CZECRIN
CZECH CLINICAL RESEARCH INFRASTRUCTURE NETWORK

MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY

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ecrin

Challenges of new clinical trial designs

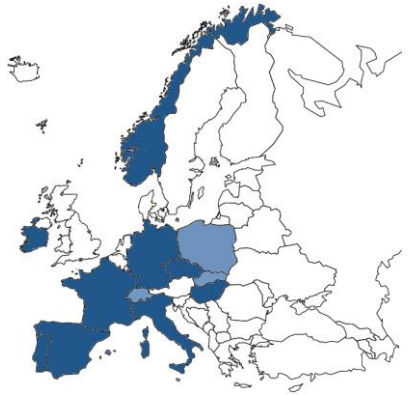
Jacques Demotes

Brno, June 9th 2022

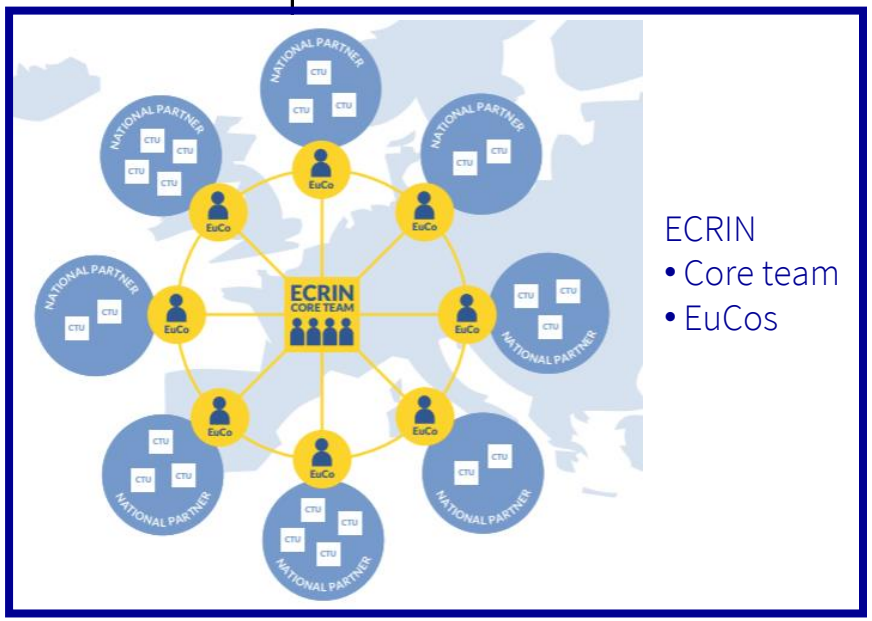
ECRIN, a distributed infrastructure supporting multinational clinical research in Europe

1. support **multinational trials** in Europe (SME-sponsored and investigator-initiated trials) through services to **trial management** tasks : regulatory, ethics, monitoring, vigilance, data management

2. develop tools for multinational trials (ethical / regulatory database, data centre certification, data sharing tools, personalised medicine, platform trials)



CZECRIN Czech Clinical Research Infrastructure Network
F.CRIN French Clinical Research Infrastructure Network
HECRIN Hungarian-European Clinical Research Infrastructure Network
KKS Netzwerk Koordinierungszentren für Klinische Studien
ItaCRIN Italian Clinical Research Infrastructure Network
Health Research Board NCTO National Clinical Trials Office
PtCRIN Portuguese Clinical Research Infrastructure Network
SLOVACRIN Slovak Clinical Research Infrastructure Network
NorCRIN Norwegian Clinical Research Infrastructures Network
SCReN Spanish Clinical Research Network
swiss clinical trial organisation
POLCRIN Polish Clinical Research Infrastructure Network



ECRIN
- Core team
- EuCos

ESFRI Projects Landmarks ROADMAP 2016
évaluation et qualité Hcéres
afaq ISO 9001 Qualité AFNOR CERTIFICATION

Lessons learned from COVID-19 Crisis

- Multinational trials
- Platform trials
- Repurposing
- Pragmatic trials
- Preparedness
- Fast-track approval
- Coordination
- Prioritization
- Funding

Clinical Pharmacology & Therapeutics

REVIEW | Open Access

Clinical trials for Covid-19: can we better use the short window of opportunity?

Hans-Georg Eichler, Marco Cavaleri, Harald Enzmann, Francesca Scotti, Bruno Sepodes, Fergus Sweeney, Spiros Vamvakas, Guido Rasi

First published:14 May 2020 | https://doi.org/10.1002/cpt.1891

What have we learned from the therapeutics RCTs?

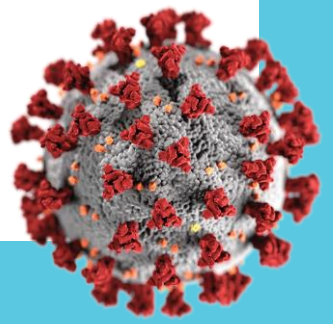
A worldwide effort to conduct RCTs. BUT, coordination and size not optimal

Studies registered	1178
Completed	15
Recruiting	644
Not recruiting	515
Suspended	2
Terminated	2

Sample sizes (ranging from 30 – 10000) and endpoints

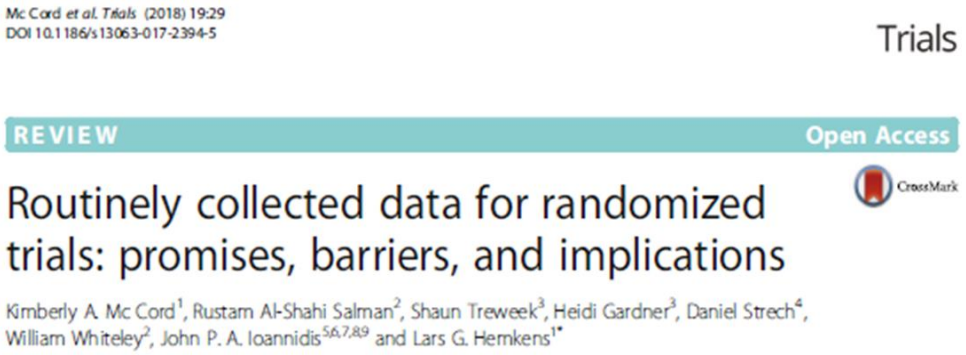
https://www.covid-nma.com/dataviz/

Both researchers and regulators must reflect on the need for large collaborative RCTS



Digital revolution in clinical research

- High throughput –omics data generation
- Multi-modal data management
- Artificial intelligence stratification
- Secondary use of EHRs



Mc Cord et al. Trials (2018) 19:29
DOI 10.1186/s13063-017-2394-5

Trials

REVIEW Open Access

Routinely collected data for randomized trials: promises, barriers, and implications

Kimberly A. Mc Cord[1], Rustam Al-Shahi Salman[2], Shaun Treweek[3], Heidi Gardner[3], Daniel Strech[4], William Whiteley[2], John P. A. Ioannidis[5,6,7,8,9] and Lars G. Hemkens[1*]

EUROPEAN COMMISSION

Strasbourg, 3.5.2022
COM(2022) 196 final

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

A European Health Data Space: harnessing the power of health data for people, patients and innovation

New frontiers in clinical research

- Platform trials
- Trials within cohorts
- Personalised medicine research

Platform trials

- are infrastructures
- testing multiple treatments
- master protocol, and amendment for new arms / domains
- shared control arm ?

- save time
- (save patients)
- contain costs
- allow multiple comparisons

REMAP-CAP

EU RESPONSE

ECRAID

VACCELERATE

EU-PEARL
EU PATIENT-CENTRIC CLINICAL TRIAL PLATFORMS

REVIEW ARTICLE

THE CHANGING FACE OF CLINICAL TRIALS

Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., and Janet Woodcock, M.D., *Editors*

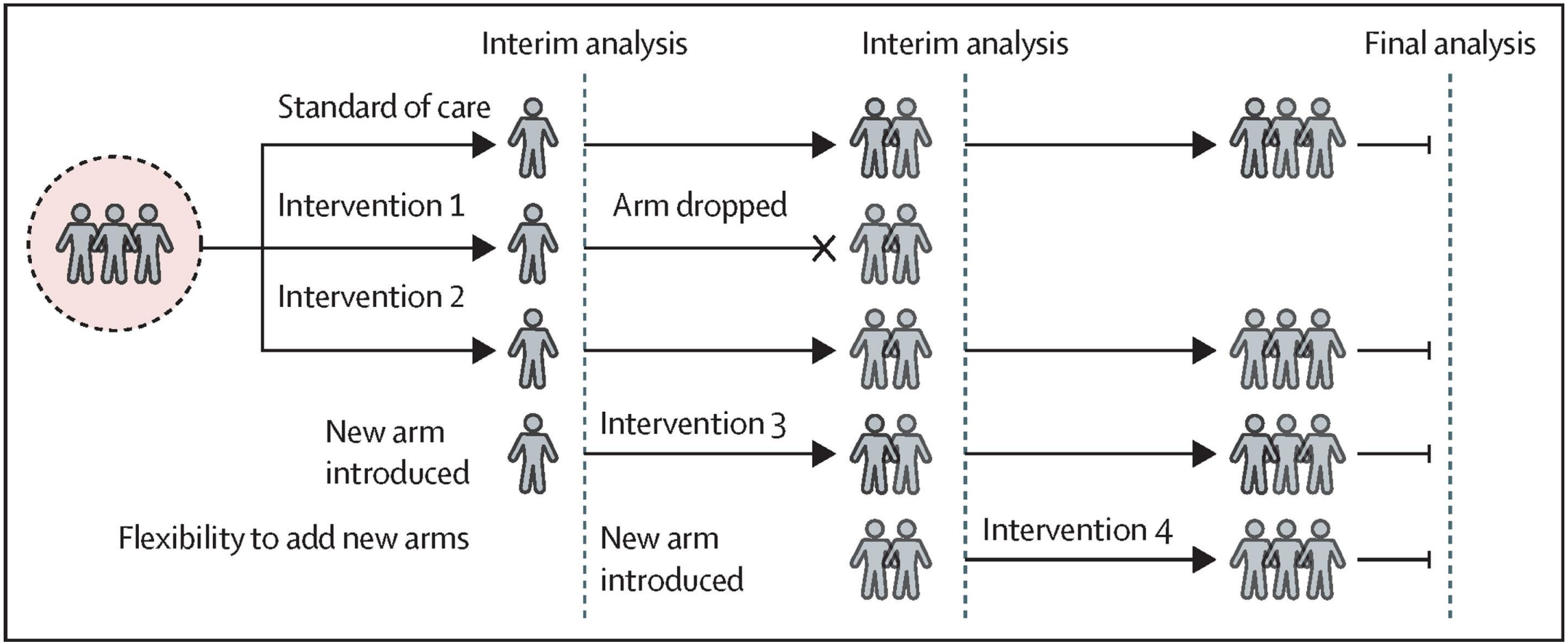
Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both

Janet Woodcock, M.D., and Lisa M. LaVange, Ph.D.

Table 1. Types of Master Protocols.

Type of Trial	Objective
Umbrella	To study multiple targeted therapies in the context of a single disease
Basket	To study a single targeted therapy in the context of multiple diseases or disease subtypes
Platform	To study multiple targeted therapies in the context of a single disease in a perpetual manner, with therapies allowed to enter or leave the platform on the basis of a decision algorithm

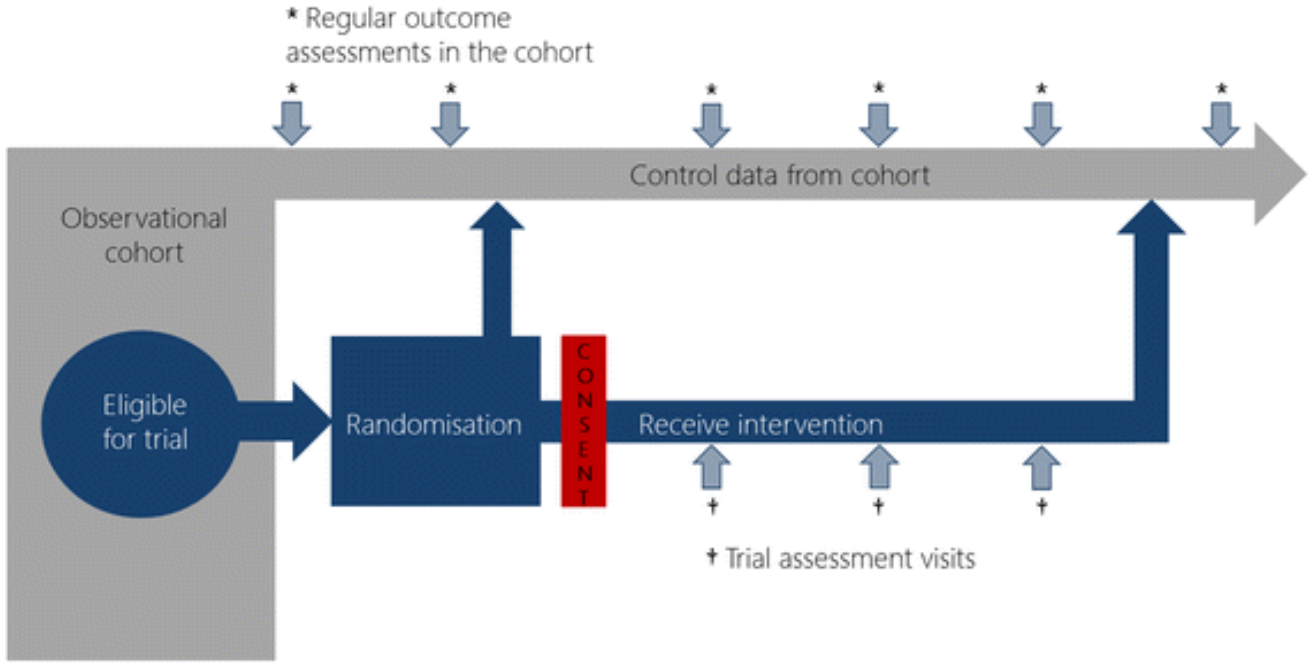
Platform trial



Considerations for using the ‘Trials within Cohorts’ design in a clinical trial of an investigational medicinal product.

Anna C. Bibby, et al. Trials. 2018;19:18

Schematic representation of the TwiC design



Secondary use of EHRs

- Interoperability of data standards ?
  - OMOP, CDISC
- Under EHDS Regulation (2023 ?)
  - HealthData@EU infrastructure
    - Federation of national health data hubs
- Under GDPR
  - Data reused in a protected environment
  - Unless anonymised
    - Risk of reidentification ?
    - Attempts to re-identify prohibited by law

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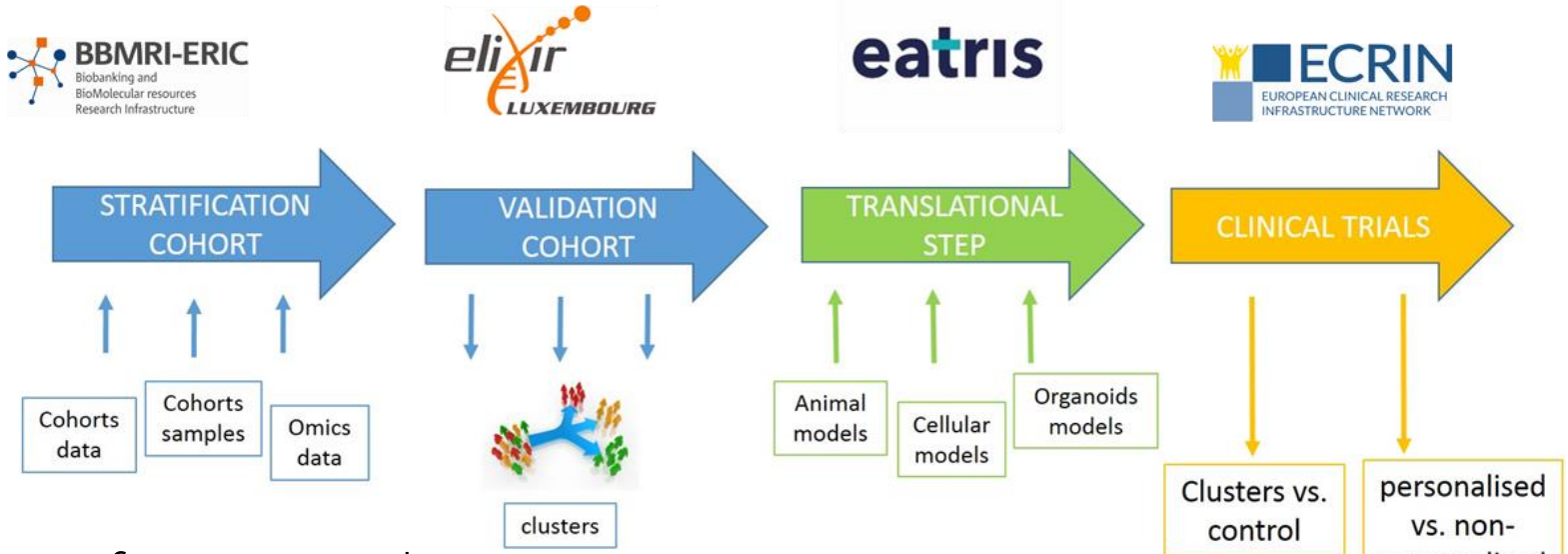
PERMIT : methodological standards for personalised medicine pipeline

PERMIT
PERsonalised MedicIne Trials

https://permit-eu.org/



- Stratification cohorts
- Stratification methods / algorithms
- Preclinical stratified models
- Personalised medicine trials

PERMIT
PERsonalised MedicIne Trials

- Review of methods
- Methodological recommendations
- Regulatory ecosystem
- Training material

Journal of *Personalized Medicine*
MDPI

Review

Methods for Stratification and Validation Cohorts: A Scoping Review

Teresa Torres Moral [1,2,3], Albert Sanchez-Niubo [1,4,5,*], Anna Monistrol-Mula [1], Chiara Gerardi [6], Rita Banzi [6], Paula Garcia [7], Jacques Demotes-Mainard [7], Josep Maria Haro [1,4] and the PERMIT Group

Open access Original research

BMJ Open

Biomarker discovery studies for patient stratification using machine learning analysis of omics data: a scoping review

Enrico Glaab [1], Armin Rauschenberger [1], Rita Banzi [2], Chiara Gerardi [2], Paula Garcia,[3] Jacques Demotes [3]

Open access Original research

BMJ Open

Study designs for clinical trials applied to personalised medicine: a scoping review

Cecilia Superchi [1], Florie Brion Bouvier [1], Chiara Gerardi [2], Montserrat Carmona [3,4] Lorena San Miguel [5], Luis María Sánchez-Gómez [3,4] Iñaki Imaz-Iglesia [3,4] Paula Garcia,[6] Jacques Demotes [6], Rita Banzi [2], Raphaël Porcher [1], the PERMIT Group

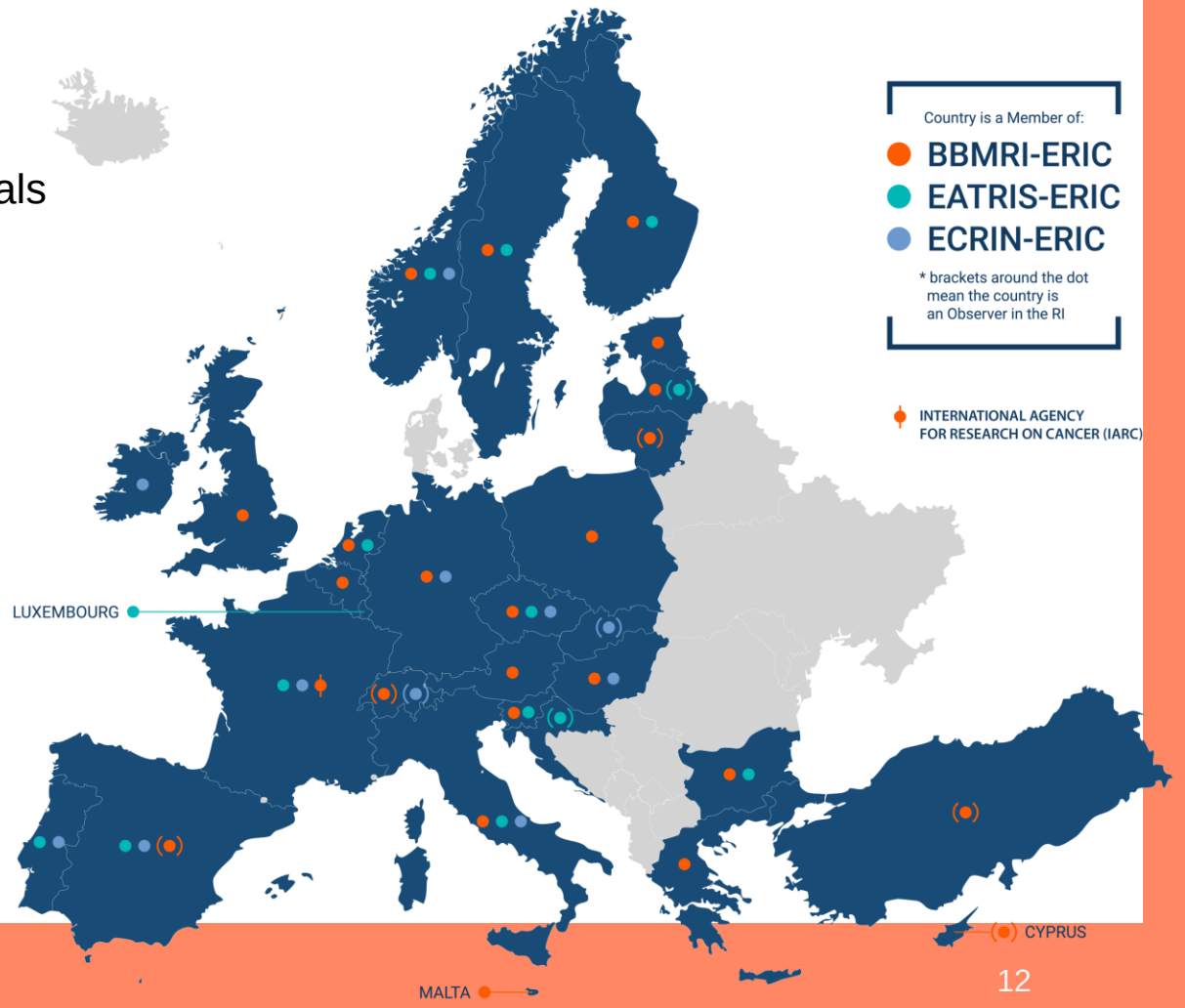
THE EUROPEAN ALLIANCE OF MEDICAL RESEARCH INFRASTRUCTURES – www.eu-amri.org

Who we are

- Over 700+ research institutions and university hospitals
- EU-AMRI members started operations in 2014
- **29 European Countries** as Members or Observers

3 areas of focus

- Biobanking & Biomolecular Resources
- Translational research
- Multinational clinical trials



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