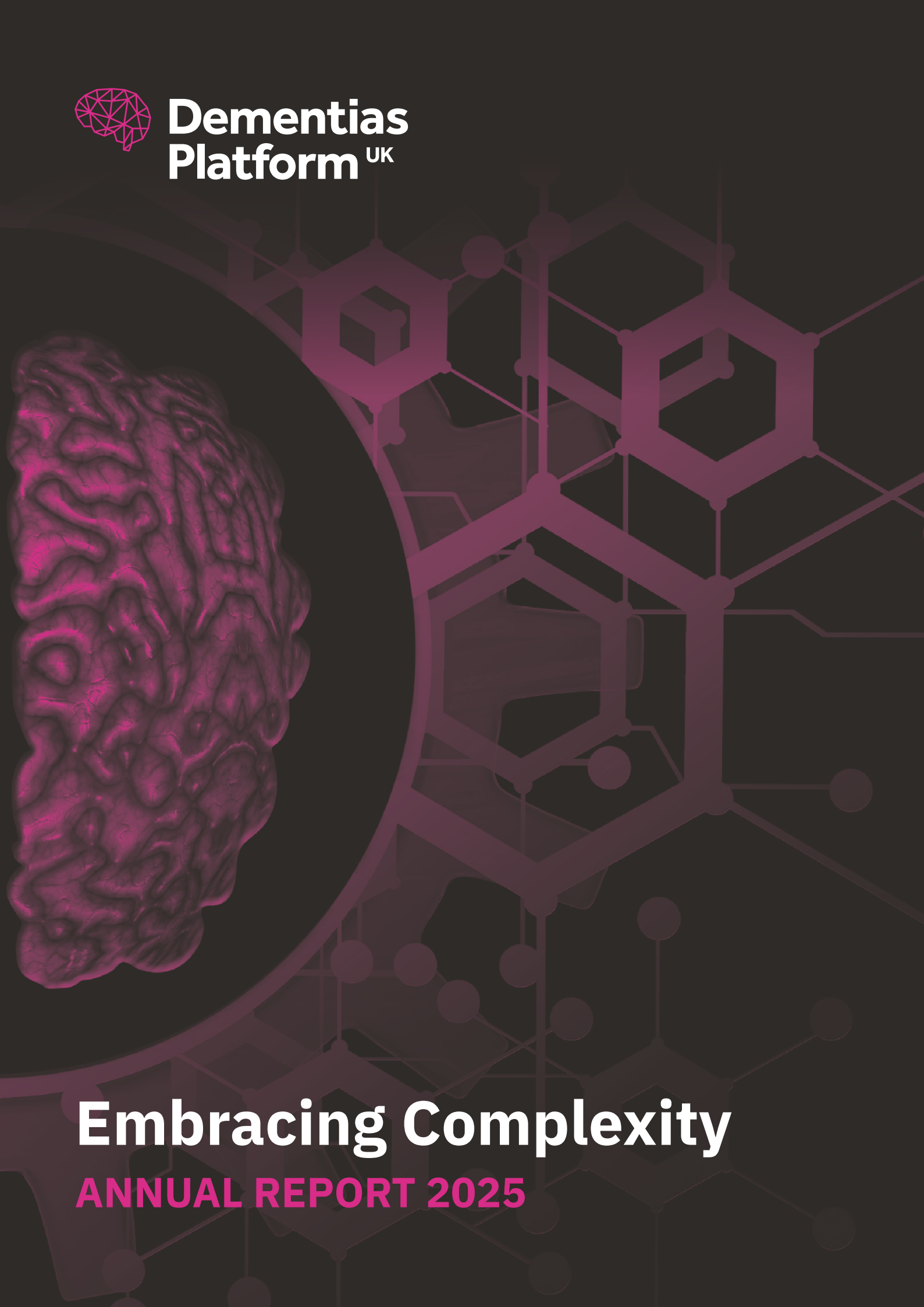
Dementias Platform UK



Embracing Complexity

ANNUAL REPORT 2025

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Introduction

Welcome to the 2025 DPUK Annual Report. Our theme this year is **"embracing complexity."**

In last year's report, Professor David Bennett explored the biological complexity of Alzheimer's disease. This year, we turn our attention to DPUK's growing role in developing what we call **complex knowledge**—insights that emerge when different fields of expertise connect and strengthen one another.

Complex knowledge describes the productive interplay between knowledge domains. When separate areas of science and technology inform each other, the result is a "force multiplier" for discovery, enabling more meaningful interpretation of data and expanding opportunities for innovation. The rapid rise of AI, with its capacity to integrate diverse data types and knowledge systems, further underscores the importance of building and sustaining such interconnected understanding.

Throughout this funding cycle, DPUK's strategy has focused on enabling complex knowledge to flourish by developing specialist research communities supported by open knowledge architectures.

Research Communities

Scientific progress is cumulative: new ideas and technologies emerge from the recombination of existing knowledge. This happens most effectively when researchers with shared interests and complementary skills can collaborate easily. These research communities accelerate the creation of both domain-specific and cross-cutting knowledge.

Through our research hub and collaborative space programmes, DPUK has supported research communities across a wide range of technology-led and mechanism-led areas.

- Technology-led hubs include research and clinical imaging (QMIN-MC), genomics, and neurological tissue banks (p20). We also highlight trials delivery—an often under-recognised technology area. Through the DPUK Trials Delivery Framework, we now support the UK's largest trials-site network, working with more than 70,000 members registered for research participation.
- Mechanism-led hubs and collaborative spaces include our experimental medicine themes in synaptic function, neuroimmunology, and neurovascular health (p15-17), as well as hubs focused on traumatic brain injury and motor neurone diseases (p22). DPUK supports these communities by providing mature, cost-effective informatics solutions that help them collaborate, share data, and grow.

Open Knowledge Architectures

The creation of complex knowledge depends on strong connections between research communities. Open knowledge architectures improve interoperability between datasets, tools, and research groups—expanding the potential for new insights to emerge.

These shared systems also reduce duplication, support better data quality, and offer cost efficient and environmentally sustainable solutions. Such benefits become even more important as the volume, velocity, and variety of research data continue to increase. The DPUK Data Portal has become a leading example of this approach. It now hosts more than 100 datasets and supports researchers in 43 countries (p18-19). By providing streamlined, standardised and cost-effective end-to-end solutions for multimodal data management, the Portal creates the conditions needed for complex knowledge to develop.

Looking ahead, DPUK is anticipating emerging data needs, by advancing standardised research ready data, enabling federation across platforms, supporting the use of synthetic data, and engaging with both the opportunities and risks presented by AI. Through this work, DPUK is helping to shape the global research data environment (p24, 25, 35).

> "It's not about the technology; it's about the people."

How We Achieve Impact

Our commitment to openness, partnership, and shared purpose is central to how DPUK continues to advance scientific discovery and accelerate progress for the dementia research community.

Our progress has relied on developing a high trust, pre-competitive environment in which collaboration thrives. As we emphasised at a recent NIH Dementia Summit: "It's not about the technology; it's about the people".

Professor John Gallacher,
Director, Dementias Platform UK

Contents

Snapshot

A look at DPUK in numbers

DATA PORTAL

2,690
Data Access Requests

107
Datasets

43
Countries

1,313
Users

6
Associated Hubs

7
Collaborative Spaces

TRIALS DELIVERY

71,794
Register participants

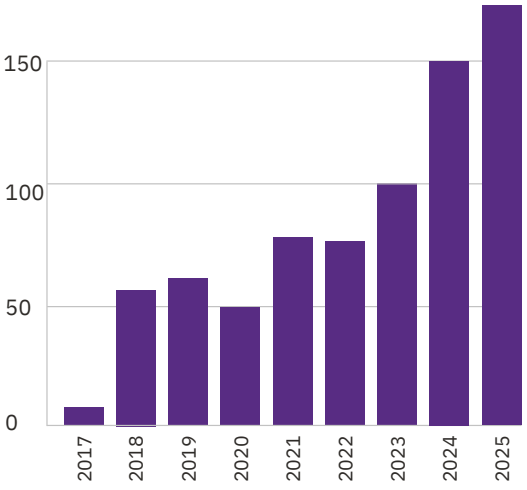
13,461
Great Minds register

36
Ongoing studies

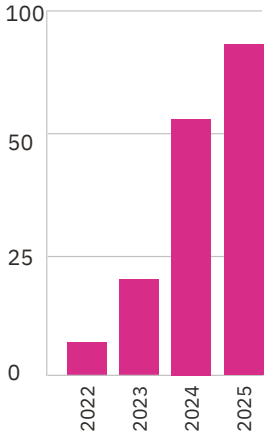
25,296
APOE data

>2,000
(at 30 sites)
FAST study participants

Data Portal applications per year

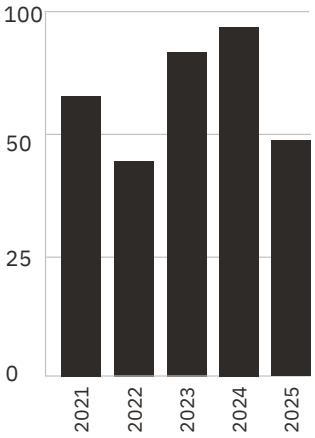


TDF sites across the UK



Publications

Academic papers published in last 5 years citing Dementias Platform UK



The power of collaboration: making a difference in human-based dementia research for over a decade

Small beginnings

From a simple idea of bringing data together to support trials, DPUK has grown to be one of the world's largest repositories of cohort data and one of the UK's largest trials infrastructures. Since 2014, when the then Government Life Sciences Minister, George Freeman MP, spoke at our Royal Society launch, DPUK has become an integral part of the dementia research landscape. George Freeman captured our ethos:

"Collaboration first, competition later. That I think, will be a key part of 21st century landscape. We need to build new models of collaborative working, whether that's pre-competitive research or shared IP. Translational medicine is far less about the 'eureka moment' of discovery that can be immediately owned and patented. There's a collaborative element to this which I think is really key."

Starting with this mission, DPUK has brought a community together around pre-competition; sharing ideas, technologies, and best practice. From data, through mechanistic studies to trials, the key has been building an environment that creates opportunity. From core MRC funding of £19.5m, this community has leveraged >£100m from industry, charities (including AD Data Initiative, Alzheimer's Society, ARUK), and from research councils. Overall, DPUK's resources have led to more than 4,870 research outputs and enabled 46 Studies.

Building the community

Our data portal is central to this collaborative approach. To improve discovery and accessibility of multiple complex datasets, data are curated to a single common data model (C-Surv) using modality-specific pre-processing pipelines. Data are then made freely available at point of use. We have received >2,600 access requests from >1,300 users in 43 countries, accessing 107 datasets describing >3m individuals. For experimental medicine, so vital to early-stage drug discovery, industry partnerships focussing on neuroimmunology, vascular health, and synaptic function have helped identify more closely mechanisms underlying pathology. We have worked with GSK, Astra Zeneca, and Johnson and Johnson on experimental medicine studies and with 32 partners overall. Our trials delivery framework has expanded to include early clinical as well as pre-clinical populations with >71,000 individuals consented for recontact.

Expanding the community

In a fast-changing ecosystem, pursuing pre-competitive partnerships which benefit everyone requires flexibility. With UK Government funding, partnerships are moving away from large platform programmes towards precision question-driven projects. In response, building on the advanced informatics of the Data Portal, DPUK is diversifying to address questions around discovery, early detection, and trials capacity. (See figure).

For the Data Portal, this has meant supporting a growing number of technology and pathology-specific communities. Examples include brain imaging technology, traumatic brain injury and motor neuron disease pathologies. These communities are provided with the full benefits of a trusted research environment at a fraction of the cost and risk. Apart from avoiding duplication and unwanted variation in practice, this incentivises collaboration and innovation, accelerating the creation of complex knowledge.

Our experimental medicine theme has expanded into drug repurposing through analysis of big-data, as well as blood biomarker research with our READ-OUT study, utilising over 30 clinical sites across the UK. The intention here is to inform the design and conduct of precision trials, as well as de-risking trials for industry. In partnership with Lilly, we are developing a pathway for accurate, early diagnosis of Alzheimer's disease AD, including biomarker assessment through cerebrospinal fluid (CSF).

For trials, diversification has meant enhancing our research registers to include stratification for pre-clinical and early clinical trials, alongside streamlining phenotyping and genotyping through the FAST and Great Minds studies. We have also expanded our trials capacity beyond traditional academic centres to create a network of 81 sites from Shetland to Cornwall and Kent to Northern Ireland, supported by an 8-site PET/MR imaging network.

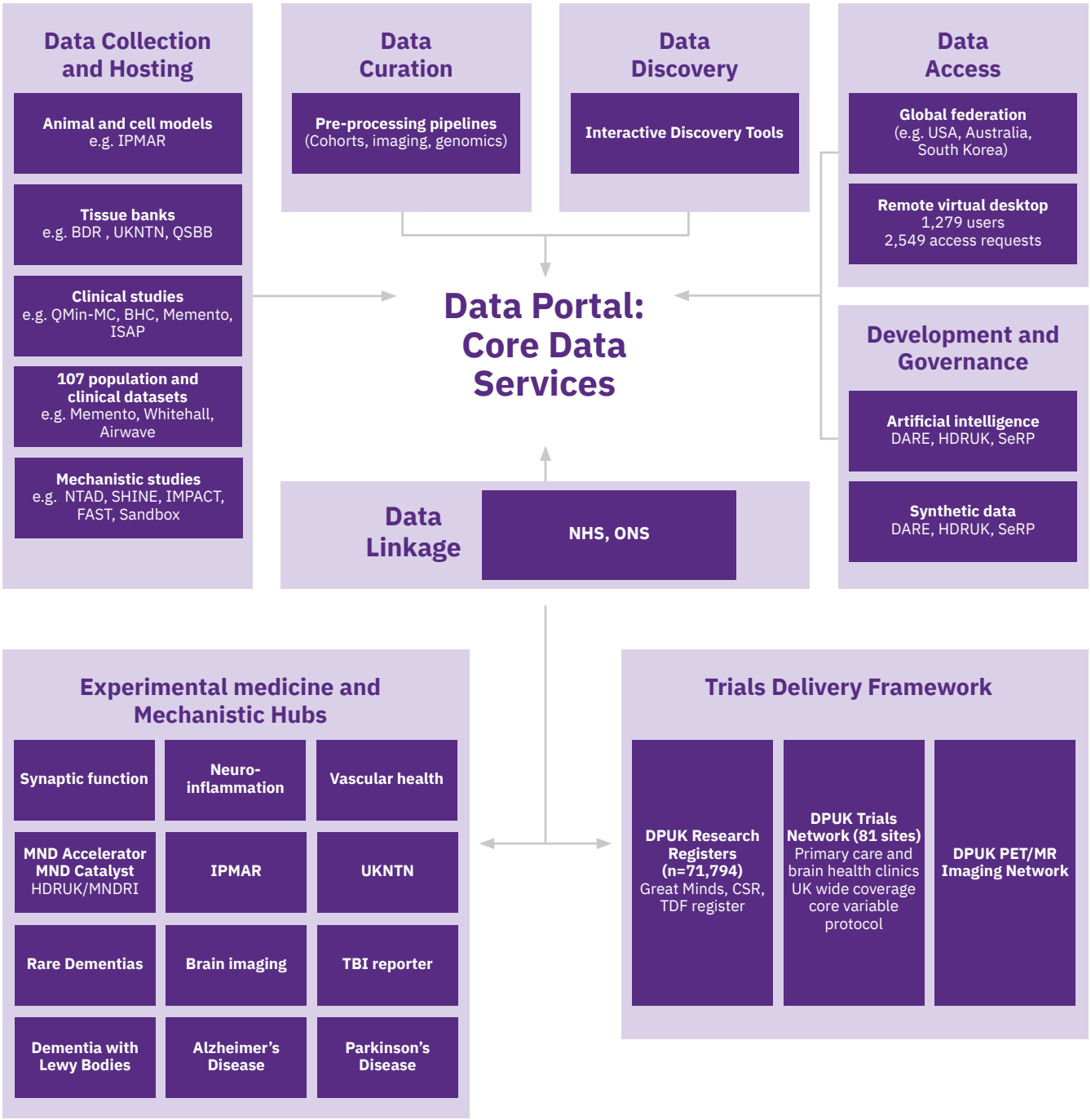
Looking ahead

For data, the future is augmentation, AI, and federation. DPUK is AI ready, at the cutting edge of federation with an international coalition of data platforms and is working with UK providers to link research data with electronic health records.

For mechanistic studies, DPUK will expand and extend our support for specific scientific communities, such as Parkinson's disease and rare dementias, giving funders cost-efficient options for integrated data management.

For trials, we look forward to supporting the Neurodegeneration Initiative, so the UK becomes a centre of innovation and best practice, as we anticipate the next generation of disease modifying therapies.

As DPUK moves forward, we expect the founding principle of success through collaboration to continue as we pursue our underlying programme of improved data access, support for mechanistic studies, and trials delivery.



DPUK News

Dr Simon Young of DPUK celebrating with our partners at the awards ceremony in London

Top partnership award for DPUK, Lilly UK and NHS trusts

DPUK, Lilly UK and four NHS Trusts had reason to celebrate at the HSJ Awards when their collaborative biomarker pilot project scooped the prestigious Partnership of the Year Award 2025.

The organisers called it a 'transformative project with the potential to revolutionise the diagnostic landscape for AD in the UK.'

The study is testing the scalability of biomarker diagnostics across diverse communities and piloting a clinical pathway for the early and accurate diagnosis of AD. This includes biomarker assessment via cerebrospinal fluid (CSF).

Dr Simon Young from Dementias Platform UK joined Lilly UK and others from the collaborative project team to collect the award in London.

The four NHS Trusts enrolled from the DPUK Trials Delivery Framework are: Greater Manchester Mental Health Foundation Trust, Oxford Health Foundation Trust, University Hospitals Sussex Foundation Trust, and Sheffield Teaching Hospital Foundation Trust.

DPUK leads charge in groundbreaking MND Research Data Catalyst Initiative

DPUK is playing a pivotal role in a new initiative to accelerate research into motor neurone disease (MND), known as the MND Research Data Catalyst. Led jointly by Health Data Research UK (HDR UK) and DPUK, the collaborative initiative is founded on participation by the wider MND research community.

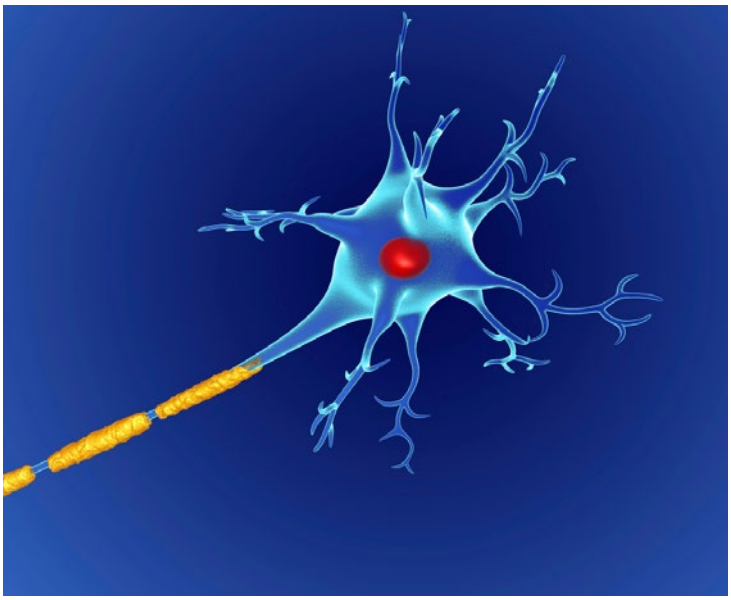
This ambitious programme aims to harness the power of data to unlock new insights into the causes, progression, and treatment of MND.

DPUK, bringing its powerful data infrastructure and expertise, is central to the project. The organisation will standardise and host large-scale datasets on its secure Data Portal—powered by SeRP—enabling FAIR (Findable, Accessible, Interoperable, Reusable) access, underpinned by user-centred design principles

Professor John Gallacher, Director of DPUK, highlighted the importance of the project: "Data is the key to understanding complex neurodegenerative diseases like MND. By making data more accessible and usable, the MND Research Data Catalyst will enable researchers to ask bigger questions and find answers faster."

The initiative is part of a wider strategy to coordinate MND research efforts and attract greater investment into the field. It also supports the UK government's ambition to find a cure for MND within a decade.

The enhanced data access will enable research using DPUK's secure, scalable digital platform, ensuring MND's scientific community has the tools needed to drive innovation, deepen understanding, and ultimately, improve outcomes for people living with MND.



Conference focus on looking to the future of people-centred research

The Translation 2025 conference held at the Congress Centre in central London, delivered a busy programme centred on its theme 'Embracing Complexity' (which we are also using as the title for this Annual Report). The scope of the conference ranged across developments in trials delivery, exciting advances in blood biomarkers and the value of taking a global approach to informatics in Alzheimer's Disease and related dementias.

250 delegates heard leading figures from dementia research and translational medicine speak about advances in data, blood biomarkers and trials delivery. Watch the speakers online.

Keynote speakers included Professor Art Toga (University of Southern California) who provided an intriguing review of the Global Approach to Informatics in ADRD; Professor Cath Mummery (UCL) who is leading a Clinical Trials initiative that is complementary to DPUK's Trials Delivery Framework; and Professor Donna Wilcock (School of Medicine and Indiana University) talking about the State of the Science of Plasma Biomarkers of ADRD.

A popular additional session focused on the opportunities for early career researchers in dementia and how they can access powerful resources.

AD-SMART to test two repurposed AD treatments

DPUK has partnered with ACORD (A Collaboration of Groups Developing, Running and Reporting Multi-Arm Multi-Stage (MAMS) Platform Trials in Neurodegenerative diseases) - a group looking at designing and running clinical trials in multiple sclerosis, Parkinson's, MND, dementia and other neurodegenerative diseases. Along with other members of the dementia trials community, it aims to develop a planned multi-arm, multi-stage trial for clinical Alzheimer's disease.

Co-led by Professor Paresh Malhotra (Imperial), Professor Vanessa Raymont (Oxford), and Professor James Carpenter (UCL), the platform (AD-SMART) is planned to commence in 2026. It will start by testing the efficacy of two repurposed treatments in Alzheimer's disease. It will look for evidence of long-term effects on cognition and activities of daily living.

Its development has been supported by the NIHR, the UK Dementia Trials Accelerator, and Alzheimer's Research UK.

New research projects and capacity-building in Korea

Researchers at Yonsei University and the Korea Brain Research Institute are to play an active role in a brain health study using the DPUK data portal as part of a knowledge-sharing initiative. Professor Sarah Bauermeister describes the core training programme as 'learning-by-experience'. It is expected that the work will lead to joint publications. The initiative is the latest in a growing number of links developed with Korean researchers.

Three additional joint projects are also progressing which include research on environmental exposure and brain health as part of the MODIFY programme, a new project with the KBRI to understand the biological mechanistic pathways in early adversity and brain health, and an AI programme.

DPUK addresses NIH at its Dementia Summit

In May 2025, DPUK was invited to give a presentation at the NIH Dementia Summit in Bethesda, Virginia. This strategy-framing meeting aimed to inform the US National Institute for Health on national research recommendations for dementia.

The meeting focussed on Alzheimer's disease and related dementias including frontotemporal degeneration, Lewy body, multiple aetiology dementias, and vascular contributions to cognitive impairment and dementia. Part of the meeting focussed on data management, discovery and access.

Of particular interest to the meeting was DPUK's ability to process and rapidly make available large and complex datasets. In commenting about our capabilities, the median access decision-time of 21 days was considered impressive, as well as our truly global reach and the range of users. Our strategic focus on creating opportunity was encapsulated by our key message: "it's not about the technology, but about the people".

The value of industry–academic collaboration: an imaging and data science perspective

Dementias Platform UK has partnerships with industry embedded in its mission. Major pharmaceutical and medical technology businesses have contributed including Astra Zeneca, GSK, and Johnson & Johnson. **Robin Wolz**, Chief Scientific Officer at leading neuroscience imaging and biomarker analytics company IXICO, reflects on the value to research of academia-industry partnerships.

From the perspective of a specialist neuroimaging and data science company, collaboration with academic researchers is fundamental to advancing dementia research. The scientific and operational challenges in this field — disease heterogeneity, slow progression, and the need for sensitive biomarkers — demand approaches that are both methodologically rigorous and practically deployable at scale. These requirements are best met when industry and academic institutions work together in a sustained and structured way.

One of the clearest benefits of collaboration is the ability to develop and validate advanced imaging and analytical methods in real research settings. Academic partners often lead in defining novel hypotheses, phenotyping strategies and outcome measures, while industry contributes experience in standardisation, quality control and scalability. For a company focused on qMRI, PET and multimodal biomarkers, access to deeply characterised cohorts and longitudinal data is invaluable in ensuring that analytical tools are not only innovative, but robust, reproducible and clinically meaningful.

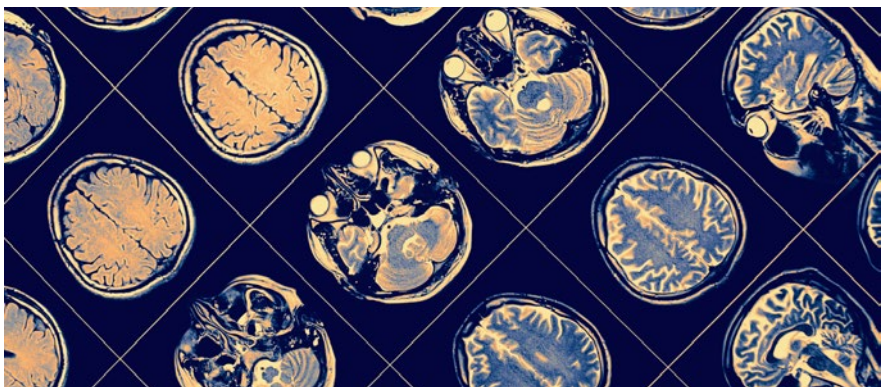
Such partnerships also support the translation of imaging science into clinical trials. Imaging biomarkers that appear promising in small or single-centre studies frequently fail to generalise when deployed across large, multi-site trials. Working closely with academic researchers allows early identification of sources of variability, optimisation of acquisition protocols, and refinement of analytical pipelines before these tools are embedded in pivotal studies. This iterative development process significantly improves confidence in biomarker performance and downstream trial decision-making.

Another important advantage is the opportunity to address pre-competitive challenges collectively. Many of the hardest problems in dementia research — including disease stratification, progression modelling and endpoint sensitivity — are shared across the entire field. Collaborative environments enable industry to contribute technical expertise while benefiting from shared learning, including negative results that are rarely visible in more traditional research models. This reduces duplication of effort and accelerates methodological convergence.

Without this kind of partnership, much of this work would be slower, more fragmented and more expensive. Building sufficiently large, harmonised datasets, testing new analytical approaches across populations, or exploring novel trial-enabling technologies is rarely feasible for a single organisation alone. Collaboration allows industry to engage earlier in the research lifecycle, improving the relevance and readiness of methods that later support therapeutic development.

More broadly, industry attitudes toward academic collaboration have evolved significantly. There is increasing recognition that long-term, trust-based partnerships are essential for progress in complex diseases such as dementia. For companies operating at the interface of technology, data and clinical research, there remain substantial opportunities to deepen collaboration — particularly through multimodal data integration, advanced analytics and responsible use of AI.

Ultimately, effective industry–academic collaboration enables better science, better trials and, most importantly, a clearer path towards delivering meaningful benefits for patients.



Trials Delivery

Expanding reach and growing use of TDFs UK-wide network

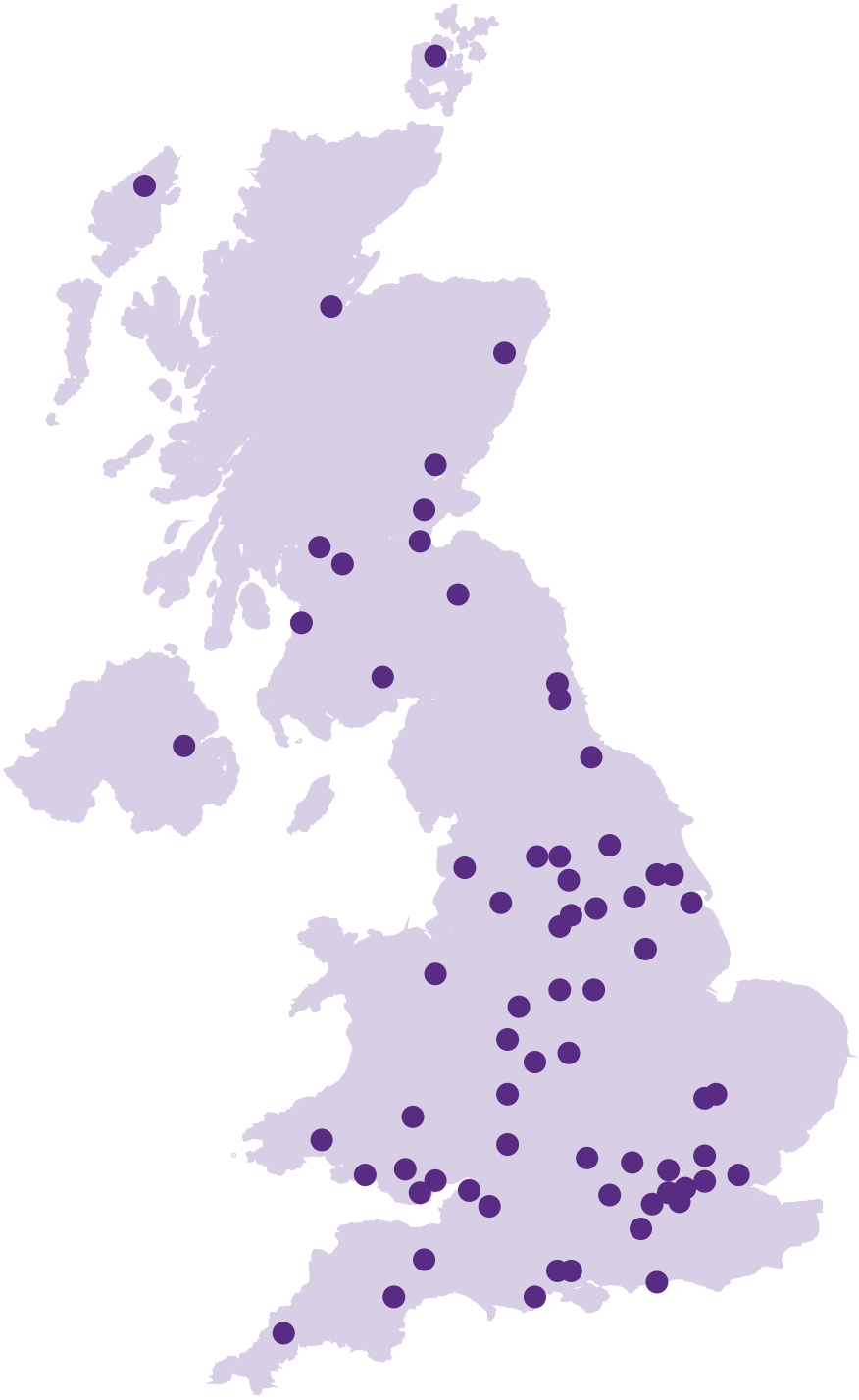
Professor Vanessa Raymont leads the Trials Delivery Workstream

The Trials Delivery Framework's clinical network has expanded further this year and it is now the largest dementia-focused network in the UK. There are 81 sites spanning all devolved nations, consisting of all UK brain health clinics, a broad and representative range of memory clinics, and two primary care networks. It covers more than 25% of all GP practices and 25% of all NHS Trusts.

The framework offers a variety of commercial, non-commercial (GOTCHA, MCI Core Outcomes) and real world evidence study opportunities (such as our work with IQVIA) to its sites. Regular meetings with network sites have enabled the Trials Delivery Framework (TDF) to establish agreement from sites to deliver a unified cognitive data collection plan, using our TDF register (TDF-R). This allows us to leverage existing NHS data-linked local research registries.

READ-OUT (REAl world Dementia OUTcomes) is a key project for the Trials Delivery Network (See page 29). It is part of the ARUK-Alzheimer's Society £4.9m joint-funded Blood Biomarker Challenge, and has opened in 31 TDF sites. More than 20 of these clinical locations have already begun working with participants. They are testing existing and novel blood biomarkers (BBMs) which can identify multiple diseases leading to dementia. The outcomes will have real-world implications, determining how a panel of blood biomarkers could accurately indicate dementia risk at an early stage, and add economic value to the NHS for scalable implementation.

In addition, we have managed to make the most of the funding received by working with external industry partners (including Roche Diagnostics, CFDX, Eisai, Diadem, Marker Diagnostics AG, Capitainer, Tasso, AlamarBio, uMed and Sterilab Services) to enable the addition of study enhancements, including facilitating experimental biomarker and genetic testing.



VIEW OUR INTERACTIVE MAP HERE

Enhancement to the framework in 2024-5

Under-represented groups

Blood biomarkers have been collected from many under-represented groups at scale through the READ-OUT and FAST blood biomarker studies.

Minimal Common dataset collection

By aligning the roll-out of the clinical register, we are collecting a 'minimal common dataset' of clinical diagnosis, medical comorbidities, demographics, genetics and blood biomarkers. We plan to expand this to more than 3,000 real-world memory clinic patients and are enhancing this with data from other existing DPUK biomarker studies to provide an enriched dataset in clinical subgroups, which will include MRI, PET, CSF and some exploratory biomarker data.

Pharma relationships

Negotiations have been completed with one large pharma company to use READ-OUT BBM data to pre-screen for their clinical trials and also deliver a functional imaging site network, with template contracts and protocols, a live database of scanner capacity and capability, and preferential access to PET ligands. We are discussing similar work with three other large pharma companies.

Digital cognition test

The Dementia GOALS Programme is funding a digital cognitive bolt-on study to READ-OUT. This is delivering a System Preparedness project in collaboration with the Davos Alzheimer's Collaborative. Two separate cognitive tests will be conducted across 10 READ-OUT sites.

CSF project

A collaboration with Lilly UK and four TDF sites is driving a wider clinical roll-out of blood biomarkers. The Cerebrospinal Fluid project aims to make CSF biomarker testing more accessible by expanding test capacity and staff expertise along with the development of a service model toolkit which other NHS organisations can adopt at scale. The piloting programme is at four TDF sites in Manchester, Oxford, Sheffield, and Sussex. The protocol that has been developed for a wider roll-out, has already led to a cost saving of £645 per patient at one site. The collaborative study won the 'Partnership of the year' award at the HSJ Partnership Awards in 2025, underlying its potential to influence national healthcare policies and practices.

Pipeline for recruitment

The TDF is developing a pipeline for well-characterised recruitment to UK clinical trials, with a focus on industry studies using the 'minimal' and 'enriched' datasets collected from DPUK registers and associated studies.

New ventures

- Along with sites in Europe, we are committed to developing plans for specific recruitment to vascular trials.
- DPUK is part of a British Heart Foundation application (LACI-Cog) for a trial of repurposed cardiac drugs for vascular cognitive impairment.
- The TDF will be the main recruiting route for the AD-SMART dementia trials platform (Professor Vanessa Raymont is co-leader with Professor Paresh Malhotra).
- In collaboration with InRAD and the Dementia Trials Network, we are developing harmonisation procedures across registers.

Great Minds

Great Minds register continues rapid growth

The Great Minds register, a core component of DPUK's Trials Delivery Framework, now includes 13,461 volunteers, providing an unprecedented resource for targeted recruitment. Of these, 4,279 participants have contributed genetic samples and 903 have worn actigraphs, enabling valuable insight into circadian patterns and lifestyle data. These well-characterised participants allow for more precise study enrolment and reduce trial delays by connecting researchers with individuals most likely to benefit from early intervention.

Enrolment momentum continues beyond the 10,000-milestone reached in early 2024, positioning Great Minds as a leading UK-wide platform for pre-clinical dementia research and trial readiness.

Great Minds Live' events have an audience attending at the venue and a substantial audience of hundreds online.

FAST Brain Health

Dr Ivan Koychev (Imperial College London) leads the FAST study

The FAST Brain Health study is progressing well across 30 clinical sites in the UK. The study is designed to evaluate the feasibility of collecting remote cognitive testing data and blood-based biomarkers (e.g. phosphorylated tau-217, plasma β-amyloid) at scale to enable earlier and more efficient dementia risk profiling.

Participants undergo online cognitive testing and blood sampling at baseline and again at 12 months. These real-world, scalable approaches will inform the development of large-scale, remote-ready trials.

The FAST study is embedded within DPUK's digital infrastructure, including Great Minds, and will ultimately support faster, more inclusive trials by validating biomarker-based stratification approaches.

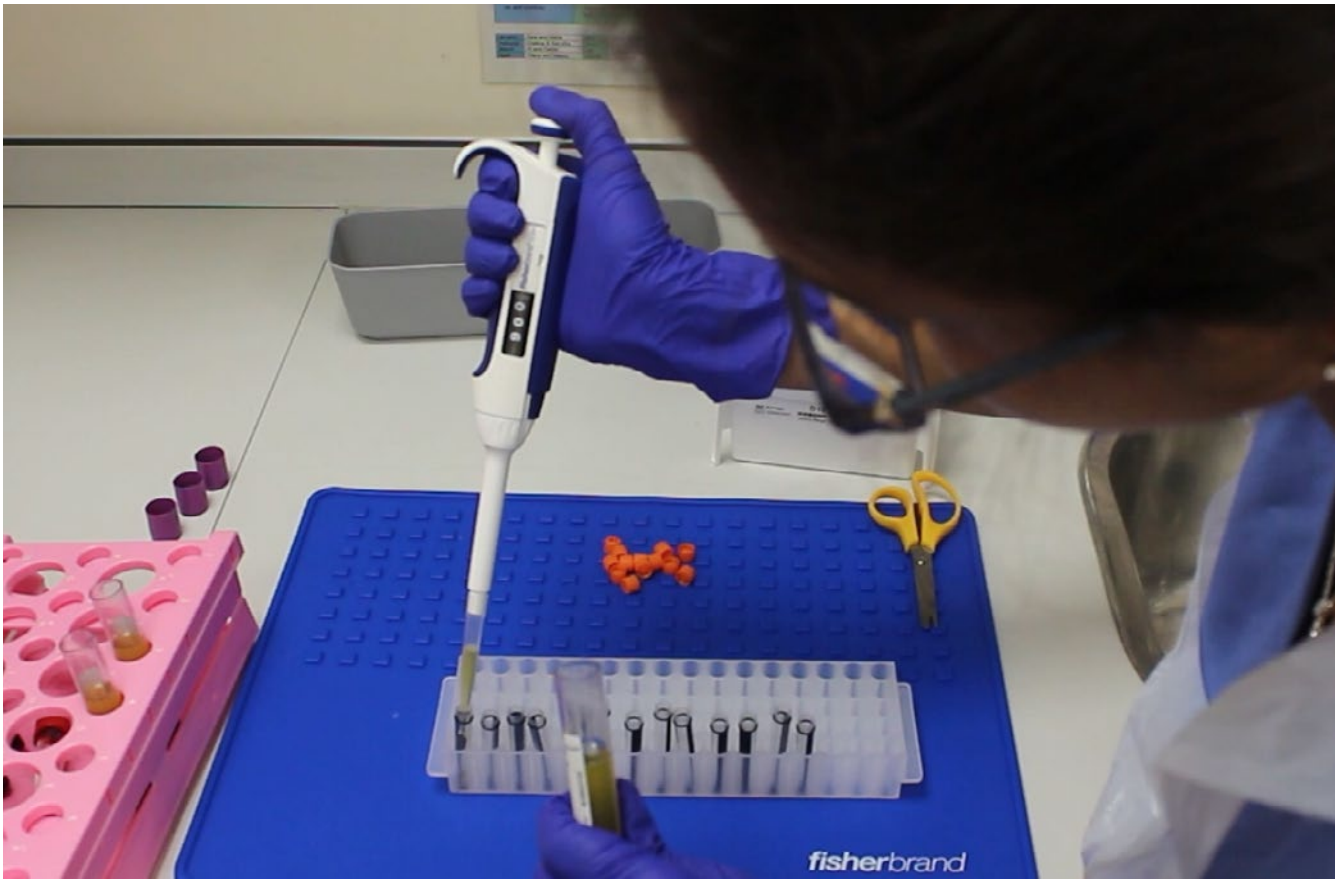
By the end of 2025 more than 2,000 participants have been recruited, including:

1,088
cognitively healthy adults

116
with subjective cognitive impairment

145
with mild cognitive impairment (MCI)

236
living with dementia



Experimental Medicine

There have been exciting developments in the Experimental Medicine Incubator, with progress in major studies and strong signals in the literature. Our programmes in Neuroimmunology, Vascular Health and Synaptic Health mirror prominent targets in the Cummings annual review of global Alzheimer's disease trials (Alzheimer's Disease Drug Development Pipeline: 2025, *Alzheimer's & Dementia: Translational Research & Clinical Interventions*).

The ON-FIRE research team

Neuroimmunology and inflammation

Professor John O'Brien leads the team in our Neuroim-munology theme.

The IMPRINT study of inflammatory and immune changes in people with early Alzheimer's disease and early dementia with Lewy bodies has recruited over 200 participants. Led by Professor John O'Brien, IMPRINT has already completed 18-month follow-ups for over 90 people. Following IMPRINT's blood and CSF approach, our second study, IMPACT, which is using Positron Emission Tomography (PET) to investigate the role of brain inflammation, began scanning its first participants at the start of 2025.

In this work, we have:

- Shown that inflammation is a potentially modifiable risk factor for cognitive decline in people with rheumatic diseases. Read more.
- Reported evidence for the association between inflammation and neuropsychiatric symptoms in dementia. Read more.
- Discovered links between innate immune changes in blood and poor outcome in terms of reduced survival across several neurodegenerative diseases, suggesting that different diseases may have shared inflammatory mechanisms that contribute to poor outcome. Read more.
- Released genetic (polygenic) risk scores for multiple cohorts in the Dementias Platform UK Data Portal. This is allowing scientists to determine which particular mechanisms are associated with the development of different degenerative diseases and dementia. Read more.

Looking beyond Alzheimer's disease, our investigators launched the ON-FIRE study of frontotemporal dementia in 2024. This work is being undertaken across 22 sites in the UK, and the number of these actively recruiting is rapidly rising. These sites reflect the diversity of the UK population and see all types of presentation of frontotemporal dementia. The ON-FIRE lead, Dr Maura Malpetti, and her co-authors were awarded the 'ISTAART FTD Professional Interest Area Publication of the Year Award' for their work.

Vascular Health

Professor Atticus Hainsworth, co-leads our Vascular Health theme.

The Vascular Health theme in our Experimental Medicine Incubator has been exceptionally busy during 2024 and 2025, demonstrating that collaborative working accelerates progress in research.

Vascular Drug Targets

DPUK's Vascular Health group brought the academic and industry communities together in October 2024 with the aim of prioritising Vascular Drug Targets in Dementia. Led by Professor Atticus Hainsworth (City St George's University), the event was jointly hosted by the Alzheimer's Society and DPUK. Attending were delegates from pharma companies (AstraZeneca, Eisai, Eli Lilly, GSK, Takeda), consultancies (RDP LifeSciences, TPB Ventures), enablers (BNA, DDF, DDI, ELRIG, Medicines Discovery Catapult, NHS-England), funders (Alzheimer's Society, BHF) and representatives from DPUK's academic sites. At this productive meeting our Vascular team reported on interlinked work packages, using the extensive data in UK Biobank. These are designed to identify molecular targets related to vascular disease, for possible use in dementia research.

Collaboration

DPUK Vascular Health members Professor Stuart Allan (Manchester) and Professor Atticus Hainsworth (City St George's University), in collaboration with Dr Laura Ajram and Dr Ekta Patel of the Medicines Discovery Catapult, produced a new roadmap on "Collaborative Opportunities in Vascular Dementia". This followed a cross-sector workshop that brought together DPUK, the UK DRI, NHS, pharma industry, government, and medical research charities.

Viva la VIDA

VIDA (Vascular and Immune contributions to DementiA) is a new multi-institutional partnership. It is amongst the first Alzheimer's Society's Doctoral Training Centres to be created. Led by Professor Stuart Allan (University of Manchester), Professor Atticus Hainsworth (City St George's), Dr Fatemeh Geranmayeh (Imperial College London) and Professor Anna Williams (Edinburgh DRI), the VIDA Doctoral Training Centre will develop a new generation of scientists to improve understanding of the mechanisms behind cardiovascular and immune system contributors to dementia. The objective is to accelerate target prioritisation and facilitate the development of future treatments. The first cohort of PhD students began their studies in September 2024, and the first in-person VIDA symposium was held in Manchester in January 2025.

Other workstreams

Professor Joanna Wardlaw's team (University of Edinburgh) are progressing with recruitment to LACI-3, one of the few phase-III clinical trials worldwide in vascular contributions to dementia. LACI-3 grew out of the DPUK Vascular theme and includes several of the DPUK Vascular team as co-investigators (Professor Philip Bath, Professor David Werring).

Professor Wardlaw's team has also made progress in characterising perivascular spaces around blood vessels in the brain, as a possible marker of dementia.

Professor Hugh Markus (University of Cambridge) and his team have made substantial progress in identifying therapeutic targets in cerebral small vessel disease using advanced genetics methods. Small vessel disease is the foremost vascular cause of dementia in older people.

Optimizing treatment of cardiovascular risk factors in cerebral small vessel disease using genetics

Professor Terry Quinn (Glasgow University) has screened a large archive of cardiovascular drug prescribing, in people within the UK Biobank study, looking for potential candidates to treat causes of dementia. His team discovered an exciting link to a thiazide diuretic agent, which would offer an entirely novel approach to dementia treatment. This was presented to an international audience at the 2025 VasCog conference in Southampton UK.

Misha Ramesh is a PhD student in the first cohort of the VIDA doctoral training centre. She works on automated retinal imaging at St George's with Professor Christopher Owen (City St George's).

VasCog25 conference

Synaptic Health

Professor James Rowe, Associate Director, and lead of the Experimental Medicine Incubator workstream.

The Synaptic Health theme brings together PET-imaging of synaptic density, magnetoencephalography (MEG) of neurophysiological function, and proteomic markers of synaptic injury, in longitudinal studies of early-stage Alzheimer's disease (mild cognitive impairment or early dementia).

Our New Therapeutics in Alzheimer's Disease (NTAD) study, led by James Rowe (University of Cambridge) has demonstrated the reliability of MEG and the ability to discern receptor specific effects of disease from brain imaging signals. Read more.

Several papers currently under review, demonstrate the sensitivity of MEG to the presence of Alzheimer's disease, its severity and progression. Changes in MEG are not confined to Alzheimer's disease, but are readily identified in frontotemporal dementia. Read more.

This work has led to another major study which is now underway, Synaptic Health in Neurodegeneration (SHINE). The team is examining the link between brain function (cognition and MEG) and biological markers of disease measured from blood, cerebrospinal fluid and specialised PET imaging of synapses. The severity and distribution of synaptic loss distinguished Alzheimer's disease pathology from corticobasal degeneration syndromes, as the two main causes of corticobasal syndromes. Read more.

It is not practical to study brain cells (neurons, microglia or astrocytes) from people living with Alzheimer's disease, but by induced pluripotent stem cells (iPSCs) from people with Alzheimer's disease, one can then transform the stems cells into neurons or astrocytes. Such iPSC-derived astrocytes from people with Alzheimer's disease mirror the pathophysiological features observed in those same people. Read more. This offers an exciting new way to study Alzheimer's, both for stratifying patients into specific treatments, and for screening potential new drugs. Similar methods are now being used to study iPSC-derived neurons, from people with Alzheimer's disease who have had MEG scanning in DPUK studies.

Some of the DPUK team at the University of Cambridge

The Data Portal

As an innovative 'open knowledge architecture' (page 3), the Data Portal is at the centre of DPUK's programme. By supporting end-to-end management for over 100 datasets and trials delivery, the Portal is an unparalleled asset to the UK dementia research infrastructure.

Professor Simon Thompson leads the Data Portal workstream.

As a trusted research environment with ISO 27001, DEA accreditation, our centralised data management strategy delivers secure, cost-efficient, low-carbon solutions that better meet the needs of a global scientific community. It simplifies the data environment, providing standard streamlined approaches to provenance, governance, curation, discovery, access, and analysis pipelines. This reduces the burden on individual research groups, freeing them to focus on science. Our strategy has led to DPUK becoming a global brand with over 2,500 access requests from over 1,200 users in 43 countries. Key features include:

Breadth and depth of data with over 65 cohorts with epidemiologic and clinical data (n>3.5m), >300,000 neuroimaging scans across 20 cohorts, and genomic data for >140,000 participants from 16 cohorts.

Powerful data discovery tools ranging from high-level overviews to in-depth variable discovery, with variables curated to a common data standard for research readiness.

Accelerated access using centralised access requests for multiple datasets with a median response time of 21 days.

Secure access using remote virtual desktops with two-factor authentication to ensure data do not leave the secure environment.

Pre-loaded analysis software including general statistical (including R, Stata, Python, Jupyter) and modality-specific packages (imaging, genomics).

Multi-modal analysis using pre-processing pipelines enabling both specialist and generalist access to complex epidemiologic, clinical, imaging and functional genomics data.

High-level compute including HPC and GPU access.

Research hubs as cost-effective and rapid solutions for specialist communities to develop their own brand identity and international profile within a trusted research environment. Examples include brain imaging, genomics, traumatic brain injury, motor neurone disease, iPSCs and neurological tissue, and adolescent mental health (pages 20-21).

Collaborative spaces as private spaces for consortia to develop their data assets in preparation for onward sharing.

Federation as the solution to international data access across platforms and secure data environments.

Synthetic data, available at a range of fidelities, offers rapid and risk-free access to complex data for training and code testing. This is particularly useful for federated analyses.

Global network of data platforms established through partnership and collaboration with AD Workbench, GAAIN, Ontario Brain Institute, France Cohortes, Korea Brain research Institute, Yonsei University, Dementia Platform Australia, Fraunhofer Institute and AI-MIND.

AI readiness through emerging governance and risk assessment frameworks that support responsible AI research. This is particularly important for safe model development within trusted research environments, addressing privacy and public trust considerations.

Global data discovery using the ADDI-funded Data Landscape Report covering translational-relevant cohorts, trials, and research registers.

Trials recruitment using our three trials registers covering preclinical populations (Great Minds, Clinical Trials Register) and early clinical populations (TDF Clinical register).

Trials delivery using our network of over 80 clinical, academic and industry sites throughout the UK.

Training for analysing complex and longitudinal data within a trusted research environment is becoming essential for developing next-generation analysts.

2025 reflections

Although 2025 has seen increases in our data portfolio and access requests, highlights orbit the breadth and quality of our collaborations. Advanced data management is complex but requires streamlining and standardisation for the efficient and timely creation of complex knowledge. The Data Portal is privileged to work with a wide range of stakeholders, sharing technologies, learnings and best practice. 2025 has seen many of our collaborations come to fruition.

The increase in Research Hubs and Collaborative Spaces has demonstrated the value of supporting distinct research communities as a strategy for attracting increasing dementia translation capacity.

The Alzheimer's Data Initiative has been a major partner in supporting data standardisation using the C-Surv model, developing data federation and funding the Dementia data Landscape report.

We have worked closely with HDR-UK on the MND Research Data catalyst and with DARE on the development of federation and synthetic data.

Global federation provides a unique opportunity to align data standards and access protocols. Our coalition of federation partners will specifically address ethnicity-bias in dementia data. We are delighted to be working with a such a generous and broad-based coalition to achieve this.

The SeRP infrastructure team have been critical to our success. The partnership of informatics innovation and real-world application is a winning combination. We look forward to extending this in support of the UK Neurodegeneration Initiative.

Looking ahead the global federation coalition will extend its activity to include cross-platform metadata discovery, and alignment of federation and federated-learning tools. Using AI to automate pre-processing pipelines will accelerate the availability of research-ready data.

Find out more about the Data Portal

Hubs and collaborative spaces

There is a growing number of studies and programmes using the DPUK Data Portal as a central resource. Here we highlight some of them, demonstrating the breadth of research enabled by the portal.

Hubs are wholly project-branded Trusted Research Environment (TRE) spaces on DPUK's portal, with all of the functionality and specific utilities they need. However, each of them saves time and significant costs because they have not had to design and build a space themselves from scratch. They share governance, data processing and analysis pipelines that were originally created for the wider DPUK portal.

Projects also use the portal to host their own collaborative space, accessing their own data inside a TRE. It is a single space for partners to work together with secure data management.

Here are some of the projects which have created their own hubs.

UK Nervous Tissue Network (UKNTN) hub

A one-stop-shop for neurological tissue research

The UKNTN was set up to bring together expertise from Newcastle, Oxford, Swansea, Exeter, King's College London and University College London to provide high quality tissue, cells and data to neuroscientists around the world.

The aim is to enhance our ability to understand the many pathologies underlying neurodegeneration.

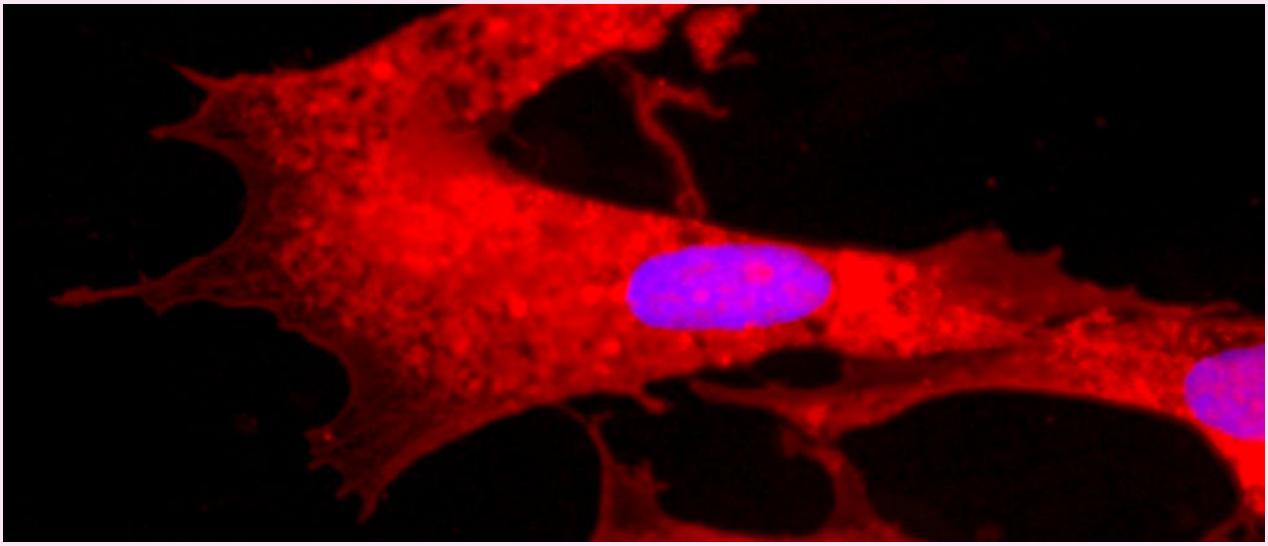
Aspects of this project include:

- recruitment of potential donors and collection of post mortem tissue from mental health and neurology;
- collection of samples from multiple organs from post mortem donors;
- development of novel methods of tissue processing e.g. Tissue Micro Array which provides samples from multiple brain areas on a single block;
- production of stem cells from donated tissue, conversion to hiPSC in selected cases and production of organoids;
- development of methods of collecting and using excess neurosurgical tissue in research;
- linkage of research data to NHS donor data.

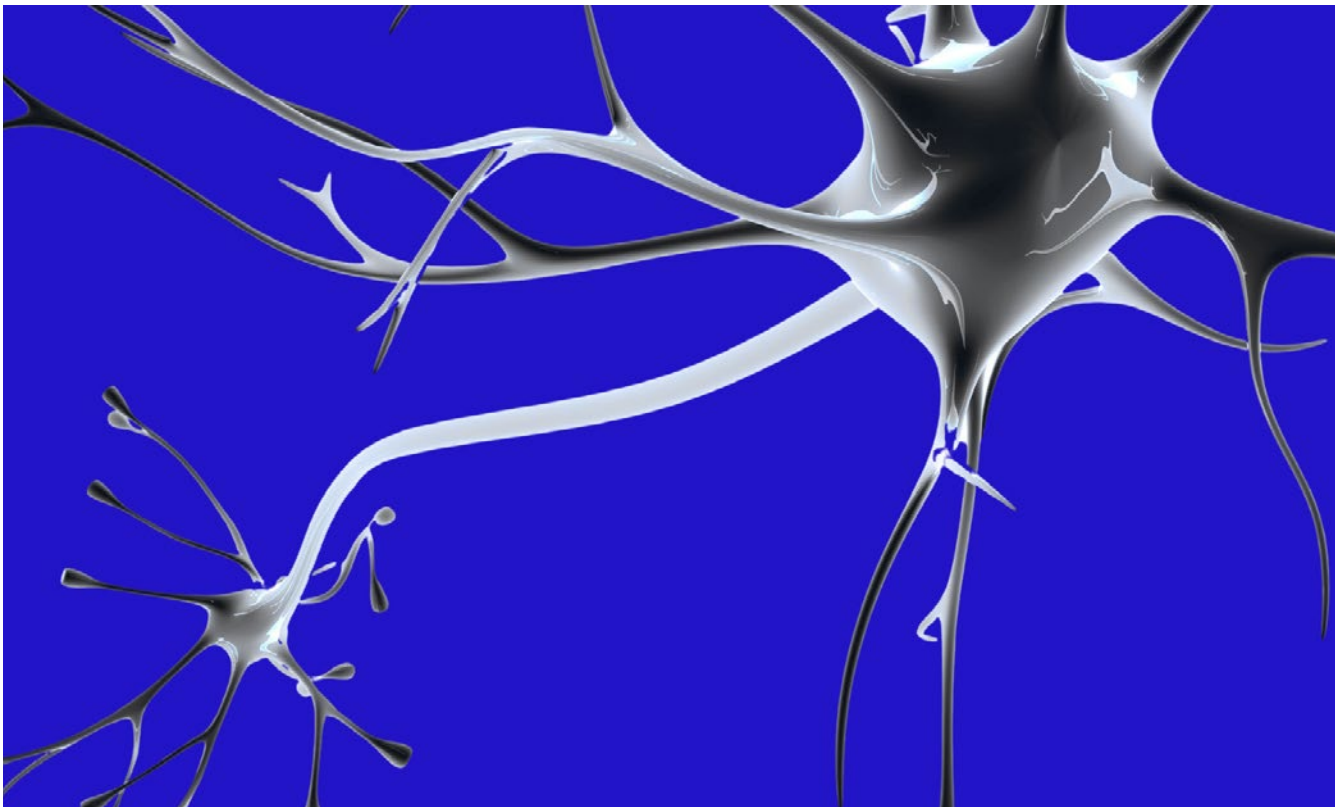
The group's ambition is to provide a one-stop-shop for researchers from academia and industry enabling them to both identify and apply to use data and materials. Read more.

UKNTN uses DPUK infrastructure to manage the data which is now being produced.

A UKNTN hub has been created within the DPUK Data Portal where genomic, epigenomic, and NHS data will be brought together and linked to individuals within a secure environment. This data will, in turn, be linked to donated nervous tissue and its derivatives. These materials will be stored in Human Tissue Authority approved tissue banks and will be made accessible to the wider scientific community.



DPUK accelerates national effort to transform MND research



DPUK is playing a pivotal role to accelerate research into motor neurone disease (MND) through two complementary initiatives: the MND Research Data Catalyst (MND RDC) and the MND Translational Accelerator (MNDAcc) both with hubs on the DPUK Data Portal.

MND Research Data Catalyst

Led jointly by Health Data Research UK (HDR UK) and Dementias Platform UK (DPUK), and supported by the wider MND research community, the MND Research Data Catalyst (MND RDC) aims to harness the power of data to unlock new insights into the causes, progression, and treatment of MND.

DPUK brings its powerful data infrastructure and expertise, standardising and hosting large-scale datasets on its secure Data Portal—powered by the Secure eResearch Platform (SeRP)—to enable FAIR (Findable, Accessible, Interoperable, Reusable) access, underpinned by user centred design principles. By enhancing data accessibility and useability, the MND RDC will ensure the scientific community has the tools needed to drive innovation, deepen understanding, and ultimately, improve outcomes for people living with the disease.

Professor John Gallacher, Director of DPUK, highlighted the importance of the project: "Data is the key to understanding complex neurodegenerative diseases like MND. By making data more accessible and usable, the MND Research Data Catalyst will enable researchers to ask bigger questions and find answers faster."

MND Translational Accelerator (MNDAcc) Hub

Complementing this data-driven approach is MNDAcc, a £6 million investment by the Medical Research Council and the National Institute for Health and Care Research, managed by DPUK. MNDAcc aims to accelerate the development of treatment for MND and related conditions such as frontotemporal dementia, providing infrastructure, specialist facilities, and rapid funding distribution to support high-quality in-human research.

Twelve projects have received MNDAcc funding, covering trial methodology, genetics, physiology, proteomics, and biomarkers. These projects are now underway, with the key goal of translating scientific discoveries into tangible therapeutic advances.

Together, the MND Research Data Catalyst and MNDAcc form a unified strategy to transform MND research. These initiatives form part of a broader national strategy to coordinate research—supporting the UK government's ambition to find a cure for MND within a decade, an ambition driven by the patient-led United to End MND campaign.

By integrating enhanced data access with accelerated translational projects, DPUK is helping to build a research ecosystem capable of delivering breakthroughs faster and more efficiently, and improving outcomes for those affected by this devastating disease.

MND ACCELERATOR

TBI-REPORTER hub

A one-stop-shop for neurological tissue research

UK-TBI REpository and data PORTal Enabling discoveRy (UK-TBI REPORTER), led by Professor David Menon at the University of Cambridge, is a £10 million project, funded by a consortium of UK research funders led by the Medical Research Council. It is continuing to make excellent progress.

The TBI-REPORTER Experimental Medicine Network has begun recruitment to the 3P (Prospective Proof of Principle) cohort. This in turn will generate bio samples for the National Biomarker resource and clinical data and neuroimaging data (CT, 3T and 7T MRI, and PET) for the Data Hub.

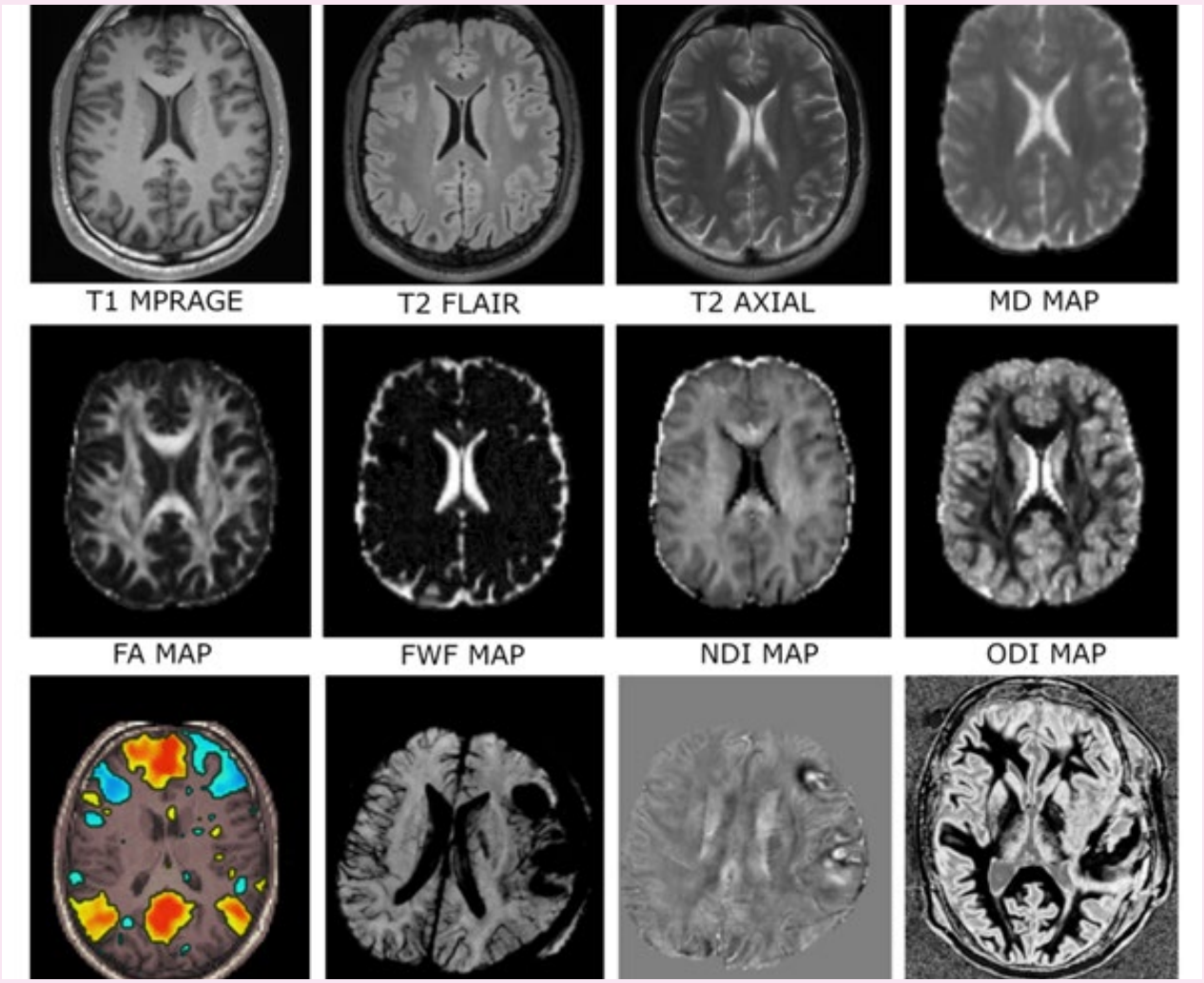
The National Biomarker resource has coordinated and developed pipelines for the collection of human biofluids at scale. It is also coordinating and harmonising neuroimaging data collection analysis, as well as standardising accrual and archiving of postmortem and surgical tissue samples.

The Data Hub continues to receive large datasets from a variety of pipelines. It provides a current, fully auditable, remote access 'sandbox' trusted research environment, facilitating data analysis via a virtual desktop. This includes multiple statistical and data management packages alongside the capability to integrate bespoke analysis tools.

The TBI-REPORTER Patient and Public Involvement and Engagement panel has a broad remit, and it helps to prioritise research areas of value to patients. The panel ensures the operation of the platform and that the sharing of resources is ethical and informed by lived experience. It also supports the efficient dissemination of the platform's impact to patients and the general public.

The TBI-REPORTER infrastructure has catalysed TBI research in the UK, as evidenced by the growing list of affiliated studies. These studies will generate data and samples for legacy use and enable analyses (such as genome-wide association studies) impossible with any single project.

TBI-REPORTER was delighted to have been awarded the NeuroRehab Times Global Impact Award 2024.



Professor Art Toga addressing the Translation 2025 conference.

AI in dementia research: opportunities, challenges, and a vision for the future

Professor David Llewellyn, Professor of Clinical Epidemiology and Digital Health at the University of Exeter Medical School says DPUK's approach to data is already offering valuable tools and assets which can give dementia researchers confidence in a world where Artificial Intelligence is playing a huge role.

Artificial Intelligence (AI) has the potential to transform dementia and brain health research. AI can detect subtle patterns in complex biomedical data, enabling earlier diagnosis, more personalised interventions, and deeper insights into disease mechanisms. These advances arrive as dementia prevalence rises due to global ageing. While the potential benefits are profound, AI introduces thorny challenges around data quality, bias, transparency, and ethics. DPUK, with its secure data infrastructure, commitment to responsible data sharing, and collaborative ethos, is uniquely positioned to help dementia researchers navigate these opportunities and challenges.

Generative AI refers to models such as variational Autoencoders and Generative Adversarial Networks (GANs) that can create synthetic data reflecting the statistical properties of real datasets. In dementia research, generative AI allows researchers to generate realistic brain scans or clinical datasets, augment underrepresented groups, and simulate disease trajectories. Crucially, synthetic data can be shared and analysed in less restricted environments than real patient data, accelerating research while protecting privacy. DPUK is investing in synthetic data tools within its Trusted Research Environment (TRE) and exploring governance frameworks to support safe and effective use. These advances will enable AI models to be developed and tested in silico before being applied to sensitive real-world data. Synthetic data also offers opportunities for wider participation in research, for example through education and capacity building in low-resource settings.

Explainable AI (XAI) is increasingly important in dementia research. While deep learning models can offer high predictive accuracy, they are often opaque. XAI techniques such as SHAP (SHapley Additive Explanations) or explainable boosting machines help reveal which features contributed most to a model's decision. Ultimately this may help clinicians trust AI outputs and uncover new scientific insights. Causal AI complements this by modelling not just associations but causal pathways, enabling virtual experiments on observational data. For example, it can help estimate whether

modifying a risk factor (e.g. midlife hypertension) is likely to reduce dementia risk. These approaches require rich longitudinal datasets and collaborative environments - a core strength of DPUK. Through promoting transparency and interpretability, DPUK supports the development of AI tools that are not only powerful but usable and trustworthy in real-world settings.

Multimodal machine learning is a natural fit for dementia research, where neuroimaging, genomics, biomarkers, and clinical data must be integrated to characterise disease progression and heterogeneity. AI can excel at combining such diverse data types to improve stratification, diagnosis, and prognosis. DPUK enables this by providing secure access to harmonised multimodal datasets from more than 50 cohorts. This positions DPUK as a key enabler of next-generation multimodal AI in dementia. Future opportunities include developing models that can generate individualised risk profiles and identify early markers of specific dementia subtypes, supporting both research and clinical decision-making.

Large language models (LLMs) also hold potential for dementia research. These models can synthesise findings across large volumes of scientific literature or extract structured information from unstructured clinical notes. In future, fine-tuned bespoke LLMs may assist with patient stratification, clinical trial recruitment, or real-time clinical decision support. Their deployment, however, requires rigorous validation and safeguarding of patient data. DPUK's secure analytical environment provides a platform to evaluate LLMs safely and at scale. Open source LLMs, such as Llama 4, may be particularly useful in that they allow access to the code and weights and are more transparent, accessible, reproducible and controllable than closed-source proprietary models such as GPT-4. Through partnership with leading academic institutions and the private sector, DPUK is well placed to assess and shape how LLMs can be ethically and effectively applied in dementia research.

The Deep Dementia Phenotyping (DEMON) Network is a key DPUK partner. The DEMON Network brings together over 1,600 data scientists, clinicians, and researchers across disciplines to develop, apply and share AI methods for dementia. Working with DPUK, the DEMON Network community co-develop tools, host training events, and contribute to governance and best practices. This partnership connects methodological innovation with data access and translation. It ensures that novel models are developed in dialogue with users and beneficiaries, accelerating their uptake and impact. It also plays a crucial role in identifying priority areas, fostering cross-sector collaboration, and building capacity globally.

To realise AI's promise, DPUK provides more than data. It offers a robust TRE, cloud-based computing, synthetic data tools, and a governance framework for responsible AI. It enables rapid, secure access to curated datasets, reducing duplication and levelling the playing field for researchers. DPUK also supports training and engagement, convening stakeholders through datathons, webinars, and international collaborations. Through these efforts, DPUK is nurturing a community of practice that combines technical excellence with a deep understanding of clinical and ethical issues in dementia research.

Looking ahead, DPUK will support the co-development of interpretable, multimodal, and causally robust AI models. It will host benchmark datasets, support model development, and promote the development of synthetic populations for simulation studies. It will also prioritise inclusive datasets and bias auditing to ensure equity in AI outcomes. Through partnership with the DEMON Network and others DPUK will continue to drive responsible, translational AI research in dementia. This includes supporting research into generalisability and robustness, ensuring that AI models trained in one population perform reliably in others, and enabling the development of tools that can be safely deployed in routine clinical practice.

> **The future of dementia research will be shaped by our ability to use AI to make sense of complexity. DPUK is laying the groundwork for this transformation. Its data infrastructure, secure computing environment, and collaborative ethos are creating the conditions for AI to accelerate discovery, optimise care, and ultimately change the trajectory of dementia worldwide.**

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Multi-site study prepares ground for next generation large-scale neuroimaging

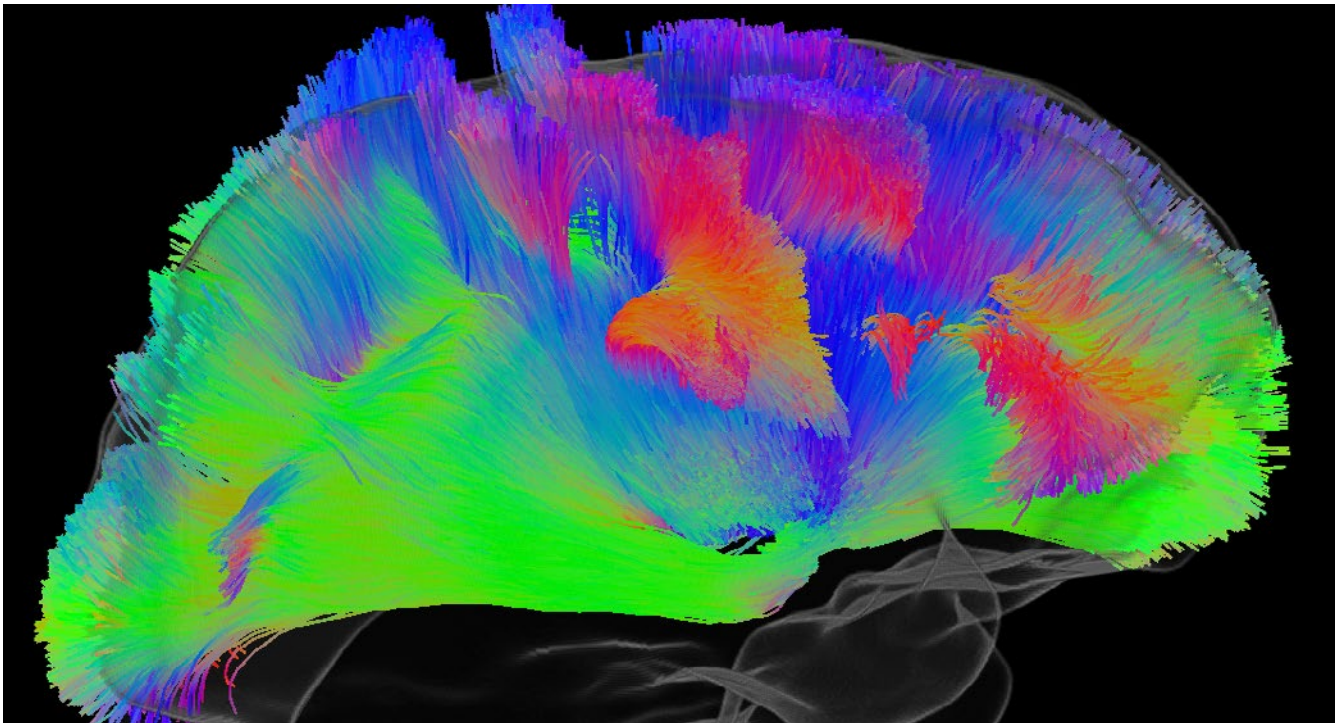
DPUK's Imaging Network is led by **Dr Pawel Markiewicz**, University College London. There has been significant growth in the images available on the Data Portal, and the Imaging Network is continuing to develop its capabilities through harmonisation across its sites.

We conducted a large MRC-funded multi-site harmonisation and test-retest study across eight DPUK imaging centres equipped with hybrid PET/MR scanners from Siemens and GE.

This work establishes a robust foundation for large-scale, high-quality neuroimaging studies, paving the way for the next generation of multi-site imaging trials in dementia. It involved healthy older adults (aged 65-90) undergoing two amyloid PET/MR scans following a fully harmonised protocol designed to assess repeatability and reproducibility both within and across scanner models and sites.

Two amyloid radiotracers—[18F] flutemetamol and [18F]florbetaben—were used with matched doses and acquisition methods. The study achieved an excellent test–retest reliability (r = 0.98) across the national network, demonstrating the high consistency achievable in multicentre PET/MR dementia studies.

All image analysis was performed using our open-source AmyPET software, developed in collaboration with the European Consortium AMYPAD (now Euro-PAD), providing an end-to-end PET imaging solution for dementia research. Importantly, all imaging data, including raw PET data, will be made



The brain's communication network (corticostriatal tracts) mapped out using Constrained Spherical Deconvolution from diffusion MR imaging. This image is taken from the Quantitative MRI in NHS Memory Clinics project that explores new ways to use brain imaging for use in memory clinics with AI and advanced imaging techniques. Image supplied courtesy of Tim Rittman and Tatjana Schmidt, University of Cambridge.

available on the DPUK data portal for sharing and furthering innovation in neuroimaging research.

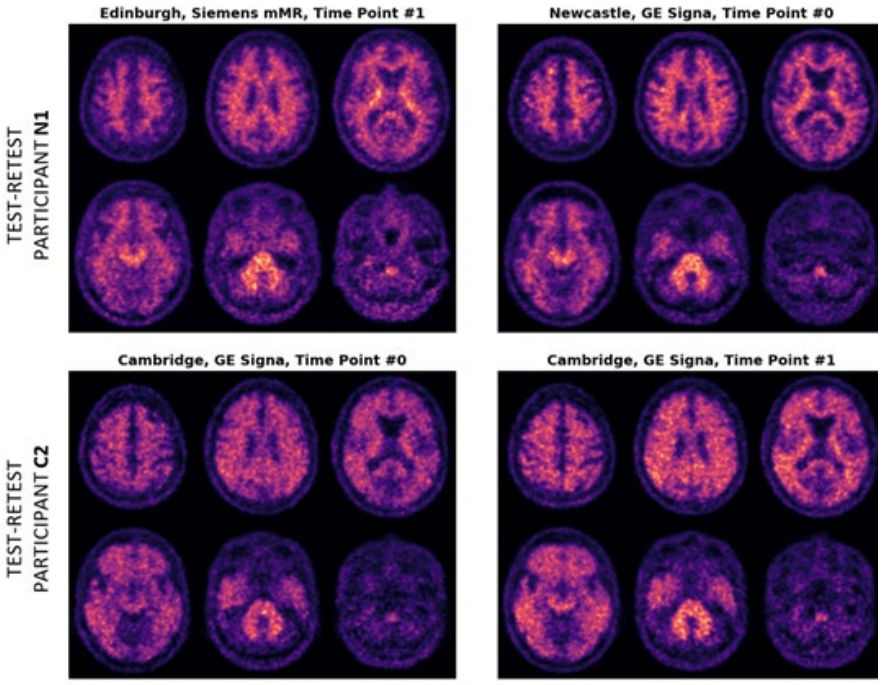
An example of test-retest PET scans of amyloid negative (top row) and amyloid positive scans (bottom row) can be seen in the image (right).

With recent breakthroughs in Alzheimer's treatment—particularly the new drugs lecanemab and donanemab—we are now seeing that memory and thinking abilities can be preserved for years, while the investigational drug trontinemab is showing rapid amyloid clearance with minimal side effects (**Alzheimer's Research UK, 2025**).

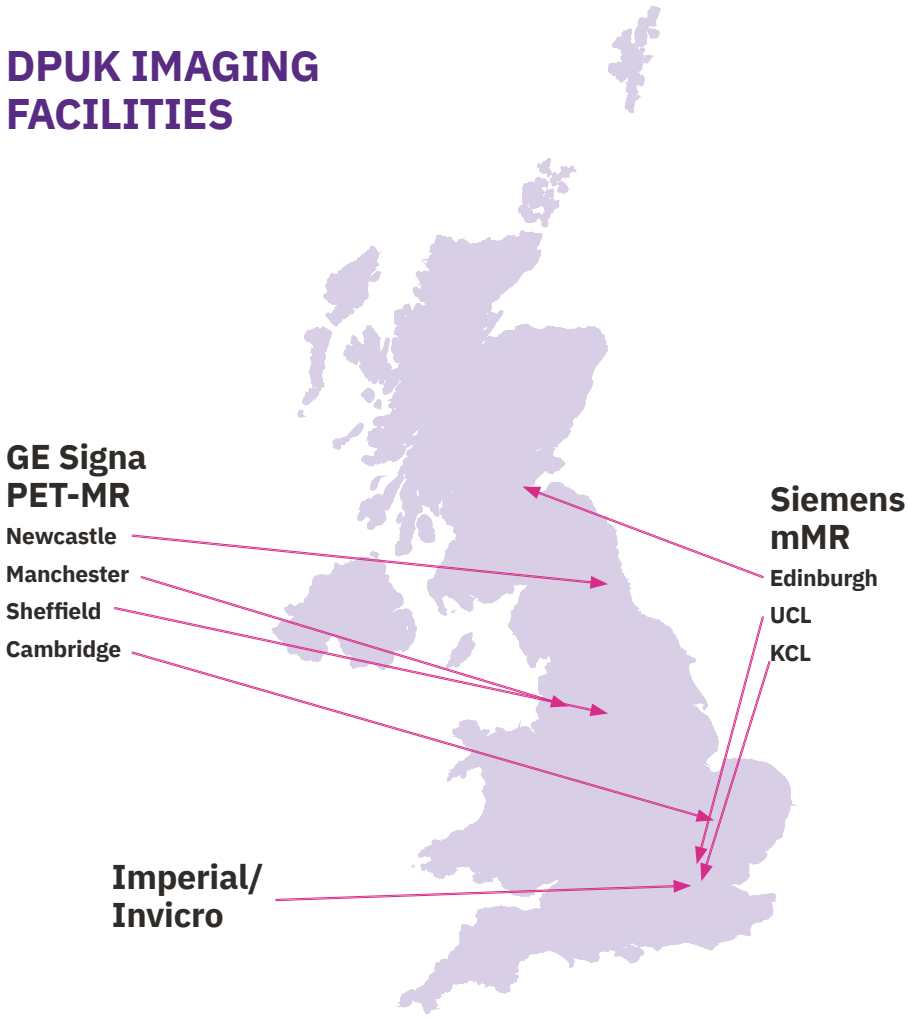
The greatest benefits of these therapies occur when treatment begins early, underscoring the urgent need for faster and more accurate diagnosis. This is where PET and MRI imaging, alongside emerging blood biomarkers, play a crucial role.

Despite significant UK investment in total-body PET scanners and the establishment of the National PET Imaging Platform (NPIP)—offering unprecedented image resolution and lower radiation exposure—the availability of PET imaging and radiotracer production still lags behind demand. Expanding this capacity is essential to meet the growing need for clinical trials, diagnosis, and therapy monitoring. Encouragingly, new, more affordable dedicated brain PET scanners are emerging on the market, which may help widen access to PET imaging across the UK.

Looking ahead, the next phase of DPUK will integrate NPIP's advanced PET infrastructure with DPUK's powerful data and trials ecosystem, enabling precision recruitment, biomarker validation, and early-phase experimental medicine.



DPUK IMAGING FACILITIES



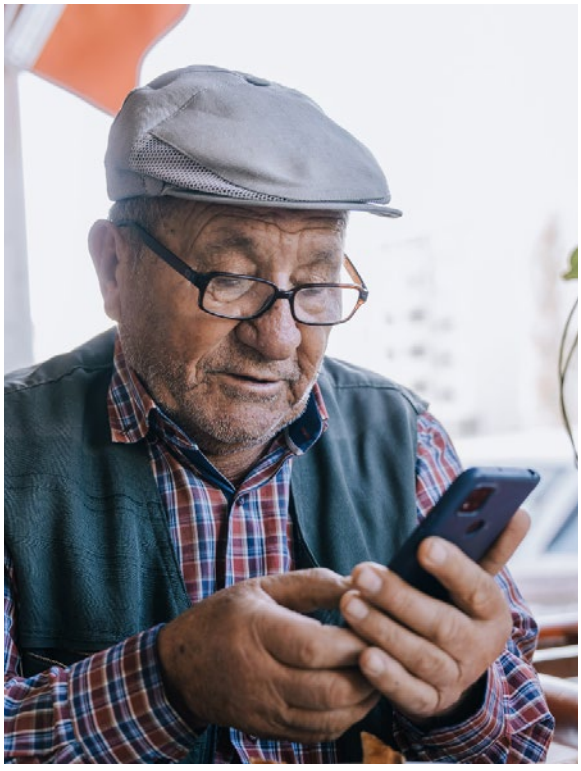
Fluid Biomarkers – DPUK is driving the How, What and Where

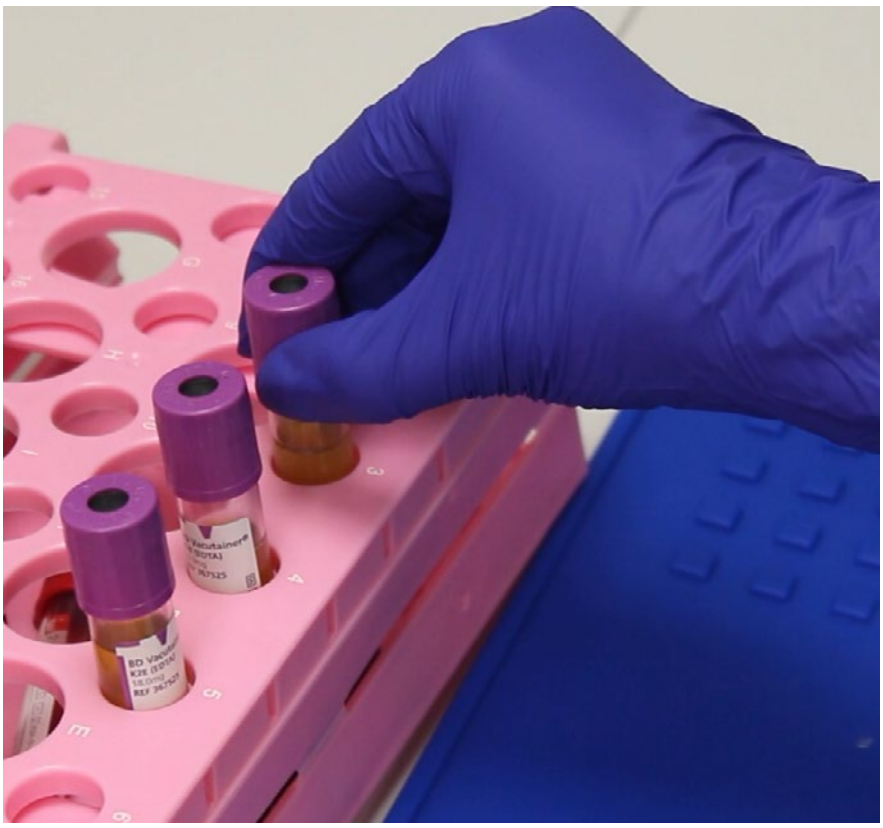
Professor Vanessa Raymont reviews current blood biomarker research in DPUK and what the future may hold.

The diagnosis of memory disorders is undergoing rapid transformation at a time of rising global need. Nearly a million people in the UK live with dementia, and worldwide cases are projected to triple by 2050. The arrival of Alzheimer's disease–modifying therapies offers real prospects for treatment, but these advances depend on accurately identifying patients who are likely to benefit. Yet diagnosis remains inconsistent: more than 30% of people with dementia in the UK lack a formal diagnosis, and fewer than 2% currently access gold-standard PET imaging or cerebrospinal fluid (CSF) testing. Despite repeated guidance from national bodies and charities, biomarkers remain underused in routine care.

Blood-based biomarkers (BBMs) have emerged as a promising solution. They are less invasive, more scalable, and substantially cheaper than PET and CSF biomarkers. The most studied markers include amyloid-β (Aβ42, Aβ40) and phosphorylated tau (p-tau181, p-tau217 and p-tau231), reflecting the core pathological features of Alzheimer's disease. Other markers such as neurofilament light (NfL) and glial fibrillary acidic protein (GFAP) offer insight into neurodegeneration and astroglial injury. However, much existing research is based on small or unrepresentative samples and often focuses solely on Alzheimer's disease. Further work is needed to confirm how BBMs perform across diverse populations and across all major causes of dementia. Key challenges remain, including assay platform variability and the need for consensus on diagnostic thresholds.

DPUK is addressing these gaps through several major programmes. The READ-OUT (REAl world Dementia OUTcomes) study, part of the ARUK–Alzheimer's Society Blood Biomarker Challenge and led by Vanessa Raymont, James Rowe and Ivan Koychev, aims to determine whether BBMs can accurately and affordably identify Alzheimer's disease, vascular dementia, frontotemporal dementia and dementia with Lewy bodies in real-world memory services. Recruiting across 33 UK Trial Delivery Framework sites, READ-OUT aims to collect data from 3,165 people, including 30% from under-represented groups. BBMs are being tested across three tiers: Tier 1 includes biomarkers closest to clinical readiness; Tier 2 represents widely used research markers; and Tier 3 incorporates exploratory approaches such as proteomics, lipidomics, metabolomics, genomics and





epigenomics. Sub-studies are assessing at-home collection, sample processing delays and test-retest reliability. A subsequent 880-participant randomised controlled trial will evaluate whether sharing BBM results with clinicians and patients improves decision-making, cost-effectiveness and care pathways.

DPUK is also working with Roche Diagnostics to broaden access to BBM assays nationwide and to integrate BBMs with imaging and digital cognitive assessment via the DPUK Imaging Network. This collaboration aligns with the UK Dementia Goals Programme and the Davos Alzheimer's Collaborative, ensuring that emerging biomarker pathways support both clinical care and trial readiness.

Complementing READ-OUT, the FAST Brain Health Study, led by Ivan Koychev, is examining whether BBMs and remote cognitive assessments can be delivered at scale. Meanwhile, DPUK's collaborative CSF project with Eli Lilly is addressing longstanding inequalities in access to CSF biomarker testing, particularly in mental health Trust-based memory clinics. Early results show substantial benefits: one site has already achieved a £645 saving per patient.

Looking ahead, blood biomarkers may reshape not only diagnosis, but the entire clinical pathway for memory disorders. While current recommendations prioritise their use in patients with existing cognitive symptoms, BBMs could eventually support earlier case identification, population-level screening, disease monitoring and personalised treatment planning. They may also help address health inequalities by providing more accessible diagnostic options.

DPUK is expanding its research beyond Alzheimer's disease to include biomarkers for vascular, inflammatory and other non-AD dementias, recognising their substantial and often overlooked contribution to cognitive decline. John O'Brien and Atticus Hainsworth are leading efforts to develop novel BBMs targeting vascular pathology and inflammatory mechanisms—areas with high clinical need and significant potential for therapeutic innovation.

In summary, biomarker research is set to transform the future of memory assessment and dementia care. By making diagnosis earlier, more accurate and more accessible, BBMs and related biomarker technologies have the potential to revolutionise how dementia is detected, managed and treated across the UK and beyond.

Digital 'Bolt-on' test to READ-OUT biomarker study

An additional study is being conducted as part of the DPUK READ-OUT programme. Funded with a £2 million injection of funding from Innovate UK, it will assess digital tests for cognitive function.

Part of the Government's Dame Barbara Windsor Dementia Goals programme, it will look at potentially quick and easy digital tests for patients' cognitive functions which will take only 10 minutes to complete. The digital test will be used alongside blood biomarker tests which the READ-OUT team is already studying as part of the Blood Biomarker Challenge.

The digital cognitive tests will also be part of the Davos Alzheimer's Collaborative Healthcare System Preparedness Project in the UK.

Speaking at the World Dementia Council Summit in London, in April 2025, Science Minister Lord Vallance said:

"Dementia is an incredibly cruel disease, affecting nearly every family in some way. As a life sciences world leader, the UK is uniquely placed to bring innovative technologies to the frontline of the fight against dementia."

This addition to the READ-OUT study allows the team to assess if a combination of tests could be helpful and cost effective in clinical settings if they were to be rolled out across NHS memory clinics and beyond. Read more.

People's experiences are essential in creating and delivering successful research

The views and comments of people with a health condition play a vital role in helping DPUK to create and deliver studies and trials. Hearing and understanding how someone feels about an approach, procedure or timescale of a study can make a considerable difference to the way a team approaches a project.

Now, collaborations with patients or participants can boost the quality and outcomes of our work. As Professor Sarah Bauermeister explains "it is a question of learning from people who have experience. People who have a condition can directly comment about the feasibility of an approach. Equally, someone who has previously taken part on a trial will be more likely to see where modifications will transform participants' experiences. There is no doubt it leads to better decision making."

READ-OUT

Our most recently launched large research study, READ-OUT, demonstrates the approach we are taking. From the beginning of its development, a group recruited and led by Dr Ben Underwood and Linda Pointon at the University of Cambridge has focused on Public Participation Inclusion and Engagement. They have engaged at each stage of the study, offering opinions from people with relevant lived experiences.

Ben Underwood said: "Engaging people with lived experience always improves research. The READ-OUT study is intended to change practice for thousands of people coming to clinic who might get a blood test to support their diagnosis. Making sure we get it right for people in this study is therefore even more important, and we are much more likely to get it right if we involve people right from the start."

Their insights have been crucial in shaping the study's development. Contributions have been instrumental in refining key study documents and offering thoughtful feedback on operational processes.

Most recently, a member of the READ-OUT PPIE group played a central role on the selection panel for digital patient assessments and was integral to the final decision regarding the inclusion of the digital cognitive assessment component of the study.

Volunteer Registers

DPUK maintains three volunteer registers and public opinion was sought and incorporated into the development of each register. Within the Great Minds register there is also a panel of volunteers who have agreed to be approached about new dementia-related studies or initiatives. This panel has provided input on a number of new developments within Great Minds, helping to ensure they are developed in an inclusive way.

Motor Neurone Disease Initiatives

PPIE is central to the MND Accelerator, with lay members, who either have MND or have been affected by it, involved in every stage of grant review. This has ensured funding decisions reflect community priorities. These members also contribute to the Executive Committee and Scientific Steering group, helping review project progress through regular updates and site visits, and informing decision-making. Likewise, the MND Research Data Catalyst has established a Patient Advisory Group to guide the initiative and ensure it addresses the real needs of those living with MND.

Data Portal Initiatives

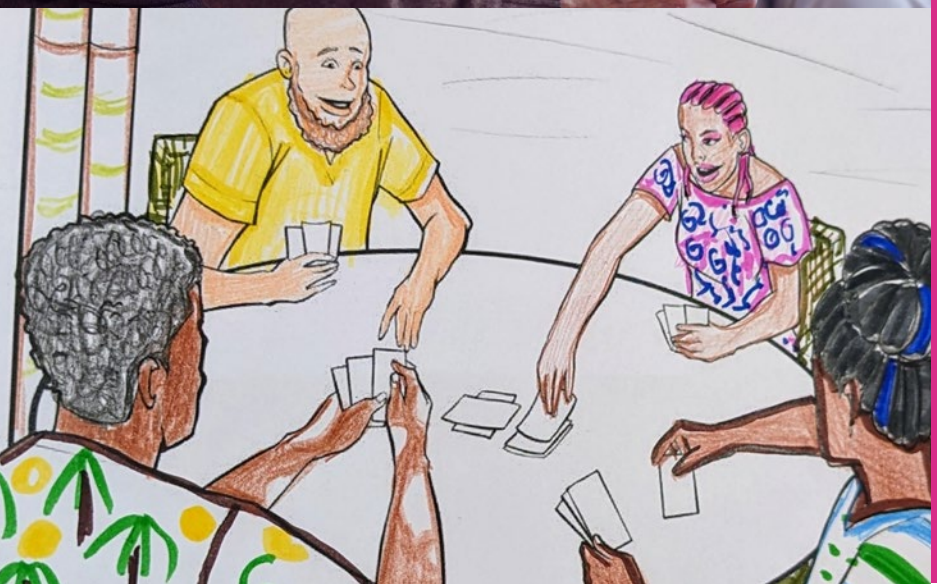
The DPUK Data Portal team has formed Community groups for two of their initiatives relating to artificial intelligence. Both the AI Risk Evaluation project and the Synthetic Data project have consulted a range of stakeholder groups, including representatives of the public and patients.

People's Voice

Professor Sarah Bauermeister has taken innovative approaches to community engagement at design and implementation stages in several recent studies.

"DPUK is committed to the importance of diversity and inclusivity in research which directly and indirectly feeds into providing datasets to researchers that better represent communities."

It is a priority to integrate diversity programmes into DPUK's core aims and strategies. Our People's Voice Engagement Programme will, for the next few years, focus on outreach programmes based on ethnicity, gender and age.



Innovative Approaches to participation and involvement

Addressing the issue of inclusion and engaging hard-to-reach communities has led DPUK to innovate in order to recruit to registers, studies and activities.

Your Beautiful Brain
In 2022, we were awarded an ARUK Inspire fund grant for 'Your Beautiful Brain' – which used Art Workshops to promote research participation and brain health education in the Black African and Caribbean communities'. The People's Initiative now continues within the DPUK People's Voice Engagement Programme in local communities with the goal of using creative arts (art, dancing, music) to promote brain health (cognition and mental health).

Great Minds diversity initiative
Further outreach work with south Asian communities has been undertaken with the aim of broadening participation in registers of people available to studies. Working closely with neighbourhood leaders in Wolverhampton, DPUK piloted a community event-based outreach to assess the most effective ways of boosting recruitment to our Great Minds register. This included bilingual contributions from our research team.

Blossom
The DPUK-supported Blossom Early Adversity and Brain Health Programme, led by DPUK Senior Scientist Professor Bauermeister, has its own PPIE group, 'Blossom Friends'. This has attracted individuals with experience of early adversity. Known as its Friends group, it is supporting the programme in applications for grants as well as being consulted on the direction and priorities of research.

'Not Just a Missing Number' (N-Jam)
This is a programme of work focused on increased research participation in dementia and cognition research by LGBTQIA+ communities, specifically Trans communities. These groups often describe themselves as isolated from mental health and neurodegenerative research because there is a lack of gender categorisation. Additionally, the 'shaping' of appropriate questions can imply a sense of exclusion. The aim of N-Jam is to create a longitudinal cohort informed by these communities to achieve more inclusive and all-embracing questions.

How DPUK is powering international dementia research

DPUK has evolved from a national initiative into a global leader in data-driven dementia research. Its advanced Data Portal is accessible worldwide. Researchers can securely explore high-quality cohort data and collaborate internationally. This growth is rooted in strong UK foundations but now extends to partnerships across North America, Europe, Asia, and Australasia. In this conversation, **Professor Sarah Bauermeister** explains how DPUK's infrastructure and global connections are transforming dementia science.

What makes DPUK such a strong facilitator of international collaboration?
DPUK's appeal stems from a richness and diversity of data, mature data management solutions for discovery, and secure systems for global access. With multi-modal data from >100 datasets and community-specific hubs, DPUK provides a uniquely wide range of scientific opportunity. This is of particular value to early career researchers who have limited access to high-quality data.

What makes DPUK's Data Portal distinctive?
One of DPUK's distinctives is how researchers interact with the platform. By bringing researchers to the data, DPUK provides a secure environment which gives data owners confidence that their data will be used responsibly and ethically. Our ontology expertise and pre-processing pipelines provide research-ready data which are accessible by experts and generalists alike. By providing generic analytic tools such as SAS, R, SPSS, STATA and Jupyter notebooks, as well as bespoke specialist software, we give >1300 users in 43 countries confidence that they can be at the scientific cutting-edge. The Data Portal is also flexible, using our research hubs to give scientific communities their own online identity and research space. This enables consortia to generate competitive proposals with low-cost, low-risk, but high-end informatics. the Data Portal is a research engine, rather than merely a data repository.

How has DPUK pioneered interoperability between platforms?
DPUK is a global leader in data federation. Through a partnership with the Alzheimer's Disease Data Initiative (ADDI), and using software developed with SeRP in Swansea, researchers can now view and apply for data across ADDI and DPUK. To improve data discovery across platforms we are harmonising a core variable set optimised for dementia. To expand this capability, DPUK is building automated data-curation pipelines based on a standard data model developed at Oxford. Automation will streamline dataset standardisation, accelerate federation work, and broaden global research participation.

What about DPUK's other international work?
DPUK believes federation is the future as it addresses complex issues around governance and sovereignty. We are piloting federation with partners in Australia, including the University of New South Wales and Dementia Platform Australia. By testing hypotheses across datasets like the Sydney Memory and Ageing Study and ELSA UK, the collaboration aims to validate a federation model that can be widely adopted.

In South Korea, DPUK works with the Korean Brain Research Institute (KBRI) and Yonsei University. The intention is to link pre-clinical and clinical data within a secure hub, enabling novel translation that bridges animal and human studies.

Central to efficient federation are synthetic data and AI. For training and code testing, DPUK has synthetic data at varying levels of fidelity, and is AI ready to maintain the security and confidentiality of our data systems. In Canada we are working closely with the Ontario Brain Institute to develop safe federated learning models.

More widely, DPUK embodies collaborative science — breaking down silos, connecting global partners, and doing the heavy-lifting so that research becomes more effective and efficient globally. Public benefit is emphasised at every stage. It is a commitment that has earned global respect and led to participation in the International Hundred Cohorts (IHC) initiative.

CASE STUDY

Open collaboration with DPUK

International collaboration has never been more important to dementia research than it is today. **Professor Martin Hoffmann-Apitius** is adept at bringing together individuals, wherever they are, to build effective research teams. The overriding motivation is to create collaborative partnerships, capable of delivering the highest quality research.

Here, Martin summarises how his COMMUTE study is using DPUK's research strengths in the team to investigate the consequences of the COVID pandemic on the risk of individuals developing neurodegenerative diseases.

COMMUTE is a European collaborative project which relies on the strength of its international collaborations to integrate individual expertise within and across the neurodegenerative disease data landscape. The project brings together an impressive consortium that combines data-driven approaches with the expertise of experimental research laboratories from both clinical research and biotechnology backgrounds. This unique infrastructure allows us to test and validate associations and patterns beyond a single mono-cultural specialism and towards a multi-disciplinary approach which transcends borders.

Key to the data-driven approaches in COMMUTE are our international "data custodians", including DPUK. These are partners that have access to relevant data and the permission to use them. In COMMUTE, we bring together leading data custodians across Europe with a broad spectrum of population data, observational study data, clinical study data and real-world-data.

DPUK is one of the key partners in COMMUTE with access to a wide spectrum of population and clinical data resources readily used in the secure research environment developed and maintained by DPUK.

Joint preparatory work between the teams at Fraunhofer Institute for Algorithms and Scientific Computing (SCAI) and the team at Oxford University paves the way for building effective partnerships delivering high quality research with integrated international data resources.

For example, with the focus of DPUK on the consequences of psycho-social interventions (so-called non-pharmaceutical interventions, NPIs; lock-downs and social deprivation are examples for this), we are able to address an increasingly important aspects of the pandemic: the effects of measures taken to prevent further spreading of the virus and the consequences of psychological stress on the dementia risk.

AI-Mind & European partners: accelerating trustworthy, cross-border data use for dementia research

Professor Ira Haraldsen of Oslo University, Principal Investigator for AI-Mind, emphasises that international collaboration is essential for accelerating progress in dementia research. Through partnership with DPUK, she believes it is possible to advance more quickly from data to trustworthy AI tools and ultimately to real-world clinical trials. Together, EU infrastructures and DPUK's translation engine create value while maintaining high levels of data protection for research participants.

AI-Mind is a European consortium developing AI-enabled tools to analyse brain connectivity and estimate dementia risk among people with mild cognitive impairment. The network brings together university hospitals, clinical neuroscientists, data scientists and businesses across Europe to translate electrophysiology, digital cognitive testing, blood biomarkers and imaging into usable clinical insights. This type of work is increasingly important as the landscape for international data access and trial delivery evolves rapidly.

Within DPUK, the growing emphasis on translating research at both pace and scale means accelerating secure data access via trusted research environments (TREs) and guiding the responsible use of AI. Ensuring standards-based, privacy-preserving data exchange within Europe has become even more critical for scientific resilience and sovereignty, including maintaining strong UK–EU collaboration through interoperable platforms and aligned safeguards.

Several developments are enabling this kind of cross-border research. AI-Mind is adopting an approach that complements DPUK's TRE by integrating with EBRAINS, a European research platform for modelling and simulating the human brain. This enables the harmonisation of clinical data without physical data movement, allowing researchers to share model-based representations of brain function through General Data Protection Regulation (GDPR) -compliant infrastructures. The result is a "GDPR-by-design" approach that keeps participant data protected while enabling discovery, analysis and simulation across borders.

AI-Mind is also developing methodological bridges with DPUK for EEG/MEG and blood-biomarker pipelines. These align with DPUK's focus on scalable biomarkers, cohort interoperability and responsible AI model stewardship. By adopting shared data models and governance patterns, the consortium accelerates safe data reuse and secondary analyses. In parallel, AI-Mind is implementing trust and risk-mitigation practices aligned with DPUK's AI-risk framework, including documenting potential attack surfaces, strengthening privacy-preserving workflows through federation and synthetic data evaluation, and establishing robust model-auditing procedures.

During the past 12 months, AI-Mind has streamlined multi-site data harmonisation with EU partners, enabling prospective validation of EEG-connectivity risk indices and blood biomarker panels for both triage and pre-screening in clinical trials. Cross-platform discovery processes have been designed to support reproducibility and regulatory traceability, using privacy-respecting analytics to generate measurable outcomes in neurophysiology and patient health.

Looking ahead, the consortium plans to pilot EU–UK interoperability by aligning a small set of de-identified cohorts across DPUK's Data Portal and EU nodes (AI-Mind–EBRAINS). This will test end-to-end discoverability, access brokering and reproducible AI workflows for dementia risk stratification, supported by shared metadata and audit trails.

The long-term aim is to achieve biomarker translation at scale, extending joint evaluation of blood-based, imaging and neurophysiology markers within TREs. This supports the UK Dementia Goals programme's focus on scalable diagnostics and more efficient trial recruitment. AI-Mind also seeks to establish governance exemplars that can be used across other disease areas, providing a practical blueprint for international research governance—including consent mapping, DPIA alignment and model-risk documentation.

DPUK leading experimental medicine for dementia in vital areas of research

Associate Director **Professor James Rowe** leads the Experimental Medicine Incubator theme at DPUK. Here, he considers how Experimental Medicine is making an impact in translating early research into clinical therapeutics for dementia.

The Experimental Medicine (EM) programme was established to bring together academic and industry partners to de-risk clinical trials – to make trials shorter and cheaper to know which drugs to prioritise for investment and which to set aside. The focus of EM is very much on human studies. This is because the move from animal research to clinical trials sees a severe reduction in the likely success of a drug, and a rapid rise in costs. This creates a "valley of death" for many aspiring drugs, even those that might work if used for the right patients in the right way.

Several things are needed to reduce the risks of trials, over and above a good drug. We need certainty on who is to take part, with the right diagnosis. This calls for good diagnostic biomarkers. We need to know how to show the drug is working, with biomarkers that prove target engagement in the brain, improvement in brain function, and slowing biological measures of disease. Only when that is achieved, is it realistic to take a drug forward to the cost, time and effort of clinical efficacy trials.

EM aims to improve the successes and lessons learned from early-phase human studies. Success can mean a better understanding of human disease mechanisms, validating preclinical concepts or demonstrating critical mechanisms for human disease. Success also means the proof of concept for a drug, with positive signs that increase the likelihood of success in a later phase trial.

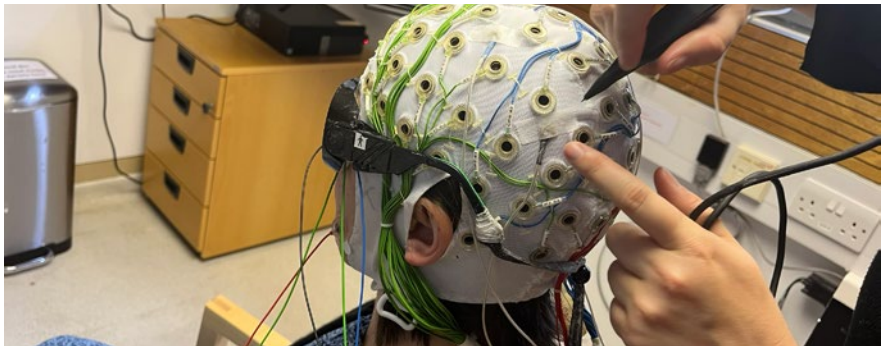
So, EM studies are not merely trials, they are experiments. We use EM to test specific hypotheses about the mechanism of action of a drug in people and/or the importance of a given target for disease onset and progression. EM can also be used to develop new biomarkers, and validate new technologies that shed light in mechanisms needed for later efficacy trials.

The DPUK team has led many EM studies, in Alzheimer's disease, mild cognitive impairment, Dementia with Lewy Bodies, and Vascular Dementia. Our Synaptic Health studies NTAD and SHINE tested new ways to measure how Alzheimer's disease affects synapses and the impact this has on cognition. We showed that magnetoencephalography scanning is sensitive to the presence, stage and progression of Alzheimer's. And it reveals the impact of Alzheimer's disease on specific layers of the cortex, and specific neurotransmitters. PET scans with a special 'dye', have shown that dementias reduce the number of synapse connections in the brain, even when the brain cells are still alive. In DPUK's IMPACT and IMPRINT studies, the Neuroimmunology team has used a different 'dye' with PET scans, to measure brain inflammation, and tested whether simpler cheaper blood tests can detect the inflammation.

The Neuroimmunology team has also investigated the genetic risks of brain inflammation, as a way in to identify and treat new targets to reduce the risk and rates of dementia. Our Vascular Health team has taken a complementary approach, using the "big data" of UK Biobank and the R4VaD post-stroke observational trial, to understand how vascular brain injury leads to cognitive change. They have shown that some common medications have a beneficial "side effect" to reduce the risk of dementia.

Working with the DPUK Trial Delivery Framework, the EM teams at DPUK are now working on the READOUT study (for *REAl World Dementia OUTcomes*), to find blood tests that diagnose and predict different types of dementia among people of all different backgrounds.

Successful EM requires collaboration, with Universities, Memory Clinics, Pharma and Biotech companies, and above all the support from patients and families. We are very grateful for the commitment from all those who have taken part, to accelerate the development of new treatments for dementia.



Training

Our DPUK Training Programme is continuing to nurture and inspire the next generation of cohort data analysts. It is a vital aspect of our programme, particularly as the complexity of data-based dementia research continues to increase. To date, more than 300 people have undertaken training with us since we first began.

Training the dementia data analysts of tomorrow involves inducting researchers new to data analysis, as well as enhancing the skill and expertise of existing researchers.

All DPUK courses are affordable and online, making it easy for widespread participation. This opens the opportunities to anyone, particularly internationally, and supports equality of opportunity globally.

Participants on each course experience working with cohort data, providing them with skills needed to work on complex and multimodal data. The emphasis in all 3 courses is on working with longitudinal, largescale datasets.

All events run over 5-days in either Spring, Summer or Autumn. Each provides teaching and informative lectures.

The Elementary Academy

Presented in conjunction with the University of Edinburgh, this is a 5-day course for researchers new to cohort data analysis. The teaching is focused on essential skills for statistical work and analysis for researchers. It is for both people new to the field and *and* those wanting to refresh their core skills.

The Advanced Academy

For more experienced data analysts, this is a 5-day online event. Participants get an in-depth insight into cohort analysis techniques including linear/logistic regression, machine learning, survival analysis, and latent growth curve models. The course features expert tutors and group working.

Datathon

This is a flagship event, popular with people already working in some way with data. Researchers join multidisciplinary teams to generate valuable new findings in dementia research using datasets in the DPUK Data Portal and retain access to the data afterwards to generate valuable findings and even published research.

THE TUTOR:
"One of the great things about tutoring as part of the 'hands-on' approach at the Data Academies is the progress people make in a short time. They are transformed from being new to data research into very capable researchers".

THE PARTICIPANT:
"The best parts of the data academy were 1) learning techniques and practicing them straight away with real-life relevant dementia data, and 2) learning alongside peers in similar career stages. It was also a great opportunity to form collaborations with others".

Maria Bunyan

Acknowledgements

DPUK is grateful to all its partners and collaborative organisations as well as many individuals offering their support for our work. We need them all to realise our goal of enabling vital breakthroughs in dementia research and benefit from the endeavours of experts drawn from many fields working towards this goal. All of them make significant contributions, here in the UK and globally.

In particular, we want to thank our research project and network leads, together with those helping to oversee the governance and scientific direction of DPUK.

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Professor John Gallacher (Director)
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Professor Simon Thompson

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Natasha Jardine (Programme Manager for Neurological Disorders)

SCIENTIFIC PROJECT LEADS

Professor Simon Thompson leads the Data Portal workstream

Professor Simon Thompson leads Work Package 21: Data Portal enhancements

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

Professor Sarah Bauermeister leads Data Curation programme

Professor Vanessa Raymont leads the Trials Delivery Framework workstream

Dr Ivan Koychev leads Work Package 23a: Clinical Studies Register

Dr Ivan Koychev leads Work Package 23b: Great Minds

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

Professor James Rowe leads the Experimental Medicine Incubator workstream

Professor Atticus Hainsworth leads the Vascular Health theme

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

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

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

Professor James Rowe leads the Synaptic Health theme

Professor James Rowe leads the Work Package 26a: Synaptic loss and its functional consequences in early Alzheimer's disease, using pre-synaptic markers and magnetoencephalography

Professor James Rowe leads the Work Package 26b: Synaptic loss and its functional consequences in early Alzheimer's disease, using a new postsynaptic TARP γ8 AMPAR ligand

Professor John O'Brien leads the Neuroimmunology theme

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

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

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

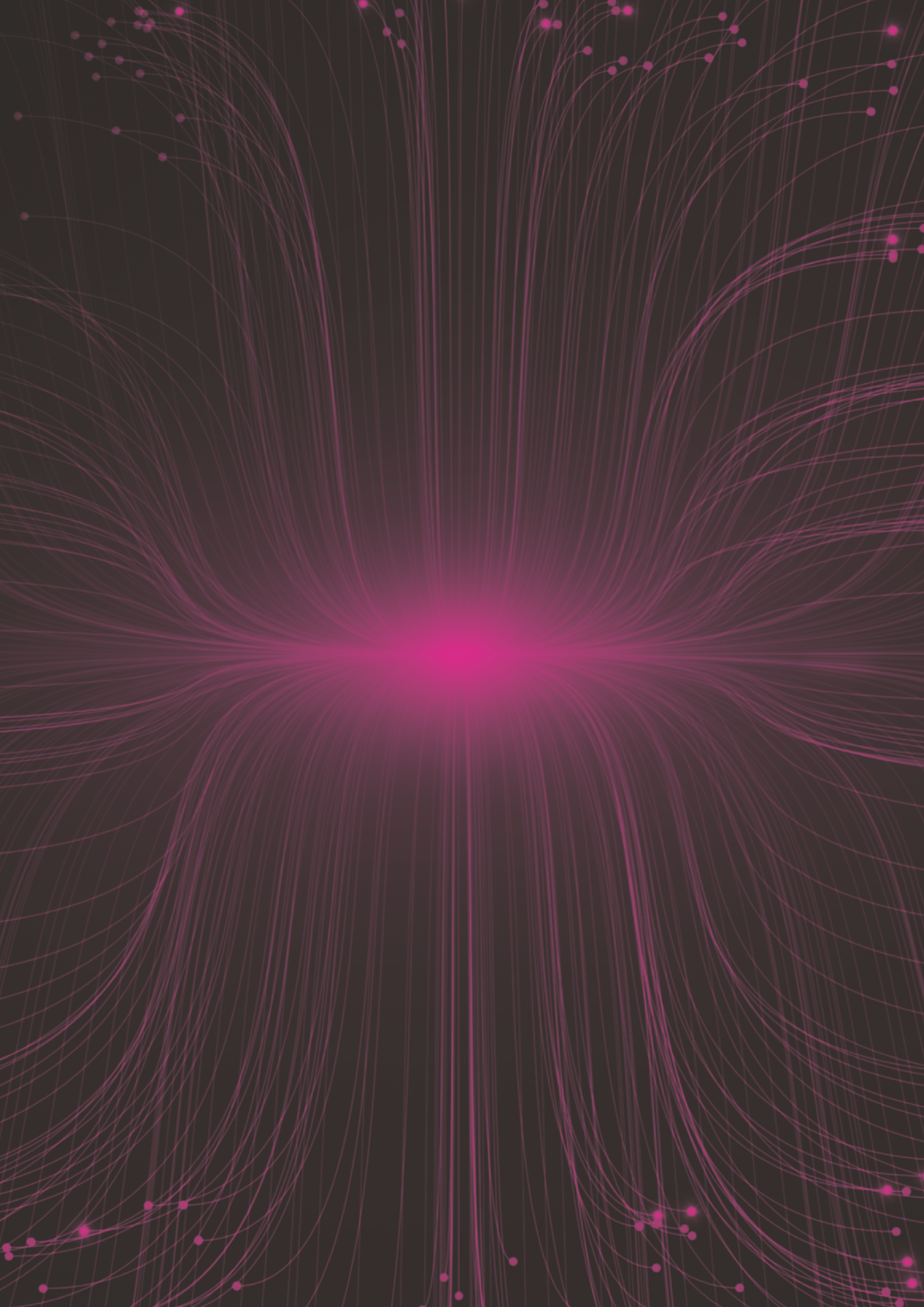
Professor Vanessa Raymont leads the Deep and Frequent Phenotyping study workstream

Professor Richard Wade-Martins leads the Stem Cell Network

Dr Pawel Markiewicz leads the Imaging Network

Professor Sarah Bauermeister leads the data analyst training programme

Our partners



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