



Institute
and Faculty
of Actuaries

Big health data: perspectives across the patient journey from linking multiple record sources

Harry Hemingway FFPH, FRCP

Professor of Clinical Epidemiology

Director, Farr Institute of Health Informatics Research, UCL

15-17 September 2014, Birmingham

Outline

- What are big health data?
- Why me – personal journey
- What are big data good for?
 - Discovery
 - Trials
 - Outcomes, risk prediction and clinical decision making
 - Public health
- What is the role of the Farr Institute?

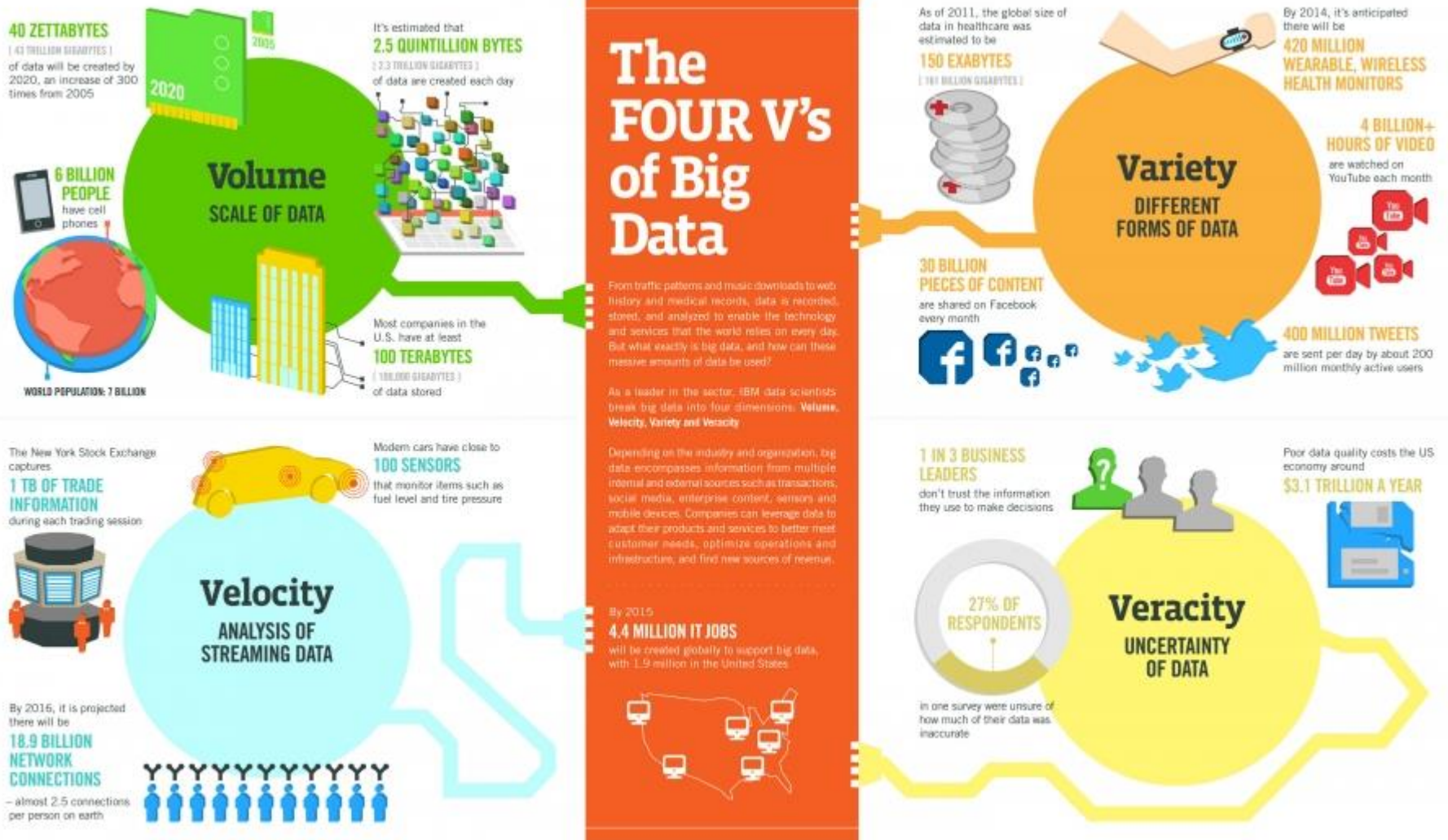
What are big data?

Big data

like teenage sex ‘everyone talks about it,
nobody really knows how to do it,
everyone thinks everyone else is doing it,
so everyone claims they are doing it’

Dan Ariely

What is big data?



How do we scale science in record linkages?

National sources of health record data

NCRS eg

- Personal Demographics Service
- Personal Spine Information Service
- Transaction Messaging Service
- Secondary Uses System
- NN48 / Central Issuing System
- Choose & Book, Payment by Results, GP2GP, etc
- Electronic Prescriptions

NHS National Collections eg

- Commissioning Datasets
- Mental Health Minimum Data
- QOF / QMAS

Specialist Collections eg

Cancer / Diabetes/ Renal Audit; waiting times; workforce

Office of National Statistics

- Births, Deaths, Termination, Marriages
- Census & Special Surveys
- Eg HSE, NDNS, GHS CEMACH, CEPOD, Infant Feeding, etc

UNIQUE IDENTIFIER

@ BIRTH / ARRIVAL in UK
NHS NUMBER
CHILD MOTHER
FATHER

Primary care

GPRD, EMIS, THIN et al.
Child health records
Immunisations [COVER]

Hospital Care Records

Hospital inpatient records
Community 'tail'
Specialist clinics & services
Fertility (NHS/private)
Genitourinary medicine
Intensive care

Devices/prescribing

Cochlear implants
Hip/knee replacement
MHRA systems

Diagnostic/Imaging

Ultrasound/Xray [PACS]
Mammography
Cytology/Pathology
Haematology
Chemical Pathology
Virology/Microbiology
Blood Transfusion
Screening programmes
HPA

Registers/databases

Cancer registers
Diabetes register
Renal register
Congenital rubella register
Pharmacoepidemiology register
Cerebral palsy registers
Down syndrome register
Congenital rubella register
HIV database
Newborn screening databases
NICOR
Juvenile chronic arthritis
Inflammatory bowel disease
Dysmorphology database
Rare disorders
Public Health Observatories

Cohorts/Biobanks

1946 1958 1970 Millennium
ALSPAC, ELSA
MidSpan, Aberdeen, Walker
Generation Scotland
UK Biobank
Newborn Biobank

Environment

UK Air Quality Archive
Environmental Agency [Landfill]
Environment Water Inspectorate
Natural Resources Institute
Geological Survey
GIS data [mobile phone masts]
Superoutput areas/small area microdata

Social Care

Child Protection, In Care/ Adopted
Elderly Care

Income & Benefits

Benefits, Housing, Income

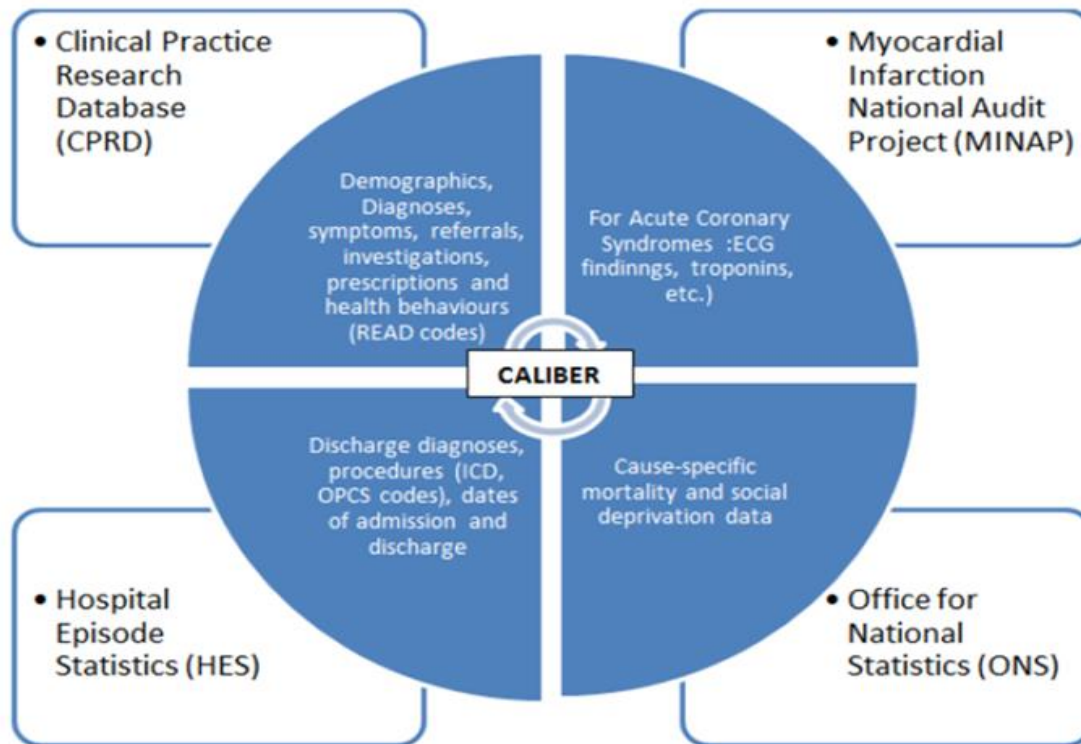
Education & Employment

Preschool/day care
Special Educational Needs
Pupil Level Annual School Census [PLASC] eg SATS scores
GCSE, GCE, Higher education
Occupations and Employment

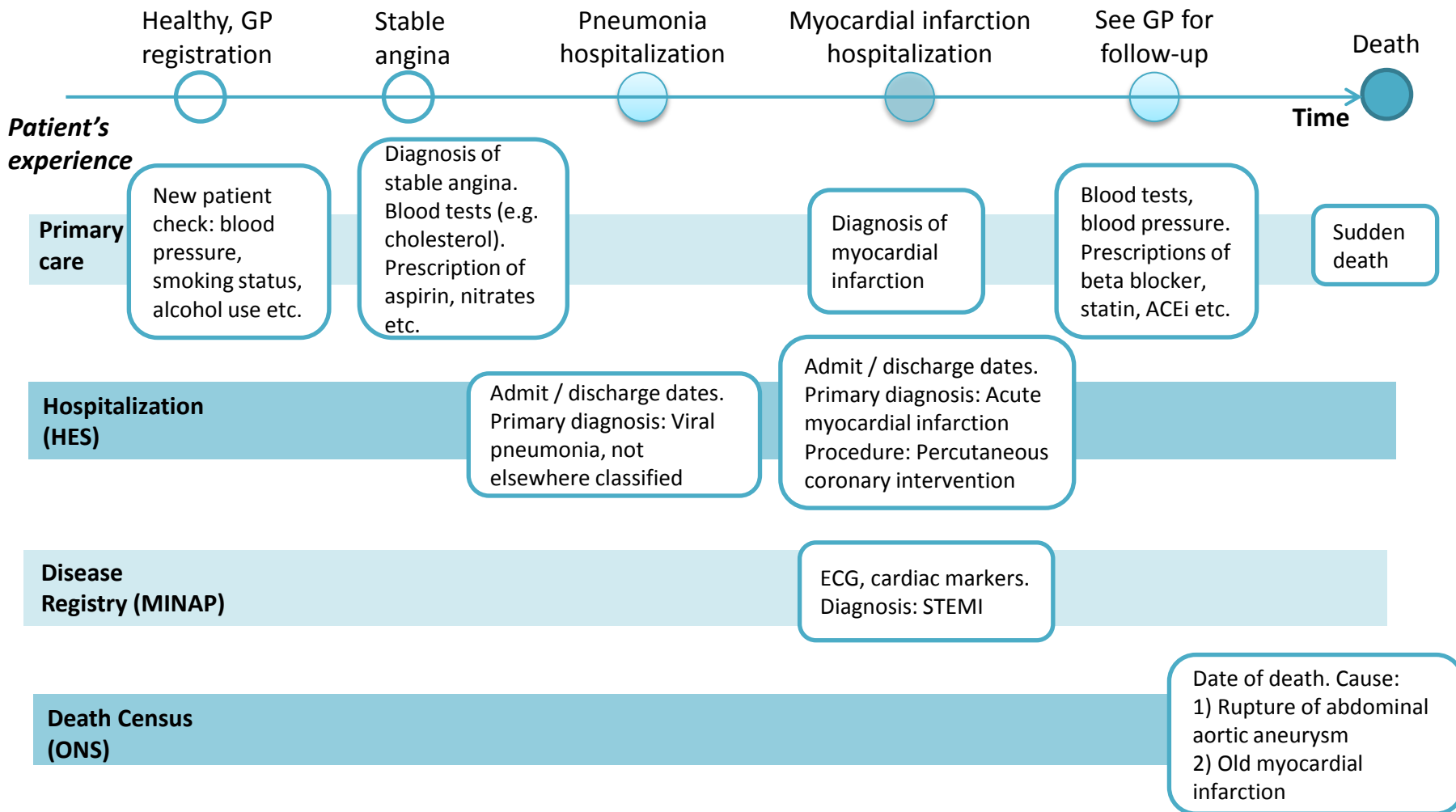
Not available in US or Scandinavia
But many UK national record sources are not linked

Multiple Record Linkages...needs expansion across NICOR registries

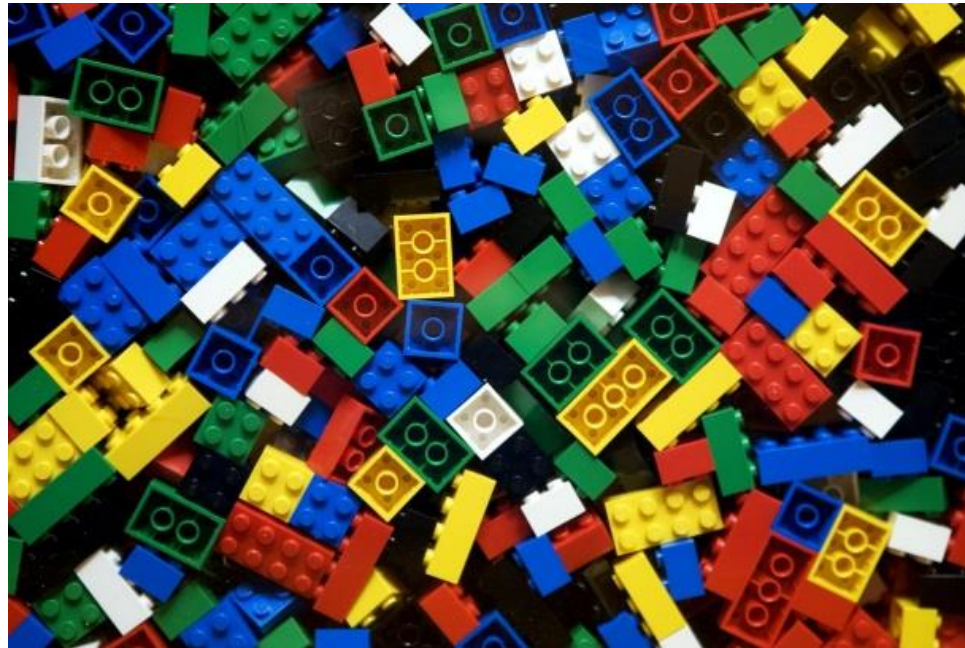
The CALIBER platform



Four nationwide EHR sources linked



What does linked record data look like?



**To get at big
data...need tools**

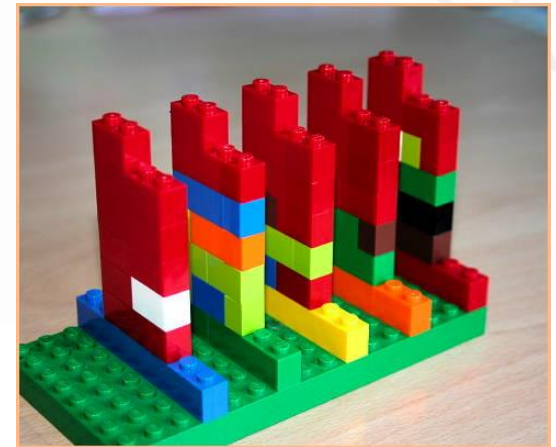
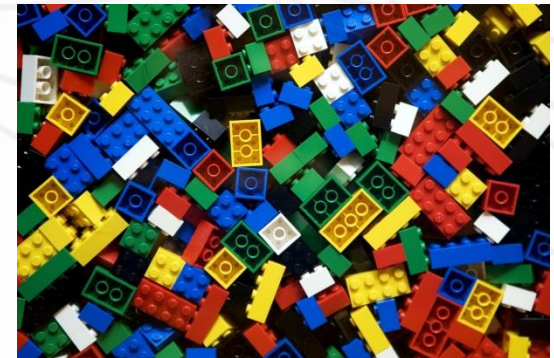
How to define phenotypes using multiple EHR data sources?

ATRIAL FIBRILLATION AND FLUTTER

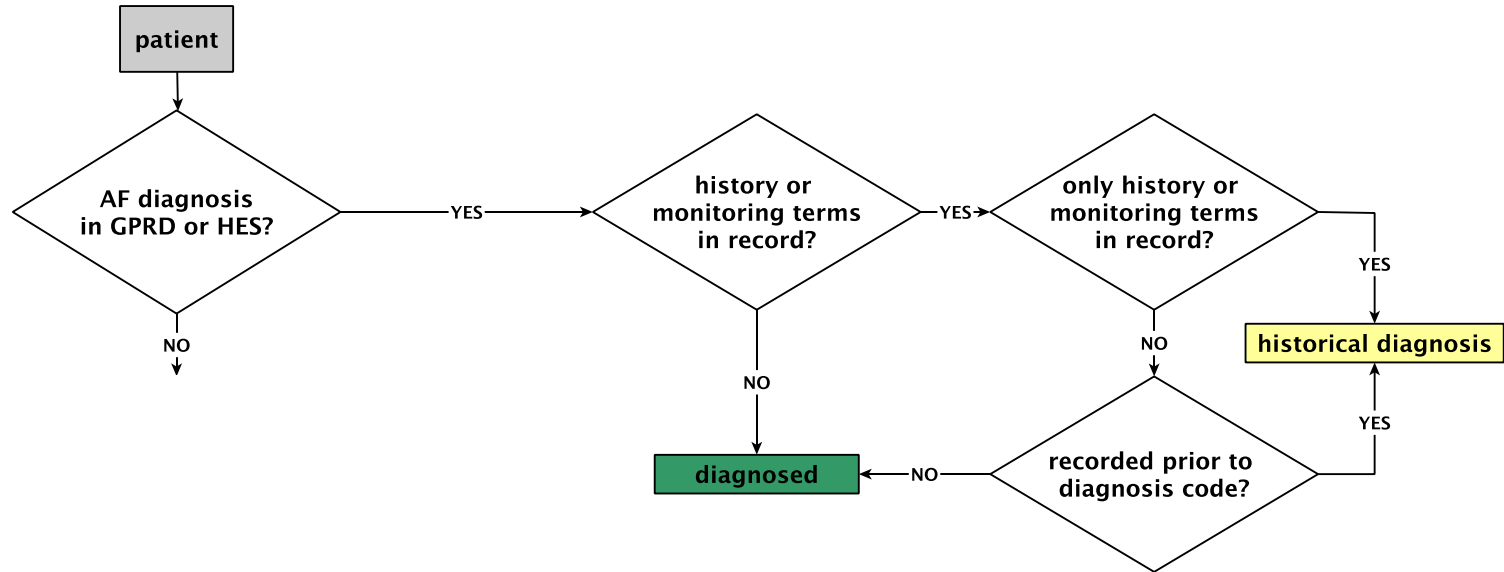
1001, 2000-01-01, 23,1,NULL,I48
1001, 1994-08-11,1234,1,3,7L1H300
1001, 1993-01-01, 253,1,1,793Mz00
1231, 2012-03-03, 23,1,123,K65
1121, 2013-05-04, 7,1,3,5,14AN.00
1121, 2011-05-21, 81,1,9, G573100
1511, 1993-01-11, 91,1,6,9hF1.00
1511, 199-03-11, 91,1,6, G573100
9913, 2012-05-21, 81,1,9, G573100
67222, 1994-11-01,1234,1,3,7L1H300
67222, 1995-12-21,1234,1,3,7L1H300
67222, 1991-03-03,1234,1,3,7L1H310
682444, 1993-01-01, 253,1,1,793Mz00

1001, 2000-01-01, **af_gprd=1**
1231, 2012-03-03, **af_hes=3**
1121, 2013-05-04,
af_procs_gprd=1
1511, 1993-01-11,
heart_valve_gprd=2
9913, 2012-05-21, **af_hes=1**
67222, 1994-08-11, **af_hes=1**
682444, 1993-01-01,
heart_valve_hes=2

af=1,
af_diag_source="primary
care" af_diag_date=2001-
12-01



AF algorithm



Definition

Sources

Implementation

Files

Publications

Genomics

Trials

Atrial Fibrillation

Name	af		
Chapter	Circulatory disease/Atrial fibrillation		
Definition	Diagnosis of atrial fibrillation.		
Data Type	Categorical		
Data sources	GPRD, HES		
Dictionaries	Read, ICD10, BNF, Free text		
Authors	K. Morley (UCL), Shah A. (UCL), Patel R. (UCL), Liam Smeeth (LSHTM), R. Schilling (St Bartholomews & The Royal London Hospital), R. Hunter (St Bartholomews & The Royal London Hospital)		
Agreed	01/02/2013 (Revision 1)		
Category	Definition		
1	Historic AF diagnosis		
2	AF diagnosis inferred		
3	AF diagnosis confirmed		
Source variables	Description	Source	Variable
	Atrial fibrillation diagnosis	Primary care	af_gprd
	Atrial fibrillation diagnosis	Secondary care	af_hes
	Atrial fibrillation procedures	Primary care	af_proc_gprd
	Atrial fibrillation procedures	Secondary care	af_proc_opcs
	AF medication	Primary care	af_drugs_gprd
	warfarin or digoxin prescription	Primary care	af_warfarin_digoxin
	Deep vein thrombosis	Primary care	dvt_gprd
	Deep vein thrombosis	Secondary care	dvt_hes
	Pulmonary embolism	Primary care	pe_gprd
	Pulmonary embolism	Secondary care	pe_hes
	ECG Text/Notes text mining	Secondary care	Algorithm

CALIBER Data Portal

- Online data discovery tool **caliberresearch.org**
- Access to *all* CALIBER phenotypes, algorithms and implementation details and scripts (SQL,R, Stata)
 - 45 users, 4 institutions, 538 phenotypes, >15,000 clinical diagnostic codes curated
- Standardization
 - Frontend is ICD10, backend becoming SNOMED-CT, LOINC
- A community rather than a static resource
 - Researchers contribute phenotypes and algorithms
 - Other researchers validate/enhance/correct them

Why me?

Why me?



The NEW ENGLAND JOURNAL of MEDICINE

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SPECIAL ARTICLE

Underuse of Coronary Revascularization Procedures in Patients Considered Appropriate Candidates for Revascularization

Harry Hemingway, M.R.C.P., Angela M. Crook, M.Sc., Gene Feder, F.R.C.G.P., Shrilla Banerjee, M.R.C.P., J. Rex Dawson, F.R.C.P., Patrick Magee, F.R.C.S., Sue Philpott, M.Sc., Julie Sanders, B.Sc., Alan Wood, F.R.C.S., and Adam D. Timmis, F.R.C.P.
N Engl J Med 2001; 344:645-654 | [March 1, 2001](#) | DOI: 10.1056/NEJM200103013440906

**What's wrong
that big data
might help fix?**

Cardiovascular diseases global #1

- Cause of death/premature death/disability adjusted life years
- So what has gone wrong?
 - **wrong prevention**
 - **wrong treatments**
 - **wrong diagnoses / wrong names for diseases**
 - **wrong health systems (and too costly)**
 - **wrong relations to data, information and knowledge**
 - **wrong relations with patients**
- **wrong science! (done by the wrong people!)**

Might big data help right these wrongs?

Yes!

Mike Lauer, Director Division of Cardiovascular
Sciences National Institutes of Health

EDITORIAL

Editorials represent the opinions
of the authors and JAMA and
not those of the American Medical Association.

Time for a Creative Transformation of Epidemiology in the United States

JAMA 2012

***“US models are being
eclipsed by non-US studies
that are much larger, yet
considerably less
expensive”***

Yes!

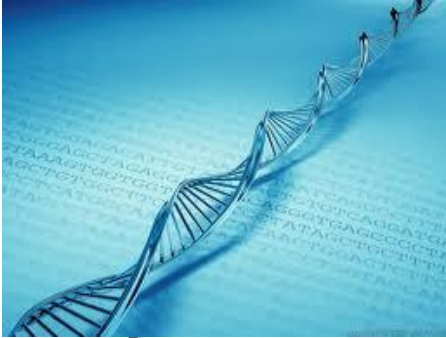
Eric Topol 'wireless and genomic medicine'



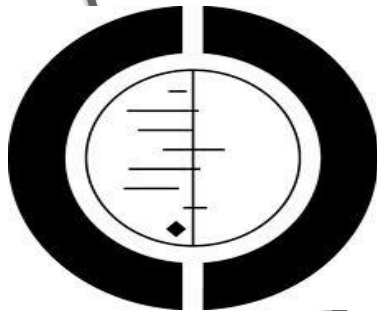
Pace and scale of translation

Discovery

Public health and clinical
decisions → **health gain**



Big data / Health records



Trials



Outcomes & quality research

Discovery

Genomics



500k participants, 47 baseline biomarkers and custom gene array data available in 2014, cardiac and brain imaging in 100k underway

Open access

Scalable approaches to disease phenotypes (startpoints or endpoints) based on linked electronic health record resources

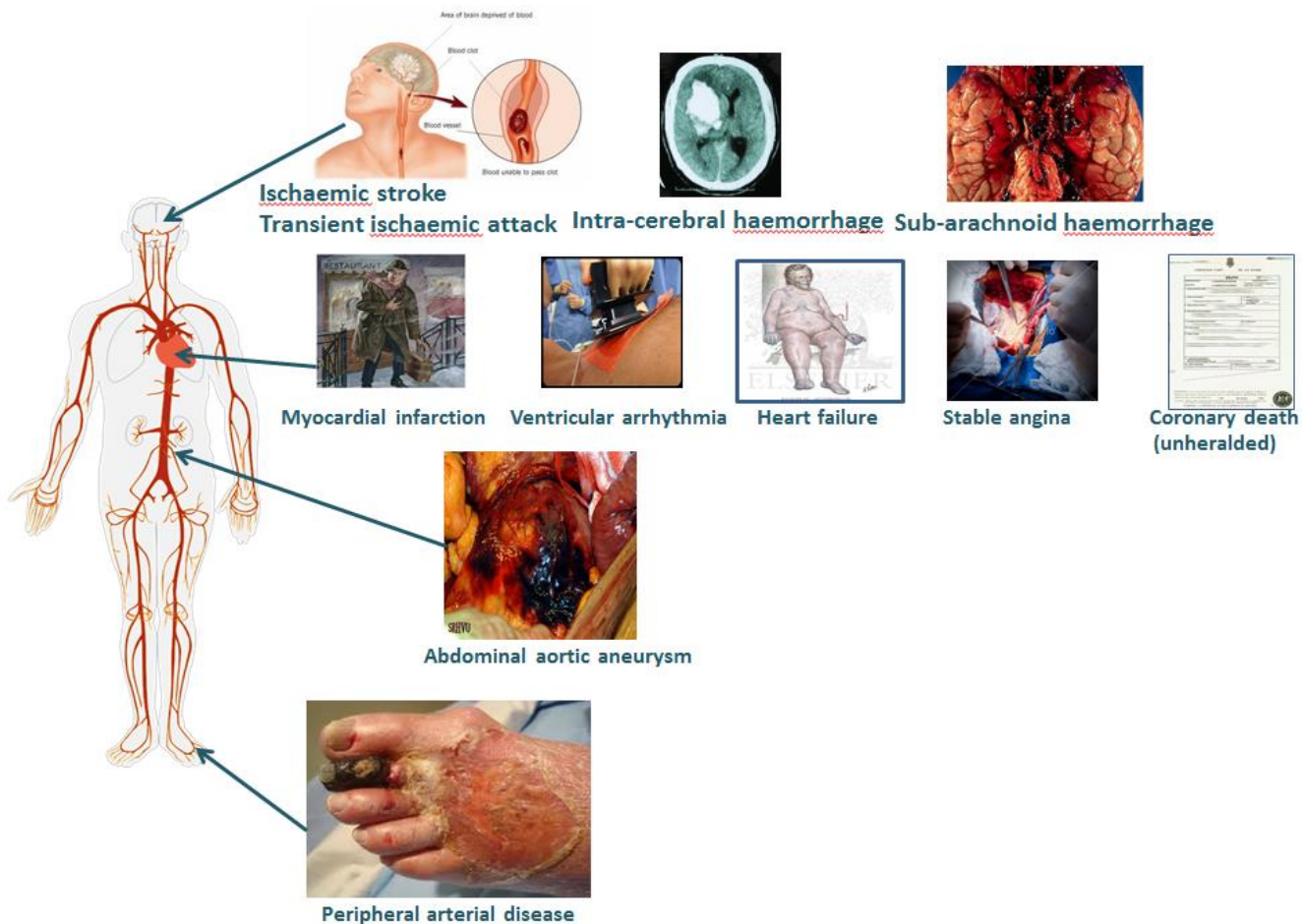
- cardiac
- diabetes
- stroke
- cancer

Example of Farr Institute working across Wales, Scotland and England

Discovering new risk factor associations:

CVD aggregates vs specific diseases

Are the risk factors the same?



To answer this question reliably we need

- **Scale:** e.g. >1 million adults followed for 5 years
- **Phenotypic resolution:**
 - Baseline risk factors
 - Follow up for disease outcomes

Cost to research funder of such data collection?

£0.00

The research costs are substantial

Information governance

**Store, share, harmonise,
analyse EHR data.....with
scalable tools**

**And develop pool of clinical
expertise**

THELANCET-D-13-09219

S0140-6736(14)60685-1

Embargo: [add date when known]

Funding: MRC, NIH, WT

[A: We have edited your paper to avoid repetition, enhance readability, reduce length, and achieve consistency with *Lancet* style]

13TL9219

Articles

KG

Version 1

This version saved: 12:14, 13-May-14

Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people



Eleni Rapsomaniki, Adam Timmis, Julie George, Mar Pujades-Rodriguez, Anoop D Shah, Spiros Denaxas, Ian R White, Mark J Caulfield, John E Deanfield, Liam Smeeth, Bryan Williams, Aroon Hingorani, Harry Hemingway



Summary

Background The associations of blood pressure with the different manifestations of incident cardiovascular disease in a contemporary population have not been compared. In this study, we aimed to analyse the associations of blood pressure with 12 different presentations of cardiovascular disease. [A: we have added a study aim here. Please amend if you wish]

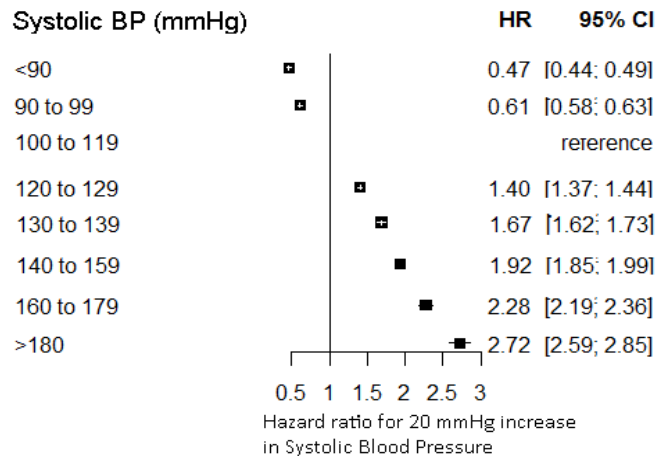
Methods We used linked electronic health records from 1997 to 2010 in the CALIBER (Cardiovascular research using Linked Bespoke studies and Electronic health Records) programme to assemble a cohort of 1.25 million patients, 30 years of age or older and initially free from cardiovascular disease, a fifth of whom received blood pressure-lowering treatments. We studied the heterogeneity in the age-specific associations of clinically measured [A: OK?] blood pressure with 12 acute and chronic cardiovascular diseases, and estimated the lifetime risks (up to 95 years of age) and cardiovascular disease-free life-years lost adjusted for other risk factors at index ages 30, 60, and 80 years. This study is registered at ClinicalTrials.gov, number NCT01164371.

The Farr Institute of Health Informatics Research, London, . UK (E Rapsomaniki PhD, Prof A Timmis FRCP, J George PhD, M Pujades-Rodriguez PhD, A D Shah MRCP, S Denaxas PhD, Prof M J Caulfield MD, Prof J E Deanfield FRCP, Prof L Smeeth FRCP, Prof B Williams FRCP, Prof A Hingorani FRCP, Prof H Hemingway FRCP); Epidemiology and Public Health (E Rapsomaniki, J George, M Pujades-Rodriguez & A D Shah)

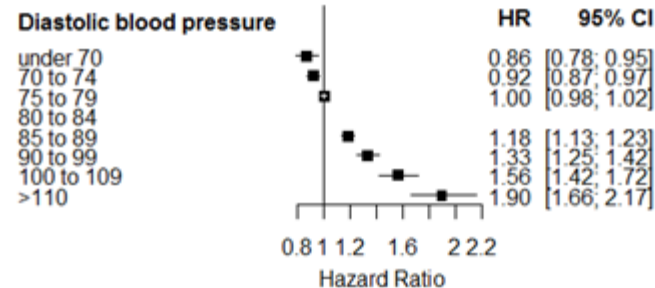
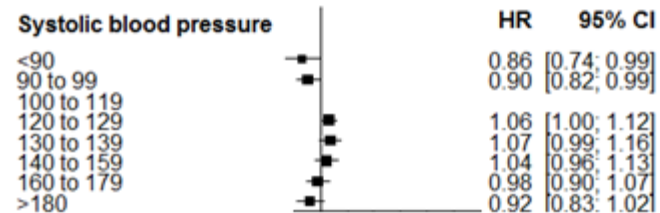
Higher resolution epidemiology: blood pressure and 12 cardiovascular diseases

Cohort N \approx 2 million adults, >100,000 disease events

Myocardial infarction



Abdominal aortic aneurysm



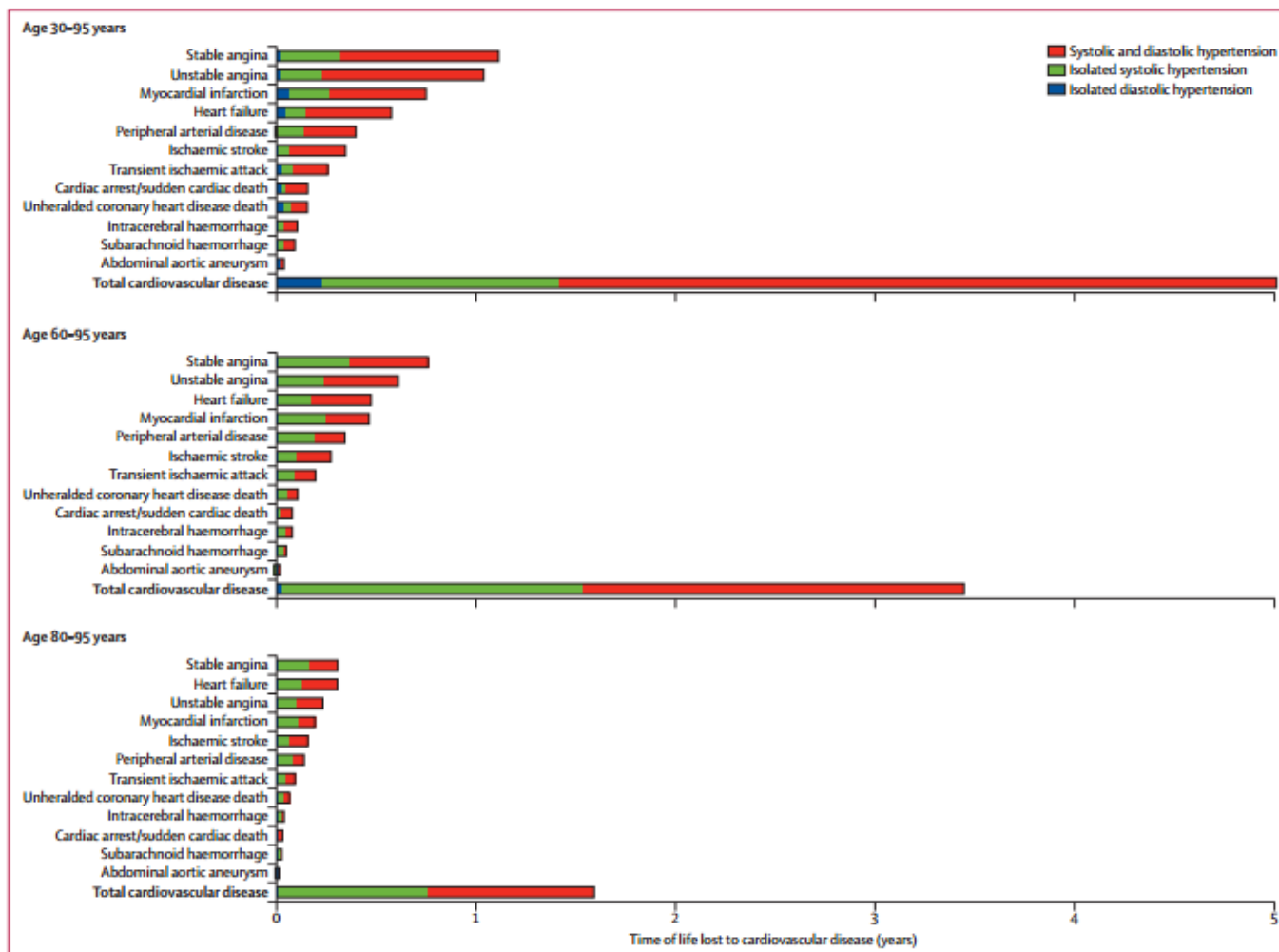
Confirms what we know from combining
multiple expensive studies

Adds resolution

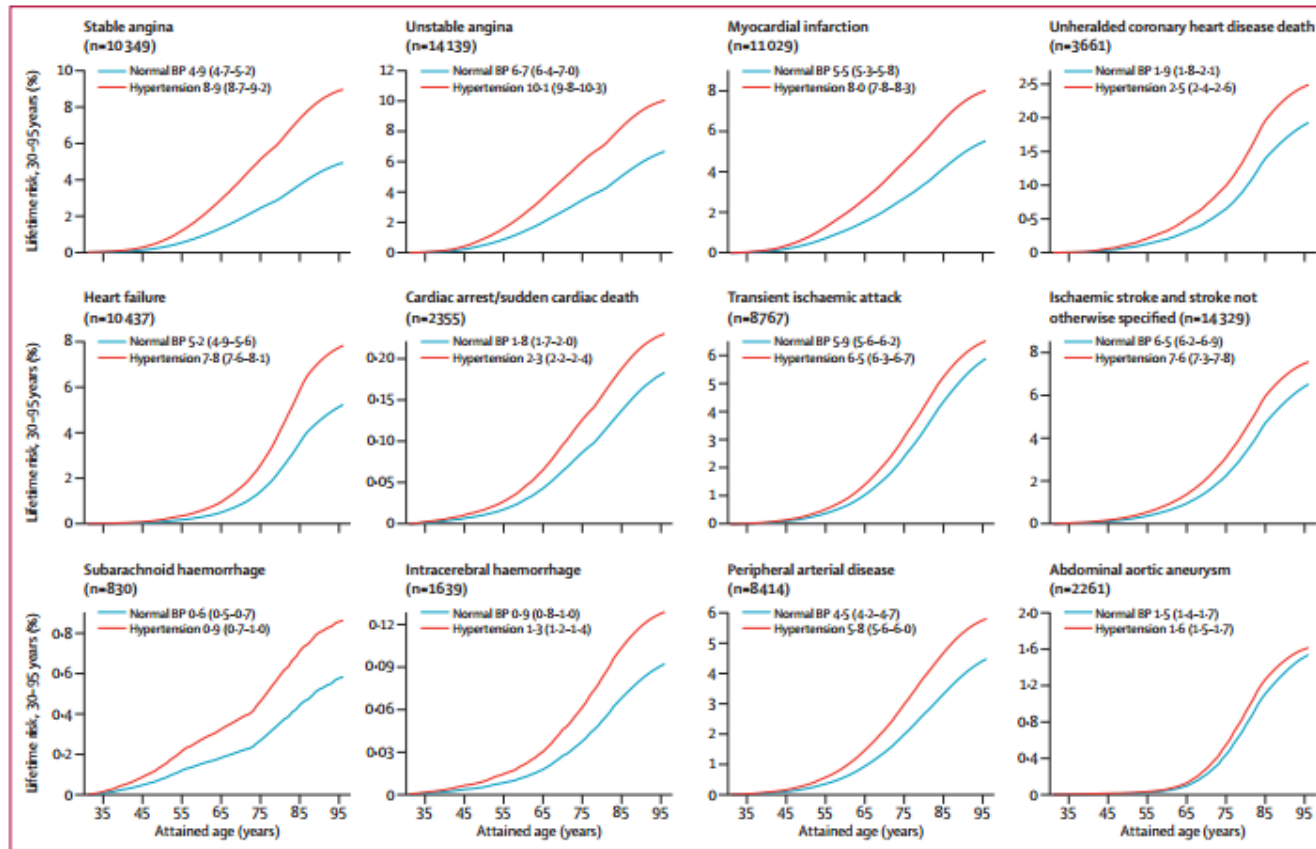
New knowledge

....a challenge for experimental medicine

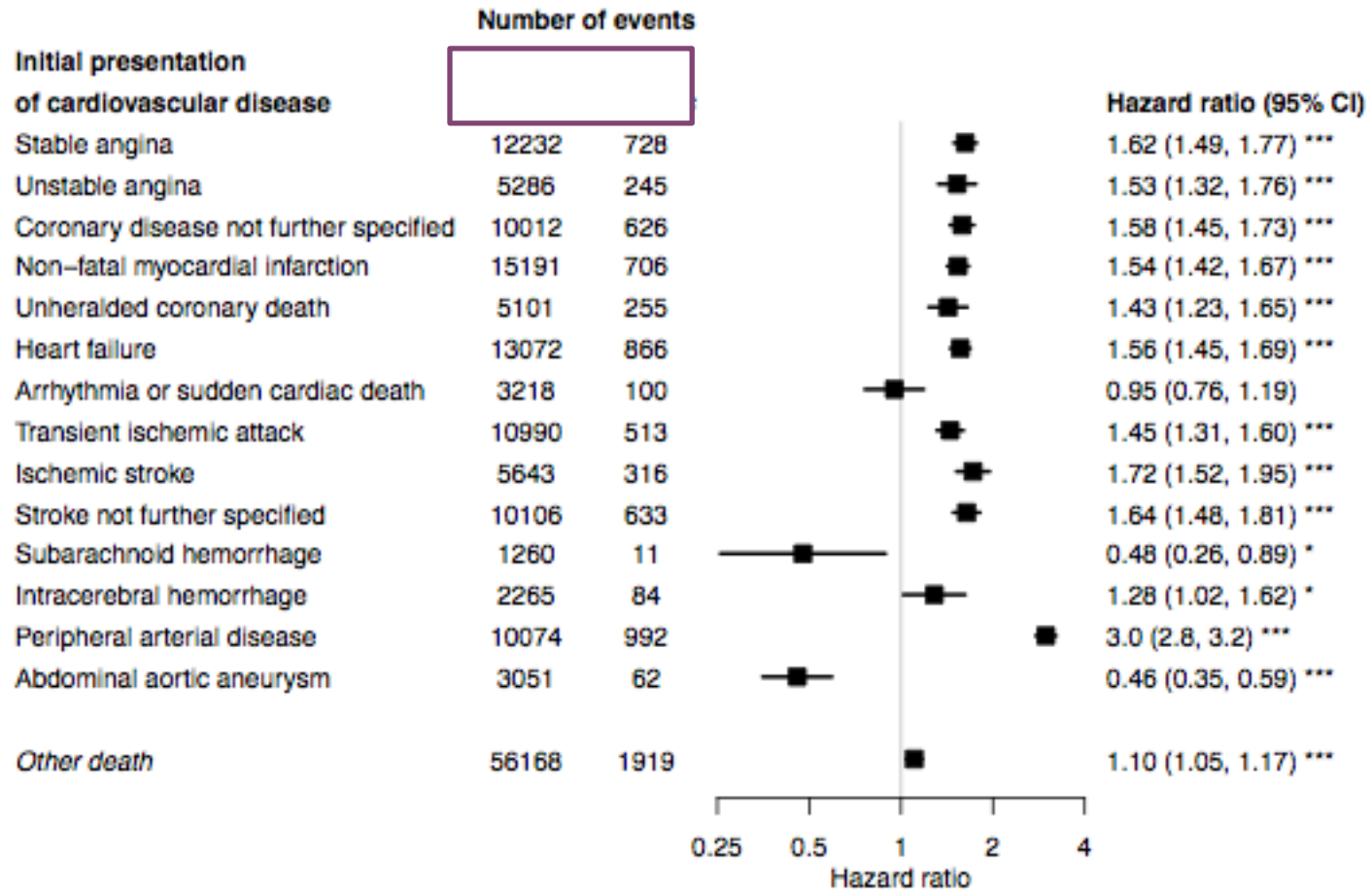
Years of life lost to CVD



Cumulative life time risk of 12 cardiovascular diseases



Inverse, null, weak and strong...what's the 'risk factor'?



‘Higher resolution’ approaches: implications

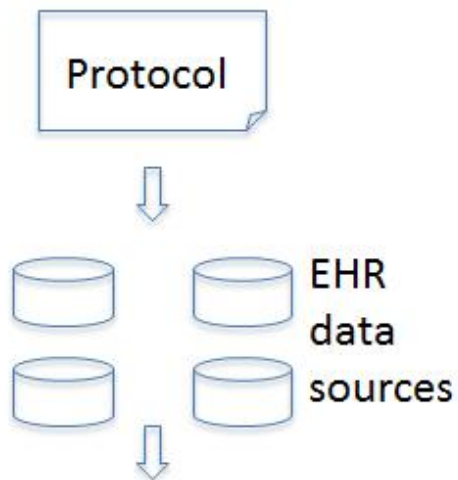
- Disease mechanism
- Trial design
- Screening and risk prediction

Discovery Trials

Developing informatics platforms for stratified trials

**Rapid
feasibility**

**EHR-based
eligibility counts**



Recruiting

EHR randomisation

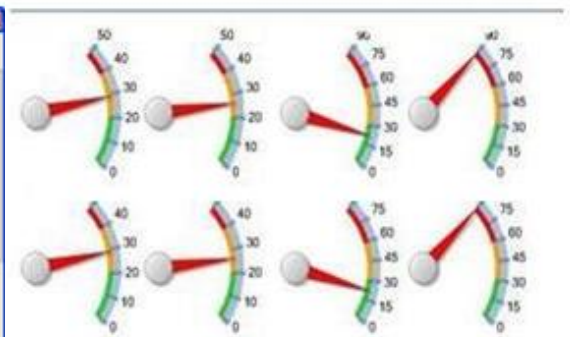
A screenshot of a software interface titled "LEPIS: Patient Eligible for Trial". The main heading is "Patient is Eligible for Trial". Below this, it says "GPRD Test Trial" and "Looking for pat ID Matt A, Aaron Elliot and Karl Aaron". There are several buttons: "Recruit Patient" (green checkmark), "Patient Wants Time to Think" (blue speech bubble), "Patient Not Interested" (red X), "Do not Disturb me for 2 Hours" (red X), "Patient Not Eligible" (purple circle), and "Close for this Patient" (purple circle). At the bottom, there is a dropdown menu for "Other Actions" with the text "Patient not interested in ever participating in trials" and a "Perform" button.

UCLP eConsent



**Following up
& safety**

**Real-time outcome
dashboards**



Embedded eCRF

A screenshot of a web-based form titled "NON-SERIOUS ADVERSE EVENT". The form contains several sections with checkboxes and text input fields. The sections include: "Diagnosis Only (if known) Otherwise Signs/Symptoms", "Onset Date", "Outcome - End Date", "Frequency", "Medication Severity", and "Action Taken with Investigational Product(s) as a Result of the AE". Each section has a "Yes/No" column with checkboxes.

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

OCTOBER 24, 2013

VOL. 369 NO. 17

Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction

Ole Fröbert, M.D., Ph.D., Bo Lagerqvist, M.D., Ph.D., Göran K. Olivecrona, M.D., Ph.D., Elmir Omerovic, M.D., Ph.D., Thorarinn Gudnason, M.D., Ph.D., Michael Maeng, M.D., Ph.D., Mikael Aasa, M.D., Ph.D., Oskar Angerås, M.D., Fredrik Calais, M.D., Mikael Danielewicz, M.D., David Erlinge, M.D., Ph.D., Lars Hellsten, M.D., Ulf Jensen, M.D., Ph.D., Agneta C. Johansson, M.D., Amra Kåregren, M.D., Johan Nilsson, M.D., Ph.D., Lotta Robertson, M.D., Lennart Sandhall, M.D., Iwar Sjögren, M.D., Ollie Östlund, Ph.D., Jan Harnek, M.D., Ph.D., and Stefan K. James, M.D., Ph.D.

METHODS

We conducted a multicenter, prospective, randomized, controlled, open-label clinical trial, with enrollment of patients from the national comprehensive Swedish Coronary Angiography and Angioplasty Registry (SCAAR) and end points evaluated through national registries. A total of 7244 patients with STEMI undergoing PCI were randomly assigned to manual thrombus aspiration followed by PCI or to PCI only. The primary end point was all-cause mortality at 30 days.

RESULTS

No patients were lost to follow-up. Death from any cause occurred in 2.8% of the

Discovery

Trials

Outcomes research/real world evidence

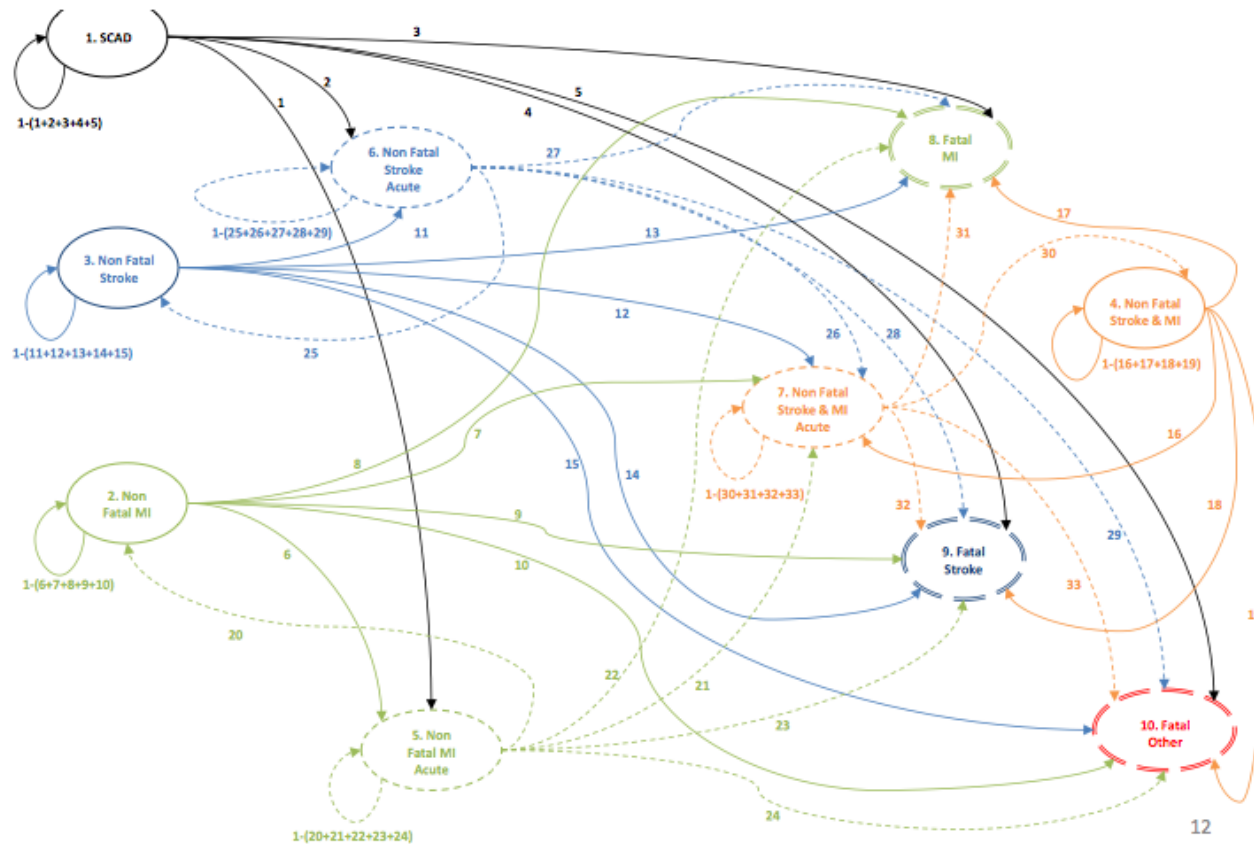
Temporal resolution

....with 'big data' can study both



Outcomes research: capturing clinically meaningful complexity

one startpoint to many types of endpoint



Acute myocardial infarction: a comparison of short-term survival in national outcome registries in Sweden and the UK

Sheng-Chia Chung, Rolf Gedeberg, Owen Nicholas, Stefan James, Anders Jeppsson, Charles Wolfe, Peter Heuschmann, Lars Wallentin, John Deanfield, Adam Timmis, Tomas Jernberg, Harry Hemingway

Lancet 2014; 383: 1305-12

THE LANCET

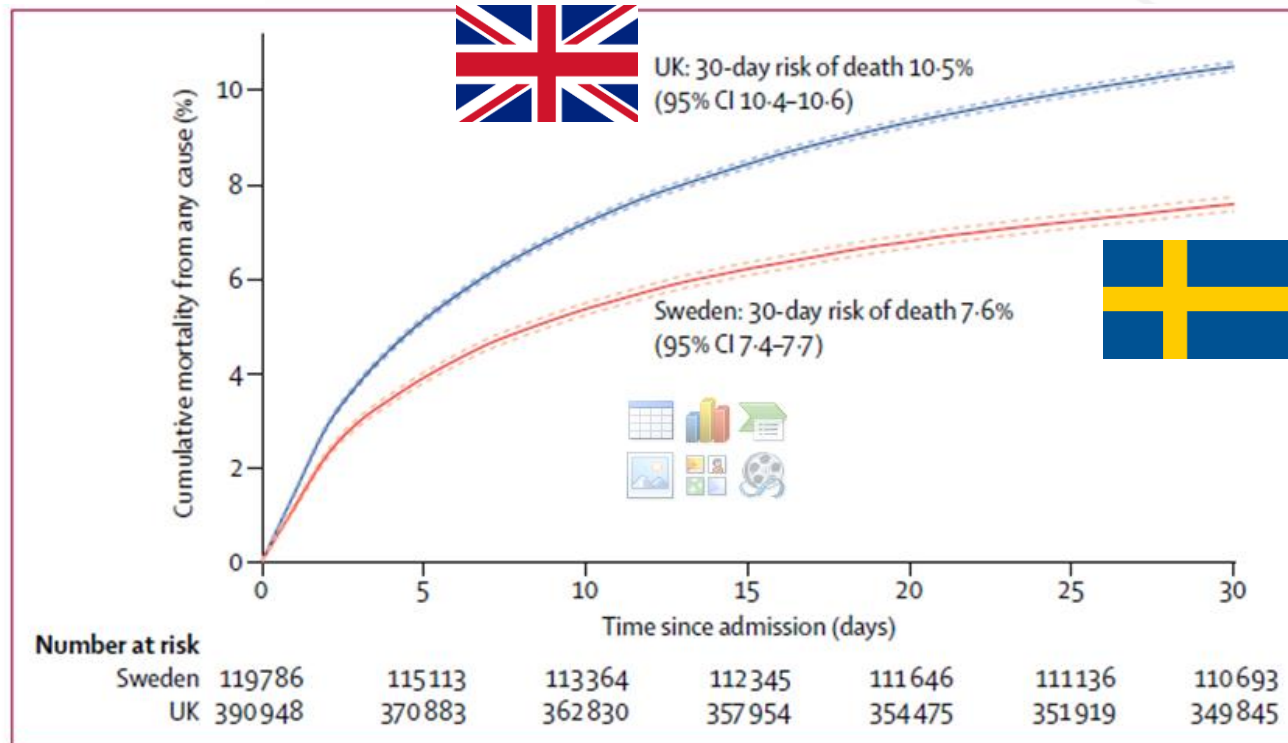
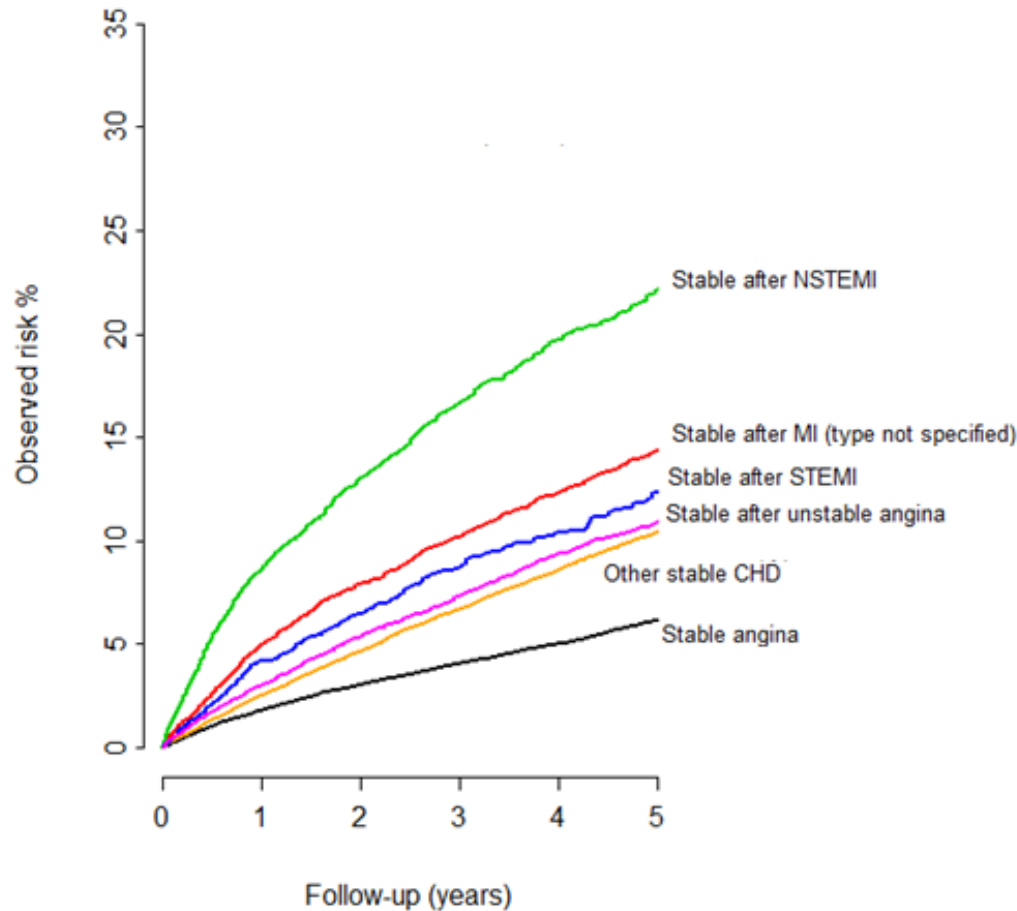


Figure 3: Kaplan-Meier curves for cumulative mortality at 30 days after admission with acute myocardial infarction in Sweden and the UK

‘Real world’ prognosis of stable CAD

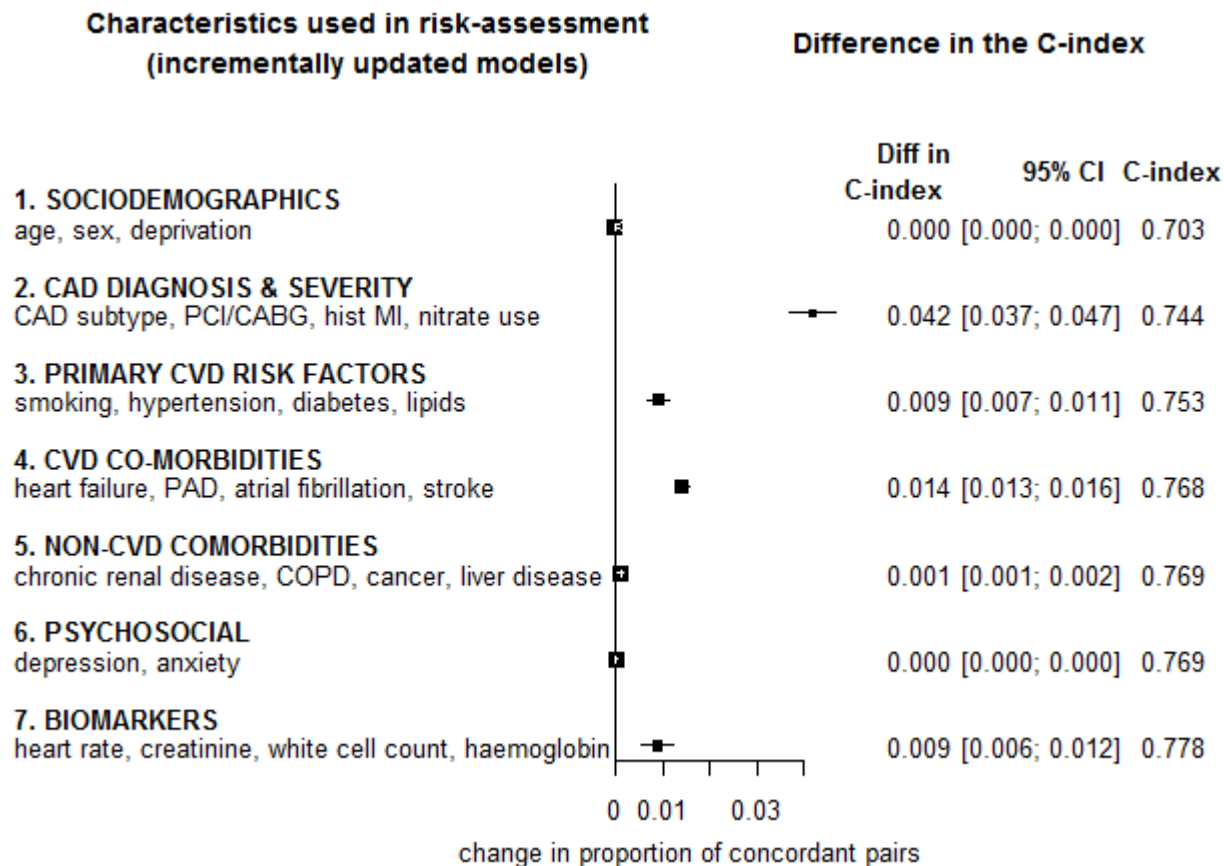
(n=102, 023) and 5 yr risk of coronary death + non-fatal MI (n=8,856)



A ‘gold standard’ for estimating relevant risks?

Prognostic models using linked EHR:

Which *clinically recorded* factors add to discrimination?



Origin of data is EHR therefore implementation of risk prediction models in decision support tools (with evaluation) is feasible

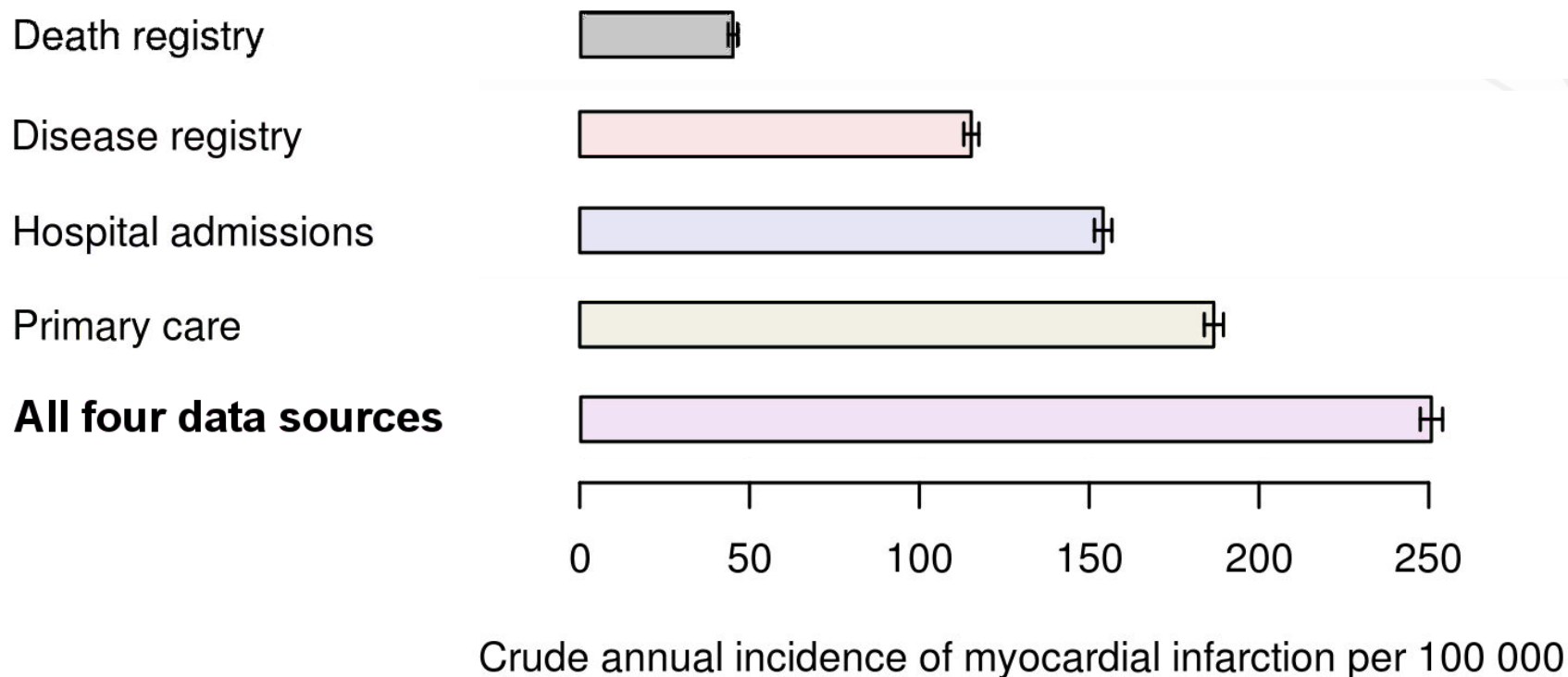
Discovery

Trials

Outcomes research/real world evidence

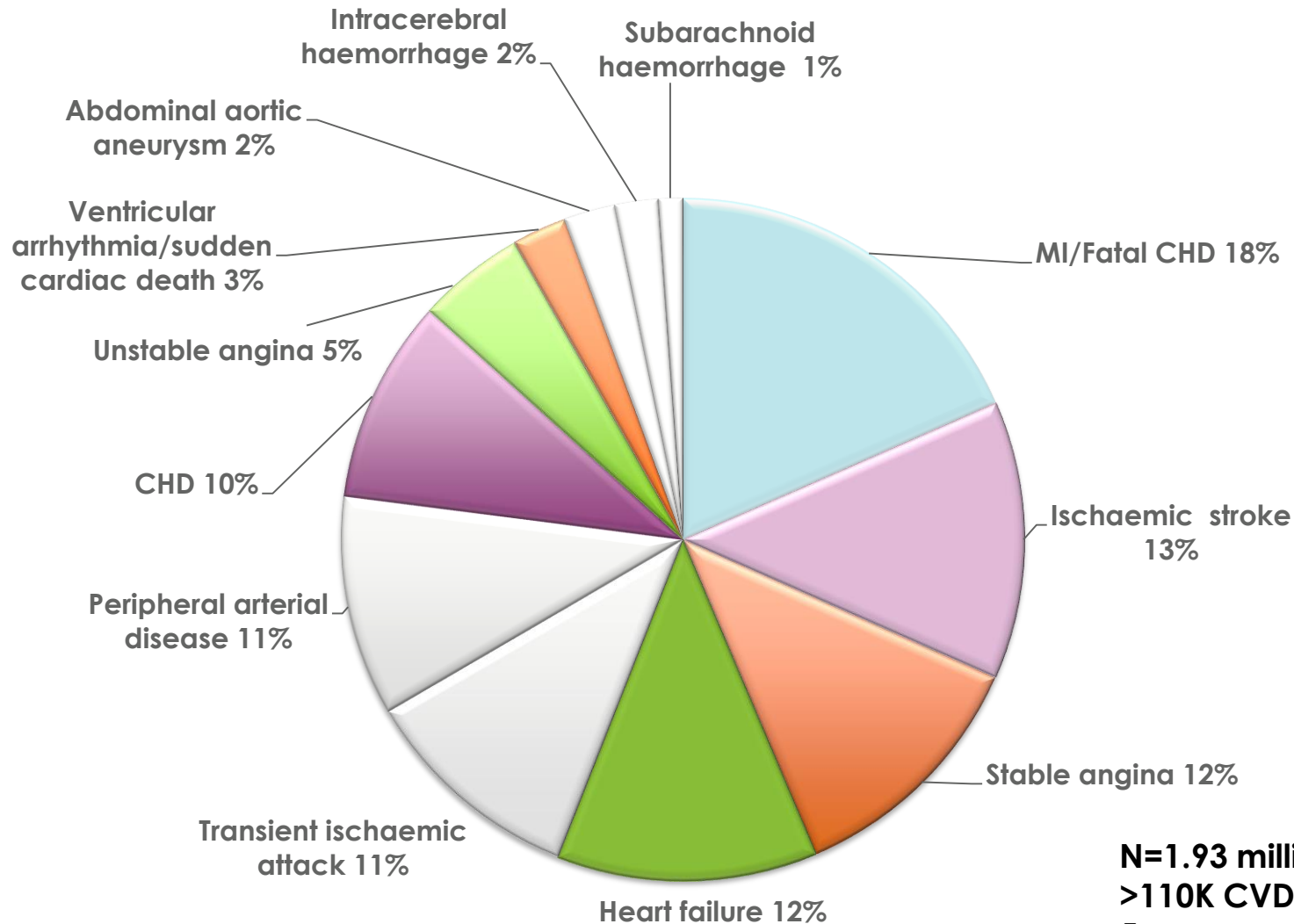
Public Health

Outcomes assessment: importance of linking multiple record sources



How does CVD first present?

In the real world, today



**N=1.93 million patients
>110K CVD events
5 year median follow-up**

Discovery

Trials

Outcomes research/real world evidence

Public Health

What is the role of the Farr Institute?

Drought



- **Data**

- Need much wider national record linkages – CPRD-NICOR-HES
- Need to liberate ‘submerged’ deeper hospital phenotypes
- Need to converge EHR, omics and imaging

- **Tools**

- Health informatics ‘20 years behind bioinformatics’
- And UK 20 yrs behind US?

- **People**

- (re) building **public trust** (care.data)
- Not nearly enough **clinicians** with the training and opportunity to drive improvements in care (and research) through data (cf new US sub-specialty)
- Careers for technical staff
- **Interdisciplinarity**

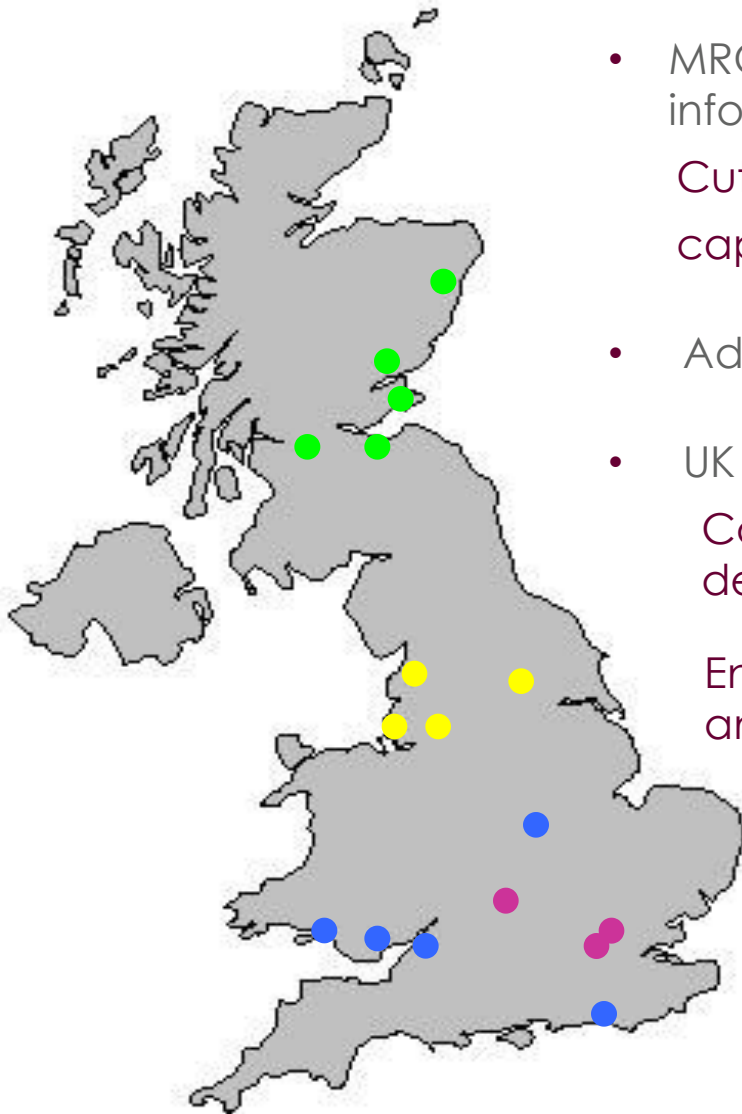
Strengthening health informatics research



Engineering and Physical Sciences Research Council



Arthritis Research UK
Providing answers today and tomorrow



- MRC coordinated 10-partner **£19m** call for e-health informatics research centres across the UK

Cutting edge research using data linkage
capacity building

- Additional **£20m** capital to create Farr Institute

- UK Health Informatics Research Network

Coordinate training, share good practice and
develop methodologies

Engage with the public, collaborate with industry
and the NHS

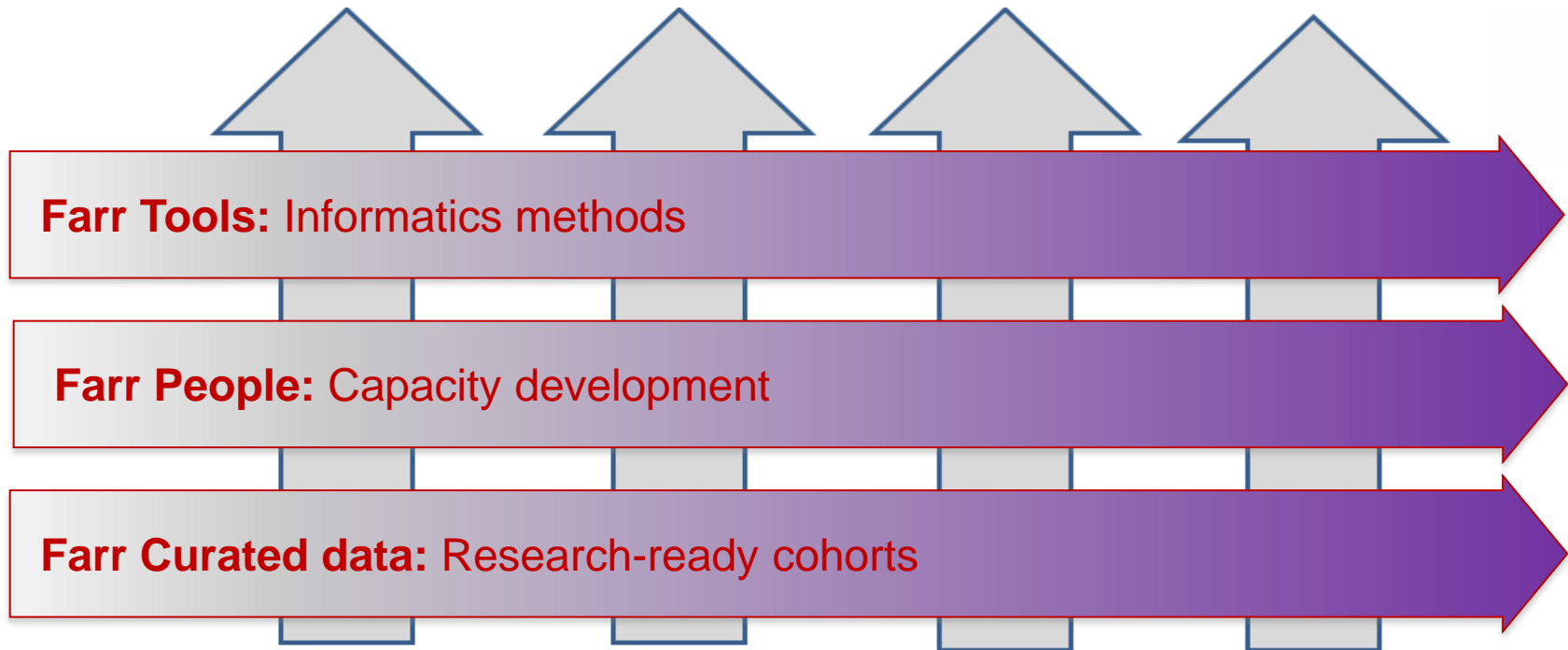
- **Farr London**
- **Farr Scotland**
- **Farr at Swansea, Wales**
- **Farr N8, Manchester**

What are the aims?

= research along the translational pathway



Cardiometabolic Infection Mother and Child Health | Phase 2: Cancer, Neuroscience, Eyes, Musculoskeletal



Rapid evolution of initiatives: emphasis on infrastructure



JULY 2013



JULY 2013



OCTOBER 2013



November 2013
Health Informatics Collaboration
(sharing hospital data across 5
Biomedical Research Centres)



February 2014
Medical Bioinformatics Awards



Who was William Farr?



“Diseases are more easily prevented than cured and the first step to their prevention is the discovery of their exciting causes.”

1807-1883

**Compiler of Scientific Abstracts at
General Register Office
...aka ‘Big data health’**

**Gave us cause of death and
International Classification of
Disease**

Local actions e.g. Victoria Park

Conclusion

- Most of what we know about mortality and morbidity has come from much 'smaller' data than is currently available to researchers
- Personalisation is a secular phenomenon across multiple sectors in society: Medicine offers vanguard and laggard examples!
- If informatics is about data, tools and people – then it is the people which need most urgent development.

Farr London (original) Investigators

CARDIOVASCULAR

- **Mike Barnes**, Director of Bioinformatics
- **James Carpenter**, Professor of Medical Statistics
- **John Deanfield**, Professor of Paediatric Cardiology
- **Mark Caulfield**, Professor Clinical Pharmacology
- **Spiros Denaxas**, Health Informatics Senior Research Associate
- **Nicholas Freemantle**, Professor of Clinical Epidemiology and Biostatistics
- **Harry Hemingway**, Professor of Clinical Epidemiology
- **Aroon Hingorani**, Professor of Genetic Epidemiology
- **Steffen Petersen**, Reader in Advanced Cardiovascular Imaging
- **John Robson**, GP, Clinical lead for the Clinical Effectiveness Group
- **Liam Smeeth**, Professor of Epidemiology
- **Adam Timmis**, Professor of Clinical Cardiology

INFORMATICS

- **Anne Blandford**, Professor of Human-Computer Interaction
- **Peter Coveney**, Professor of Physical Chemistry
- **James Freed**, Head of Health Intelligence and Standards
- **Dipak Kalra**, Professor of Health Informatics
- **John Shawe-Taylor**, Professor of Computing
- **Paul Taylor**, Reader in Health Informatics
- **Alan Wilson**, Professor of Urban Regional Systems

MOTHER & CHILD

- **Peter Brocklehurst**, Professor of Women's Health
- **Tito Castillo**, Chief Operating Officer, LIFE Study
- **Carol Dezateux**, Professor of Paediatric Epidemiology
- **Ruth Gilbert**, Professor of Clinical Epidemiology
- **Irene Petersen**, Senior Lecturer Epidemiology and Medical Statistics
- **Judith Stephenson**, Professor of Reproductive and Sexual Health
- **Phil Koczan**, Chief Clinical Information Officer
- **Irwin Nazareth**, Professor of Primary Care and Population Science
- **Max Parmar**, Director of MRC Clinical Trials Unit

INFECTION

- **Mike Catchpole**, Head of Epidemiology and Surveillance
- **Andrew Hayward**, Senior Clinical Lecturer in Infection
- **Richard Pebody**, Head of the Seroepidemiology Programme
- **Deenan Pillay**, Professor of Virology

PHASE 2 CLINICAL WORKSTREAMS

- **Andy Goldberg**, Senior Lecturer in Trauma and Orthopaedics
- **Anthony Moore**, Professor of Ophthalmology
- **Kathy Pritchard-Jones**, Professor of Paediatric Oncology
- **Martin Rossor**, Professor of Neurology & Director of DeNDRON