Investing in clinical trials infrastructure for dementia: a network approach

Our vision of a network for dementia clinical trials

A growing treatment pipeline in Alzheimer’s and dementia, combined with recent regulatory approvals in the USA, means that dementia research will likely see growing investment from the life sciences industry over the next few years. The UK, with its traditional leadership in both dementia and clinical research, has the potential to benefit from this new wave of investment. Even more importantly, it could mean that people living with dementia in the UK are among the first to benefit from new treatments. However, the last five years have seen a decline in both the number of trials being initiated in the UK and in the number of patients recruited into trials across disease areas, putting us at risk of falling behind our global competitors. This is compounded by long-standing challenges in dementia clinical research, not least in identifying eligible candidates for trials. Alzheimer’s Research UK is recommending a number of actions to realise the UK’s full potential in this space.

We believe the recently launched Dementia Mission should work with industry and the National Institute for Health and Care Research (NIHR) to map out and pump-prime potential trial site capacity and seek to future-proof our clinical trials infrastructure. To support this, Alzheimer’s Research UK has proposed that the UK develop a network of high-performing clinical trial sites to drive increased speed and scale in clinical trials. We are pleased therefore that work is now ongoing, led by NIHR, to build on the Dementia Translational Research Collaborative (D-TRC) of Biomedical Research Centres, which will form the basis for this. We believe it is vital that the new chair of the D-TRC works in close collaboration with the Dame Barbara Windsor Dementia Mission to deliver on the potential of the network.

In this document, we set out the key issues, and Alzheimer’s Research UK’s view on the main requirements and objectives of a clinical trials network for dementia.

The need

There are currently over 4,000 dementia clinical trials registered, of which, only 7% are taking place in the UK and just over 50 of these are actively recruiting\(^1\). The UK is falling behind, averaging only a 3.6% share of global clinical trials in all disease areas in 2020, a decline from 6.8% in 2015\(^2\). For Phase II and III trials the UK ranks fifth globally\(^3\) and has the highest percentage of missing enrolment targets (13.7%)\(^4\). The benefits of hosting clinical trials are convincing - in 2019, the total estimated income for the NHS from delivering commercial clinical trials across all disease areas was £355 million, and an estimated 47,500 jobs were generated\(^5\). There are also clear benefits to patients in taking part in clinical trials, including access to otherwise unavailable drugs, a more bespoke package of care and monitoring, and a higher level of autonomy over their treatment.

Dementia research has specific and complex challenges, particularly around screening and recruitment. There is a distinct lack of clear diagnosis in the early stages of Alzheimer’s disease progression and diagnostic tests are in high demand. Recruitment of patients for research is often not a priority in clinics that are facing a rising demand for care. Furthermore, lengthy study set-up times and bureaucratic procedures mean that many identified, screened, and eligible patients become ineligible to take part by the time studies are able to start.

Nearly a million people are living with dementia in the UK, but only 2% of those with a diagnosis are registered to hear about dementia clinical trials\(^6\), and far fewer than this will end up taking part. In 2021/22, just 61 patients were recruited to late-stage dementia drug trials supported by the NIHR
Clinical Research Network, 100 times fewer than for cancer drug trials and 10 times fewer than for stroke or coronary heart disease. Dementia patients in the UK are not offered enough opportunities to take part in research and clinical trials, both in comparison to other health conditions and to other countries. Patients who are not engaged with research miss out on the opportunity to receive a higher standard of tailored healthcare. Those who are involved can make a valuable contribution to the development of life-changing treatments that will ultimately change the outlook of those diagnosed with dementia in the future. Alzheimer’s Research UK’s survey found that 69% of people would consider taking part in medical research for dementia. A US study found that 77% of patients with dementia would be “very likely” to participate in an approved clinical trial, as would 56% of those with mild cognitive impairment (MCI) and 32% of people without cognitive deterioration.

The focus of the network

There will no doubt be a number of models which could be applied to form the basis of a network. We set out thoughts on this below, however, what is crucially important to deliver success is that the new network has the right leadership, focus and objectives.

The overarching goal and primary key performance indicator (KPI) of the clinical trials network must be to support greater industry investment in the UK, to increase the percentage of trials with sites in the UK and the number of UK patients enrolled into international trials - goals which align with the objectives of the Dementia Mission. Clear, measurable KPIs are needed, which are ambitious but grounded in a realistic sense of what is deliverable and employ an approach that can be developed over time with industry and other stakeholders.

Five key tests

1. **Speed** – the network will need to focus on how study set-up can be accelerated. The network should feature a model that is aligned around ethical approval and contracting, which can enable faster set-up.

2. **Finding eligible participants** – the focus should be on agreeing on a minimum clinical data set across the network and sharing this data so that there is a better understanding of the location of patients, allowing them to be moved into screening quickly and efficiently.

3. **A federated model** – a central “hub” which will offer support and best practice sharing but not seek to standardise or create unnecessary bureaucracy. The network would need to agree on key themes for collaboration and best practices - including supporting diverse participation across dementia clinical research.

4. **An inclusive network** – that should look to support a range of sites, both geographically and in their research activities, from leading well-established research centres to those that are less active but looking to increase their activity and build greater capacity. The right governance structures will need to be put in place to enable this.

5. **Aligned with wider activity in this space** – crucially with the wider Dementia Mission, but the network will also need to work closely with other relevant initiatives both in the UK (e.g., Dementia Platform UK’s Trial Delivery Network and Brain Health Clinics) and globally (e.g., Global Alzheimer’s Platform Foundation trial sites).
Outcomes checklist

- Increase the UK’s global share of clinical trials in dementia.
- Increase the number of industry-led clinical trials in the UK.
- Attract more industry partners to the UK.
- Reduce screen rate failure.
- Share clinical skills and infrastructure across sites to support wider geographical reach.
- Develop a faster approach to the set-up time, focusing on commonly approved protocols and making further changes through amendments.
- Work collectively with other established initiatives to speed up the development of early-stage research into clinical trials.
- Increase the diversity of participants involved in dementia research through improving engagement with primary care and outreach to underrepresented communities.
- Enable creative and innovative approaches to clinical trial design and delivery.

Learning from and building on existing initiatives

Several other initiatives have been set up for dementia and other health conditions to achieve coordinated support for new treatments and clinical trials. Future projects must learn from the successes and downfalls of previous initiatives and continue to build on the available infrastructure.

As well as learning from these initiatives, the new network should seek to work closely with industry partners and other initiatives, including the DAVOS Alzheimer’s Collaborative, the Global Alzheimer’s Platform, the Alzheimer’s Disease Data Initiative, the World Dementia Council and the World Health Organisation.

Setting clinical targets

Identification of suitable patients for dementia trials is one of the major barriers to successful trials in the UK currently. The Trial Discovery Framework (TDF)\textsuperscript{12} and European Prevention of Alzheimer’s Dementia (EPAD)\textsuperscript{13} have both independently put efforts into setting up phenotyped, trial-ready cohorts of patients at different stages of dementia progression and have found that this has not been a viable solution to the recruitment issues faced by clinical trials. Dementia cohorts are difficult and costly to maintain due to the slow set-up of trials, and, as mentioned earlier, many patients become ineligible for studies before they can be offered a position in a trial. An alternative proposal would be for the network to implement a minimum clinical data set and agree to share data to enable faster and more efficient screening when trials begin recruitment.

Trial finder for clinicians

Clinical time with patients is increasingly limited and pressured, particularly since the backlog created by COVID-19. In addition to this, it is difficult for clinicians to have oversight of what trials are currently recruiting, and which would be suitable for their patients. The Experimental Cancer Medicines Centre (ECMC)\textsuperscript{14} have developed the Experimental Cancer Trial Finder Database\textsuperscript{15}, a free, easy, and fast method for clinical staff to identify trials for their patients. The benefits of the database were piloted and showed a 55% increase in the feasibility of matching patients to trials over six months, and particular benefits were mentioned in recruitment for more complicated trials.

The Trial Finder was originally piloted by 200 NHS users before being rolled out to leads and coordinators. The tool is now available to all NHS staff, and further information about it is published
through Cancer Research UK. The network should explore the potential for a similar approach for dementia clinical trials, working alongside patient databases such as Join Dementia Research.

**Evolving trial-ready sites**

The Clinical Research Network (CRN) is a group of 15 local networks and 30 specialities across England, with dementias and neurodegeneration being one of the specialities. The network should look to work with these established resources, rather than replacing or replicating them. Utilising sites which are set up to deliver earlier phase trials, particularly phase II, and establishing a pipeline to develop them into delivering phase III and IV trials is a more sustainable approach than trying to establish a large number of late-stage trial-ready sites early on.

**Leadership and governance**

The network needs to have strong representative leadership that is responsible for oversight, join-up and inclusion. Within this, the central leadership should look to align the sites to achieve agreed KPIs, without over-regulating or putting unnecessary governance structures in place. The aim of the network should be on innovation and fluidity, allowing sites and site managers to be creative about solutions and practices that will lead to the KPIs and endpoints.

**Workforce needs and benefits**

The network should seek to invest in the entire workforce required for trial completion, without only emphasising clinical and research roles. “Frontline” staff, including data managers and trial practitioners, are integral to the delivery of clinical research, particularly for non-commercial studies, as well as research nurses who provide the vital link between study delivery and patient care. There should be clear plans set out for how the network will support skill development and staff retention.

Additional benefits for the workforce include the sharing of best practices, knowledge and specialist skills and increased collaboration, achieved through better join-up of sites. Through the creation of a network, there will be less risk of study duplication and better infrastructure for researchers to share results and data. Clinicians with less research involvement will benefit from the increased use and availability of diagnostic tools from site join-up and from having more support and skills for interpreting molecular data and neuroimaging scans from increased collaboration.

**Streamline administrative procedures**

For the UK to be in the best position to attract industry partners and further our international reach the network should ensure that the bureaucratic measures that currently hinder and slow dementia clinical trials are kept to an absolute minimum going forward. There needs to be a careful balance between what is needed for the proposal while allowing for innovation and new approaches.

**Memorable terminology**

Consistency in the use of terminology around the network will significantly impact memorability and the ease with which clinicians and researchers refer to it in their daily language. We feel that the current title and acronym of the network (D-TRC-DN) are too lengthy and complicated. We propose simplifying the title of the network to “Dementia Clinical Trials Network” to increase memorability and ease of reference.
Conclusion

A clinical trials network for dementia has huge potential to dramatically change the landscape for dementia research. The network’s main goals and deliverables should be aligned with the suggestions set out in this document and coordinated with the Dementia Mission. The UK will then be in a unique position to make real headway towards finding life-changing treatments for people living with dementia and raising the UK’s profile in clinical research on the global stage.

Our suggestions above are ones we believe could work and that will help to ensure the success of a future network. However, we are not fixed on a particular structure or model, instead, we are driven by the outcomes, focus and leadership of the chosen approach, aspects which will determine the overall success of the initiative.

Further considerations

We recognise that more work will be required to help establish the network. Below are some further key considerations:

- What will be the overarching aims and KPIs of the network? Are they both ambitious and deliverable?
- How will we best organise the structures?
- How will the central leadership balance aligning site goals while allowing for flexibility and innovation?
- How many sites will be engaged with for the roll-out of the network? Will there be a range of sites, from well-established sites to those that wish to build on their research engagement? How will more established sites be encouraged to support others?
- How can we ensure join-up with previously established initiatives?
- What else can we learn and build on from previous initiatives?
- What should the minimum clinical dataset consist of? How will clinicians have access to it?
- Will the network consider implementing a “Trial Finder” approach to aid clinicians in identifying trials for patients?
- What approaches will we take to increase diversity in trial participation?

References

1. Clinical Trials (NIHR)
2. UK share of global clinical trial activity in 2020 (Clinical Trials Arena)
3. An opportunity for growth: Clinical research in the UK (ABPI)
4. UK clinical trials: the data behind a slow post-pandemic recovery (Clinical Trials Arena)
5. National Institute for Health Research - clinical research benefits the UK economy (NIHR)
6. Updates from Join Dementia Research (NIHR)
7. Clinical Research Network (NIHR)
8. Parliamentary question for DHSC on clinical trial recruitment
9. Embedding a research culture (NIHR)
10. Dementia Attitudes Monitor (Alzheimer’s Research UK)
11. Attitudes towards clinical trials across the Alzheimer’s disease spectrum
12. Trials Delivery Framework — (DPUK)
14. Experimental Cancers Medicines Centre (ECMC)
15. Experimental Cancers Trial Finder (ECMC)
16. Join Dementia Research - register your interest in dementia research (NIHR)