“HEALTH MEETS RESEARCH”
Concept of a long term follow up instrument for critically ill patients

Univ. Prof. Dr. Ruth Ladenstein
St. Anna Children’s Hospital &
Children’s Cancer Research Institute,
Vienna /Austria
eHealth for Research

“……….eHealth is the cost-effective and secure use of information and communications technologies in support of health and health-related fields, including health-care services, health surveillance, health literature, and health education, knowledge and research”

WHO, WHA58.28, eHealth, The Fifty-eighth World Health Assembly, 25. 05. 2005
Directive 2011/24/EU of patients' rights in cross-border healthcare

focussing on patients' rights & healthcare across the Union:

- Right to choose and be reimbursed, under certain circumstances for, healthcare provided by public or private providers located in the EU.

- More transparency about their rights, treatment options or, the quality and safety levels of healthcare providers.

- Strong focus on cooperation among Member States.

Entry into force at National level 25 October 2013
THE EUROPEAN UNION VISON
Telemedicine and other IT solutions and tools are the basis

Remote guidance and Diagnosis
Remote training
Secure exchange of Patient information, databases/registries
Remote monitoring and follow-up
Tele-radiology
Tele-surgery
Tele-imaging
Tele-dermatology
Tele-consultation

Local Healthcare Provider
Member
Member
Virtual clinical/tumour boards
Member
Member
ADSL

European Reference Networks
Paediatric Cancer is a public health challenge

- > 12,000 children and young people diagnosed in Europe each year
- 60 different types of cancer, > if biological markers considered
- 6000 die each year

- The quality and availability of paediatric cancer care widely varies across Europe
- 10% to 20% of them die from curable forms of cancer where quality care is not easily accessible.
- The outcome gap is even larger for paediatric cancers with poor outcomes
- In 2020 - 500,000 survivors: 2/3 late effects
European Expert Paediatric Oncology Reference Network for Diagnostics and Treatment
Stakeholders

ExPO-r-Net is a 3.5 year project (03.2014 - 09.2017) to build and structure a European Reference Network for Paediatric Cancer (PaedCan ERN)

- Project Coordination: CCRI /Vienna-AT
- More than 60 Partners (Health care professionals, Hospitals, Institutes) from 17 countries
  - 18 core partners from 9 EU countries
  - > 50 Collaborating professional partners

### Collaborating partners

<table>
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<tr>
<th>Number</th>
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<tr>
<td>Eastern European</td>
<td>20%</td>
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<tr>
<td>Western European</td>
<td>80%</td>
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</table>

- Involving parents and patients
- 8 Work Packages
Childhood Cancer

- Rare Disease Definition: 1 in 2000  www.eurordis.org
- Childhood ( < 15 years) Cancer Incidence in Europe: 1 in 6250


**Brain Tumours** 19%

**Soft Tissue Sarcoma**

**Other (VRT)** 8%

**Neuroblastoma** 8%

**Liver Tumours** 1%

**Retinoblastoma** 3%

**Bone Tumours** 5%

**Wilms Tumour** 6%

**Lymphoma** 13%

**Leukaemia** 30%

Deutsches Kinderkrebsregister Mainz / 2000 New Cases / year
ExPO-r-Net: PaedCan ERN Roadmap

- Healthcare cooperation and resolving expert fragmentation

- **Identifying special therapeutic needs** of young people with cancer requiring high expertise interventions with ECTG
  
  Examples: special surgery, radiotherapy (proton therapy), stem cell transplants

- **Identifying European institution ready to engage as reference centres** by establishing and/or rolling out virtual tumour boards for cross border advice

- **Identifying European Institutions /hospitals offering top level expertise** for special therapeutic interventions and referrals

Guidance for Health Care Providers

Increased Transparency for Affected Families
European Clinical Trial Groups
International Coordinating Sites (PI)
Hubs of Coordination

- Already in Expo-r-Net
  - Acute Lymphoblastic Leukemia (ALL2009, IntreALL, Interfant, ALL-SCT)
  - Brain Tumours (div. entities)
  - Ewing Sarcoma
  - Hepatoblastoma
  - LCH
  - Lymphoma (NHL, Hodgin)
  - Neuroblastoma
  - Osteosarcoma
  - Soft Tissue sarcomas (CWS, EpSSG)
  - Wilms Tumour
  - Very Rare Tumours – paediatric age

- Invited
  - AML
  - Lymphoma Groups (NHL, Hodgkin)
1) The Survivorship Passport is an innovative patient-centered web platform that provides a ‘Patient Summary’ with relevant information on the medical history and treatment undergone by patients.

2) The goal is to empower patients and make them aware of the potential risks or late effects stemming from the previous diseases and treatments received.

3) It also includes recommendations for a personalized long-term follow-up, based on treatment history and up-to-date clinical guidelines, in collaboration with EU-Pancare experts.
Survivorship Passport: A life-long cancer-related patient-centered repository

Life-long data preservation

The long-term Cancer History

First Cancer
Follow-ups
Secondary Cancer or other diseases
Follow-ups
....

Survivorship Passport Platform

Survivorship Passport First Version
Survivorship Passport Second Version
Survivorship Passport Third Version
Survivorship Passport Fourth Version
Structure

- Demographics
- Diagnosis
- Frontline treatment
- Chemotherapy
- HSCT
- Radiotherapy
- Surgery
- Relapse/Progression
- Other relevant clinical events
- Medical suggestions
- Relapse after 1st end of therapy
- Notes

ICD-O (WHO or Cancer registries)

New coding (215 variables)

ATC

420 variables

Before 2013 2014 2015
January-June July-December January-June July-December January-July
Cardiomyopathy SMN breast cancer
Coronary / vascular disease CV risk / Metabolic syndrome
Models of care / transition
Female gonadal toxicity Male gonadal toxicity
Neurocognitive deficits, fatigue Thyroid cancer/ dysfunction
Bone CNS & other vasculopathy GH deficiency Hearing disabilities
Tubular/glomerular injury Other secondary neoplasms Miscellaneous Group 1 Miscellaneous Group 2

IGHG EBM method
IGH & PCSF collabor EBM method
PCSF alone "Pragmatic method focused on education"

14 IGHG+PCSF (2 completed + 3 ≈completed)
3 PCSF alone (transition + 2 miscellaneous)
may also gather medical images (e.g. Radiotherapy)
Survivorship Passport Data Schema

Demographic data

Tumor description

Front line treatment

Relapse/Progression

Chemotherapy

Stem Cell Transplantation

Radiation Therapy

Surgery

Other relevant clinical events

Recommendations for follow-up

Second tumor

...

Other relapses

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

New recommendations for follow-up

Recommendations for follow-up

Second tumor

Other relapses

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

New recommendations for follow-up

Relapse/Progression

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

Other relapses

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

New recommendations for follow-up

Relapse/Progression

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

Other relapses

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

New recommendations for follow-up

Relapse/Progression

Chemotherapy

Stem cell transplantation

Radiation therapy

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Other relevant clinical events

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Stem cell transplantation

Radiation therapy

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Other relevant clinical events

New recommendations for follow-up

Relapse/Progression

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

Other relapses

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

New recommendations for follow-up

Relapse/Progression

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

Other relapses

Chemotherapy

Stem cell transplantation

Radiation therapy

Surgery

Other relevant clinical events

New recommendations for follow-up
Guideline example (English version)

The risk of second malignant tumours

The risk of cancer increases for everyone as they get older. As a survivor of childhood cancer you may have a slightly higher risk of developing a cancer in adulthood compared to people of similar age in the general population. There are several factors that can affect this:

Radiotherapy: receiving radiotherapy, especially at a young age and in a large dose, increases the risk of developing a second cancer in the area of the radiation. These cancers are unlikely to develop until 10 years after treatment. The most common sites include the skin, the breasts, the bones, the brain, and the thyroid.

Treatment with certain chemotherapy drugs: there is a small risk of developing leukaemia after treatment with certain drugs e.g. etoposide, cyclophosphamide and drugs like adriamycin. If leukaemia does develop this is usually within 10 years of treatment.

People who have a history of cancer in their family: some patients have inherited gene changes (mutations) that increase the chances of getting a second cancer.

Inherited gene changes are quite uncommon and affect less than 10% of people diagnosed with childhood cancer. If the same or different cancers have occurred in several family generations, particularly at young ages, there may be a genetic link. A review of your family medical history will help decide if genetic counselling or testing is advisable.

Breast Cancer Screening

www.siope.eu
www.pancare.eu
www.ighg.org
encca.cineca.org/passport

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Yes, Go do it

It is reasonable to do
More research required

It might be considered to be done
More Research required

Stop, Don’t do it

No specific recommendation can be made since further studies are needed

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Manche Krebsbehandlung kann die Herzfunktion beeinträchtigen.

Die Probleme können mehrere Jahre nach Therapieende auftreten.

Diese Broschüre gibt eine Übersicht:
- Wie das Herz funktioniert
- Wichtige Zeichen und Symptome für kardiale Beeinträchtigung
- Empfehlungen für regelmäßige kardiologische Untersuchungen für jene Patienten, die bei ihrer Krebsbehandlung potentiell geschädigende Medikamente erhalten haben.

Das Herz ist ein kraftiger Muskel, der das Blut durch den ganzen Körper pumpet. Das Blut liefert Sauерstoff und Nährstoffe in den Körper und transportiert Kohlendioxid und Abfallprodukte ab. (siehe Abbildung)

Das Blut wird durch zwei Gefäße vom Herzen in den Körper gepumpt: die Aorta und die Pulmonalarterien. Es wird in zwei großen Gefäßen wiede zurück zum Herzen geführt: die obere und untere Hohlvenen.

Das Herz ist in vier Kammern unterteilt:
- Den rechten und linken Vorhof, sowie die rechte und linke Herzkammer. Durch die Vorhöfe kommt das Blut ins Herz und die Kammerpumpen es wieder aus dem Herzen.

Es gibt 4 Herzklappen, welche den Blutfluß in eine Richtung lenken.


Schließlich wird das Herz von einer schützenden Hülle, dem Herzbauwinkel umgeben.
### SUMMARY OF CANCER TREATMENT

"This Survivorship Passport is a short summary extracted from the information reported in the medical record. It describes the disease and its clinical course as well as the treatments you received. This document does not replace the medical record that is always available at our center."

Marie DOE  
Passport Number: IT1201505211

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<td><strong>Hereditary Cancer Predisposition Syndrome</strong></td>
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<td><strong>Other medical conditions, cancer associated</strong></td>
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<tr>
<td><strong>Other medical conditions, not cancer associated</strong></td>
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<th>FRONT LINE TREATMENT</th>
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<td><strong>The treatment has been executed following</strong></td>
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<tr>
<td><strong>Summary of major treatments</strong></td>
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<td><strong>Chemotherapy</strong></td>
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<tr>
<td><strong>Stem Cell transplantation</strong></td>
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<td><strong>Major Surgery</strong></td>
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<tr>
<td><strong>Progression/recur during frontline treatment</strong></td>
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The Survivorship Passport: 2 sides of the same coin

Care

- Empowerment of survivors
- Risk adapted personalized follow-up
- Homogeneous follow-up
- Guidelines available to survivors and GP
- Appropriate use of NHS resources

Research

- Early identification of «epidemic» of emerging rare events
- Identification of risk factors
- Move from «cure at any price» to «cure at least price»
- Design of new treatment strategies
A. Clinician registers the patient in the Patient Registration form
B. During the registration process, the system requests the EUPID code for the Patient
C. In the Diagnostic Data area the clinician can collect all the relevant clinical information
D. Therapy Information are important for the generation of guidelines
E. The system generates the Passport and related Guidelines
Already available Tools from ENCCA

- **EUPID - European Unified Patient IDentity Management Service**
  - [www.eupid.eu](http://www.eupid.eu) (beta)

- **Survivorship Passport – Patient Summary**

Each Context needs 1 Informed Consent (i.e Trial A)

Given Name, Surname, Date of Birth

Same Patient
New Context ➔ New Pseudonym PSN₂

• No Double Registration
• Data Matches
• Re-Identification

EUPID itself not visible to the outside world

Input (GUI): accessible (Output) inaccessible (internal)
Secondary Use of Data Pilot Neuroblastoma Data Integration

KEY and UNIQUE to EUPID:
No central personal data storage in Europe!
*Personal Data stays with Health Care Providers only*

The Survivorship Passport Data Flow

- National/Hospital Electronic Health Records or other Healthcare data (data transfer via HL7, IHE, ...)

- Patient-based Survivorship Passport (printable PDF)
- Patient-based Survivorship Passport (web-based version)

Clinician Data Input
Survivorship Passport Data Access: Future

Patient will have the possibility to view and share his own data during lifetime.

Legenda
- View data
- Update data

Data Input (Hospital)
- Patients
- National Authorities
- Oncologists, GPs,
Future planned Developments

- The possibility of a mobile app for the passport is under consideration
  - Passport download and/or search for specific information
  - Possibility of pop-up memos according to guidelines

- SU-PP Concept part of Austrian National Cancer Plan
  - Implementation with the Austrian electronic health records
  - European eHealth based long term follow up and advisory health surveillance instrument solution for a moving population
Long Term Follow Up
Integration in new Clinical Trials

- Identification of Core data set for LTFU (eHealth compatible)
- Integration of LTFU diagnostic test in clinical trials
- Data linkage of data bases and LTFU registries via EUPID
- Secondary Use of data via eHealth /Research platform integrating the eHealth Survivorship Passport
ExPO-r-Net: Key Benefits

- **Improved visibility and access to expert care and advise in Europe:** A ‘roadmap’ of centres to allow medical teams to find expert sites for given conditions for advise and patient referral if indicated.

- **Information on cross-border treatment modalities:** in another EU –Member State accessing healthcare or advice received and reimbursement for advise.

- **Possibility to be treated at home or abroad:** Mechanisms to facilitate movement of information and knowledge rather than patients whenever possible.

- **Progress in instituting virtual late effects centre:** incl. operationalising Survivorship Passport.

- **Elevated standards of treatment and care across all of Europe**
PaedCan ERN

THANK YOU!

The project ExPO-r-Net has received funding from the European Union in the framework of the Health Programme (2008-2013), grant agreement nr. 2013 12 07. The content represents the views of the author and is his sole responsibility and it can in no way be taken to reflect the views of European Union bodies. The European Commission and/or Chafea do not accept responsibility for any use that may be made of the information it contains.
PaedCan ERN ExPo-r-Net Roadmap Hepatoblastoma

**Background**

- Annual hepatoblastoma incidence: 1-1.5 case / million, thus expected number of hepatoblastoma cases annually in Europe is 120-180

- Childhood Liver Tumours Strategy Group SIOPEL: European platform with 211 members and global partners to discuss paediatric liver tumours

- SIOPEL therapy Guidelines:
  - Standard risk SIOPEL3 cisplatin monotherapy
  - High risk non-metastatic SIOPEL3 SuperPLADO
  - High risk metastatic SIOPEL4 dose intensive cisplatin
  - HCC – in preparation
PaedCan ERN
ExPo-r-Net Roadmap
Subentityity Hepatoblastoma

Impact

• Network of European centres of expertise in the treatment of paediatric liver tumors
• Access to equipment and experience in unique treatment modalities:
  • Liver transplantation (LTX)
  • Chemoembolization (HACE)
  • Radiofrequency ablation (RFA)
  • Complicated liver resections with vascular reconstructions
• Fully operational Virtual Consultation Forum
• Standardized consultation and referral criteria
• European state-of-the-art in hepatoblastoma
Hepatoblastoma
Hubs of Coordination

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Advantages

- Provide access to global expertise to support clinicians in managing challenging cases, particularly in rare diseases
- Opportunity to update clinicians on new developments in diagnosis, risk stratification and treatment approaches
- Cases storage for training purposes

Workflow
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<td>Universitätsklinikum Frankfurt</td>
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European Clinical Trial Groups
International Coordinating Sites (PI)
Hubs of Coordination

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  - Soft Tissue sarcomas (CWS, EpSSG)
  - Wilms Tumour
  - Very Rare Tumours – paediatric age

- Invited
  - AML
  - Lymphoma Groups (NHL, Hodgkin)
Peadiatric Haematology Oncology Clinical Centres in European Countries with Low Health Expenditure Rates (LHEAR)

**Preparation of a checklist enabling self-assessment by treatment centres of their compliance with the European Standards**

- Identification of centres in Central/Eastern Europe, which meet specified criteria to fulfil the Standards of Care
- They will become visible internationally and may in the future interact with “hubs of coordination” via virtual tumour boards.
- These identified centres should be able to do baseline care for the patients, with help and advice from tumour boards.
LHEAR Countries in Europe

- **>2000 U$**: Czech Rep., Slovakia, Slovenia
- **1400 – 1800 U$**: Croatia, Estonia, Hungary, Lithuania, Poland
- **1100-1200 U$**: Bulgaria, Latvia, Serbia
- **< 1000 U$**: Belarus, Bosna-Herzegovina, Macedonia, Romania, Ukraine
Self Assessment Questionnaire based on the Standards of Care Requirements in PHO

- “Assessment test run”
  - UCL London
  - IGR Villejuif
  - Erasmus Rotterdam
  - Milano
  - Kiel

- LHEAR Countries
  - Sofia, Bulgaria
  - Bucharest, Romania
Childhood Cancer International Europe (CCI Europe) is instrumental in feeding the needs of childhood cancer parents organisations and survivor groups to the project.

- **Example**: Participation to questionnaires and site visits to centres with the potential to link to the PO-ERN based on European Standards of Care for Children with Cancer.
LHEAR – National Centres Identification ongoing

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Planned after site evaluation:

- Affiliation of LHEAR Hocs with PaedCan ERN Hocs as needed
  - For VTB
  - For optional CBHC referrals