Improving time to dementia diagnosis through new insights from big data

Dementia is the leading cause of death in the UK

Today, there are over 8.7 million people living with dementia across Europe[1]. With an ageing population and no effective treatments, this number is set to rise to 152 million globally by 2050, highlighting the huge unmet need of this condition. In the UK, the health and social care costs of dementia are more than cancer and coronary heart disease combined. The sheer number of people living with dementia and the associated health and social care costs make dementia one of the greatest medical challenges of our time.

Emerging potential of big data in healthcare

In healthcare, decisions on patient treatment and care are made based on several pieces of information, whether that be based on clinical examinations, blood test or scans. However, as we get more and more data about an individual from genetic information, scans to patient records and the literature, we need new ways to organise and derive insights across these many diverse pieces of information. This is where machine learning and algorithms are needed to 'crunch' the data and reveal new insights. Moreover, when these algorithms are tested across thousands of people, we can start to move from a healthcare where 'one-size-fits-all', towards a system of predictive, preventive, and precision care.

Paving the way for personalised medicine approaches

The diseases that cause dementia, such as Alzheimer's, present an key example of the need for a precise, person-specific approach, by virtue of the fact that its biology and pathophysiology is so varied and so subject to the influence of different factors, including but not limited to those associated with comorbidity, lifestyle, and genetics.

iASiS (Integration and analysis of heterogeneous big data for precision medicine) is a European-funded research project that seeks to pave the way for precision medicine approaches by utilising insights from patient and open data. It has combined information from medical records, imaging databases and genomics data to facilitate a personalised approach for diagnosis of the diseases that cause dementia, as well as diagnostic and treatment approaches in lung cancer.

We have developed a novel knowledge-driven framework that uses knowledge graphs and machine learning to understand and predict patterns within these diverse datasets. Moreover, it has utilised advances in Artificial Intelligence (AI) to not only understand and predict patterns between these diverse data sets, but also to provide a context and rationale around each of the discoveries and contributory factors within the knowledge graph. Collectively, this approach is giving us a more holistic characterisation of lung cancer and dementia.

The method of clinical assessment by which contributory factors are identified also offers ways of making a range of simple quantitative judgements about a patient's cognitive ability. Not surprisingly, the simplest cognitive assessment tools (e.g. the Mini Mental State Examination) are also the most commonly used, and allow long and short-term memory, attention, orientation, verbal and visuospatial abilities to be individually examined. Given the inherent variability of the underpinning diseases, it is hardly surprising that no single measure or observation has ever proved to be necessary and sufficient for a diagnosis of dementia. Large numbers of datapoints taken from

a large longitudinal cohort, however, has defined ways in which this kind of information can be used to identify not only the presence and absence of dementia at a given assessment but the risks of developing dementia over the following five years with accuracies considerably above chance. The results of these analyses indicate that, along with recent improvements in disease biomarker identification, simple clinical observations remain a central component to the rapid, efficient, accurate and specific diagnosis.

Improving prediction of those who will go onto develop dementia

Earlier diagnosis of the diseases that cause dementia would enable people to start making lifestyle changes, such as a healthy diet and exercise, that could help to maintain their brain health as well as giving them the opportunity to participate in clinical trials, an opportunity which is too often already closed to those diagnosed at a later stage of the disease.

Mild cognitive impairment (MCI) is a term used to describe early memory and thinking problems in older people. It is not a disease in itself. MCI can be caused by a range of conditions, which can make it challenging to identify those people who may go on to develop Alzheimer's disease. Evidence suggests that each year, around one in 10 people with a diagnosis of MCI develop dementia[2,3], although the time this takes to develop dementia can vary from one person to another[2]. Factors such as older age, depression, diabetes,[2] smoking and high blood pressure may increase the likelihood that someone with MCI will go on to develop a form of dementia.

Moreover, the drugs in late stage clinical trials are looking at delaying the progression of the Alzheimer's disease, the most common cause of dementia. Scientific evidence suggests that these are most likely to be effective at the earliest stages of the disease, or when people are experiencing Mild Cognitive Impairment (MCI).

In clinical trials conducted on potential disease-modifying treatments, people are normally tested for one of the hallmark proteins of Alzheimer's disease, amyloid, but there could be other factors that may also indicate progression to Alzheimer's disease. The iASiS model suggests that these may actually be considerably simpler, and ascertainable in the context of a conventional clinical assessment. A combination of age and the presence or absence of comorbid cerebrovascular disease present a high risk of early progression in people with low overall cognitive function, while later progressors are identifiable on the basis of performance in the specific domains of praxis (complex task performance), attention and language production. These findings underline the importance of contextual health-related information, and suggest that predictive accuracy may be improved if the MMSE were to be replaced by a rather more detailed cognitive assessment approach which incorporated tests of language, orientation and praxis.

Enabling an accurate diagnosis

A key focus of the UK government's Challenge on Dementia 2020 has been on improving diagnosis rates and access to a timely diagnosis. Since 2010/11 the diagnosis rate has increased from 42% to 67% in England, but there is still more to do. The recent London Memory Clinic Audit highlighted that people are currently waiting between 4-15 weeks to be seen by a memory clinic[4].

Currently, most people living with dementia are diagnosed when either they or a loved one started to notice changes in their memory, orientation or behaviour, all common symptoms associated with dementia. Because dementia is a progressive condition, the diseases that cause it develop slowly, and unforgivingly, attack people's ability to think, move and communicate over time.

However, as the wealth and breadth of information about patients is increasing with data stemming from medical records, scans, genetic tests as well as all the latest scientific literature, we need to find new ways to integrate all this big data into a form that is useful for clinicians. This has been the focus of the iASiS project, and the approach has revealed the importance of psychiatric comorbidities (anxiety and depression), and the specific cognitive domains of long-term memory, attention and orientation to be the most important clinical pointers

Promoting data sharing

Alongside investment in research, we need to facilitate data sharing from research cohorts and clinical trials among the research community so that we can glean additional insights and make further progress through this data. The complexity of the disease means that data from clinical trials and longitudinal cohorts may help unlock new insights into the disease and new treatments. While protection of this data and appropriate consent must be upheld, the benefits of using this wealth of information to make progress in dementia research cannot be understated. People living with dementia and who have taken part in these research studies have been generous with their time to help advance research, and we owe it to them to ensure that we learn as much as we can from this data to improve the lives of people affected by this condition.

In the coming era of medications potentially being licensed for disease modifying treatments, the heterogeneous data integration approach taken by iASiS and other big data models, will help to ensure that as large as possible a proportion of the right patients are identified and started on the best dose of the right drug at the most appropriate time.

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