EMBRYONAL TUMOURS

100%
OF EMBRYONAL TUMOURS ARE RARE

INCIDENCE

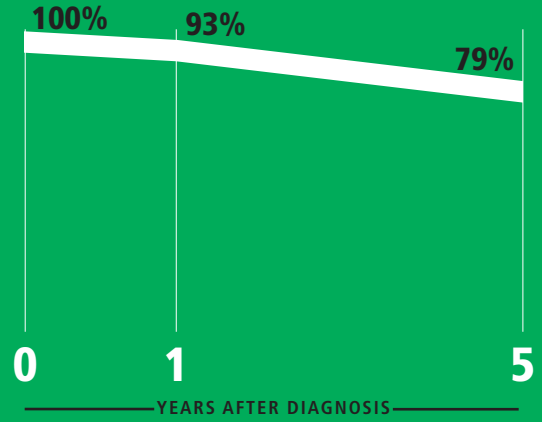
234
ESTIMATED NEW CASES
ITALY, 2015

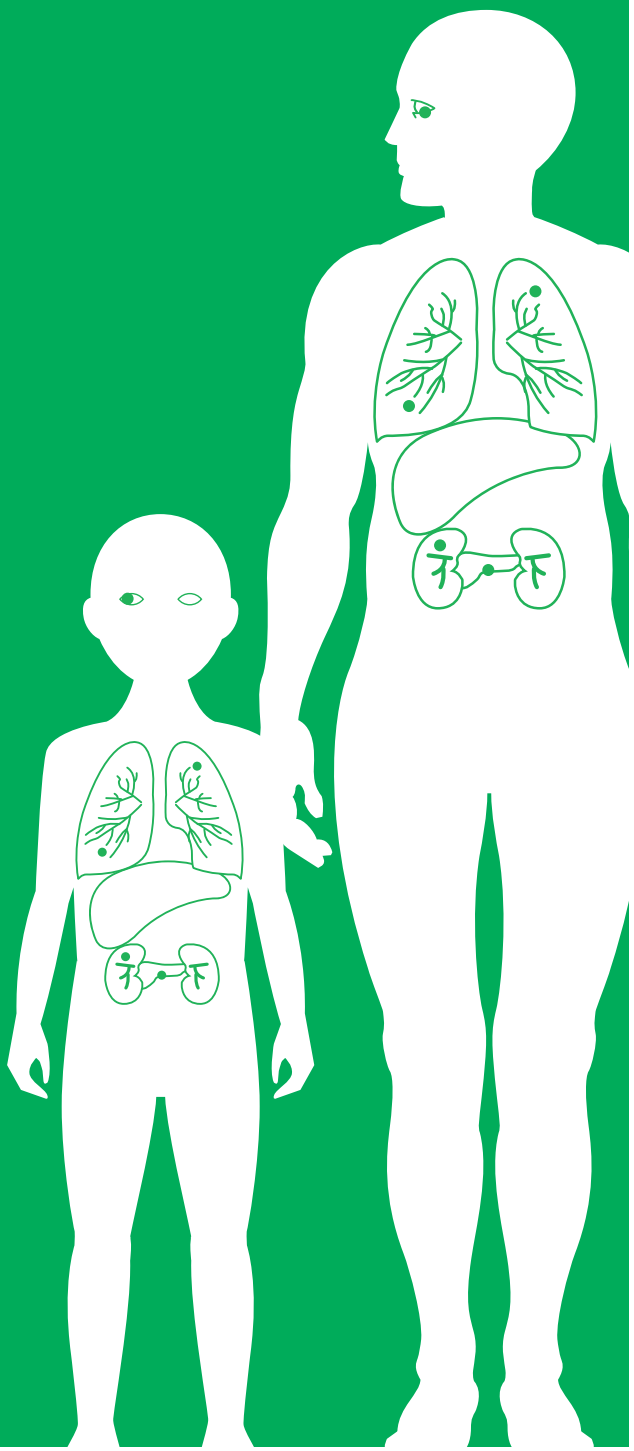
99	NEUROBLASTOMA AND GANGLIONEUROBLASTOMA
68	NEPHROBLASTOMA
30	RETINOBLASTOMA
11	HEPATOBLASTOMA
1	PLEUROPULMONARY BLASTOMA
1	PANCREATOBLASTOMA
20	OLFACTORY NEUROBLASTOMA
4	ODONTOGENIC MALIGNANT TUMOURS

PREVALENCE

6 085
ESTIMATED PREVALENT CASES
ITALY, 2010

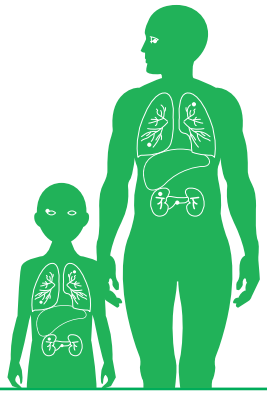
SURVIVAL





SOURCE: AIRTUM. ITALIAN CANCER FIGURES–REPORT 2015

EMBRYONAL TUMOURS



INCIDENCE

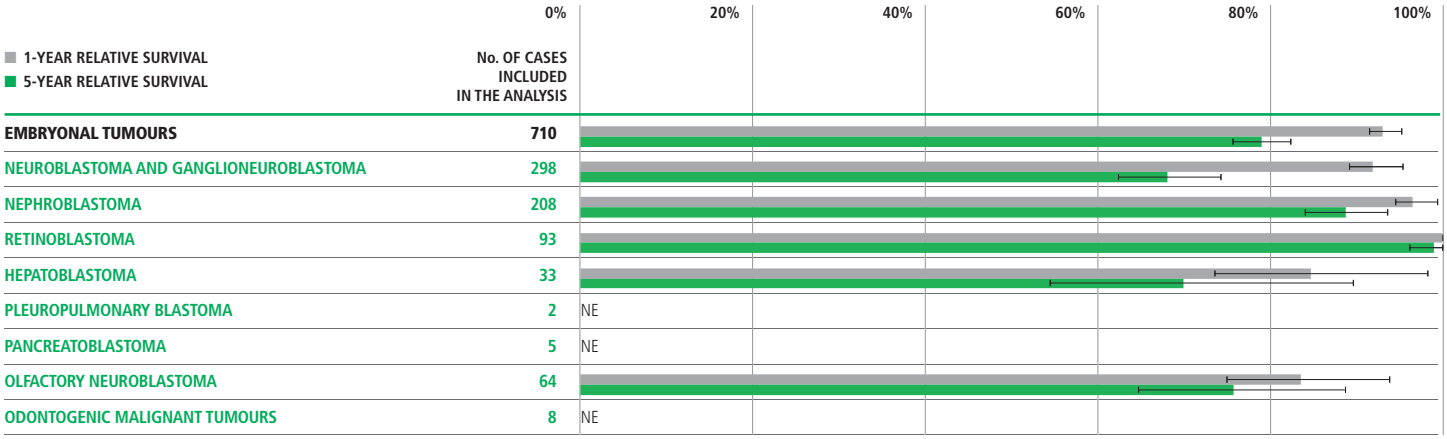
EMBRYONAL TUMOURS. Crude incidence (rate per 100,000/year) and 95% confidence interval (95% CI), observed cases and proportion of rare cancers on all (common + rare) cancers by site. Rates with 95% CI by sex and age. Estimated new cases at 2015 in Italy.

	AIRTUM POOL (period of diagnosis 2000-2010)														ITALY
					SEX				AGE						
					MALE		FEMALE		0-4 yrs		5-14 yrs		15+ yrs		
	RATE	95% CI	OBSERVED CASES (No.)	RARE CANCERS BY SITE (%)	RATE	95% CI	RATE	95% CI	RATE	95% CI	RATE	95% CI	RATE	95% CI	ESTIMATED NEW CASES 2015
EMBRYONAL TUMOURS	**0.39**	**0.36-0.41**	**859**	**100%**	**0.41**	**0.37-0.45**	**0.37**	**0.34-0.41**	**5.92**	**5.46-6.41**	**0.65**	**0.54-0.77**	**0.06**	**0.05-0.07**	**234**
NEUROBLASTOMA AND GANGLIONEUROBLASTOMA	0.17	0.15-0.18	370	NA	0.19	0.16-0.22	0.15	0.12-0.17	2.88	2.56-3.23	0.29	0.22-0.38	<0.01	0.00-0.01	99
NEPHROBLASTOMA	0.11	0.10-0.13	248	NA	0.10	0.08-0.12	0.12	0.10-0.15	1.67	1.43-1.94	0.30	0.23-0.38	<0.01	0.00-0.01	68
RETINOBLASTOMA	0.05	0.04-0.06	111	NA	0.05	0.04-0.06	0.05	0.04-0.07	1.03	0.84-1.24	0.02	0.01-0.06	0.00	–	30
HEPATOBLASTOMA	0.02	0.01-0.02	40	NA	0.02	0.01-0.03	0.01	0.01-0.02	0.28	0.19-0.40	0.02	0.01-0.06	<0.01	0.00-0.01	11
PLEUROPULMONARY BLASTOMA	<0.01	0.00-0.00	2	NA	NE	–	NE	–	NE	–	NE	–	NE	–	1
PANCREATOBLASTOMA	<0.01	0.00-0.01	5	NA	NE	–	NE	–	NE	–	NE	–	NE	–	1
OLFACTORY NEUROBLASTOMA	0.03	0.03-0.04	71	NA	0.04	0.03-0.05	0.03	0.02-0.04	0.02	0.00-0.07	<0.01	0.00-0.03	0.04	0.03-0.05	20
ODONTOGENIC MALIGNANT TUMOURS	<0.01	0.00-0.01	12	NA	NE	–	NE	–	NE	–	NE	–	NE	–	4

NE: not estimable because 15 or less incident cases were observed **NA:** not applicable

SURVIVAL

EMBRYONAL TUMOURS. One and 5-year relative survival. Error bars are 95% confidence interval. Cohort approach (complete analysis), period of diagnosis 2000-2008.



	No. OF CASES INCLUDED IN THE ANALYSIS
EMBRYONAL TUMOURS	**710**
NEUROBLASTOMA AND GANGLIONEUROBLASTOMA	298
NEPHROBLASTOMA	208
RETINOBLASTOMA	93
HEPATOBLASTOMA	33
PLEUROPULMONARY BLASTOMA	2
PANCREATOBLASTOMA	5
OLFACTORY NEUROBLASTOMA	64
ODONTOGENIC MALIGNANT TUMOURS	8

NE

NE

NE

NE: not estimable because 30 or less incident cases were observed

PREVALENCE

EMBRYONAL TUMOURS. Observed prevalence (proportion per 100,00 and 95% confidence interval - 95% CI) by duration (≤2, 2-5, ≤15 years) prior to prevalence date (1st January 2007), and complete prevalence. Estimated prevalent cases in 2010 in Italy.

	AIRTUM POOL								ITALY
	OBSERVED PREVALENCE BY DURATION						COMPLETE PREVALENCE		
	≤2 YEARS		2-5 YEARS		≤15 YEARS				
	PROPORTION	95% CI	PROPORTION	95% CI	PROPORTION	95% CI	PROPORTION	95% CI	ESTIMATED PREVALENT CASES 2010
EMBRYONAL TUMOURS	**0.76**	**0.59-0.96**	**0.87**	**0.69-1.09**	**3.74**	**3.35-4.17**	**9.46**	**3.78-15.15**	**6 085**
NEUROBLASTOMA AND GANGLIONEUROBLASTOMA	0.38	0.26-0.53	0.34	0.23-0.49	1.47	1.23-1.75	2.89	1.78-3.99	1 922
NEPHROBLASTOMA	0.17	0.10-0.28	0.24	0.15-0.37	1.16	0.94-1.41	2.36	1.41-3.31	1 638
RETINOBLASTOMA	0.08	0.03-0.16	0.09	0.04-0.18	0.53	0.39-0.70	0.70	0.40-1.00	543
HEPATOBLASTOMA	0.05	0.01-0.12	0.08	0.03-0.17	0.18	0.11-0.30	2.63	0.00-8.08	1 474
PLEUROPULMONARY BLASTOMA	0.01	0.00-0.06	NE	–	0.01	0.00-0.06	0.01	0.00-0.01	6
PANCREATOBLASTOMA	NE	–	NE	–	0.01	0.00-0.06	0.34	0.00-1.01	180
OLFACTORY NEUROBLASTOMA	0.05	0.01-0.12	0.11	0.06-0.21	0.36	0.24-0.51	0.47	0.30-0.64	276
ODONTOGENIC MALIGNANT TUMOURS	0.02	0.00-0.08	NE	–	0.02	0.00-0.08	0.06	0.00-0.15	47

NE: not estimable in observed prevalence if no cases were observed within ≤2, 2-5, ≤15 years prior to prevalence date, in complete prevalence if the 15-year prevalence is NE

Embryonal cancers are a heterogeneous group of cancers. They occur mainly in children, with the exception of some very rare types (olfactory neuroblastoma, odontogenic tumours). Several studies indicate that the incidence of embryonal cancer is increasing.[1-3] The risk of developing embryonal cancer is higher in children with certain genetic syndromes or congenital malformations,[4-6] which account for no more than 5% of all cases. Environmental factors, such as ionising radiation, toxic therapies, herbicides, tobacco smoke, and diet, have been investigated as potential causes of embryonal cancers, particularly for exposure in the womb or at a very young age.[1,2,7] Changing foetal growth conditions related to increasing age at first pregnancy, exposure to sex hormones, and increasing birth weight have also been investigated.[7] Childhood cancers such as nephroblastoma and retinoblastoma have been intensely studied: their clinical and biological characteristics are well known and numerous clinical trials have been conducted by cooperative groups, resulting in the development of effective therapies. By contrast, hepatoblastoma, pulmonary blastoma, pancreatoblastoma, olfactory neuroblastoma, and odontogenic tumours are rare, even among childhood cancers;[8] nevertheless, they, too, have been investigated by cooperative research programs[9] either in the context of rare paediatric tumours as a group, or as individual entities.

The embryonal tumours considered in this monograph are:

- **neuroblastoma and ganglioneuroblastoma;**
- **nephroblastoma;**
- **retinoblastoma;**
- **hepatoblastoma;**
- **olfactory neuroblastoma;**
- **pleuropulmonary blastoma;**
- **pancreatoblastoma;**
- **odontogenic tumours.**

NEUROBLASTOMA AND GANGLIONEUROBLASTOMA

Incidence

About 100 new diagnoses are estimated in 2015 in Italy. Incidence is 10% more frequent in boys than girls (not significant). The majority of cases occurs in children aged <5 years, with an incidence rate (IR) of 2.9 per 100,000. The annual crude IR is 0.2 per 100,000, higher than the IR observed if the European RARECAREnet database (www.rarecarenet.eu) (0.1 per 100,000). In Europe, incidence in children significantly increased between 1978 and 1997.[10]

Survival

Survival significantly drops after the first year of diagnosis, from 92% to 68% at 5 years. Data from EUROCARE-5[11] show 5-year relative survival (RS) to be excellent in infants (91%) and worse in children 1-14 years of age, between 52% and 59%. Actually, the majority of low-risk neuroblastomas are among infants, most likely for the propensity of neuroblastomas of infancy to undergo spontaneous regression. According to the RARECAREnet database, 5-year RS in children is slightly better in Italy than in Europe (71% vs. 79%). In Europe from 1999 to 2007 no progress was reported for neuroblastoma in children.[11]

Prevalence

Around 2,000 patients were estimated to be living with a diagnosis of neuroblastoma and ganglioblastoma in 2010. Almost 50% of prevalent cases were diagnosed 15 or more years before the prevalence date.

NEPHROBLASTOMA

Incidence

In Italy, about 70 children and adults are diagnosed with nephroblastoma each year; most (99%) nephroblastomas are diagnosed in children aged less than 5 years. The highest IR is in the first 2 years of life. Thus, the annual IR per 100,000 decreases from 1.7 to 0.01 across ages.

Incidence is slightly higher among females than males. European childhood IRs significantly increased among girls and among children aged 5 or less years only.[10]

According to the RARECAREnet database (www.rarecarenet.eu), there are no differences between Italian and European rates.

Survival

One- and 5-year RS are 97% and 89%, respectively. In Europe, 5-year RS is better in children (92%) than in adults (64%).[12] According to the RARECAREnet database, there are no differences in prognosis between Europe and Italy, for the period 2000-2007.

Prevalence

Around 1,600 people were estimated to be living with a diagnosis of nephroblastoma in 2010. Almost 50% of prevalent cases were diagnosed 15 or more years before the prevalence date.

RETINOBLASTOMA

Incidence

In Italy, approximately 30 children are diagnosed with retinoblastoma each year, with almost 95% occurring before five years of age. The annual IR per 100,000 for the period 2000-2007 is 1.0, in children <5 years of age. There are no differences between genders. The overall IR is 0.05 per 100,000 in Italy and Europe, according to the RARECAREnet database. In Europe, age-standardized rates were higher in Northern and Southern Europe and in the UK and Ireland.[12]

Survival

The outcome of children diagnosed with retinoblastoma in the period 2000-2007 is favourable, with 99% alive five years after diagnosis.

Prevalence

Slightly more than 500 people were estimated to be living with a diagnosis of retinoblastoma in 2010.

HEPATOBLASTOMA

Incidence

About 10 new cases are diagnosed in Italy each year, all occurring in children. The peak is in those aged <5 years, with an IR of about 3 cases per million. Incidence is slightly higher among boys than girls. There are no differences between the Italian and European rates, according to the RARECAREnet database. The incidence of hepatoblastoma increased during the period 1975-1995 in the US, while no increment was reported for Europe.[10,13]

Survival

Based on 33 cases, 1- and 5-year RS are 85% and 70%, respectively. According to the RARECAREnet database, RS is slightly lower in Italy than Europe (76% at 5 years). There was an impressive progress in Europe: 5-year RS increased from 59% (1995-1999) to 82% (2004-2007). Cooperative research programs, such as the International Childhood Liver Tumour Strategy Group (SIOPEL), on hepatoblastoma are responsible for the excellent progress.[9]

Prevalence

Around 1,500 children were estimated to be living with a diagnosis of hepatoblastoma in Italy in 2010; most of them were diagnosed 15 or more years before the prevalence date.

OLOFACTORY NEUROBLASTOMA

Incidence

In Italy, about 20 cases of olfactory neuroblastoma are diagnosed each year.

Survival

Based on 64 cases, 1- and 5-year RS are 86% and 76%, respectively. According to the RARECAREnet database, RS is slightly better in Italy than Europe (1- and 5-year RS: 81% and 64%, respectively).

Prevalence

Around 300 persons were estimated to be living with a diagnosis of olfactory neuroblastoma in Italy in 2010.

PLEUROPULMONARY BLASTOMA, PANCREATOBLASTOMA, AND ODONTOGENIC TUMOURS

These tumours are so rare that in 11 years (2000-2010) in the AIRTUM dataset only 2, 5, and 12 cases, respectively, were observed. In the RARECAREnet database, in the period 2000-2007, there were 9, 39, and 69 cases. It is not possible to provide estimates of survival for these tumours on the basis of the Italian data. According to the RARECAREnet database, 5-year RS for pancreatoblastoma is 34% (based on 35 cases) and for odontogenic tumours it is 62% (based on 69 cases).

REFERENCES

1. Kaatsch P. Epidemiology of childhood cancer. *Cancer Treat Rev* 2010;36(4):277-285.
2. Ries LAG, Smith MA, Gurney JG, et al (eds). *Cancer incidence and survival among children and adolescents: United States SEER Program 1975-1995.* NIH Pub. No. 99-4649. Bethesda, National Cancer Institute, 1999.
3. Baade PD, Youlden DR, Valery PC, et al. Trends in incidence of childhood cancer in Australia, 1983-2006. *Br J Cancer* 2010;102(3):620-626.
4. Lindor NM, McMaster ML, Lindor CJ, Greene MH; National Cancer Institute, Division of Cancer Prevention, Community Oncology and Prevention Trials Research Group. Concise handbook of familial cancer susceptibility syndromes – second edition. *J Natl Cancer Inst Monogr* 2008;38:1-93.
5. Narod SA, Hawkins MM, Robertson CM, Stiller CA. Congenital anomalies and childhood cancer in Great Britain. *Am J Hum Genet* 1997;60(3):474-485.
6. Scott RH, Stiller CA, Walker L, Rahman N. Syndromes and constitutional chromosomal abnormalities associated with Wilms tumour. *J Med Genet* 2006;43(9):705-715.
7. Pritchard-Jones K, Kaatsch P, Steliarova-Foucher E, Stiller CA, Coebergh JW. Cancer in children and adolescents in Europe: developments over 20 years and future challenges. *Eur J Cancer* 2006;42(13):2183-2190.
8. Ferrari A, Bisogno G, De Salvo GL, et al. The challenge of very rare tumours in childhood: the Italian TREP project. Eur J Cancer 2007;43(4):654-659.
9. Perilongo G, Maibach R, Shafford E, et al. Cisplatin versus cisplatin plus doxorubicin for standard-risk hepatoblastoma. *N Engl J Med* 2009;361/17):1662-1670.
10. Kaatsch P, Steliarova-Foucher E, Crocetti E, Magnani C, Spix C, Zambon P. Time trends of cancer incidence in European children (1978-1997): report from the Automated Childhood Cancer Information System project. *Eur J Cancer* 2006;42(13):1961-1971.
11. Gatta G, Botta L, Rossi S, et al. Childhood cancer survival in Europe 1999-2007: results of EUROCARE-5 – a population-based study. *Lancet Oncol* 2014;15(1):35-47.
12. Gatta G, Ferrari A, Stiller CA, et al. Embryonal cancers in Europe. *Eur J Cancer* 2012; 48(10):1425-1433.
13. Bulterys M, Goodman MT, Smith MA, Buckley JD. Hepatic tumours. In: Ries LAG, Smith MA, Gurney JG, et al (eds). *Cancer incidence and survival among children and adolescents: United States SEER Program 1975-1995.* NIH Pub. No. 99-4649. Bethesda, National Cancer Institute, 1999.