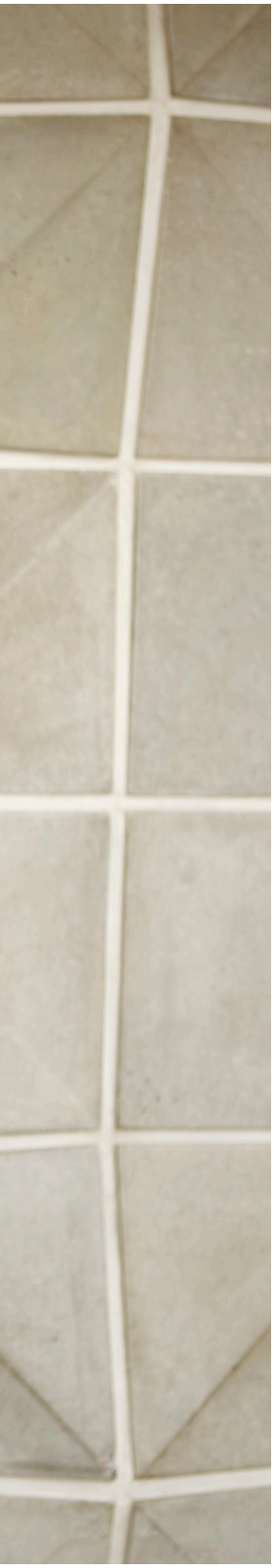
Photo by Tynan Studio

Bruna DiMonte, BScN, RN
Jason D. Pole, PhD
Mohammad Agha, PhD
Mark L. Greenberg, OC, MB, ChB, FRCPC



2

POGONIS: Methods and Data Sources

Pediatric Oncology Group of Ontario Networked Information System (POGONIS)

History

In response to concern over published incidence rates of childhood cancer in Ontario, an early objective of the Pediatric Oncology Group of Ontario (POGO) was to clarify these rates.

A pediatric cancer registry, designed to record new incident cases by active registration, was created and began capturing data in 1985. The registry used a standardized paper registration form completed by a funded dedicated data manager in each tertiary care centre. Data elements were restricted to demographic and diagnostic information and were entered into a simple electronic database. Increased accuracy and specificity of diagnoses resulted. Comparison with the Ontario Cancer Registry revealed that a proportion of children were being treated at institutions other than the 5 pediatric tertiary centres.

In 1995, the data scope was extended to encompass key outcomes and standardized treatment information on all registered cases. The registry was converted to an electronic networked database, the Pediatric Oncology Group of Ontario Networked Information System (POGONIS). The system was developed in collaboration with Artificial Intelligence in Medicine Inc., a Canadian software engineering company with expertise in cancer informatics. POGONIS was structured as a relational database with meticulously defined data elements and architecture. The Ontario Ministry of Health and Long-Term Care financially supported the creation of POGONIS.

In 2008, POGONIS was reorganized as a patient/event driven model, enabling capture of key events in diagnosis, treatment and outcomes, including survival and other late effects, in a chronological record. The patient/event data model also provides specific data management tools that facilitate more timely, accurate and complete data capture.

The new POGONIS platform has enhanced functionality for retrieving and exporting data in various formats, which enhances inter-operability with other data management and analysis software systems, permitting increased utility for external researchers requesting data sets. POGONIS also provides enhanced management controls for data quality, accuracy and completeness and for data security to ensure compliance with provincial and federal privacy standards. Direct access to POGONIS is limited to a select group of authorized users and user actions. Any changes made in POGONIS are recorded in an audit log.

Between 2010 and 2013, POGO retrospectively collected treatment data not captured on the original cohort registered between 1985 and 1995. This effort was funded by operating grants from the Canadian Institutes of Health Research and the Canadian Cancer Society, Ontario Division. POGONIS now contains detailed demographic, diagnostic, treatment and outcome data for the entire cohort, starting in 1985, enhancing POGONIS's usefulness for the study of many population-based outcomes. The additional treatment data were not available for inclusion in this Atlas (hence all treatment information presented starts with diagnoses in 1995).

Prospective Data Collection

Funded, dedicated data managers/clinical research associates actively collect POGONIS-standardized data at each tertiary hospital using hospital chart review, internal hospital information systems and direct connections with the patient's health care team. The data are remotely entered into POGONIS via a virtual private network. POGONIS is physically housed on a dedicated server in the POGO office.

POGONIS also prospectively captures data on late effects for the population it encompasses. Although this component of the data is not used in this Atlas, the longitudinal commitment to the collection of expert-selected data elements and the data's availability

for research purposes make it a unique resource for studies of this population. These factors also create unique potential to improve both the care of future generations of childhood cancer patients and the ongoing care and quality of life of current patients and survivors and their families.

POGONIS Centralized Support

Beyond the physical hardware and information technology support required to operate POGONIS, POGO continues to provide oversight and resources for POGONIS, including the following:

- Clinical oversight, which ensures ongoing review and updating of all data element definitions, with resultant data standardization
- Continual (re)alignment of registration conventions to international cancer reporting schemas
- Continuity of the data via linkage to other databases to identify key events occurring either beyond the childhood age range or unrecorded in hospital charts, including death and development of subsequent primary cancers
- Ongoing knowledge transfer and education for data managers

Childhood Cancer Nomenclature and Classification System

A standardized system of tumour classification is at the heart of any cancer registry and is essential for the comparison of incidence and survival across countries and time periods. Classification systems for childhood cancers differ substantially from those used in adult cancer: the latter are anatomically classified, while the childhood classification is based on morphology of the tumour tissue.

Since its inception, POGONIS has used a common system for the classification of childhood cancer, based on morphology. As with all data elements in POGONIS, the classification system has been modified as needed as disease classifications have changed. Initially, POGONIS adopted the informal classification and nomenclature system developed internally by the former Childhood Cancer Study Group. The schema defined 10 diagnostic groups and assigned a 4 digit diagnosis code to each specific diagnosis. This classification system mapped onto other diagnostic schema, such as the one adopted by the International Agency for Research on Cancer and the subsequently developed International Classification of Childhood Cancer (ICCC).[1] The ICCC updated the widely used Birch and Marsden classification scheme to a schema defining 12 main diagnostic groups with multiple subgroups.[2] The ICCC first requires each tumour to be assigned to the appropriate International Classification of Diseases for Oncology (ICD-O) code,[3] after which the ICD-O codes are grouped into main and subgroups. In 2000, evolving diagnostic methods, including molecular, genetic and pathologic studies, prompted the development of the third edition of the ICD-O, which introduced numerous new morphology codes and revisions to the ICCC, now defined as ICCC-3.[4] POGONIS has adopted the ICCC-3 standard.

Data Quality

The accuracy and completeness of the data in a database, and the timeliness with which it is entered, can be measured and improved. The mechanisms POGO has in place to ensure the quality of the information stored in the POGONIS database are identified below.

Accuracy

- The standardized nomenclature and coding system for classification of childhood cancer entities is regularly adjusted to meet evolving standards for classification and is mapped to the ICCC system.
- POGONIS data are collected and entered only by designated data managers/clinical research associates, who are responsible for the collection, integrity, quality and transfer of data to POGONIS. POGO's senior database administrator provides this designated staff with detailed initial and ongoing training and support.

- Data managers are provided with written reference documents, policies and procedures to support their data gathering, entry and transfer responsibilities.
- Interactive and intelligent architecture with embedded data coding standards are in place to assist with option selection.
- A Data Quality Committee is in place to define the quantifiable measures for the evaluation of data quality and to report on the quality of the data in POGONIS.
- Random data audits are routinely conducted on a percentage of cases registered in POGONIS. Selective random re-verification is the preferred method for performing data audits. Such audit routines provide data quality surveillance by employing a variety of methodologies for identifying inaccuracies.
- POGO conducts annual comparison reviews of all registrations in POGONIS with Cancer Care Ontario's Cancer Registry under a data sharing agreement. These reviews assist in mutual data quality assurance.
- POGO routinely reviews specific disease events (e.g., relapses) and treatments (e.g., radiation) as a component of particular analytic projects. Algorithms have been written that specify mandatory correlations between treatment patterns and disease stage or clinical status. These reviews may reveal data that do not pass face validity tests and that therefore require data managers to re-verify the data against paper and electronic chart review.

The existing POGONIS structure and data policies and procedures are regularly reviewed to identify and introduce technical upgrades that will further enhance the data quality assessment process.

Completeness

The data managers/clinical research associates are responsible for ensuring the completeness of data transferred to POGO.

The POGO Data Quality Committee monitors the accuracy and completeness of the data by routinely identifying data fields with missing or improbable values. In POGONIS, data elements are organized within event-driven forms. For example, for a treatment event, there are forms for chemotherapy, surgery, radiation, bone marrow transplant, etc. Each form has required and optional data fields. On completion of a form, data managers are required to sign off on the form as complete, not applicable or pending completion. This step ensures that all required elements are entered for each form. Reports are generated to determine any errors or omissions and are provided to institutional data managers, along with a schedule of deadlines to populate the fields in which values are missing or corrections are required. In addition, embedded data edits identify fields with missing data elements, which are then brought to the attention of data managers.

Timeliness

Data on new incident cases, including demographic, diagnostic and an identified subset of treatment information, for each calendar year must be entered into POGONIS by March 31st of the following year.

Annual updates of information (diagnostic, treatment, outcome and service delivery) for each patient file are required by June 30th of the following year.

POGONIS Linkage with Other Data Sources

Under the *Ontario Personal Health Information Protection Act*, POGO is a "prescribed entity" and is authorized to collect, use and disclose personal health information (PHI) for the purposes of analysis or compiling of statistical information with respect to the management, evaluation or monitoring of the allocation of resources to, or planning for, all or part of the health system, including the delivery of services. PHI must be held, used and disclosed under the strict security specifications outlined and enforced by the office of Ontario's Information and Privacy Commissioner. POGO has created and operationalized detailed policies and procedures

that govern all aspects of the collection, use and disclosure of PHI. These are detailed in POGO's Privacy and Data Security Code and its Procedures.

Additionally, this designation permits POGO to establish linkages between POGONIS and other large designated administrative and purposed databases, creating the potential for more in-depth epidemiologic, outcome, service utilization and health economic studies than previously possible. Thus POGONIS's intrinsic potential can be amplified substantially by linkage to such databases as the Ontario Health Insurance Plan (OHIP) claims database, the Discharge Abstract Database (a record of all hospitalizations), the Registered Persons Database (which tracks eligibility for OHIP and related demographic data) and others.

To systematically capture deaths in the entire cohort regardless of location and age at death (specifically outside the pediatric period), death information is identified via annual record linkage to the Ontario Cancer Registry and the Ontario Registrar General Death File under a data sharing agreement with Cancer Care Ontario. This agreement also allows the identification of subsequent malignant neoplasms among the POGONIS cohort that develop after POGONIS patients have left the pediatric care system.

Potential Limitations of POGONIS

POGONIS is an active database, dependent on identification of all patients diagnosed and treated in pediatric hospitals. The capture of new cases in the 0–14 year age range has been cross validated against the Ontario Cancer Registry; the congruence is 98% in this age range.[5] By contrast, in the 15–19 year age range, completeness of ascertainment is substantially lower, with progressive decreases by successive years of age at diagnosis. On average POGONIS captures only 50% of patients diagnosed in this age range. This lower capture rate is the result of referral patterns in the community: older adolescents whom family practitioners suspect of having cancer are referred for diagnosis and treatment to adult cancer facilities. Accordingly, only the 0–14 years cohort is analyzed in this Atlas.

As indicated, classification of diseases in POGONIS follows the International Classification of Childhood Cancers, third edition.[4] This classification, updated in 2005, is related but not identical to the topography-based ICD-O 3 schema used for adult malignancies. Additionally, entities not included in ICD-O are included in the morphology-based ICCC. In particular, certain categories of brain neoplasms not identified in ICD-O 3 as malignant are included in the ICCC.

Advances in laboratory diagnostic techniques over the past 2 decades have been substantial and transformative. The evolution of immunohistochemistry (IHC), and more recently of molecular diagnostics, has confirmed the separate identity of clinically identified disease subsets and uncovered new diagnostic categories. An example is the identification of atypical teratoid/rhabdoid tumour (ATRT) within medulloblastoma and renal tumours, particularly in younger children. ATRT was originally suggested by the clinical observation of a lethal illness in younger patients diagnosed with medulloblastoma.[6] Atypical histology was then confirmed,[7] with the evolution of IHC, by the identification of polyphenotypic expression of epithelial, neurofibrillary and muscle elements. Ultimately, identification of somatic mutation in chromosome 22q11.2 and absence of expression of the INI 1 protein product[8] culminated in a specific diagnostic profile, now considered mandatory for the diagnosis.

This profile was not sought in the patients diagnosed in the early part of the period under consideration in this Atlas, and thus it is likely that some cases classified as either primitive neuroectodermal tumour/medulloblastoma or choroid plexus carcinoma might in reality have been examples of ATRT. The classification of lymphomas has similarly evolved with specific diagnostic translocations or molecular gene expression, such as *ALK 1* in anaplastic large cell lymphoma. Again, retrospective reclassification is not within the scope of this Atlas.

Research Applications

POGONIS has become a valuable tool for population-based planning, policy development and research in Ontario, across Canada and abroad. The richness of POGONIS's data supports POGO and its partners in planning for childhood cancer control in Ontario and is a critical resource for the work of the POGO Research Unit.

POGONIS is designed to routinely monitor

- The province-wide incidence and prevalence of childhood cancer
- The demand for care from and workload of pediatric oncology programs and staff
- The nature and specifics of treatment
- Patient outcomes
- Demography and the strategic placement of treatment facilities to enable care closer to home
- Long-term effects of childhood cancer and its treatment
- Health economics

In concert with this policy agenda, POGONIS is readily available for use by bona fide researchers to explore studies that would benefit from population-based data or from circumscribed subgroups in the database. To enable such research proposals, approval from a Research Ethics Board of record and a formal application process is required. Details can be found on the POGO website at www.pogo.ca.

References

1 Kramarova E, Stiller CA. The international classification of childhood cancer. Int J Cancer. 1996 Dec 11;68(6):759-65. [review]

2 Birch JMH. A classification scheme for childhood cancer. Int J Cancer. 1987 Nov 15;40(5):620-4.

3 Fritz A, Percy C, Jack A, Shanmugaratna K, Sobin L, Parkin MD, et al. International classification of diseases for oncology, 3rd ed. World Health Organization; 2000.

4 Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International classification of childhood cancer, third edition. Cancer. 2005 Apr 1;103(7):1457-67.

5 Greenberg ML, Barr RD, DiMonte B, McLaughlin E, Greenberg C. Childhood cancer registries in Ontario, Canada: lessons learned from a comparison of two registries. Int J Cancer. 2003 May 20;105(1):88-91.

6 Burger PC, Yu IT, Tihan T, Friedman HS, Strother DR, Kepner JL, et al. Atypical teratoid/rhabdoid tumor of the central nervous system: a highly malignant tumor of infancy and childhood frequently mistaken for medulloblastoma: a Pediatric Oncology Group study. Am J Surg Pathol. 1998 Sep;22(9):1083-92.

7 Rorke LB, Packer RJ, Biegel JA. Central nervous system atypical teratoid/rhabdoid tumors of infancy and childhood: definition of an entity. J Neurosurg. 1996 Jul;85(1):56-65.

8 Biegel JA, Zhou JY, Rorke LB, Stenstrom C, Wainwright LM, Fogelgren B. Germ-line and acquired mutations of INI1 in atypical teratoid and rhabdoid tumors. Cancer Res. 1999 Jan 1;59(1):74-9.

Published by the Pediatric Oncology Group of Ontario (POGO)

Pediatric Oncology Group of Ontario
480 University Avenue, Suite 1014
Toronto, Ontario M5G 1V2
info@pogo.ca

Canadian cataloging in publication data:

Atlas of Childhood Cancer in Ontario
Includes bibliographical references.
ISBN: (Print) **978-0-9939255-0-4**
ISBN: (Online) **978-0-9939255-1-1**

How to cite this publication:

The production of *Atlas of Childhood Cancer in Ontario* was a collaborative venture. Accordingly, to give credit to individual authors, please cite individual chapters and title, in addition to editors and book title.

For example: Pole JD, Greenberg ML, Sung L, Agha M, Riehl, M. Survival. In: Greenberg ML, Barnett H, Williams J, editors. Atlas of Childhood Cancer in Ontario. Toronto: Pediatric Oncology Group of Ontario; 2015.

This document is available at www.pogo.ca and www.ices.on.ca