



# Dementia research opportunities in the UK

The Translational Research Collaboration in dementia, the UK Dementia Platform, and experimental medicine research at Oxford



# The problem





# The problem

- 44 million affected people
- 800,000 in UK
- The only disease with increasing deaths since 2000
- Current spend > \$600b
- 135 million cases by 2050
- Projected spend > \$1 trillion by 2050



*The banker*  
**Andrea Ponti**  
JP Morgan

*The pharma CEO*  
**Paul Stoffels**  
Johnson & Johnson

*The funder*  
**Francis Collins**  
NIH

*The clinician  
researcher*  
**Ed Richard**  
Amsterdam

*The regulator*  
**Maria Issac**  
EMA





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## G8 becomes the G7 as leaders kick Russia out: It's not a big problem, says Putin's foreign minister

- World leaders said it was up to Putin to 'change course'
- Leaders of the countries agreed to meet again without Russia
- David Cameron made it 'clear' this summer's G8 summit was cancelled

By TAMARA COHEN

PUBLISHED: 00:38, 25 March 2014 | UPDATED: 20:31, 25 March 2014



# No longer a Cinderella subject

## Dementia funding opportunities to April 2016 .....

- |                       |                                     |       |
|-----------------------|-------------------------------------|-------|
| • Alzheimer's Society | Doctoral Training centre            | £600k |
| • Alzheimer's Society | Drug Development programme          | £800k |
| • Alzheimer's Society | ADDF Drug repurposing programme     | £2m   |
| • ARUK                | Alzheimer's Drug Development Centre | £10m  |
| • MRC                 | Dementia capital                    | £15m  |
| • MRC                 | UK Dementia Platform                | £12m  |
| • MRC                 | Deep and Frequent Phenotyping       | £6m   |
| • EU                  | IMI-EPOC                            | €60m  |

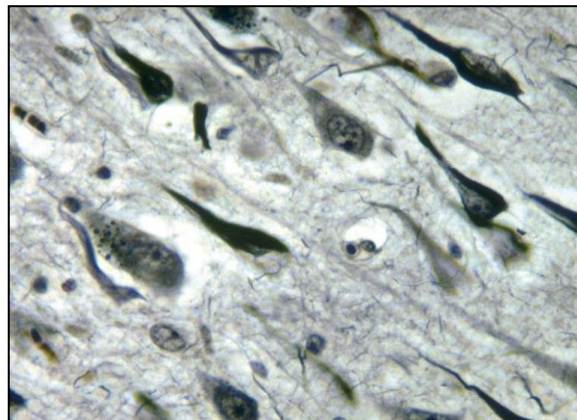
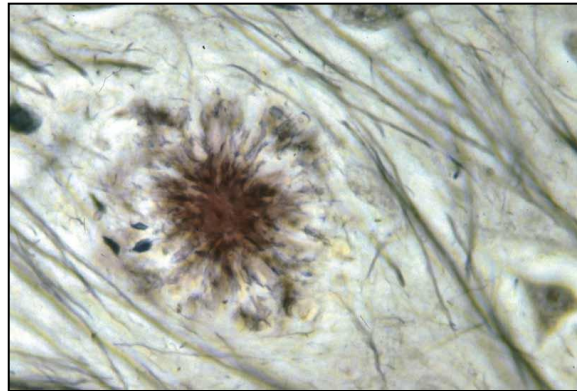
..... approximately £ 100,000,000



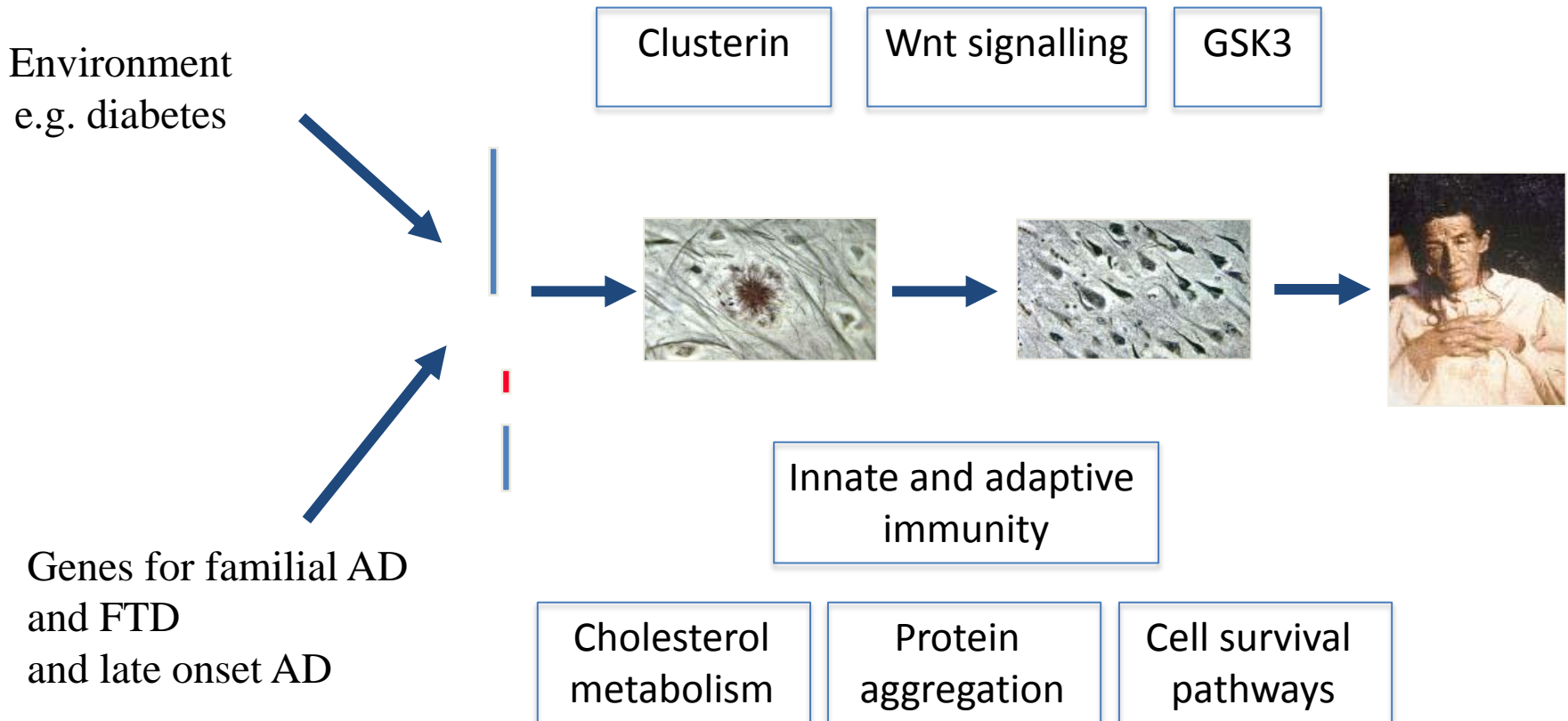


# Alzheimer's disease – What do we know?

# Alzheimer's pathology

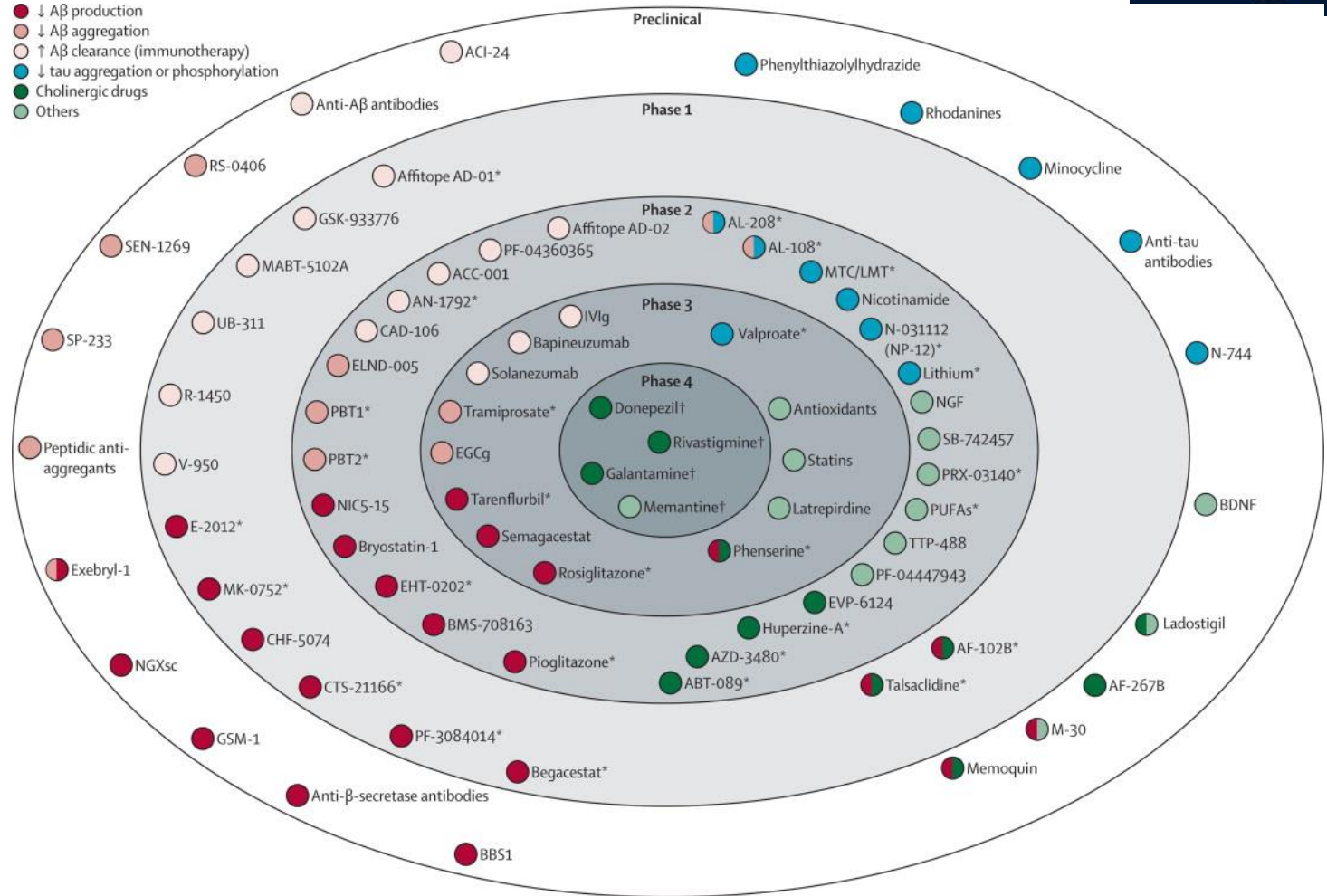


# The amyloid cascade hypothesis – 2014





# No shortage of therapeutic possibilities

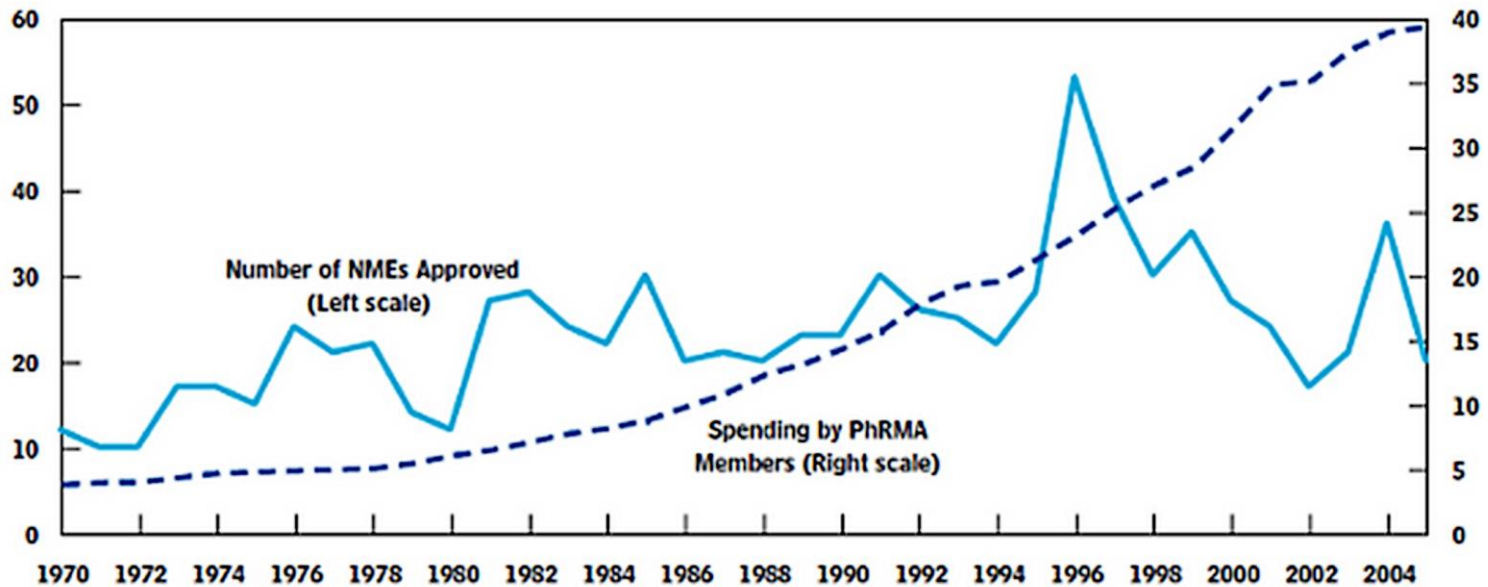




But the trials are failing !



# Not confined to dementia





## But worse for dementia

- Pathways less defined
- Brain less accessible
- Outcomes more uncertain
- Clinical trials more difficult
  
- Prodromal disease – challenge and opportunity



# The solution/opportunity

- Diversify target development
- Develop therapeutics *with PoC in models and man*
- Rapid trials with early read-outs
- Trials in prodromal or preclinical disease

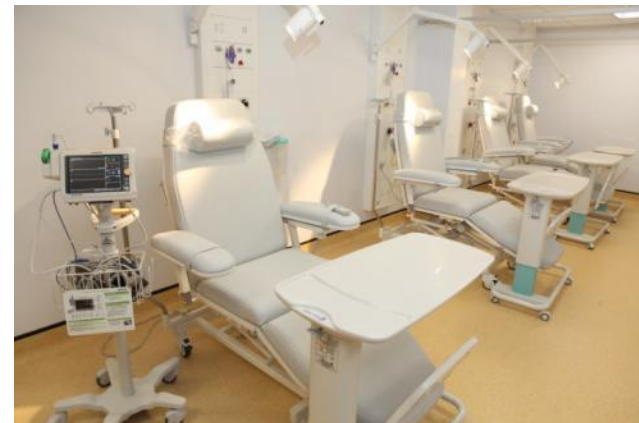


# NIHR Translational Research Collaboration in Dementia



- Newcastle / NTT
- Cambridge / Addenbrookes
- Imperial / IHC
- UCL / UCLH
- KCL/ Maudsley
- Oxford / OUH / OH

Substantial core funding



outstanding experimental medicine facilities



# TRC-D; aims and ambitions

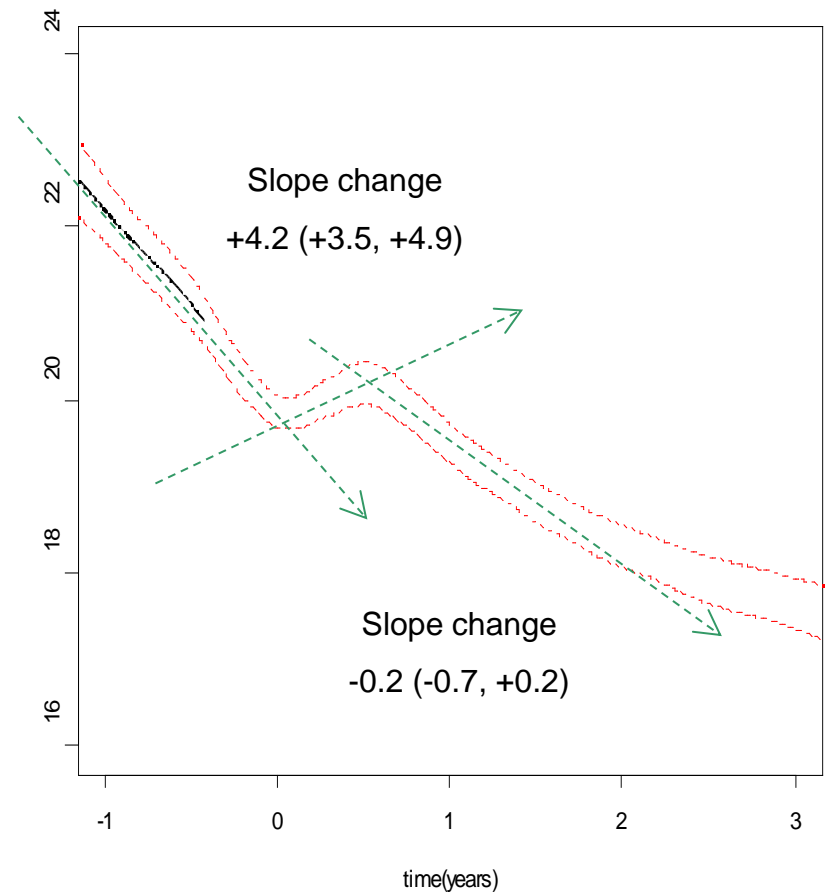
- A collaboration between BRCs and BRU-Ds
- Working with industry
  - Single point of contact and contract negotiation
- Harmonisation and avoiding duplication
  - Subgroups in MRI, PET and iPSCs
  - Use of EMRs in mental health and dementia
- New projects
  - Shared informatics – imaging (Oxford; Mackay)
  - PD dementia biomarkers (Oxford; Lovestone)
  - UK Dementia Platform and experimental medicine (Cardiff; Gallacher)
  - Deep and frequent phenotyping in Alzheimer's disease (Oxford; Lovestone)



# EMR 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



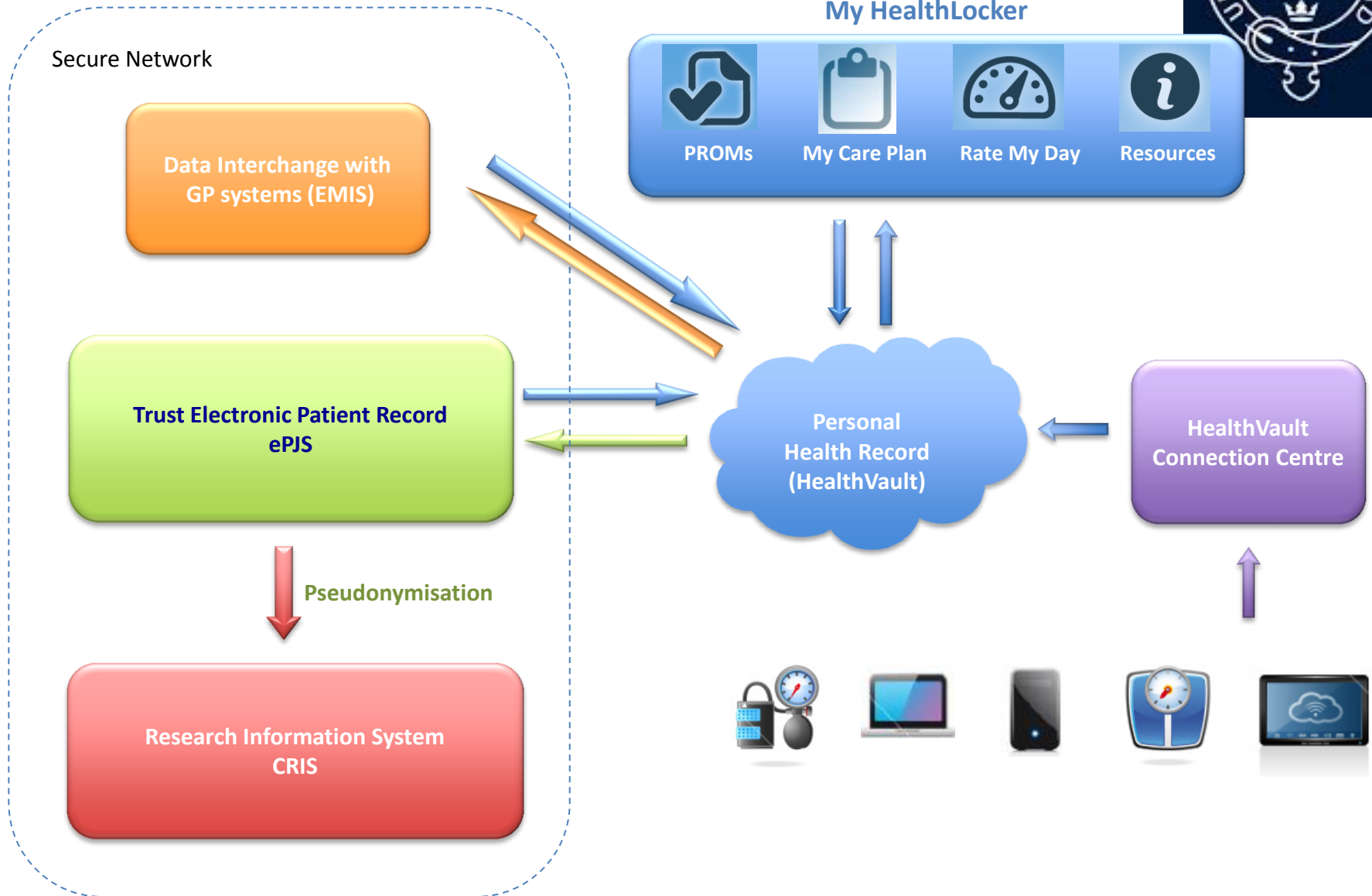


# D-CRIS and then UK-CRIS



- D-CRIS
  - Cambridge & Peterborough, Oxford Health, West London, Camden and Islington
  - NIHR funding; completion 04/2014
  - 1 million plus patients
  - SWAT team 2014-15
- UK-CRIS
  - 10 site extension
  - Proposal in UKDP Capital bid

# eMPOWERMENT Connected Health Model

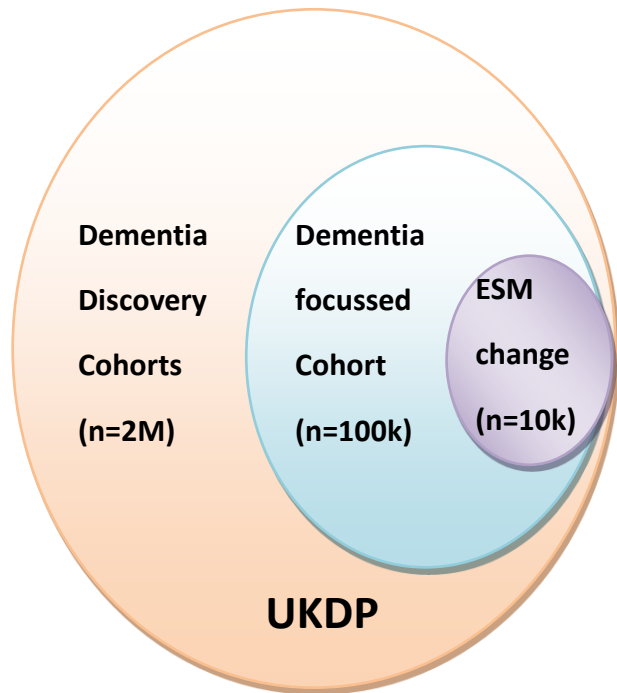




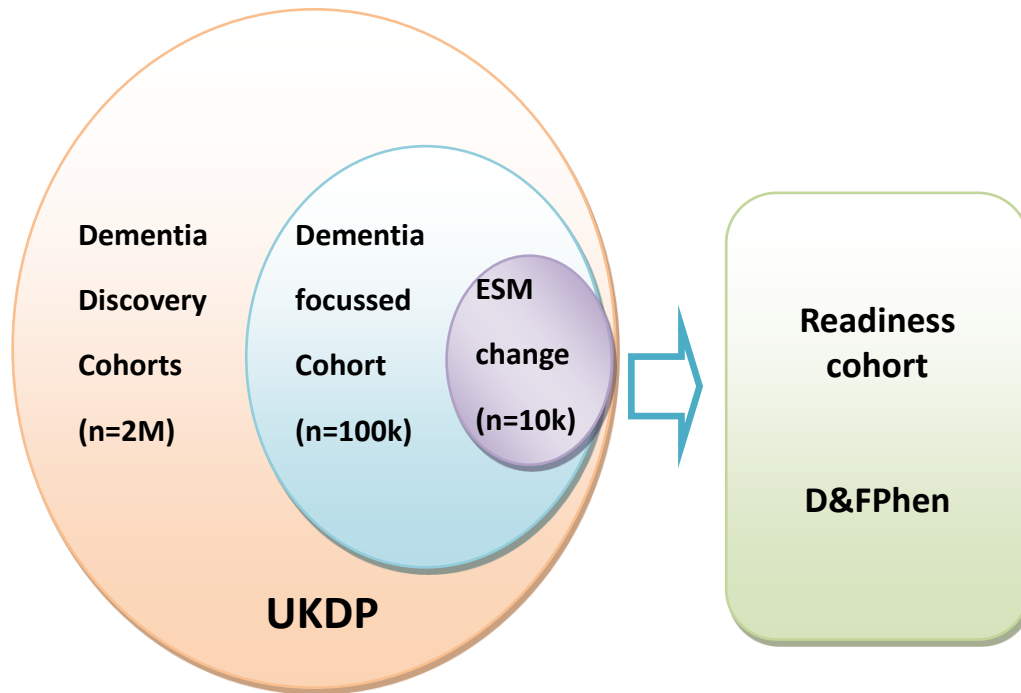
# UK Dementia Platform

- Epidemiologic platform: 21 cohorts (n=2M)
  - Familial, ‘case-rich’ and prodromal populations
- Informatics platform
  - Single portal for access to all cohorts
- Experimental platform
  - UK Biobank imaging cohort (n=100,000):
    - 3T Brain (1.5T chest) MRI, Dxa, 3D carotid Ultra-sound
    - Concurrent imaging, cognitive testing, bio-sampling
  - 10,000 repeat assessment after two years
  - Lead in data for early susceptibility markers
  - Consent for consent for a range of studies

# Moving from risk through biomarkers to experimental medicine



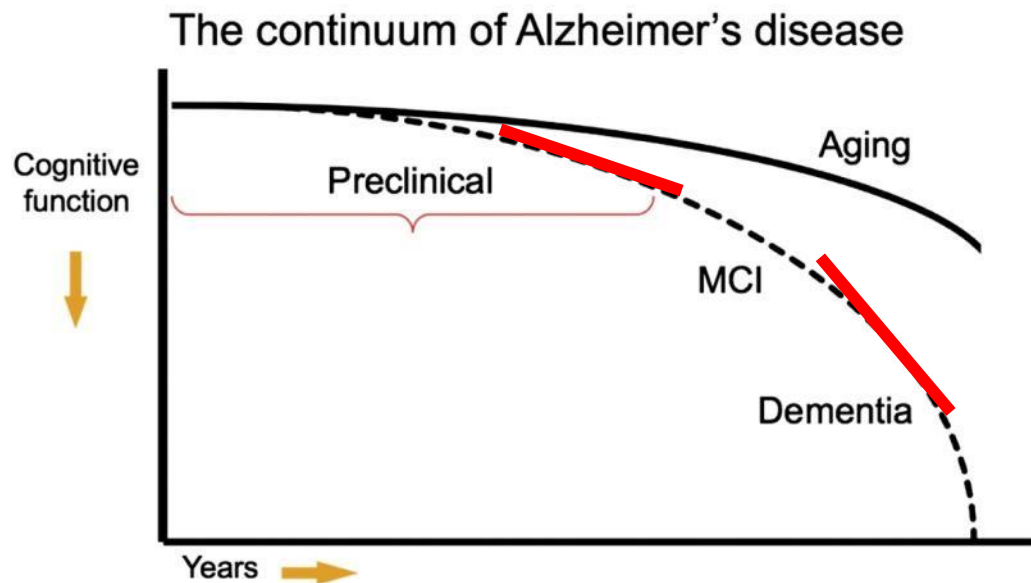
# Moving from risk through biomarkers to experimental medicine





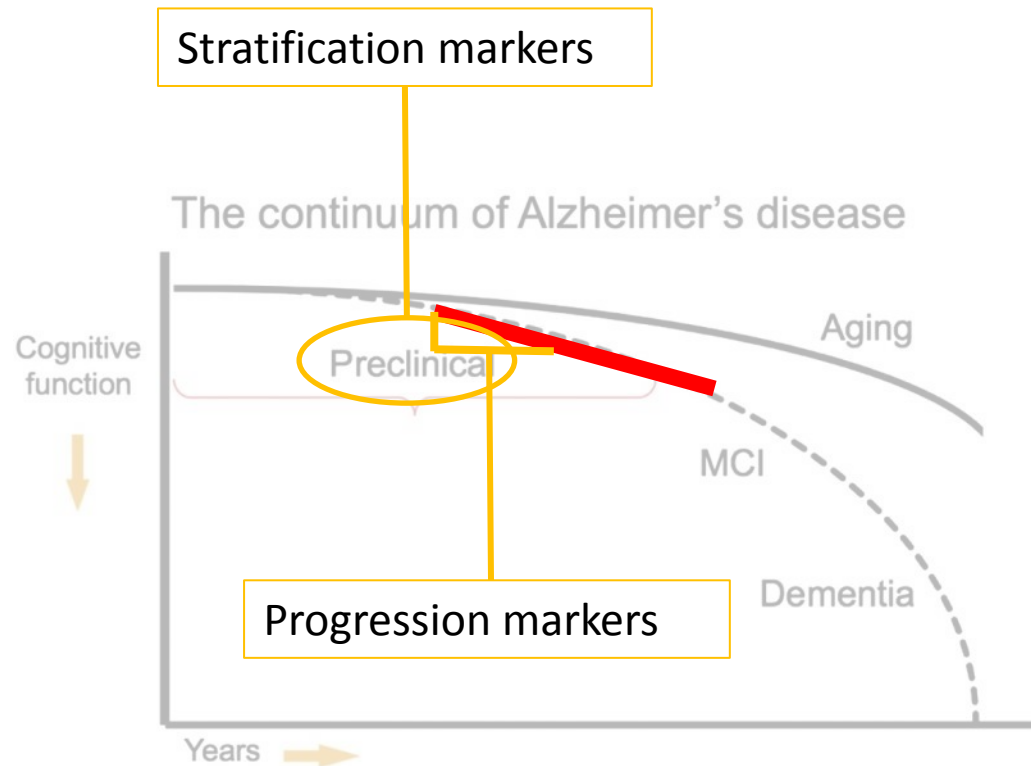


# Trials are conducted too late





# Biomarkers for secondary prevention





# Deep and Frequent Phenotyping

## Deep phenotyping

- PET *A $\beta$  and tau tracers*
- CSF *repeated measures*
- MRI *serial imaging with noise reduction strateg*
- Electrophysiology *EEG and MEG*
- Peripheral markers *noise reduction, change measurement*
- Cognitive markers *computerised batteries, web testing integration*
- novel markers *retinal imaging, quantitative gait measures*

## Frequent phenotyping

- Test the limits of acceptability *monthly, bi-monthly ?*



# Aims and objectives

## 1) determine participant acceptability

- very extensive (deep) and repeated (frequent) phenotyping

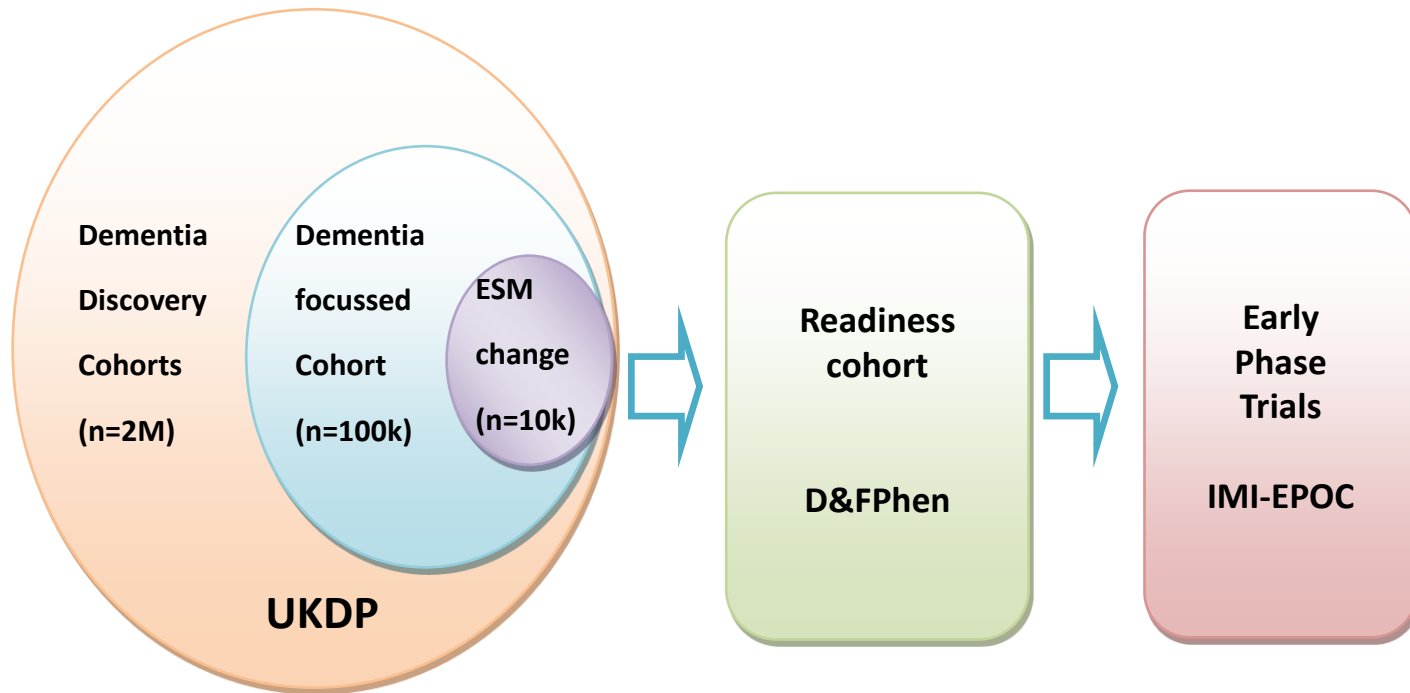
## 2) establish the operational practicability

- Including standardization of acquisition, quality control (QC) and analysis

## 3) prepare for a full trial

- utilising the NIHR TRC-D infrastructure
- establishing protocols
- set-up processes including ethics and approvals
- data management and trials governance.

# Moving from risk through biomarkers to experimental medicine





# European Proof of Concept for prevention IMI-EPOC



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## Prevention of Alzheimer's – What will it take?

June 10-13 2013

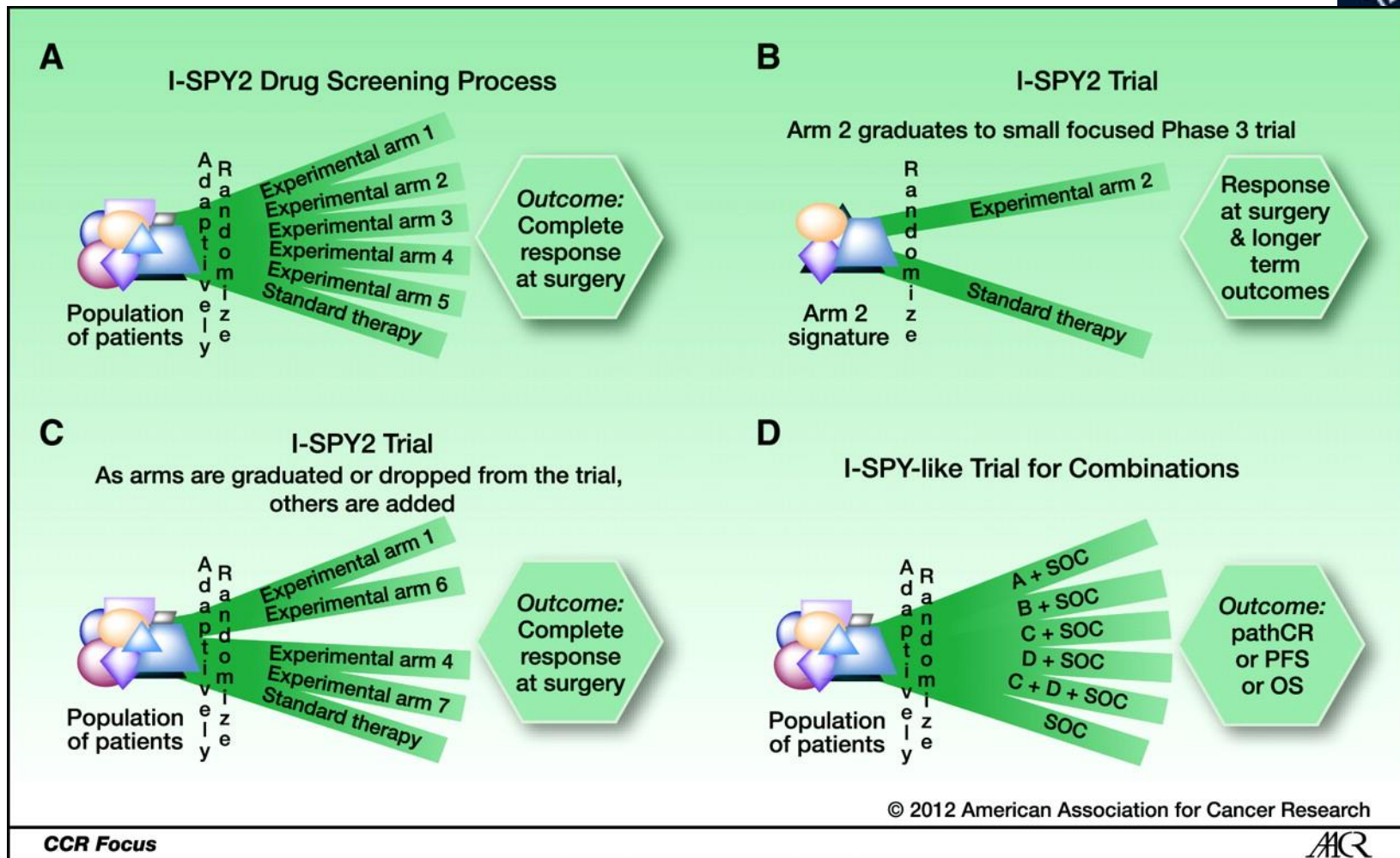
<http://www.nyas.org/publications/EBriefings>



# European Proof of Concept for prevention IMI-EPOC

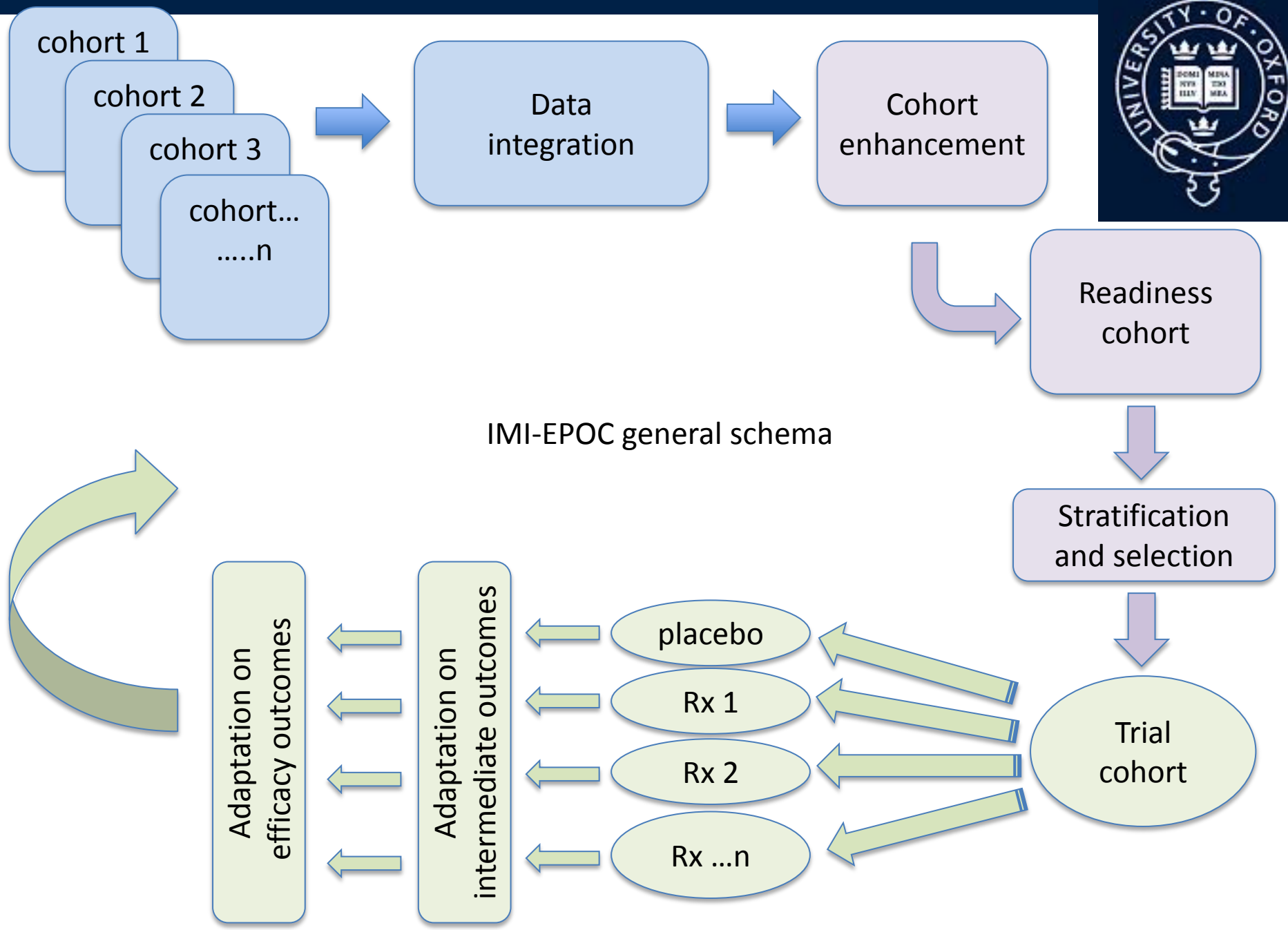
- 11<sup>th</sup> call of Innovative Medicines Initiative
- €60m Public Private Partnership
- EFPIA members led by J&J
- Academic consortium being established
  - Leads Ritchie(Imperial) and Lovestone (Oxford)
  - UK partners based around TRC-D and UKDP
  - European partners from France, Spain, Sweden, Finland, Germany, Holland.....
  - Non-EFPIA industry partners
  - Advisors include Esserman and Berry

# I-SPY 2 schema.

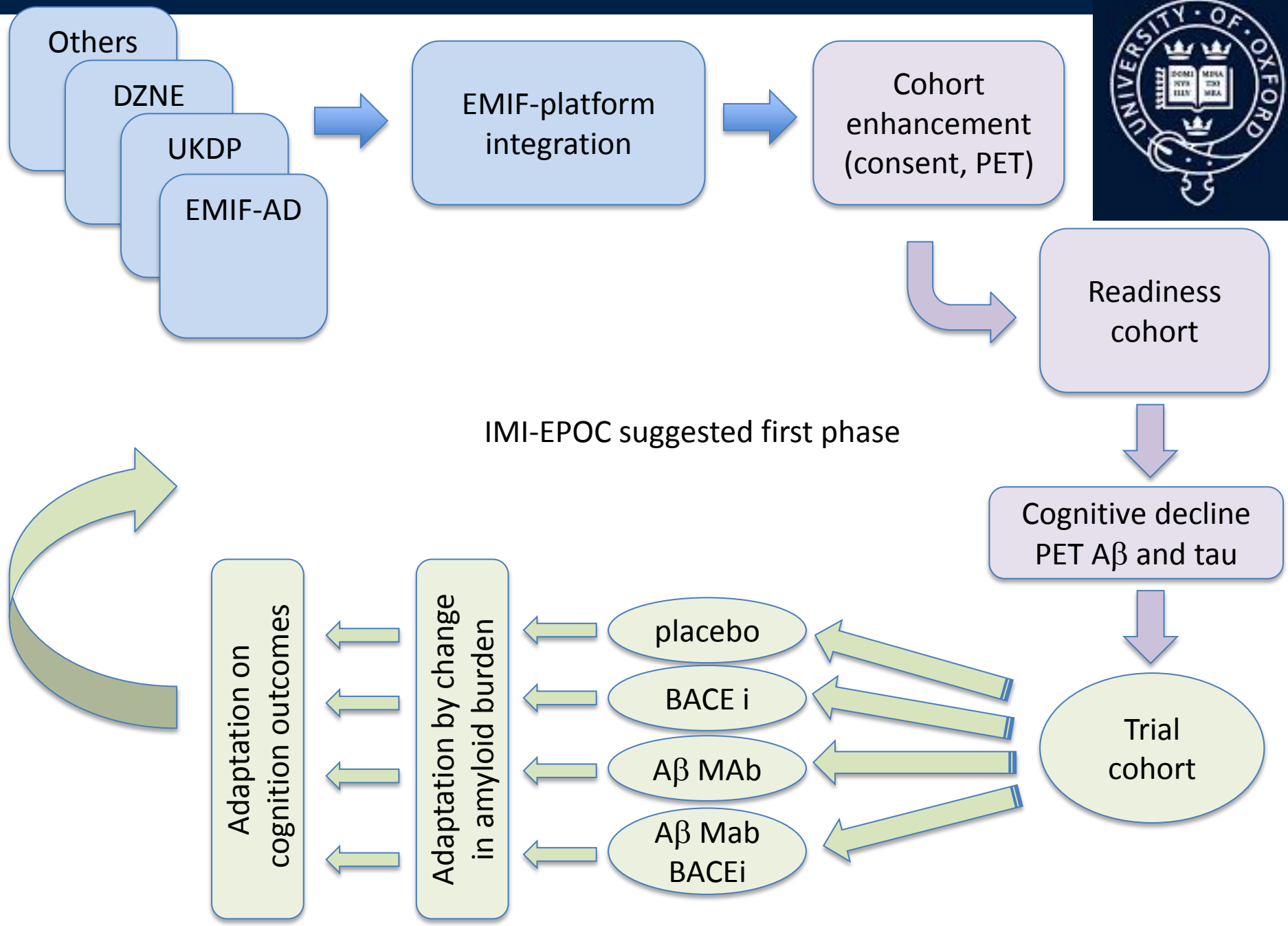


Berry D A et al. Clin Cancer Res 2012;18:638-644

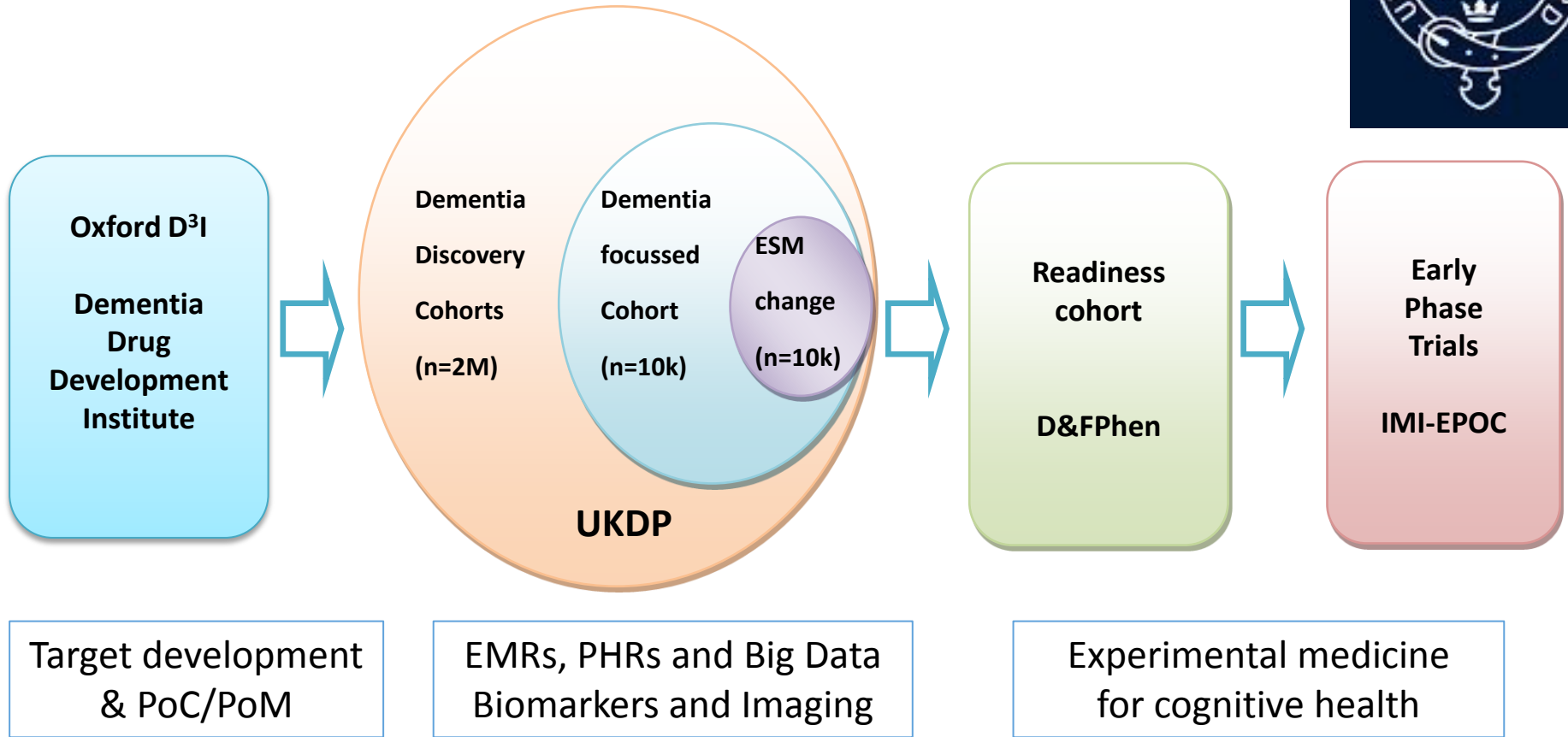




IMI-EPOC general schema



# The opportunity for Oxford



Its about preventing dementia

