European Journal of Cancer (2012) xxx, xxx–xxx

Available at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.ejconline.com

Childhood cancer: Incidence and early deaths in Argentina, 2000–2008

Florencia Moreno [a,*], Dora Loria [b,c], Graciela Abriata [c], Benedetto Terracini [d], ROHA network

[a] *Argentinean Oncopediatric Registry, National Cancer Institute, Buenos Aires City, Argentina*
[b] *Angel Roffo Institute of Oncology, Research Area, Buenos Aires City, Argentina*
[c] *Surveillance and Epidemiological Analysis, National Cancer Institute, Buenos Aires City, Argentina*
[d] *University of Turin, Turin, Italy*

KEYWORDS
Cancer childhood incidence
Epidemiology
Population registries
Survival
Early death

Abstract ***Introduction:*** Knowledge on the epidemiology of childhood cancer in Latin America is limited. The Argentinean Oncopaediatric Registry (ROHA) has been active since 2000. Data for 2000–2008 are described in the present work.
Materials and methods: ROHA is fed from a network of paediatric units and population-based cancer registries. Cases are coded by the International Classification of Childhood Cancer.
Results: A total of 11447 children aged 0–14 diagnosed with cancer were reported. Histologically verified cases and cases identified only through death certificates were respectively 91% and 6%. The annual age of standardised incidence rate of all cancers was 128.5 per million. Proportions of leukaemia's, lymphoma's and Central Nervous System tumours were 37%, 13% and 18%. The distribution of rates of acute lymphatic leukaemia by the year of age showed a peak around age 3. Eighty percent of the patients are treated in public hospital and around 35% migrate for some of the treatment. Deaths within a month of diagnosis were 5% in 2000 and 3% in 2008.
Conclusions: Childhood cancer incidence in Argentina is somewhat lower than in North American and in Western European countries: the deficit is mainly due to tumours of the Central Nervous system and other solid tumours. Childhood cancer incidence did not show any tendency to increase. The possible excess of Hodgkin lymphoma in the Northeast region requires additional studies. Early deaths after diagnosis indicate an unsatisfactory state of the overall organisation of childhood cancer care. Data from ROHA are used for decision making at local and national levels.

* *Corresponding author:* Address: ROHA, Av. Julio A Roca 781, Piso 11, C1067ABC, CABA, Argentina. Tel.: +54 11 5235 7555; fax: +54 11 5235 7553.
E-mail address: roha@roha.org.ar (F. Moreno).

0959-8049/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ejca.2012.08.001

1. Introduction

The primary purpose of population-based childhood cancer registries is twofold. On one hand, the identification of differences in incidence within and between populations may provide aetiological clues. In addition, since nowadays most children with cancer can be cured, survival rates and other population-based clinical indicators provide information on the quality of cancer care given to the paediatric population served by registry. Childhood cancers are rare (in the Western world, approximately one child in 500 develops a cancer by age 15), so that reliable figures can be obtained only from relatively large paediatric population. Out of 13 cancer registries serving Latin American areas included in 'Cancer Incidence in Five Countries, Volume IX',[1] and in 'International Incidence of childhood Cancer, Volume II'[2] only those of Costa Rica, Peru and Sao Paulo (Brazil) estimate incidence rates from paediatric populations larger than one million.

A nationwide childhood cancer registry in Argentina (Registro Oncopediatrico Hospitalario Argentino, ROHA) was implemented in the late nineties through a network of hospitals. ROHA has adopted standard methods on cancer registration,[3] which are applicable for registration in public and private hospitals, thus allowing for analyses and use for decision making both at the local and national levels.

Incidence of childhood cancer in Argentina between 2000 and 2008 is reported in the present study. Attention is given to indicators of quality of registration and their distribution over the country. Data on deaths occurring early after diagnosis are presented, which provide some indication on the quality of childhood cancer care in Argentina.

ROHA was a part of Kaleidos Foundation (www.fundacionkaleidos.org). Since 2011 it is part of the newly created Argentinean National Cancer Institute. ROHA information can be found at www.roha.org.ar.

2. Methods

Argentina comprises 24 political units, 23 provinces and the city of Buenos Aires, capital of the country, which is a political unit separated from the province of Buenos Aires. The political units are commonly grouped in five major geographic areas ('regions') as shown in the map (Fig. 1). In 2000, the country population aged 0–14 was 10.2 millions with 60% living in the Central Region (CeR), 14% in the North-western Region (NW), 12% in the North-eastern Region (NE), 8% in the Cuyo Region (CuR) and 6% in the Patagonia Region (PR).

In 2007 the overall infant mortality rate was 13.3 per 1000 born alive with a range between 22.9 per 1000 in Formosa (province included in NE region) and 8.4 per 1000 born alive in Buenos Aires City.

ROHA is fed through different sources. Most cases are forwarded from a network of 49 oncological paediatric units (OPU), mainly located in the central region. During 2000–2008, 86% of cases were reported to ROHA from the OPU network. In addition, ROHA obtains information from 12 traditional (non-exclusively paediatric) population-based cancer registries serving 30% of the population of Argentinean corresponding regions: CeR 14%, NW 74%, NE 29% CuR 55% PR 90%. A 3% of data included in ROHA comes from population-based cancer registries as the only source.

At regular intervals, cases are reported to ROHA, where duplicates and prevalent cases are identified and diagnoses are coded. Data reported for each patient include: patient's name and surname, number of identification cards, date of birth, diagnosis, sex, province of residence, address, histopathology, tumour site and basis of diagnosis. Cases are coded according the Third edition of the International Classification of Diseases for Oncology (ICD-O3)[4] and the International Classification of Childhood Cancer third edition (ICCC-3).[5] Benign tumours

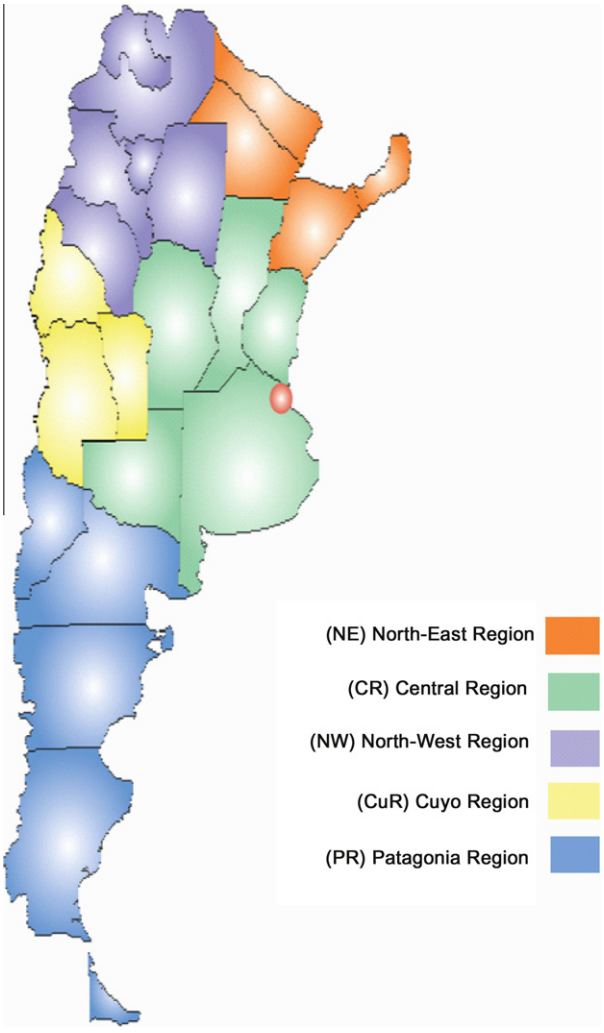

Fig. 1. Argentina by regions.

Please cite this article in press as: Moreno F. et al., Childhood cancer: Incidence and early deaths in Argentina, 2000–2008, *Eur J Cancer* (2012), http://dx.doi.org/10.1016/j.ejca.2012.08.001

are excluded from the computation of rates, with the exception of those of the Central Nervous System (CNS).

For each of the 24 political units, the National Institute of Statistics and Census provided yearly death certificate cases for all causes of death. The population data are from the 2001 census and the annual inter-census estimates; from 2000 and 2002 through 2008. Age-adjusted incidence rates were estimated by the direct method using the world standard population.

Each OPU takes care of the clinical follow up of each child and forwards to ROHA periodical updates of his/her clinical conditions. For the ascertainment of the follow up information for children who are not seen at OPU we cross all ROHA's data with the database of the People National Registry and confirm the children's status yearly. In order to estimate the mortality/incidence ratio (M/I) as an index of quality of ROHA, rates of mortality from cancer in the paediatric age were obtained from the Statistical Office of the Ministry of Health.

3. Results

3.1. Quality of registration

A total of 11447 children aged 0–14 diagnosed a cancer in 2000–2008 were reported to ROHA, corresponding to an average of 1272 cases per year. In 2000 and 2001, the first two years in which ROHA was active, recorded cases were respectively 1208 and 1290. The proportion of cases confirmed through microscopical examination and the proportion of cases reported to the registry only through the death certificate were respectively 91% and 6% with no relevant differences among the regions of the country. The percentage of cases that were only reported through a general cancer registry is 3%.

Given the distribution of the OPUs, referral of children with cancer to hospitals located outside the province of residence is not uncommon. During the period covered by the present study, 57% of children were taken care of in hospitals located in their province of residence, 37% in the City of Buenos Aires and 6% in hospitals located in provinces other than that of residence.

During the same period, the M/I ratio ($\times$100) was 35.3. It peaked to 41.3 in NE region where the ratios for leukaemias and CNS tumours were also higher than in the rest of the country (respectively 41.7 versus 35.3 and 57.1 versus 52.7).

Within the limits of ICCC-3 categories, precision of diagnosis was good. Only 87 out of 11447 (0.8%) cases were classified in the major category XII 'Other and unspecified tumours' (Table 1). Within major categories, leukaemias, lymphomas, renal and liver tumours, these cases were around 1%. Subtype 'unspecified' cases in categories in tumours of bone tumours and soft tissue ranged between 4% and 5%, and in tumours of CNS and carcinomas were respectively 23% and 42% (Table 1).

3.2. Incidence rates

All cancers: Table 1 describes age-standardised incidence rates (ASR) for each of the categories of childhood cancer.

Overall ASR ranged between 119 and 134 per million per year by region. Major categories contributing to the lower overall rates were CNS tumours in the NW and NE and leukaemias in CuR (Table 2).

Crude and ASR for all cancers and for all leukaemias as well as their 95% CI were estimated for children reporting residence in each of the 24 political units in a previous publication.[6]

Rates did not differ between the three triennia covered by this study (Table 3).

Leukaemias: Out of 4207 cases, 79%, 19% and 1% respectively were Acute Lymphocytic (ALL), Acute non-lymphocytic and other/unspecified (Table 1). The distribution of ALL by year of age showed the typical peak at age 2–3 (Fig. 2).

Lymphomas (n: 1454): This group includes 43% Hodgkin's lymphomas (HL), 29% non-Hodgkin lymphomas, 17% Burkitt tumours and 11% 'lymphoreticular tumours' (Table 1). The main subtype of the HL is nodular sclerosis for the entire country. In the NE region, the incidence rate of Childhood lymphomas was 20.4 (12.1–28.6) versus 15.8 (13.2–18.0) in the whole country. Most of the excess was due to Hodgkin's lymphoma, for which the annual age-standardised rate was 8.7, i.e. higher than the upper limit of the 95% confidence interval of the national rate (4.9–7.9). For the 10–14 age group the specific rates were 9.5 and 7.4 per million for the country and NE region respectively. In particular, in age 0–9, we registered 9 cases (annual average for the NE) versus an expected figure of 5, whose Age Standardized Incident Rate (ASR) was 1.8 (2.2; 1.4).

Tumours of the Central Nervous System (n: 2122): rates were lower in the NE and NW regions (Table 2). Astrocytomas were 27%, embryonal tumours 23%, ependymomas 12%, other gliomas 6%, other specified tumours 9% and unspecified tumours 23% (Table 1). As shown in Table 2, rates were lower in the NE and NW regions.

Other cancer types: ASR for sympathetic nervous system tumours (most of them neuroblastoma) was lower in the NE and NW regions than in the rest of the country (Table 2). Out of 395 registered cases of retinoblastoma, 7% were unknown, 68% monolateral and 25% bilateral. Twenty-three percent of the former and 54% of the latter were diagnosed during the first year of life. Three-hundred and twenty-five bone cancers were diagnosed as osteosarcomas versus 176 Ewing's sarcomas. Among the 697 tumours of the soft tissues, 48% were

Please cite this article in press as: Moreno F. et al., Childhood cancer: Incidence and early deaths in Argentina, 2000–2008, *Eur J Cancer* (2012), http://dx.doi.org/10.1016/j.ejca.2012.08.001

Table 1
Numbers of cases (n) by age at diagnosis, sex ratio, annual crude and standardised incidence rates by diagnostic group. Argentina, 2000–08.

ICCC-3 diagnostic group[a]	*n*				Rel. freq. (%)				Rates per Million				
	0	1–4	5–9	10–14	All	M/F[b]	Overall	Group	0–4	5–9	10–14	Crude	ASR[c]
I Leukaemia	240	1705	1204	1058	4207	1.2	36.8	100.0	64.7	38.9	34.1	45.7	47.5
Lymphoid	135	1431	981	780	3327	1.2	29.1	79.1	52.1	31.7	25.1	36.2	37.7
Acute non-lymphocytic	99	260	203	266	828	1.1	7.2	19.7	11.9	6.6	8.6	9.0	9.2
Other specified	6	14	20	12	52	3.0	0.5	1.2	0.7	0.6	0.4	0.6	0.6
II Lymphomas	58	346	517	533	1454	2.1	12.7	100.0	13.4	16.7	17.2	15.8	15.6
Hodgkin' s disease	4	96	246	272	618	2.6	5.4	42.5	3.3	8.0	8.8	6.7	6.4
Non-Hodgkin lymphomas	7	77	157	184	425	1.9	3.7	29.2	2.8	5.1	5.9	4.6	4.4
Burkitt's lymphoma	–	82	95	64	241	2.3	2.1	16.6	2.7	3.1	2.1	2.6	2.6
Miscellaneous lymphoreticular neoplasms	47	88	12	8	155	1.0	1.4	10.7	4.5	0.4	0.3	1.7	1.9
Unspecified	–	3	7	5	15	14.0	0.1	1.0	0.1	0.2	0.2	0.2	0.2
III Brain and spinal neoplasms	158	650	753	561	2122	1.3	18.5	100.0	26.9	24.4	18.1	23.1	23.5
Ependymoma	25	112	75	43	255	1.4	2.2	12.0	4.6	2.4	1.4	2.8	2.9
Astrocytoma	38	158	199	176	571	1.2	5.0	26.9	6.5	6.4	5.7	6.2	6.2
Primitive neuroectodermal tumours	32	167	194	102	495	1.6	4.3	23.3	6.6	6.3	3.3	5.4	5.5
Other gliomas	4	27	44	41	116	1.1	1.0	5.5	1.0	1.4	1.3	1.3	1.2
Other specified	12	44	64	73	193	1.6	1.7	9.1	1.9	2.1	2.4	2.1	2.1
Unspecified	47	142	177	126	492	1.0	4.3	23.2	6.3	5.7	4.1	5.3	5.5
IV Sympathetic nervous system tumours	189	322	92	38	641	1.1	5.6	100.0	17.0	3.0	1.2	7.0	7.9
Neuroblastoma	188	317	86	33	624	1.1	5.5	97.3	16.8	2.8	1.1	6.8	7.7
Other	1	5	6	5	17	1.4	0.1	2.7	0.2	0.2	0.2	0.2	0.2
V Retinoblastoma	125	238	27	5	395	1.2	3.5	100.0	12.1	0.9	0.2	4.3	5.0
VI Renal tumours	95	320	121	31	567	1.0	5.0	100.0	13.8	3.9	1.0	6.2	6.9
Wilms' tumour	95	314	116	19	544	1.0	4.8	95.9	13.6	3.8	0.6	5.9	6.7
Renal carcinoma	–	3	2	12	17	0.7	0.1	3.0	0.1	0.1	0.4	0.2	0.2
Unspecified	–	3	3	–	6	2.0	0.1	1.1	0.1	0.1	–	0.1	0.1
VII Hepatic tumours	45	64	20	30	159	1.5	1.4	100.0	3.6	0.6	1.0	1.7	1.9
Hepatoblastoma	43	60	10	10	123	1.4	1.1	77.4	3.4	0.3	0.3	1.3	1.5
Hepatic carcinoma	1	4	9	20	34	2.1	0.3	21.4	0.2	0.3	0.6	0.4	0.3
Unspecified	1		1	–	2	1.0	0.0	1.3	–	–	–	–	–
VIII Malignant bone tumours	4	40	151	347	542	1.3	4.7	100.0	1.5	4.9	11.2	5.9	5.4
Osteosarcoma	1	16	80	228	325	1.2	2.8	60.0	0.6	2.6	7.3	3.5	3.2
Chondrosarcoma	–	2	1	4	7	2.5	0.1	1.3	0.1	–	0.1	0.1	0.1
Ewing's sarcoma	2	19	58	97	176	1.3	1.5	32.5	0.7	1.9	3.1	1.9	1.8
Other specified	–	–	3	6	9	0.3	0.1	1.7	–	0.1	0.2	0.1	0.1
Unspecified	1	3	9	12	25	2.1	0.2	4.6	0.1	0.3	0.4	0.3	0.3
IX Soft tissue sarcomas	80	190	199	228	697	1.4	6.1	100.0	9.0	6.4	7.3	7.6	7.7
Rhabdomyosarcoma	39	119	105	72	335	1.6	2.9	48.1	5.3	3.4	2.3	3.6	3.8
Fibrosarcoma	17	20	28	52	117	1.4	1.0	16.8	1.2	0.9	1.7	1.3	1.3
Other specified	19	41	56	93	209	1.1	1.8	30.0	2.0	1.8	3.0	2.3	2.2

Unspecified	5	10	10	11	36	1.0	0.3	5.2	0.5	0.3	0.4	0.4	0.4
X Germ cell and gonadal neoplasms	52	105	52	161	370	0.9	3.2	100.0	5.2	1.7	5.2	4.0	4.1
Intracranial and intraspinal germ cell	3	2	13	49	67	1.6	0.6	18.1	0.2	0.4	1.6	0.7	0.7
Other and unspecified non–gonadal germ cell	22	23	7	8	60	0.4	0.5	16.2	1.5	0.2	0.3	0.7	0.7
Gonadal germ cell	25	71	30	90	216	0.9	1.9	58.4	3.2	1.0	2.9	2.3	2.4
Gonadal carcinoma	–	–	–	11	11	0.1	0.1	3.0	–	–	0.4	0.1	0.1
Other and unspecified	2	9	2	3	16	1.0	0.1	4.3	0.4	0.1	0.1	0.2	0.2
XI Carcinomas and epithelial neoplasms	6	27	41	132	206	0.9	1.8	100.0	1.1	1.3	4.3	2.2	2.1
Adrenocortical	2	8	4	5	19	0.1	0.2	9.2	0.3	0.1	0.2	0.2	0.2
Thyroid	–	3	8	16	27	0.4	0.2	13.1	0.1	0.3	0.5	0.3	0.3
Nasopharyngeal	–	–	5	19	24	1.4	0.2	11.7	–	0.2	0.6	0.3	0.2
Melanoma	2	7	6	17	32	1.1	0.3	15.5	0.3	0.2	0.5	0.3	0.3
Skin	–	2	6	8	16	2.2	0.1	7.8	0.1	0.2	0.3	0.2	0.2
Other and unspecified	2	7	12	67	88	1.0	0.8	42.7	0.3	0.4	2.2	1.0	0.9
XII Other and unspecified neoplasms	25	26	9	27	87	1.0	0.8	100.0	1.7	0.3	0.9	0.9	1.0
Other specified	4	7	2	4	17	0.9	0.1	19.5	0.4	0.1	0.1	0.2	0.2
Other unspecified	21	19	7	23	70	1.1	0.6	80.5	1.3	0.2	0.7	0.8	0.8
Total	1077	4033	3186	3151	11447	1.3	100.0	100.0	170.0	103.0	101.5	124.4	128.5

[a] ICCC-3: International Classification of Childhood Cancer Third Edition.
[b] M/F: sex ratio.
[c] ASR: age standardised incidence rate per 1000,000 population aged 0–14 years.

rabdo- and embryonal sarcomas, 17% fibrosarcomas and neurofibrosarcomas, 30% other specified histological types and 5% were unspecified.

3.3. Early deaths after diagnosis

Out of 11447 cases notified during the period, post diagnosis information on clinical course was available for 9653 children, 85% of the whole series. The proportions of cases dying within one month and within 12 months of diagnosis by the year of diagnosis are described in Fig. 3.

Early deaths after diagnoses were more frequent in residents in the NE and NW regions. For all cancers, in these regions, proportions of deaths within one month after diagnosis were respectively 9% and 8% versus 3.4% among residents in the CeR.

4. Discussion

ROHA represents an attempt to create and maintain a nation-wide population registry of childhood cancer in children in Latin America. In Argentina, as well as in other South American countries, data bases for an exhaustive ascertainment of cancer cases are not as much developed as in Europe and North America. In particular, there is no quality controlled centralised systematic registration of hospital discharges and services of pathology using electronic databases are limited. The willingness of the oncological paediatric units to join into a network has been vital for ROHA.

Cancer registries in developing countries are vulnerable to several common technical problems which could jeopardise the quality of the data collected.[7] However, the overall quality of the ROHA registration seems acceptable. The stability of the number of cases registered per year indicates that erroneous recording of prevalent cases, if any, is negligible.

Conventional indicators of quality used by cancer registries are the proportion of cases confirmed through a histological (or bone marrow) examination and the proportion of cases reported to the registry only through the death certification, DCO cases.[8] The proportions of microscopically confirmed and DCO cases are satisfactory. These indicators were uniform over the country and over the period covered by registration.

Within each major diagnostic category of the ICCC, with the exception of CNS tumours and carcinomas, the proportion of cases coded within the group 'XII Other and Unspecified Malignant Neoplasms' is small (0.8%). Contrary to observations in other developing countries,[9] there is no suggestion of under-registration of cancer in girls.

ROHA has made no attempt to confirm the child's province of residence provided by his/her relatives at the time of hospitalisation. In some instances, while collecting individual data, confusion between permanent

Table 2
Standardised incidence rates at age 0–14 years and major diagnostic group by regions. Argentina, 2000–08.

ICCC-3 diagnostic group[a]	Central ASR[b]	Northeast ASR[b]	Northwest ASR[b]	Cuyo ASR[b]	Patagonia ASR[b]	Country ASR[b]
I. Leukaemia	48.2	50.4	45.9	40.4	48.6	47.5
II. Lymphomas and Reticuloendothelial Neoplasms	15.2	20.4	14.4	13.8	14.9	15.6
III. CNS and Miscellaneous Intracranial and Intraspinal Neoplasms	25.4	18.7	19.5	22.8	24.4	23.5
IV. Sympathetic Nervous System Tumours	9.6	4.9	3.2	6.4	9.7	7.9
V. Retinoblastoma	5.6	4.0	3.8	4.9	4.1	5.0
VI. Renal Tumours	7.1	7.6	6.0	7.5	5.2	6.9
VII. Hepatic Tumours	1.9	1.3	2.8	1.1[a]	1.9	1.9
VIII. Malignant Bone Tumours	5.4	4.5	5.3	6.3	5.5	5.4
IX. Soft-Tissue Sarcomas	8.4	5.7	6.7	7.7	7.3	7.7
X. Germ Cell, Trophoblastic and Other Gonadal Neoplasms	4.0	4.2	4.2	4.5	3.1	4.1
XI. Carcinomas and Other Malignant Epithelial Neoplasms	2.3	1.5	1.0	2.5	2.5	2.1
XII. Other and Unspecified Malignant Neoplasms	1.2	0.6[c]	0.8[c]	0.9[c]	0.4[c]	1.0
Total	134.3	123.7	113.6	119.1	127.5	128.5

[a] ICCC-3: International Classification of Childhood Cancer Third Edition.
[b] ASR: age standardised rate per 1000,000 population aged 0–14 years.
[c] Less than 10 cases registered over the whole period.

Table 3
Standardised incidence rates at age 0–14 years and major diagnostic group by triennium. Argentina, 2000–08.

ICCC-3 diagnostic group[a]	ASR[b] 2000–02	ASR[b] 2003–05	ASR[b] 2006–08
I. Leukaemia	47.2	47.2	46.7
II. Lymphomas and Reticuloendothelial Neoplasms	15.5	15.7	15.3
III. CNS and Miscellaneous Intracranial and Intraspinal Neoplasms	22.9	23.8	23.3
IV. Sympathetic Nervous System Tumours	7.6	7.8	7.9
V. Retinoblastoma	4.3	5.0	5.4
VI. Renal Tumours	6.2	7.4	6.7
VII. Hepatic Tumours	1.8	1.9	1.9
VIII. Malignant Bone Tumours	5.7	5.6	5.0
IX. Soft-Tissue Sarcomas	7.1	8.2	7.6
X. Germ Cell, Trophoblastic and Other Gonadal Neoplasms	3.1	4.5	4.5
XI. Carcinomas and Other Malignant Epithelial Neoplasms	1.7	2.7	1.8
XII. Other and Unspecified Malignant Neoplasms	0.7	1.1	1.2
TOTAL	123.8	130.9	127.3

[a] ICCC-3: International Classification of Childhood Cancer Third Edition.
[b] ASR: age standardised incidence rate per 1000,000 population aged 0–14 years.

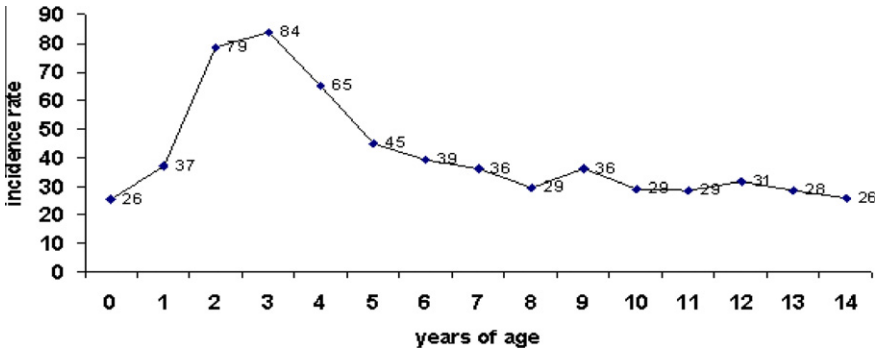

Fig. 2. Age specific acute lymphoblastic leukaemia incidence rates (per 1000,000 population) by age. Argentina 2000–08.

address and temporary domicile during the child's hospitalisation may have occurred. Thus, the apparent excess of incident cases in the city of Buenos Aires may be an artefact because of the concentration of

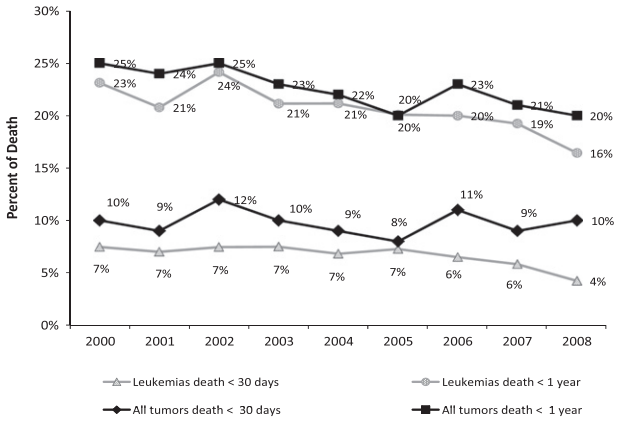

Fig. 3. Children diagnosed with tumours (all types) and leukaemias dying within 1 month or within 1 year after diagnosis (DCO cases are excluded). Argentina 2000–2008.

referral hospitals in this city. The contribution to incidence rates of children of other nationalities being treated for cancer in hospitals located in Argentina is negligible.

The ratio between mortality and incidence rates (M/I) obtained from two independent sources of case ascertainment is commonly used by conventional cancer registries.[10] Its usefulness to assess the quality of childhood cancer registration is questionable, since mortality rates are largely affected by the extent to which children with cancer can take advantage of the effective (and expensive) therapeutic protocols which have been developed.

Compared to developed countries, the M/I ratio of 35.3 in Argentina is high. For instance, in Italy it is 18.8.[11] This reflects a high mortality rate, most likely attributable to late diagnosis and/or inadequate access to effective therapeutic protocols.

This ratio is fairly uniform over the country, but for the NE region is higher than elsewhere: this might indicate either under-registration or an increased mortality rate (most likely attributable to late diagnosis and/or inadequate access to effective therapeutic protocols).

Argentine rates presented in this paper are compared with those from other countries prior periods (Table 4) corresponding to the ones available to date. In Argentina, as in other Latin American countries, the overall picture of childhood cancer incidence is similar to those of Western countries. They differ from those corresponding to the U.S, which exceeds the incidence in Argentina (Table 4). The variation in total rates for Latin American countries in comparison is less than the variation shown by the record rates of European regions for the Period 1988–1997.[12,13]

The Argentinean population is largely of European descent. Table 4 shows that for all cancers considered together, as well as for leukaemias and most solid tumours, age-standardised incidence rates in Argentina in the early 2000 are similar to those of Europe in the late 90s. However, tumours of the Central Nervous System and possibly those of the sympathetic nervous system seem to be under registered. Present data do not suggest that childhood cancer incidence in Argentina showed any tendency to increase during the period for which data are available. Reports from Europe[14–16] and from the US[17] estimated an increase in the order of 1% per year until the beginning of new millennium, for periods which did not overlap with the activity of ROHA. Indeed, the increment was hardly visible in Spain.[19]

The shape of the distribution of ALL by year of age and the typical peak around age 3 are similar to those observed in Europe in recent years. The peak emerged in the UK and in the US white population early in the 20th century.[18] It is believed to reflect the association between affluence and risk for common ALL.[19] Between 1970 and 2000, the peak has been less marked in Eastern than in Western European countries, but the gap has become progressively less obvious.[15]

As for internal comparisons, the lower incidence rates among children living in the NE and NW regions might reflect the relatively poor quality of registration in these regions (associated to the possibility of misrecording the province of residence in children being treated in hospitals outside their province of residence). Given the overall under registration in the NE region, the high incidence rate of lymphomas and particularly of HL in this region is unlikely to be a chance finding. NE is among the poorest regions of Argentina and an accelerated onset of HL in poor socioeconomic environments with a peak in age 5–9 (perhaps in relation to Epstein Barr virus) has been suggested elsewhere.[20] Altogether, however, variation of rates within Argentina seems more limited than in Brazil.[7]

Early deaths after diagnosis reflect inadequacies in the detection and appropriate referral of cases. Major causes of early deaths are delay in diagnosis, sepsis, toxicity of chemotherapy and surgical complications. The separate weight of these events cannot be analysed through the data collected by ROHA, which nevertheless indicate an unsatisfactory situation, in spite of an improvement over the years. In the SEER series in the United States, deaths within a month of diagnosis decreased from 3.1% in 1973–77 to 1.5% in 1993–1995.[21] Similarly, among cases reported to the Piedmont childhood cancer registry in Italy, deaths within a month of diagnoses decreased from 10.8% for cases diagnosed in the 70s to 1.8% for cases diagnosed in the 90s.[22] The latter study also showed a higher risk of early death for children referred to non-specialised centres.

The activities of a population-based cancer registry include evaluation of the effects of early diagnosis and treatment. Compared to clinical trials, registries collect less individual data on factors related to prognosis

Please cite this article in press as: Moreno F. et al., Childhood cancer: Incidence and early deaths in Argentina, 2000–2008, *Eur J Cancer* (2012), http://dx.doi.org/10.1016/j.ejca.2012.08.001

Table 4
Standardised incidence rates, relative frequencies at age 0–14 years and major diagnostic groups by countries.

ICCC -3 diagnostic group[a]	EUROPE (14) 1988–97		USA SEER & (15) 1975–05		ARGENTINA 2000–08		ECUADOR(2) 1985–92		URUGUAY(2) 1988–1992		Mexico(12) 1996–2002	
	ASR[b]	%RF[c]	ASR[b]	%RF[c]	ASR[b]	%RF[c]	ASR[b]	%RF[c]	ASR[b]	%RF[c]	ASR[b]	%RF[c]
I. Leukaemia	44.0	28.5	52.0	32.4	47.5	36.8	56.3	44.6	44.0	36.8	55.4	45.8
II. Lymphomas and Reticuloendothelial Neoplasms	15.2	13.3	15.8	10.1	15.6	12.7	21.1	17.4	19.6	16.7	12.8	11.1
III. CNS and Miscellaneous Intracranial and Intraspinal Neoplasms	29.9	21.7	41.0	24.7	23.5	18.5	13.3	10.6	23.0	19.2	14.4	12.0
IV. Sympathetic Nervous System Tumours	11.2	8.1	10.2	6.2	7.9	5.6	3.2	2.4	3.2	2.6	6.3	2.7
V. Retinoblastoma	4.1	2.4	4.1	2.5	5.0	3.5	7.4	5.4	2.7	1.9	5.5	4.0
VI. Renal Tumours	8.8	4.3	7.4	4.5	6.9	5.0	3.6	2.7	7.1	5.3	5.2	4.1
VII. Hepatic Tumours	1.5	1.0	2.7	1.6	1.9	1.4	1.5	1.1	0.8	0.6	2.5	1.8
VIII. Malignant Bone Tumours	5.5	6.3	6.7	4.0	5.4	4.7	5.5	4.6	6.2	5.6	6.3	5.7
IX. Soft-Tissue Sarcomas	9.1	6.7	10.7	6.5	7.7	6.1	4.9	3.8	7.7	6.4	6.8	5.5
X. Germ Cell, Trophoblastic and Other Gonadal Neoplasms	4.5	2.8	5.7	3.4	4.1	3.2	4.4	3.5	3.1	2.4	7.9	6.4
XI. Carcinomas and Other Malignant Epithelial Neoplasms	4.1	4.4	6.4	3.9	2.1	1.8	4.1	3.5	2.6	2.4	1.0	0.9
XII. Other and Unspecified Malignant Neoplasms	0.6	0.3	0.4	0.2	1.0	0.8	0.3	0.3	0.2	0.2	–	0.0
Total	138.5	100.0	165.8	100.0	128.5	100.0	125.6	100.0	120.2	100.0	121.5	100.0

[a] ICCC-3: International Classification of Childhood Cancer Third Edition.
[b] ASR: age standardised rate per 1000,000 population aged 0–14 years.
[c] RF: Relative frequencies (%).

Please cite this article in press as: Moreno F. et al., Childhood cancer: Incidence and early deaths in Argentina, 2000–2008, *Eur J Cancer* (2012), http://dx.doi.org/10.1016/j.ejca.2012.08.001

(extent of disease, response to treatment, etc.). On the other hand, patients are enrolled in clinical trials only after a diagnosis has been established: therefore, events occurring between diagnosis and entry into a trial (including death, if any) might be underreported in clinical series.[23] The present study confirms the assessment of paediatric oncology in Argentina made several years ago by a senior paediatrician oncologist in that country.[24] More in general, population-based cancer registries have a great potential for measuring overall quality of care, through the use of specific indicators (such as early death in various periods, geographical differences, diagnostic groups and hospital categories). ROHA is in condition of offering the database required for those purposes.

Conflict of interest statement

None declared.

Acknowledgements

The Fondo Anglesio Moroni, Turin, Italy (www.anglesiomoroni.org) generously supported the sojourn of Prof. Benedetto Terracini in Buenos Aires for the present work.

References

1. Curado MP, Edwards B, Shin HR et al. editors. *Cancer incidence in five continents*, vol. IX. IARC Scientific Publ No. 160. Lyon, France: International Agency for Research on Cancer; 2007.
2. Parkin DM, Kramárová E, Draper GJ, et al. editors. *Incidence of childhood cancer*, vol. 2. IARC. Scientific Publ No. 144. Lyon: IARC; 1998.
3. Jensen OM, Parkin DM, Maclennan R, et al. *Cancer registration: principles and methods*. IARC Scientific Publ No. 95, Lyon, France: International Agency for Research on Cancer; 1991.
4. Fritz A, Percy C, Jack A, et al. *International classification of diseases for oncology*. 3rd ed. Geneva: World Health Organization; 2000.
5. Kramarova E, Stiller CA, Ferlay J, et al. *International classification of childhood cancer*. IARC technical Report No. 29. Lyon: International Agency for Research on Cancer; 1996.
6. ROHA – *Fundación Kaleidos. Registro Oncopediátrico Argentino Resultados* 2000–2008. Available from: <http://www.fundacionkaleidos.org/Roha_publicaciones/roha2008.pdf> 2011 [accessed 15.11.2011].
7. De Camargo B, De Oliveira Santos M, Rebelo MS, et al. Cancer incidence among children and adolescents in Brazil: first report of 14 population – based cancer registries. *Int J Cancer* 2010;**126**(3):715–20.
8. Bray F, Parkin M. Evaluation of data quality in the cancer registry: principles and methods. Part I. Comparability, validity and timeliness. *Eur J Cancer* 2009;**45**:747–55.
9. Pearce MS, Parker L. Childhood cancer registrations in the developing world: still more boys than girls. *Int J Cancer* 2001;**91**:402–6.
10. Parkin M, Bray F. Evaluation of data quality in the cancer registry: principles and methods. Part II completeness. *Eur J Cancer* 2009;**45**:756–64.
11. AIRTUM working group. Italian cancer figures. Childhood cancer incidence, survival, trend. *Epidemiol Prev* 2008;**21**(suppl):1–111.
12. Fajardo-Gutierrez A, Juarez-Ocaña S, Gonzalez-Miranda G, et al. Incidence of cancer in children residing in ten jurisdictions of the Mexican Republic: importance of the cancer registry (a population-based study). *BMC Cancer* 2007;**7**:68. Available from: <http://www.biomedcentral.com/1471-2407/7/68>.
13. Stiller C, Marcos-Grager R, Ardanaz E, et al. Geographical patterns of childhood cancer incidence in Europe, 1988–1997. Report from the Automated Childhood Cancer Information System project. *Eur J Cancer* 2006;**42**:1952–60.
14. Kaatsch P. Epidemiology of childhood cancer. *Cancer Treat Rev* 2010;**36**:277–85.
15. Steliarova-Foucher E, Stiller C, Kaatsch P, et al. Geographical patterns and time trends of cancer incidence and survival among children and adolescents in Europe since the 1970 (the ACCIS project): an epidemiological study. *Lancet* 2004;**364**:2097–105.
16. Kaatsch P, Steliarova-Foucher E, Crocetti E, Magnani C, Spix C, Zambon P. Time trends of cancer incidence in European children (1978–1997): report from the Automated Childhood Cancer Information System protect. *Eur J Cancer* 2006;**42**(13):1961–71.
17. Ries LAG, Melbert D, Krapcho M, Stinchcomb DG, Howlader N, Horner MJ, et al. *SEER Cancer statistics review*. Bethesda, MD: National Cancer Institute; 1975–2005.
18. Peris-Bonet R, Salmerón D, Martínez-Beneito MA, Galceran J, Marcos-Gragera R, Felipe S. Childhood cancer incidence and survival in Spain. *Ann Oncol* 2010;**21**(Suppl 3):103–10.
19. Court Brown WM, Doll R. Leukaemia in childhood and young adult life. *Br Med J* 1961;**1**(5231):981–8.
20. Stiller CA. Epidemiology and genetics of childhood cancer. *Oncogene* 2004;**23**:6429–44.
21. Hamre MR, Williams J, Chuba P, Bhambhani K, Ravindranath Y, Severson RK. Early deaths in childhood cancer. *Med Pediatr Oncol* 2000;**34**:343–7.
22. Pastore G, Viscomi S, Mosso ML, et al. Early deaths from childhood cancer. *Eur J Pediatr* 2004;**163**:313–9.
23. Riley LC, Ha JM, Wheatley H. Treatment-related deaths during induction and first remission of acute myeloid leukaemia in children treated on the Tenth Medical Research Council acute myeloid leukaemia trial (MRC AML10). *Br J Haematol* 1999;**106**:436–44.
24. Scopinaro MJ, Casak SJ. Pediatric oncology in Argentina: medical and ethical issues. *Lancet Oncol* 2002;**3**:111–7.