

FINAL MINUTES, JARC workshop, Brussels, 5-6 March 2019

JARC joint workshop WP4 and WP7 to discuss results of the pilot project to apply the Toronto staging principles by cancer registries and next steps.

Date: March 5-6 2019, Venue: SIOPe offices, Brussels.

Attendees

Name and Surname	Country	Name of organisation/registry
Nancy Van Damme (Day 2 only)	Belgium	Belgian Cancer Registry
Liesbet van Eycken	Belgium	Belgian Cancer Registry
Kathy Pritchard-Jones	England	University College London (clinical registries) & representing Public Health England
Kaire Innos	Estonia	National Institute for Health Development
Keiu Paapsi	Estonia	National Institute for Health Development
Emmanuel Desandes	France	Registre National des Tumeurs Solides de l'Enfant, CHRU Nancy, France
Jacqueline CLAVEL	France	INSERM, Registre national des cancers de l'enfant
Claudia Spix	Germany	German Childhood Cancer Registry
Eleni Petridou	Greece	National and Kapodistian University of Athens Medical School: Nationwide Registry of Childhood Hematological Malignancies and Solid Tumors (NARECHEM-ST)
Gemma Gatta	Italy	fondazione IRCCS Istituto Nazionale Tumori
Patrizia Piga	Italy - Campania	REGISTRO TUMORI INFANTILI DELLA REGIONE CAMPANIA (ITALIA)
Fabio Savoia	Italy - Campania	Childhood cancer registry of Campania
Laura Botta	Italy - INT	Istituto Nazionale dei Tumori Milano
Carmen Martos	JRC - EU	Joint Research Centre, Ispra, Cancer Information Group
Ieva Vincerzevskiene	Lithuania	Lithuanian Cancer Registry, National Cancer Institute
Otto Visser (Day 1 only)	Netherlands	Netherlands Cancer Registry abd ENCR co-chair
Bernward (Bem) Zeller	Norway	Oslo University Hospital/Norwegian Cancer Registry
Gabriela Caldas	Portugal	Portuguese Pediatric Oncology Registry
Daniela Coza	Romania	Cluj Regional Cancer Registry - Oncology Institute Cluj-Napoca
Mihaela Bucurenci	Romania	Romanian Society of Pediatric Onco-Hematology/ Romanian National Child Cancer Registry
Alina Patrahau	Romania	Romanian National Child Cancer Registry
Vesna Zadnik	Slovenia	Slovenian Cancer Registry, Institute of Oncology Ljubljana
ADELA CAÑETE	Spain	La FE / RETI-SEHOP - clinical registries
Antonia Sánchez Gil	Spain- Murcia	Registro de Cáncer de la Región de Murcia, Servicio de Epidemiología, Consejería de Salud, Murcia, España
Shelagh Redmond	Switzerland	Swiss Childhood Cancer Registry

Day 1, Tuesday 5th March

1. Welcome and introductions

Kathy Pritchard-Jones and Gemma Gatta welcomed everyone to the meeting and introductions were made. Apologies were noted from the following Francesco Vetrano (Campania, Italy), Filippa Nyboe Norsker and Jeanette Falck Winther (Denmark), Brigitte Lacour (France), Kamila Kepska (Poland), Martin McCabe and Lucy Irvine, (Public Health England), Zsuzanna Jakab (Hungary), Rafael Peris-Bonet (Spain).

2. Objectives of the workshop

The objectives of the workshop were discussed in the wider context of the aims of the epidemiology WP4 of the JARC, namely to improve data quality and cancer intelligence on rare cancers and to support the Expert Reference Networks (ERNs) in evaluating their work. The specific aims of the workshop were agreed as:

- to review the results of the pilot project to apply the Toronto staging principles and to formulate a plan for publication,
- to understand the capabilities and resource requirements of each registry, whether or not they were able to participate in the pilot, to contribute to a future larger collaborative study of more cases diagnosed over a longer time period
- to identify potential funding opportunities for a joint collaborative grant application.

3. Presentation of JARC pilot study

GG then presented the JARC pilot study results. Data has been received from cases diagnosed over a time period of 2000-2016, according to the size of the registry, with smaller registries having to provide several years of data in order to have 10 cases of each tumour type. Most contributing registries were national registries. Overall, 24 registries from 14 countries provided data on 499 cases of neuroblastoma and 387 cases of nephroblastoma (Wilms tumour) diagnosed consecutively. 3 year follow up data were available for the majority but not all cases. The distribution of age at diagnosis was as expected from previous EURO CARE studies. The Toronto stage was provided for 97% of cases, for which all registries were congratulated. The source of data used had been clinical records and/or pathology report in the majority of cases. For neuroblastoma, the proportion with metastatic disease at diagnosis was >50% in those aged over 1yr compared to only 12% in those diagnosed as infants < 1yr. For Wilms tumour, 14% had metastases at diagnosis. 76% of the Wilms tumours were noted to have been treated according to SIOP protocols (i.e. with elective pre-operative chemotherapy recommended for the majority of clinical scenarios). There was evident variation in stage distribution by country. The overall survival for each tumour type was as expected from EURO CARE. Whilst some exploratory analyses of correlations of survival by country and by stage distribution were presented, it was agreed that the cohorts would need to be larger for any statistically robust comparisons. Several countries had provided data on treatment and relapse, very few had data on imaging used for staging purposes or metastatic response.

Claudia Spix commented that it was important to report *incidence* of stage by age group. There was a discussion about variation in age and stage at diagnosis and how this might be related to child health practices in each country. She also noted that in Germany, just as they ended the neuroblastoma screening programme, a national programme of hip ultrasound at age 3 months was introduced which may explain why they continued to see incidentally identified cases.

4. Presentation (verbal or slides) by each cancer registry on their methodology, resources required and any enablers or challenges to their participation in the pilot study

Most registries had required more than one data source to complete the Toronto stage. All had had to go back to existing records and/or obtain new data sources in order to perform the task.

Belgium: (Nancy van Damme) Achieved 100% completeness. Obtained data by sending the patient file data they held back to the clinical centres (8 in total) and asking them to complete the staging and imaging data (CR is not allowed to send registry staff to the hospitals to see patient records). Required data management time at the cancer registry (CR) and at the hospitals - Pediatric oncologists filled in the data. Don't yet hold Toronto Stage at the CR but want to introduce it directly in future registrations. From the administrative data, they know if an exam (i.e. CT) was done but not the result. Registrars will be able to go back to this information but needs to be discussed hospital by hospital.

Option: ask to fill in the Toronto stage during collection for the new cases in the legal format and send it to the CR. Information on multidisciplinary team will be available at the CR but we are dealing with the government for that because we need funding to do this, is not available in the CR.

Estonia: The CR staff went to the hospitals (n = 2) to examine the Medical records and pathology reports. CR staff filled in the forms with the oncologist at hand. Problems: difficult to follow the timeline, dates were missing, information on imaging difficult to find (the MD stated "I remember but is not in the case report"). For future: We can do but takes time. Oncologist don't have the experience of the Toronto staging principles.

France: the French national registry of childhood cancers (RNCE) has had a single database since 2013 for both childhood haematological and solid tumours. They can view medical reports electronically, meeting reports and path reports. They extracted all cases of NBL and WT diagnosed in 2014 and a single person assigned the Toronto stage from the compiled information. Took about 10 minutes per case. Only 2 cases of NBL were missing stage, and 19% of WTs – partly because of missing pathology reports after delayed nephrectomy. 14% cases of neuroblastoma without CT and MRI. Actively research to collect the data. In the hospital they have Quality control for stage registration for all cases from 2016. Traceability for validation, using the Toronto guidelines. They plan to automatically generate the Toronto stage, both tier 1 and tier 2, through use of an algorithm. They are in the process of apply the Toronto staging to cases diagnosed 2000-2015. Done for leukaemia and NBL, WT is in progress, will do sarcomas next (as research projects). They have Clinical Research Assistants (CRAs) funded from the RNCE project who work in the treatment centres and collect data for the RNCE.

Greece: taking part in the pilot has facilitated conversations with the treatment centres. There is a centralised system of childhood cancer treatment centres (n = 7) who collaborate with the CR. However, for CNS tumours, these are often managed by private hospitals and it is more difficult to obtain data from them. Actively collected the data required for the Toronto stage by a CR staff member going to the 3 Athens centres or having a phone conversation with the others and speaking to the oncologist. It was a lot of effort to collect the staging data on the retrospective cohort but the clinicians were willing to provide the data with the correct format. Now the CR is routinely collecting it on prospective cases from 2017 onwards. As the CR is not a government organization but a university led initiative, they need parental permission for data collection and it is collected with consent.

Italy (Campania regional registry): the CR is located in the Children's regional hospital. They contributed ~30 cases diagnosed 2011-12. Regarding neuroblastomas, when they are able to acquire the medical records, they had no difficulty in staging the cases. It was more difficult for patients without access to the clinical record or imaging (about 30% of the NBL cases). Staging was possible for all 14 WTs as the medical record or pathology report was available and contained the information. The feasibility of applying the Toronto guidelines in practice, in their experience, depends on the availability of the required information and on the time spent to track and acquire these records. More easy dealing with the most recent cases. They work with a strong health migration out of the Campania region (about 30%).

Norway: -there are about 120 childhood cancers a year from a population of 5 million, treated across 4 hospitals and large geographic distances. The one centre in Oslo sees ~ 55% patients. The CR holds few variables, but from the year 2000 they have also had a clinical database for pediatric solid tumors that includes more variables, but not the Toronto stage. Registry staff are not allowed to go and examine

medical records, hence for the pilot study, some effort was needed and data were obtained by linking to clinical study data. E.g. LINES + Neuroblastoma.

Future: Possible to obtain stage as numbers of cases are small. However obtaining the necessary permissions for retrospective data collection takes a long time and it will be difficult to provide stage for EUROCARE 6. Perhaps from 2020 clinical + CR childhood will be only one registry -> collecting this data prospectively will be easier.

Portugal: There are about 400 new cases/yr under 18 y from a total population of 10.5 million (1.9 million under 18 y). Until the end of 2017, there were 4 regional CRs in Portugal with different databases but now there is a complete national cancer registry, that is mandated by law. The National Cancer Registry (RON) is available from January 2018

Treatment of pediatric cancer patients are centralized in 4 pediatric oncology units. Since 2014 there is a National Pediatric Cancer Registry. Data on patients aged up to 18 yrs are entered into a clinical registry by pediatric oncologists and cancer registries, working together. The database is the same as the national CR but layout and diagnostic, classification (ICCC 3) and staging system are adequate to each pediatric tumor group. There are some obligatory fields, including classification and staging, so the case can't be saved without their correct completion. However, pediatric oncologists find it difficult to have time to complete all the fields and maintained the registry up to date. It is not difficult to have access and collect clinical data, including staging adequate to each tumour. It would be easy to add the Toronto Stage as an obligatory field of the pediatric registry. The main problem is the manpower, which is not solved, with few registry staff and registries are delayed.

In the Pilot study we used regional registry data from the South area, but now we can have the data from the whole country.

Spain: Murcia regional registry: CR used hospital discharge and pathology reports as data sources for the Toronto stage. In general, these records do not provide sufficient info to produce the Toronto stage, therefore they had to make active efforts for CR clinical nurse staff members to look at medical records to be able to assign tumour stage. Takes time and resources but they are able to stage.

Slovenia: 2 million population with 300,000 aged 0-14yrs or 400,000 aged 0-19yrs. Their first question was to which age group to apply the Toronto staging guidelines? They have a single national cancer centre for children and adolescents that performs all diagnostic procedures and treatment other than radiotherapy which is done at the Institute of Oncology, home of the national cancer registry and the long term clinical follow up services. Data sources used were the standard notifications received by the CR for tier 1 stage, whereas tier 2 required extra specific efforts and was not possible for all cases – successful in 8 out of 10 WTs and 10/11 NBL, using mainly medical records as data source. Participation in the pilot made it clear that tier 2 staging requires both extra effort by personnel and additional data sources to those collected routinely by the CR. They are soon moving to active registration direct from clinical sources and hope to begin Toronto staging prospectively for new cases quite soon.

Switzerland: Data are sent, with parent consent, to the national CR from 9 paediatric oncology clinical centres. The CR records which reports have been received (e.g. diagnostic imaging, pathology, molecular info and hospital discharge) and use secure email to chase missing data. They also have information on clinical trial participation (50% in trial, 25% treated as trial but not in the trial). For the pilot, the central coder received relevant documents and assigned the stage. This was easy to do for 10 NBL and 12 WTs though only 6 clinics responded (1-6 cases/clinic) and took between 1d and 8 weeks (mean 34 days) to send the additional reports requested. Thought it would be useful to have some "test cases" across all registries or training days on how to assign stage from info contained within admin reports as this can be difficult. For the future studies, it will be difficult to provide stage for EUROCARE 6 because cases are retrospective. From 2020 onwards, will be better as there will be a national platform for new cancer registrations aged 0-19 yrs and Shelagh has helped with inclusion of the Toronto staging guidelines within this. Staging data collection will be mandatory.

5. Presentation (verbal or slides) by each cancer registry who was not able to contribute data to the pilot study, including barriers and future enablers.

Spain: national: Adela Canete spoke on behalf of the national children's cancer registry (led by Rafael Peris-Bonet) and the neuroblastoma national clinical registry held in Valencia. Stage was too incomplete in the national registry, whilst clinical stage is a 'must' for the clinician. They decided to focus on improving prospective collection rather than trying to go retrospectively. Later in the agenda, she described a separate linkage project between the neuroblastoma clinical registry and the national childhood cancer registry. To do another retrospective study would be impossible for them.

UK: Since 2012, the national cancer registration and analysis system (NCRAS) of Public Health England is on a single database, into which the childhood cancer registry records for England have been migrated. Hospitals are mandated to submit a cancer services and outcomes dataset that includes tumour stage. (The devolved nations of the UK (N Ireland, Scotland, Wales) have their own systems which are following similar principles). However, for NBL and WT cases in 2014, staging completeness was low, though this is improving over time (80% for NBL and 30% for WT cases diagnosed in 2015). It was not possible to join the pilot due to the incompleteness of staging data held in the registry and the length of time and resources needed to obtain necessary permissions to link to stage data held in a clinical registry (WT) or by going back to treatment centres (NBL). In the future, routine data feeds direct from multi-disciplinary team meeting information systems is expected to be more robust and complete. Hence, PHE keen to contribute to next phase of joint working. Scotland, Wales and N Ireland were not yet approached but likely to be interested.

Germany: the national cancer registry is an epidemiological rather than a clinical registry. While stage forms part of the expected national CR record, it is often incomplete. Tumour stage and other clinical info can be obtained from the many national clinical study registries that exist for all tumour types and which are led from various hospitals in Germany. There are more than 50 hospitals treating pediatric oncology (expected to reduce to ~40 over time) and over 30 clinical studies where 98% of patients are enrolled or treated according to standardized protocols. Data exchange with the clinical study registries is possible but often slow to happen for various reasons – e.g. no staff time, data needs 'cleaning' before sending, etc. It may be possible to provide some stage data for EURO CARE 6 for some tumour types. It would also be helpful to ask for stage and other clinical outcome indicators such as relapse in the call for data, as this would encourage the clinical registries for joint working and would also help the CR check its data on relapse. CR staff are not permitted to go to the hospitals to view records due to data privacy rulings by hospital administrators. In the future, aiming to move to electronic notification through a portal (not before 2 yrs from now). Had considered including more clinically inputted data but probably won't do this now due to differences at the federal versus state level of what data items are permitted. Another player in the field is the German Cancer Society which is offering an accreditation scheme for which hospitals can apply. The GCS is willing to work with the CR to avoid triple reporting requirements (state health services, CR, GCS) for the hospitals.

Lithuania: -main challenge is the law. Cancer registration legal status and authorization was only signed off by the government in 2016. This includes authorization for the variables to be collected, but if we want to add something, we have to change the law because it stated clearly which variables we have to collect. Also the CR does not sit under the Minister of Health but under the Minister of Education, Science and Sports. The CR collects TNM. There are two clinical registries in hospitals created by doctors for their own use but are full of mistakes and under register.

Netherlands: The national CR did have sufficient stage data to assign tier 1 but didn't participate as they didn't have the time/resources to collect the additional data required for tier 2 Toronto staging. They have since applied tier 1 staging to all cases in the CR (only 3% unstaged). For solid cancers diagnosed 2014-17, they hold data on extent of disease and presence of metastases. There is a specific clinical registry that collects data on relapse so this is not collected by the CR.

Romania: there are 8 regional adult cancer registries. In 2009, there was an initiative to start a national childhood cancer registry from scratch. Staff in all 13 pediatric cancer treatment centres were trained to input data. Cases diagnosed in 2010-2015 already done and now collecting 2016. They are now compiling their first analyses of incidence. Staging data are not yet available. They are planning to use an online portal to report the general cancer cases and have started from the most basic items recommended by ENCR. For cases from 2018 onwards, they intend to add more clinical information and may be able to do this retrospectively within the frame work of this pilot. In 2014, 11/22 NBL cases were staged. For WT, among the average of 17 cases/yr 2010-15, 40% had missing stage in the CR. Adult cancer registration is mandatory by law but the childhood cancer registry is voluntary and not supported by the government. Its development has been supported by a charity working with the national PHO society.

Everyone congratulated the Romanian team for their successful efforts to establish a national childhood cancer registry.

6. Linkage between clinical and/or administrative data bases and population-based cancer registries for collection of stage and other clinical parameters

Spain: Adela Canete presented a project in that aims to test linkage of clinically collected/scrutinised data in a tumour-specific clinical registry and unselected population data through close collaboration between paediatric oncologist-led and epidemiologist-led (population-based) cancer registries. The pilot linkage project focused on neuroblastoma, for which the Spanish neuroblastoma clinical registry is held at La Fe hospital, Valencia. Nationally, there are 38 Paediatric haemato-oncology units (PHU). There is a national childhood cancer registry (RETI-SHOP) that collects population-level data from the regional, all-age, cancer registries. There are 13 regional registries that cover ~32% of the Spanish population, 10 registries participated in the pilot linkage project for neuroblastoma. All cases aged 0-14 yrs with neuroblastoma registered 1999-2017 were cross-referenced (n = approx. 1,500 cases). It was found that, although there are tools that permit automatic linkage, with the available software (DALINK) and permitted personal identification details, a manual cross-check must be carried out in ~54% of the matches from the clinical registry to the population-based cancer registries. Linkage was hampered by the lack of a unique personal identifier at the national level. The human resources required for this pilot were 2 persons for 2 months. The sustainability of these semi-automatic procedures is doubtful and they recommend that there should be a unique identifier (national / European) that could “track” the patient from the moment he/she enters the Health System.

France and Greece mentioned that their countries do have unique patient identifiers in the healthcare system but they are not allowed to use it. Their national registry presentations on efforts on data linkage with clinical registries were postponed to day two.

7. Presentation on activities of the European Joint Research Centre, Ispra

Carmen Martos presented the current and planned activities for cancer registration of the JRC, Ispra, Italy. Following the first call for data in 2015, there are now about 34.5 million records in the entire European Cancer Information System (ECIS), that comprise a mixture of core and optional variables. The current European cancer registration coverage is provided by 136 CRs, 13 specific, across 34 countries. There is ~60% population coverage overall, with ~72% for childhood cancers. Reported incidence for all cancers, 2008-2012, is lower in eastern regions. There was a public launch of ECIS in Feb 2018. ECIS currently reports incidence and mortality (from IARC) and survival from EURO CARE 5 but there will be a new call for data in 2020. Hence, now is the time to ask as the paediatric oncology community, if we want to add Toronto stage into the data collection protocol. The request should go via the ENCR steering committee who are next meeting in May 2019.

When registries provide their data to the JRC, they state which projects they wish to participate in, e.g. EURO CARE 6; European cancer incidence and mortality analyses, etc.

The 2014 JRC Technical Report provide for one common procedure for cancer registration with agreement on common standards. It is planned to provide training for cancer registries on the Toronto staging principles as part of the next JRC-ENCR training workshop – to be held 5-6th June 2019, Ispra. The JRC gives some financial support for registries who cannot access training easily.

8. Update on ENCR plans to support improvement in childhood cancer registration at a European level.

Otto Visser, co-chair of the ENCR, gave a brief update. Data quality is an issue and whilst ENCR can make recommendations and offer training, the needs of each cancer registry can be very different. He suggested for each CR to ask ENCR if they have a specific problem. For children's cancers, the ICCC classification should be used. He welcomed that we should submit a request to include Toronto staging in the next (2020) call for data. Whilst many registries said they wouldn't be able to provide stage for any but the most recent cases, it was welcomed that including stage in the call would be a stimulus for the registries to find means to collect and share these data.

Day two, Wed 6th March 2019

1. **Liesbet van Eycken (Belgium)** gave a description of the approach to training for cancer registries provided by ENCR who see a need for and wish to support both basic registration training and specialist courses. The next course at the JRC, Ispra, is not specific for childhood cancer but will include training on implementing the Toronto guidelines. The workshop is aimed at those responsible for coding and with some coding experience. She emphasized the importance of training general cancer registration staff in the Toronto guidelines since the majority of childhood cancer cases were captured through this route. The workshop will have an interactive training format, with anonymous voting and feedback on coding real cases that include challenging or 'grey area' decision making. She requested that the childhood cancer registries help by providing some real-life difficult examples that would be useful in this context for the training workshop. A similar approach will be used for other rare cancers, e.g. sarcomas, brain and neuro-endocrine tumours.

The training workshop faculty will be Francesco Giusti, Otto Visser, Liesbet van Eycken, Nadya Dimitrova and Carmen Martos. **The workshop dates are 5-6th June, JRC, Ispra. Deadline for applications is 3rd May.** She noted that the Toronto guidelines have been endorsed by ENCR on their website since February 2019 and it is expected that all registries will make efforts to use them. It will be good if Toronto stage can be included in the 2020 call for data, even as an optional item, to stimulate its use by registries.

Vesna Zadnik proposed a 5 day course in October to be run with ENCR involvement and to be held in Slovenia aimed at South and Eastern registries. It would be a mixture of basic and specialist registration training and would include a focus on childhood cancer.

Continuation of item 6 from day 1: national registry presentations on efforts on data linkage with clinical registries:

Jacqueline Clavel (France) described the set up of the French national registry of childhood tumours (RNCE) as a collaboration between the INSERM and the Societe Francaise des Cancers d'Enfant (SFCE). This had been in response to a government-backed call to establish an infrastructure for research in childhood cancer that would be systematic, permanent and nationwide, include all types of childhood and adolescent cancers, integrate clinical, biological and follow-up data and be open to researchers under required regulations (ethical, security and privacy, GDPR). Initial funding provided ~300,000 euro per year for 10 years. She described an ambitious portfolio of projects underway and planned.

The RNCE was created in 2013 by bringing together the pre-existing certified structures: the National Registry of Childhood Hematopoietic malignancies (RNHE, based in Paris and active since 1990) and the National Registry of Childhood Solid Tumors (RNTSE, based in Nancy and active since 2000) into a combined

effort that continues to operate from Paris and Nancy. They have built a pooled database containing all cases diagnosed up to age 18yrs from 2000 onwards. This is approx. 30,000 cases with multisource standardized data that includes detailed information on diagnosis, stage, grade, basic data on treatments, response to 1st line therapy, vital status and cause of death. They can geolocalize all cancer patients aged 0-19 years old. Treatment data has been recorded prospectively since 2013 and they are aiming to go back retrospectively to 2000, aiming to extract cumulative doses of chemotherapy and radiotherapy and response to each line of treatment. They have established COHOPER as an exhaustive database on 22,000 survivors with systematic follow up for 5yrs from diagnosis. Data sources are obtained through linkage with health insurance and hospital databases and include all hospital visits, screening examinations and use of specific algorithms to detect relapse – the latter is also notified directly to the RNCE, along with second cancer occurrences.

It took 2 years to get all necessary permissions for data access and handling in place. They don't have visibility of the patients' national health insurance number but it is used in a non-disclosive way for linkage to routine health care records. Patient data are linkable to a virtual biobank. The Toronto staging is integrated for cases since 2016 using routine healthcare reports. About 90% of cases have enough information to be staged. In France nothing is mandatory, but the clinical centres must open the files when asked for info by the RNCE. They have relapse free survival by stage.

From Oct 2019, they are starting a questionnaire study of 10,000 survivors that will have elements in common for comparison with a contemporaneous cohort of 200,000 volunteers in the same age group completing a questionnaire on lifestyle, quality of life, occupation, health, disabilities, medical care (CONSTANCES study).

Eleni Petridou (Greece) presented NARECHEM-ST (National registry for childhood haematological malignancies and solid tumours). This collects data on 6 cancer types diagnosed since 1996 (haematological malignancies) neuroblastoma and Wilms tumour since 2009, CNS tumours since 2010 and liver tumours (with the exception of one treatment centre still pending) since 2000. They have blood samples stored on some cases in Athens. Registration is with consent as this is not a governmental but an academic-led registry. They are conducting a sub-analysis of liver tumours (approx. 58 cases) and aim to obtain PRETEXT staging retrospectively which will require important clinical interactions. Taking part in the Toronto pilot has stimulated greater collective standardization of approach to data collection and even of clinical adherence to protocols. There was a brief discussion on how PRE-TEXT staging for liver tumours is not part of the Toronto guidelines. KPJ explained that this was because it was a clinical staging system used by the SIOPEL group to determine pre-treatment extent of disease and hence the type of surgical approach that should be planned. As other clinical groups (e.g. COG) used other staging systems, it had not been included in the Toronto guidelines. However, the Toronto meeting had recognized that staging systems would evolve over time as they incorporated a more integrated overall 'risk classification' approach that is most useful clinically. Hence, it was important that the guidelines were reviewed periodically and since it was now nearly 5 years since their publication, KPJ volunteered to enquire from Dr Sumit Gupta, Toronto, if and when such a review was planned. She also informed Eleni that there was a global initiative between clinical study groups in childhood liver cancers to build a global database for these rare tumours. She recommended that NARECHEM-ST considered offering to share their data with PRETEXT stage in this context, for international benchmarking of stage and extent of disease at diagnosis in Greek patients.

Australian Cancer Registry TorontoStage App: Laura Botta (Italy, Gemma Gatta's research group) gave a presentation that she had received from Joanne Aitken (Director of the Australian Children's Cancer Registry) and Jad Goss (solution development lead) to demonstrate the functioning of their bespoke app, designed to incorporate the Toronto Staging principles. The App allows data managers to enter results of various diagnostic and imaging tests as well as information on staging found in doctors' letters. It then provides a stage based on the information inputted and highlights any conflicts or difficulties in assigning a stage. The app has gone through several iterations during its development and is now being used routinely by the Australian registration staff. They are very keen to share their experience and the App itself if useful

in other countries. Anyone interested in signing up for an account to use the demonstration site (<https://stardemo.azurewebsites.net>) should contact Laura.Botta@istitutotumori.mi.it

3. Discussion on next steps for JARC recommendations and opportunities for further joint projects

Romania (Mihaela Bucurenci): as their registry is based on voluntary reporting without government involvement, they have had a problem with frequency of reporting by the treatment centres and also with losing patients to follow up when children transition to adult (15-19yrs) as they are no longer in the pediatric oncology hospitals. Since 2018, they have established more regular reporting with an estimated number of 400 new cases/year nationally. However, tumour stage is missing in 59% of reported cases. The old registration form had only TNM. She emphasised the importance of a statement on a minimum set of variables that have to be collected by all the registries for childhood cancer cases, not only adult cancers. This should specify the staging system to be used and we have the Toronto guidelines ready to propose for this purpose.

ENCR/ECIS in response to a question about how data provided by registries are used, they establish a data protection agreement registry by registry, valid for at least for 10 years. The 2020 call for data is under discussion and will be finalized at the June meeting of the ENCR. The time period over which cases will be requested has not yet been decided, nor the time interval from data call to data provision. There will be some quality control work undertaken before the 2020 data call to improve data comparability. There was agreement amongst attendees that for any comparisons of tumour stage by childhood cancer, at least three years of incident cases would be needed for the analysis. There was a recap of discussion from day 1 regarding the efforts required to obtain tumour stage retrospectively over a longer time period than in the pilot:

- Belgium - prospectively they are collecting Toronto from 2018, retrospectively feasible but with money
- France – estimate it would require 14 person-months to code for staging of all cases for 2010-2016. They have the data for cases from 2016 onwards.
- Germany – rely on clinical registries to provide tumour stage. Could be requested and provided if Toronto stage is included in the ENCR 2020 data call.
- Some registries could provide data on tumour stage for cases diagnosed 2015 onwards (Murcia, Slovenia, Estonia) whereas others are planning to have this for 2018 cases onwards (Romania, Spain and others). Lithuania - need to check what will be available with the head of the CR. Greece - routinely collected for neuroblastoma and nephroblastoma, other tumors need money. UK – high proportion of missing stage info on retrospective cases but expected to be much improved for prospective cases and can be provided.

All agreed it would be very helpful to have a statement from SIOP Europe endorsing the importance of clinical centres and clinical registries cooperating with their population based cancer registries to make staging data available.

There was a discussion on the feasibility and value of additional data items:

- Belgium, difficult to have relapse. Imaging used to stage is a new variable that we want to include.
- France collect treatment but is unable to give it to the ENCR.
- Biological subgroups are becoming standard of care and no longer research items. They have been included in pathology reports for several years in many tumour types but don't have a specific code in the ICD0 and are therefore difficult to register. Switzerland and France have these data items.
- Data on biology and other clinically important data used for risk stratification are more about relapse free than overall survival (i.e. optimizing the success rates of first line therapy to reduce late effects). Therefore will be important to have data on relapse.

Agreement that we need to keep it simple and take an incremental approach, with Toronto staging being the most important first step for all registries, and ambition to collect/option to provide other data items for shared projects where feasible.

Discussion on publication of the pilot study:

Main message is about the feasibility of provision of tumour stage by many registries for a collaborative study and the effort required and data sources used. Romania thought they might be able to provide their 2014 cases to the pilot if they can be accepted in the necessary timescale. Mihaela will liaise with Gemma on this point. Claudia Spix emphasized that we needed to think about recommending some form of quality checks for the Toronto stage implementation if it is to be included in the ENCR guidelines, as well as TNM checks, although the latter apply to fewer childhood cancers. The paper should be useful to clinicians, to highlight the potential for future comparative studies of survival to be able to show them what type of patients they are treating and to show survival rates stratified by stage.

Gemma to lead on drafting the full paper. Suggested that journal for publication should be one that reaches both clinicians and epidemiologists/registries.

Discussion on possibility of funding for future projects:

Recognised that having data on tumour stage would be useful for evaluation of impact of twinning programmes and comparing the data of eastern European countries. As discussed above, even if Toronto staging is included in the ENCR 2020 data call, without additional funding, registries will only be able to provide data they already hold or have easy access to for the likely time period of diagnosed cases with sufficient follow up. Whilst ENCR has funding from the European Commission, it has no funds for projects. There is a current call open from Children with Cancer UK and Gemma/Kathy will explore whether this might be suitable – however noted that their grant call website emphasizes a focus on adolescent cancers, of which we had few in our pilot.

Conclusions

1. The pilot study of the feasibility of implementing the Toronto staging guidelines by cancer registries had been successful.
2. It had highlighted the most useful data sources, the methodology and effort required, both for registries who had been able to provide cases for the pilot and those who had not, for a variety of reasons.
3. All were supportive of including Toronto stage for prospective cases diagnosed from 2018 onwards, there was variable and limited capability to stage retrospective cases over a short time period back to ~ 2015.
4. Inclusion of Toronto stage in the ENCR 2020 data call would be a useful stimulus to strengthen joint working with clinical treatment centres and clinical registries. This group should submit a formal request to the ENCR steering committee to include the guidelines and to SIOP Europe asking for their endorsement of their use.
5. The workshop had highlighted the increasing capability of registries to include 'enhanced' clinical data items in their registration processes and their willingness to use these in joint projects to improve interpretation of international survival comparisons and the European cancer intelligence system for children's cancers. However, specific funding would be needed to enable registries to contribute cases for a larger joint project in the near term.

ACTIONS

	Action	Owner	Date for completion
1	Claim travel expenses – max. 1 person per registry	All	25.03.2019
2	Feedback comments on minutes	All	25.03.2019
3	To note dates of next ENCR workshop, Ispra (5-6th June) and that deadline for applications is 3rd May.	All	03.05.2019 to apply
4	To provide 'grey cases' as coding examples for implementing the Toronto guidelines for the ENCR training workshop – send to Liesbet van Eycken elizabeth.vaneycken@kankerregister.org	All	Before early May 2019
5	Draft full paper on pilot study and invite comments	GG	Tbc by GG
6	Submit formal request to ENCR steering committee to include Toronto stage in 2020 data call	GG/KPJ	April 2019
7	Review possibility of submitting a grant call to CWC, UK	KPJ/GG	Asap
8	Request SIOP Europe to endorse Toronto staging guidance	KPJ	April 2019
9	Romanian CR to liaise with Gemma Gatta regarding inclusion of their staged cases in the pilot study	MB/GG	Completed 13.03.2019
10	KPJ to enquire from Dr Sumit Gupta, Toronto, if and when a review of the Toronto guidelines was planned	KPJ	19.03.2019

Note added post-meeting:

The conveners of the original Toronto staging guidelines development workshop (Lindsay Frazier, Boston, and Sumit Gupta, Toronto) are planning to hold an update session in conjunction with IARC during the SIOP annual congress in Lyon, Oct 2019, to both update the staging guidelines and to discuss whether there are additional prognosticators that population-based registries with sufficient resources should collect.

Workshop attendees day 2

