Smoking and dementia

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Key points:

- dementia is not a normal part of ageing[1]; approximately 3,000 people in Scotland have early onset (under age 65) dementia[2]
- whilst it is possible to live, and in many cases live well, for many years with dementia, it is an incurable and terminal condition[3]
- almost one third of people in the UK who died over the age of 65 years have had some form of dementia[4]
- smoking is a risk factor for Alzheimer's disease and other forms of dementia[5, 6, 7]
- emerging evidence[8] suggests that exposure to second-hand smoke may be a risk factor for dementia
- smoking and exposure to second-hand smoke are risk factors for cardiovascular disease, diabetes and stroke which are in turn underlying risk factors for dementia[9]
- the risk of developing dementia may be up to 70% higher in current heavy smokers than in non-smokers[10]
- age-related cognitive decline may be accelerated by smoking[11]
- a 2011 YouGov poll[12] found that 31% of those surveyed feared dementia more than cancer or death so there may be smokers for whom dementia risk reduction is an incentive to quit
- giving up smoking improves health and may reduce the risk of dementia.

This specialist briefing is aimed at professionals and policy makers. It reviews the evidence on smoking and an increased risk of Alzheimer's disease and other forms of dementia, and cognitive impairment. This briefing also examines how continued smoking or exposure to second-hand smoke may affect people with dementia and their carers.

Introduction

Dementia is a complex illness that impacts on the lives of 84,000 people in Scotland with the condition, their families and carers. According to Alzheimer Scotland[13], based on current estimates the number of people with dementia will double within the next 25 years. Epidemiological studies have consistently linked smoking to an increased risk of developing dementia[14], and long-term cohort studies suggest that the risk for dementia in former smokers (after several years of not smoking) approaches that of never smokers[15]. This suggests that smoking could be an important modifiable lifestyle risk factor for dementia.

What is dementia?

Alzheimer Scotland[16] describes dementia as '*a term for a range of illnesses. The most common type is Alzheimer's disease, in which brain cells deteriorate through the build-up of a protein. Vascular dementia is the second most common type of dementia and is caused by problems in the supply of blood to brain cells. About 75% of people who are diagnosed with dementia will have either Alzheimer's or vascular dementia, or a combination of the two.'*

'People develop dementia as a result of degeneration and death of brain cells. In the case of Alzheimer's disease, a protein called amyloid builds up in deposits in the brain (known as plaques) and tiny filaments in brain cells form what are known as tangles.'

'Dementia is a major cause of disability in people aged over 60. It contributes 11.2% of all years lived with disability, more than stroke (9%), musculoskeletal disorders (8.9%), cardiovascular disease (5%) and all forms of cancer (2.4%).'

'Although there are many different forms of dementia, the thing they all have in common is that they progressively damage the brain. In most cases, the key symptom of dementia is serious memory loss, but others include losing track of the time, getting lost in familiar places and changes in behaviour. Additionally, people with dementia are likely to lose their ability to reason clearly, and may find making decisions very hard. Dementia can also cause personality changes, which can be particularly distressing for those who care for a person with the illness.'

Smoking and dementia risk

Brain cell degeneration – amyloid plaques and tau tangles

Cigarette smoking is a risk for Alzheimer's disease[17, 18,] the pathological hallmark of which is the amyloid-β (Aβ) deposits found in the brain. Whilst more research is needed it has been speculated[19] that the mechanism underlying the epidemiological association of cigarette smoking with Alzheimer's disease might involve the effect of cigarette smoke on amyloid precursor protein processing, a reduction of Aβ clearance by microglia (immune cells in the brain and spinal system), and/or an increased microglial proinflammatory response. Research published in February 2013[20], which analysed the brains of transgenic mice exposed to cigarette smoke, also suggests that smoking increases the severity of abnormalities typical of Alzheimer's disease, including amyloidogenesis (the production of amyloid), neuroinflammation and tau phosphorylation (this causes tangles within nerve cells). Cigarette smoking may therefore both hasten the onset of Alzheimer's disease and exacerbate its features.

Cardiovascular disease

Several studies[21, 22, 23] have found that the risks of Alzheimer's disease (AD) and dementia are increased with smoking. A meta-analysis of 19 prospective studies[24] with a total of 26,374 participants reported that the risk of developing dementia was up to 70% higher in current smokers than in non-smokers. According to a review in the Lancet Neurology[25] '*the most likely mechanism underlying the association between smoking and AD is vascular disease. Smoking contributes to a variety of subclinical and clinical vascular disorders including atherosclerosis and cerebrovascular disease, which, in turn, could lead to increased risk of AD. However, tobacco smoke also contains hundreds of neurotoxins and could contribute to AD risk through oxidative stress, inflammatory processes, or other mechanisms*'. Optimal management of cardiovascular risk factors may therefore improve cognition and delay onset of dementia[26].

Diabetes and insulin resistance

Many studies have identified a positive association between smoking and the incidence of diabetes[27, 28, 29, 30, 31] and between diabetes and dementia[32, 33, 34]. Nicotine promotes insulin resistance[35] also called pre-diabetes (again a risk factor for cardiovascular disease), and there may be a link between pre-diabetes and an increased risk of dementia and Alzheimer's disease[36]. It has also been found[37] that diabetes and prediabetes substantially accelerated the progression from mild cognitive impairment (MCI) to dementia.

Stroke

Smoking is known to increase the risk of stroke[38] and consequently may increase the risk of developing vascular dementia. Pooled data from a meta-analysis of studies of pre- and post-stroke dementia[39] estimate that 1-in-10 patients have dementia prior to first stroke, 1-in-10 develop new dementia soon after first stroke, and over 1-in-3 develop dementia after a recurrent stroke. For Alzheimer's disease too there is increasing evidence to suggest that it is '*a neurovascular disease, with macrovascular events such as heart attack and stroke causing sustained hypoxia preceding disease onset, although some cases of AD lack a vascular component*'[40].

A 2012 report from the World Health Organization and Alzheimer's Disease International[41] observed that '*as research into identifying risk factors for dementia is in its infancy primary prevention should focus on preventing risk factors for vascular disease, diabetes, midlife hypertension, midlife obesity, smoking, and physical inactivity*'. An international study[42] which analysed the proportion of cases of Alzheimer's disease in the population that might be prevented if the risk factor could be removed entirely concluded that the most promising strategies for prevention were the elimination of physical inactivity (12.7% prevented), smoking (13.9% prevented), and low education (19.1% prevented). Reduction in blood pressure, lipid levels, blood sugar, weight, alcohol intake and smoking may also improve cognitive function and prevent or delay the progression of dementia[43].

There is sufficient evidence to conclude that current smokers have an increased risk of any dementia, Alzheimer's disease, vascular dementia and cognitive decline compared to non-smokers[44, 45], and that this risk is greatly increased for heavy* midlife smokers[46].

Dementia risk and exposure to second-hand smoke

A 2013 study from China[47] concluded that second-hand smoke should be considered an important risk factor for severe dementia syndromes, and that avoidance of second-hand smoke might reduce the rates of severe dementia syndromes worldwide. This cohort study assessed almost 6,000 older adults in China, examining their mental state to see if they had dementia and questioning their exposure to second-hand smoke during their lifetime. This study had some limitations, including the uncertainty both of the dementia diagnoses and the self-recall of exposure to second-hand smoke; more research is needed.

However, established research on endothelial dysfunction of the coronary circulation in healthy young non-smokers[48, 49, 50] has repeatedly demonstrated that exposure to second-hand smoke can cause measurable changes to the vascular system, suggesting a mechanism by which second-hand smoke causes disease[51]. Exposure to second-hand smoke is associated with an increased risk of cardiovascular disease[52, 53] and stroke[54] which are themselves associated with an increased risk of cognitive impairment and dementia[55, 56]. Similarly, studies suggest that second-hand smoke exposure increases the risk of developing diabetes[57,58, 59]and a review of several large prospective cohort studies estimated that diabetes increased the risk of Alzheimer's disease by 50–100 per cent and of vascular dementia by 100–150 per cent[60].

Smoking and the risk of developing cognitive impairment

Decreased brain function (as opposed to the degeneration and death of brain cells in dementia) is a natural part of ageing[61], although it can develop into dementia. Research using data from the Whitehall II Cohort study[62] found that compared with never smokers, middle-aged male smokers experienced faster cognitive decline in global cognition and executive function; in ex-smokers with at least a 10-year cessation there were no adverse effects on cognitive decline. Similarly, in a prospective cohort study of men and women aged between 43 and 53 smoking was associated with faster declines in verbal memory and with slower visual search speeds[63]; these effects were largely accounted for by individuals who smoked more than 20 cigarettes per day and were independent of sex, socioeconomic status, previous (adolescent) cognitive ability, and a range of health indicators. In a 2012 population based cohort study[64] which explored the association between cardiovascular risk and cognitive decline in adults aged 50 and over, smoking was consistently associated with lower performance on the cognitive outcomes measured. A 2004 prospective multi-centre

* More than two packs a day

cohort study[65] (European Community Concerted Action Epidemiology of Dementia [EURODEM]) found higher rates of decline by smoking in men and women over 65, persons with and without family history of dementia, and in three of four participating studies, and that higher cigarette pack–year exposure was correlated with a significantly higher rate of decline. All of the above support the theory that age-related cognitive decline is accelerated by smoking[66].

Cognitive impairment and exposure to second-hand smoke

A cross sectional analysis of a national population based study in England reported that exposure to second-hand smoke may be associated with increased odds of cognitive impairment[67].

Nicotine as a protective factor

As there are nicotinic acetylcholine receptors throughout the cholinergic system which can bind to nicotine, the idea of nicotine as a mechanism for aiding cognitive function is entirely plausible[68, 69] although not using cigarettes as the delivery method. Yet there has been some research to suggest[70, 71, 72] that smoking could have a protective effect for some forms of Alzheimer's disease, nicely summed up in the journal Nature as 'A puff a day keeps the plaque away?'[73]. By 2008 a study of nicotine dependence in the journal Human Genetics was even declaring that *'epidemiological studies reveal that cigarette smoking is inversely associated with AD*'[74]. However, a 2010 analysis which controlled for tobacco industry affiliation[†], study design and other factors concluded that smoking is not protective against Alzheimer's disease but is instead a significant and substantial risk factor[75].

Nevertheless, interest remains in the idea that nicotine, a cholinergic agonist, could counteract the cholinergic dysfunction in cognitive impairment[76]. Research published in 2012 in the journal Neurology[77] suggested that wearing a nicotine patch might help improve memory loss in non-smoking older adults with mild cognitive impairment, and this may be because nicotine stimulates receptors in the brain which are important for thinking and memory. However, whilst the association between nicotinic acetylcholine receptor (nAChR) dysfunction and cognitive decline in Alzheimer's disease may yet have therapeutic potential a great deal of research is still needed. Cigarettes kill half of lifelong regular smokers, and of those an average of 22 years life expectancy will be lost,[78] so research into protective factors is likely to focus on nicotine rather than tobacco smoking.

[†] defined as current or past funding, employment, paid consultation, collaboration, or co-authorship on the included study with someone with then-current or previous tobacco industry funding (within ten years of publication).

When people with dementia smoke

Smoking and dementia are uneasy bedfellows. Many smokers will have occasionally left a lit cigarette unattended; indeed in 2011 – 2012 45% of fatal house fires in Scotland were caused by matches and smokers' materials[79]. The risk for people with impaired memory and reasoning seems likely to be much higher.

According to the Alzheimer's Society[80] there are recorded instances where a person with dementia no longer remembers they smoke if their access to cigarettes is gradually reduced. However, it is important to take the views of the person with dementia into consideration and if they want to continue to smoke, to support them to do so in safety. Simply stopping the supply of cigarettes could result in serious withdrawal symptoms, unless treated, and perhaps interfere with medication. When attempting to give up smoking it is best to get professional advice and support to do so, as this increases the chance of success[81].

Many people with dementia have other medical conditions which can make their dementia worse and lead to hospital admissions. Not smoking is an important part of staying well for as long as possible yet there is a lack of research about helping people with dementia to stop smoking, or finding ways of limiting exposure to second-hand smoke.

Giving up smoking for people with dementia

For those who manage to give up smoking the risk of dying from lung cancer halves within ten years[82]. A June 2012 systematic review[83] suggests that the benefits of giving up smoking are evident in all age groups, including subjects 80 years and older. As with the general population, giving up smoking confers both immediate and long-term health benefits from improved blood pressure and lung function to decreased cancer and stroke risk[84].

Smoking and dementia medication

There is some evidence[85] that smoking predicts poor response to treatment with cholinesterase inhibitors (such as donepezil, rivastigmine, and galantamine for mild to moderate Alzheimer's disease). Confusingly, there is also emerging interest in the idea of using cholinesterase inhibitors as an aid to giving up smoking[86].

Smoking affects the metabolism of various medications, including diazepam, haloperidol (partial), olanzapine (partial), clozapine, mirtazapine (partial), tricyclic antidepressants, barbiturates and benzodiazepines. Smoking cessation may improve the effectiveness of medication and reduce the amount needed.

Giving up smoking and decreasing the risk of dementia

The Whitehall II Cohort study found that in ex-smokers with at least a 10-year cessation, there were no adverse effects of their past smoking on cognitive decline[87]. Other long-term cohort studies also suggest that the risk for dementia in former smokers (after several years of not smoking) approaches that of never smokers[88]. Giving up smoking confers both immediate and long-term health benefits from improved blood pressure and lung function to decreased cancer and stroke risk[89].

People with dementia, carers and exposure to second-hand smoke

Direct exposure to second-hand smoke can cause many of the same diseases as active smoking[90]. Whilst less is known about indirect exposure to second-hand smoke, tobacco smoke is a toxic substance with no safe level of exposure although the risks from exposure are largely dose-related[91, 92]. Even low levels of exposure may cause irritation to eyes and lungs, nausea and headaches as well as creating an unpleasant smell. The 2006 report from the US Surgeon General concluded that *'second-hand smoke is not a mere annoyance. It is a serious health hazard that leads to disease and premature death in children and non-smoking adults'*[93].

Inhaling second-hand smoke can cause cancer in non-smokers and many of the cancer-causing chemicals are present in higher concentrations than in the smoke inhaled by the smoker themselves[94]. Research[95] indicates that non-smokers' heart arteries show a reduced ability to dilate when exposed to tobacco smoke, diminishing the ability of the heart to get blood. In addition, the same half hour of second-hand smoke exposure activates blood platelets, which can initiate the process of atherosclerosis (blockage of the heart's arteries) that can lead to heart attacks. These effects may explain other research showing that non-smokers regularly exposed to SHS suffer death or disease rates 30% higher than those of unexposed non-smokers[96].

People with dementia already have compromised health and whilst they should avoid exposure to second-hand smoke may be unable to remove themselves from smoky settings. Similarly, when people with dementia smoke this may cause carers to be exposed and they too may be reluctant or unable to remove themselves from this situation. Caring for someone with dementia can be a very intensive, challenging, rewarding and at times stressful experience and carers may forget that it's important to look after themselves. Caring for someone with dementia is more stressful than caring for physically impaired older adults[97] and the strains of caregiving can have an impact on the health of carers[98].

Professional carers

Even though second-hand smoke is a known health hazard, many community staff still find themselves regularly exposed to it on home visits. They may find it difficult to ask clients not to smoke in their own homes and it is therefore vital that managers and employers have a clear policy on how to protect staff from the harms of second-hand smoke. For examples of best practice on domiciliary visits see The Royal College of Nurses guidance: www.rcn.org.uk/__data/assets/pdf_file/0006/78702/003043.pdf
and NHS Tayside's protocol on passive smoking for home visits by staff and volunteers: www.nhstayside.scot.nhs.uk/about_nhstay/commitees/06_pchp/19092006/68990.pdf

Recommendations

Although there is sufficient evidence to conclude that current smokers have an increased risk of any dementia, Alzheimer's disease, vascular dementia and cognitive decline compared to non-smokers[99,100] and emerging evidence of exposure to second-hand smoke as a risk factor, there is little awareness of these connections and lingering confusion about smoking having a protective effect. Alongside a need for improved awareness of the links between smoking and dementia there therefore lies a need to develop preventive population strategies similar to those already in place for cancer and heart disease. Information about the benefits of giving up smoking and the health risks of exposure to second-hand smoke should be incorporated into guidelines for the management of dementia and raised with people who have a diagnosis of dementia, their families, and their carers at every suitable opportunity in the care pathway. There should also be an increase in the number of healthcare professionals trained to deliver smoking cessation for people with a diagnosis of dementia and those who care for them, and research into how best to support their quit attempts.

Dedicated specialist smoking cessation support should be made available within the hospital/acute setting and integrated with community-based cessation services. According to a May 2012 updated Cochrane Review of interventions for smoking cessation in hospitalised patients[101] '*high intensity behavioural interventions that begin during a hospital stay and include at least one month of supportive contact after discharge promote smoking cessation among hospitalised patients. The effect of these interventions was independent of the patient's admitting diagnosis and was found in rehabilitation settings as well as acute care hospitals. There was no evidence of effect for interventions of lower intensity or shorter duration. This update found that adding NRT to intensive counselling significantly increases cessation rates over counselling alone*'. In short, every memory clinic and assessment centre, day care facility and care resource, including carer education, should reinforce the message that smoking and exposure to second-hand smoke have implications for the health of people with dementia, and have help available to support people to stop, including advice, behavioural support and referral pathways.

Key messages for the general public

- smoking increases the risk of developing dementia
- one of the mechanisms via which smoking increases the risk of developing dementia is through the impact of smoking on blood flow to the heart and brain
- second-hand smoke is a known health hazard
- the sooner you quit the better, but it's never too late and it will have immediate health benefits

Key messages for people with dementia and their carers

- smoking is bad for your health and the health of those around you
- smoking materials are a fire hazard
- the sooner you quit the better, but it's never too late and it will have immediate health benefits
- exposure to second-hand smoke is harmful to you if you have a diagnosis of dementia, and even more so you have underlying health conditions
- giving up smoking is an important part of staying healthy for as long as possible

Further information and support

Alzheimer Scotland's 24 hour, freephone Dementia Helpline is for people with dementia, those who care for them and anyone with a concern or query regarding dementia. Also see the Alzheimer Scotland website at: www.alzscot.org

Support to stop smoking

Most pharmacies/local chemists are able to provide quit smoking advice and support. Where appropriate, the pharmacist can identify the most suitable form of nicotine replacement therapy (NRT) and some pharmacies run NHS-funded stop smoking services. NRT is available on NHS prescription in Scotland.

People who smoke have a much better chance of giving up smoking if they get support to do so and there are lots of different ways to find support:

- through the local doctor's surgery
- phone free to Smokeline on **0800 84 84 84** (9am to 9pm, seven days a week) Smokeline advisers provide free advice and information for anyone who wants to stop smoking, or who wants to help someone to quit. Smokeline also provides information about the free stop smoking services provided by every health board in Scotland
- request stop smoking leaflets, a magazine and a DVD from Smokeline either by calling the helpline, or by texting 'QUIT' to 83434
- visit www.canstopsmoking.com and enter a postcode to find the nearest stop smoking service or use web chat support (9am to 9pm) at www.canstopsmoking.com/Web-Chat

Short and long term benefits of quitting

20 minutes after quitting	heart rate and blood pressure drop
12 hours after quitting	the blood carbon monoxide level drops to normal
2 weeks to 3 months after quitting	circulation improves and lung function increases
1 to 9 months after quitting	coughing and shortness of breath decrease; cilia (tiny hair-like structures that move mucus out of the lungs) start to regain normal function in the lungs, increasing the ability to handle mucus, clean the lungs, and reduce the risk of infection
1 year after quitting	the excess risk of coronary heart disease is half that of a continuing smoker's
5 years after quitting	risk of cancer of the mouth, throat, oesophagus, and bladder are cut in half. Cervical cancer risk falls to that of a non-smoker. Stroke risk can fall to that of a non-smoker after 2-5 years
10 years after quitting	the risk of dying from lung cancer is about half that of a person who is still smoking. The risk of cancer of the larynx (voice box) and pancreas decreases
15 years after quitting	the risk of coronary heart disease is that of a non-smoker's.

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