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Short Communication

Patterns of domestic migrations and access to childhood cancer care centres in Italy: A report from the hospital based registry of the Italian Association of Pediatric Hematology and Oncology (AIEOP)

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ABSTRACT

Tertiary care centres, grouped in the Italian Association of Paediatric Haematology and Oncology (AIEOP) are unevenly distributed across the country. In an attempt to describe their perceived efficacy, we matched the residence and the location of the treatment centre in 18,441 patients aged ⩽15 years treated in the AIEOP network between 1989 and 2005. Overall, centres located in the central and southern regions were less appealing than those located in the North, although this trend decreased over the study period. Patients with solid tumours migrated more frequently than those with leukaemia or lymphoma. Information resulting from better knowledge of the non-random migrations for treatment of children with cancer will be useful to refine planning of the national paediatric haematology-oncology network with social and economic implications.

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1. Introduction

Approximately 1,500 children younger than 15 years of age are diagnosed with cancer each year in Italy.[1] The Italian Association of Pediatric Hematology and Oncology (AIEOP) has played a major role in the design and implementation of nationwide controlled clinical trials in Italy since the 1970's. Such collaborative work has been instrumental in raising the standards for diagnosis and treatment of childhood cancer throughout the country, allowing risk-directed treatment and a total cure approach for a continuously increasing proportion of children.[2–4]

Survival rates are commonly considered the best indicator of the quality of care. Yet, the accessibility to specialist support, in terms of distance, time, cost, and transport [5,6] has a deep impact on the quality of life of children and their families; thus, the geographical pattern of access to care services may be an informative tool for health care planning and evaluation.

The aim of this study was to evaluate the AIEOP efficiency in terms of geographical accessibility to its clinical units measuring the migratory phenomenon. Analyses are based on children diagnosed with cancer before the age of 15 at any of the AIEOP centres between 1989 and 2005.

2. Patients and methods

Since 1989, all centres participating in the AIEOP (see Appendix for the list) were asked to register any child with a malignant tumour. Data on demographic (gender, town and date of birth, town of residence at diagnosis) and clinical (date of diagnosis, cancer site, morphology and stage, centre where diagnosis was made and therapy implemented) features were collected. Data collection was performed through an ad-hoc form (Model 1.01) in cooperation with CINECA (Centro Interuniversitario del Nord Est italiano per il Calcolo Automatico), as previously reported.[7] This dataset collects about 75% of all national childhood cancer (80% in Northern and Central regions, 65% in Southern regions), on estimates of the number of expected cases in Italy (on average, 1600 cancer cases are expected to occur yearly).[1] The coverage is higher for leukaemias and lymphomas (85%) than for solid tumours (64%). Central nervous system tumours (CNS) have the lowest coverage (45%).

The database used for this study included 18,776 children (0–14 years) diagnosed between January 1st, 1989 and December 31st, 2005. Children with benign histiocytosis and mesoblastic nephroma have been excluded from the present analyses, as well as the cases diagnosed at older age (15+ year). Cases with unknown residence locations at diagnosis and those residing abroad were excluded from the analysis (this amounted to 335 patients uniformly distributed over the study period and histological type). Tumour types were grouped according to the International Childhood Cancer Classification (ICCC).[8]

In order to describe the possible migration of patients from their residences to the site of care, we grouped the Italian regions into three macro-areas (North, Centre, South-Isles). The agreement between the macro-areas of the family residence and the AIEOP centre where the therapy program was implemented was calculated through the weighted Cohen's kappa coefficient.[9]

Furthermore, for each of the 3 Italian macro-areas (North, Centre, South-Isles), we calculated three indicators of access to AIEOP care services:

a. the capability to keep (KEEP) children in clinical units within the macro-area, expressed as the proportion of children residing within the macro-area who are treated in centres operating within the macro-area;
b. the capability to attract (ATTRACT) children residing outside the macro-area to their clinical units, expressed as the proportion of children non-resident in the macro-area who are treated in centres operating within the macro-area;
c. the burden of cases (BURDEN) loaded onto the clinical units of other macro-areas, expressed as the proportion of children treated in centres outside the macro-area of their residence. Even largely populated regions that are capable of attracting many cases may exert a substantial burden on other macro-areas if a sizable fraction of their cases migrate to other macro-areas.

The trend in the three indicators (KEEP, ATTRACT and BURDEN) across periods of diagnosis was tested applying the Breslow-Day test.[10]

Analyses were carried out stratifying the histological type into hemo-lymphoproliferative disorders (including leukaemia, lymphoma and reticuloendothelial neoplasms and myelodysplastic syndrome) and solid tumours. The period of diagnosis was also broken down into four time intervals (1989–93, 1994–97, 1998–01, 2002–05).

3. Results

Among the 18,441 children included in this study, 5076 (27.5%), 4256 (23.1), 4389 (23.8) and 4720 (25.6) were diagnosed during 1989–93, 1994–97, 1998–01, and 2002–05, respectively. Due to the reduction of the birth rate, the Italian child population decreased over the study period from approximately 9,200,000 in 1989–93 to approximately 8,200,000 in 2002–05.

Leukaemia (38.1%), central nervous system and miscellaneous intracranial and intraspinal neoplasms (13.9), lymphoma and reticuloendothelial neoplasms (13.6), and sympathetic nervous system tumour (8.9) were the largest groups, followed by soft-tissue sarcomas (5.9), renal tumours (5.4) and malignant bone tumours (4.8).

Table 1 shows the distribution of children according to the macro-area of residence at diagnosis and the location of the AIEOP clinical units where treatment was implemented. Over the four time periods of diagnosis, the weighted Cohen's kappa coefficients calculated between the residence and AIEOP centre location areas were 0.74, 0.77, 0.73, and 0.79 among children with hemo-lymphoproliferative disorders For solid tumours, the weighted Cohen's kappa coefficients consistently increased during the study period from 0.41 during 1989–93 to 0.53 during 2002–05. For central nervous system

Table 1 – AIEOP database, 1989-2005–Estimated weighted Cohen's kappa (K) agreement coefficient between residence at diagnosis and AIEOP centre location for children (0–14 years) included in the study by period of diagnosis and histological type

Period of diagnosis	Hemo-lymphoproliferative disorders*					Solid tumours				
	Residence area	AIEOP centre location				Residence area	AIEOP centre location			
1989-93		North	Centre	South & Isles	Italy		North	Centre	South & Isles	Italy
	North	1118	3	1	1122	North	905	13	2	920
	Centre	60	461	5	526	Centre	124	360	2	486
	South & Isles	248	91	768	1107	South & Isles	481	88	346	915
	Italy	1426	555	774	2755	Italy	1510	461	350	2321
	K = 0.74					K = 0.41				
1994-97		North	Centre	South & Isles	Italy		North	Centre	South & Isles	Italy
	North	939	5	2	946	North	819	9	2	830
	Centre	48	384	2	434	Centre	94	308	5	407
	South & Isles	177	58	622	857	South & Isles	365	84	333	782
	Italy	1164	447	626	2237	Italy	1278	401	340	2019
	K = 0.77					K = 0.48				
1998-01		North	Centre	South & Isles	Italy		North	Centre	South & Isles	Italy
	North	936	3	3	942	North	840	18	1	859
	Centre	47	386	1	434	Centre	88	332	17	437
	South & Isles	227	52	673	952	South & Isles	352	82	331	765
	Italy	1210	441	677	2328	Italy	1280	432	349	2061
	K = 0.73					K = 0.49				
2002-05		North	Centre	South & Isles	Italy		North	Centre	South & Isles	Italy
	North	1021	4	3	1028	North	981	40	1	1022
	Centre	33	464	3	500	Centre	69	373	10	452
	South & Isles	175	57	673	905	South & Isles	331	133	349	813
	Italy	1229	525	679	2433	Italy	1381	546	360	2287
	K = 0.79					K = 0.53				

* leukaemia, lymphoma and reticuloendothelial neoplasms, myelodysplastic syndrome.

tumours, kappa coefficients decreased over time from 0.45 during 1989–93 and 1994–97, to 0.42 and 0.41 during 1998–01 and 2002–05, respectively.

The macro-area estimates of the three indicators, KEEP, ATTRACT and BURDEN, for each time period of diagnosis for hemo-lymphoproliferative disorders and solid tumours are reported in Table 2. The clinical units located within the Northern regions showed increased capability to keep children and to attract children residing outside of the region. Additionally, the Northern region centres provided a lower burden of cases loaded onto the clinical units of other regions compared to those from the Central and Southern regions. Over the study periods, the capability to attract children showed a decreasing trend for the centers located in the Northern part of Italy, while the centers of Central and Southern regions showed increasing trends in their capability to keep children and a decrease burden of cases onto the clinical units of Northern Italy. These geographical and temporal differences were particularly marked among children with solid tumours.

4. Discussion

The access of Italian children with cancer to AIEOP tertiary care centers was evaluated throughout the analysis of the AIEOP hospital-based registry. We first estimated the agreement between the area of residence at diagnosis and the location of the AIEOP centre where the children were treated through the Cohen's kappa coefficient. This agreement coefficient can be considered a valuable indicator of how frequently Italian children access clinical units operating in the same geographical area where they live. According to Landis and Koch's interpretation,[11] the agreement was substantial (K = 0.63) for all tumours types combined throughout 1989-05. Among children with hemo-lymphoproliferative disorders, the agreement was already high in 1989–93 (K = 0.74) and showed further improvement in 2002–05 (K = 0.79). Despite an increasing trend in location agreement coefficients during the study period, concordance was inferior for patients with solid tumours. In particular, the migration phenomenon seems to be more associated with CNS tumours than other solid tumours. This could be due to referral to a few neurosurgeons specially dedicated to pediatric brain tumours. As a result, since some of them do not fully share the AIEOP data-reporting system, we have a higher rate of migration and a lower rate of accuracy of reporting for brain tumours than other solid tumours in our country. This bias is partly corrected by data rescue in those CNS tumour subtypes requiring also radiotherapy and chemotherapy, while data of subtypes such as low-grade ones, treated only by neurosurgeons and never referred to pediatric hematology/oncology centers, are missing.

If we assume that the proportion of patients attending the AIEOP centre located within its macro-area may reflect

Table 2 – AIEOP database, 1989–2005 – Macro-area indicators for hemo lymphoproliferative disorders (leukaemia, lymphoma and reticuloendothelial neoplasms, myelodysplastic syndrome and solid tumours by period of diagnosis

	Macro-area	KEEP[a]				ATTRACT[b]				BURDEN[c]			
		1989–93	1994–97	1998–01	2002–05	P[d]	1989–93	1994–97	1998–01	2002–05	P[d]	1989–93	1994–97	1998–01	2002–05	P[d]
Hemo-lymphoproliferative disorders	North	0.996	0.993	0.994	0.993	0.388	0.189	0.174	0.198	0.148	0.027	0.003	0.007	0.005	0.006	0.391
	Centre	0.876	0.885	0.889	0.928	0.009	0.042	0.035	0.029	0.032	0.033	0.030	0.028	0.025	0.019	0.030
	South & Isles	0.694	0.726	0.707	0.744	0.038	0.004	0.003	0.003	0.004	0.027	0.171	0.146	0.169	0.132	0.011
Solid tumours	North	0.984	0.987	0.979	0.960	<0.001	0.432	0.386	0.366	0.316	<0.001	0.018	0.015	0.024	0.045	<0.001
	Centre	0.741	0.757	0.760	0.825	0.004	0.055	0.058	0.062	0.094	<0.001	0.068	0.061	0.064	0.045	0.011
	South & Isles	0.378	0.426	0.433	0.429	0.029	0.003	0.006	0.014	0.007	0.040	0.289	0.267	0.254	0.241	<0.001

a capability to keep children in clinical units within the macro-area (proportion of children residing within the macro-area who are treated in centres operating within the macro-area).
b capability to attract children residing outside the macro-area to their clinical units (proportion of children non-resident in the macro-area who are treated in centres operating within the macro-area).
c burden of cases loaded onto the clinical units of other macro-areas (proportion of children treated in centres outside the macro-area of their residence).
d P-value for trend across periods of diagnosis.

their perceived quality, this analysis of migrations may provide useful information on several issues for the AIEOP network and highlight situations in which AIEOP centres could be improved. We produced macro-area indicators of the capability of centres to keep children within their territory, to attract children residing outside of their macro-area, and the burden of cases loaded onto the clinical units of other macro-areas.

Our results show that the AIEOP centres located in the Northern regions were perceived as more appealing, as suggested not only by their higher capability to keep their own patients, but also to attract cases from the Centre and the South (including isles). The trial entry could be considered a possible explanation of the migration of children from Southern regions to centres located in Northern regions. In Italy, the paediatric clinical working groups adopted different therapeutic strategies over the years, both developing national protocols and taking part in international trials. Patients not enrolled in AIEOP protocols were treated according to a single institution's own protocol, received individualized treatments or were included in international cooperative protocols not formally defined as AIEOP trials. We explored the proportion of children entered into AIEOP clinical trials (data not shown) and found no association with the clinical migration phenomenon. Remarkably, this phenomenon decreased over the study period. This may reflect the continuous effort made by AIEOP to develop and support clinical units to insure the best quality of care near to the family home in Central and Southern Italy, where 54% of the centres are currently located (27% and 27%, respectively) and approximately 58% of Italian children live. Nowadays, centres located in Central and Southern regions have the capacity to treat all patients, based on the evaluation of the amount of cases provided by each region. However, the perceived quality of care can yet be considered a strong driver for migration towards Northern Italy.

Treatment of pediatric – as well as adult – cancer is completely free of charge in the Italian health care system, based on public hospitals. In this frame, the AIEOP network provides the opportunity to deliver optimal cancer-directed therapy at a reasonable distance from the family living place, thus reducing the social impact and costs of the disease. This may result in a considerable support not only for the affected family, but for the national economy as well. Continuous monitoring of 'migrations' for medical reasons may impact the design of health care interventions and the allocation of resources.

Conflict of interest statement

None declared.

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Appendix F. List of the chairpersons within the AIEOP Centres, as of December, 2005

Northern Italy: Madon E (Torino), Pastore G (Vercelli), Dini G (Genova), Carnelli V, Fedeli F, Fossati Bellani F (Milano), Masera G (Monza), Locatelli F (Pavia), Cornelli PE (Bergamo), Notarangelo L (Brescia), Nespoli L (Varese), Bagnulo S (Chiari), Carli M (Padova), Marradi P (Verona), Musi L, Rodeghiero F (Vicenza), Grotto P (Belluno), Rossetti F (Monselice), Battisti L (Bolzano), Tamaro P (Trieste), Mascarin M (Pordenone), Nocerino A (Udine), Izzi G (Parma), Paolucci P (Modena), Ambrosioni G, Pession A, Picci P (Bologna), Borgna Pignatti C (Ferrara), Vecchi V (Rimini);

Central Italy: Bernini G (Firenze), Morgese G (Siena), Favre C (Pisa), Zucchetti P (S. Sisto), Pierani P (Ancona), Felici L, Visani G (Pesaro), Di Bartolomeo P (Pescara), Ballati G, Castello MA, De Rossi G, Donfrancesco A, Foà R, Menichelli A, Riccardi R (Roma);

Southern Italy: Di Tullio MT F, Fiorillo A, Poggi V (Napoli), Amendola G (Nocera Inferiore), Ladogana S (S Giovanni Rotondo-FG), Ruggiero L (Tricase), Pozzi S (Lecce), De Mattia D (Bari), Magro S (Catanzaro), Nobile F (Reggio Calabria), Sperlì D (Cosenza), Aricò M (Palermo), Schilirò G (Catania), Gallisai D (Sassari), Biddau P (Cagliari).

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