Collecting Pediatric Stage and Non-Stage Prognosticators in Cancer Registries

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Outline

- The challenge of childhood cancer in population-based cancer registries (PBCRs)
- The importance of stage and non-stage prognosticators
- The Toronto Staging Guidelines – Development and implementation
- Adding non-stage prognosticators

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The Challenge of Children

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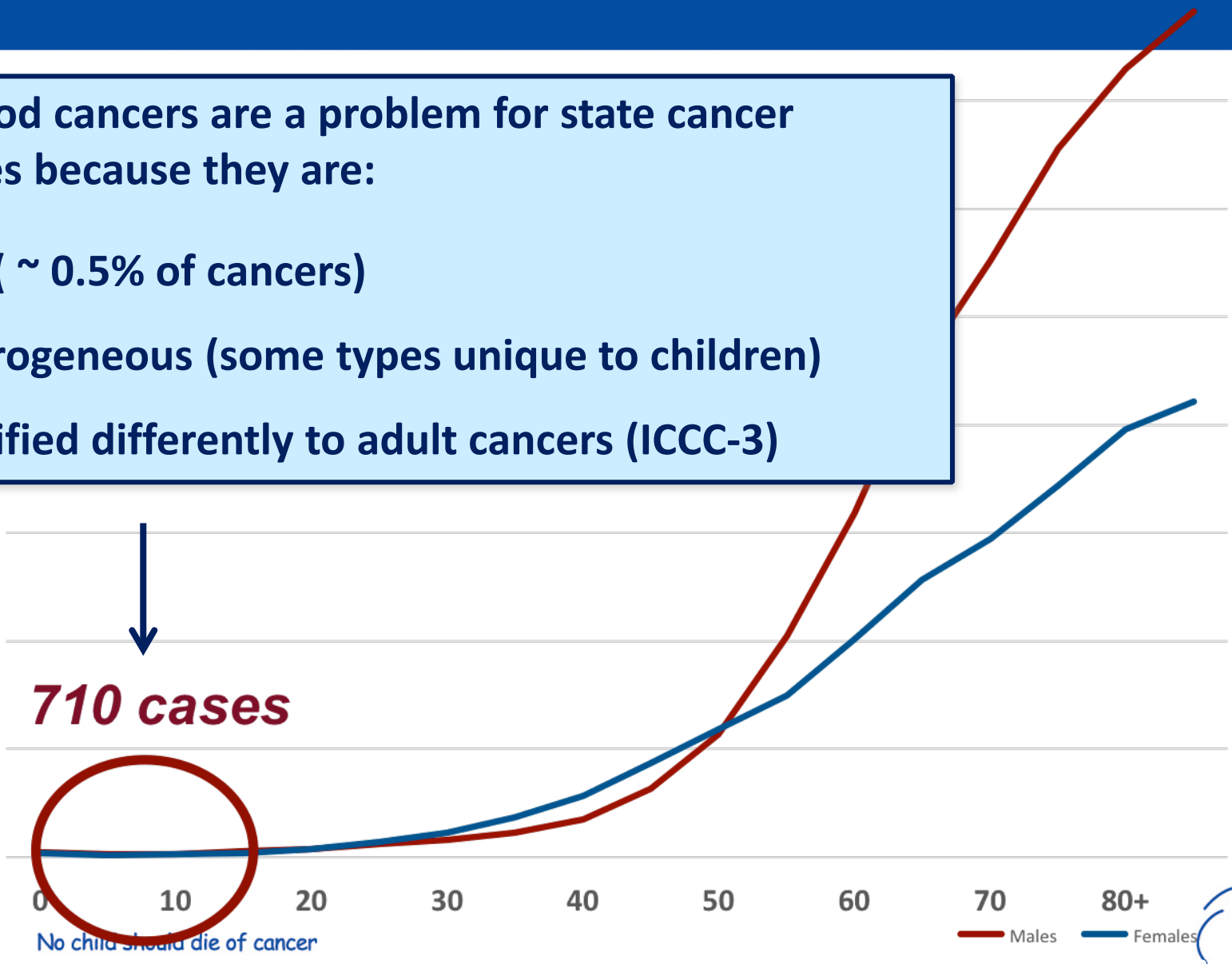
Childhood cancers are a problem for state cancer registries because they are:

- **rare (~ 0.5% of cancers)**
- **heterogeneous (some types unique to children)**
- **classified differently to adult cancers (ICCC-3)**



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The Importance of Collecting Prognosticators

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Importance of Prognosticators

- For adult cancer, incidence is a key cancer control metrics that can be decreased through:
  - Risk reduction
  - Screening
- Very few, if any modifiable risk factors for cancer incidence exist in children
- The key cancer control metric in children is therefore mortality/survival

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Importance of Prognosticators

- Being able to compare mortality/survival between populations, either across jurisdictions or over time, requires that important prognosticators be collected

- Stage at diagnosis, in addition, has been proposed as a cancer control metric itself as a proxy for time to diagnosis
  - Strength of association between time to diagnosis and stage at diagnosis varies by setting and malignancy
  - Particularly relevant to low- and middle-income countries?

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The Toronto Staging Guidelines

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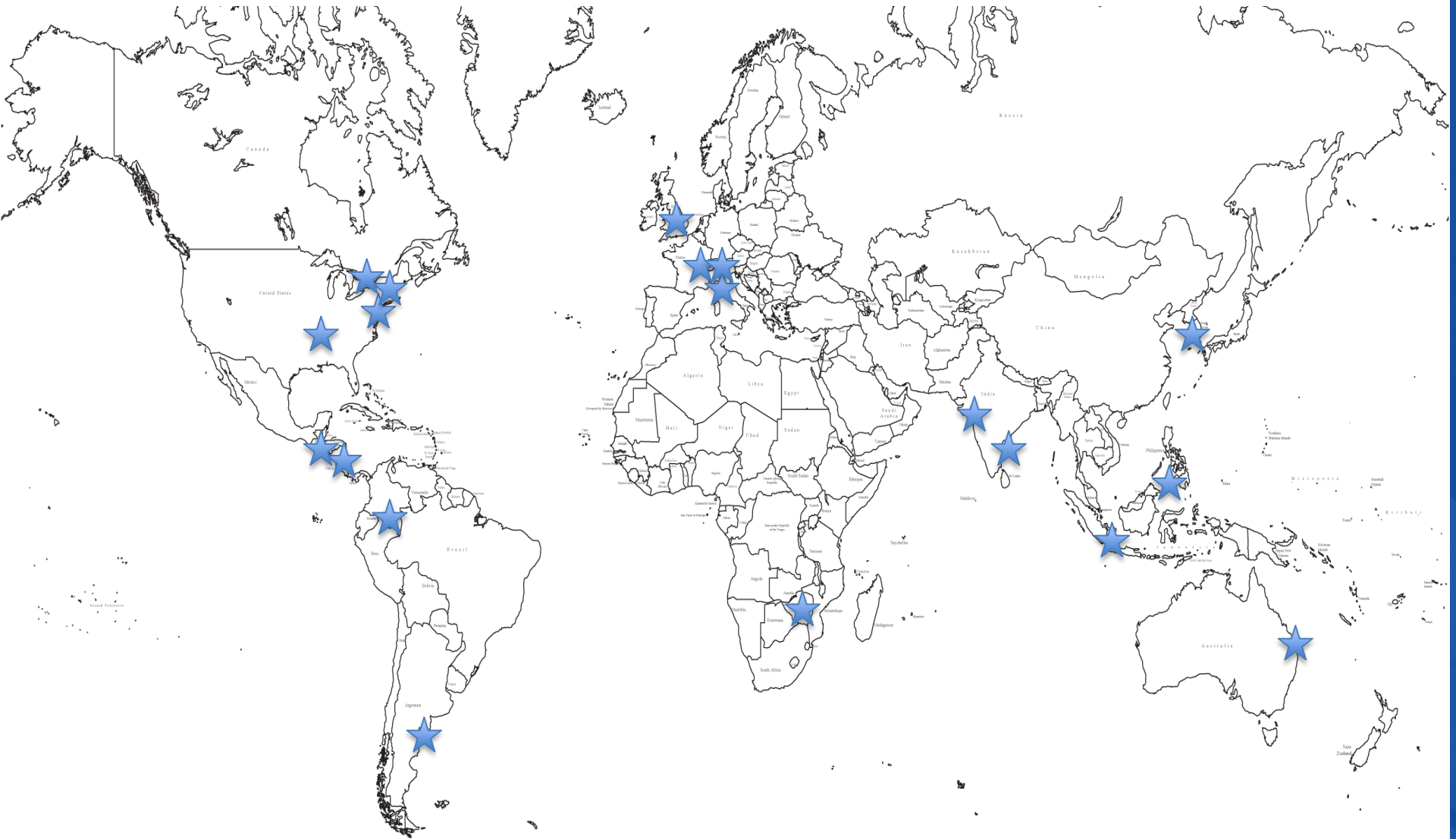
Challenges of pediatric stage

- Most registries do not collect stage, and even fewer collect pediatric stage:

1. Staging for childhood cancer is complex (not just TNM)
2. Stage is rarely documented in the medical record
3. Staging systems vary by cooperative trial group
4. Staging system used rarely documented

Assembled consensus panel of global experts in pediatric oncology, cancer registration, cancer epidemiology, and the key stakeholders in cancer registration



Staging systems recommended for:

Acute lymphoblastic leukaemia

Acute myeloid leukaemia

Hodgkin lymphoma

Non-Hodgkin lymphoma

Neuroblastoma

Wilms tumour

Rhabdomyosarcoma

Non-rhabdomyosarcoma soft tissue tumours

Osteosarcoma

Ewing sarcoma

Retinoblastoma

Hepatoblastoma

Testicular

Ovarian

Medulloblastoma

Ependymoma

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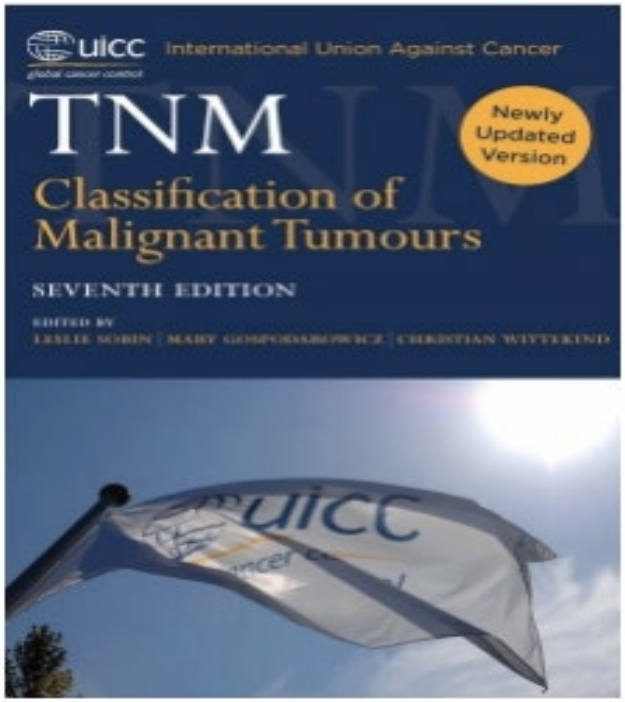
- Outline
- Challenge
- Importance of Prognosticators
- TSG
- Non-Stage Prognosticators
- Future Directions

Review

Paediatric cancer stage in population-based cancer registries: the Toronto consensus principles and guidelines

Sumit Gupta, Joanne F Aitken, Ute Bartels, James Brierley, Mae Dolendo, Paola Friedrich, Soad Fuentes-Alabi, Claudia P Garrido, Gemma Gatta, Mary Gospodarowicz, Thomas Gross, Scott C Howard, Elizabeth Molyneux, Florencia Moreno, Jason D Pole, Kathy Pritchard-Jones, Oscar Ramirez, Lynn A G Ries, Carlos Rodriguez-Galindo, Hee Young Shin, Eva Steliarova-Foucher, Lillian Sung, Eddy Supriyadi, Rajaraman Swaminathan, Julie Torode, Tushar Vora, Tezer Kutluk, A Lindsay Frazier



Non-Hodgkin lymphoma	Limited	St Jude/Murphy—stage I[32]	Tier 1 advanced stage indicates CNS or bone marrow involvement; although some clinicians will use Ann Arbor staging for non-Hodgkin lymphoma, St Jude/Murphy more often used in paediatric populations; Ann Arbor stage IV will often correspond to Tier 1 advanced stage disease; whether Ann Arbor or St Jude/Murphy staging systems were used by clinicians can be difficult to ascertain from medical charts
	Limited	St Jude/Murphy—stage II	
	Limited	St Jude/Murphy—stage III	
	Advanced	St Jude/Murphy—stage IV	
Neuroblastoma	Localised	INRGSS—localised L1[33]	MS disease refers to children younger than 18 months with metastases confined to skin, liver, or bone marrow; the first two stages of the Tier 1 system are intended to be simplified proxies of INRGSS L1 and L2 not dependent on adequate assessment of imaging-defined risk factors
	Locoregional	INRGSS—locoregional L2	
	Metastatic	INRGSS—metastatic M	
	INRGSS—MS disease	INRGSS—MS disease	
Wilms' tumour	Localised	Stage I[35]/y-stage I[15]	y designates that staging assessment was performed after neoadjuvant therapy was given, which allows the staging system to accommodate both SIOP and COG/NWTSG-based treatment strategies;[15] in cases of bilateral disease the stage of the most advanced kidney should be recorded
	Localised	Stage II/y-stage II	
	Localised	Stage III/y-stage III	
	Metastatic	Stage IV	
Rhabdomyosarcoma	Localised	TNM stage 1[27]	Rhabdomyosarcoma overall stage incorporates both TNM staging and site of disease; as registries collect primary disease site, overall rhabdomyosarcoma stage may be approximated with either tier staging system; for very high-resourced registries, a Tier 3 system that incorporates site of metastases could be considered
	Localised	TNM stage 2	
	Localised	TNM stage 3	
	Metastatic	TNM stage 4	

- Joanne Aitken and the Australian National Pediatric Cancer Registry ***offered to put these staging guidelines to the test in the field***

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Cancer Council Queensland

Australian Government Cancer Australia

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Childhood cancer staging for population registries

according to the

Toronto Childhood Cancer Stage Guidelines[1]

HEP - Hepatoblastoma

Case ID	Hospital	Hospital record number	Gender	DOB (d/m/y)	Age at diagnosis	Status	Tier 1 stage	Tier 2 stage
20090639	Sydney Children's Hospital	8693214	Female		4	Completed	Metastatic	Metastatic

Diagnostic imaging results

Imaging type	Source	Report #	Report date
CT	Original report	POWERCHART	15/09/2009

Site	Involvement
Lung	Metastatic

Haematology results (bone marrow)

Cytology results

Histology results

Edit

Assessing the feasibility and validity of the Toronto Childhood Cancer Stage Guidelines: a population-based registry study

Joanne F Aitken, Danny R Youlden, Andrew S Moore, Peter D Baade, Leisa J Ward, Vicky J Thursfield, Patricia C Valery, Adèle C Green, Sumit Gupta, A Lindsay Frazier

160 cases (10 of each of the 16 malignancies) selected at random

2 or 3 expert reviewers staged each case independently

***96% agreement* between computer algorithm and expert reviewers**

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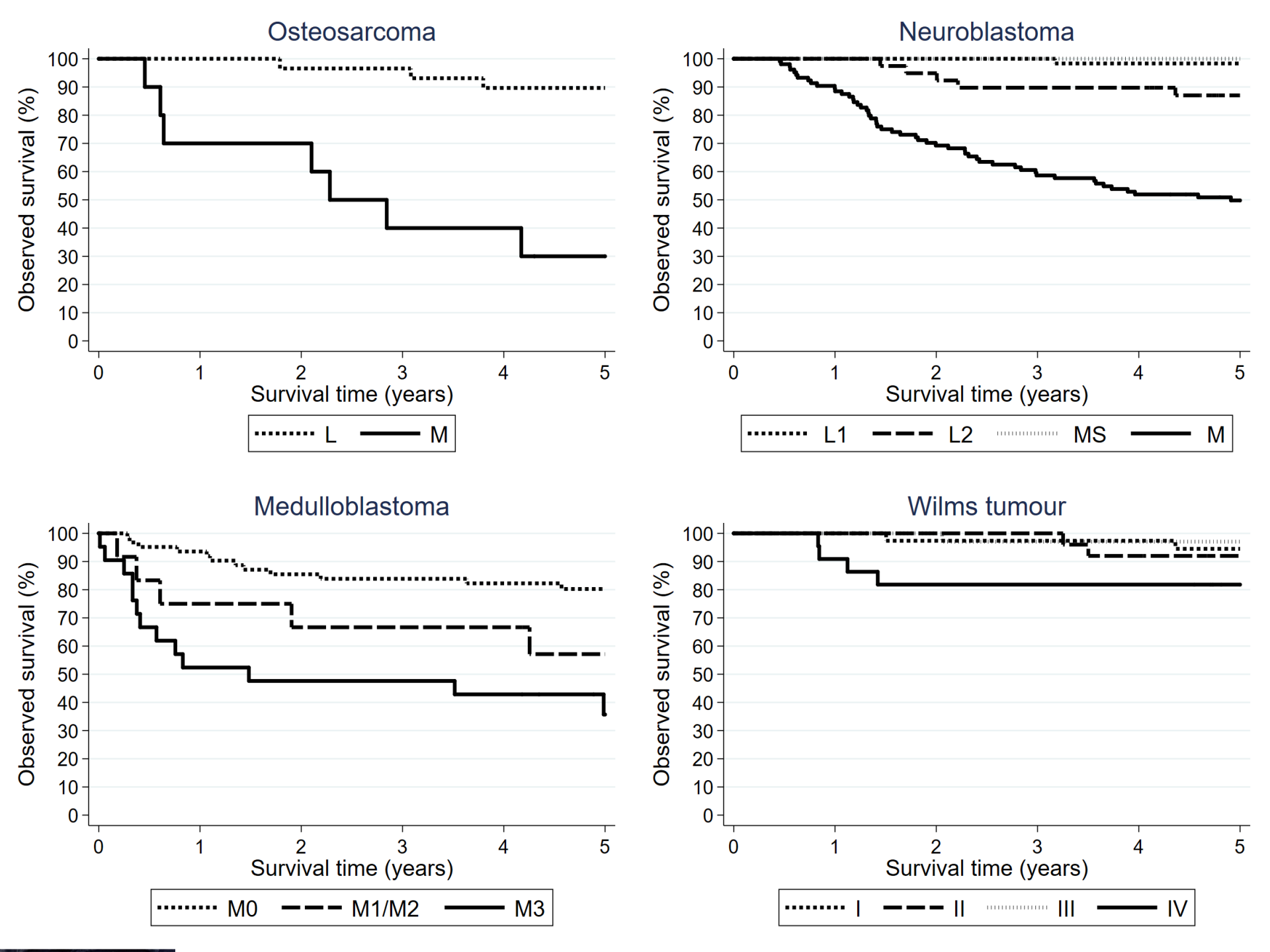
- Excellent agreement between computer algorithm and expert assessment
- 18 minutes average per case
- Physician documented stage was present in the chart in only 39% of cases, and was often inconsistent


Osteosarcoma
Observed survival (%)
0
10
20
30
40
50
60
70
80
90
100
0
1
2
3
4
5
Survival time (years)
L
M
Neuroblastoma
Observed survival (%)
Survival time (years)
L1
L2
MS
M
Medulloblastoma
Observed survival (%)
Survival time (years)
M0
M1/M2
M3
Wilms tumour
Observed survival (%)
Survival time (years)
I
II
III
IV


Greenland
Canada
United States
Mexico
Brazil
Peru
Bolivia
Paraguay
Argentina
Russia
Kazakhstan
Mongolia
China
Iran
Afghanistan
Pakistan
India
Algeria
Libya
Egypt
Mauritania
Mali
Niger
Chad
Sudan
Saudi Arabia
Yemen
Ethiopia
South Sudan
Nigeria
Angola
Namibia
Botswana
Zimbabwe
Mozambique
Madagascar
South Africa
Tanzania
Seychelles
Maldives
Philippines
Micronesia
Kiribati
Nauru
Tuvalu
Solomon Islands
Vanuatu
New Caledonia
Fiji
Tonga
Samoa
New Zealand
Northern Mariana Islands
Guam
Palau
French Polynesia

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Inclusion of Non-Stage Prognosticators

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Non-stage prognosticators

- Many important prognosticators in childhood cancer that go beyond stage
- In order to confidently compare outcomes across populations, need to collect these non-stage prognosticators (NSPs) as well
- In 2019, repeated the Delphi consensus process in Lyon (hosted by IARC) focused on which NSPs should be collected by PBCRs

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Non-stage prognosticators

- Similar to UICC/TNM, categorized NSPs as "Essential" vs. "Additional" vs. "New and Promising"
- Many of the most important NSPs already theoretically collected by PBCRs (e.g. histology, cytogenetics, molecular info) though in reality often not complete or valid
- Guidelines can help PBCRs prioritize
- Response to treatment and host factors not considered

Malignancy	Essential	Additional	New and Promising	Comments
ALL	Age Initial WBC Lineage	Cytogenetics	-	1. Lineage can be divided into precursor B-cell vs. precursor T-cell (using ICD-O-3.2 categories) 2. Cytogenetic categories using ICD-O-3.2 classification 3. MRD not considered (response to therapy)
AML	-	Cytogenetics	-	1. Cytogenetic categories using ICD-O-3.2 classification; most relevant discussed in text. 2. MRD not considered (response to therapy)
CML	-	-	-	
HL	-	-	-	
NHL	Histology	-	-	1. Most common subtypes in childhood (see text) have unique ICD-O-3.2 codes
Neuroblastoma	-	N-myc	-	
Wilms tumour	Histology	-	1p, 16q, 1q	1. Histologic sub-classification will depend on if assessed before or after adjuvant chemotherapy; see text for details
Rhabdomyosarcoma	Histology Anatomic location	Cytogenetics	-	1. Histologic categories based on ICD-O-3.2 classification 2. Anatomic location captured through ICD-O-3.2 topography codes
Non-rhabdomyosarcoma soft tissue sarcomas	-	-	-	
Osteosarcoma	-	-	-	
Ewing sarcoma	-	-	-	
Retinoblastoma	-	-	-	
Hepatoblastoma	-	-	-	
Testicular	-	-	-	
Ovarian	-	-	-	
Astrocytoma	Histology/Grade Anatomic location	H3K27M mutation	BRAF status	1. Histologic categories/grade based on ICD-O-3.2 classification

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Future Directions

- Further implementation by other cancer registries globally, including the NCCR
- Development of implementation plans for non-stage prognosticator collection
- Comparison of distribution of stage, non-stage prognosticators, and stratified outcomes across jurisdictions (already happening in Europe)

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QUESTIONS?