ECRIN
Facilitating European Clinical Research

http://www.ecrin.org

ECRIN
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

NEURON-EBRA Workshop
22 January 2019, Bonn, Germany
Christian Ohmann, ECRIN

Aim of the presentation

- Introduction
- ECRIN
  - infrastructure
  - results achieved so far
- Outlook
- Summary & conclusions

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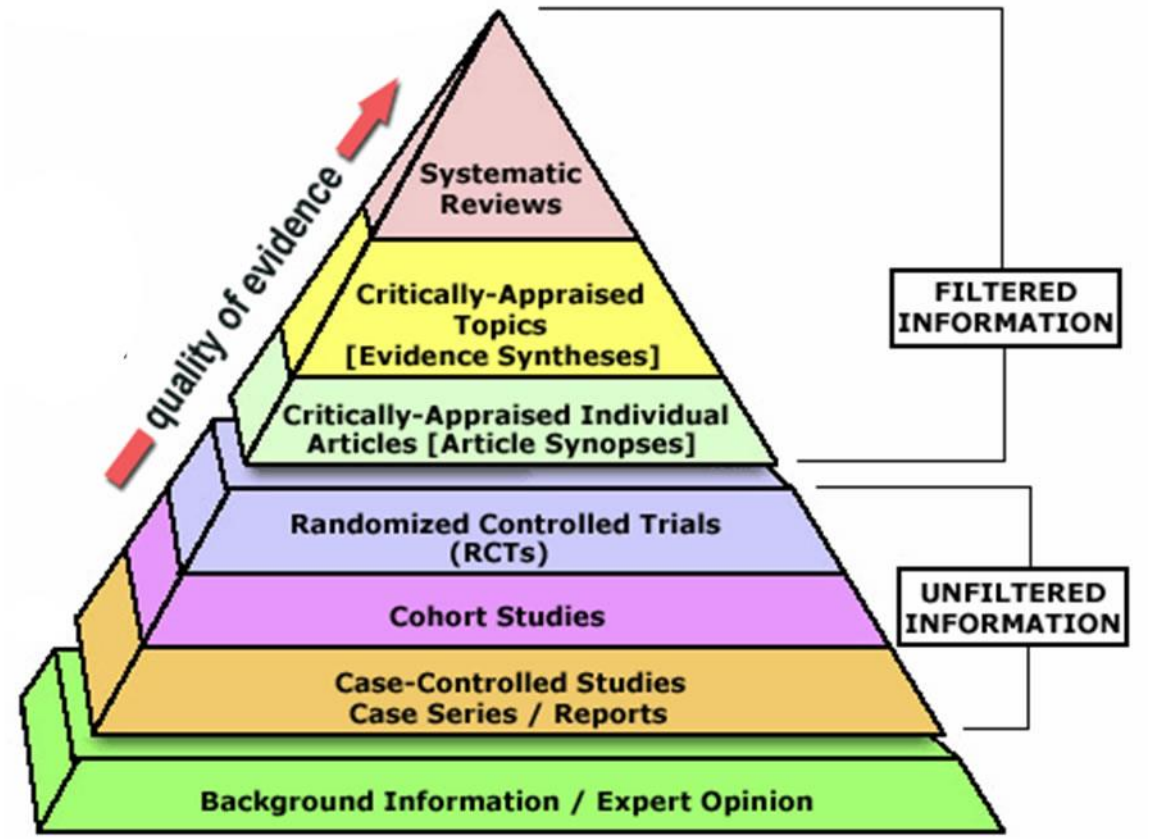
Levels of scientific evidence*



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**Glover et al., EBM Pyramid and EBM Page Generator, copyright 2006 Trustees of Dartmouth College and Yale University*

Product centred vs. patient centred research

Investigator-driven multinational clinical trials: Rationale and definition

Scientific Workshop ERA-Net NEURON
3.5.2011
Villa Vigoni, Lake Como, Italy

Registration trials
Repurposing trials

Mostly industry

Comparative effectiveness
Personalized medicine

Mostly academic

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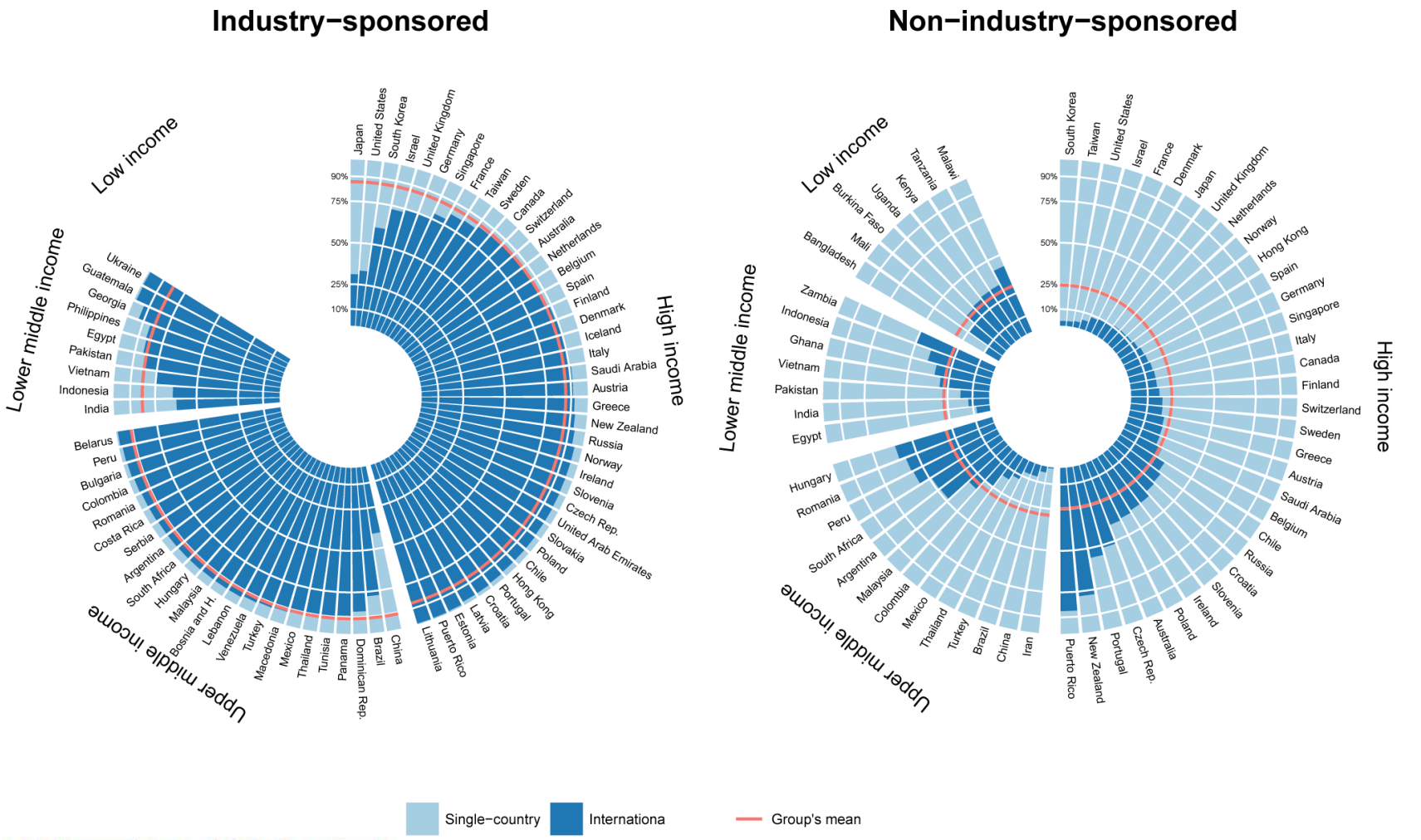
International cooperation*



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*Atai et al., PLOS One, 2015, 10(12): e0145122

History of ECRIN

EU-funded projects

- 2004 ECRIN-RKP
- 2006 ECRIN-TWG
- 2008 ECRIN-PPI
- 2012 ECRIN-IA
- 2017 PedCRIN

ESFRI-ERIC infrastructure

ECRIN-*ERIC* 2013

ESFRI Projects Landmarks ROADMAP 2016

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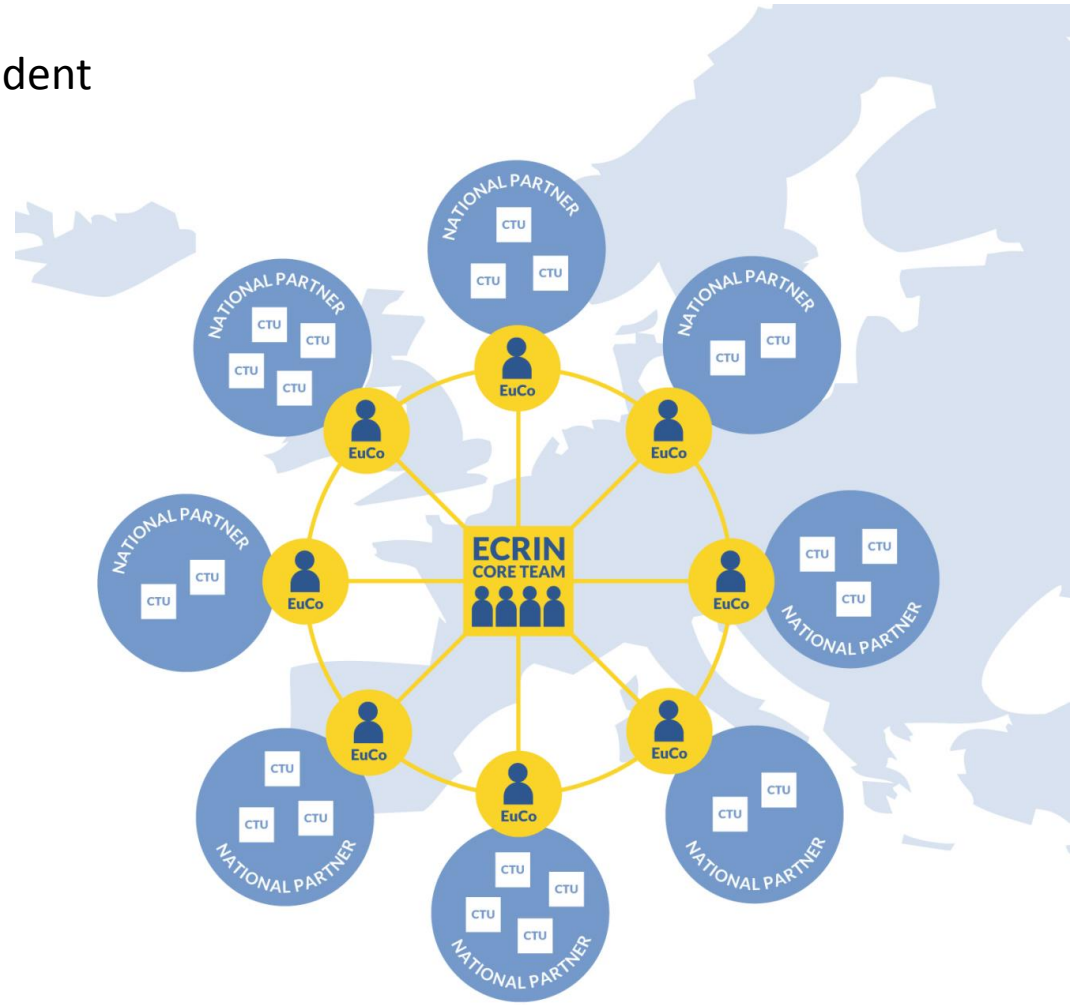
ECRIN a distributed infrastructure

EuCo = European Correspondent
CTU = Clinical Trial Unit



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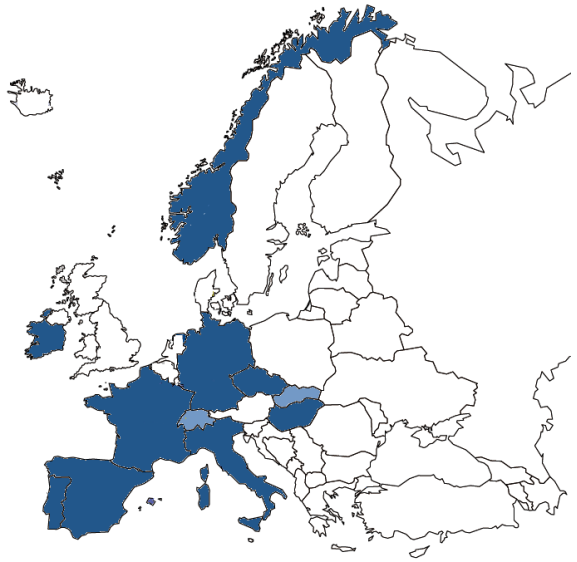
ECRIN and its national scientific partners

Country	*National hub*	*Nat. CTU-Network*	*Host Institution (linked third party)*
Czech Rep.	Brno	CZECRIN	Masaryk University
Germany	Berlin	KKSN	KKSN
Spain	Barcelona	SCReN	ISCIII
France	Toulouse	F-CRIN	INSERM
Hungary	Pecs	HECRIN	University of Pecs
Ireland	Dublin	CRCI	HRB
Italy	Rome	ItaCRIN	ISS
Norway	Trondheim	NORCRIN	St Olaf Hospital
Portugal	Lisbon	PtCRIN	Nova University
Slovakia	*Kosice*	*SlovaCRIN*	*Kosice University*
Switzerland	*Berne*	*SCTO*	*SCTO*



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ECRIN trial support services

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- ✓ Eligibility : multinational
  - ○ > 2 member or observer
- ✓ Access : Scientific Board
  - ○ collaboration committee
  - ○ peer-review committee
- ✓ Coordinating EuCo

ECRIN tools

- guidance on methodological design
- regulatory / ethics database (‘Campus’)
- risk-based monitoring toolkit
- data centre certification procedure
- recommendatinos and tools for data sharing

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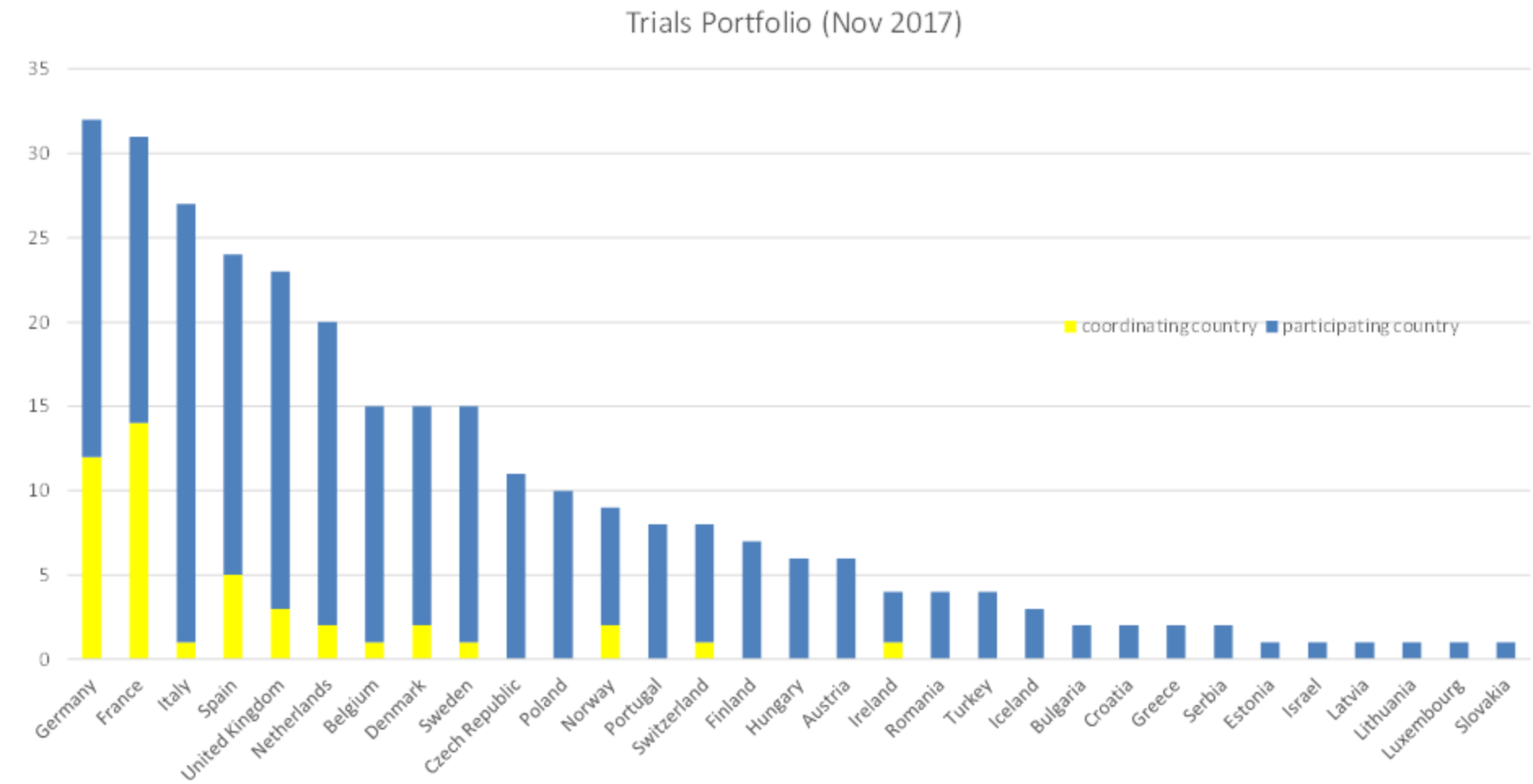
ECRIN trials portfolio



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ECRIN support of ERA-Net E-Rare trials

Trial	Title	ECRIN - services
HCQ4Surfdefect	Hydroxychloroquine (HCQ) in pediatric interstitial lung diseases *(Dr von Hauner Children´s Hospital, University of Munich Munich, Germany)*	Country- specific funding of ECRIN services, German ECRIN partner subcontractor of lead CTU in Germany
NICOFA	Nicotinamide for the treatment of Friedreich ataxia *(RWTH Aachen University Hospital Aachen, Germany)*	Contract between ECRIN and the sponsor for ECRIN services, Distribution to national ECRIN partners

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E-Rare

ECRIN tools: Guidance on methodological design

European Journal of Internal Medicine 32 (2016) 13–21

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Review Article

Evidence-based clinical practice: Overview of threats to the validity of evidence and how to minimise them

Silvio Garattini [a], Janus C. Jakobsen [b,c], Jørn Wetterslev [b], Vittorio Bertelé [a], Rita Banzi [a], Ana Rath [d], Edmund A.M. Neugebauer [e], Martine Laville [f], Yvonne Masson [f], Virginie Hivert [f], Michaela Eikermann [g], Burc Aydin [h], Sandra Ngwabyt [d], Cecilia Martinho [i], Chiara Gerardi [a], Cezary A. Szmigielski [j], Jacques Demotes-Mainard [k], Christian Gluud [b,*]

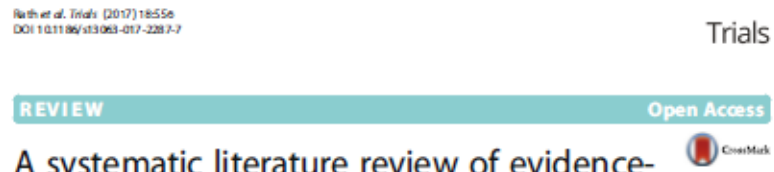
Djurisic et al. Trials (2017) 18:360
DOI 10.1186/s13063-017-2099-9

Trials

REVIEW Open Access

Barriers to the conduct of randomised clinical trials within all disease areas

Snezana Djurisic[1*], Ana Rath[2], Sabrina Gaber[3], Silvio Garattini[4], Vittorio Bertele[4], Sandra-Nadia Ngwabyt[2], Virginie Hivert[5], Edmund A. M. Neugebauer[6], Martine Laville[7], Michael Hiesmayr[8], Jacques Demotes-Mainard[3], Christine Kubiak[3], Janus C. Jakobsen[1,9] and Christian Gluud[1*]



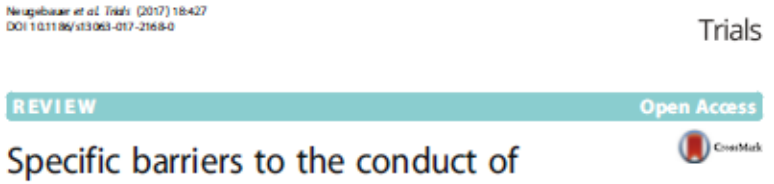
Rath et al. Trials (2017) 18:556
DOI 10.1186/s13063-017-2287-7

Trials

REVIEW Open Access

A systematic literature review of evidence-based clinical practice for rare diseases: what are the perceived and real barriers for improving the evidence and how can they be overcome?

Ana Rath[1], Valérie Salamon[1], Sandra Peixoto[1], Virginie Hivert[2], Martine Laville[3], Berenice Segrestin[3], Edmund A. M. Neugebauer[4], Michaela Eikermann[5], Vittorio Bertele[6], Silvio Garattini[6], Jørn Wetterslev[7], Rita Banzi[6], Janus C. Jakobsen[7,8], Snezana Djurisic[7*], Christine Kubiak[8], Jacques Demotes-Mainard[8] and Christian Gluud[7*]



Neugebauer et al. Trials (2017) 18:427
DOI 10.1186/s13063-017-2168-0

Trials

REVIEW Open Access

Specific barriers to the conduct of randomised clinical trials on medical devices

Edmund A. M. Neugebauer[1], Ana Rath[2], Sunya-Lee Antoine[3], Michaela Eikermann[3], Doerthe Seidel[3], Carsten Koenen[3], Esther Jacobs[3], Dawid Pieper[3], Martine Laville[4], Séverine Pitel[5], Cecilia Martinho[6], Snezana Djurisic[7*], Jacques Demotes-Mainard[8], Christine Kubiak[8], Vittorio Bertele[9], Janus C. Jakobsen[7,10], Silvio Garattini[9] and Christian Gluud[7*]

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ECRIN tools: Data centre certification procedure

ECRIN Certified data centres

DM center Unit	Country
Uppsala Clinical Research Centre*	SW
Düsseldorf KKS*	DE
ISPED Bordeaux	FR
Study Centre, Freiburg	DE
Mario Negri, Milan	IT
GIMEMA, Rome	IT
Aibili, Coimbra	PT
Ospedale Pediatrico, Rome	IT
Mainz IZKS	DE
UPCET, Lyon	FR
Marburg IZKS	DE
Dresden KKS	DE
Heidelberg KKS	DE

**now elapsed*

ECRIN Certification structure

- ECRIN standards
  (ECRIN DM standards v4.0, April 2018 revised https://zenodo.org/record/1240941#.W9F9_HszaUk)
- Auditors
- Independent Certification Board (ICB)
- ICB secretariat
- System development and maintenance

ECRIN Assessment of certification procedure

Raising standards in clinical research – The impact of the ECRIN data centre certification programme, 2011–2016

C. Ohmann [a,*], S. Canham [b], J. Demotes [c], G. Chêne [d], J. Lauritsen [e], H. Martins [f], R.V. Mendes [g], E.B. Nicolis [h], A. Svobodnik [i], F. Torres [j]

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ECRIN tools: Data sharing*

Open Access Research

BMJ Open

Sharing and reuse of individual participant data from clinical trials: principles and recommendations

Christian Ohmann,[1] Rita Banzi,[2] Steve Canham,[3] Serena Battaglia,[4] Mihaela Matei,[4] Christopher Ariyo,[5] Lauren Becnel,[6] Barbara Bierer,[7] Sarion Bowers,[8] Luca Clivio,[2] Monica Dias,[9] Christiane Druml,[10] Hélène Faure,[11] Martin Fenner,[12] Jose Galvez,[13] Davina Ghersi,[14] Christian Gluud,[15] Trish Groves,[16] Paul Houston,[6] Ghassan Karam,[17] Dipak Kalra,[18] Rachel L Knowles,[19] Karmela Krleža-Jerić,[20] Christine Kubiak,[4] Wolfgang Kuchinke,[21] Rebecca Kush,[22,23] Ari Lukkarinen,[5] Pedro Silverio Marques,[24] Andrew Newbigging,[25,26] Jennifer O'Callaghan,[27] Philippe Ravaud,[28] Irene Schlünder,[29] Daniel Shanahan,[11,30] Helmut Sitter,[31] Dylan Spalding,[32] Catrin Tudur-Smith,[33] Peter van Reusel,[6] Evert-Ben van Veen,[34,35] Gerben Rienk Visser,[36] Julia Wilson,[8] Jacques Demotes-Mainard[4]

To cite: Ohmann C, Banzi R, Canham S, *et al*. Sharing and reuse of individual participant data from clinical trials: principles and recommendations. *BMJ Open* 2017;**7**:e018647. doi:10.1136/bmjopen-2017-018647

► Prepublication history and additional material for this paper are available online. To view these files, please visit

ABSTRACT

Objectives We examined major issues associated with sharing of individual clinical trial data and developed a consensus document on providing access to individual participant data from clinical trials, using a broad interdisciplinary approach.

Design and methods This was a consensus-building process among the members of a multistakeholder task force, involving a wide range of experts (researchers, patient representatives, methodologists, information technology experts, and representatives from funders,

Strengths and limitations of this study

- ► An effective and formal consensus-building process among a large group of very experienced researchers and others involved in clinical trials.
- ► A unique perspective: Europe-wide, non-commercial, with a focus on the particular needs of researchers.
- ► A large number of practical recommendations set against an overarching framework of principles.
- ► The recommendations now need to be implemented and tested in practice, and feasibility and usability

- ✓ data protection, GDPR
- ✓ informed consent
- ✓ anonymized / pseudonymized
- ✓ access (open vs. controlled)
- ✓ standard data format
- ✓ security
- ✓ type of repositories

development of data sharing plans, tools and services

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**doi:10.1136/bmjopen-2017-018647*

ECRIN capacity projects (infrastructure development)

Partnership with medical specialties	Data structure/sharing	International cooperation
H2020 PedCRIN*	H2020 CORBEL	H2020 RISCAPE
H2020 EPTRI	H2020 EOSC-Hub	H2020 RI-VIS**
IMI c4c	H2020 EOSC-Pilot	H2020 EULAC PerMed**
H2020 EJP RD**	H2020 EOSC-Life**	EDCTP TESA II
H2020 TRANSVAC-II	H2020 XDC	CRIGH
H2020 ECRAID **	H2020 SYNCHROS**	
H2020 EBRA**		
H2020 TB-Med**		

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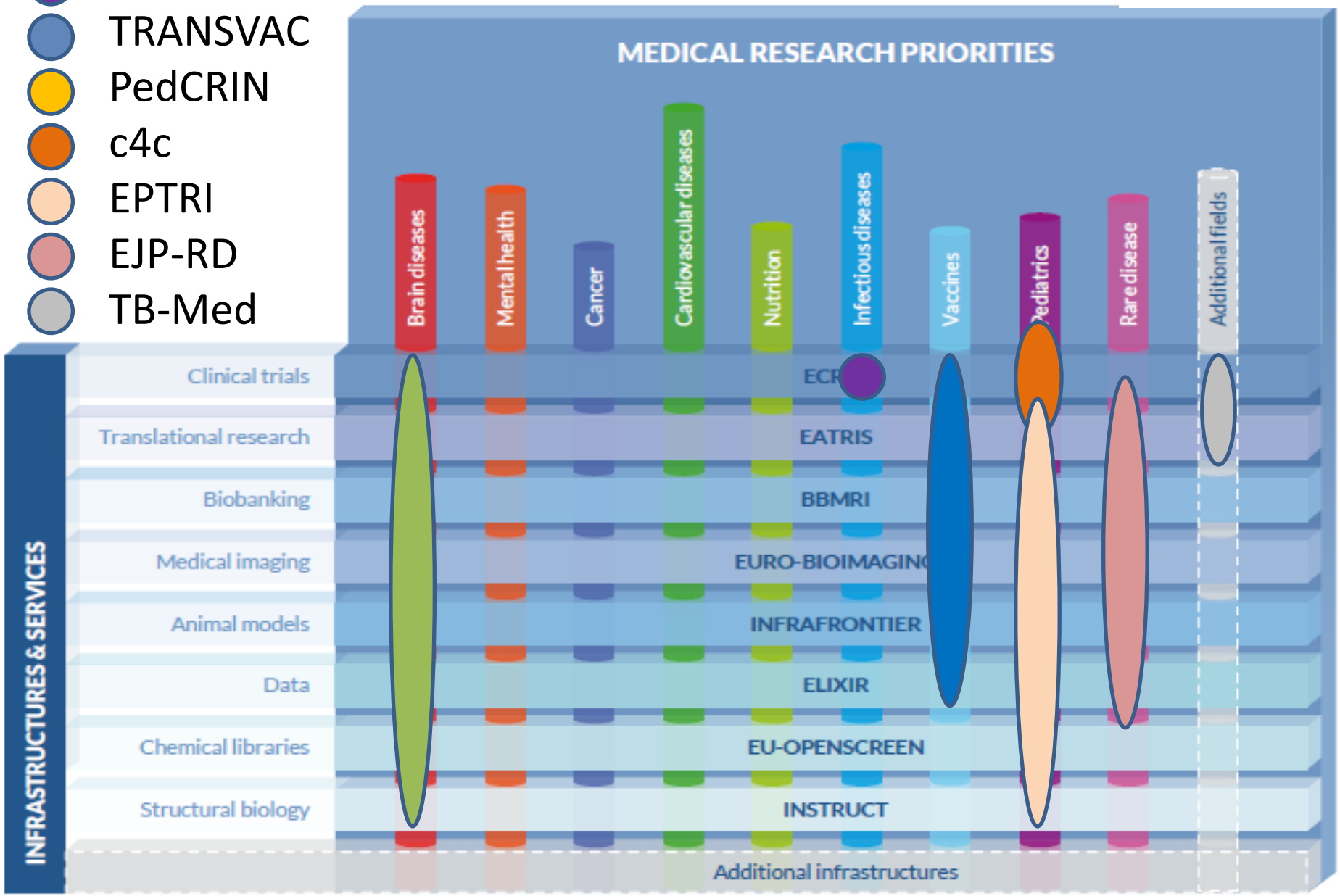
** ECRIN coordinator, ** start in 2019*

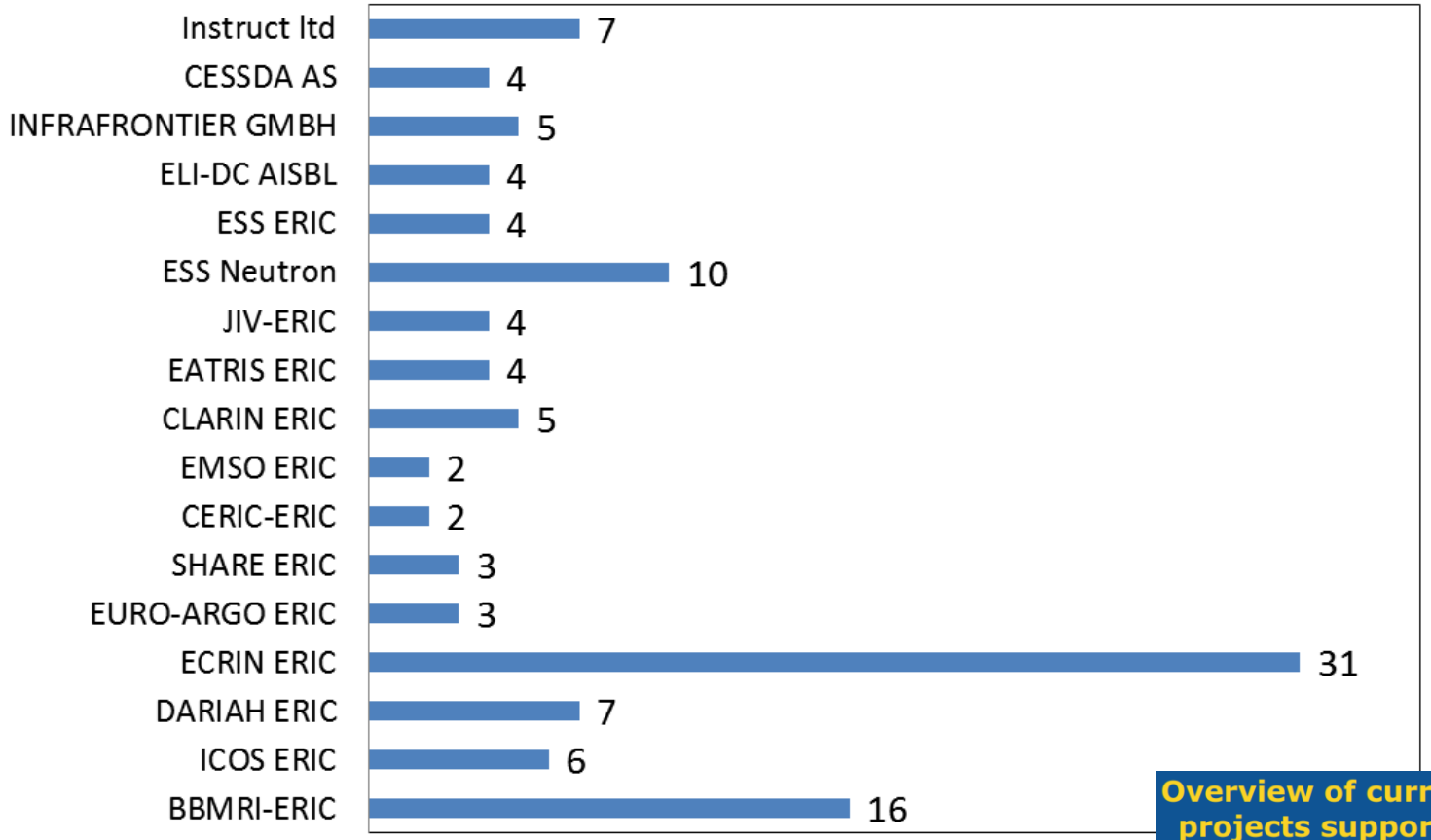
E-Rare

Medical Infrastructures / Users Forum

- EBRA
- ECRAID
- TRANSVAC
- PedCRIN
- c4c
- EPTRI
- EJP-RD
- TB-Med



ERIC participation in selected proposals



Overview of current portfolio of projects supported in DG RTD under H2020 including ERIC and ESFRI participation

Lorenza Saracco

European Commission – DG Research & Innovation
Research Infrastrusctures

PC RI meeting 9 February 2018

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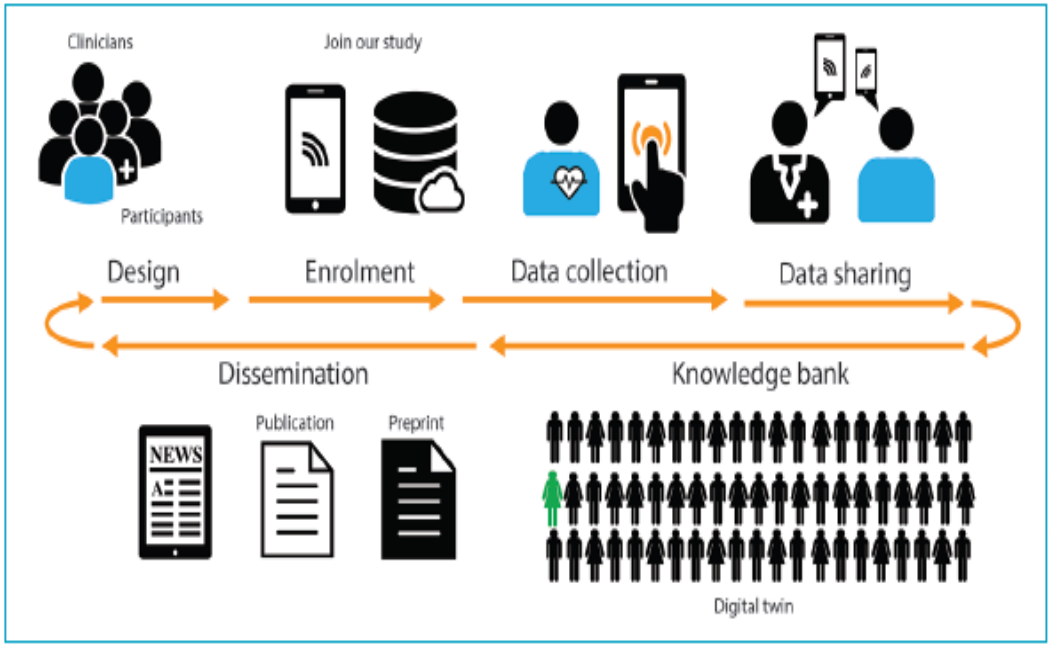
Funding for multinational clinical trials

The digitised clinical trial

- Protocol design
- Site selection
  - patients ?
  - investigator ?
- Patient selection
- Informed consent
- Data from cohorts / registries
- Electronic health records
- Electronic data capture
- Data from national databases
- Data sharing for meta-analyses, re-analyses, secondary use

- Data reuse
- High-throughput –omics
- Imaging data
- Patient stratification studies
- Multimodal data management



Lancet 390:2137 (2017)

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International cooperation : CRIGH

Clinical Research Initiative for Global Health

- Secretariat NIH + ECRIN (OECD and WHO partners)

- **projects**
  - Infrastructure and funding
  - Global core competencies
  - Research ethics
  - Patient involvement
  - Comparative effectiveness research
  - Regulatory awareness
  - Data

OECD Recommendation on the Governance of Clinical Trials

OECD

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www.crigh.org

Nature 545:289 (2017)

Summary and conclusions

- Investigator-initiated trials important contributor to scientific evidence
- International investigator-initiated trials underrepresented
- ECRIN implemented as an ERIC infrastructure, following a series of EU-funded projects
- ECRIN currently supports around 40 multinational clinical trials (mostly academic) with services
- ECRIN has developed a series of open tools to support clinical trials
- ECRIN is trying to structure the landscape of clinical research via funded capacity projects
- Major challenges for the future are funding mechansims for multinational clinical trials, the digitised clinical trial and worldwide cooperation in clinical research

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