed in 1993–1999, exhibited a borderline significantly higher five-year survival rate (91% (95% CI 85–97%)).

4. Discussion

Although our study includes small numbers, our observations are rather unique as the Eindhoven Cancer Registry was the only registry of solid childhood cancers in the Netherlands before 1989.

The patterns of increased incidence rates of childhood cancer and cancer in young adults roughly corresponds with that in other Western populations [3–7,11,12,23]. The increase in incidence of cancer has been more marked for young adults than for children, and can be attributed to increased incidence rates of testicular carcinomas and melanomas. Increased incidence rates may be partly explained by improved completeness of the registry since the 1980's, but may also be related to new diagnostic tools and a change in classification from benign to malignant (brain tumours). The registry was probably incomplete for tumours of the CNS before 1980 when the neurosurgical centre in Tilburg started collaborating with the registry.

The incidence of ALL was not as markedly increased as in some other European studies [3–5,11]. After the increase in the late 1970's and early 1980's, across the Netherlands [24] the incidence rate recurred, but seemed to increase again in the period 1993–1999, at least for boys.

Increasing parental age, decreasing parity, (high) birthweight and infections have been found to be related to the occurrence of ALL [25–27].

The apparent increase in ALL incidence among women aged 20–24 years is presently difficult to explain.

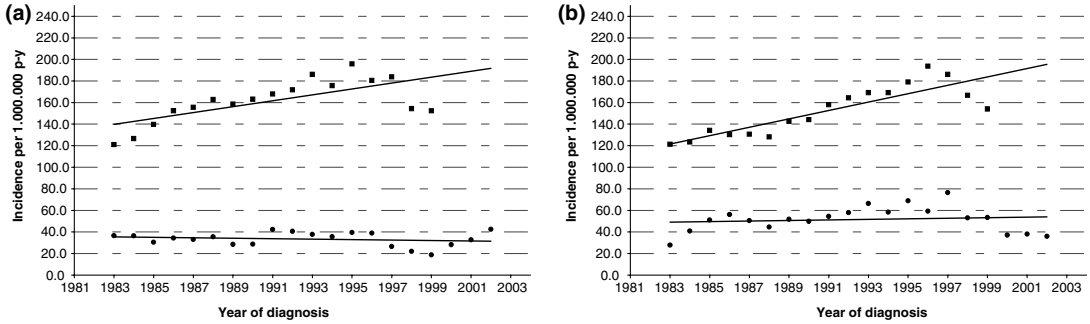

Fig. 1. (a) and (b) Three-year moving world standardised incidence and mortality rates, represented per 1,000,000 person–years (p–y). Incidence rates (squares) and mortality rates (dots) calculated for children (a) and young adults (b). For children the EAPC in incidence is 3.1% ($P = 0.66$).

An increase in the incidence of HD among children and young adults was also seen in the United States, England and Sweden [3,5]. A few cases of HD may have been classified as NHL during the 1970's [28], which disappeared later on with improvements in haematopathology. However, part of the increase in the incidence of

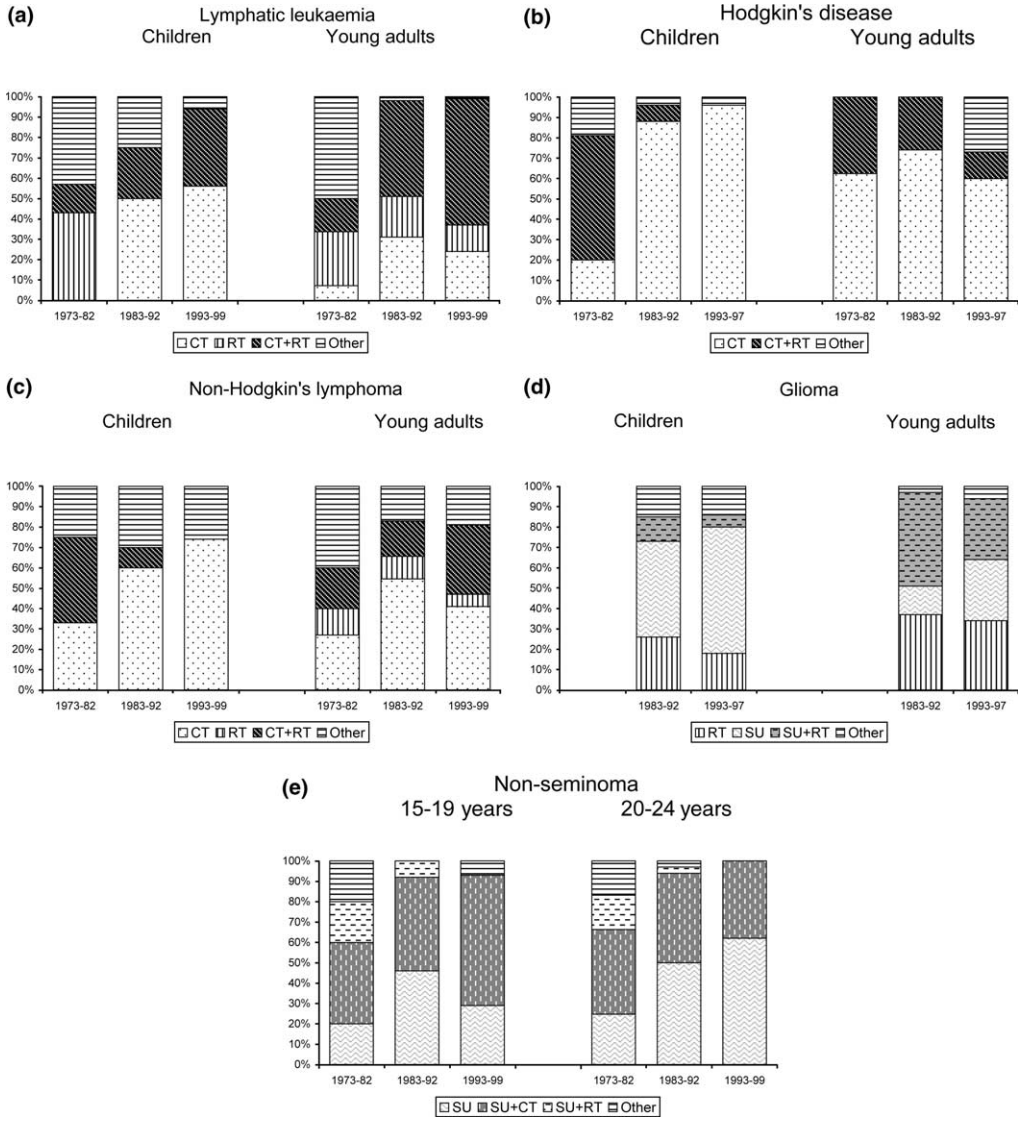

Fig. 2. (a)–(e) Changes in initial treatment over time for children (0–14 years) and young adults (15–24 years): CT, chemotherapy; RT, radiotherapy; SU, surgery.

Table 3A
Trends in crude survival (%) of children (0–14 years) diagnosed with cancer in Southern Netherlands between 1973 and 1999

Children boys ans girls	Survival after:		1 year		3 years		5 years		10 years		15 years		20 years	
	Period	No.	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
ALL	1973–82	54	87	(77–97)	67	(55–79)	61	(47–75)	57	(43–71)	57	(43–71)	57	(43–71)
	1983–92	66	92	(86–98)	83	(73–93)	77	(67–87)	76	(66–86)	73	(61–85)		
	1993–99	82	95	(91–99)	88	(80–96)	85	(77–93)						
HD	1973–82	8	88[a]	(64–100)	75[a]	(46–100)								
	1983–92	15	100	(–)	93	(79–100)	86	(68–100)	86	(68–100)				
	1993–99	18	100	(–)	100	(–)	94	(82–100)						
NHL	1973–82	16	63	(39–87)	50	(25–75)								
	1983–92	22	77	(59–95)	68	(48–88)	68	(48–88)	68	(48–88)				
	1993–99	20	90	(76–100)	90	(76–100)	85	(69–100)						
CNS tumours	1978–82													
	1983–92	62	73	(61–85)	68	(56–80)	63	(51–75)	61	(49–73)				
	1993–99	58	76	(64–88)	53	(39–67)	52	(38–66)						
All malignancies	1973–82	183	75	(69–81)	61	(53–69)	56	(48–64)	53	(45–61)	53	(45–61)	53	(45–61)
	1983–92	310	83	(79–87)	75	(71–79)	69	(63–75)	68	(62–74)	68	(62–74)		
	1993–99	326	87	(83–91)	77	(73–81)	75	(71–79)	75	(69–81)				

95% CI, 95% confidence interval.
[a] Effective sample size <10.

Table 3B
Trends in crude survival (%) of young adults (15–24 years) diagnosed with cancer in Southern Netherlands between 1973 and 1999

Young adults males and females	Survival after:		1 year		3 years		5 years		10 years		15 years		20 years	
	Period	No.	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
HD	1973–82	44	95	(86–100)	93	(85–100)	88	(78–98)	75	(61–89)	75	(61–89)	70	(56–84)
	1983–92	52	96	(90–100)	90	(82–98)	86	(76–96)	84	(74–94)	84	(74–94)		
	1993–99	68	100	(–)	91	(85–97)	91	(85–97)						
NHL	1973–82	15	60[a]	(35–85)	47[a]	(22–72)								
	1983–92	37	76	(62–90)	56	(40–72)	56	(40–72)	56	(40–72)				
	1993–99	32	78	(64–92)	63	(45–81)	63	(45–81)						
CNS tumours	1973–82													
	1983–92	47	83	(73–93)	66	(52–80)	55	(41–69)	43	(29–57)				
	1993–99	35	94	(86–100)	71	(55–87)	71	(55–87)						
Non–seminoma	1978–82	20	88	(72–100)	81	(61–100)	81	(61–100)						
	1983–92	63	96	(90–100)	92	(84–100)	90	(82–98)	90	(82–98)	87	(77–97)		
	1993–99	64	100	(–)	100	(–)	100	(–)						
Melanoma	1973–82	16	88	(72–100)	81	(61–100)	74	(52–96)						
	1983–92	50	100	(–)	92	(84–100)	87	(77–97)	85	(75–95)				
	1993–99	66	97	(93–100)	94	(88–100)	94	(88–100)						
All malignancies	1973–82	205	83	(77–89)	68	(62–74)	64	(58–70)	57	(49–65)	57	(49–65)	55	(47–63)
	1983–92	470	87	(83–91)	74	(70–78)	70	(66–74)	68	(64–72)	66	(62–70)		
	1993–99	465	92	(90–94)	83	(79–87)	82	(78–86)	81	(77–85)				

[a] Effective sample size <10.

HD might be real, because the incidence continued to increase in the 1990's. Infections may play a role in the same way as for leukaemias [3].

The increase in the incidence of gliomas and other CNS tumours seems largely attributable to refinements in diagnostic approaches [2]. However, the diagnostic approaches did not change that much in the 1990's whereas the incidence continued to increase for some groups during the 1990's. Recently, two inconsistent papers were published about birth characteristics in relation to brain tumours in children. A positive association between CNS tumours and low birth-weight (<2500 g) was found [29], but high birth-weight (>4000 g) also seemed associated with an increased risk for astrocytomas, the main subgroup of gliomas [30].

In 15–24-year-old girls, there was a large increase in the incidence of melanomas, for which the most likely explanation is increasing exposure to ultraviolet (UV) radiation due to intermittent sunbathing and sunburn [31].

In 15–24-year-old boys there was an increase in the incidence of testicular carcinomas, which seems to be a worldwide phenomenon [32]. Except for cryptorchism [32], potential risk factors should be mainly found in maternal exposures during pregnancy [33].

At the end of the 1970's, policies regarding cancer therapy may have changed due to the introduction of chemotherapy and new combinations thereof [34]. The prognosis for children with a malignancy improved considerably due to these improvements in therapy. Information about specific combinations of chemotherapy is only available in the cancer registry more recently. As effective, but aggressive, therapeutic protocols may have side-effects, of which second malignancies are the most severe [9], the major objective of treatment since the mid-1980's has been a reduction in treatment-related side-effects and a focus on quality of life. A 5.2% standardised incidence ratio was found for the development of any second malignancy after megavoltage radiation for paediatric tumours in 1954–1980 [35]. A significantly increased risk for the development of any second malignant neoplasm after childhood cancer was found for children treated with different chemotherapeutic agents in 1980–1998 [9].

We confirm that survival of children and young adults with a malignancy has improved considerably in the past 25 years in our area [2,7,8,15,36–38]. Besides more effective treatment protocols, improved diagnostic techniques probably contributed to the better prognosis for children and young adults. With these techniques, adequate therapy could be initiated earlier during the disease evolvement [34]. The overall 5-year survival for children with cancer in the southern part of the Netherlands (75%) was about average compared with rates in Europe [8].

The overall 5-year survival rate for young adults with a malignancy (82%) corresponds with the 5-year survival rate for the same age group in some Nordic countries (80% or more) [16].

Improvement in survival for childhood ALL probably resulted from improved access to care, introduction of nationwide protocols and better adherence to protocols and surveillance [39].

Survival rates for children with HD were high and stable during the study period. The weighted European 5-year survival rate for 1985–1989 was 93% [37]. The survival rate in our study was somewhat lower (86%) in 1983–1992, but improved to 94% in 1993–1999. In our study, 5-year survival rates for young adults with HD were similar to those for the children younger than 15 years. For the period 1990–1994, the pooled European five-year survival rate for young adults with HD was 89% [16].

Due to refinement of treatment strategies the prognosis for children with NHL has improved. The weighted European survival rate for 1985–1989 was 74% [37]. The 5-year survival rate in our study improved from 68% in 1983–1992 to 85% in 1993–1999. The explanation for the inferior survival of young adults with NHL must be sought in differences in the biological behaviour of cancers in young adults versus cancers in children [16], or in reported differences in treatment. Compared with children, a substantial proportion of the young adults received chemotherapy in combination with radiotherapy in the last time period.

The weighted European 5-year survival rate for children with a CNS tumour in 1985–1989 was 61% [38]. The 5-year survival rate in our study was 63%, for the period 1983–1992. Only in Northern Europe were the survival rates slightly higher for this time period, but it is known that incidence rates were also higher due to the inclusion of more benign tumours. For young adults, the 5-year survival rate found in our study (71%) for the period 1993–1999, corresponds with the pooled European 5-year survival rate (66%) [16].

The favourable prognosis for non-seminoma in young adults, 100% five-year survival, was also found in Europe [16]. Since the late 1970's, most patients with non-seminoma can be cured by surgery alone or in combination with chemotherapy and survival has improved ever since. For melanomas, the European five-year survival rate was somewhat lower (89%) than in our study (94%). This could be due to earlier detection as a result of more publicity about the risks of sunbathing and skin cancer within the Dutch population [40].

In conclusion, this study showed an increasing trend in cancer incidence for young adults ($P = 0.06$). Mainly due to changes in treatment, a positive trend in crude overall survival was found for children and young adults ($P < 0.05$ for both groups).

Conflict of interest statement

None declared.

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