Enhancing clinical trials

The use of Electronic Medical Records and pre-existing data integration
Collaboration for translational research in dementia

Alzheimer’s Research UK Oxford Drug Development Institute
Wellcome Trust Strategic awards:
Target Enabling Packages
Neuroinflammation

Dementias Platform UK
Dementia Discovery cohorts (n=2m)
Dementia UK BioBank cohort (n=10k)
Deep and Frequent Phenotyping cohort

IMI-EPAD
European Prevention of Alzheimer’s disease
Readiness register, cohort and Early Phase Trials

Pre-competitive data driven drug development
Pre-competitive cohort repurposing for experimental medicine
Pre-competitive reutilisation of research and real-world data
Pre-competitive data driven PoC/PhII
Cohort A
Cohort B
Cohort C

EPAD Registry
integration

Readiness cohort

Selection criteria

Trial cohort

placebo
Rx 1
Rx 2
Rx ... n

Adaptation by change in intermediate phenotype
Adaptation on cognition outcomes
Biomarkers for secondary prevention

Stratification markers

Progression markers

Adapted from Sperling et al (2011) Alzheimer’s and dementia 7 280-92
Dementias Platform UK

BEATING DEMENTIAS TOGETHER

The Dementias Platform is a coordinated and integrated way of doing dementia research. By helping world-leading experts to work together to do better studies more quickly and at a lower cost, we will accelerate progress in dementia research.

READ MORE

TWITTER

10 year old becomes new face of national #dementia campaign after watching his gran suffer - http://t.co/qR6yRpZh4 http://t.co/1Tlb31uBpX

49 minutes ago

MRC’s Dementias Platform UK supports new European research initiative for the prevention of Alzheimer’s dementia

EPAD, the European Prevention of Alzheimer’s Dementia Consortium will follow in the footsteps of the MRC’s Dementias Platform UK (DPvC),

READ MORE

http://www.dementiasplatform.uk/
UK Biobank for Dementia Research

- 500,000 participants; baseline assessments 2005-8
- Web-based questionnaires for additional exposures and outcomes (cognition, mental health, occupation..)
- Multimodal imaging in 100,000 - brain, cardiac and body fat MRI; bone & joint DEXA; 3D carotid ultrasound
- Repeat Neuroimaging, cognition and sampling in 20,000
- Genotyping of all participants (820,000 SNPs)
- Connectivity to EMRs for mental health
Use of EMRs for research

- 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
CRIS – core functionality

EHR Data Source → De-identification → Processing pipeline → CRIS SQL → CRIS front end
CRIS Security

- Researcher
- Trust contract
- Project
- Audit log
- CRIS
- RIO
- Pseudonymisation
- Firewall
- Output
- Managed by Stakeholder-led oversight committee
- Findings
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.
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
Data available through consortium

- Large variety in “types” of data

- Data is available from more than 53 million subjects from seven EU countries, including

  - >40,000 subjects in AD cohorts
  - >90,000 subjects in metabolic cohorts
EMIF Catalogue

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Research cohorts on AD or aging

• Type of cohorts:
  – Population-based cohorts
  – Clinical cohorts
  – National multicenter studies
  – European multicenter studies
  – Clinical trial cohorts
Data available through cohorts in catalogue

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<thead>
<tr>
<th>Number of subjects</th>
<th>Controls</th>
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<th>MCI</th>
</tr>
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<td>11976</td>
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<td>EEG</td>
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Either access to results from analysis or access to samples/scans
# Available EMR data sources – EMIF-Platform

<table>
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<tr>
<th>Database name</th>
<th>total (cumulative) # of subjects</th>
<th># of active patients in January 2012</th>
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<tbody>
<tr>
<td>Aarhus (DK)</td>
<td>2.3 million</td>
<td>1.8 million</td>
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<tr>
<td>Regional DB Tuscany (IT)</td>
<td>4.8 million</td>
<td>3.8 millions</td>
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<tr>
<td>GePaRD (DE)</td>
<td>17 million</td>
<td>12,655,616 (Jan 2007)</td>
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<tr>
<td>THIN (UK)</td>
<td>&gt; 11 million</td>
<td>3.8 million (Sept 2012)</td>
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<tr>
<td>IPCI (NL)</td>
<td>2.9 million</td>
<td>1.6 million</td>
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<tr>
<td>Health Search (IT)</td>
<td>&gt; 2 million</td>
<td>930,000</td>
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<tr>
<td>Pedianet (IT) {0 to 14 years}</td>
<td>400,000</td>
<td>150,000</td>
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<tr>
<td>Pharma (NL)</td>
<td>&gt; 7 million</td>
<td>5 million</td>
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<td>Birth Cohort (UK)</td>
<td>1,184</td>
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<td>Salford Diabetes registry (UK) TBC</td>
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<td>IMASIS (ES)</td>
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<td>EGCUT (ES)</td>
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<td><strong>TOTAL</strong></td>
<td><strong>~ 48 million</strong></td>
<td><strong>~ 17 million</strong></td>
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Private Remote Research Environments

Local DBs

Data Storage

Project 1

Project n

Data Analysis

Project 1

Project n

Remote Users

Remote Research Environment
Readiness register
Modeling cohort
Standing PoC adaptive trial
With thanks to....

> 50 executive members
> 150 principal investigators
> 500 scientists
> 1500 collaborators
> 50,000 volunteers
> 50,000,000 individuals contributing data
> 200,000,000 euros from funders
Data Interchange with
GP systems

Patient Portal

PROMs  My Care Plan  Rate My Day  Resources  True Colours  ESilverBook

Secure Network

Personal Health Record

Data Interchange with
GP systems

AHSN

OHFT/OUH
Trust Electronic
Patient Record

Research
Information
System (HIC/CRIS)

Mike Denis