Paediatric clinical trials: challenges and opportunities The contribution of PedCRIN

Mark Turner

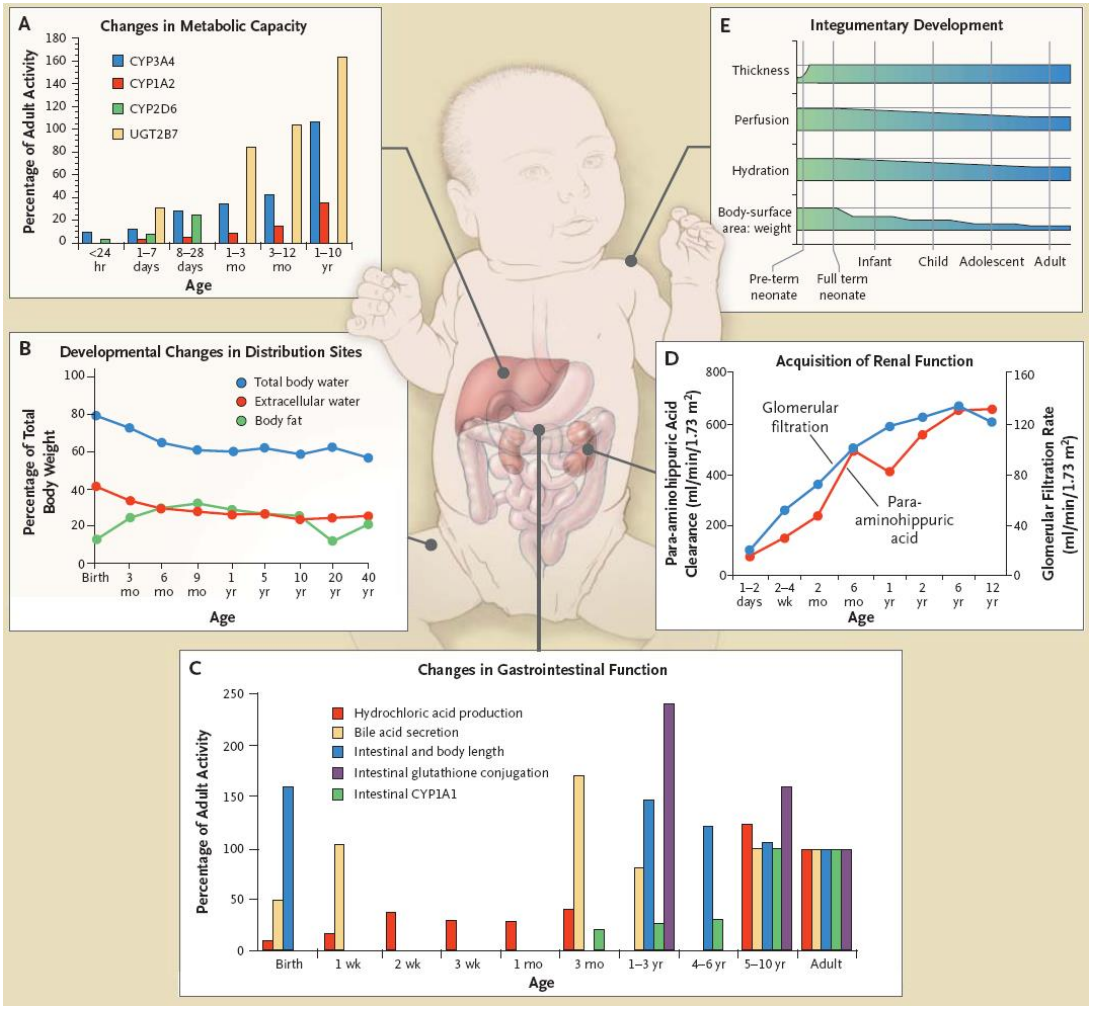
Declaration of interests

- My employers have received funds for clinical studies from: Roche, Chiesi, Johnson & Johnson, Pfizer, EC FP7, NIHR, BLISS, MRC, AMR
- My employers receive funds for consultancy from Chiesi, BMS, Novartis, Shire, Janssen, Grunenthal
- Lead for International Liaison, National Institute for Health Research, Children's Theme
- Co-Coordinator, Global Research in Paediatrics (GRiP)
- Chair, European Network for Paediatric Research at the European Medicines Agency
- Co-Director, International Neonatal Consortium

Topics

- Paediatric trials
- Challenges
- Opportunities
- PedCRIN

Developmental physiology



Developmental Pharmacology — Drug Disposition, Action, and Therapy in Infants and Children Kearns et al., N Engl J Med 2003;349:1157-67

Challenges 1

- Children
  - Different responses (PD)
  - Different drug handling (PK)

- Study procedures
  - Consent / Assent
  - Blood volumes and sampling methods
  - Outcomes

Challenges 2

- Poor delivery
- Poor design
- Fragmentation
- Inefficiency
- Poor engagement
- Poor feasibility

Challenges 3

Involvement of multiple countries in clinical trials

- Participants in paediatric trials can be rare
- Single countries may not be big enough to enrol all participants in a trial with appropriate power
- There are considerable barriers to opening clinical trials in extra countries
  - Particularly for publically-funded trials

Opportunities

- Improved understanding of how to do trials
  - Trial design
  - Trial management
- Paediatric Regulation

Industry Clinical Trials for Children

Table 13 - Paediatric clinical trials by year of authorisation (or, if not available, by year of protocol upload into EudraCT).

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Paediatric[1] trials	340	362	342	407	391	372	401	344	434	763
Total number of trials (adults and / or children)	4272	4855	4640	4555	4134	3971	3865	3576	3588	4242
Proportion of paediatric trials of all trials (%)	8.0	7.5	7.4	8.9	9.5	9.4	10.4	9.6	12.1	18
Exclusively[2] paediatric trials	196	188	185	241	230	218	257	211	284	473

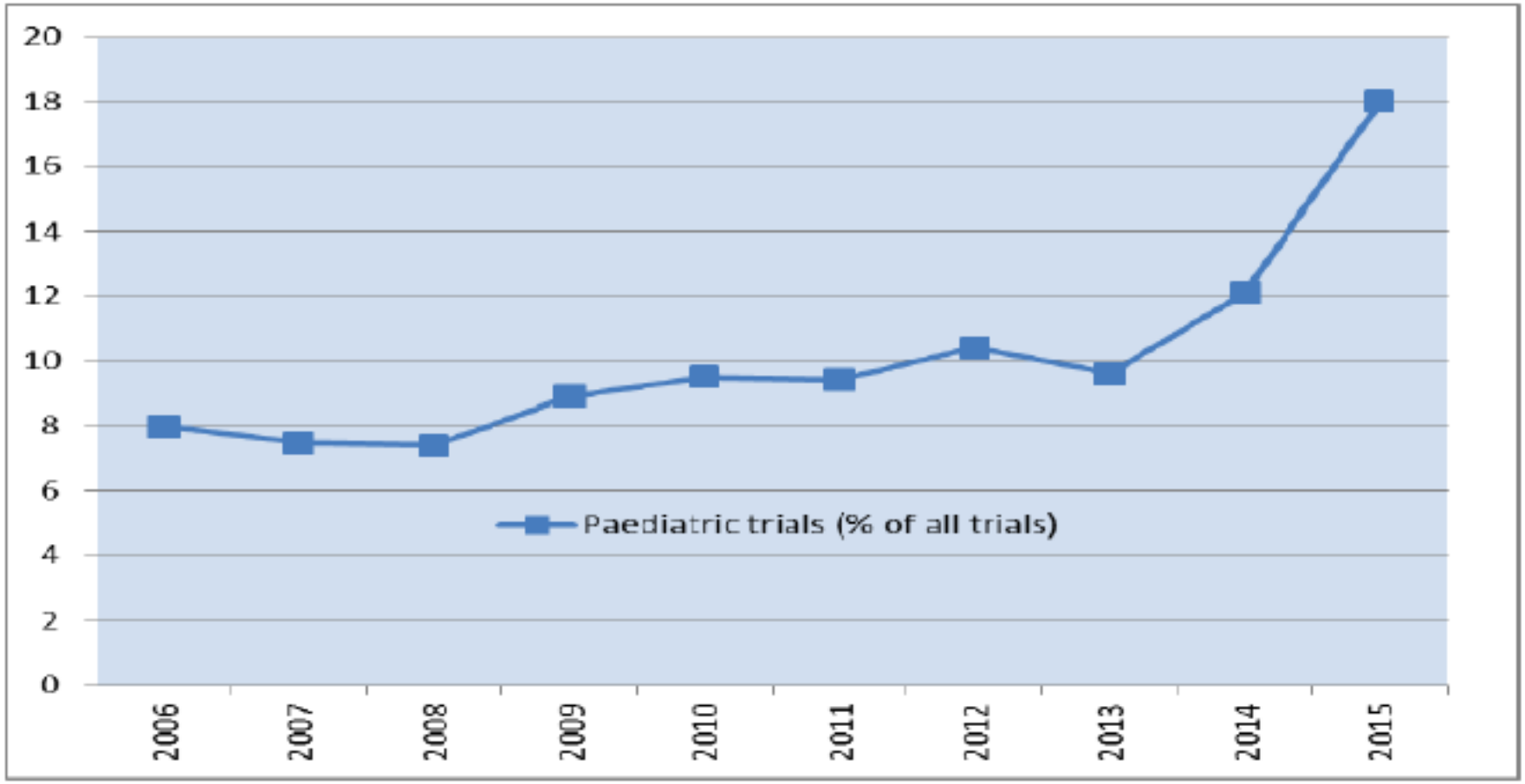
Source: EudraCT Data.

[1] A paediatric trial is a trial that includes at least one participant < 18 years of age

[2] An exclusively paediatric trial is a trial that includes only participants < 18 years of age

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Proportion of paediatric clinical trials of all trials (by year of authorisation).



Number of children planned to be enrolled in clinical trials, by age by year of authorisation of the trial (or, if not available, by year of protocol upload into EudraCT).

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Preterm neonates	0	0	0	327	82	2,527	1,552	3,634	4,997	1,979
Term neonates	0	98	5	184	169	1,353	2,283	1,488	2,168	1,749
Infants and toddlers	530	119	20	54,715	2,224	13,318	62,226	17,772	39,095	122,295
Children	2,683	706	270	5783	2,771	21,665	30,831	27,994	65,824	48,358
Adolesecents	435	36,458	285	5801	4,869	20,206	22,680	17,628	45,717	36,921
Total	3,648	37,381	580	66,810	10,115	59,069	119,516	68,516	157,261	211,302

Opportunities

Precision Medicine

Repurposing

Biologics

Methods

PK/PD

Design

Extrapolation

Devices

Apps

European Strategy Forum
on Research Infrastructures

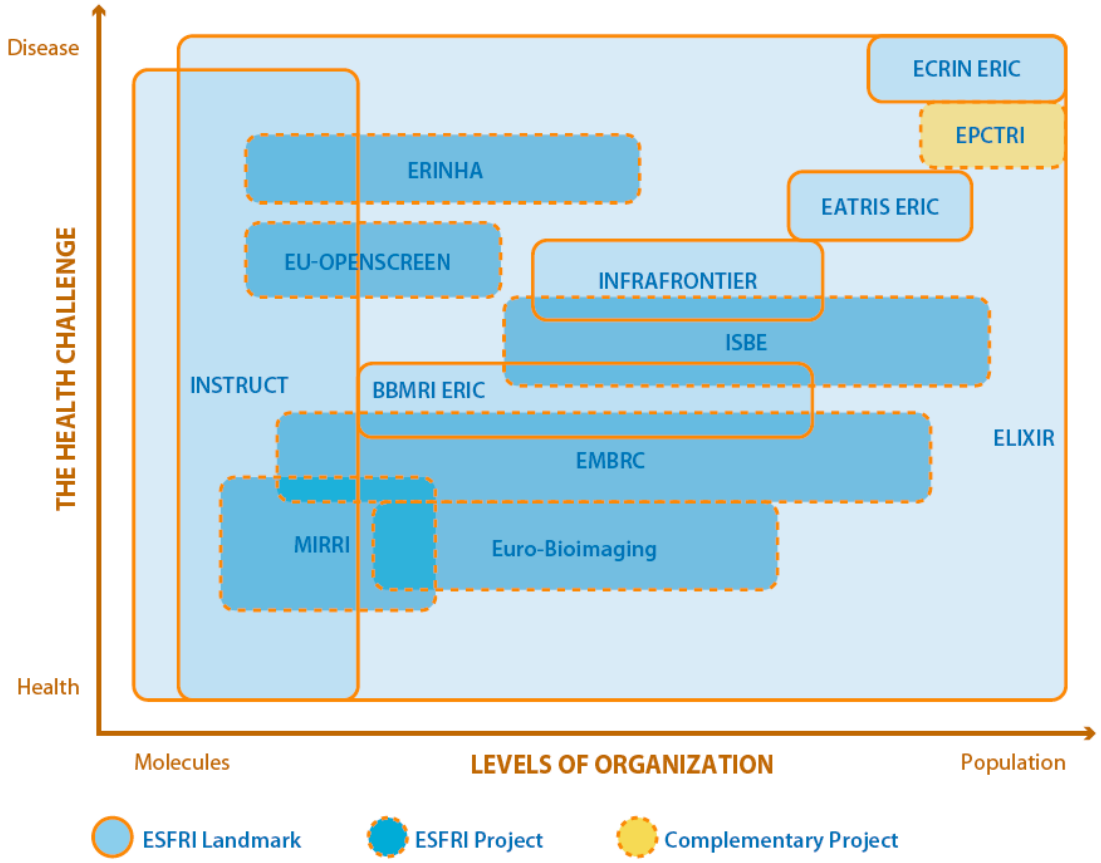
ESFRI

STRATEGY REPORT ON RESEARCH INFRASTRUCTURES

ROADMAP 2016

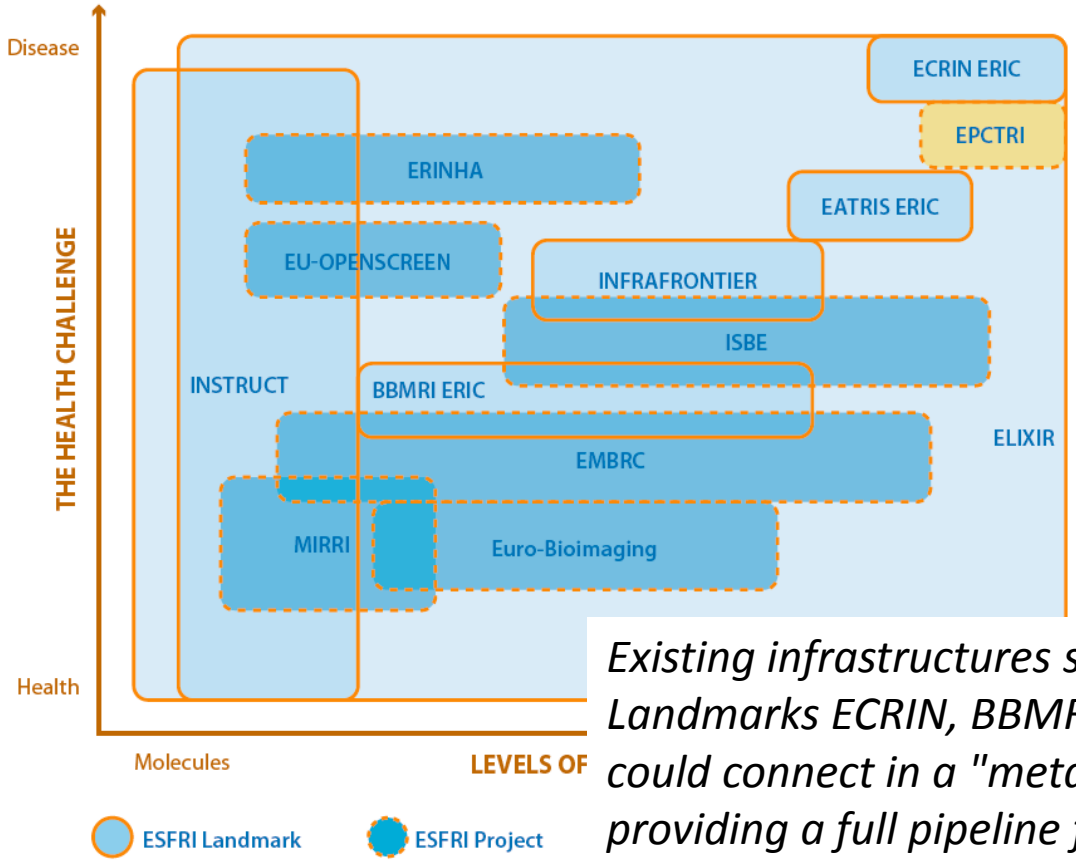
EPCRTI

Figure 3: the indicative position of ESFRI RIs relative to the different levels of organisation in the Health domain.



EPCRTI

Figure 3: the indicative position of ESFRI RIs relative to the different levels of organisation in the Health domain.



Existing infrastructures such as the ESFRI Landmarks ECRIN, BBMRI, EATRIS and others could connect in a "meta-structure" aiming at providing a full pipeline for drug development.

PedCRIN

Participant No	Participant organisation name	Acronym	Country
1 (Coordinator)	European Clinical Research Infrastructure Network - ERIC	ECRIN	FR
2	The University of Liverpool	ULIV	UK
3	Consorzio per Valutazioni Biologiche e Farmacologiche	CVBF	IT
4	Radboud University	RUMC	NL
5	Institut National de la Santé et de la Recherche Médicale	INSERM	FR
6	Hospital District of Helsinki and Uusimaa	HUS-FI	FI
7	Fundacio San Joan de Deu	FSJD	ES
8	Swiss Clinical Trial Organisation	SCTO	CH
9	Karolinska Institutet	KI	SE
10	Helse Bergen HF Haukeland University Hospital	HUS-NO	NO
11	Tartu Ulikool	UTartu	EE
12	Aristotelio Panepistimio Thessalonikis	AUTH	GR
13	OKIDS GmbH	OKIDS	AT
14	The National Children's Research Centre	NCRC	IRL
15	Vereniging Samenwerkende Ouder – en Patientenorganisaties	VSOP	NL

Project partners
BBMRI-ERIC
EATRIS-ERIC

UNIVERSITY OF LIVERPOOL | DEPARTMENT OF WOMEN'S AND CHILDREN'S HEALTH

Liverpool Women's

PedCRIN

WP1

- Management and coordination of PedCRIN

WP2

- Business case and Strategy for PedCRIN.

WP3

- Locate, Adapt, Develop and Adopt measures for management of multinational paediatric trials

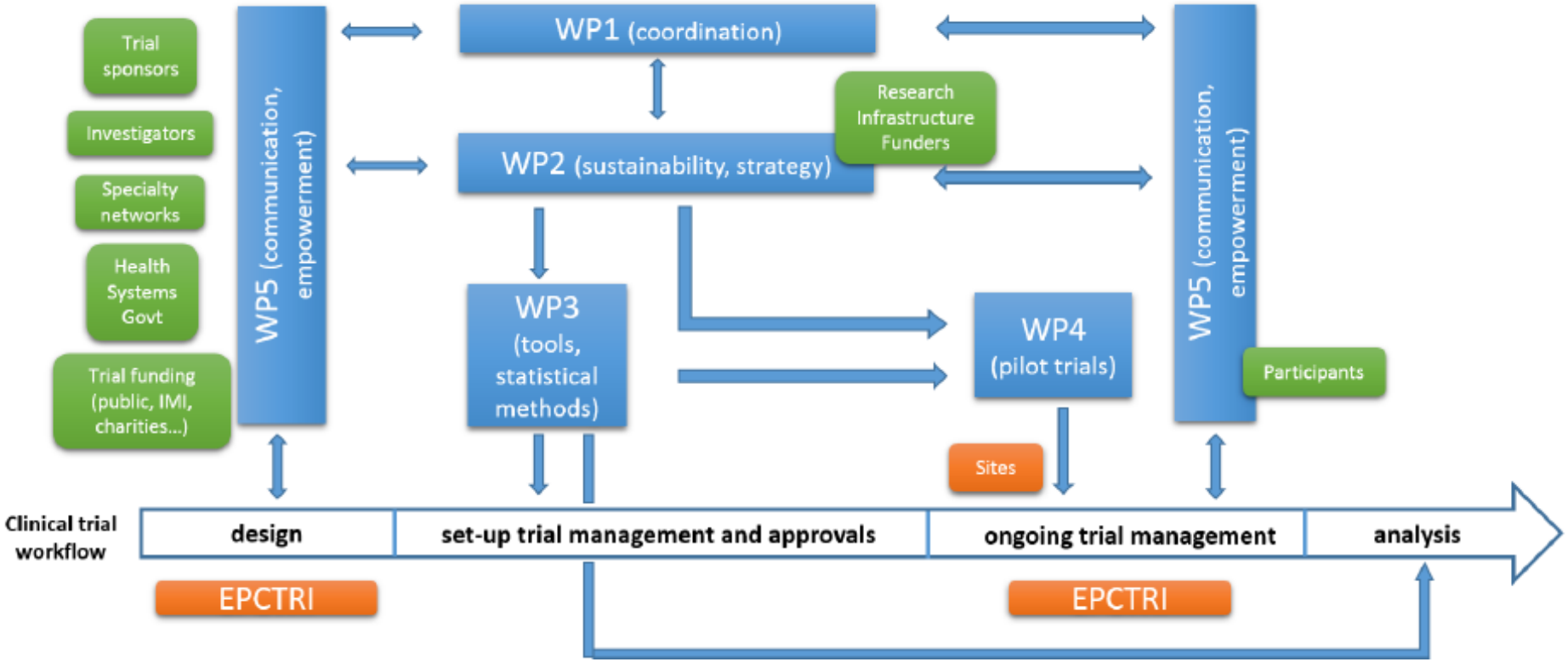
WP4

- Attract new studies in paediatrics and treat these studies as pilots for the upgrade to ECRIN.

WP5

- Communication and Empowerment

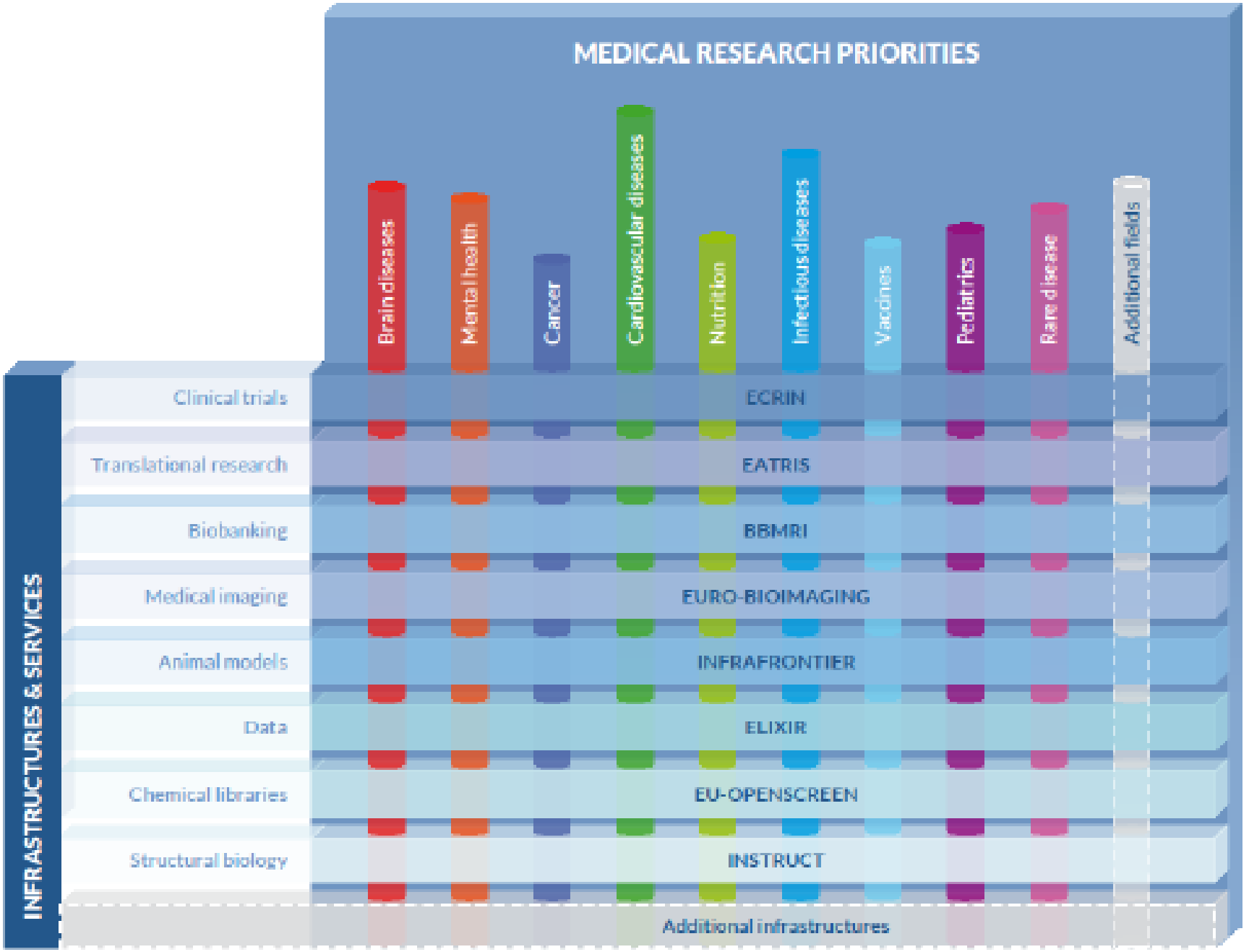
PedCRIN



Project partners
BBMRI-ERIC
EATRIS-ERIC

UNIVERSITY OF LIVERPOOL
DEPARTMENT OF WOMEN'S AND CHILDREN'S HEALTH
Liverpool Women's

RI activity	Summary
ECRIN OnBoard	A free advice service provided to ECRIN members to help multinational, clinical research projects improve the quality of their applications for multinational funding (e.g., Horizon 2020, E-Rare).
ECRIN Regulatory and Ethical Requirements database	A central resource for information about CT regulatory and ethical requirements covering over 22 European countries and multiple study types such as clinical drug trials, clinical investigations of medical devices, combination drug-device studies and nutritional studies.
Regulatory and Ethical Requirements in Medical Device Studies: Toolkits	Toolkits have been prepared for various countries to provide country-specific information on regulatory and ethical requirements in medical device studies.
Centre Locator for Nutrition	enables users to identify research centres based on study type and other relevant information (e.g., type of subjects, research tools). Descriptions are provided for more than 80 centres across Europe.
Risk Based Monitoring Toolbox	Provides information on tools available for risk assessment, monitoring and study conduct,
ECRIN Guidance Document on Risk Assessments	List of 19 study characteristics to be considered during risk assessment, with comments and examples
Medical Device Outcome Measure Database	Supports researchers to plan and conduct clinical trials and health technology assessments (HTA) of medical devices by providing a comprehensive view of outcome measures.
Trial Preparation - Advice and Consultancy	ECRIN offers advice on running the trial in multiple sites and countries and potential sites; meeting regulatory and ethical requirements in different countries; Insurance and related costs in each country; evaluating costs and budget preparation; contracting
Trial Management Support	ECRIN ensures support throughout project implementation. It offers investigators and project coordinators various trial management services.
Trial Management - Instructions for Applicants	ECRIN trial management services are provided at not-for-profit rates to projects approved after a scientific evaluation by the ECRIN Scientific Board and a logistical assessment by the ECRIN European Correspondents. The approval procedure takes seven weeks from protocol submission
Trial Management Application checklist	Checklist
Data Centre Certification	Process that identifies data centres providing high-quality, efficient and compliant data and information technology (IT) management for multinational clinical research.
Quality Management System for ECRIN Supported Trials	Established to implement the quality policy, to meet requirements for research and processes and to continually optimise the performance.

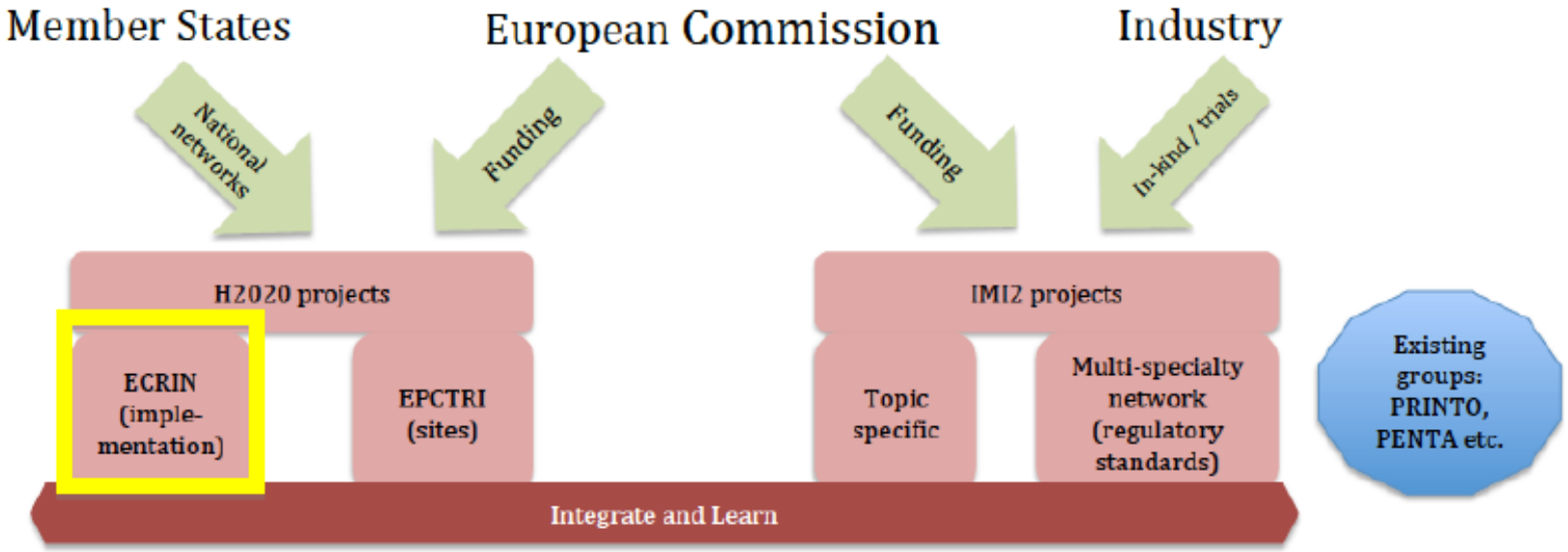

MEDICAL RESEARCH PRIORITIES
Brain diseases
Mental health
Cancer
Cardiovascular diseases
Nutrition
Infectious diseases
Vaccines
Pediatrics
Rare disease
Additional fields
INFRASTRUCTURES & SERVICES
Clinical trials
ECRIN
Translational research
EATRIS
Biobanking
BBMRI
Medical imaging
EURO-BIOIMAGING
Animal models
INFRAFRONTIER
Data
ELIXIR
Chemical libraries
EU-OPENSCREEN
Structural biology
INSTRUCT
Additional infrastructures

PedCRIN

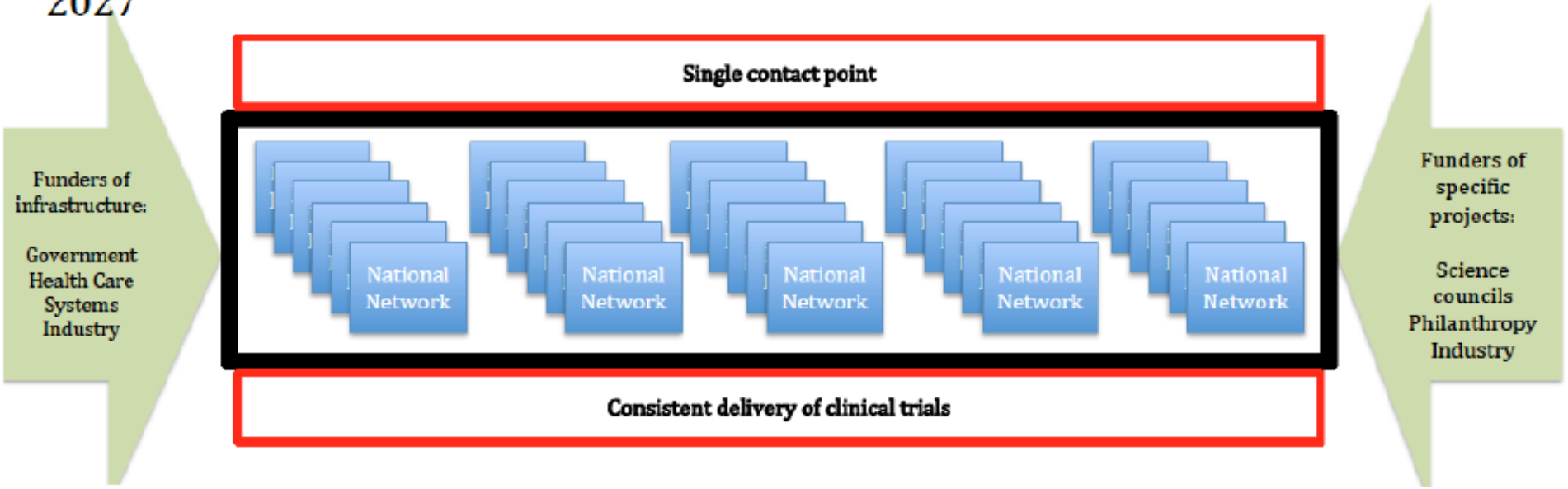
Good opportunity to test joint working

- National vs Specialty networks
  - Differentiation not competition
  - Consistent
  - Comprehensive
  - Reduce duplication by sites and funders
- Main competition is the status quo
  - Need to overcome costs of collaboration

2017

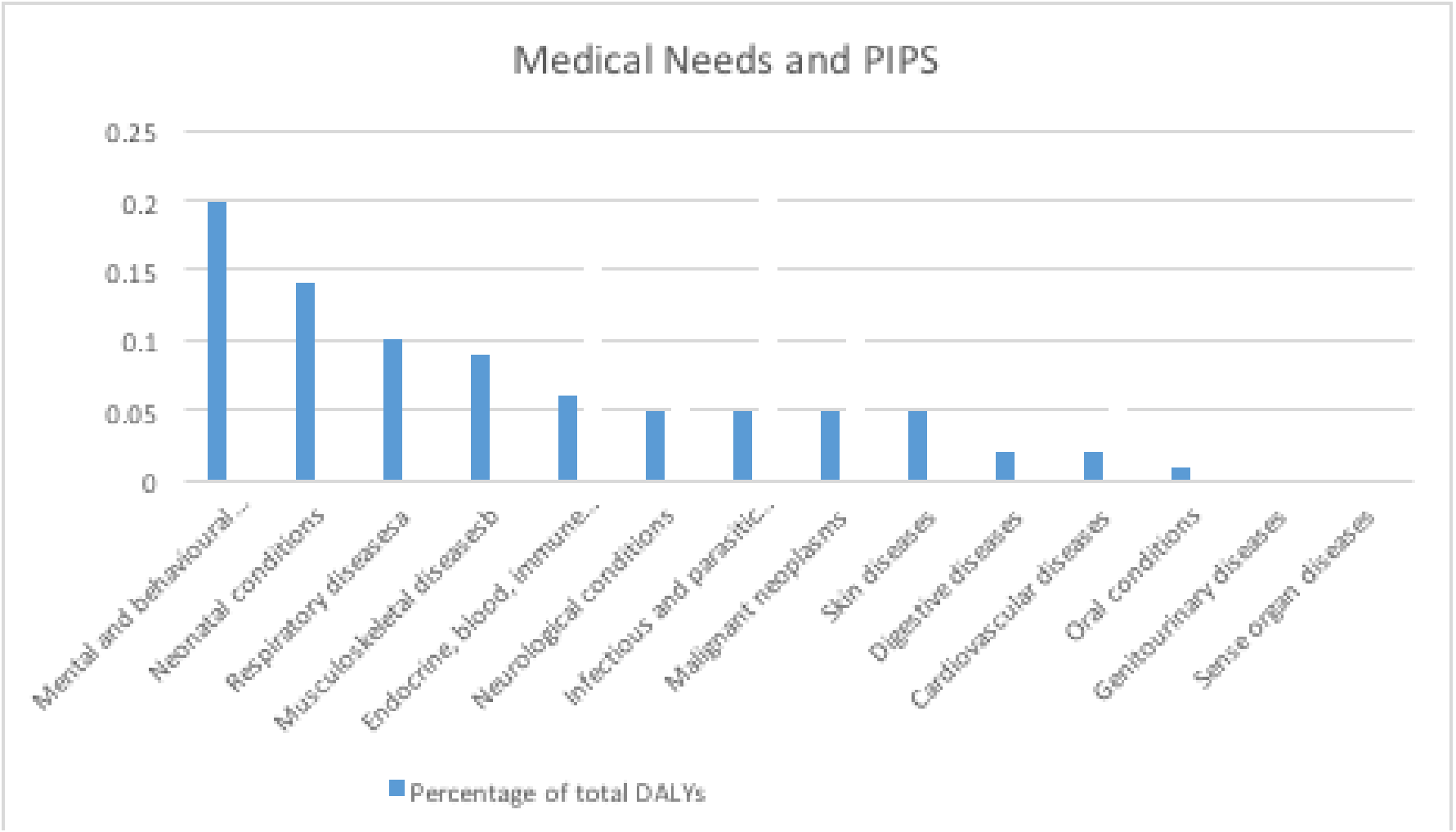

Member States
European Commission
Industry
National networks
Funding
Funding
In-kind / trials
H2020 projects
IMI2 projects
ECRIN (imple-mentation)
EPCTRI (sites)
Topic specific
Multi-specialty network (regulatory standards)
Existing groups: PRINTO, PENTA etc.
Integrate and Learn

2027


Funders of infrastructure:
Government
Health Care
Systems
Industry
Single contact point
National Network
National Network
National Network
National Network
National Network
Consistent delivery of clinical trials
Funders of specific projects:
Science councils
Philanthropy
Industry

State of the Art

In Western Europe, much of the burden of childhood disease is amenable to drug therapy



State of the Art

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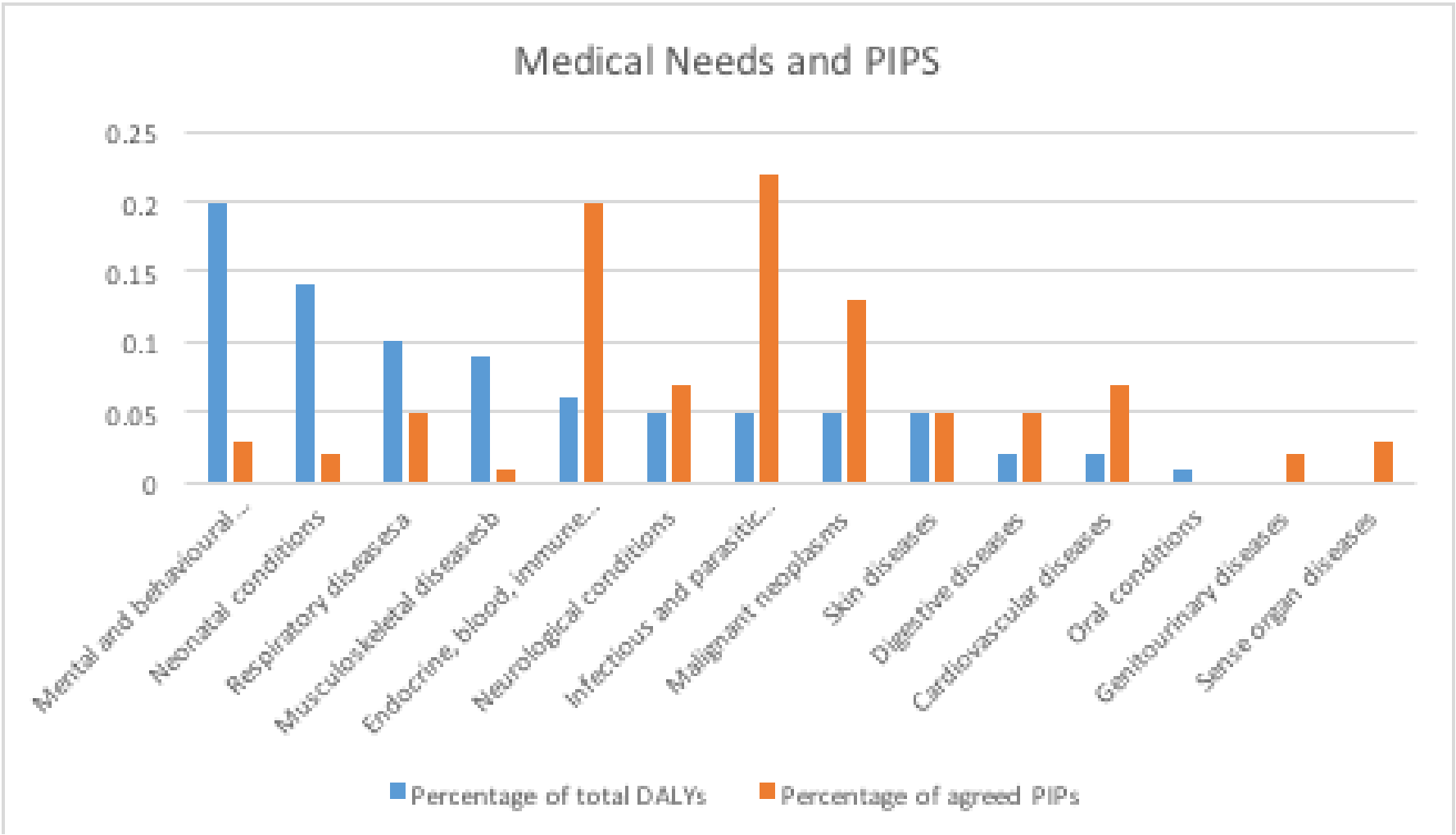

PedCRIN

- Allow publically-funded trials to open in multiple countries
- Promote shared working
  - Integrated product development for publically-funded studies
  - Collaboration between national and specialty networks
- Improve child heath through improved access to information about medicines