Childhood Cancer Incidence and Survival in Sweden 1984-2010

Report 2013

From the Swedish Childhood Cancer Registry

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Förord

Det Svenska Barncancerregistret har successivt byggts upp från att enbart innefatta barn med leukemi från början av 70-talet, till registrering av samtliga solida tumörer, inklusive tumörer i centrala nervsystemet (CNS-tumörer) från början av 80-talet.
Registret är ett viktigt verktyg för barn-onkologerna i arbetet med utvärdering av behandlingsresultat och data från registret utgör en viktig del av underlaget vid utarbetande av nya behandlingsprotokoll.
Vidare utgör den en informationskälla med patientuppgifter för ett flertal forsknings-projekt, såväl pågående som planerade inom barncanceområdet.
Årliga rapporter har kontinuerligt utarbetats inom de separata barnonkologiska arbetsgrupperna men en översiktlig sammanställning över alla aktuella incidens - och överlevnads - data sammanställdes första gången 2007.
Denna rapport är en uppdatering av sammanställningen från 2007 och innehåller alltså data från ytterligare 5 års rekrytering och uppföljning och sammanfattar incidens- och överlevnadsdata för såväl gruppen som helhet som för de tolv undergrupperna av diagnoser som används vid den internationella klassificeringen av barncancer (1,2,3).
Genom denna uppdatering redovisas, med ett populationsbaserat perspektiv, den aktuella utvecklingen i Sverige för såväl barncancergruppen som helhet, som för enskilda diagnoser.
Ekonomiskt bidrag för drift och utveckling av det Svenska Barncancerregistret har sedan 1982 kontinuerligt lämnats av Svenska Barncancerfonden.
Sedan 2012 är Svenska Barncancerregistret också Nationellt Kvalitetsregister med stöd från Sveriges Kommuner och Landsting (SKL).

Stockholm, februari 2013.
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Foreword

The Swedish Childhood Cancer Registry started with registration of children with leukaemia in the early 1970s to complete registration of all solid tumours, including tumours of the central nervous system (CNS-tumours) from the beginning of the 1980s.
The registry is an important tool for the evaluation of treatment outcome by paediatric oncologists and data from the registry provides the foundation for the development of new treatment protocols. Furthermore, the database serves as a basic source of information, identifying patients for on-going and planned research projects within the childhood cancer research field.
Annual reports have continuously been produced within the separate childhood cancer working groups. However, a complete compilation of all incidence – and survival-analyses was reported for the first time in 2007.

This report is an update of this compilation and contains data from another 5 years of recruitment and follow – up. It includes complete incidence – and survival data for, both the whole group of cancer diseases, as well as for the twelve subgroups used in the international classification of childhood cancer (1,2,3)
Through this update, the recent development of treatment results in Sweden is shown from a population-based perspective, both for the childhood cancer group as a whole and for single diagnoses.
Financial support for the development and running costs of the Swedish Childhood Cancer registry has been obtained from the Swedish Childhood Cancer Foundation since 1982.
Since 2012, the Swedish Childhood Cancer Registry is a National Quality Registry with support also from the Swedish Association of Local Authorities and Regions (SKL).

Stockholm, February 2013.
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1. Introduktion och organisation

Rapporten omfattar uppgifter på samtliga barn med cancer diagnostiserade i Sverige åren 1984 -2010.

I kapitel 1 ges en presentation av nuvarande barnonkologiska organisation med sektion, arbetsgrupper, barnonkologiska centra och staben vid Barncancerepidemiologiska forskningsenheten vid Karolinska Institutet, som ansvarat för utgivningen av rapporten.

Kapitel 2 redovisar materialet, metod för insamling av data samt de statistiska metoder som använts vid analyserna.

Resultaten presenteras i kapitel 3 med primärt en översikt av de tre stora diagnosgrupperna (leukemier, solida tumörer och CNS- tumörer) följt av separata analyser för varje underdiagnos av barncancer.
För att kunna presentera prognosutvecklingen inklusive tidsperioden innan uppgifter fanns i vår egen databas har data från Svenska Cancerregistret använts.
Klassificeringen av diagnoserna baseras ursprungligen på WHO:s ICD - koder (1) som har anpassats till Birch-Marsden klassifikationen för barncancer som först publicerades 1987 (2) senast reviderad 2005 (3).

I kapitel 4 diskuteras klassificering av sjukdomarna och prognosutvecklingen över tiden och resultaten i det aktuella materialet jämförs med andra internationella publicerade data.

Publikationslistan omfattar internationella artiklar som helt eller delvis baseras på data från Svenska Barncancerregistret.
I Appendix redovisas i detalj det basala patientmaterialet.

1. Introduction and organisation

This report contains information on all children with cancer diagnosed in Sweden between 1984 and 2010.

Chapter 1 presents the childhood cancer organisation in Sweden including section, working groups, regional centres and the staff of the Childhood Cancer Epidemiology Research Unit at Karolinska Institutet which has been responsible for the report.

In chapter 2 we report the material and methods for collection of data and the statistical methods used in the analyses.

The results are presented in chapter 3 with an initial survey of the three main diagnostic groups (leukaemias, solid tumours and CNS-tumours) followed by analyses of the separate sub diagnoses in childhood cancer.
In order to present the development of prognosis including the time period before our own database existed, we have used data from the Swedish Cancer Registry.
The classification of the diagnoses are originally based on WHO:s ICD – codes (1), which have been adjusted to the Birch – Marsden classification for childhood cancer first published in 1987 (2), last revised 2005 (3).

The classification of the diseases and survival over time is discussed in chapter 4 and the results in the present material are compared with international results.
The list of publications includes international articles completely or partly based on data from the Swedish Childhood Cancer Registry.
The appendix contains basic patient data.

Barncancerverksamhetens organisation i Sverige
Childhood Cancer Organization in Sweden

Sektionen för Barncancer inom Svenska Barnläkarföreningen
Section for Childhood Cancer in the Swedish Pediatric Society

Chair:	Stefan Söderhäll	Stockholm
Secretary:	Torben Ek	Halmstad
Treasurer:	Hartmut Vogt	Linköping
Members:	Mikael Behrendtz	Linköping
	Christina Botvid	Karlskrona
	Britt-Marie Frost	Uppsala
	Arja Harila-Saari	Stockholm
	Mats Heyman	Stockholm
	Lars Hjorth	Lund
	Stefan Holm	Stockholm
	Gustaf Ljungman	Uppsala
	Karin Mellgren	Göteborg
	Kristina Nilsson	Uppsala
	Ulrika Norén-Nyström	Umeå
	Jacek Toporski	Lund

Regionala Barncancercentra i Sverige
Childhood Cancer Regional Centers in Sweden

Karolinska Solna: Arja Harila-Saari, Karin Belander-Strålin, Klas Blomgren, Göran Carlsson, Christina Egnell, Tony Frisk, Pernilla Grillner, Tatiana von Bahr Greenwood, Göran Gustafsson, Jan-Inge Henter, Mats Heyman, Stefan Holm, Åke Jakobson, Jonas Karlén, Per Kogner, Anna Lindblom, Johan Malmros, Niklas Pal, Trausti Óskarsson, Cecilia Petersen, Susanna Ranta, Stefan Söderhäll, Catarina Träger

Karolinska Huddinge: Jacek Winiarski, Britt Gustafsson, Peter Priftakis, Mikael Sundin

Lund: Jacek Toporski, Helga Björgvinsdóttir, Anders Castor, Marie-Eliasson-Hofvander, Nadine Gretenkort Andersson, Lars Hjorth, Rolf Ljung, Annika Mårtensson, Helena Mörse, Kees-Jan Pronk, Patrik Romerius, Ulf Tedgård, Dominik Turkiewicz, Ingrid Öra

Uppsala: Britt-Marie Frost, Johan Arvidson, Per Frisk, Clary Georgantzi, Fredrik Hedborg, Gustaf Ljungman, Josefine Palle, Susan Pfeifer, Annika Englund, Anders Öberg

Gothenburg: Karin Mellgren, Jonas Abrahamsson, Margareta Bergkvist, Magnus Göransson, Marianne Jarfelt, Cecilia Langensköld, Birgitta Lannering, Lene Karlsson, Mirka Pinkava, Magnus Sabel, Elisabeth Schepke, Gustaf Österlundh

Umeå: Ulrika Norén-Nyström, Per-Erik Sandström, Erik Forestier, Ulf Hjalmars, Caroline Björklund, Mattias Mattson, Owe Ljungdahl, Frans Nilsson

Linköping Mikael Behrendtz, Irene Devenney, Britt-Marie Holmqvist, Lisa Törnudd, Hartmut Vogt

Barncancerepidemiologiska Forskningsgruppen vid Karolinska Institutet
Childhood Cancer Epidemiology Research Group at Karolinska Institutet

Head:	Mats Heyman
Research secretary:	Jenny Juhlin
Statistician:	Matteo Bottai (Karolinska Institutet core-facility for Biostatistics)
Developers:	Anders Larsson, Omid Mavadati, Mats Nordström
PhD student:	Trausti Óskarsson
Postdoc:	AnnaCarin Horne
Senior researcher:	Göran Gustafsson

Regionala registrerare
Regional registrators

Eva Franzén	Stockholm
Carina Rinaldo	Uppsala/Stockholm
Gunnel Hedblom	Uppsala
Anna Schröder-Håkansson	Göteborg
Carina Hallberg	Göteborg
Birgitta Hellström	Linköping
Ingrid Hagelin	Lund
Ingrid Colberger	Lund
Rut-Inger Enryd	Umeå
Lotta Paulsson Ödmark	Umeå
Camilla Ernstsson	Umeå
Britt Fällman	Umeå

Arbetsgrupper inom Sektionen
Working groups within the Section

SBLG (Svenska Barnleukemigruppen)
SBLG (Swedish Childhood Leukaemia and Lymphoma Group)

Chair:	Britt-Marie Frost	Uppsala
Secretary:	Mikael Behrendtz	Linköping
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	Anders Castor	Lund
	Mats Heyman	Stockholm
	Ulrika Noren-Nyström	Umeå
	Margareta Stenmarker	Jönköping
	Arja Harila-Saari	Stockholm
	Jacek Winiarski	Huddinge
	Johan Malmros	Stockholm
	Dominik Turkiewicz	Lund
	Lene Karlsson	Skövde
	Karin Mellgren	Göteborg
Adjungerade:	Erik Forestier	Umeå
	Stefan Söderhäll	Stockholm
	Jesper Heldrup	Lund

VSTB (Vårdplaneringsgruppen för Solida Tumörer hos Barn i Sverige)
Swedish Childhood Solid Tumours Working Group

Chair:	Gustaf Ljungman	Uppsala
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	Torben Ek	Halmstad
	Kristina Nilsson	Uppsala
	Ulf Hjalmars	Umeå
	Lars Hjorth	Lund
	Mats Heyman	Stockholm
	Per Kogner	Stockholm
	Otte Brosjö	Stockholm
	Bengt Sandstedt	Stockholm
	Gustaf Österlundh	Göteborg
	Vladimir Gatzinsky	Göteborg
	Pär-Johan Svensson	Stockholm
	Erik Sköldenberg	Uppsala
	Zahra Taheri-Kadkhoda	Göteborg
	Marie Sandgren	Linköping

VCTB (Vårdplaneringsgruppen för CNS Tumörer hos Barn i Sverige)
Swedish Childhood CNS Tumours Working Group

Chair:	Stefan Holm	Stockholm
Secretary:	Magnus Sabel	Göteborg
Members:	Birgitta Lannering	Göteborg
	Helena Mörse	Lund
	Irene Devenney	Linköping
	Susan Pfeifer	Uppsala
	Fredrik Hedborg	Uppsala
	Per-Erik Sandström	Umeå
	Mattias Mattsson	Umeå
Neurosurgery:	Bengt Gustavsson	Stockholm
	Pelle Nilsson	Uppsala
	Peter Siesjö	Lund
	Jörgen Elfversson	Göteborg
Neurology:	Olof Rask	Lund
	Pernilla Grillner	Stockholm
	Christoffer Ehrstedt	Uppsala
	Erik Stenninger	Örebro
Radiotherapy:	Ulla Martinsson	Uppsala
	Gun Wickart-Johansson	Stockholm
	Per Bergström	Umeå
Neuropatohlogy:	Irina Alafuzoff	Uppsala
	Olivera Casar-Borota	Uppsala
	Jurate Asmundsson	Stockholm
Neuroradiology:	Daniel Martin Munoz	Stockholm
	Evaldas Laurencikas	Uppsala
Registration:	Mats Heyman	Stockholm
Consultant nurse:	Charlotte Castor	Lund

BMT-Gruppen (Benmärgstransplantationsgruppen)
BMT Group (Bone Marrow Transplantation Group)

Chair:	Karin Mellgren	Göteborg
Members:	Johan Arvidson	Uppsala
	Niklas Pal	Stockholm
	Johan Malmros	Stockholm
	Ulrika Norén-Nyström	Umeå
	Jacek Toporski	Lund
	Jacek Winiarski	Huddinge

SALUB (Svenska Arbetsgruppen för Långtidsuppföljning efter Barncancer)
(Swedish Working Group for Long-term Follow-up after Childhood Cancer)

Chair:	Lars Hjorth	Lund
Secretary:	Mikael Behrendtz	Linköping
Members:	Johan Arvidson	Uppsala
	Per Frisk	Uppsala
	Ulla Martinsson	Uppsala
	Marianne Jarfelt	Göteborg
	Birgitta Lannering	Göteborg
	Ulrika Norén-Nyström	Umeå
	Per-Erik Sandström	Umeå
	Stefan Söderhäll	Stockholm
	Cecilia Petersen	Uppsala/Stockholm
	Mats Heyman	Stockholm

Svenska Radioterapigruppen för Barn med Cancer
Swedish Radiotherapy Group for Children with Cancer

Chair:	Kristina Nilsson	Uppsala
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	Per Bergström	Umeå
	Anna-Maja Svärd	Umeå
	Ulla Martinsson	Uppsala
	Petra Witt Nyström	Uppsala
	Gun Wickhart Johansson	Stockholm
	Gunilla Frykholm Jansson	Stockholm
	Teresa Calero Herlestam	Stockholm
	Claes Mercke	Stockholm
	Måns Agrup	Linköping
	Hedda Haugen	Göteborg
	Charlotta Fröjd	Göteborg
	Malin Blomstrand	Göteborg
	Karin Belfrage	Lund
	Jacob Engelau	Lund
	Sven Börje Ewers	Lund
	Ingrid Kristensen	Lund
	Per Nilsson	Lund

2. Material och Metoder

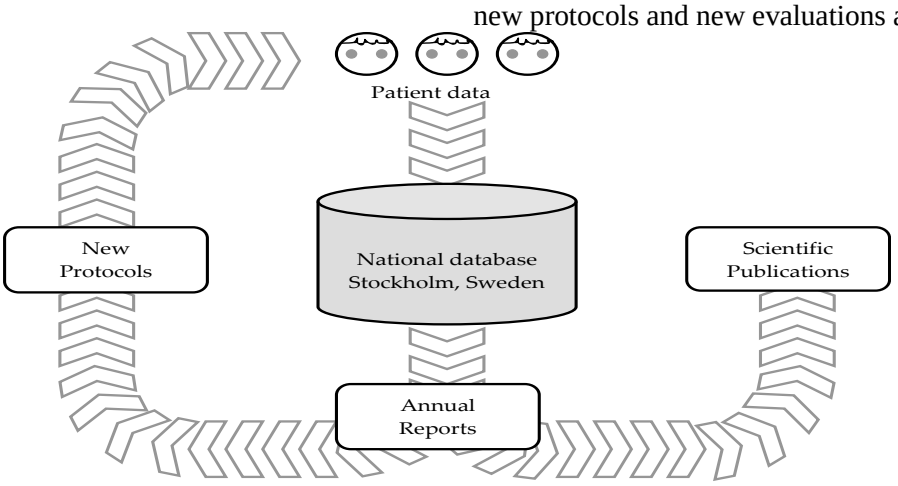
2.1. Material och databaser

Det populationsbaserade Svenska Barncancerregistret innehåller 8 279 barn med diagnos under tidsperioden 1.1.1984–31.12.2010.
965 barn 15- 20 år vid diagnos, 193 barn bedömda som benigna tumörer och
56 barn som dubbelregistrerats exkluderades från analyserna som således baseras på kvarvarande 7 065 barn. Databasen frystes 1.1.2012.
Klassifikationen av cancerdiagnoser på barn baseras på morfologiska fynd och inte som för vuxna på lokalisation av tumören. Den första accepterade klassifikationen av barncancer presenterades 1987 (2) och baserades på WHO:s ICD- koder som reviderats vid flertal tillfällen (1). Diagnoserna indelades i 12 huvudgrupper. Senaste förslag till indelning av barncancer publicerades 2005- ICCC-3 (3), vilket innebar en vidare subklassificering av de tolv huvudgrupperna. Denna utgör underlag för klassifikation av föreliggande patientmaterial. Inrapportering och uppföljning av patienter sker helt via ett webbaserat system.
Flödet av patientinformation från regionala barncancercentra till den centrala databasen och vidare flöden illustreras av nedanstående figur. Loopen till vänster i figuren illustrerar det kontinuerliga flödet av information som leder till nya protokoll med nya utvärderingar.

2. Material and Methods

2.1. Material and data bases

The populations based Swedish Childhood Cancer Registry contains 8 279 children with a diagnosis between 1.1. 1984 to 31.12.2010.
965 children 15-20 years of age at diagnosis, 193 children classified as having a benign tumour and 56 children who were registered twice were excluded from the analyses, thus leaving 7 065 left for the study. The database was frozen at January, 1 2012.
The classification of cancer in childhood is based on morphologic findings and not, as in adults, on primary site of organ. The first general accepted classification of childhood cancer was published in 1987 (1-Birch) an was based on WHO:s ICD- codes, later revised several times (1). The diagnoses were divided into twelve main groups. The latest proposal for classification of childhood cancer was published in 2005 – ICCC-3 (3), where the twelve diagnostic groups were further sub-divided into subgroups. This classification forms the basis for classification of the actual patient material. Information and follow up data of the patients are reported via a national Webb based system. The flow of information from the regional childhood cancer centres to the central database and further flow of information is illustrated in the figure below. The loop to the left in the figure shows the continuous flow of information resulting in new protocols and new evaluations and so on.



Barn med leukemi i det Svenska Barncancerregistret utgör sedan 1981 del av det Nordiska Barnleukemiregistret. Detta skapades och har utvecklats vid BCFE och har utgjort viktig basinformation för ett flertal forskningsprojekt som bedrivits inom NOPHO.

Children with leukaemia in the Swedish Childhood Cancer Registry constitute since 1981 part of the Nordic Childhood Cancer Registry. This was created and has been developed at BCFE and has also served as basic patient information for several research projects within NOPHO.

2.2. Statistiska mått och metoder i denna rapport

För incidensberäkningar behövs en klar definition av diagnosen. Detta innefattar både detektion av ursprungligt fall samt hur man ska tackla pågående eller kroniska tillstånd där det kan finnas latens-, remissions-, bot/behandlings - samt återfallsproblematik. Det är viktigt att fullständigt besvara de till synes enkla frågorna ’vad är en åkomma?’ och ’när är en åkomma?’ före man beräknar dessa storheter.

Incidenssiffror beräknas för fall som insjuknat mellan 1 januari, 1984 och 31 december, 2010 bland barn (ej fyllda 15 år) boende i Sverige vid tiden för diagnos, diagnosticerade på något behandlande centra och räknas som insjuknade vid tidpunkten för diagnos. Incidenssiffror presenteras per 100 000.

2.2.1 Incidens – Åldersspecifikt mått

Precis som hos vuxna varierar cancerincidensen hos barn med ålder och kön på barnet. ALL hos barn är till exempel tre gånger så vanligt i åldersgruppen två till fyra år jämfört med övriga åldrar. Den åldersspecifika incidensen för olika cancerformer är det observerade antalet nya fall, vägda mot den observerade riskpopulationen och sedan multiplicerat med 100 000. Den åldersspecifika incidensen för klass i är

$r_i = \frac{d_i}{Y_i} \cdot 100\,000$; där

d_i är antalet fall i varje åldersklass

Y_i är observerat antal personår.

2.2.2 Incidens – Åldersstandardiserat mått

Det är vanligt att rapportera incidens i åldersstandardiserade tal för att underlätta jämförelser mellan riskgrupper eftersom måttet inte påverkas av skillnader i åldersfördelning mellan grupperna. Medan det åldersspecifika måttet viktas enbart med riskpopulationen är det åldersstandardiserade måttet på incidens det åldersspecifika måttet viktat med ännu en gång med användande av en standardpopulation. På så vis blir det åldersstandardiserade måttet ett mer sammanfattande mått som underlättande jämförelse mellan många olika grupper. I

2.2. Statistical methods used in this report

In incidence a clear definition is required for the condition. This includes the detection as well as how to deal with on-going or chronic conditions where there may be issues of latency, remission, cure/treatment, and recurrence.
Answering the seemingly simple questions 'What is a condition?' and 'When is a condition' before starting a study is important.

Incidence figures are calculated on cases included between January 1, 1984 and December 31, 2010 among children (below 15 years of age) living in Sweden at the time of diagnosis, diagnosed at one of the treating centers in Sweden and are counted as a case at the time of diagnosis. Incidence figures are presented per 100,000.

2.2.1 Incidence - Age-specific rates

Just as among adults, cancer incidence in different types of cancers among children varies with age and sex. ALL in childhood is i.e. three times more common in children between two and four years old compared to other ages. The age-specific rates for various cancers are the observed number of new cases, weighted by the observed population at risk and multiplied by a factor of 100,000. The age-specific rate for class i is

$r_i = \frac{d_i}{Y_i} \cdot 100{,}000$; where

d_i is the number of events in each age class

Y_i is the observed person-years.

2.2.2 Incidence - Age-standardized rates

It is common practice to report incidence figures as age-standardized rates so as to enable comparison of risk between different risk groups, since it is not affected by age. Whereas the age-specific incidence is weighted by the population at risk, the age-standardized rates are the age-specific rates weighted yet again by a standard population, making this a summary measure especially when it comes to comparing many sets of incidence rates. In this report the so called world standard population, as it is presented by Doll et al., is used as a standard population. The world standard population is presented in table 3.2.1. The

denna rapport används som standardpopulation den s.k. världsstandardpopulationen (the world standard population), såsom den presenterats av Doll et al. Världsstandardpopulationen presenteras i tabell 3.2.1. Den svenska barnpopulationen återfinns i 3.2.2.

Den åldersstandardiserade incidensen per 100 000 invånare beräknas:

$$ASR = \frac{\sum_i r_i w_i}{\sum_i w_i} \cdot 100\,000$$; där w_i är vikten i den i :te åldersklassen. Graferna över incidens visar ett 3-års glidande medelvärde för att släta ut kurvan. För år *y* kallas detta glidande medelvärde I_y^{MA}, vilket är medelvärdet av incidensen året före år y, incidensen år y samt incidensen året efter år y, således fås

$$I_y^{MA} = \frac{\sum_{i=-1}^{1} I_i}{3}$$; där I_i är incidensen år *i*.

Swedish child population can be found in table 3.2.2.

The age-standardized incidence per 100,000 is calculated as:

$$ASR = \frac{\sum_i r_i w_i}{\sum_i w_i} \cdot 100{,}000$$; where w_i is the weight in the i th age class. The graphed incidence shows a 3-year moving average of the incidence in order to smooth the curve. The 3-year moving average value for year *y*, denoted I_y^{MA}, is the mean value of the incidence the year before year *y*, the incidence at year *y* and the incidence the year after year *y*, thus

$$I_y^{MA} = \frac{\sum_{i=-1}^{1} I_i}{3}$$; where I_i is the incidence at year *i*.

Tabell 2.2.1 / Table 2.2.1
Världsstandardpopulationen / The world standard population (Doll et al., 1966)

Ålder/age	Population		
(år/years)	Män/males	Kvinnor/females	Totalt/total
0	1,200	1,200	2,400
1-4	4,800	4,800	9,600
5-9	5,000	5,000	10,000
10-14	4,500	4,500	9,000
Totalt/total	15,500	15,500	31,000

Tabell 2.2.2 / Table 2.2.2
Den svenska barnpopulationen / The Swedish child population (Statistiska Centralbyrån (SCB) / Statistics Sweden (SCB))

Ålder/age	Medelpopulation över de studerade åren / Mean population during the years studied		
(år/years)	Män/males	Kvinnor/females	Totalt/total
0	53,013	50,219	103,232
1-4	212,728	201,887	414,615
5-9	270,994	257,413	528,406
10-14	278,718	264,697	543,415
Totalt/total	815,453	774,215	1,589,668

2.2.3 Överlevnadsanalys

Med användande av metoder inom överlevnadsanalys är det möjligt att studera och analysera inte bara tid till en händelse (ett event) utan även den förväntade kvarvarande livstiden för en person vid en given tidpunkt. Metoder inom överlevnadsanalys tillämpas vanligen inom cancerforskning för att jämföra två eller fler grupper med avseende på överlevnad, med eller utan hänsyn taget till andra kovariater som kan tänkas påverka (4).

I denna rapport kommer främst så kallade Life tables att presenteras. Skillnader mellan grupper testas med logrank-testet, ett test som simultant tar hänsyn till skillnader över hela överlevnadskurvan, inte enbart skillnader vid slutpunkten av överlevnadskurvan.

2.2.4 The Kaplan-Meier product limit estimate

Antag *n* oberoende observationer som betecknas (t_j, δ_j) för $j = 1, \ldots, n$ där t_j är tiden i studien för den *j*:te individen och δ_j är en händelseindikator. Multipliceras överlevnadstiderna över alla observationer fås överlevnadsfunktionen

$$\hat{S}(t) = \prod_{j=1}^{t} [(n-j)/(n-j+1)]^{\delta(j)} ;$$

där $\hat{S}(t)$ är den skattade överlevnads-funktionen; *n* är antalet fall $\delta(j)$, händelseindikatorn, är en konstant som antar värdet 1 om det *j*:te fallet är ocensurerat (har komplett uppföljningstid) och som antar värdet 0 om värdet är censurerat (dvs. har fallit bort före uppföljningstiden är fullföljd) (5).

2.2.5 Logrank-testet (eller 'the Mantel-Haenszel test' eller 'the Mantel-Cox test')

Låt $j = 1, \ldots, J$ vara distinkta tider för observerade händelser i båda grupper. För varje tidpunkt *j*, låt N_{1j} och N_{2j} vara antalet individer som ännu ej haft ett event eller censurerats vid början av period *j* i respektive grupp. Låt $N_j = N_{1j} + N_{2j}$. Låt O_{1j} och O_{2j} vara observerat antal events i respektive grupp vid tidpunkten *j*, och sätt $O_j = O_{1j} + O_{2j}$. Givet O_j events som inträffat över båda grupperna vid tidpunkten *j*, under nollhypotesen att O_{1j} följer den

2.2.3 Survival analysis

By survival analysis methods it is possible to measure and estimate not only the time to event but also the expected remaining lifetime of a person at a certain time. Survival analysis methods are commonly used in cancer research to compare two or more groups with regard to their survival pattern, with or without taking additional covariates into account (4).

In this report the main survival analysis method used is Life tables. Differences between groups are tested by the log rank test, which simultaneously takes differences over the whole survival curve into account, not only the differences at the end point of the curve.

2.2.4 The Kaplan-Meier product limit estimate

Assume *n* independent observations denoted (t_j, δ_j) for $j = 1, \ldots, n$ where t_j is the time on the study for the *j*th individual and δ_j is the event indicator. Multiplying the survival times over each single observation we get the survival function

$$\hat{S}(t) = \prod_{j=1}^{t} [(n-j)/(n-j+1)]^{\delta(j)} ;$$

where $\hat{S}(t)$ is the estimated survival function *n* is the total number of cases $\delta(j)$, the event indicator, is a constant equal to 1 if the *j*th case is uncensored (has complete follow-up time) and equal to 0 if it is censored (5).

2.2.5 The logrank test (or the Mantel-Haenszel test or the Mantel-Cox test)

Let $j = 1, \ldots, J$ be the distinct times of observed events in either group. For each time *j*, let N_{1j} and N_{2j} be the number of subjects "at risk" (have not yet had an event or been censored) at the start of period *j* in the groups respectively. Let $N_j = N_{1j} + N_{2j}$. Let O_{1j} and O_{2j} be the observed number of events in the groups respectively at time *j*, and define $O_j = O_{1j} + O_{2j}$. Given that O_j events happened across both groups at time *j*, under the null hypothesis O_{1j}

hypergeometriska fördelningen med parametrar N_j, N_{1j}, och O_j. Den här fördelningen har förväntat värde

$$E_j = O_j \frac{N_{1j}}{N_{1j}}$$ och variansen

$$V_j = \frac{O_j \left(N_{1j} / N_j\right)\left(1 - N_{1j} / N_j\right)\left(N_j - O_j\right)}{N_j - 1}$$

Logrank-teststatistikan jämför varje O_{1j} med dess förväntade värde E_j under nollhypotesen och definieras som

$$Z = \frac{\sum_{j=1}^{J} O_{1j} - E_j}{\sqrt{\sum_{j=1}^{J} V_j}}$$

Om båda grupper har samma överlevnadsfunktion så följer logrank-teststatistikan approximativt den standardiserade normalfördelningen. Vid ett enkelsidigt test på α-nivån förkastas nollhypotesen om $Z >$ den övre α:te quartilen i den standardiserade normalfördelningen.

follows the hypergeometric distribution with parameters N_j, N_{1j}, and O_j. This distribution has expected value

$$E_j = O_j \frac{N_{1j}}{N_{1j}}$$ and variance

$$V_j = \frac{O_j \left(N_{1j} / N_j\right)\left(1 - N_{1j} / N_j\right)\left(N_j - O_j\right)}{N_j - 1}$$

The logrank statistic compares each O_{1j} to its expectation E_j under the null hypothesis and is defined as

$$Z = \frac{\sum_{j=1}^{J} O_{1j} - E_j}{\sqrt{\sum_{j=1}^{J} V_j}}$$

If the two groups have the same survival function, the logrank statistic is approximately standard normal. A one-sided level α test will reject the null hypothesis if $Z >$ the upper α quantile of the standard normal distribution.

3.1 Resultat - översikt

Under tidsperioden 1.1.1984 – 31.12.2010 diagnosticerades 7 065 barn (<15 år vid diagnos; 3 805 pojkar, 3 260 flickor; M/F ratio 1.17) med primär cancersjukdom i Sverige. Det motsvarar en årlig incidens på 16.0 nyinsjuknade/100 000 barn < 15 år.
Fördelningen mellan diagnoserna visas i Fig 3.1.1 Leukemier utgör 30 %, CNS tumörer 28 % och övriga solida tumörer 42 % av maligniteterna.
Ålderfördelningen vid de olika diagnoserna (Fig. 3.1.2-3) visar den välkända incidenstoppen mellan 2-4 år vid ALL medan hjärntumörernas har en mer jämn ålderfördelning. Den vanligaste diagnosen för barn < 1 år vid diagnos är neuroblastom som har en topp i denna åldersgrupp för att snabbt sjunka i frekvens ner till 5-6 års ålder. Barn med Germinalcellstumörer är vanligast under första levnadsåren och senare under tonåren. Bentumörer drabbar mest tonåringar.

965 barn var 15-<20 år vid diagnos och redovisas enbart i Appendix där barnen är uppdelade i de olika diagnosgrupperna.
Den positiva utvecklingen mätt som 5-års överlevnad under de senaste 5 decennierna visas översiktligt i figur 3.1.4 där data från första tidsperioderna baseras på uppgifter från Svenska Cancerregistret. De mest dramatiska förbättringarna av prognosen inträffade under 70-och 80-talen, mest påtagligt för ALL och NHL. Under den senaste 15 - års perioden verkar resultaten för överlevnad ha stabiliserats. Data talar således för att vi nu verkar ha nått en platå utan påtaglig förbättring av överlevnaden. Prognosen för CNS tumörer och neuroblastom verkar dock ha förbättrats även under senaste diagnostiska tidsperioderna.
Tendensen till stagnation var tydlig också vid inventeringen för fem år sedan, men ser alltså ut att etablera sig. Sannolikt krävs kvalitativt nya strategier för att

3.1 Results - survey

During the time period from 1.1.1984-31.12.2010, there were 7 065 children (<15 years of age at diagnosis; 3 805 boys, 3 260 girls; M/F ratio 1.17) diagnosed with primary cancer in Sweden. This corresponds to an annual incidence of 16.0 /100 000 children<15 years.
The distribution of the diagnoses is shown in fig 3.1.1. The leukaemias constitute 30%, CNS tumours 28% and the solid tumours 42% of the malignancies.
The age distribution for different diagnoses (Fig 3.1.2-3) shows the well-known incidence peak for ages 2-4 years for ALL, while brain tumours have a more even distribution. Neuroblastoma is the most common diagnosis among infants (< 1 years of age) with decreasing numbers to ages 5-6. Children with germ cells tumours are more frequent during the first years of life and among teenagers. Bone tumours mostly affect teenagers.

965 children aged 15-<20 years at diagnosis are only reported in the Appendix, where the children have been classified in the different sub diagnoses.
The positive development of 5-years survival during the last 50 years is shown in figure 3.1.4, where information from the first time periods is based on data from the Swedish Cancer Registry. The most dramatic improvements in survival occurred during the 1970s and 1980s, most pronounced among children with ALL- and NHL.
During the last fifteen years the survival figures seem to have stabilized. Thus, data seems to indicate that we have now reached a plateau. However, the prognosis for CNS tumours and neuroblastom seems to have improved also during the last diagnostic periods.
The tendency to stagnation in the results was clear also in the inventory five years ago, but seems now to be well established. It is likely that qualitatively new strategies are necessary to change this pattern

ändra detta mönster.
Figur 3.1.5 och Tabell 3.1.1 visar ålderfördelningen vid uppföljningen för alla levande patienter totalt och uppdelat efter diagnosgrupper.

Figure 3.1.1 and Table 3.1.1 show the age distribution at follow up among surviving patients in all and subdivided into diagnostic subgroups.

Distribution of childhood malignancies in Sweden diagnosed 1984-2010
< 15 years of age at diagnosis (n= 7 065)

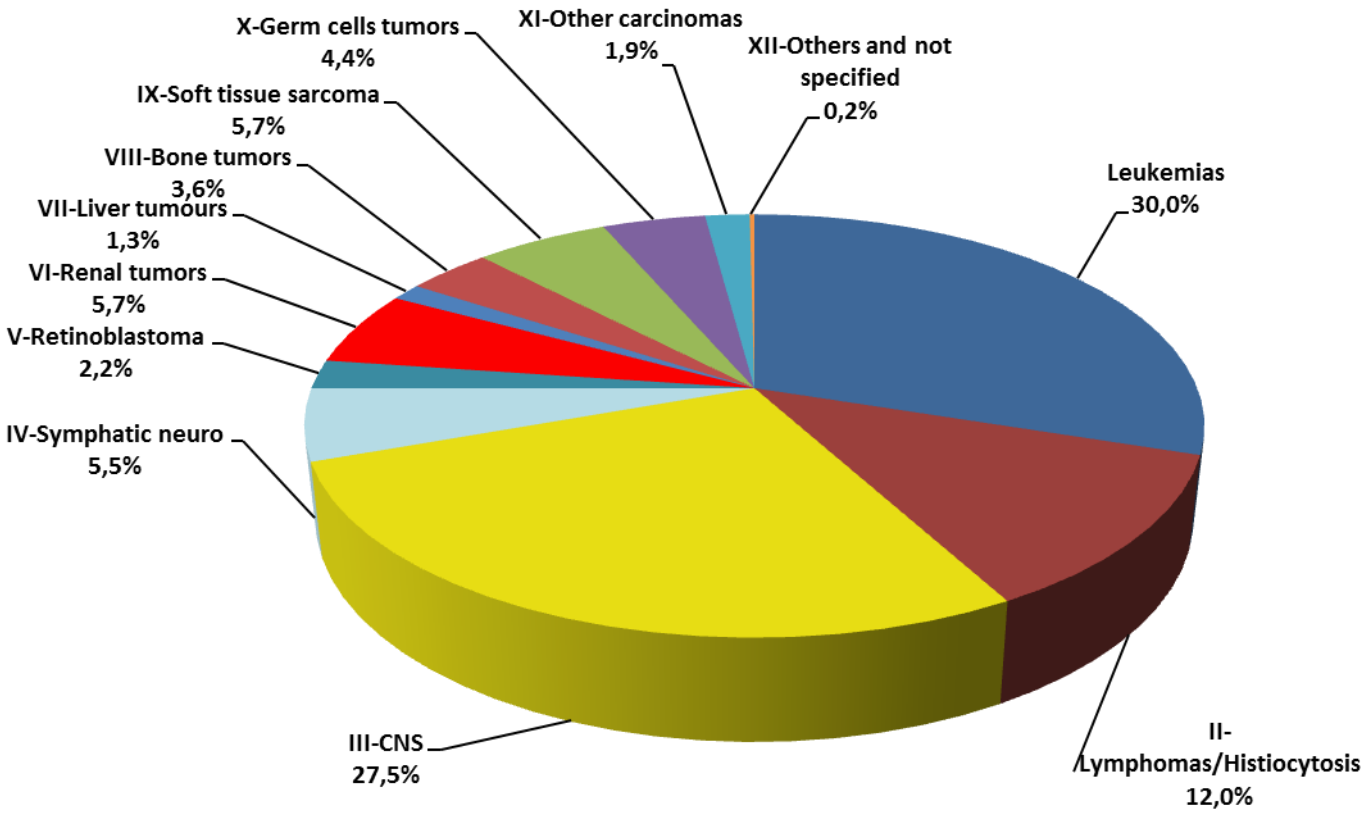


Figure 3.1.1. The diagnoses are stratified according to the WHO ICCC3 classification from 2005. Leukaemias, CNS-tumours and Lymphomas constitute 70% of the children and the other nine diagnoses account for 30%.

Age distribution by diagnosis in childhood malignancies
< 15 years of age at diagnosis (n= 7 065)

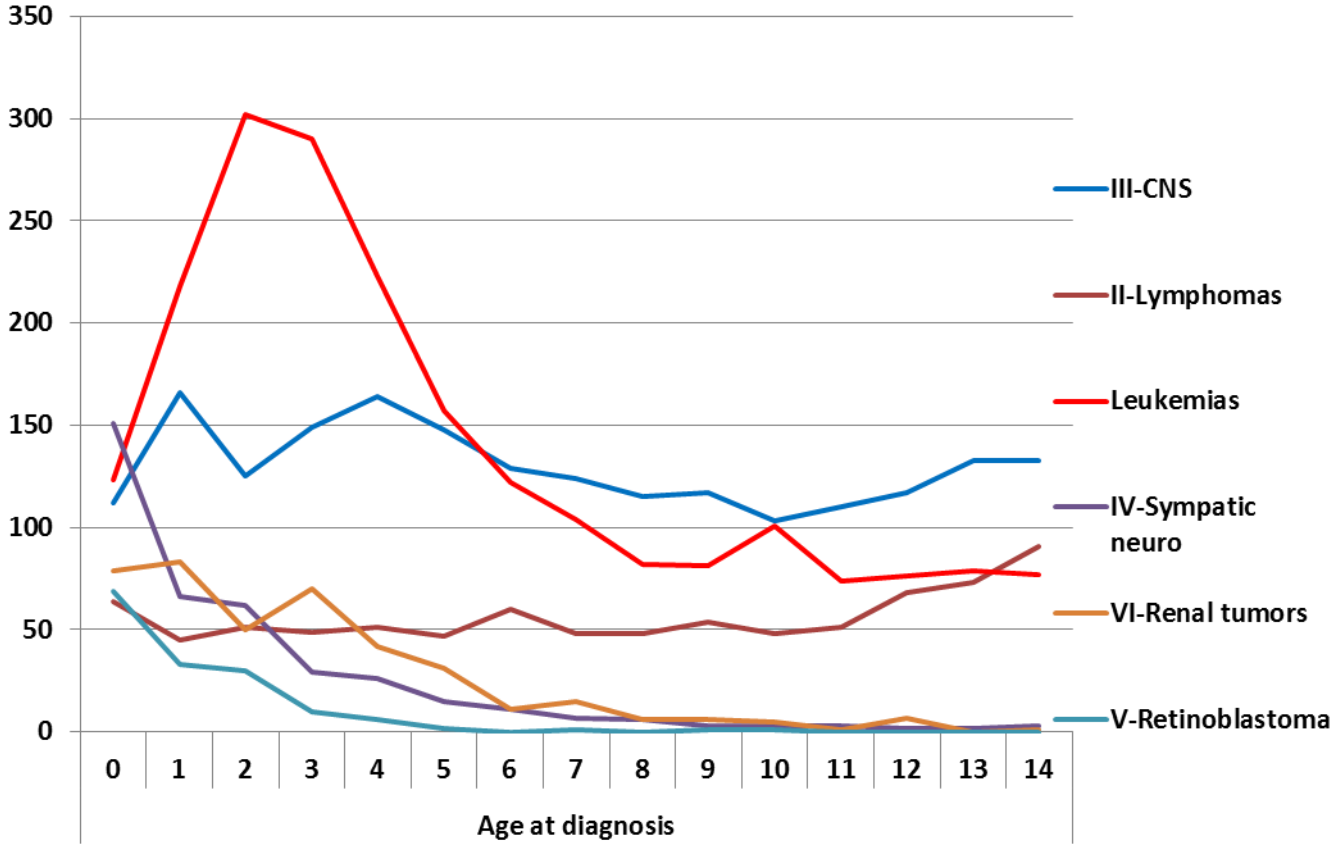


Figure 3.1.2.

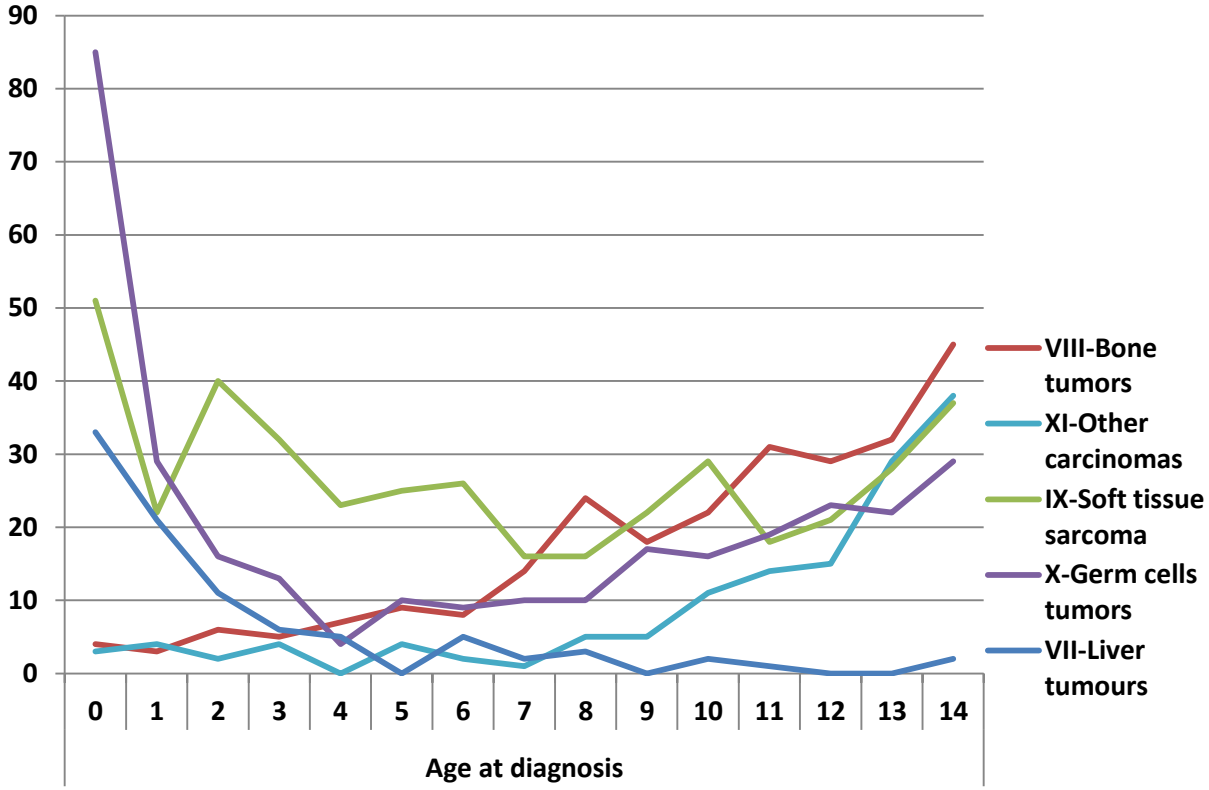


Figure 3.1.3.

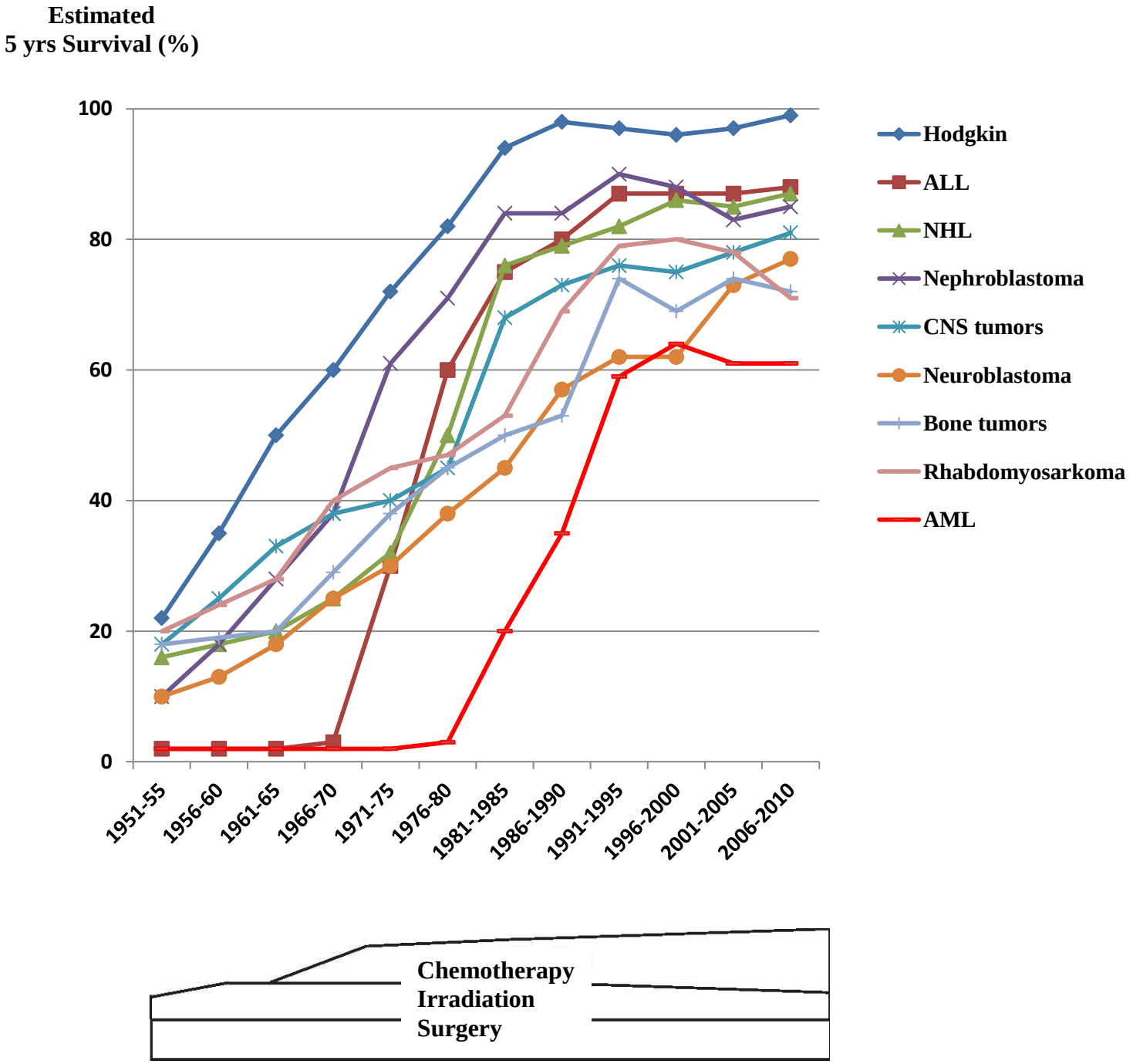


Figure 3.1.4. The estimated prognosis (5-years survival) over time for selected diagnostic groups. The prognosis improved considerably during time period 1970-1995. The results during the last decades seem to have reached a plateau, although neuroblastoma and CNS-tumours seem to have a continued improved 5-years survival.

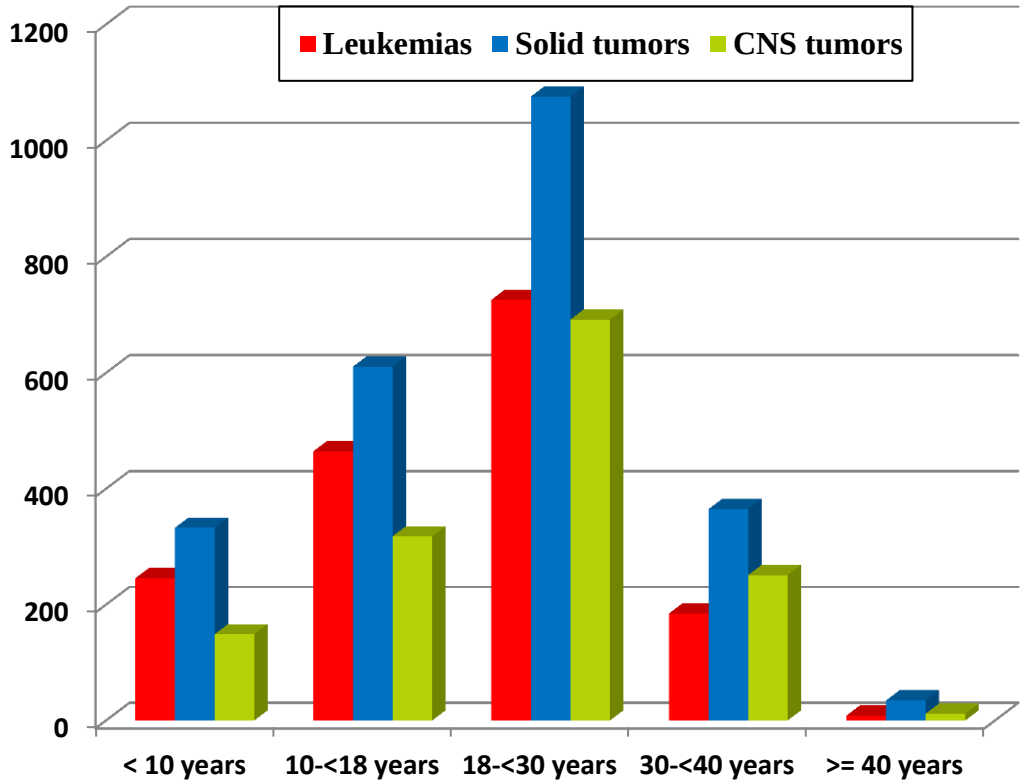


Fig 3.1.5.Age distribution at FU for all living patients by diagnostic group (n=5 473).

	Age at Follow Up					Total
	< 10 years	10-<18 years	18-<30 years	30-<40 years	>= 40 years	
Leukemias	246	465	726	185	9	1631
II-Lymphomas/Histiocytosis	56	161	340	167	15	739
III-CNS	149	318	692	251	12	1422
IV-Symphatic neuro	64	86	92	9	0	251
V-Retinoblastoma	39	47	61	3	0	150
VI-Renal tumours	75	91	149	29	0	344
VII-Liver tumours	19	24	25	2	0	70
VIII-Bone tumuors	7	45	78	35	4	169
IX-Soft tissue sarcoma	30	83	132	48	5	298
X-Germ cells tumours	37	52	141	42	3	275
XI-Other carcinomas	3	18	57	30	8	116
XII-Others and not specified	3	4	1	0	0	8
	728	1394	2494	801	56	5473

Tabell 3.1.1. Age distribution at FU for all living patients by diagnostic group (n=5 473)

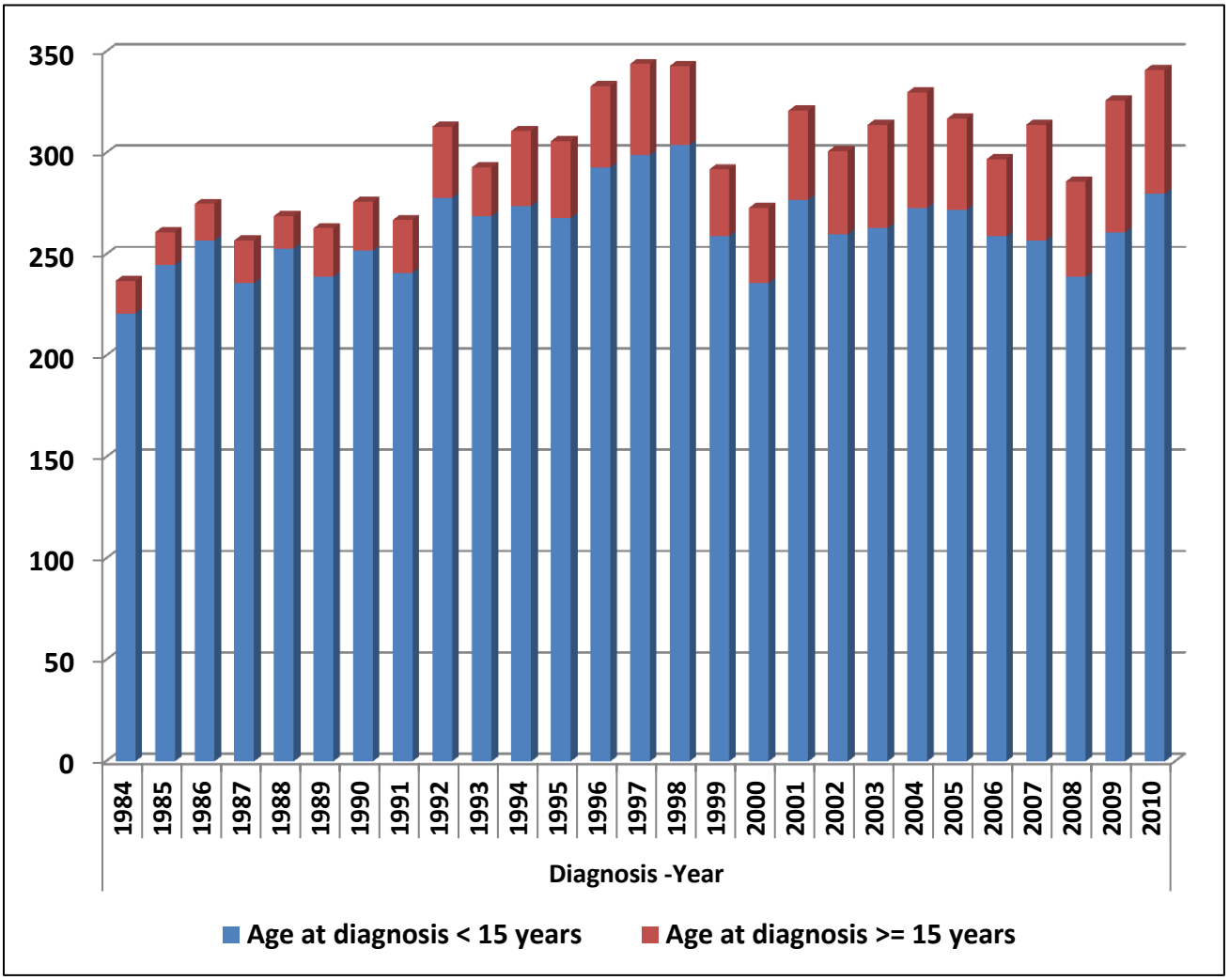


Fig 3.1.6. All reported patients annually 1984-2010

3.2.1 Alla maligniteter

Den genomsnittliga årliga incidensen för all form av barncancer under tidsperioden 1984-2010 var 16,0 fall/100 000 barn < 15 år vid diagnos, 16,9 för pojkar och 15,0 för flickor. (Appendix 1.1).
Ingen signifikant incidensökning har skett under tidsperioden.

Könsfördelningen visar att fler pojkar än flickor insjuknar i cancer med ett M/F Ratio = 1.17. Vidare framgår att cancer är vanligast under de 5-6 första levnadsåren.

Överlevnaden har ökat signifikant efter 1990 vilket framgår av figur 3.2.1.1.

Det är ingen skillnad i överlevnad mellan pojkar och flickor och prognosen för olika åldersgrupper är lika med undantag av barn>= 10 år vid diagnos som har sämre prognos än övriga ålders grupper. (Fig 3.2.1.2)

Figur 3.2.1.3 visar motsvarande analysresultat för leukemier.
Figur 3.2.1.4 visar översiktliga resultat för solida tumörer sammanslagna och figur 3.2.1.5 motsvarande för CNS-tumörer.

3.2.1 All malignancies

The mean annual incidence rate for the whole group of childhood cancer diagnosed 1984 through 2010 was 16,0 cases/100 000 children < 15 years of age at diagnosis, 16,9 for boys and 15,0 for girls. (Appendix 1.1).
No significant increase of incidence has occurred during the time period.

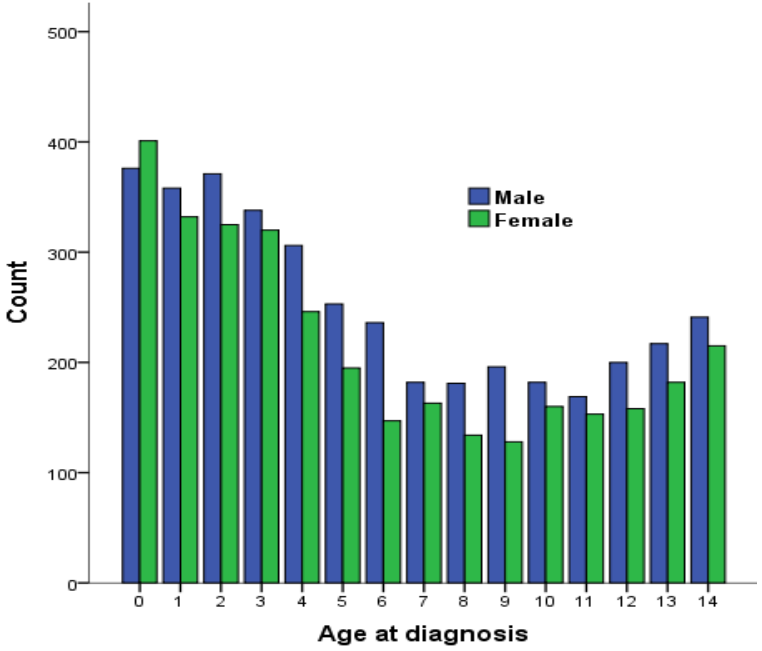
The age-and sex-distribution shows that cancer is more common among boys with a M/F Ratio = 1.17. Furthermore, cancer is most common in children aged 5-6 years at diagnosis.
The survival figures have increased significantly after 1990 which is shown in adjoining life table in figure 3.2.1.1.
There is no difference in prognosis between boys and girls and the prognosis is equal for different age groups except for children >= 10 years of age who have an inferior prognosis. (Fig 3.2.1.2).

Fig 3.2.1.3 shows the corresponding analyses for all leukemia.
Figure 3.2.1.4 shows the survey analyses for solid tumours and figure 3.2.1.5 the corresponding results for CNS tumours.

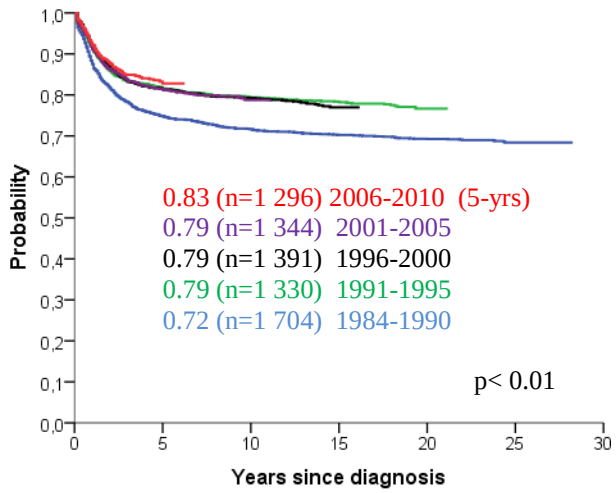
Fig 3.2.1.1.
All Malignancies in Sweden 1984-2010.
Selected criteria Total numbers of children: 7 065

Number/Relative frequency		7 065= 100 %		
	Number	Alive	Dead	% Alive
Boys	3 805	2 950	856	77,5
Girls	3 260	2 523	736	77,4
Ratio boys/girls	1.17			
< 1 year	776	585	191	75,4
1-4 yrs	2 596	2 049	547	78,9
5-9 yrs	1 816	1 407	409	77,5
10-14 yrs	1 877	1 432	445	76,3

Age- and sexdistribution.



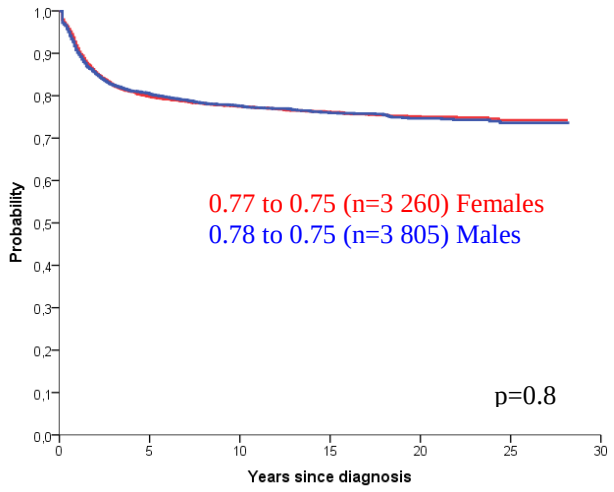
Survival probability at 10 years by years of diagnosis.



The prognosis has improved significantly after 1990. No significant difference during later time periods.

Fig 3.2.1.2.
All Malignancies in Sweden 1984-2010 (continued).
Total numbers of children: 7 065

Survival probability at 10 and 20 years by gender



Survival probability at 20 years by age

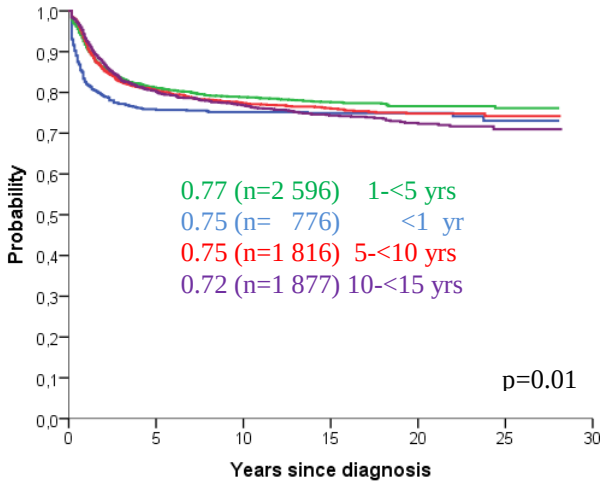
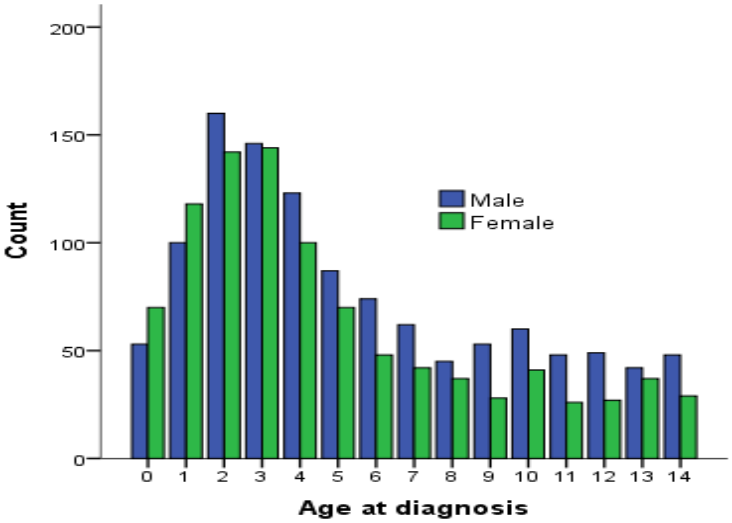


Fig 3.2.1.3.
All Leukemias diagnosed 1984-2010.

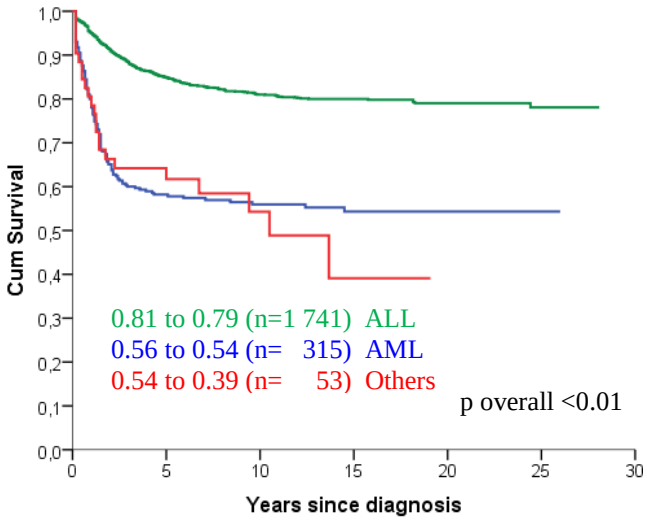
Selected criteria Total number of children:2 109

Relative frequency	2 109/7 065= 29.9 %			
	Number	Alive	Dead	% Alive
Subdiagnosis				
ALL	1 741	1 422	319	81,7
ANLL	315	179	136	56,8
Others	53	30	23	56,6
Boys	1 150	897	253	78,0
Girls	959	734	225	76,5
Ratio boys/girls	1.20			
< 1 year	122	62	60	50,8
1-4 yrs	1 034	863	171	83,5
5-9 yrs	545	433	112	79,4
10-14 yrs	408	273	135	66,9

Age- and sexdistribution.



Survival probability at 10 and 20 years. Subdiagnosis.



Survival probability at 10 years. Time of diagnosis

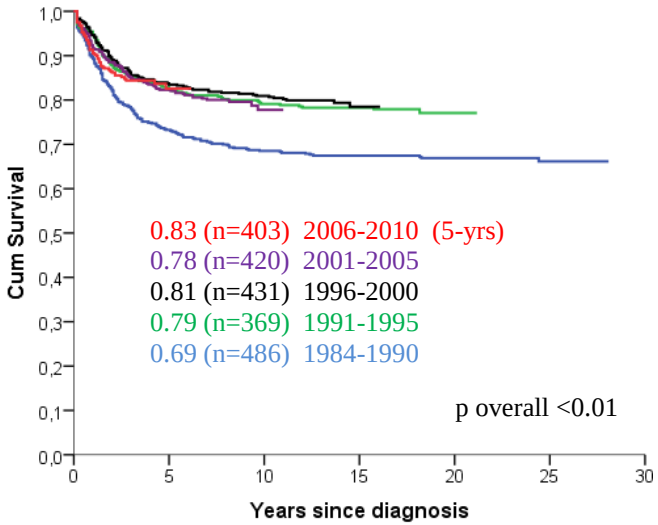
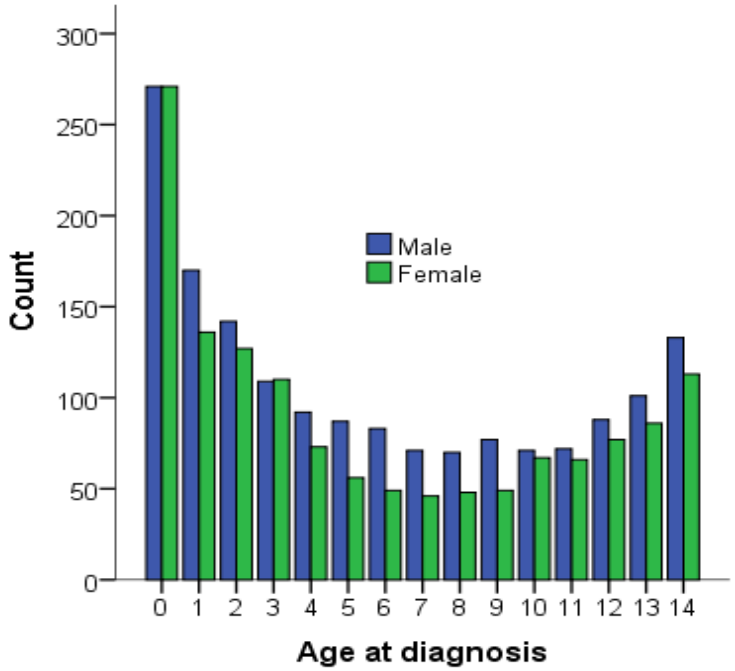


Fig 3.2.1.4.
All Solid tumors diagnosed 1984-2010
Selected criteria Total number of children: 3 011

Relative frequency		3 011/7 065=42.6 %		
	Number	Alive	Dead	% Alive
Boys	1 637	1 305	332	79,7
Girls	1 374	1 115	259	81,1
Ratio boys/girls	1.19			
< 1 year	542	455	87	83,9
1-4 yrs	959	753	206	78,5
5-9 yrs	637	517	120	81,2
10-14 yrs	873	695	178	79,6

Age- and sexdistribution.



Survival probability at 10 years

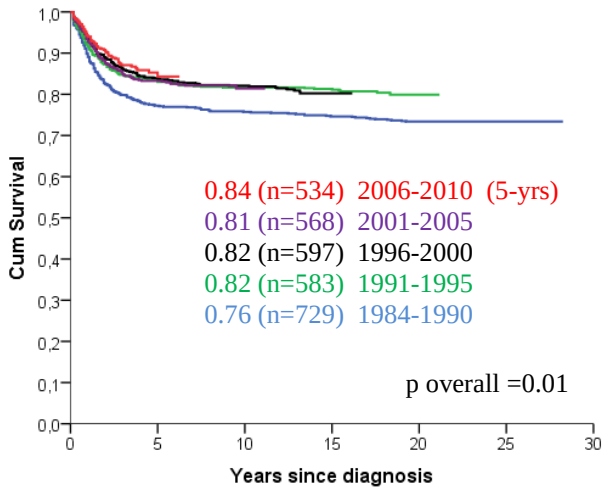
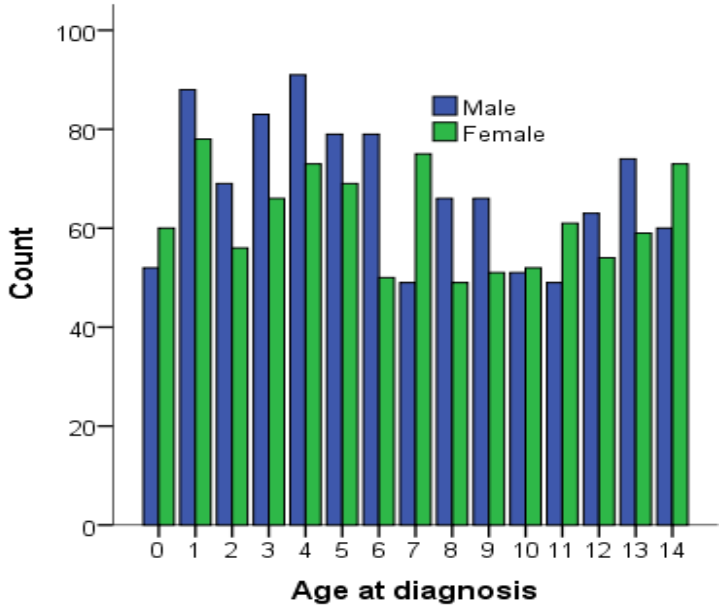


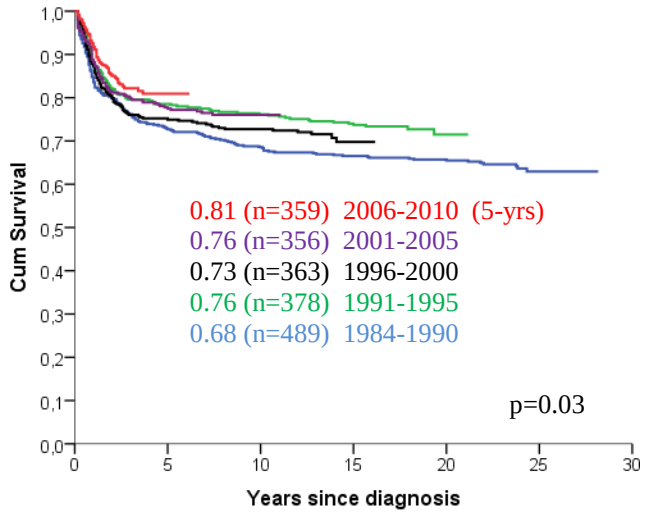
Fig 3.2.1.5.
All CNS tumors diagnosed 1984-2010
Selected criteria Total number of children: 1 945

Relative frequency		1 945/7 065=27.5 %		
	Number	Alive	Dead	% Alive
Boys	1 019	748	271	73,4
Girls	926	674	252	72,8
Ratio boys/girls	1.10			
< 1 year	112	68	44	60,5
1-4 yrs	603	433	170	71,8
5-9 yrs	634	457	177	72,1
10-14 yrs	596	464	132	77,9

Age- and sexdistribution.



Survival probability at 10 years



3.3.1.1 Leukemi- ALL

Den genomsnittliga årliga incidensen för samtliga leukemier under tidsperioden 1984-2010 var 5,0/100 000 barn < 15 år vid diagnos, 5,4 för pojkar och 4,6 för flickor.
Motsvarande incidenssiffra för ALL patienter var 4,2/100 000 barn.
Incidensen har en topp i gruppen 1-<5 år vid diagnos motsvarande den väl kända incidenstoppen vid ALL. AML är vanligast bland barn < 1 år vid diagnos. (Appendix 1.1). Prognosutvecklingen vid leukemier och särskilt ALL har varit mycket dramatisk och utgör det bästa exemplet på den framgångsrika behandlingen vid barncancer som skett under de senaste fem decennierna. Detta illustreras i nedanstående figur som inkluderar alla barn med ALL diagnostiserade i Sverige 1968-2010. Det har varit en kontinuerlig förbättring av prognosen fram till senaste 15 åren, varefter resultaten tycks ha stabiliserats. För mer detaljer om ALL behandlingen i Norden hänvisas till Referenser.

3.3.1.1 Leukemia - ALL

The mean annual incidence rate for all leukaemias diagnosed 1984 through 2005 was 5,0 cases/100 000 children < 15 years of age at diagnosis, 5,4 for boys and 4,6 for girls. Corresponding incidence rate for ALL patients was 4,2/100 000 children.
There is an incidence peak between 1-<5 years of age at diagnosis which illustrates the well-known peak in ALL. AML is most common among children < 1 year of age at diagnosis (Appendix A1.1). The increased survival in leukaemia and especially in ALL-children has been dramatic and is the best example of the successful development in childhood cancer that has occurred during the last five decades. This is shown in the historical figure below where all Swedish children with ALL diagnosed 1968 through 2010 are included. The survival rates have increased over time until the last 15 years when a stabilization of the results seems to have occurred.
For more details concerning ALL-treatment in the Nordic countries- see references.

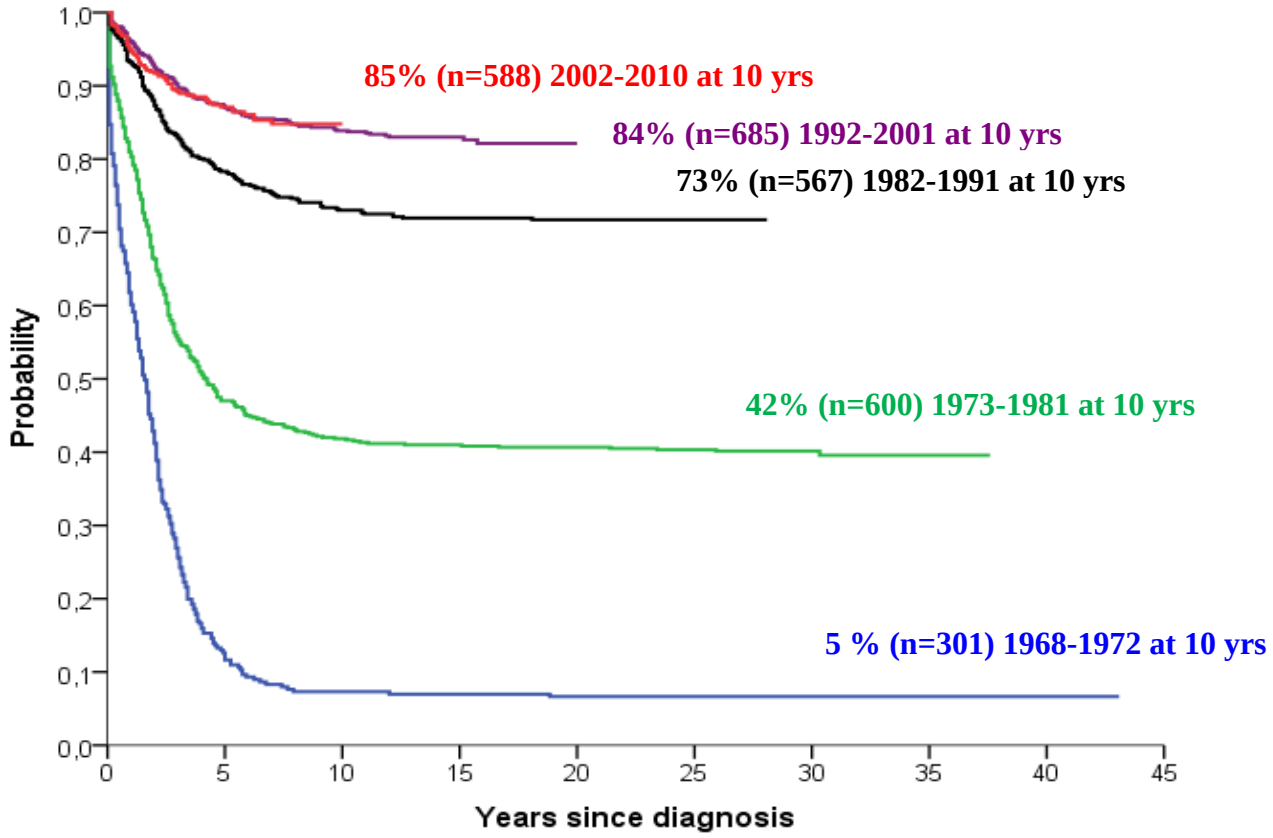


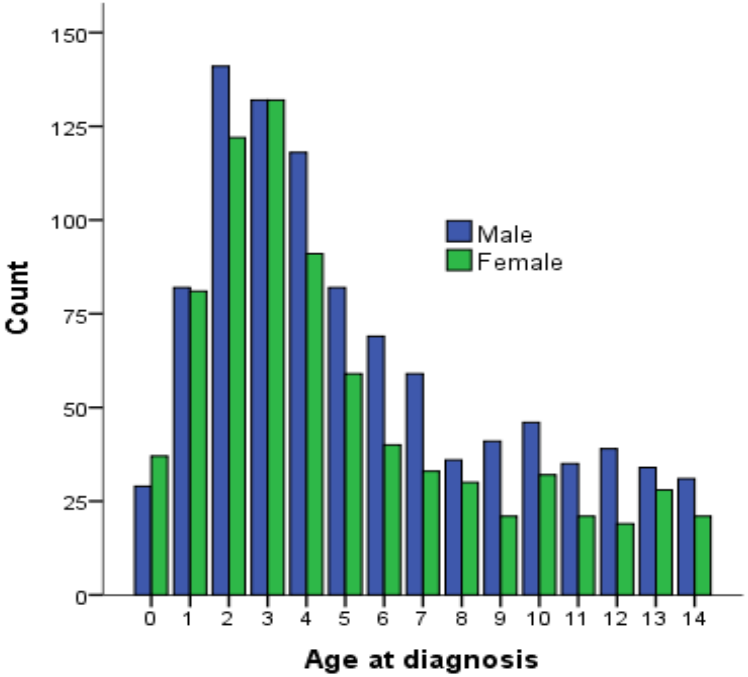
Fig 3.3.1.1

I a. Acute lymphoblastic leukemia. Diagnosed 1984-2010

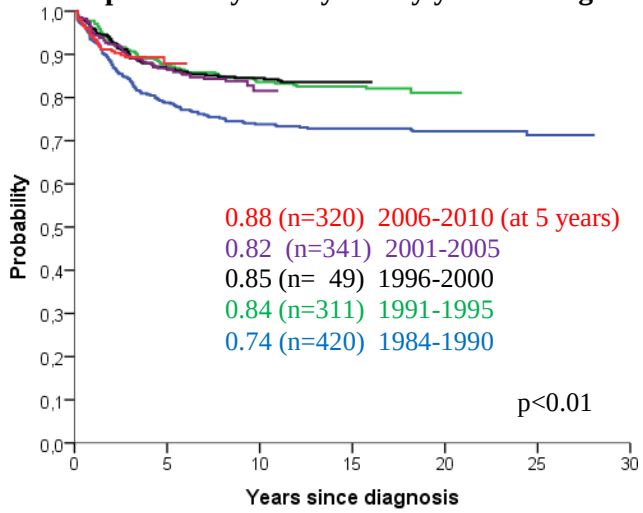
Selected criteria Total number of children:1 741

Relative frequency		1 741/7 065= 24.6 %		
	Number	Alive	Dead	% Alive
Boys	974	798	176	81,9
Girls	767	624	143	81,4
Ratio boys/girls	1.26			
< 1 year	66	31	35	47,0
1-4 yrs	899	786	113	87,4
5-9 yrs	470	388	82	82,6
10-14 yrs	306	217	89	70,9

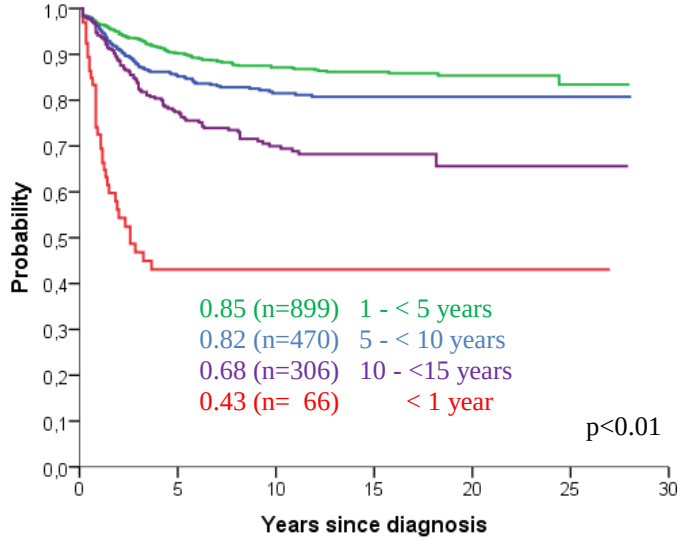
Age- and sexdistribution.



Survival probability at 10 years by years of diagnosis



Survival probability at 20 years by age at diagnosis



3.3.1.2 Leukemi- AML

Incidensen för AML patienter var 0,7/100 000 barn.
Sjukdomen är vanligast under de två första levnadsåren med övervikt för flickor.

Prognosförbättringen vid AML har som vid ALL varit dramatisk men inträffade ca 10 år efter genombrottet vid ALL.
AML hör fortfarande till gruppen av barn med en allvarlig prognos.

Förbättringen av prognosen sammanfaller med införande av gemensamma Nordiska behandlingsprotokoll 1984. Dessa har senare reviderats vid flertal tillfällen.
Ett fynd som tidigt iakttogs vid AML var att 10-15% av barnen som insjuknade var barn med Mb Down som även visade sig ha en mycket god prognos om de behandlades adekvat.
AML resultaten på Nordisk nivå har publicerats vid flertal tillfällen - se Referenser.

3.3.1.2 Leukemia - AML

The incidence rate for AML patients was 0,7/100 000 children.
The disease has the highest frequency during the first two years of life.

The improved prognosis in AML has like in ALL has been dramatic but occurred some 10 years later after the ALL breakthrough. Children with AML still belong to the group of children with a serious prognosis.
The improvement of prognosis coincides with introduction of common Nordic treatment protocols in 1984. The protocols have been modified at several time points.
A special feature which was early recognized in AML was that 10-15 % of the children were children with Mb Down. These children had an excellent prognosis if they received an adequately treatment.
The Nordic AML results have been published in several papers- See References.

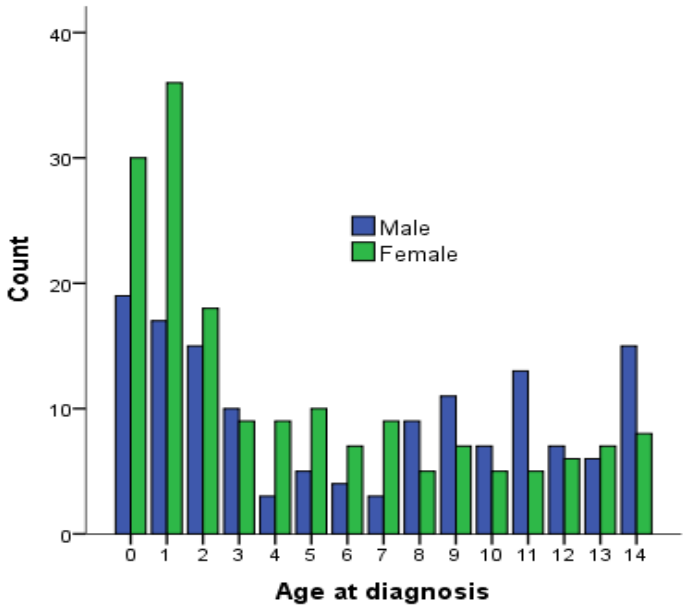
Fig 3.3.1.2

I b. Acute non-lymphoblastic leukemia
Diagnosed 1984-2010.

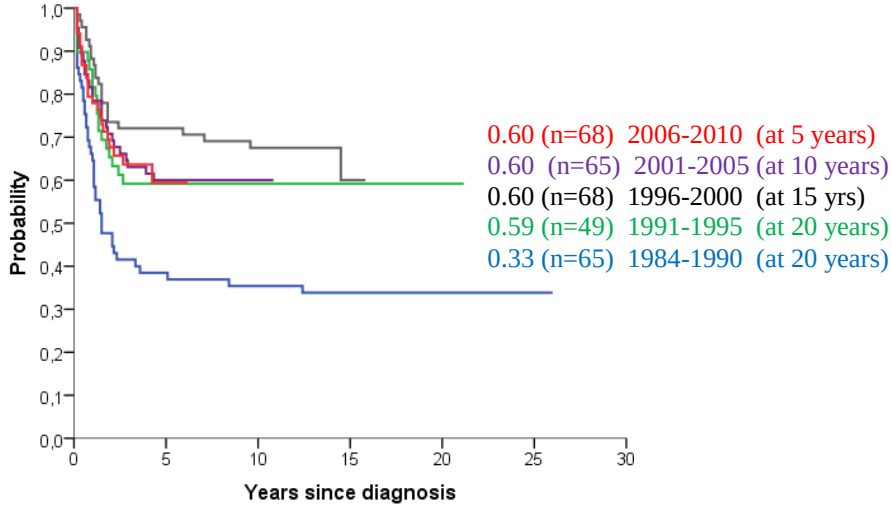
Selected criteria Total number of children: 315

Relative frequency		315/7 065= 4.5 %		
	Number	Alive	Dead	% Alive
Boys	144	84	60	58,3
Girls	171	95	76	55,6
Ratio boys/girls	0.85			
< 1 year	49	29	20	59,2
1-4 yrs	117	68	49	58,1
5-9 yrs	69	40	29	58,0
10-14 yrs	80	42	38	52,5

Age- and sexdistribution.



Survival probability by diagnostic period



3.3.1.3 Andra former av leukemi

53 barn utgör en liten grupp med varierande diagnoser (JMML, CMML, MDS).
Dessa barn har en allvarlig prognos och endast 23/53 (43 %) var i livet vid senaste uppföljningen.

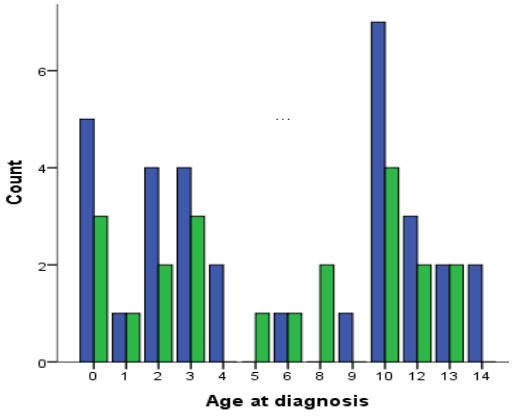
3.3.1.3 Other leukemias

53 children constitute a small group with different diagnoses (JMML, CMML, MDS).
These children have a serious prognosis and only 23/53 (43%) were alive at last follow up.

Fig 3.3.1.3
Ic. Other mixed forms
Diagnosed 1984-2010
Selected criteria Total number of children: 53

Relative frequency		53/7 065= < 0.1 %		
	Number	Alive	Dead	% Alive
CML,JMML	40	21	19	52,5
MDS	13	9	4	69,2
Boys	32	15	17	46,9
Girls	21	15	6	71,4
Ratio boys/girls	1.5			
< 1 year	7	2	5	28,6
1-4 yrs	18	9	9	50,0
5-9 yrs	6	5	1	83,3
10-14 yrs	22	14	8	63,6

Age- and sexdistribution.



3.3.2 Lymfom

Den genomsnittliga årliga incidensen för Lymfom under tidsperioden 1984-2010 var 2,0 fall/100 000 barn < 15 år vid diagnos, 2,6 för pojkar och 1,3 för flickor. (Appendix 1.1.)
Motsvarande incidenser vid Hodgkins sjukdom var 0,5/100 000, vid Non-Hodgkins lymfom (NHL) 0,8 vid Burkitt's lymfom 0,2 och för gruppen histiocytoser 0,5/100 000 barn.

Vid Hodgkins sjukdom ökar incidensen med stigande ålder. På grund av de höga överlevnadssiffrorna vid Hodgkins sjukdom (95 %) inriktas framtida protokoll på att reducera behandlingsintensiteten för att reducera långsiktiga biverkningar från framför allt strålbehandlingen.

Behandlingen av barn med NHL har framgångsrikt samordnats på Nordisk nivå med gemensamma behandlings-rekommendationer och uppföljningar av utfall. Prognosen har successivt förbättrats efter 1990. På senare år har Sverige anslutit sig till fr a tyska behandlingsstudier.
Gruppen histiocytoser består av en mycket liten grupp patienter hemofagocyterande lymfhistiocytos (HLH) med mycket allvarlig prognos och en till antalet helt dominerande grupp av patienter med Langerhans cell histiocytos (LCH) - med mycket bättre prognos. Sistnämnda patientgrupp exkluderas i vissa rapporter om cancer och redovisas separat, men är inkluderade i denna rapport.

3.3.2 Lymphomas

The mean annual incidence rate for all lymphomas diagnosed 1984 through 2010 was 2,0 cases/100 000 children < 15 years of age at diagnosis, 2,6 for boys and 1,3 for girls. (Appendix 1.1).
Corresponding incidence rates were for Hodgkin's disease 0,4, for Non-Hodgkin's lymphoma 0,8 for Burkitt's lymphoma 0,2 and for the group histiocytosis 0,5/100 000 children.

The incidence rates for Hodgkin's disease increase with increasing ages. Due to the high survival figures for Hodgkin's disease (95 %), future protocols have the intention to reduce the treatment intensity in order to reduce long time side effects especially from irradiation.

The treatment of children with NHL has been coordinated with common Nordic protocol recommendations and survival analyses. The prognosis in NHL has improved since 1990. In later years, Sweden has joined and treated the patients according to German protocols.

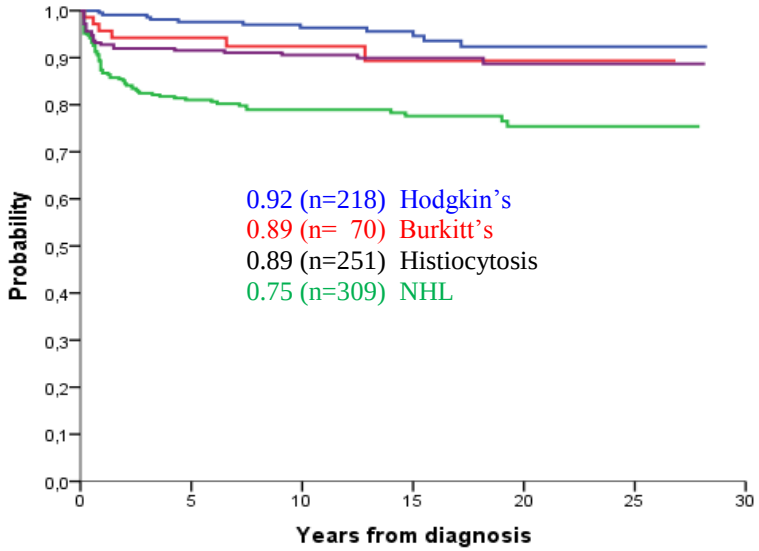
The histiocytoses consist of a smaller group of patients: hemophagocytic lymph histiocytosis (HLH) with a very serious prognosis and the larger group of patients with Langerhan's cell histiocytosis (LCH) - with much better prognosis. These patients are sometime excluded from analyses of cancer materials and are reported separately, but are included in the present compilation.

Fig 3.3.2 Group II. Lymphomas and reticuloendothelial neoplasms. Diagnosed 1984-2010

Selected criteria Total number of children: 848

Relative frequency	848/7 065 = 12.0%			
	Number	Alive	Dead	% Alive
Diagnosis				
Hodgkin's	218	207	11	95,0
Non-Hodgkin's	309	242	67	78,3
Burkitt's	70	64	6	91,4
Histiocytosis (LCH/HLH)	251	226	25	90,0
Boys	565	488	77	86,4
Girls	283	251	32	88,7
Ratio boys/girls	2.0			
< 1 year	64	53	11	82,8
1-4 yrs	196	164	32	83,7
5-9 yrs	257	229	28	89,1
10-14 yrs	331	293	38	88,5

Survival probability at 20 years



Age- and sex distribution

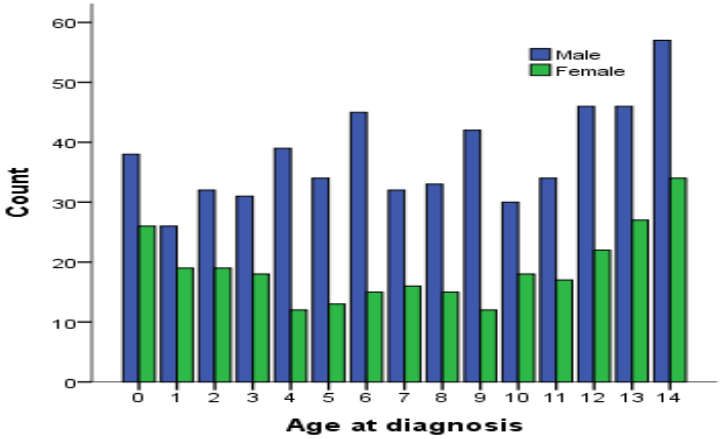


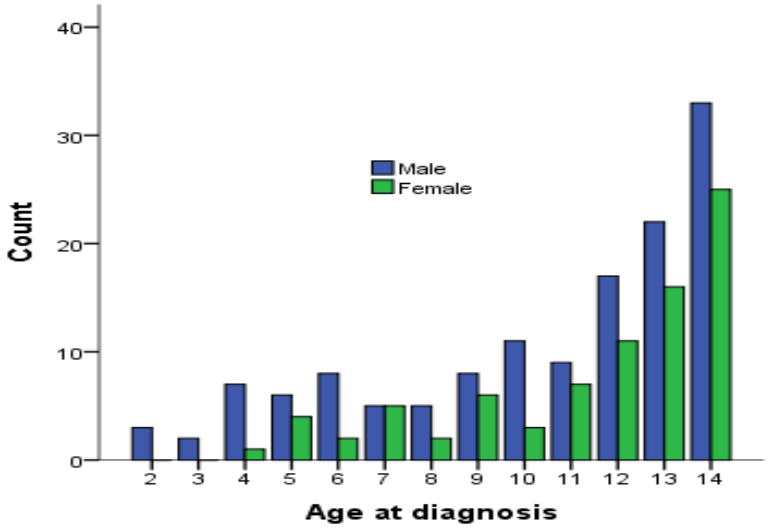
Fig 3.3.2.1

Group IIa. Hodgkin's disease. Diagnosed 1984-2010

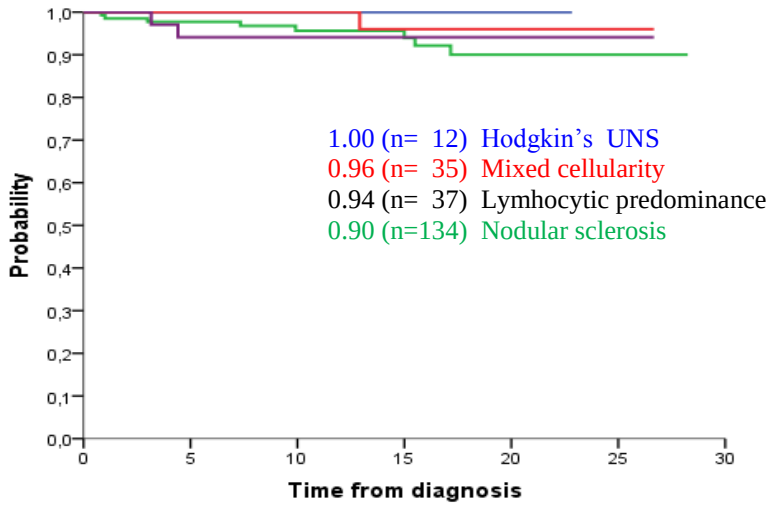
Selected criteria Total number of children: 218

Relative frequency		218/7 065 = 3.1 %		
	Number	Alive	Dead	% Alive
Boys	136	129	7	94,9
Girls	82	78	4	95,1
Ratio boys/girls	1.7			
< 1 year	0			
1-4 yrs	13	12	1	92,3
5-9 yrs	51	48	3	94,1
10-14 yrs	154	147	7	95,5

Age- and sexdistribution



Survival probability at 20 years- PAD



Survival probability at 10 years by diagnostic period

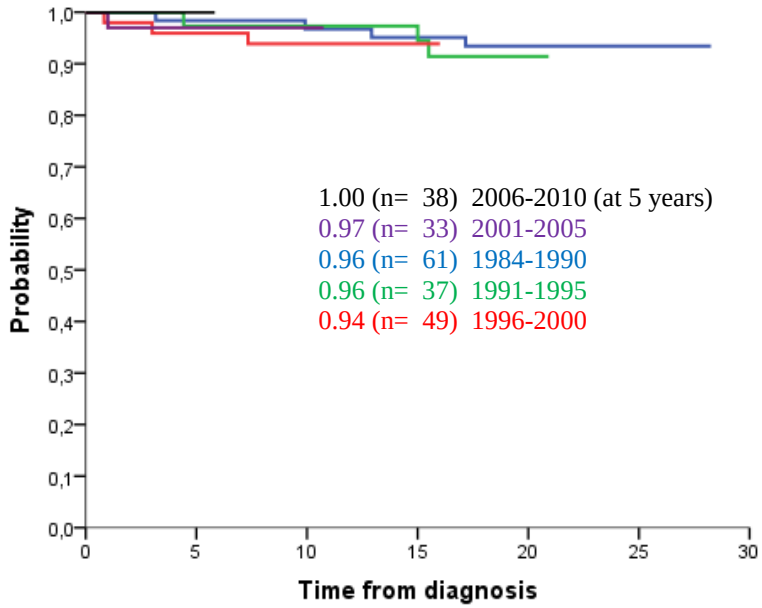
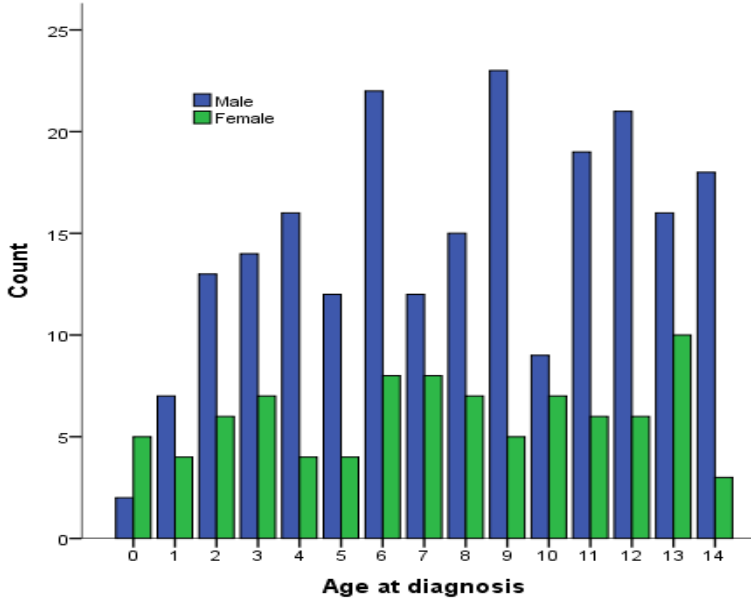


Fig 3.3.2.2
Group IIb. Non-Hodgkin's disease
Diagnosed 1984-2010

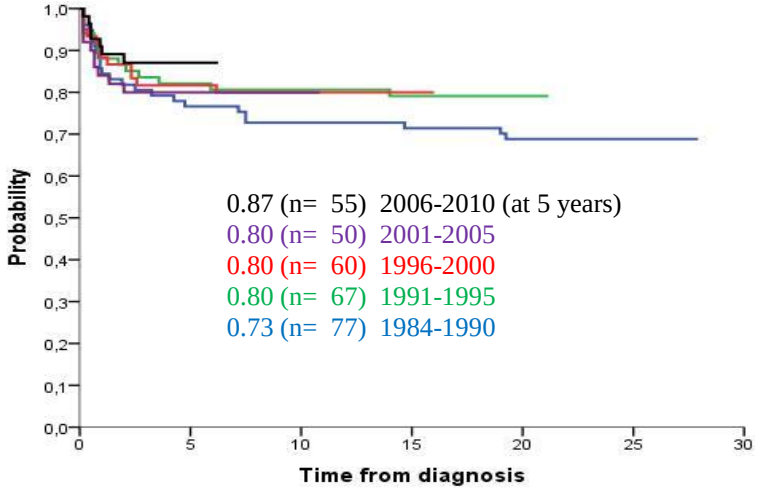
Selected criteria Total number of children: 309

Relative frequency		309/7 065= 4.4 %		
	Number	Alive	Dead	% Alive
Boys	219	172	47	78,5
Girls	90	70	20	77,8
Ratio boys/girls	2.4			
< 1 year	7	3	4	42,9
1-4 yrs	71	54	17	76,1
5-9 yrs	116	95	21	81,9
10-14 yrs	115	90	25	78,3

Age- and sexdistribution



Survival probability at 10 years by diagnostic period



Survival probability at 20 years by PAD

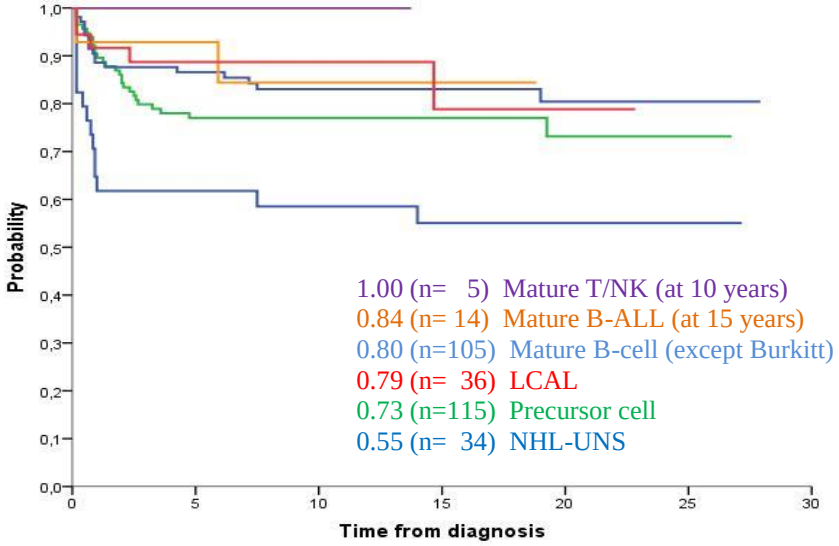


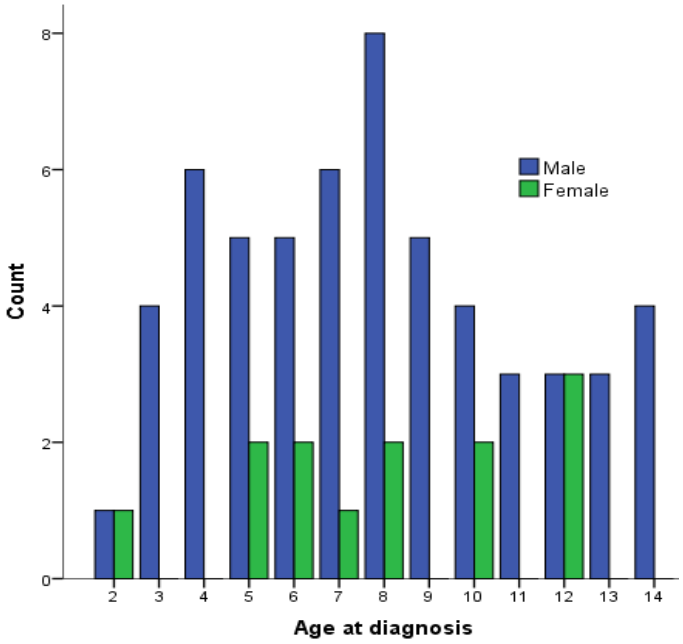
Fig 3.3.2.3

Group IIc. Burkitt's lymphomas diagnosed 1984-2010

Selected criteria Total number of children: 70

Relative frequency		70/7 065= 1.0 %		
	Number	Alive	Dead	% Alive
Boys	57	53	4	93,0
Girls	13	11	2	84,6
Ratio boys/girls	4.4			
< 1 year	0			
1-4 yrs	12	12	0	100
5-9 yrs	36	35	1	97,2
10-14 yrs	22	17	5	77,3

Age- and sexdistribution



Survival probability at 10 years by diagnostic period

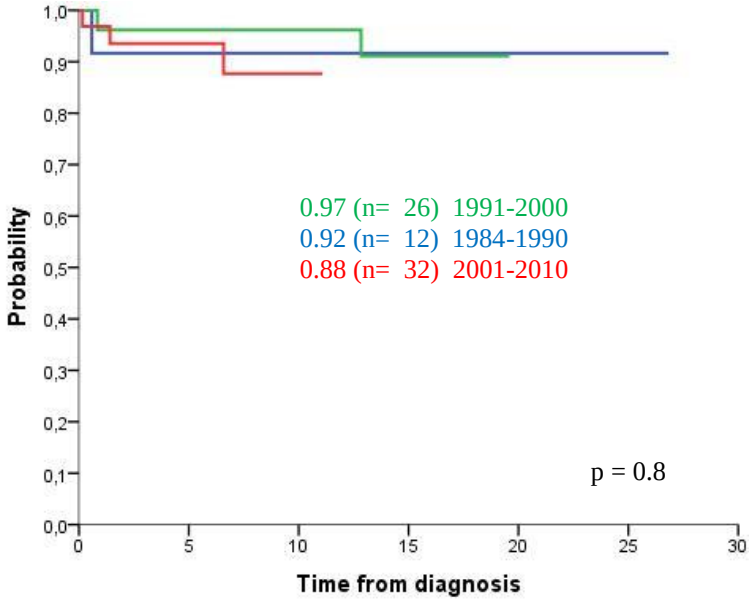


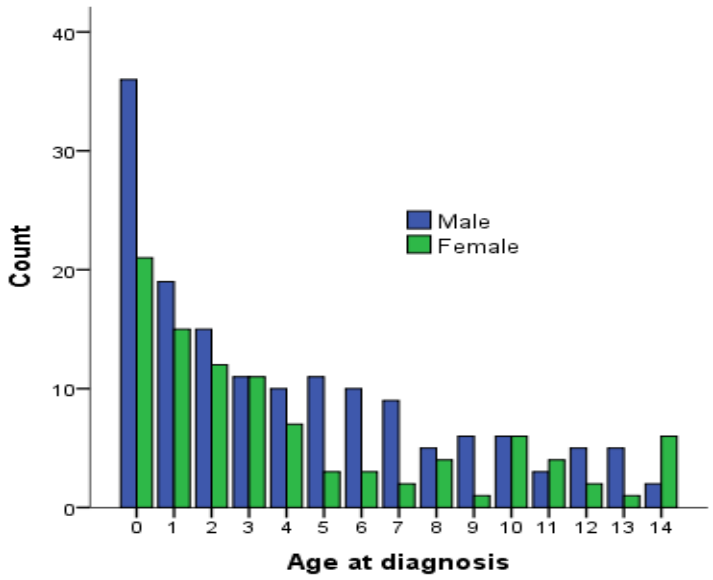
Fig 3.3.2.4

Group IId. Histiocytosis. Diagnosed 1984-2010

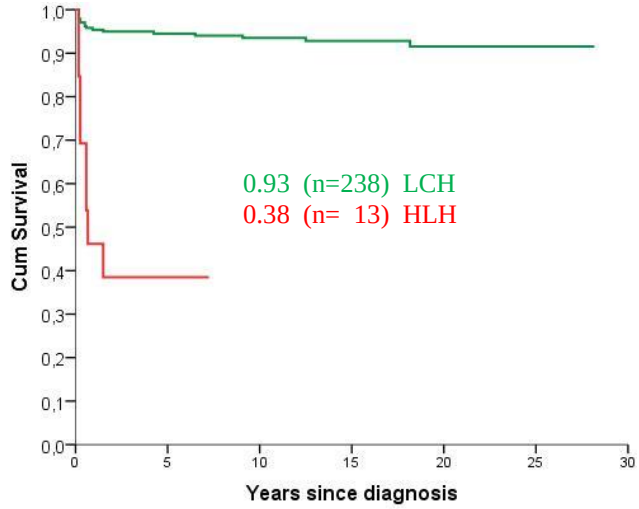
Selected criteria Total number of children: 251

Relative frequency		251/7 065= 3,6 %		
	Number	Alive	Dead	% Alive
LCH	238	221	17	92,9
HLH	13	5	8	38,5
Boys	153	134	19	87,6
Girls	98	92	6	93,9
Ratio boys/girls	1.6			
< 1 year	57	50	7	87,7
1-4 yrs	100	86	14	86,0
5-9 yrs	54	51	3	94,4
10-14 yrs	40	39	1	97,5

Age- and sexdistribution



Survival probability at 5 and 20 years.



3.3.3 CNS tumörer

Den genomsnittliga årliga incidensen för CNS-tumörer under tidsperioden 1984-2010 var 4,6 fall/100 000 barn < 15 år vid diagnos, 4,7 för pojkar och 4,5 för flickor. Incidensen har varit stabil under hela tidsperioden vid analys av gruppen som helhet. Åldersfördelningen vid CNS-tumörer är relativt jämnt fördelad utan någon påtaglig incidenstopp.(Appendix 1.1)

Figur 3.3.3 visar översiktligt alla CNS-tumörer indelade i undergrupper. Prognoserna skiljer sig avsevärt mellan de olika undergrupperna med skillnader i överlevnadssiffror mellan 40-80 %. Vidare framkommer i överlevnadsfigurerna att sena dödsfall är relativt vanligt förekommande även 10-20 år efter diagnos. Detta skiljer sig från våra erfarenheter vid leukemier och merparten av solida tumörer där en klar majoritet av dödsfallen sker inom 10 år efter diagnos.
Prognosen över tiden har dock förbättrats över hela tidsperioden.

På följande sidor visas resultaten för barn med CNS-tumörer.
Fig. 3.3.3.2 visar de markant olika överlevnadsresultaten för undergrupperna av astrocytom.
I fig. 3.3.3.3.2 framkommer att prognosen för barn med embryonala CNS-tumörer under perioden 1984-1990 tycks vara bättre än under senare perioder vilket möjligen kan förklaras med att högre stråldoser gavs under den tidigare tidsperioden. Flickorna är färre, men har bättre prognos vid denna tumörtyp.
I fig. 3.3.3.4 ingår som undergrupp oligodendrogliom och patienter med ponsgliom med en i de flesta fall fatal utgång.
Fig. 3.3.3.5 visar prognos för olika tumörer i denna grupp, bland annat kranio-faryngeom.

3.3.3 CNS tumours

The mean annual incidence rate for CNS-tumours diagnosed 1984 through 2010 was 4,6 cases/100 000 children < 15 years of age at diagnosis, 4,7 for boys and 4,5 for girls. The incidence rates have been stabile during the study period for the whole group of patients. The age distribution in CNS-tumours has a relatively even distribution without evident peaks (Appendix 1.1).

Figure 3.3.3 shows an overview of all CNS-tumours classified into subgroups. The different diagnoses have marked differences in survival figures fluctuating between 40-80%.
Late deaths even after 10-20 years from diagnosis occur in a relative high frequency among CNS-tumour patients. This is in contrast with our experiences from leukaemias and most solid tumours where a clear majority of the deaths occur within 10 years after diagnosis.
Anyhow, the prognosis over time has improved.

The results for the different sub diagnoses of CNS-tumours are shown in the following pages.
Fig 3.3.3.2 shows the highly different survival figures for the subgroups of astrocytomas.
Figure 3.3.3.3.2 shows that the prognosis for children diagnosed with Embryonal CNS-tumours during the time period 1984-1990 seems to be better compared to later years, which may be explained by higher radiation doses given during this earlier time period. Girls are fewer but have better prognosis for this group of tumours.
Figure 3.3.3.4 illustrates the survival for patients with oligodendrogliomas and patients with pontine gliomas who have a dismal outcome in most cases.
Figure 3.3.3.5 shows prognosis for different types of tumours in this group, inter alia for craniopharyngeomas.

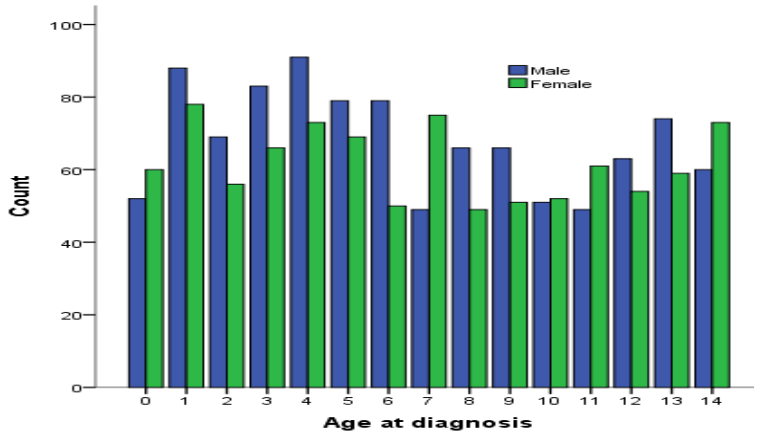
Fig 3.3.3

Group III. Intracranial/intraspinal neoplasms 1984-2010.

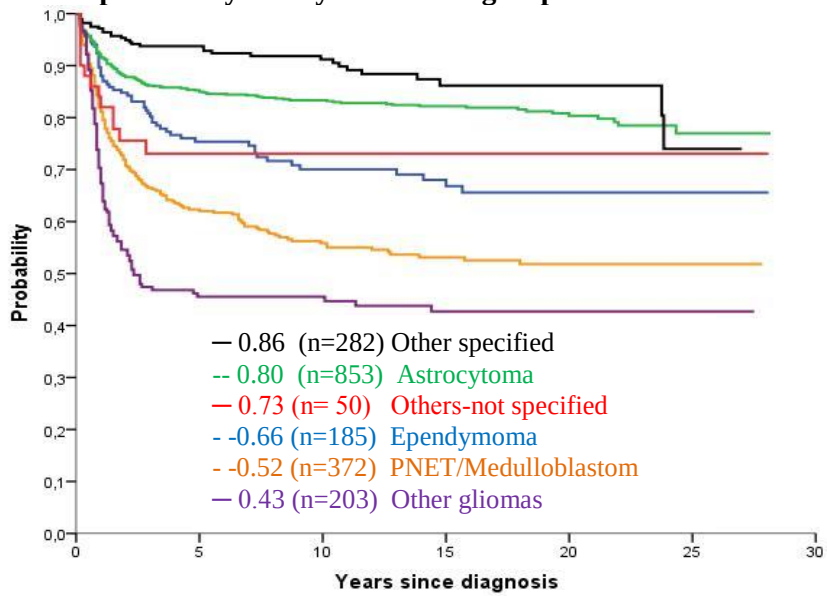
Selected criteria Total number of children: 1 945/ 7 065

Relative frequency	1 945/7 065 =27.5 %			
	Number	Alive	Dead	%Alive
Subdiagnosis				
a. Ependymoma	185	130	55	70,3
b. Astrocytoma	853	702	151	82,3
c. Embryonal tumour	372	208	164	55,9
d. Other gliomas	203	93	110	45,8
e. Others specified	282	252	30	89,4
f. Others nonspec.	50	37	13	74,0
Boys	1019	748	271	73,4
Girls	926	674	252	72,8
Ratio boys/girls	1.1			
< 1 year	112	68	44	60,7
1-4 yrs	603	433	170	71,8
5-9 yrs	634	457	177	72,1
10-14 yrs	596	464	132	77,9

Age- and sexdistribution



Survival probability at 20 years- WHO group



Survival probability at 10 years by diagnostic period

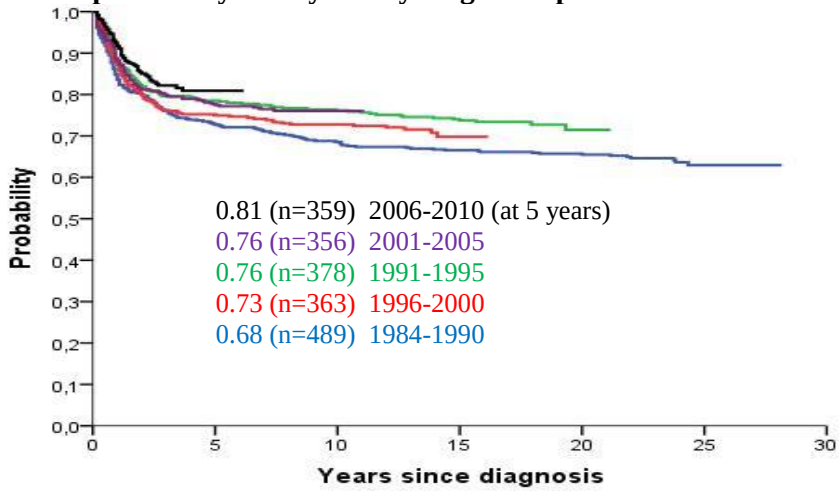


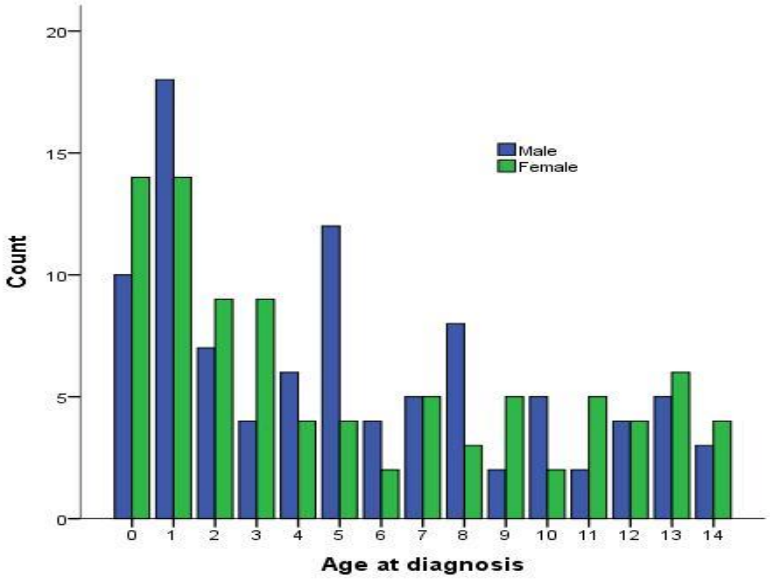
Fig 3.3.3.1

Group IIIa. Ependymoma. Diagnosed 1984-2010

Selected criteria Total number of children: 185

Relative frequency	185/7 065 =2,6 %			
	Number	Alive	Dead	% Alive
Ependymoma	149	97	52	65,1
Plexus choroideus	36	33	3	91,7
Boys	95	67	28	70,5
Girls	90	63	27	70,0
Ratio boys/girls	1.1			
< 1 year	24	18	6	75,0
1-4 yrs	71	39	32	54,9
5-9 yrs	50	38	12	76,0
10-14 yrs	40	35	5	87,5

Age- and sexdistribution



Survival probability at 20 years

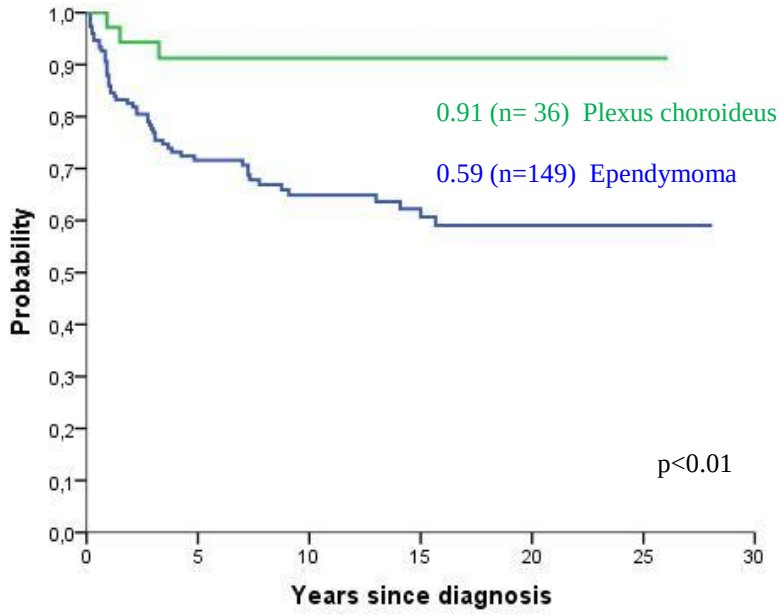
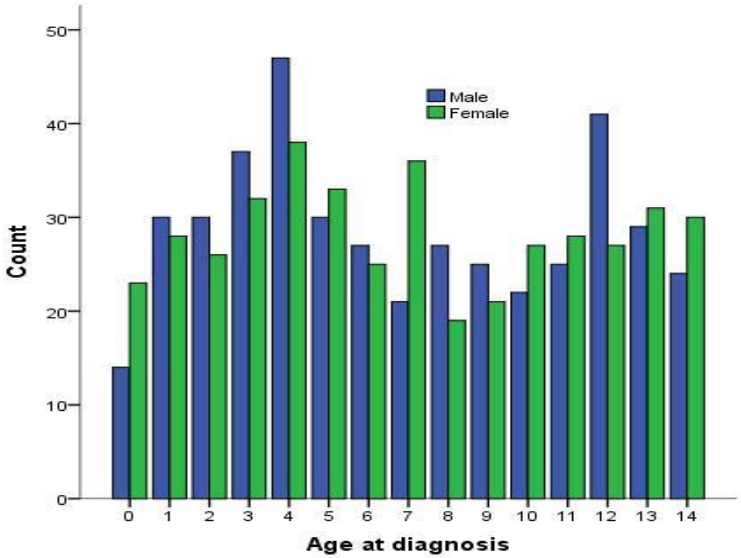


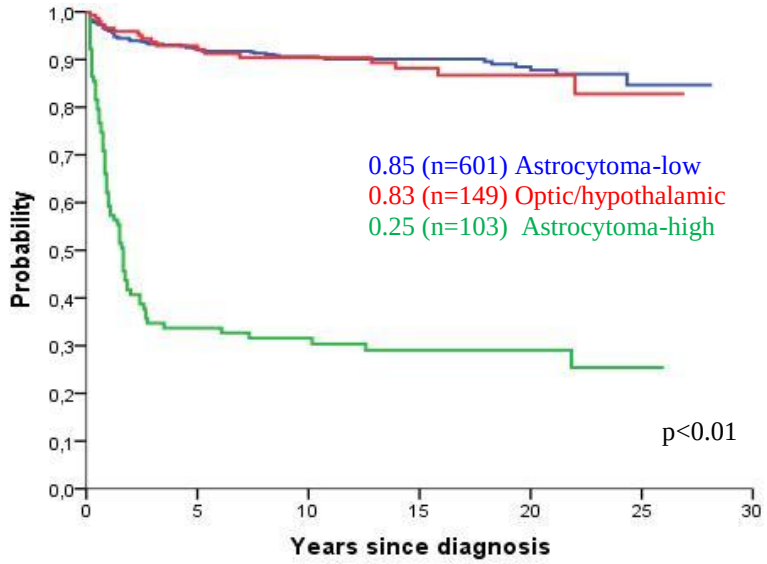
Fig 3.3.3.2
Group IIIb. Astrocytoma. Diagnosed 1984-2010.
Selected criteria Total number of children: 660

Relative frequency	853/7 065 =12,1 %			
	Number	Alive	Dead	% Alive
Astrocytoma-low	601	540	61	89,9
Astrocytoma-high	103	30	73	29,1
Optic/hypothalamic	149	132	17	88,6
Boys	429	361	68	84,1
Girls	424	341	83	80,4
Ratio boys/girls	1.01			
< 1 year	37	23	14	62,2
1-4 yrs	268	231	37	86,2
5-9 yrs	264	219	45	83,0
10-14 yrs	284	229	55	80,6

Age- and sexdistribution



Survival probability at 20 years



Survival probability at 10 years by diagnostic period

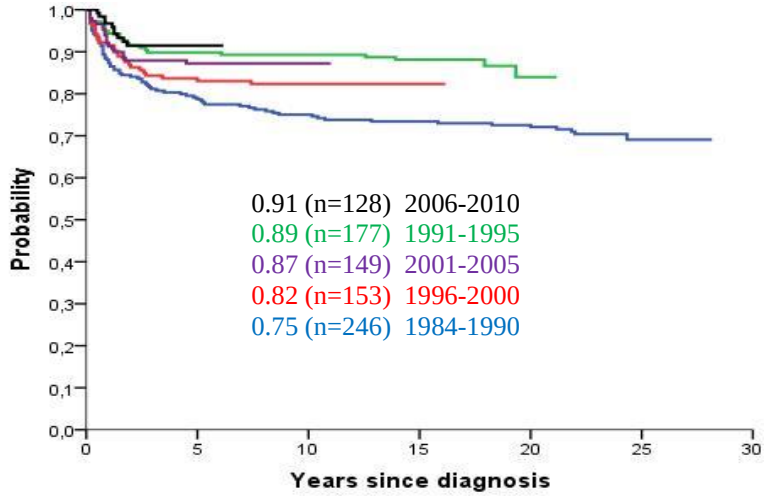
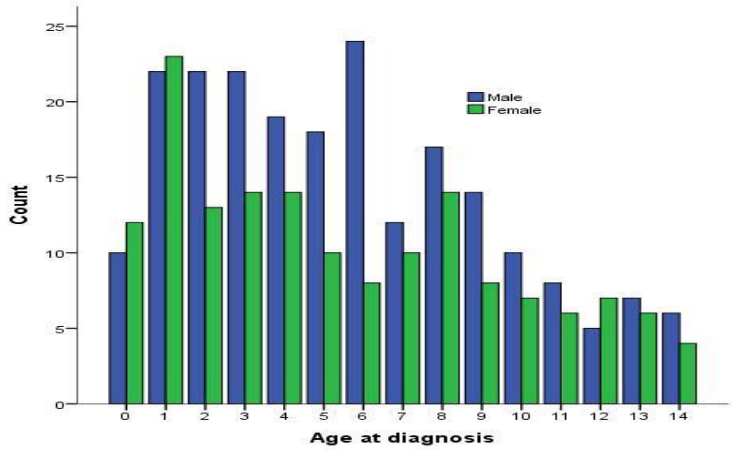


Fig 3.3.3.3.1
Group IIIc. Embryonal tumours.
Diagnosed 1984-2010.

Selected criteria. Total number of children: 372

Relative frequency	372/7 065 =5,3 %			
	Number	Alive	Dead	% Alive
Medulloblastoma	296	174	122	58,8
PNET	63	27	36	42,9
AT/RT	9	4	5	44,4
Medulloepithelioma	4	3	1	75,0
Boys	216	112	104	51,9
Girls	156	96	60	61,5
Ratio boys/girls	1.38			
< 1 year	22	8	14	36,4
1-4 yrs	149	84	65	56,4
5-9 yrs	135	80	55	59,3
10-14 yrs	66	36	30	54,5
Infratentoriell	242	142	100	58,7
Supratentoriell	69	28	41	40,6
Brain stem	12	4	8	33,3
Spinal	5	1	4	20,0
Unknown loc.	44	33	11	75,0

Age- and sex distribution



Survival probability at 20 years

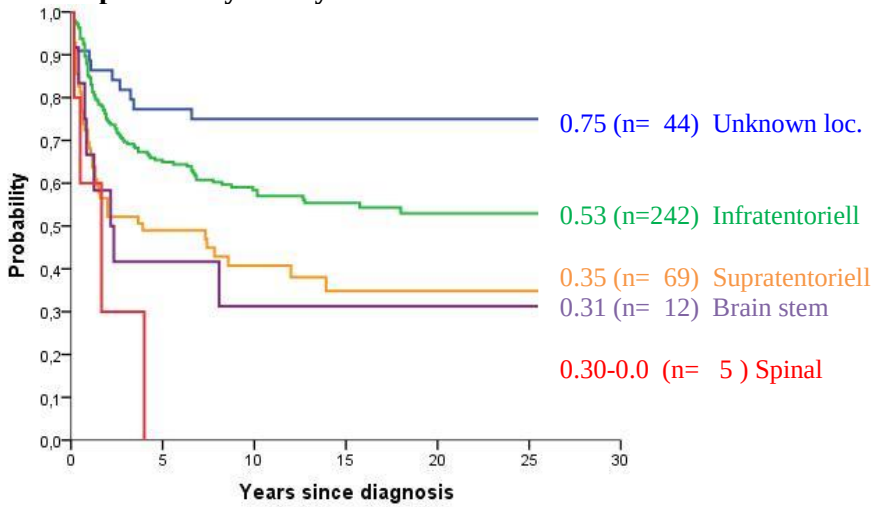
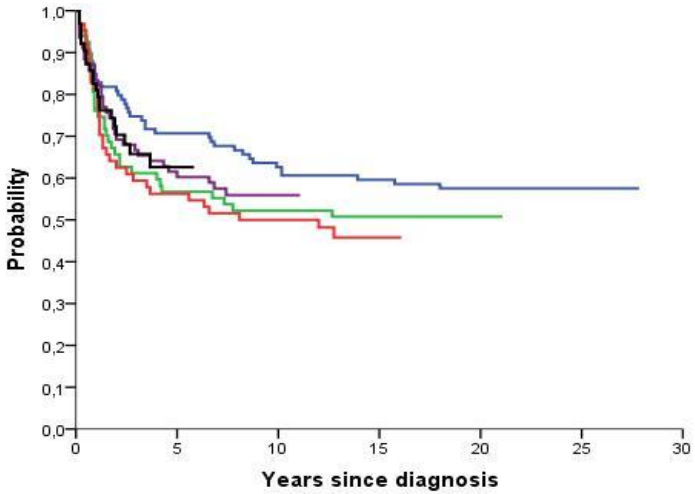
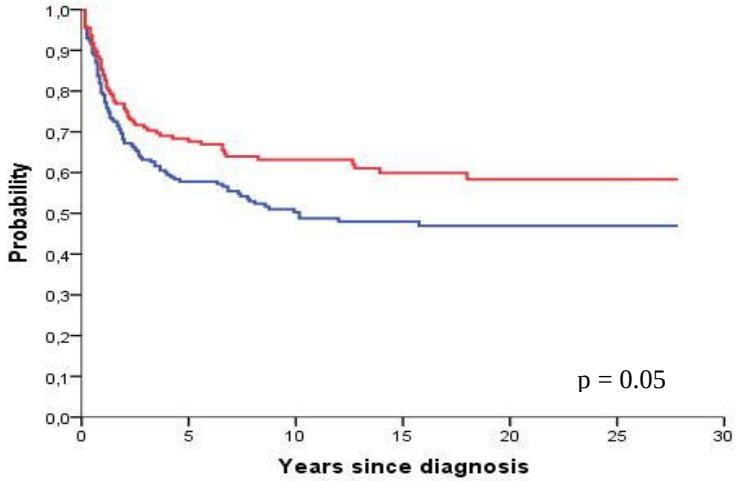


Fig 3.3.3.3.2
Group IIIc. Embryonal tumours (continued)
Survival probability at 10 years by diagnostic period



0.63 (n=64) 2006-2010 (at 5 years)
0.63 (n=99) 1984-1990
0.56 (n=78) 2001-2005
0.52 (n=67) 1991-1995
0.50 (n=64) 1996-2000

Survival probability at 20 yrs - Gender



0.58 (n=156) Females

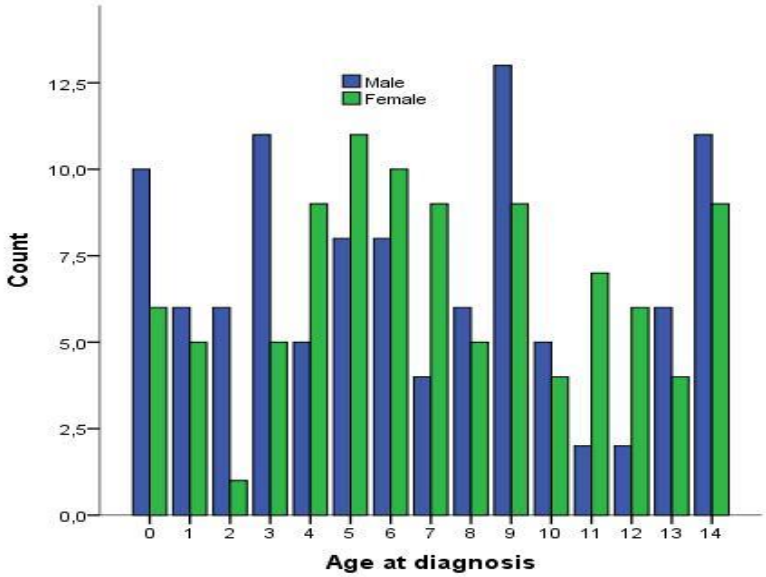
0.47 (n=216) Males

Fig 3.3.3.4
Group IIId. Other gliomas
Diagnosed 1984-2010.

Selected criteria Total number of children: 203

Relative frequency	203/7 065 =2,8 %			
	Number	Alive	Dead	% Alive
Oligodendrogliom	41	31	10	24,3
Mixed and unspec gliomas	102	51	51	50,0
Neuroepitelial glial- or uncertain origin	60	11	49	18,3
Boys	103	37	37	50,0
Girls	100	27	47	63,5
Ratio boys/girls	1.0			
< 1 year	16	11	5	68,8
1-4 yrs	47	24	23	51,1
5-9 yrs	84	31	53	36,9
10-14 yrs	56	27	29	48,2

Age-and sexdistribution



Survival probability at 20 years

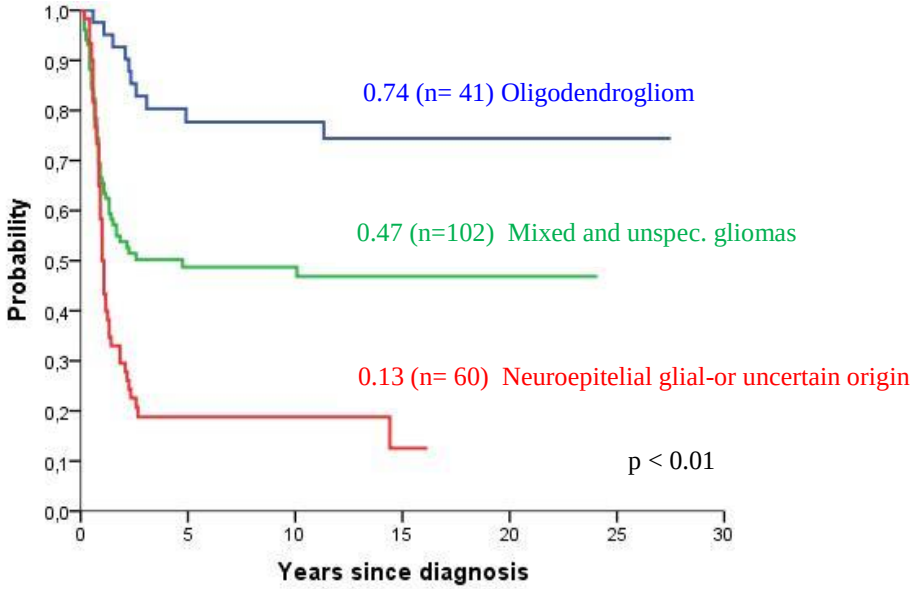


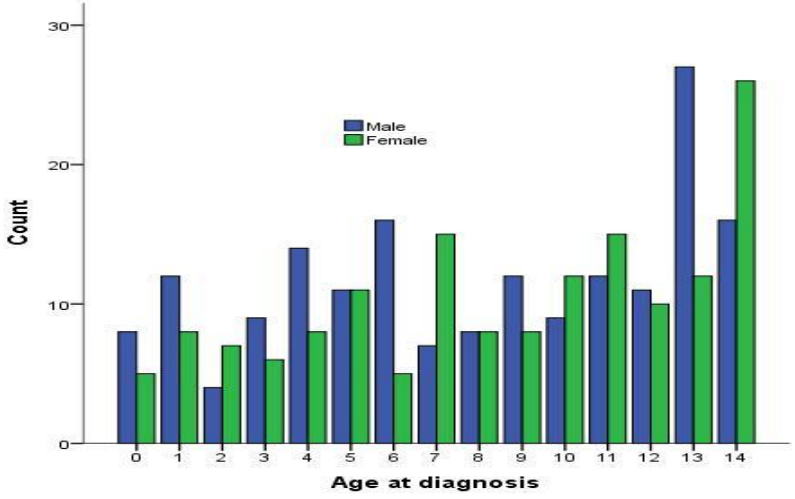
Fig 3.3.3.5

Group IIIe+f. Others specified and unspecified neoplasms.

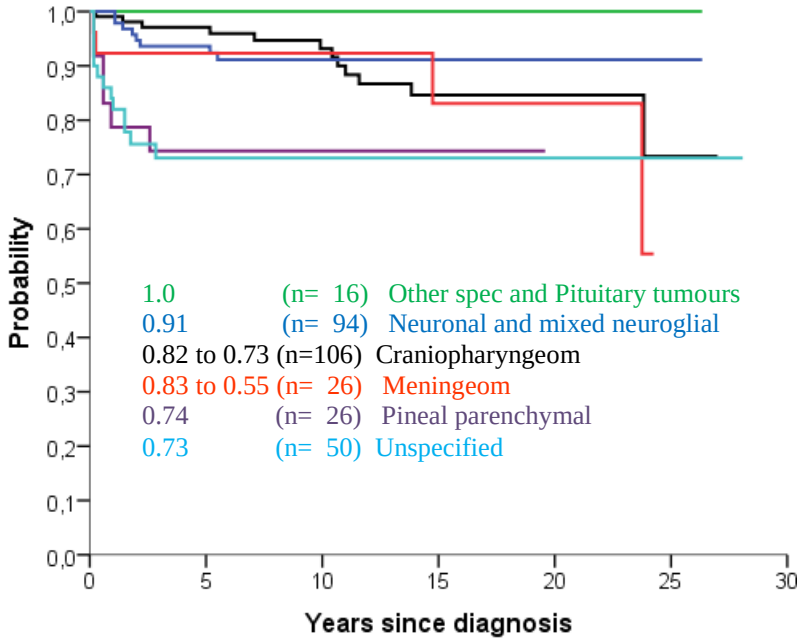
Selected criteria Total number of children: 332

Relative frequency	332/7 065 =4,7 %			
	Number	Alive	Dead	%Alive
Pituitary adenomas/carcinomas	16	16	0	100
Craniopharyngeoma	106	94	12	88,7
Pineal parenchymal tumours	26	20	6	76,9
Neuronal and mixed neuronglial	94	86	8	91,5
Meningeomas	26	22	4	84,6
Other specified	14	14	0	100
Unspecified intracranial/spinal	50	37	13	74,0
Boys	176	153	23	86,9
Girls	156	136	20	87,2
Ratio boys/girls	1.1			
< 1 year	13	8	5	66,6
1-4 yrs	68	55	13	84,2
5-9 yrs	101	89	12	91,2
10-14 yrs	150	137	13	91,2

Age-and sexdistribution.



Survival probability at 20 years



3.3.4 Neuroblastom

Den genomsnittliga årliga incidensen för barn med neuroblastom under tidsperioden 1984-2010 var 0,7 fall/100 000 barn < 15 år vid diagnos. Incidensen är högst under första levnadsåret för att sedan successivt sjunka med stigande ålder.

Neuroblastom är vanligare hos pojkar med ett M/F ratio på 1,22.
Den viktigaste kliniska prognostiska faktorn vid neuroblastom är ålder vid diagnos vilket klart framgår av figur 3.3.4.1 med bättre överlevnad för barn <18 månader vid diagnos.

Det har skett en signifikant förbättring av överlevnaden bland dessa barn efter 2001 vilket framgår av figur 3.3.4.2.
Detta sammanfaller med en förbättrad förståelse av sjukdomen och påtagligt ökad behandlingsintensitet med införande av nya behandlingsformer för barn med högriskneuroblastom.

3.3.4 Neuroblastoma

The mean annual incidence rate for children with neuroblastoma diagnosed 1984 through 2010 was 0,7 cases/100 000 children < 15 years of age at diagnosis. The incidence rate is highest during the first year of life with decreasing incidence with increasing age.
Neuroblastoma is more common among boys, with M/F ratio of 1.22.
The most important clinical prognostic factor in children with neuroblastoma is the age at diagnosis which is evident in the figure 3.3.4.1 with better survival for children <18 months at diagnosis.
The survival rates have improved significantly for these children after 2001, which is shown in figure 3.3.4.2.
This coincides with an improved understanding of the disease and significantly increased treatment intensity with introduction of novel treatment modalities for children with high-risk neuroblastoma.

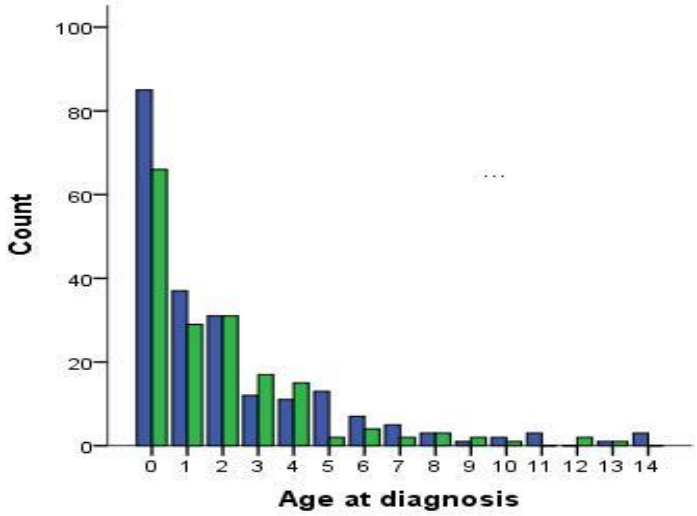
Fig 3.3.4.1

Group IV. Symphatetic nervous system tumors. Diagnosed 1984-2010

Selected criteria Total number of children: 389

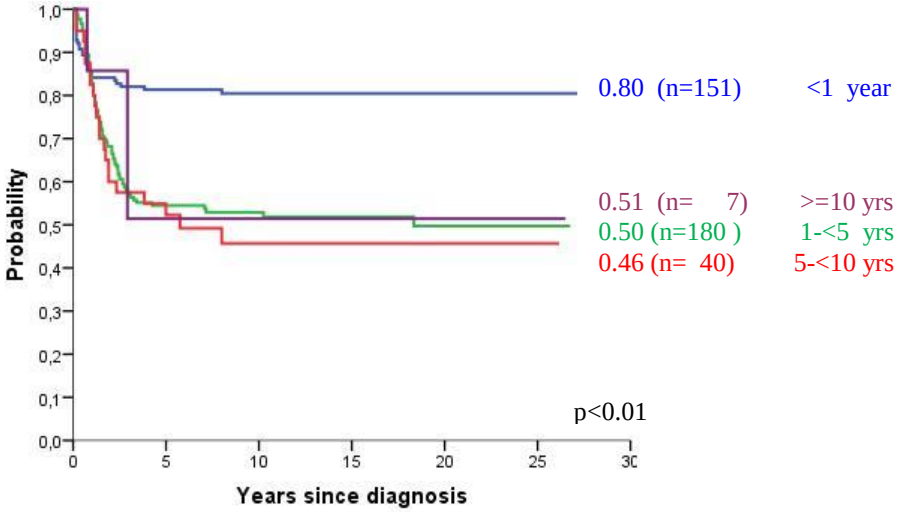
Relative frequency	389/7 065 = 5.5 %			
	Number	Alive	Dead	% Alive
Diagnoses				
a. Neuroblastom	378	241	137	63,8
b. Others	11	10	1	90,9
Boys	214	131	83	61,2
Girls	175	120	55	68,6
Ratio boys/girls	1.22			
< 1 year	151	122	29	80,8
1-4 yrs	183	99	84	54,1
5-9 yrs	42	21	21	50,0
10-14 yrs	13	9	4	69,2

Age- and sexdistribution



Neuroblastoma. Different age at diagnosis.

Total number of children: 378



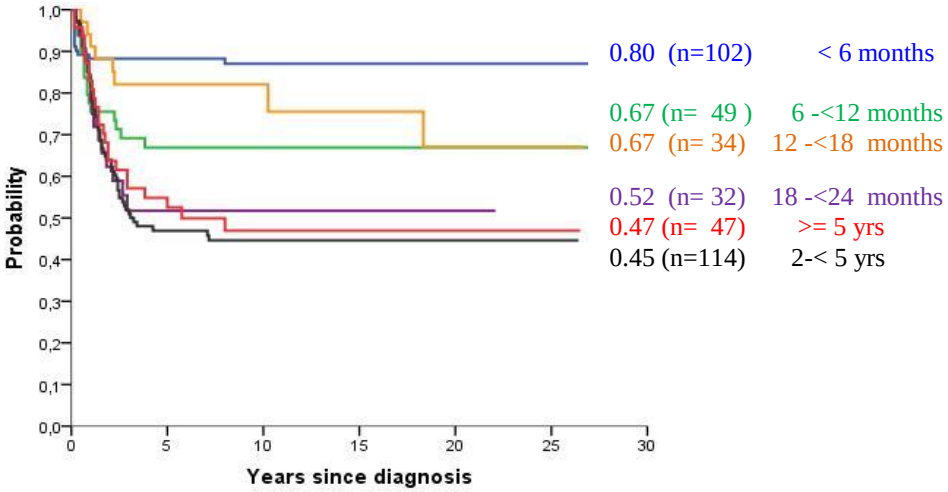
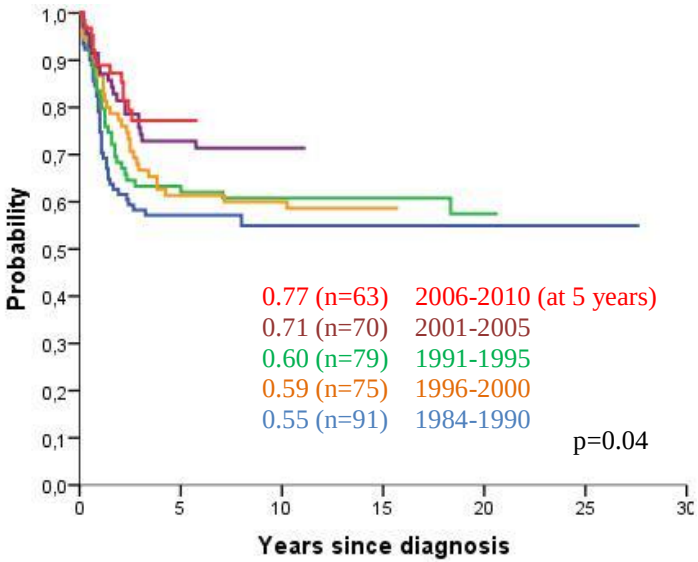


Fig 3.3.4.2 (continued)
Survival probability at 10 years by diagnostic period – all ages



The prognosis has improved over time, most pronounced after 2001.

3.3.5 Retinoblastom

Den genomsnittliga årliga incidensen för retinoblastom under tidsperioden 1984-2010 var 0,25 fall/100 000 barn < 15 år vid diagnos. Sjukdomen är vanligast under första levnadsåret för att därefter snabbt sjunka i frekvens och är ovanlig hos barn över 5 års ålder (5/153).
Det är en svag övervikt av flickor med ett M/F Ratio=0.7.

Av 153 barn hade 33 barn tumör i båda ögonen, hos 76 var ett öga engagerat och i 44 fall saknades denna uppgift.

Behandlingen av denna sjukdom har sedan många år varit centraliserad till ett sjukhus i Sverige.

Prognosen för dessa barn är mycket god och endast tre av barnen har hittills rapporterats som avlidna.

3.3.5 Retinoblastoma

The mean annual incidence rate for children with retinoblastoma diagnosed 1984 through 2010 was 0,25 cases/100 000 children < 15 years of age at diagnosis. The incidence rate is highest during the first year of life with decreasing incidence with increasing age and is a rarity in children more than 5 years of age. (5/153).
There is a slight overweight of girls with a M/F Ratio = 0.7.
Of 153 children the disease was bilateral in 33 children, unilateral in 76 children and in 44 this information was missing.

The treatment of this disease has since many years been centralized to one hospital in Sweden.

The prognosis for these children is very good and only three children have so far been reported as deceased.

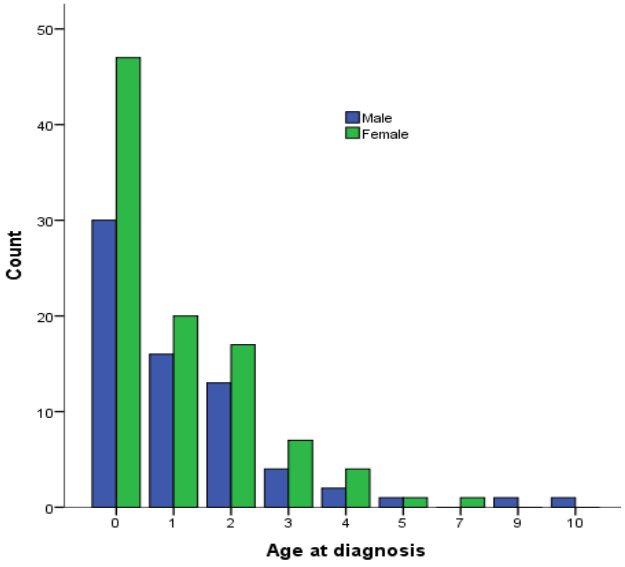
Fig 3.3.5

Group V. Retinoblastoma. Diagnosed 1984-2010.

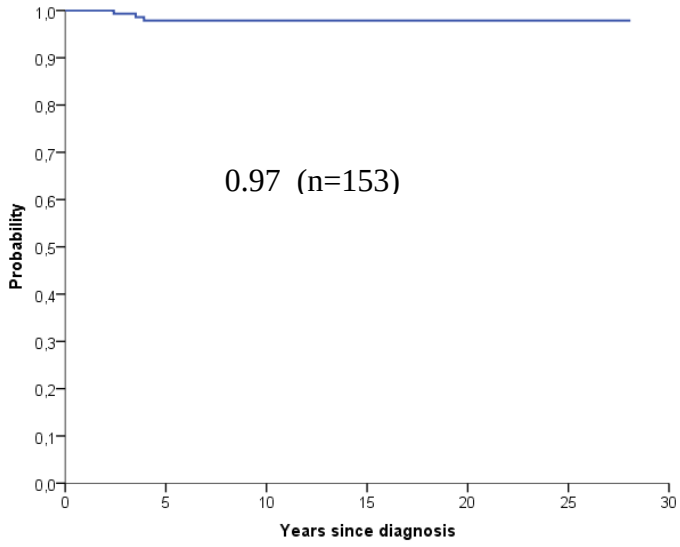
Selected criteria Total number of children: 153

Relative frequency	153/7065= 2,2 %			
	Number	Alive	Dead	% Alive
Boys	62	61	1	98,4
Girls	91	89	2	97,8
Ratio boys/girls	0.7			
< 1 year	69	67	2	97,1
1-4 yrs	79	78	1	98,7
5-9 yrs	4	4	0	100
10-14 yrs	1	1	0	100
Unilateral	76	75	1	98,7
Bilateral	33	32	1	97,0
Unknown	44	43	1	97,7

Age- and sexdistribution



Survival probability at 20 years



3.3.6 Njurtumörer

Den genomsnittliga årliga incidensen för njurtumörer under tidsperioden 1984-2010 var 0,9 fall/100 000 barn < 15 år vid diagnos med högst incidens < 5 års ålder vid diagnos. (Appendix 1.1).

Åldern är en prognostisk faktor vid denna tumörform med sämre prognos för äldre barn. (Fig 3.3.6.2).

Gruppen utgörs till största delen av Wilms tumörer med en historiskt sett god prognos. Dessa barn har under många år med stor framgång behandlats enligt protokoll i SIOP:s regi. Tidigt uppnåddes höga överlevnadssiffror vilket ledde till att man under strikt kontrollerade former har kunnat reducera behandlingen.

Detta kan vara anledningen till de något lägre överlevnadskurvorna under senare tidsperioder.(Fig 3.3.6.2).

3.3.6 Renal tumours

The mean annual incidence rate for children with renal tumours diagnosed 1984 through 2010 was 0,9 cases/100 000 children < 15 years of age at diagnosis. (Appendix 1.1).

Age is a prognostic factor among these children with worse prognosis for older children (Fig 3.3.6.2).

The group of patients consists mainly of patients with Wilms' tumour who have had a good prognosis. The children have since many years been treated according to SIOP – protocols. Good survival figures were established early which has led to a successive reduction of treatment duration and intensity in the protocols under strictly controlled forms. This may explain the slight decrease in the survival during later time periods. (Fig 3.3.6.2).

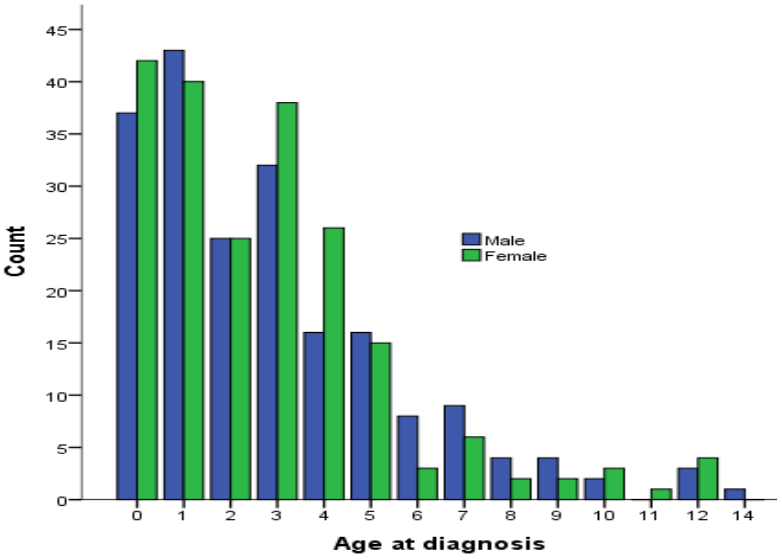
Fig 3.3.6.1

Group VI. Renal tumours. Diagnosed 1984-2010

Selected criteria Number of children: 407

Relative frequency	407/7 065= 5,8 %			
	Number	Alive	Dead	%Alive
Diagnosis:				
Wilms'	400	338	62	84,5
Renal Carcinoma	7	6	1	86,0
Boys	200	171	29	85,5
Girls	207	173	34	83,6
Ratio boys/girls	0.9			
0 < 1 year	79	68	11	86,1
1-4 yrs	245	213	32	86,9
5-9 yrs	69	53	16	76,8
10-14 yrs	14	10	4	71,4

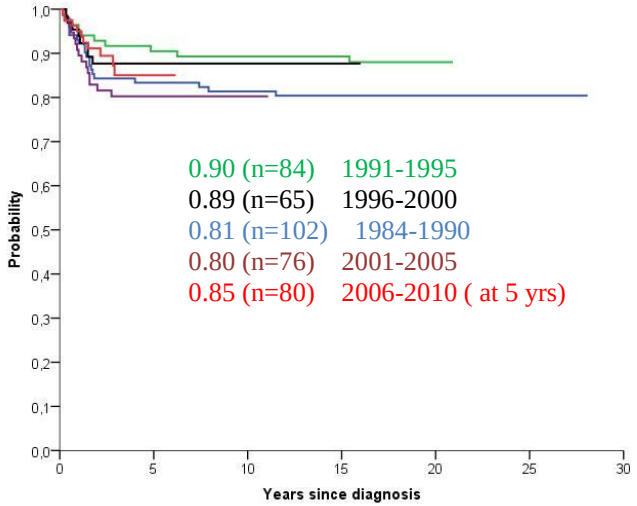
Age- and sexdistribution.



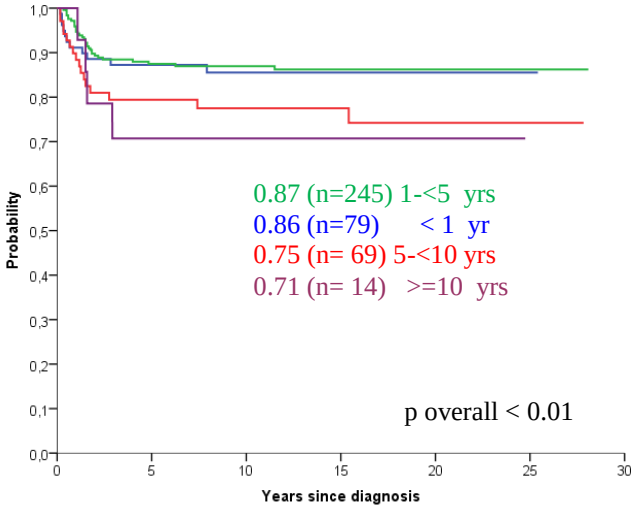
The tumors were further sub classified into 4 groups in 35 patients.

	Alive	Dead	Total
VIa1. Nephroblastoma-UNS	314	51	365
VIa2. Rhabdoid renal tumors	**1**	**7**	**8**
VIa3. Kidney sarcomas (CCSK)	**8**	**2**	**10**
VIa4. pPNET of kidney	**2**	**2**	**4**
VIa5. Mesoblastiskt nephrom (GG)	**13**	**0**	**13**
VIb. Renal carcinomas	6	1	7
Total	344	63	407

Fig 3.3.6.2 (continued)
Survival probability at 10 years by diagnostic period



Survival probability at 20 years- Age at diagnosis



3.3.6 **Levertumörer**

Den genomsnittliga årliga incidensen för levertumörer under tidsperioden 1984-2010 var 0,2 fall/100 000 barn < 15 år vid diagnos. Denna ovanliga tumör är vanligast förekommande under de första två levnadsåren.

Hepatoblastom utgör flertalet inom denna tumörgrupp och bland dessa barn har det skett en signifikant prognosförbättring över tiden. (Figur 3.3.7)

Orsaker till förbättringen står att finna i förbättrade och standardiserade stadieindelnings och handläggnings kriterier, förfinade kirurgiska metoder kombinerat med effektivare cytostatikabehandling.

3.3.7 Hepatic tumours

The mean annual incidence rate for children with hepatic tumours diagnosed 1984 through 2010 was 0,2 cases/100 000 children < 15 years of age at diagnosis. The incidence rate is highest during the first two years of life with decreasing incidence with increasing age.
Hepatoblastoma constitute the majority of patients within this diagnostic group and the prognosis among these children has improved significantly over time.
(Fig 3.3.7)

The reasons for the improved results are standardized staging and management of these patients, refined surgical techniques in combination with more effective chemotherapeutic treatment.

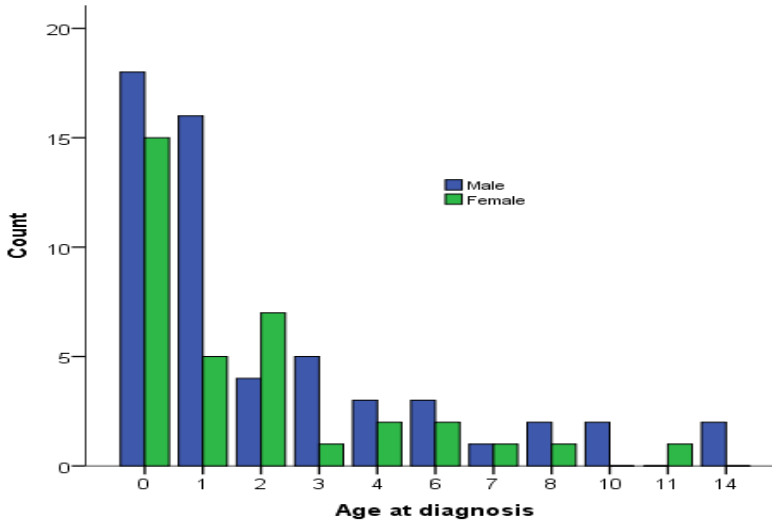
Fig 3.3.7

Group VII. Hepatic tumours. Diagnosed 1984-2010

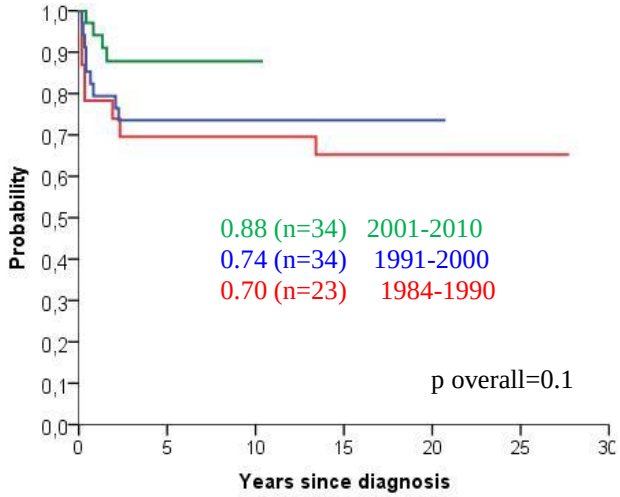
Selected criteria Total number of children: 91

Relative frequency	91/7 065= 0,1 %			
	Number	Alive	Dead	% Alive
Diagnoses				
a. Hepatoblastoma	78	64	14	82,1
b. Hepatic carcinoma	9	4	5	44,4
c. Others	4	2	2	50,0
Boys	56	42	14	75,0
Girls	35	28	7	80,0
Ratio boys/girls	1.6			
< 1 year	33	27	6	81,8
1-4 yrs	43	32	11	74,4
5-9 yrs	10	7	3	70,0
10-14 yrs	5	4	1	80,0

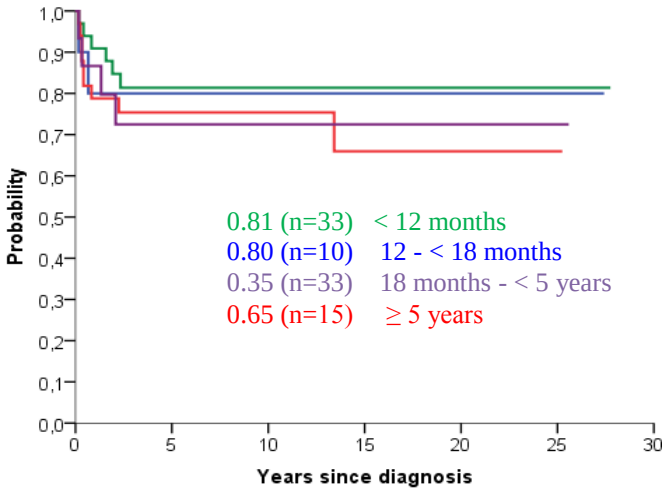
Age- and sex-distribution



Survival probability at 10 years by diagnostic period.



Survival probability at 20 years- Age at diagnosis



3.3.8 Bentumörer

Den genomsnittliga årliga incidensen för barn med bentumörer under tidsperioden 1984-2010 var 0,6 fall/100 000 barn < 15 år vid diagnos. Incidensen ökar med stigande ålder och bland barnen är bentumörer vanligast i tonåren. Gruppen består av två huvudgrupper - osteosarkom och Ewings sarkom. Särskilt osteosarkom blir mycket vanligare under pubertetens tillväxtspurt än i de yngre åldrarna (Fig 3.3.8.1).

Behandlingen består ofta av en kombination av kirurgi och kemoterapi med hög intensitet samt ibland strålning fr a för Ewings sarkom. Prognosen har inte signifikant förbättrats sedan 1990, men en tendens till fortsatt förbättring kan skönjas fr a för Ewings sarkom (Fig 3.3.8.2).

3.3.8 Bone tumours

The mean annual incidence rate for children with bone tumours diagnosed 1984 through 2010 was 0,6 cases/100 000 children < 15 years of age at diagnosis. The incidence rate increases with increasing age and is most common among teenagers.

The diagnostic group consists of two main diagnoses- osteosarcoma and Ewing's sarcoma. In particular osteosarcoma becomes much more common during the growth velocity peak of puberty compared to younger ages (Fig 3.3.8.1).

The children are mostly treated with a combination of surgery and intensive chemotherapy and sometimes radiation, particularly for Ewing's sarcoma. The prognosis has not improved significantly since 1990, but a slight improvement may be seen in Ewing's sarcoma (Fig 3.3.8.2).

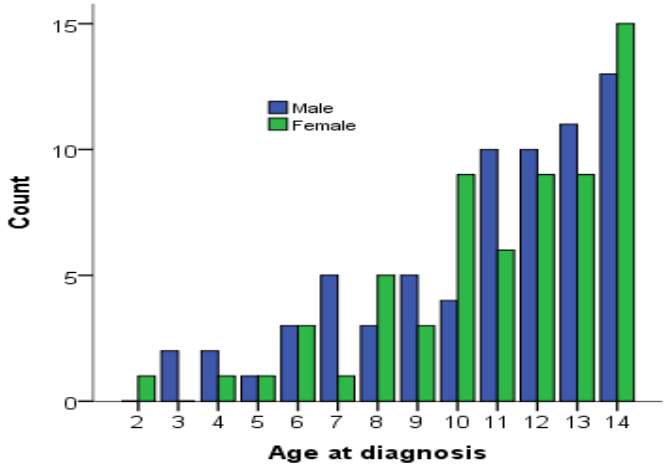
Fig 3.3.8.1

Group VIII. Malignant bone tumors. Diagnosed 1984-2010

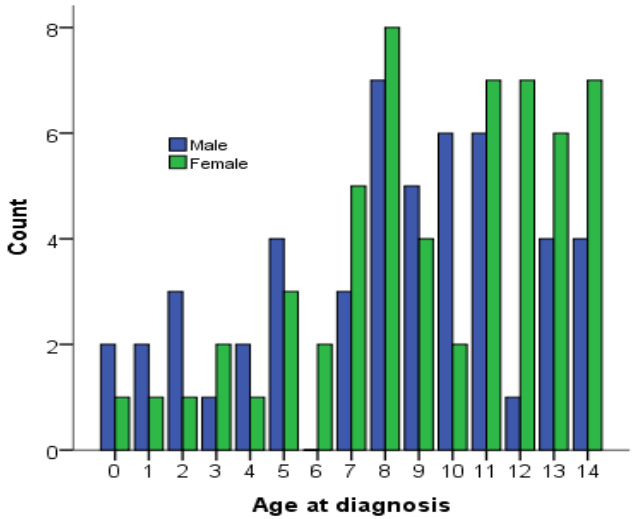
Selected criteria Total number of children:257

Relative frequency	257/7 065= 3,6 %			
	Number	Alive	Dead	%Alive
Diagnoses				
Osteosarcoma	132	87	45	65,9
Chondrosarcoma	7	6	1	85,7
Ewing's sarcoma	107	67	32	62,6
Others	11	9	2	81,8
Boys	129	80	49	62,0
Girls	128	89	39	69,5
Ratio boys/girls	1.0			
< 1 year	4	4	0	100
1-4 yrs	21	14	7	66,7
5-9 yrs	73	52	21	71,2
10-14 yrs	159	99	60	62,3

Age- and sex distribution- Osteosarcomas

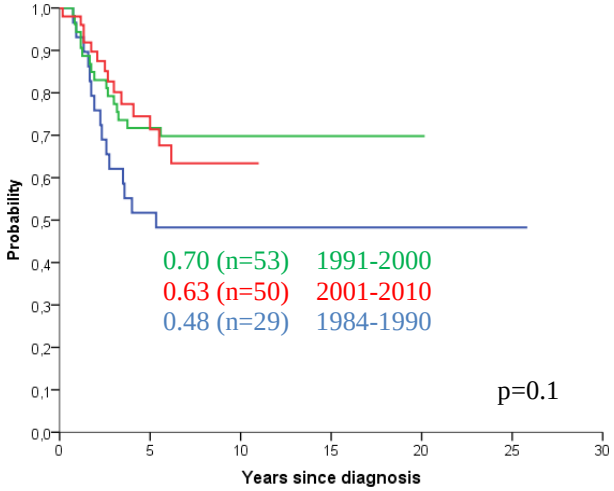


Age- and sex distribution- Ewing's

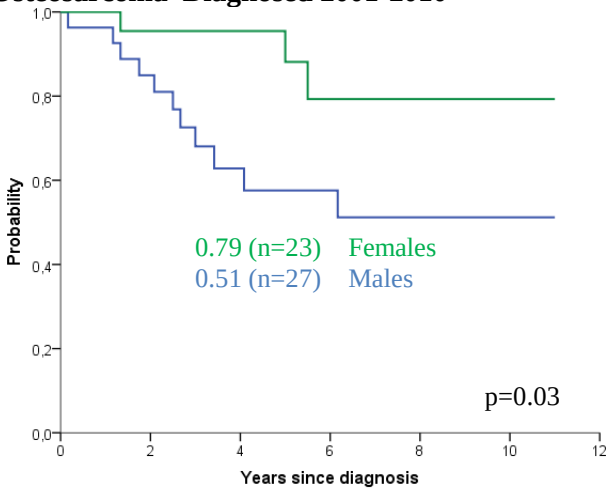


Male/Female Ratio – Osteosarcoma 69/63 (Ratio 1.1)
-"- Ewing's 50/57 (Ratio 0.9)

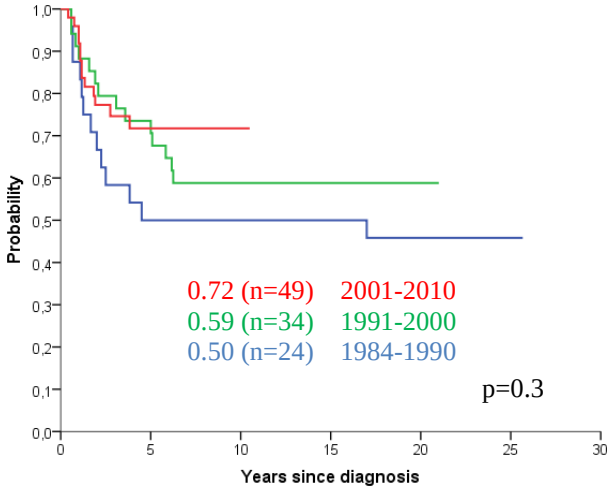
Fig 3.3.8.2 (continued)
Survival probability at 10 years by diagnostic period.
Osteosarcoma



Survival probability at 10 years- Gender
Osteosarcoma Diagnosed 2001-2010



Survival probability at 10 years- Years of diagnosis
Ewing's



No difference between males-females among the Ewing's.

Older patients ≥ 10 years of age at diagnosis (both osteosarcomas and Ewing's) have an inferior prognosis compared to younger children. (See table)

The difference in prognosis between genders has become more evident during the last diagnostic period (figure to the left).

3.3.9 Mjukdelstumörer

Den genomsnittliga årliga incidensen för mjukdelstumörer under tidsperioden 1984-2010 var 0,9 fall/100 000 barn < 15 år vid diagnos.
Gruppen består av tre större under-grupper varav majoriteten utgörs av rhabdomyosarkom. I denna diagnosgrupp har pojkarna en signifikant bättre prognos jämfört med flickor vilket är ett ovanligt fynd vid barncancer.

Prognosen för hela gruppen har inte förbättrats under senare tidsperioder.

Snarare tycks en viss försämring av prognosen ha inträffat. (Fig 3.3.9.2)

En djupare analys av denna diagnos-grupp och prognosförändringen över tiden kommer att utföras av VSTB-gruppen.

3.3.9 Soft Tissue Tumours

The mean annual incidence rate for children with soft tissue tumours diagnosed 1984 through 2010 was 0,9 cases/100 000 children < 15 years of age at diagnosis.
The diagnostic group consists of three major sub groups, the majority of which are rhabdomyosarcoma. Boys have a superior prognosis compared to girls in this diagnostic subgroup, which is an unusual finding among childhood cancer patients.

The prognosis has not improved during the last time periods.

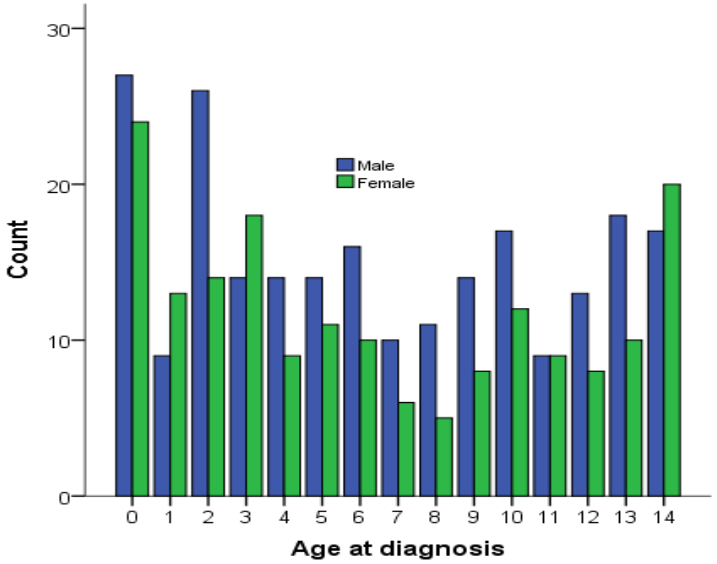
Instead, a decrease in prognosis seems to have occurred during the last decades (Fig 3.3.9.2).
A deeper analysis of this diagnostic group and the change of prognosis will be performed of the VSTB-group.

Fig 3.3.9.1

Group IX. Soft tissue sarcomas. Diagnosed 1984-2010

Selected criteria Total number of children: 406

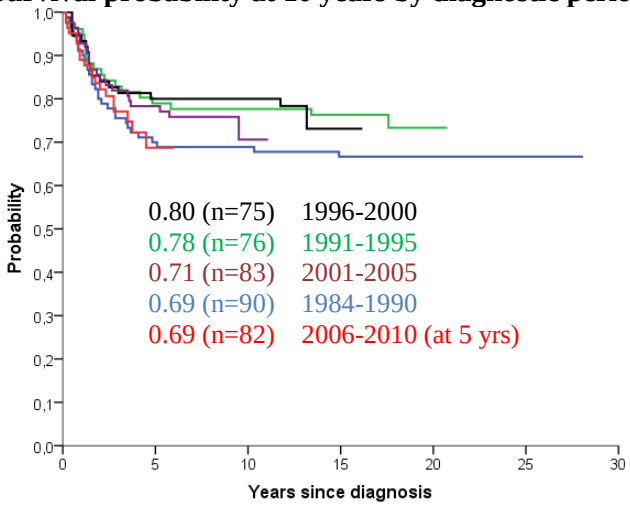
Relative frequency	406/ 7 605= 5.7 %			
	Number	Alive	Dead	%Alive
Diagnoses				
a. Rhabdomyosarcoma	218	154	9	61,2
b. Fibrosarcomas	91	77	7	78,1
c. Kaposi sarcoma	1	0	1	-
d. Other soft tissue sarc.	90	62	28	68,9
e. Unspec. soft tissue sarc.	6	5	1	,3
Boys	229	177	52	7,3
Girls	177	121	56	68,4
Ratio boys/girls	1.3			
< 1 year	51	33	18	64,7
1-4 yrs	117	85	32	72,6
5-9 yrs	106	86	20	81,2
10-14 yrs	132	94	38	71,2



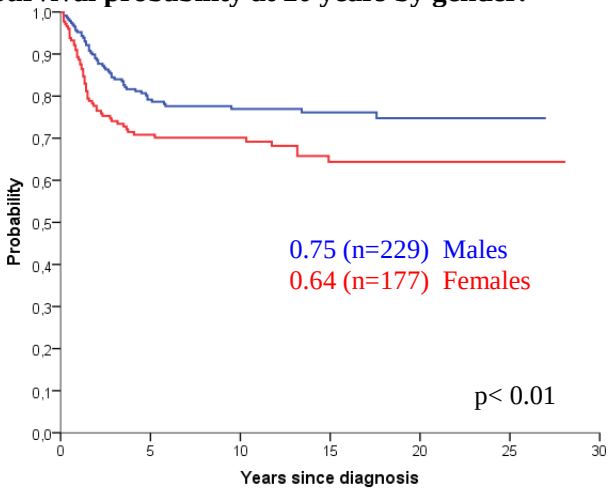
	Number	Alive	Dead	%Alive
Sub - Diagnoses				
b1. Fibroblastic tumors	24	22	2	91,7
2. Nerve sheet tumors	43	33	10	76,7
3. Other fibromatous neo	13	11	2	84,6
4. Acusticusneurinom	11	11	0	100
d1. Ewing and Askim	5	3	2	60,0
2. pPNET of soft tissue	21	11	10	52,4
3. Extra renal	1	1	0	100
4. Liposarcoma	3	2	1	66,7
5. Fibrohistocytic	10	9	1	90,0
6. Leiomyosarcoma	4	3	1	75,0
7. Synovial sarcoma	21	17	4	81,0
8. Blodd vessel tumors	2	2	0	100
9. Misc soft tissue sarc.	22	14	8	63,6
10. Others	1	0	1	100

Fig 3.3.9.2 (continued)

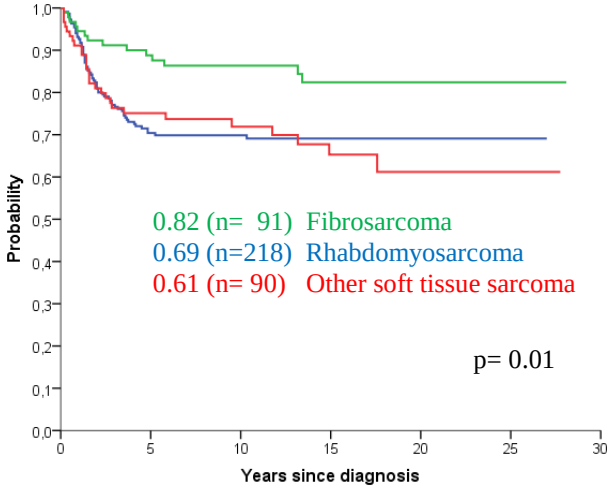
Survival probability at 10 years by diagnostic period.



Survival probability at 20 years by gender.



Survival probability at 20 years. Sub-diagnoses.



Children with fibrosarcomas have the best prognosis. The group – "other soft tissue sarcoma" is a very heterogeneous group with different prognosis for different sub diagnoses.

There is a significant difference in prognosis between males and females. This is the case for the whole group and for the three main subgroups.(left figure)

For all Soft tissue tumours: The prognosis seems to have decreased during the last decade.

3.3.10 Germcellstumörer

Den genomsnittliga årliga incidensen för germcellstumörer under tidsperioden 1984-2010 var 0,6 fall/100 000 barn < 15 år vid diagnos. De flesta barnen är < 1 år vid diagnos. M/F Ratio= 0.7.

Gruppen är heterogen med tre större huvudgrupper: intrakraniella/intraspinala, non-gonadala och gonadala GC.

Överlevnaden vid dessa tumörer är överlag hög och överstiger 80 % med undantag av de intrakraniella/intraspinala GC med en långtidsöverlevnad på drygt 60 %.

Barnen behandlas oftast efter internationella protokoll.

3.3.10 Germ cell tumours

The mean annual incidence rate for children with germ cell tumours diagnosed 1984 through 2010 was 0,6 cases/100 000 children < 15 years of age at diagnosis. Most children are < 1 year of age at diagnosis. M/F Ratio=0.7.
This is a heterogeneous group with three main sub groups: intracranial/intraspinal, non-gonadal and gonadal GC.

The survival figures for these patients are good and exceed 80 % except for the intracranial/intraspinal GC with a long term survival rate of 60%.

The children are mostly treated according to international protocols.

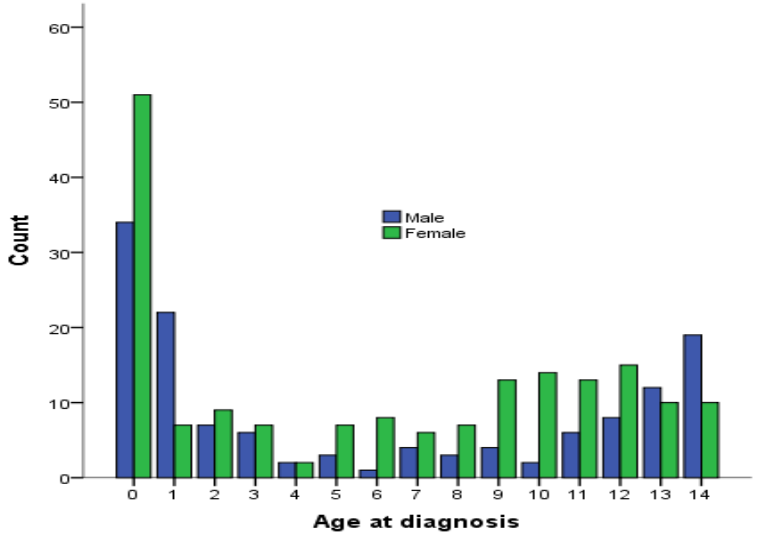
Fig 3.3.10

Group X. Germ cell tumors. Diagnosed 1984-2010

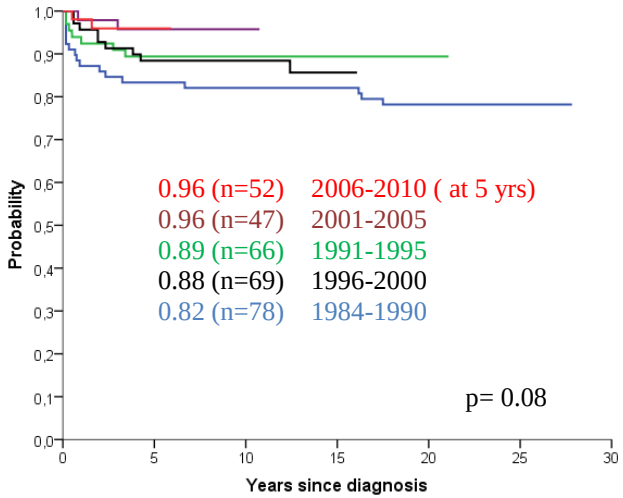
Selected criteria Total number of children: 312

Relative frequency	312/7 065= 4.4 %			
	Number	Alive	Dead	%Alive
a.Intracran./intraspin. GC	50	34	16	68,0
b.Non-gonadal GC	79	71	8	89,9
c.Gonadal GC	171	160	11	93,6
d.Gonadal carcinoma	2	1	1	50,0
e.Other and unspec GC	10	9	1	90,0
Boys	133	116	17	87,2
Girls	179	159	20	91,3
Ratio boys/girls	0.7			
< 1 year	85	76	9	89,4
1-4 yrs	62	57	5	91,9
5-9 yrs	56	46	10	82,1
10-14 yrs	109	96	13	88,7

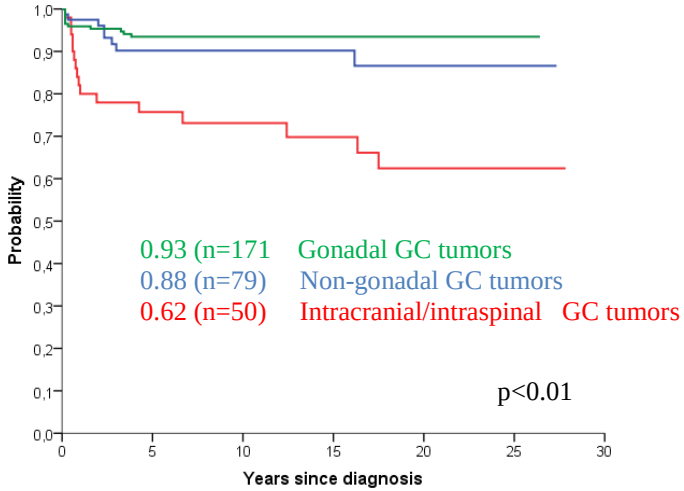
Age- and sexdistribution



Survival probability at 10 years



Survival probability at 20 years



3.3.11 Carcinom

Den genomsnittliga årliga incidensen för gruppen carcinom under tidsperioden 1984-2010 var 0,3 fall/100 000 barn < 15 år vid diagnos. Sjukdomen drabbar främst barn över 10 år och är vanligare bland flickor.

Gruppen är en till antalet liten grupp bestående av 137 patienter med skiftande lokalisation av tumörerna.

Prognosen för patienterna i denna grupp ligger på drygt 80 % och har inte förändrats över tiden.

3.3.11 Carcinoma

The mean annual incidence rate for children with soft tissue tumours diagnosed 1984 through 2005 was 0,2 cases/100 000 children < 15 years of age at diagnosis and more often girls. Most children are more than 10 years of age at diagnosis
This diagnostic group is small and contains only 72 patients with different localizations of the tumours.

The children in this group have a good prognosis exceeding 80 % which has not changed over time.

3.3.12 Andra och ospecificerade maligniteter

Gruppen utgörs av 11 barn med tumörer där närmare klassifikation av tumören inte varit möjlig eller saknas.

8 av de 11 barnen levde vid uppföljning.

3.3.12 Others and unspecified malignant neoplasms

This group consists of 11 children with tumours where detailed classification of the tumours has not been possible or is missing.

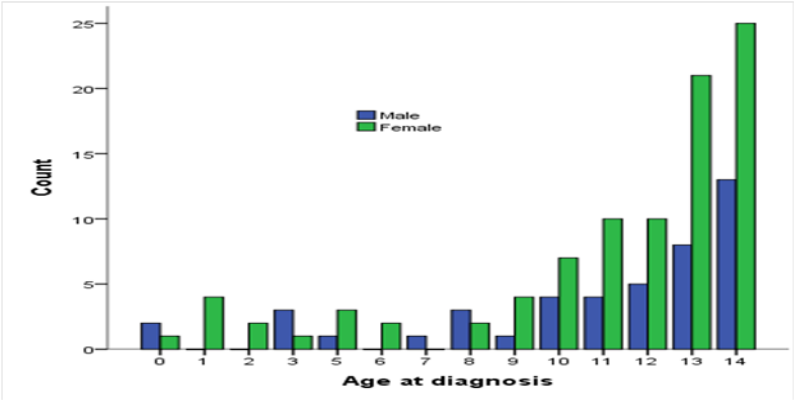
8 out of 11 children were alive at follow up.

Fig 3.3.11
Group XI. Carcinomas and other malignant epithelial neoplasms. Diagnosed 1984-2010.

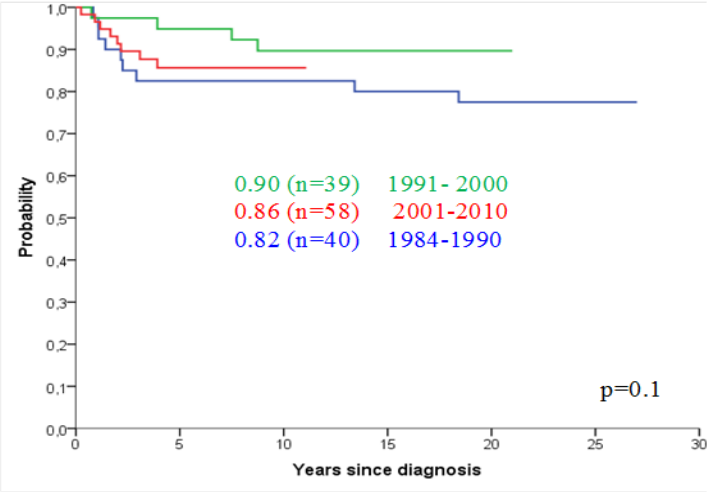
Selected criteria Total number of children: 137

Relative frequency	137/7 065=1.9 %			
	Number	Alive	Dead	%Alive
Sub diagnosis				
Adrenocortical carcinoma	11	9	2	81,8
Thyroid carcinoma	46	45	1	97,8
Nasopharyngeal carc.	12	12	0	100
Melanomatous carc.	34	28	6	82,4
Other carcinoma	34	22	12	64,7
Boys	45	37	8	82,2
Girls	92	79	13	85,9
Ratio boys/girls	0.49			
< 1 year	3	3	0	100
1-4 yrs	10	9	1	90,0
5-9 yrs	17	16	1	94,1
10-14 yrs	107	88	19	82,2

Age- and sexdistribution



Survival probability at 10 years by diagnostic period.



5. Diskussion

Cancer hos barn motsvarar mindre än 2 % av all cancer, men består av ett stort antal olika sjukdomar som signifikant skiljer sig från cancer hos unga och äldre vuxna (6). Cancer är fortfarande den sjukdom som orsakar flest dödsfall bland barn >1år i den rika delen av världen (7).

Under de senaste 10 åren har ett flertal publikationer redovisat incidens- och överlevnadssiffror avseende barn med cancer (< 15 år) från ett flertal länder. EUROCARE-3 har sammanställt data från populationsbaserade cancer register i 20 europeiska länder (8, 9) och ACCI (Automated Childhood Cancer Information) presenterade i september numret 2006 av Eur J Cancer ett flertal artiklar angående incidens- och översiffror vid barncancer från 35 europeiska länder omfattande 50 000 barn med cancer (10, 11, 12).
Svenska Cancerregistret har deltagit med data till vissa av studierna. Genomgående resultat från dessa arbeten visar att det har skett en årlig incidensökning av barncancer på cirka 1 % under de senaste 4-5 decennierna vilket även gällt under de två senaste decennierena (10, 11)
Incidenssiffrorna varierar kraftigt mellan länder från 1,3/100 000 barn till 16,0 /100 000 barn < 15 års ålder, den senare siffran härrör från de Nordiska länderna. Medel incidensen ligger på 13,8 fall/100 000.
Flera studier har visat en incidensökning under senaste 30-40 åren (10, 11, 13, 14) vilket har förklarats med förbättrade registreringar och känsligare diagnostiska metoder såsom immun histokemiska analyser, ultraljud, CT och MRI.
I en publicerad studie från Japan fann man en stadigt ökande incidens från 1970-talet fram till slutet av 1980-talet varefter en minskning av incidensen inträffade (5). Detta fenomen förklarades inte av

5. Discussion

Although childhood cancer represents less than 2% of human cancers, they are histologically very diverse and differs in types and distributions from those found in young and old adults (6). Cancer is still the most common cause of death from disease in children older than 1 year (7).

Several publications from various countries have reported incidence and survival for children <15 years at diagnosis with cancer during the last 10 years. The EUROCARE-3 study has compiled data from population-based cancer registries in 20 European countries (8, 9) and several papers containing the same type of information from 50000 children with cancer in 35 countries and was produced from Automated Childhood Cancer Information (ACCI) and appeared in Eur J Cancer in September 2006 (10, 11, 12).
The Swedish Cancer registry has contributed data to some of these studies. The results generally shows a yearly increase in overall incidence of childhood cancer of approximately 1% during the last 4-5 decades and also for the last 20 years (10, 11).
The incidence varies greatly between the different countries, from 1.3/100000 children to 16.0/100000 children <15 years of age. The latter figure reflects the situation in the Nordic countries. The average incidence is 13.8 cases/100000 children.
Several studies have thus detected an increase in the incidence of childhood cancer during the last 30-40 years (10,11,13, 14), which has been explained by improved coverage of the registration as well as more sensitive diagnostic methods, such as immunohistochemistry, ultrasound, computerised tomography (CT) and magnetic resonance imaging (MRI).
A study from Japan detected an increasing

införandet av neuroblastom screening då samma trender observerades även efter exklusion av neuroblastomgruppen. Sammanställning av data ur det Svenska Barn Cancer Registret visar att vi har en hög incidensen av barncancer i Sverige som legat stabilt under hela tidsperioden 1984 till 2010.

Det har skett en successiv förbättring av prognosen av samtliga diagnoser av cancer sedan 1970-talet. (7, 8, 9, 12, 13, 15). Det mest påtagliga genombrottet ägde rum under 70-och 80 talen då behandling intensifierades med kombinationer av kirurgi, strålning och cytostatika som alltmer kom att dominera de nya behandlingsprotokollen. Den så kallade ”Total Therapy” som infördes vid leukemibehandlingen under 70-talet ledde till snabbt ökade överlevnadssiffror för denna tidigare undantagslöst fatala sjukdom.

I en studie som redovisar barn med cancer från 20 europeiska länder diagnostiserade 1990-94, visas att resultaten i de Nordiska länderna har de högsta överlevnadssiffrorna överlag samt i fyra av sju diagnoser som analyserats mer i detalj (njurtumörer, ALL, AML och CNS-tumörer) (7). Slutsatsen i artikeln blir att: ”The Nordic countries represent a survival gold standard to which other countries can aspire”. Även om ökad överlevnad ofta kan kopplas till introduktion av nya specifika behandlingar betonas i en annan internationell jämförelse just betydelsen av registrering och uppföljning av behandlingsresultat så som det tidigt infördes i det nordiska samarbetet (9).

Behandlingsresultaten i Sverige har följt de internationella trenderna. Den mest påtagliga prognosförbättringen skedde under 1970- och 1980 talen med en ökning av 5-års överlevnaden från ca 40

incidence from the 1970s to the end of the 1980s and then a decline (13). This finding was not explained by the introduction of screening for neuroblastoma, since the same pattern was observed even when the cases of neuroblastoma were excluded from the analysis.
The compilation of data from the Swedish Childhood Cancer Registry shows that Sweden has a high incidence of childhood cancer, which has been stable from 1984 to 2010.

There has been a gradual improvement of the outcome for all diagnoses of childhood cancer since the 1970s (7, 8, 9, 12, 13, 15). The most prominent breakthrough occurred in the 1970s
and 1980s, when the therapy was intensified with combinations of surgery, irradiation and chemotherapy as a part of the new treatment protocols. The “Total Therapy” developed during the 1970s for the treatment of Leukaemia led to quickly increasing survival for this until then uniformly fatal disease.
A study reporting results from the treatment of children with cancer diagnosed 1990-1994 from 20 European countries showed the highest survival in the Nordic countries, both overall and in four out of seven diagnoses analysed in more detail (kidney tumours, ALL, AML and CNS-tumours) (7). The conclusion of the paper was that: ”The Nordic countries represent a survival gold standard to which other countries can aspire”. Although improved cancer survival often can be linked to the introduction of novel more effective treatments another international evaluation emphasised the importance of registration and evaluation of treatment results as it was early introduced in the Nordic collaboration (9).

% till ca 80 % med fortfarande relativt stora variationer mellan olika diagnosgrupper (Fig 3.1.4).
Sedan 1990 verkar prognosutvecklingen ha planar ut och legat relativt konstant i likhet med andra länder i västvärlden (7, 16) men med några undantag. Prognosen för barn med neuroblastom har klart förbättrats sedan början av 2000-talet, och då särskilt för barn med den svåraste formen, högrisk-neuroblastom. Detta torde kunna förklaras både med en ökad biologisk förståelse av sjukdomens olika former och därigenom bättre handläggning av patienterna, men också med en påtaglig intensifiering av behandlingen, framförallt för barn med högrisk form av sjukdomen där även nya behandlingsmöjligheter introducerats.

Prognosen för barn med hjärntumörer har också fortsatt förbättrats de senaste decennierna troligen beroende på en kombination av förbättrad diagnostik och behandling inom ramen för ett multidisciplinärt samarbete.
Prognosen för barn med mjukdelssarkom visar en trend till försämring under det senaste decenniet. Orsakerna till denna förändring är oklar varför en noggrann genomgång av denna patientgrupps diagnostik och behandling har inletts.
Den stora utmaningen för framtiden blir att utarbeta nya behandlingsmetoder för att bota fler barn men samtidigt reducera de toxiska långtidseffekterna av given behandling. Just utprövandet av nya behandlingsformer kräver stora resurser och ett nära samarbete mellan klinisk och translationell forskning ofta i ett brett internationellt samarbete (17).
Nya strålbehandlingsmetoder kommer att bli tillgängliga inom en snar framtid, vilket kommer att medföra mer skonsam behandling särskilt vid behandling av barn med CNS-tumörer.

The treatment results in Sweden have mirrored the international trends. The most pronounced improvement of the prognosis occurred in the 1970s and 1980s with an increase in the 5-year survival from about 40% to around 80% with still relatively pronounced variation between different diagnostic groups (Fig 3.1.4).
Since 1990 the prognosis has been relatively stable seemingly reaching a plateau similar to other countries (7, 16) but with a few exceptions. The outlook for children with neuroblastoma has improved markedly from the beginning of the 21st century, and then in particular for the worst subset, with high-risk neuroblastoma. This is likely due to significant advances in the biological understanding of the different forms of neuroblastoma leading to a better management and stratification of the patients, but also a substantial intensification of the treatment, mostly for children with high-risk disease and introduction of several new treatment modalities.

The prognosis for children with brain tumours has also improved over the last decades, which probably is the result of a combination of improved diagnostic measures and treatment within the framework of a multi-disciplinary collaboration.
The outcome for children with soft tissue sarcomas shows a trend towards worse results during the last ten years. The reason for this decline in prognosis is unclear and a thorough survey of the clinical characteristics and treatment of this patient group has been started.
The greatest challenge for the future will be the preparation and implementation of new treatment methods to cure more children while at the same time reducing the toxic long-term side effects of the treatment. The development of novel therapies requires

Pågående långtidsuppföljningar som kartlägger livskvaliteten hos vuxna som i barndomen genomgått behandling och överlevt en cancersjukdom får allt större betydelse. Drygt 850 av patienterna i Barn Cancer Registret är idag 30 år eller äldre (Fig 3.1.6). Information från dessa studier kommer att utgöra viktiga komponenter vid utarbetande av framtida behandlingsprotokoll.

Genom mer sofistikerade diagnostiska analysmetoder kommer behandlingen i framtiden att bli mer stratifierad och anpassad till väl definierade grupper av patienter och mer individualiserad för vissa patienter.

Denna sammanställning presenterar det aktuella nuläget vid behandling av barn med cancer i Sverige. Den framtida utvecklingen måste följas noggrant med återkommande uppföljningar, men med fokus även inriktat på livskvalitet hos de barn som behandlats för cancer.

extended resources and a close interplay between clinical and translational research often in extensive international collaborative efforts (17).

New methods for irradiation will be available soon, which will result in less toxic treatment, particularly for the treatment of children with CNS-tumours. Ongoing long-term follow-up studies focusing on the quality of life of adults who have survived treatment for cancer during childhood will gain in importance. Slightly more than 850 patients in the Swedish Childhood Cancer Registry are more than 30 years old today (fig 3.1.6). Information from these studies will add important components to the development of future treatment protocols. With the use of more sophisticated analytical methods the treatment will become more stratified and adapted to well defined sub-groups of patients and possibly even individualised for some patients. This compilation presents the current situation for the treatment of childhood cancer in Sweden. The future development must be followed closely with repeated surveys, but with the focus also directed towards quality of life of children treated for cancer.

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7. Appendix

Table Appendix 1.1	Numbers and incidence vs age for different diagnoses. (1984-20010)							
Diagnoses	**Sex**	**Age - Number of cases**					**Number of cases 15-<20 years years**	**Incidence rates/100 000**
		<1 year	**1-<5 yrs**	**5-<10 yrs**	**10-<15 yrs**	**0-<15 yrs**		**0-<15 years**
All malignancies	**Total**	**776**	**2597**	**1816**	**1876**	**7065**	965	**15,99**
	Males	377	1371	1048	1009	3805	543	16,95
	Females	399	1226	768	867	3260	422	14,98
I Leukemias	**Total**	**122**	**1035**	**545**	**407**	**2109**	163	**5,00**
	Males	54	528	320	247	1149	97	5,35
	Females	68	507	225	160	960	66	4,63
Acute Lymphoblastic Leukemia	Total	66	899	470	306	1741	105	4,20
Acute Myeloblastic Leukemia	Total	49	117	69	80	315	49	0,73
JMML, CMML, MDS	Total	7	18	6	22	53	10	0,13
II Lymphomas	**Total**	**64**	**196**	**257**	**331**	**848**	225	**1,96**
	Males	38	128	186	213	565	127	2,57
	Females	26	68	71	118	283	98	1,32
Hodgkin´s disease	Total	0	12	51	153	216	141	0,52
Non-Hodgkin Lymphoma	Total	7	71	116	115	309	63	0,75
Burkitt's lymphoma	Total	0	12	36	22	70	12	0,17
LCH	Total	48	95	53	40	236	11	0,50
HLH	Total	8	4	1	0	13	2	0,02
Other	Total	**1**	**1**	**0**	**0**	2	0	**0,00**
III CNS tumours	**Total**	**112**	**603**	**634**	**596**	**1945**	240	**4,59**
	Males	52	330	340	297	1019	126	4,72
	Females	60	273	294	299	926	114	4,46
Ependymom	Total	24	71	50	40	185	19	0,41
Astrocytom	Total	37	268	264	284	853	95	2,03
Medulloblastoma/PNET	Total	22	149	135	66	372	29	0,89
Other gliomas	Total	16	47	84	56	203	17	0,47
Other specified CNS tumors	Total	9	55	86	132	282	67	0,67
Unspecified CNS tumors	Total	4	13	15	18	50	13	0,12

Diagnoses	Sex	Age - Number of cases					Number of cases 15-<20 years years	Incidence rates/100 000
		<1 year	1-<5 yrs	5-<10 yrs	10-<15 yrs	0-<15 yrs		0-<15 years
IV Symphatetic nervous system tumours	**Total**	**151**	**183**	**42**	**13**	**389**	4	**0,69**
	Males	85	91	29	9	214	2	0,73
	Females	66	92	13	4	175	2	0,64
Neuroblastoma	Total	150	180	40	7	378	3	0,66
Other symp nervous system tumors	Total	0	3	2	6	11	1	0,03
V-Retinoblastomas	**Total**	**69**	**79**	**4**	**1**	**153**	0	**0,25**
	Males	26	33	2	1	62		0,21
	Females	43	46	2	0	91		0,30
Retinoblastoma, unilateral	Total	31	41	4	1	76		0,13
Retinoblastoma, bilateral	Total	21	12	0	0	33		0,04
Retinoblastoma, unspec	Total	17	26	0	1	44		0,08
VI Renal tumours	**Total**	**79**	**245**	**69**	**14**	**407**	11	**0,87**
	Males	37	116	41	6	200	3	0,84
	Females	42	129	28	8	207	8	0,90
Nephroblastom	Total	79	244	65	12	400	10	0,85
Renal carcinoma	Total	0	1	4	2	7	1	0,02
Other and unspec.	Total							0,00
VII Hepatic tumours	**Total**	**33**	**43**	**10**	**5**	**91**	4	**0,16**
	Males	18	28	6	4	56	3	0,21
	Females	15	15	4	1	35	1	0,12
Hepatoblastom	Total	32	38	5	3	78	0	0,13
Hepatocellular carcinoma	Total	0	3	4	2	9	4	0,02
Other and unspec.	Total	1	2	1	0	4		0,01

Diagnoses	Sex	Age - Number of cases					Number of cases	Incidence rates/100 000
		<1 year	1-<5 yrs	5-<10 yrs	10-<15 yrs	0-<15 yrs	15-<20 years years	0-<15 years
VIII Bone tumours	**Total**	**4**	**21**	**73**	**159**	**257**	133	**0,61**
	Males	2	14	37	76	129	85	0,60
	Females	2	7	36	83	128	48	0,63
Osteosarcoma	Total	0	6	30	96	132	88	0,32
Chondrosarcoma	Total	0	0	1	6	7	2	0,02
Ewings	Total	3	13	41	50	107	39	0,26
Other and unspec.	Total	1	2	1	7	11	4	0,02
IX Soft tissue tumours	**Total**	**51**	**117**	**106**	**132**	**406**	83	**0,90**
	Males	27	63	65	74	229	46	1,00
	Females	24	54	41	58	177	37	0,80
Rhabdomyosarkoma,embr. sarc. soft tis	Total	25	85	70	38	218	32	0,50
Fibrosarkoma, neurofibrosarkoma,other	Total	19	9	18	45	91	17	0,19
Kaposi's sarkom	Total	0	0	0	1	1	0	0,00
Other soft tissue sarkoma	Total	7	22	15	46	90	33	0,20
Unspec soft tissue sarkoma	Total	0	1	3	2	6	1	0,01
X Germ cells tumours	**Total**	**85**	**62**	**56**	**109**	**312**	69	**0,61**
	Males	34	37	15	47	133	38	0,51
	Females	51	25	41	62	179	31	0,71
Intracranial/intraspinal germ cells	Total	2	4	13	31	50	23	0,12
Non-gonadal germ-cell and trophoblastic	Total	45	22	2	10	79	8	0,11
Gonadal germ-cell and trophoblastic	Total	37	34	36	64	171	37	0,35
Gonadal carcinoma	Total	0	0	0	2	2	1	0,00
Other and unspec mal gonadal tumors	Total	1	2	5	2	10		0,02

Diagnoses	Sex	Age - Number of cases					Number of cases	Incidence rates/100 000
		<1 year	1-<5 yrs	5-<10 yrs	10-<15 yrs	0-<15 yrs	15-<20 years years	0-<15 years
XI Carcinomas	**Total**	**3**	**10**	**17**	**107**	**137**	25	**0,32**
	Males	2	3	6	34	45	11	0,20
	Females	1	7	11	73	92	14	0,44
Adrenocarcinoma	Total	1	5	3	2	11	1	0,03
Thyroid carcinoma	Total	0	2	7	37	46	9	0,11
Nasopharyngeal carcinoma	Total	1	0	0	11	12	2	0,03
Melanomatous neoplasma	Total	1	1	3	29	34	3	0,08
Other and unspec.carcinomas	Total	0	2	4	28	34	10	0,08
XII-Others and not specified	**Total**	**3**	**3**	**3**	**2**	**11**	4	**0,02**
	Males	2	0	1	1	4	4	0,01
	Females	1	3	2	1	7	0	0,03

Table Appendix 1.2	Numbers, relative frequencies and survival figures for different diagnoses. (1984-2010)								
Diagnoses	**Sex**	**Number**	**Relative**	**Group**	**Ratio**	**Age**	**Survival**		
			%	**%**	**M/F**	**Mean/Md**	**5-yrs**	**10-yrs**	**20 yrs**
All malignancies	**Total**	**7065**	**100**	**100**	**1.17**	**5.9/5**	**79±1**	**77±1**	**75±1**
	Males	3805	53.8	53.8		6.0/5	79±1	77±1	75±1
	Females	3260	46.2	46.2		5.7/5	80±1	77±1	75±1
I Leukemias	**Total**	**2109**	**29.9**	**100**	**1.20**	**5.2/4**	**79±1**	**76±1**	**74±1**
	Males	1149	16.3	54.5		5.6/4	79±1	77±1	75±1
	Females	960	13.6	45.5		4.8/4	78±1	75±1	73±2
ALL	Total	1741	24.6	82.6		5.2/4	84±1	81±1	79±1
AML	Total	315	4.6	15.7		5.5/4	59±3	55±3	53±3
JMML,CMML,MDS	Total	53	0.6	1.7		5,6/4	59±9	45±13	37±11
II Lymphomas	**Total**	**848**	**12.0**	**100**	**2.00**	**7.5/8**	**89±1**	**88±1**	**85±1**
	Males	565	8.0	66.6		7.6/8	88±2	88±1	84±2
	Females	283	4.0	33.3		7.5/8	91±2	89±2	87±2
Hodgkin´s disease	Total	216	3.1	25.5		10.8/12	98±1	96±1	92±2
Non-Hodgkin Lymphoma	Total	309	4.4	36.4		7.8/8	81±2	79±2	75±3
Burkitt's lymphoma	Total	70	1.0	8.3		7.9/8	94±3	92±3	90±4
LCH	Total	236	3.5	29.6		4.2/3	92±2	91±2	89±2
HLH	Total	13							
Other	Total	2				1.5/1			

Diagnoses	Sex	Number	Relative	Group	Ratio	Age	Survival		
			%	%	M/F	Mean/Md	5-yrs	10-yrs	20 yrs
III CNS tumours	**Total**	**1945**	**27.5**	**100**	**1.10**	**6.7/6**	**76±1**	**73±1**	**70±1**
	Males	1019	14.4	52.4		6.7/6	76±1	73±1	70±2
	Females	926	13.1	47.6		6.8/7	76±1	73±2	70±2
Ependymom	Total	185	2.6	9.5		5.2/4	75±3	70±4	66±4
Astrocytom	Total	853	12.1	43.9		7.0/7	85±1	83±1	80±2
Medulloblastoma/PNET	Total	372	5.3	19.1		5.6/5	62±3	55±3	52±3
Other gliomas	Total	203	2.9	10.4		6.9/7	45±4	44±4	43±4
Other specified	Total	282	4.0	14.5		8.4/9	92±2	89±2	86±3
CNS-Unspecified	Total	50	0.7	2.5		7.1/6	73±6	73±6	73±6
IV Symphatetic nervous system tumours	**Total**	**389**	**5.5**	**100**	**1.22**	**2.1/1**	**66±2**	**64±3**	**62±3**
	Males	214	3.0	55.0		2.2/1	61±3	60±3	60±3
	Females	175	2.5	45.0		1.9/1	71±3	68±4	65±4
Neuroblastoma	Total	378	5.4	97.2		1.9/1	65±2	63±3	62±3
Other symp nervous system tumors	Total	11	0.2	2.8		8.9/11			
V-Retinoblastomas	**Total**	**153**	**2.2**	**100**	**0.68**	**1.2/1**	**98±1**	**98±1**	**98±1**
	Males	62	0.9	40.5		1.3/1	98±2	98±2	98±2
	Females	91	1.3	59.5		1.1/1	98±2	98±2	98±2
Retinoblastoma, unilateral	Total	76	1.1	49.7		1.2/1			
Retinoblastoma, bilateral	Total	33	0.5	21.5					
Retinoblastoma, unspec	Total	44	0.6	28.9					
VI Renal tumours	**Total**	**407**	**5.8**	**100**	**0.97**	**2.8/2**	**85±2**	**84±2**	**83±2**
	Males	200	2.8	49.1		2.9/2	86±3	86±3	85±3
	Females	207	3.0	50.9		2.7/2	85±3	83±3	82±3
Nephroblastom	Total	400	5.7	98.2		2.7/2	85±2	84±2	83±2
Renal carcinoma (1/7 dead)	Total	7	0.1	1.8		8.1/9			

Diagnoses	Sex	Number	Relative	Group	Ratio	Age	Survival		
			%	%	M/F	Mean/Md	5-yrs	10-yrs	20 yrs
VII Hepatic tumours	**Total**	**91**	**1.3**	**100**	**1.60**	**2.3/1**	**78±4**	**78±4**	**75±5**
	Males	56	0.8	61.5		2.5/1	74±6	74±6	74±6
	Females	35	0.5	38.5		1.9/1	83±6	83±6	77±8
Hepatoblastom	Total	78	1.1	85.7		1.7/1	83±4	83±4	80±5
Hepatocellular carcinoma (5/9 dead)	Total	9	0.1	9.8		7.2/6			
Other and unspec. (2/4 dead)	Total	4	0.1	4.3		3.0/3			
VIII Bone tumours	**Total**	**257**	**3.6**	**100**	**1.00**	**10.0/11**	**66±3**	**63±3**	**62±3**
	Males	129	1.8	50.1		9.7/11	64±4	61±4	59±5
	Females	128	1.8	49.9		10.2/11	69±4	66±4	66±4
Osteosarcoma	Total	132	1.9	51.4		10.8/12	65±4	64±4	64±4
Chondrosarcoma (1 dead)	Total	7	0.1	2.7		12.6/13			
Ewings	Total	107	1.5	41.6		8.8/9	64±5	61±5	58±6
Other and unspec.	Total	11	0.2	4.3		9.2/11			
IXSoft tissue tumours	**Total**	**406**	**5.7**	**100**	**1.29**	**6.5/6**	**74±2**	**74±2**	**70±3**
	Males	229	3.2	56.4		6.6/6	78±3	77±3	75±3
	Females	177	2.5	43.6		6.4/5	70±4	69±4	64±4
Rhabdomyosarkoma,embr. sarc. soft tis	Total	218	3.1	53.7		5.3/4	70±3	69±3	69±3
Fibrosarkoma, neurofibrosarkoma,other	Total	91	1.3	22.4		7.7/10	86±4	86±4	82±4
Kaposi's sarkom	Total	1	<0.1	0.2		10.0/10			
Other soft tissue sarcoma	Total	90	1.3	22.2		7.9/10	74±5	72±5	61±7
Unspec soft tissue sarkoma	Total	6	0.1	1.5		9.2/9			

Diagnoses	Sex	Number	Relative	Group	Ratio	Age	Survival		
			%	%	M/F	Mean/Md	5-yrs	10-yrs	20 yrs
X Germ cells tumours	**Total**	**312**	**4.4**	**100**	**0.74**	**6.0/5**	**89±2**	**89±2**	**86±6**
	Males	133	1.9	42.6		5.8/3	89±3	89±3	85±3
	Females	179	2.5	57.4		6.1/6	90±2	89±2	86±3
Intracranial/intraspinal germ cells	Total	50	0.7	16.0		9.8/10	76±6	73±6	62±8
Non-gonadal germ-cell and trophoblast	Total	79	1.1	25.3		2.3/2	90±4	90±4	87±5
Gonadal germ-cell and trophoblastic n	Total	171	2.4	54.8		6.4/6	93±2	93±2	93±2
Gonadal carcinoma	Total	2	<0.1	0.6		13/13			
Other and unspec mal gonadal tumors	Total	10	0.1	3.2		6.6/7			
Diagnoses	**Sex**	**Number**	**Relative**	**Group**	**Ratio**	**Age**	**Survival**		
			%	%	M/F	Mean/Md	5-yrs	10-yrs	20 yrs
XI Carcinoma	**Total**	**137**	**1.9**	**100**	**0.49**	**10.9/12.0**	**87±3**	**85±5**	**82±4**
	Males	45	0.6	32.8		10.8/12	84±6	84±6	79±7
	Females	92	1.3	67.2		11.0/12	89±3	86±4	83±5
Adrenocarcinoma	Total	11	0.2	8.0		4.9/3	90±9	90±9	45±32
Thyroid carcinoma	Total	46	0.7	33.6		11.2/12	98±2	98±2	98±2
Nasopharyngeal carcinoma	Total	12	0.2	8.8		11.3/12	93±2	93±2	93±2
Melanomatous neoplasma	Total	34	0.5	24.8		11.8/13	88±6	81±7	81±7
Other carcinoma	Total	34	0.5	24.8		11.4/13	67±8	67±8	60±10
XII-Others and not specified	**Total**	**11**	**0.2**	**100**	**0.57**	**4.8/4**			
	Males	4	0.1	36.4		4.8/4			
	Females	7	0.1	63.6		4.7/4			