Creating the context for a new generation of highly targeted, highly informative clinical trials
The precision medicine challenge
The experimental medicine challenge

Identify early determinants
Identify early treatments to delay onset
Identify treatments To relieve symptoms and slow progression

Cognitive Health

Preclinical
Prodromal
Dementia
Core enabling utilities

• Identification of highly characterised participants
  – Recruitment of stratified samples
  – Discovery studies, trials, in-silico experiments

• Technology capacity building:
  – Imaging, stem cells, bioinformatics:
    • Sharing best practice, niche expertise
    • Standardising protocols, streamlining governance

• Rapid data access:
  – Triangulation between multiple independent datasets
  – >30 cohorts: 2M participants
Integrated Infrastructure

Informatics

>30 Cohort Studies

Cohort Integration

Informatics Platform

DPUK

Data Portal

Dementia Resources

- Trials Readiness Cohort
- Amyloid Cohort
- Familial Disease Cohort
- Biomarker Discovery Cohort

Methods Development

- Biostatistics
- Dementia Outcomes
- Cognitive Assessment
- Trials Recruitment
- ELSI
- Brain Donation

Research Networks

- Molecular and Structural Imaging
- Induced Pluripotent Stem Cells
- Bio-Informatics

Experimental Medicine

- Synaptic Health
- Innate and Adaptive Immunity
- Vascular Disease Mechanisms
- Deep and frequent Phenotyping
Rapid Data Access

UKSeRP

cohort controlled
secure storage space

cohort 1
complete
data instance

cohort 2
complete
data instance

cohort 3
partial
data instance

cohort 4
partial
data instance

remotely accessed
secure analytic space

approved
project

approved
project

approved
project

report

report

report
7 site PET/MR imaging network

- Step change in molecular imaging capability
- Lowering barriers to, and increasing the impact of, imaging studies
  - Economies of scale
  - Knowledge sharing and standardisation of protocols
  - Recruitment of highly characterised cohort participants
6 centre iPS Cells network

• Provide neuronal models of clinical phenotypes
• Preserve cell lines from cohorts
• Develop cellular basis of disease stratification
• Interrogate pathogenic pathways
• Early drug development studies
5 centre Informatics network

- >30 Cohorts (Swansea)
- Imaging and EHR linkage (Oxford)
- Wearable and other Devices (Manchester)
- Genomics (Cardiff)
- Tissue and Brain banking (Bristol)
Highly characterised trials recruitment

- Informatics Platform (>30 cohorts n=2M)
- UKB baseline (inc. genetics n=500K)
- 3T brain and body imaging (n=100K)
- 2 yr repeat imaging (n=10K)

Deep and Frequent Phenotyping study
EPAD adaptive trial
## Risk stratification for clinical studies (and in silico experiments)

<table>
<thead>
<tr>
<th>Sample</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>UKB base population</td>
<td>502,713</td>
</tr>
<tr>
<td>Episodic memory</td>
<td>498,053</td>
</tr>
<tr>
<td>Episodic memory &gt;2 SD below mean</td>
<td>17,096</td>
</tr>
<tr>
<td>...... plus age 55 years+</td>
<td>12,447</td>
</tr>
<tr>
<td>...... plus APOE4 carrier (20%)</td>
<td>2,489</td>
</tr>
</tbody>
</table>
Opportunities: collaboration

• Data access
  – Register as a scientist through the website
  – Apply for data access through the portal
  – Portal goes live imminently

• Cross-initiative partnerships
  – Canada: CCNA, CLSA
  – USA: ADNI, GAAIN
  – Europe: MEMENTO, DZNE, ROADS