

A large, stylized graphic element consisting of a central orange triangle pointing to the right, surrounded by a white outline that forms a larger, irregular shape. The background is white with faint orange lines.

Smoking and MS

Review of the evidence on
smoking and MS

October 2021

Let's stop MS **together**



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Executive Summary

Tobacco use is one of the leading causes of death, illness and inequality. In 2018 the world health organisation estimated that there were 1.3 billion smokers worldwide and over 8 million tobacco related deaths³⁹. While the number of smokers is reducing, there is still a large number of people with MS who smoke in the UK.⁶²

Growing evidence links smoking to increased disability in people with MS^{18, 29, 33} and Magnetic Resonance Imaging (MRI) scans show greater numbers of lesions in people with MS who smoke^{1, 2, 8, 12, 15}. Smoking in people with MS is linked to a greater number of relapses^{34, 35} and quicker progression from relapsing remitting MS (RRMS) to secondary progressive MS (SPMS)^{5, 6, 11, 13, 14, 16}.

Smoking is also linked to increased risk of getting MS, and passive smoking may have a similar effect^{4, 25, 37, 38, 44, 45, 46, 47, 59}. But there is some good news, studies have found reduced effects in those who have stopped smoking, including reduced disability accumulation^{18, 33}, clinical prognosis¹⁶ and increased time to conversion from RRMS to SPMS^{5, 13}. One study even found that for those quitting in the year after first diagnosis, the time to SPMS increased by approximately 8 years, compared to those who continued smoking⁵.

The National Institute for Health and Care Excellence (NICE) produces guidelines that advise health professionals on the best practices for treating patients. NICE guidelines recommend that people with MS do not smoke, as it may increase the accumulation of disability⁴⁰.

1 Smoking and MS

The UK Office for National Statistics (ONS) report a steady decline in smoking over the last 30 years. Figures from 2019 estimates that there are currently 6.9 million (14%) smokers across the UK. This is down from 20% in 2010. Of the constituent countries, 14% of adult respondents in England stated they smoked compared with 15% in Scotland, 16% in Wales and 16% in Northern Ireland. This data also shows that men are more likely to smoke than women⁴¹.

It's widely acknowledged that more wealthy people are less likely to smoke¹. A report by the Institute of Health Equality showed that in 2007, 12% of men and 10% of women in higher professional households were smokers, compared to 31% of men and 27% of women in routine and manual households⁴².

Figures published in 2020 by Public Health England estimate 23% of men with MS currently smoke. This is higher than the proportion among men without MS (19%). They estimate 15% of women with MS are currently smoke, similar to the proportion among women without MS (14%)⁶².

1.1 The effects of smoking, and passive smoking, on the risk of getting MS

There is a substantial amount of evidence indicating smoking is a risk factor for MS. This relates to people who currently smoke, rather than those who have quit smoking^{1, 4, 37, 38}. Two large reviews both estimated that the relative risk of smokers developing MS is around 50% higher than for non-smokers^{37, 38}. A study which identified a 40% increase in risk of being diagnosed with MS for current smokers, found those who had stopped smoking showed a reduction to the same level of risk of those who had never smoked¹⁴.

One large review of the research looked at the quality of evidence, and whether this showed smoking was a cause of increased risk. They identified strong evidence to support a causal relationship between smoking and the risk of getting a MS diagnosis⁴. However, two studies using a very different method tried to determine whether smoking was a cause of increased risk. These used genetic variants as a proxy for smoking. They didn't find clear evidence that genetically predicted smoking initiation or lifetime smoking were associated with MS risk^{64, 65}. Instead one suggested that rather than a causal relationship between smoking and MS risk, smoking instead accelerates the disease process in those that would have already developed MS. It's worth noting that these studies did not look at current smoking separately, as others have done.

Numerous studies have shown that nicotine itself is not the cause of an increased risk of MS^{17, 21, 22, 47}. There are many theories as to how smoking effects MS risk, but no definitive evidence of the mechanism.

There are very few studies that examine the links between passive smoking and MS risk. Those that do show that how passive smoking contributes to MS risk changes depending on the amount of exposure. Exposure to passive smoking for a greater number of years increased the risk of being diagnosed with MS^{25, 44, 45, 46, 47}.

As there is some risk of getting MS passed on through genetics, the risk associated with smoking or passive smoking is especially important for those already at increased risk, such as the mother, father, brother, sister or child of someone who has been diagnosed with MS^{46, 47, 59}.

1.2 The effects of smoking on conversion of CIS to MS

Few studies have examined the impact of smoking on the conversion from early MS or Clinically Isolated Syndrome (CIS) to Clinically Definite MS (CDMS). Those that have used varied methodologies and provide varied results.

A meta-analysis in 2017 found no strong evidence, due to the small number of studies⁴. Seven studies that examined conversion from CIS to CDMS were identified^{1, 2, 3, 8, 9, 10, 12}. Two used a similar approach to measure smoking at CIS diagnosis, to determine if it was a predictor of future CDMS diagnosis. One found smoking did predict conversion to CDMS, although it did not for ex-smokers¹. The study did not find smoking predictive of conversion to CDMS².

1.3 The effects of smoking on disability progression

There is a growing evidence base that supports the link between smoking and faster disease progression in MS. The Expanded Disability Status Scale (EDSS) is a method used in clinical assessment of people with MS to quantify disability and monitor the accumulation of disability over time, where a higher score represents greater disability on a scale from 0 to 10. Many of the studies reported here use EDSS to measure disability.

A number of studies have found that people with MS who are current smokers are more likely to reach a higher EDSS compared to both those who have never smoked and those who have stopped smoking^{18, 29, 33}. These studies included people with primary progressive MS (PPMS), RRMS and SPMS. Some earlier studies did not find any link between smoking and disability progression^{7, 16, 29, 30}. However these studies mostly compared those who had smoked at any point in their lives, even if they had now stopped, to those who had never smoked. This means they did not account for the benefits gained by those who had stopped smoking.

Many of the studies compare smokers with non-smokers. But researchers are also examining the benefits of stopping smoking for people with MS. One study found that each 'smoke-free year' is associated with a reduction in risk of an increase in EDSS¹⁸. This includes those who had only stopped smoking for one year. Another study, using two different measures of disability, also found that when smokers quit there is a slowing in the rate of disability deterioration, that matches that of people who have never smoked. This suggests quitting smoking benefits people with MS⁶⁶.

Similar effects of giving up smoking have also been linked to reduced psychological impact of MS^{18, 29, 33}. But there is less research that addresses the damaging effects of smoking on MS-specific symptoms.

1.4 The effects of smoking on MS symptoms

A review of the literature completed in 2010³¹ identified three studies that examined the MS-specific effects of smoking on symptoms. One study reported an increased sensitivity to the effects of smoking during an MS relapse. This may accentuate symptoms such as mental confusion, blurred or double vision, vertigo and or ataxia (lack of voluntary coordination of muscle movements), paraesthesia (an abnormal sensation, typically tingling or pricking or 'pins and needles'), motor weakness, lassitude and fatigue. The other two studies found similar effects. One showed reduction in the ability to do upper body motor tasks immediately after smoking in people with MS. The other reported more red/green colour vision defects in smokers following recovery from an optic neuritis attack.

A more recent study found increased cognitive impairment in current heavy smokers with MS, compared to non-smokers with MS²⁰. And another found smokers with MS had more severe fatigue and depression symptoms and poorer quality of life compared to non-smokers.⁶³

There isn't enough evidence to make any definitive conclusions. But this does suggest that smoking cessation could have a beneficial effect on the symptoms experienced by people with MS.

1.5 The effects of smoking on progression to SPMS

Multiple studies have reported quicker progression from RRMS to SPMS among people who smoke^{5, 6, 11, 13, 14, 16}. This appears to be linked to the number of cigarettes smoked i.e. the more cigarettes smoked the greater the effect⁶. A meta-analysis combining three studies⁴ showed a significant effect of smoking on conversion from RRMS to SPMS, but only rated the evidence for causality as 'moderate'.

Starting smoking at an early age (and therefore increasing the number of years smoked) has also been linked to increased risk of a more quickly progressing MS¹¹. Each additional year of smoking following diagnosis of MS was found to result in accelerated time to conversion from RRMS to SPMS⁵. However, quitting can change this prognosis. One study found that SPMS occurred approximately four years earlier in people who had smoked at some point in their lives. But another study that examined the effects in those who had stopped smoking, found that those who quit at diagnosis reached a SPMS diagnosis eight years later than those who continued to smoke^{5, 13}.

Studies examining the effects of smoking on the type of MS first diagnosed did not find any link between smoking and an increased risk of diagnosis of RRMS or PPMS^{7, 11, 13, 14, 16, 37}.

1.6 The effects of smoking on the brain in MS

When examining disease progression clinicians often look for evidence of brain lesions or brain atrophy as well as the clinical characteristics, or symptoms, of MS. Gadolinium enhanced MRI is a form of MRI where dye (gadolinium) is injected into the blood stream and if it is then seen in the brain this suggests that there is a breakdown in the barrier between the brain and the rest of the body. This barrier is known as the Blood Brain Barrier (BBB). A breakdown in the BBB is often linked to increased inflammatory activity in people with MS and can correspond to a relapse or show underlying inflammatory activity in the absence of a noticeable relapse.

A different type of MRI scan, referred to as a T2 scan, uses a mathematical methodology to determine where there are lesions within the brain. While gadolinium enhanced MRI can highlight damage to the BBB and therefore indicate active inflammation, lesions detected using T2 MRI scans are a sign of myelin damage.

Studies looking at the effects of smoking on disease progression have used these T2 type MRI scans to determine the myelin damage that has occurred in people with MS who smoke and those who have never smoked. A number of MRI studies link smoking with increased brain lesions and increased brain atrophy^{1, 2, 8, 12, 15}.

One early study, which found no difference in EDSS progression between smokers and non-smokers, identified an increase in brain lesions and brain atrophy in current smokers when compared to non-smokers¹⁶. This may reflect damage that is occurring in the brain, but is not experienced as physical disability, as captured by EDSS.

Some studies have found that lesions and atrophy in the brains of people with MS increase at a similar rate in those who smoke and those who don't. This suggests that the damage from smoking could have taken place before MS was diagnosed, leaving the brain more susceptible to damage^{8, 12, 16}. Regardless of the initial cause, this reduced brain volume may mean less ability to fight MS, or earlier experience of worsening symptoms for people with MS. When ex-smokers were examined, no significant differences in brain lesions or brain atrophy were found in those who had stopped smoking, compared to those who had never smoked. This suggests that the brain can begin to heal itself once the threat of smoking has been removed¹⁶.

1.7 The effects of smoking on MS treatments

Disease modifying treatments (DMTs) aim to reduce the number of relapses and slow down disease progression. Studies have shown that the effectiveness of two DMTs appears to be inhibited by smoking. The reasons for this are still unclear but two studies, looking at beta interferon treatments and natalizumab, found that the relapse rate during treatment was higher in smokers compared to non-smokers^{34, 35}.

1.8 The effect of vaping on MS

There is growing evidence that nicotine does not have a negative impact on risk of being diagnosed with MS, disability accumulation or disease progression in MS^{17, 21, 22, 47}. There are a number of theories as to why smoking may affect people with MS, but there is no clear evidence that identifies how smoking exerts its effects³¹. This makes it difficult to interpret wider evidence about vaping.

Two studies examining the effects of cigarette smoke and e-cigarette vapour condensate on the cells that separate the brain from the rest of the body, the Blood Brain Barrier cells, and the lung cells, found that nicotine-free cigarette smoke and nicotine-free vapour condensate both caused cell damage^{24, 36}. The study examining the effects of the vapour condensate found that the unheated liquid was much less damaging to cells compared to the heated vapour condensate (or vaped liquid), suggesting that heating the liquid to a certain temperature may activate components of the substance that increases the harm caused³⁶.

So while vaping is a useful tool to aid quitting smoking, we don't know enough about it and how it may affect MS.

1.9 The effect of smoking cannabis on MS

We want to see cannabis for medicinal use available on the NHS. But we strongly advise against smoking cannabis, because of the risk associated with smoking and MS.

2 Support to stop smoking

Nicotine is extremely addictive and most smokers find it hard to give up without help. There are a number of reasons for this. In general the most common barriers to people giving up smoking are:

- Reliance on smoking to relieve stress, depression or anxiety
- Smoking for pleasure
- Social norming (friends, family, partners who smoke)

Only about 5% of unaided quit attempts result in smokers giving up for good. But with effective smoking cessation support people can be more than four times as successful in quitting⁶⁰.

The research available on this subject is vast. But there is a lack of research specific to people who have long-term health conditions.

3 Conclusions and recommendations

While it can be difficult to stop smoking, doing so has a number of health benefits for people with MS. Smoking is a modifiable behaviour that is linked to quicker disability accumulation, faster disease progression and increased risk of developing MS. This is one piece of the puzzle that people can take control of. Further research is needed to draw definitive conclusions about how smoking impacts MS risk, symptoms, and the underlying processes. But overall the evidence shows that there is a negative impact and that quitting can dramatically reduce these effects.

Our own research suggests that people with MS are not familiar with the risks of smoking related to MS. We found that people with MS who smoke reported not having been told about the importance of quitting by their healthcare professionals. Nor had many seen any information from other sources. This is despite the fact that NICE guidelines state that people with MS should be advised not to smoke.

We are taking a position to inform people with MS of the links between smoking and MS. Our recommendations are:

1. For charities, including the MS Society: Promote smoking cessation amongst people with MS, highlighting the risks involved and promoting the importance of quitting
 - Opportunities to signpost people to support to stop smoking should be used, as people are more likely to quit with support

- People with MS should be able to access the most up to date information on smoking and MS
 - Those related to someone with MS are more likely to be diagnosed with MS, and smoking may increase this risk further. Highlight this risk in information resources to encourage people at greater risk of an MS diagnosis to
2. For people with MS:
 - Vaping should be considered as a route towards quitting only rather than a replacement to smoking long term
 - Cannabis should not be smoked by people with MS to relieve their symptoms, whether vaping cannabis is appropriate is an issue which will need to be considered as access to cannabis progresses
 3. For health professionals: Bring up the importance of giving up smoking as soon as appropriate near the time of diagnosis and at annual reviews.
 4. For the UK government: Reverse cuts to public health funding for local authorities to allow people to access smoking cessation services.

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