COLLECTIVE INTELLIGENCE

Managing Alzheimer's Therapy Expectations: A View from the Lab

Interview with incoming Director of the UK Dementia Research Institute Professor Siddharthan Chandran

Ben Hirschler
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New disease-modifying drugs that target sticky amyloid plaques in the brain have been hailed as a turning-point in treating Alzheimer's. Yet important questions remain over access, identifying those patients who will benefit, developing improved healthcare infrastructure and monitoring potentially dangerous side effects.

Finding the right balance in communicating today's advances presents a major challenge for biopharmaceutical companies and healthcare providers as they seek to manage the expectations of a wide range of stakeholders – from patients, carers and healthcare professionals to investors, regulators and payers.

The task starts with setting clear parameters for what has been achieved and what remains to be done. As clinician-scientist and incoming Director of the UK Dementia Research Institute Siddharthan Chandran explains to Brunswick's Ben Hirschler, three central messages shine through:

1. **The latest drugs are pathfinders, not the endgame.**
2. **Simpler and earlier diagnosis is urgently needed.**
3. **Integrated research and patient data are key to better care.**

Where are we on the road to treating Alzheimer's disease, given the trial success of the anti-amyloid drugs donanemab and lecanemab?

What the lecanemab and donanemab studies do for the first time is unequivocally demonstrate that the problem of the diseased aging brain and Alzheimer's is tractable. That's the key.

This is the beginning of something important and it will come to be seen, I think, as a watershed moment over the next decade. It is a tipping point because it shows that if you identify the right people at the

right stage, you can not only reduce brain amyloid plaque but also have some measurable functional benefit at the level of the individual.

It shows what is possible even in the brain, which has long been considered a graveyard for pharmaceutical discovery.

There's an analogy here with multiple sclerosis, which used to be managed symptomatically until beta-interferons came along, opening up a raft of investment. Today, there are many licensed multibillion-dollar drugs for MS and the outlook for newly diagnosed patients in 2023 is like night and day compared to 2000.

Amyloid therapies appear only modestly effective, slowing cognitive decline by around 30 percent. How do you interpret this level of efficacy?

The challenge is to manage expectations. We've seen a hugely important development in the field, but there is more to do. The latest drugs are the beginning of something rather than the summit. Pharma companies will now rush into this field because they can see it's tractable – and there is going to be a vast market for anyone who can identify effective treatments.

But Alzheimer's is a complex disease. It's not only about amyloid. It's also about other stuff, so I think treatments will be additive. Other diseases show the way on this, whether it is cancer or HIV or TB, all of which are treated with combinations of drugs.

There are also practical issues about identifying the right people for treatment and having a healthcare infrastructure that can do that, as well as delivering treatment safely and monitoring people for side effects, such as inflammation or bleeding in the brain. Currently, you need either PET (positron emission tomography) scans or lumbar punctures, and offering that at a population level is going to be a struggle.

What are the prospects for more effective and earlier diagnosis?

We need diagnostics and biomarkers that are scalable and cost-effective. You need to be able to identify dementia in people when it emerges and identify people at high risk. Blood tests are the obvious way to go. We already have simple cholesterol tests for assessing risk of heart disease, and we want the same thing for dementia.

In the future, I believe, there will be a predictive algorithm based on a blood test that measures brain health and genetic risks, together with a set of simple cognitive evaluations that you can do on an app on your phone. The result will be an aggregate score that will guide an individual's treatment plan, which will probably be a mix of lifestyle advice and drugs.

How will perceptions of dementia change with the rollout of new drugs?

Scientific advances are going to radically change perceptions around dementia. I think it will gradually become destigmatized. Whereas before people may have said there's no point seeing a doctor or a neurologist because there is nothing that can be done, that idea will start to change.

These things take time to land but it will happen. If a proportion of people with dementia can live better and more independent lives for even one, two or three years, then I challenge anyone to tell them or

their loved ones that treatment is not for them. It's not a question of affordability; it is about a nation's priorities.

What role can the UK play in the dementia fight?

There is amazing research in many parts of the world. What makes the UK stand out is the totality of the offering, in terms of the integration of world-class research with world-class NHS (National Health Service) data assets.

That was demonstrated in the COVID-19 pandemic, where Britain led the way in the RECOVERY trial by using the NHS patient infrastructure to gain crucial insights into which treatments worked. Now we have the same opportunity to lead the way for a different sort of pandemic – called dementia – by doing population-level screening to identify those people at higher risk, who then become a trial-ready cohort for clinical studies.

If the UK wants to remain in what you can think of as the peloton of dementia research, we need sustained investment at a decent level. This is a bet that the UK should take because it will pay off handsomely, both in terms of generating jobs, retaining talent and growing the economy, as well as doing the right thing.

Professor Chandran will take over on October 1 as the new Director of the UK Dementia Research Institute, the UK's leading biomedical institute dedicated to better understanding the underlying causes of neurodegenerative disease and changing the lives of the millions affected by dementia. He is Dean of Clinical Medicine, Director of Edinburgh Neuroscience, the Euan MacDonald Centre for Motor Neuron Disease Research and the Anne Rowling Regenerative Neurology Clinic at the University of Edinburgh.

To continue the conversation

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