

国立大学病院臨床研究推進会議
第12回 第12回総会シンポジウムプログラム
---社会基盤としての臨床試験体制の強化に向けて---

マスタープロトコル試験の現状と課題 －欧州の状況－

European Clinical Research Infrastructure Network

Clinical Scientist/ Project manager

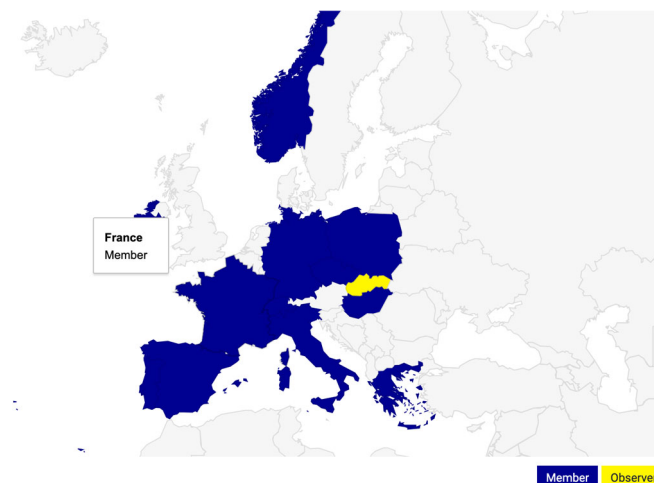
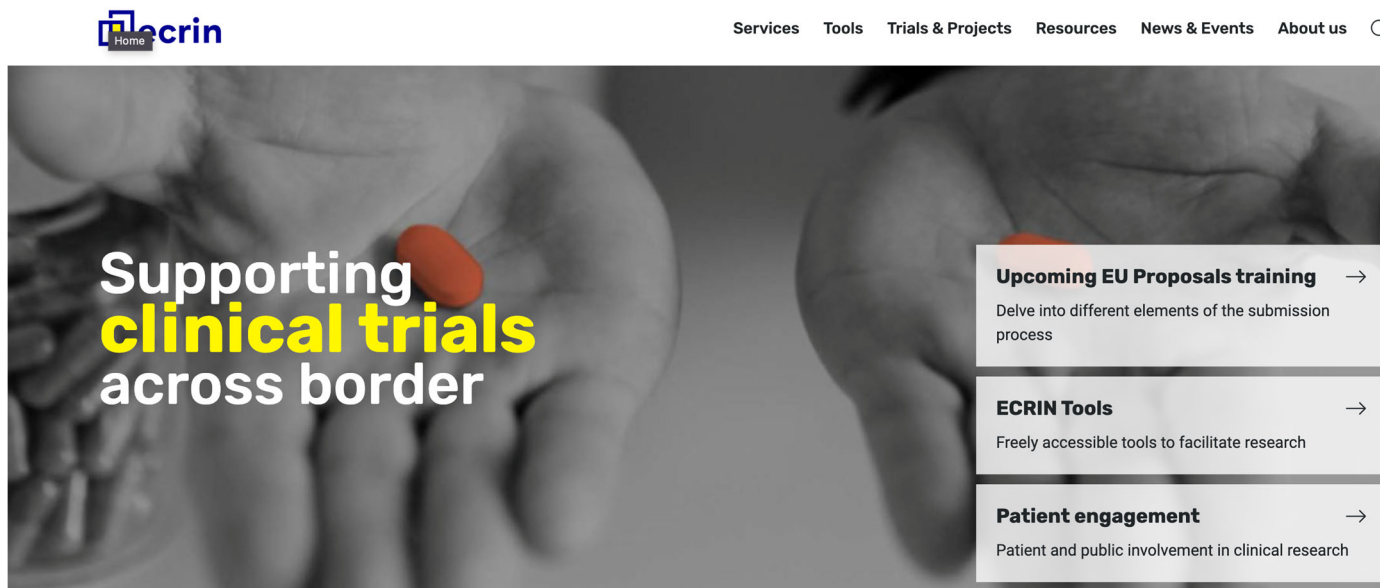
上田恵子

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本発表に関する利益相反はありません。

また、発表内容は個人の見解であり、組織の公式見解ではありません。

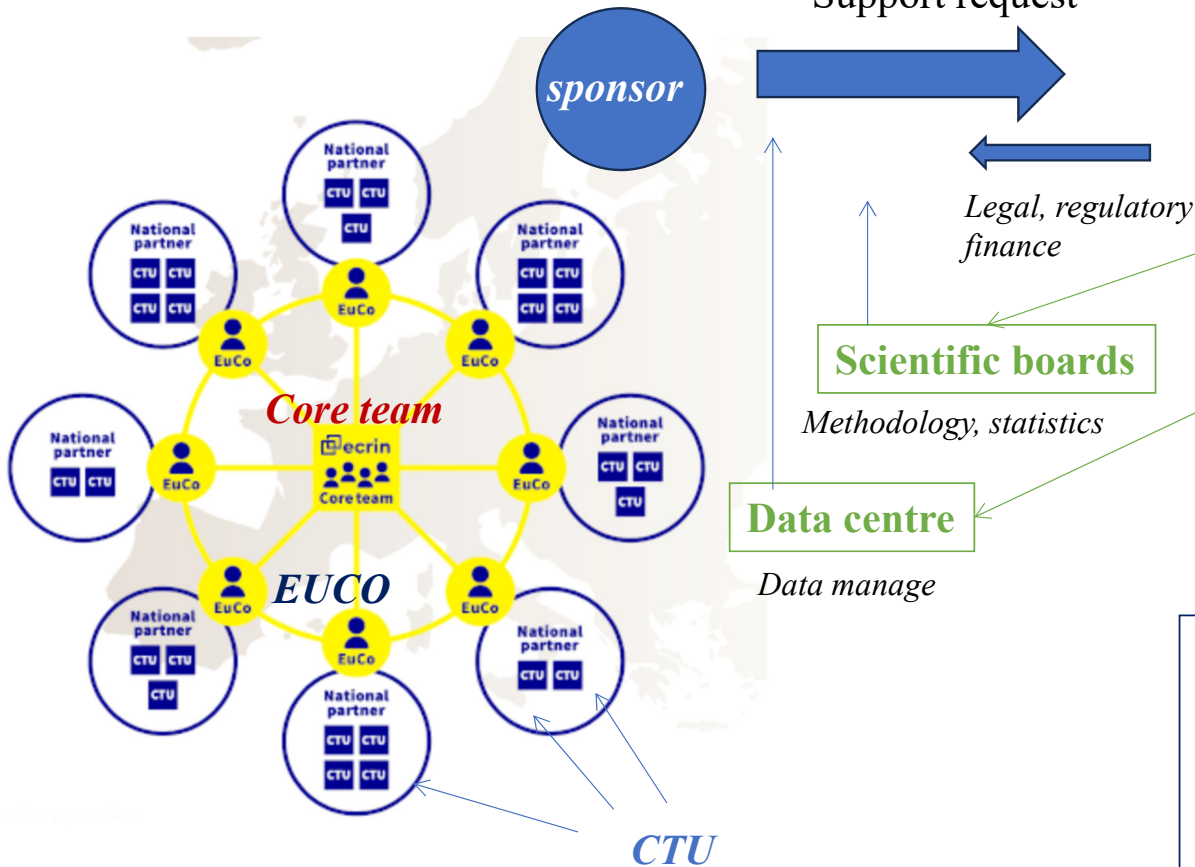
ECRIN (European Clinical Research Infrastructure Network)



- Infrastructure network, European commission legal entity
- EU-funded project for European clinical trial
- Member country+ observer country
- Core team member+ European correspondents (EUCCO)
Single partner (National based network) Contact

■ Member Country 12
■ Observer Country 1
Dec 2023

<https://ecrin.org/>



ECRIN Core team, Paris, France

- Director general 1
- Clinical Operation 4+ EuCo
(Project manager/ Clinical scientist)
- Capacity building 11
(Project manager/ Data scientist)
- Human resources 1
- Communication 3
- Quality 2
- IT 1
- Finance 1
- Legal 1
- Executive assistant 2

- EUCO representatives of each country 18**
- Coordinator of national clinical trial unit (CTU)
- CTU**
- Local project manager
 - Clinical research associate
 - Pharmacovigllance

COVID: Lessons- Learned in EU/EEA

Preparedness for health emergency, 2003-

Pandemic declaration, Mar 2020

ECDC/ EMA (task force)/ EC, Health Emergency Preparedness and Response Authority (HERA)

The guidance on the management of clinical trial during COVID-19 pandemic



WHO Solidarity- master protocol

EMA workshop, June 2023; Lessons –learned from COVID

- 18000以上の臨床試験が登録したが、90%が失敗
 - * 成功の定義 = 完遂し、医療現場にエビデンスをもたらしたものの
- 10%の成功した臨床試験は大規模 **Platform試験**であった
- Prioritisation/ Optimizationを強化する必要がある
- Interpandemic coordination; EMA, HERA, ECDC, ECRIN, Patient Eng.
- 資金源の確保、迅速なファンディング

Why multicenter/ global trial?

- WHA 75.8 resolution



World Health
Organization

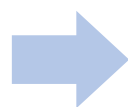
SEVENTY-FIFTH WORLD HEALTH ASSEMBLY
Agenda item 16.2

WHA75.8
27 May 2022

**Strengthening clinical trials¹ to provide high-quality
evidence on health interventions and to improve
research quality and coordination**

Well-designed, Well-implementad clinical trials

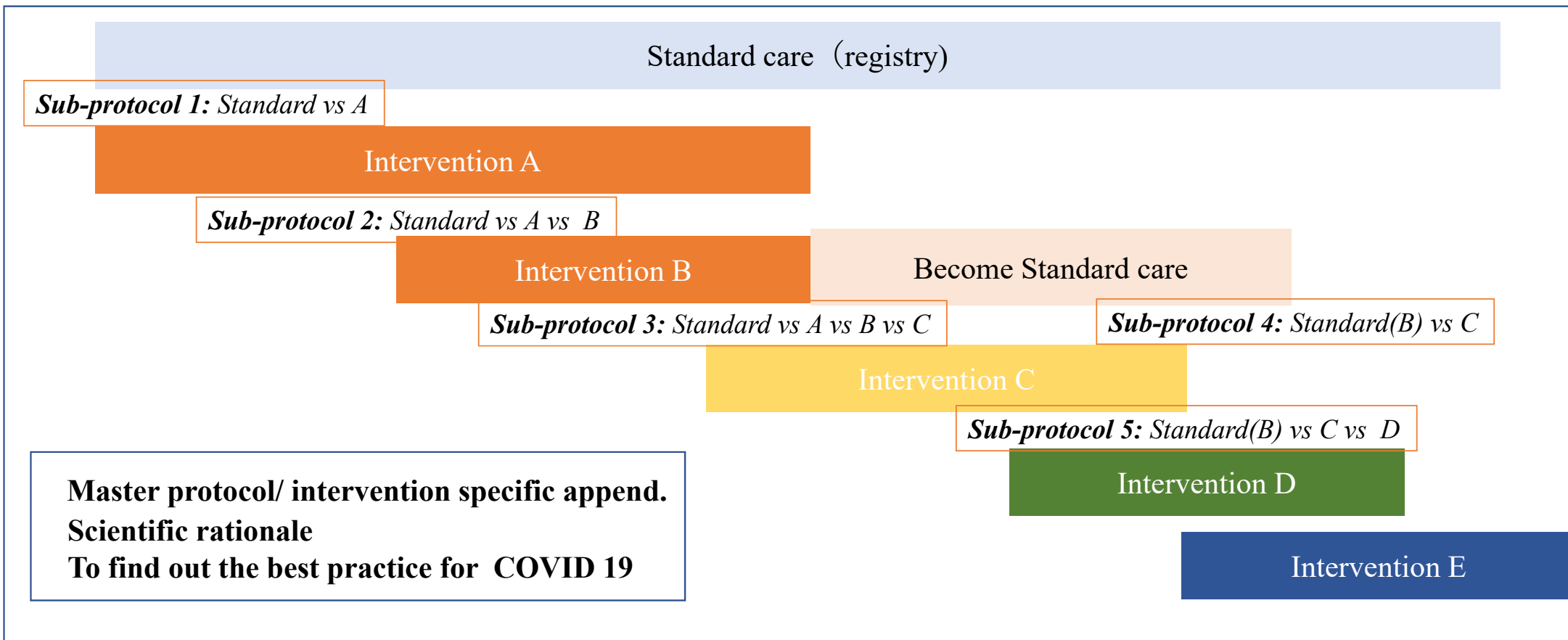
- 類似試験の競合をさける
- 結果の出ない小規模試験へのリソースや資金分散は批判的
- **Public health** ニーズによる国内での研究及び研究資金の **prioritisation**
- 国内リソース把握と調整に基づく、国際インフラネットワーク(エコシステム)推進
- 基礎研究に基づく科学的妥当性への見極めを促進



WHO draft guidance for best practice for clinical trials

Improve efficacy and minimize research waste

Complex trial design: Plat form trial



Platform trial for COVID-19/ EU

WHO Solidarity - Discovery(French), Recovery (UK) etc.



	REMAP CAP	EU-SOLIDA _c T	ECRAID PRIME	VACCERELATE
Sponsor	U. Utrecht/ UK (Europe)	U. Oslo	ECRAID/U. Utrecht	U. Cologne (G)
Target population	ICU/ severe	hospitalized (moderate, severe)	Primary care	Healthy volunteer
target	treatment	treatment	Early treatment Post-ex prophylaxis	Vaccine optimization
Intervention	64 intervention steroid, HCQ etc)	Baricitinib AXL	NONS, xx	4 vaccines
Site	300 in 25 countries	No, A, B, CR, F, G, Gr, H, Ir, It, Lx, P, Sl, Sp, Sw, Tu etc	Ne, B, E, No	G, B, No, Ir, S, Li, D, F, Ne

Success case? – UK example

Adaptive Platform Trial & National priority study

HOME PARTICIPANT INFORMATION FOR HEALTHCARE PROFESSIONALS NEWS COMMUNITY OUTREACH
SHARE ACKNOWLEDGEMENTS

HELP FIND EFFECTIVE EARLY TREATMENTS FOR COVID-19

Recruitment
Participants: 28,601
Sites: 65

Click to find out more

All of the UK Chief Medical Officers and the NHS England Medical Director have broadcast that this trial is a national priority (Oxford population health)

<https://www.gov.uk/government/publications/commercial-clinical-trials-in-the-uk-the-lord-oshaughnessy-review/commercial-clinical-trials-in-the-uk-the-lord-oshaughnessy-review-final-report>

HOME RESULTS NEWS

HELP FIND EFFECTIVE EARLY TREATMENTS FOR COVID-19

Recruitment
Participants: 28,601
Sites: 65

Click to find out more

- Primary care対象 (molnupiravir, Paxlovid etc)
- PANORMIC 22700, PRINCIPLE 11000
- オンライン登録（かかりつけ医登録可）
- 自宅参加（薬剤投与及びデータ提出（デジタル、電話））

<https://www.principletrial.org/>
<https://www.panoramictrial.org/>

Coordination of Platform trials- JAAM and TCB

- **JAAM-COVID platform trial**の窓口として発足した第三者会議
3つのEU platform (REMAP-CAP, SolidAct, RECOVER) のガバナンス体制

2024 Jan より CODIV以外に拡大、HERA/EMA連携強化

New JAAM composition

- 1) 第2相後期以降が対象、参加申込
- 2) Secretariat (ECRIN) が科学的評価
- 3) 専門家会議 (methodology, virology, Clinician, immunology, preclinical, HTA)
- 4) 優先度、科学的根拠が議論され、platformに追加することが妥当と判断されたら recommendation letter
- 5) 各自、各グループと交渉開始

#COVID-19 #JAAM/TCB #Platform Trial

Published on 24/01/2022



- **TCB-コンソーシウム**による進捗共有 (UK,US, Africa, Latin america)

Support Tools for EU platform trial –EUPEARL



PROJECT ▾ WHY PLATFORM TRIALS? ▾ RESULTS ▾ EU-PEARL COMMUNITY OTHER



Advancing Collaborative
Platform Trials to accelerate
the development of medicines

D2.6 Final Generic Master Protocol Template and Appendix for IRPs

853966 – EU-PEARL

EU Patient-cEntric clinicAl tRIal pLatforms

WP2 –Scientific, Regulatory and Operational Methodology

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Other contributors	Franz König, Martin Posch (4 – MUW); Tom Parke, Scott Berry (14 – Berry); Clelia Di Serio, Paola Rancoita (7 – USR); Olga Sánchez-Maroto, Juan

- Collaborative project, patient centered platform trial
- Develop tools for APT
- 4 case studies, not oncology, not COVID
 - * MDD, TB, NF NASH

- Master protocol
- Intervention specific appendix
- Template for DMC
- Template for SAP
- Template for cover letter
- Best practice tools

<https://eu-pearl.eu/>

Support tools for EU platform trial –APT toolbox



The adaptative platform trial toolbox

This toolbox aims to collect the accumulated knowledge, experience, & resources from multiple projects and trials into a practical and guided toolbox to facilitate planning & conduct of future APTs in any therapeutic area.

The toolbox has been structured with different categories and subcategories to facilitate the navigation of the over 130 resources. Each tool is presented with a brief explanation indicating the tool's format and level of validation. The tools can also be searched by their type, year of publication or more generally by keywords. The link to access the outside source is included. If you want to download a list of key references to have on hand you can select them and download them directly.

Introduction & design elements	Regulatory	Statistics & data management	Trial conduct & documents	From recent & ongoing trials
<ul style="list-style-type: none">Complex innovative designConsideration for particular fieldPatient	<ul style="list-style-type: none">Document from European ProjectEuropeInternationalUSA	<ul style="list-style-type: none">Data managementData monitoring committeeGuidance supportMethodology	<ul style="list-style-type: none">Case study / Lessons learnedReportingTemplates / Guide for developing	<ul style="list-style-type: none">CancerCovidOther

2020年に作成、今年度更新

- 131 tools
- tools;
 - documents, deliverable, software, aide
 - webpage, published paper, template
- category
 - introduction and design element
 - regulatory
 - trial conduct and document
 - statistics and data management
 - From recent and ongoing trials
- whole fields(70%-COVID)

NEXT STEP of Platform trials in Europe

- COVID対策で立ち上げたプラットフォーム試験は転換時期
- Sustainability の議論
 - レジストリの継続
 - データ共有、サンプル共有からのバイオマーカー 研究
 - 対象疾患を広げてplatformを維持
- 感染症以外の分野への展開（Platform trialの社会的意義）
 - 小規模試験乱立、競合によるリソースの浪費や経験の分散、エビデンスの観点から見た失敗試験をさける
 - 個人研究者、個別施設のネットワークではなく Nation based infrastructure network

Platform試験の展開に向けた今後の議論

- Platform 試験の目的
 - Comparative effectivenessやデータ共有がメイン
- どのような分野が適しているか
 - データの多様性、全般化可能性を必要とする分野
 - リアルワールドデータの必要性（DCT等methodology）
- SME以外の企業参画の難しさ
 - 開発の守秘、費用負担、HTAの観点