DIGICORE 2024 Research priorities and working groups

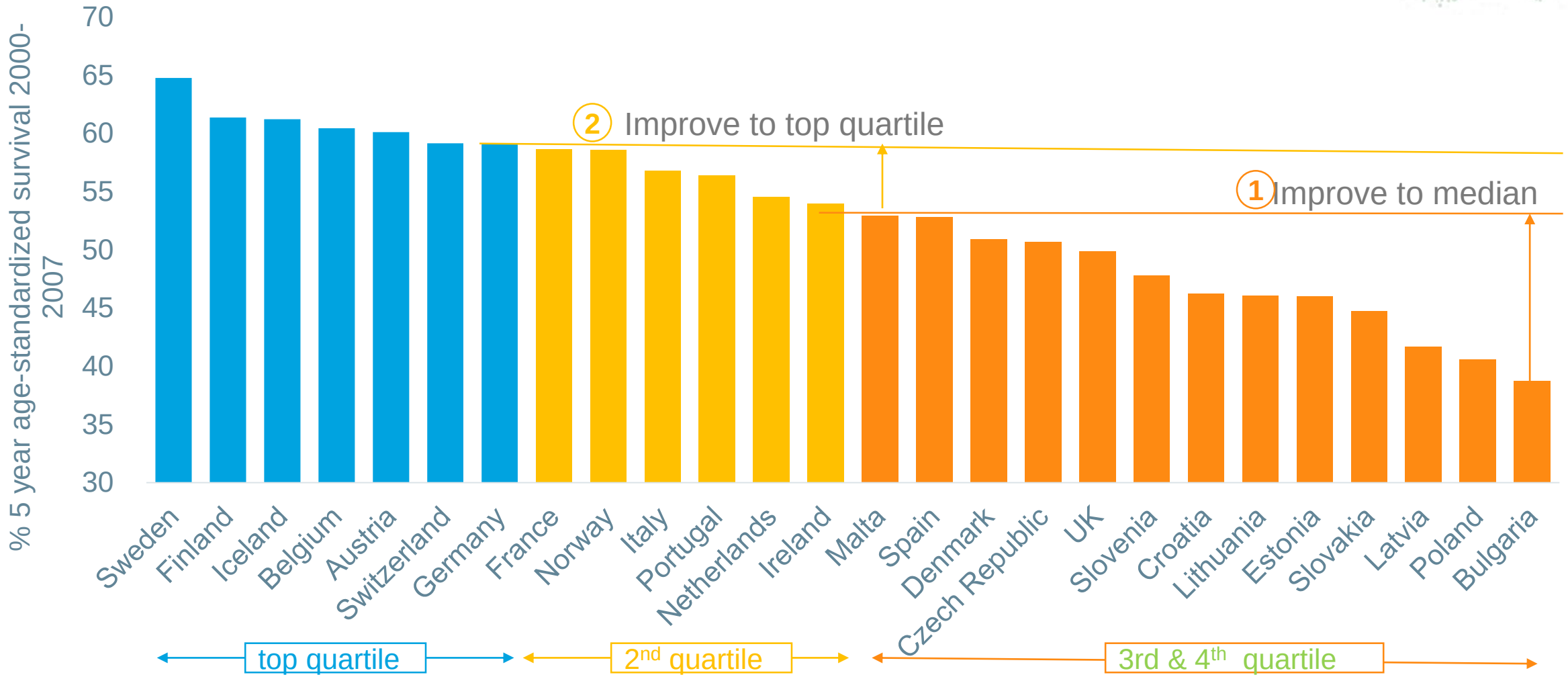
13 November 2023

The Digital Institute for Cancer Outcomes Research

Objectives

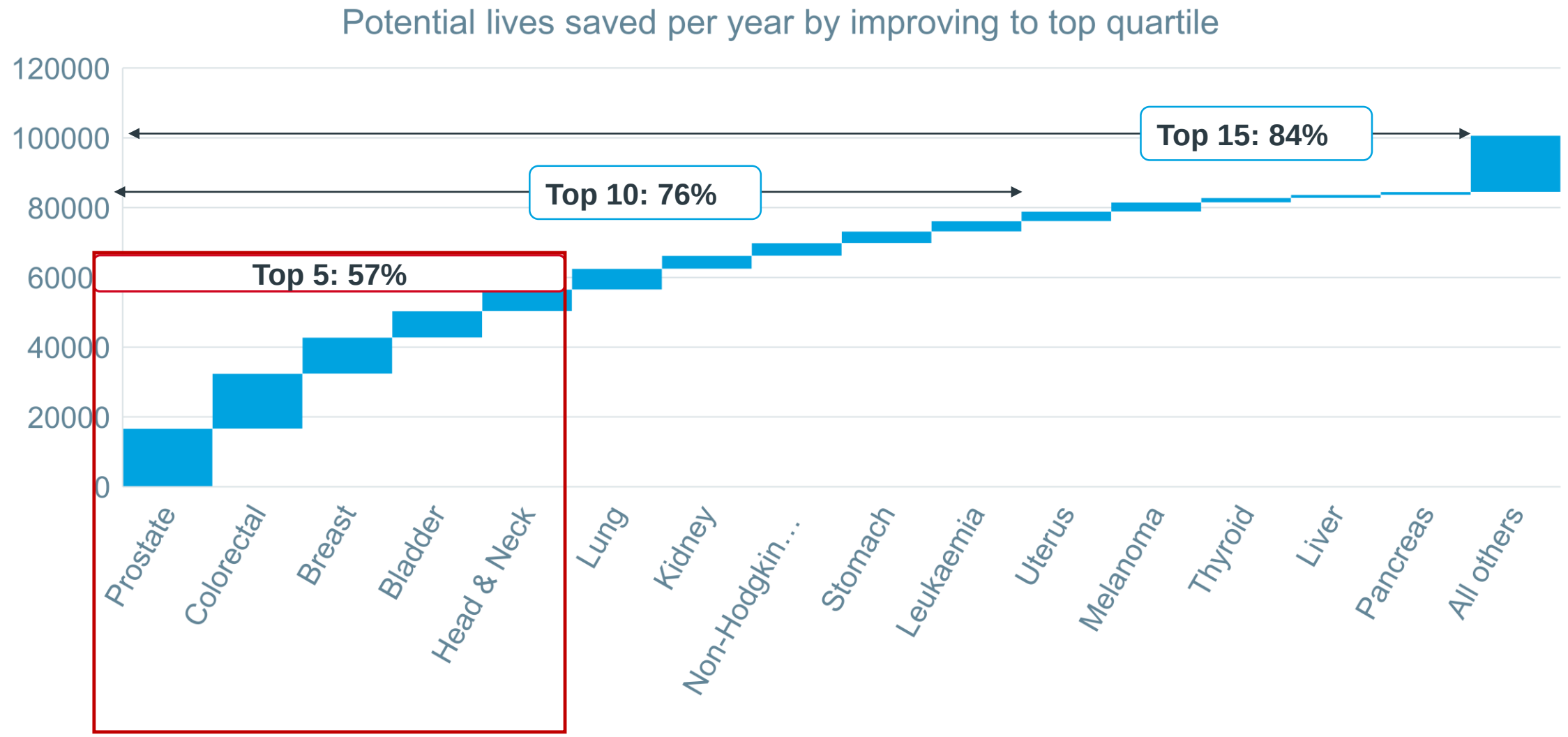
• Given you context to the working groups	Piers	10 minutes
• Share example pilot Cancer OMOP study concepts	Piers / Aslaug / Cedric	15 minutes
• Propose how we set up working groups	Adriana	15 minutes
• Discuss next steps	all	15 minutes

From the epidemiological registries we can measure the potential lives lost due to variation in care quality across Europe



Source: EUROCARE-5 5-year survival by tumor and country based on 2000-2007

Perhaps 100,000 lives p.a. could be saved by getting all of Europe to top quartile today, with 57% of this concentrated in 5 cancers



Source: EUROCARE-5 5-year survival by tumor and country based on 2000-2007, IARC Cancer incidence by site and country and projections 2020

IQVIA INSTITUTE

Theoretically, the technology we are putting into DIGICORE hospitals could study any cancer, but the researchers / questions are more cancer specific

Digital Research infrastructure
(the digital microscope)

- Covers **all cancers** treated in a cancer centre
- Integrates **multi-modal** treatment and outcome data
- **Easy to extend** to co-morbidities (e.g. cardiotoxicity)
- **Engineered for high quality, reusable data** with appropriate **privacy controls** (makes research easier)

Digital Researcher Community
(the social research network)

- Tends to be **cancer specific** (e.g. a lung specialist)
- Often focused on a **specific treatment modality** (e.g. radiotherapy or surgery)
- Need to **work in teams** to bring **multi-disciplinary, multi-centre consortia** together to answer **joint research questions**

Where are we in mobilising these cancer specific working groups?

Cancer	WG volunteers		IDEAL4RWE trainees*		Protocol status on first studies
	# centres	*# people*	*# centres*	*# people*	
Breast	13	14	8	9	IDEAL4RWE: Data analysed DINASTY-OMOP: ethics approved
Prostate / Urology	6	10	8	10	IDEAL4RWE: Data analysed
Lung	14	16	3	3	DINASTY-OMOP: data in prep
Colorectal	6	8	2	2	IDEAL4RWE: protocol designed
Head & neck	6	10	5	5	IDEAL4RWE: poster at ESMO ‘23
Upper GI	6	7	-	-	
Melanoma	-	-	4	4	
OBGYN (not breast)	6	7	-	-	ORWIC: papers published DINASTY-OMOP: protocol at ethics
Haem	7	9	-	-	

*Clinical specialties of individuals, not necessarily projects completed

DigiCore

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As we automate study delivery, we will need to run a pilot study to validate the methods and data in every cancer

THE 'MANUAL' STUDY WORLD TODAY

PILOT OMOP-NLP STUDIES

DIGICORE's FUTURE…

Traditional eCRF outcomes study	Semi-automated outcomes study	Automated a Cancer outcomes study
• Manual retype post consent into central eCRF • Centralised data = trial like statistical methods possible	• Protocol specific Ccmmon data models* • Direct extraction from EHR + manual abstraction free text • Meta-analysis	• Network wide studies in cancer OMOP • Data "ready" before protocol in RDR • Use both ETL and NLP Federated to allow detailed insights
• *Post-approval safety studies* • *Traditional clinical registry (etype)*	• *ORWIC (ovarian)* • *IDEAL4RWE*	• *DINASTY: Disease natural history and outcomes with care quality assessment*

- Patterns / cost of care
- Care quality benchmarking
- Comparative effectiveness
- Patient finding
- Trial planning analytics
- Long term safety
- Digital pragmatic trial
- Biomarker validation
- Discovery -omics

Key: Future users

- HTA / health systems / Gov
- Trialist and regulatory
- Diagnostics / discovery

These are the OMOP studies under development

	Pan cancer	mNSCLC	mBC	EOC
PI	Elin Hallan Naderi, Oslo University Hospital, Norway	Åslaug Helland, Oslo University Hospital, Norway	Cédric van Marcke, Cliniques Universitaires Saint-Luc, Belgium	Geoff Hall, Leeds Teaching Hospital NHS Trust, UK
Title	Impact of COVID-19 on cancer care in European centres based on number of new diagnoses and 12-month survival	A disease natural history and outcomes study with care quality assessment (DINASTY) in patients with metastatic NSCLC	DINASTY in patients with HR positive HER2 negative metastatic breast cancer	DINASTY in patients with epithelial ovarian cancer
# centres committed	5	5	4	4
Estimated cohort size	124,000	9,500	3,000	1,500
# EC approvals	5	2	*Not yet submitted*	*Not yet submitted*
Contact point	Project Manager: Rosie McDonald, IQVIA, rosie.mcdonald@iqvia.com			

Cancer specific pilot studies are using an innovative guideline compliance research on large cohorts concept called DINASTY using Cancer OMOP

DINASTY: **DI**sease **NA**tural Hi**ST**ory with care qualit**Y** assessment
(mNSCLC quality assessment example)

Diagnosis	cfDNA liquid biopsy for all patients	**1st Tx**	Proximity of 1st line Tx to Dx
	Pts with a negative cfDNA blood test have a tissue biopsy		Pts with driver mutation: 1st line Tx ESMO-guideline recommended based on the test result
	IHC for subtyping of NSCLC		
Testing	Proportion tested for PD-L1 and proximity to Dx. Repeat for..		Squamous-cell carcinoma patients, 1st line chemo immune checkpoint inhibitors in line with ESMO recommendations
	EGFR		
	ALK		
	ALK	**Later add..**	2nd and subsequent Tx lines are ESMO-guideline recommended
	ROS1		
	KRAS		Frequency of scheduled appointments
	etc		

Why is it a good place to start?

- **Focus on care quality assessment** – appropriate to get ethics without study specific consent (like clinical audit)
- **Establishes interoperability** - solves many of our data issues (and measures data quality)
- **Covers all treatment & diagnostic modalities** (at low resolution)
- **Enabler of future research -** Builds large cohorts for future in-depth research questions

Summary of disease natural history and outcomes study with care quality assessment (DINASTY) in metastatic NSCLC

Cohorts

Diagnosed with metastatic NSCLC between 1st November 2018 – 30th November 2023

Subgroups

- Patients with metastases at index date (metastatic NSCLC diagnosis) in each of the following locations: brain, liver, adrenal gland, bone, lung, other single site, multiple sites of metastases
- Patients prescribed immunotherapies as 1st LoT for metastatic NSCLC

Research Objectives (abbreviated)

Primary Objective: Describe the demographic and clinical characteristics, molecular and genetic phenotype, re-biopsy rates, and treatment received for NSCLC in the 5 years prior to index date.

Secondary Objectives:

- Describe treatment patterns by 1st and 2nd LoT
- Assess OS and TtNT by 1st and 2nd LoT including adjustment for prognostic characteristics
- Describe duration of treatment, drug dose and frequency, BMI (and so dose intensity) by age and gender in patients prescribed immunotherapies as 1st LoT
- Benchmark care quality between the centres using ESMO guidelines

Highlights: Subgroups defined by location of metastases = many subgroups; Limits to treatments in 1st LoT and 2nd LoT; focus on immunotherapies as 1st LoT and on dose intensity of immunotherapies

Summary of DINASTY in HR positive/HER2 negative metastatic breast cancer

Cohorts

Diagnosed with HR+/ HER2− mBC between 1st November 2018 – 30th November 2023

Subgroups

- De novo mBC
- Recurrence after locoregional disease
- Within and across these cohorts, further compare HER2-low and HER2-zero

Research Objectives (abbreviated)

Primary Objective: Describe proportion of patients re-biopsied at index date and concordance between phenotype at locoregional disease and at metastatic disease (ER, PR and HER2).

Secondary Objectives:

- Describe the demographic, clinical characteristics, molecular phenotype, somatic and germline NGS testing.
- Compare known menopausal status to proxies of menopausal status (such as anti-cancer treatment or age) thereby evaluating the accuracy of these proxies.
- Benchmark care quality between the centres using EUSOMA guidelines.

Highlights: Reduced focus on Tx (exploratory objectives), instead focus on re-biopsies and accuracy of menopause data; subgroups defined by stage at initial BC diagnosis and by HER2 levels

Summary of DINASTY in epithelial ovarian cancer

Cohorts

Diagnosed with EOC between 1st January 2019 – 30th November 2023

Subgroups

- Patients prescribed PARPi

Research Objectives (abbreviated)

Primary Objective: Describe the demographic, clinical characteristics (including tumour stage, morphology, grade, presence of other cancers), molecular and genetic phenotype

Secondary Objectives:

- Describe non-surgical treatment patterns by LoT
- Describe surgical treatment patterns including the use of exploratory/diagnostic laparoscopy, the timing and extent of 'debulking' surgery including lymphadenectomy, bowel resection and stoma formation or primary anastomosis
- Assess OS and TtNT by LoT including adjustment for prognostic characteristics
- Benchmark care quality between the centres using NCCN guidelines

Highlights: Focus on surgery and outcomes of surgery; Does not restrict to a particular stage therefore more heterogeneous cohort and Tx; All Tx included and don't restrict LoT groupings

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We have modelled the process to set-up the working groups on the success of World Sarcoma Network

World Sarcoma Network Magic Recipe

1. Find a small group of passionate researchers with similar interests (RWE methods, cancer type)
2. Help them connect, organise and get set-up
3. They meet informally at the main congresses to plan research together
4. Together, they hunt grant funding – with rules for fair division of reward

This is the proposed process to connect researches and get them set-up

Nov 2023: Madrid

- Propose process
- Finalise mailing lists / volunteers

Early Q1 24: Cancer WG introductory kick-off

- *Peer to peer introductions*
- *Share protocols if they exists, clarify "rules"*
- *Agree which conferences to meet at*

This is the proposed process to connect researches and get them set-up

Jan 24: Virtual Science symposium

- 90 minute showcase on existing studies
- Explain process & invite participation

By Easter: informal in-person events at conferences

- Informal peer-to-peer meetings in person at disease
- Specific conferences like ESMO breast, ELCC

This is the proposed process to connect researches and get them set-up

Q2 24: Working groups elect co-chairs, plan

- Co-chairs elected to coordinate that WG
- Meeting frequency agreed
- 2024 objectives discussed

WGs self-organise
(under their co-chairs)

Nov 24: Working groups report on progress
(at Connect to win 2024)

- We suggest every WG prepares a position paper on their research plan, potentially for publication

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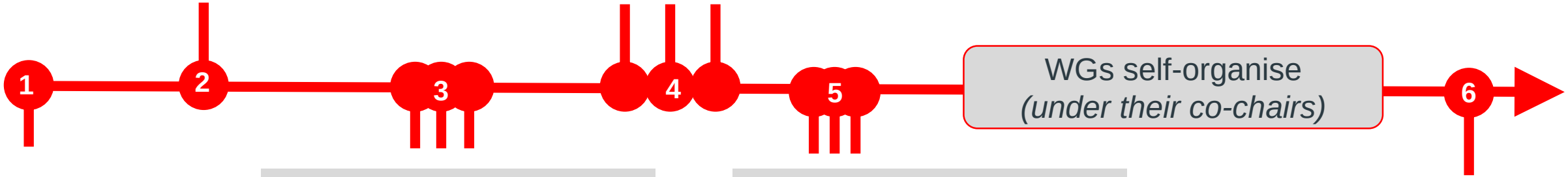
Jan 24: Virtual Science symposium
90 minute showcase on existing studies
Explain process & invite participation

By Easter: informal in-person events at conferences
Informal peer-to-peer meetings in person at disease specific conferences like ESMO breast, ELCC



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Nov 24: Working groups report on progress (at Connect to win 2024)

We suggest every WG prepares a position paper on their research plan, potentially for publication

Key: All cancer events | Cancer specific events (virtual unless stated otherwise)

Proposed dates for cancer specific working groups (for discussion)

Virtual science symposium

- **Friday 19 January 1500-1700 CET**

Cancer	Cancer WG introductory kick-off (on Thursdays)	Possible conference meet-up options in Q1/2	Working groups elect their co-chairs
Breast	February 1st	ESMO breast 15-17 May	March 8th
Prostate / Urology	February 8th	EAU 5-8 April (PIONEER)	March 15th
Lung	February 1st	ELCC 21-24 Feb ESMO lung 20- 23 March	March 8th
Colorectal	February 8th	ECC spring 14-17 April	March 15th
Head & neck	February 1st	ICHNO 21-23 March	March 8th
Upper GI	February 15th	ESMO upper GI 26-29 June	April 9th
Melanoma	February 15th	EADO 4-6 April	April 9th
OBGYN (not breast)	February 8th	ESGRO 7-10 March	March 15th
Haem	February 15th	EHA 13-16 June	March 15th

Possible future non-pathology working groups could be created if there is sufficient interest from cancer centers across DIGICORE

- Radiotherapy
- Cardiotoxicity
- Gender & outcomes
- Geriatric outcomes / formularies
- Biomarker validation / new test validation
- Descaltion / dose optimisation in chemo
- Digital pragmatic trials methods

What are the benefits of joining or leading a cancer working group?

NOW

- **Unique research opportunities:** only European *"cancer x digital outcome research"* community
- **~20 hospitals (and more) with right technology investment**: Federated cancer OMOP + NLP
- **Training programmes + competitive seed funding:** get proof of concept for future grants
- **Potential future commercial studies or academic grants:** funding for research
- **Digital infrastructure & some administrative support:** mailing lists, newsletters, meeting schedulin

FUTURE

- **Access to IQVIA support for proven teams:** project mgmt., medical writers, bid support
- **Expanding technology capabilities:** somatic data, chemo / surgery / radio, PROMs etc

Proposed DIGICORE working group rules (to optimize scientific production)

- **Every working group is led by 2 co-chairs** who set the DIGICORE agenda in that cancer
- **Co-chairs must be from cancer centres in different countries** and only from DIGICORE members or associate member. We **strongly** recommend 1 senior, 1 early career
- **Democratically elected by DIGICORE cancer centres** (either members or associate members)
  - 1 vote per legal entity in the working group (*not per individual)*
- **Co-chairs set the research strategy for their WG and meeting frequency**, in consultation with their member. If there is disagreement (e.g. priorities), we operate democratically
- **Co-chairs re-elected annually and must report on progress to Board 1x a year** (there will be an "co-chair council" to share best practice between working groups)
- **Working groups must operate within the legal statutes of DIGICORE**, especially on respecting institutional research autonomy (no one forced to do a study)
- **Non-members of DIGICORE only have observer status** (can't vote or propose studies)

Proposed next steps

By Cancer Centre leadership

- Brief your research community: this is coming
- Check if others want to join (now you know more)
- Promote the virtual kick-off events
- Promote the training programmes

By DIGICORE

- Set-up cancer specific mailing lists (make peer to peer connection easy)
- Schedule and advertise virtual kick-off events
- Where possible, find some speakers on RWE “in that cancer type” for the kick-off events

Thank you!

Discussion topics on the way

End Section One: Context

- How do we **balance cancer specific research and "cross-cutting" research themes** like, precision medicine, gender or toxicity research?
- How can DIGICORE **support member cancer centres to mobilize the right researchers**?

End Section Two: Initial Studies

- How do we get people engaged and trained in these new digital research methods / protocols?

End Section Three: Setting-up Working Groups

- Do we think **this set-up process could work**? Any improvements / suggestions?
- How should we **work with / build links to other clinical informatics initiatives** like HDR-UK, German Informatics Initiative or Million European Genomes or OHDSI?