Platform trials in a confirmatory regulatory setting – generating thoughts and directions

Wolfgang Jacquet
Benjamin Hofner

18 September 2023

Disclaimer

- What follows is not the position of the FAGG –AFMPS the PEI nor the EMA.
- It is solely intended as a basis for reflection on ethics, clinical trials and decisions.

Causality

Causality

Probability Experiment

Randomized Clinical Trials (RCT's) with an ***internal concurrent control*** arm are considered the standard in trial design where ***appropriate and feasible***.

Clinical trials: Two aims!!!

Robust **decision making** and **precise estimation**

- Complex Designs
- Artificial Intelligence (AI)
- Real World Data (RWD)

How to move forward?

Two aims!!!

Robust **decision making** and **precise estimation**

- ICH E9
- CTR
- …

Clinical Trial?

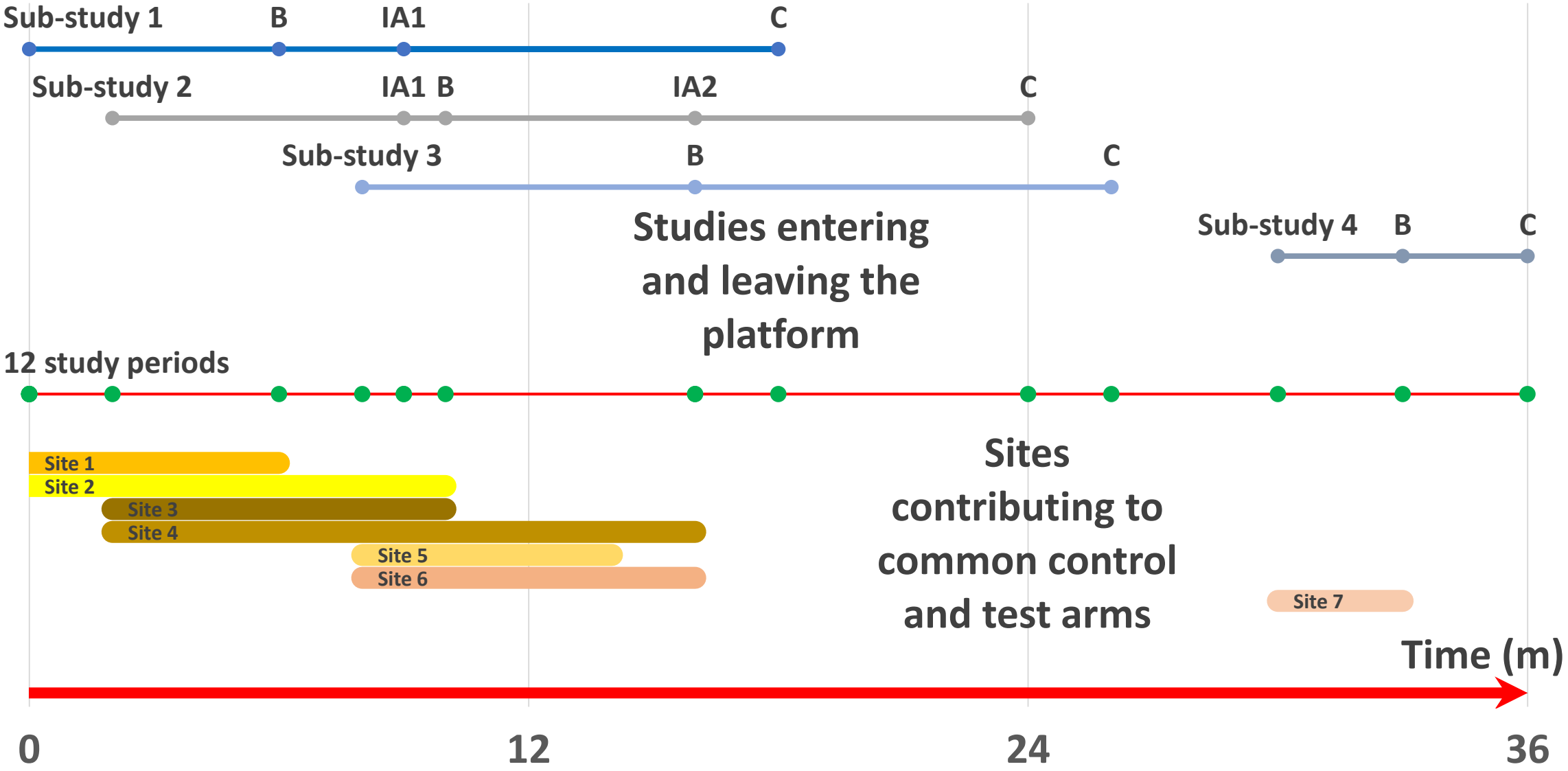
What is a complex (clinical) trial?

- CTR -> Clinical Trial
- Complex trial???
- Platform trial???

Why the Covid-19 experience is not a good reference - template for confirmatory platform trial design

Platform Trials

A platform example



Platform Trial – Some Examples From Practice Set the Stage

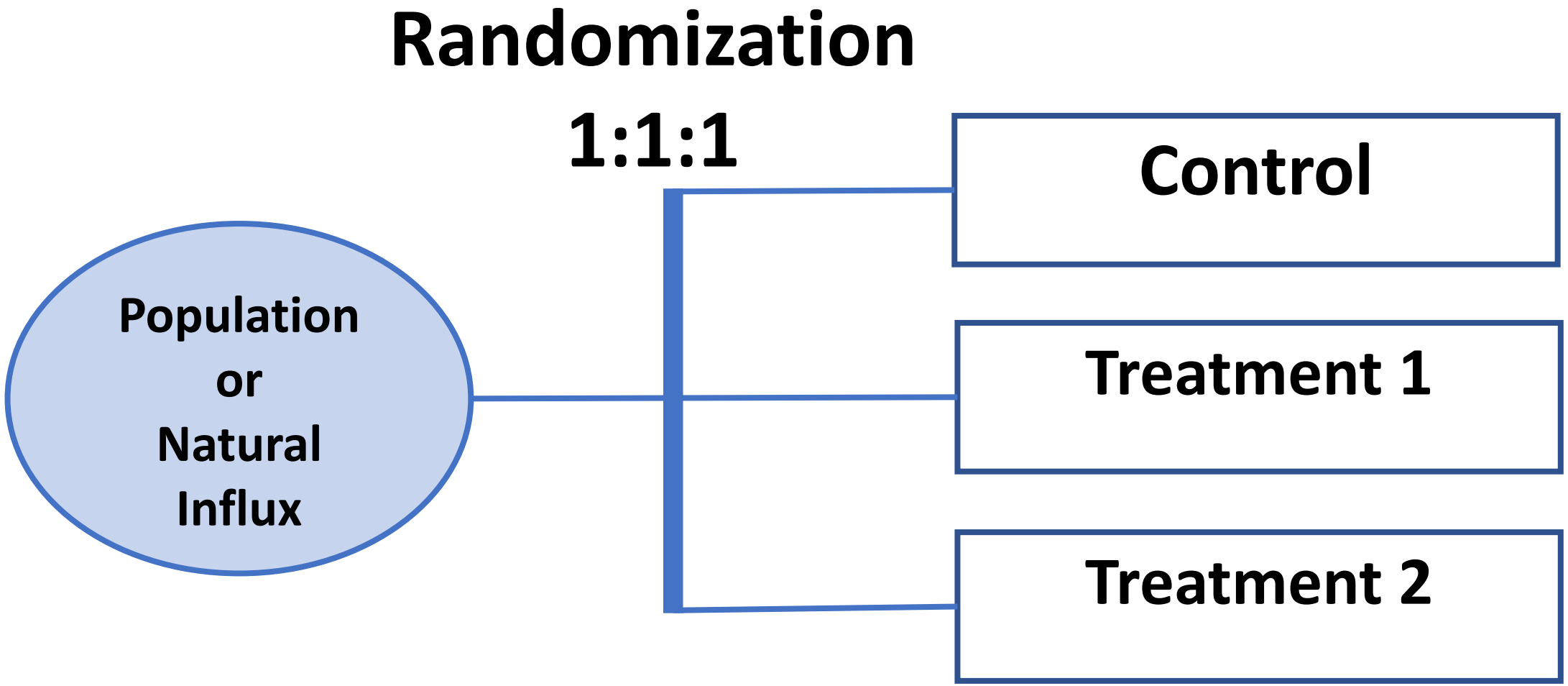
Independence.

Independence?

Independence!

« Reculer pour mieux sauter »

One indication – a proposed trial

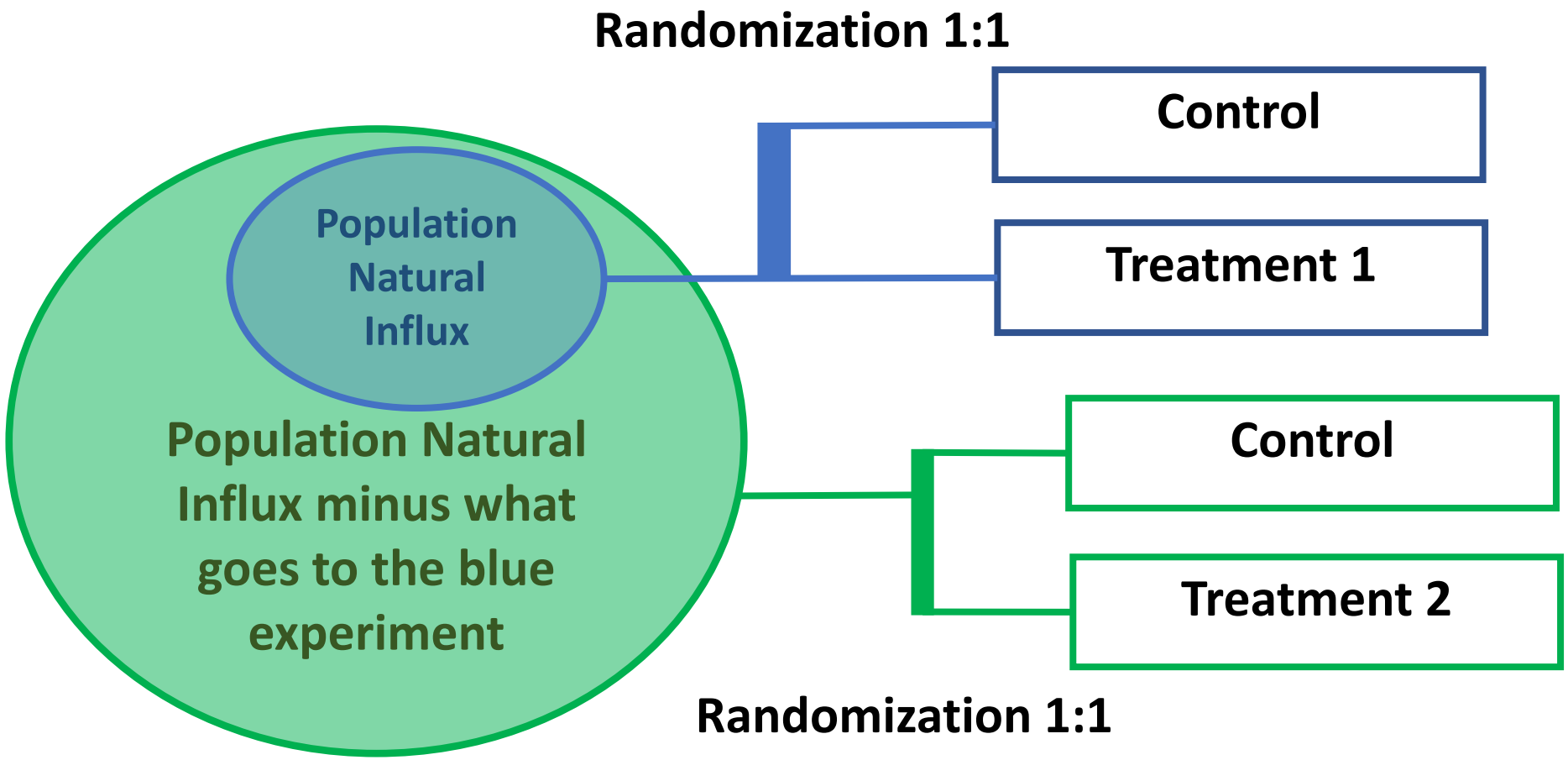


The Type I_r is controlled at $\alpha_r = 0.05$

Are there remaining problems?

Dependency a problem?

Subpopulation – a proposed trial



Probabilistic Independence.

Independent modes of action.

Different sponsors.

Bias - Corrections

How linear can a human be!

Adapted decision making?
Pragmatic platform trials?

Data scientists

- Bio-statisticians
- Data scientist
- AI community

Are all data scientists.

EU-PEARL

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What is EU-PEARL?

NB:
Funding for EU-PEARL ended in April 2023

EU-PEARL is an IMI funded public-private partnership
and a strategic alliance between the public and private sectors to:

by developing a common framework for platform clinical trials and integrated research platforms (IRPs)

Who was involved?

EUROPEAN UNIVERSITY HOSPITAL ALLIANCE (EUHA) HOSPITALS

Vall d'Hebron Institut de Recerca
Vall d'Hebron
Erasmus MC
Assistance Publique Hôpitaux de Paris
UniSR Università Vita-Salute San Raffaele
Medizinische Universität Wien
King's College London
KU Leuven
Charité Universitätsmedizin Berlin

OTHER HOSPITALS

LMU Klinikum der Universität München

UNIVERSITIES

University of Oxford
Manchester 1824 The University of Manchester
Università degli Studi di Milano
Newcastle University
Tartu Ülikool 1632 Universitas Tartuensis

PATIENT ORGANISATION

EPF European Patients Forum

DATA, STATISTICS

The European Institute For Innovation Through Health Data
Berry Consultants Statistical Innovation
CUSTODIX

REGULATORY / HTA

Paul-Ehrlich-Institut
euroscan

PROJECT MANAGEMENT

teamit Research

EUROPEAN RESEARCH INFRASTRUCTURES

eatris
ECRIN European Clinical Research Infrastructure Network

BIOPHARMACEUTICAL COMPANIES / EFPIA / ASSOCIATED PARTNERS

AstraZeneca
Novartis
Janssen Johnson & Johnson
Allergan
novo nordisk
Otsuka
teva
Sanofi
Pfizer
TB Alliance Global Alliance for TB Drug Development
SpringWorks Therapeutics
Children's Tumor Foundation Ending NF Through Research
Servier

EU-PEARL's structure

DISEASE-AGNOSTIC WORK PACKAGES

WP1 IRP Governance, Quality, Sustainability	WP2 Scientific, Regulatory and Operational Methodology	WP3 Clinical network and patient level data	WP8 Project Oversight, Project Management and Outreach
	Qualitative Methods and Statistical Design Regulatory Aspects Clinical Operational Best Practices (Master Protocol Template)		

DISEASE-SPECIFIC WORK PACKAGES

WP4 IRP for Major Depressive Disorder (MDD)	WP5 IRP for Tuberculosis (TB)	WP6 IRP for Non-Alcoholic Steatohepatitis (NASH)	WP7 IRP for NeuroFibromatosis (NF)
Define scientific challenges for each disease area Design Master Protocol (disease specific) Establish operational requirements for the implementation of specific IRPs Endorsement of Master Protocols by regulatory and ethics			

NB:
Trials were not executed within EU-PEARL

Further recourses

Generic Tools and Resourc

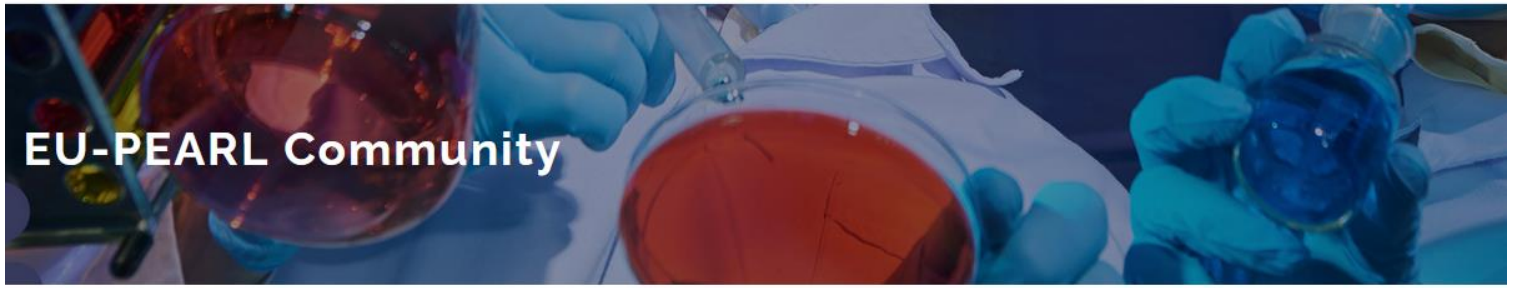
View and employ the innovative and **gener**
methodology and **toolbox** developed by E
collaborative platform trials. Take advantag
real-world data management, protection
guidelines and templates to facilitate the d
this type of trials.

most to patients are embedded in the trial design.

Source: https://eu-pearl.eu

Source: https://eu-pearl.eu/tools/

EU-PEARL community



Be part of the EU-PEARL Community!

Experts and organisations that participated in EU-PEARL have come together in a vibrant community of practice. They have the critical knowledge, services and resources around IRPs to ensure that adaptive platform trials can thrive in future.

Other organisations active in innovative clinical research and interested in advancing platform trials are welcome to become part of the EU-PEARL Community. Please feel in the form below and let us know a little bit more about your interest in EU-PEARL.

Name

Surname

Source: https://eu-pearl.eu/community-of-practice/