News from Platinum & Clinical Informatics Interoperability Working Group

Dr Piers Mahon & Prof. Giovanni Tonon

A Chinese proverb …updated for digital research

Lao Tzu

“Give a man a fish, and you feed him for a day

Teach a man to fish, and you feed him for life”

The Matrix

“Give a hospital a study grant, and get a single paper”

Teach a hospital to build its digital research infrastructure, and they shall publish forever”

DigiCore

Your speakers today

Dr. Piers Mahon

- **“Facts of life”** on large scale digital research networks
- Review of **DIGICORE progress in 2022** in clinical informatics
- Progress **creating digital interoperability** in European oncology

Dr. Richard Bergstrom

- **Personal perspective** on why digital research networks matter
- **The Big Reveal:** who has got Platinum funding?

- **Panel discussion** from senior clinicians in the funded hospitals

Prof. Giovanni Tonon

- Looking ahead: **plans for 2023** & discussion

Reminder: Multi-centre real world evidence is a specialised form of protocolised research using hospital EHR, with 3 classic study types today

Evidence Platforms

Objective

Recurring natural history and outcome studies to understand evolving patterns of care and identify best practice pathways

Examples

- IO-Optimise NSCLC

Precision Oncology

Objective

Characterize outcomes today on narrow biomarker RWE sub-cohorts

Examples

- HER2+ vs - NSCLC
- P53 +/- -and radiotherapy

External Comparators

Objective

Case match controls vs. single arm interventional trial data

Examples

- Multiple heam studies on breakthrough drugs

All operate **after ethics approval** of a specific protocol

DigiCore

But the reality of European hospital EHR today makes delivery hard: every hospital has a unique “data language” creating a Tower of Babel

The Tower of Babel

Pieter Bruegel the Elder

- ✕ We speak **multiple languages**
- ✕ We **practice medicine differently**
- ✕ Most of the data in a hospital is **unstructured**
- ✕ **Critical data is missing**
- ✕ We have **bespoke IT systems** and vendors in every hospital with **proprietary data formats**
- ✕ We have **different clinical coding standards and claims systems** in every country
- ✕ We have different **national care quality** agendas
- ✕ We have **different national (and local) interpretations of GDPR** & privacy requirements

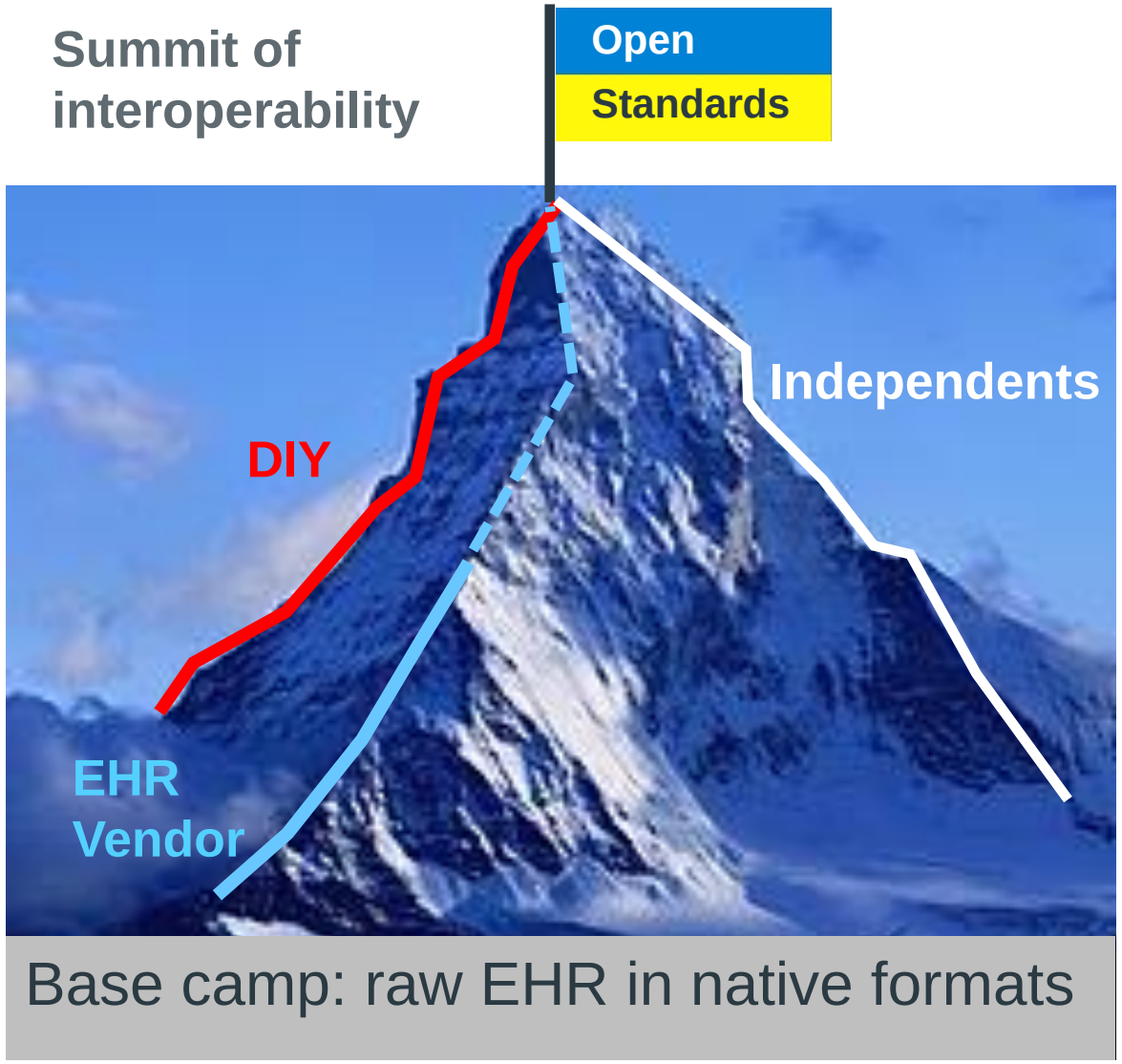
Data science standardised data to get to digital interoperability

Data item	Data model	Extraction "Tooling"	Conformed research data repository
• Specific medical concept that can be measured in data, a "protocol element"	• A conceptual schema for storing data elements in standardised ways, in standardised units for reliable analysis	• Software to "pull" data from existing messy storage, clean it, standardise and "push" into a data model	• The result: clean data in a standardised format in a robust data model held under hospital control for research use

An analogy…

Cars	Empty Car Park	Car Park Attendants	Filled, Neat Car Park
			

Open standards are essential to a competitive market in digital interoperability, and broadly there are three ways for a hospital to get there



- DIY: Do-it-yourself using Open Source tools (The IT version of climbing with no guide)
- EHR vendor supported (e.g. EPIC, Varian, Daedelus, Cerner etc)
- But will they get beyond a Clinical Data Warehouse in a proprietary data model?

Independent specialist systems integrators (IQVIA, EHDEN accredited SI vendors)

It is going to be expensive, so who is going to pay, and how does DIGICORE help its members get those funds?

Cost per Hospital

€500K

(and 10% maintenance p.a. thereafter)

Cost for a Network

- **€15M**
  (30 hospitals)
- **€50M**
  (100 hospitals)
- **€125M**
  (representative sample)
- **€1B+**
  (all major chemo centres)

Observations

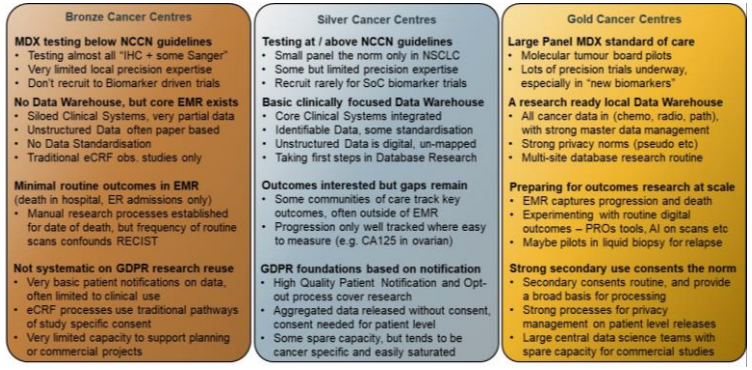
- It **isn't** HORIZON
- It **isn't** Industry
- DIGICORE **Must Coordinate**
- DIGICORE must **shape policy agenda**

What I am going to cover

- “Facts of life” on large scale digital networks
- Progress of DIGICORE’s clinical informatics community in 2022
- Deep Dive on creating digital interoperability on oncology EHR: Platinum and the DIGI-ONE prototype / pilot federated network

Three major planning activities in 2022 across the network

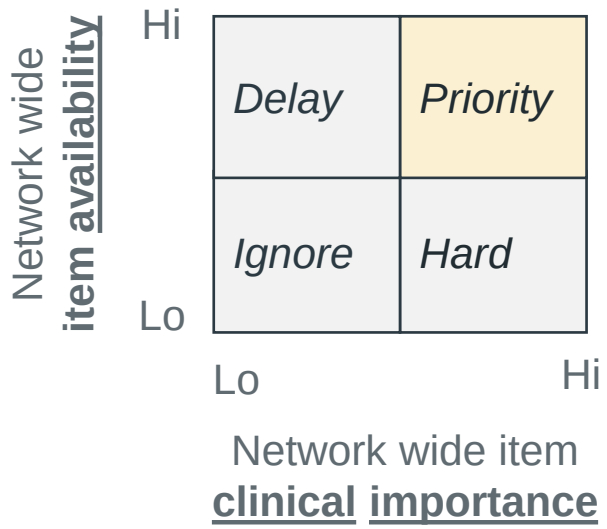
1. Mapping Our Digital Research Readiness



2. Mapping our Cohorts and PIs

Average DIGICORE Centre	
Cancer group	**# new Dx p.a.**
Big 4	2,013
Less common solid	1,972
Haem	308
Total	**4,293**

3. European consensus on a minimal digital description of cancer



A BIG THANK YOU to the 26 hospitals that participated

N#	Cancer Centre	Country	OECI Status	Research Readiness Survey	PI & Cohort Survey	Consensus on essential data for cancer
1	**Biobank Innsbruck**	Austria	n/a	Yes		*
2	**Charité, Berlin**	Germany	Other member	Yes		Yes
3	**Cliniques Universitaires Saint-Luc**	Belgium	Other member	Yes	Yes	Yes
4	**Institut Curie, Paris**	France	Certified Comprehensive CC	Yes	Yes	Yes
5	**Institut De Cancerologie de l'Ouest**	France	Member in the A&D process	Yes		Yes
6	**Institute of Oncology, Ljubljana**	Slovenia	Member A&D certified CC	Yes	Yes	Yes
7	**IPO Porto**	Portugal	Certified Comprehensive CC	Yes	Yes	
8	**Istituto Nazionale dei Tumori, Milan**	Italy	Certified Comprehensive CC	Yes	Yes	
9	**Istituto Nazionale Tumori Regina Elena**	Italy	Certified Comprehensive CC	Yes	Yes	Yes
10	**Istituto Romagnolo "Dino Amadori"**	Italy	Other member	Yes	Yes	
11	**Karolinska Comprehensive CC**	Sweden	Certified Comprehensive CC	Yes		
12	**Leeds Teaching Hospitals NHS Trust**	UK	n/a	Yes	Yes	Yes
13	**Maastricht Comprehensive CC**	Netherlands	Certified Comprehensive CC	Yes	Yes	Yes
14	**Masaryk Memorial CI, Brno**	Czechia	Member A&D certified CC	Yes	Yes	
15	**Oslo University Hospital CC**	Norway	Certified Comprehensive CC	Yes	Yes	Yes
16	**Ospedale San Luigi Gonzaga, Turin**	Italy	n/a	Yes		
17	**Ospedale San Raffaele, Milano**	Italy	Member in the A&D process	Yes	Yes	Yes
18	**Policlinico San Matteo, Pavia**	Italy	Other member	Yes	Yes	
19	**Sestre milosrdnice University Hospital**	Croatia	Other member	Yes	Yes	Yes
20	**START Madrid**	Spain	n/a	Yes		
21	**Tartu University Hospital**	Estonia	Member A&D certified CC	Yes	Yes	Yes
22	**Tays CC**	Finland	Member A&D certified CC	Yes	Yes	Yes
23	**Trinity St James's Cancer Institute**	Ireland	Member A&D certified CC	Yes	Yes	Yes
24	**Universitäts Klinikum Frankfurt**	Germany	Other member	Yes	Yes	Yes
25	**Vall d'Hebron University hospital**	Spain	Member in the A&D process	Yes		Yes
26	**Vejle Hospital**	Denmark	Member A&D certified CC	Yes	Yes	

1. Digital research readiness builds from the framework we shared in Paris

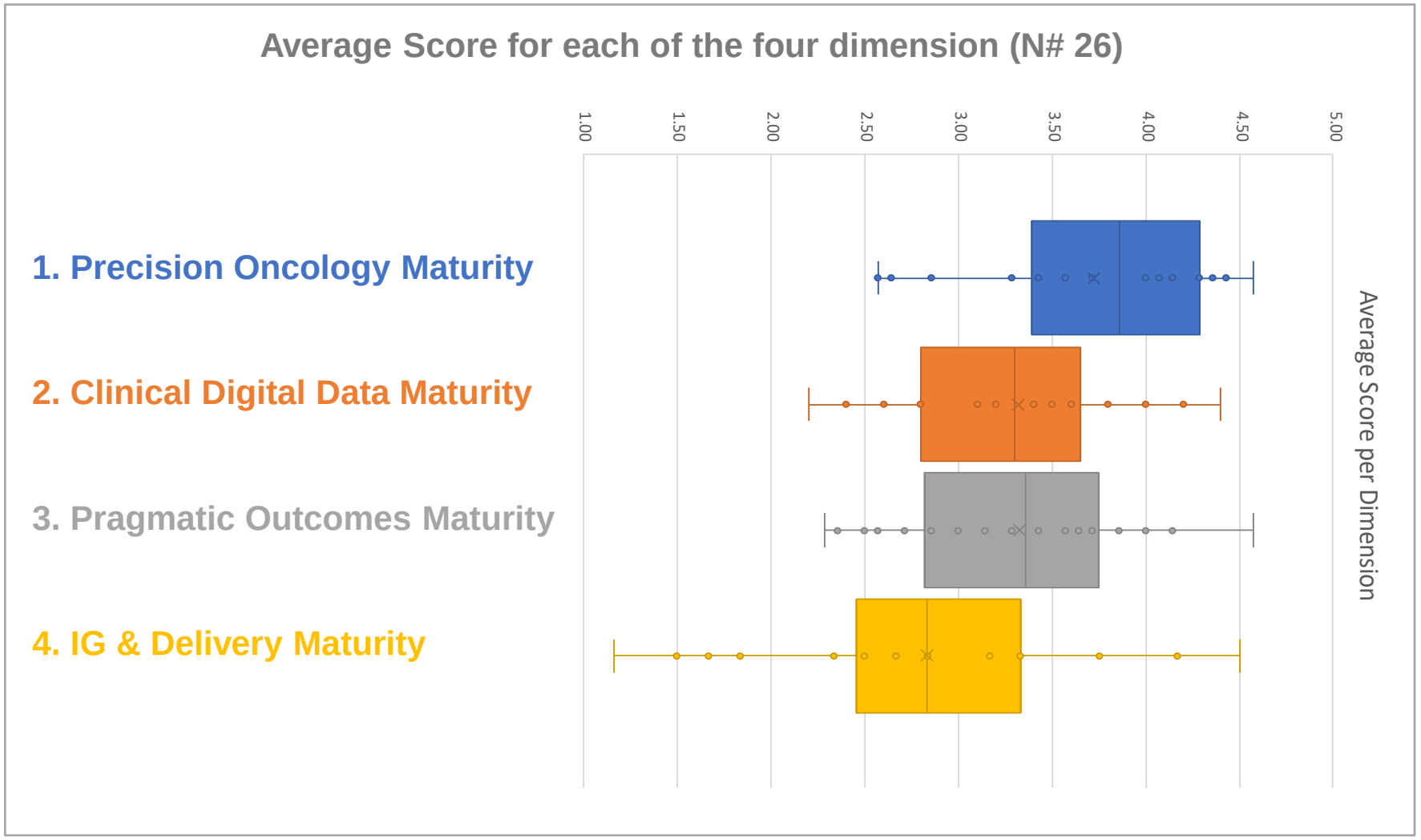
	Bronze Cancer Centres	Silver Cancer Centres	Gold Cancer Centres
1. Precision oncology research maturity	**MDX testing below NCCN guidelines** • Testing almost all "IHC + some Sanger" • Very limited local precision expertise • Don't recruit to Biomarker driven trials	**Testing at / above NCCN guidelines** • Small panel the norm only in NSCLC • Some but limited precision expertise • Recruit rarely for SoC biomarker trials	**Large Panel MDX standard of care** • Molecular tumour board pilots • Lots of precision trials underway, especially in "new biomarkers"
2. Routine clinical data digital research maturity	**No Data Warehouse, but core EMR exists** • Siloed Clinical Systems, very partial data • Unstructured Data often paper based • No Data Standardisation • Traditional eCRF obs. studies only	**Basic clinically focused Data Warehouse** • Core Clinical Systems integrated • Identifiable Data, some standardisation • Unstructured Data is digital, un-mapped • Taking first steps in Database Research	**A research ready local Data Warehouse** • All cancer data in (chemo, radio, path), with strong master data management • Strong privacy norms (pseudo etc) • Multi-site database research routine
3. Pragmatic outcomes maturity	**Minimal routine outcomes in EMR** (death in hospital, ER admissions only) • Manual research processes established for date of death, but frequency of routine scans confounds RECIST	**Outcomes interested but gaps remain** • Some communities of care track key outcomes, often outside of EMR • Progression only well tracked where easy to measure (e.g. CA125 in ovarian)	**Preparing for outcomes research at scale** • EMR captures progression and death • Experimenting with routine digital outcomes – PROs tools, AI on scans etc • Maybe pilots in liquid biopsy for relapse
4. Information Governance & Delivery Maturity	**Not systematic on GDPR research reuse** • Very basic patient notifications on data, often limited to clinical use • eCRF processes use traditional pathways of study specific consent • Very limited capacity to support planning or commercial projects	**GDPR foundations based on notification** • High Quality Patient Notification and Opt-out process cover research • Aggregated data released without consent, consent needed for patient level • Some spare capacity, but tends to be cancer specific and easily saturated	**Strong secondary use consents the norm** • Secondary consents routine, and provide a broad basis for processing • Strong processes for privacy management on patient level releases • Large central data science teams with spare capacity for commercial studies

DigiCore

We have developed a 25 question semi-structured expert self-assessment

Dimension	# Q	Example question		
1. Precision medicine	1.3	**Molecular Diagnostics (MDx) Access** - Which of the following options best describe the centre's maturity of Molecular Diagnostics focused on somatic biomarker mutations?		
		1 = Our center doesn't perform molecular tests for the moment (for instance due to lack of funding)	**3** = Testing according to national/ESMO guidelines, but behind US NCCN guidelines	**5** = Large panel (>=50 genes) standard of care for a few cancers, e.g. NSCLC.
2. Clinical data	2.5	**RWE maturity** - Which of the following statements best describes the level of sophistication possible at your centre with regard to routine retrospective observational Medical Research?		
		1 = eCRF based studies only, with clinician re-type	**3** = Multi-centre, relatively simple academic database studies (e.g. OMOP studies)	**5** = Multi-centre, complex RWE for commercial sponsors with regulatory audit
3. Pragmatic outcomes	3.4	**Line of therapy and start of next therapy** - How easy is it to call line of therapy locally, and get a date of next therapy start (so that time to next treatment is possible)?		
		1 = Line of therapy is hard to resolve in most patients on retrospective data alone	**3** = Line of therapy can be resolved manually in over half of cancers using established rules	**5** = Line of therapy is routinely resolved in structured data on all patients with robust dates
4. Information governance and research operations	4.2	**Use of patient level data in collaborative research** - In what circumstances can patient level data be shared with other organisations for the purpose of research **without** study specific consent?		
		1 = No data release is possible without study specific consent, let alone patient level	**3** = We have procedures in place to allow strong privacy protections for release of (near)-anonymous data	**5** = Our routine consents allow pseudonymised data to leave the center and EU for all types of protocolised research

Overall results suggest network strongest on precision medicine, with most work to do on information governance



	Average
1. Precision Oncology	3.72
2. Clinical Digital Data	3.32
3. Pragmatic Outcomes	3.33
4. IG & Delivery Maturity	2.83

Measuring digital maturity can help DIGICORE members in 5 ways

1. Direct Institutional Benchmark

Hold up a mirror to internal views on progress your centre is making to digitize, and where to focus efforts

2. Publication of Results

Survey and its development are a natural publication

3. Identify European Best Practice

Identify institutions which are best practice in particular elements of digital research as “sources of expertise” to others

4. Catalyse Collaborative Research

Enable collaborative research projects within DigiCore to come together between “expert centres” to develop new clinical informatic solutions

5. Track our digital progress

Repeat the surveys in 18 months to 2 years to track progress in digitization

As an example, these are our expert centres – how do we best use their expertise to lift up others?

Top 5 hospitals in each dimension, listed alphabetically.

1. Precision Oncology

Top 5

Cliniques Universitaires Saint Luc

Institut Curie

Oslo

San Raffaele

Anonymous

2. Overall Routine Clinical Data/Digital Research

Top 5

Cliniques Universitaires Saint Luc

Institut Curie

San Raffaele

Sestre milosrdnice UH

Tays - Tampere

3. Pragmatic Outcomes

Top 5

Cliniques Universitaires Saint Luc

MaastrichtCCC

San Raffaele

Sestre milosrdnice UH

Anonymous

4. IG & Research Operations

Top 5

Leeds Teaching Hospitals NHS

Oslo

San Raffaele

Universitäts Klinikum Frankfurt

Anonymous

Total Overall

Top 5

Cliniques Universitaires Saint Luc

San Raffaele

Sestre milosrdnice UH

Universitäts Klinikum Frankfurt

Anonymous

*Anonymous hospitals didn't explicitly agree to share their results within DigiCore

Our research communities have the information they need to start planning studies – we just need to "connect the PIs" and set-up more working groups

Cancer	Overall New Dx / P.A* (in 19 CC)	DIGICORE's 34 CC (estimate)	# centers with an interested PI*	New Dx p.a. with an interested PI**	Working group being set-up?
Breast	15,667	28,036	14	8,858	Yes
Prostate	7,941	14,210	14	4,601	
Lung	8,137	14,561	16	6,509	Yes
Colorectal	6,507	11,644	16	5,604	
Skin	8,680	15,533	10	4,395	
Gynaecological	5,698	10,196	16	4,376	
Other Solid	23,086	41,312	Typically 11 to 12	15,808 (all)	
Lymphomas	3,551	6,354	10	2,106	Yes
Other haem	2,295	4,107	Typically 6 to 7	873	
Total	**81,562**	**145,953**	***12**	**53,130**	

*in the 19 DIGICORE members that have completed these surveys

** i.e. in the 19, not only is there a local cohort, there is a named individual willing to lead research on that cohort

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Platinum fund: up to €3M* for technology investment in a proof of concept federated network to help members access follow-up funds

Objectives for the Platinum Fund

**half cash, half in-kind labour*

1. Define a **scalable common international minimum dataset for cancer**, building from French OSIRIS
2. **Achieve interoperability and high data quality** on that dataset between 6 centres across Europe under GDPR
3. **Federate those centres** to allow aggregated statistics like counts and to answer simple research questions, with appropriate information governance and contracting
4. **Link routine molecular and clinical data** (despite the format challenges on molecular PDFs)
5. **Demonstrate commercial real world evidence possible** in a broader range of European countries than today
6. Work out how to **scale up digitally less mature hospitals** with a **variety of technologies and vendors** in DIGICORE's learning – by- doing community

We have built international consensus across 16 hospitals in 13 countries to define a minimum data model for cancer: MEDOC

1. National cancer datasets

- UK COSD (~1200)
- German ADT (~300)
- French OSIRIS (105) (smallest + has best biomarker plan)

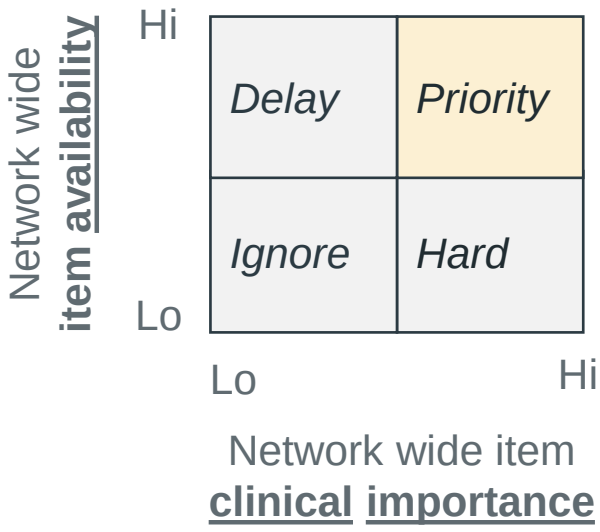
2. Experience from international RWE

- Detailed under-standing of data availability in hospitals
- Detailed understanding of data item research importance, e.g. ECOG for risk normalisation and trial matching

3. Expert hypothesis modified from OSIRIS

- Input from experts in France, Italy, Germany, UK to
  - "Slim down" OSIRIS where possible
  - Identify gaps (e.g. weight for cachexia, or chemotherapy dosing)

4. Clinical priority / feasibility trade-offs by e–survey



5. Traditional consensus process on the "contentious items"

- Item by item discussion on the "Hard" variables to agree pragmatic solutions
- For example, focus on the CCI co-morbidities, not all co-morbidities
- Result: MEDOC a *"**m**inimal **e**ssential **d**escription **o**f **c**ancer"* 40% easier to implement than OSIRIS

Some important features of MEDOC

1. **Primary use case is care quality management**, secondary use case is research
2. **Tailored for realities of European data** (e.g. not dependent on US step-edits in claims)
3. **Minimal = implementable** (~40% smaller than OSIRIS)
4. **Emphasis on data quality and completeness**
5. **Precision Oncology ready under GDPR** (no nucleic acid strings)
6. **Modular & extensible:** we can extend from this “minimal core” over time within OMOP

Taster on the results:

Representation of real data from 16 completed Data Item Surveys.

1 Date of birth (year)	**15** Metastasis presence	**29** Radiotherapy Start Date
2 Sex	**16** Metastasis location	**30** Radiotherapy type
3 Weight/dates	**17** Biomarker name, type	**31** Radiotherapy End Date
12 Disease stage	**26** based treatment	**40** clinical trial status
13 Histological cell type	**27** Treatment dose	
14 Core routine biochemical blood tests	**28** End Date of the drug based treatment	

Withheld until publication

40 clinical data items made the cut, and became the target specification for hospitals to build for high quality, high completeness, near real time data

Patient Registration & Consent	Clinical Diagnosis & Clinical Phenotype	Biomarkers & tissue samples	Treatment	Outcomes
Birth date (to nearest month - data item 3.1)	**Confirmation of diagnosis type / method)** (data items 10.1)	**Biomarker type name** (data items 13.1, 13.2)	**Treatment type** (data item 11.1)	**Date of death** (item 4.3) *Where routine death linkage allowed by local law*
			Treatment start & end	

Withheld until publication

Key: Black = in OSIRIS, Red = additional data items not in OSIRIS, yellow = likely national / locally tailored data elements
Notes: numbers like "3.1" refer to the numbering in official OSIRIS data schema

16 hospitals went through an intensive 2 stage bid development process

1. Expressions of Interest – 7 July

1.1 Official non-binding letter saying your CC wants to participate, appointing *name X & name Y* to lead your bids' technical and legal planning over the summer. If you want to use 3rd party or IQVIA support please register this in this letter for capacity planning & coordination reasons

1.2 Digital maturity survey* to benchmark your molecular, clinical and outcome data maturity, as well as your information governance – needs cross-functional input

1.3. Data importance / availability survey** – get clinical input on the critical clinical elements to capture for care quality management + engage senior clinicians in bid

1.4. IT systems landscape * – work out where your key data lies, in which vendors and engage your IT team

2. Formal bid submission – 14 September

2.1 A data sourcing and deployment plan that is thoughtful, pragmatic and coherent as to how your centre will meet the MEDOC specification with high data quality

2.2. 10 page core application, covering team, track record, legal basis and proposed plan

2.3 Key appendices: CVs, detail on sourcing 5 "harder" data items, budgets

2.4 **Reviewed draft contract** that allows studies and funding to sites to proceed.

We asked applicants to “throw every technology” at getting to high quality, near real time structured data conformed to MEDOC and in OMOP

Molecular data example

NGS routine testing pipeline

A) For 95% centres with only PDF access

PDFs

OCR

B) For 4% centres with a helpful lab

XML summary equivalent to results in the PDF report

NLP

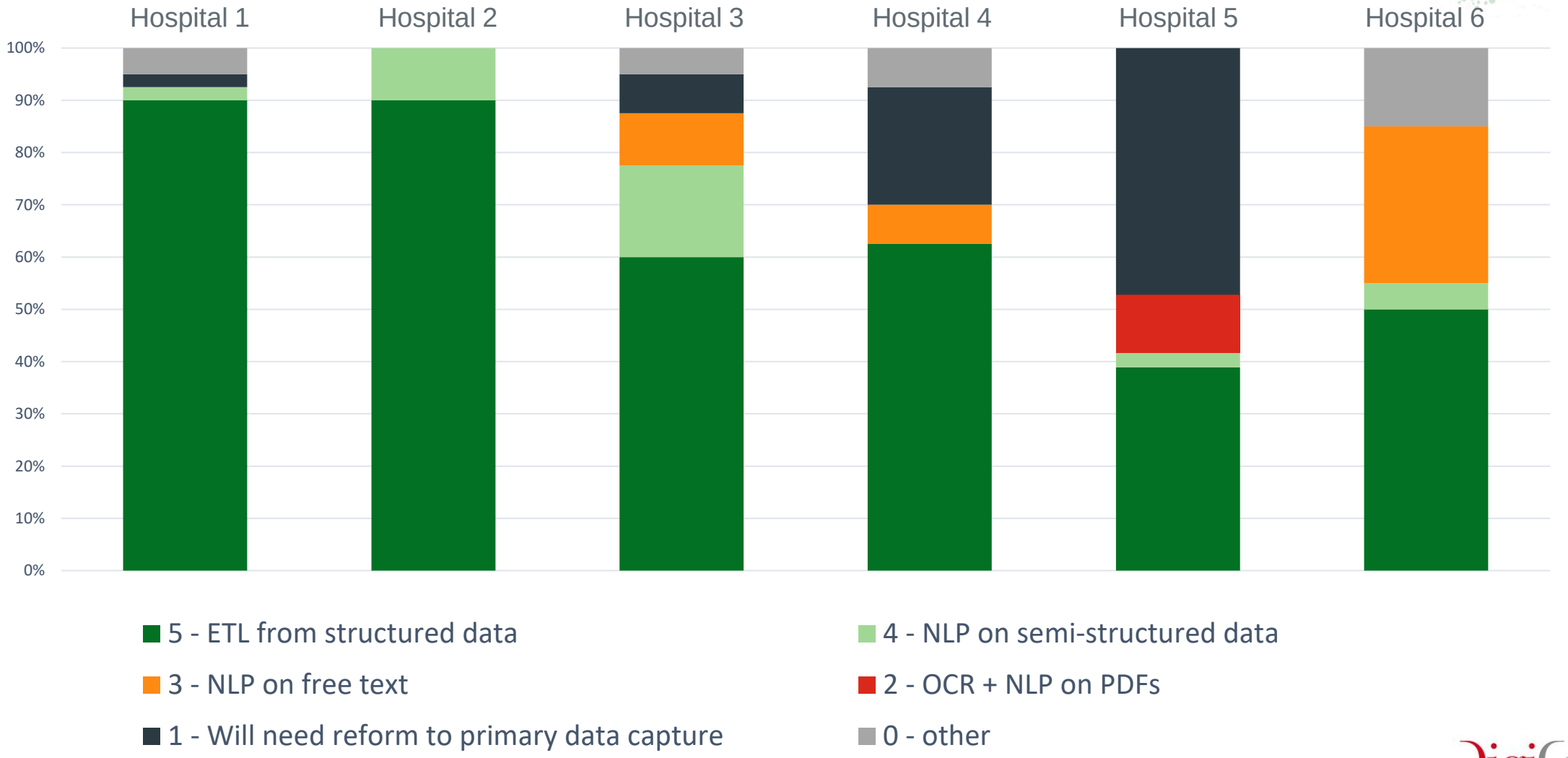
Structured Data in OSIRIS - omics format

Storage
OMOP
OSIRIS

C) For 1% centres with in-house bioinformatics*

Upgrade the data flow pipeline – structured test data to OSIRIS

The six winners took a variety of approaches, tailored to their existing local IT ecosystem and current data availability



Results have already been reused in DIGICORE's I3 bid to ERDF that - if successful - would get another 15 hospitals to the common standard

27 partners

Coordinator (EEIG)

DigiCore

Q-Helix Partner

EuroScan International Network

Oncology Research Partner

IQVIA

IQVIA Cancer Research BV

Hospitals

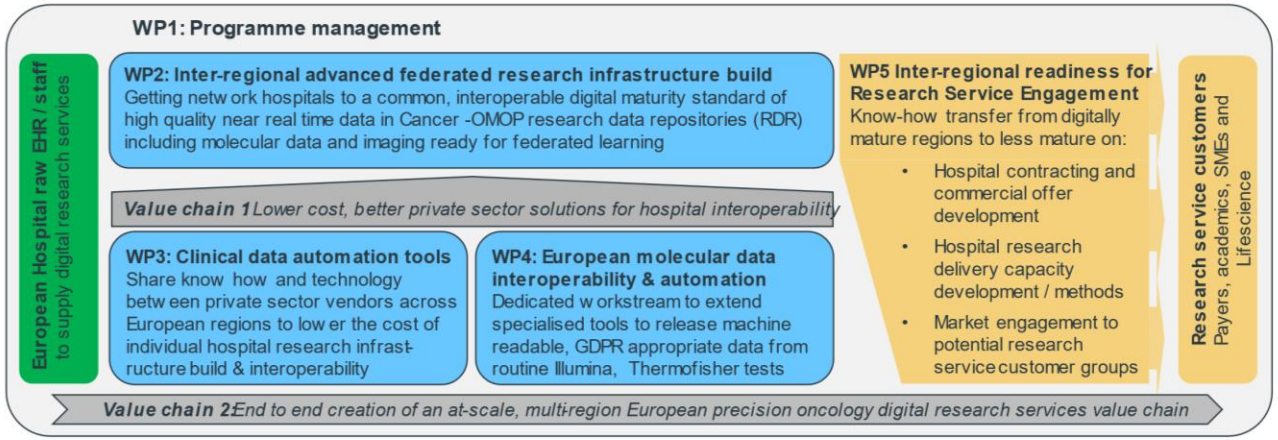
Belgium	Grand Hôpital de Charleroi
Czechia	Masaryk Memorial Cancer Institu
Estonia	The Cancer Centre of Tartu Univ
Germany	Charité – Universitätsmedizin Be
	Dresden university hopsital
	Greifswald University Hospital
Ireland	Trinity St. James's Cancer Institut
Italy	Istituto Nazionale Tumori Regina
	Ospedale San Raffaele
Lithuania	Vilnius University Hospital Santa
Netherlands	University Medical Center Groni
	Maastricht University Medical Ce
Poland	Central Clinical Hospital of the M
	Maria Sklodowska-Curie Nationa

IT Partners

The Digital Institute for Cancer Outcomes Research

Work packages

Digital Oncology Network for Europe bid to the I3 scheme to scale up our pilot (€12M)



DigiCore 3

The Digital Institute for Cancer Outcomes Research

Thank you…

- The teams at the 16 hospitals

- Coordinating team
  - Anthony Guerthert
  - Carlos Berenguer Albinana
  - Davide Ugolini

- Selection Committee
  - Ashley Woolmore
  - Marie Lamott
  - Adrian McKemey
  - Mariana Guergova-Kuras
  - Thorsten Duseberger
  - Bettina Ryll

… and welcome

Dr. Richard Bergstrom,
VP European Affairs, IQVIA

Former Director EFPIA

Panel discussion

People

- **Prof. Dr. Janne Vehreschild,** Frankfurt University hospital
- **Prof. Geoff Hall,** Leeds UTH
- **Prof. Andre Dekker,** Maastricht UHT
- **Prof. Åslaug Helland,** Oslo Cancer Centre
- **Dr. Joëlle Thonnard**, Cliniques Universitaires Saint-Luc (UCLouvain)
- **Prof. Giovanni Tonon**, Ospedale San Raffaele University

Topics for discussion

- Why DIGI-ONE matters
  (to them, to research, to patients)
- What was challenging, and what they learnt during the process
- Where their centre can help, and where they need help

DigiONE will transform cancer research and care

DigiCore

0. Digital care quality management applications

(e.g. guideline compliance apps, automating clinical audit)

1. International outcomes research

2. Biomarker discovery and validation

3. RWE for trials, such as case matched controls or digital screening solutions

4. Ultimately, digital pragmatic trials (randomise in research data repository)

Proposed Clinical Informatic 2023 objectives

- **Make Platinum implementation a success**, and share learnings quickly with rest of DIGICORE

- Drive **clinical informatic publications** from the design work in Platinum, **get conference speaking slots**
  - Workout which conferences matter (OHDSI Europe, HIMMS?)

- **Secure non-HORIZON grants to expand the # of centers on the common data model**
  (won't be TRL 1-3, will have to get average = > good therefore won't be HORIZON eligible)

- Work out what we have in **our best centres & set them up as "centres of excellence" others can consult**
  - "New abstracts for old papers" to find good open-source code

- **Set-up 2023 virtual seminar series to share lessons / best practice**
  - Try different formats, including "every one speaks a bit" – e.g. "what outcomes can your centre get to"
  - Consider detailed seminars on highly technical topics for example:
    - Cancer OMOP, molecular data, federation software options etc