Childhood Cancer International EUROPE

Big Data and AI application in paediatric oncology

What could be the impact of Big Data and AI application in paediatric oncology?

Pamela Kearns, Patrick Kemmeren,
Franck Devaux

14.10.2024
17:00-18:30

www.ccieurope.eu

HOUSEKEEPING ITEMS

1. Smile! The webinar is being recorded ☺
2. Use the chat for your burning questions
3. We'd love to hear from you! We are going to address all your written and oral questions in the Q & A session at the end of the presentation

#CCIEGOLD WEBINARS

Childhood Cancer International EUROPE

CONTENT

1. Big Data and AI
2. Big Data and AI in childhood cancer research and diagnostics
3. Ethical implications
4. Q&A

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Childhood Cancer International EUROPE

We have some questions for you ☺

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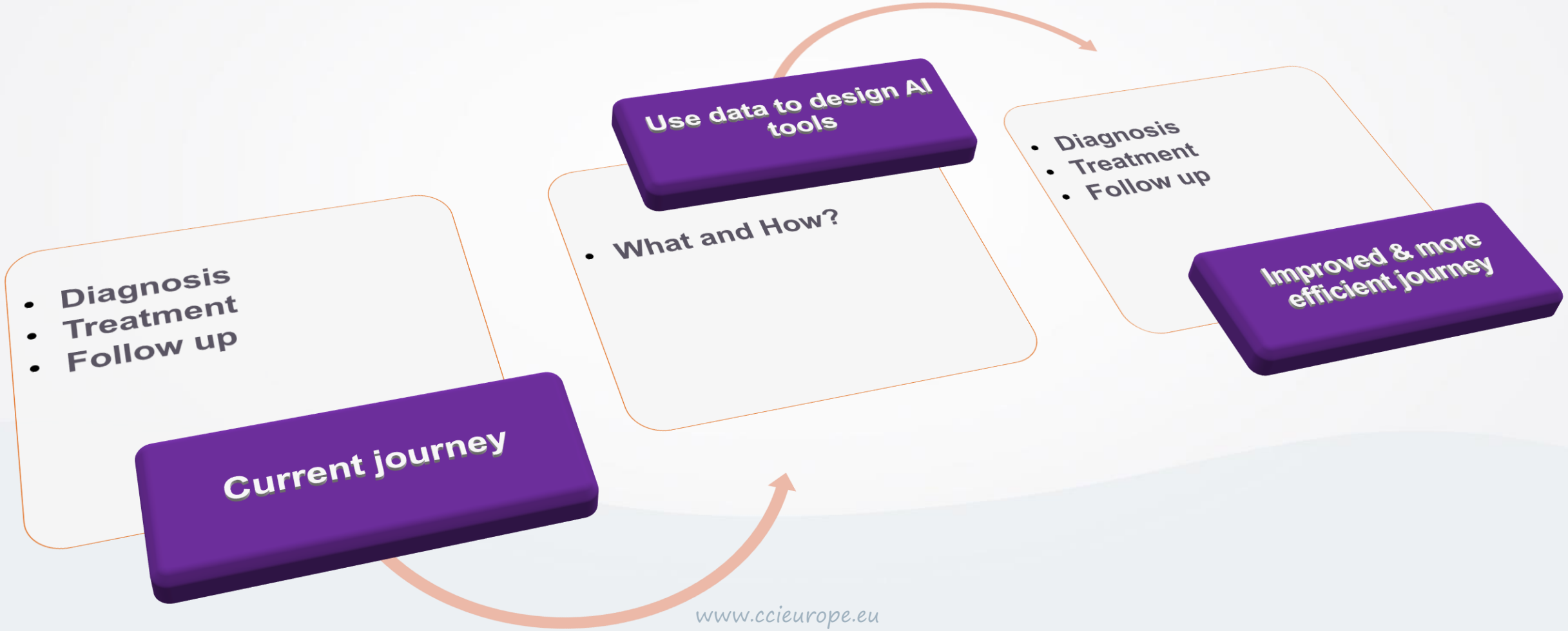
Big Data and AI in paediatric oncology

Pamela Kearns
Emeritus Professor
University of Birmingham, UK

Can we improve the childhood cancer patient journey through machine learning and artificial intelligence?



How?

Starting Point:

Multi-modality, multi-site data

Destination:

Clinically-implementable AI tool

Data Reality in Paediatric Oncology

- **35,000 children are diagnosed with cancer across Europe each year**

- **100+ individual cancer types:**

- each subdivided by
  - Histopathology
  - Stage
  - Biology
  - other validated disease-specific risk stratifications

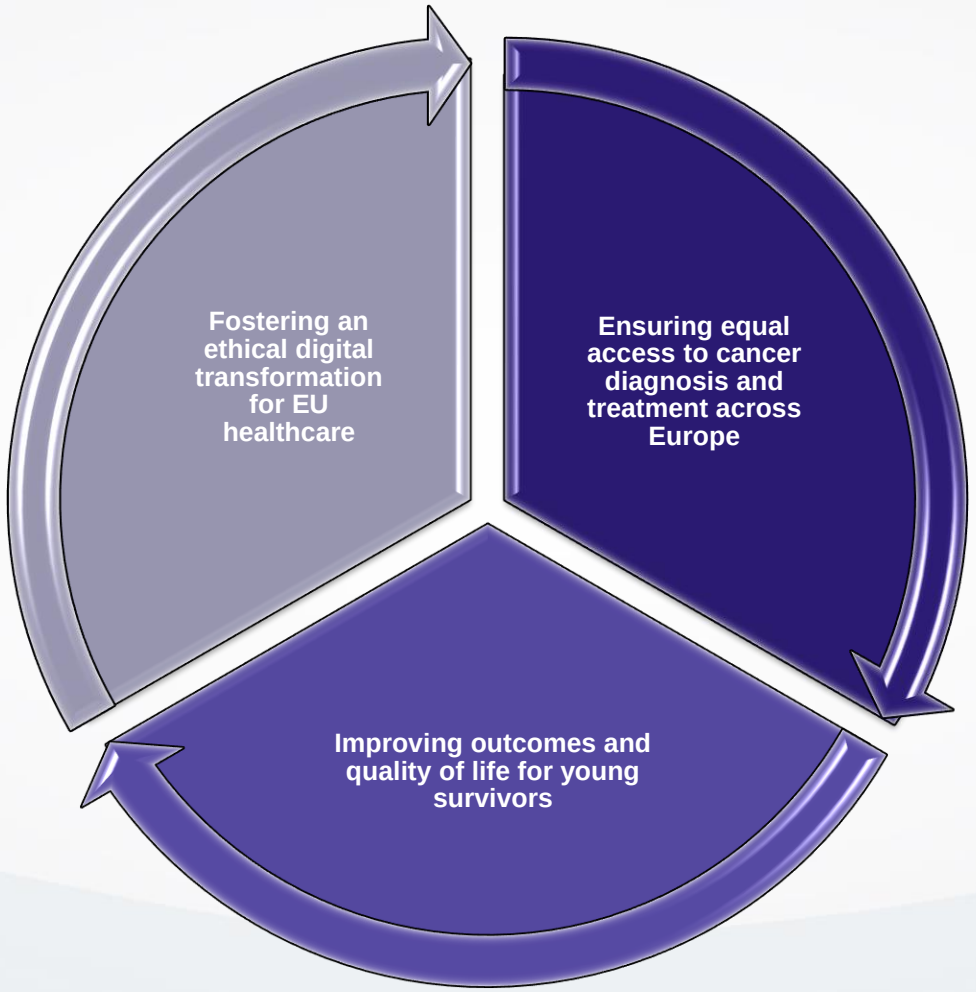
- **Individual patient-specific treatment pathway**

- clinical standards of care pathway
- participation in a clinical trial
- and/or multiple biological studies

- **No single /unified European data framework**

- Site/ hospital and country specific systems
- Complex data protection, legal and ethical dimensions to data sharing and usage

UNICA4EU: An EU funded pilot project to understand how to achieve application of AI to childhood cancers



UNICA4EU receives funding from the European Union's Call for Pilot Projects and Preparatory Actions (PPPA) under Grant Agreement No. 101052609

UNICA4EU Aims

Understand the landscape and the multi-stakeholders' perspectives

Build a set of **clinical use cases** that endorse **trustworthy and reliable AI** and address the inherent challenges in data homogenization, interoperability, processing and federation

Keep a **patient centric approach** with sight of the fundamental **ethical, personal** and **legal** rights

UNICA4EU Objectives

Map

the existing

multi-disciplinary and multi-national platforms/datasets and registries

Propose a prototype European point of access to multimodal health data of different nature and origins

Create multidisciplinary guidelines for data curation and AI in childhood cancer

Promote the outcomes towards standardization to reaching research, Industrial and clinical and regulatory communities

Collaborate with Big Data initiatives; EU4CHILD, PARTNER, & PRIMAGE

Plus Partners SIOPE, ERN-PaedCan & CCI Europe

to s share of best practices and dissemination

UNICA4EU Partners

Multi-dimensional Stakeholders

- ❑ Healthcare providers
- ❑ AI and Technology Providers
- ❑ Patient Representation
- ❑ Advocate Ecosystems
- ❑ Policy Makers

The challenges to meet the objectives are many and complex!

- Data digitisation: different levels of digitisation among entities in Europe
- Data collection:
  Data collected from children is scarce
- Data anonymization: The strategies to ensure that there is no way to individualise data
- Data Harmonisation & curation: Due to the multiple modalities and characteristics of the data collected
- Data interoperability: Data silos and reluctance to be shared
- Extraction, Loading, transformation and integration of data
- AI application for Paediatric cancer pathways
- Reliability and acceptance of AI: Can a diagnostic be confirmed by AI?
- Innovative treatments and precision medicine: How can AI support it?
- Going beyond clinical trials: adding new data sources
- Quality Standards: for medical data collection and AI results interpretation
- Data ownership: who owns the data? Is it the patient, the person who collected the data, or nobody?
- Informed consent and re-consent
- Data re-use

The challenges to meet the objectives are many and complex!

The Data

The Regulations

The Utility

The Implementation

The Data

Types of data collected throughout the patient journey

- **Patient data and electronic health records (EHRs)**
- **Patient-derived research data (clinical trials)**
- **Patient reported outcomes and measures (PROs, PROMs)**
- **Public health data**
  - *Data about disease prevalence, population health trends etc*
- **Mobile health (mHealth) and sensor health data**
  - *Data collected from wearables, sensors etc*
- **Social media data**
  - *Data from various social media*
- **Social determinants of health (SDOH) data**
  - *Conditions that impact health outcome including economic stability, …*

Multiple Potential Sources of Childhood Cancer Data

SIOP Europe
the European Society for Paediatric Oncology

Childhood Cancer International EUROPE

European Reference Network
for rare or low prevalence complex diseases
Network Paediatric Cancer (ERN PaedCan)

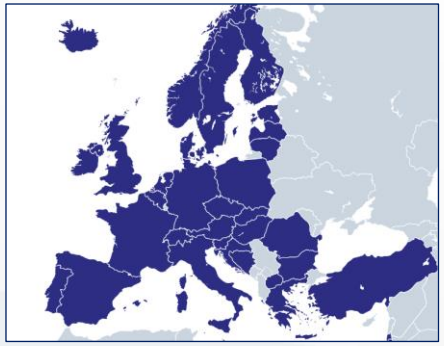
All European Clinical Trial Groups (**ECTGs**)

National Paediatric Haemato-Oncology Societies (**NaPHOS**) or paediatric oncology centres

35 countries incl. all EU Member States

67 **Patient**, **Parent** and **Survivor Organisations**

34 countries incl. most EU Member States



- Memorandum-based core partnerships
- Cooperation with industry
- EU projects and platforms
- Joint Strategy

JARC JOINT ACTION ON RARE CANCERS

European Commission

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

SIOP Europe
Clinical Research Council

www.ccieurope.eu

Data Challenges in Childhood Cancer

Do we have access to robust data

Is it fair? Do we have potential bias

Are our clinical services ready?

Digitalised Landscape

- Imaging
- Pathology
- Electronic Health Records
- Paper Clinical records
- Genomics
- Trials Data

Implementable AI tools

Challenges

- **Volume of Data**
  - Small patient populations
- **Fairness**
  - Inclusivity
  - Diversity
  - Ethics
- **Data Access**
  - Privacy
  - IP
- **Interoperability**
  - Sites
  - Systems
- **Commercialisation**

The Regulations

Data Handling Steps are all Regulated

- Prevention
- Detection
- Diagnosis
- Treatment
- Long-term survival
- Palliative care

Data

- **Collection**
- **Processing**
- **Curation**
- **Integration**

Regulatory Frameworks for Collecting and Processing the Data

- **Informed Consent**
- **Re-consent (at age of majority)**
- **Data Quality**
  - ***Reliability, accuracy, completeness, consistency, relevance***
- **Data Standardisation**
- **Data Harmonization**
- **Data Interoperability**
- **Data Privacy and Security**
  - **Data Access**
    - *Harmonized data access agreements (**DDAs**)*
    - *General Data Protection Regulation (**GDPR**)*

All need to consider potential specificities for children and young people (with cancer)

The Utility

Can AI enhance early detection, risk stratification, clinical decision making and support treatment?

UNICA4EU Use Cases:

DIAGNOSTIC PATHOLOGY

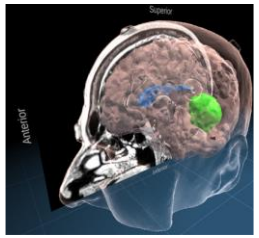
WG, WE, RNA-seq + Histopathology

AI Tumor classification

IMAGING BIOMARKERS

Harmonization

1) HQ MRI
2) Image feat or MRI + Clinical Endpoints & Biomarkers



Treatment

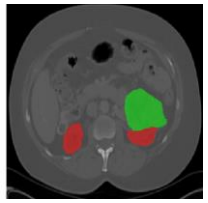
Tumor segmentation

OPTIMISING CLINICAL PATHWAY

Histopathological classification

Tumor characteristics

&



AI- based tumor/tissue delineation

QUALITY OF LIFE WITH EPRO

ePRO

QoL indicators Interventions

The Implementation

Patient, Parent, Advocate Survey and Focus Groups on Perspectives about using AI in Childhood Oncology

- Over **300 respondents** from diverse background, age groups and countries

- What did it tell us:
  - At a high level; probably a good idea but
    - It is a new topic to most
    - Majority had a lack of any or detailed knowledge and understanding of AI
    - Need more certainty and transparency to build trust
    - More information and education needed

Hyseni-Bocolli et al EJCPO 2024

The Next Steps

To exploit the potential for AI to meet the needs of children and young people with of cancer we need:

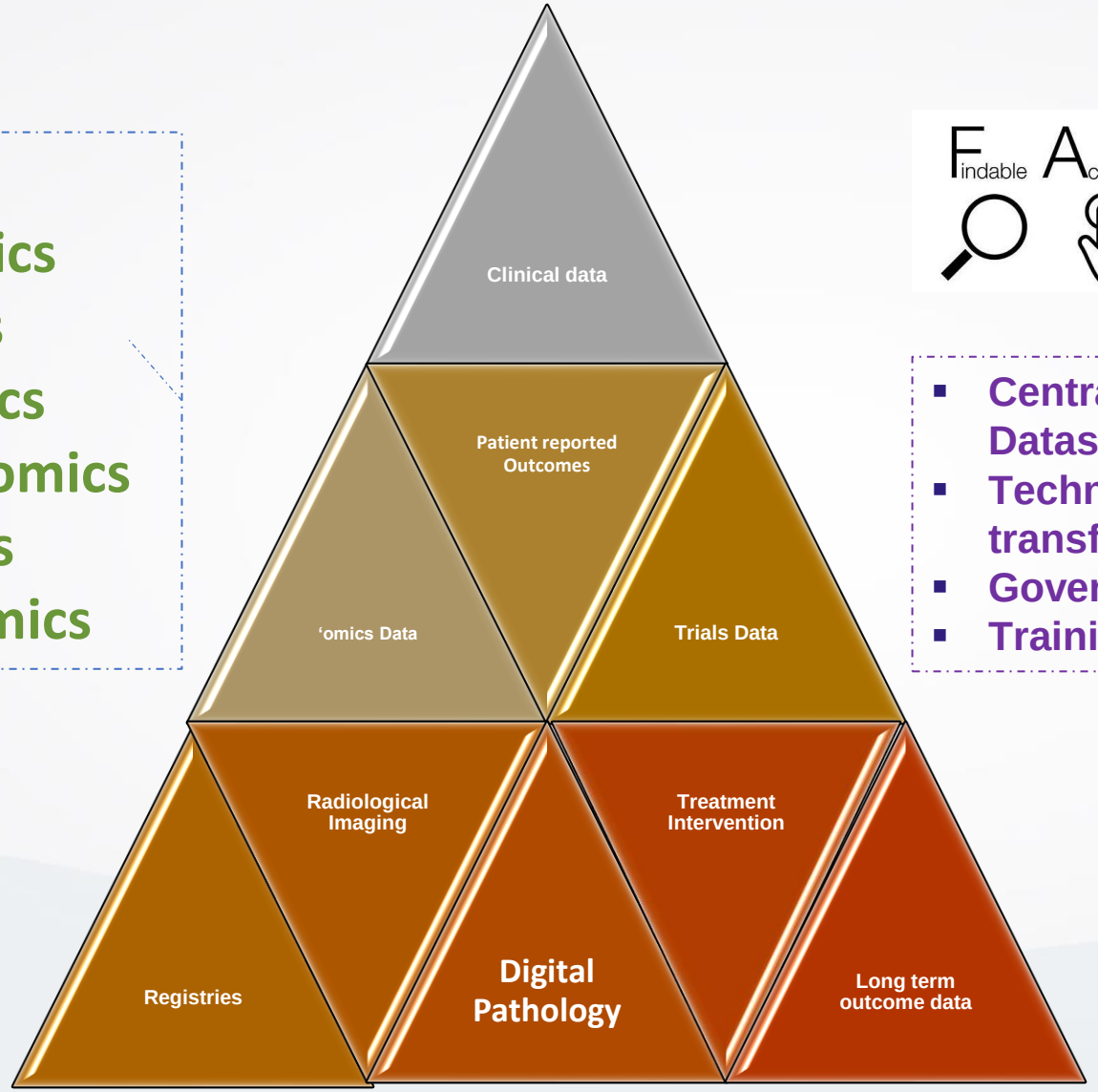
- **Robust, generalisable AI models based on representative training data, ideally sourced from multiple, independent sources**

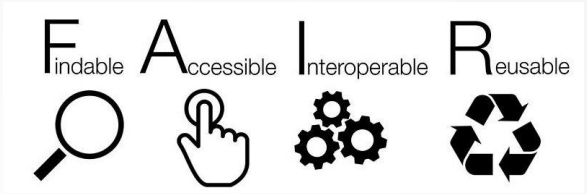
- **Evaluation of models for overall accuracy, potential bias and clinical benefit**
  - Clinical Trials using CONSORT-AI reporting
  - Real World Data

- **Clinical Preparedness**
  - Clinicians / healthcare professionals
  - Patients and families
  - Clinical systems /workflows

We need a European Childhood Cancer Data Initiative to enable a European Childhood Cancer Big Data Gateway

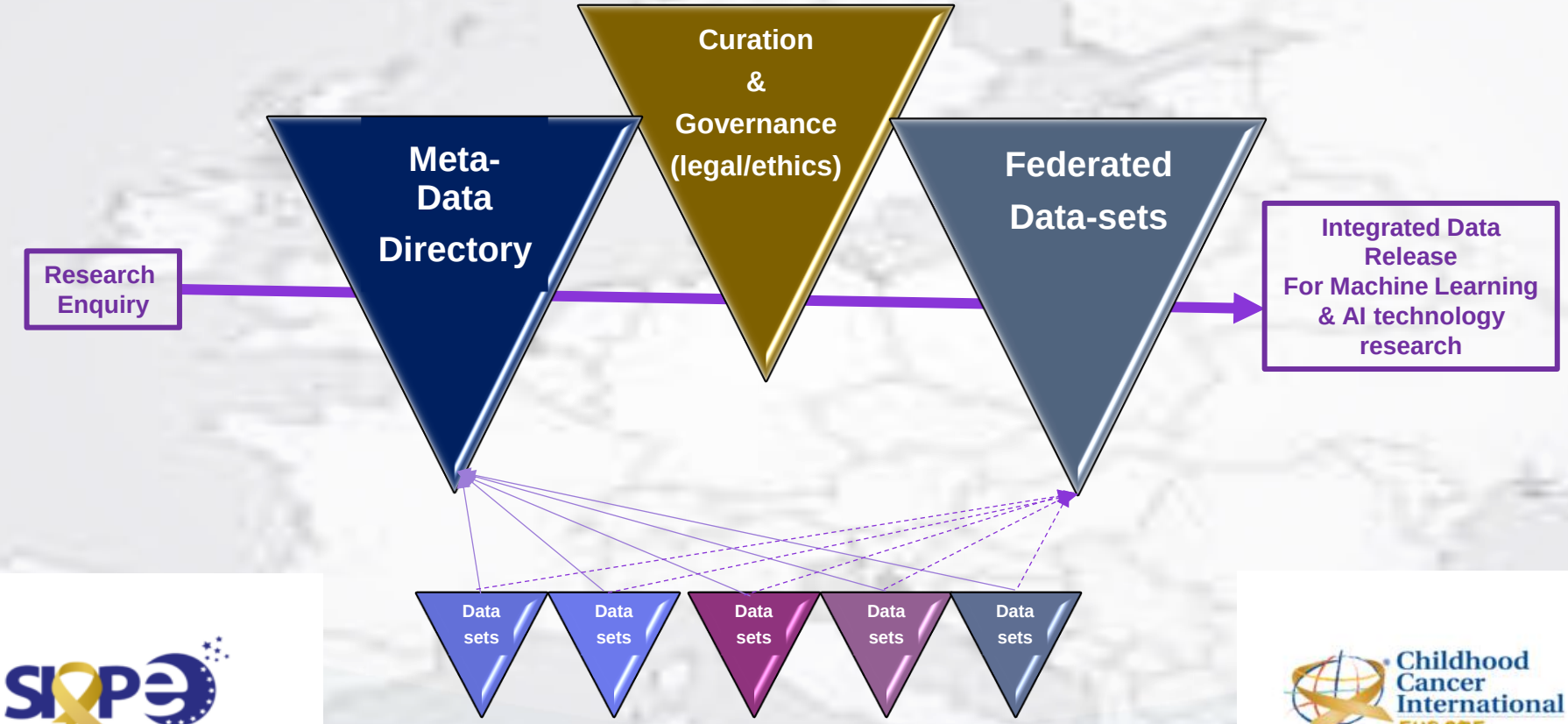
- Genomics
- Immunomics
- Phenomics
- Epigenomics
- Transcriptomics
- Proteomics
- Metabolomics





- Centralised Directory of Discoverable Datasets
- Technology platform(s) for data transformation for interoperability
- Governance and Oversight Framework
- Training Programmes

A Potential Model for a European Childhood Cancer Big Data Gateway

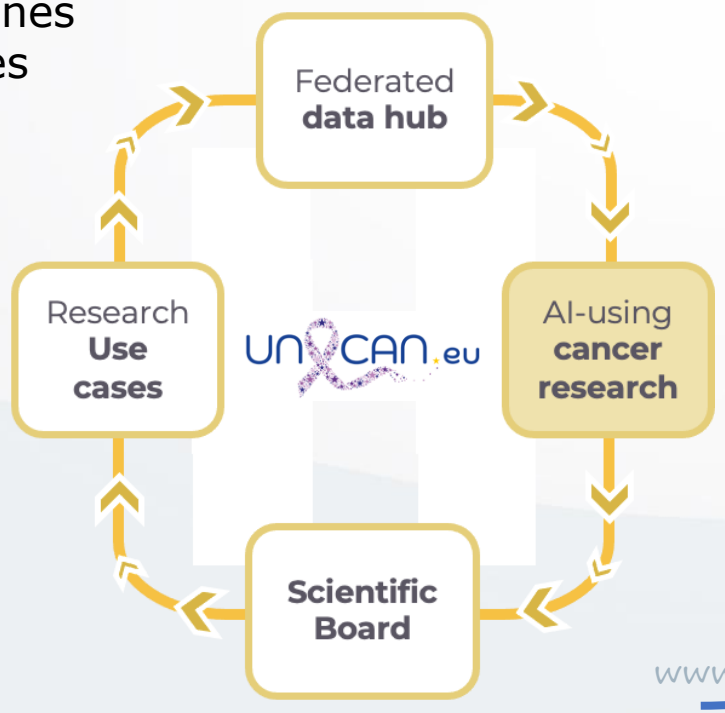


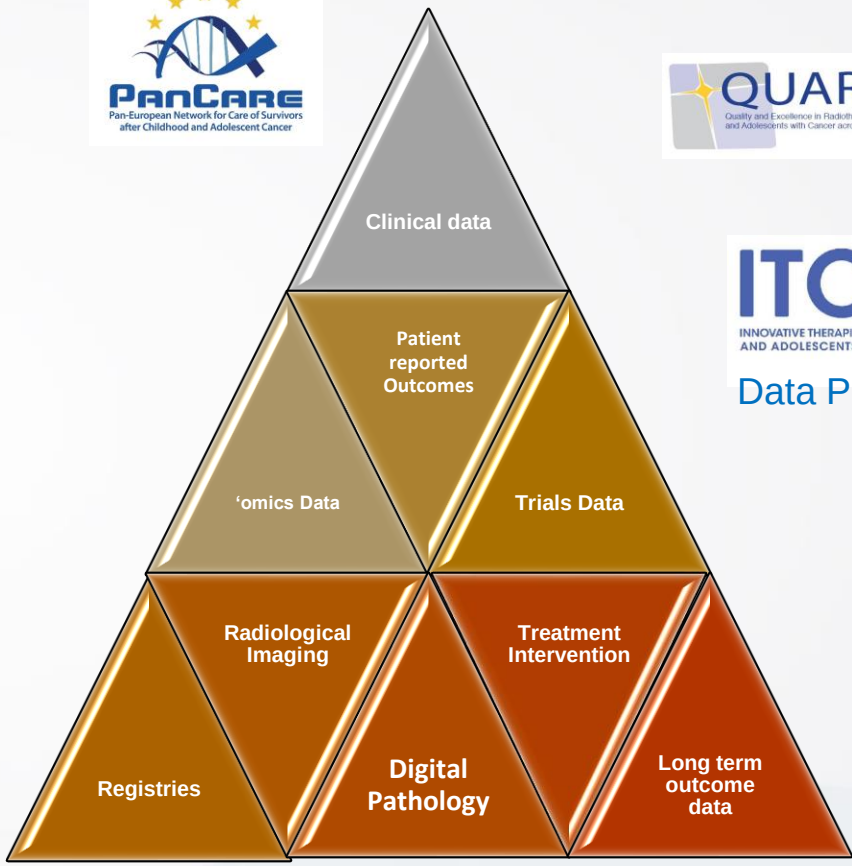
SIOP Europe
the European Society for Paediatric Oncology

Childhood Cancer International EUROPE

European Health Data Strategy
promoting health data exchange and supporting research and innovation on treatments, medicines and medical devices

Data **A**nalysis **R**eal **W**orld **I**nterrogation **N**etwork -federated data from network or regulators





Data Portal

A European Childhood Cancer Data Strategy

Summary

- **Paediatric Oncology AI could be possible with leverage of our diverse data sources**

- **AI could be applied it the data can be accessed and curated:**
  - to improve diagnostic and therapeutic approaches
  - to provide follow-up support for childhood cancer patients

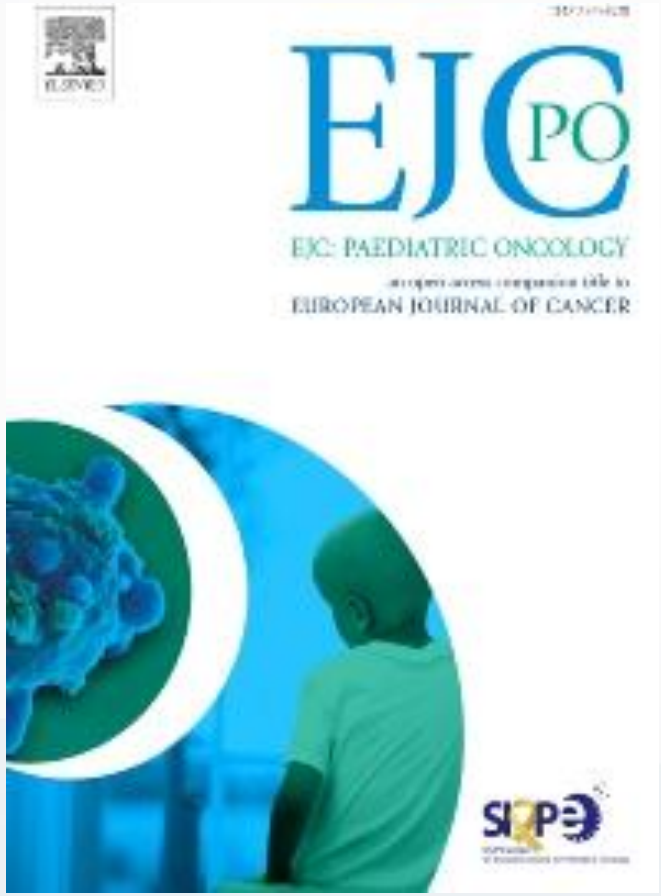
- **Regulatory and Ethics legislation**
  - ***Specificities for paediatric oncology*** need to be incorporated

- **Comprehensive guidance** is required
  - for collecting and handling patients' data
  - For all aspects of implementing AI in paediatric oncology

- Accessible **Education and Training essential; tailored for each stakeholders** needs

Special Edition of the European Journal of Cancer –Paediatric Oncology: coming soon

Collection of White Papers and Manuscripts agreed to be published of the outputs from UNICA4EU



for listening

Thank you to everyone who contributed to UNICA4EU

UNICA4EU receives funding from the European Union's Call for Pilot Projects and Preparatory Actions (PPPA) under Grant Agreement No. 101052609

Big Data and AI in childhood cancer research and diagnostics

Patrick Kemmeren
Princess Máxima Center for Pediatric Oncology

Biobank & diagnostics

For care and research

Broad informed consent

@Princess Máxima Center:
Data of >2500 patients,
DNA characterized for ~1500 patients

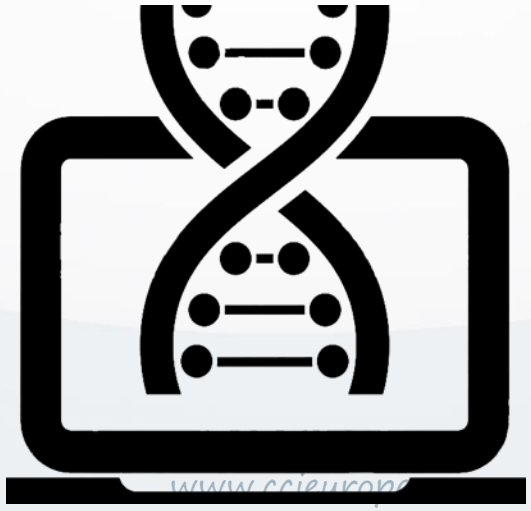
Biobank & Data Access Committee (BDAC)

DNA & research

DNA is **large**

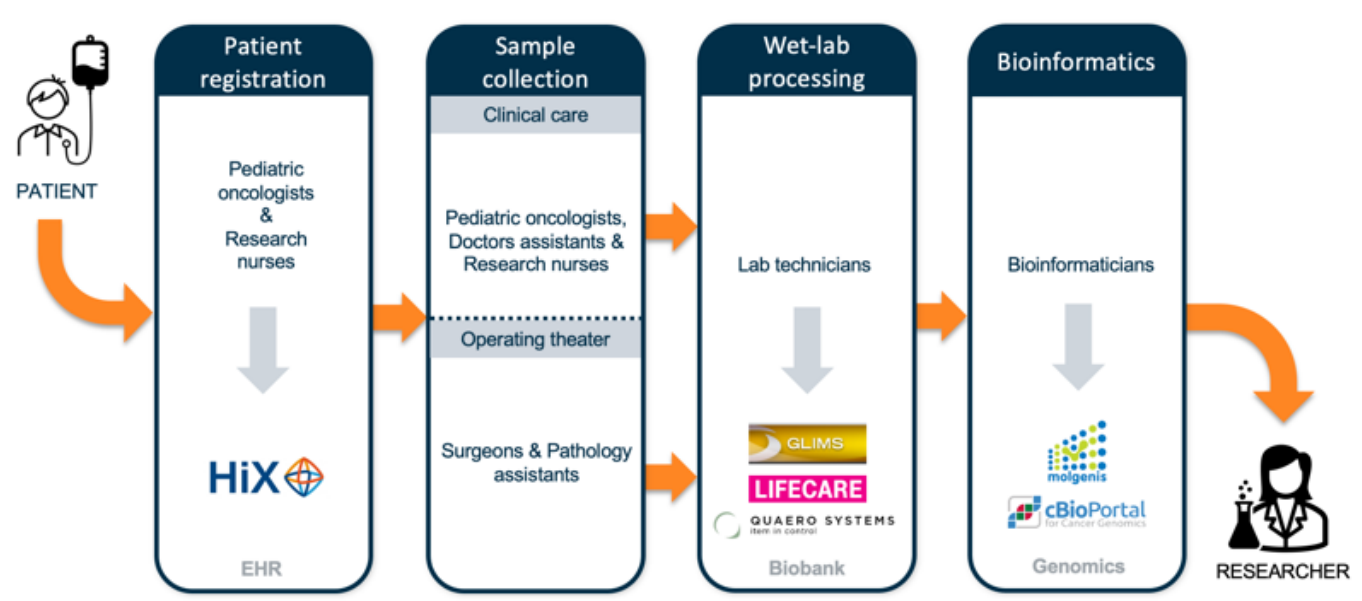
- DNA within a cell approximately 2 meters
- ≈ 130 books

Advanced algorithms and large computers



Biobank & diagnostics

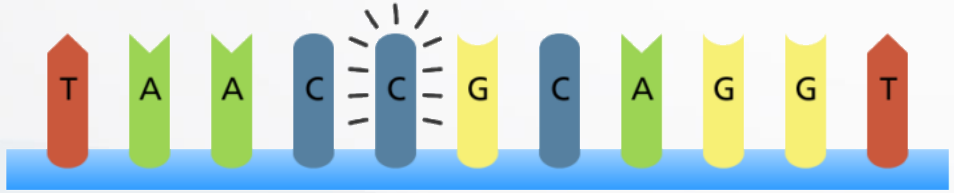
Clinical translation of research results



Diagnostics
WES
RNA-seq
DNA methylation

Research
WGS
RNA-seq
DNA methylation

Compare DNA between healthy and tumor cells



Search through 3 billion letters for differences in DNA

Biobank & diagnostics

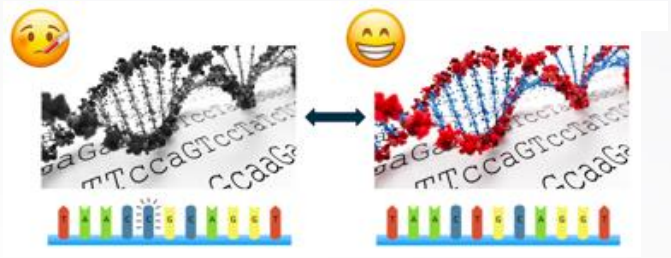
Clinical translation of research results

Clinical research

Healthcare

Diagnostics

Preclinical research



Compare DNA sequence

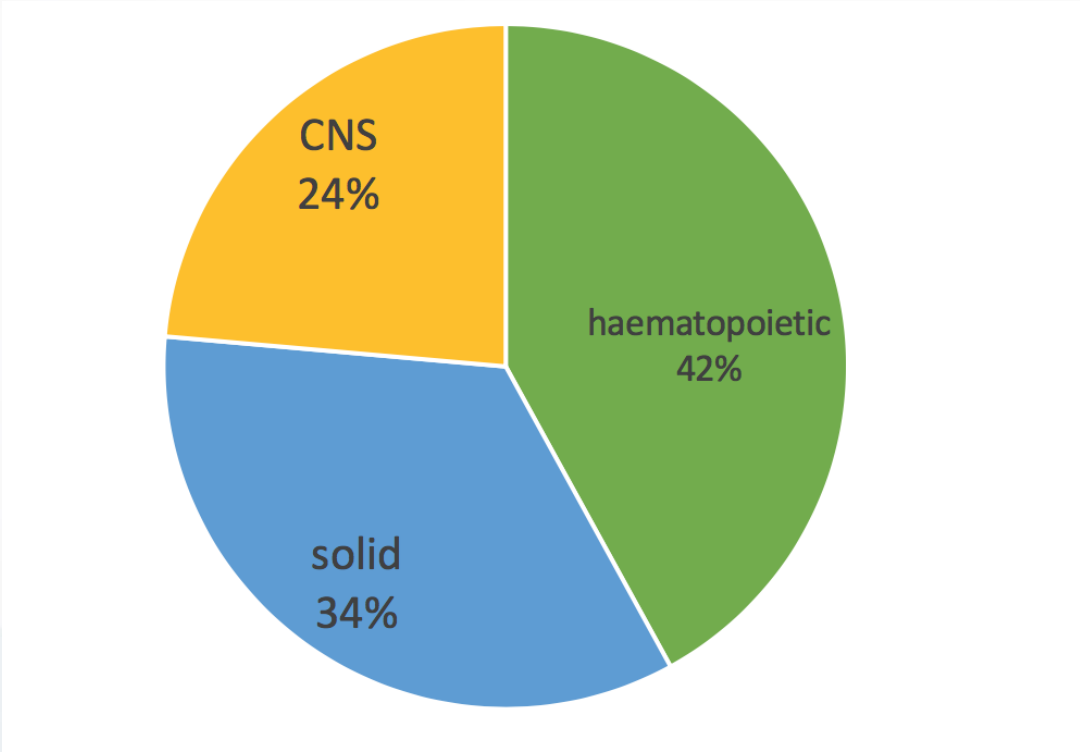
List of abnormalities in tumor DNA: Single base substitutions, gene fusions, copy number changes

Diagnosis

RNA-seq gene fusion detection for precision oncology & precision medicine

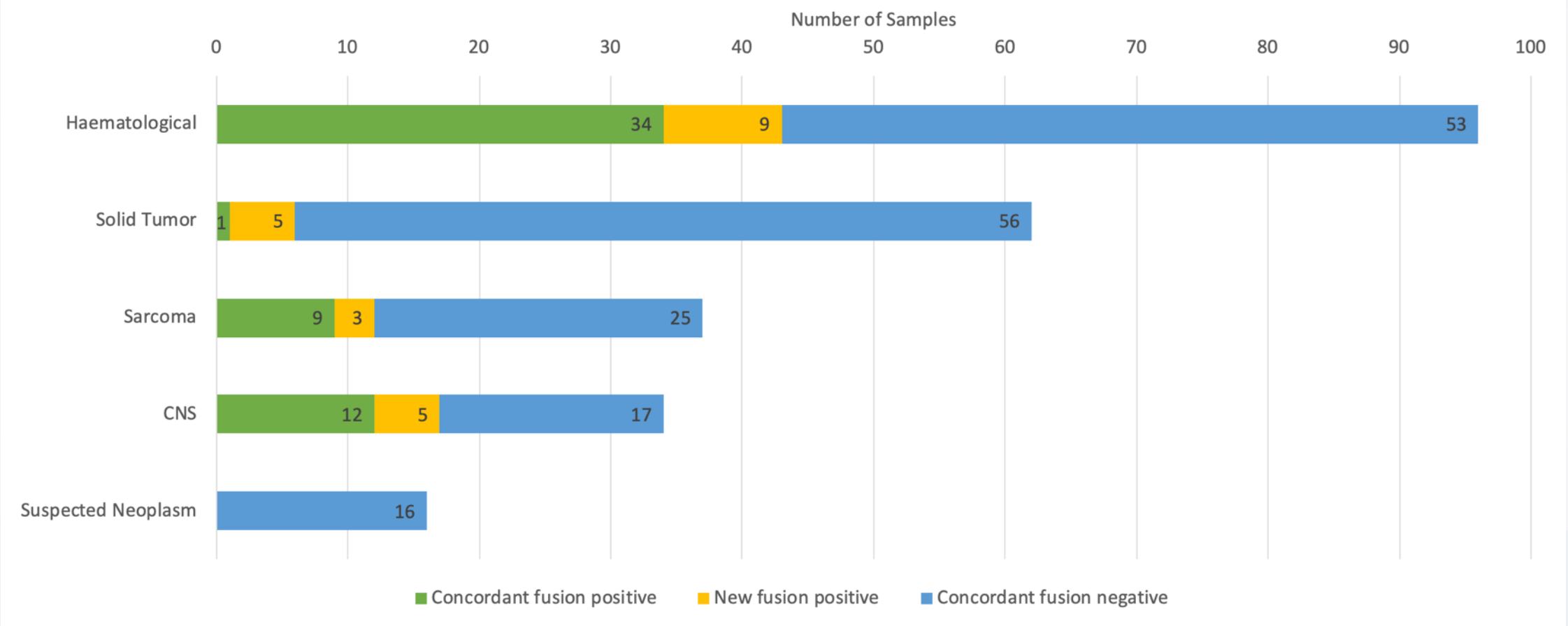
RNA-seq gene fusion detection in diagnostics

257 consecutive patients from 1st December 2018 until 31 May 2019



RNA-seq gene fusion detection in diagnostics

Increased sensitivity of clinically relevant events



No events missed

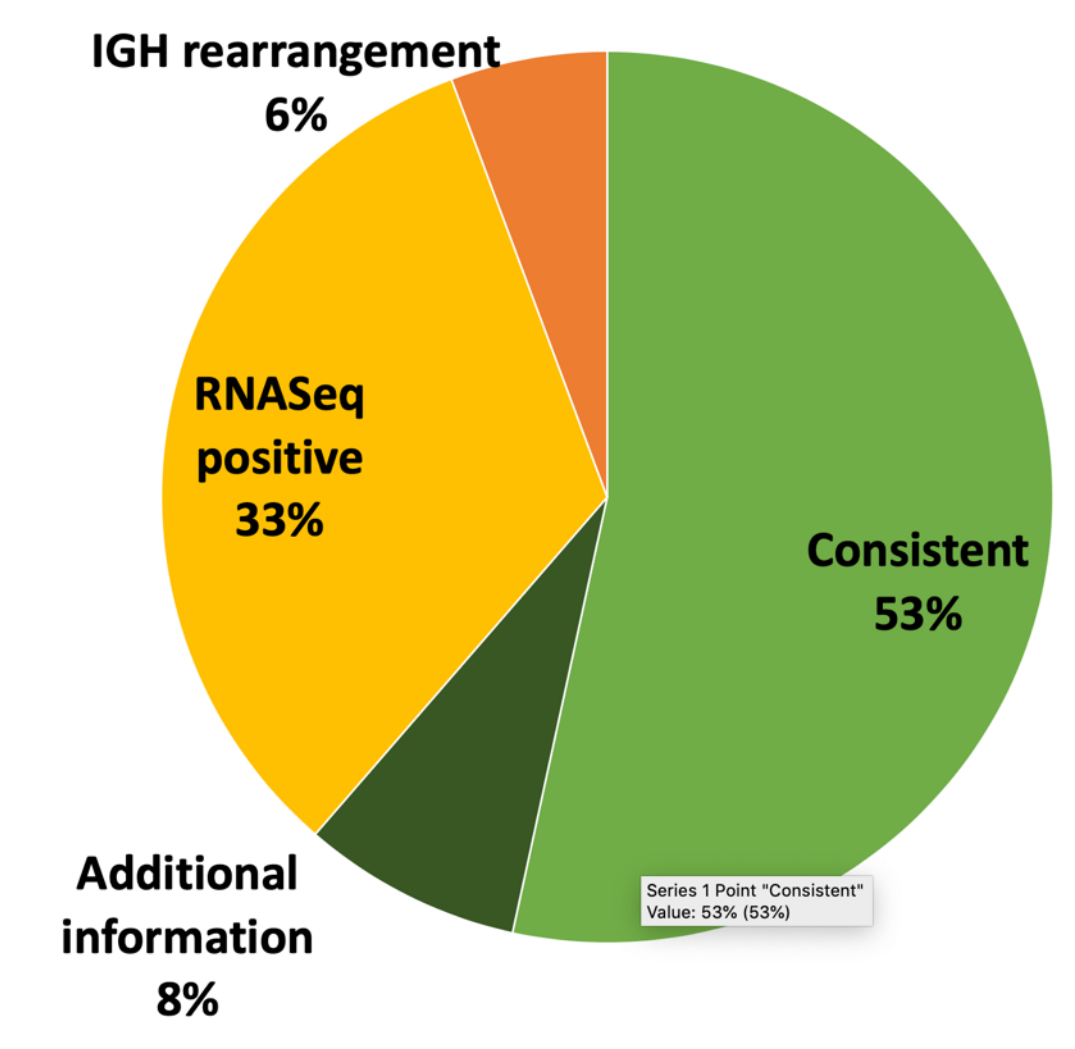
>40% increase in clinically relevant events (22%-> 36%)

RNA-seq gene fusion detection in diagnostics

The fusion positive cases

Additional information
- Fusion partner
- More accurate breakpoint

Additional events
- Not tested
- Atypical breakpoints
- IGH rearrangements

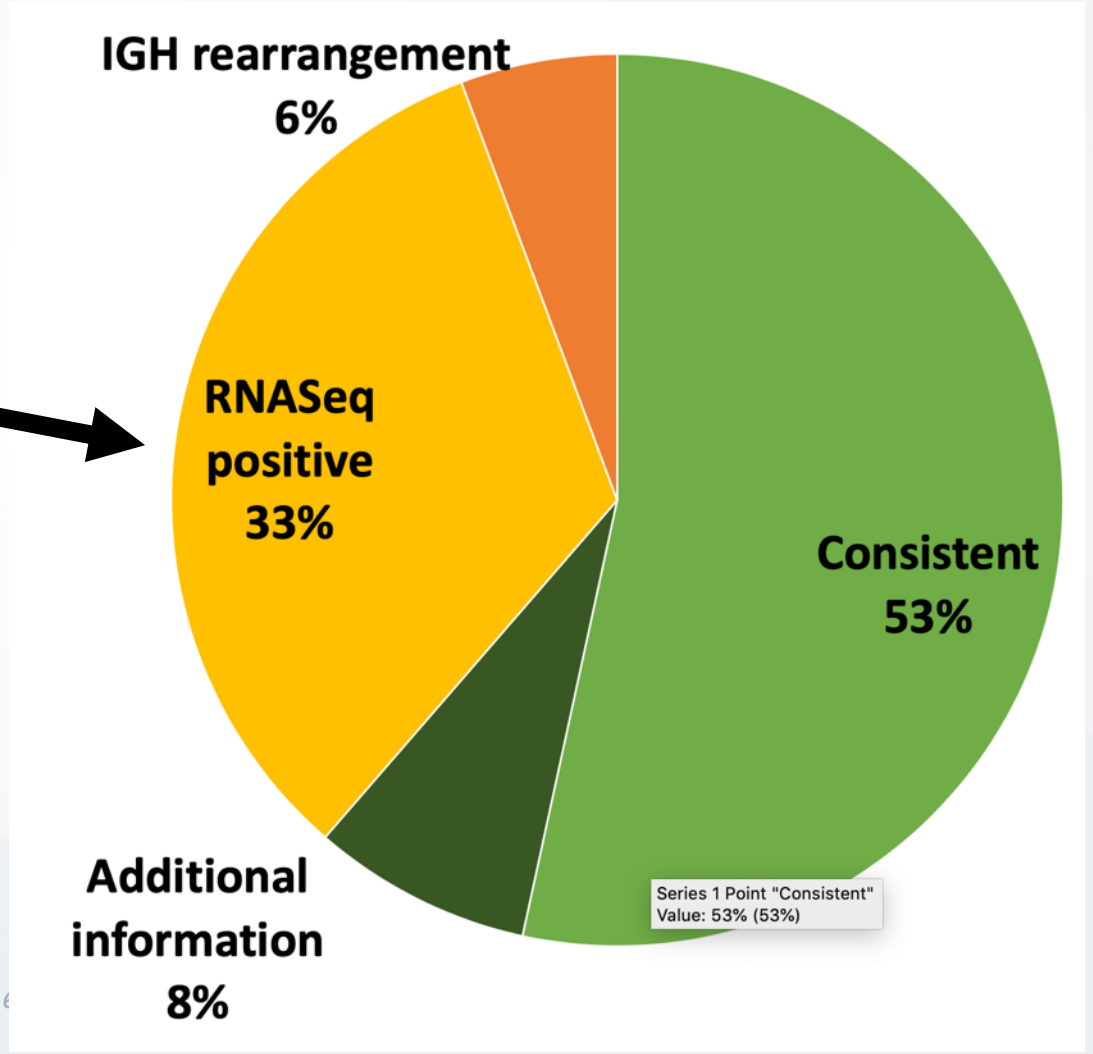


RNA-seq gene fusion detection in diagnostics

The fusion positive cases

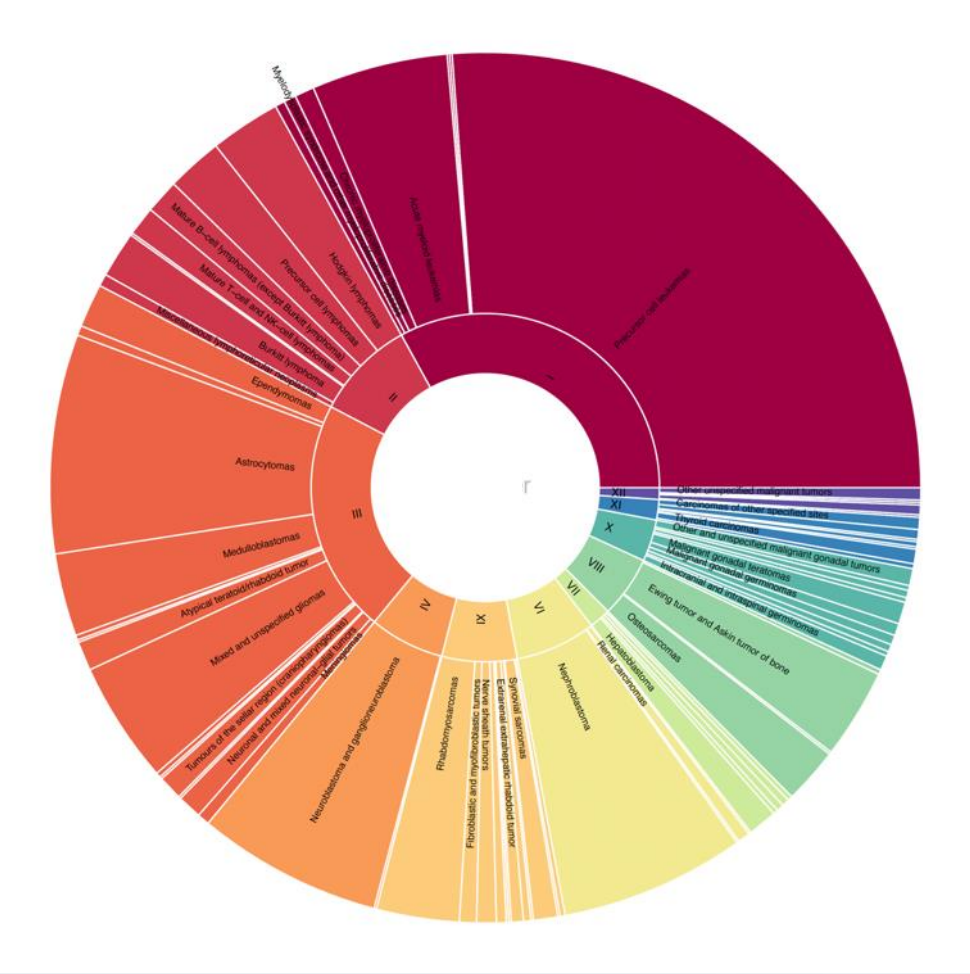
4 new druggable gene fusions

- ZCCHC8-ROS1
- PPP1CB-ALK
- EML4-ALK
- EML4-NTRK3

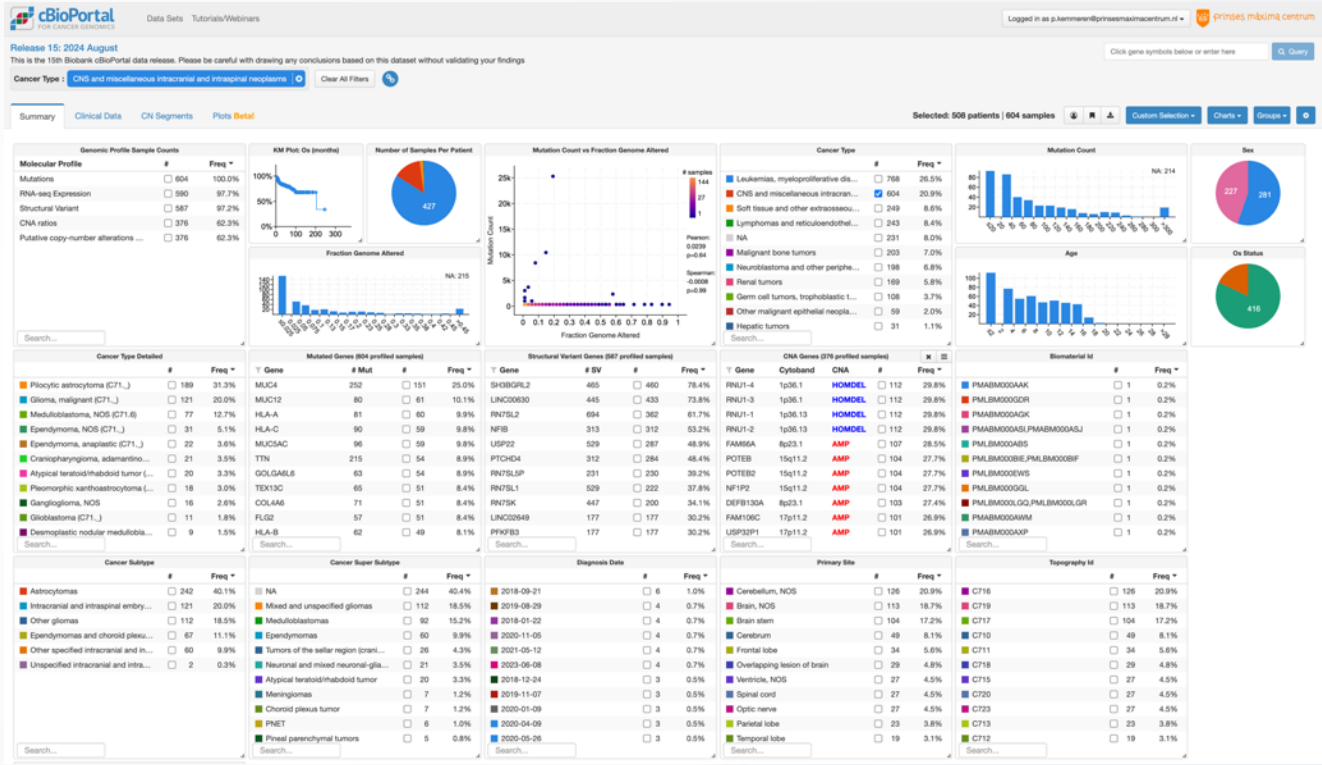


Dutch Comprehensive Childhood Cancer Commons

A data collection of 4,000 pediatric cancer genomes



~1200 pediatric cancer genomes in the cloud



Tooling to explore relevant mutations

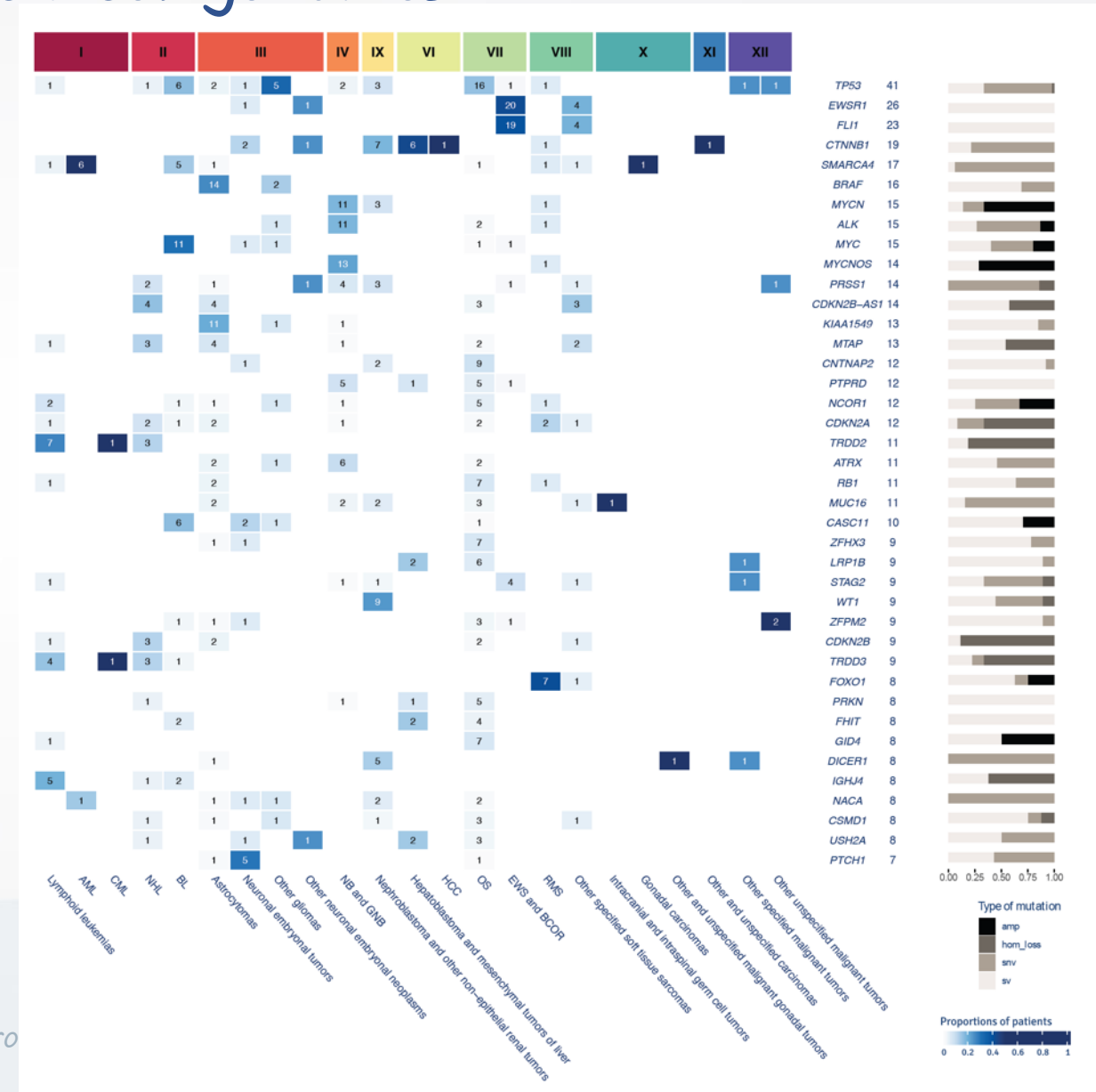
Dutch Comprehensive Childhood Cancer Commons

A data collection of 4,000 pediatric cancer genomes

Predicting role in cancer of different mutations types

Cloud speeds-up analyses

Bioinformatic analyses performed on ~1000 patient samples in 2 weeks compared to >6 months on-prem



International Classification of Childhood Cancer, Third edition (ICCC-3)

- I.Leukemias
- II.Lymphomas
- III.CNS, intracranial
- IV.Neuroblastoma, peripheral
- VI.Renal tumors
- VII.Hepatic tumors
- VIII.Bone tumors
- IX.Soft tissue, sarcomas
- X.Germ cell, gonads
- XI.Other epithelial, melanomas
- XII.Other and unspecified

Global data access

A federated landscape of childhood cancer data nodes

Germany

France

UK

>5000 retrospective cases
>1000 new patients per year

Netherlands

Australia

Canada

Denmark

AI initiatives

Creating impact through data & AI

Capricorn: AI to aid tumor board interpretation & decision making

AI initiatives

Creating impact through data & AI

Sturgeon: Intra-operative identification of brain tumors

Article

Ultra-fast deep-learned CNS tumour classification during surgery

https://doi.org/10.1038/s41586-023-06615-2

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Open access

Check for updates

C. Vermeulen[1,2,6], M. Pagès-Gallego[1,2,6], L. Kester[3], M. E. G. Kranendonk[3], P. Wesseling[3,4], N. Verburg[5], P. de Witt Hamer[5], E. J. Kooi[4], L. Dankmeijer[4,5], J. van der Lugt[3], K. van Baarsen[3], E. W. Hoving[3], B. B. J. Tops[3]✉ & J. de Ridder[1,2]✉

Central nervous system tumours represent one of the most lethal cancer types, particularly among children[1]. Primary treatment includes neurosurgical resection of the tumour, in which a delicate balance must be struck between maximizing the extent of resection and minimizing risk of neurological damage and comorbidity[2,3]. However, surgeons have limited knowledge of the precise tumour type prior to surgery. Current standard practice relies on preoperative imaging and intraoperative histological analysis, but these are not always conclusive and occasionally wrong. Using rapid nanopore sequencing, a sparse methylation profile can be obtained during surgery[4]. Here we developed Sturgeon, a patient-agnostic transfer-learned neural network, to enable molecular subclassification of central nervous system tumours based on such sparse profiles. Sturgeon delivered an accurate diagnosis within 40 minutes after starting sequencing in 45 out of 50 retrospectively sequenced samples (abstaining from diagnosis of the other 5 samples). Furthermore, we demonstrated its applicability in real time during 25 surgeries, achieving a diagnostic turnaround time of less than 90 min. Of these, 18 (72%) diagnoses were correct and 7 did not reach the required confidence threshold. We conclude that machine-learned diagnosis based on low-cost intraoperative sequencing can assist neurosurgical decision-making, potentially preventing neurological comorbidity and avoiding additional surgeries.

AI initiatives

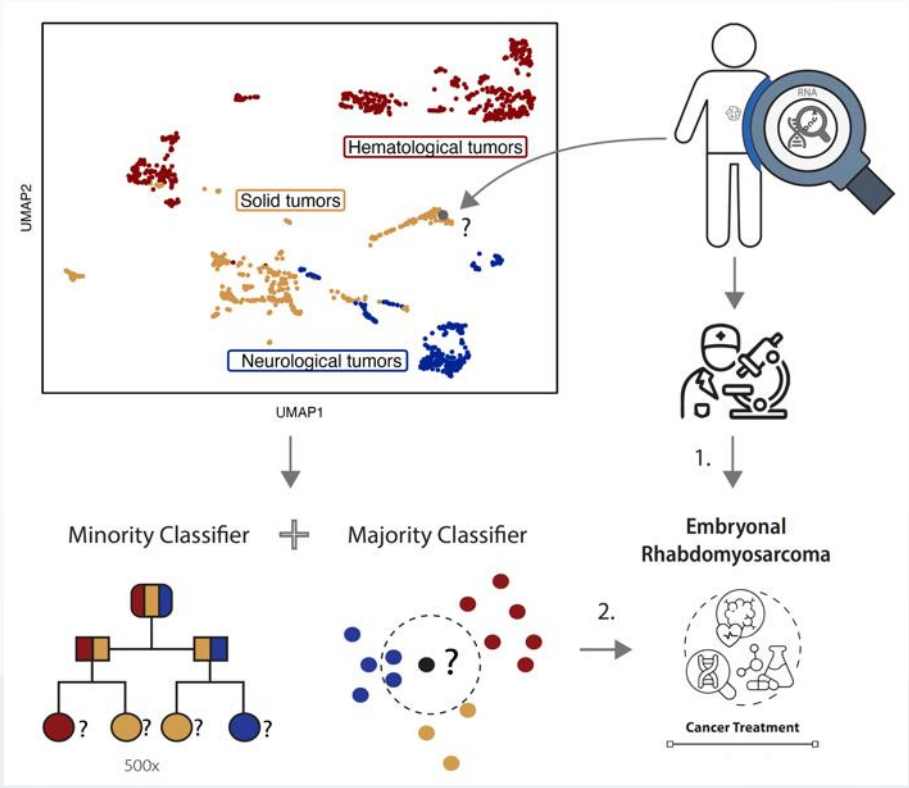
Creating impact through data & AI

Apple Vision Pro: Improved surgical precision using augmented reality

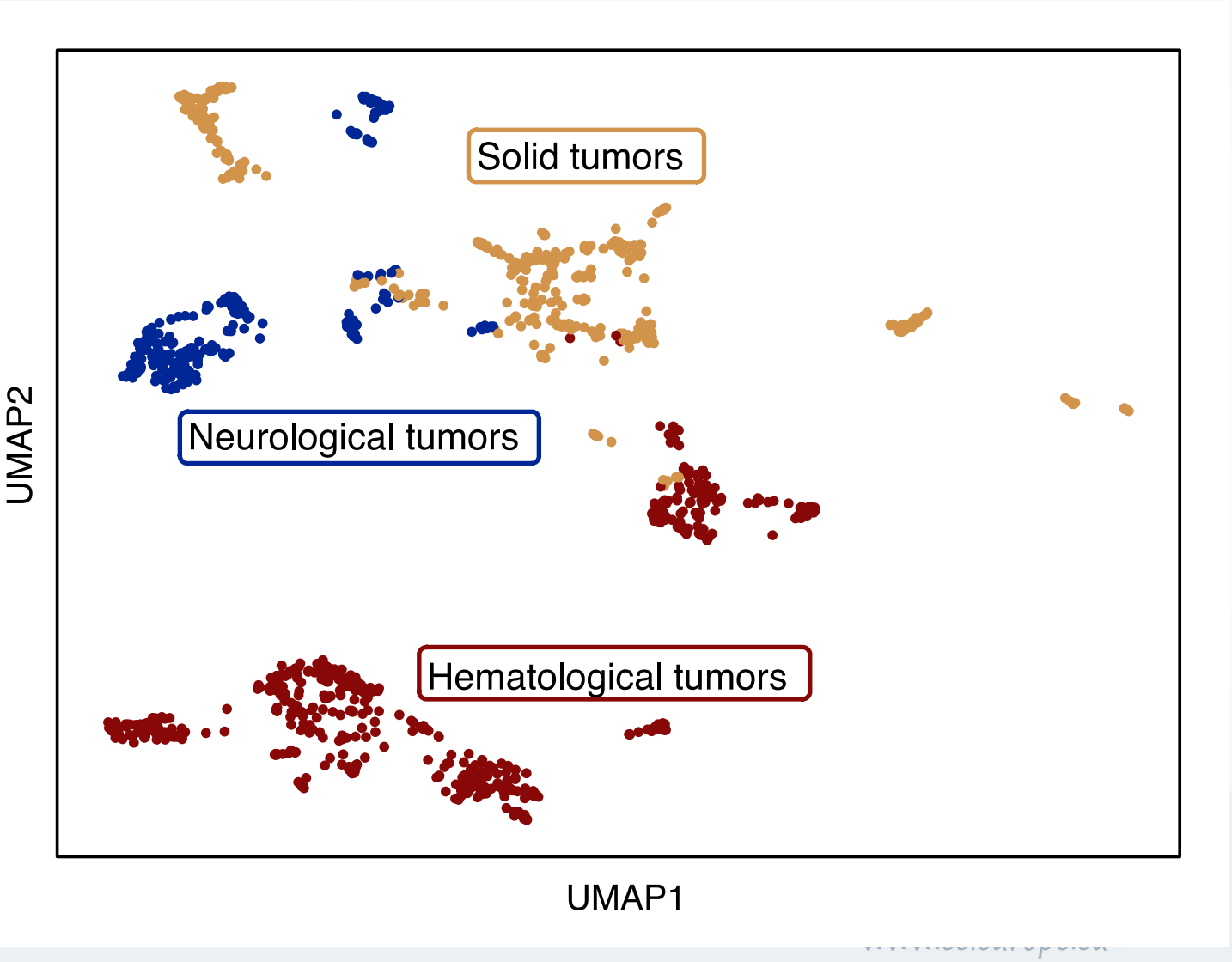
AI initiatives

Creating impact through data & AI

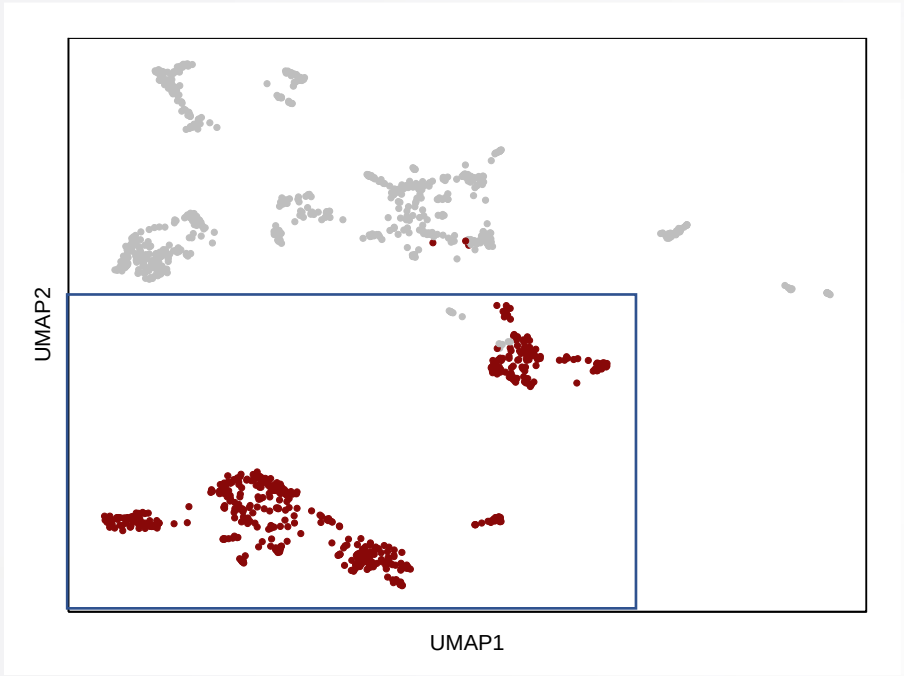
M&M: Accurate pan-cancer classification of pedatric tumor types

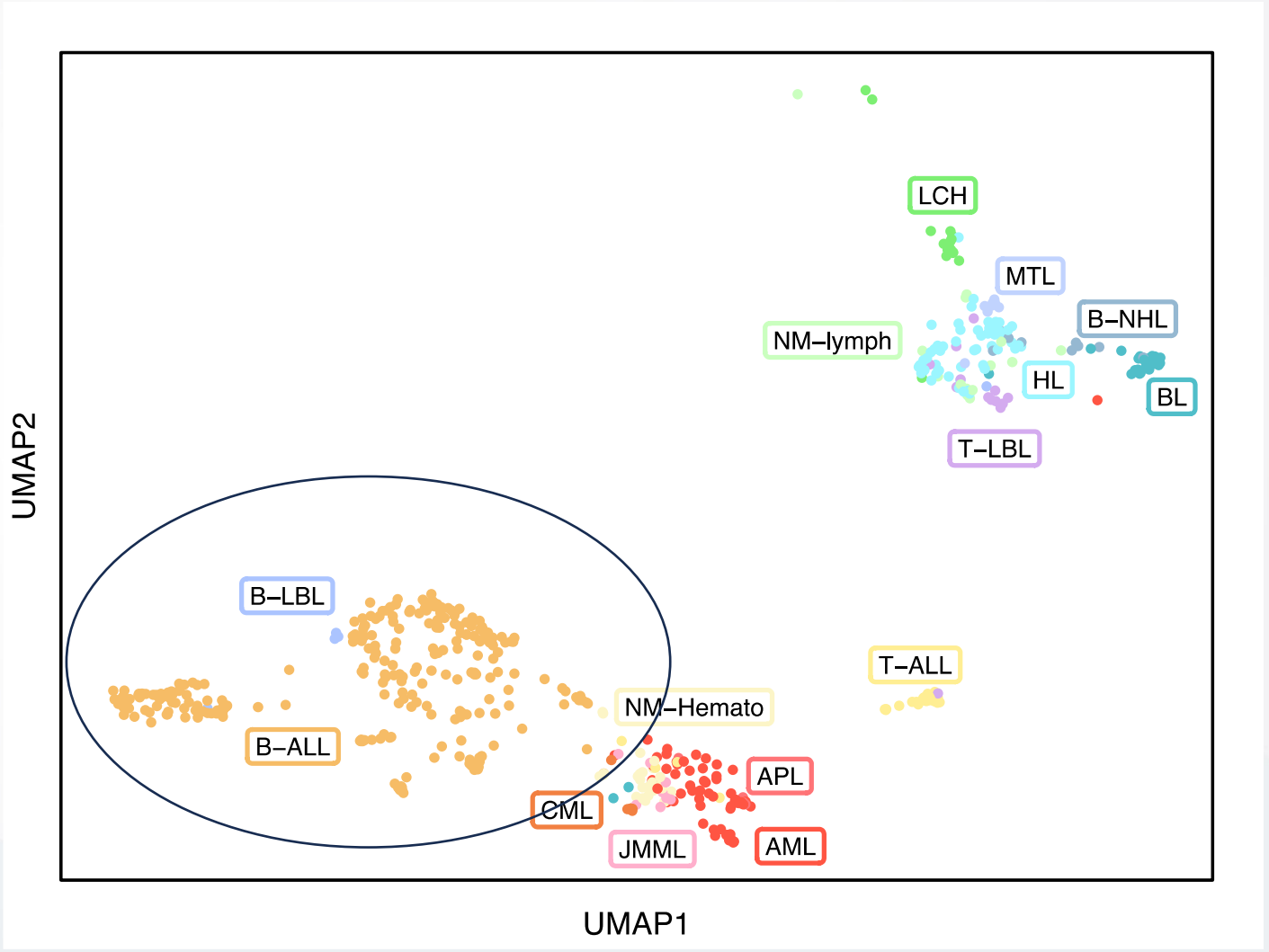


Cohort overview

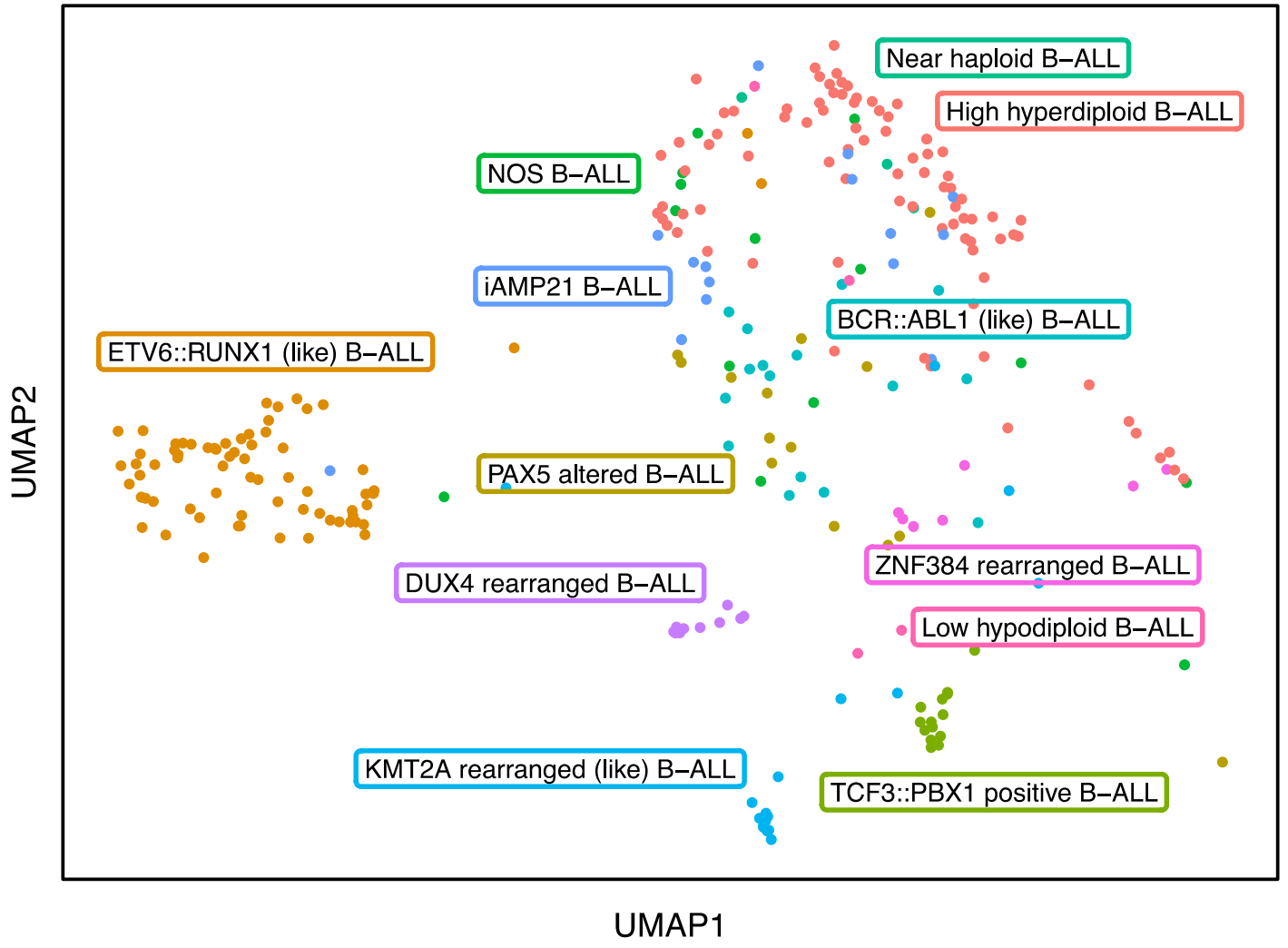


Hematological tumor types



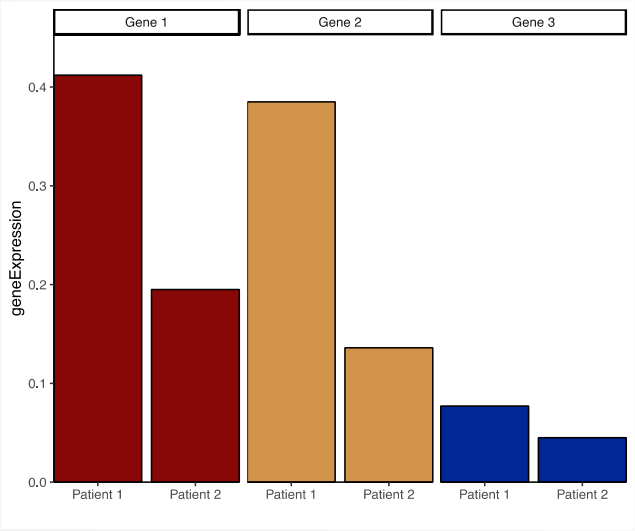


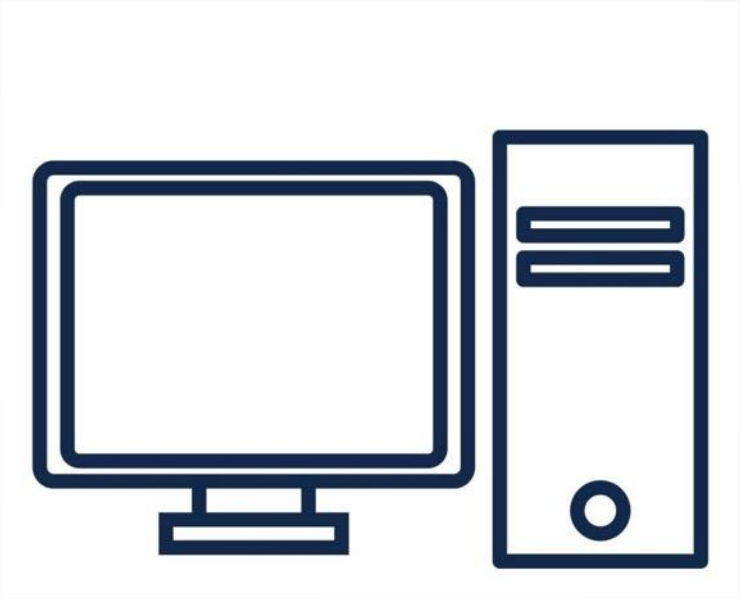
Hematological tumor subtypes



Added value RNA-seq for diagnostics

Pan-cancer classifier





Contribute towards **quick** and **accurate** diagnosis

- *Confirms* expected diagnosis
- Push diagnostic process in *different direction*

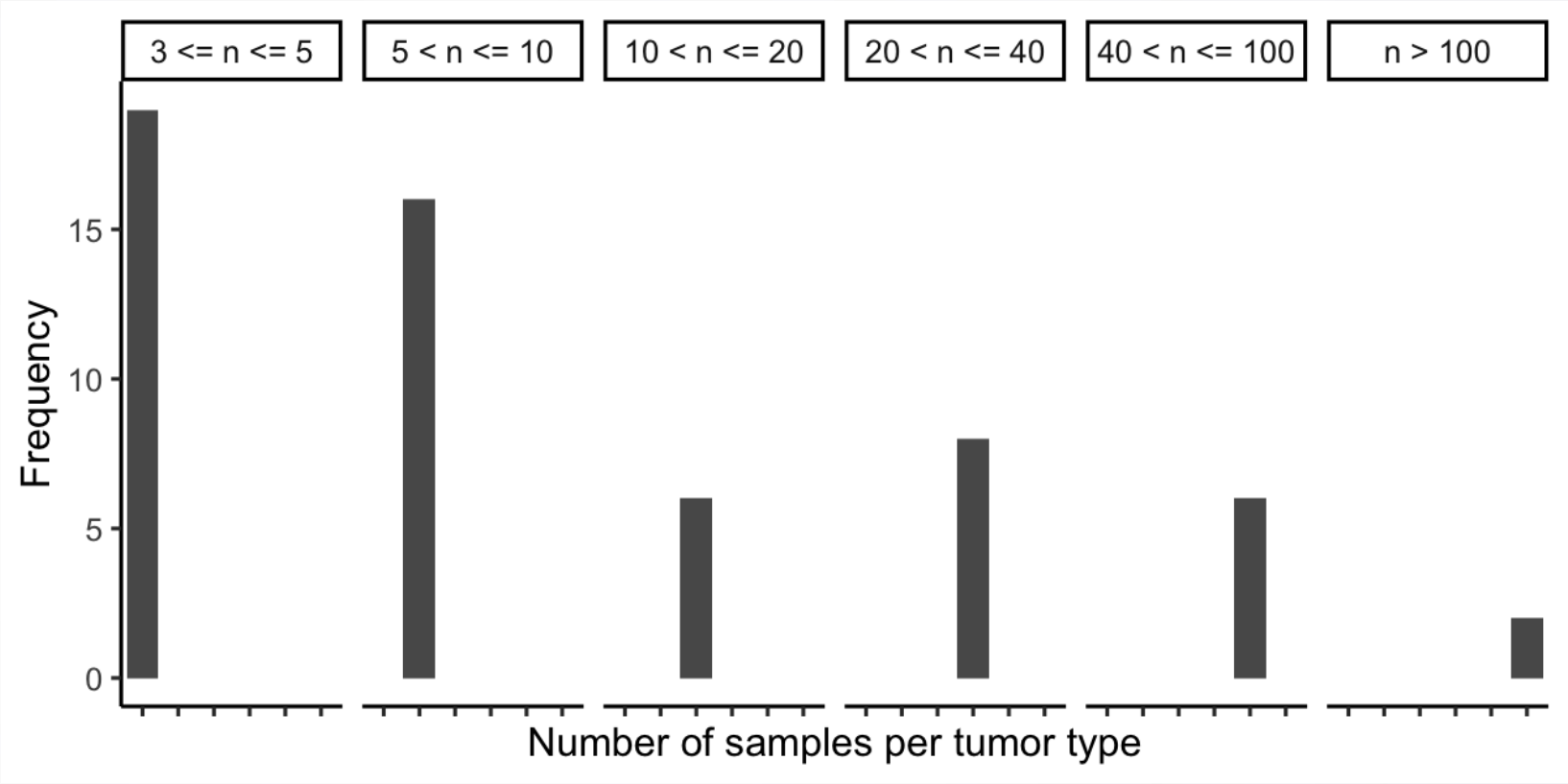
Challenges pediatric cancer dataset

Severe **class imbalance**

Many classes

> 50 tumor types

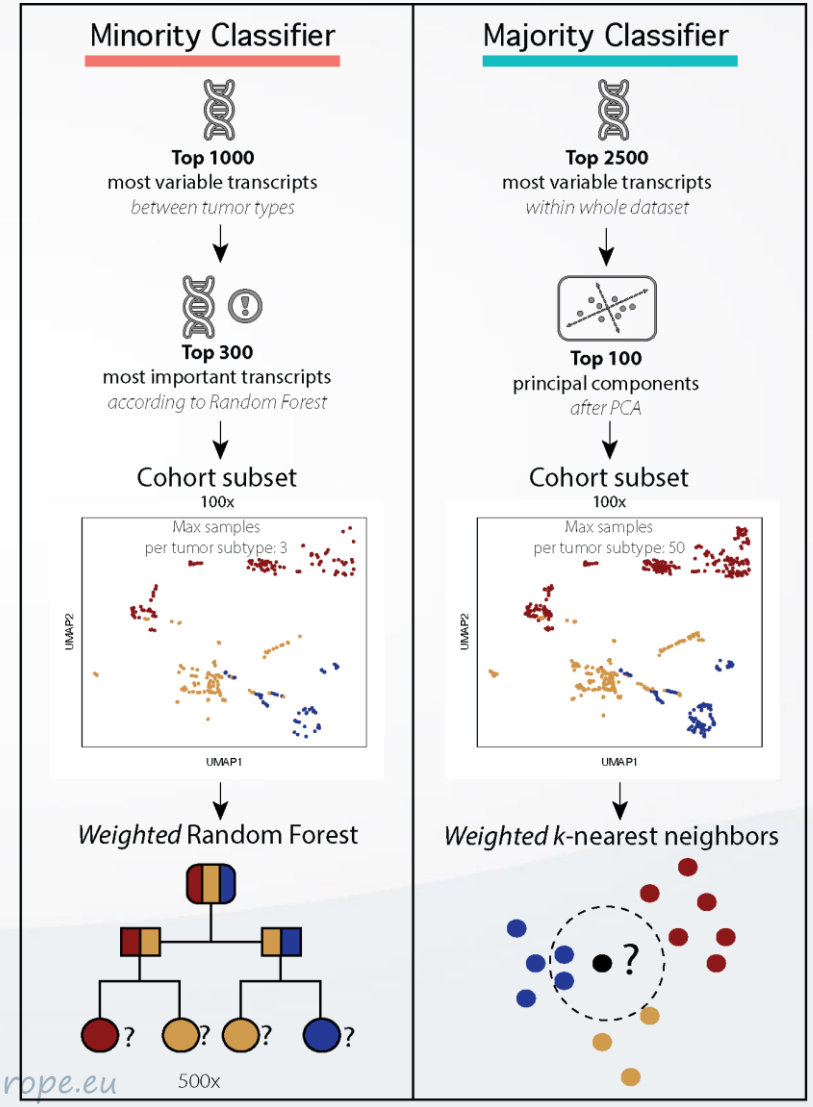
> 100 tumor subtypes



Minority + Majority classifier

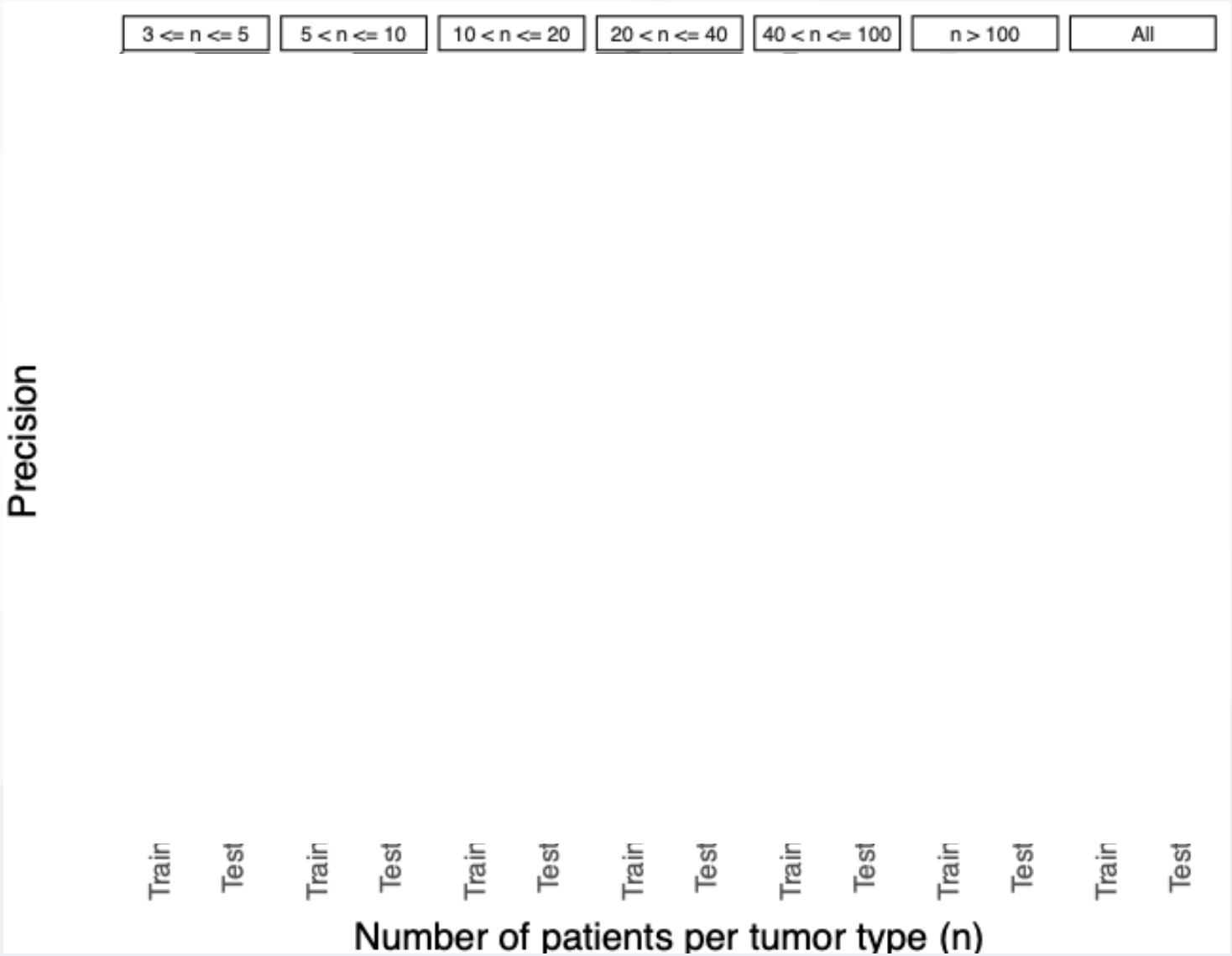
Minority
Focus on low-frequency tumor (sub)types

Majority
Focus on high-frequency tumor (sub)types



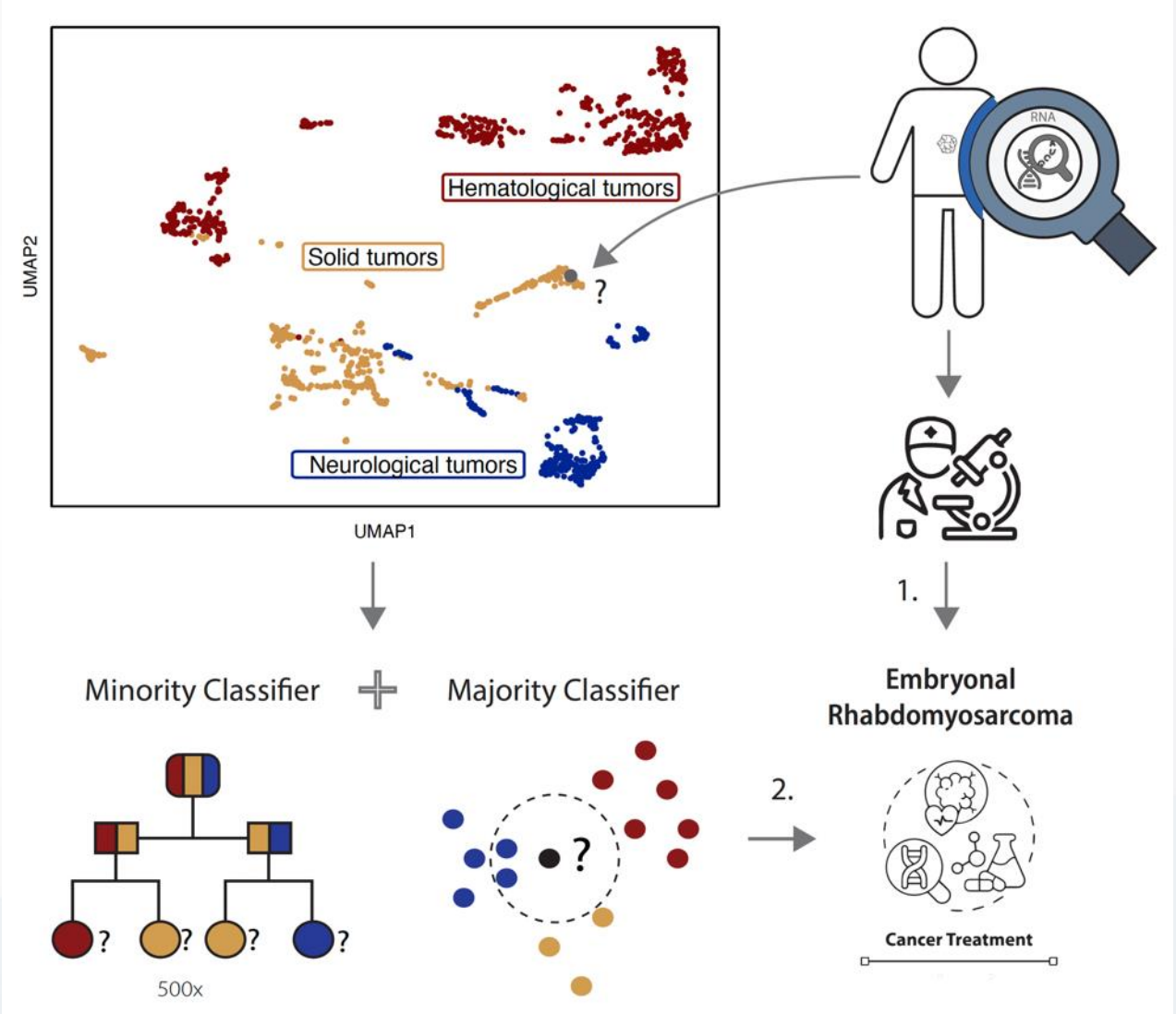
Classification performance across cohort

Did we manage to tackle the class imbalance issue? ✓



M&M: Accurate pan-cancer classification of pediatric tumor types

AI as a decision support system can aid the diagnostic process for accurate pediatric tumor identification



Big Data and AI in paediatric oncology
Ethical Implications

Franck Devaux
Universitate Libre de Bruxells

1 Ethical issues : aim for the head

- An AI answers, but doesn't listen
- Patients overflow their data (till singularity at least)
- How to still be able to listen to « real life » / empathic data ?
- How to mind the gap in study desgin ?

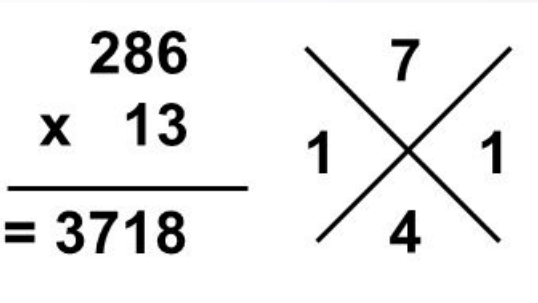
2 Scientificity of doubt

- An AI answers, but doesn't doubt even when it's wrong
- Medicine is an art enlighted by science and reason
- How to avoid black-box effect and keep human perspective at core and stake ?

3 AI and Skills

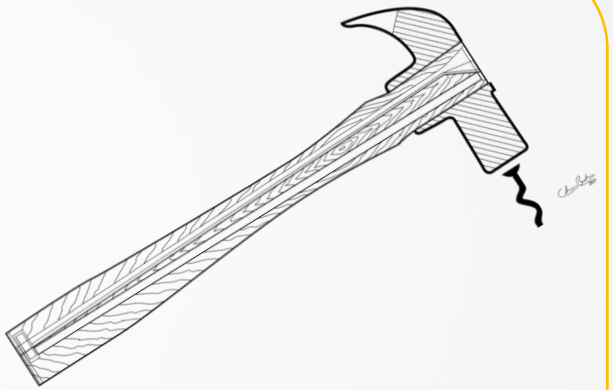
- Does AI support human skills, replace them, or create new ones?
- At the end, passed the « honey moon » of AI's, will we enhance our skills or weakend them ?
- How to avoid a black-box effect and keep human perspective at core and stake ? What might be lost in translation ?

Still able to do « Casting out nine »?



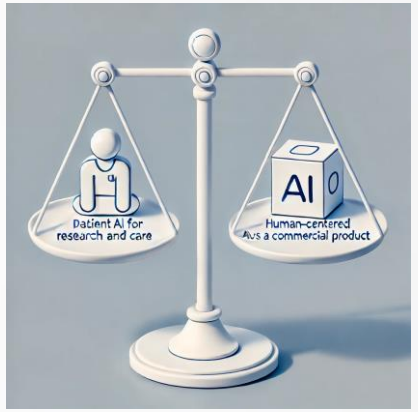
4 Is AI the New Hammer in town ?

- « If the only tool you have is an hammer everything will look like a nail »
- Risk of novelty bias, excitement of new resources
- Importance of maintaining a personalized and nuanced approach despite the use of AI.
- How to keep interdisciplinarity at the core of care ?



5 What will we care for ?

- What's important for an AI : the data, the cancer, the patient, the person of their own ?
- How to teach AI the paediatric population specificities (vulnerabilities and needs) ? How to avoid them to forget it ?
- How to avoir a purely predictive medicine ? « You didn't answer well to the predictions ? - the good patient paradox »?
- How to avoid restricted access to free trials and inovative treatments ?
- How to balance inclusivity and filtered populations while reducing risks.
- AI for research and care or AI as competitive commercial product ?
- How to manage time, training and costs for clinical teams ?
- What might be lost in translation ? between AI data analysis and human care?
- Does an AI even care ?



6 AI Opportunities & Hopes

- Enhanced econsent and empowerment through adaptative GPT-like information and FAQ
- Real-time chatbot to prepare questions and feddback for the clinical teams
- Performative PREM's and PROM's ressources
- Ease and encourage ancillary psycho-social research
- Ease master-protocol managment and development
- Reduce the need for double-blind vs placebo project
- Real-Time predictive SAE-prevention based on ongoing data

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Any questions?

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Conclusions!

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Give us your feedback

What could be the impact of Big Data and AI application in paediatric oncology?

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NEXT WEBINAR IS:

Advance Your Knowledge: How to develop and translate a multidisciplinary Psycho-Oncology Model of Care into real action?

18.11.2024

17:00-18:30 CET

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Thank you for your time !

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