

Risk Factors and Lifestyle

Although there is no magic bullet for preventing Alzheimer's, it has been suggested that up to one-in-three cases could be prevented if people led different lifestyles. The seven main risk factors for developing Alzheimer's disease are:

- Physical inactivity (lack of exercise)
- Smoking
- Lack of education
- Midlife hypertension (stress)
- Midlife obesity
- Diabetes
- Depression

Of the seven risk factors for Alzheimer's, the four main risk factors for the disease are a lack of exercise, smoking, depression and poor education. Although there is no single way to treat dementia, we may be able to take steps to reduce our risk of developing dementia at older ages. Simply tackling physical inactivity, for example, will reduce levels of obesity, hypertension and diabetes, and prevent some people from developing dementia. Whilst age is the biggest risk factor for most cases of Alzheimer's, lifestyle and general health factors could increase or decrease a person's chances of developing the disease. The single biggest contributor to Alzheimer's disease is age, but because we get older doesn't mean we have to become unhealthy. Simple daily exercises will go a long way to helping fight off the disease as we get older. The current wisdom on the sensible precautions you might wish to take could be broadly summed up in the thought that what's 'good for your heart' also appears to be 'good for your brain'. And, reduced to a maxim, it would be 'moderation is good': moderation in what you eat, and moderation in everything.

Risk factors for cardiovascular disease (like heart disease and stroke) are also risk factors for all dementia. So it's a good idea to keep healthy by:

- Exercising regularly
- Not smoking
- Achieving and maintaining a healthy weight
- Controlling high blood pressure
- Reducing your cholesterol level
- Controlling your blood glucose if you have diabetes
- Eating a healthy, balanced diet with lots of fruit and vegetables and low amounts of saturated fat
- Only drinking alcohol within the recommended limits

Some studies suggest that enjoying an active life, with lots of interests and hobbies might be beneficial. Other researchers have found that spending more time in education is associated with a lower risk. It's not yet known whether eating oily fish or taking B vitamins can reduce the risk of dementia as studies so far have had mixed results. It is not advised to take NSAIDs (non-steroidal anti-inflammatory drugs like aspirin or ibuprofen) or HRT (hormone replacement therapy) to protect against dementia but research is continuing in this area. Despite occasional publicity, research has shown that aluminium, eating meat or living close to power lines are not risk factors for dementia. There is also no evidence that turmeric, ginkgo, ginseng, statins or coffee can protect against dementia.

The World Alzheimer's Report 2014 on dementia and risk reduction summarises the risk factors issue as follows:-

The strongest evidence for possible causal associations with dementia are those of low education in early life, hypertension in midlife, and smoking and diabetes across the life course. Improved detection and treatment of diabetes and hypertension, and smoking cessation, should be prioritised, including for older adults who are rarely specifically targeted in prevention programs. Increased physical activity and reduction in levels of obesity are also important. There is considerable potential for reduction in dementia incidence associated with global improvements in access to secondary and tertiary education. There is also consistent evidence from several studies for an inverse association between cognitive activity in later-life and dementia incidence. However, this association may not be causal, and the benefits of cognitively stimulating activities need to be tested in randomised controlled trials. While cardiovascular health is improving in many high income countries, it is deteriorating elsewhere. Many low and particularly middle income countries show a pattern of increasing cardiovascular conditions, hypertension and

diabetes. The largest increase in dementia prevalence in the coming decades will be in the low and middle income countries, where the risk factors identified in this report present an increasing problem. There is no evidence strong enough at this time to claim that lifestyle changes will prevent dementia on an individual basis, but combining efforts to tackle the global burden is important

Eat Well

You'd do well to avoid excess consumption of carbohydrates and sugar: tracking over a thousand elderly people for four years revealed that those with the highest carbohydrate intake were nearly twice as likely to develop mild cognitive impairment (MCI - which can lead to symptoms of dementia) as participants with the lowest portions of carbohydrate on their plates. Those eating food with the highest levels of sugar showed a 50 per cent increase in the risk of developing MCI, but those on diets highest in fat saw a 42 per cent reduction in that risk.

Lose Weight

Keeping trim in your 30s, 40s and 50s could reduce the risk of dementia later in life. Confirming earlier data, a Swedish study found that people classed as overweight or obese in middle age had an 80 per cent higher risk of developing dementia, even when other contributory factors - such as vascular disease and diabetes - were taken into account. Yes, 80 (not 8) per cent!

Avoid Stress

Lack of sleep and stress may of course be connected, but stress really slows us down. It can prevent the working memory from retaining information required for tasks in hand, exciting extra action in neurons in the prefrontal cortex but actually reducing their focus. Acute stress has been shown to trigger the release of hormones in the hippocampus, which interfere with the brain's collection and storage of memories. Research suggests that fitter people are more capable of managing stress than those who do not get enough exercise. A good walk for half an hour three times a week can make a real improvement in stress levels.

Reduce Blood Pressure

High blood pressure in early middle age has been shown to cause damage to the brain, making the brains of younger people 'age' more quickly and shrink - MRI scans showed that the brains of subjects with high blood pressure had shrunk by an average of 9 per cent, compared to the brains of people with normal blood pressure. Watch what you eat: try more foods such as oats, bananas, lean meat and low-fat dairy products, and less saturated fat, salt and added sugar. Lose weight if you are overweight, take more exercise and be prepared to cut down on excessive alcohol consumption.

Diabetes

Research is uncovering more suggestions of links between Type 2 diabetes and Alzheimer's disease, including evidence that higher levels of two of the established pointers towards the presence of Alzheimer's - the beta-amyloid and tau proteins that seem to malfunction to form the plaques and tangles in brain cells - are found in the brains of animals with diabetes. The brains of people with diabetes in middle age have been shown to shrink faster, especially in the hippocampus - an area associated with memory function. Type 2 diabetes significantly and independently increases the risk of Alzheimer's disease but many people with diabetes will not go on to develop dementia. Researchers are working to unravel the link between these two conditions with the hope that it might help us develop new dementia therapies. Although it is not yet understood why people with diabetes are at an increased risk of dementia, research suggests that people with early stage Alzheimer's might benefit from treatment with a diabetes drug called Liraglutide.

Sleep Medications

Benzodiazepines are a class of drugs used to treat short-term insomnia, anxiety, and sometimes epilepsy, ie. alprazolam, diazepam, flurazepam, lorazepam, temazepam etc. Although clinical guidelines recommend against the long-term use of benzodiazepines, particularly in elderly people with a greater risk of side effects, chronic benzodiazepine use is common in older populations. A new study reported that people who had used benzodiazepines for more than three months had almost a 50% higher risk of Alzheimer's disease over the following six years, an association that has been reported in previous publications as well. Short-term use of benzodiazepines (less than 90 daily doses) did not raise the risk for Alzheimer's but, beyond that point, with longer use came greater risk. The associated risk was observed even in people who had previously used a benzodiazepine for at least six months but had stopped using it at least a year before their diagnosis of dementia. Despite these studies, it is not clear if the risk comes from benzodiazepines or from the health conditions for which benzodiazepines are regularly

prescribed. Both anxiety and sleep disorders are potential risk factors for dementia. The scientists leading the study did attempt to control for these risk factors yet still observed an increased risk from benzodiazepine use. No strong scientific rationale has been identified to explain why benzodiazepines might accelerate the development of Alzheimer's disease.

Alcohol-related dementia

This has been described as the silent epidemic, because most people are unaware that the decline in cognitive functions seen in dementia can also be triggered by the persistent over-consumption of alcohol. The long-term misuse of alcohol interferes with the body's ability to use or store vitamins, particularly vitamin B1, which affects the functioning of the nervous system and the brain, leading to memory loss and personality changes. Unlike other forms of dementia, if caught soon enough, alcohol-related dementia can be reversed: a quarter of people with alcohol-related dementia recover completely, but another quarter are permanently damaged. Drinking that falls short of alcohol abuse but is habitually above the recommended levels is said to be a contributory factor in between 20 and 25 per cent of all dementia cases, and there are fears that a growing number of young people will be affected.

Genetics

Risk genes increase the likelihood of developing a disease, but do not guarantee it will happen. A small but growing number of genes have now been identified which affect – to different degrees – the chances of developing late onset Alzheimer's. The effects of these genes are subtle, with variations acting to increase or decrease the risk of developing Alzheimer's disease, but not directly to cause it. The gene with the greatest known influence on the risk of developing late onset Alzheimer's disease is called apolipoprotein E (Apo-E). This is a major cholesterol carrier that supports lipid transport and injury repair in the brain. This gene is found on chromosome 19 and comes in three forms:-

ApoE-e2. This is rare. The e2 form of the gene is mildly protective against Alzheimer's: people with it are slightly less likely to develop the disease. In the general population, 11 per cent has one copy of ApoE-e2 together with a copy of ApoE-e3, and one in 200 (0.5 per cent) has two copies of ApoE-e2.

ApoE-e3. Most common. It has no effect on the risk of developing Alzheimer's dementia. About 60 per cent of the population has a 'double dose' of the ApoE-e3 gene and is at 'average' risk. Up to half of this group develops Alzheimer's disease by their late 80s.

ApoE-e4. ApoE-e4 is associated with a higher risk of Alzheimer's. About a quarter of the general population inherits one copy of the ApoE-e4 gene. This increases their lifetime risk of developing Alzheimer's disease by up to four times. About 2 per cent of the population gets a 'double dose' of the ApoE-e4 gene – one from each parent. This increases their risk of developing Alzheimer's disease by between 10 and 30 times or more by the age of 75. However, even then, they are not certain to develop Alzheimer's. Whilst the exact mechanism of how E4 causes such dramatic effects remains to be fully determined, evidence has been presented suggesting an interaction with the peptide beta-amyloid. Apolipoprotein E enhances the break-down of this peptide, both within and between cells. Some researchers think that ApoE-e4 does not affect whether a person will get Alzheimer's disease but the age at which they get it.

Everyone inherits a copy of some form of ApoE from each parent. Those who inherit one copy of ApoE-e4 have an increased risk of developing Alzheimer's. Those who inherit two copies have an even higher risk, but not a certainty. In addition to raising risk, ApoE-e4 may tend to make symptoms appear at a younger age than usual. Scientists estimate that ApoE-e4 is implicated in about 20 percent to 25 percent of Alzheimer's cases. High education, active leisure activities, or maintaining vascular health seems to reduce the risk of dementia related to APOE-e4. The e4 carriers with these characteristics appear to have similar dementia-free survival time to non-e4 carriers.

Ecstasy

The drug known as Ecstasy has become a relatively common drug among adolescents today. Ecstasy is known as 3, 4-methylenedioxymethamphetamine or MDMA for short. It is a synthetic drug that can act as both a stimulant and hallucinogenic drug that enhances sensory processing, and is known to cause major changes the level of neurotransmitters in the brain, such as serotonin and dopamine, which control our mood and behaviours. Amphetamines such as MDMA cause the release of serotonin in the body, and there is a suggestion, expressed by some medical professionals, that the long-term Ecstasy use may cause irreversible brain damage, which may potentially trigger Alzheimer's disease. This does not mean that Ecstasy users are at risk of dementia, but that there's a loss of brain efficiency in both Ecstasy users and early Alzheimer's patients. This shift in cortical excitability may be chronic, long-lasting, and even permanent, which is a real worry. A study in 2011 found a definite brain drain

in ten long-time Ecstasy users: their hippocampus measured, on average, more than 10% smaller than that of non-users. Several researches have suggested that people who use ecstasy can develop serious memory problems.

Drug Abuse

Young people who abuse heroin may suffer brain damage similar to what's seen in the early stages of Alzheimer's disease, according to UK researchers. Comparing autopsied brain tissue from young heroin abusers and non-drug users, UK researchers found that before they died, the drug users had begun to develop damage in brain areas involved in learning, memory and emotion. Specifically, they had heightened levels of two proteins that contribute to the plaques and tangles that build up in the brains of people with Alzheimer's. Drug users in this study showed higher levels of an abnormal, insoluble form of tau that is seen the tangles that mark Alzheimer's and other forms of dementia. Since abnormal tau is clearly linked to dementia in a number of other conditions, there is cause for worry about accelerated aging of the brain in people who start to abuse opiates at a young age. Young drug abusers are up to three times more likely to suffer brain damage, than those who did not use drugs.

Anaesthesia

Elderly patients often exhibit a condition called postoperative cognitive decline in which they experience lapses in memory and attention, but it usually does not last for more than a few weeks. Because anaesthesia affects so many diverse brain processes and areas, some researchers worry that it may have unforeseen consequences. The molecules in anaesthesia can trigger other mechanisms that have nothing to do with anaesthesia itself including processes that may be linked to neurodegeneration. At the cellular level, anaesthesia can set off a chemical cascade triggering the release of microglia, immune cells normally deployed to fight infections in the brain. When microglia are activated for long periods of time they can inflame brain tissue, which is thought to contribute to the cognitive problems associated with Alzheimer's. However, examining links between anaesthesia and dementia risk has given mixed results. Of 2030 elderly volunteers in France who developed dementia, those who had a general anaesthetic, rather than local, during the time of the study, had a 35% higher risk of dementia than those without anaesthesia.

The results are in favour of an increased risk of dementia several years after general anaesthetic. However, it is not thought that anaesthesia and surgery actually *cause* Alzheimer's or *cause* dementia, rather that it interacts with individual vulnerabilities if you're already predisposed to getting something like dementia, anaesthesia just speeds it up.

Dental Amalgam Fillings

This is a controversial area. Dental amalgam fillings contain powdered silver, tin, and copper combined with metallic mercury. The components, mixed together in the dentist's immediately before use, form a hard, stable material. These fillings have been used since the nineteenth century and are widely used because they are strong and so provide durable chewing surfaces. They can be inserted more quickly than some other types of fillings, they are less expensive to place than other types of fillings and they usually last longer. In recent decades, composite filling materials have become available.

Now on the face of it, why would you want toxic metals in your mouth? Mercury is more toxic than any other heavy metal. There is approximately 1g of mercury in the typical filling. This is nearly one million times more mercury than is present in contaminated sea food. Most people don't realize that the mercury amalgams slowly release mercury vapour. Every time you chew, mercury vapour is released and quickly finds its way into your bloodstream, where it causes oxidative processes in your tissues. Mercury vapour is the form of mercury most easily absorbed by your body. National and international bodies have determined that the use of mercury-containing dental amalgams is safe. Researchers have determined that there is no relationship between brain mercury levels or Alzheimer's disease and the presence of dental amalgam fillings, regardless of their number, size, or length of time present in a person's mouth. However, scientists have shown that trace amounts of mercury can cause the type of damage to nerves that is characteristic of the damage found in Alzheimer's.

This does not mean you should have mercury fillings removed, you can be exposed to significant amounts of mercury vapours if the dentist doesn't know what he or she is doing by taking correct precautions.

Anticholinergic Medication

An anticholinergic agent is a substance that blocks the neurotransmitter acetylcholine in the central and the peripheral nervous system. Long term use increases the risk of both mental and physical decline. It is unclear if they affect the risk of death. Possible effects of anticholinergics include dementia, they are known to cause confusion, memory loss, worsening of mental function, and other cognitive effects in the elderly. These medicines include some antihistamines, antidepressants and drugs for an overactive bladder. That said, a well-designed US study suggested those taking the highest levels of anticholinergic prescribed medicines were at a higher risk of developing dementia compared with those not taking any. Importantly, the increased risk was only found in people

who took these medicines at the equivalent of once every day for more than three years. No link was found at lower levels. However, these are not unrealistic doses of medicines, so the results may be applicable to a significant proportion of older adults. Furthermore, it's not possible to say if reducing the amount of anticholinergic medicines will reduce the risk of dementia to normal. Anticholinergics are not usually prescribed to older people. The elderly are more sensitive to their effects compared to younger adults. Over-the-counter medicines identified were Benadryl (USA only), Nytol and Piriton. Some examples of prescription medications with anticholinergic properties are as follows:-

ANTIHISTAMINES (H-1 BLOCKERS); chlorpheniramine cyproheptadine diphenhydramine hydroxyzine

ANTIDEPRESSANTS; amoxapine amitriptyline clomipramine desipramine doxepin imipramine nortriptyline
protriptyline paroxetine

CARDIOVASCULAR MEDICATIONS; furosemide digoxin nifedipine disopyramide

GASTROINTESTINAL MEDICATIONS; Antidiarrheal Medications: diphenoxylate atropine

Antispasmodic Medications: belladonna clidinium chlordiazepoxide dicyclomine
hyoscyamine propantheline

Antiulcer Medications: cimetidine ranitidine

ANTIPARKINSON MEDICATIONS; amantadine benztropine biperiden trihexyphenidyl

MUSCLE RELAXANTS; cyclobenzaprine dantrolene orphenadrine

ANTIVERTIGO MEDICATIONS; meclizine scopolamine

ANTIPSYCHOTIC MEDICATIONS; chlorpromazine clozapine olanzapine thioridazine

URINARY INCONTINENCE; oxybutynin probantheline solifenacin tolterodine trospium

PHENOTHIAZINE ANTIEMETICS; prochlorperazine promethazine

