Appendix 3

ACCIS – Automated Childhood Cancer Information System

Rationale

In the European Union about 1% of all cancers occur in children under 15 years of age, corresponding to an estimated 11,000 new cases per year. This number may seem insignificant in comparison with the total of 1.6 million new cancer cases of all ages (Ferlay *et al.*, 1999). However, cancer is the second cause of death (after injuries) in children between 1 and 14 years of age, despite the considerable success achieved in its treatment over the last 30 years (Draper *et al.*, 1982; Capocaccia *et al.*, 2001). Even though almost 75% of childhood cancer patients survive five years after diagnosis, many of these survivors bear consequences in terms of physical, mental or reproductive impairment throughout their life.

Preventive measures are non-existent, largely because of uncertainty about the causes of cancer in childhood. The short exposure period suggests that genetic factors play a role, although the proportion of childhood tumours due to known genetic abnormalities is estimated to be less than 5% Narod *et al.*, 1991).

An important obstacle to study of the etiology of tumours in children is their rarity and the diverse spectrum of morphological tumour types. While over 80% of malignancies in adults are carcinomas, in childhood these represent less than 10%. Common childhood tumour types are sarcomas (45%), leukaemias (30%) and lymphomas (15%) (Miller & Myers, 1983; Parkin *et al.*, 1997). Presumably, the different morphology is a reflection of different histogenesis and probably also its etiology and cause. To address the importance of a separate study of clearly defined tumour groups, a specific International Classification of Childhood Cancer (ICCC) is used (Kramárová & Stiller, 1996).

Large geographical areas or long time periods are needed to permit the collection of enough cases for a study to have sufficient power to give answers to specific hypotheses of causality. Sources of standardized data on childhood cancer incidence are the two volumes of *International Incidence of Childhood Cancer* (IICC) produced by IARC (Parkin *et al.*, 1988, 1998). Survival of children with cancer was uniformly analysed within the EUROCARE study and published as a special issue of the *European Journal of Cancer* (Capocaccia *et al.*, 2001) for a large number of tumour groups.

The aim of the ACCIS project is to collect, standardize, interpret and disseminate data on indicators of cancer burden in the childhood population of Europe. These objectives are being achieved by:

1. Construction of the ACCIS database containing information on incidence and survival of childhood cancer patients in Europe.

2. Development of the ACCISpass software designed for storage, analysis, presentation, interpretation and dissemination of the collected data.

3. Setting up an Internet site for wide distribution of information on the ACCIS project and the collected data.

4. Evaluation and interpretation of results of data analyses.

With some 160,000 cancer cases registered in Europe over the last 30 years and the population at risk of around 2.6 billion person-years, the ACCIS database is the largest database of young cancer patients in the world. ACCISpass accommodates the ACCIS database and permits analysis of groups of patients selected with great flexibility. Continuous updating and exploration of the database will ensure that ACCIS becomes the reference source of data and expertise on childhood cancer, not only in Europe, but worldwide.

The ACCIS database

Eighty population-based cancer registries in 30 countries of Europe have provided data for the construction of the ACCIS database, which includes all cases of cancer incident before the age of 20 years. Traditionally, the specialized paediatric cancer registries

provided cancer data only for patients younger than 15 years of age at diagnosis.

Every registry provided a list of individual records of cancer cases with a standard set of variables. The data were validated to limit coding errors, to allow standard interpretation of the results obtained and to evaluate the overall comparability of the data-sets (Parkin *et al*., 1994). Questions concerning the data were resolved in collaboration with the participating registries. At IARC, all records were classified into ICCC (Kramárová & Stiller, 1996) categories using the Child-Check program (Kramárová *et al*., 1996). Length of survival time was calculated for each case where the follow-up information was available: date of death for the deceased patients or date of last contact for patients who were still alive.

The population data file ideally contained the number of residents in the registration area in each calendar year of the reported period, by sex and single year of age. For registries that were not able to provide population data in the required detail, the missing data were estimated at IARC.

All participants also completed a questionnaire, which provided the coordinating centre with information on the registry and its registration and coding practices.

The ACCIS Scientific Committee examined and commented on each dataset. Any issues possibly influencing the interpretation of the results are documented within the ACCIS database. With the exception of a few submitted data-sets (missing mandatory variables or clearly incomplete coverage), virtually all were included in the ACCIS database. The latter is destined for dissemination to the contributing registries within ACCISpass. The majority of the data-sets were also considered sufficiently comparable for display to the general public on the Internet site. Regional registries with a relatively small number of cases are not presented on the Internet in detail, although they contribute to the national estimates. This cautious approach was adopted in order to avoid misinterpretation by a lay user of naturally large variations of statistics based on small numbers.

ACCISpass

ACCISpass is the software designed to accommodate the ACCIS database and present the collected data. ACCISpass was developed jointly by IARC and Lambda[+], the company involved in the development of the EUROCIM software (European Network of Cancer Registries, 2001). It was therefore possible to adapt the modules developed within EUROCIM for incorporation into ACCISpass.

The most important asset of ACCISpass is the usage of the database of individual records for data analysis and presentation. This novelty in comparison with EUROCIM allows maximum flexibility in the creation of groups of cases. This potential is fully exploitable (within the confidentiality restrictions) starting with ACCISpass version 2.00.

Another important feature is a distinction between two types of data-set, according to the age-range of the cases. Paediatric data-sets cover the age-range 0–14, while the general cancer registries include all cancer cases aged 0–19.

A further useful function of ACCISpass is the availability of observed survival proportions for the datasets with complete follow-up.

ACCISpass provides fast access to a comprehensive overview of the childhood cancer indicators for data-sets defined by the combination of a registry and a period, using the options "standard incidence tables" and "standard survival tables".

Finally, the results of the review of the datasets have become part of the software as "commentaries". The aim of these comments is to provide guidance to the user in interpretation of the results, especially because virtually no quality-based selection was made among the submitted data-sets for their inclusion in the ACCIS database.

ACCISpass is destined for free distribution to all the contributors to the ACCIS database.

Internet site

An Internet site was developed to present the ACCIS project, display the conditions for contribution, give information about participants in the study, link to resources of data on (childhood) cancer and, most importantly, disseminate data on childhood cancer incidence and survival, together with help in the interpretation of the results. The user is able to consult incidence rates and survival proportions of childhood cancer cases in those registries whose data-sets were chosen for display on the Internet, by the ICCC diagnostic group and five-year age group. The tables are displayed in PDF format. The web

page can be explored at the address http://www-dep.iarc.fr/accis.htm.

Data protection

Since the ACCIS database contains individual cancer records, precautions have been taken against possible misuse of the data. The level of detail for data dissemination is defined by the ACCIS Scientific Committee, which in turn respected the wishes of the individual contributors.

On the Internet, only aggregated data are displayed.

The ACCIS database, disseminated with ACCISpass, is encoded and readable only within the software. The coded database contains no names and the dates of birth, diagnosis and death are in general trimmed to the format MMYYYY, unless more strict conditions apply for a particular data-set.

In addition, the ACCIS software that allows detailed exploration of the ACCIS database is being distributed only to the registries whose data-sets form part of this database.

The future of the ACCIS project

The ACCIS database was established with a view to continuous updating. In parallel with the database, all other aspects of the project evolve to make full use of this precious data source. Envisaged directions of growth include:

1. Analysis, interpretation and dissemination of the accumulated information through scientific publications.

2. Further development of the ACCISpass software, notably the inclusion of a period-survival method and calculation of the years of life lost.

3. Further development of the Internet site.

4. Implementation of automatic procedures for data validation, to speed up the process of updating of the ACCIS database.

5. Enlargement of the ACCIS database by incorporating more recent data-sets from the current participants and inviting new participants possibly also from outside Europe to strengthen the power of future studies.

Provision of up-to-date information on childhood cancer incidence and survival will have an impact on public health policy, both directly and indirectly. The explanation of the registration techniques permits the data users to become familiar with the significance and limitations of the observed results. This will clearly demonstrate the value of data collection and hopefully relieve anxiety about data abuse and breaching of confidentiality laws.

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ACCIS participants

The existence of this project depends upon the collaboration of the European population-based cancer registries, the members of European Network of Cancer Registries (Table 1).

All aspects of the development of the ACCIS project are directed by the ACCIS Scientific Committee, an international group of scientists with relevant experience. They advise on methodology of analysis, and on data protection and dissemination, and evaluate the submitted data-sets.

The members of the ACCIS Scientific Committee are:

Franco Berrino	Director, Epidemiology Unit, National Cancer Institute, Milan, Italy
Jan Willem Coebergh	Research Director of Eindhoven Cancer Registry, Consulting Epidemiologist to the Dutch Childhood Leukaemia Study Group, Eindhven, The Netherlands
Peter Kaatsch	Director, German Childhood Cancer Registry, University of Johannes Gutenberg, Mainz, Germany (since 2002)
Brigitte Lacour	Coordinator of the French National Registry of Childhood Solid Tumours, Children's Hospital, Vandoeuvre, France (since 2002)
Joerg Michaelis	Director, Institute of Medical Statistics and Documentation, German Childhood Cancer Registry, University of Johannes Gutenberg, Mainz, Germany (until 2001)
Max Parkin	Chief, Unit of Descriptive Epidemiology, International Agency for Research on Cancer, Lyon, France
Charles Stiller	Research Officer, Childhood Cancer Research Group, Department of Paediatrics, University of Oxford, Oxford, United Kingdom

The ACCIS project is coordinated within the Unit of Descriptive Epidemiology at the International Agency for Research on Cancer:

Eva Šteliarová-Foucher	Scientific coordinator of the ACCIS project
Sue Dunderdale	Secretary
Nicolas Mitton	Database manager
Trinidad Valdivieso	Webmaster

ACCISpass is developed by the Lambda[+] company, Gembloux, Belgium.

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Table 1. List of the population-based cancer registries contributing data to the ACCIS database

Country	Registry	Country	Registry
AUSTRIA	National Cancer Registry	ITALY	Veneto Cancer Registry
BELARUS	National Childhood Cancer Subregistry	LATVIA	National Cancer Registry
BELGIUM	National Cancer Registry	LITHUANIA	National Cancer Registry
BULGARIA	National Cancer Registry	MALTA	National Cancer Registry
CROATIA	National Cancer Registry	NETHERLANDS	National Cancer registry
CZECH REPUBLIC	National Cancer Registry	NETHERLANDS	Eindhoven Cancer Registry of CCC South (IKZ)
DENMARK	National Cancer Registry	NETHERLANDS	Dutch Childhood Leukaemia Study Group (DCLSG)
ESTONIA	National Cancer Registry	NORWAY	National Cancer Registry
FINLAND	National Cancer Registry	POLAND	Cracow City and District Cancer Registry
FRANCE	Childhood Cancer Registry of Brittany	POLAND	Regional Cancer Registry of Kielce
FRANCE	Childhood Cancer Registry of Lorraine	PORTUGAL	Coimbra Oncology Centre (Central Zone)
FRANCE	Cancer Registry of Provence, Alps, Côte d'Azur and Corsica	PORTUGAL	Cancer Registry of Northern Region (Porto)
FRANCE	Children's Cancer Registries of the Rhône Alps Region	PORTUGAL	Cancer Registry of Southern Region (Lisbon)
FRANCE	Cancer Registry of Calvados	ROMANIA	Cancer Registry of Bihor County
FRANCE	Doubs Cancer Registry	SLOVAKIA	National Cancer Registry
FRANCE	Hérault Cancer Registry	SLOVENIA	National Cancer Registry
FRANCE	Isère Cancer Registry	SPAIN	National Childhood Cancer Registry (RNTI-SEOP)
FRANCE	Cancer Registry of La Manche	SPAIN	Albacete Cancer Registry
FRANCE	Bas-Rhin Cancer registry	SPAIN	Asturias Cancer registry
FRANCE	Haut-Rhin Cancer Registry	SPAIN	Cancer Registry of the Basque Country
FRANCE	Somme Cancer Registry	SPAIN	Cancer Registry of the Canary Islands
FRANCE	Tarn Cancer Registry	SPAIN	Girona Cancer Registry
GERMANY	National Registry of Childhood Malignancies	SPAIN	Granada Cancer Registry
GERMANY	National Cancer Registry of the former GDR	SPAIN	Mallorca Cancer Registry
HUNGARY	National Paediatric Cancer Registry	SPAIN	Navarra Cancer Registry
ICELAND	National Cancer Registry	SPAIN	Tarragona Cancer Registry
IRELAND	National Cancer Registry	SPAIN	Cancer Registry of Zaragoza
ITALY	Childhood Cancer Registry of Piedmont	SWEDEN	National Cancer Registry
ITALY	Childhood Cancer Registry of the Marche Region	SWITZERLAND	Basel Cancer Registry
ITALY	Ferrara Cancer Registry	SWITZERLAND	Geneva Cancer Registry
ITALY	Cancer Registry of the Latina Province	SWITZERLAND	Cancer Registry of Graubünden and Glarus
ITALY	Ligurian Cancer Registry	SWITZERLAND	Cancer Registry of St. Gallen-Appenzell
ITALY	Lombardy Cancer Registry	SWITZERLAND	Cancer Registry of Valais
ITALY	Parma Province Cancer Registry	TURKEY	Izmir Cancer Registry
ITALY	Piedmont General Cancer Registry	UNITED KINGDOM	Childhood Cancer Registry of England and Wales
ITALY	Ragusa Cancer Registry	UNITED KINGDOM	Cancer Registry of Northern Ireland
ITALY	Sassari Cancer Registry	UNITED KINGDOM	Cancer Registry of Scotland
ITALY	Tuscany Cancer Registry	YUGOSLAVIA	Cancer Registry of Central Serbia
ITALY	Cancer Registry of Umbria	YUGOSLAVIA	Cancer Registry of Vojvodina