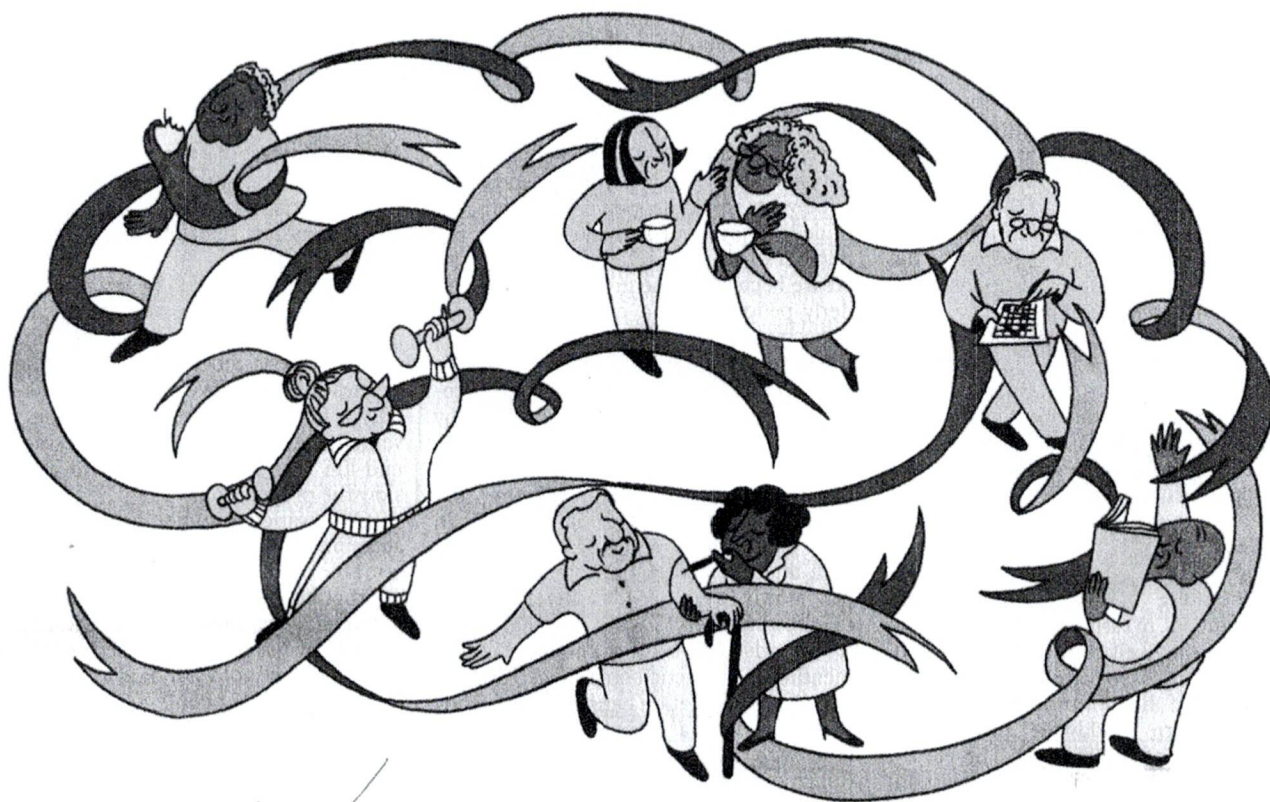


Briefing Dementia



Brain gain

HELSINKI

The world is making heady progress in the fight against dementia

WHEN ERIC STALLARD, an actuary and academic, began looking into the incidence of dementia among elderly Americans, he was so stunned by his findings that he held off publishing his first paper on the subject for two and a half years while he double-checked his work. "I wanted to be absolutely certain," he recalls, since the numbers defied all expectation. Instead of confirming the received wisdom that America faced an intensifying plague of the condition, they showed that the proportion of old people succumbing to it was in fact shrinking fast. "I was shocked by the declines," he says.

Mr Stallard has been working for a decade to corroborate this revelation. His findings have, if anything, become even more striking. Last year he and some colleagues published research in the *Journal of the American Medical Association* showing that, whereas 40 years ago three in every ten Americans aged 85-89 had dementia, by 2024 just one in ten had it (see chart

1 on next page). What is more, America is not the only beneficiary of this trend. Between 1988 and 2015 the share of older people being diagnosed with dementia fell by 13% a decade across six countries in North America and Europe, according to a study of almost 50,000 people by Frank Wolters of the Erasmus Medical Centre in Rotterdam, and colleagues.

Some smaller studies have also found big declines. Data from the Framingham Heart Study, which has tracked three generations in an American town, show an average drop in new dementia cases of 20% per decade over almost 40 years between the late 1970s and early 2010s. Those who were entering their dotage when Daft Punk's "Get Lucky" was topping the charts (2013) were 44% less likely to have dementia than those who were doing so when Sting was urging Roxanne to switch off her red light (1978).

Whereas most earlier studies had simply pooled elderly people and then applied

a statistical adjustment for age, Mr Stallard looked at narrow bands of ages to compare different cohorts of people over 50 years. By examining the changes between each successive cohort, he calculates that dementia rates have been declining by 2.5-3% for each calendar-year cohort. "In my view it was the Copernican revolution in the field," he says, turning assumptions about dementia's spread upside down. Similar cohort studies in various European countries and Japan have found comparable trends there, too.

Making memories

Big questions remain about why dementia rates are falling and whether they will continue to drop. The growing number of old people in most countries and increasing longevity mean that overall case numbers are still rising, even if a smaller share of the elderly are afflicted. And the good news is largely confined to rich countries, at least for now. But the fear that an epidemic of ►►

dementia will soon be running out of control, blighting ever more lives and placing an impossible burden on health systems, is mercifully overblown.

The single biggest risk factor for dementia is age. Prevalence doubles roughly every five years after 70. In America in 2016, for instance, just 4% of people aged 70-74 had dementia, but the rate jumped to 9% for those who were 75-79 and again to 18% for 80- to 84-year olds. More than a quarter of those over 85 had the condition.

This near-exponential pattern, combined with the rising life expectancy, has long fuelled alarming predictions. In a study published last year in the journal *Nature Medicine* Josef Coresh, Michael Fang and their co-authors projected that the number of new cases in America would double from around 500,000 a year in 2020 to 1m a year by 2060. A study published in 2022 calculated that the global population of people with dementia will almost triple from around 57m people in 2019 to 153m people in 2050.

Mind-bending

Such numbers, in turn, feed frightening estimates of the likely future cost of dementia. The direct cost of care (including informally in the home) probably came to around \$1.3trn worldwide in 2019 (or roughly 0.8% of global GDP). The burden becomes even greater if one accounts for indirect costs such as patients' diminished quality of life. These added up to around \$781bn last year in America alone (or about 2.5% of GDP), according to a model funded by America's National Institutes of Health. A paper by Arindam Nandi of the Population Council, David Bloom at Harvard University and others uses an even broader measure that tries to put a price on patients' suffering (by estimating a willingness to pay to prevent it). It put the global cost of dementia at \$2.8trn in 2019 increasing to \$4.7trn by 2030, \$8.5trn in 2040 and \$16.9trn by 2050.

Yet such terrifying projections are almost certainly wrong, at least with respect to rich, Western countries. Almost all are based on models in which there is little, if any, reduction in the age-adjusted rate of dementia over the coming decades. Since there will be growing numbers of old people in most Western countries in the coming years, and since those old people will live longer, such assumptions lead to gigantic increases in the projected number of dementia cases. Yet even relatively small annual changes in the rate of dementia, when compounded over 30 years, can lead to much happier outcomes.

To show this Chiara Celine Brück and her co-authors at the Erasmus Medical Centre built a detailed computer simulation of 10m Dutch people and then looked at how dementia would progress under

two different scenarios. In the first they assumed there would be no change in the underlying risk of dementia over time (other than from ageing) and found, as other mainstream projections have, that the number of Dutch people with dementia would more than double by 2050. In another, they used the research of their co-author, Mr Wolters, who found that the incidence of dementia had been falling by 13% a decade after adjusting for age, and simulated what would happen if the trend continued. They found that, although the number of dementia cases would still increase because of the growing ranks of elderly people, instead of more than doubling by 2050, it would grow by just 43% from the level of 2020.

To be more confident about such projections, researchers must determine why so many more people have been keeping their wits and so be able to make a more reasoned judgment about whether the trend will continue. That is not easy, in large part because dementia is a condition with multiple causes that typically develops slowly over decades before clearly manifesting itself.

Scientists have long known that dementia has a genetic component. Roughly 25% of the population carries a single copy of a gene known as ApoE4, which is associated with a risk of getting Alzheimer's (much the most common of the dozens of diseases that can cause dementia) that is 2-3 times greater than the norm. For the 2-3% of the population with two copies of this gene, the risk is 10-15 times greater.

Yet many people without these genes get dementia and many who have them do not. The search for other causes of the condition was given a boost in the 1970s in North Karelia, a remote and hard-living region of Finland which had one of the world's highest rates of heart attacks. To reduce this scourge, health authorities discouraged smoking, monitored blood pres-

sure and encouraged healthy eating. The public-health campaign eventually cut deaths from heart attacks by 84%. An unexpected benefit, says Tiia Ngandu, a researcher at the Finnish Institute for Health and Welfare, was the opportunity for researchers to examine some 40 years of detailed health records for a large population.

Memory laws

The result was a groundbreaking series of observational studies showing that high blood pressure, high cholesterol, obesity and poor fitness in mid-life all increased the risks of dementia 20 years later. "It really changed the way we think about dementia," says Miia Kivipelto of the Karolinska Institute in Stockholm, who led some of these studies. "We saw that it was not only a late-life disease that can't be prevented, but more of a process that starts in mid-life with the possibilities to at least slow the progression."

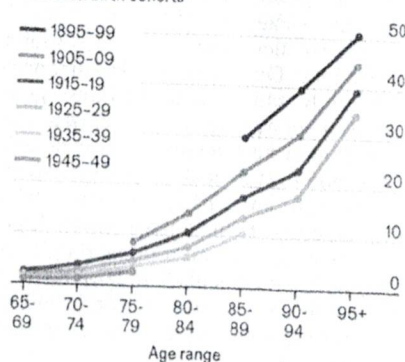
Observational studies, however, cannot account for variables that researchers are not able to (or do not think to) measure, but that may nonetheless contribute to the outcome. The best way of eliminating these is by using a randomised controlled trial (RCT), the gold standard in clinical research, in which people are divided into two groups, only one of which receives the intervention being tested. In 2009 Dr Ngandu and a team led by Ms Kivipelto began the world's first big RCT to see whether two years of healthy eating, exercise, cognitive training and heart treatment could reduce dementia among old people at high risk of it. Sure enough, the results of FINGER (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability), which were published in 2015, proved that people could significantly diminish the risk of cognitive decline by adopting a healthy lifestyle.

Several similar RCTs have found significant benefits from such changes in lifestyle in America, Australia and Japan, among other places. Because these studies are comparable, pooling their results has also given researchers a big enough sample group to study interactions between lifestyle and genes. This has produced a particularly hopeful result for those with the ApoE4 gene, who saw a bigger benefit from the interventions than those without. "You can't change your genes," says Ms Kivipelto, "but you can do things to postpone the onset of the disease or reduce the effect of genetics."

The implications are vast. The Lancet Commission on Dementia, an international collaboration of leading experts, reckons that as many as 45% of dementia cases worldwide could be delayed or prevented through addressing 14 "modifiable risk factors" at various stages in life. These range from better schooling for children (insuffi-

Cognitive coup

United States, % with dementia by age
Selected birth cohorts



Source: "Changing story of the dementia epidemic", by E. Stallard et al., *Journal of the American Medical Association*, May 2025

cient education is associated with a 60% higher risk of dementia), to treating deafness, high cholesterol and depression in mid-life and avoiding social isolation when older (see chart 2).

The commission's findings offer important lessons for policymakers about how to reduce the incidence (and cost) of dementia. The first is not to focus exclusively on the factors with the strongest association with dementia, such as untreated depression (which brings a 120% bigger risk of developing the condition than the norm). Instead, attending to factors that are associated with lower risk but are more common can have a bigger impact. Treating people with hearing loss and high cholesterol, for instance, could cut total dementia cases by 14%, the commission finds.

Mind control

Such advances help explain why the incidence of dementia has fallen so rapidly over the past 40 years. Improvements in education and successful efforts to reduce heart disease and strokes have also, by happenstance, improved brain health. "When I graduated from medical school, which was quite a long time ago, we thought that dementia was just like one of these things that hit you from outer space in a totally random fashion," says Gill Livingston of University College London, who leads the Lancet Commission. "It is hugely positive and hopeful that we now know that policy and individuals can do a huge amount to change that."

Researchers continue to discover new risk factors. In 2024, for instance, the Lancet Commission added untreated vision loss and high levels of LDL, a type of cholesterol. Among the bewildering array of possible additions researchers are examining are some that can be easily acted on, such as regularly flossing teeth (inflammation from infected gums may harm the brain). Others, such as poor sleep, may simply give anxious insomniacs one more thing to lie awake worrying about. And some may prove to be double-edged swords, says Ms Kivipelto. People with demanding and engaging jobs (such as medical researchers and journalists, she says, perhaps a little generously) have little need to do extra cognitive exercises to keep their brains nimble. But such jobs may also be more stressful, which may well turn out to be a risk factor, too.

Research is also revealing unexpected interventions that help to keep ageing minds sharp. One of the most promising derives from an analysis by Pascal Geldsetzer of Stanford University and his team of a natural experiment in Wales. In 2013 the British region started offering people aged 70-79 free vaccinations through the public-health system. This change resembled an RCT, in that a large number of peo-

ple were separated almost at random into two groups: those who had already turned 80 in the weeks before the programme started, and so were not eligible to be jabbed; and those who turned 80 in the weeks after, roughly half of whom were duly vaccinated.

The study found that a vaccine intended to prevent shingles, a form of chickenpox, suffered chiefly by the elderly, also reduced the risk of developing dementia by 20% for at least seven years after it was administered. This conclusion has been validated by similar studies in Australia and Canada. "We were super-excited by this finding," says Mr Geldsetzer, "because it showed that such a simple and cheap intervention could potentially avert one-fifth of cases." A more recent study by the same team suggests that the vaccine also slows the progression of dementia in people who already have it before they get vaccinated.

These results are not only encouraging in themselves, but also raise tantalising prospects of further benefits. Should people be jabbed at a younger age—50, say—given that dementia can take years to manifest? Should the elderly receive regular booster vaccines over the years?

The news regarding treatments developed expressly for dementia is less heartening. Until recently the most promising drugs were thought to be antibodies such as Lecanemab and Donanemab that bind to and clear out amyloid-beta, a protein that clogs up the brains of people with Alzheimer's. But studies suggest they offer modest real-world benefits and carry hefty risks of bleeding or swelling in the brain, especially for people with the ApoE4 gene. In other words, the people most in need of

these drugs are also at greatest risk of being harmed by them. For some, these findings also call into question the hypothesis that tangles of amyloid cause Alzheimer's and that clearing them could cure it. Others argue that these drugs need to be given earlier in life to have an impact.

Some observers hope that GLP-1s, weight-loss drugs often heralded as a miracle cure for practically everything, might make brains as trim as they do waistlines. An RCT has found that it offers no benefits to people who already have Alzheimer's, although earlier observational studies had suggested that people on these sorts of drugs had a lower risk of getting dementia in the first place.

Trials are under way to test lots of drugs as treatments for dementia, including many that were originally developed for other ailments. In the EasyFit gym in central Helsinki, a group of grey-haired women clad in lycra are in the vanguard of this effort. They start their warm-up exercises at the gentle cajoling of a physiotherapist. For the next hour they lift weights, swing kettlebells, horse around and laugh heartily, as part of an RCT. "Alzheimer's is a real problem," says Riita, aged 77. "If something can be done to improve the methods of helping people I would very much like to be part of it."

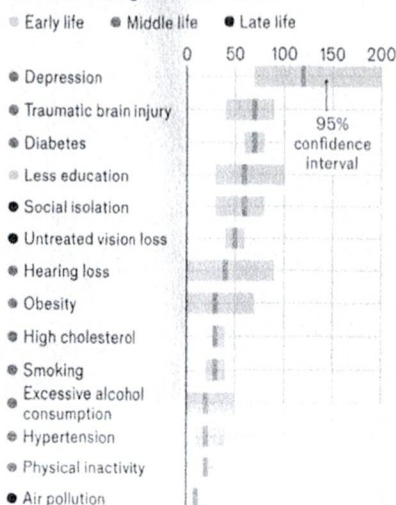
Riita and her buddies are among almost 600 people in three countries taking part in the MET-FINGER study, which combines healthier lifestyles with metformin, a diabetes drug, to see if these can prevent or at least delay the onset of various sorts of dementia. Other studies are examining activities from saunas to ice baths in search of methods to sharpen the mind.

For now even the most optimistic projections still entail a rise in the total number of dementia cases over the coming decades, albeit at a far slower rate than before, as the ranks of the elderly grow. Yet there are good reasons to hope that a combination of drugs, vaccinations, lifestyle and policy changes could bend this curve further. It is even possible that the total number of people with dementia may soon begin to fall in rich countries.

Mr Livingston and Ms Kivipelto both point out that the grim arithmetic whereby dementia rates double every five years after the age of 70 also offers huge possibilities. Simply delaying the average onset of dementia by five years would cut the total number of cases by around 50%. "I'm optimistic it's possible," says Mr Livingston. So is Lisa, a 66-year-old working out in the gym in Helsinki. She lifts weights or exercises five times a week, motivated, in part, by personal experience. "It's not nice to see your own mother becoming a different person," she says. "I know Alzheimer's can come to anyone, so it is good to do these things if you can." ■

Mind map

Potentially modifiable risk factors for dementia, higher relative risk, %



Source: "Dementia prevention, intervention and care", Lancet Commission report, 2024