Lightning Talks Session

Adoption of the OMOP-CDM

The European Health Data & Evidence Network

What is it?

Nigel Hughes

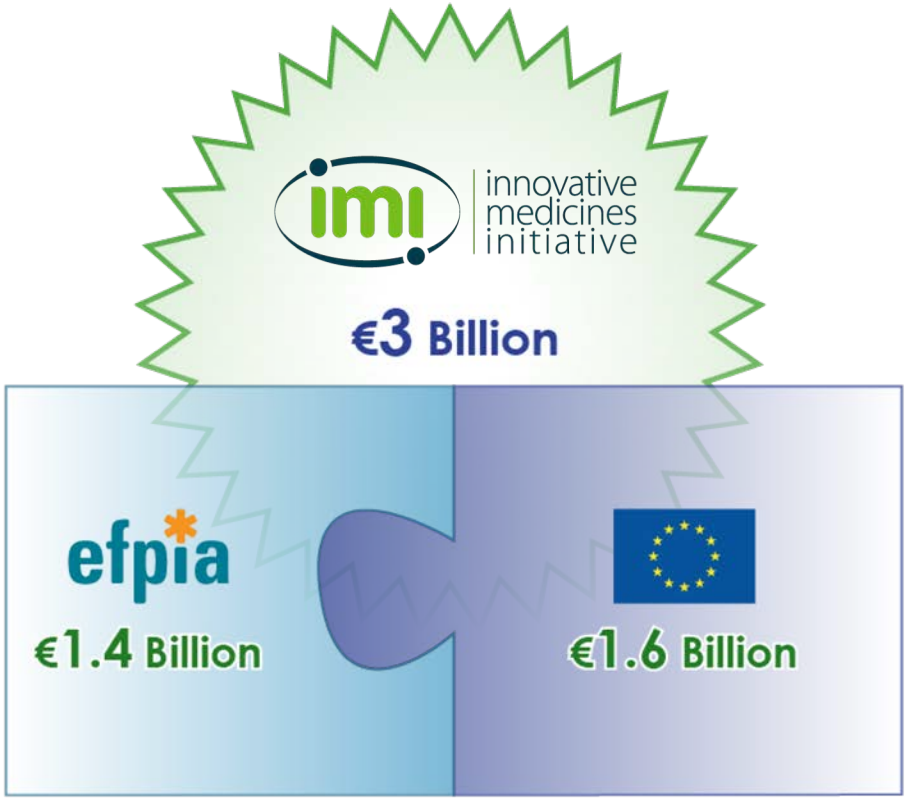
EFPIA Coordinator

Scientific Director, JCI Patient Data for Research, Janssen

All too often real world research is a challenging journey….

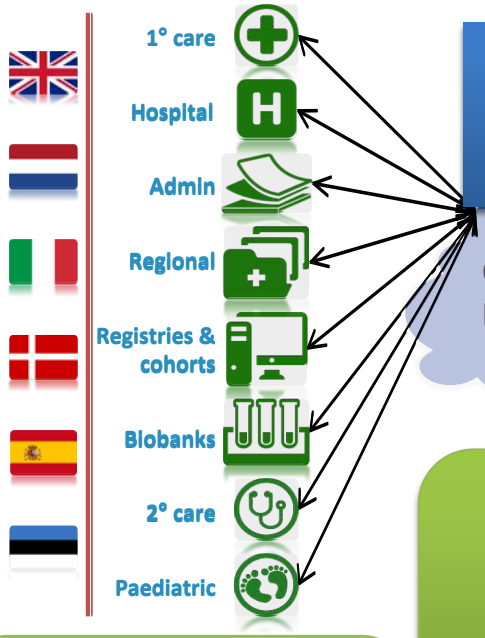
What we need is infrastructure and a network to conduct real world research in the 21st Century….

Innovative Medicines Initiative



IMI: a unique Public-Private Partnership (PPP) between the pharmaceutical industry represented by the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the European Union represented by the European Commission.

Federated distributed data networks reflect real world patients with greater phenotypic resolution: 'big data'



OMOP Common Data Model

COMMON DATA PLATFORM

RWD is about diversity of source as no one data source is the whole truth. A **federated data network** retains local provenance and governance while facilitating remote connectivity with RWD for research reuse

A federated data network is based around a **common platform** to facilitate bi-directional data flow, data harmonisation (from diverse sources) and connectivity for research reuse; supported by a harmonisation fund and certified/qualified SME network

There are a multitude of use cases for RWD, but the more reflective of populations, cohorts and real world patient trajectories **the more reliability can be attributed to RWD/RWE**

- **Academia**
  - Collaborative research
  - Pharmaco-epidemiology
  - Basic science
- **Discovery**
  - Natural history
  - Translational research
  - Biomarker development
- **Development**
  - Study feasibility
  - Strategic site/participant selection
  - Adaptive/pragmatic/platform studies
- **Post-Authorisation**
  - Regulatory commitments
  - Pharmaco-vigilance
  - License extensions
- **HTA/Outcomes**
  - HEMAR
  - Health service planning
  - Outcomes, value-based contracting

For value and outcomes patients, their treatment episodes, and outcomes need to be **tracked longitudinally** across health domains

Key Components of Collaborative Data Projects….

EHDEN Public & EFPIA Consortium Working on Full Project Proposal

Institute	Country
Erasmus MC	The Netherlands
Synapse Research Management	Spain
Oxford University	UK
Tartu Ulikool	Estonia
University of Aveiro	Portugal
The Hyve	The Netherlands
Odysseus Data Services	Czech Republic
European Patients Forum	Luxembourg
National Institute for Health and Care Excellence (NICE)	UK
Stiftelsen WHO Collaborating Centre for International Drug Monitoring	Sweden
International Consortium for Health Outcomes Measurement (ICHOM)	UK

Current Progress on EHDEN - 2018

- EHDEN is an IMI flagship project
- Key stakeholders and actors in this domain recognise the RWD→RWE process in the EU is inadequate
- For the coming year pre-project preparation is critical for a Q4 start

Key Activities Q1-Q3

Consortium Development

Vision Alignment

Work Packages

- Advancing Short Project Proposal
- Aligning Consortium
- Linkage with e.g. OHDSI
- Developing 'The Plan'

Final Project Proposal

What is the European Health Data & Evidence Network (EHDEN)?

The aim is to map 100 million health records across the EU via a common data model (OMOP), supporting research, the BD4BO IMI2 programme, and **outcomes-based** healthcare

- Advance the skill base in the EU via certified& qualified SMEs
- Harmonisation fund to support mapping to CDM

- Building on prior and current (IMI) projects
- Accelerate the platform and supporting research process

- A federated network of increasing number of Data Custodians and Sources
- Evaluation and incorporation of 'novel' data sources
- Utilisation of FAIR Principles

- Incorporation of outcome standards (e.g. ICHOM)
- Supporting the evidence base in the EU for outcomes-based research and medicine

EHDEN will be an IMI consortium of 12 EFPIA partners and a public consortium of 11 partners , commencing c. October 2018

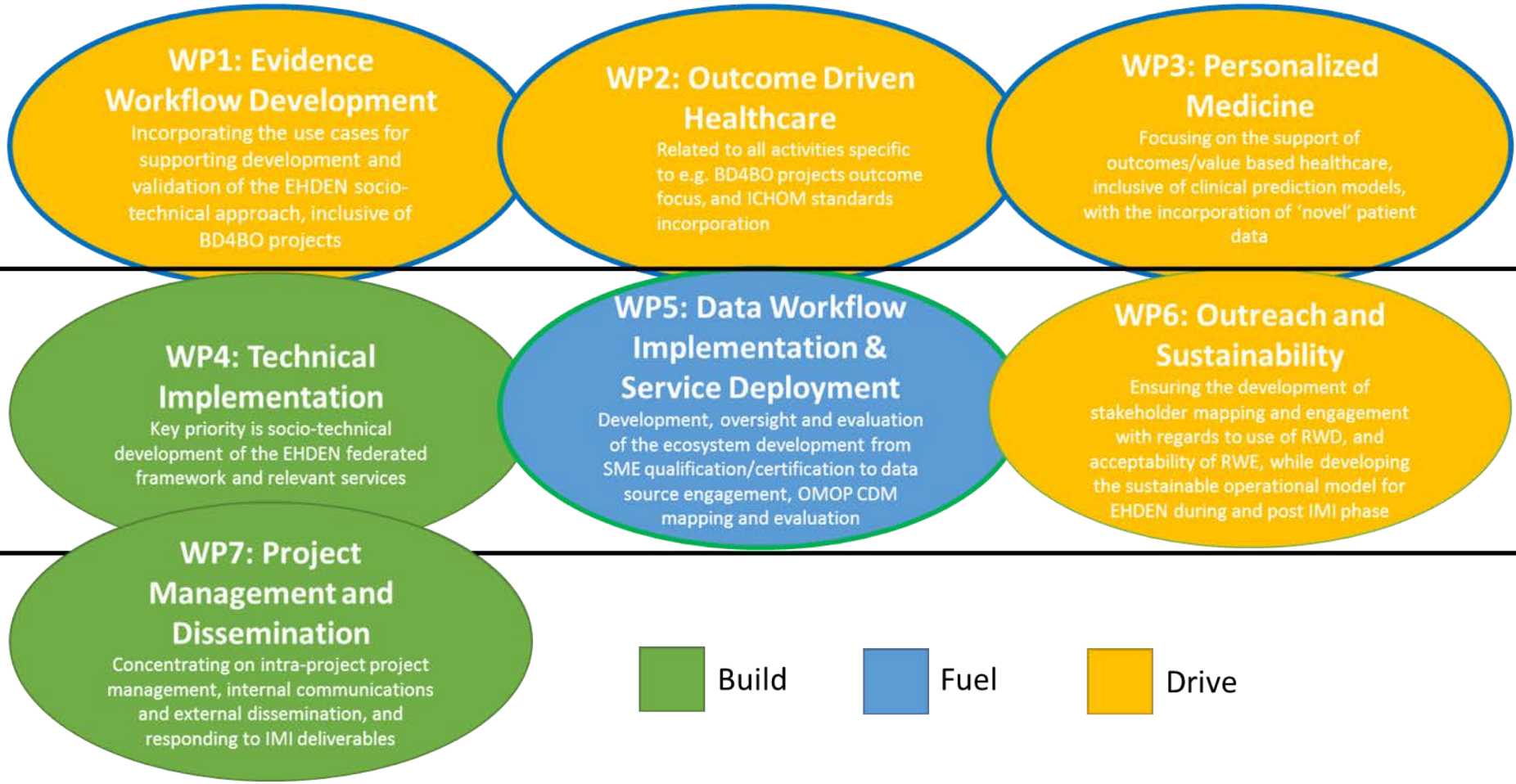
EHDEN: Vision, Mission & Values

Vision: **The European Health Data & Evidence Network (EHDEN) aspires to be the trusted observational research ecosystem to enable better health decisions, outcomes and care**

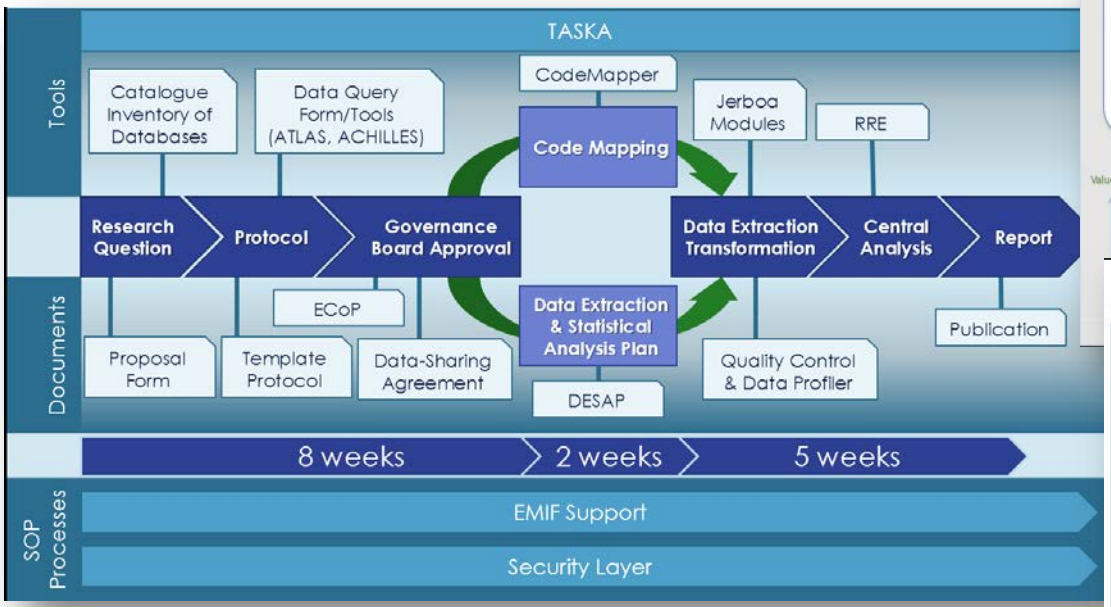
Mission: **Our mission is to provide a new paradigm for the discovery and analysis of health data in Europe, by building a large-scale, federated network of data sources standardised to a common data model**

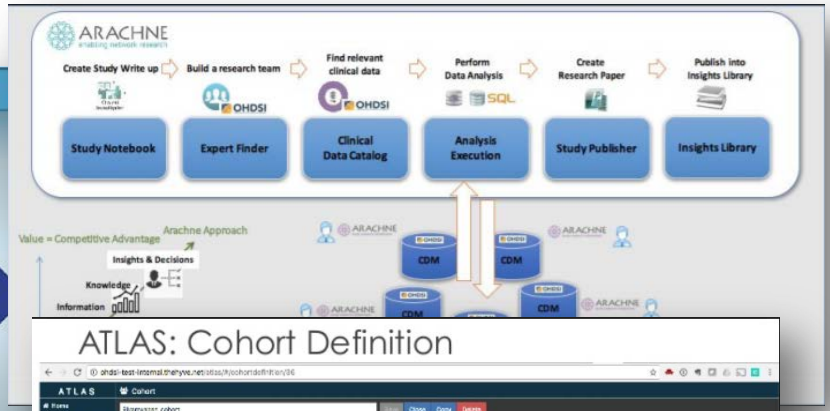
Values:

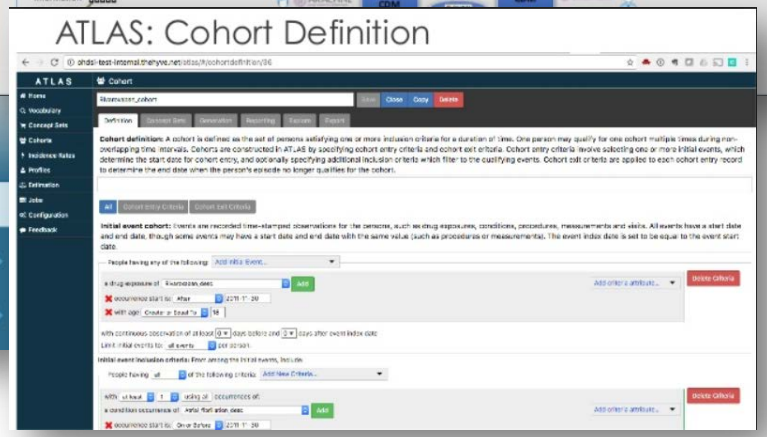
EHDEN Proposed Work Packages



EHDEN is not a blank canvas project….

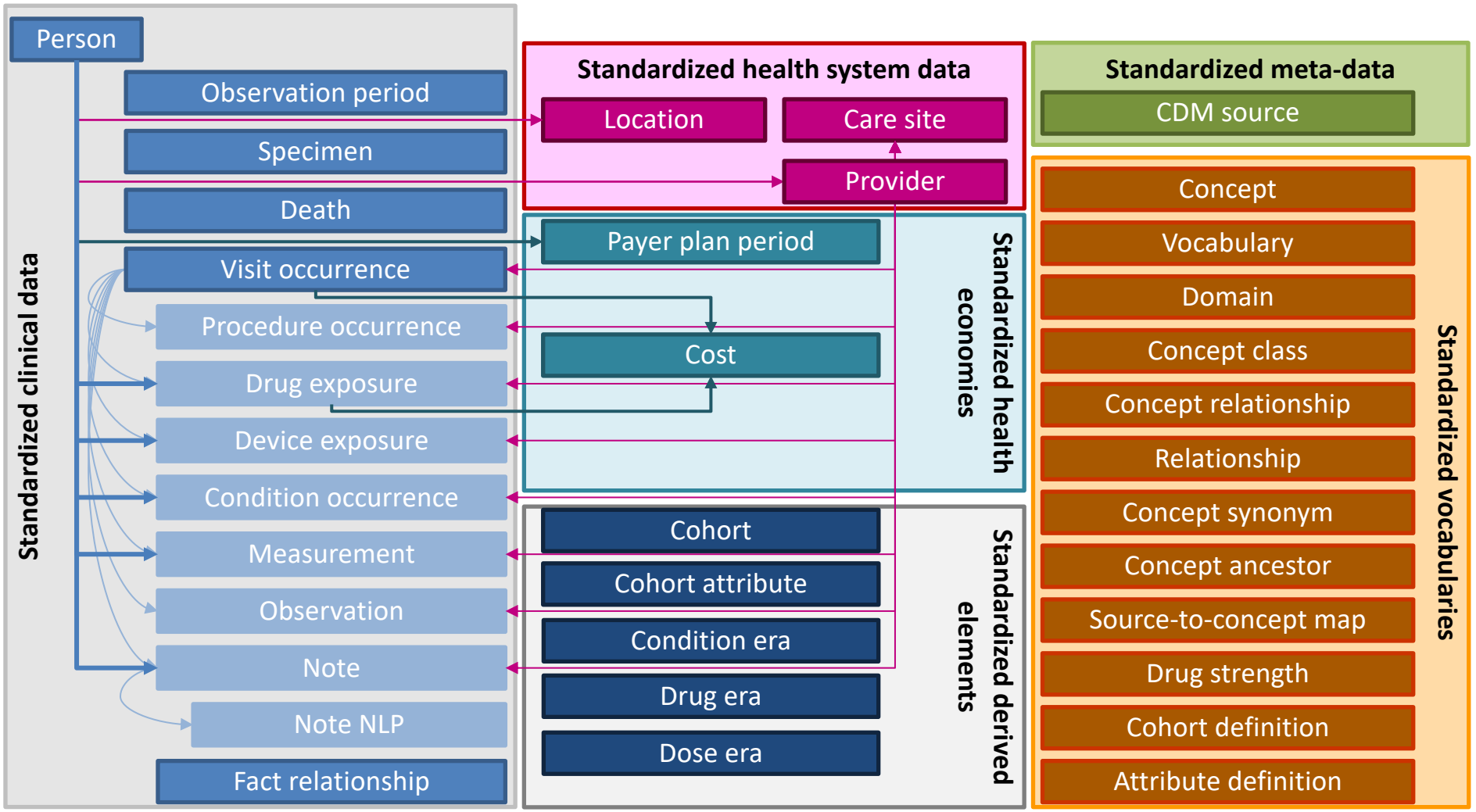






- EHDEN will utilise the best from prior and current (IMI) projects and platforms to develop its own infrastructure
- It will be developing its federated framework, but also analytical tooling and processes to support observational research in the EU, closely associated with the OHDSI EU/Global Open Science/Open Source collaboration

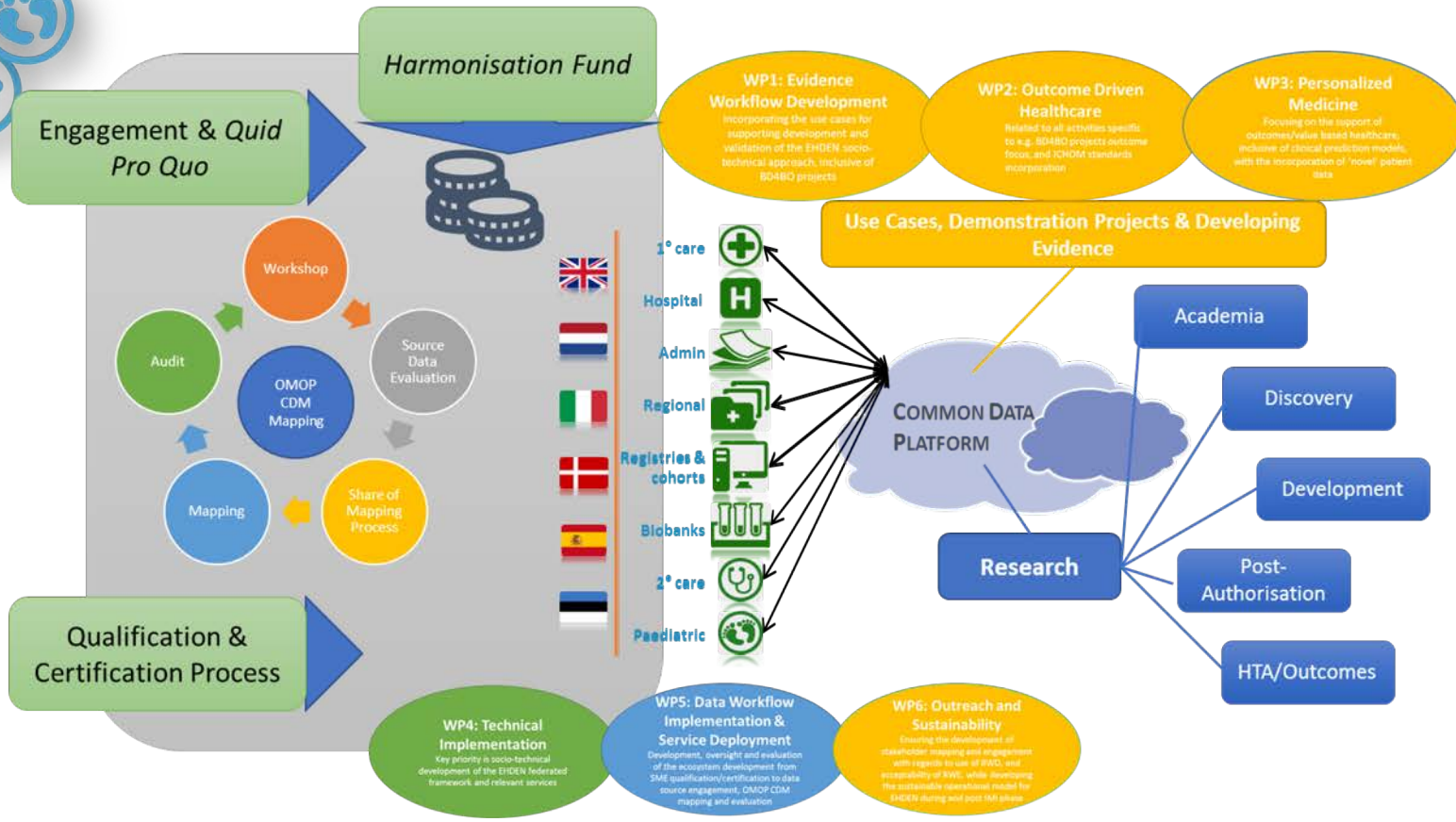
Critical at the heart of EHDEN is the OMOP CDM and OHDSI Collaboration



What is the flow through EHDEN?

A multitude of data sources in the EU

Developing the SME domain in the EU



EHDEN: In Summary

- EHDEN is a bold step in recognising that a flagship project is needed to address conducting real world research for the 21st Century

- At its heart is the acknowledgement that we need to develop a community via a federated network, within an ecosystem, all based on a *quid pro quo* around data for research use

- The Open Science/Open Source community of OHDSI, and the OMOP CDM are critical enablers and partners for EHDEN in this endeavour

Federal Ministry
of Education
and Research

miracum

Medical Informatics for Research and Care in University Medicine

The German Data Network

Martin Sedlmayr[1], Christian Maier[2], Thomas Ganslandt[3], Hans-Ulrich Prokosch[2]

on behalf of the MIRACUM consortium

[1]Institute for Medical Informatics and Biometry, TU Dresden
[2]Chair of Medical Informatics, FAU Erlangen-Nürnberg
[3]Department of Biomedical Informatics, University Medicine Mannheim, Ruprecht-Karls-University Heidelberg

Motivation

- We need
  - coordinated
  - secure
  - data protected
  - governed
- access to data and tools
- based on a trustworthy framework of technologies and policies

The German Medical Informatics Funding Scheme

- Improve **research opportunities** and **patient care** through innovative IT solutions (initially at university hospitals)
- Intensify the **exchange and sharing of data** between the research community and the health care delivery system
- Position medical informatics as a progressive field in research, **teaching and continuing education**
- As a key element of the funding scheme **data integration centres** are to be set up and interlinked by the university hospitals

MEDIZIN INFORMATIK INITIATIVE

The initiative so far...

Bild: Bundesforschungsministerin Wanka auf der MEDICA (Bildquelle: Messe Düsseldorf / ctillmann)

Announcement 2015

Conceptual Phase 2016-2017


10.07.2017 | PRESSEMITTEILUNG: 083/2017

Bessere Therapien dank Medizininformatik

BMBF fördert Medizininformatik mit über 150 Millionen Euro / Wanka: "Patientinnen und Patienten noch besser beraten und behandeln"

Bundesforschungsministerin Johanna Wanka und Alexander Hörbst mit den Vertretern der vier Konsortien, die für eine Förderung vorgesehen sind. v.l.: Alexander Hörbst (Vorsitzender des Gutachterkreises), Klaus A. Kuhn (DIFUTURE), Markus Löffler (SMITH), Roland Eils (HiGHmed), Johanna Wanka, Hans-Ulrich Prokosch (MIRACUM)

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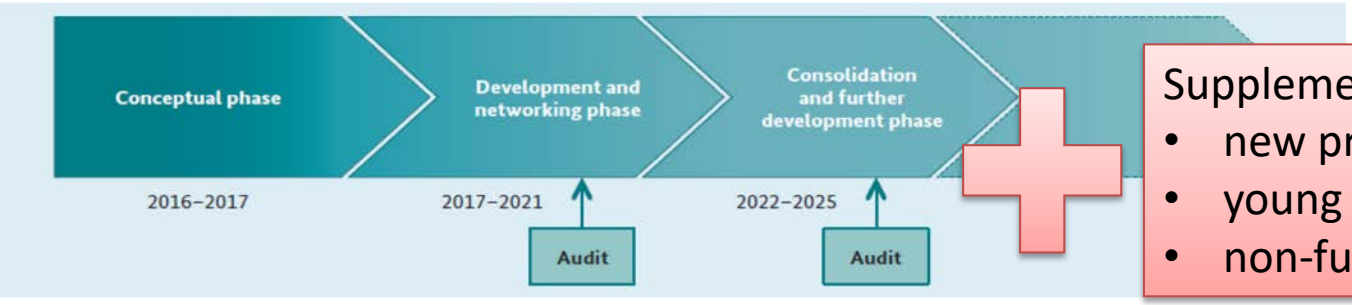
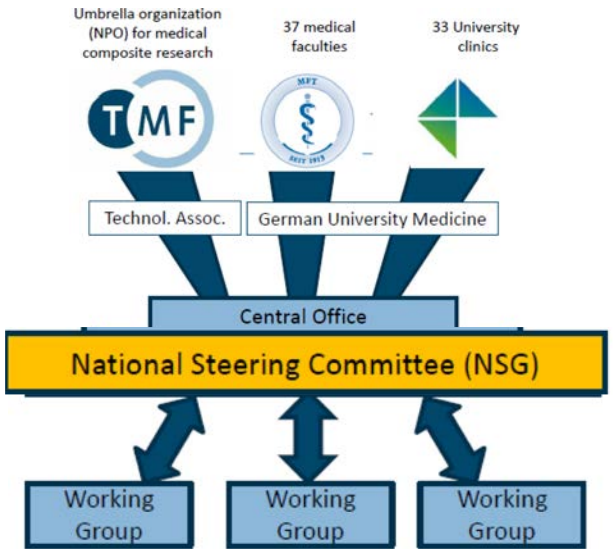
Development and Networking Phase 2018-2021



Supplementary Funding for
- new professorships
- young researcher groups and
- non-funded university hospitals

Governance of the MI-I



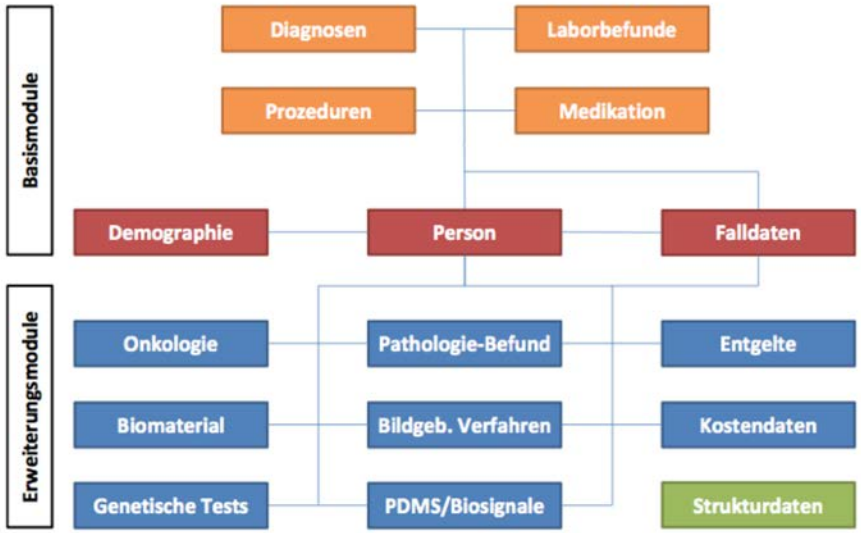
Working Groups

- Interoperability
- Data Sharing
- Consent
- ...

- TMF
  - Umbrella organization for networked medical research in Germany
- VUD
  - Association of the 33 German University Hospitals
- MFT
  - Association of the 37 German Medical Faculties
- NSG
  - PIs of the funded consortia
- Working Groups
  - Members of the funded consortia

Working groups foster harmonisation on a national level

- Interoperability
  - Core Dataset
  - Terminologies
  - Technologies (IHE, FHIR)
- Consent / eConsent
  - Modular, research friendly
- Use and Access Policies
  - UAC Committees
  - Registry of studies



The MIRACUM consortium

- Medical Informatics in Research and Care in University Medicine
  - eight University Hospitals and Medical Faculties, two Universities of Applied Science, and one industrial partner
  - across five German States
  - associated with four German Health Research Networks

- comprising ¼ of all German University Hospitals
- handling clinical and research data of
  more than 10 Mio patients

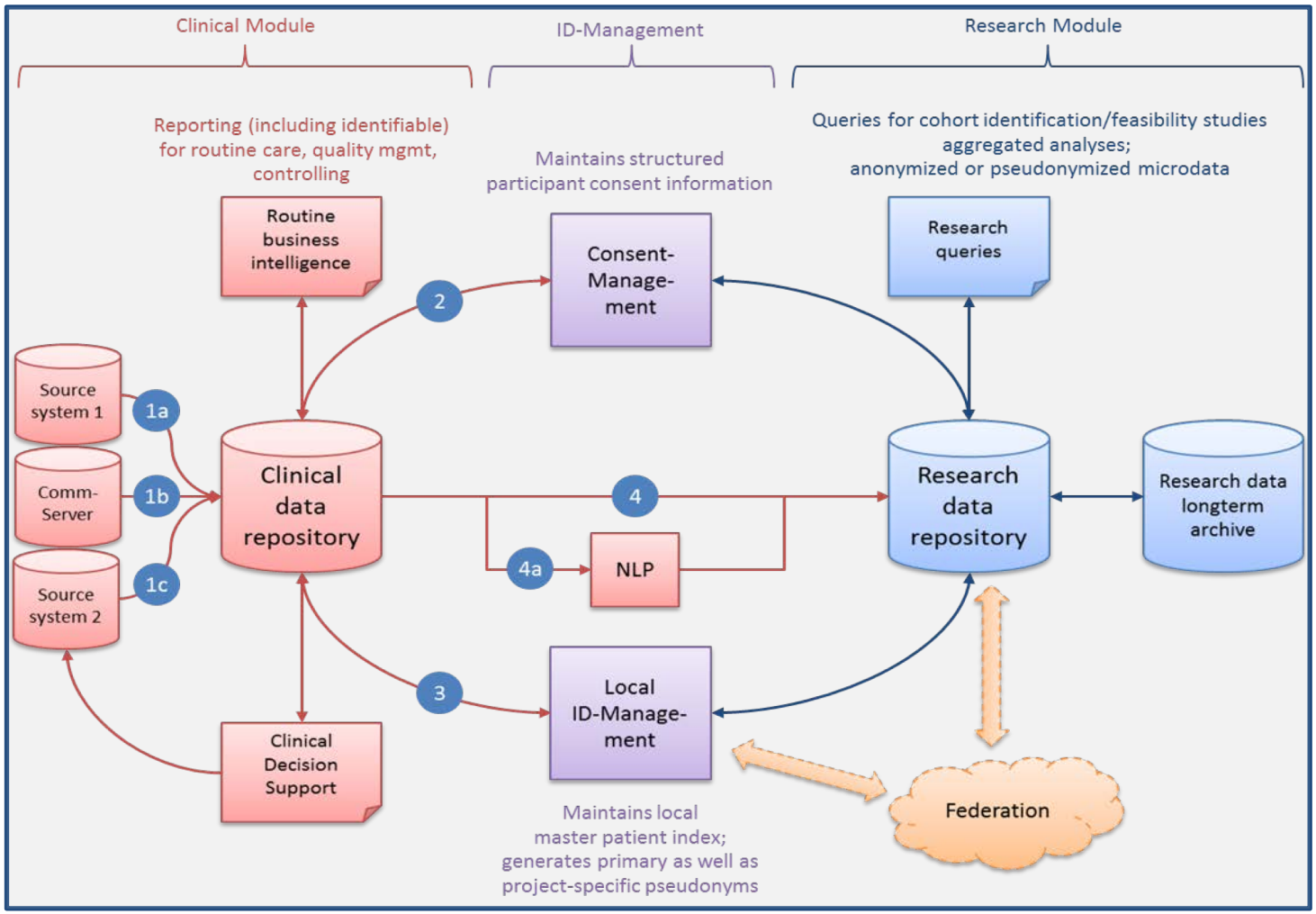
Usecases of MIRACUM

Alerting in Care	• *IT Support for Patient Recruitment* • Medical Informatics / Clinical Trials
From Data to Knowledge	• *Clinico-molecular Predictive Knowledge Tool* • Biostatistics / Prediction Models / Med. Inf.
From Knowledge to Action	• *Support for Molecular Tumor Boards* • Bioinformatics / Medical Informatics / Precision Medicine

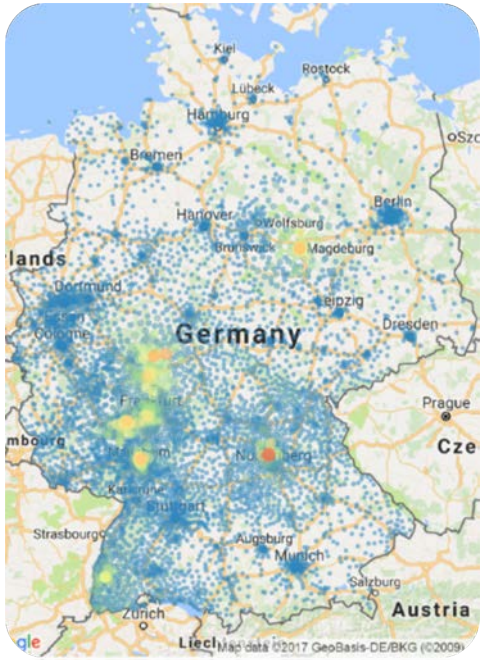
The MIRACUM ecosystem

- Medical Informatics ReusAble eCosystem of Open source Linkable and Interoperable software tools – X
  - MIRACOLIX
- MIRACOLIX is
  - pragmatic
  - modular
  - reusable
  - open source
  - interoperable
  - federated

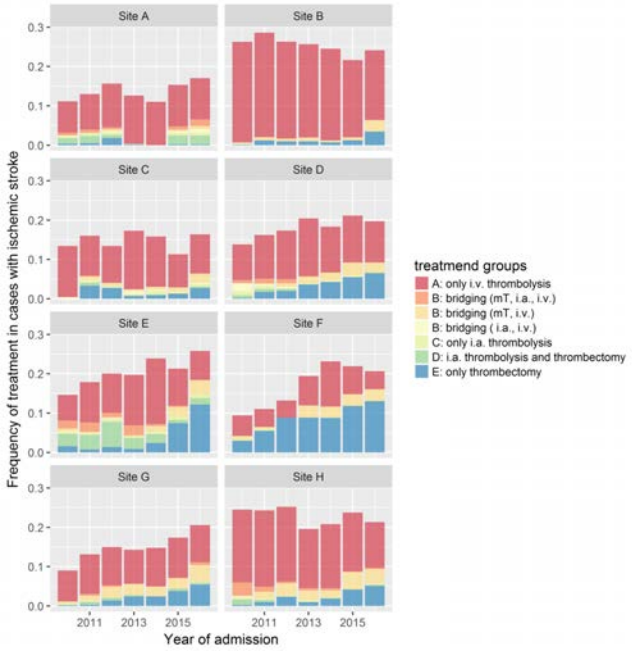
Architecture of MIRACUM Data Integration Centers



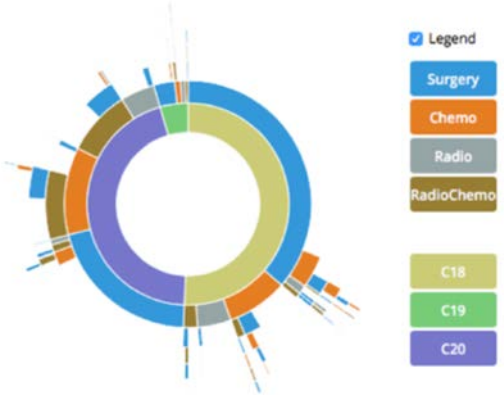
Example: Feasibility



Catchment Area of MIRACUM Partners



Application of Thrombectomy over Time



Treatment of Colorectal Cancer

- 3,3 Mio Patients
- 30 Mio Diagnoses
- 23 Mio Procedures

- Haverkamp Ch, Gansland T, Horki P, Boeker M, Dörfler A, Schwab S, Berkefeld J, Pfeilschifter W, Niesen W-D, Egger K, Kaps M, Brockmann M, Neumaier-Probst E, Szabo K, Skalej M, Bien S, Best C, Prokosch U, Urbach H. Regional differences in thrombectomy rates: Secondary use of Billing Codes in the MIRACUM Consortium. Clin Neuroradiol 2018 Jan 8
- Maier C, Lang H, Storf H, Vormstein P, Bieber R, Bernarding J, Herrmann T, Haverkamp C, Horki P, Laufer J, Berger F, Höning G, Fritsch HW, Schüttler J, Ganslandt T, Prokosch HU, Sedlmayr M: Towards implementation of OMOP in a German university hospital consortium. Applied clinical informatics 9.2018,1: 54-61.

Summary

- The Medical Informatics Initiative (MI-I)
  - towards a German Health Data Network
  - Data integration centers and nationally harmonized policies
- MIRACUM is the largest consortium
  - 1/3 of all university hospitals
  - Strongly committed to open source tools
  - MIRACOLIX infrastructure
  - i2b2 & OMOP appliances provided to all partner sites and other consortia
- Harvest “low hanging fruits” by queries on the reduced basic core dataset
- Full basic core dataset planned for end of 2018
  - Finalization of the specification
  - Mapping of data (especially not annotated data)
  - National SNOMED license (not really) on the way
- Advancing MIRACOLIX with OMOP
  - Privacy preserving distributed computing
  - “omics” data and imaging data integration

MEDICAL INFORMATICS INITIATIVE GERMANY

http://www.medizininformatik-initiative.de/en

miracum
Medical Informatics for Research and Care in University Medicine

http://www.miracum.org

Thank you!

miracum
Medical Informatics for Research and Care in University Medicine

MEDIZIN INFORMATIK INITIATIVE

Federal Ministry of Education and Research

UKGM University Medical Center Giessen and Marburg
UMM Universitätsmedizin Mannheim
Universitätsmedizin Mainz
Medizinische Fakultät Mannheim der Universität Heidelberg
Universitätsklinikum Mannheim
Universitätsklinikum Erlangen
FAU Friedrich-Alexander Universität Erlangen-Nürnberg
Universitätsklinikum Freiburg
Universitätsklinikum Frankfurt Goethe-Universität
Otto von Guericke Universität Magdeburg
Justus-Liebig-Universität Giessen
Philipps Universität Marburg
THM Technische Hochschule Mittelhessen
Fachbereich Medizin Frankfurt Goethe-Universität
hochschule mannheim

Device Safety Data Network

Daniel Prieto

Associate Professor & NIHR Clinician Scientist

Oxford University, UK

CENTRE for STATISTICS in MEDICINE

NDORMS
NUFFIELD DEPARTMENT OF ORTHOPAEDICS, RHEUMATOLOGY AND MUSCULOSKELETAL SCIENCES

UNIVERSITY OF OXFORD

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

DEVICE SAFETY DATA NETWORK

Dani Prieto-Alhambra, *MD MSc(Oxf) PhD*

Associate Professor, Theme Lead for Observational Research

Centre for Statistics in Medicine, NDORMS, University of Oxford

Scope

- To study the **use** and **risk/benefit** of medical **devices,** when used in the wider community (*'as far as possible' from RCT settings/participants*)
- To develop and validate clinical and/or classification tools/algorithms for outcome prediction
- To **improve the existing methods for the analysis of routinely collected data** for the purposes above

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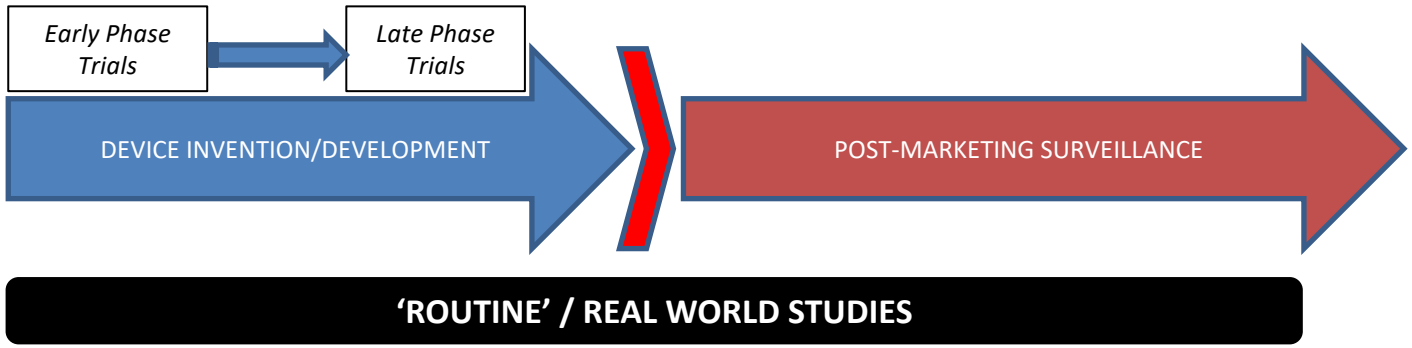
REMIT: Where does this fit?



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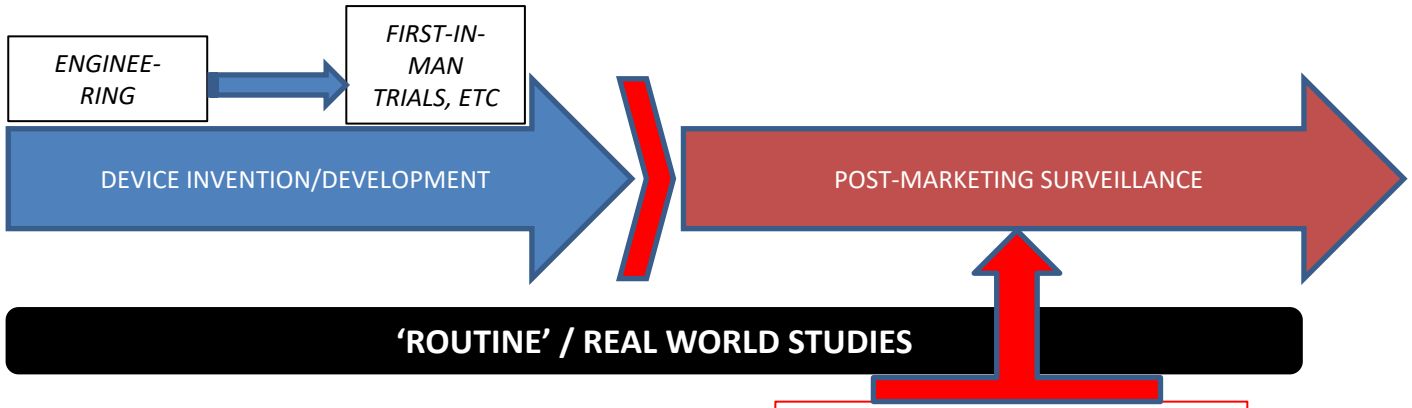
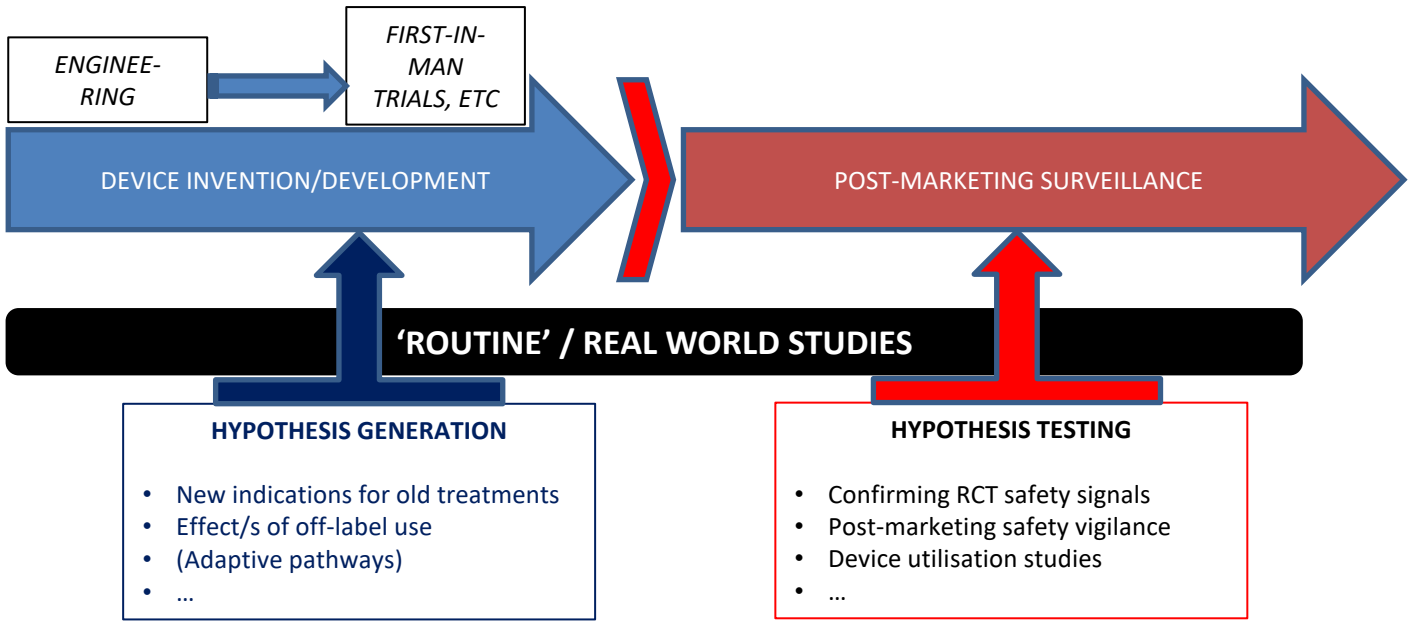


HYPOTHESIS TESTING

- Confirming RCT safety signals
- Post-marketing safety vigilance
- Device utilisation studies
- …

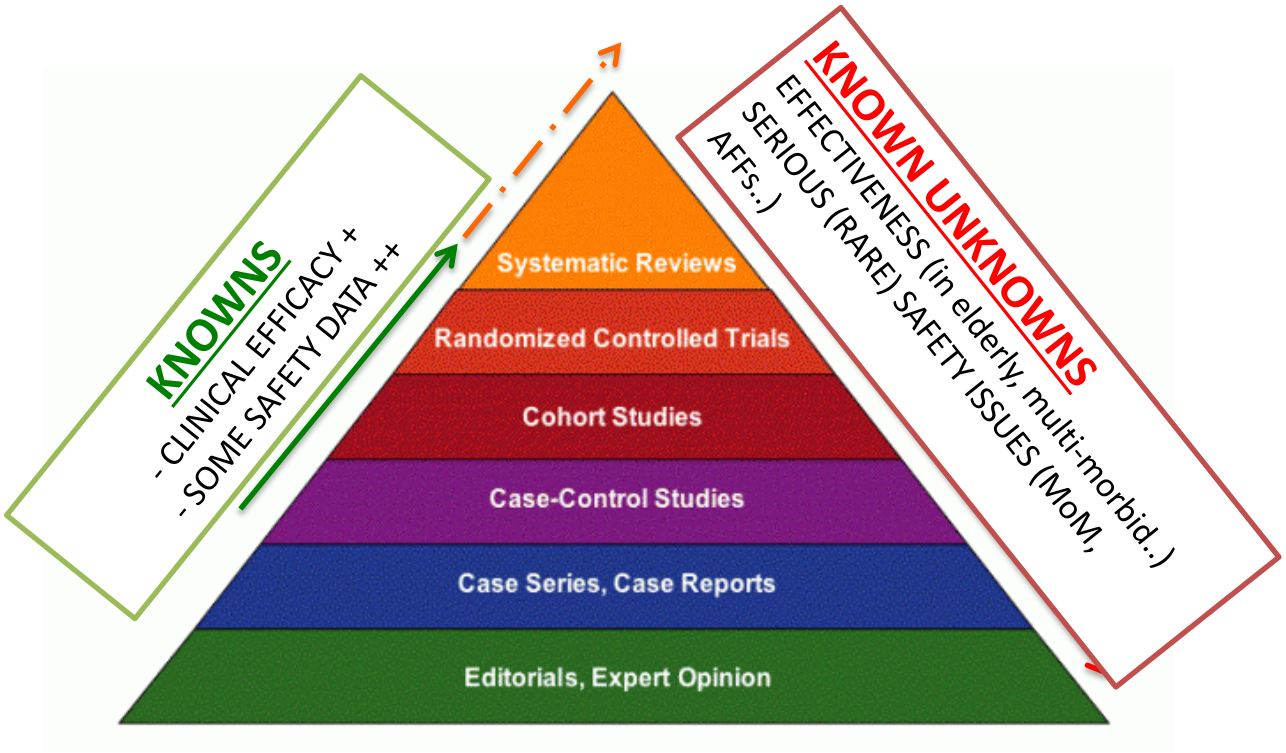
REMIT: Where does this fit?



EXPERTISE REQUIREMENTS

1. Pharmaco- and *Device Epidemiology*
2. Causal Inference Methods
3. Machine Learning & Predictive Modelling

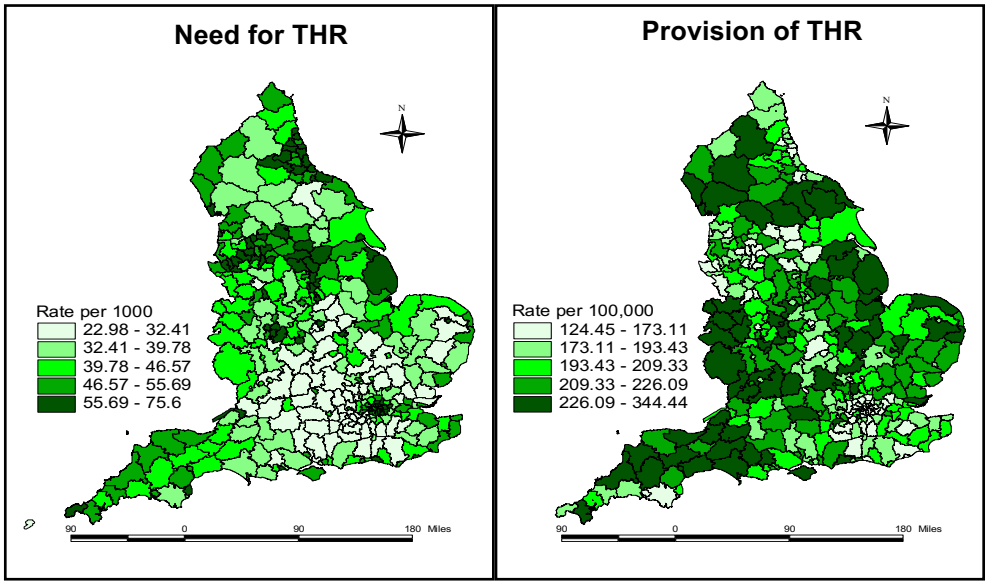
MOTIVATION: The 'KNOWN UNKNOWNS'



ORTHOPAEDIC DEVICES
(an example)

RECENT OUTPUTS
(and data used)

Outputs (1) – UK HES (hospital inpatient)
Equity: THR - Need vs Provision of care



Outputs (2) : CPRD (GP EMR)
Lifetime Risk/s of Revision vs Age

The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study

Lee E Bayliss, David Culliford, A Paul Monk, Sion Glyn-Jones, Daniel Prieto-Alhambra, Andrew Judge, Cyrus Cooper, Andrew J Carr, Nigel K Arden, David J Beard, Andrew J Price

Bayliss L et al. Lancet 2017

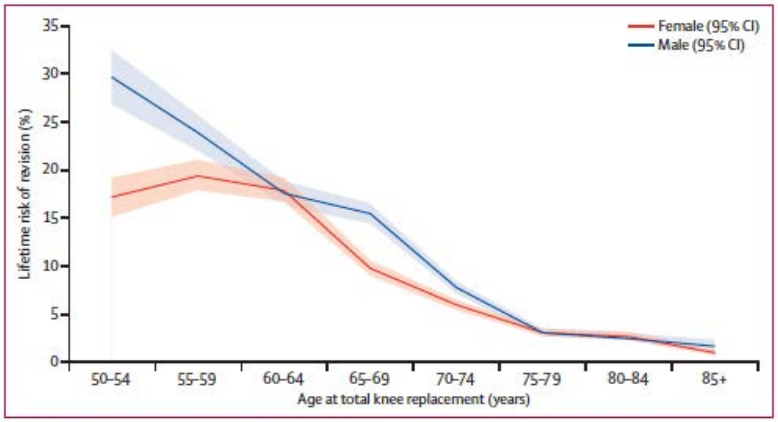
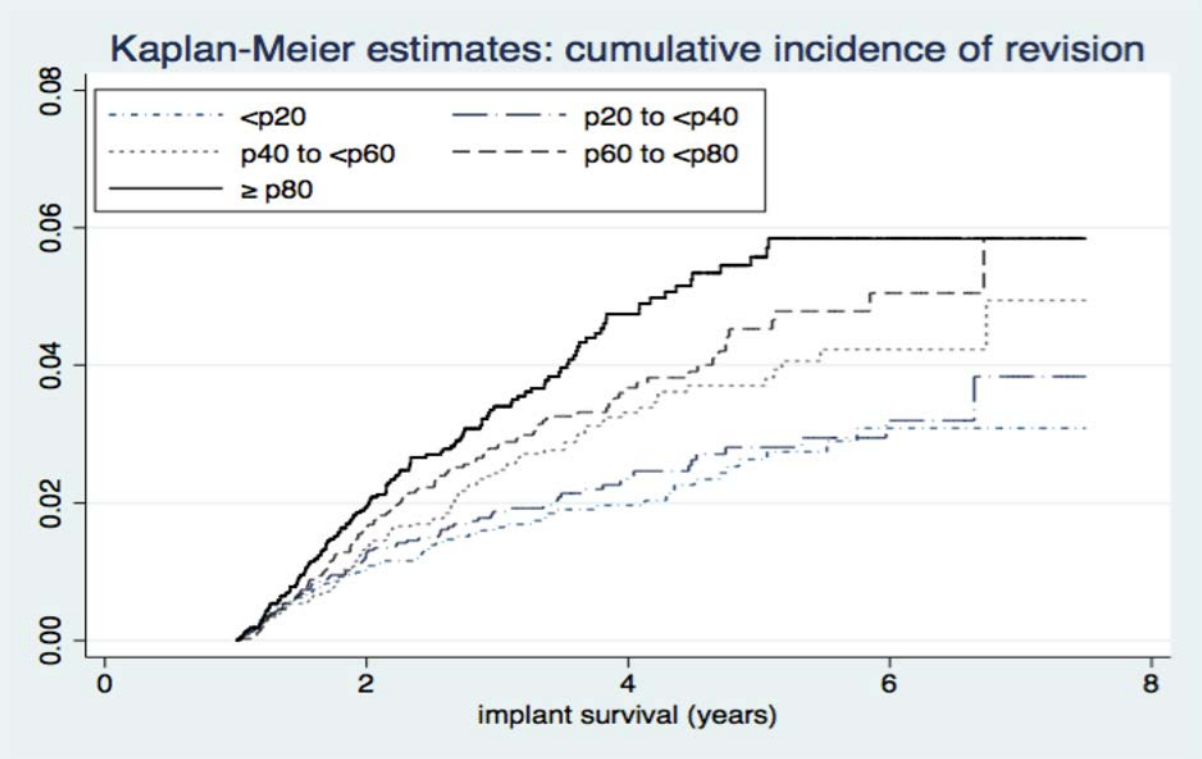


***Figure 2*: Lifetime risk of revision after total hip replacement**
Plot showing estimates of lifetime risk of total hip replacement revision against age at the time of total hip replacement primary surgery (in 5-year age bands) and stratified by sex (results adjusted for lost and censored population).

Outputs (3) – Catalan Registry + linked GP EMR (SIDIAP)
Early Surrogate/s of Implant Failure



Malak T et al.
[Unpublished]

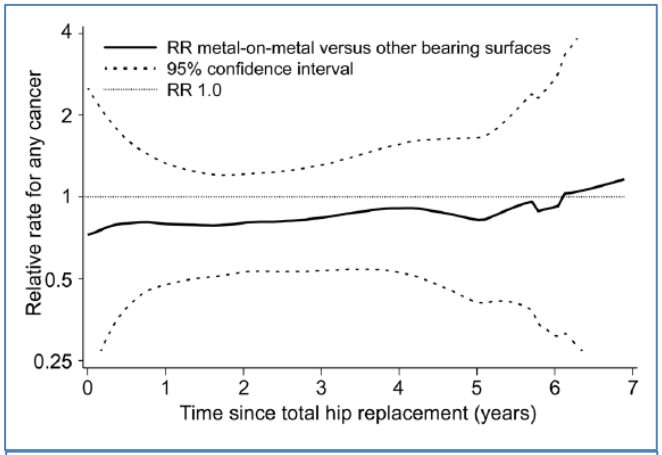
Outputs (4): UK CPRD linked to NJR Data Safety: MoM THR and Cancer Risk

	THR patients		Control patients		Compared with no THR Adjusted relative	
	n cases	rate	n cases	rate	rate (95% CI) (a)	
All total hip replacements						
Any cancer	75	1.33	611	1.82	0.74	(0.57–0.95)
By bearing surface type						
Stemmed metal-on-metal	3	0.84	29	0.94	0.80	(0.23–2.76)
Resurfacing	1	0.26	17	0.62	0.39	(0.05–3.12)
Other bearing surfaces	71	1.51	565	1.99	0.75	(0.59–0.96)
Haematological cancer	10	0.18	39	0.12	1.41	(0.67–2.98)
Malignant melanoma	1	0.02	19	0.06	0.26	(0.03–1.99)
Prostate cancer	12	0.21	62	0.18	1.14	(0.59–2.20)
Renal cancer	5	0.09	39	0.12	0.82	(0.31–2.16)
Other cancer	47	0.83	452	1.34	0.63	(0.46–0.86)

OPEN ACCESS Freely available online PLOS ONE

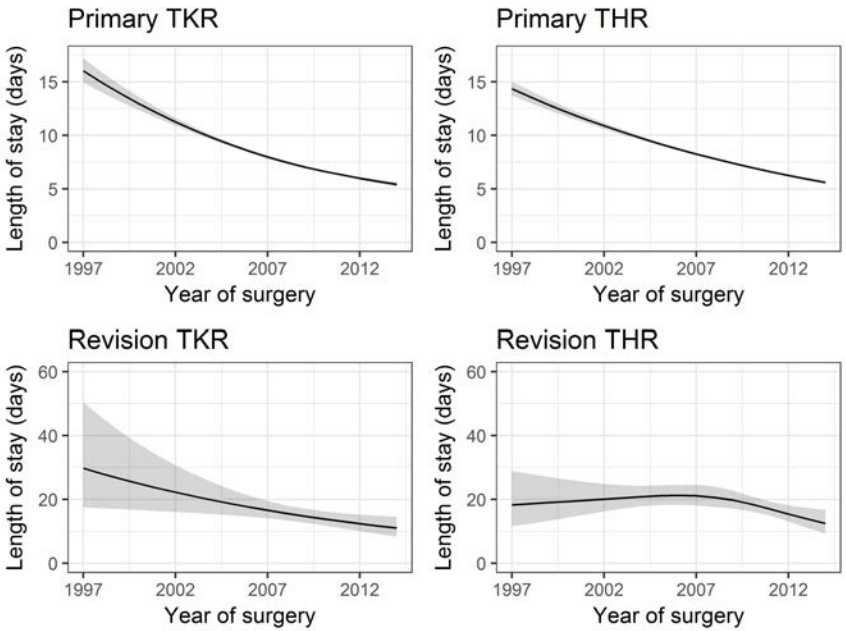
Patterns of Risk of Cancer in Patients with Metal-on-Metal Hip Replacements versus Other Bearing Surface Types: A Record Linkage Study between a Prospective Joint Registry and General Practice Electronic Health Records in England

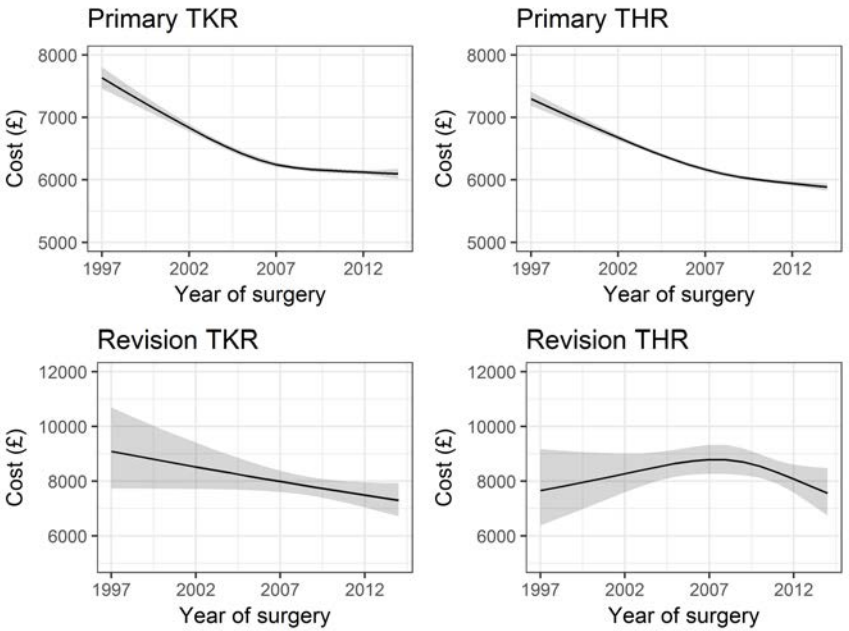
Arief Lalmohamed[1,2], Alexander J. MacGregor[3], Frank de Vries[1,4,5,6], Hubertus G. M. Leufkens[1], Tjeerd P. van Staa[1,4,7]*



CPRD/HES = non-THR controls (counter-factual)

Outputs (5) – CPRD linked to HES Health Economics





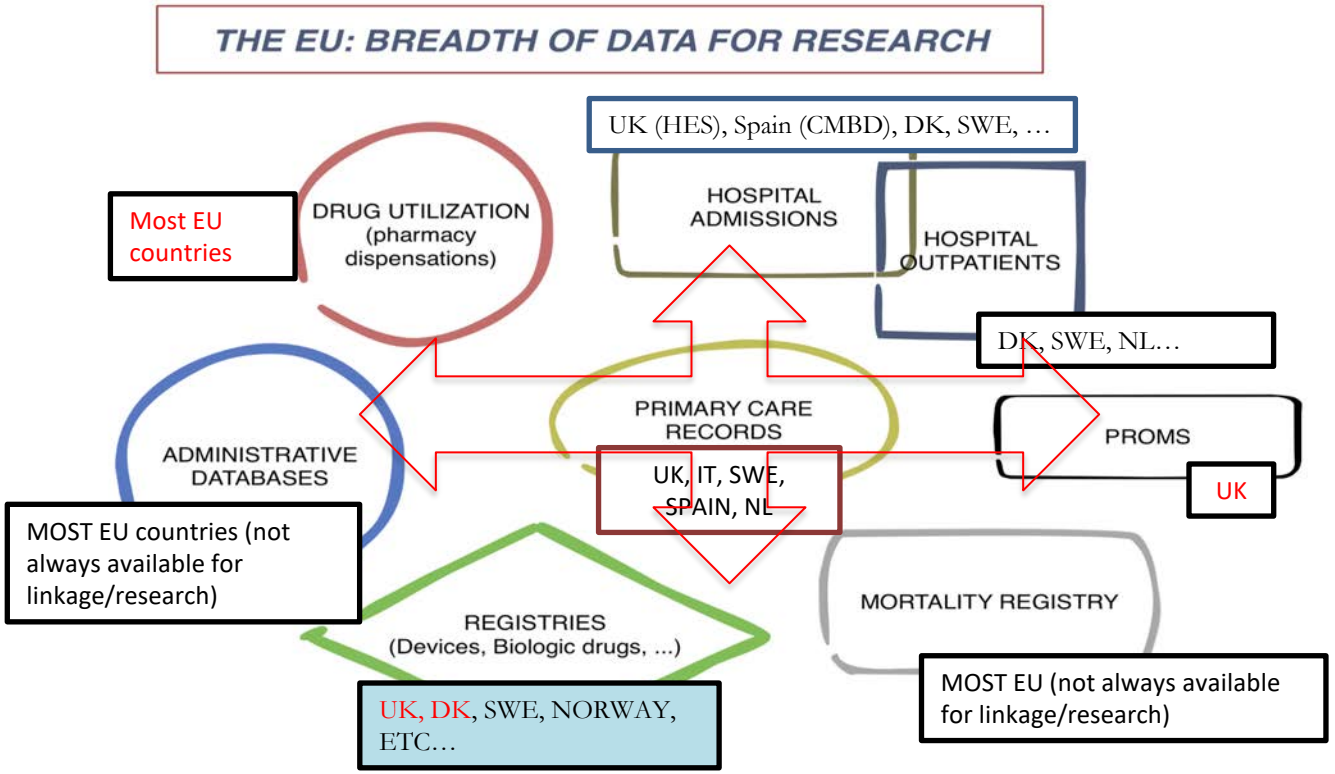
E Burn et al. BMJ Open 2017

OHDSI - TAKING THIS..
TO ANOTHER LEVEL

’Real World’ Data NEEDS

- European **Primary Care EMR**
  - Linked to Hospital Records
  - Lined to Mortality Registry/ies
- European **National Joint (Arthroplasty) Registry**
  - Linked to Hospital Records
  - Linked to Patient Reported Outcomes
- European **National Audit/s**
  - National Hip Fracture Database
  - National Trauma Database
  - National Renal Registry
  - …

EU-wide Device Registries linked to patient EMR data …



THE DREAM (OF A DEVICE EPIDEMIOLOGIST) …
*WITH A **COMMON DATA MODEL** ☺*

ONGOING WORK, AND NEXT STEPS

Uni vs Total Knee Replacement in patients with multiple co-morbidities: **UTMOST**

- UK NIHR funded project started Nov/2017, running for 2y

- Aim/s
  - To replicate an on going RCT comparing UKR vs TKR in patients eligible for the RCT (ASA Grade <3) using observational (NJR) data and methods
  - To use ‘validated’ methods to study the risk-benefit and comparative costs of UKR vs TKR in patients with high co-morbidity, not eligible for RCT (ASA 3+)

EHDEN & ERC Grant Applications (Awaiting Outcome) – AIM/s

- To create a framework for post-marketing device surveillance research, including:
  1. Mapped EU-wide EMR linked to national/local Device Registry/ies, all in the OMOP CDM
  2. Federated network of data custodians/analysts willing to contribute to such research
  3. Validated methods/analytical tools for comparative device risk-benefit and HE

CENTRE for STATISTICS in MEDICINE

NDORMS
NUFFIELD DEPARTMENT OF ORTHOPAEDICS, RHEUMATOLOGY AND MUSCULOSKELETAL SCIENCES

UNIVERSITY OF OXFORD

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

THANK YOU!

Dani Prieto-Alhambra, *MD MSc(Oxf) PhD*

Associate Professor, Theme Lead for Observational Research

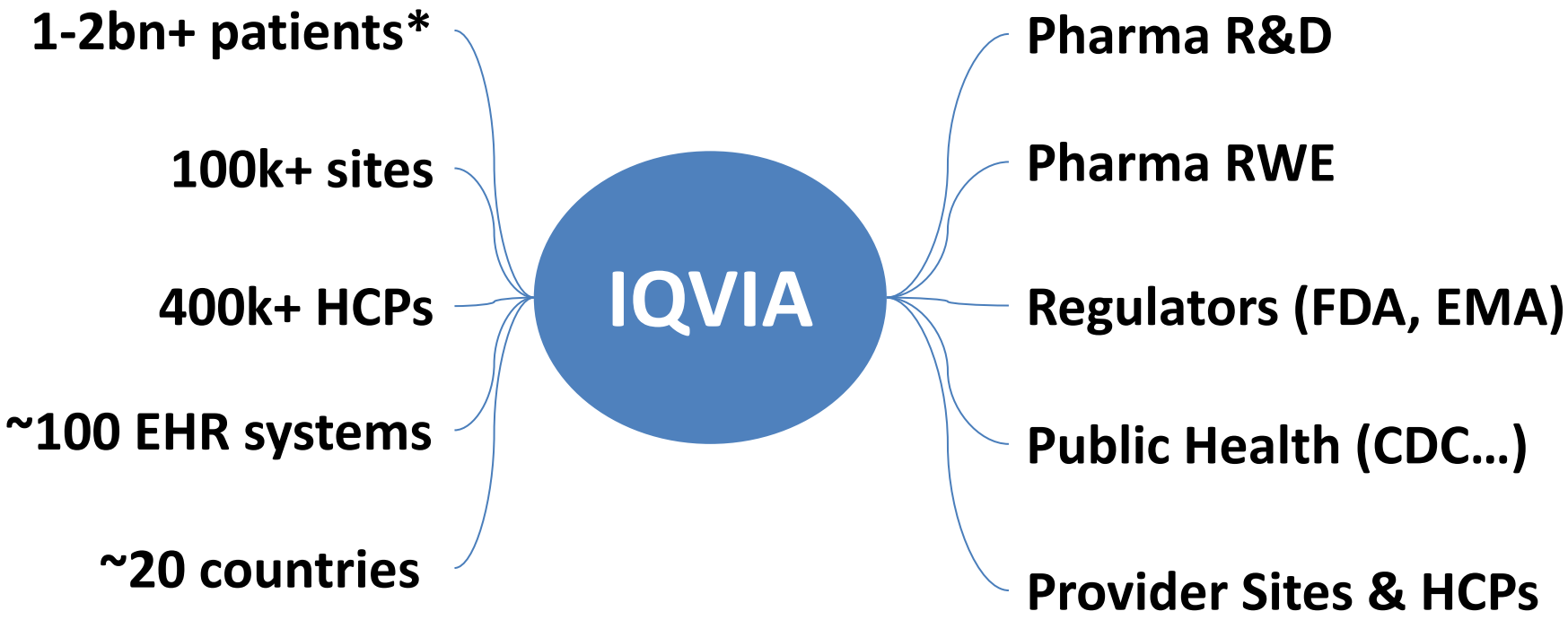
Centre for Statistics in Medicine, NDORMS, University of Oxford

NDORMS
NUFFIELD DEPARTMENT OF ORTHOPAEDICS, RHEUMATOLOGY AND MUSCULOSKELETAL SCIENCES
UNIVERSITY OF OXFORD

Adopting OMOP in IQVIA's scaled ecosystem

Dr. Benjamin Hughes, PhD, MBA, MRes, MSc
SVP, Global Head of Strategy & Technology
IQVIA Real World & Analytics Services (RWAS)

IQVIA's OHDSI context (1/2)



Global network for various organization's critical decisions
x10 next biggest organization's data ecosystem

*Fully anonymized patient level data; range indicates unique active records vs total processed

IQVIA's OHDSI journey

	# IQVIA DBs In OMOP	# trainings / hacks given	# Vocab. submitted	# network partners
2014 Workshop's with 6 clients on OMOP	2	0	0	0
2015 CEO OMOP investment approval Christian Reich joins IQVIA	4	0	2	0
2016 Build up of IQVIA OMOP team Deeping relationship with Odysseus	8	3	3	0
2017 OHDSI an independent product line FDA BEST network	12	13	5	5
2018 Expansion of network efforts Scaling of software investment	15	27	7	10

~$10m IQVIA investment in OMOP & OHDSI over 4 years

Learnings “OMOPing“ 12+ datasets

Different Healthcare Systems

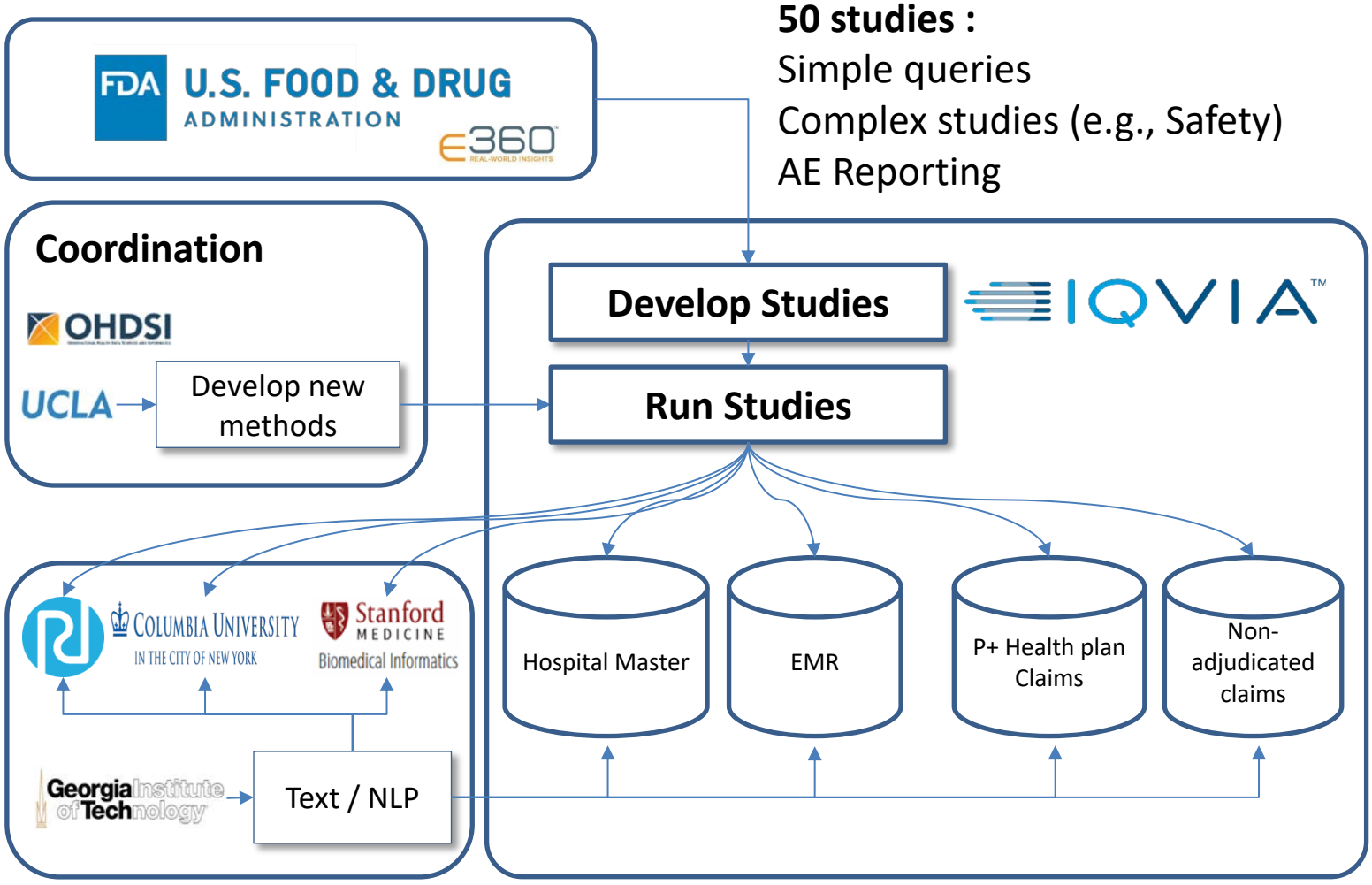
- Payers
- Healthcare institutions
- Specialties
- Visits
- Cost
- Referrals
- Prescriptions (days supply vs fixed packages)

Vocabularies

- Languages
- Drugs: only 30-50% overlap among the 100-300k products
- Conditions: ICD10≠ICD10
- Procedures: Wild west
- Lab tests: Wild west
- Units: traditional vs. SI

“OMOPing” iterative and intensive work,
with huge potential for analytics industrialization

FDA Best & Network development



Exciting developments in Surveillance & networks in general

IQVIA OMOP Status – Overall & EU

Country	Type	Patients*
FRA	IQVIA Ambulatory & Specialty EHR	14 M
GER	IQVIA Ambulatory & Specialty EHR	32 M
UK	IQVIA Ambulatory EHR	16 M
BEL	IQVIA Ambulatory EHR	1.1 M
ITA	*IQVIA Ambulatory EHR*	*2 M*
CAN	IQVIA Ambulatory EHR	1 M
AUS	IQVIA Ambulatory EHR	4 M
Global	IQVIA Oncology Survey	n/a
US	IQVIA Ambulatory EHR	38 M
US	IQVIA P+ Health claims	142 M
US	IQVIA Oncology EHR	140 K
US	MMI Specialty EHR Enhanced	350 K
US	IQVIA Hospital Charge Master	16 M
US	IQVIA Open Source claims	243 M

France validation study:

Next effort in EU (or CPRD v5? Or other client ask?)

Also engaging EU actors (e.g., EMIF / EHDN) on collaborations

***Fully anonymized patient level data**

Balanced view of where we are

Glass half full	Glass half empty
Clients: Growing # of engaged & happy	Cost: $100m+ for IQVIA to deploy fully
Partnerships: New models & partners	Adoption: difficult for most
Collaboration: community participation	Security & Privacy: not @IQVIA level
Long-term: industrialization of analytics	Networks: shared economic model

Optimistic on OMOP but with challenges to address

IQVIA path forward

Definitely

More IQVIA data conversions

Further vocab releases

OHDSI / Public interest scientific studies

Partner outreach for networks (~30 conversations)

Software investments to reduce OMOP costs

Maybe

Commercial research / consortium provider & pharma

Data nodes for general access / network studies

Privacy software for networks

IQVIA Oncology network inclusion

IQVIA ML algorithms on OMOP

Ongoing investment OMOP and iterative & collaborative approach

Adoption of the OMOP-CDM: Industry perspective of using the OMOP-CDM

23-March-2018

Erica A. Voss, MPH, PMP [1,2,3]

[1]Janssen Research and Development, Raritan, NJ, USA
[2]Observational Health Data Sciences and Informatics (OHDSI), New York, NY, USA
[3]Erasmus University Medical Center, Rotterdam, Netherlands

Who We Are

- Mission to help people everywhere live longer, healthier, happier lives.

- **3 Sectors:**
  - Consumer Products
  - Medical Devices
  - Pharmaceutical Products

- **Epidemiology's focus:** generating ***real world evidence*** that will benefit patients and consumers who use our company's products every day

Opportunities for Real World Evidence across Research & Development

- Disease natural history
- Treatment pathways
- Safety Surveillance
- Comparative effectiveness
- Prediction Modeling

Many questions types with global products requires **lots of different types of data**

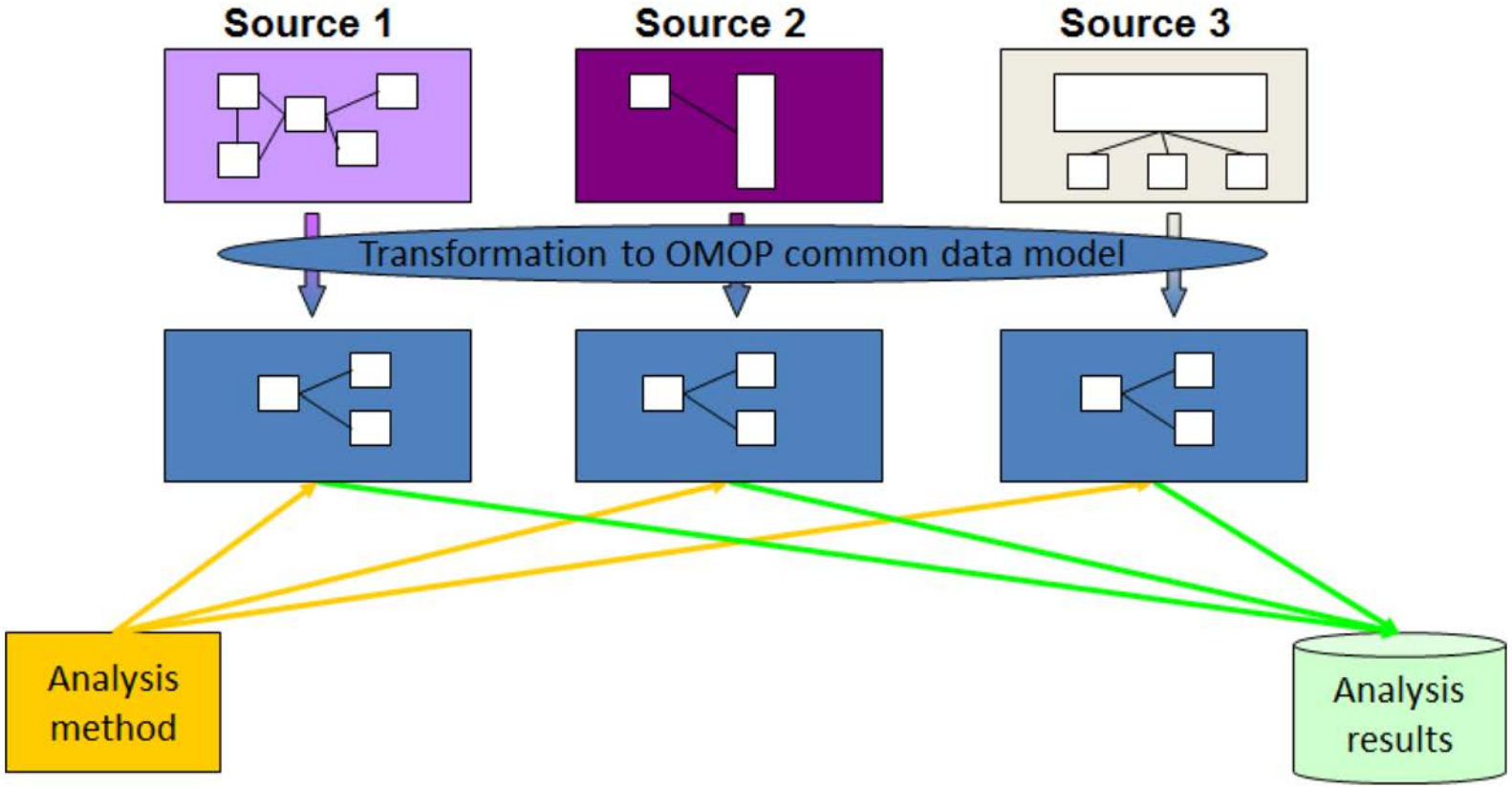
Insurance Claims	Medical Records	Hospital	Other
Optum Clinformatics	Optum Pan-Therapeutic	Premier	NHANES
Truven MarketScan Commercial	CPRD	HCUP	Registries
Truven MarketScan Medicare Suppl	IMS EMR Australia	Cerner HealthFacts	SEER Medicare
Truven MarketScan Medicaid	IMS DA France		
JMDC	IMS DA Germany		

In total, Janssen Epidemiology Analytics conducts research on more than 400+ million patient records from across US, Europe and Asia-Pacific

Strategy to Achieve This?

Standardized Data

Standardized Analysis



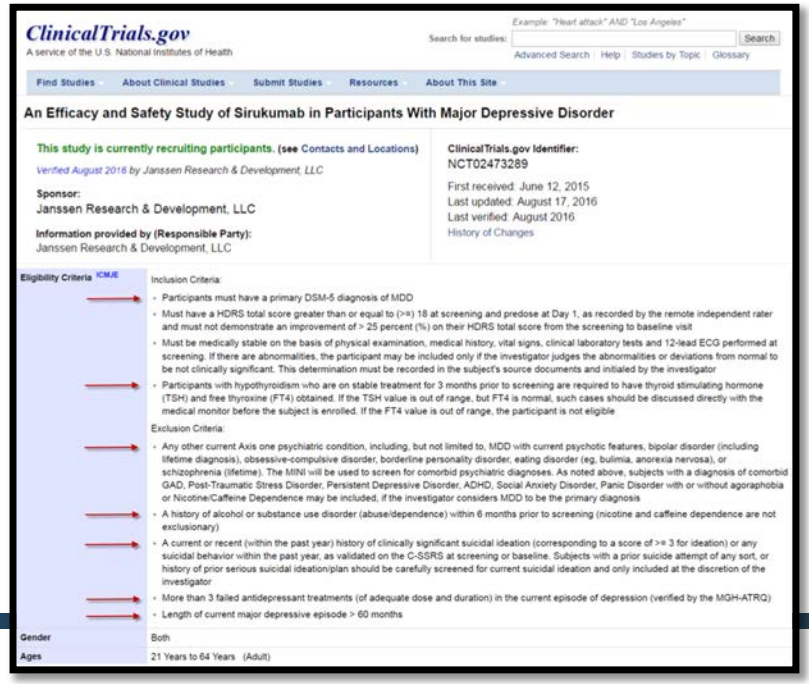
Use Case: Cohort Identification

Using OHDSI tools to conduct clinical trial feasibility

Rupa Makadia, MS[1,2], Jamie B. Forlenza[1], PharmD, MS[1], Frank J. DeFalco[1,2], Chris Knoll[1,2], Patrick B. Ryan, PhD[1,2,3]

[1]Janssen Research & Development, LLC, Titusville, NJ [2]OHDSI collaborators, Observational Health Data Sciences and Informatics (OHDSI), New York, NY [3]Columbia University, New York, NY

1. Protocol evaluated
2. Concept sets created in ATLAS
3. Inclusion rules created in ATLAS
4. Results generated in ATLAS on databases
5. Results shared with clinical teams



ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Search for studies: Search

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

An Efficacy and Safety Study of Sirukumab in Participants With Major Depressive Disorder

This study is currently recruiting participants. (see Contacts and Locations)

Verified August 2016 by Janssen Research & Development, LLC

Sponsor:
Janssen Research & Development, LLC

Information provided by (Responsible Party):
Janssen Research & Development, LLC

ClinicalTrials.gov Identifier:
NCT02473289

First received: June 12, 2015
Last updated: August 17, 2016
Last verified: August 2016
History of Changes

Eligibility Criteria

Inclusion Criteria:

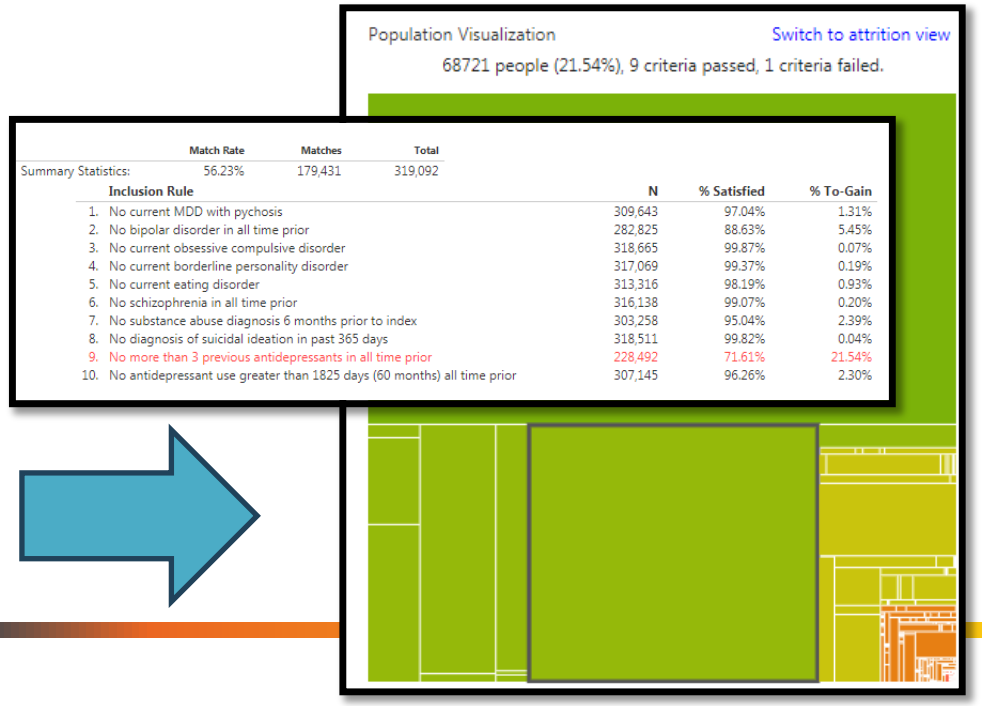
- Participants must have a primary DSM-5 diagnosis of MDD
- Must have a HDRS total score greater than or equal to (>=) 18 at screening and predose at Day 1, as recorded by the remote independent rater and must not demonstrate an improvement of > 25 percent (%) on their HDRS total score from the screening to baseline visit
- Must be medically stable on the basis of physical examination, medical history, vital signs, clinical laboratory tests and 12-lead ECG performed at screening. If there are abnormalities, the participant may be included only if the investigator judges the abnormalities or deviations from normal to be not clinically significant. This determination must be recorded in the subject's source documents and initialed by the investigator
- Participants with hypothyroidism who are on stable treatment for 3 months prior to screening are required to have thyroid stimulating hormone (TSH) and free thyroxine (FT4) obtained. If the TSH value is out of range, but FT4 is normal, such cases should be discussed directly with the medical monitor before the subject is enrolled. If the FT4 value is out of range, the participant is not eligible

Exclusion Criteria:

- Any other current Axis one psychiatric condition, including, but not limited to, MDD with current psychotic features, bipolar disorder (including lifetime diagnosis), obsessive-compulsive disorder, borderline personality disorder, eating disorder (eg, bulimia, anorexia nervosa), or schizophrenia (lifetime). The MINI will be used to screen for comorbid psychiatric diagnoses. As noted above, subjects with a diagnosis of comorbid GAD, Post-Traumatic Stress Disorder, Persistent Depressive Disorder, ADHD, Social Anxiety Disorder, Panic Disorder with or without agoraphobia or Nicotine/Caffeine Dependence may be included, if the investigator considers MDD to be the primary diagnosis
- A history of alcohol or substance use disorder (abuse/dependence) within 6 months prior to screening (nicotine and caffeine dependence are not exclusionary)
- A current or recent (within the past year) history of clinically significant suicidal ideation (corresponding to a score of >= 3 for ideation) or any suicidal behavior within the past year, as validated on the C-SSRS at screening or baseline. Subjects with a prior suicide attempt of any sort, or history of prior serious suicidal ideation/plan should be carefully screened for current suicidal ideation and only included at the discretion of the investigator
- More than 3 failed antidepressant treatments (of adequate dose and duration) in the current episode of depression (verified by the MGH-ATRQ)
- Length of current major depressive episode > 60 months

Gender: Both

Ages: 21 Years to 64 Years (Adult)



Population Visualization — Switch to attrition view

68721 people (21.54%), 9 criteria passed, 1 criteria failed.

	Match Rate	Matches	Total
Summary Statistics:	56.23%	179,431	319,092

	Inclusion Rule	N	% Satisfied	% To-Gain
1.	No current MDD with pychosis	309,643	97.04%	1.31%
2.	No bipolar disorder in all time prior	282,825	88.63%	5.45%
3.	No current obsessive compulsive disorder	318,665	99.87%	0.07%
4.	No current borderline personality disorder	317,069	99.37%	0.19%
5.	No current eating disorder	313,316	98.19%	0.93%
6.	No schizophrenia in all time prior	316,138	99.07%	0.20%
7.	No substance abuse diagnosis 6 months prior to index	303,258	95.04%	2.39%
8.	No diagnosis of suicidal ideation in past 365 days	318,511	99.82%	0.04%
9.	No more than 3 previous antidepressants in all time prior	228,492	71.61%	21.54%
10.	No antidepressant use greater than 1825 days (60 months) all time prior	307,145	96.26%	2.30%

Use Case: Population-Level Effect Estimation

DIABETES, OBESITY AND METABOLISM
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

Open Access Creative

ORIGINAL ARTICLE

Risk of lower ext
diabetes mellitus
transporter-2 inh
study

Zhong Yuan MD, PhD,
Martijn J. Schuemie PhD,
Norm Rosenthal MD

3.3 | Comparative analysis

Of the 72 797 users of canagliflozin and 225 627 users of non-SGLT2 inhibitor AHAs with no history of BKLE amputation and ≥1 day at risk who were eligible for inclusion in the comparative analysis, 63 845 pairs were formed based on matching of EPS (Figure 1). All baseline characteristics were well balanced after EPS matching (Figure 2), and patient demographics (age and sex), key comorbid conditions (including CV disease) and medications of interest (eg, commonly reported in patients with T2DM) for the treatment cohorts are presented in Table 2. The median (interquartile range [IQR]) duration of index therapy was 0.43 (0.17, 0.94) years with canagliflozin

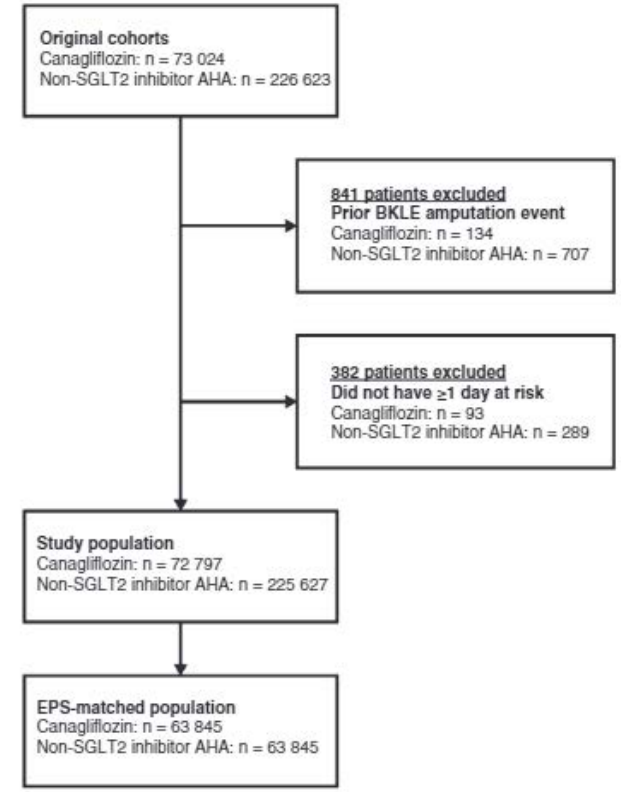


FIGURE 1 Attrition diagram for the comparative analysis

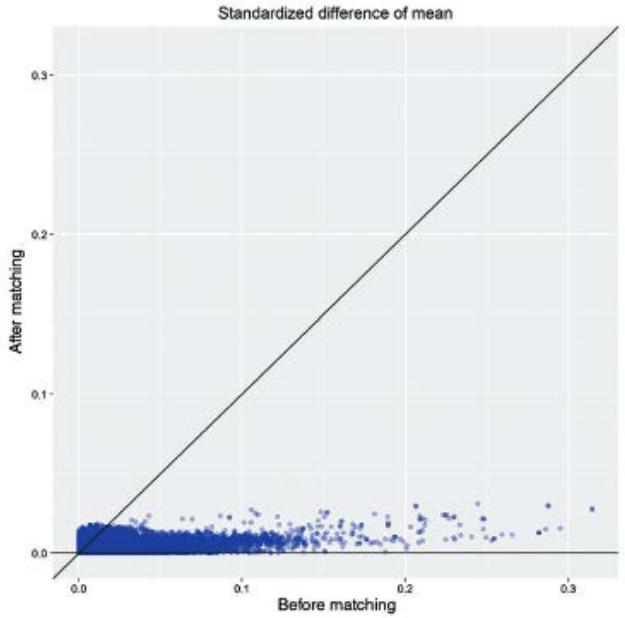


FIGURE 2 Diagnostics of EPS matching performance

Use Case: Patient-Level Prediction

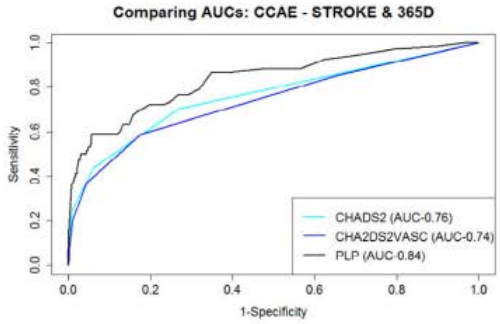
Journal of Stroke and Cerebrovascular Diseases
Volume 26, Issue 8, August 2017, Pages 1721-1731

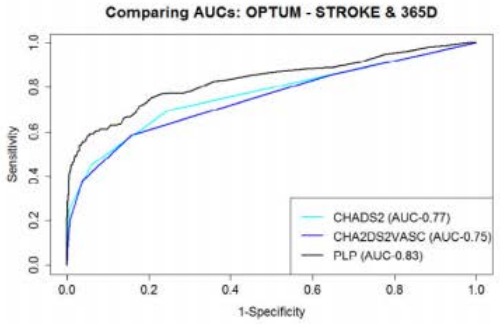
Risk Prediction for Ischemic Stroke and Transient Ischemic Attack in Patients Without Atrial Fibrillation: A Retrospective Cohort Study

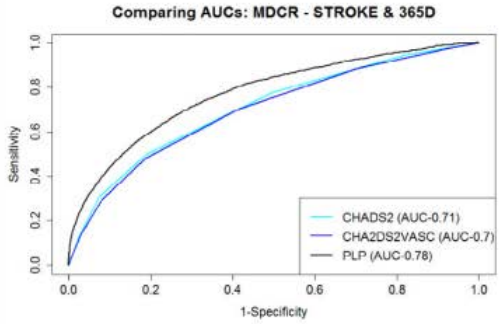
Zhong Yuan MD, PhD* ✉
PhD*, Daniel Yannicelli MD

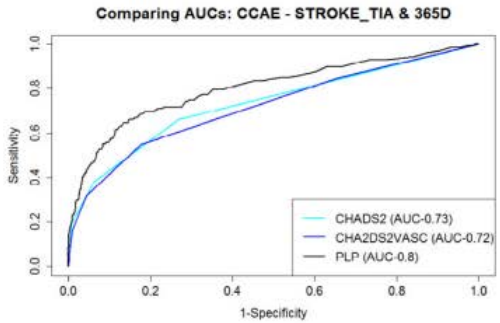
A

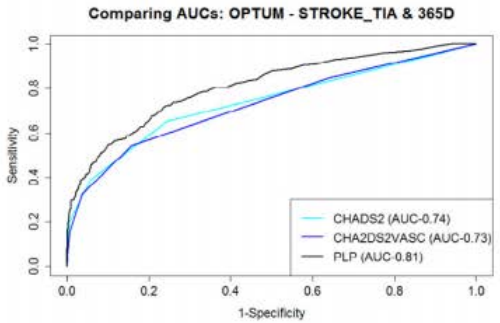
CCAE	OPTUM	MDCR

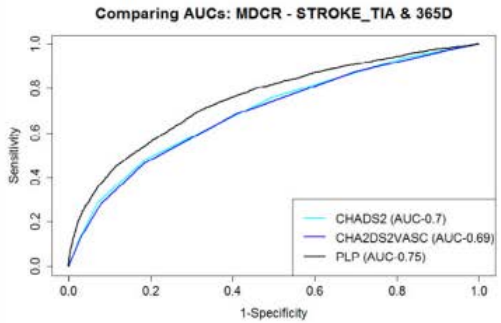












OMOP CDM and OHDSI are Critical to our Success

- Real world data:
  - increasingly important part of evidence generation
  - working with data takes substantial investment

- Our experience investing in OMOP / OHDSI has a strong return; **the more we invest the more we get out of it**

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

A Mental Health Data Platform

Simon Lovestone

Professor of Translational Neuroscience

Oxford University, UK

Clinical Records Interactive Search (CRIS)

- Mental Health and Dementia clinical services in the UK and the benefits of being Cinderella!
- Generating access for research
- OMOP and future directions

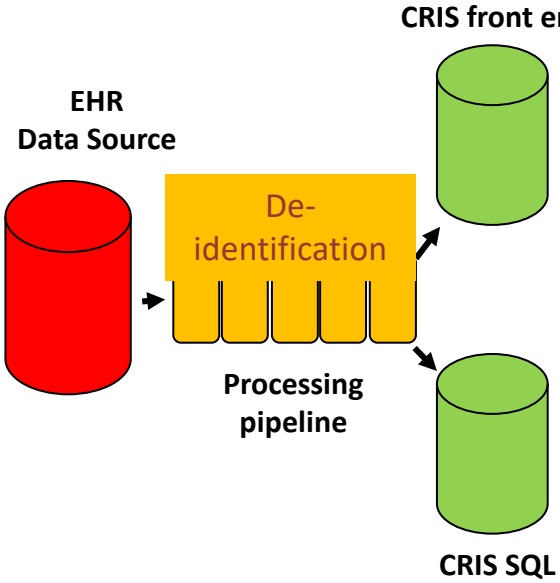
Clinical Records Interactive Search (CRIS)

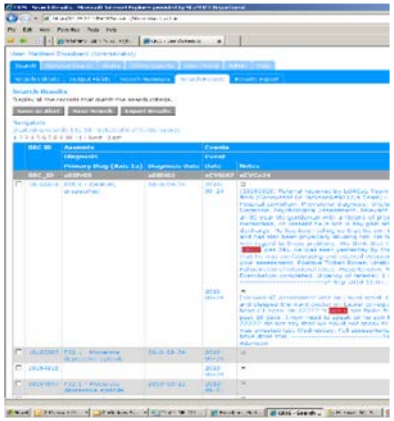
- SLaM CRIS
  - South London and Maudsley NHS BRC implementation
- D-CRIS
  - Cambridge & Peterborough, Oxford Health, West London, Camden and Islington
  - 1 million plus patients
- UK-CRIS
  - 10 site extension
  - Connectivity to UK BioBank

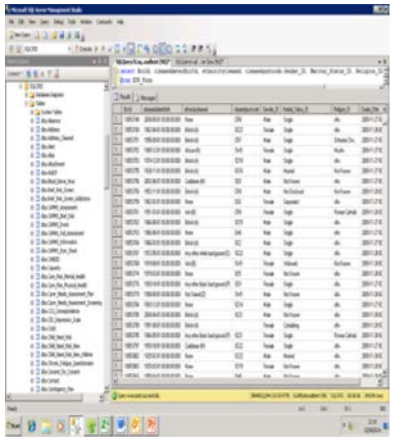
Mike Denis and Simon Lovestone

Dementias Platform UK
Medical Research Council

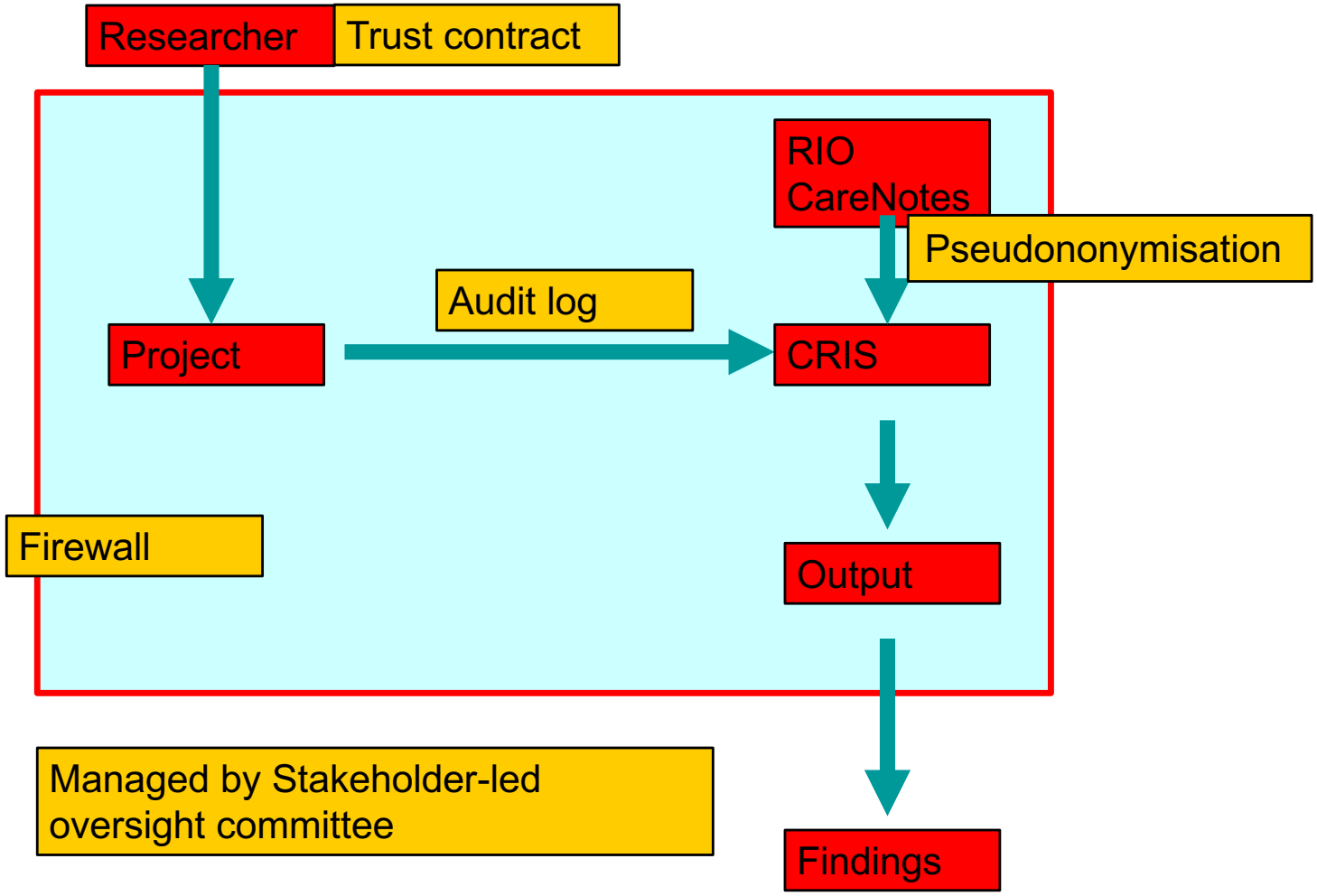
CRIS – core functionality







CRIS Security



Deriving information from data

FAST enables **information retrieval**, i.e. search and retrieval by matching against user defined strings;

GATE enables **information extraction**, i.e. extracts ‘meaning’ (structure) from free text context

Neural Networks for **advanced and automated** search and extraction for data exploration

EHR-data re-use for research (Cholinesterase inhibitors and Alzheimer's disease)

- Phase IV of AChEI

  > 2500 patient years of therapy

  > 8 fold dataset compared to Cochrane

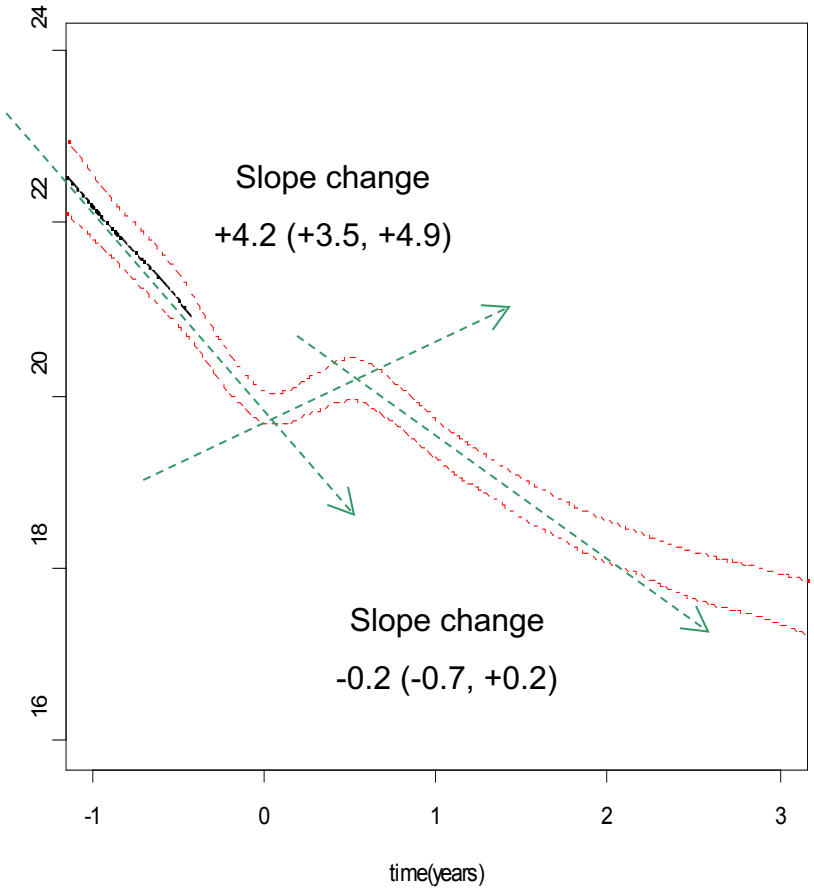
- Costs and effectiveness

  precompetitive collaboration with pharma

  Text mining derivation of service utilisation and costs

- Predictors of response

  Biomarkers and clinical

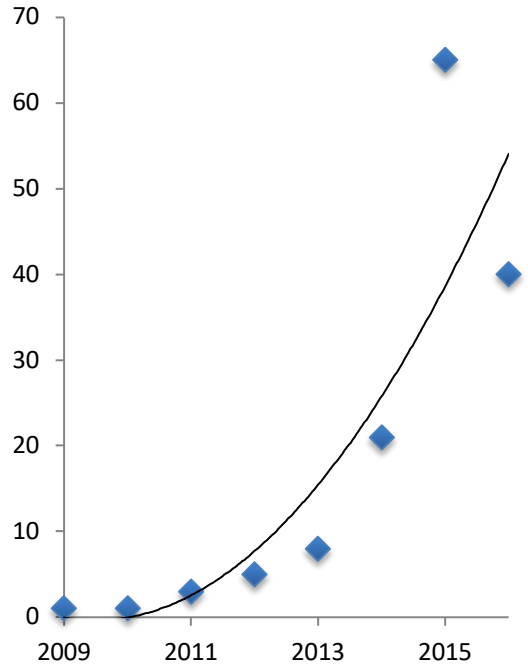


Data from Robert Stewart, KCL

Real world data reutilisation for research

- EMIF publications
  - http://www.emif.eu/results
    - or search EMIF EU references
  - > 85 papers 2012-2017

- CRIS publications
  - http://www.maudsleybrc.nihr.ac.uk/facilities/clinical-record-interactive-search-cris/cris-publications/
    - or search CRIS BRC references
  - > 65 papers 2009-2017



National Clinical Records Interactive Search (UK- CRIS)

14

NHS Mental Health Trusts across the UK

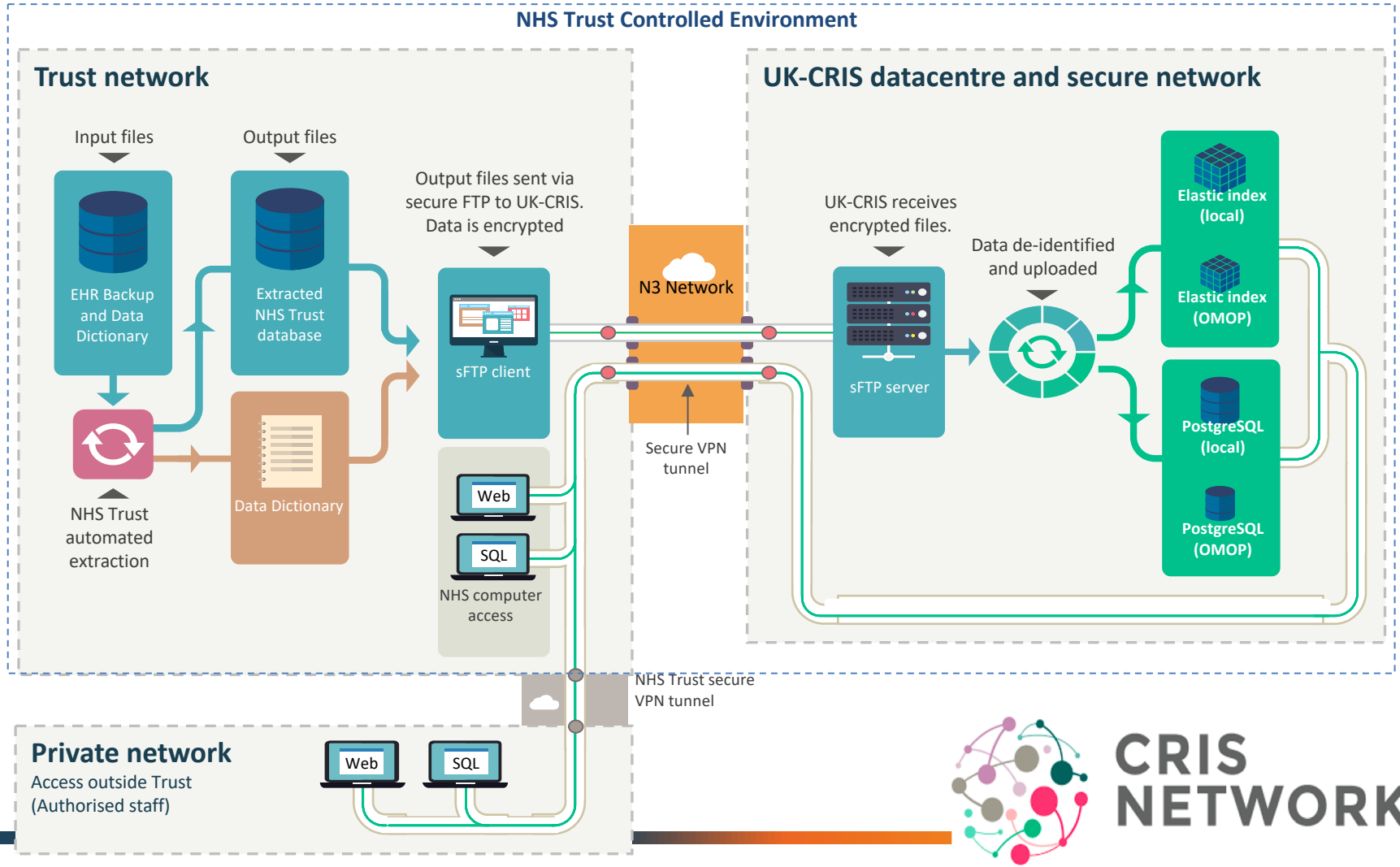
2.5m+

De-identified electronic patient records

1. Avon and Wiltshire Mental Health Partnership NHS Trust
2. Cambridgeshire and Peterborough NHS Foundation Trust
3. Camden and Islington NHS Foundation Trust
4. Devon Partnership NHS Trust
5. Kent and Medway NHS and Social Care Partnership Trust
6. Mersey Care NHS Foundation Trust
7. North East London Foundation Trust
8. Nottinghamshire Healthcare NHS Foundation Trust
9. Northumberland, Tyne and Wear NHS Foundation Trust
10. Oxford Health NHS Foundation Trust
11. Southern Health NHS Foundation Trust
12. South London and Maudsley NHS Foundation Trust
13. South West London and St George's NHS Foundation Trust
14. West London Mental Health NHS Trust

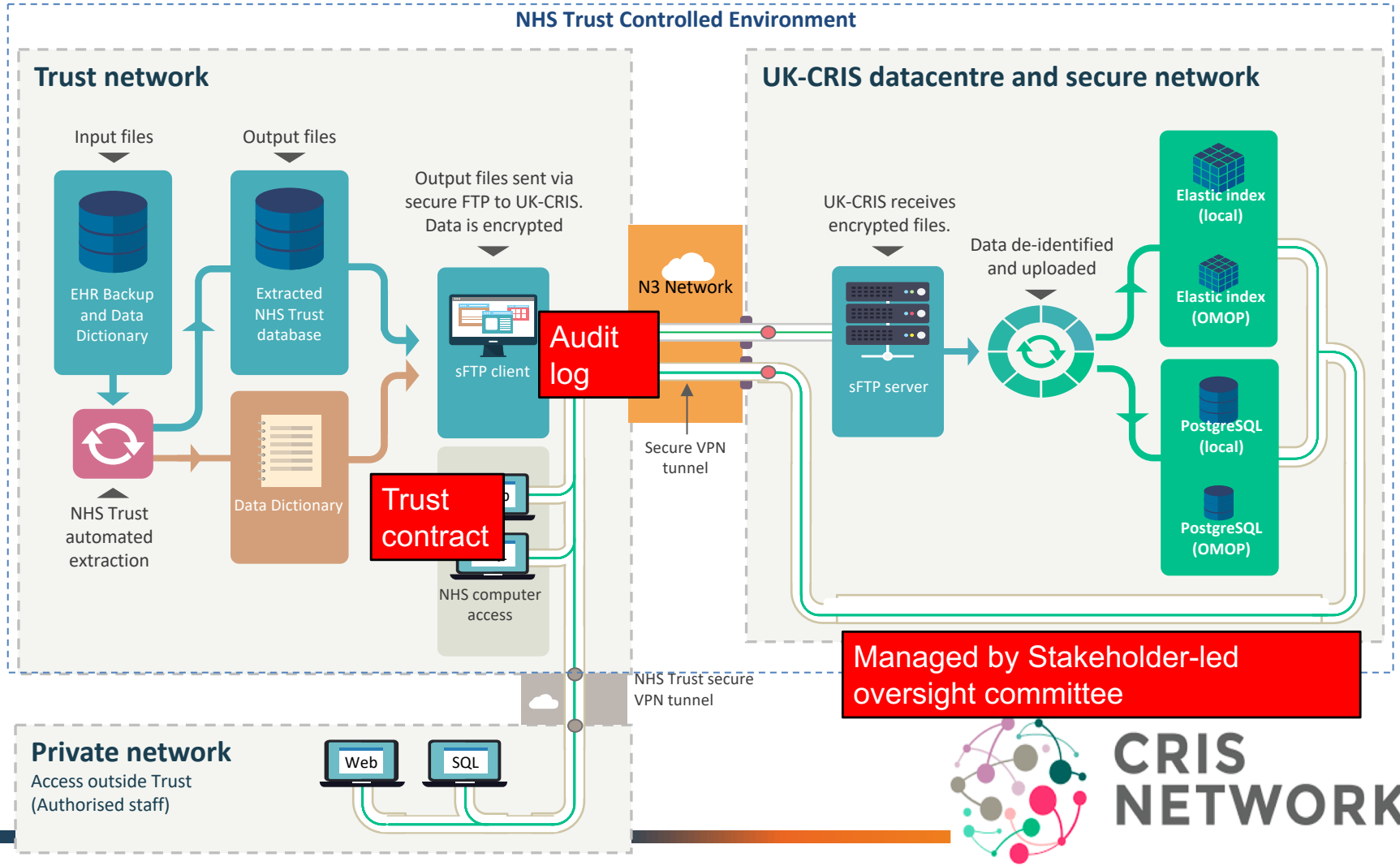
CRIS NETWORK

UK-CRIS: safe, secure and ***complete***



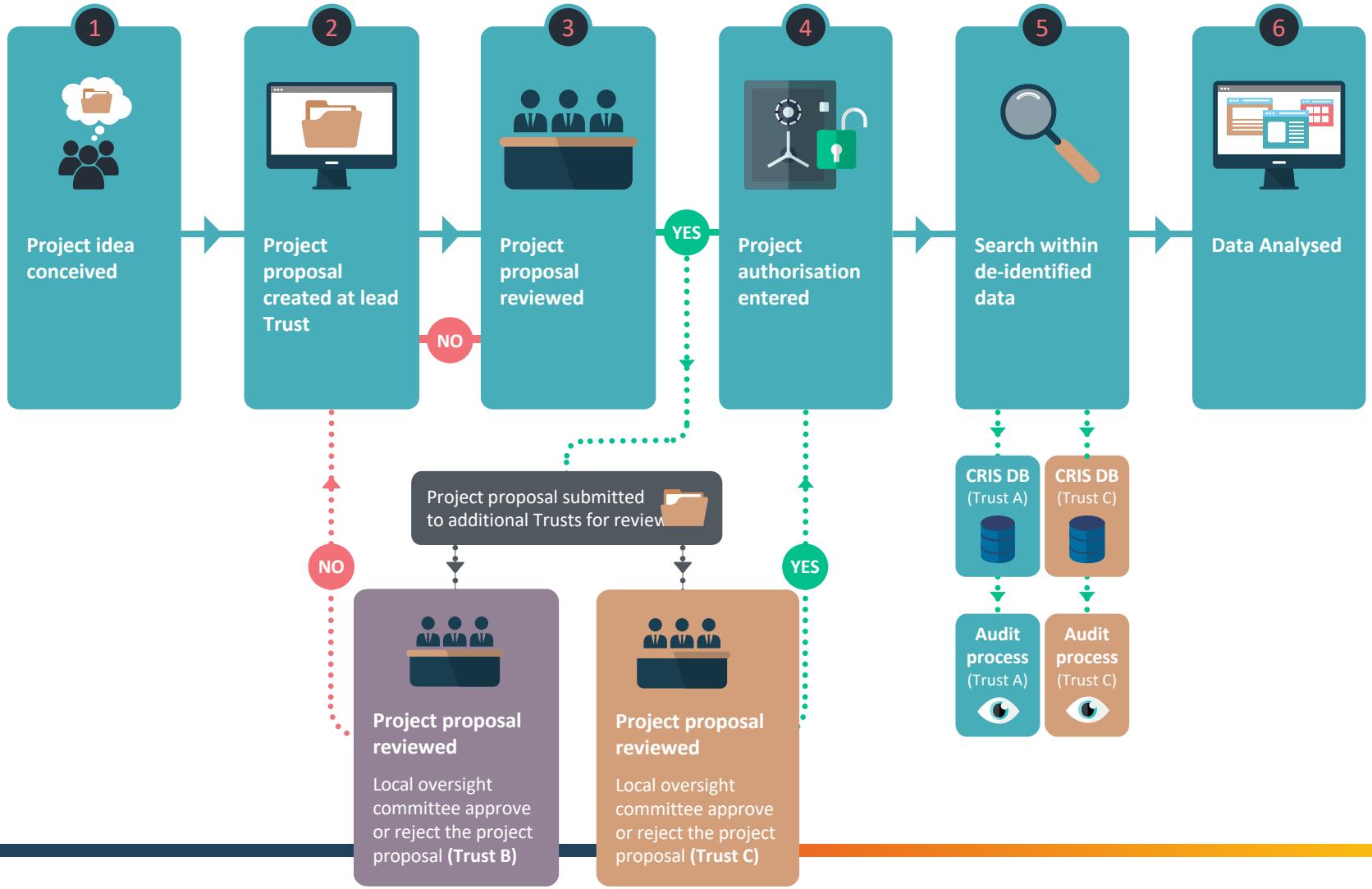
CRIS NETWORK

UK-CRIS: safe, secure and ***complete***



CRIS NETWORK

Federated access studies



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UK Biobank is a national and international health resource with unparalleled research opportunities, open to all bona fide health researchers. UK Biobank aims to improve the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses – including cancer, heart diseases, stroke, diabetes, arthritis, osteoporosis, eye disorders, depression and forms of dementia. It is following the health and well-being of 500,000 volunteer participants and provides health information, which does not identify them, to approved researchers in the UK and overseas, from academia and industry. Scientists, please ensure you read the background materials before registering. To our participants, we say thank you for supporting this important resource to improve health. Without you, none of the research featured on this website would be possible.

Read more about Biobank UK

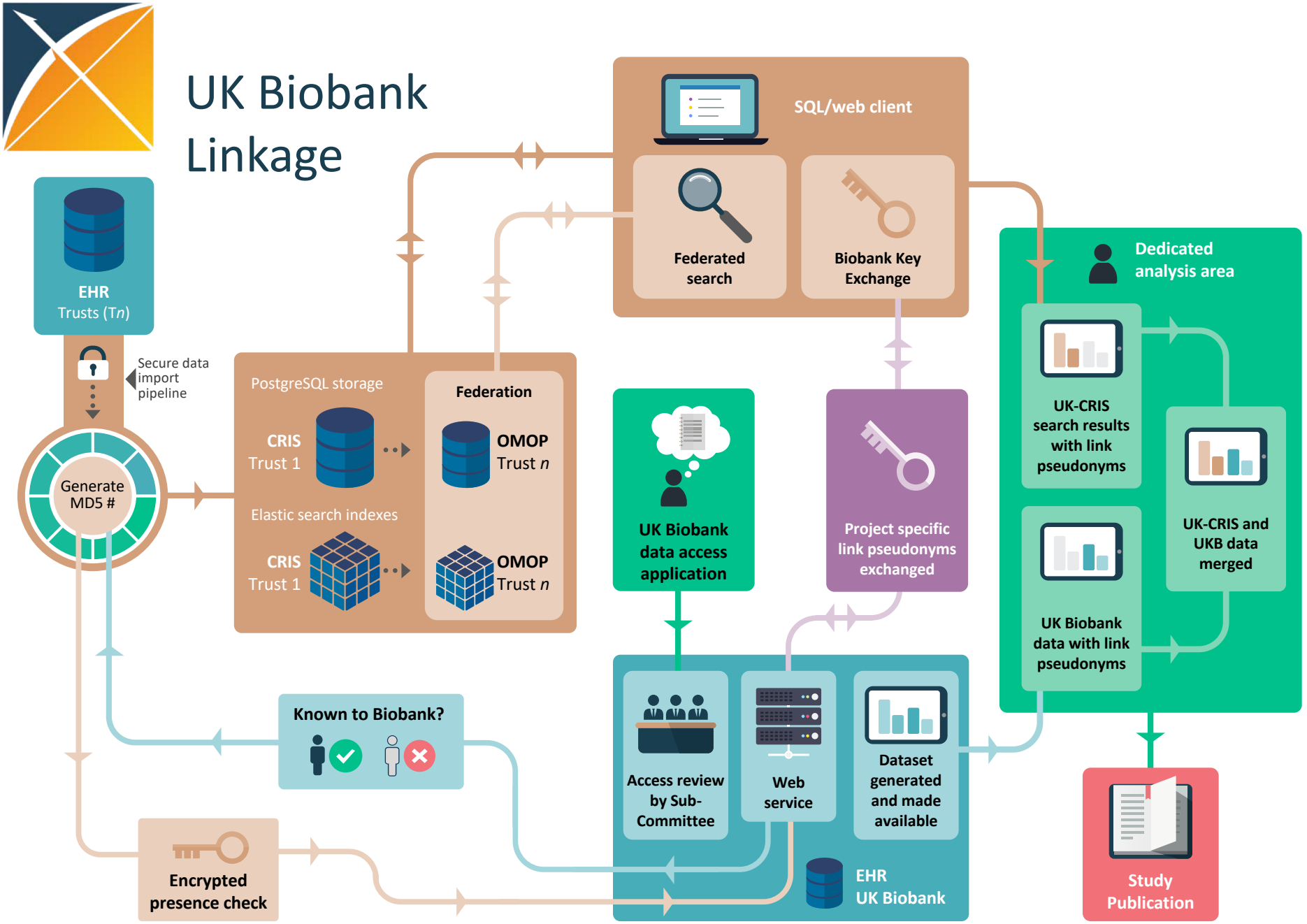
UK Biobank – Enhancements

- Web-based questionnaires for additional exposures and outcomes (cognition, mental health, occupation..)
- Wrist-worn accelerometers mailed to 100,000 participants to measure physical activity
- Multimodal imaging in 100,000
- Repeat Neuroimaging in 10,000
- Genotyping of all participants (820,000 SNPs)
- Repeat cognition, sampling
- Connectivity to EMRs for mental health

Dementias Platform UK
Medical Research Council


1
Simon Lovestone @Simon_Lovestone · 29 Jun 2014
Proud to be wearing #UKBioBank movement measuring device.
Volunteer reseach to prevent dementia and other diseases.
biobank
2
9
7

UK Biobank Linkage

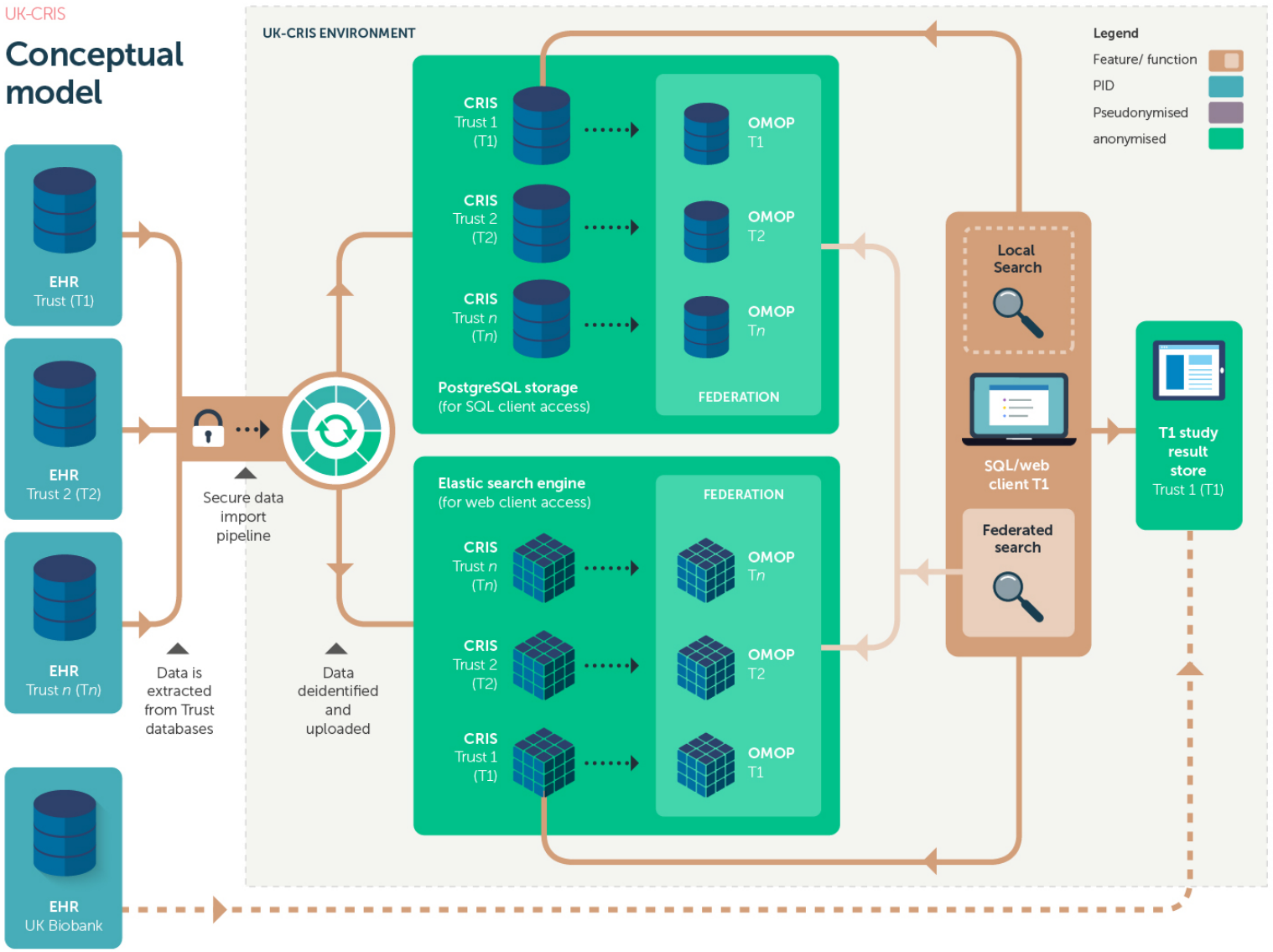


UK- CRIS to UK-biobank

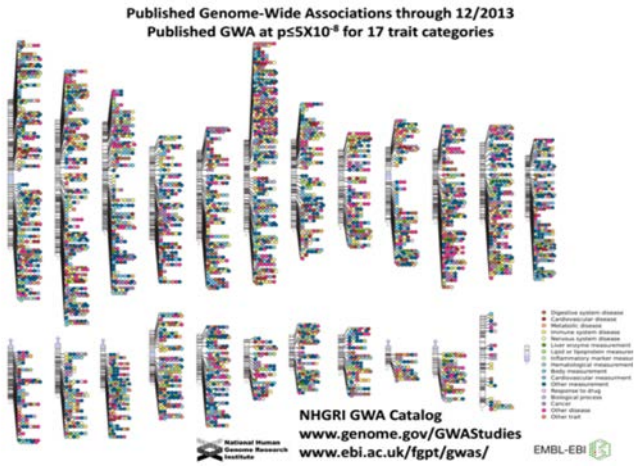
- First ten NHS Trusts linked 2017
- >15,000 shared individuals

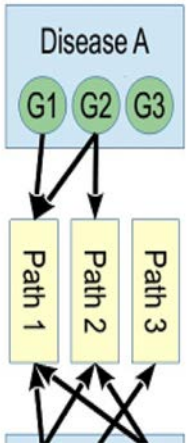
NHS Trust	Oxford Trust coded **diagnosis**	A	B	C	D	E	F	G	H	I	J	K	TOTAL
Patient numbers		131041	125239	238018	288285	210021	249117	110023	155877	193418	179389	330000	**2210428**
UK Biobank match		731	152	1,053	3,964	40	2,894	63	62	1,528	1,450	3,161	**15,098**
Anxiety	**8 %**	*56.9*	*11.8*	*82.0*	*308.8*	*1.8*	*225.4*	*4.9*	*4.8*	*119.0*	*112.9*	*246.2*	***1175***
Bipolar	**9 %**	*66.1*	*13.7*	*95.2*	*358.6*	*3.6*	*261.8*	*5.7*	*5.6*	*138.2*	*131.2*	*285.9*	***1366***
Schizophrenia	**5 %**	*33.1*	*6.9*	*47.6*	*179.3*	*19.0*	*130.9*	*2.8*	*2.8*	*69.1*	*65.6*	*143.0*	***700***
Cognitive disorder	**41 %**	*303.1*	*63.0*	*436.5*	*1643.4*	*16.6*	*1199.8*	*26.1*	*25.7*	*633.5*	*601.1*	*1310.5*	***6259***
Depression	**22 %**	*161.6*	*33.6*	*232.8*	*876.5*	*8.8*	*639.9*	*5.6*	*13.7*	*337.8*	*320.6*	*698.9*	***3330***
Other	**15 %**	*110.2*	*22.9*	*158.7*	*597.6*	*6.0*	*436.3*	*9.5*	*9.3*	*230.4*	*218.6*	*476.5*	***2276***

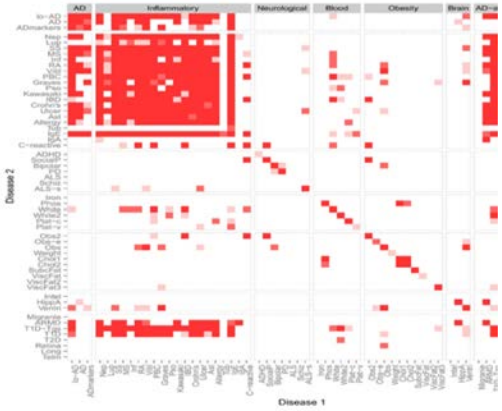
Mapping to the OMOP CDM

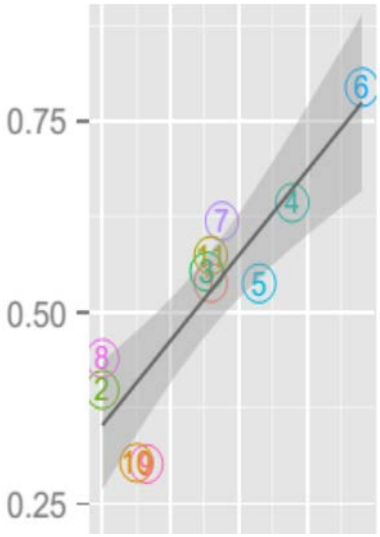


Target nomination





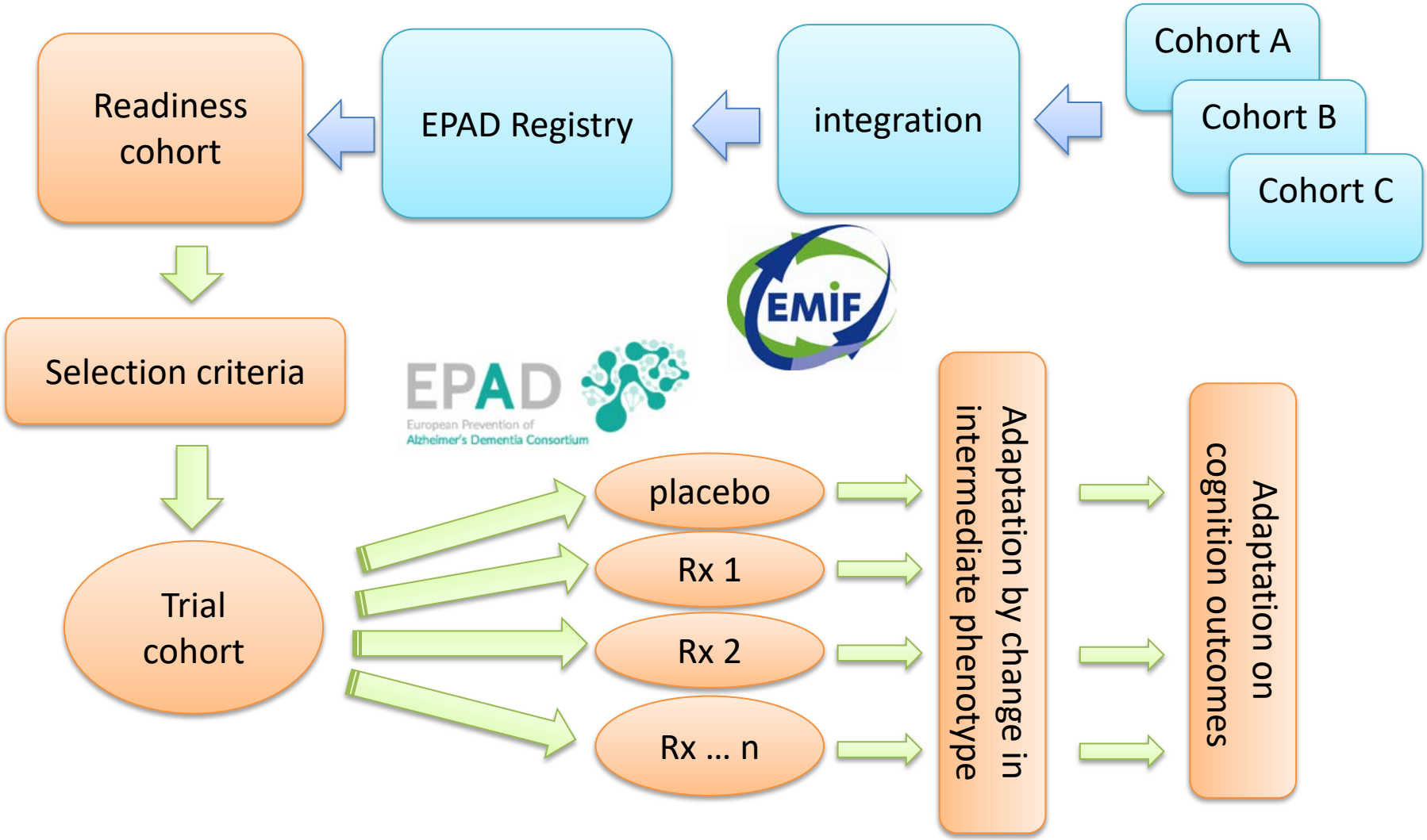




- Generate pathways from complete GWAS datasets and perform clustering analysis for shared pathways
- Correlate pathway load per disease with risk relationship between disease and Alzheimer's ***from real world data***
- Perform proof of concept in human samples ***using EMIF catalogue***

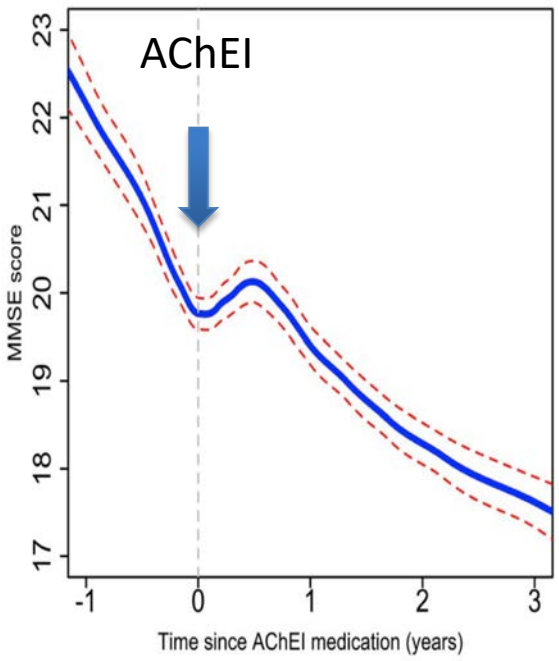
Nevado-Holgado et al (2017) https://www.biorxiv.org/content/early/2017/08/21/179267

Participant identification and recruitment



Post-licensing / ‘Phase IV’

Potential to deliver post-marketing data at scale and in real-world contexts

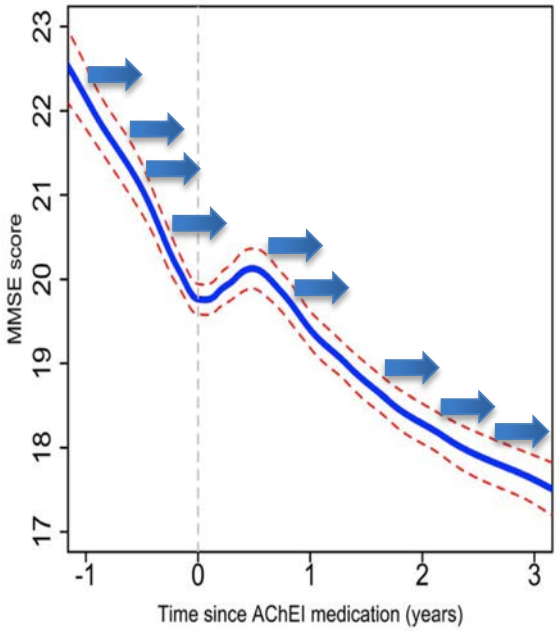


- South London & Maudsley NHS FT ***CRIS*** data
- n=2460; dementia treatment with AChEIs
- MMSE derived from **coded and uncoded** data
- Improvement by 4.2 units per year in first 6 months
- Predictors of response:
  - Better early response in non-white patients
  - Worse early response in vascular dementia

G. Perera, *et al.*, Factors associated with response to acetylcholinesterase inhibition in dementia: a cohort study from a secondary mental health care case register in London. *PLoS One* **9**, e109484 (2014).

Payer approval

Beyond research data modeling - using CRIS for real-world, individual level costs



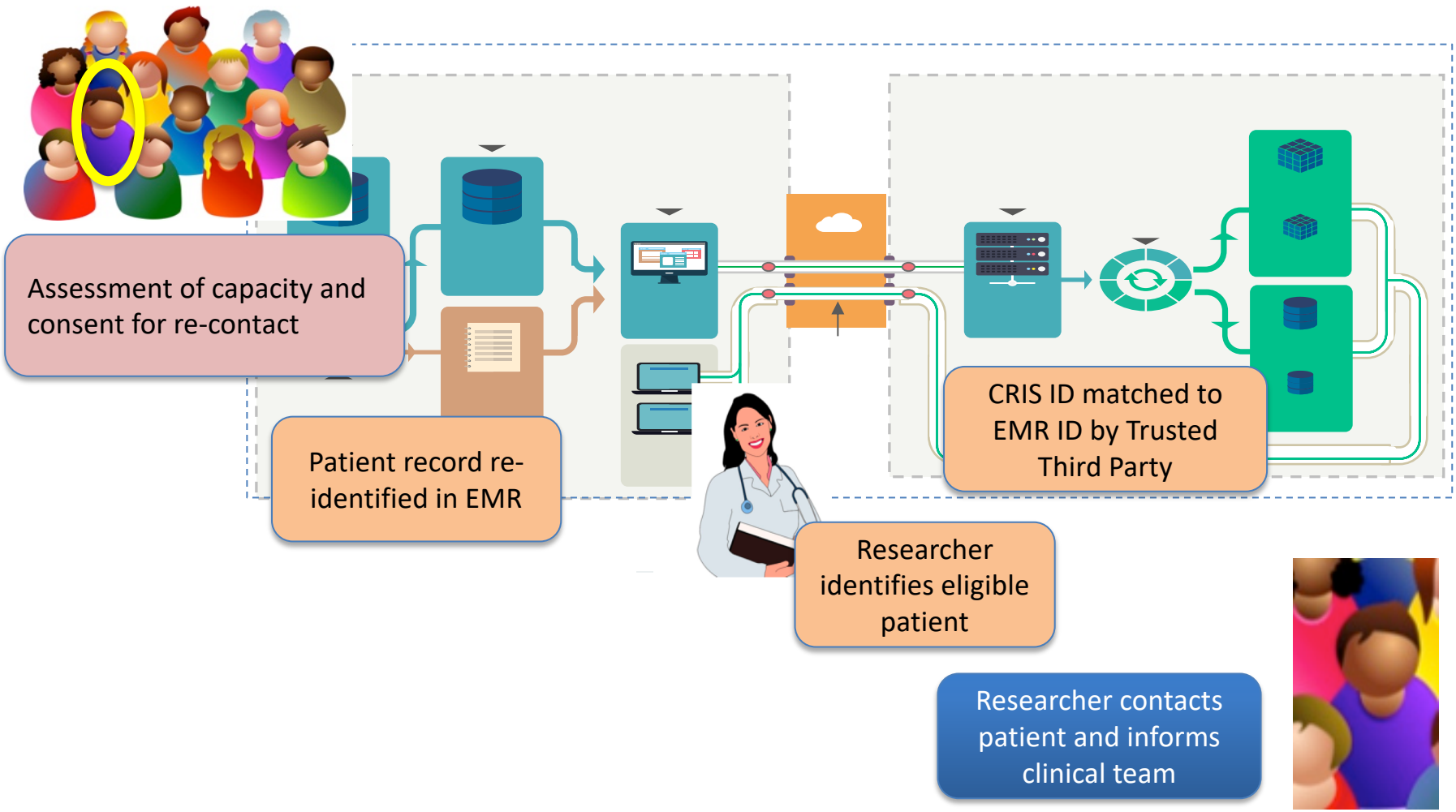
- Destination from uncoded data and linkage
- N=3075 (5624 6m windows)
  - 25% alone; 52% ADL problems
  - 37% physical illness; 45% moderate severity
- Mean costs of severe dementia >2x that for mild
- Increased care costs associated:

  with severity, functional problems, agitation, living alone

  but not physical illness, depression or gender

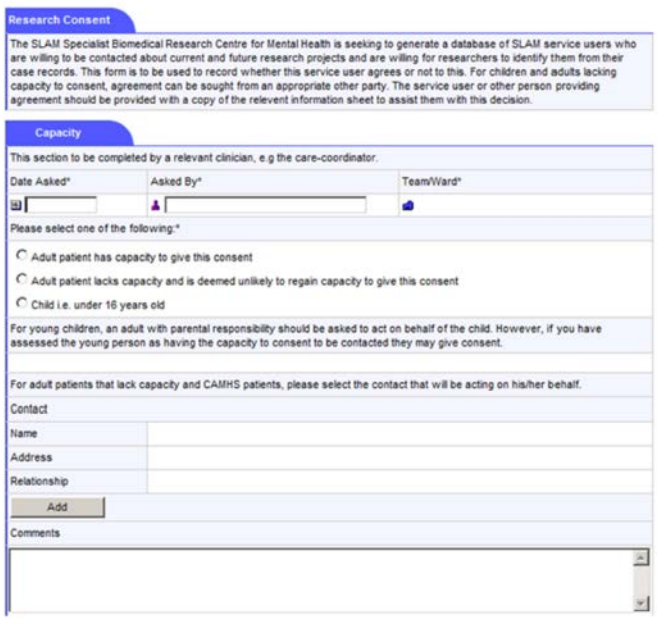
M. Knapp *et al.*, Predictors of care home and hospital admissions and their costs for older people with Alzheimer's disease: findings from a large London case register. *BMJ open* **6**, e013591 (2016).

CRIS consent for contact model



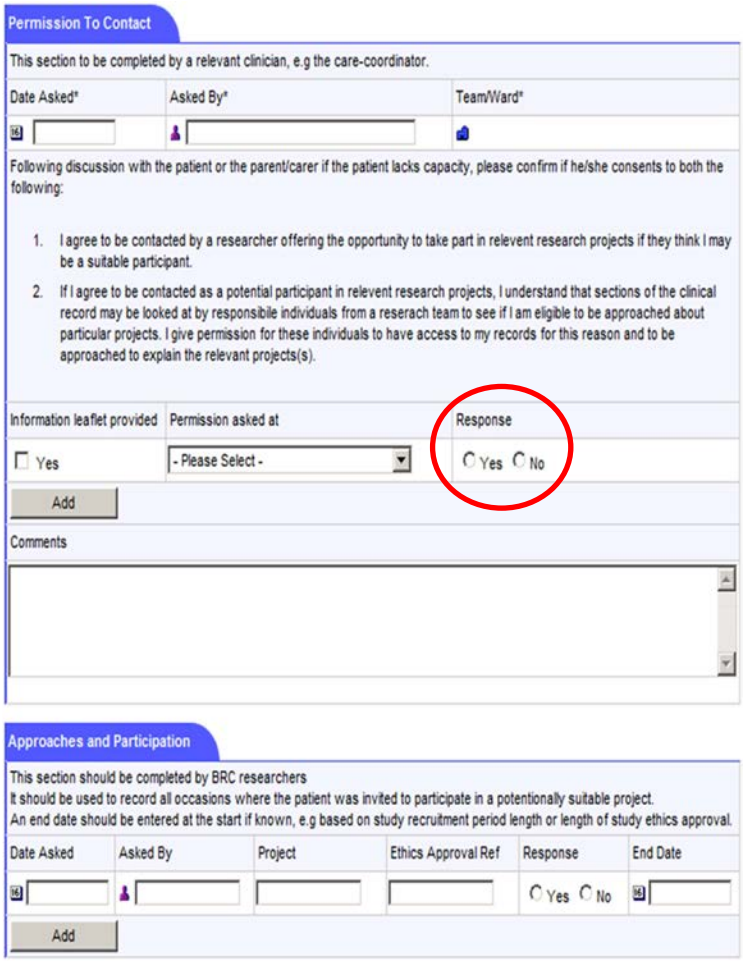
Callard et al. Developing a new model for patient recruitment in mental health services: a cohort study using Electronic Health Records. BMJ open. 2014;4:e005654

CRIS consent for contact model



74% agreement

20,000 consents and samples in 3 years



Callard et al. Developing a new model for patient recruitment in mental health services: a cohort study using Electronic Health Records. BMJ open. 2014;4:e005654.

Next steps

- UK-CRIS expansion, renewal and sustainability
- Linkage
  - Other large scale / population cohorts
  - Primary care
  - Secondary acute care
  - Improving Access to Psychological Therapies (IAPT)
- Using UK-CRIS
  - for target identification, drug repurposing and understanding risk of disease
  - for trials platforms
  - to improve health care (algorithms and decision support)
- An ecosystem for patient empowerment
  - Patient health records / medical records
  - Connected devices for PROMs

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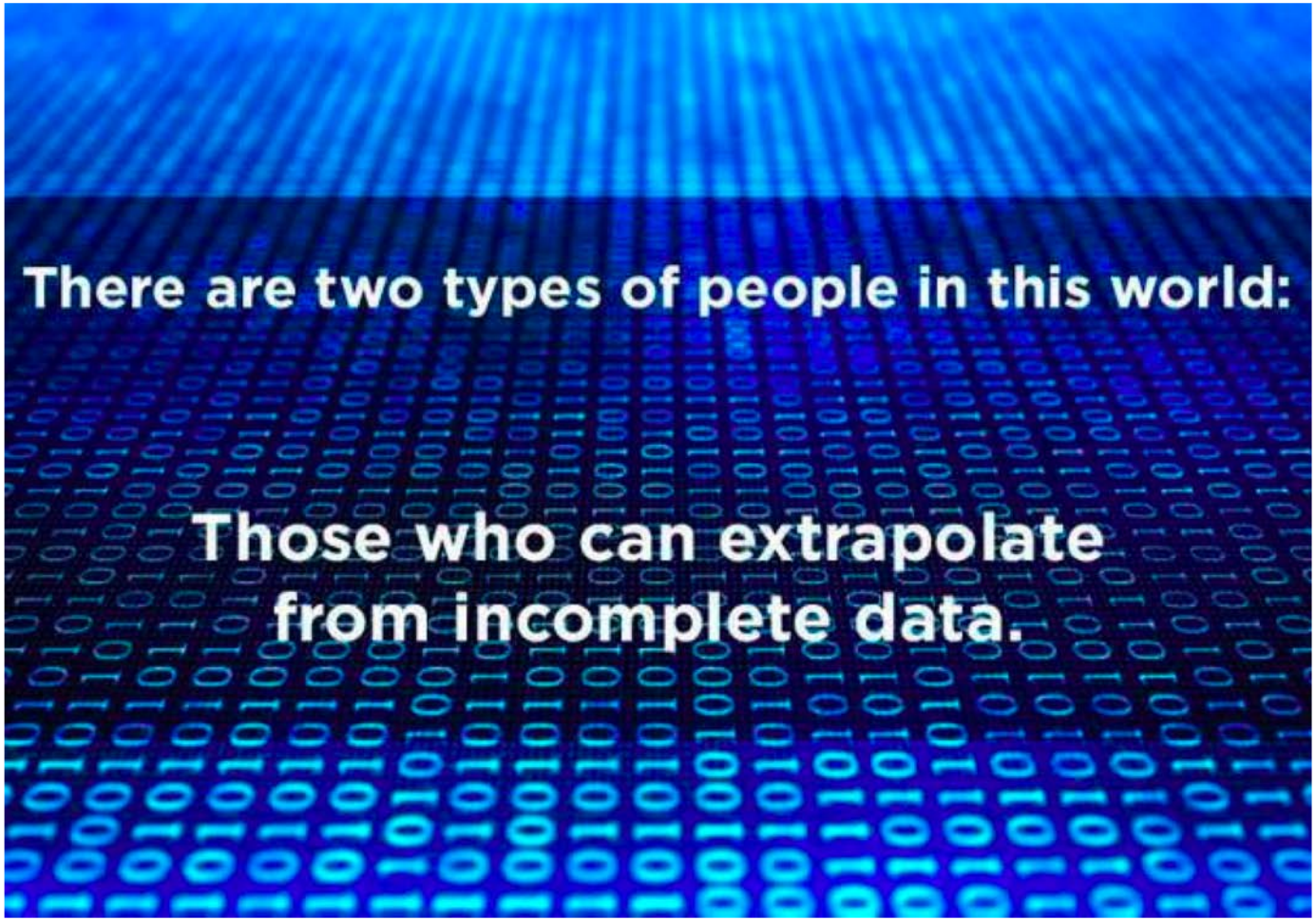
- SLaM team: Robert Stewart and Matthew Broadbent
- UK-CRIS team: Mike Denis and David Newton
- OxCRIS: Tanya Smith and Alejo Nevado

- UK CRIS network

- Funders : NIHR and MRC


There are two types of people in this world:
Those who can extrapolate
from incomplete data.

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

13:00 – 14:45 OHDSI Collaborator Showcase

A success story: The adoption of the OMOP-CDM in South Korea

Rae Woong Park

Ajou University School of Medicine, South Korea

SLIDES TO ADD

Coffee Break