increased the risk of stroke far more (66% increase *vs* people with healthy lifestyles) than genetic risk factors did (35% increase *vs* people without high genetic risk).[11]

Cognitive impairment and dementia are arguably the commonest manifestations of cerebrovascular disease. Regardless, vascular disease is still low priority among Alzheimer's disease researchers, even though vascular disease is preventable and treatable, whereas thus far Alzheimer's disease is not. Conversely, cognitive consequences of stroke still do not receive enough research or clinical attention. One factor that might help increase researchers' interest in stroke is that, as of 2018, stroke is no longer classed as a brain disease, but is officially a neurological disease according to WHO; however, arguably, given the diversity and size of its burden, stroke should be in a category of its own.

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Dementia research 2018: current and future population relevance

When asked to select the most important advances in dementia in 2018, as seen through a small number of papers (out of the tens of thousands published), I was presented with a challenge. Dementia research spans a huge range of subject areas, such as ageing, gerontology, developmental research, neuroscience, social science, ethics, law, engineering, architecture, and even environmental research. The academic literature reports on prevention, screening, early detection, treatment of symptoms, and end-of-life care. No one researcher can cover all these territories, and the meaning of best will vary hugely accordingly to an investigator's discipline and overall perspective. Given this complexity, I have chosen to reflect on changing approaches to dementia and have selected papers that use different methodologies and come from different disciplines.


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At present, the dominant approaches in dementia research include data science, imaging, and biomedicine (especially –omics). These approaches are being brought together as powerful methods to understand human disease, with neuroscience at the forefront. Artificial intelligence will be in the background, measuring, analysing, defining, and nudging our lives in directions that might or might not be transparent. Artificial intelligence techniques are being explored to incorporate the neglected area of small vessel disease into more accurate ways of linking brain imaging to clinical states.[1] However, major concerns remain about

the ability of cognitive neuroscience to reduce the human lived experience to data interpreted by artificial intelligence.[2]

The ability to do more detailed investigations has led to the massive expansion and push for early diagnosis. Research into fundamental neurobiological and neuropathological drivers of dementia is reaching earlier and earlier into people's lives, with implications for regular testing of populations for multiple types of risk, decades before dementia onset. This approach requires detailed societal, ethical, and legal considerations alongside that of value to society and evidence on benefit and harm. Such work is rare at present, despite its importance to the dementias and other fields, such as cancer. The long-term implications for society of screening and early diagnosis need to be thoroughly considered.[3]

Primary (upstream) prevention is known to provide more value, over a longer time frame, than secondary (screening and early detection) and tertiary (mitigation once present) prevention. Investment in secondary and tertiary prevention, while having a place, does not provide the same reduction of risk for the whole population. Modelling studies[4] published in 2018, as part of an extensive exercise drawing on the UK's population studies, are beginning to provide robust predictions of future population care needs, including dementia. These reports emphasise the urgent need for rebalanced investments in research on whole populations to reduce risk for dementia, in parallel with biomedical investments.

A policy paper for the National Health Service (NHS) England highlights a move towards a prevention approach, with the aim of extending healthy life expectancy by 5 years.[5] This is an admirable goal, but the means to achieve it are promoted, again, as early detection through technology and biomedical advances, with the assumption of evidence-based interventions. This assumption has profound implications for costs and potential lost opportunities through resource diversion. The balance between different types of prevention needs to be understood for the short, medium, and longer term. Health checks in the UK are now incorporating areas relevant to dementia risk. None of these has been tested in trials, even though national and local systems, and businesses, already have the opportunity to roll out new approaches in an experimental and evaluative manner. Enthusiasm for individually based approaches needs to be contextualised alongside the potential for community and population change. Evidence for these approaches needs to be robust and honest. For example, the HATICE trial[6] tested a coach-supported internet platform for older, at-risk individuals aiming to reduce their cardiovascular risk to change dementia risk profiles. These changing behaviours are needed in the face of continuing trials of pharmacological approaches. Such approaches need to be integrated with future trials of existing and novel agents and physical activity, nutrition, and social engagement interventions.

Another important topic is the recognition that, in many countries, age-for-age dementia has declined over the past two decades, probably reflecting improvements on life-course health. Brain development sets the scene for our whole lifespans. Children continue to be born and grow up without the physical, social, and emotional environments to sustain and optimise their brain development, which remains a global scandal of inequity within and across countries. About 202 million children younger than 5 years were estimated to have stunting or wasting in 2018.[7] Studies that capture the sequelae of these poor childhoods provide evidence of their effect on later life cognition and dementia. Physical measures of body size have repeatedly been found to be associated with these outcomes.[8]

Such evidence confirms the need for major population and life-course approaches to reduce the risk for dementia. In high-income countries, risk reductions have been seen not because of pharmaceuticals, but as the result of whole societal shifts in health. Such broad approaches need to be sustained, rather than reversed, and must include research that supports people with dementia and their families, including at the patient's end of life. The need for a global research agenda in dementia that is rounded and considers the challenges facing humankind, as captured in the Sustainable Development Goals, is urgent—closer to that described in the Alzheimer's Society-led roadmap for dementia research than the limited drive for pharmaceutical discovery.[9]

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The most important advances in headache research in 2018

In 2018, many advances were made in headache research. In my view, one of the major advances was the publication of the third edition of the The International Classification of Headache Disorders (ICHD-3), which includes new diagnostic criteria for migraine with aura that better distinguish it from transient ischaemic attacks.[1] These criteria were previously in the appendix of the ICHD-2 and have now been included in ICHD-3. Patients with aura should now report at least three of the following six characteristics: 1) at least one aura symptom spreads gradually over at least 5 min; 2) two or more aura symptoms occur in succession; 3) each individual aura symptom lasts 5–60 min; 4) at least one aura symptom is unilateral; 5) at least one aura symptom is positive; 6) the aura is accompanied, or followed within 60 min, by headache. The classification of trigeminal neuralgia has also changed: trigeminal neuralgia is now subdivided into classical trigeminal neuralgia (neurovascular compression with morphological changes in the trigeminal root shown by MRI or during surgery) and idiopathic trigeminal neuralgia (no abnormalities by electrophysiological tests or MRI) on the basis of presence of degree of neurovascular contact; trigger factors are now required to establish a diagnosis; the absence of sensory abnormalities is no longer required for diagnosis; and the diagnosis of secondary trigeminal neuralgia (caused by an underlying disease) is now accepted.

Development and introduction of monoclonal antibodies against calcitonin gene-related peptide (CALCA; also known as CGRP) or the CGRP receptor are the most important advances in migraine therapy in decades. Three double-blind, randomised, placebo-controlled phase 3 trials[2-4] reported on the safety and efficacy of this new drug class. One trial assessed 875 patients with episodic migraine who received subcutaneous fremanezumab monthly (225 mg) or quarterly (675 mg), or placebo.[2] The study excluded patients who had previous treatment failure with two classes of anti-migraine medications. Compared with placebo, fremanezumab significantly reduced the mean number of migraine days over 12 weeks by 1·5 days (95% CI 0·93–2·01) with the monthly regimen and 1·3 days (0·72–1·79) with the quarterly regimen.[2] In the EVOLVE-1 trial,[3] 858 patients with episodic migraine received subcutaneous galcanezumab (120 mg or 240 mg) or placebo once per month for 6 months. Both galcanezumab doses significantly reduced monthly migraine days compared with placebo

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