

LSHTM Research Online

Girardi, Fabio; Allemani, Claudia; Coleman, Michel P; (2019) Worldwide Trends in Survival From Common Childhood Brain Tumors: A Systematic Review. Journal of Global Oncology, 5. pp. 1-25. DOI: https://doi.org/10.1200/jgo.19.00140

Downloaded from: http://researchonline.lshtm.ac.uk/id/eprint/4655001/

DOI: https://doi.org/10.1200/jgo.19.00140

Usage Guidelines:

Please refer to usage guidelines at https://researchonline.lshtm.ac.uk/policies.html or alternatively contact researchonline@lshtm.ac.uk.

Available under license: http://creativecommons.org/licenses/by/2.5/

Worldwide Trends in Survival From Common Childhood Brain Tumors: A Systematic Review

Fabio Girardi, MD¹; Claudia Allemani, PhD¹; and Michel P. Coleman, MD¹

PURPOSE The histology of brain tumors determines treatment and predicts outcome. Population-based survival reflects the effectiveness of a health care system in managing cancer. No systematic review of worldwide variation and time trends in survival from brain tumors in children is currently available.

PATIENTS AND METHODS We considered longitudinal, observational studies comprising children diagnosed with intracranial astrocytic or embryonal tumors. We searched six electronic databases from database inception to September 30, 2018, using complex search strategies. The outcome measure was 5-year survival, estimated through a time-to-event analysis. This study is registered with PROSPERO, number CRD42018111981.

RESULTS Among 5,244 studies, we identified 47 eligible articles that provided 228 survival estimates. Only five studies were entirely or partially conducted in low-income or middle-income countries. Five-year survival from embryonal tumors increased from 37% in 1980 to approximately 60% in 2009. Although survival for medulloblastoma improved substantially (from 29% to 73% during 1959-2009), survival for primitive neuro-ectodermal tumors wavered over time (1973-2009) and between countries. Five-year survival from astrocytoma changed very little over the 27 years between 1982 and 2009 (from 78% to 89%). Interpretation of the literature was made difficult by the heterogeneity of study designs.

CONCLUSION Survival has improved for embryonal tumors, but little change has been observed for astrocytic tumors. We found a striking gap in knowledge about survival from childhood brain tumor subtypes in middle-income and low-income countries, where half of these tumors are diagnosed. Larger studies are needed, including in under-represented countries and based on standardized data collection, to provide up-to-date survival estimates.

J Global Oncol. © 2019 by American Society of Clinical Oncology

Licensed under the Creative Commons Attribution 4.0 License

INTRODUCTION

Primary tumors of the CNS in children are rare. The estimated world-standardized incidence rate in 2018 was 12 cases per million, ranging from 1.8 in Melanesia to 36.0 in North America.¹ Despite their rarity, primary CNS tumors were estimated to be the second most important cause of childhood cancer–related deaths after leukemia. The estimated world-standardized mortality rate in 2018 was 0.7 deaths per million, varying between 0.04 in Tanzania and 2.4 in Honduras.¹

Incidence and mortality are essential indicators of the cancer burden in a given population, but the duration of survival also accounts for the dynamic nature of the process between diagnosis and death. Therefore, population-based survival is the most appropriate measure to assess the overall effectiveness of a health care system in managing a given cancer.^{2,3} The third cycle of the CONCORD program (CONCORD-3) found

wide disparities in survival among more than 700,000 patients who were diagnosed with a primary brain tumor in 58 countries worldwide during the 15-year period of 2000-2014. Five-year net survival for all childhood brain tumors combined ranged from 29% in Brazil to approximately 80% in several European countries.⁴ International disparities in survival may result from obstacles in access to surgery, radiotherapy, and chemotherapy.⁵⁻⁸ Such inequalities will inevitably result in failure to diagnose and treat brain tumors adequately, ultimately leading to premature deaths.⁹

CNS tumors comprise tumors of the brain, the spinal cord, and the meninges, but brain tumors are by far the largest group. Brain tumors vary widely in terms of histology and clinical behavior. Histology plays a pivotal role in treatment planning, and treatment needs are specific to each tumor subtype. Therefore, a breakdown of the observed disparities in survival by

ASSOCIATED CONTENT Appendix

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on August 20, 2019 and published at ascopubs.org/journal/ jgo on November 4, 2019: DOI https://doi. org/10.1200/JG0.19. 00140



Journal of Global Oncology®

CONTEXT

Key Objective

To explore what is known about time trends and global variation in population-based survival from common childhood brain tumors.

What Is Known

Five-year survival from medulloblastoma increased from 23% to 73% during 1960-2010, while survival from astrocytoma (nonmalignant and malignant combined) persisted in the range of 80%-90% (1970-2010). Scarce data were available from low-income and middle-income countries, where most childhood brain tumors are currently diagnosed.

Relevance

Our systematic review of real-world, population-based survival estimates may inform clinicians about expected outcomes in unselected populations of children with brain tumor. The available estimates, however, do not cover countries with limited resources, where obstacles in access to care may result in suboptimal treatment. Global initiatives aiming to improve survival of children with brain tumor are underway, and they require a more recent, wide-ranging survival benchmark, which can be obtained only through larger studies using the same protocol for data collection, centralized data quality checks, and the same statistical methodology.

histology is warranted to help shape cancer control plans. In the fifth cycle of the EUROpean CAncer REgistry based study on survival and care of cancer patients (EUROCARE-5) study, which involved children diagnosed during 2000-2007 in 27 European countries, the average 5-year observed survival was 95% for children diagnosed with pilocytic astrocytoma and 65% for those affected by medulloblastoma. This study showed very wide international disparities. For instance, among children diagnosed with a brain tumor defined as WHO grade III or IV, 5-year survival ranged from 36% in Bulgaria to 66% in Finland.¹⁰

To our knowledge, no summary of the scientific evidence on population-based survival for the main subtypes of brain tumor in children is available. We aimed to fill this gap in knowledge by conducting the first systematic review on time trends and geographic variation in survival from brain tumors.

PATIENTS AND METHODS

We considered longitudinal, observational studies that provided estimates of population-based survival, by histology, for children (mainly those age 0-14 years) diagnosed with a primary brain tumor, either malignant or nonmalignant. We excluded studies that only included patients with a CNS tumor in anatomic sites other than the brain because of their rarity and the paucity of data. We also excluded studies that only presented survival estimates for all histologies combined. Studies had to be based on primary data drawn from population-based cancer registries. To maximize geographic coverage, we did not discard studies presenting hospital-based estimates if those estimates were likely to be representative of a given country or territory (eg, a single referral center or a comprehensive network of referral centers) and if no population-based estimate was available. We also excluded clinical trials or

clinical series, because these study designs only include selected patients. Studies were eligible if they included estimates of the survival probability from a time-to-event analysis. To improve comparability between studies, only those presenting survival estimates at 5 years after the diagnosis were included.

We searched six databases (Dissertation and Theses Global, Embase, Medline, Open Grey, Scopus, and Web of Science) from database inception to September 30, 2018, using predefined search strategies that included terms related to the disease under study, the statistical method, and the study design. A professional librarian at the London School of Hygiene and Tropical Medicine reviewed the search strategies (Appendix Table A1).

There were no restrictions relating to language or publication status. However, we excluded studies published before 1995, because the versions of the reference classifications were too early to allow comparability with subsequent editions.

According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (ie, PRISMA) approach (Fig 1),¹¹ potentially eligible studies were evaluated at three progressive levels: title, abstract, and full text. When eligibility was unclear, we reached an agreement through discussion.

For each eligible study, we extracted data on the tumor subtypes included and the reference classification used for tumor definitions (eg, International Classification of Diseases for Oncology, third edition [ICD-O-3]).¹² We collected, when available, specifications of data quality indicators: the proportions of microscopically verified tumors, poorly specified/unspecified morphologies, patients lost to follow-up, and whether diagnoses based on death certificate only or autopsy were excluded. We recorded the



FIG 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.

5-year survival probabilities for each eligible subtype and, when available, the corresponding survival estimates for each calendar period. Last, for each cancer registry, we sought information on the proportion of the population covered and on the completeness of ascertainment.

For studies considering several calendar periods, we abstracted each survival estimate separately. The calendar periods examined varied widely between studies, so we described trends by using the middle year of the corresponding time interval. Given the sparseness of data for some very rare subtypes, we focused on the most frequent morphologies, namely astrocytic and embryonal tumors. Morphologic groupings and definitions also differed between studies. We combined different definitions for the same subtype under a common descriptor (Appendix Table A2).

RESULTS

We assessed 5,244 records for eligibility. Forty-seven studies were included in the systematic review. For each study, we detailed the following: location, completeness of ascertainment, population covered, calendar period for incident cases, age range, quality indicators available, reference classification, and outcome measure (Table 1).

In thirty studies (64%), patients were age 0-14 years; they were 0-15 years in four studies and were 2 years or younger in three studies. Nine studies (19%) included individuals age 20 years or younger, and the upper age limit in one

TABLE 1. Studies It	ncluded in th	le Systematic Revie	We						
First Author	Year of Publication	Countries	Completeness of Ascertainment	Population Coverage	Calendar Period for Incident Cases and End of Follow-Up	Age Span (years)	Quality Indicators	Reference Classification (with edition, if applicable)	Outcome Measure
Kramarova et al²⁰	1996	Slovakia	Not specified	National	1968-1987, 1988	0-14	Proportion of microscopically verified tumors, proportion of patients lost to follow-up	Birch and Marsden	Observed survival
Ilveskoski et al ⁴⁸	1997	Finland	Not specified	Not specified	1975-1993, not specified	0-2	Not specified	Rorke and Kernohan	Observed survival
Magnani et al ³²	1997	Italy	Not specified	Not specified	1978-1989, 1994	0-14	Proportion of microscopically verified tumors, exclusions, proportion of patients lost to follow-up	ICD-0, not further specified	Observed survival
Davis et al ³¹	1998	United States	Not specified	Regional (9.5%, SEER 9)	1973-1991, not specified	0-20	Not specified	ICD-0-2	Observed survival
Agerlin et al ²⁸	1999	Denmark	Not specified	Not specified	1960-1984, 1996	0-14	Proportion of microscopically verified tumors	Not specified	Observed survival
Kaatsch et al ³⁶	2001	Germany	95%	Not specified	1980-1999, not specified	0-14	Not specified	ICCC-2	Observed survival
Alston et al ²⁷	2003	England	95%	Regional (Manchester)	1954-1997, not specified	0-15	Not specified	Not specified	Observed survival
Dama et al ³⁰	2005	Italy	Not specified	Regional (Piemonte)	1970-2001, 2004	0-14	Proportion of microscopically verified tumors, exclusions, proportion of patients lost to follow-up	Iccc-2	Observed survival
Gatta et al ¹⁹	2005	EUROCARE-3 consortium*	Not specified	Regional and national (12%-100%)	1983-1994, not specified	0-14	Proportion of microscopically verified tumors, exclusions, proportion of patients lost to follow-up, proportion of unspecified morphologies	Iccc-2	Observed survival
Berger et al ³⁷	2006	France	Not specified	Regional (Rhone-Alpes)	1987-1999, 2004	0-14	Not specified	ICD-0-2	Observed survival

(Continued on following page)

 ${\bf 4} \, \, {\ensuremath{\mathbb C}}$ 2019 by American Society of Clinical Oncology

Outcome Measure	Observed survival	Observed survival	Observed survival	Observed survival	Observed survival	Observed survival	Observed survival	Observed survival	Observed survival	
Reference Classification (with edition, if applicable)	ICCC-2	ICD-O, not further specified	Not specified	ICCC-3	WHO, 4th edition	ICCC-3	ICD-0-3	ICD-0-2	ICD-0-2	
Quality Indicators	Proportion of microscopically verified tumors, exclusions, proportion of patients lost to follow-up/censored before 5 years, proportion of unspecified morphologies	Exclusions	Proportion of microscopically verified tumors	Proportion of microscopically verified tumors, exclusions	Not specified	Proportion of patients lost to follow-up	Proportion of microscopically verified tumors, proportion of patients lost to follow-up	Proportion of microscopically verified tumors	Proportion of microscopically verified tumors, exclusions, proportion of patients lost to follow-up	
Age Span (years)	0-14	0-14	0-15	0-19	0-15	0-14	0-14	0-15	0-14	
Calendar Period for Incident Cases and End of Follow-Up	1978-1997, not specified	1971-1990, 1995	1997-2005, not specified	1994-2003, 2003	1990-2004, not specified	1990-1999, 2006	1975-1999, not specified	1975-1996, not specified	1990-2001, 2003	ollowing page)
Population Coverage	Regional and national	National	National	Regional (Quebec excluded)	Regional (Institute of Neurosurgery of Tunis)	Regional (24%, Auvergne- Limousin, Bretagne, Lorraine, Rhone-Alpes, Valde-Marne)	Regional (14%, SEER 13)	Regional (Alberta)	Regional (Chennai)	(Continued on fi
Completeness of Ascertainment	Not specified	95%	Not specified	Not specified	Not specified	Not specified	98%	Not specified	Not specified	
Countries	ACCIS consortium†	England, Wales	Singapore	Canada	Tunisia	France	United States	Canada	India	
Year of Publication	2006	2006	2007	2007	2008	2008	2008	2008	2008	
First Author	Magnani et al ¹⁸	Tseng et al ³³	Chan et al ⁴³	Ellison et al ²⁴	Bellil et al ¹³	Desandes et al ³⁸	Linabery et al ⁵¹	Roldan et al ³⁴	Swaminathan et al ¹⁵	

TABLE 1. Studies Included in the Systematic Review (Continued)

Outcome Measure	bbserved survival)bserved survival	kelative survival)bserved survival)bserved survival	bserved survival)bserved survival)bserved survival)bserved survival	kelative survival)bserved survival	
Reference Classification (with edition, if applicable)	1000-3	ICCC-3 C	ICCC-3 F	ICCC, not further C specified	ICCC-3	Iccc-3	ICCC-3	Not specified C	ICD-0-3	ICD-0-3 F	Not specified C	
Quality Indicators	Proportion of microscopically verified turnors, exclusions, proportion of unspecified morphologies	Not specified	Proportion of microscopically verified turnors, exclusions	Not specified	Proportion of patients lost to follow-up	Proportion of microscopically verified tumors, exclusions, proportion of patients lost to follow-up/censored before 5 years, proportion of unspecified morphologies	Proportion of microscopically verified tumors	Not specified	Proportion of microscopically verified tumors	Not specified	Not specified	
Age Span (years)	0-14	0-14	0-14	0-19	0-14	0-14	0-14	0-1	0-19	0-19	0-19	
Calendar Period for Incident Cases and End of Follow-Up	1995-2002, 2003	1984-2005, 2007	1983-2006, 2006	1998-2007, not specified	1968-2005, not specified	1994-2005, 2006	2003-2008, 2008	1973-2006, 2008	1999-2004, 2009	2000-2006, not specified	1988-2009, not specified	ollowing page)
Population Coverage	Regional and national	Not specified	National	Not specified	Regional (Northumberland, Tyne and Wear, Durham, Teesside and Cumbria)	National	Regional (11 registries)	Regional (SEER 17)	National	Regional (25%, SEER 17)	Regional (California)	(Continued on fo
Completeness of Ascertainment	Not specified	Not specified	Not specified	Not specified	98%	Not specified	Not specified	Not specified	Not specified	98%	Not specified	
Countries	EUR OCARE-4 consortium‡	Sweden	Australia	Israel	England	Ireland	Italy	United States	South Korea	United States	United States	
Year of ublication	2009	2009	2010	2010	2011	2011	2012	2012	2012	2012	2013	
First Author P	Gatta et al ²³	Lannering et al ⁴⁰	Baade et al ²¹	Ben Arush et al ⁴⁴	Basta et al ⁵⁰	Walsh et al ²²	Associazione Italiana Registri Tumori ²⁶	Bishop et al ⁵³	Jung et al ⁵⁵	Smoll et al ⁴⁵	Flores et al ⁵²	

 ${\bf 6}~{\odot}$ 2019 by American Society of Clinical Oncology

TABLE 1. Studies Included in the Systematic Review (Continued)

Outcome Measure	Observed survival	Observed survival	Relative survival	Relative survival	Observed survival	Observed survival	Observed survival	Relative survival	Observed survival	Observed survival	Observed survival	
Reference Classification (with edition, if applicable)	ICCC-3	ICCC-3	Not specified	ICD-0-2	ICCC-3	CCC-3	Not specified	ICD-0-3	ICCC-3	Iccc-3	ICCC-3	
Quality Indicators	Proportion of patients lost to follow-up	Proportion of microscopically verified tumors	Proportion of microscopically verified tumors	Proportion of microscopically verified tumors	Not specified	Proportion of microscopically verified tumors, exclusions, proportion of patients lost to follow-up, proportion of unspecified morphologies	Not specified	Not specified	Proportion of microscopically verified tumors, proportion of patients lost to follow-up	Proportion of microscopically verified tumors, proportion of patients lost to follow-up	Not specified	
Age Span (years)	0-14	0-14	0-14	0-19	0-14	0-14	0-19	0-19	0-14	0-28 days	0-24	
Calendar Period for Incident Cases and End of Follow-Up	2000-2009, 2013	1996-2005, not specified	2002-2012, not specified	2007-2011, not specified	1986-2009, not specified	1983-2014, 2014	2001-2004, not specified	2001-2010, 2011	1991-2010, 2010	2000-2009, 2011	1990-2013, 2014	ollowing page)
Population Coverage	Not specified	United Kingdom: national; United States: regional (SEER 18)	Not specified	National	Regional (Auvergne- Limousin)	Regional and national	Not specified	Regional (26%, SEER 18)	National	Not specified	Regional (Yorkshire, Northumberland, Tyne and Wear, Durham, Teesside, and Cumbria)	(Continued on fo
Completeness of Ascertainment	Not specified	%66	Not specified	Not specified	Not specified	Not specified	Not specified	98%	Not specified	Not specified	100%	
Countries	France	United Kingdom, United States	Uganda	England	France	SEE consortium§	Japan	United States	Germany	France	England	
Year of ⁹ ublication	2014	2014	2014	2015	2015	2015	2015	2015	2015	2016	2016	
First Author	Desandes et al ²⁵	Mathew et al ⁴²	Stagno et al ¹⁶	Brodbelt et al ^{58a}	Coll et al ²⁰	Karalexi et al ¹⁴	Narita et al ⁵⁸	Ostrom et al ⁵⁴	Tulla et al ³⁹	Desandes et al ⁴⁹	Fairley et al ⁴¹	

TABLE 1. Studies Included in the Systematic Review (Continued)

7

					Calendar Period for	Ауе		Reference Classification (with	
First Author	Year of Publication	Countries	Completeness of Ascertainment	Population Coverage	Incident Cases and End of Follow-Up	Span (years)	Quality Indicators	edition, if applicable)	Outcome Measure
Park et al ¹⁷	2016	South Korea	80%-90%	National	1993-2011, 2012	0-14	Not specified	ICCC-3	Relative survival
Trama et al ⁴⁷	2016	EUROCARE-5 consortium	Not specified	Regional and national (12%-100%)	2000-2007, 2008	0-14	Proportion of microscopically verified tumors, exclusions, proportion of lost to follow-up, proportion of unspecified morphologies	ICD-0-3	Relative survival
Gatta et al ¹⁰	2017	EUROCARE-5 consortium	Not specified	Regional and national	2000-2007, 2008	0-14	Proportion of microscopically verified tumors, exclusions, proportion of patients lost to follow-up/censored before 5 years, proportion of unspecified morphologies	ICD-0-3	Observed survival
Georgakis et al ⁵⁷	2017	SEE consortium§, United States	Not specified	SEE consortium: regional and national; United States: regional (29%, SEER 18)	SEE: 1983-2014, not specified; SEER: 1973- 2012, not specified	0-14	Proportion of microscopically verified tumors	ICCC-3	Observed survival
Khanna et al ⁴⁶	2017	United States	Not specified	Regional (28%, SEER 18)	2001-2013, not specified	0-14	Not specified	ICD-0-3	Relative survival
Schindler et al ³⁵	2017	Switzerland	91%	National	1984-2013, 2013	0-14	Proportion of microscopically verified tumors, proportion of unspecified morphology	ICCC-3	Observed survival
Abbreviations: AC	Cols, Automat	ted Childhood Cance	er Information Syste	m; EUROCARE, EUROpean	CAncer REgistry based study	on surviv	al and care of cancer patier	nts; ICCC, International	Classificatior

of Unidnood Cancer; ICU-U, International Glassification of Diseases for Uncology; SEE, Southern and Eastern Europe.

*EUROCARE-3 consortium: Austria, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Italy, Malta, Netherlands, Norway, Poland, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales.

#EUROCARE-4 consortium: Austria, Belgium, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, Netherlands, Northern Ireland, Norway, Poland, +ACCIS consortium: Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Italy, Netherlands, Slovakia, Slovenia, Spain, Switzerland, United Kingdom, Norway.

Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales.

§SEE consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine.

IIEUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales.

TABLE 1. Studies Included in the Systematic Review (Continued)

Emboral Lance 97 980 Observed Magmin is al (EURCARE-3, 2006) Europe 48 1980 Observed Magmin is al (ACCIS, 2006) Europe 48 1980 Observed Magmin is al (ACCIS, 2007) Europe 48 1980 Observed Magmin is al (ACCIS, 2007) Europe 48 1980 Observed Gatte al (EURCARE-3, 2007) Europe 48 1980 Observed Bade of al (2017) Europe 48 1980 Observed Bade of al (2017) Catter al (EURCARE-2, 2007) Europe 48 1980 Observed Gatter al (EURCARE-2, 2007) Kantelak Catter al (EURCARE-2, 2007) Catter al (EURCARE-2, 2007) Europe 48 1980 Observed Gatter al (EURCARE-2, 2007) Kantelak Europe 49 1980 Observed Gatter al (EURCARE-2, 2007) Kantelak Europe 40 1980 Observed Gatter al (EURCARE-2, 2007) Kantelak Europe 40 1980 Observed	HISTOLOGY AND FIRST AUTHOR	LOCATION	FIVE-YE	AR SURVIVAL (%) AND 95% CI	%	CENTRAL YEAR	OUTCOME MEASURE	AGE RANGI (years)
Magnani et al ACCS. 20091 Europe 42 1980 Observed Magnani et al ACCS. 20091 Europe 43 1987 Observed Magnani et al ACCS. 20091 Europe 43 1987 Observed Gaits et al EUROCARES. 20091 Europe 43 1987 Observed Gaits et al EUROCARES. 20091 Europe 43 1987 Observed Magnani et al ACCS. 20091 Europe 43 1987 Observed Magnani et al ACCS. 20091 Europe 43 1987 Observed Magnani et al ACCS. 20091 South Korea 40 1987 Observed Magnani et al ACCS. 20091 South Korea 40 1987 Observed Magnani et al ACCS. 20091 Europe 50 1997 Observed Casta et al EUROCARES. 20091 Europe 50 1997 Observed Casta et al EUROCARES. 20091 Europe 50 1997 Observed Casta et al EUROCARES. 20091 Europe 50 10 10 10 <	Embryonal tumor							
Ginse and IEUROCARES. 2009) Europe 46 1986 Deserved Margan et al ALCOS. 2009) Europe 48 1980 Deserved Margan et al ALCOS. 2009) Europe 48 1980 Deserved State et al IEUROCARES. 2009) France 48 1980 Deserved Gate et al IEUROCARES. 2009) France 48 1980 Deserved Bask et al (2017) Catter at IEUROCARES. 2009) France 48 1980 Deserved Bask et al (2017) Catter at IEUROCARES. 2009) Central Europe 48 1987 Deserved Gate at al EUROCARES. 2009) Central Europe 48 1987 Deserved Gate at al EUROCARES. 2009) Central Europe 48 1987 Deserved Gate at al EUROCARES. 2009) Central Europe 48 1987 Deserved Gate at al EUROCARES. 2009 Central Europe 59 Deserved 59 Deserved Gate at al EUROCARES. 2007 Central Europe 50 Deserved 59 Deserved	Magnani et al (ACCIS, 2006) ¹⁸	Europe		🔺 i	37	1980	Observed	0-14
Magenet et al. (J.C.), 2000) Europe 48 1985 Observed Gate et al (EUROARE 5, 2007) Europe 48 1980 Observed Call et al (J.C.), 2000) Europe 48 1980 Observed Call et al (J.C.), 2000) Europe 48 1980 Observed Call et al (J.C.), 2000) Europe 48 1980 Observed Call et al (J.C.), 2000) Europe 48 1980 Observed Gate et al (J.C.), 2000) Europe 48 1980 Observed Gate et al (J.C.), 2000) Europe 58 1997 Observed Gate et al (J.C.), 2000) Europe 58 1997 Observed Gate et al (J.C.), 2000) Europe 58 1997 Observed Gate et al (J.C.), 2000) Europe 58 1997 Observed Gate et al (J.C.), 2000) Europe 59 2000 Observed Gate et al (J.C.), 2000) Europe 59 2000 Observed Gate et al (J.C.), 2000) </td <td>Gatta et al (EUROCARE-3, 2005)¹⁹</td> <td>Europe</td> <td></td> <td>📥 i</td> <td>46</td> <td>1984</td> <td>Observed</td> <td>0-14</td>	Gatta et al (EUROCARE-3, 2005) ¹⁹	Europe		📥 i	46	1984	Observed	0-14
butter en is contu-ont-5x (200) Europe 48 1977 Deserved Call et al (LDPLARE 5, 2005) Europe 48 1987 Deserved Badd et al (LDPLARE 5, 2005) Europe 48 1987 Deserved Badd et al (LDPLARE 5, 2005) Europe 48 1987 Deserved Badd et al (LDPLARE 5, 2005) Europe 48 1987 Deserved Gatt et al (LDPLARE 5, 2005) Europe 48 1987 Deserved Gatt et al (LDPLARE 5, 2005) Europe 48 1987 Deserved Gatt et al (LDPLARE 5, 2007) Europe 48 1997 Deserved Gatt et al (LDPLARE 5, 2007) Europe 48 1997 Deserved Gatt et al (LDPLARE 5, 2007) Europe 48 1997 Deserved Gatt et al (LDPLARE 5, 2007) Europe 48 1997 Deserved Gatt et al (LDPLARE 5, 2007) Europe 50 1997 Deserved Gatt et al (LDPLARE 5, 2007) Europe 50 1997 Deserved	Magnani et al (ACCIS, 2006) ¹⁰	Europe		🔺 📜	44	1985	Observed	0-14
Galls at all EURCARES, 2005" Europe 48 1933 Diserved Galls at all EURCARES, 2005" Europe 48 1933 Diserved March at all CURCARES, 2005" Europe 48 1933 Diserved March at all CURCARES, 2005" Europe 48 1933 Diserved March at all CURCARES, 2005" Europe 48 1937 Diserved Galts at all EURCARES, 2005" Southern Europe 48 1937 Diserved Galts at all EURCARES, 2005" Southern Europe 48 1937 Diserved Galts at all EURCARES, 2005" Europe 40 1939 Diserved Mark at all CURCARES, 2005" Europe 40 1939 Diserved Europe 40 1939 Diserved 53 1937 Diserved Europe 40 1939 Diserved 53 1937 Diserved Context all CONT Associal CONT South Korea 53 1937 Diserved Dasocial CONT South Korea	Gatta et al (EUROCARE-3, 2005) Magnani et al (ACCIS, 2006) ¹⁸	Europe		A	49	1987	Observed	0-14
Coll et al (2006) ¹¹ Finisher Serie A (2006) ¹¹ Park et al (2017) ¹¹ Wah et al (2017) ¹² Wah et al (2017) ¹² Serie A (2007) ¹⁴ Serie A (2007) ¹⁴ Serie A (2007) ¹⁴ Serie A (2007) ¹⁴ Serie A (2007) ¹⁴ Ellicon et al (2007) ¹⁴ Ellicon et al (2007) ¹⁴ Park et al (2014) ¹⁵ Park et al (2014) ¹⁵ Park et al (2014) ¹⁶ Park et al (2014) ¹⁶ Park et al (2014) ¹⁷ Park et al (2017) ¹⁷ Par	Gatta at al (ELIROCARE 2, 2005) ¹⁹	Europe			48	1990	Observed	0-14
Gente at ILUNCARES, 2005" Europe 62 1983 Belaive Park et al (2010" South Korea 40 1984 Belaive Gatte at al (EURCARES, 2005") Europe 61 1997 Observed Gatte at al (EURCARES, 2005") Europe 61 1997 Observed Gatte at al (EURCARES, 2005") Europe 61 1997 Observed Gatte at al (EURCARES, 2005") Europe 68 1997 Observed Gatte at al (EURCARES, 2005") Europe 68 1997 Observed Gatte at al (EURCARES, 2005") Europe 68 1997 Observed Gatte at al (EURCARES, 2005") Europe 68 2001 Observed Gatte at al (EURCARES, 2005") Europe 68 2001 Observed Cast at al (EURCARES, 2005") Europe 68 2001 Observed Cast at al (EURCARES, 2005") Europe 60 2001 Observed Cast at al (EURCARES, 2005") Europe France 52 2008 Delaiv	Coll et al (2015) ²⁰	Europe			40	1990	Observed	0-14
Park et al (2016)** South Korea 40 1956 Relative Bande et al (2016)** South Korea 40 1956 Relative Gatte et al (EURCARE + 2006)** South Korea 61 1997 Observed Gatte et al (EURCARE + 2006)** South Korea 61 1997 Observed Gatte et al (EURCARE + 2006)** South Korea 61 1997 Observed Gatte et al (EURCARE + 2006)** South Korea 53 1997 Observed Gatte et al (EURCARE + 2006)** Karakei et al (SURCARE + 2006)** 66 1997 Observed Gatte et al (EURCARE + 2006)** Karakei et al (SURCARE + 2006)** France 51 2001 Observed Gatte et al (EURCARE + 2006)** France 51 2001 Observed 52 2003 Observed Park et al (2016)** South Korea 51 2001 Observed 52 2006 Observed Park et al (2016)** France 50 2006 Observed 52 2006 Observed Coll et al (2016)** France 50 2006 Observed 50 <td>Gatta et al (EUROCARE-3, 2005)¹⁹</td> <td>Europe</td> <td></td> <td></td> <td>52</td> <td>1993</td> <td>Observed</td> <td>0-14</td>	Gatta et al (EUROCARE-3, 2005) ¹⁹	Europe			52	1993	Observed	0-14
Basde et al (2010) ¹⁷ Maran et al (2007,AEE, 2000) ¹⁷ Gatte at al (EUROCARE, 2000) ¹⁷ Carter at al (EUROCARE, 2000) ¹⁷ Eastern Europe Gatte at al (EUROCARE, 2000) ¹⁷ Europe Europe Gatte at al (EUROCARE, 2000) ¹⁷ Europe Coll et al (2011) ¹⁷ France France France France Gatte at al (2017) ¹⁷ Agenin et al (2001) ¹⁷ Agenin et al (2001) ¹⁷ Agenin et al (2001) ¹⁷ Agenin et al (2001) ¹⁷ Europe France Fran	Park et al (2016) ¹⁷	South Korea			49	1994	Relative	0-14
Magnani et al (ACCES, 2008) ¹ Europe 6 996 Observed Gatt et al (EUROCARE 2, 2008) ¹ South on Europe 6 997 Observed Gatt et al (EUROCARE 2, 2008) ¹ South on Europe 6 997 Observed Gatt et al (EUROCARE 2, 2008) ¹ Canada 5 9986 Observed Gatt et al (EUROCARE 2, 2008) ¹ Canada 6 997 Observed Far et al (CON) ¹ South on any 5 9986 Observed Gatt et al (EUROCARE 2, 2008) ¹ Europe 40 9989 Observed Gatt et al (CON) ¹ South Konae 6 2001 Observed Deands et al (CON) ¹ South Konae 57 2003 Observed Altron et al (CON) ¹ South Konae 6 2000 Observed Altron et al (CON) ¹ South Konae 6 2000 Observed Altron et al (CON) ¹ South Konae 9 9980 Observed Altron et al (CON) ¹ South Konae 9 9980 Observed </td <td>Baade et al (2010)²¹</td> <td>Australia</td> <td></td> <td></td> <td>49</td> <td>1995</td> <td>Relative</td> <td>0-14</td>	Baade et al (2010) ²¹	Australia			49	1995	Relative	0-14
Wash at al (2011) ¹⁰ 49 1977 Deserved Gatt at al (EURCARE +, 2007) ¹⁰ Extern Europe 68 1997 Deserved Gatt at al (EURCARE +, 2007) ¹⁰ Extern Europe 68 1997 Deserved Gatt at al (EURCARE +, 2007) ¹⁰ Extern Europe 68 1997 Deserved Gatt at al (EURCARE +, 2007) ¹⁰ Extern Europe 68 1997 Deserved Gatt at al (EURCARE +, 2007) ¹⁰ Extern Europe 60 1999 Deserved Gatt at al (EURCARE +, 2007) ¹⁰ Europe 50 2001 Deserved Desartest at (2016) ¹⁰ Europe 51 2001 Deserved Desartest at (2016) ¹⁰ France 52 2004 Deserved Desartest at (2016) ¹⁰ Europe 52 2004 Deserved Aution at (2007) ¹⁰ Enalor 52 2004 Deserved	Magnani et al (ACCIS, 2006) ¹⁸	Europe			52	1995	Observed	0-14
Gatta di EUROCARE 4, 2009" Central Europe 61 61 697 Observed Gatta di EUROCARE 4, 2009" UK and relamin 65 1997 Observed Gatta di EUROCARE 4, 2009" UK and relamin 65 1997 Observed Gatta di EUROCARE 4, 2009" UK and relamin 65 1997 Observed Elisor etal (2016) South Korea 55 1980 Observed Gatta di EUROCARE 4, 2009" Europe 66 1997 Observed Gatta di EUROCARE 4, 2009" Europe 66 1997 Observed Gatta di EUROCARE 4, 2009" Europe 66 2001 Observed Gatta di EUROCARE 4, 2009" Europe France 50 2000 Observed Matin di EUROTI" France 50 2000 Observed 50 2000 Observed Altron et al (2001" France 50 2000 Observed 50 2000 Observed Altron et al (2001" Europe South Korea 50 2000	Walsh et al (2011) ²²	Ireland	-		49	1997	Observed	0-14
Gatta et al (EURCARE 4, 2009)" Souther Europe Gatta et al (EURCARE 4, 2009)" Park et al (2016)" Ranadas et al (EURCARE 4, 2009)" Northern Europe Gatta et al (EURCARE 4, 2009)" Northern Europe Gatta et al (EURCARE 4, 2009)" Northern Europe Canada Hand 1000 at al (2017)" Park et al (2016)" Desended et al (2014)" Park et al (2016)" Canada Altron et al (2016)" Ranadas et al (2016)" Canada Call et al (2016)" Ranadas et al (2016)" Canada Call et al (2016)" Ranadas et al (2016)" Canada Altron et al (2006)" Ranadas et al (2016)" Call et al (2016)" Ranadas et al (2016)" Canada Call et al (2016)" Ranadas et al (2016)" Call et al (2016)" Ranadas et al (2016)" Call et al (2016)" Ranadas et al (2016)" Call et al (2017)" Call et al (2016)" Call et al (2016)" Call et al (2016)" Call et al (2017)" Call et al (2016)" Call et al (2016)" Call et al (2017)" Call et al (2016)" Call et al (2017)" Call et al (2016)" Call et al (2017)" Call et al (Gatta et al (EUROCARE-4, 2009)	Central Europe		I	61	1997	Observed	0-14
Gente ai (EURCARE 4, 2009)" Eastern Europe 46 1997 Observed Gante ai (EURCARE 4, 2009)" South Kora 55 1997 Observed Rankei ai (12016) South Kora 55 1997 Observed Ellion ei al (2007) Canada 60 1999 Observed Deandes et al (2014) France 57 2008 Relative Deandes et al (2014) France 57 2008 Relative Commende et al (2014) France 57 2008 Relative Commende et al (2014) France 58 2007 Observed Park et al (2014) France 58 2007 Observed Matton et al (2003) ^T France 58 2008 Observed Altron et al (2003) ^T France 59 2008 Relative Altron et al (2003) ^T France 59 2008 Relative Altron et al (2003) ^T France 59 2008 Relative Down et al (2003) ^T France 59 2008 Relative Apprint et al (2004) ^T <	Gatta et al (EUROCARE-4, 2009) ²³	Southern Europe			58	1997	Observed	0-14
Gath and BUND-ANE-2, 2009) Uk and relation South forma Fark et al (2016) ¹⁰ South forma South forma Kanadox et al (SEE, 2019) ¹⁰ Europe Gate at al (EUROCARE - 2009) ¹⁰ Cante at al (2010) ¹⁰ Fance South forma Park et al (2010) ¹⁰ Fance South forma Cante at al (2016) ¹⁰ South forma South forma Park et al (2010) ¹⁰ Fance South forma Cante at (2016) ¹⁰ South forma South forma Park et al (2016) ¹⁰ Fance South forma Desnodes et al (2014) ¹⁰ France South forma Park et al (2016) ¹⁰ South forma South forma Auton et al (2009) ¹⁰ Fance South forma Park et al (2016) ¹⁰ South forma South forma Canter at (2009) ¹⁰ Fance South forma Dams et al (2009) ¹⁰ South forma South forma Canter at (2009) ¹⁰ England Demmark Canter at (2009) ¹⁰ England Demmark Dams et al (2009) ¹⁰ England South forma Dams et al (2009) ¹⁰ England S	Gatta et al (EUROCARE-4, 2009)23	Eastern Europe			46	1997	Observed	0-14
Same at a LUP(2) Northern Europe Be Be Descreted Ellison et al (2007) ²⁷ Canada Berrope Berrope Berrope Canada Canada Berrope Berrope <td< td=""><td>Gatta et al (EUROCARE-4, 2009)</td><td>UK and Ireland</td><td></td><td>!-</td><td>55</td><td>1997</td><td>Observed</td><td>0-14</td></td<>	Gatta et al (EUROCARE-4, 2009)	UK and Ireland		!- 	55	1997	Observed	0-14
Ease nuclear Land Core Duration of Linear Core Duration of Linear Core Gatts at al (EUROCARS - 2009) ¹ Europe France South Core Desandes et al (Core) ¹ France South Core South Core Call et al (Core) ¹ France South Core South Core Call et al (Core) ¹ France South Core South Core Call et al (Core) ¹ France South Core South Core Desandes et al (Core) ¹ France South Core South Core Matton et al (Core) ¹ France South Core South Core Matton et al (Core) ¹ South Core South Core South Core Matton et al (Core) ¹ South Core South Core South Core Dama et al (Core) ¹ South Core South Core South Core Dama et al (Core) ¹ South Core South Core South Core Dama et al (Core) ¹ South Core South Core South Core Dama et al (Core) ¹ South Core South Core South Core Dama et al (Core) ¹ South Core South Core South Core Dama et al (Core) ¹ <td>Gatta et al (EURUCARE-4, 2009)</td> <td>Northern Europe</td> <td></td> <td></td> <td>56</td> <td>1997</td> <td>Observed</td> <td>0-14</td>	Gatta et al (EURUCARE-4, 2009)	Northern Europe			56	1997	Observed	0-14
Ellison et al (2027)* Canada ed 990 Observed Gata et al (2014)* France 51 2001 Observed Main et al (2014)* France 51 2001 Observed Desandes et al (2014)* France 51 2001 Observed Desandes et al (2014)* France 52 2004 Observed Desandes et al (2014)* France 52 2004 Observed Altrot et al (2014)* France 52 2000 Observed Altrot et al (2014)* England 53 2000 Observed Altrot et al (2005)* England 53 2005 Observed Altrot et al (2005)* England 53 2005 Observed Altrot et al (2005)* England 53 2005 Observed Agein et al (2005)* England 53 2005 Observed Agein et al (2005)* England 53 1372 Observed Agein et al (2005)* England 54 <t< td=""><td>Fark et al (2016) Karalovi et al (SEE 2015)¹⁴</td><td>South Korea</td><td></td><td></td><td>20</td><td>1998</td><td>Obsorved</td><td>0-14</td></t<>	Fark et al (2016) Karalovi et al (SEE 2015) ¹⁴	South Korea			20	1998	Obsorved	0-14
Gatta et al (EU/00CARE_4.2009) ¹⁰ Europe image: al (EU/00CARE_4.2009) ¹⁰ Europe Wath et al (2011) ¹⁰ France 59 2000 Observed Park et al (2016) ¹⁰ France 59 2000 Observed Coll et al (2015) ¹⁰ France 59 2000 Observed Destandse et al (2014) ¹⁰ France 59 2000 Observed Park et al (2014) ¹⁰ France 50 2000 Observed Destandse et al (2014) ¹⁰ France 50 2000 Observed Park et al (2016) ¹⁰ South Korea 50 2000 Relative Mation et al (2003) ¹⁰ Figland 50 2000 Relative Alston et al (2003) ¹⁰ Figland 50 2000 Relative Darna et al (2006) ¹⁰ Figland and Wales 3 1970 Observed Darna et al (2006) ¹⁰ Figland and Wales 1 1980 Observed Darna et al (2006) ¹⁰ Figland and Wales 1 1980 Observed Darna et al (2006) ¹⁰ Figland and Wales 1 1980 Observed <td>Ellicon et al (2007)²⁴</td> <td>Canada</td> <td></td> <td></td> <td>60</td> <td>1999</td> <td>Observed</td> <td>0.19</td>	Ellicon et al (2007) ²⁴	Canada			60	1999	Observed	0.19
Deandes et al (2014) Park et al (2015) Park et al (2014) France Park et al (2014) France Fr	Gatta et al (EUROCARE-4, 2009) ²³	Europe			66	2001	Observed	0-13
Wideh trail (2011) ²¹ train d 59 2003 Observed Described at (2014) ²¹ France 53 2004 Observed Coll et al (2014) ²¹ France 53 2004 Observed Described at (2014) ²¹ France 53 2004 Observed Park et al (2016) ²¹ France 53 2004 Observed Park et al (2016) ²¹ South Korea 61 2008 Observed Action et al (2003) ²¹ France 61 2008 Relative Action et al (2003) ²¹ South Korea 61 2009 Relative Action et al (2003) ²¹ South Korea 61 2009 Doserved Action et al (2005) ²¹ South Korea 71 1977 Doserved Action et al (2005) ²¹ Stovakia 18 1877 Doserved 1877 Doserved Action et al (2005) ²¹ Italy Stovakia 18 1877 Doserved 1870 Doserved 1870 Doserved 1870 Doserved 1870 Doserved 1870 Doserved 1870 Doserve	Desandes et al (2014) ²⁵	France			51	2001	Observed	0-14
Park et al (2016) ¹⁰ South Korea 57 2003 Relative Coll et al (2016) ¹⁰ France 53 2004 Observed Altton (2017) ²⁰ France 53 2004 Observed Park et al (2016) ¹⁰ South Korea 59 2005 Observed Mediobletona 50 2007 Observed 50 2008 Observed Mediobletona 50 2008 Observed 50 2009 Relative Mediobletona 50 2004 Observed 50 2008 Observed Marnorova et al (1990) ¹⁰ South Korea 50 2008 Observed 50 2008 Observed Marnorova et al (1990) ¹⁰ South Korea 50 2008 Observed 31 3070 Desved Maranova et al (1990) ¹⁰ Stovata 51 Stovata 31 3100 Desved 31 3100 Desved 31 310 31 310 31 310 31 310 31 310 31 310 31 310 31 310	Walsh et al (2011) ²²	Ireland			59	2003	Observed	0-14
Desandes et al (2014) ¹⁰ France France 53 2006 Observed AITUM (2012) ¹⁰ France France 53 2006 Observed South Kores 54 2001 Park et al (2014) ¹⁰ France 53 2006 Observed France 64 2009 Relative Meduciolationa Altion et al (2037) ¹⁰ Altion et al (2037) ¹⁰ Altion et al (2037) ¹⁰ Altion et al (2037) ¹⁰ Altion et al (2037) ¹⁰ Kramarova et al (2037) ¹⁰ Haly Maganit et al (1999) ¹⁰ Divis et al (1999) ¹⁰ Charles 4 11999) ¹⁰ Divis et al (1999) ¹⁰ Divis et al	Park et al (2016) ¹⁷	South Korea			57	2003	Relative	0-14
Coll et al (2015) ¹⁰ AltrUM (2014) ¹⁰ Park et al (2014) ¹⁰ France Franc	Desandes et al (2014) ²⁵	France			53	2004	Observed	0-14
AlfTUM (2012) ²⁷ Park et al (2016) ¹⁷ France South Korea France Fra	Coll et al (2015) ²⁰	France			50	2005	Observed	0-14
Desandes et al (2014) ¹⁶ Park et al (2016) ¹⁷ South Korea South K	AIRTUM (2012) ²⁶	Italy			62	2006	Observed	0-14
Park et al (2016) ¹⁷ Park et al (2003) ²⁷ Alkton et al (2003) ²⁷ Apprint et al (1999) ¹⁰ Common et al (2005) ¹⁹ Damie at al (2005) ¹⁹ Common et al (2005) ¹⁹ Kramerova et al (1997) ¹⁰ Kramerova et al (1997) ¹⁰ Common et al (2006) ¹⁹ Common et al (2007) ¹⁷ Kramerova et al (1999) ¹⁰ Common et al (2007) ¹⁹ Common et al (2007) ¹⁹ Kramerova et al (1999) ¹⁰ Common et al (2007) ¹⁹ Common et al (2007) ¹⁹ Ridy Magnani et al (1997) ¹⁹ Ridy Magnani et al (2007) ¹⁹ Common et al (2007) ¹⁹ Ridy Magnani et al (2007) ¹⁹ Ridy Common et al (2007) ¹⁹ Ridy	Desandes et al (2014) ²⁵	France			58	2007	Observed	0-14
Park et al (2016) ¹⁷ South Korea 60 2009 Relative Maduliobiastoma Alton et al (2003) ¹⁷ England 1959 Observed Alton et al (2005) ¹⁶ England 1977 Observed 1970 Observed Davis et al (1999) ¹⁷ United States 1977 Observed 1977 Observed Maganit et al (1997) ¹⁶ Haly Haly 1977 Observed 1970 Observed Jorne et al (2005) ¹⁶ Haly Finland 11 1972 Observed Jorne et al (2005) ¹⁶ Haly Finland 11 1972 Observed Jorne et al (2005) ¹⁶ Haly Finland 11 1972 Observed Agrint et al (1997) ¹⁶ Finland 11 1972 Observed Agrint et al (1997) ¹⁶ Haly Denmark 00 00 00 00 Davis et al (1998) ¹⁷ Novakia Gandad 1977 1983 Observed Maganit et al (1997) ¹⁷ Stavkia Gandad 197 1988 Observed Maganit et al (1997) ¹⁷ Stavkia <td>Park et al (2016)</td> <td>South Korea</td> <td></td> <td></td> <td>61</td> <td>2008</td> <td>Relative</td> <td>0-14</td>	Park et al (2016)	South Korea			61	2008	Relative	0-14
Medialobiastoma Agerin et al (1998) ¹¹ Kramarova et al (1996) ¹² Dama et al (2005) ¹² Kramarova et al (1996) ¹³ Dama et al (1997) ¹⁴ Mited States Taeny et al (1998) ¹⁵ United States Taeny et al (2006) ¹² Taeny et al (2007) ¹³ Taeny et al (2007) ¹³ T	Park et al (2016)	South Korea		i 🔺	60	2009	Relative	0-14
Akton et al (2003) ¹⁷ Agerin et al (1999) ¹⁸ Bouwak Aranarova et al (1996) ¹⁹ Dona et al (2005) ¹⁹ The y Magrani et al (1997) ¹⁹ Hely Magrani et al (2005) ¹⁹ France Franc	Medulloblastoma			1				
Agerin et al (1999) ^a Demmark 3 1952 Observed Kramarova et al (1996) ^a Slovakia 1 1972 Observed Dans et al (205) ^a Italy Slovakia 1 1972 Observed Dans et al (206) ^a United States 22 1977 Observed Magnani et al (1996) ^a Italy Slovakia 22 1977 Observed Kramarova et al (1996) ^a Italy Slovakia 22 1977 Observed Magnani et al (1996) ^a Italy Slovakia 22 1987 Observed Temp et al (2060) ^a England and Wales 26 1980 Observed Agerin et al (1997) ^a Italy 46 1982 Observed Kramarova et al (1997) ^a Italy 46 1982 Observed Magnani et al (1997) ^a Italy Slovakia 26 1986 Observed Magnani et al (1997) ^a Italy Slovakia 66 1986 Observed Magnani et al (1997) ^a Italy Italy 50 Slovakia 50 1989 Obs	Alston et al (2003)27	England –	_		29	1959	Observed	0-15
Kramarova et al (1969) ¹⁶ Slovakia 1 1970 Observed Davis et al (1989) ¹⁶ United States 67 1977 Observed Dama et al (2065) ¹⁶ Haly 1 1970 Observed Magnani et al (1997) ¹⁶ Finland 71 1980 Observed Trans et al (2065) ¹⁶ Haly 1 1980 Observed Agerin et al (1999) ¹⁶ England and Wales 21 1980 Observed Dama et al (2065) ¹⁶ Haly 36 1982 Observed Magnani et al (1997) ¹⁶ United States 21 1980 Observed Magnani et al (1997) ¹⁶ United States 26 1982 Observed Magnani et al (1997) ¹⁶ Italy Canada 71 1983 Observed Magnani et al (1997) ¹⁶ Stotakia 66 1982 Observed Canada 73 1980 Observed 78 1980 Observed Germany Stotakia 73 1980 Observed 78 1980 Observed Jotast al (2006) ¹⁷ Finlond <td>Agerlin et al (1999)²⁸</td> <td>Denmark</td> <td></td> <td>1</td> <td>8</td> <td>1962</td> <td>Observed</td> <td>0-14</td>	Agerlin et al (1999) ²⁸	Denmark		1	8	1962	Observed	0-14
Dama et al (1990) ¹⁰ Haly 1 1972 Observed Dama et al (1990) ¹⁰ United States 67 1977 Observed Magnani et al (1997) ¹⁰ Haly 22 1980 Observed Magnani et al (1997) ¹⁰ Haly 36 1980 Observed Treng et al (2006) ¹⁰ England and Wales 41 1980 Observed Dama et al (2006) ¹⁰ England and Wales 41 1980 Observed Magnani et al (1997) ¹⁰ Haly 41 1980 Observed Magnani et al (1997) ¹⁰ Haly 41 1980 Observed Magnani et al (1997) ¹⁰ Haly 56 1984 Observed Magnani et al (1997) ¹⁰ Haly 56 1986 Observed Magnani et al (1997) ¹⁰ Haly 58 1988 Observed Magnani et al (1997) ¹⁰ Haly 53 1980 Observed Magnani et al (1997) ¹⁰ Haly 53 1980 Observed Magnani et al (2001) ¹⁰ Germany 53 1980 Observed Not et al (1997	Kramarova et al (1996) ²⁹	Slovakia 🔺			3	1970	Observed	0-14
Kramarova et al (1999) ¹⁰ Slovakia 18 1975 Observed Dama et al (2005) ¹⁰ Italy 22 1977 Observed Kramarova et al (1999) ¹⁰ Italy 36 1980 Observed Kramarova et al (1997) ¹⁰ Finland 11 1980 Observed Kramarova et al (1997) ¹⁰ Finland 11 1980 Observed Agerin et al (1997) ¹⁰ Finland 41 1981 Observed Agerin et al (1997) ¹⁰ England and Wales 23 1982 Observed Agerin et al (1997) ¹⁰ United States 73 1982 Observed Magmani et al (1997) ¹⁰ United States 76 1986 Observed Davis et al (1997) ¹⁰ Kaity 78 1987 Observed Davis et al (1997) ¹⁰ Kaity 78 1987 Observed Davis et al (1997) ¹⁰ Kaity 78 1987 Observed Schindler et al (2017) ¹⁰ Switzerland 10 1980 Observed Desandes et al (2005) ¹⁰ France 1980 Observed 1980 O	Dama et al (2005) ³⁰	Italy		1	1	1972	Observed	0-14
Davis et al (1999) ^a United States Haly Kramarova et al (1997) ^a Haly Kramarova et al (1997) ^a Haly Kramarova et al (1997) ^a Haly Kramarova et al (1997) ^a Haly Haly Conserved Haly Kramarova et al (1997) ^a Haly Haly Haly Haly Haly Haly Kramarova et al (1997) ^a Haly Haly Haly Haly Kramarova et al (1997) ^a Haly Haly Haly Kramarova et al (1997) ^a Haly Haly Haly Haly Haly Haly Kramarova et al (1997) ^a Haly Ha	Kramarova et al (1996) ²⁹	Slovakia		i	18	1975	Observed	0-14
Dama et al (2005) ^a , Italy Magnani et al (1997) ^a , Finland Kramarova et al (2005) ^a , England and Wales Italy Agentin et al (1997) ^a , England and Wales Italy Dama et al (2005) ^a , England and Wales Italy Dama et al (2005) ^a , England and Wales Italy Dami et al (2005) ^a , England and Wales Italy Davis et al (1997) ^a , England and Wales Italy Agentin et al (1997) ^a , England and Wales Italy Davis et al (1997) ^a , England and Wales Italy Agentin et al (1997) ^a , England and Wales Italy Agentin et al (1997) ^a , England and Wales Italy Davis et al (1997) ^a , England and Wales Italy Agentin et al (1997) ^a , England and Wales Italy Davis et al (1997) ^a , England and Wales Italy Davis et al (1997) ^a , England Scharda Davis et al (1997) ^a , England Scharde Davis et al (1997) ^a , England Scharde Davis et al (1997) ^a , England Scharde Scharde Scharder et al (2006) ^a , England Scharder et al (2007) ^a , England Scharder	Davis et al (1998) ³¹	United States		i 🔺	67	1977	Observed	0-20
Magnani et al (1997)* Italy 36 1980 Observed Kramarova et al (1990)* Finland 22 1980 Observed Dama et al (2005)* England and Wales 46 1982 Observed Dama et al (1997)* United States 71 1983 Observed Davis et al (1997)* United States 71 1983 Observed Ramarova et al (1990)* Bonmark Donmark 28 1982 Observed Magnani et al (1997)* Italy Canada 28 1982 Observed Magnani et al (1997)* Canada 28 1982 Observed Magnani et al (1997)* England 48 51 1980 Observed Dama et al (2005)** Italy Canada 53 1980 Observed Schindler et al (1997)** Italy Finlend 53 1980 Observed Nieskoki et al (2005)** France 53 1980 Observed 1989 Observed Lanarering et al (2005)** France 51 1990 Observed 1990 Observed	Dama et al (2005) ³⁰	Italy			22	1977	Observed	0-14
Ilveskoski et al (1997)*** Finland 11 1980 Observed Kramarova et al (1996)** England and Wales 41 1981 Observed Agerini et al (1996)** England and Wales 41 1981 Observed Agerini et al (1996)** Denmark 36 1982 Observed Magnani et al (1997)** Italy Stowakia 56 1984 Observed Kramarova et al (1996)** Conada 56 1984 Observed Roidon et al (2005)** Canada 56 1986 Observed Schndler et al (1997)** Italy Stowakia 72 1987 Observed Davis et al (1989)** United States 1 72 1989 Observed Nutzerland United States 1 72 1989 Observed Davis et al (1989)** Finland 43 1980 Observed Nutzerland Intel States 1 72 1989 Observed Ratoch et al (2005)** France 51 1992 Observed Ratoch et al (2005)** France 51	Magnani et al (1997) ³²	Italy		▲ I	36	1980	Observed	0-14
Kramarova et al (1996) ² Slovakia 22 1980 Observed Dama et al (2005) ⁿ England and Wales 46 1982 Observed Agerini et al (1999) ² Denmark 0nited States 71 1983 Observed Rinardova et al (1996) ² Dinted States 71 1983 Observed Rovakia 71 1983 Observed Observed Rovakia 71 1983 Observed Observed Rovakia 71 1983 Observed Observed Magnani et al (2005) ⁿ Canada 26 1986 Observed Dama et al (2007) ⁿ Haty 72 1989 Observed Magnani et al (1997) ⁿⁱ United States 72 1989 Observed Diveskoki et al (1998) ⁿⁱ United States 72 1989 Observed Ratach et al (2005) ⁿⁱ France 53 1990 Observed Lannering et al (2005) ⁿⁱ France 51 1992 Observed Lannering et al (2005) ⁿⁱ Germany France 1997 Observed	Ilveskoski et al (1997) ⁴⁸	Finland		1	11	1980	Observed	0-2
Teeng et al (2006)* England and Wales 41 1981 Observed Agerfin et al (1999)* Denmark 36 1982 Observed Magnani et al (1997)* United States 71 1983 Observed Kramarova et al (1996)* Slovakia 26 1986 Observed Barger et al (2005)* Italy 26 1986 Observed Magnani et al (1997)* Italy 26 1986 Observed Schindler et al (2005)* Italy 78 1987 Observed Magnani et al (1997)* Italy 10 78 1987 Observed Daws et al (1997)* Italy Inited States 72 1988 Observed Daws et al (1997)* Finand 73 2990 Observed 73 Magnani et al (2006)* France 71 1982 Observed Daws et al (2006)* France 51 1992 Observed Dama et al (2005)* France 51 1992 Observed Dama et al (2005)* France 51 1992 Observed Lannering et al (2005)* France 51 1992 Observed Lannering et al (2005)* France 1992 O	Kramarova et al (1996)	Slovakia		_ I	22	1980	Observed	0-14
Dama et al (2005) ¹⁶ , Laly Agerilin et al (1997) ²⁰ , Laly Magnani et al (2005) ¹⁶ , Canada Davis et al (1998) ¹⁷ , Laly Kramarova et al (1996) ¹⁹ , Canada Davis et al (1997) ²⁰ , Laly Magnani et al (2005) ¹⁶ , Laly Switzerland Davis et al (1997) ²⁰ , Laly Kastsch et al (2001) ²⁰ , France Desandes et al (2003) ²⁰ , France Desandes et al (2003) ²⁰ , France Davis et al (2003) ²⁰ , France Davis et al (2003) ²⁰ , France Desandes et al (2003) ²⁰ , England Cannering et al (2003) ²⁰ , France Tulla et al (2005) ²⁰ , France Berger et al (2003) ²⁰ , France Cannering et al (2003) ²⁰ , France Carmany Cannering et al (2003) ²⁰ , France Carmany Cannering et al (2003) ²⁰ , France Carmany Carmany Carmany Carmany Cannering et al (2003) ²⁰ , France Carmany Cannering et al (2003) ²⁰ , France Carmany	Tseng et al (2006)	England and Wales		- A , I	41	1981	Observed	0-14
Agerin et al (1999) Davis et al (1996) ¹⁷ Kramarova et al (1996) ¹⁹ Slovakia Roldan et al (2005) ¹⁹ Laly Magnani et al (2005) ¹⁹ Laly Canada Dame et al (2005) ¹⁹ Laly Canada Dame et al (2005) ¹⁹ Laly Canada Dame et al (2005) ¹⁹ Laly Liskowitzerland Dovis et al (1997) ¹⁰ Switzerland Cermany	Dama et al (2005)	Italy			46	1982	Observed	0-14
Davis et al (1996) Magnanie et al (2006) ¹⁰ Canada Sovakia Canada Sovakia Canada Sovakia Canada Sovakia Canada Sovakia Canada Sovakia Canada Sovakia Canada Sovakia Canada Sovakia Canada Sovakia Canada Sovakia Canada Soverved Sovakia Canada Soverved Soverved Sovakia Canada Soverved	Agerlin et al (1999)	Denmark		A !	36	1982	Observed	0-14
Magnetic et al (200) ¹⁶ Early Kramarova et al (200) ¹⁷ Silvakia Dara et al (200) ¹⁶ Early Magnani et al (200) ¹⁷ Italy Magnani et al (200) ¹⁷ Switzerland Davis et al (1998) ¹⁷ United States Ilveskoski et al (2005) ¹⁷ Finland Berger et al (2005) ¹⁷ France Dara et al (2005) ¹⁷ France Dara et al (2005) ¹⁷ France Deserved 49 1990 Deserved 51 1992 Deserved 52 1992 Deserved 51 1992 Deserved 52 1992 Deserved 53 1996 Deserved 55 1995 Deserved 50 1997 Deserved	Magnani et al (1996)	United States			56	1903	Observed	0-20
Roldan et al (2009) ⁴ Roldan et al (2009) ⁴ Laly Schindler et al (2017) ⁴ Schindler et al (2017) ⁴ Schindler et al (2017) ⁴ United States Desandes et al (2009) ⁴ France Desandes et al (2009) ⁴ France Fran	Kramarova et al (1997)	Slovakia	A		26	1904	Observed	0-14
Dama et al (2005) ⁶⁰ Magnani et al (1997) ²⁰ traly Magnani et al (1997) ²⁰ Lance tal (2007) ²⁰ Katsch et al (2007) ²⁰ France Dama et al (2005) ²⁰ France Chan et al (2005) ²⁰ France	Boldan et al (2008) ³⁴	Canada			56	1986	Observed	0-14
Magnani et al (1997) ¹⁰ Italy 55 1988 Observed Schindler et al (1993) ¹⁰ United States 1 72 1988 Observed Juss et al (1993) ¹⁰ United States 1 72 1988 Observed Kastsch et al (2001) ¹⁰ Germany 53 1990 Observed Berger et al (2006) ¹⁰ France 43 1990 Observed Desandes et al (2003) ¹⁰ England 52 1992 Observed Alston et al (2005) ¹⁰ Italy 63 1993 Observed Camering et al (2006) ¹⁰ England 55 1992 Observed Camering et al (2005) ¹⁰ England 55 1992 Observed Dama et al (2005) ¹⁰ England 56 1995 Observed Para et al (2006) ¹⁰ England 56 1995 Observed Dama et al (2005) ¹⁰ England 56 1995 Observed Bellit et al (2005) ¹⁰ England 57 1997 Observed Dama et al (2005) ¹⁰ Italy France 56 1997	Dama et al (2005) ³⁰	Italy			78	1987	Observed	0-14
Schindler et al (2017) ³⁶ Davis et al (1999) ³⁷ Liveskoski et al (1999) ³⁷ Linked States Hinland Germany Desandes et al (2008) ³⁶ France Haly Alston et al (2008) ³⁷ Linked States Haly Alston et al (2009) ⁴⁷ England Germany Lannering et al (2009) ⁴⁶ Berger et al (2009) ⁴⁷ France Haly Alston et al (2009) ⁴⁷ England Germany Lannering et al (2009) ⁴⁷ France Haly Lannering et al (2009) ⁴⁷ Berger et al (2009) ⁴⁷ France Haly Lannering et al (2009) ⁴⁷ Berger et al (2009) ⁴⁷ France Haly Lannering et al (2009) ⁴⁷ France Haly Lannering et al (2009) ⁴⁷ France Haly Lannering et al (2009) ⁴⁷ France Haly Haly Lannering et al (2009) ⁴⁷ France Haly Haly Lannering et al (2009) ⁴⁷ France Haly Haly Lannering et al (2009) ⁴⁷ France Haly Haly Haly Lannering et al (2009) ⁴⁷ France Haly Haly Haly Haly Haly Haly Haly Lannering et al (2009) ⁴⁷ France Haly France Haly Ha	Magnani et al (1997) ³²	Italy		i – 🗖 🔺	85	1988	Observed	0-14
Davis et al (1999) ¹¹ Ilveskoski et al (1997) ¹⁴ Kaatsch et al (2001) ¹⁷ Berger et al (2006) ¹⁰ Trance Alston et al (2005) ¹⁰ France Desandes et al (2006) ¹⁰ France Alston et al (2005) ¹⁰ Tulla et al (2005) ¹⁰ France Alston et al (2005) ¹⁰ France Tulla et al (2005) ¹⁰ France Alston et al (2005) ¹⁰ France France Alston et al (2005) ¹⁰ France Cermany France Alston et al (2005) ¹⁰ France France Alston et al (2005) ¹⁰ France France Alston et al (2005) ¹⁰ France France Cermany France Alston et al (2005) ¹⁰ France France Alston et al (2005) ¹⁰ France France Cermany France France Alston et al (2005) ¹⁰ France France France Alston et al (2005) ¹⁰ France France France Alston et al (2005) ¹⁰ France France France France Alston et al (2005) ¹⁰ France Fr	Schindler et al (2017) ³⁵	Switzerland			50	1989	Observed	0-14
Ilveskoski et al (1997) ⁴⁸ Finland 43 1990 Observed Kaatsch et al (2001) ³⁰ Germany 53 1990 Observed Desandes et al (2003) ³⁰ France 51 1990 Observed Dama et al (2003) ³⁰ England 52 1992 Observed Alston et al (2006) ³⁰ England 52 1992 Observed Lannering et al (2006) ³⁰ Sweden 63 1995 Observed Paral et al (2006) ³⁰ Germany 1 64 1997 Observed Berger et al (2006) ³⁰ Germany 1 64 1997 Observed Dama et al (2006) ³⁰ France 1 64 1997 Observed Dama et al (2006) ³⁰ Italy 1 61 1997 Observed Dama et al (2006) ³⁰ Italy 1 59 1997 Observed Belli et al (10x17) ⁴⁰ Italy 1 61 1997 Observed Mathew et al (2017) ⁴⁰ United Kingdom 63 1990 Observed 63 Mathew et al (2015) ⁴⁰ <t< td=""><td>Davis et al (1998)³¹</td><td>United States</td><td></td><td>T 🔺</td><td>72</td><td>1989</td><td>Observed</td><td>0-20</td></t<>	Davis et al (1998) ³¹	United States		T 🔺	72	1989	Observed	0-20
Kaatsch et al (2001) ³⁶ Germany 53 1990 Observed Berger et al (2008) ³⁷ France 49 1990 Observed Dama et al (2003) ³⁷ England 52 1992 Observed Alston et al (2001) ³⁷ England 52 1992 Observed Tulla et al (2005) ³⁷ Germany 63 1992 Observed Lannering et al (2009) ⁴⁰ Germany 63 1995 Observed Berger et al (2006) ³⁷ France 63 1995 Observed Berger et al (2006) ³⁷ France 64 1997 Observed Desandes et al (2006) ³⁷ France 61 1997 Observed Desandes et al (2006) ³⁷ France 61 1997 Observed Bellit et al (2017) ⁶¹ Singapore 61 1997 Observed Schindler et al (2017) ⁶¹ Singapore 51 2001 Observed Germany Germany 63 1992 Observed Mathew et al (2017) ⁶¹ Singapore 51 2001 Observed Fairley et al (2016)	llveskoski et al (1997) ⁴⁸	Finland	-		43	1990	Observed	0-2
Berger et al (2006) ³⁷ Tulla et al (2005) ³⁷ Tulla et al (2005) ³⁷ Tulla et al (2005) ³⁷ Tulla et al (2005) ³⁷ France France Fairley et al (2006) ³⁷ Tulla et al (2017) ⁴⁶ Smoll et al (2017) ⁴⁶ Smoll et al (2017) ⁴⁶ Smoll et al (2017) ⁴⁶ Smoll et al (2017) ⁴⁶ France Fra	Kaatsch et al (2001) ³⁶	Germany			53	1990	Observed	0-14
Desindes et al (2006) ³⁰ France 51 1992 Observed Dama et al (2005) ³⁰ Italy 56 1992 Observed Tulla et al (2015) ³⁰ Germany 52 1992 Observed Lannering et al (2006) ³⁰ Sweden 63 1993 Observed Fairley et al (2016) ³¹ England 55 1995 Observed Berger et al (2006) ³² France 46 1997 Observed Desandes et al (2006) ³¹ France 59 1997 Observed Desandes et al (2006) ³² France 149 59 1997 Observed Desandes et al (2007) ³³ Switzerland 58 1997 Observed Mathew et al (UK + US, 2014) ⁴² United Kingdom 68 1997 Observed Mathew et al (2017) ⁴⁵ Singapore 51 2001 Observed France United States 71 2001 Observed Smoll et al (2010) ⁴⁴ Instel States 71 2001 Observed Smoll et al (2012) ⁴⁵ United States 72 2004 Relative	Berger et al (2006) ³⁷	France		<u>_</u>	49	1990	Observed	0-14
Dama et al (2005) ³⁰ Alston et al (2009) ⁵⁰ Tulla et al (2009) ⁵⁰ Sweden Fairley et al (2006) ⁵⁰ Berger at al (2008) ³⁰ Shindler et al (2017) ⁵⁰ Mathew et al (UK + US, 2014) ⁴² Tulla et al (2017) ⁵⁰ Served Ben Arush et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2016) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2016) ⁵⁰ Trama et al (2016) ⁵⁰ Trama et al (2016) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2016) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Smoll et al (2017) ⁵⁰ Trama et al (2017) ⁵⁰ Smoll et al (2017)	Desandes et al (2008) ³⁸	France		<u>_</u>	51	1992	Observed	0-14
Alston et al (2005) ³⁷ England Lannering et al (2015) ³⁹ Germany Hair et al (2015) ³⁹ Germany Bergler et al (2015) ³⁹ France Desandes et al (2005) ³⁰ Italy Desandes et al (2008) ³⁰ France Hair et al (2015) ³⁰ France Berli et al (2015) ³⁰ France Chan et al (2017) ³⁰ Switzerland Mathew et al (UK + US, 2014) ⁴² United Kingdom Mathew et al (UK + US, 2014) ⁴² United Kingdom Mathew et al (UK + US, 2014) ⁴² United Kingdom Mathew et al (UK + US, 2014) ⁴² United States Smoll et al (2017) ⁴⁵ Singapore Bengland Smoll et al (2017) ⁴⁵ Singapore Bengland Smoll et al (2017) ⁴⁵ United States Desandes et al (2017) ⁴⁵ Conserved Mathew et al (UK + US, 2014) ⁴² United States Desandes et al (2017) ⁴⁵ Singapore Bendle al (2017) ⁴⁵ Conserved Smoll et al (2017) ⁴⁵ Conserved Smoll et al (2017) ⁴⁵ Conserved Mathew et al (UK + US, 2014) ⁴² United States Desandes et al (2017) ⁴⁵ Conserved Smoll et al (2017) ⁴⁵ Conserved Smoll et al (2017) ⁴⁵ Conserved Mathew et al (UK + US, 2014) ⁴² United States Desandes et al (2017) ⁴⁵ Conserved Smoll et al (2017) ⁴⁵ Conserved Mathew et al (UK + US, 2014) ⁴² United States Desandes et al (2017) ⁴⁵ Conserved Mathew et al (UK + US, 2014) ⁴² Conserved Smoll et al (2012) ⁴⁵ Conserved Mathew et al (UK + US, 2014) ⁴² Conserved Mathew et al (2017) ⁴⁵ Conserved Mathew et al (UK + US, 2014) ⁴² Conserved Smoll et al (2012) ⁴⁵ Conserved Mathew et al (UK + US, 2014) ⁴² Conserved Mathew et al (UK + US, 2014) ⁴² Conserved Mathew et al (UK + US, 2014) ⁴² Conserved Mathew et al (2017) ⁴⁵ Conserved Mathew et al (2017) ⁴⁵ Conserved Mathew et al (2017) ⁴⁶ Cons	Dama et al (2005) ³⁰	Italy		U. 📕 📥 👘	56	1992	Observed	0-14
Tulla et al (2015) ¹⁷ Germany 63 1993 Observed Lannering et al (2009) ⁴⁰ Sweden 63 1995 Observed Fairley et al (2015) ⁴¹ England 55 1995 Observed Berger et al (2008) ⁴⁰ France 46 1997 Observed Desandes et al (2008) ⁴⁰ France 46 1997 Observed Bellil et al (cot5) ⁴⁰ Italy 59 1997 Observed Bellil et al (cot5) ⁴⁰ Tunisia 27 1997 Observed Mathew et al (UK + US, 2014) ⁴² United Kingdom 66 1999 Observed Mathew et al (2015) ⁴³ United Kingdom Germany 65 2001 Observed Chan et al (2007) ⁴³ Singapore 51 2001 Observed Smoll et al (2012) ⁴⁵ United States 72 2004 Relative Smoll et al (2012) ⁴⁵ United States 72 2004 Relative Smoll et al (2012) ⁴⁵ United States 72 2004 Relative Smoll et al (2012) ⁴⁵ United States 69 2004	Alston et al (2003) ²⁷	England	-	<u> </u>	52	1992	Observed	0-15
Lannering et al (2009) ⁷⁷ Sweden Fairley et al (2016) ⁸¹ England Tulla et al (2015) ⁸⁹ Germany Berger et al (2006) ⁸¹ France Bellil et al (hospital-based, 2008) ³³ France Schindler et al (2017) ⁸¹ Mathew et al (UK + US, 2014) ⁶² United Kingdom Mathew et al (UK + US, 2014) ⁶² United Kingdom Mathew et al (UK + US, 2014) ⁶² United Kingdom Mathew et al (UK + US, 2014) ⁶² United Kingdom Mathew et al (UK + US, 2014) ⁶² United Kingdom Mathew et al (2017) ⁶¹ England France France Tulla et al (2017) ⁶¹ England Bendler et al (2017) ⁶² United States Trama et al (EUROCARE-5, 2017) ⁶¹ Europe Berandes et al (2016) ⁶¹ France Tulla et al (2017) ⁶⁴ United States Trama et al (2017) ⁶⁴ United States Trama et al (2017) ⁶⁴ United States Trama et al (2017) ⁶⁴ United States Tulla et al (2017) ⁶⁴ United States Trama et al (2017)	Tulla et al (2015) ³⁷	Germany		· · · · · · · · · · · · · · · · · · ·	63	1993	Observed	0-14
Fairley et al (2015) ³⁰ England 55 1995 Observed Berger et al (2006) ³⁷ France 46 1997 Observed Desandes et al (2008) ³⁰ Italy France 61 1997 Observed Bellit et al (hospital-based, 2008) ³¹ Tunisia 58 59 1997 Observed Schindler et al (2017) ³⁶ Switzerland 68 1997 Observed Mathew et al (UK + US, 2014) ⁴² United Kingdom 68 1999 Observed Mathew et al (2015) ⁴⁶ Germany Germany 68 1999 Observed Pairley et al (2016) ⁴¹ Singapore Fairley et al (2016) ⁴¹ Israel 68 2000 Observed Smoll et al (2012) ⁴⁴ United States United States 72 2004 Relative Smoll et al (2012) ⁴⁵ United States United States 72 2004 Relative Desandes et al (2016) ⁴¹ Israel Germany 63 2004 Relative Smoll et al (2012) ⁴⁵ United States France 72 2004 Relative Desandes et a	Lannering et al (2009)	Sweden			63	1995	Observed	0-14
Luna et al (2015) ³⁰ Germany Germany 64 1997 Observed Dema et al (2006) ³⁰ Italy 59 1997 Observed Dema et al (2006) ³⁰ Tunisia 59 1997 Observed Belili et al (hospital-based, 2008) ³⁰ Tunisia 27 1997 Observed Mathew et al (UK, + US, 2014) ⁴² United Kingdom 0hited States 66 1997 Observed Mathew et al (UK, + US, 2014) ⁴² United States 0hited States 71 2001 Observed Germany Germany Germany 63 2002 Observed Smoll et al (2015) ⁴³ Germany Germany 63 2002 Observed Smoll et al (2012) ⁴⁵ United States 72 2004 Relative Smoll et al (2015) ⁴⁵ United States 72 2004 Relative Gatta et al (EUROCARE-5, 2017) ¹⁰ Europe Germany 63 2004 Observed Junited States Germany France 69 2004 Relative Desandes et al (2017) ⁴⁶ United States 65 2004	Fairley et al (2016)	England			55	1995	Observed	0-24
berger et al (2005) ¹⁰ Dama et al (2005) ¹⁰ Belili et al (hospital-based, 2008) ¹³ Schindler et al (2017) ¹⁶ Mathew et al (UK + US, 2014) ²⁰ United Kingdom Mathew et al (UK + US, 2014) ²⁰ United Kingdom Mathew et al (UK + US, 2014) ²⁰ United Kingdom Chan et al (2017) ⁴¹ Singapore Bendrat et al (2017) ⁴¹ Singapore Bendrat et al (2012) ⁴⁵ Trama et al (2012) ⁴⁵ Trama et al (2012) ⁴⁵ Desarved States Desardes et al (2016) ⁴¹ France Tulla et al (2017) ⁴¹ Singapore Bendrat et al (2012) ⁴⁵ Trama et al (2012) ⁴⁵ Desarved States Desardes et al (2016) ⁴¹ Khanna et al (2017) ⁴⁶ Khanna et al (2017) ⁴⁶ States Khanna et al (2017) ⁴⁶ States	i ulla et al (2015) Person et al (2000) ³⁷	Germany			64	1997	Observed	U-14
Desandes et al (2009) ³⁸ Belailie et al (2019) ⁴⁰ Schindler et al (2017) ⁴⁰ Mathew et al (UK + US, 2014) ⁴² Mathew et al (UK + US, 2014) ⁴² United States Singapore Ben Arush et al (2017) ⁴³ Smoll et al (2017) ⁴⁴ Smoll et al (2012) ⁴⁵ Smoll et al (2012) ⁴⁵ Trama et al (EUROCARE-5, 2016) ⁴⁷ Smoll et al (2012) ⁴⁶ Desandes et al (2016) ⁴¹ Trama et al (EUROCARE-5, 2016) ⁴⁷ Smoll et al (2012) ⁴⁵ Trama et al (2016) ⁴⁴ Trama et al (2016) ⁴⁴ Smoll et al (2012) ⁴⁵ Trama et al (2016) ⁴⁴ Trama et al (2016) ⁴⁴ Smoll et al (2012) ⁴⁵ Trama et al (2016) ⁴⁵ Trama et al (2016) ⁴⁶ Smoll et al (2012) ⁴⁵ Trama et al (2016) ⁴⁷ Smoll et al (2017) ⁴⁶ United States Desandes et al (2016) ⁴⁷ France France France Smoll et al (2017) ⁴⁶ United States United States Smoll et al (2017) ⁴⁶ United States Smoll et al (2017) ⁴⁶ United States Smoll et al (2017) ⁴⁶ United States Smoll et al (2017) ⁴⁶ Trama et al (2017) ⁴⁶ Smoll et al (2017) ⁴⁶ Trama et al (2017) ⁴⁶ States S	Dema et al (2005) ³⁰	FidilCe			46	1997	Observed	0-14
Belili et al (hospital-based, 2008) ¹³ Schindler et al (2017) ²⁶ Mathew et al (UK + US, 2014) ²⁰ United States Traina et al (2017) ²⁶ Switzerland Mathew et al (UK + US, 2014) ²⁰ United States United States Traina et al (2017) ⁴⁶ Smoll et al (2012) ⁴⁶ Traina et al (2012) ⁴⁶ United States Traina et al (2016) ⁴⁷ Smoll et al (2012) ⁴⁶ Traina et al (2016) ⁴⁷ Smoll et al (2016) ⁴⁷ Smoll et al (2017) ⁴⁶ Smoll et al (2017) ⁴⁶ Smoll et al (2017) ⁴⁶ Smoll et al (2017) ⁴⁶ Smoll et al (2016) ⁴⁷ Smoll et al (2017) ⁴⁶ Smoll et al (2017) ⁴⁶ Smoll et al (2016) ⁴⁷ Smoll et al (2016) ⁴⁷ States Smoll et al (2016) ⁴⁷ Traina et al (2016) ⁴⁷ States Smoll et al (2017) ⁴⁶ States Smoll et al (2017) ⁴⁶ States	Desandes et al (2009)	France		<u> </u>	09 61	1997	Observed	0-14
Schindler ei (2017) ⁴⁰ Mathew et al (2017) ⁴¹ Smoll et al (2017) ⁴⁵ Smoll et al (2012) ⁴⁵ Trama et al (2017) ⁴⁵ Smoll et al (2012) ⁴⁵ Trama et al (2017) ⁴⁵ Trama et al (2017) ⁴⁶ Trance Tran	Bellil et al (hospital-based 2009) ¹³	Tunisia		1	27	1997	Observed	0-14
Mathew et al (UK + US, 2014) ⁴² United States Mathew et al (UK + US, 2014) ⁴² United States Mathew et al (UK + US, 2014) ⁴² United States Tulla et al (2015) ⁴³ Singapore Fairley et al (2016) ⁴¹ England Ben Arush et al (2010) ⁴⁴ Inited States Smoll et al (2012) ⁴⁵ United States Smoll et al (2012) ⁴⁶ United States Trame at al (EUROCARE-5, 2016) ⁴⁷ Europe Smoll et al (2012) ⁴⁶ United States Trame at al (EUROCARE-5, 2017) ⁴⁰ Europe Smoll et al (2012) ⁴⁶ United States Trame at al (EUROCARE-5, 2017) ⁴⁰ Europe Smoll et al (2012) ⁴⁶ United States Desendes et al (2016) ⁴¹ England Smoll et al (2017) ⁴⁶ United States Desendes et al (2016) ⁴¹ England Lunited States France Fairley et al (2016) ⁴¹ England Khanna et al (2017) ⁴⁶ United States Khanna et al (201	Schindler et al (2017) ³⁵	Switzerland		! _	68	1999	Observed	0-14
Mathew et al (UK + US, 2014) ⁴² United States 71 2001 Observed Chan et al (2007) ⁴³ Singapore 80 2001 Observed Fairley et al (2016) ⁴¹ England 63 2002 Observed Ben Arush et al (2010) ⁴⁴ Israel 63 2002 Observed Smoll et al (2012) ⁴⁵ United States 42 2004 Relative Gatta et al (EUROCARE-5, 2016) ⁴⁷ Europe Europe 63 2004 Relative Desandes et al (2015) ⁴⁸ United States	Mathew et al (UK + US. 2014)42	United Kingdom			65	2001	Observed	0-14
Tulla et al (2015) ³⁶ Germany 80 2001 Observed Chan et al (2017) ⁴⁶ Singapore 51 2001 Observed Fairley et al (2012) ⁴⁶ United States 42 2004 Relative Smoll et al (2012) ⁴⁶ United States 72 2004 Relative Gatta et al (2016) ⁴⁷ Europe Europe 63 2004 Relative Desandes et al (2016) ⁴⁷ Europe Europe 65 2004 Relative Desandes et al (2016) ⁴⁷ Europe Europe 65 2004 Relative Desandes et al (2016) ⁴⁷ Germany France 50 2005 Observed 0 Fairley et al (2016) ⁴⁷ England England 62 2007 Relative 0 0 0 Fairley et al (2017) ⁴⁶ United States 71 2007 Observed 0 0 0 0 Khanna et al (2017) ⁴⁶ United States 75 2007 Relative 80 2007 Relative Khanna et al (2017) ⁴⁶ United States 77 2007	Mathew et al (UK + US, 2014) ⁴²	United States		!	71	2001	Observed	0-14
Chan et al (2007) ⁶³ Singapore Fairley et al (2016) ⁶⁴ Israel Ben Arush et al (2010) ⁶⁴ United States Smoll et al (2012) ⁶⁵ United States Trama et al (EUROCARE-5, 2016) ⁷⁷ Europe Gatta et al (EUROCARE-5, 2016) ⁷⁰ Europe Smoll et al (2012) ⁶⁵ United States Desandes et al (2016) ⁶⁶ France Europe Benders et al (2016) ⁶⁶ France Stand et al (2016) ⁶⁶ Erope Khanna et al (2017) ⁶⁶ United States Chana et al (2017) ⁶⁶ Chana et al (2017) ⁶⁶ Chan	Tulla et al (2015) ³⁹	Germany		!	80	2001	Observed	0-14
Fairley et al (2010) ⁴⁴ England 63 2002 Observed Ben Arush et al (2010) ⁴⁴ Israel 63 2003 Observed Smoll et al (2010) ⁴⁴ United States 42 2004 Relative Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe 63 2004 Relative Gatta et al (EUROCARE-5, 2017) ⁴⁷ United States 69 2004 Relative Desandes et al (2016) ⁴⁸ Germany 65 2004 Relative Trama et al (2017) ⁴⁶ United States 69 2004 Relative Desandes et al (2016) ⁴⁸ Germany 77 2005 Observed Taile et al (2017) ⁴⁶ United States 62 2007 Relative Khanna et al (2017) ⁴⁶ United States 62 2007 Relative Khanna et al (2017) ⁴⁶ United States 62 2007 Relative Khanna et al (2017) ⁴⁶ United States 62 2007 Relative Khanna et al (2017) ⁴⁶ United States 75 2007 Relative Schindler et al (2017) ⁴⁶ United States 75	Chan et al (2007) ⁴³	Singapore		▲	51	2001	Observed	0-15
Ben Arush et al (2010) ⁴⁴ Israel Smoll et al (2012) ⁴⁵ United States Desandes et al (2012) ⁴⁶ United States Desandes et al (2012) ⁴⁶ Europe Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe United States Desandes et al (2015) ⁴⁷ France Tulla et al (2015) ⁴⁷ England Khanna et al (2017) ⁴⁶ United States Khanna et al (2017) ⁴⁶ United States Stagno et al (congradue) States Stagno et al (2017) ⁴⁶ United States Stagno et al (2017) ⁴⁶ United States Stagno et al (2017) ⁴⁶ United States Stagno et al (2017) ⁴⁶ States Stagno et al (2017) ⁴⁶ United States Stagno et al (2017) ⁴⁶ States Sta	Fairley et al (2016) ⁴¹	England			63	2002	Observed	0-14
Smoll et al (2012) ⁴⁵ Smoll et al (2012) ⁴⁵ Gatta et al (2012) ⁴⁵ United States Lurope	Ben Arush et al (2010) ⁴⁴	Israel		· · · · · · · · · · · · · · · · · · ·	69	2003	Observed	0-19
Smoll et al (2012) ⁷⁰ United States 72 2004 Relative Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe Europe 63 2004 Relative Gatta et al (EUROCARE-5, 2017) ⁴⁷ United States 69 2004 Relative Desandes et al (2015) ⁴⁸ Germany 77 2005 Observed 0 Tulla et al (2017) ⁴⁶ United States 77 2005 Observed 0 Khanna et al (2017) ⁴⁶ United States 48 2007 Relative Khanna et al (2017) ⁴⁶ United States 48 2007 Relative Khanna et al (2017) ⁴⁶ United States 48 2007 Relative Stagno et al (2017) ⁴⁶ United States 48 2007 Relative Schindler et al (2017) ⁴⁶ United States 48 2007 Relative Schindler et al (2017) ⁴⁶ United States 75 2007 Relative Schindler et al (2017) ⁴⁶ United States 73 2009 Observed Observed Germany 73 2009 Observed	Smoll et al (2012)	United States		<u></u>	42	2004	Relative	0-1
Trama et al (EUROCARE-5, 2016) ⁷⁰ Europe Smoll et al (2012) ⁴⁶ United States Tulla et al (2017) ⁴⁶ United States Khanna et al (2017) ⁴⁶ United States Khanna et al (2017) ⁴⁶ United States Khanna et al (2017) ⁴⁶ United States Schindler et al (2017) ⁴⁶ United States Schindler et al (2017) ⁴⁶ Switzerland Tulla et al (2017) ⁴⁶ Conserved Khanna et al (2017) ⁴⁶ Conserved States States Schindler et al (2017) ⁴⁶ Conserved Germany Conserved States Schindler et al (2017) ⁴⁶ Conserved Conserved Conserved Conserved States Stat	Smoll et al (2012) ⁴⁵	United States		i . — 📥 —	72	2004	Relative	1-9
Gatta et al (EUROCARE-5, 2017) Smoll et al (2012) ⁴⁶ United States Khanna et al (2017) ⁴⁶ Khanna et al (2017) ⁴⁶ Khanna et al (2017) ⁴⁶ Khanna et al (2017) ⁴⁶ Conserved	Trama et al (EUROCARE-5, 2016) ⁴⁷	Europe		i 📥	63	2004	Relative	0-14
Smoll et al (2012) United States Germany Fairley et al (2016) ⁴⁶ France 50 2005 Observed 0 Observed 1 (2016) ⁴⁷ England 41 (2017) ⁴⁶ United States 48 2007 Relative Atlana et al (2017) ⁴⁶ United States 48 2007 Relative Stagno et al (2016) ⁴⁶ United States 48 2007 Relative Stagno et al (2017) ⁴⁶ United States 48 2007 Relative Stagno et al (2017) ⁴⁶ United States 48 2007 Relative Stagno et al (2017) ⁴⁶ United States 48 2007 Relative Stagno et al (2017) ⁴⁶ United States 48 2007 Relative Stagno et al (2017) ⁴⁶ Switzerland 75 2007 Relative Stagno et al (2017) ⁴⁶ Switzerland 73 2009 Observed 73 2009 Observed 73 2009 Observed 74 2005 Observe	Gatta et al (EUROCARE-5, 2017) ¹⁰	Europe		i 📥 📩	65	2004	Observed	0-14
Uesandes et al (2015) ¹⁶ France 50 2005 Observed C Fairley et al (2015) ¹⁶ Germany England 77 2005 Observed C Khanna et al (2017) ⁴⁶ United States 48 2007 Relative Khanna et al (2017) ⁴⁶ United States 62 2007 Relative Khanna et al (2017) ⁴⁶ United States 62 2007 Relative Stagno et al (cospital-based, 2014) ⁴⁶ United States 80 2007 Relative Schindler et al (2017) ³⁶ Germany Germany 64 2009 Observed	Smoll et al (2012) ²⁵	United States		_	69	2004	Relative	10-19
I uila et al (2015) Germany Fairley et al (2016) ⁴⁶ England Khanna et al (2017) ⁴⁶ United States Khanna et al (2017) ⁴⁶ United States Khanna et al (2017) ⁴⁷ United States Khanna et al (2017) ⁴⁷ United States Khanna et al (2017) ⁴⁷ United States Stagno et al (hospital-based, 2014) ⁴⁷ Uganda Schindler et al (2017) ⁵⁸ Switzerland Tulla et al (2015) ³⁹ Germany	Desandes et al (2016)	France			- 50	2005	Observed	U-28 days
Fairley et al (2010) England 71 2007 Observed Khanna et al (2017) ⁴⁶ United States 48 2007 Relative Khanna et al (2017) ⁴⁶ United States 62 2007 Relative Khanna et al (2017) ⁴⁶ United States 75 2007 Relative Stagno et al (bspital-based, 2014) ¹⁶ United States 80 2007 Relative Schnidler et al (2017) ²⁶ Germany 64 2009 Observed	I ulla et al (2015) ²⁷	Germany		, <u> </u>	77	2005	Observed	0-14
Khana et al (2017) ⁴⁶ United States 48 2007 Relative Khana et al (2017) ⁴⁶ United States 62 2007 Relative Khana et al (2017) ⁴⁶ United States 75 2007 Relative Stagno et al (2017) ⁴⁶ United States 1 2007 Relative Stagno et al (2017) ⁴⁶ Switzerland 64 2009 Observed Tulla et al (2015) ⁵⁹ Germany 73 2009 Observed	Fairley et al (2016) Khappa et al (2017) ⁴⁶	England		<u> </u>	/1	2007	Upserved	0-24
Khanna et al (2017) ⁴⁶ United States 62 2007 Relative Khanna et al (2017) ⁴⁶ United States 75 2007 Relative Stagno et al (2017) ⁴⁶ United States 1 2007 Relative Stagno et al (2017) ⁴⁶ United States 1 2007 Relative Schindler et al (2017) ⁴⁶ Switzerland 64 2009 Observed Tulla et al (2015) ³⁹ Germany 73 2009 Observed	Kiidnna et al (2017) Khappa et al (2017) ⁴⁶	United States			48	2007	Relative	0-1
Khana et al (2017) ⁴⁶ United States Stagno et al (2017) ⁴⁶ United States Schindler et al (2017) ⁵⁶ Switzerland Tulla et al (2015) ⁵⁹ Germany A 2007 Relative States Tulla et al (2015) ⁵⁹ Germany	Khappa et al (2017)	United States			52	2007	Relative	1-4
Stagno et al (2017) ³⁶ Switzerland Tulla et al (2015) ³⁶ Germany 73 2009 Observed	Khanna et al (2017) ⁴⁶	United States			10	2007	Relative	5-9 10-14
Schindler al (2017) ⁵⁵ Switzerland Tulla et al (2015) ³⁹ Germany Germany	Stanno et al (2017)				8U 1	2007	Relative	0.14
Tulla et al (2015) ³⁹ Germany 1 - 73 2009 Observed	Schindler et al (2017) ³⁵	Switzerland		_	6/	2007	Observed	0-14
	Tulla et al (2015) ³⁹	Germany			73	2009	Observed	0-14
			,			_,,,,		
0 25 50 75		0	25	50 75				

FIG 2. Five-year survival (%) from embryonal tumors and medulloblastoma. Automated Childhood Cancer Information System (ACCIS) consortium: Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Italy, Netherlands, Slovakia, Slovenia, Spain, Switzerland, United Kingdom (UK), Norway. EUROpean CAncer REgistry based study on survival and care of cancer patients (EUROCARE)-3 consortium: Austria, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Italy, Malta, Netherlands, Norway, Poland, Scotland, (continued on following page)

study was 24 years. Studies using nonstandard age definitions were included here, because the study populations comprised mainly children.

Nineteen studies (40%) had regional population coverage, 10 (21%) were based on nationwide registries, eight (17%) were international studies based on both regional and national registries, and the information was not available in 10 studies. Only five studies were entirely or partially conducted in low-income or middle-income countries.¹³⁻¹⁶ The calendar period for incident cases ranged from 1954 to 2014 (Table 1). The eligible studies collectively provided 228 survival estimates.

For patients diagnosed with embryonal tumors as a broad histology group, 5-year survival increased substantially during the 30 years between 1980 and 2009, from 37% in 1980 to approximately 60% in 2009.^{14,17-26} In most countries, the survival probability was 50% or lower until 1997.¹⁷⁻²⁶ Despite this positive trend, there were remarkable geographic disparities. Around 2000, there was a 26% gap in 5-year survival between the Southern and Eastern Europe (SEE) consortium, including middle-income countries such as Belarus, Bulgaria, and Ukraine (40%),¹⁴ and the EUROCARE-5 consortium, which includes all of the most affluent European countries (66%; Fig 2).²³

Five-year survival from medulloblastoma increased from 29% to 73% during the 50 years between 1959 and 2009.²⁷⁻⁴⁶ In Denmark, Italy, and Slovakia, survival was 10% or less until 1972. In Denmark and Italy, survival increased sharply during the following decade (approximately 40% in 1982), while survival in Slovakia was still 26% in 1985.²⁸⁻³⁰ In most of the European countries, the survival probability was 60% or more after 1992^{10,27,35,38-42,47}; in the United States, similar or higher values were observed in 1977.³¹ Five-year survival from medulloblastoma in Tunisia was less than 27% in 1997, and it was zero in Uganda in 2007 (n = 14 patients).^{13,16} Survival in children younger than age 2 years was 50% or lower and did not change over time (Fig 2).^{45,46,48,49}

Five-year survival from primitive neuroectodermal tumors (PNETs) fluctuated in the range of 27%-52% in most European countries (1973-2009) without a monotonic trend.^{10,35,36,38-42,45,50-52} In two studies conducted in England and France, survival values were not in line with those observed in other European countries, but CIs were

wide.^{39,50} In the United States, 5-year survival ranged between 47% and 81% during 1977-2009.^{42,45,51,52} These values were higher than those observed in Europe during the four decades between 1973 and 2009 (24%-47%). Five-year survival from PNET in infants (age 1 year or younger) varied between zero and 33% (1990-2004), but data were scant and inconsistent (Fig 3).^{45,49,53}

For children diagnosed with atypical teratoid/rhabdoid tumor, a rare subtype of embryonal tumor, 5-year survival in Germany increased from 21% to 42% during 2001-2009, but Cls overlapped.³⁹ In the United States⁵⁴ and the EUROCARE-5 consortium,¹⁰ the survival probability during 2004-2008 was 30% or less (Fig 3).

Astrocytoma as a broad histology group was the most commonly adopted definition. Five-year survival was 71% or lower during 1970-1980.^{29,30,32,50,51} and it increased slightly over three decades, from 78% in 1982 to 89% in 2009.^{14,17,19,20,22-25,29-32,35,37,47,50,51,55} During 1982-1996, when the ICD-O-2 was in force,⁵⁶ 5-year survival for astrocytoma ranged between 72% and 82% in most countries.^{19,21,30-32,35,38,50,51} In the EUROCARE-4 study²³ (which used the ICD-O-3¹²), 5-year survival for astrocytoma (1995-2002) in Central Europe, Northern Europe, Southern Europe, the United Kingdom, and Ireland was also approximately 75% when all behaviors were considered, but it decreased by 10% when nonmalignant tumors were excluded. In Eastern Europe, the survival probability was approximately 65% regardless of tumor behavior.²³ Similarly, in the EUROCARE-5 study, 5-year survival for malignant astrocytoma was in the range of 60%-65% during 2000-2007.⁴⁷ Five-year survival from astrocytoma in India was 39% in 1996, whereas survival in the SEE consortium was similar to that of other European regions (Fig 4).^{14,15}

Five-year survival for low-grade astrocytoma (WHO grades I and II combined) was 80% or more in Europe, the United States, and Israel,^{25,36,40,44} but it was slightly less than 80% in Tunisia.¹³ For patients diagnosed with pilocytic astrocytoma during 1981-1991, 5-year survival was in the range of 88%-91% in England, Wales, the United States, and Southeastern Europe. During 1995-2004, 5-year survival from pilocytic astrocytoma increased to 95% or more in the United States, Israel, and the EUROCARE-5 consortium,^{10,42,44,52,57} but it remained unchanged in Southeastern Europe.⁵⁷ Five-year

FIG 2. (Continued). Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales. EUROCARE-4 (continued on following page)consortium: Austria, Belgium, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales. Southern and Eastern Europe (SEE) consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine. AIRTUM (Associazione Italiana Registri Tumori). EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales. The CI is not displayed when the study did not provide it.

HISTOLOGY AND FIRST AUTHOR	LOCATION	FIVE-YEAR SURVIVAL (%) AND 95% CI	CENTRAL % YEAR	OUTCOME	AGE RANGE (years)
Primitive neuroectodermal tumor					
Basta et al (2011) ⁵⁰	England	<u>_</u> 2	4 1973	Observed	0-14
Linabery et al (2008) ⁵¹	United States		7 1977	Observed	0-14
Basta et al (2011) ⁵⁰	England		5 1983	Observed	0-14
Linabery et al (2008) ⁵¹	United States		4 1987	Observed	0-14
Schindler et al (2017) ³⁵	Switzerland	<u>+</u>	3 1989	Observed	0-14
Bishop et al (2012) ⁵³	United States	A i s	5 1990	Observed	0-1
Kaatsch et al (2001) ³⁶	Germany		2 1990	Observed	0-14
Desandes et al (2008) ³⁸	France	<u>_</u> 2	9 1992	Observed	0-14
Tulla et al (2015) ³⁹	Germany	i 3	3 1993	Observed	0-14
Basta et al (2011) ⁵⁰	England		3 1993	Observed	0-14
Lannering et al (2009) ⁴⁰	Sweden	<u></u>	7 1995	Observed	0-14
Fairley et al (2016) ⁴¹	England		6 1995	Observed	0-24
Tulla et al (2015) ³⁹	Germany		5 1997	Observed	0-14
Desandes et al (2008) ³⁸	France	3	0 1997	Observed	0-14
Linabery et al (2008) ⁵¹	United States	! 6	5 1997	Observed	0-14
Schindler et al (2017) ³⁵	Switzerland		7 1999	Observed	0-14
Flores et al (2013) ⁵²	United States	ء 🔺	1 1999	Observed	0-19
Mathew et al (UK + US, 2014) ⁴²	United States	ά 🔺 ε	7 2001	Observed	0-14
Mathew et al (UK + US, 2014) ⁴²	United Kingdom	▲ 3	2 2001	Observed	0-14
Tulla et al (2015) ³⁹	Germany	i 3	5 2001	Observed	0-14
Basta et al (2011) ⁵⁰	England	e	3 2002	Observed	0-14
Fairley et al (2016) ⁴¹	England	2	7 2002	Observed	0-14
Smoll et al (2012) ⁴⁵	United States	1	4 2004	Relative	0-1
Smoll et al (2012) ⁴⁵	United States	¦ <u> </u>	4 2004	Relative	1-9
Gatta et al (EUROCARE-5, 2017) ¹⁰	Europe	<u> </u>	1 2004	Observed	0-14
Smoll et al (2012) ⁴⁵	United States		7 2004	Relative	10-19
Desandes et al (2016) ⁴⁹	France	▲ i	1 2005	Observed	0-28 days
Tulla et al (2015) ³⁹	Germany		4 2005	Observed	0-14
Fairley et al (2016) ⁴¹	England	! 3	0 2007	Observed	0-24
Schindler et al (2017) ³⁵	Switzerland		0 2009	Observed	0-14
Tulla et al (2015) ³⁹	Germany	e	1 2009	Observed	0-14
Atypical teratoid/rhabdoid tumor					
Tulla et al (2015) ³⁹	Germany	<u>2</u>	1 2001	Observed	0-14
Gatta et al (EUROCARE-5, 2017) ¹⁰	Europe	2	3 2004	Observed	0-14
Desandes et al (2016) ⁴⁹	France	▲	1 2005	Observed	0-28 days
Tulla et al (2015) ³⁹	Germany		8 2005	Observed	0-14
Ostrom et al (2015) ⁵⁴	United States	2	8 2008	Relative	0-19
Tulla et al (2015) ³⁹	Germany		2 2009	Observed	0-14
		1 1 1 1 1 0 25 50 75			

FIG 3. The 5-year survival (%) from primitive neuroectodermal tumor and atypical teratoid/rhabdoid tumor. EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales. The CI is not displayed when the study did not provide it. UK, United Kingdom.

survival for diffuse astrocytoma was in the range of 60%-78% in Europe and Japan during 1981-2004 (Fig 5). 10,33,58

Five-year survival for high-grade astrocytoma (WHO grades III and IV combined) was 20%-30% in France, Germany, and Sweden (1990-2004).^{25,36,40} Five-year survival probability for anaplastic astrocytoma was 30% or lower in Europe,^{10,33,42} Japan,⁵⁸ South Korea, and the United States,^{42,55} but it was 55% in Israel.⁴⁴ Five-year survival for glioblastoma was in the range of 8%-20% in Europe,^{10,33} Israel,⁴⁴ Japan,⁵⁸ South Korea, and the United States^{31,42,55} (Fig 5). For both low-grade and high-grade astrocytomas, there was no improvement in the observed outcomes during the 25 years between 1981 and 2004.

Among 47 studies, only 11 (23%) specified the completeness of case ascertainment. One third (36%) did not provide details on data quality. Twenty-six studies (55%) specified at least the proportion of microscopically verified tumors, and seven of them only included patients with microscopically verified tumors (Appendix Table A3). Four of the eight international studies specified the proportion of histologically confirmed brain tumors, ^{10,14,42,57} whereas the others reported a proportion for all childhood tumors combined (Appendix Table A3).^{18,19,23,47} Seven studies (15%) did not specify the reference classification, and two did not clarify the version of the ICD-O or the International Classification of Childhood Cancer (ICCC) that was used

Attractyons thread group View of the second group View of the second group View of the second group Remarces et al (2001) ¹⁰ England View of the second group View of the second group Contract et al (2001) ¹⁰ Italy View of the second group View of the second group Lunabery et al (2005) ¹⁰ Italy View of the second group View of the second group Magnani et al (1997) ¹⁰ Italy View of the second group View of the second group Dawis et al (2005) ¹⁰ Italy View of the second group View of the second group Dawis et al (1997) ¹⁰ Italy View of the second group View of the second group View of the second group Remarces et al (1997) ¹⁰ Italy A 74 1982 Catt at al (EUROCARE 3, 2005) ¹⁰ Europe 74 1987 Linabery et al (2006) ¹¹ United States 74 1987 Linabery et al (2006) ¹¹ United States 74 1987 Dama et al (2006) ¹¹ United States 74 1982 Dama et al (2006) ¹¹ Europe 74 1982 Dama et al (2006) ¹¹ Europe 74 1	OUTCOME MEASURE	INCLUSION OF E NONMALIGNANT TUMORS	AGE RANGE (years)
Kramarova et al (1990) ²⁰ Slovakia 41 40 1972 Basta et al (2011) ²⁰ England 60 1933 Kramarova et al (1990) ²¹ Slovakia 71 1975 Linabery et al (2005) ²⁰ United States 68 1977 Linabery et al (2005) ²⁰ Italy 68 1980 Magnani et al (1997) ²¹ United States 72 1982 Basta et al (2011) ²⁰ England 72 1982 Basta et al (2011) ²⁰ England 72 1982 Gata at al (UBOCARE-3, 2005) ¹⁰ Europe 72 1984 Kramarova et al (1997) ²¹ Italy 74 1987 Dama et al (2005) ²⁰ Europe 73 1983 Gata at el (UBOCARE-3, 2005) ¹⁰ Europe 74 1987 Inabery et al (2005) ²⁰ Italy 74 1987 Dama et al (2005) ²⁰ Europe 73 1983 Schindler et al (2017) ²¹ State al (EUROCARE-3, 2006) ¹⁰ Europe 73 1983 Dama et al (2005) ²⁰ France 63 1992 1983 <			
Dama et al (2005) ¹⁶ Italy 41 1972 Basta et al (2005) ¹⁶ England 60 1973 Kramerova et al (2005) ¹⁷ Italy 68 1977 Magnani et al (2005) ¹⁷ Italy 68 1977 Magnani et al (1990) ¹⁷ Italy 68 1980 Dama et al (2005) ¹⁶ Italy 68 1980 Daris et al (1990) ¹⁷ Italy 72 1982 Davis et al (1990) ¹⁷ England 72 1982 Catta et al (CONCARE 3, 2005) ¹⁸ Europe 72 1984 Kramerova et al (1997) ²⁷ Italy 75 1984 Kramerova et al (2005) ⁶⁰ Italy 73 1987 Gatta et al (EUROCARE 3, 2005) ¹⁸ Europe 74 1987 Dama et al (2005) ¹⁰ Italy 73 1987 Schindler et al (2017) ¹⁸ Switcerland 74 1982 Dama et al (2005) ¹⁸ France 74 1982 Dama et al (2005) ¹⁸ France 74 1982	Observed	not specified	0-14
Basta et al (2011) ¹⁰ England 60 1973 Kramarova et al (2006) ¹⁰ United States 61 1977 Linabury et al (2006) ¹⁰ United States 63 1977 Dama et al (2006) ¹⁰ Italy 63 1980 Kramarova et al (1997) ²⁰ Stovakia 72 1982 Davis et al (1996) ¹¹ United States 72 1982 Basta et al (2011) ¹⁰ England 73 1984 Gatta et al (EUROCARE-3, 2006) ¹¹ Europe 74 1987 Casta et al (EUROCARE-3, 2006) ¹¹ United States 73 1987 Dama et al (2005) ¹² Italy 74 1987 Dama et al (2005) ¹⁷ France 73 1984 Descript et al (2006) ¹⁷ France 73 1993 Gatta et al (EUROCARE-3, 2006) ¹⁸ Italy 88 <	Observed	yes	0-14
Kramzova et al (1996) ^{an} Italy 71 1975 Linabery et al (2006) ^{an} Italy 66 1980 Magnani et al (1996) ^{an} Italy 78 1982 Davis et al (1998) ^{an} United States 78 1982 Davis et al (1998) ^{an} United States 78 1982 Davis et al (1997) ^{an} Italy 78 1982 Davis et al (1997) ^{an} Italy 78 1983 Magnani et al (1997) ^{an} Italy 78 1984 Kramzova et al (2005) ^{an} Europe 72 1984 Kramzova et al (1997) ^{an} Italy 73 1987 Junaber et al (2005) ^{an} Italy 74 1967 Linabery et al (2006) ^{an} Italy 74 1987 Schindler et al (2006) ^{an} France 71 1989 Derane et al (2006) ^{an} France 71 1982 Derane et al (2006) ^{an} France 71 1982 Derane et al (2006) ^{an} France 71 1982 Derane et al (2006) ^{an} France 73 1987	Observed	yes	0-14
Dama et al (2005) ¹⁰ Italy 68 1977 Magnani et al (1990) ¹⁰ Italy 65 1980 Kramsrova et al (1996) ¹⁰ Slovakia 56 1980 Davis et al (1996) ¹⁰ United States 72 1982 Davis et al (1996) ¹⁰ Linkey et al. (1997) ¹⁰ Italy 78 1983 Magnani et al (1997) ¹⁰ Italy 78 1983 Magnani et al (1996) ¹⁰ Lincope 72 1983 Magnani et al (1996) ¹⁰ Italy 75 1987 Catta et al (EUROCARE-3, 2005) ¹⁰ Europe 75 1987 Catta et al (EUROCARE-3, 2005) ¹⁰ United States 73 1987 Magnani et al (2005) ¹⁰ Italy 76 1988 Schindler et al (2007) ¹⁰ Italy 76 1988 Darma et al (2005) ¹⁰ Italy 77 1980 Desrades et al (2005) ¹⁰ France 73 1987 Darma et al (2005) ¹⁰ France 74 1982 Darma et al (2005) ¹⁰ France 74 1982 Darma et al (2005) ¹⁰ France 78 1983 Gatta et al (EUROCARE-3, 2005) ¹⁰ France 78 1983 Gatta et al (EUROCARE-4, 2005) ¹⁰ </td <td>Observed</td> <td>not specified</td> <td>0-14</td>	Observed	not specified	0-14
Linbary et al (2006)" Italy Kramorov at al (1990)" Stovkia 55 1980 Dama et al (2007)" Italy 78 1982 Dama et al (2007)" Italy 78 1983 Gata et al (2017)" England 79 1983 Gata et al (2017)" England 79 1983 Gata et al (2007)" England 79 1983 Gata et al (2007)" Italy 79 1984 Kramorov at al (1997)" Italy 79 1984 Gata et al (2007)" Italy 79 1984 Gata et al (2007)" Italy 79 1984 Gata et al (2007)" Italy 79 1987 Linbary et al (2008)" Italy 79 1987 Linbary et al (2008)" Italy 70 1987 Dama et al (2008)" Italy 70 1987 Dama et al (2008)" Italy 70 1987 Gata et al (2007)" Italy 70 1989 Berger et al (2006)" Italy 70 1989 Berger et al (2006)" France 73 1987 Dama et al (2006)" France 73 1989 Gata et al (2007)" France 73 1989 Desandes et al (2007)" France 73 1989 Gata et al (2007)" France 73 1989 Desandes et al (2007)" France 73 1989 Gata et al (2007)" France 74 1989 Gata et al (2007)" France 74 1989 Gata et al (2007)" France 74 1989 Gata et al (2007)" France 75 1987 Gata et al (2007)" France 76 1987 Gata et al (2007)" France 76 1987 Gata et al (2007)ACRE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe 78 1987 Gata et al (EUROCARE 4, 2009)" Central Europe	Observed	yes	0-14
Magnani et al (1990) ¹⁰ Ialy 65 1980 Daras et al (2005) ¹⁰ Ialy 78 1982 Davis et al (1990) ¹¹ United States 72 1982 Basta et al (2011) ¹⁰ England 75 1984 Karamcrova et al (1996) ¹¹ Ialy 76 1982 Gatta et al (EUROCARE-3, 2005) ¹⁰ Europe 76 1984 Karamcrova et al (1996) ¹¹ Inited States 73 1987 Linabery et al (2005) ¹⁰ Iurope 76 1987 Darna et al (2007) ¹⁰ Ialy 76 1988 Schindler et al (2017) ¹⁰ Switzerland 78 1980 Desandes et al (2006) ¹⁰ France 63 1980 Desandes et al (2006) ¹⁰ France 63 1980 Desandes et al (2006) ¹⁰ Ialy 88 1982 Desandes et al (2006) ¹⁰ Ialy 88 1982 Dark et al (2006) ¹¹ Raly 88 1982 Stort at al (EUROCARE-4, 2006) ¹² France 63 1983 Gatta et al (EUROCARE-4, 2006) ¹² Central Europe 78<	Observed	yes	0-14
Kramarova et al (1996)" Slovakia 5 1980 Davis et al (1998)" United States 72 1982 Basta et al (2011) ⁶⁰ England 79 1983 Magnani et al (1997) ⁷¹ Italy 75 1984 Kramarova et al (1996) ⁷¹ Slovakia 66 1985 Gatta et al (EUROCARE3, 2005) ⁷¹ Europe 72 1984 Kramarova et al (2005) ⁷² Italy 74 1987 Dama et al (2005) ⁷¹ United States 73 1987 Magnani et al (2007) ⁷¹ Italy 74 1987 Catta et al (EUROCARE3, 2005) ⁷¹ Europe 71 1980 Desandes et al (2007) ⁷¹ France 63 1983 Desandes et al (2007) ⁷¹ France 63 1983 Gatta et al (EUROCARE3, 2005) ⁷¹ France 74 1982 Dama et al (2007) ⁷¹ France 74 1982 Dama et al (2007) ⁷¹ Europe 74 1983 Gatta et al (EUROCARE3, 2005) ⁷¹ France 78 1983 Gatta et al (EUROCARE4, 2006) ⁷¹ Italy 7	Observed	no	0-14
Dams et al (2005) ^{III} United States 78 1982 Basta et al (2011) ^{IIII} England 72 1982 Gatta et al (EUROCARE3, 2005) ^{III} Europe 75 1984 Kramarova et al (2006) ^{III} United States 76 1987 Linabery et al (2006) ^{III} United States 76 1987 Linabery et al (2006) ^{III} United States 73 1987 Linabery et al (2006) ^{III} United States 73 1987 Magnani et al (1997) ^{III} United States 73 1987 Schindler et al (2006) ^{III} United States 73 1987 Dergor et al (2006) ^{III} France 74 1982 Desma et al (2006) ^{III} England 72 1983 Coll et al (2016) ^{III} England 73 1983 Dams et al (2006) ^{III} India 88 1982 Data et al (2006) ^{III} England 74 1982 Catta et al (EUROCARE4, 2006) ^{III} Katal (2006) ^{III} India 79 South Korea E	Observed	not specified	0-14
Davis et al (1996)" United States 72 1982 Basta et al (2011)"6 England 76 1984 Kramaroxa et al (1996)" Slovakia 66 1985 Gatta et al (EUROCARE-3, 2005)" Europe 72 1984 Kramaroxa et al (1996)" Slovakia 66 1985 Dama et al (2005)" United States 73 1987 Linabery et al (2006)" United States 73 1987 Magnani et al (1997)" Italy 76 1988 Schindler et al (2006)" United States 77 1980 Desandes et al (2007)" France 63 1990 Desande et al (2005)" France 63 1993 Colt et al (EUROCARE-3, 2005)" France 63 1993 Colt et al (2017)" Europe 74 1993 Colt et al (2016)" Italy 88 1992 Baste et al (2011)" England 72 1993 Colt et al (2006)" Krance 63 1993 Gatt et al (EUROCARE-4, 2009)" Central Europe 74 1992	Observed	yes	0-14
Basta et al (2011) ⁶ Magnani et al (1997) ⁷ Gatta et al (EUROCARE-3, 2005) ⁷ Europe Eur	Observed	no	0-20
Magnani et al (1997)" Italy 75 1994 Gatta et al (EUROCARE-3, 2005)" Europe 75 1994 Kramarova et al (1990)" Slovakia 56 1995 Gatta et al (EUROCARE-3, 2005)" Italy 71 1997 Linabery et al (2005)" Italy 71 1998 Schindler et al (2017)" Trance 71 1998 Gatta et al (2006)" France 71 1990 Desandes et al (2006)" France 73 1990 Desandes et al (2006)" France 74 1992 Dama et al (2006)" France 74 1992 Dama et al (2006)" France 74 1992 Dama et al (2006)" France 73 1993 Gatta et al (EUROCARE-3, 2005)" France 78 1993 Gatta et al (EUROCARE-3, 2006)" France 78 1993 Sowaninathan et al (2007)" Australia 79 1995 Swaminathan et al (2007)" Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009)" Central Europe 63 1997	Observed	yes	0-14
Gatt at al (EUROCARE-3, 2005) ¹⁰ Europe 72 1994 Kramarova et al (2005) ^{an} Europe 75 1967 Dama et al (2005) ^{an} Italy 76 1987 Linabery et al (2006) ^{an} United States 76 1987 Schindler et al (2007) ^{an} Switzerland 76 1988 Schindler et al (2007) ^{an} Europe 77 1990 Gatta et al (EUROCARE-3, 2005) ^{an} Europe 77 1990 Dema et al (2005) ^{an} France 63 1990 Dema et al (2005) ^{an} Europe 78 1983 Cell et al (2015) ^{an} France 78 1993 Gatta et al (2006) ^{an} France 78 1993 Gatta et al (2016) ^{an} South Korea 75 1994 Bada et al (2010) ^{an} Australia 79 1995 Swaminathan et al (2006) ^{an} France 78 1997 Gatta et al (EUROCARE-4, 2009) ^{an} Central Europe 68 1997 Gatta et al (EUROCARE-4, 2009) ^{an} Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ^{an}	Observed	no	0-14
Kramarova et al (1996)" Slovakia 56 1995 Gatta et al (EUROCARE-3, 2005)" Europe 74 1967 Linabery et al (2005)" United States 73 1997 Magnani et al (1997)" Italy 74 1967 Schindler et al (2017)"S Switzerland 22 1989 Gatta et al (EUROCARE-3, 2005)" Europe 74 1987 Derager et al (2006)" France 74 1982 Dama et al (2006)" England 72 1993 Coll et al (2015)" England 72 1993 Catta et al (EUROCARE-3, 2005)" Europe 78 1992 Basta et al (2006)" South Korea 63 1993 Badde et al (2010)" Australia 79 1995 Swaninathan et al (2008)" Ireland 79 1997 Gatta et al (EUROCARE-4, 2009)" Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009)" Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009)" Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009)" Cent	Observed	no	0-14
Gatta et al (EUROCARE-3, 2005) ¹⁰ Europe 76 1987 Dama et al (2005) ¹⁰ United States 73 1987 Linabery et al (2006) ¹⁰ United States 73 1987 Schindler et al (2017) ¹⁸ Switzerland 77 1989 Gatta et al (EUROCARE-3, 2005) ¹⁰ France 71 1990 Desandes et al (2006) ¹⁰ France 73 1997 Call et al (2006) ¹⁰ France 73 1993 Call et al (2006) ¹⁰ France 73 1993 Call et al (2016) ¹⁰ Europe 78 1993 Call et al (2016) ¹⁰ France 63 1993 Swaminathan et al (2006) ¹⁰ France 78 1993 Swaminathan et al (2006) ¹⁰ India 39 1996 Swaminathan et al (2006) ¹⁰ France 68 1997 Gatta et al (EUROCARE-4, 2009) ¹⁰ Central Europe 68 1997 Gatta et al (EUROCARE-4, 2009) ¹⁰ Central Europe 68 1997 Gatta et al (EUROCARE-4, 2009) ¹⁰ Central Europe 63 1997 Gatta et al (EUROC	Observed	not specified	0-14
Dame et al (2005) ¹⁰ Italy 74 1987 Linabery et al (2006) ¹¹ United States 76 1988 Schindler et al (2017) ¹⁶ Switzerland 82 1989 Gatta et al (EURCCARE-3, 2005) ¹⁰ Europe 74 1982 Desandes et al (2008) ¹⁰ France 74 1982 Desandes et al (2008) ¹⁰ France 74 1982 Dama et al (2005) ¹⁰ Europe 74 1982 Dama et al (2008) ¹⁰ England 72 1993 Coll et al (2010) ¹⁰ South Korea 33 1993 Back et al (2000) ¹⁰ India 39 1996 Berger et al (2006) ¹⁷ France 78 1993 Swaminathan et al (2001) ¹⁰ Australia 79 1995 Swaminathan et al (2001) ¹⁰ Australia 79 1997 Gatta et al (EUROCARE-4, 2009) ¹⁰ Central Europe 68 1997 Gatta et al (EUROCARE-4, 2009) ¹⁰ Central Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ¹⁰ Central Europe 65 1997 Gatta et al (EUROCARE-4, 200	Observed	no	0-14
Linabery et al (2009) ¹¹ United States 1 1 1 1 1 1 1 1 1 1	Observed	yes	0-14
Magnani et al (1997)Italy761988Schindler et al (2017)Switzerland761989Gatta et al (EUROCARE-3, 2005)Europe771990Desandes et al (2006)France731990Dama et al (2005)Europe741992Basta et al (2017)England721993Coll et al (2015)France781993Coll et al (2015)Europe781993Park et al (2006)France781993Park et al (2016)South Korea551994Badde et al (2011)Australia791995Swaminathan et al (2006)France821997Gatta et al (EUROCARE-4, 2009)Central Europe681997Gatta et al (EUROCARE-4, 2009)Central Europe681997Gatta et al (EUROCARE-4, 2009)Eastern Europe631997Gatta et al (EUROCARE-4, 2009)France681997Gatta et al (EUROCARE-4, 2009)Northern Europe651997Gatta et al (EUROCARE-4, 2009)Northern Europe651997Gatta et al (EUROCARE-4, 2009)Southern Europe651997Gatta et al (EUROCARE-4, 2009)UK and Ireland791997Gatta et al (EUROCARE-4, 2009)Southern Europe651997Gatta et al (EUROCARE-4, 2009)Southern Europe651997Gatta et al (EUROCARE-4, 2009)UK and Ireland791997Gatta et al (EUROCARE-4, 2009)UK and Irelan	Observed	yes	0-14
Schindler et al (2017) ²⁶ Switzerland 4 82 1989Gatta et al (EUROCARE-3, 2005) ¹⁷⁰ France 63 1990Desandes et al (2006) ²⁷⁰ France 63 1992Daras et al (2005) ²⁷⁰ Italy 63 1993Gatta et al (EUROCARE-3, 2005) ¹⁷⁰ France 63 1993Coll et al (2016) ²⁷⁰ France 63 1993Gatta et al (EUROCARE-3, 2005) ¹⁷⁰ Europe 78 1993Back et al (2010) ²⁷¹ Australia 79 1995Swaminathan et al (2008) ¹⁷⁰ India 39 1996Berger et al (2010) ²⁷¹ France 63 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ Central Europe 68 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ Central Europe 68 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ Eastern Europe 65 1997Desandes et al (2006) ²⁷⁰ France 63 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ Eastern Europe 65 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ Eastern Europe 65 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ Southern Europe 65 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ Southern Europe 65 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ Northern Europe 65 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ Southern Europe 65 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ South Korea 75 1997Gatta et al (EUROCARE-4, 2009) ²⁷⁰ <td>Observed</td> <td>no</td> <td>0-14</td>	Observed	no	0-14
Gatta et al (EUROCARE-3, 2005) ¹⁰ Europe 77 1990 Desandes et al (2006) ³⁷ France 74 1992 Dama et al (2005) ³⁰ Italy 88 1992 Basta et al (2011) ³⁰ England 72 1993 Coll et al (2015) ³⁰ France 63 1993 Gatta et al (EUROCARE-3, 2005) ³⁰ Europe 78 1993 Swaminathne et al (2016) ³⁷ South Korea 55 1994 Baade et al (2010) ¹⁷¹ Australia 39 1995 Berger et al (2006) ¹⁷⁰ Ireland 39 1996 Barger et al (2006) ¹⁷⁰ France 81 1997 Gatta et al (EUROCARE-4, 2009) ¹⁷⁰ Central Europe 81 1997 Gatta et al (EUROCARE-4, 2009) ¹⁷⁰ Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹⁷⁰ Eastern Europe 63 1997 Desandes et al (2006) ¹⁸⁰ Italy 79 1997 Gatta et al (EUROCARE-4, 2009) ¹⁷⁰ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹⁷⁰ Northern Europe 65 1997 <tr< td=""><td>Observed</td><td>not specified</td><td>0-14</td></tr<>	Observed	not specified	0-14
Berger et al (2006) ¹⁰ France 63 1990 Desandes et al (2006) ¹⁰ France 63 1992 Dans et al (2006) ¹⁰ England 72 1993 Coll et al (2015) ¹⁰ France 63 1992 Basta et al (EUROCARE-3, 2005) ¹⁰ Europe 78 1993 Park et al (2016) ¹⁰ South Korea 55 1994 Baade et al (2016) ¹¹ Australia 79 1995 Swaminathan et al (2006) ¹³ India 39 1996 Berger et al (2006) ¹³ France 81 1997 Gatta et al (EUROCARE-4, 2009) ¹²⁰ Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹²⁰ Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹²⁰ Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹²⁰ Karen Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹²⁰ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹²⁰ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹²⁰ Southern Europe 63 1997 </td <td>Observed</td> <td>no</td> <td>0-14</td>	Observed	no	0-14
Desandes et al (2006) ³⁰ France 74 1992 Dama et al (2005) ³⁰ Italy 88 1992 Basta et al (2011) ³⁰ England 78 1993 Coll et al (2015) ⁷³ France 63 1993 Gatta et al (2016) ⁷¹ Australia 79 1993 Swaminathan et al (2008) ¹³ India 39 1996 Berger et al (2011) ²² Ireland 39 1997 Gatta et al (EUROCARE-4, 2009) ²⁰ Central Europe 81 1997 Gatta et al (EUROCARE-4, 2009) ²⁰ Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²⁰ Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²⁰ Eastern Europe 63 1997 Deande et al (2006) ³⁰ Italy 79 1997 Gatta et al (EUROCARE-4, 2009) ²⁰ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²⁰ Northern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ²⁰ Northern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ²⁰ Southern Europe 65 1997 <td>Observed</td> <td>yes</td> <td>0-14</td>	Observed	yes	0-14
Dama et al (2005) ³⁰ Italy 88 1992 Basta et al (2011) ³⁰ England 72 1993 Gatta et al (2016) ³⁰ France 78 1993 Park et al (2016) ³¹ South Korea 55 1994 Basde et al (2010) ³¹ Australia 39 1995 Berger et al (2006) ³⁷ France 82 1997 Walsh et al (2011) ²² Ireland 39 1996 Gatta et al (EUROCARE-4, 2009) ³² Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³² Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³² Eastern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³² Eastern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³² Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³² Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³² Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ³² Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ³² Southern Europe 63	Observed	yes	0-14
Basta et al (2011) ¹⁰ England 72 1993 Coll et al (2015) ¹⁰ France 63 1993 Gatta et al (EUROCARE-3, 2005) ¹⁸ Europe 78 1993 Baade et al (2016) ¹⁷ South Korea 55 1994 Baade et al (2006) ¹⁷ India 39 1995 Swaminathan et al (2006) ¹⁷ France 78 1995 Gatta et al (EUROCARE-4, 2009) ¹² Central Europe 81 1997 Gatta et al (EUROCARE-4, 2009) ¹² Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹² Eastern Europe 63 1997 Desandes et al (2006) ⁶³ France 81 1997 Gatta et al (EUROCARE-4, 2009) ¹² Eastern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹² Northern Europe 83 1997 Gatta et al (EUROCARE-4, 2009) ¹² Northern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ¹² Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ¹² Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ¹² UK and Ireland	Observed	yes	0-14
Coll et al $(2015)^{70}$ France 63 1993 Gatta et al $(EUROCARE:3, 2005)^{18}$ Europe 78 1993 Park et al $(2016)^{17}$ South Korea 55 1994 Baade et al $(2010)^{11}$ Australia 39 1996 Berger et al $(2008)^{17}$ France 82 1997 Gatta et al $(EUROCARE:4, 2009)^{12}$ Central Europe 68 1997 Gatta et al $(EUROCARE:4, 2009)^{12}$ Central Europe 63 1997 Gatta et al $(EUROCARE:4, 2009)^{12}$ Central Europe 63 1997 Gatta et al $(EUROCARE:4, 2009)^{12}$ Central Europe 63 1997 Gatta et al $(EUROCARE:4, 2009)^{12}$ Eastern Europe 63 1997 Desandes et al $(2005)^{30}$ Italy 79 1997 Gatta et al $(EUROCARE:4, 2009)^{12}$ Northern Europe 63 1997 Gatta et al $(EUROCARE:4, 2009)^{12}$ Northern Europe 63 1997 Gatta et al $(EUROCARE:4, 2009)^{12}$ Northern Europe 63 1997 Gatta et al $(EUROCARE:4, 2009)^{12}$ Southern Europe 65 1997 Gatta et	Observed	yes	0-14
Gatta et al (EUROCARE-3, 2005) ¹⁹ Europe 78 1993 Park et al (2016) ¹⁷ South Korea 55 1994 Baade et al (2010) ¹¹ Australia 79 1995 Swaminathan et al (2008) ¹⁵ India 79 1997 Bata et al (2010) ²¹ France 82 1997 Gatta et al (EUROCARE-4, 2009) ²² Central Europe 81 1997 Gatta et al (EUROCARE-4, 2009) ²² Eastern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²² Eastern Europe 65 1997 Dama et al (2005) ²⁸ Italy 79 1997 Gatta et al (EUROCARE-4, 2009) ²² Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Southern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ²⁴ UK and Ireland 1997 1997 Linabery et al (2016) ¹⁷ South Korea	Observed	not specified	0-14
Park et al (2016)South Korea551994Baade et al (2001)Australia791995Swaminathan et al (2006)India391996Berger et al (2006)Ireland791997Gatta et al (EUROCARE-4, 2009)Central Europe811997Gatta et al (EUROCARE-4, 2009)Central Europe681997Gatta et al (EUROCARE-4, 2009)Eastern Europe681997Desandes et al (2006)Eastern Europe681997Gatta et al (EUROCARE-4, 2009)Eastern Europe681997Desandes et al (2006)Italy791997Gatta et al (EUROCARE-4, 2009)Eastern Europe631997Gatta et al (EUROCARE-4, 2009)Northern Europe631997Gatta et al (EUROCARE-4, 2009)Southern Europe651997Gatta et al (EUROCARE-4, 2009)Southern Europe651997Gatta et al (EUROCARE-4, 2009)Southern Europe651997Gatta et al (EUROCARE-4, 2009)UK and Ireland611997Inabery et al (2005)UK and Ireland611997Linabery et al (2005)UK and Ireland611999Schindler et al (2016)Europe632001Desandes et al (2017)South Korea642001Basta et al (2016)Europe641999Schindler et al (2017)South Korea652002Desandes et al (2011)France622004Desandes et al (2014) <t< td=""><td>Observed</td><td>no</td><td>0-14</td></t<>	Observed	no	0-14
Baade et al $(2010)^{21}$ Australia791995Swaminathan et al $(2006)^{37}$ India391996Berger et al $(2006)^{37}$ France821997Gatta et al $(EUROCARE-4, 2009)^{22}$ Central Europe811997Gatta et al $(EUROCARE-4, 2009)^{22}$ Central Europe631997Gatta et al $(EUROCARE-4, 2009)^{22}$ Eastern Europe631997Desandes et al $(2005)^{30}$ ItalyFrance811997Gatta et al $(EUROCARE-4, 2009)^{22}$ Eastern Europe631997Gatta et al $(EUROCARE-4, 2009)^{23}$ Northern Europe631997Gatta et al $(EUROCARE-4, 2009)^{22}$ Northern Europe631997Gatta et al $(EUROCARE-4, 2009)^{22}$ Northern Europe631997Gatta et al $(EUROCARE-4, 2009)^{22}$ Southern Europe651997Gatta et al $(EUROCARE-4, 2009)^{22}$ UK and Ireland611997Linabery et al $(2005)^{51}$ United States491998Ellison et al $(2007)^{54}$ Canada431999Schindler et al $(EUROCARE-4, 2009)^{22}$ UK and Ireland411997Linabery et al $(2015)^{54}$ Europe632001Desandes et al $(2014)^{22}$ France431999Schindler et al $(EUROCARE-4, 2009)^{22}$ Europe632001Desandes et al $(2014)^{26}$ France532001Desandes et al $(2014)^{26}$ France532003Desandes et al $(2014)^{27}$	Relative	not specified	0-14
Swaminathan et al (2008) ¹⁵ India 39 1996 Berger et al (2006) ¹⁷ France 82 1997 Gatta et al (EUROCARE-4, 2009) ¹² Central Europe 81 1997 Gatta et al (EUROCARE-4, 2009) ¹² Central Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹² Eastern Europe 63 1997 Dasandes et al (2008) ³⁰ France 63 1997 Gatta et al (EUROCARE-4, 2009) ¹² Eastern Europe 63 1997 Dasande et al (EUROCARE-4, 2009) ¹² Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹² Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹² Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ¹² Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ¹² Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ¹² Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ¹² Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ¹² United States 85 1997 Par	Relative	yes	0-14
Berger et al (2006) ³⁷ France 82 1997 Walsh et al (2011) ²² Ireland 79 1997 Gatta et al (EUROCARE-4, 2009) ³⁷ Central Europe 68 1997 Gatta et al (EUROCARE-4, 2009) ³⁷ Eastern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³⁸ Eastern Europe 63 1997 Desandes et al (2006) ³⁰ Italy 79 1997 Gatta et al (EUROCARE-4, 2009) ³⁷ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³⁷ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³⁷ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³⁷ Northern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ³⁷ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ³⁷ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ³⁷ UK and Ireland 79 1997 Linabery et al (2007) ³⁴ Canada 83 1999 Schindler et al (2017) ³⁵ Switzerland 61 1999 Gatta et al (EUROCARE-4, 2009) ³² <td>Observed</td> <td>not specified</td> <td>0-14</td>	Observed	not specified	0-14
Walsh et al $(2011)^{12}$ Ireland791997Gatta et al $(EUROCARE-4, 2009)^{12}$ Central Europe811997Gatta et al $(EUROCARE-4, 2009)^{12}$ Central Europe631997Gatta et al $(EUROCARE-4, 2009)^{12}$ Eastern Europe651997Desandes et al $(2005)^{30}$ Italy791997Gatta et al $(EUROCARE-4, 2009)^{12}$ Northern Europe631997Gatta et al $(EUROCARE-4, 2009)^{12}$ Southern Europe651997Gatta et al $(EUROCARE-4, 2009)^{12}$ UK and Ireland19971997Linabery et al $(2006)^{13}$ UK and Ireland791997Linabery et al $(2007)^{14}$ Canada831999Schindler et al $(EUROCARE-4, 2009)^{12}$ Witzerland611999Gatta et al $(EUROCARE-4, 2009)^{14}$ Urope611999Gatta et al $(2010)^{17}$ South Korea491999Gatta et al $(2010)^{16}$ Europe611999Gatta et al $(2010)^{16}$ France442001Desandes et al $(2011)^{26}$ France522002Walsh et al $(2011)^{26}$ France522004Desandes et al $(2011)^{26}$ France502004Coll et al $(2011)^{26}$ France5020	Observed	yes	0-14
Gatta et al (EUROCARE-4, 2009) ²³ Central Europe 81 1997 Gatta et al (EUROCARE-4, 2009) ²³ Central Europe 68 1997 Gatta et al (EUROCARE-4, 2009) ²³ Eastern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Eastern Europe 63 1997 Desandes et al (2005) ³⁰ Italy 79 1997 Gatta et al (EUROCARE-4, 2009) ²³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ²³ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ²³ UK and Ireland 79 1997 Linabery et al (2016) ¹⁷ South Korea 49 1998 Ellison et al (2017) ²⁴ Canada 48 31 1999 Gatta et al (EUROCARE-4, 2009) ²³ Europe 61 1999 Gatta et al (EUROCARE-4, 2009) ²⁴ Europe 63 2001 G	Observed	yes	0-14
Gatta et al (EUROCARE-4, 2009) ³² Central Europe 68 1997 Gatta et al (EUROCARE-4, 2009) ³³ Eastern Europe 63 1997 Desandes et al (2005) ³⁰ Italy France 81 1997 Gatta et al (EUROCARE-4, 2009) ³³ France 81 1997 Gatta et al (EUROCARE-4, 2009) ³³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³³ Southern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³³ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ³⁴ Southern Europe 61 1997 Linabery et al (2006,1 ⁵¹ United States 85 1997 Park et al (2016) ¹⁷ South Korea 49 1998 Ellison et al (2017) ³⁶ Europe 63 2001 Gatta et al (EUROCARE-4, 2009) ³³ Europe 63 2001 Gatta et al (2010) ³⁶ Europe 63 2001 Gatta et al (2010) ²⁶	Observed	yes	0-14
Gatta et al (EUROCARE-4, 2009) ²³ Eastern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Eastern Europe 65 1997 Desandes et al (2008) ³⁰ France 4 1997 Gatta et al (EUROCARE-4, 2009) ²³ Korthern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ²³ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ²³ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ²³ UK and Ireland 61 1997 Gatta et al (EUROCARE-4, 2009) ²³ UK and Ireland 61 1997 Linabery et al (2001) ³¹ United States 61 1999 Schindler et al (2017) ³⁴ Canada 63 2001 Gatta et al (EUROCARE-4, 2009) ²³ Switzerland 63 2001 Desandes et al (2011) ³⁵ Switzerland 63 2001 Gatta et al (EUROCARE-4, 2009) ²³ Europe 63 2001 Desandes et al (2011)	Observed	no	0-14
Gatta et al (EUROCARE-4, 2009) ³⁸ France 65 1997 Desandes et al (2008) ³⁸ France 81 1997 Dama et al (2005) ³⁰ Italy 79 1997 Gatta et al (EUROCARE-4, 2009) ³⁸ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³⁰ Northern Europe 63 1997 Gatta et al (EUROCARE-4, 2009) ³⁰ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ³⁰ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ³⁰ Southern Europe 65 1997 Gatta et al (EUROCARE-4, 2009) ³⁰ UK and Ireland 79 1997 Linabery et al (2007) ³¹ United States 45 1997 Park et al (2017) ³⁵ Switzerland 43 1999 Schindler et al (2017) ³⁵ Switzerland 44 1999 Gatta et al (EUROCARE-4, 2009) ²³ Europe 61 1999 Schindler et al (2017) ³⁵ Switzerland 44 1999 Gatta et al (EUROCARE-4, 2009) ²³ Europe 61 1999 Gatta et al (EUROCARE-4, 2009) ²³ Europe	Observed	no	0-14
Desandes et al (2006) ³⁸ France811997Dama et al (2005) ³⁰ Italy791997Gatta et al (EUROCARE-4, 2009) ³⁰ Northern Europe631997Gatta et al (EUROCARE-4, 2009) ³⁰ Northern Europe651997Gatta et al (EUROCARE-4, 2009) ³⁰ Southern Europe651997Gatta et al (EUROCARE-4, 2009) ³⁰ UK and Ireland611997Gatta et al (EUROCARE-4, 2009) ³⁰ UK and Ireland791997Gatta et al (EUROCARE-4, 2009) ³⁰ UK and Ireland791997Linabery et al (2007) ³⁴ Southern Europe4831999Raralexi et al (2017) ³⁵ South Korea4911998Ellison et al (2017) ³⁵ Switzerland4841999Gatta et al (EUROCARE-4, 2009) ²³ Europe611997Gatta et al (EUROCARE-4, 2009) ²³ Europe611999Schindler et al (2017) ³⁵ Switzerland484Basta et al (2014) ²⁵ France42001Desandes et al (2011) ²⁶ South Korea752002Walsh et al (2011) ²⁶ South Korea752002Walsh et al (2011) ²⁶ France902004Coll et al (2016) ¹⁷ South Korea752003Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe622004Desandes et al (2014) ⁴⁵ France902004Coll et al (2015) ⁴⁶ France902004Desandes et al (2016) ⁴⁶ France8	Observed	yes	0-14
Dama et al (2005)Italy791997Gatta et al (EUROCARE-4, 2009)Northern Europe631997Gatta et al (EUROCARE-4, 2009)Northern Europe631997Gatta et al (EUROCARE-4, 2009)Southern Europe651997Gatta et al (EUROCARE-4, 2009)Southern Europe651997Gatta et al (EUROCARE-4, 2009)UK and Ireland611997Gatta et al (EUROCARE-4, 2009)UK and Ireland791997Linabery et al (2006)United States851997Park et al (2016)South Korea491998Ellison et al (2017)South Korea431999Gatta et al (EUROCARE-4, 2009)Europe611999Schindler et al (2017)Switzerland481999Gatta et al (EUROCARE-4, 2009)Europe632001Gatta et al (EUROCARE-4, 2009)Europe632001Gatta et al (2017)Switzerland442001Desandes et al (2011)England772002Jung et al (2011)England772002Jung et al (2011)Ireland632003Park et al (2016)France622004Desandes et al (2011)France902004Coll et al (2016)France902004Desandes et al (2016)France502005Desandes et al (2016)France502005Desandes et al (2016)France502005Desandes et al (2016)<	Observed	yes	0-14
Gatta et al (EUROCARE 4, 2009)Northern Europe831997Gatta et al (EUROCARE 4, 2009)Northern Europe631997Gatta et al (EUROCARE 4, 2009)Southern Europe631997Gatta et al (EUROCARE 4, 2009)Southern Europe651997Gatta et al (EUROCARE 4, 2009)UK and Ireland611997Catta et al (EUROCARE 4, 2009)UK and Ireland791997Linabery et al (2006)UK and Ireland791998Ellison et al (2007)South Korea491998Batta et al (EUROCARE 4, 2009)Canada611999Varialexi et al (SEE, 2015)Europe611999Schindler et al (2017)South Korea491998Batta et al (EUROCARE 4, 2009)Europe632001Gatta et al (EUROCARE 4, 2009)Europe632001Gatta et al (EUROCARE 4, 2009)Europe632001Gatta et al (EUROCARE 4, 2009)Europe632001Desandes et al (2011)England752002Jung et al (2011)Ireland632003Park et al (2011)France632003Trama et al (EUROCARE 5, 2016)France90Desandes et al (2016)France90Desandes et al (2016)France90Desandes et al (2016)France90Desandes et al (2016)France87Desandes et al (2016)France87Desandes et al (2016)France87	Observed	yes	0-14
Gatta et al (EUROCARE-4, 2009)Northern Europe631997Gatta et al (EUROCARE-4, 2009)Southern Europe651997Gatta et al (EUROCARE-4, 2009)UK and Ireland651997Gatta et al (EUROCARE-4, 2009)UK and Ireland761997Inabery et al (2006)UK and Ireland771997Linabery et al (2007)South Korea491998Ellison et al (2007)South Korea491999Schindler et al (2017)South Korea631997Gatta et al (EUROCARE-4, 2009)Europe611999Schindler et al (2017)South Korea491999Gatta et al (2017)Switzerland632001Gatta et al (EUROCARE-4, 2009)Europe632001Desandes et al (2011)England772002Jung et al (2011)England772002Valsh et al (2011)Europe632001Desandes et al (2011)England772002Valsh et al (2011)Europe632001Desandes et al (2011)Europe622004Desandes et al (2011)Europe622004Oral det al (2011)France902004Coll et al (2015)France902004Desandes et al (2016)France502005Desandes et al (2016)France502005Desandes et al (2016)France502005Desandes et al (2016)France50<	Observed	yes	0-14
Gatta et al (EUROCARE 4, 2009)Southern Europe761997Gatta et al (EUROCARE 4, 2009)Southern Europe651997Gatta et al (EUROCARE 4, 2009)UK and Ireland611997Gatta et al (EUROCARE 4, 2009)UK and Ireland791997Linabery et al (2008)UK and Ireland791997Park et al (2016)UK and Ireland791997Batta et al (2007)South Korea491998Ellison et al (2007)Canada611999Schindler et al (2017)Switzerland632001Gatta et al (EUROCARE 4, 2009)Europe632001Gatta et al (EUROCARE 4, 2009)Europe632001Gatta et al (2017)France772002Jung et al (2011)England772002Unals et al (2011)Europe632001Basta et al (2011)England772002Unals et al (2011)England772002Unals et al (2011)Europe622004Desandes et al (2011)France902004Coll et al (2015)France902004Desandes et al (2016)France902005Desandes et al (2016)France902005Desandes et al (2016)France902005Desandes et al (2016)France872005Desandes et al (2016)France872005Desandes et al (2016)France872005	Observed	no	0-14
Gatta et al (EUROCARE-4, 2009) Gatta et al (EUROCARE-4, 2009) Tarma et al (2011)Southern Europe651997Gatta et al (EUROCARE-4, 2009) UK and Ireland UK and Ireland UK and IrelandVK and Ireland791997Linabery et al (2006) Park et al (2016) Schindler et al (2017) Schindler et al (2011) Schindler et al (2011) S	Observed	yes	0-14
Gatta et al (EUROCARE-4, 2009)UK and IrelandImage: fill and fill an	Observed	no	0-14
Gatta et al (EUROCARE-4, 2009)UK and Ireland791997Linabery et al (2008)United States851997Park et al (2016)South Korea491998Ellison et al (2007)Canada331999Karalexi et al (SEE, 2015)Europe611999Schindler et al (2017)South Korea491998Gatta et al (EUROCARE-4, 2009)Europe632001Gatta et al (EUROCARE-4, 2009)Europe632001Desandes et al (2011)England772002Jung et al (2011)South Korea752002Walsh et al (2011)Ireland832003Park et al (2011)South Korea752002Urante et al (EUROCARE-5, 2016)France622004Desandes et al (2014)France902004Coll et al (2015)France902004Desandes et al (2014)France902004Desandes et al (2014)France902004Desandes et al (2016)France902005Desandes et al (2016)France90Desandes et al (2016)Fr	Observed	no	0-14
Linabery et al (2008) ⁵¹ United States 85 1997 Park et al (2016) ¹⁷ South Korea 49 1998 Ellison et al (2007) ²⁴ Canada 83 1999 Karalexi et al (SEE, 2015) ¹⁴ Europe 61 1999 Schindler et al (2017) ⁵⁵ Switzerland 44 1999 Gatta et al (EUROCARE-4, 2009) ²³ Europe 63 2001 Desandes et al (2014) ⁵⁵ France 84 2001 Basta et al (2011) ⁵⁵ South Korea 77 2002 Jung et al (2011) ⁵⁵ South Korea 75 2002 Walsh et al (2016) ¹⁷ South Korea 57 2003 Trama et al (2016) ¹⁷ South Korea 57 2003 Trama et al (2014) ⁵⁶ France 90 2004 Coll et al (2015) ⁵⁰ France 92 2005 Desandes et al (2014) ⁵⁶ France 92 2005 Desandes et al (2014) ⁵⁶ France 92 2005 Desandes et al (2016) ⁶⁹ France 92 2005 Desandes et al (2016) ⁶⁹ France 92 </td <td>Observed</td> <td>yes</td> <td>0-14</td>	Observed	yes	0-14
Park et al (2016)South Korea491998Ellison et al (2007)Canada \checkmark 831999Karalexi et al (SEE, 2015)Europe611999Schindler et al (2017)Switzerland \checkmark 841999Gatta et al (EUROCARE-4, 2009)Europe632001Desandes et al (2014)France842001Basta et al (2011)England \checkmark 772002Jung et al (2011)South Korea772002Walsh et al (2011)Ireland832003Park et al (EUROCARE-5, 2016)France \checkmark 622004Desandes et al (2014)France \checkmark 902004Coll et al (2015)France \checkmark 902004Desandes et al (2014)France \checkmark 902004Desandes et al (2014)France \checkmark 902004Desandes et al (2014)France \checkmark 902004Coll et al (2015)France \checkmark 902005Desandes et al (2014)France \checkmark 872007	Observed	ves	0-14
Ellison et al $(2007)^{24}$ Canada 83 1999 Karalexi et al $(SEE, 2015)^{14}$ Europe 61 1999 Schindler et al $(2017)^{26}$ Switzerland 84 1999 Gatta et al $(EUROCARE-4, 2009)^{23}$ Europe 63 2001 Gatta et al $(EUROCARE-4, 2009)^{23}$ Europe 63 2001 Desandes et al $(2014)^{26}$ France 84 2001 Basta et al $(2011)^{50}$ England 77 2002 Jung et al $(2012)^{25}$ South Korea 75 2002 Walsh et al $(2016)^{17}$ South Korea 75 2003 Trama et al (EUROCARE-5, 2016)^{67} Europe 62 2004 Desandes et al $(2014)^{55}$ France 90 2004 Coll et al $(2015)^{70}$ France 90 2004 Desandes et al $(2016)^{19}$ France 90 2005 Desandes et al $(2016)^{19}$ France 90 2005 Desandes et al $(2016)^{19}$ France 90 2005	Relative	not specified	0-14
Karalexi et al (SEE, 2015) ¹⁴ Europe 61 1999 Schindler et al (2017) ³⁵ Switzerland 4 1999 Gatta et al (EUROCARE-4, 2009) ²³ Europe 63 2001 Gatta et al (EUROCARE-4, 2009) ²³ Europe 63 2001 Desandes et al (2014) ³⁵ France 4 2001 Basta et al (2011) ³⁶ England 77 2002 Jung et al (2012) ³⁶ South Korea 75 2003 Park et al (2016) ¹⁷ South Korea 57 2003 Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe 62 2004 Desandes et al (2014) ³⁶ France 90 2004 Desandes et al (2016) ¹⁹ France 90 2005 Desandes et al (2016) ¹⁹ France 90 2005 Desandes et al (2016) ¹⁹ France 90 2005	Observed	ves	0-19
Schindler et al (2017) ³⁵ Switzerland 4 1999 Gatta et al (EUROCARE-4, 2009) ³³ Europe 63 2001 Gatta et al (EUROCARE-4, 2009) ²³ Europe 63 2001 Desandes et al (2014) ²⁵ France 4 4 2001 Jung et al (2011) ²⁶ South Korea 77 2002 Jung et al (2012) ²⁶ South Korea 75 2002 Park et al (2011) ²⁷ Ireland 83 2003 Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe 62 2004 Desandes et al (2014) ²⁵ France 90 2004 Desandes et al (2014) ²⁶ France 90 2005 Desandes et al (2016) ⁴⁷ France 90 2005	Observed	no	0-14
Gatta et al (EUROCARE-4, 2009) ²³ Europe 63 2001 Gatta et al (EUROCARE-4, 2009) ²³ Europe 78 2001 Desandes et al (2014) ²⁵ France 84 2001 Basta et al (2014) ²⁵ England 77 2002 Jung et al (2012) ²⁶ South Korea 75 2002 Walsh et al (2011) ²² Ireland 83 2003 Park et al (2016) ¹⁷ South Korea 57 2003 Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe 62 2004 Coll et al (2015) ²⁰ France 90 2004 Coll et al (2016) ¹⁹ France 92 2005 Desandes et al (2016) ¹⁴⁹ France 50 2005 Desandes et al (2016) ¹⁴⁹ France 50 2005	Observed	not specified	0-14
Gatta et al (EUROCARE 4, 2009) ²³ Europe 78 2001 Desandes et al (2014) ²⁵ France 84 2001 Basta et al (2012) ²⁵ South Korea 77 2002 Jung et al (2011) ²⁶ South Korea 75 2002 Walsh et al (2011) ²⁷ Ireland 83 2003 Park et al (2016) ¹⁷ South Korea 57 2002 Ubesandes et al (2014) ²⁵ France 90 2004 Coll et al (2015) ²⁰ France 90 2004 Coll et al (2016) ¹⁹ France 92 2005 Desandes et al (2016) ¹⁶⁹ France 92 2005 Desandes et al (2016) ¹⁶⁹ France 92 2005	Observed	no	0-14
Desandes et al (2014) ⁴⁵ France 84 2001 Basta et al (2011) ⁶⁰ England 77 2002 Jung et al (2012) ⁵⁵ South Korea 75 2002 Walsh et al (2016) ¹⁷ South Korea 77 2003 Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe 62 2004 Desandes et al (2014) ⁵⁶ France 90 2004 Coll et al (2015) ⁷⁰ France 92 2005 Desandes et al (2016) ⁴⁹ France 50 2005 Desandes et al (2016) ⁴⁵ France 50 2005	Observed	ves	0-14
Basta et al (2011) ⁵⁰ England 77 2002 Jung et al (2012) ⁵⁵ South Korea 75 2002 Walsh et al (2011) ⁵¹ Ireland 83 2003 Park et al (2011) ⁵² Ireland 57 2003 Trama et al (EUROCARE-5, 2016) ⁵⁷ Europe 62 2004 Desandes et al (2014) ⁵⁵ France 90 2004 Desandes et al (2016) ⁵⁹ France 50 2005 Desandes et al (2014) ⁵⁵ France 50 2005	Observed	Ves	0-14
Jung et al (2012) ⁸⁶ South Korea 75 2002 Walsh et al (2011) ²² Ireland 83 2003 Park et al (2016) ¹⁷ South Korea 57 2003 Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe 62 2004 Desandes et al (2014) ⁵⁶ France 90 2004 Coll et al (2015) ²⁰ France 92 2005 Desandes et al (2016) ⁴⁹ France 50 2005 Desandes et al (2016) ⁴⁹ France 50 2005	Observed	, V@e	0_14
Walsh et al (2011) ¹² Ireland 1 1 83 2003 Park et al (2016) ¹⁷ South Korea 57 2003 Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe 62 2004 Desandes et al (2014) ²⁵ France 90 2004 Coll et al (2015) ³⁰ France 92 2005 Desandes et al (2016) ⁴⁸ France 50 2005 Desandes et al (2014) ²⁵ France 50 2005	Observed	100	0.14
Park et al (2016) ¹⁷ South Korea 57 2003 Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe ▲ 62 2004 Desandes et al (2014) ⁵⁵ France ▲ 90 2004 Coll et al (2015) ⁵⁰ France ▲ 90 2004 Desandes et al (2016) ⁶⁹ France ▲ 90 2005 Desandes et al (2014) ⁵⁵ France ▲ 50 2005 Desandes et al (2014) ⁵⁵ France ▲ 87 2007	Oheanuad	Ver	0-19
Trama et al (EUROCARE-5, 2016) ⁴⁷ Europe 1 62 2004 Desandes et al (2014) ⁵⁶ France 1 49 2005 Desandes et al (2016) ⁶⁹ France 50 2005 Desandes et al (2014) ⁵⁵ France 50 2005 Desandes et al (2014) ⁵⁵ France 50 2005	Relativo	yes not enertified	0-14
Desandes et al (2014) ²⁶ France ↓ <td>Relative</td> <td>not specified</td> <td>0-14</td>	Relative	not specified	0-14
Coll et al (2015) ²⁰ France 1 4 90 2004 Desandes et al (2016) ⁴⁹ France 1 4 92 2005 Desandes et al (2014) ²⁵ France 50 2007	Observed	NOC	0-14
Constant (2016) France 1 92 2005 Desandes et al (2016) ¹⁹ France 50 2005 Desandes et al (2014) ²⁵ France 4 87 2007	Observed	yes	0-14
Desandes et al (2014) ²⁵ France 50 2005 Desandes et al (2014) ²⁵ France & 87 2007	Observed	not specified	U-14
Desances et al (2014) France	Observed	yes	0-20 uays
	Del	yes	0-14
Park et al (2017) South Korea 54 2008	Relative	not specified	0-14
Schindler et al (2017) Switzerland	Ubserved	not specified	0-14
rark et al (2016) South Korea 👗 51 2009	Relative	not specified	0-14
I			

FIG 4. Five-year survival (%) from astrocytoma (broad group). EUROpean CAncer REgistry based study on survival and care of cancer patients (EUROCARE-3) consortium: Austria, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Italy, Malta, Netherlands, Norway, Poland, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales. EUROCARE-4 consortium: Austria, Belgium, Czech (continued on following page)

Survival From Astrocytic and Embryonal Brain Tumors in Chil	dren
---	------

HISTOLOGY AND FIRST AUTHOR	LOCATION	FIVE-YEAR SURVIV	VAL (%) AND 95% CI	%	CENTRAL YEAR	OUTCOME MEASURE	AGE RANGE (years)
Astrocytoma WHO grade I/II			i I				
Kaatsch et al (2001) ³⁶	Germany		I 📥	82	1990	Observed	0-14
Lannering et al (2009)40	Sweden		.¦	93	1995	Observed	0-14
Bellil et al (hospital-based, 2008) ¹³	Tunisia		. ▲	78	1997	Observed	0-15
Ben Arush et al (2010)44	Israel		i 🔺	82	2003	Observed	0-19
Desandes et al (2014) ²⁵	France		1 A	94	2004	Observed	0-14
Pilocytic astrocytoma			1				
Tseng et al (2006) ³³	England and Wales		▲ · · ·	88	1981	Observed	0-14
Georgakis et al (SEE + US, 2017) ⁵⁷	United States		i 📥	91	1981	Observed	0-14
Davis et al (1998) ³¹	United States		1 	89	1982	Observed	0-28
Georgakis et al (SEE + US, 2017) ⁵⁷	Europe		! 📥	88	1991	Observed	0-14
Georgakis et al (SEE + US, 2017) ⁵⁷	United States		▲ .	98	1995	Observed	0-14
Flores et al (2013) ⁵²	United States		▲	99	1999	Observed	0-19
Mathew et al (UK + US, 2014) ⁴²	UK		i 🔺	96	2001	Observed	0-14
Mathew et al (UK + US, 2014) ⁴²	United States		1 🔺	97	2001	Observed	0-14
Georgakis et al (SEE + US, 2017) ⁵⁷	Europe		- <u>-</u>	92	2002	Observed	0-14
Ben Arush et al (2010) ⁴⁴	Israel		▲ ·	95	2003	Observed	0-19
Gatta et al (EUROCARE-5, 2017) ¹⁰	Europe		i 🔺	95	2004	Observed	0-14
Georgakis et al (SEE + US, 2017) ⁵⁷	United States		. ▲	98	2006	Observed	0-14
Diffuse astrocytoma			1				
Tseng et al (2006) ³³	England and Wales			71	1981	Observed	0-14
Tseng et al (2006) ³³	England and Wales		i 🔺	78	1981	Observed	0-14
Narita et al (hospital-based, 2015) ⁵⁸	Japan		1	60	2003	Observed	0-19
Gatta et al (EUROCARE-5, 2017) ¹⁰	Europe		! 🔺	74	2004	Observed	0-14
Gatta et al (EUROCARE-5, 2017) ¹⁰	Europe			75	2004	Observed	0-14
Astrocytoma WHO grade III/IV			l l				
Kaatsch et al (2001) ³⁶	Germany		1	24	1990	Observed	0-14
Lannering et al (2009)40	Sweden		1	28	1995	Observed	0-14
Desandes et al (2014) ²⁵	France			22	2004	Observed	0-14
Ananlastic astrocytoma			1				
Tseng et al (2006) ³³	England and Wales			19	1981	Observed	0-14
Mathew et al (UK + US, 2014) ⁴²	UK		1	19	2001	Observed	0-14
Mathew et al (UK + US, 2014)42	United States	A	i	30	2001	Observed	0-14
Jung et al (2012) ⁵⁵	South Korea	A	1	21	2002	Observed	0-19
Ben Arush et al (2010) ⁴⁴	Israel		!	55	2003	Observed	0-19
Narita et al (hospital-based, 2015) ⁵⁸	Japan	A	1 -	18	2003	Observed	0-19
Gatta et al (EUROCARE-5, 2017) ¹⁰	Europe	- <u>+</u> -	1	21	2004	Observed	0-14
Glioblastoma			1				
Tseng et al (2006) ³³	England and Wales	A	1	20	1981	Observed	0-14
Davis et al (1998) ³¹	United States		1	21	1982	Observed	0-20
Brodbelt et al (2015) ^{58a}	England		i	15	1990	Relative	0-19
Mathew et al $(UK + US 2014)^{42}$	LIK		1	.0	2001	Observed	0-14
Mathew et al (UK + US 2014) ⁴²	United States	_	1	22	2001	Observed	0-14
Jung et al (2012) ⁵⁵	South Korea		1	19	2002	Observed	0-19
Ben Arush et al (2010) ⁴⁴	Israel		i i	15	2003	Observed	0-19
Narita et al (hospital-based 2015) ⁵⁸	Janan	_	1	.5	2003	Observed	0-19
Gatta et al (EUROCARE-5, 2017) ¹⁰	Europe		1	14	2004	Observed	0-14
			1				
		0 25	+ i i 50 75 100)			
		5 25	55 75 TO				

FIG 5. Five-year survival (%) from astrocytoma WHO grade I and II, pilocytic astrocytoma, diffuse astrocytoma, astrocytoma WHO grade III and IV, anaplastic astrocytoma, and glioblastoma. EUROpean CAncer REgistry based study on survival and care of cancer patients (EUROCARE-5) consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales. The CI is not displayed when the study did not provide it. SEE, Southern and Eastern Europe; UK, United Kingdom.

(Table 1). Five of the 22 studies using the definition "astrocytoma" (broad histology group) did not elucidate whether they included only malignant tumors or both malignant and nonmalignant tumors (Appendix Table

A3).^{15,17,20,29,35} Thirty-nine studies (83%) provided estimates of all-cause survival (ie, observed). Only eight provided relative survival estimates, adjusted for background mortality (Table 1).

FIG 4. (Continued). Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, (continued on following page)Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales. Southern and Eastern Europe (SEE) consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine. EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales. The CI is not displayed when the study did not provide it. UK, United Kingdom.

DISCUSSION

To our knowledge, this is the first systematic review synthesizing trends and geographic variation in survival for the most common morphologic subtypes of brain tumor in children. Five-year survival for embryonal tumors increased remarkably during the 1980s and the 2000s, and the change was driven mostly by an improvement in the outcome of patients diagnosed with medulloblastoma. Survival from astrocytic tumors changed very little, regardless of WHO grade.

Only five studies included patients diagnosed in lowincome or middle-income countries (Belarus, Bulgaria, India, Montenegro, Romania, Serbia, Tunisia, Turkey, Uganda, Ukraine).¹³⁻¹⁶ In this setting, the magnitude of the survival gap depended on country and histology, albeit the largest deficit was seen for embryonal tumors. In highincome countries, where nearly all of the studies were conducted, outcomes were similar. However, in the United States, survival from the most common embryonal tumors improved earlier than elsewhere.

Low-grade gliomas represent approximately one third of all CNS tumors in children. They are biologically distinct from low-grade gliomas seen in adults, and progression to highergrade lesions rarely occurs.⁵⁹ Pilocytic astrocytoma is the most common glioma subtype in children.⁶⁰ We adopted different levels of granularity in the histology definitions, but data for specified astrocytic tumors were sparse. Most studies presented survival estimates on the basis of the second tier of the ICCC, group IIIb (ie, astrocytoma).⁶¹ For tumors defined as astrocytoma (broad group), corresponding to the ICCC group IIIb, 5-year survival was approximately 90% during 2004-2009. During a comparable period, survival from pilocytic astrocytoma (WHO grade I) was nearly 100%. Pilocytic astrocytoma therefore is probably responsible for the favorable outcome observed in the broader group, because diffuse astrocytoma, anaplastic astrocytoma, and glioblastoma combined only constituted approximately 30% of astrocytic tumors in children.¹⁰

The current recommendation is to present survival in children separately for each ICCC group. Even though pilocytic astrocytoma is predominant in children, we believe that the adoption of a broad category, such as astrocytoma (ICCC-3 group IIIb), does not fully account for international variations in survival, and it may actually attenuate the observed trends and differences. We chose to report survival at 5 years, because that is the most commonly reported time landmark, and to facilitate comparisons between studies. Low-grade gliomas are often indolent tumors that progress slowly, even after partial resection or biopsy.⁶² In a large US study that included nearly 3,500 children (age 0-20 years) diagnosed with low-grade gliomas during 1973-2005, the survival probability at 10 years for WHO grade I and grade II tumors was approximately 90% and 80%, respectively.⁶³ Therefore, outcomes for this cancer subtype may be better described with longer-term survival estimates.

A remarkable proportion of studies adopting the definition of astrocytoma (as a broad histology group) did not clarify the tumor behavior. This information is necessary to interpret trends correctly. In the second edition of the ICD-O (in force from 1990),⁵⁶ pilocytic astrocytoma was coded as malignant (behavior code 3), but, in the third edition (in force from 2000), it was attributed a borderline behavior (code 1).¹² In studies considering patients diagnosed during 1982-1996, which used ICD-O-2, survival from astrocytoma was likely to be high as a result of the inclusion of pilocytic astrocytoma, which was defined at that time as a malignant tumor. In brain tumors, location is more important than it is for tumors at other anatomic sites, because location affects clinical presentation, diagnosis, treatment, and morbidity. Therefore, though pilocytic astrocytoma was reclassified as a nonmalignant tumor in ICD-O-3, most studies published after 2000, when ICD-O-3 was adopted, included all brain tumors, regardless of behavior. As a result, survival estimates from these studies were in fact comparable to those in earlier reports that were based on ICD-O-2. In EUROCARE-5, however, survival from astrocytoma in Eastern Europe was similar, regardless of whether tumors with borderline behavior were included or not.²³ This finding suggests under-registration of nonmalignant brain tumors in Eastern Europe.

Medulloblastoma is the most common embryonal tumor, with a peak incidence at approximately 7 years of age. Treatment includes a combination of surgery, craniospinal irradiation, and chemotherapy. In this review, the steepest gain in survival from medulloblastoma occurred before 1992, possibly reflecting improvement in radiotherapy techniques.⁶⁴ The effect of adding chemotherapy with lomustine, cisplatin, and vincristine after radiotherapy was first assessed in a phase II trial in the 1990s.⁶⁵ In light of the observed benefit, the use of chemotherapy became standard. In the 1990s and 2000s, 5-year survival increased from approximately 60% to 70%. This finding may be the joint result of improved surgical management and incorporation of chemotherapy into routine clinical practice.⁶⁶ Survival from medulloblastoma was much lower in low-income and middle-income countries than in highincome countries. This disparity may reflect the lack of access to optimal multimodality treatment.5-8

In three studies, medulloblastoma was grouped with PNETs, even though ICD-O-3 was given as the reference classification.⁵⁰⁻⁵² As a result, survival estimates were higher than those for PNET only.^{35,38,41,42} Infratentorial medulloblastoma and supratentorial PNET are distinct entities, described as separate morphologies in the second edition of the WHO classification of CNS tumors (2002).⁶⁷ Because medulloblastoma has a more favorable outcome than PNET, its inclusion in a wider group mislabeled as PNET will bias the survival estimates upward.

Two studies defined astrocytoma, not otherwise specified (NOS), as a separate morphologic entity, perhaps to allow for a generic diagnosis of unspecified astrocytic tumor.^{10,33} In the United States, the proportion of astrocytic tumors registered as astrocytoma NOS decreased from 47% to 13% during 1973-2005.⁶³ The WHO classification does not recognize astrocytoma NOS as a distinct definition. Diffuse astrocytoma and astrocytoma NOS share the same ICD-O-3 code, but the WHO classification retains only the first of the two descriptors.^{12,60} Therefore, we grouped together the survival estimates, which proved comparable (70%-80%).^{10,33}

In most of the studies reviewed here, indicators of data quality were often missing or incomplete. The proportion of tumors that had been microscopically verified was the most widely available parameter. Few studies reported any additional descriptors, such as the proportion of patients who were lost to follow-up before the end of the study. The proportion of microscopically verified tumors pertains not only to disease management, namely whether surgery or biopsy was performed, but also to whether the cancer registry had access to pathology reports.⁶⁸ The proportions of microscopically verified brain tumors were in the range of 73%-93% in the SEE consortium (1983-2014) and 71%-100% in the EUROCARE-5 study (2000-2007).^{10,14}

The proportion of brain tumors that are microscopically verified is typically lower than for other types of cancer, because brain tumors are more lethal and patients are often too unwell to undergo an invasive diagnostic procedure; advanced surgical expertise also is required. If the proportion of tumors that are histologically unclassified is high, survival estimates for specific morphologies may be biased, because patients with histologically confirmed disease are likely to have higher survival than those whose tumors could not be pathologically confirmed.

Similarly, information on the completeness of ascertainment of brain tumors was very often missing. In most of the studies for which this information was available, it was usually reported as nearly complete (95% or more). This parameter is important to assess whether the patients included in the study are representative of all patients with brain tumors in the population of a given region or country.⁶⁹

In most of the studies (83%), survival was reported only as observed survival, without taking into account death as a result of causes other than the brain tumor (background mortality). If competing risks of death are not properly accounted for, survival estimates will be biased downward. Background mortality also varies widely between countries and over time, so valid international comparisons require that background mortality is incorporated in the survival estimates. However, nearly all of the studies were conducted in affluent countries, where background mortality in children has generally been very low for several decades.

The distortion in international comparisons of brain tumor survival in children is thus likely to be small.

This systematic review was affected by several limitations. First, we aimed to give a comprehensive account of variations in brain tumor survival by including all of the relevant histology categories. However, very few studies were available for some categories, precluding robust conclusions on time trends and geographic variations in survival. Second, almost all the studies were based on regional rather than national data. Assuming that regional survival estimates are applicable to the whole country may not be wise in the presence of regional disparities in access to or provision of treatment within a given country. However, data from most of these regions were later included in wider studies with national or international coverage. Survival estimates from those studies were in line with those previously reported at regional level, suggesting that findings from the earlier, smaller studies were indeed generalizable to the country. Finally, the dates and the length of calendar periods in which the patients had been diagnosed also varied widely between studies. To allow an orderly presentation of time trends, we referred to the central year for any given time interval, but we were not able to compare the average annual increment or decrement in survival between calendar periods of different, and often overlapping, lengths. Improvements in survival were nevertheless limited mainly to embryonal tumors, and they occurred over an extended period, so the international comparisons may be considered reasonably informative.

In conclusion, there is a staggering gap in evidence about survival from the most common types of childhood brain tumor in low-income and middle-income countries. Interpretation of the literature is hampered by the very wide heterogeneity between the designs of the various studies and by the quality of the available data.

We highlight the fact that the ICCC does not allow accurate description of variation in survival from astrocytic tumors, because it does not encompass stratification by grade. The goal of the WHO Global Initiative for Childhood Cancer is to improve survival worldwide for six cancer subtypes, including low-grade gliomas.⁷⁰ In the context of brain tumors, future assessment of the progress of this global effort will require that an informative, up-to-date survival benchmark for low-grade gliomas is set. Ultimately, the ICCC should be revised.

The 2016 WHO classification of Tumors of the Central Nervous System has redefined or replaced several diagnostic entities or subgroups by incorporating molecular classifiers.⁷¹ For instance, PNET is no longer included in the diagnostic dictionary, and medulloblastoma is now genetically defined. Future comparisons of survival will have to account for these changes, but capacity-building and resources are needed to extend the use of this classification, both in clinical practice and in cancer

Downloaded from ascopubs.org by 82.60.182.79 on November 5, 2019 from 082.060.182.079 Copyright © 2019 American Society of Clinical Oncology. All rights reserved.

registries, especially in low-income and middle-income countries.

Larger international studies that include currently underrepresented countries are warranted, and robust survival estimates are only possible through use of the same

AFFILIATION

¹London School of Hygiene and Tropical Medicine, London, United Kingdom

CORRESPONDING AUTHOR

Fabio Girardi, MD, Cancer Survival Group, Noncommunicable Disease Epidemiology Department, London School of Hygiene and Tropical Medicine, Keppel St, London WC1E 7HT, United Kingdom; Twitter: @FabioGir22; e-mail: fabio.girardi@lshtm.ac.uk.

SUPPORT

Supported by the Davidson and O'Gorman Fellowship (to F.G.) from Children with Cancer UK.

AUTHOR CONTRIBUTIONS

Conception and design: All authors Collection and assembly of data: Fabio Girardi Data analysis and interpretation: All authors Manuscript writing: All authors Final approval of manuscript: All authors Agree to be accountable for all aspects of the work: All authors protocol for data collection, centralized and stringent data quality checks, and application of the same statistical methodology—including appropriate life tables to correct for the risk of death as a result of causes other than cancer.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs. org/jgo/site/misc/authors.html.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

No potential conflicts of interest were reported.

ACKNOWLEDGMENT

We thank Audrey Bonaventure, MD, for her advice on the systematic review design.

REFERENCES

- 1. International Agency for Research on Cancer: Global Cancer Observatory; Cancer Today. 2018. http://gco.iarc.fr/today/home.
- 2. Coleman MP: Cancer survival: Global surveillance will stimulate health policy and improve equity. Lancet 383:564-573, 2014
- 3. Coleman MP, Allemani C: Cancer: The elephant in the room. Lancet 385:1047-1048, 2015
- 4. Allemani C, Matsuda T, Di Carlo V, et al: Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): Analysis of individual records for 37,513,025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 391:1023-1075, 2018
- 5. Cohen P, Friedrich P, Lam C, et al: Global access to essential medicines for childhood cancer: A cross-sectional survey. J Glob Oncol 4:1-11, 2018
- 6. Atun R, Jaffray DA, Barton MB, et al: Expanding global access to radiotherapy. Lancet Oncol 16:1153-1186, 2015
- 7. Alkire BC, Raykar NP, Shrime MG, et al: Global access to surgical care: A modelling study. Lancet Glob Health 3:e316-e323, 2015
- 8. International Atomic Energy Agency: Inequity in Cancer Care: A Global Perspective. Vienna, IAEA (International Atomic Energy Agency), 2011.
- 9. Bhakta N, Force LM, Allemani C, et al: Childhood cancer burden: A review of global estimates. Lancet Oncol 20:e42-e53, 2019
- 10. Gatta G, Peris-Bonet R, Visser O, et al: Geographical variability in survival of European children with central nervous system tumours. Eur J Cancer 82:137-148, 2017
- 11. Moher D, Liberati A, Tetzlaff J, et al: Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 6:e1000097, 2009
- 12. Fritz A, Percy C, Jack A, et al (eds): International Classification for Diseases in Oncology, (ed 3). Geneva, WHO, 2013.
- 13. Bellil S, Limaiem F, Mahfoudhi H, et al: Descriptive epidemiology of childhood central nervous system tumours in Tunisia: Experience of a single institution over a 15-year period (1990-2004). Pediatr Neurosurg 44:382-387, 2008
- 14. Karalexi MA, Papathoma P, Thomopoulos TP, et al: Childhood central nervous system tumour mortality and survival in Southern and Eastern Europe (1983-2014): Gaps persist across 14 cancer registries. Eur J Cancer 51:2665-2677, 2015
- 15. Swaminathan R, Rama R, Shanta V: Childhood cancers in Chennai, India, 1990-2001: Incidence and survival. Int J Cancer 122:2607-2611, 2008
- Stagno V, Mugamba J, Ssenyonga P, et al: Presentation, pathology, and treatment outcome of brain tumors in 172 consecutive children at CURE Children's Hospital of Uganda: The predominance of the visible diagnosis and the uncertainties of epidemiology in sub-Saharan Africa. Childs Nerv Syst 30:137-146, 2014
- 17. Park HJ, Moon EK, Yoon JY, et al: Incidence and survival of childhood cancer in Korea. Cancer Res Treat 48:869-882, 2016
- Magnani C, Pastore G, Coebergh JW, et al: Trends in survival after childhood cancer in Europe, 1978-1997: Report from the Automated Childhood Cancer Information System project (ACCIS). Eur J Cancer 42:1981-2005, 2006
- 19. Gatta G, Capocaccia R, Stiller C, et al: Childhood cancer survival trends in Europe: A EUROCARE Working Group study. J Clin Oncol 23:3742-3751, 2005
- Coll G, Combes JD, Isfan F, et al: Incidence and survival of childhood central nervous system tumors: A report of the regional registry of childhood cancers in Auvergne-Limousin. Neurochirurgie 61:237-243, 2015

- 21. Baade PD, Youlden DR, Valery PC, et al: Population-based survival estimates for childhood cancer in Australia during the period 1997-2006. Br J Cancer 103:1663-1670, 2010
- 22. Walsh PM, Byrne J, Capra M, et al: Childhood cancer survival in Ireland: Temporal, regional and deprivation-related patterns. Eur J Cancer 47:1852-1862, 2011
- 23. Gatta G, Zigon G, Capocaccia R, et al: Survival of European children and young adults with cancer diagnosed 1995-2002. Eur J Cancer 45:992-1005, 2009
- 24. Ellison LF, Pogany L, Mery LS: Childhood and adolescent cancer survival: A period analysis of data from the Canadian Cancer Registry. Eur J Cancer 43:1967-1975, 2007
- Desandes E, Guissou S, Chastagner P, et al: Incidence and survival of children with central nervous system primitive tumors in the French National Registry of Childhood Solid Tumors. Neuro-oncol 16:975-983, 2014
- 26. AIRTUM Working Group; CCM; AIEOP Working Group: Italian cancer figures, report 2012: Cancer in children and adolescents. Epidemiol Prev 37:1-225, 2013
- 27. Alston RD, Newton R, Kelsey A, et al: Childhood medulloblastoma in northwest England 1954 to 1997: Incidence and survival. Dev Med Child Neurol 45:308-314, 2003
- Agerlin N, Gjerris F, Brincker H, et al: Childhood medulloblastoma in Denmark 1960-1984: A population-based retrospective study. Childs Nerv Syst 15:29-36, 1999;discussion 36-37
- 29. Kramarova E, Plesko I, Black RJ, et al: Improving survival for childhood cancer in Slovakia. Int J Cancer 65:594-600, 1996
- Dama E, Pastore G, Mosso ML, et al: Time trends and prognostic factors for survival from childhood cancer: A report from the Childhood Cancer Registry of Piedmont (Italy). Eur J Pediatr 165:240-249, 2006
- 31. Davis FG, Freels S, Grutsch J, et al: Survival rates in patients with primary malignant brain tumors stratified by patient age and tumor histological type: An analysis based on Surveillance, Epidemiology, and End Results (SEER) data, 1973-1991. J Neurosurg 88:1-10, 1998
- 32. Magnani C, Pastore G, Verdecchia A, et al: Survival of childhood cancer patients in Italy, 1978-1989. Tumori 83:426-489, 1997
- Tseng JH, Tseng MY: Survival analysis of children with primary malignant brain tumors in England and Wales: A population-based study. Pediatr Neurosurg 42:67-73, 2006
- 34. Roldán G, Brasher P, Vecil G, et al: Population-based study of medulloblastoma: Outcomes in Alberta from 1975 to 1996. Can J Neurol Sci 35:210-215, 2008
- 35. Schindler M, Belle FN, Grotzer MA, et al: Childhood cancer survival in Switzerland (1976-2013): Time-trends and predictors. Int J Cancer 140:62-74, 2017
- 36. Kaatsch P, Rickert CH, Kühl J, et al: Population-based epidemiologic data on brain tumors in German children. Cancer 92:3155-3164, 2001
- 37. Berger C, Trombert-Paviot B, Mitton N, et al: Les cancers de l'enfant de la région Rhône-Alpes: Incidence et survie 1987-1999 [in French]. Arch Pediatr 13:121-129, 2006
- 38. Desandes E, Berger C, Tron I, et al: Childhood cancer survival in France, 1990-1999. Eur J Cancer 44:205-215, 2008
- 39. Tulla M, Berthold F, Graf N, et al: Incidence, trends, and survival of children with embryonal tumors. Pediatrics 136:e623-e632, 2015
- 40. Lannering B, Sandström PE, Holm S, et al: Classification, incidence and survival analyses of children with CNS tumours diagnosed in Sweden 1984-2005. Acta Paediatr 98:1620-1627, 2009
- 41. Fairley L, Picton SV, McNally RJQ, et al: Incidence and survival of children and young people with central nervous system embryonal tumours in the North of England, 1990-2013. Eur J Cancer 61:36-43, 2016
- 42. Mathew RK, O'Kane R, Parslow R, et al: Comparison of survival between the UK and US after surgery for most common pediatric CNS tumors. Neuro-oncol 16:1137-1145, 2014
- 43. Chan MY, Teo WY, Seow WT, et al: Epidemiology, management and treatment outcome of medulloblastoma in Singapore. Ann Acad Med Singapore 36:314-318, 2007
- 44. Ben Arush M, Rabinowicz R, Ramu N, et al: Incidence and survival of first pediatric primary malignant central nervous system tumors in Israel, 1998-2007. Neuro-oncol 12:ii46, 2010
- 45. Smoll NR: Relative survival of childhood and adult medulloblastomas and primitive neuroectodermal tumors (PNETs). Cancer 118:1313-1322, 2012
- 46. Khanna V, Achey RL, Ostrom QT, et al: Incidence and survival trends for medulloblastomas in the United States from 2001 to 2013. J Neurooncol 135:433-441, 2017
- 47. Trama A, Botta L, Foschi R, et al: Survival of European adolescents and young adults diagnosed with cancer in 2000-07: Population-based data from EUROCARE-5. Lancet Oncol 17:896-906, 2016
- Ilveskoski I, Pihko H, Sankila R, et al: Improving outcome of malignant brain tumours in very young children: A population-based study in Finland during 1975-93. Acta Paediatr 86:724-729, 1997
- 49. Desandes E, Guissou S, Ducassou S, et al: Neonatal solid tumors: Incidence and survival in France. Pediatr Blood Cancer 63:1375-1380, 2016
- 50. Basta NO, James PW, Gomez-Pozo B, et al: Survival from childhood cancer in northern England, 1968-2005. Br J Cancer 105:1402-1408, 2011
- 51. Linabery AM, Ross JA: Childhood and adolescent cancer survival in the US by race and ethnicity for the diagnostic period 1975-1999. Cancer 113:2575-2596, 2008
- 52. Flores K, Crawford J, Piccioni D, et al: Survival factors in children with central nervous system brain tumors in California between 1988 and 2009. Neuro-oncol 15:iii32, 2013
- 53. Bishop AJ, McDonald MW, Chang AL, et al: Infant brain tumors: Incidence, survival, and the role of radiation based on Surveillance, Epidemiology, and End Results (SEER) Data. Int J Radiat Oncol Biol Phys 82:341-347, 2012
- 54. Ostrom QT, Chen Y, M de Blank P, et al: The descriptive epidemiology of atypical teratoid/rhabdoid tumors in the United States, 2001-2010. Neuro-oncol 16:1392-1399, 2014
- 55. Jung KW, Yoo H, Kong HJ, et al: Population-based survival data for brain tumors in Korea. J Neurooncol 109:301-307, 2012
- 56. Percy C, Van Holten V, Muir C (eds): International Classification of Diseases for Oncology, (ed 2). Geneva, WHO, 1990.
- 57. Georgakis MK, Karalexi MA, Kalogirou El, et al: Incidence, time trends and survival patterns of childhood pilocytic astrocytomas in Southern-Eastern Europe and SEER, US. J Neurooncol 131:163-175, 2017
- Narita Y, Shibui S: Trends and outcomes in the treatment of gliomas based on data during 2001-2004 from the Brain Tumor Registry of Japan. Neurol Med Chir (Tokyo) 55:286-295, 2015
- 58a. Brodbelt A, Greenberg D, Winters T, et al: Glioblastoma in England: 2007-2011. Eur J Cancer 51:533-542, 2015
- 59. Sturm D, Pfister SM, Jones DTW: Pediatric gliomas: Current concepts on diagnosis, biology, and clinical management. J Clin Oncol 35:2370-2377, 2017
- 60. Louis DN, Ohgaki H, Wiestler OD, et al (eds): WHO Classification of Tumours of the Central Nervous System (ed 4). Geneva, WHO, 2007.

Girardi et al

- 61. Steliarova-Foucher E, Stiller C, Lacour B, et al: International classification of childhood cancer, third edition. Cancer 103:1457-1467, 2005
- 62. Stokland T, Liu JF, Ironside JW, et al: A multivariate analysis of factors determining tumor progression in childhood low-grade glioma: A population-based cohort study (CCLG CNS9702). Neuro-oncol 12:1257-1268, 2010
- 63. Qaddoumi I, Sultan I, Gajjar A: Outcome and prognostic features in pediatric gliomas: A review of 6212 cases from the Surveillance, Epidemiology, and End Results database. Cancer 115:5761-5770, 2009
- 64. Hershatter BW, Halperin EC, Cox EB: Medulloblastoma: The Duke University Medical Center experience. Int J Radiat Oncol Biol Phys 12:1771-1777, 1986
- 65. Packer RJ, Sutton LN, Elterman R, et al: Outcome for children with medulloblastoma treated with radiation and cisplatin, CCNU, and vincristine chemotherapy. J Neurosurg 81:690-698, 1994
- 66. Packer RJ, Gajjar A, Vezina G, et al: Phase III study of craniospinal radiation therapy followed by adjuvant chemotherapy for newly diagnosed average-risk medulloblastoma. J Clin Oncol 24:4202-4208, 2006
- 67. Kleihues P, Louis DN, Scheithauer BW, et al: The WHO classification of tumors of the nervous system. J Neuropathol Exp Neurol 61:215-225, 2002
- 68. De Angelis R, Francisci S, Baili P, et al: The EUROCARE-4 database on cancer survival in Europe: Data standardisation, quality control and methods of statistical analysis. Eur J Cancer 45:909-930, 2009
- 69. Lorez M, Bordoni A, Bouchardy C, et al: Evaluation of completeness of case ascertainment in Swiss cancer registration. Eur J Cancer Prev 26:S139-S146, 2017
- 70. WHO: Global initiative for childhood cancer. https://www.who.int/cancer/childhood-cancer/en/.
- 71. Louis DN, Perry A, Reifenberger G, et al: The 2016 World Health Organization Classification of Tumors of the Central Nervous System: A summary. Acta Neuropathol 131:803-820, 2016

APPENDIX

TABLE A1. Strategy for Searching Embase Search Term and Order

Exposu	re domain: central nervous system tumor
1	"central nervous system tumo?r*".mp.
2	"central nervous system cancer*".mp.
3	"central nervous system neoplasm*".mp.
4	"brain cancer*".mp.
5	"brain tumo?r*".mp.
6	"brain neoplasm*".mp.
7	"cns cancer*".mp.
8	"cns tumo?r*".mp.
9	exp central nervous system neoplasms
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
Outcom	ne domain: survival
11	"survival".mp.
12	"survival analysis".mp.
13	exp survival rate
14	11 or 12 or 13
Study d	lesign domain: longitudinal observational studies
15	"cancer registr*".mp.
16	"international comparison*".mp.
17	exp epidemiology
18	exp life tables
19	exp registries
20	15 or 16 or 17 or 18 or 19
21	exp clinical trial, phase i or exp clinical trial, phase ii or exp clinical trial, phase iii or exp clinical trial, phase iv or exp controlled clinical trial or exp randomized controlled trial or exp double-blind method or exp random allocation or exp single-blind method
22	"randomized controlled trial".mp.
23	"clinical trial".mp.
24	"clinical trial, phase i".pt.
25	"clinical trial, phase ii".pt.
26	"clinical trial, phase iii".pt.
27	"clinical trial, phase iv".pt.
28	"controlled clinical trial".pt.
29	"randomized controlled trial".pt.
30	"clinical trial".pt.
31	21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32	20 not 31

(Continued in next column)

TABLE A1. Strategy for Searching Embase (Continued) Search Term and Order

Combin	ation of the above domains
33	10 and 14 and 32
34	"comment".pt.
35	"letter".pt.
36	"editorial".pt.
37	exp case reports
38	exp comment
39	exp letter
40	exp editorial
41	34 or 35 or 36 or 37 or 38 or 39 or 40
42	33 not 41
43	animals
44	humans
45	43 not 44
46	42 not 45

Abbreviations: mp, multi-purpose (the database looks for the keywords in the default set of fields); exp, explosion (the database searches not only for the medical subject heading but also for many related terms); pt, publication type.

TABLE A2. Morphology Grouping Strategy in the Systematic Review Morphology Grouping Strategy in the Systematic Review	Definitions As Adopted in the Studies
Embryonal tumor	Embryonal tumor
Medulloblastoma	Medulloblastoma Ependymoma and medulloblastoma
Primitive neuroectodermal tumor	PNET Supratentorial PNET
Atypical teratoid/rhabdoid tumor	AT/RT
Astrocytoma (broad group)	Astrocytoma Astrocytoma + pilocytic astrocytoma IIIb (ICCC-3)
Astrocytoma WHO grade I/II	Astrocytoma WHO grade I/II Astrocytoma low grade
Pilocytic astrocytoma	Astrocytoma WHO grade I Pilocytic astrocytoma
Diffuse astrocytoma	Astrocytoma WHO grade II Diffuse astrocytoma Fibrillary astrocytoma Astrocytoma NOS
Astrocytoma WHO grade III/IV	Astrocytoma WHO grade III/IV Astrocytoma high grade Glioblastoma and anaplastic astrocytoma
Anaplastic astrocytoma	Anaplastic astrocytoma Astrocytoma WHO grade III
Glioblastoma	Glioblastoma

Abbreviations: ICCC-3, International Classification of Childhood Cancer, third edition; NOS, not otherwise specified.

First Author and Year of Publication	Quality Indicators	Outcome Measure	5-Year Survival (95% Cl)
Agerlin et al. (1999) ²⁸	MV: 100%	Observed survival	Medulloblastoma: 1960-1964: 8%; 1980-1984: 36%
Associazione Italiana Registri Tumori (2012) ²⁶	MV: 90%-94% DCO and autopsy only excluded	Observed survival	Embryonal tumor: 62% (53% to 70%)
Alston et al (2013) ²⁷	Not specified	Observed survival	Medulloblastoma: 1954-1964: 29% (SE, 7.3%); 1987-1997: 52% (10.4%)
Baade et al (2010) ²¹	MV: 95% DCO and autopsy only excluded	Relative survival	Astrocytoma: 79% (75% to 82%) Embryonal tumor: 49% (43% to 54%)
Basta et al (2011) ⁵⁰	Lost to follow-up: $< 1\%$	Observed survival	Astrocytoma: 1968-1977: 60% (46% to 72%); 1978-1987: 79% (65% to 88%); 1988-1997: 72% (59% to 81%); 1998-2005: 77% (63% to 87%) PNET: 1968-1977: 24% (11% to 41%); 1978-1987: 45% (27% to 61%); 1988-1997: 43% (23% to 62%); 1998-2005: 63% (39% to 80%)
Bellil et al (2008) ¹³	Not specified	Observed survival	Astrocytoma (Iow grade): 78% Medulloblastoma: 27% Hospital-based estimates
Ben Arush et al (2010) ⁴⁴	Not specified	Observed survival	Astrocytoma (WHO grade I/II): 82% Astrocytoma (WHO grade III): 55% Pilocytic astrocytoma: 95% Medulloblastoma: 69% Glioblastoma multiforme: 15%
Berger et al (2006) ³⁷	Not specified	Observed survival	Astrocytoma: 1987-1993: 63% (52% to 72%); 1994-1999: 82% (68% to 90%) Medulloblastoma: 1987-1993: 49% (34% to 61%); 1994-1999: 46% (23% to 67%)
Bishop et al (2012) ⁵³	Not specified	Observed survival	Supratentorial PNET: 35%
Brodbelt et al (2015) ^{58a}	MV: 90%	Relative survival	Glioblastoma: 15%
Chan et al (2007) ⁴³	MV: 100%	Observed survival	Medulloblastoma: 51%
Coll et al (2015) ²⁰	Not specified	Observed survival	Astrocytoma (behavior not specified): 1986-1999: 63% (52% to 72%); 2000-2009; 92% (77% to 97%) Embryonal tumor: 1986-1999: 45% (24% to 64%); 2000-2009: 50% (25% to 70%)
Dama et al (2005) ³⁰	MV: 79% DCO excluded Lost to follow-up: 0.9%	Observed survival	Astrocytoma: 1970-1974: 41%; 1975-1979: 58%; 1980-1984: 78%; 1985-1989: 74%; 1990-1994: 88%; 1995-1999: 79% Medulloblastoma: 1970-1974: 0%; 1975-1979: 22%; 1980-1984: 46%; 1985-1989: 78%; 1990-1994: 56%; 1995-1999: 59%
	(Con	ntinued on following page)	

TABLE A3. Studies Included in the Systematic Review

First Author and Year of Publication	Quality Indicators	Outcome Measure	5-Year Survival (95% CI)
Davis et al (1998) ³¹	Not specified	Observed survival	Glioblastoma: 21% (15% to 27%) Astrocytoma (only malignant): 72% (69% to 74%) Pilocytic astrocytoma: 89% (84% to 93%) Medulloblastoma: 1973-1980: 67% (66% to 68%); 1981-1985: 71% (70% to 72%); 1986-1991: 72% (71% to 73%)
Desandes et al (2008) ³⁸	Lost to follow-up: 2.6%	Observed survival	Astrocytoma: 1990-1994: 74% (68% to 81%); 1995-1999: 81% (68% to 81%) Medulloblastoma: 1990-1994: 51% (38% to 64%); 1995-1999: 61% (49% to 74%) PNET: 1990-1994: 29% (9% to 48%); 1995-1999: 30% (9.9% to 50%)
Desandes et al (2014) ²⁵	Lost to follow-up: 7.5%	Observed survival	Astrocytoma: 2000-2002: 84% (80% to 87%); 2003-2005: 90% (87% to 93%); 2006-2008: 87% (83% to 90%) Astrocytoma (low grade): 94% (92% to 95%) Astrocytoma (high grade): 22% (15% to 29%) Embryonal tumor: 2000-2002: 51% (45% to 57%); 2003-2005: 53% (46% to 58%); 2006-2008: 58% (51% to 64%)
Desandes et al (2016) ⁴⁹	MV: 80% Lost to follow-up: 0.3%	Observed survival	Astrocytoma: 50% (15% to 77%) Medulloblastoma: 50% (0.5% to 91%) PNET: 0% AT/RT: 0%
Ellison et al $(2007)^{24}$	MV: 89% DCO and autopsy only excluded	Observed survival	Astrocytoma: 83% (79% to 86%) Embryonal tumor: 60% (52% to 66%)
Fairley et al (2016) ⁴¹	Not specified	Observed survival	Medulloblastoma: 1990-1999: 55% (44% to 64%); 2000-2013: 71% (61% to 79%) Medulloblastoma: 0-14 years: 63% (55% to 70%) PNET: 1990-1999: 36% (19% to 53%); 2000-2013: 30% (15% to 48%) PNET: 0-14 years: 27% (15% to 41%)
Flores et al $(2013)^{52}$	Not specified	Observed survival	Pilocytic astrocytoma: 99% PNET: 81%
Gatta et al (2005) ¹⁹	MV: 95% DCO and autopsy only excluded Lost to follow-up: 1.5% < 4 years of follow-up: 4% Unspecified morphology: 3.5%	Observed survival	Astrocytoma (only malignant): 1983-1985: 72%; 1986-1988: 75%; 1989-1991: 77%; 1992-1994: 78% Embryonal tumor: 1983-1985: 46%; 1986-1988: 49%; 1989-1991: 48%; 1992-1994: 52%
Gatta et al (2009) ²³	MV: 95% DCO and autopsy only excluded < 5 years of follow-up: 2.6% Unspecified morphologies: 3.8%	Observed survival	Astrocytoma (only malignant): 1995-1999: Northern Europe: 63% (53% to 74%). UK and Ireland: 61% (57% to 66%), Central Europe: 68% (64% to 72%), Southern Europe: 65% (58% to 72%); Eastern Europe: 63% (47% to 79%); 2000-2002: 63% (57% to 68%) Astrocytoma (including pilocytic astrocytoma): 1995-1999: Northern Europe: 83% (78% to 89%), UK and Ireland: 79% (76% to 81%), Central Europe: 65% (50% to 81%); 2000-2002: 78% (73% to 82%) Embryonal tumor: 1995-1999: Northern Europe: 65% (50% to 81%); 2000-2002: 78% (73% to 82%) Embryonal tumor: 1995-1999: Northern Europe: 61% (57% to 65%), UK and Ireland: 55% (50% to 66%), Central Europe: 61% (57% to 65%), Southern Europe: 66% (60% to 71%)

 ${\bf 22} \ \ \odot \ 2019$ by American Society of Clinical Oncology

TABLE A3. Studies Included in the Systematic Review (Continued)

First Author and Year of Publication	Quality Indicators	Outcome Measure	5-Year Survival (95% CI)
Gatta et al (2017) ¹⁰	MV: 87% DCO and autopsy only excluded < 5 years of follow-up: < 4% Unspecified morphology: 5.6%	Observed survival	Pilocytic astrocytoma: 95% (94% to 96%) Diffuse astrocytoma: 75% (67% to 81%) Astrocytoma NOS: 74% (71% to 77%) Anaplastic astrocytoma: 21% (16% to 26%) Glioblastoma: 14% (11% to 18%) Medulloblastoma: 65% (62% to 67%) PNET: 41% (36% to 45%) AT/RT: 23% (18% to 29%)
Georgakis et (2017) ⁵⁷	MV: 97%	Observed survival	Pilocytic astrocytoma: SEE: 1983-1999: 88% (8% to 92%); 2000-2004: 92% (88% to 94%); SEER: 1973-1989: 91% (86% to 95%); 1990-1999: 98% (96% to 99%); 2000-2012: 98% (97% to 98%)
llveskoski et al (1997) ⁴⁸	Not specified	Observed survival	Medulloblastoma: 1975-1985: 11% (0% to 32%); 1986-1993: 43% (17% to 68%)
Jung et al (2012) ⁵⁵	MV: 100%	Observed survival	Astrocytoma (only malignant): 75% Anaplastic astrocytoma: 21% Glioblastoma: 19%
Kaatsch et al (2001) ³⁶	Not specified	Observed survival	Astrocytoma (WHO grade I/II): 82% (80% to 84%) Astrocytoma (WHO grade III/IV): 24% (17% to 32%) Medulloblastoma: 53% (49% to 57%) Supratentorial PNET: 52% (46% to 59%)
Karalexi et al (2015) ¹⁴	MV: 58%-91% DCO excluded Lost to follow-up: 0%- 3.6% Unspecified morphology: 0%-37%	Observed survival	Astrocytoma (only malignant): 61% (58% to 63%) Embryonal tumor: 40% (37% to 43%)
Khanna et al (2017) ⁴⁶	Not specified	Relative survival	Medulloblastoma: <1 year: 48% (33% to 62%); 1-4 years: 62% (56% to 67%); 5-9 years: 75% (70% to 79%); 10-14 years: 80% (72% to 86%)
Kramarova et al (1996)≊	MV: 98% Lost to follow-up: 6.5%	Observed survival	Ependymoma and medulloblastoma: 1968-1972: 2.7%; 1973-1977: 18%; 1978-1982: 22%; 1983-1987: 26% Astrocytoma (behavior not specified): 1968-1972: 40%; 1973-1877: 71%; 1978-1982: 55%; 1983-1987: 56%
Lannering et al (2009) ⁴⁰	Not specified	Observed survival	Astrocytoma (low grade): 93% (1%) Astrocytoma (high grade): 28% (5%) Medulloblastoma: 63% (4%) Supratentorial PNET: 47% (7%)
Linabery et al (2008) ⁵¹	MV: 95% Lost to follow-up: 14%	Observed survival	Astrocytoma: 1975-1979: 69% (64% to 73%); 1985-1989: 73% (69% to 77%); 1995-1999: 85% (82% to 89%) PNET: 1975-1979: 47% (39% to 55%); 1985-1989: 54% (47% to 62%); 1995-1999: 65% (59% to 71%)
	(Cont	tinued on following page)	

TABLE A3. Studies Included in the Systematic Review (Continued)

First Author and Year of Publication	Quality Indicators	Outcome Measure	5-Year Survival (95% CI)
Magnani et al (1997) ³²	MV: 64%-94% DCO and autopsy only excluded Lost to follow-up: 1.3%	Observed survival	Astrocytoma (only malignant): 1978-1981: 65%; 1982-1985: 75%; 1986-1989: 76% Medulloblastoma: 1978-1981: 36%; 1982-1985: 56%; 1986-1989: 85%
Magnani et al (2006) ¹⁸	MV: 86% DCO excluded < 5 years of follow-up: 1%-74% Lost to follow-up: 4% Unspecified morphology: 0%-16%	Observed survival	Embryonal tumor: 1978-1982: 37%; 1983-1987: 44%; 1988-1992: 48%; 1993-1997: 52%
Mathew et al (2014) ⁴²	MV: 100%	Observed survival	Pilocytic astrocytoma: NRCT: 96%; SEER: 97% Anaplastic astrocytoma: NRCT: 19%; SEER: 30% Glioblastoma: NRCT: 8%; SEER: 22% Medulloblastoma: NRCT: 65%; SEER: 71% PNET: NRCT: 32%; SEER: 57%
Narita et al (2015) ⁵⁸	Not specified	Observed survival	Diffuse astrocytoma: 60% Anaplastic astrocytoma: 18% Glioblastoma: 7.8 % Hospital-based estimates
Ostrom et al (2015) ⁵⁴	Not specified	Relative survival	AT/RT: 28% (21% to 36%)
Park et al (2016) ¹⁷	Not specified	Relative survival	Astrocytoma (behavior not specified): 1993-1995: 55%; 1996-2000: 49%; 2001-2005: 57%; 2006-2010: 54%; 2007-2011: 51% Embryonal tumor: 1993-1995: 49%; 1999-2000: 55%; 2001-2005: 57%; 2006-2010: 61%; 2007-2011: 60%
Roldan et al (2008) ³⁴	MV: 100%	Observed survival	Medulloblastoma: 56% (36% to 75%)
Schindler et al (2017) ³⁵	MV: 94% Unspecified morphology: 1.4%	Observed survival	Astrocytoma (behavior not specified): 1984-1993: 82% (71% to 89%); 1994-2003: 84% (77% to 90%); 2004-2013: 89% (82% to 94%) Medulloblastoma: 1984-1993: 50% (36% to 62%): 1994-2003: 68% (55% to 77%); 2004-2013: 64% (52% to 75%) PNET: 1984-1993: 33% (17% to 51%); 1994-2003: 37% (22% to 51%); 2004-2013: 30% (19% to 42%)
Smoll et al (2012) ⁴⁵	Not specified	Relative survival	Medulloblastoma: <1 year: 42% (22% to 61%); 1-9 years: 72% (66% to 77%); 10-19 years: 69% (58% to 78%) PNET: <1 year: 14% (2% to 39%); 1-9 years: 64% (54% to 72%); 10-19 years: 57% (41% to 70%)
Stagno et al (2014) ¹⁶	MV: 100%	Relative survival	Medulloblastoma: 0%
Swaminathan et al (2008) ¹⁵	MV: 95% DCO excluded Lost to follow-up: 15%	Observed survival	Astrocytoma (behavior not specified): 39%
	(Con	ntinued on following page)	

TABLE A3. Studies Included in the Systematic Review (Continued)

TABLE A3.Studies Included in tFirst Author and Year of	he Systematic Review (Continued)	:	
Publication	Quality Indicators	Outcome Measure	5-Year Survival (95% CI)
Tseng et al (2006) ³³	DCO and autopsy only excluded	Observed survival	Pilocytic astrocytoma: 88% Astrocytoma NOS: 71% Diffuse astrocytoma: 78% Anaplastic astrocytoma: 19% Glioblastoma: 20% Medulloblastoma: 41%
Trama et al (2016) ⁴⁷	MV: 84%-100% DCO, autopsy only, or zero survival excluded Lost to follow-up: 0%-9.7% Unspecified morphologies: 0%-18%	Relative survival	Astrocytoma (only malignant): 62% (1.1%) Medulloblastoma: 63% (1.3%)
Tulla et al (2015) ³⁹	MV: 100% Lost to follow-up: 4%	Observed survival	Medulloblastoma: 1991-1994: 63% (57% to 68%); 1995-1998: 64% (58% to 70%); 1999-2002: 80% (74% to 85%); 2003-2006: 77% (72% to 83%); 2007-2010: 73% (67% to 79%) PNET: 1991-1994: 33% (23% to 44%); 1995-1998: 35% (23% to 46%); 1999-2002: 35% (23% to 47%); 2003-2006: 44% (30% to 58%); 2007-2010: 61% (44% to 78%) AT/RT: 1999-2002: 21% (7% to 34%); 2003-2006: 28% (15% to 42%); 2007-2010: 42% (28% to 57%)
Walsh et al (2011) ²²	MV: 93% DCO and autopsy only excluded Lost to follow-up: 0% Follow-up < 5 years: 35% Unspecified morphology: 5.1%	Observed survival	Astrocytoma: 1994-1999: 79% (70% to 86%); 2000-2005: 83% (72% to 90%) Embryonal tumor: 1994-1999: 49% (32% to 63%); 2000-2005: 59% (35% to 77%)
Abbreviations: AT/RT, atypical	teratoid/rhabdoid tumor; DCO, death certificate only; MV	/, microscopic verification; N	RCT, National Registry of Childhood Tumors; NOS, not otherwise specified; PNET,

primitive neuroectodermal tumor; SE, standard error; SEE, Southern and Eastern Europe; UK United Kingdom. ULLY; IVIV, ILLIC DOO, UCALL CEL 5 2 2 Ŋ ADDREVIATIONS: ATTRT, ALYPICAL