Dementias Platform UK

A new era of translational dementia research

DPUK report 2021/22

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Welcome

When Dementias Platform UK (DPUK) was established with funding from the MRC and partners in 2014, our vision was simple: to transform dementia research in this country by providing a new, more open and collaborative, way of doing things. Now, as DPUK’s second phase kicks into gear, there are reasons for real optimism.

Not only are we constantly learning more about the fundamentals of disease, we’re making strides in ensuring clinicians and pharmaceutical companies have the information they need to detect and treat dementia more quickly and effectively than ever before.

DPUK is at the forefront of efforts to innovate in dementia research, bringing together expert voices from across fields and sectors. In this report, you’ll read about (among much else):

- enhancements to our already world-class Data Portal
- our cutting-edge experimental studies and technology networks
- precision volunteer recruitment via our Trials Delivery Framework
- the early-career researchers who are benefiting from opportunities to forge their own paths.

I was delighted to note that DPUK has now registered nearly 3,500 outputs on the Researchfish reporting platform – including 1,267 publications, 1,188 engagement activities, 195 collaborations and partnerships, and 123 instances of policy influence. That’s testament to the hard work and success of our researchers, support staff and advocates.

What makes DPUK distinctive in the dementia research landscape is our focus on translation and our commitment to high-trust, pre-competitive partnership with industry. Fine-tuning that translational pipeline – in our case, from big data through to precision recruitment to mechanism-specific experimental medicine studies – is a high priority as we support the development of disease-modifying treatments.

The future of dementia research is collaborative: a continuum in which discovery and translation work side by side to ensure breakthroughs in the lab can lead to the new treatments we all so desperately want to see. I believe the future is in safe hands – and I’m as optimistic as ever.

Professor John Gallacher, PhD AFBPsS CPsychol FFPH
Director of DPUK

The year in brief

February 2021:

New research involving DPUK Senior Scientist Dr Sarah Bauermeister finds that people who use hearing aids to correct a hearing impairment are less likely to progress from mild cognitive impairment to dementia. The research is welcomed by hearing loss charity RNID and is featured in a number of national media outlets.

May 2021:

Professor Franklin Aigbirhio, DPUK Imaging Network lead, is elected as a Fellow of the Academy of Medical Sciences.

FEB • MAR • APR • MAY • JUN • JUL • AUG • SEP •

March 2021:

DPUK is featured as a case study in the latest report from the non-governmental organisation Alzheimer Europe. The report, titled 'Data sharing in dementia research – the EU landscape', evaluates the legal and policy landscapes that dementia researchers have had to navigate in recent years, identifying key barriers and enablers for data sharing.

May 2021:

DPUK's Data Portal welcomes its 50th cohort, with the number of individuals represented totalling around 3.5 million. Among the new additions to the Portal in 2021 is the Aberdeen Children of the 1950s cohort – a study of 12,150 people born in Aberdeen between 1950 and 1956.

June 2021:

DPUK Director Professor John Gallacher appears on The Economist podcast to provide expert commentary on the decision by US authorities to approve a new Alzheimer's treatment known as aducanumab – the first such drug to be approved in two decades.

July 2021:

DPUK signs a memorandum of understanding with the newly launched Korea Dementia Research Center. The two organisations will work together to provide shared access to data and to develop best practice in running experimental studies and recruiting participants to trials.

July 2021:

A DPUK-funded study led by Professor Paul Matthews demonstrates a method of visualising Alzheimer's progression that could also become a target for new treatments. The paper shows that a particular chemical tracer used in brain scans can highlight the activity of astrocytes – a type of cell that reacts when under attack by Alzheimer's.

September 2021:

Dementias Platform Australia is launched at UNSW Sydney's Centre for Healthy Brain Ageing to enable access to research data from dementia studies carried out in Australia, the Asia-Pacific region and beyond.

September 2021:

DPUK runs its inaugural Autumn Academy – a week-long series of in-depth workshops and lectures giving researchers the chance to hone their cohort data analysis skills.

October 2021:

A study conducted in DPUK's Data Portal by early-career researcher Dr Danielle Newby finds that people with high blood pressure tend to perform more poorly in cognitive tests.

December 2021:

Dr Ivan Koychev, Senior Clinical Researcher at DPUK, receives funding to lead a clinical trial in a collaboration between Oxford University and Novo Nordisk. It will examine whether a commonly prescribed diabetes pill can help reduce risk of Alzheimer's dementia.

OCT • NOV • DEC • JAN •

October 2021:

The Deep and Frequent Phenotyping study (the world's most detailed study of its kind into early Alzheimer's disease) welcomes its first participant for their six-month repeat baseline testing in Oxford. Several more testing sites around the UK are due to open in 2022.

December 2021:

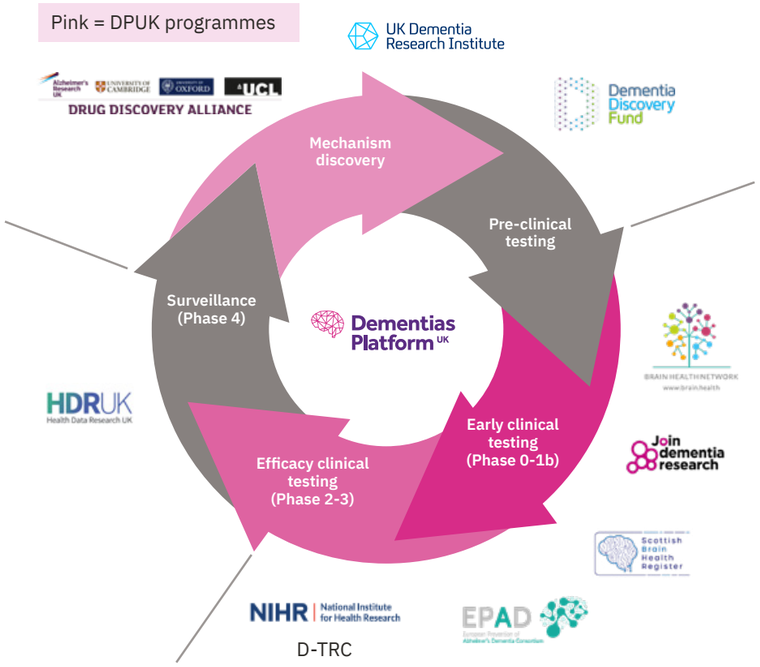
Professor Ronan Lyons, DPUK Associate Director, is awarded an honorary OBE for services to research, innovation and public health. Professor John Hardy, friend of DPUK and a pioneer of neurogenetics, receives a knighthood.

January 2022:

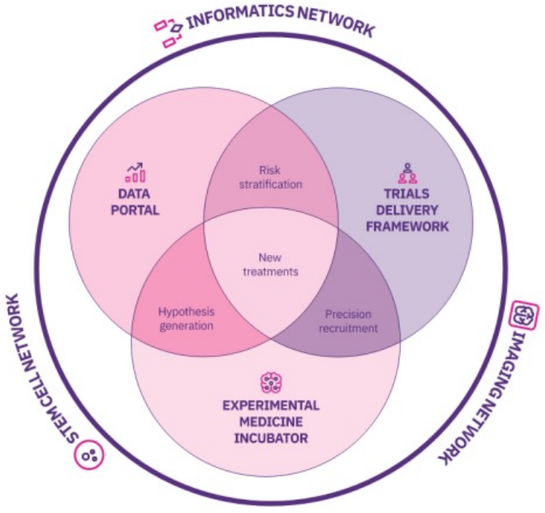
DPUK researchers and professional staff win a grant from Alzheimer's Research UK's Inspire Fund to hold a series of workshops aimed at increasing participation in dementia research among under-represented Black African and Caribbean communities in the UK.

DPUK: an overview

DPUK and the dementia research ecosystem



DPUK: a translational hub for dementia research



Our research programmes, tools and resources empower scientists to discover new ways of detecting, treating and preventing dementia.

- The **DPUK Data Portal** gives researchers rapid, secure access to millions of health research records.
- Our **Trials Delivery Framework** matches public volunteers to the right dementia studies.
- Our **Experimental Medicine Incubator** accelerates and de-risks the development of new treatments.
- Our **Stem Cell and Imaging Networks** enhance the UK's capabilities in two cutting-edge areas of research.

The DPUK Data Portal: cohort analysis for all

Fast facts

- **Free to use**
- **Requires only internet access**
- **Lifestyle, cognitive, imaging and genetic data (and more)**
- **Ideal for early-career researchers**

"The DPUK Data Portal is a ground-breaking initiative supporting dementia research. It is the only facility that offers global access to well-curated research data on millions of participants without charging access fees."

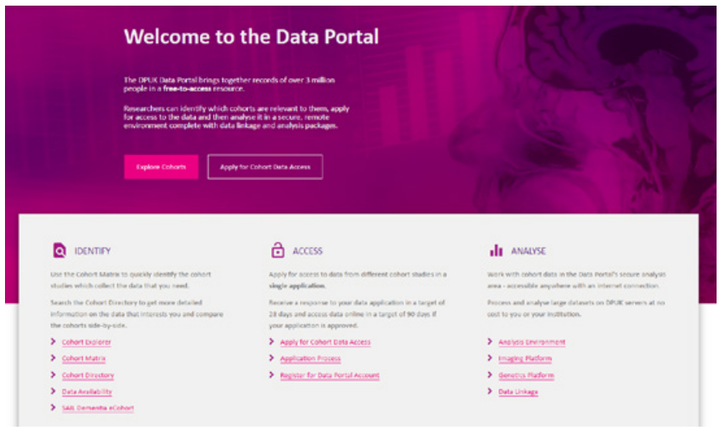
PROFESSOR RONAN LYONS & PROFESSOR SIMON THOMPSON (Swansea University), Data Portal leads

Dementias Platform UK | Data Portal

DPUK's **Data Portal** gives researchers anywhere in the world access to high-quality, multi-modal data from more than 50 population and clinical cohort studies, comprising records for over 3.5 million people.

Researchers can identify which cohorts are relevant to their proposed research question or area of study, apply for access to the data, and then analyse it in a secure, remote environment complete with analytical software and multi-cohort capability.

More than 100 studies are ongoing into the causes of and risk factors for dementia, on topics as diverse as childhood adversity and high blood pressure. A priority for DPUK is to increase the geographical spread of global data access applications.



Enhancing a world-class resource

DPUK's goals over the next 12 months include enhancing the Data Portal's capabilities in a number of key areas:

Data discovery:
By curating data and metadata to research-readiness using the C-Surv data model, and following feedback from users, DPUK will enhance its data discovery and variable selection tools.

Imaging:
Support for and maintenance of the imaging platform is being transferred to Swansea University to facilitate data integration and multi-modal analysis. The platform contains many terabytes' worth of data on more than 6,300 study participants, and there is a steady growth in the number and ambition of access requests.

Tissue discovery:
Specification for a tissue discovery platform hosted by DPUK has been developed in conjunction with the UK Dementia Research Institute's IPMAR study at Cardiff University. The platform aims to become one of the largest cellular model resources available to study Alzheimer's disease, accessible to researchers across the world. The platform will enable the analysis of stem cell lines that have been developed from biological samples and shared with the European Bank for Induced Pluripotent Stem Cells.

High-performance computing:
A high-performance computing (HPC) cluster has been made available via the DPUK Data Portal for large-scale, multi-modal data analysis. The first use case of the HPC cluster is in the development of a genomics platform of cross-cohort data being used to produce polygenic risk scores for dementia by a team at Cardiff and Oxford universities.

Data linkage:
A mechanism to link specified NHS Digital data to research data contained within the DPUK Data Portal has been developed in conjunction with Health Data Research UK and the UK Longitudinal Linkage Collaboration. A proof-of-concept study has been designed, incorporating data from the ALSPAC, ELSA, Generation Scotland and NSHD studies. On completion of this project, the ability to link data to a broader set of cohorts will be developed.

Cohort support:
DPUK is extending its work with a number of collaborating cohorts by managing increasing data access requests on their behalf. To help cohorts demonstrate the added value of data sharing, DPUK will also develop individual 'dashboards' showing access requests and ongoing research projects. And to increase the international profile of collaborating cohorts, DPUK will develop cohort-specific webpages summarising scientific mission, available data, and access procedures.

Map showing origins of data access requests

53 cohorts

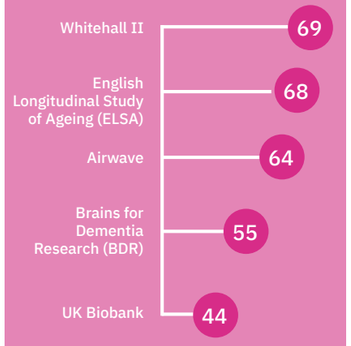
258 study applications (76 new in 2021)

949 cohort access requests

752 users

Applications from **113** organisations in **25** countries

Top 5 Data Portal cohorts by access requests from researchers:



Study spotlight:
Exploring the links between iron and dementia

The DPUK Data Portal is freely accessible to any bona fide researcher, offering excellent opportunities for those in the early stages of their careers. One postdoctoral researcher making the most of the Data Portal's capabilities is Dr Laura Winchester from the University of Oxford.

During a three-year fellowship funded by Alzheimer's Research UK, Dr Winchester will use the Data Portal's vast datasets – combined with sophisticated data analysis techniques – to improve our knowledge of whether varying levels of iron in the brain might be linked to dementia risk. Measurements of iron can be taken by blood tests, through our genes, or in brain scans.

Dr Winchester says: "This project will provide insights into the role of iron in the development of dementia. The research may also identify new ways to detect disease and serve as a foundation for future studies to determine if lowering iron levels in the brain could help prevent or treat dementia."

Training the data analysts of the future

Through our analyst training programmes, DPUK is helping to inspire a new generation of data scientists. Our well-established Datathon events give researchers the chance to work in multidisciplinary teams to tackle specific dementia research questions using cohort data within the DPUK Data Portal.

Datathons are free to attend and are ideal for early-career researchers with an interest in statistical analysis or machine learning methods. More than 170 people have taken part in our Datathons since they began in 2018.

New in 2021 was the DPUK Academy series – week-long, in-depth programmes of expert lectures, presentations, guided tutorials and group workshops. Our first Academy ran in autumn 2021 and saw 20 experienced data analysts learn new cohort analysis techniques to enhance their data science skillsets.

Since then, the Autumn Academy has been complemented by a Spring Academy aimed at beginner cohort analysts.

Trials Delivery Framework: precision recruitment in dementia research

Dementias Platform UK | Trials Delivery Framework

DPUK's **Trials Delivery Framework** is establishing an engine for testing new treatments for dementia. Its aim is to bring the **right people** to the **right place** for the **right project**.

This precision-matching of volunteers to early-phase trials based on detailed genetic and observed characteristics will ensure that researchers testing therapies and interventions can understand quickly and robustly what works – and what doesn't.

The Trials Delivery Framework is closely aligned with DPUK's Experimental Medicine Incubator, aiding with participant recruitment, stratification and case validation for pre-clinical experimental studies. It operates in conjunction with the NIHR's Join Dementia Research initiative and the Scottish Brain Health Register.

As the Trials Delivery Framework develops, it will work with clinical brain health facilities and memory clinics across the UK to create research 'centres of excellence'. This will significantly improve the process of study set-up, recruitment, retention and delivery in dementia research.

We have three sites already identified and are establishing relationships with commercial organisations to further streamline trial set-up. We are also developing collaborations with similar networks internationally to facilitate worldwide multi-site trials.

"The Trials Delivery Framework provides a crucial link between researchers, projects and precision-matched volunteers. It combines all of these aspects to deliver trials quickly, effectively and efficiently to get new dementia treatments to the public."

DR VANESSA RAYMONT (University of Oxford), Trials Delivery Framework lead

Volunteer registries: people power to beat dementia

"By using volunteers from existing cohort studies, we can identify the people who are at risk of developing dementia symptoms in the next five or ten years. We can then test what impact certain interventions will have on the path of disease progression in new, highly targeted trials."

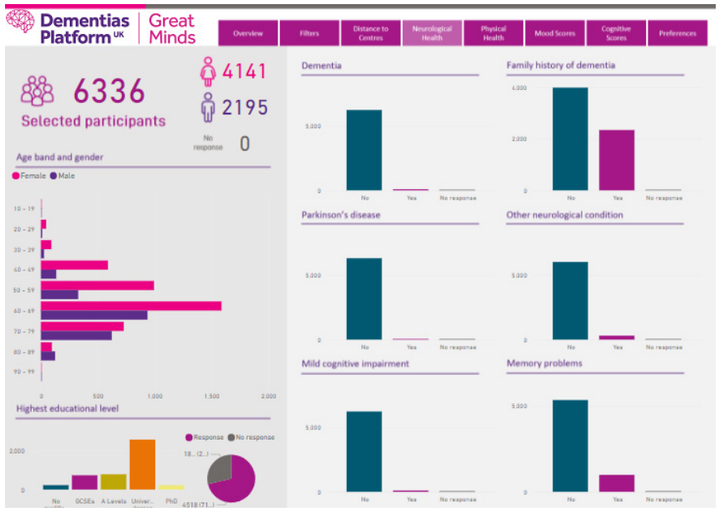
DR IVAN KOYCHEV (University of Oxford), DPUK's research volunteer registry lead

DPUK runs two registries of public volunteers: Great Minds and the Clinical Studies Register. Study sponsors can use these resources to find the right participants for their project – whether it's an experimental study or a clinical trial.

Great Minds is an opt-in pool of around 6,000 highly characterised research volunteers, primarily recruited from existing DPUK-affiliated cohort studies. These volunteers complete six-monthly questionnaires and cognitive tests.

Our **Clinical Studies Register** comprises more than 58,000 research participants who have already undergone extensive characterisation and have pre-existing consent for re-contact through their parent DPUK cohort. By combining detailed phenotyping and, where available, genomic data from cohorts, the Clinical Studies Register enables risk stratification per hypothesis at a level of detail and convenience that would not otherwise be available.

We have developed interactive feasibility tools to enable researchers to determine the number of Great Minds or Clinical Studies Register members that meet their study's requirements. This tool is accessed via the DPUK Data Portal.



Studies involving Great Minds volunteers

A smartphone app to test cognitive decline

To date, testing memory and thinking skills has not been possible without having to ask individuals to come to the clinic. The purpose of this research is to test whether a new mobile app is effective in remotely measuring cognition among healthy adults – helping to detect risk of cognitive decline and dementia as we age. The app was created by technology company Five Lives, working under the scientific guidance of researchers from Oxford University.

Detecting impairments in day-to-day function

The aim of the Remote Assessment of Disease and Relapse – Alzheimer's Disease (RADAR-AD) study is to assess the use of remote monitoring technology (RMT) such as fitness watches in detecting impairments in people's ability to function in day-to-day life. This is measured through the activities of daily living – for example, dressing oneself or preparing a meal. The RADAR-AD study will gather health data using RMT in people with Alzheimer's disease and mild cognitive impairment. Data will be compared with the normal tests these volunteers would do when they visit a hospital, and with RMT data from healthy people. The study is being carried out by researchers from Oxford University and King's College London.

Dementias Platform UK
Great Minds

Great Minds live events

Great Minds holds six-monthly events to give members an insight from leading scientists into the latest developments in dementia research.

Broadcast live on YouTube, these popular seminars have covered progress in dementia research, healthy ageing strategies, Parkinson's and related dementias, and frontotemporal dementia.

The series began in May 2020 and has, to this point, been held exclusively online because of COVID-19 restrictions. An in-person event is due to be held at the University of Bristol in June 2022.

4 online events

10 expert speakers

640 attendees

Experimental Medicine Incubator: reducing the time, cost and risk of drug development

Dementias Platform UK | Experimental Medicine Incubator

Bringing together scientists from industry and academia, DPUK's **Experimental Medicine Incubator** (EMI) is an engine for accelerating and optimising the clinical trials process in dementia. The EMI takes exciting new research prospects from pre-clinical labs and runs in-human studies to test whether a concept is likely to perform well in trials.

Our experimental programme not only investigates the feasibility of new treatments – it also develops quick and accurate methods of measuring their effectiveness in research participants. In this way, the EMI helps focus the investment of time, money and resources on treatment concepts that are most likely to succeed when tested on the wider population.

The EMI offers exciting opportunities for early-career researchers and works closely with DPUK's other workstreams: fresh ideas for research flow in from the Data Portal, and those predicted to be most effective are fast-tracked directly to our Trials Delivery Framework.

The EMI is a partnership with DPUK's industry partners, in collaboration with the UK Dementia Research Institute, Alzheimer's Research UK, and Alzheimer's Society.

"Our experimental programmes increase industry confidence in the decisions to pursue or cancel potential treatments based on early indications of their effect on disease processes in people with, or at risk of, dementia."

PROFESSOR JAMES ROWE (University of Cambridge), Experimental Medicine Incubator lead

Vascular Health

Lead: Dr Atticus Hainsworth (St George's, University of London)

Our experimental medicine studies are grouped around three core processes in Alzheimer's disease and other dementias: the loss of synapses, brain inflammation, and vascular disease.

The Vascular Health theme tests treatments that target the cardiovascular system – the human body's network of blood vessels and the heart. There is a wealth of evidence that heart health and brain health are intrinsically linked, and because cardiovascular risk can be modified by lifestyle and medication, it presents an exciting target for potential treatments for dementia.

Researchers in the Experimental Medicine Incubator's Vascular Health theme are using large datasets from the DPUK Data Portal and elsewhere to generate hypotheses, shortlist potential treatments, and optimise the design of interventional studies.

The wider DPUK Vascular Health network benefits from multidisciplinary expertise and includes international leaders in dementia and stroke medicine, neuroimaging, drug trials, neuropathology, and translational biology. The group has representation from centres of excellence across the UK and actively encourages collaboration proposals from industry.

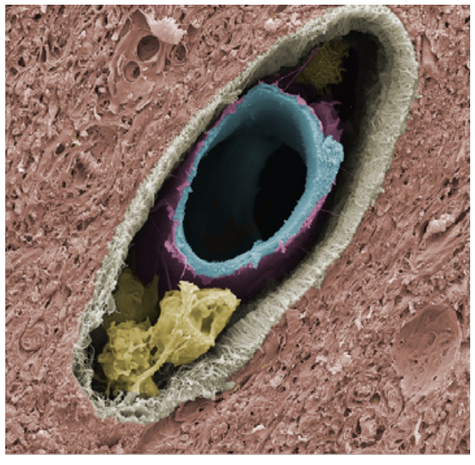


Image: Dr Matthew MacGregor Sharp (University of Southampton)

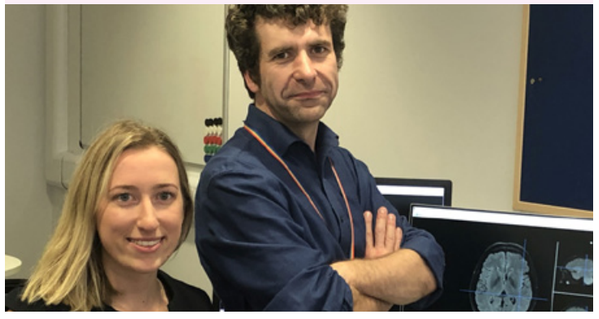
Study spotlight: Can drugs that manage heart disease be used to treat dementia?

Dr Terry Quinn and his team at the University of Glasgow are investigating whether any medications currently used to treat heart disease could also be used to treat dementia. They are scouring huge datasets from UK Biobank to find heart medications that are associated with healthier brain scans or better scores on memory assessments.

Once the researchers have identified a list of cardiovascular drugs that could offer potential cognitive benefits, they will investigate them further using richer data present in the DPUK Data Portal. This stage of the project aims to condense the 'longlist' of potential drugs into two or three with the strongest links to improved brain health. These select few will then be tested in a large, randomised clinical trial. In keeping with the aims of DPUK's Experimental Medicine Incubator, this will ensure precious time and resources are only spent on the drugs that are most likely to offer a viable treatment for the vascular aspects of dementia.

Repurposing existing drugs also helps fast-track the process because they have already been shown to be safe and effective in humans, which allows for several stages of drug development to be skipped.

Dr Quinn says: "The process of developing a new drug from scratch usually takes around 20 to 25 years. What we're doing will bring the time taken for a drug to reach clinical trials down to just two years."



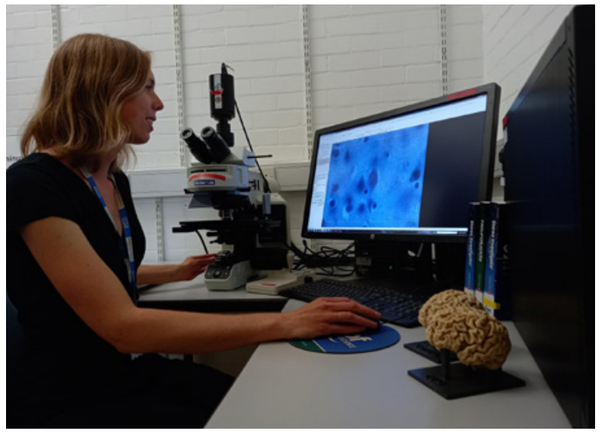
Synaptic Health

Lead: Professor James Rowe (University of Cambridge)

Synapses are the connections that carry information between brain cells (neurones). They are critical for thinking, memory, decision making, perception and movement. Synapse loss and damage has been implicated as an early indicator of the development of Alzheimer's disease and other forms of dementia.

Researchers in the Synaptic Health theme – from both academia and industry – are aiming to understand how synaptic changes lead to cognitive impairment, and how these differences can be measured in people. To quantify the loss of synapses in people with Alzheimer's disease, other forms of dementia and mild cognitive impairment (and its impact on brain function and cognition), researchers are testing cutting-edge brain scanning methods and analysis of cerebrospinal fluid (the fluid around the brain).

Understanding synaptic health – and identifying new biomarkers – may be key to better treatments in the future.



Study spotlight:
Detecting subtle markers of Alzheimer's disease

One major project within the Experimental Medicine Incubator's Synaptic Health theme is the New Therapeutics in Alzheimer's Disease (NTAD) study. The study aims to identify, using imaging techniques, the earliest signs of Alzheimer's disease in the brain – before symptoms start to show.

These sensitive measures of the early disease process will enable drug developers to test new interventions with more precision. Crucially, they will allow trials of therapies that combat dementia before the damage caused becomes irreversible.

To find these measures (known as biomarkers), researchers based at the universities of Cambridge, Cardiff and Oxford are collecting a wealth of data from volunteer participants in various stages of cognitive health. Data collected includes medical history, blood test results, amyloid protein status (from a PET scan or lumbar puncture), MRI scan, MEG scan, and neuropsychological tests. Each category involves taking multiple measurements, and the research teams are still busy collecting data from participants.

Although it is early in the NTAD study, the researchers are already seeing physiological differences between the participants with and without memory impairment. For example, the Cambridge-based team has detected subtle changes in brain cell activity that indicate early Alzheimer's disease and which could be used as a biomarker of the condition.

A new study called Synaptic Health in Neurodegeneration (SHINE) will expand on the work of NTAD by probing a larger cohort with more diverse imaging techniques, including PET-MR. The two studies will result in a rich and unique data resource offering novel research insights and early targets for development by DPUK's industry partners.

NTAD in numbers

85 participants

30 control participants

30 participants with mild cognitive impairment

25 patients with Alzheimer's disease

80% of participants returning for annual scans

25 researchers involved

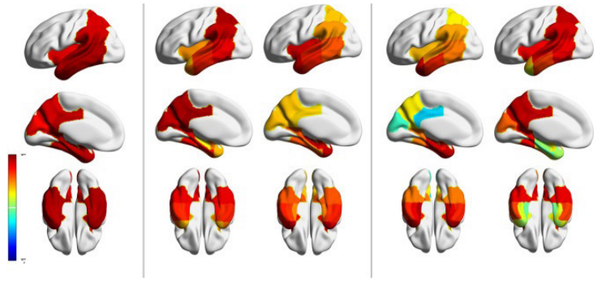
Neuroimmunology

Lead: Professor John O'Brien (University of Cambridge)

There is increasing evidence that the immune system may play an important role in the progression of dementia. Recent studies have found evidence of inflammation in the brain and changes in other parts of the immune system in the early stages of dementia. This suggests that inflammation could be an early indicator of disease, with the potential to improve diagnosis, as well as being a possible target for new treatments.

The Experimental Medicine Incubator's Neuroimmunology theme is investigating the role of the immune system and inflammation in early Alzheimer's disease and Lewy body dementia, in order to facilitate new clinical trials.

And while the evidence for neuroinflammation as a major contributor to the development of dementia is growing, there is a lot more to discover. These gaps form the key focus of the research questions being asked in the Neuroimmunology theme – the answers to which will provide more effective diagnostic and treatment targets in future clinical trials.



Study spotlight:
Predicting genetic risk of dementia

To what extent do our genes influence our risk of developing dementia as we get older? A project led by Professor Valentina Escott-Price at Cardiff University is harnessing the power of cohort studies in the DPUK Data Portal to predict how an individual's genetic make-up contributes to their dementia risk.

The team will first harmonise and unify the available genetic data to establish a common set of genetic variants – which they expect will total 40 million – across all datasets. Next, the researchers will assess the accuracy of the predicted dementia risk from their data by comparing their figures with established risk predictions of known genetic variants, such as the APOE gene.

Once complete, the team will investigate the risk of dementia associated with genes linked to the brain's immune system. Having dismissed genetic variants not predictive of increased dementia risk, they will study in detail those which do suggest an increased risk of dementia. They will also calculate whether having several genes that carry a small increase in risk could combine to give a larger risk. This is called a polygenic risk, from which the researchers hope to calculate a person's genomic risk score based on the combination of genetic variants they possess in their whole genome.

The team has so far gained permission from 11 cohorts to use their data – encompassing roughly 580,000 participants – and has embarked on the processing and analysis phases of the project.

The DPUK Imaging Network: a world-leading environment for brain scanning

"Cutting-edge brain imaging has a major role to play in beating dementia. Our aim is to create a world-leading environment for applying advanced imaging in support of experimental medicine and clinical trials in dementia research."

PROFESSOR FRANKLIN AIGBIRHIO (University of Cambridge), DPUK Imaging Network lead

At the heart of DPUK's **Imaging Network** is a group of eight state-of-the-art PET-MR brain scanners located at universities and hospitals across the UK. Synchronised to enable nationwide dementia studies and data sharing, this network of scanners is the first of its kind anywhere in the world.

The DPUK Imaging Network aims to help researchers identify the biological mechanisms underpinning dementia onset and progression, as well as the physiological markers of disease. The ultimate goal is to facilitate high-quality clinical trials to find a viable treatment for dementia.

The brain scanners in the Imaging Network use both positron emission tomography (PET) and magnetic resonance imaging (MRI) simultaneously. This enables the useful biological information from PET scans – such as blood flow and oxygen use – to be visualised over a high-resolution MRI image.

Brain imaging is one of the key tools in the fight against dementia – and the DPUK Imaging Network has huge potential to increase our understanding of disease and speed up the development of new treatments.

Imaging on the Data Portal

The Imaging Network incorporates a bespoke imaging informatics platform – accessed via the DPUK Data Portal – which allows researchers to securely store, share and analyse the brain imaging data they are working with.

A project led by Professor Clare Mackay and Dr Ludovica Griffanti (University of Oxford) is under way to adapt and optimise UK Biobank's brain MRI pipelines for cohorts in the DPUK Data Portal.

These pre-processing pipelines will derive widely used phenotypes from raw imaging data, helping researchers to interpret complex brain scans.

Study spotlight: High-tech scanners working in harmony

Before DPUK's network of PET-MR scanners can be used in national-scale brain imaging studies – rarely before seen in dementia research – they need to be properly calibrated.

A project to 'harmonise' the equipment is progressing well (despite being paused during COVID-19 restrictions) and involves scanning the brains of 45 volunteers on each of the scanners and comparing the images. Once all eight scanners are synchronised, it will allow researchers to run nationwide studies because they can guarantee that brain scans on each machine will be directly comparable to all others in the network.

Dr Julian Matthews, of the University of Manchester, is joint lead of the harmonisation project, as well as chief investigator of a clinical study that will ensure these high-specification scanners are properly calibrated and providing consistent imaging results between sites. Dr Matthews says: "This unique national network will provide accurate imaging biomarkers and thus enable highly effective clinical studies in the UK of new therapeutics in neurodegenerative disease, including – but not limited to – dementia.

"And although not yet established, this equipment has many potential benefits, such as reducing the scanning burden to patients who require both PET and MRI scans as part of their care, and being used in research where the clinical state of patients can change between scanning sessions."

Image: University of Manchester

The DPUK Stem Cell Network: powering new approaches in dementia research

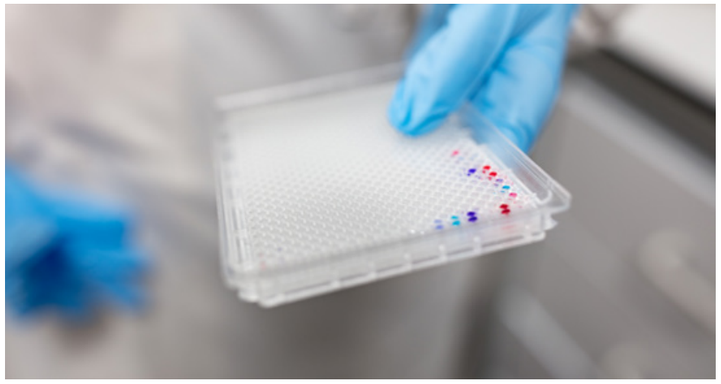
"As the field matures, it is clear that iPSC models have transformed our understanding of neurodegenerative disease. DPUK researchers are internationally leading in this area."

PROFESSOR RICHARD WADE-MARTINS (University of Oxford), DPUK Stem Cell Network lead

Induced pluripotent stem cells (iPSCs) have the ability to develop – using a process called differentiation – into all types of cell in the adult human body. They are incredibly useful tools for research.

DPUK's **Stem Cell Network** gives researchers access to technology, equipment and expertise to enable them to conduct research involving iPSCs. The network is equipped with iPSCs taken from a variety of people – including those with specific mutations to their genes – allowing researchers to choose the iPSCs most relevant to their project.

The DPUK-funded network comprises stem cell laboratories based at the following universities: Cambridge, Cardiff, Edinburgh, Manchester, Oxford and UCL. Scientists working within the Stem Cell Network have expertise across a broad range of subjects, including genetic editing, cell imaging, and the various types of cell found throughout the brain.



Study spotlight: From rescuing damaged neurones to growing 'mini-brains' for Parkinson's

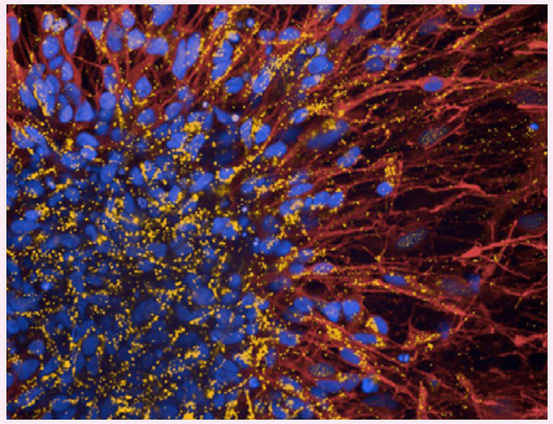
PhD students in the Wade-Martins lab in Oxford are using DPUK-funded iPSCs to investigate Parkinson's disease – a common cause of dementia.

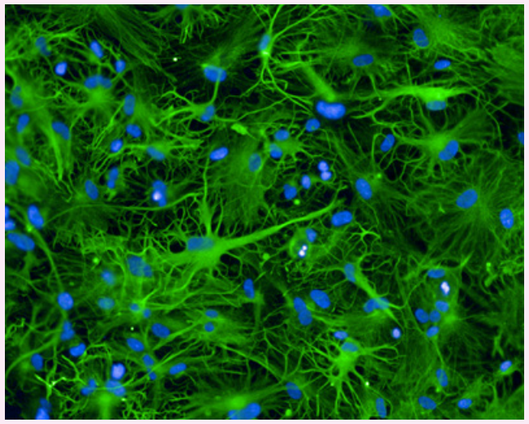
Ajantha Abey is growing iPSCs into brain cells (neurones) from a range of areas in the brain to understand why different populations of cell vary in their susceptibility to Alzheimer's and Parkinson's.

Quyen Do is investigating how neurones that are damaged by Parkinson's disease affect their neighbouring cells. To do this, she is using iPSCs to create mini-circuits of different sets of neurones, as well as 3D mini-brains that mimic the environment of the brain.

Naroa Ibarra Aizpurua is exploring how the cells that support neurones (known as glial cells) are involved in Parkinson's disease. The iPSCs she is using to grow neurones and glia have a specific genetic mutation associated with the disease.

Using iPSCs to research dementia allows scientists to develop the specific cells they need, increasing the accuracy of their studies. Plus, using these human cells ensures the results are directly applicable to real people with dementia.





The view from industry

“DPUK has revolutionised the way academic scientists work with industry in the dementia space”

Compared with when I first started working in this complex field, we now have a much better understanding of dementia – from the fundamental biology of disease to the phenotypic characteristics and biomarkers that will allow us to intervene at an earlier stage and improve countless people’s lives.

Industry and academia traditionally have different roles to play in moving forward efforts to beat a condition such as dementia. Typically, university scientists will generate insights into the basic properties of a disease, and pharmaceutical companies will use those discoveries to develop potential treatments. And then, going full circle, academia can identify suitable volunteers to help industry test whether those treatments are going to be useful.

It’s a relationship that, despite the differing roles, requires hand-in-hand co-operation. Indeed, it’s very difficult to see how we could make any progress without both parties working together and being signed up to the same goal.

DPUK has revolutionised the way academic scientists work with industry in the dementia space. It has established a consortium model in which high levels of trust, openness and collaboration are the expected norm – and it’s as much an investment of intellectual horsepower as it is a financial investment.

Take DPUK’s work in the experimental medicine arena, in synaptic and vascular health and neuroinflammation. That work is really bridging the knowledge gap between scientific discovery and the testing of new treatments. The real need in dementia is not finding new molecules for drugs to target – it’s finding those biomarkers of disease using brain imaging, blood tests, cerebrospinal fluid, cognitive assessment and so on that will tell us, yes or no, whether an intervention is working. If, at present, we can only afford to study one out of ten potential treatments, think how much of a leap forward it will be if we have quicker, cheaper and more effective ways of doing it. We could study all ten.

The promise of highly characterised research subjects and new insights into disease progression is why DPUK has proved attractive to private industry – from major pharmaceutical companies to agile biotech startups.

Co-operating across sectors and across company lines is now the only way of doing things successfully in dementia. No individual firm or academic research group is going to solve the challenges we face in dementia: the way we’re going to do it is by working side by side. And all of us will win together.

Dr Iain Chessell
Associate Director, DPUK
Global Head, Neuroscience, Biopharmaceuticals R&D, AstraZeneca

Third sector perspective

“The dementia research of the future has to take the shape of broad collaborations”

As someone who joined the fold relatively recently, what’s been immediately clear to me about DPUK is its commitment to collaboration and stakeholder input.

Why is it so important that dementia research charities like Alzheimer’s Research UK (ARUK) work alongside universities, private companies, other funding bodies, clinicians, patients and caregivers? The answer is simple: because it’s going to take a team effort to solve the complexities and challenges within dementia; to cover the gaps that exist both in our knowledge of disease and in the delivery of research.

The dementia research of the future has to take the shape of broad collaborations of the type demonstrated in this country through the DPUK model. It’s crucial to involve people and organisations from different domains, and with different backgrounds and experiences.

To make progress in the field, we need to address early detection and diagnosis of dementia. We need insights from large datasets like those in the DPUK Data Portal, and to develop new tools that we can test on groups of volunteers that DPUK can provide through its Trials Delivery Framework – the right people for the right study.

At ARUK, we’re also interested in experimental medicine that aims to make late-stage clinical trials less risky, incentivising further investment from industry and others. One of the challenges we face in dementia is that trials are very expensive and take a long time. If we’re going to develop disease-modifying treatments for people with dementia, we need to be able to carry out those trials as quickly and as cheaply as possible. The experimental medicine work within DPUK will help us define and identify which participants are likely to be suitable for different trials, and will begin to work out whether potential treatments are hitting their intended targets.

I’m really optimistic about where we’re heading in dementia research. Because of the investment from government, industry and charities, we’re seeing an explosion in new ideas and in new avenues of research. Governments, funding bodies and philanthropists around the world are taking dementia seriously as a healthcare priority, and recognising that dementia can be a treatable condition – not simply an inevitable part of ageing.

The challenge now is understanding how we can test those potential treatments in an efficient and effective way. DPUK has provided the investment and infrastructure – now it’s up to the scientific community to use those resources to their fullest potential and drive forward progress in dementia research.

Dr Susan Kohlhaas
Associate Director, DPUK
Director of Research, Alzheimer’s Research UK

An international outlook

DPUK is committed to enhancing global efforts to tackle dementia. To that end, we work with similar organisations around the world that share our goal of finding new ways to prevent and treat dementia – in particular by improving access to cohort data.

Dementias Platform AU

DPUK is delighted to support the establishment of Dementias Platform Australia (DPAU) at UNSW Sydney's Centre for Healthy Brain Ageing. DPAU's objective is to provide dementia researchers with access to data from studies carried out in Australia, the Asia-Pacific region and beyond.

KOREA DEMENTIA RESEARCH CENTER KDRC

DPUK has signed a memorandum of understanding with the newly launched Korea Dementia Research Center (KDRC), based at Seoul National University. DPUK and KDRC will share ideas and best practice around data access, experimental study design, and volunteer recruitment.

ADDI Alzheimer's Disease Data Initiative

DPUK is a founding partner in the Alzheimer's Disease Data Initiative (ADDI) and its Alzheimer's disease (AD) Workbench. ADDI is a new global effort that aims to advance innovation in Alzheimer's disease by connecting researchers with the data needed to generate insights and inform the development of improved treatments and diagnostic tools.

DPUK works in collaboration with these organisations and many more with the collective aim of accelerating discoveries in dementia.

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Professor Ronan Lyons and Professor Simon Thompson lead DPUK Work Package 21: Data Portal enhancements

Professor Clare Mackay and Dr Ludovica Griffanti lead DPUK Work Package 22: Image processing pipelines

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Dr Ivan Koychev leads DPUK Work Package 23b: Great Minds

Dr Vanessa Raymont leads DPUK Work Package 24: Clinical recruitment and research facilities

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Professor Joanna Wardlaw leads DPUK Work Package 25a: Early vascular lesion MRI biomarkers and dementia risk

Professor Hugh Markus leads DPUK Work Package 25b: Identifying potential drug targets using Mendelian randomization

Dr Terry Quinn leads DPUK Work Package 25c: Identifying the most promising cardiovascular drugs for a cognitive endpoint trial

Professor James Rowe leads DPUK's Synaptic Health theme

Professor James Rowe and Dr John Isaac lead DPUK Work Package 26a: Synaptic loss and its functional consequences in early Alzheimer's disease, using pre-synaptic markers and magnetoencephalography

Professor James Rowe and Dr John Isaac lead DPUK Work Package 26b: Synaptic loss and its functional consequences in early Alzheimer's disease, using a new post-synaptic TARP γ8 AMPAR ligand

Professor John O'Brien leads DPUK's Neuroimmunology theme

Professor Valentina Escott-Price leads DPUK Work Package 27a: Polygenic risk and inflammatory pathways

Dr Paresh Malhotra, Professor Paul Matthews, Professor John O'Brien and Dr Alastair Reith lead DPUK Work Package 27b: Prodromal dementia immunoprofiles

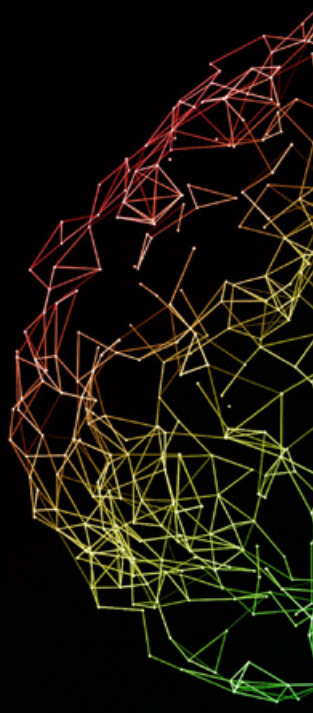
Dr Paresh Malhotra, Professor Paul Matthews, Professor John O'Brien and Dr Alastair Reith lead DPUK Work Package 27c: Dynamic PET-MR and brain inflammation

Dr Vanessa Raymont leads the Deep and Frequent Phenotyping study

Professor Franklin Aigbirhio leads the DPUK Imaging Network

Professor Richard Wade-Martins leads the DPUK Stem Cell Network

Dr Sarah Bauermeister leads DPUK's data analyst training programme



Dementias Platform UK

UKRI Medical Research Council

NIHR National Institute for Health Research