EPSRC

Engineering and Physical Sciences Research Council

Report of

EPSRC Dementia Scoping Workshop

2 SEPTEMBER 2013

Introduction and Goals of Workshop

A small scale workshop to identify challenges within Dementia was held on the 2 September 2013.

The goals of the workshop were to:

- Identify scientific research needs and challenges, through which the Engineering and Physical Sciences might be able to make a contribution to Dementia research
- Look for a "Grand challenge" i.e.
  - A large or significant problem with **long term** aims / goals
  - **A Complex problem** that will require ambitious research;
  - Long term outputs which could deliver a **step change** in current knowledge

The remit of the workshop was broad in that it allowed discussion on *all dementias for example* Alzheimers, Vascular dementia, Fronto temporal dementia, Parkinsons, Huntingtons, to name a few. Workshop attendees were asked to focus their thinking around issues of treatment and diagnosis of dementias rather than care.

The outputs from this workshop will help EPSRC identify areas in which it is well positioned to make a contribution to the challenges of Dementia, and will inform the scope of an activity in the area.

Attendees

This was a small scale workshop, and participants were invited, rather than identified through an open expression of interest. Attendees were invited from the following areas:

- Big data, data mining, computational modelling, and computational drug design.
- Non-drug interventions such as deep brain stimulation.
- Imaging technologies
- Others (users e.g. charity, industry, others e.g. TSB, STFC)

A full list of attendees is shown below:

Peter	Bath	University of Sheffield
Richard	Bayford	Middlesex University
Howard	Bowman	University of Kent
Annette	Bramley	EPSRC
Doug	Brown	Alzheimer's Society
Richard	Bryce	University of Manchester
Craig	Buckley	Siemens
Sandy	Cochran	University of Dundee
Nick	Cook	EPSRC
Gareth	Derbyshire	STFC, Daresbury Laboratory
Paul	Edison	Imperial College London
Colin	Fishwick	University of Leeds
Nick	Fox	University College London
Alejandro	Frangi	University of Sheffield
Alasdair	Gaw	Technology Strategy Board
Katherine	Giles	Medical Research Council
Nicola	Goldberg	EPSRC
Kenneth	Harris	University College London
Meilan	Huang	Queen's University Belfast
Declan	Jones	J & J London Innovation Centre
Carol	Jones	EPSRC
Marcus	Kaiser	University of Newcastle
Caroline	Low	Imperial College London
Vicky	Marlow	EPSRC
Hannah	Maytum	EPSRC
Karla	Miller	University of Oxford
Sebastian	Ourselin	University College London
Dolly	Parkinson	EPSRC
Simon	Ridley	Alzheimer's Research UK
Peter	Sawyer	Lancaster University
Bjoern	Schelter	University of Aberdeen
Francisco	Sepulveda	University of Essex
Roger	Staff	University of Aberdeen
Mark	Tarplee	EPSRC
John	Terry	University of Exeter
Gergely	Toth	University of Cambridge
Mark	van Rossum	University of Edinburgh
Richard	Wise	Cardiff University

The Workshop - Outputs

The outputs from this workshop are provided below and each section starts by briefly providing a summary of the activity in which attendees were asked to participate. Following this a short summary which identifies some of the key points raised is provided. (Full outputs are provided in the Annex 1a-3g).

Activity 1:

Activity

After a short warm up exercise, participants were asked to consider diagnosis and treatment. Specifically participants were asked to describe:

a) The ideal future state

- Where do we want to be with dementia research / diagnosis/ treatment in 25 years time?
- How would things be different if we had effective treatment and improved (early) diagnosis for dementia?
- What might that treatment and diagnosis look like?
- What would people be saying / doing differently?
- How would effective treatment and improved (early) diagnosis change things?
- How would we know the situation is better? What would have changed?
- How might developments in dementia, have an impact on other areas? E.g. our understanding of the brain? Or other neurodegenerative conditions?
- What do you think your own field / discipline could have contributed within 25 years time?

b) The present state

- What's happening now with dementia diagnosis / treatment?
- What's frustrating about the current situation?
- What is working?
- What's not working?
- How do you know this is still a major challenge?.
- How is your own field / discipline trying to make a contribution to diagnosis and treatment?

c) Barriers

- What are the critical factors in enabling the best future scenario and allowing us to progress from our current position?
- What needs to change and why can't that be done today?
- Which disciplines need to be working more closely together but aren't?

Summary for Activity 1

A summary of the key points arising from discussions is provided below, but the full outputs are provided in Annex 1a-i.

Key points arising were as follows:

- Currently diagnosis rates for dementia are poor.
- Need to differentiate the "identification/detection" of dementia from the diagnosis of the cause of the dementia

- Any improvements in diagnosis need to be cheap, non-invasive and accurate.
- Identification of dementia types was felt to be important,
- Developments in early diagnosis are currently driven by research need (i.e. attempts to understand dementia better), rather than potential use in a clinical setting.

Activity 2:

Activity
Simon Ridley, Head of Research, Alzheimer's Research UK delivered a presentation which provided background context to the challenges of dementia, and dementia research including perspectives on where Engineering and Physical Sciences might make a contribution. *Part a): Attendees where then asked to consider this presentation and review their present state and future state descriptions (activity 1), and were asked to consider current gaps in research and knowledge of dementia treatment and diagnosis.* *Part b): Participants were also asked specifically to identify the gaps in terms of science and our knowledge?*

Summary for Activity 2: part a)

A brief summary of the gaps identified is provided below. Full outputs are provided in Annex 2a-e.

Gaps from an NHS perspective:

- NHS would be expecting cost effective and robust diagnosis and treatment methods
- Cure and palliative care
- Ability to manage dementia plus co-morbidities
- Prediction about disease progression

Gaps from a patient perspective:

- Treatment options
- Prognosis and prediction – "how quickly am I going to be affected?" and "in what ways?" – often a carer's question – when will care be needed etc
- Assistive technologies to help with daily living and quality of life
- Diagnosis is not early enough – disease progression is often advanced by time of confirmed diagnosis.

Fill in the blanks:

- In 25 years' time we will successfully diagnose the at risk population if we can improve timely access to the appropriate technologies for dementia diagnostics.
- In 25 years' time we will cure Alzheimers if we can understand the biological mechanisims that underpin the clinical systems"
- "In 25 years' time we will have early diagnostics for dementia if we can identify dynamic markers in routine clinical recordings that stratify patient groups and controls"
- "In 25 years' time we will characterise different sub-types of dementia if we can identify suitable connectivity analysis techniques"

Summary for Activity 2: part b)

A brief summary of the gaps and clusters formed is provided below. Additional comments provided are shown in Annex 2 f.

The Scientific Gaps and clusters identified were:

Sensing & Imaging

- Ability to measure real time decline
- Need to know environment versus genetics
- Need to know molecular mechanisms of disease pathologies
- Measurement and sensing techniques
- Sensing and imaging (instrumentation)
- Instrumentation for cell physiology
- Imaging cell physiology in whole organs

Blood Brain Barrier

- Understanding of getting molecules across the blood-brain barrier
- Routes that facilitate blood brain barrier penetration
- Improve general CNS treatment approaches – AD not well enough understood currently

Assistive Tech

- Non-intrusive means for monitoring development of the condition and predicting its onset
- Assistive living technologies
- Develop practical engineering solutions (e.g. BCI) to assist on day to day basis
- BCI using eyes to control things
- AI to provide an environment for a patient to engage with

Early Diagnosis (Proximity to onset) & Progression (Speed/rate of deterioration)

- Improvement of specificity of diagnosis – cause(s) of the cognitive decline
- Development of new tracers
- Clearer picture of dementia as a progression and/or spectrum disorder
- Identifying the signs before getting to a clinician
- Development of apps which can monitor daily behaviour for changes (deterioration)
- Can change in pattern of use of smart phones/iPad identifying risk i.e. predictive marker
- How to use mobile technology to diagnose (and monitor and treat)

Models/Multi-scale Models

- Multivariate/multi model Phenotyping (including “what is normal”)
- Methods that combine qualitative and quantitative data
- Methods to evaluate multifactorial information
- Measure to improve outcome measures
- Understand causality using computational modelling
- Experimental data acquisition/extractions analysis is ‘primitive’ and needs developing
- Good models allow the user to identify test new parameters
- Computational modelling of lifestyle, environment
- Multi-modal biomarker development
- Understand post diagnosis progression

Basic Biology & Pathology

- Novel models for neuro-degeneration/dementia
- Better models of disease (in Silica, Vitro, Vivo)
- We don't understand the multi-scale mechanisms that ultimately give rise to the symptoms of the condition
- Multi-scale models and theories to understand dementia
- Identify signatures of abnormal brain activity in animal models – correlate these with signatures in human patients
- Is there a common network-level proximal cause of multiple dementias
- What underlies the cognitive symptoms of dementia
- Identify predictive animal models
- Basic biology → differences between ND diseases → overlap between ND diseases

In terms of non-scientific challenges the availability of long term funding, and the need to increase research community exposure to people with dementia, and to work more closely with clinicians was also highlighted (the latter with a view to ensuring clinically informed and patient relevant research).

Activity 3: Gaps in the research landscape

Activity
Bearing in mind the discussions so far participants were asked to complete templates on research challenges and specifically to generate problem statements and challenges that might be tackled. Once the templates had been completed, attendees were invited to review all of the challenges identified and then to vote for which they felt was most important.

Summary for Activity 3

A summary for Activity 3 is provided below, but the full outputs are provided in Annex 3a-g.

Research challenges were identified in the following areas:

- Basic Biology and Pathology
- Models and multi-scale
- Early diagnosis and progression
- Big data and integration
- Assistive technology
- Blood brain barrier
- Sensing and imaging

Voting

Basic Biology and Pathology	14
Models and multi-scale	12
Early diagnosis and progression	19
Big data and integration	14
Assistive technology	4
Blood brain barrier	2
Sensing and imaging	7
	72

Group size (number of attendees = 24
[3 votes per person maximum of 2 on any one proforma, or 3 votes across 3 proformas]

Conclusion

Seven research challenges have been identified, with “Early diagnosis and progression” being viewed as particularly important. There is clearly an important link between the challenge of “Early diagnosis and progression” and “Sensing and imaging”. Strength in both sensing and medical imaging means the UK is well positioned to tackle challenges in this area. Additionally delegates have also indicated that clinical engagement/input, would benefit any research in dementia, and so this should be borne in mind for any future activity. Important challenges emerging within diagnosis include instrumentation and techniques capable of identifying dementia sub-types, and also quantitative measurement of disease progression. Much of the discussion at this workshop served to highlight our lack of understanding of the brain and a

variety of neurodegenerative diseases. It may therefore be timely for EPSRC to consider how it might contribute more broadly in the area.

Annex 1a: Dementia Diagnosis

Ideal future for dementia diagnosis

- Everyone that has developed dementia is diagnosed and the diagnosis has much greater specificity – (E.g. Alzheimer's disease as primary cause with minor contribution from vascular pathology)
- Whatever the data is or what its source is, we can capture & combine it e.g. imaging, medical devices, environment…..
- Cost effective, non-invasive, accurate technology for diagnosis.
- Bringing forward point you can make diagnosis

Current situation for dementia diagnosis

- Less than half dementia sufferers diagnosed.
- Attitudes – perceived value of diagnosis
- Technology for diagnosis expensive & not there for every dementia.
- We need better (more accurate) technologies (new/improved)

Where are the barriers to achieving these futures?

- Attitudes (as above)
- Quality of data and lack of consistency in controls & study design
- There is not a "gold standard" technology for diagnosing dementia that is consistently used throughout progression of disease.

Annex 1b: Dementia Diagnosis

Ideal future for dementia diagnosis

Cheap, non-invasive test for all dementias! -> One test for all

- Imaging (non-invasive?)
- Blood test
- Genomics
- Behavioural testing

Current situation for dementia diagnosis + diagnosis

- GP – [too] late
- Memory clinic – [too] late
- Structural imaging (MRI = 20%)
- PET / SPECT
- Biomarkers
- CSF markers are now in clinical use and have reasonable sensitivity and specificity for some of the key questions: blood, urine and saliva biomarkers have little or no evidence base for utility at the moment
- Post mortem diagnosis!
- Slow diagnosis

Where are the barriers to achieving these futures?

Identifying dementia types to stratify populations for drug testing
Cost
Education – No clear route for patient -> diagnosis

Additional discussion

Diagnosis

NICE guidelines state that a patient with dementia should have a structural scan.
80% of patients have the wrong sort of scan (i.e. CT instead of MRI)
This scan "tells you nothing but is cheaper and satisfies the guideline" [This comment was the opinion of one particular attendee, an opinion not shared by all, with others feeling CT does deliver some value].
What do you tell patients if they have dementia? – *It Depends on the specifity of diagnosis – we lack prognostic markers but the most important factor is what is the cause of the dementia*
Right now, diagnosis is only once you've got it! (There is no support for screening in the absence of evidence that this improves outcomes – this has been hotly debated in the BMJ etc and has been the subject so DH meetings to discuss)
Driver for early diagnosis is research based at the moment – in order to get the data for treatment.
Can only specifically diagnose dementia type by post mortem.
"Clinical diagnostic of dementia" is what doctors tell patients.
4 BRU's in UK on dementia [See http://www.nihr.ac.uk/infrastructure/Pages/infrastructure_biomedical_research_units.aspx .]
No clear route for patients and potential patients into clinical trials (Although DeNDRoN is tasked with improving this).
Need robust treatment strategies for patients.

Annex 1c: Dementia Diagnosis

Ideal future for dementia diagnosis Blood test No diagnosis if no treatment – diagnosis if benefit Need for economic benefit Rule out other conditions more easily Patient stratification Early diagnosis, early treatment
Current situation for dementia diagnosis Diagnosis too late Coming forward → no treatment Poor stratification of types of dementia Expertise at GP patchy No good biomarkers just have to wait and see No mechanistic basis
Where are the barriers to achieving these futures? Identify biomarkers and validate Identify good drug targets Enhance non-invasive technologies → affordable point of care Understand cause, longitudinal studies Bioinformatics → linking databases + longitudinal studies Physical sciences + medicare IT infrastructure

Annex 1d: Dementia Diagnosis

Ideal future for dementia diagnosis

- Achieve intervention early through early diagnosis – using cost effective imaging or chemical tests Technologies at standard GP check-up/ screening

→Spectrum of risk + treatment

- Non invasive
- Cheap
- Pre-clinical /symptomatic
- Easy to administer
- Primary care

→Can escalate when at the risk isn't identified

- What type of dementia
- Risk category

→Personalised medicine – appropriate to risk category

- Lack of treatment

Current situation for dementia diagnosis

- Depends on presentation on how you are recognised
- Very variable Behaviour assessment is the only current method
- Inhibitors – only current drug
- Behavioural intervention – responsive

Where are the barriers to achieving these futures?

Quantifying Risk

- Reliability of biomarkers
- Bringing together a collaborative team to work together on timescales needed
- Need tech help in identifying new biomarkers
- Analysis of multiple biomarkers →risk factors
- Integration of these
- Need a larger scale collaboration/consortia/hub/centre for dementia research
- Need to understand the biology →treatment
- New techniques and technologies to understand the biology
- Better animal models
- Computational models built up to a system wide model of connectivity
- Limitations of the solution being just drug based – need to be combined with other approaches – societal level – life course approach
- Data mining
- Maths and trail design
  →reliability or biomarkers
  →biology
  →treatment strategies
- Lack of data

Annex 1e: Dementia Diagnosis

Ideal future for dementia diagnosis Presymptomatic Cheap → Screening ('Measurable') → Quantitative (objective) Leading to stratified treatment (differential diagnosis) Monitoring people via mobile phones, etc. → Speed, behaviour
Current situation for dementia diagnosis Quantitative diagnosis missing
Where are the barriers to achieving these futures? Understanding how cognitive symptoms arise from molecular/cellular pathology Volume of data for data mining, data analysis techniques Complexity, Multifunctional Loads of "good" databases (well – structured , well – annotated) Tools/infrastructure / existing disc boundaries

Annex 1f: Dementia treatment

Ideal future for dementia treatment

"Magic pill" to reverse/prevent symptoms without side effects
Personalised medicine

Current situation for dementia treatment:

Drugs to slow down – Limited effect
Treatment symptom based

Where are the barriers to achieving these futures?

Recoup R&D cost to industry
Investment
Appeal to researchers / focus
Time horizon
Results
Identifying populations for testing – interpretation of data & access to

Additional discussion

Dreamworld: pill that that reverses dementia symptoms

- Magic pill requires early diagnosis
- Diagnosis of when you have dementia already would need regenerative neuro treatment.

Dementia is not "sexy" (appeal)
Care plans / medical insurance – differs in different countries
Social issue of being told you have the gene for dementia
(society is not ready to know if you're going to get dementia when you're 45)

Brain connectivity and structure in the brain
Functional networks
Semantic tasks -> used as tests for dementia
Connections between names and things
Misuse of equipment – fishing expeditions
Common protocols not in place
Heterogenous vs. homogenous data -Common protocols would help here.
Sharing of algorithms from EPSRC research
Info needs to be in open domain

Annex 1g:

Ideal future for dementia treatment An effective treatment choice Different dementias at different stages Preventative treatments Cheap No recurrence Symptomatic + disease modifying Fast + noticabble treatment Slowing the progression Implantable devices
Current situation for dementia treatment: No disease modification treatments Only some tratments for ailments not for other dementias Onlt effective in some people for a limited time
Where are the barriers to achieving these futures? Don't know what we are trying to treat Ways to administer CHS drugs Blood brain barrier Test new treatments, identify the right people at the right time, regulatory framework not fit for purpose Drug repurposing for use at Blood brain barrier? Loss of pharma from this area Lack of private finance

Annex 1h:

Ideal future for dementia treatment Cure disease, not symptoms Stratified Reverse post symptomatic disease Shorter-term: equivalent of DBS
Current situation for dementia treatment: Carers (Cholinergic drugs/ glutamatergic) not very effective DBS for Parkinson's
Where are the barriers to achieving these futures? Early diagnosis would help Need to understand how cognitive symptoms arise from different disease mechanisms Basic research must be done Understanding? Most useful research directions Data bases/ transparency Tools & infrastructure for cross disc research

Annex 1i:

Ideal future for dementia treatment & diagnosis

Achieve intervention early through early diagnosis – using standard cost effective imaging (or chemical tests) at standard GP check-ups / screening.

➔ Spectrum of risk & treatments
- Identify vulnerable phenotypes

➔ Can escalate when an at risk person is identified
- What type of dementia
- Risk category
- Personalised medicine – appropriate to risk category

- Non invasive
- Cheap
- Pre-clinical / symptomatic
- Easy to administer
- Primary care

Lack of Treatment

Current situation for dementia treatment & diagnosis:

- Depends on presentation & how quickly you are referred
- Very variable
- Behavioural assessment only current method
- Inhibitors – only current drug
- Behavioural interventions - expensive

Where are the barriers to achieving these futures?

Quantifying risks
Reliability of bio-markers
Bringing together a collaborative team to work together on timescales needed
Need technology to help in identifying new bio-markers
Analysis of multiple bio-markers -> risk factor
- Inter-relation of these

Need a larger scale collaboration / consortia / hub / Centre for dementia research
Need to understand the biology -> treatment
- New techniques & technologies to understand the biology
- Better animal models

Computational models built up to a system wide model of connectivity
Limitations of the solution being just drug based
- Societal level
- Life – course approach

Data mining
Maths & trial design -> Reliability of Biomarkers
-> Biology
-> Treatment strategies
Lack of data

Annex 2a

What are the gaps from the perspective of the NHS?

- Treatments
  →Symptomatic
  →Disease modifying
- Cheap and robust diagnosis
  →Existing
  →Prodromal
- Cost effective ways of diagnosing and treating patients with dementia
- Cheap
- well establish

What are the gaps through the eyes of patients?

- Lack of alternatives (non-drug) treatments with fewer side effects
- Information on treatments and prognosis
- Robust treatments which are safe and effective

Fill in the blanks with a gap and a possible outcome

_[outcome]_____* if we can *_[gap to be tackled]_"

"In 25 years' time we will delay the onset of dementia symptoms by an average of 'x' years across the UK population if we can……

- Secure long term funding
- look at on-going behaviour instead of cognitive tests
- Understand the biological mechanisms of dementia symptoms
- Diagnose prior to symptoms
- Develop treatments for stratified populations
- Develop surrogate markers of clinical benefit

Annex 2b

What are the gaps from the perspective of the NHS?

Geographical variation of provision
- Neuropsych
- Neurology

Dementia is a massive cost for NHS – how limit that expense?

Cure / palliative care

What are the gaps through the eyes of patients?
Lack of suitable treatments
Developing assistive technologies
Stimulation / social interaction
Improved QOL
Prognosis progression
Aid / care in social situations (think daily living tasks)

Fill in the blanks with a gap and a possible outcome

"In 25 years' time we will ***cure Alzheimers*** if we can ***understand the biological mechanisms that underpin the clinical symptoms."***

"In 25 years' time we will ***have early diagnostics for dementia*** if we can ***identify dynamic markers in routine clinical recordings that stratify patient groups and controls"***

"In 25 years' time we will ***characterise different sub-types of dementia*** if we can ***identify suitable connectivity analysis techniques"***

Annex 2c

What are the gaps from the perspective of the NHS?

Primary care expertise
Adoption
Interoperability w/HIS
Cost effectiveness
Who is the User? – PC, Hospital or memory clinics
No clear route of adoption of new approaches – HOW, WHO, WHEN
HOSPITAL – I.T? → 1year care
Proven treatments
Lack of cost effective – Diagnosis, Treatments
Unclear? Irregular clinical care pathways

What are the gaps through the eyes of patients?

Where do we go first?
What can you do for me
How do I know?
Lack of information
Drug cures that work
Post Diagnoses support
Vagueness of symptoms
+ Objective was of knowing when to worry?
+ Confidence in reporting
Some way to improve quality of life
Prognostic → How quickly am I going to be effected
Predicting Prognosis

Fill in the blanks with a gap and a possible outcome

"In 25 years time we will have Extended 10yrs quality of life if we can achieve Early diagnosis"
"In 25 years time we will have a range of treatments & lower burden of cost on healthcare and cost to elderly If we can get people to look after themselves."
"In 25 years time we will have early diagnosis/treatments and a Better understanding of disease If we can design better clinical trials"
"In 25 years time we will Manage a healthy ageing if we can inform individuals on lifestyle decision and risks"
"In 25 years time we will be able to predict the risk of developing Dementia in X years if we can model disease mechanisms"

Annex 2d

What are the gaps we perceive **from the perspective of the NHS** and social care**?**

- Early stage diagnosis
- Standardised, well annotated databases
- Monitoring of efficacy
- Technology/process to help manage pw Dementia and all co-morbidities
- Affordable, accurate diagnostic technologies
- Access to technology
- Standardisation of data collection
- Prediction of treatment efficacy
- Efficient treatment
- Prediction about disease progression
- Access to specialist centres

What are the gaps through the eyes of patients?

- Disease progression is advanced by time of diagnosis
- Consistent level of care
- Diagnosis not early enough
- Support after diagnosis
- Lack of effective treatment
- Understanding:
    - Of the disease
    - Societal
    - Patients – "When do I start to worry" (cognitive decline: simple ageing, or worse?)
- Assistive technologies
- Access to current state of the art

Fill in the blanks with a gap and a possible outcome

"In 25 years' time we will *successfully diagnose the at risk population* **if we can** *improve timely access to the appropriate technologies for dementia diagnostics***"**

"In 25 years' time we will *provide personalised intervention throughout lifespan* **if we can** *develop early biomarkers that predict interventional (therapeutic) outcomes.***"**

Annex 2e

What are the gaps from the perspective of the NHS?

Reducing "Trial & Error"
Drug based treatments???
R+D geographically spread
100% diagnosis would make the system collapse!
Low cost for any treatment
Diagnosis without cure would put pressure on NHS
Treatment delivery in Community
Non: intravenous treatment
Diagnosis with very low leave of false positives

What are the gaps through the eyes of patients? –and Carers

Variable in approach to diagnosis
Availability of cheap and effective diagnosis and treatment
Effective drugs
Lack of understanding of the disease
Being informed that you are at risk of developing Dementia can have very negative impacts
Not enough information about the conditions

Fill in the blanks with a gap and a possible outcome

"In 25 years time…..
We will be able to use simple (oral) drugs as prophylactics for a range of dementia causes.
We will have simple, reliable, non-invasive test to detect biomarker for Alzheimers etc.
We will have cognitive stimulation / enhancement using drug based interventions
We will delay onset by 5 years and slow or stop progression using drug based interventions
We will manage the condition using drug based interventions

[No comment on gaps provided]

Annex 2f

What are the gaps in terms of science and our knowledge? [What (scientifically) needs to be achieved to address these gaps?] How might engineering and physical Science contribute?

- Early diagnosis
- Novel treatment options
- Cure disease and not symptoms
- Treatment to stop progression
    - Better trial methodologies/POC outcomes & biomarkers
    - Better understanding of mechanics of neurodegeneration in dementia
    - Patient stratification
- Greater consistency of care if we can develop cost effective measures to delay progression
- Better QOL PA Dementia (less than 2 years!)
    - Assistive technology
    - System to enable NHS/Social Care manage all PW dementia and all co-morbidities
    - Effective diagnosis
- Predict progression
    - Optimised treatment
    - Improved caring
- Prevent dementia
    - Identify all modifiable risk factors & early enough
- Monitorng
    - Patient specific treatment
- Perspective of NHS:
- Affordable technology (i.e. PET/MRI/CSF analysis cost
    - Why to diagnose early if no treatment?
- Databases
    - Improvement of algorithms
    - Early diagnosis
- An effective therapy for different disease stages if we can characterise mechanism

Annex 3a

ASSITIVE TECHNOLOGY

What is the research challenge?

- **Improve the quality of life of dementia sufferers and their carers**

Phrase the research challenge as a question(s)

- **Which technologies should be developed that enables dementia sufferers to remain independent for longer**

Why is it important?

- **Bring carers back into productive life**
- **Dementia is an evidently distressing condition for patient and carer**
- **To keep people active in society**
- **Potential to bring benefit relatively quickly**
- **Make tangible progress that evidently helps dementia sufferers**
- **Can link to monitoring condition with assistive technologies**

What disciplines should be involved?

- **Computing**
- **Electronics**
- **Robotics**
- **HCI**
- **Clinical practise → treatment + assessment**
- **Cognitive science**
- **Social sciences**

Who are the key people with an interest in this?

- **Dementia sufferers**
- **Carers**
- **Clinicians**
- **Employers (Carers)**
- **Charities**
- **Technology Companies**

What might make a good Title for this research challenge?

- **Remaining Independent for longer**

Annex 3b

BASIC BIOLOGY & PATHOLOGY

What is the research challenge?

- **How do we develop better treatments**

Phrase the research challenge as a question(s)

- **How do network models relate to molecular changes**
- **New quantitative tools/methods to monitor disease progression *Imaging/electrical/neuro chem**
- **What are the commonalities in disrupted network activity (between different dementias)**
- **How do cognitive symptoms arise from network level changes**
- **Can objectively – measureable signatures of disrupted brain activity in dementia be identified in humans? Can they be reproduced in animal models**

Why is it important?

- **Identify points of intervention**
- **Because to treat you must first understand**
- **Network – level endophenotypes provide more rigorous animal tests and may save pharma a lot of money on clinical trial failures**

What disciplines should be involved?

- **Molecular/cellular biology and neuroscience**
- **Physiology**
- **Chemistry**
- **Modelling**
- **Imaging (medical & molecular)**
- **Systems biology/medicine**
- **Systems neuroscience**
- **Cognitive neuroscience**
- **Neurology**

Who are the key people with an interest in this?

- **All those in disciplines above (academia)**
- **Patients & carers**
- **Pharma**
- **Government**
- **Research Councils**

What might make a good Title for this research challenge?

- **Making sense of dementia from molecules to systems**

Annex 3c

BLOOD BRAIN BARRIER

What is the research challenge?

- **How do we develop better treatments and diagnosis**

Phrase the research challenge as a question(s)

- **Develop new techniques for molecules to cross BBB (in context of dementia and more broadly)**
- **Can we develop a detailed understanding at the molecular level of the properties required to penetrate BBB in context of dementia**

Why is it important?

- **Gives access to portfolio of therapeutic and diagnostic agents + open avenues for new approaches**

What disciplines should be involved?

- **Animal physiology**
- **Neuropath**
- **Membrane Biology**
- **Structure/comp chemistry**
- **Molecular Imaging**
- **MRI & PET**
- **Modelling**

Who are the key people with an interest in this?

- **Pharma**
- **Academics**
- **Patent Groups (Dementia & beyond)**
- **Charities**
- **Funders**
  - **EPSRC**
  - **MRC**
  - **BBSRC**

What might make a good Title for this research challenge?

- **Bridging the Blood Brian Barrier**

Annex 3d

BIG DATA & INTEGRATION

What is the research challenge?

- **Integrated platform – in complete data – in homogeneous data**
- **Multimodal data analysis**
- **Quantitative, Qualitative Data**
- **Robust data analysis/multi-scale data analysis**
- **Need a safe haven**

Phrase the research challenge as a question(s)

- **How to optimally use the data collected for individual patient care for population level studies**
-

Why is it important?

- **Characterise, define the disease**
- **Optimal clinical care pathway**
- **Appropriate interventions**
- **Comorbidities, national health challenges**
- **Tools developed are relevant to other disciplines**

What disciplines should be involved?

- **Health informatics**
- **Computer science**
- **Mathematicians**
- **Statisticians**
- **Epidemiologists**
- **Health economists**
- **Ethics**

Who are the key people with an interest in this?

- **BBSRC**
- **MRC**
- **TSB**
- **NIHR**
- **ESRC**
- **Patient groups**
- **Research charities**
- **Pharma/biotech companies**

What might make a good Title for this research challenge?

- **Integrating patient data for population research in Dementia**

Annex 3e

SENSING & IMAGING (INSRUMENTATION)

What is the research challenge?

- **Need to image/measure real time decline**
- **Need to know environment versus genetics**
- **Need to know molecular mechanisms of disease pathologies**
- **Enhanced measurement and sensing techniques**
- **Sensing and imaging (instrumentation)**
- **Instrumentation for cell physiology**
- **Imaging cell physiology in whole organs**

Phrase the research challenge as a question(s)

- **How to use sensing and imaging to assess cognitive decline**
- **How do we get better parameters out of imaging techniques**
- **How can we combine non-imaging and imaging data**
- **How can we learn and model lifestyle factors and environmental factors from multidimensional sensors**
- **How do we relate the whole system (brain) with the molecular/cellular level**
- **Validity + selectivity + specificity of data and making sure data ties together**
- **How do you get quantitative imaging**

Why is it important?

- **Parameters needed for models**
- **Physiological data**
- **Get as much information out of the patient as possible and use this information as biomarkers**
- **Combination of sensing and imaging information**
- **Two types of sensing → In hospital and in the home**

What disciplines should be involved?

- **Bioinstrumentation**
- **Signal/image processing**
- **Statistical neuroscientists**
- **Ubiquitous sensing/wearable sensing technology**
- **Physicists and engineers**

Who are the key people with an interest in this?

- **UK Bio bank**
- **Human connectome project**
- **WT Neuro imaging Centre**

What might make a good Title for this research challenge?

- **Sensing for Dementia**

Annex 3f

MODELS/MULTISCALE MODELS

What is the research challenge?

- **Multivariate/multi model Phenotyping (including "what is normal")**
- **Methods that combine qualitative and quantitative data**
- **Methods to evaluate multifactorial information**
- **Measure to improve outcome measures**
- **Understand causality using computational modelling**
- **Experimental data acquisition/extractions analysis is 'primitive' and needs developing**
- **Good models allow the user to identify test new parameters**
- **Computational modelling of lifestyle, environment**
- **Multi-modal biomarker development**
- **Understand post diagnosis progression**

Phrase the research challenge as a question(s)

- **How do we create a predictive multi-scale physical dementia of pathophysiology which is informed by the basic biology and the imaging data for understanding the underlying mechanisms and direct treatment**
- **How to develop multi-scale models of brain ageing and pathophysiology that are mechanistic and personalised**

Why is it important?

- **To predict the onset of dementia and the level of disease progression and predict the best treatment strategy**
- **Biology alone is insufficient to provide interpretation of mechanisms**
- **Need a measure for the clinician to see them whether someone has dementia or not**
- **Classification and diagnosis**
- **Forces you to think in terms of first principles in terms of mechanisms**
- **Spanning the space between the basic biology and chemistry and the clinic**
- **Inform testing for costs of cognitive function → cycle to inform the model**

What disciplines should be involved?

- **Maths**
- **ICT Computer science**
- **Neuroscience**
- **Experimental neurophysiology**
- **Clinical input**
- **Biophysics and bioengineers**
- **Systems engineers**

Who are the key people with an interest in this?

- **Patient**
- **Experimental biologists**
- **Clinicians**
- **Pharma Companies**
- **Governance**
- **Insurance companies**
- **Carers**
- **Medical device companies**
- **Software companies**
- **Neuro-informatics researchers**
- **Human brain project**

What might make a good Title for this research challenge?

- **Computational models to understand diagnose and treat dementia**

Annex 3g

EARLY DIAGNOSIS & PROGNOSIS

What is the research challenge?

- **Development of new tracers**
- **Clearer picture of dementia as a progression and/or spectrum disorder**
- **Identifying the signs before getting to a clinician**
- **Development of apps which can monitor daily behaviour for changes (deterioration)**
- **Can change in pattern of use of smart phones/iPad identifying risk i.e. predictive marker**
- **How to use mobile technology to diagnose (and monitor and treat)**

Phrase the research challenge as a question(s)

- **How can we get to the population before symptoms are present**
- **How might we identify the underlying pathological cause of dementia (all types)**

Why is it important?

- **For predictive capability (e.g. markers) → Immediate clinical trials (clinical stratification)**
- **For making a timely diagnosis for treatment management especially for identifying pre-symptomatic patients for trials**
- **Trials can run more efficiently → leading to treatment**
- **Modifiable risk factors (and how to modify them)**
- **Patients with the right type of dementia (patients not be pre-symptomatic here)**
- **Identify quantifiably when symptoms will show these are the people we need to recruit into trials)**
- **Fluid biomarkers (CSF)**

What disciplines should be involved?

- **Industry**
  - **Pharma ADNI funded by a number of pharma companies**
  - **Roche, GSK etc.**
- **CROs who work for pharma (help with trials)**
- **GE – in the device space (dementia diagnostic team in US)**
- **Imaging**
- **Assessing cognition (neuropsychologists but being computerised) ESRC/MRC academic neuropsychologists**
- **Academic clinicians**
  - **Neurologists**
  - **Radiologists psychiatrists**
  - **Clinicians and engineers together**

Who are the key people with an interest in this?

- **Alzheimer's Research UK**
- **Alzheimer's Society**
- **WT**
- **Parkinson's Disease Society + MJ Fox Foundation**
- **CHDI (non UK based USA)**
- **Amyloid imaging → Lilly**
- **AU imaging → identifying key pathologies in Alzheimer's disease**

What might make a good Title for this research challenge?

- **Improving Diagnosis and Measure of Disease Progression ("timely diagnosis" not early)**