

The challenge of understanding modifiable risk factors in paediatric oncology and the potential role EU initiatives in addressing this

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Structure of the Presentation

1. Childhood cancer in Europe: key facts
2. Causes & prevention of paediatric cancers: current status, future orientations
3. Actions from the European Paediatric Haematology Oncology Community
4. Role of the EU in driving transformational change

1. Childhood cancer in Europe: Key facts

Leading cause of children's death by disease, with substantial morbidity in survivors

- More than 35,000 new cases diagnosed every year
- Over 100 types of childhood cancer, each individually rare
- Over than 6,000 young patients die every year
- Nearly 500,000 childhood cancer survivors, majority experience long-term adverse effects
- Substantial inequalities in access to best available care and expertise accounting for up to 20% difference in survival rates between EU countries

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2. Causes & prevention of paediatric cancers: current status, future orientations

“WHY DOES MY CHILD HAVE CANCER?”

Is a crucial question for parents, which most of the time receives no answer

Relatively few causative factors have been identified for the majority childhood cancers

Inaccurate or speculative information can cause unnecessary parental distress

Although lifestyle changes are identified that can help to reduce the risk of adults developing cancer

Today, there are no known alterable risk factors to prevent most childhood cancers

Known exposure risk factors for childhood cancer

High dose ionizing radiation & prior chemotherapy are accepted causes of childhood cancers

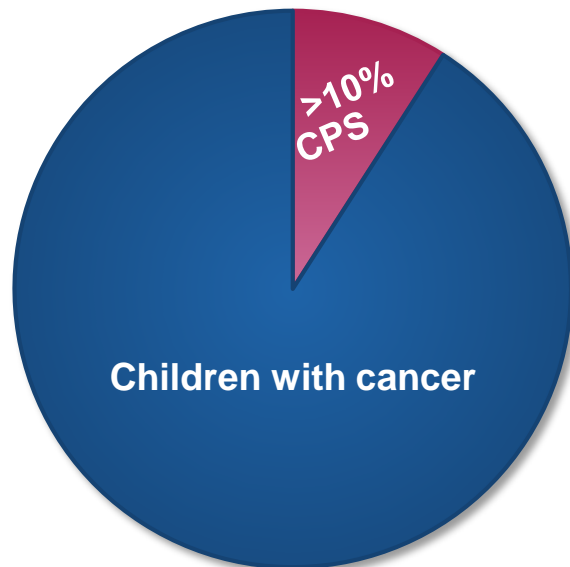
No other environmental* risk factors, have emerged as definitive causes for childhood cancers

*by which we mean any exposure which originates outside the body

What limits our ability to identify environmental risk factors of childhood cancer?

- Insufficient patient numbers to undertake meaningful prospective risk factor studies
- Most childhood cancer studies rely on retrospective case-control design
 - Accuracy and lack of bias challenging because:
 - For environmental factors such as parental diet, maternal medication, caffeine, alcohol use, and pesticide and air pollution exposure
 - Accurate exposure assessment is not possible to measure retrospectively
 - The susceptible time windows and latent periods are not known and likely to vary widely
 - There is limited knowledge of the underlying biological drivers of most childhood cancers

Genetic predisposition is the major known cause of childhood cancer



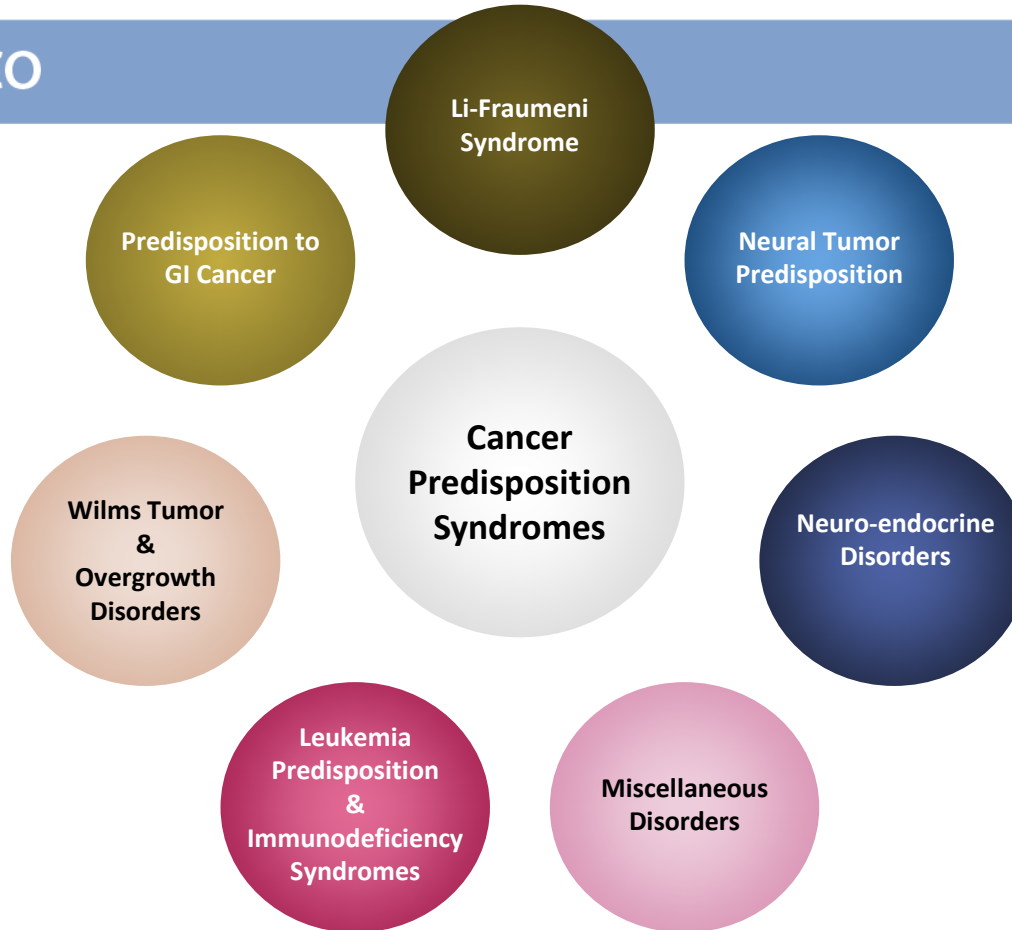
Cancer Pre-disposition Syndromes (CPS)
account for approximately 10% of childhood
cancer

CPS figures courtesy of
Prof. Christian Kratz

POLICY DEPARTMENT FOR ECONOMIC, SCIENTIFIC AND QUALITY OF LIFE POLICIES

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Li-Fraumeni Syndrome
Beckwith-Wiedemann syndrome
Bohring-Opitz syndrome
Mulibrey (muscle, liver, brain, and eye) nanism
Perlman syndrome
Trisomy 18
Simpson-Golabi Behmel syndrome
WT1-related syndromes (WAGR, Denys-Drash, Frasier)
Neurofibromatosis 1 and 2
Schwannomatosis
Predisposition to other Neural Tumors
Neuroblastoma Predisposition
Retinoblastoma Predisposition
Medulloblastoma Predisposition
Rhabdoid Tumor Predisposition
APC-related adenomatous polyposis
MUTYH-associated polyposis
Peutz-Jeghers Syndrome
Juvenile Polyposis syndrome
Constitutional Mismatch Repair Deficiency
Von Hippel Lindau
Hereditary Pheochromocytoma/Paraganglioma
Multiple Endocrine Neoplasia 1
Multiple Endocrine Neoplasia 2A and 2B

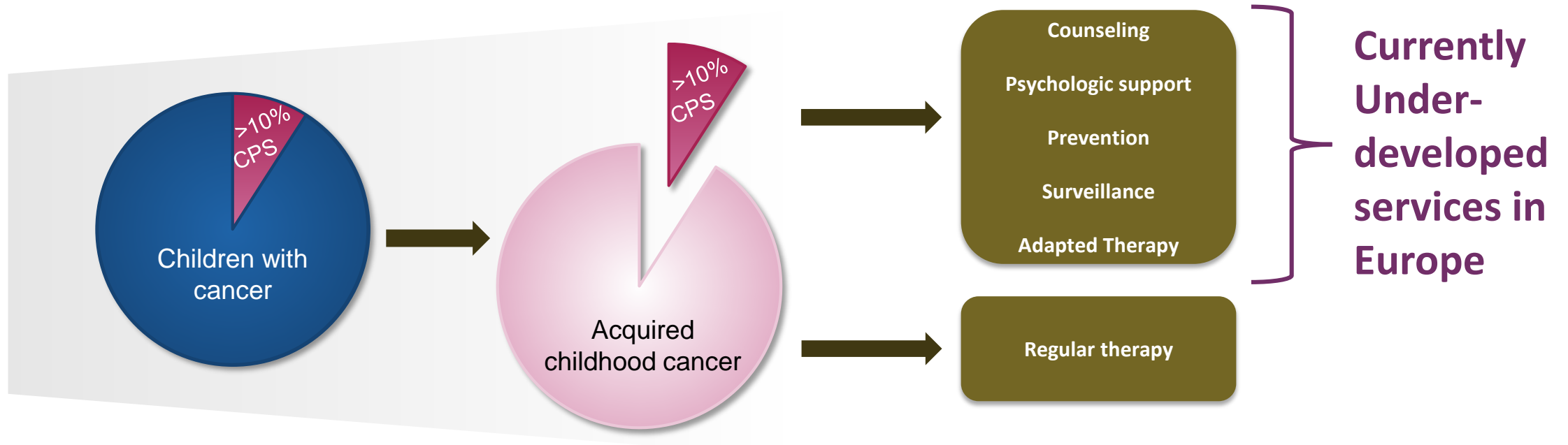


Multiple Endocrine Neoplasia 4
CDC73-Related (Hyperparathyroid-Jaw Tumor)
PAX5-Deficiency
CEBPA-Deficiency
ETV6-Deficiency
RUNX1-Deficiency
GATA2-Deficiency
Robertsonian translocation 15;21 & ring chrom 21
Ataxia Telangiectasia
Bloom syndrome
Dyskeratosis congenita
Fanconi anemia
Nijmegen breakage syndrome
Xeroderma pigmentosa
DICER1 syndrome
PTEN Hamman-Richards Tumor Syndrome
Hereditary Leiomyomatosis and Renal Cell Cancer
Rasopathies, Rubinstein-Taybi syndrome
Sotos syndrome, Weaver syndrome
Schinzel-Giedion syndrome
NKX2-1 syndrome
Ornithine Transcarbamylase Deficiency
L-2-Hydroxyglutaric Aciduria
Tyrosinemia

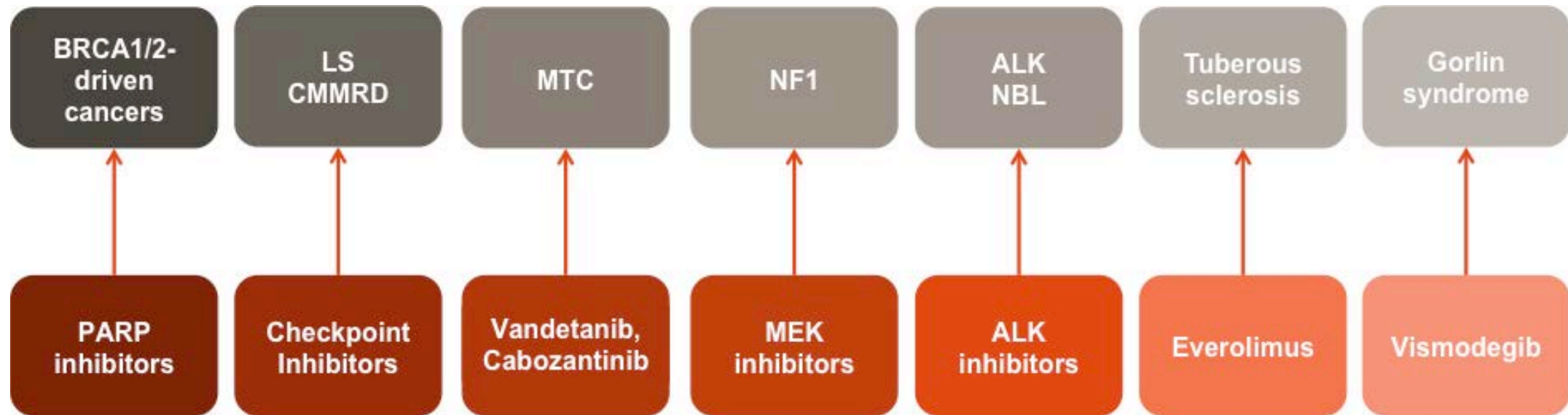
What is the Childhood Cancer Risk in CPS?

Syndrome	Defect	Risk
Beckwith Wiedemann	Subtype: GoM at IC1	28%
Li-Fraumeni Syndrome	<i>TP53</i>	40%
Perlman syndrome	<i>DIS3L2</i>	>90%
Denys Drash Syndrome	<i>WT1</i>	>90%
Hereditary Retinoblastoma	<i>RB1</i>	>90%
Multiple Endocrine Neoplasia 2B	<i>RET</i>	>90%

Why does the CPS diagnosis matter?



Potential for targeted therapy for some hereditary cancers

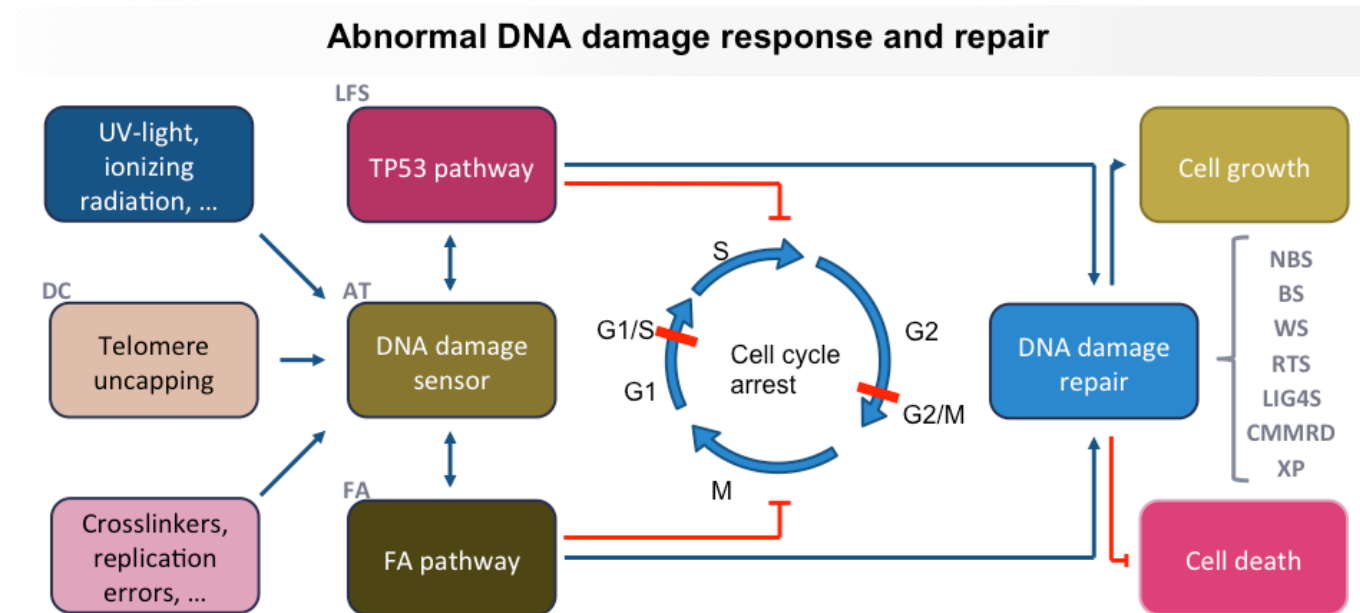


2. Causes & prevention of paediatric cancers: current status, **future orientations**

Critical need for more research on predisposition and oncogenic drivers

- Systematic whole genome sequencing to further uncover genetic predisposition to paediatric cancers
- Fundamental science needed to understand molecular and genomic drivers of paediatric cancers

2. Causes & prevention of paediatric cancers: current status, future orientations



Modified and adopted from Nat Rev Cancer. 2018;18(3):168-85.

**Fundamental science needed to
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2. Causes & prevention of paediatric cancers: current status, **future orientations**

Critical need for more research on predisposition and oncogenic drivers

- Systematic whole genome sequencing to further uncover genetic predisposition to paediatric cancers
- Fundamental science needed to understand molecular and genomic drivers of paediatric cancers
- **Address data-sharing and inter-operability and access of scientific and healthcare databases**
- **Exploit the Artificial Intelligence potential for paediatric cancers**
- **Address questions on the environmental causes of paediatric cancer through scientifically-led and evidence-based studies**

3. Actions from the European Paediatric Haematology Oncology Community

Multi-disciplinary, partnership-based, patient-centric

- **SIOP Europe (European Society for Paediatric Oncology)**
 - **Representing** 30 national societies of paediatric haemato-oncology professionals and 19 disease-specific and cross-specialty European Clinical Trial Groups
- **CCI Europe (Childhood Cancer International – Europe)**
 - Representing parents, patients and survivors
- **ERN PaedCan (European Reference Network for Paediatric Oncology)**
 - virtual network addressing inequalities in healthcare across Europe.



3. SIOP Europe Strategic Plan

7 scientific and clinical objectives:

- Introduce innovative therapies
- Foster precision medicine in healthcare
- **Increase biology knowledge of paediatric tumours**
- Ensure equal access to standard care, expertise and clinical research
- Address the needs of teenagers and young adults
- Improve the quality of survivorship
- **Understand causes of paediatric cancers and address prevention where possible**



3. SIOP Europe Host Genome Working Group

To study the **cancer epidemiology** in patients with CPS

To study CPS **biology**

To improve **psychosocial support** for patients with CPS

To improve **diagnosis** of CPS

To improve **counseling** for patients with CPS

To develop **cancer prevention** for patients with CPS

To optimize **cancer surveillance** for patients with CPS

To improve **cancer treatment** of patients with CPS by close collaboration with trial groups

To collaborate with **patient support organizations**

To study the **genetic component of adverse treatment reactions**

To harmonize **care practice and diagnostic procedures** for individuals with CPS within Europe

To **educate** families and health professionals in host genome field



4. Role of EU Policies and Programmes

The rarity of individual paediatric cancers and leading collective health burden in Europe make coordinated EU level approaches crucial

- **Europe's Beating Cancer Plan & Cancer Mission** Area are among the EU initiatives that hold the greatest promise for children and adolescents with cancer

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4. Role of EU Polices and Programmes

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- **Europe's Beating Cancer Plan & Cancer Mission Area** are among the EU initiatives that hold the greatest promise for children and adolescents with cancer
- The **SIOP Europe Strategic Plan** can serve as a **blueprint** for the elaboration of EU strategies and implementation
- **Sustained public investment** at the EU level could effect transformational change to address the urgent needs in childhood and adolescent cancers and foster positive collateral benefits in other disease areas.

**Thank you for your
attention!**