

Briefing on smoking in the UK and specifically in people with MS

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1 Evidence summary

- More people in the UK with multiple sclerosis (MS) smoke, than in the general UK population.
- Disability progresses faster in people with MS who smoke and when people stop smoking each 'smoke-free year' can reduce the risk of an increase in disability.
- An EDSS score of 6 means a person with MS requires aid to walk about 100m, with or without resting. 1-15 smoke free years can increase the time to an EDSS of 6 by 4 years, and greater than 15 smoke-free years can increase the time taken to reach an EDSS of 6 by up to 14 years.
- People with MS who smoke have increased brain lesions on MRI scans and those who have quit smoking have similar lesion volume to non-smokers.
- Smoking can increase the risk of someone with relapsing remitting MS (RRMS) getting secondary progressive MS (SPMS) sooner, and quitting can reduce this risk, meaning conversion to SPMS can happen up to 8 years later.
- There is some evidence that smoking can increase the risk of those diagnosed with Clinically Isolated Syndrome (CIS), a single episode that may or may not lead to a diagnosis of MS, going on to be diagnosed with Clinically Definite MS (CDMS).
- disease modifying therapies (DMTs) do not protect against the effects of smoking in people with MS and at least two DMTs are proven to work less well when people smoke, resulting in more relapses.
- Smoking, and in some studies passive smoking, is linked to an increased risk of getting MS.
- There is no clear evidence for how smoking causes these MS-specific detrimental effects and therefore alternatives, like vaping, may also be harmful for people with MS.

2 Background

Tobacco use is one of the leading causes of death, illness and inequality. In 2018 the world health organisation estimated that there were 1.1 billion smokers worldwide and over 7 million tobacco related deaths³⁹. While the number of those who smoke is reducing, there are still a large proportion of people with MS who smoke in the UK, larger than the population average.

Growing evidence shows that smoking increases disability accumulation 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 increases the risk of getting an MS diagnosis, 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 quitting in the year after first diagnosis can increase the time to SPMS 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 and advising patients. Based on the evidence outlined above, NICE guidelines recommend that people with MS are advised not to smoke as it may increase the accumulation of disability⁴⁰.

2.1 Smoking and MS in the UK: the numbers

In 1974 the UK Office for National Statistics (ONS) launched a national survey to monitor tobacco use, since then we have seen a steady decline in smoking habits in the general population. The most recent UK level ONS data (from the Annual Population Survey 2016) estimates that there are currently 7.6 million (15.8%) smokers across the UK. This is down from 19.9% in 2010. However, there is some variation across the nations, with 18.1% of adult respondents in Northern Ireland stating they smoked compared with 17.7% in Scotland, 16.9% in Wales and 15.5% in England. This research also found that men were still more likely to smoke than women, with 17.7% of men and 14.1% of women identifying as current smokers⁴¹.

In 2016 those aged 25-34 were most likely to identify as a current smoker (20.8%), however this age group also show the largest decrease from 2015 (23.0%). All age groups have seen a decline in smoking. Additionally more people than ever are reporting that they have never smoked⁴¹.

It is also widely acknowledged that more wealthy people are less likely to smoke, with the burden of tobacco falling more heavily on those in routine and manual households¹ compared to those in higher professional households. 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.

Despite a wealth of research into the effects of smoking in MS, estimates of the number of people with MS (and other neurological conditions) who smoke are limited. The UK MS

¹ According to the Office for National Statistics (ONS) 'routine and manual households' are classified as those households where the main income earner is employed in an occupation that is classified as lower supervisory and technical or semi-routine and routine.
<https://www.ons.gov.uk/methodology/classificationsandstandards/otherclassifications/thenationalstatisticssocioeconomicclassificationnssecbasedonsoc2010>

Register, a database of more than 17,000 people living with MS in the UK, includes a questionnaire that records smoking behaviours of its respondents. A recent analysis of the most up-to-date responses on this questionnaire, the Lifestyle questionnaire, showed that 48% of respondents never smoked, 33.5% identified as ex-smokers and 18.5% were still smoking⁴³. While the data on the UK MS Register only represents a proportion of the overall MS population in the UK, with 6,420 responses included in this analysis it does indicate that there is a higher incidence of smoking in this MS population compared to the national average, which is 15.8%⁴¹.

Further evidence of smoking prevalence in the UK MS population comes from a study conducted by the University of Nottingham. Researchers at the University of Nottingham looked at smoking and excess mortality in a cohort of 895 people with MS during the period of 1994-2013. Their research found that 57% of their cohort had considered themselves smokers at some point in their lives and were therefore 'ever-smokers'. Of this 'ever-smokers' group, 13% had quit before developing MS and 49% were smokers at the time of MS onset. Those who had stopped smoking before disease onset were diagnosed significantly later in life than those who had stopped after disease onset³³.

3 The evidence

3.1 Smoking increases disability progression in people with MS

There is a growing evidence base that supports a causal 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.

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. While some early work in this area would refute these claims^{7, 16, 29, 30}, those 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, and therefore did not account for the benefits gained by those who had stopped smoking.

A recent study specifically examined the benefits of stopping smoking in people with MS and found that each 'smoke-free year' is associated with a 4% reduction in risk of an increase in EDSS¹⁸, and, while the sooner someone stops smoking the better, the participants in this study included those who had only stopped smoking for one year.

Similar effects of giving up smoking have also been found for MS, when measured by the MS Impact Scale (MSIS), a measure of the physical and psychological impact of MS^{18, 29, 33}.

3.2 Effects of smoking on MS symptoms

While there is very little research that addresses the damaging effects of smoking on MS-specific symptoms there are some studies that it is worthwhile addressing.

A review of the literature completed in 2010 by Shirani and Tremlett³¹ identified three studies that examined the MS-specific effects of smoking on symptoms:

- One of these studies reported an increased sensitivity to the effects of smoking during an MS relapse which 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 fatigue²³.
- The other two studies found similar effects. One showed acute reduction in upper body motor performance immediately after smoking in people with MS²³. The other reported a higher incidence of red/green colour vision defects in smokers following recovery from an optic neuritis attack.

A more recent study conducted since that review has also found increased cognitive impairment in current heavy smokers with MS compared to non-smokers with MS²⁰.

While there is too little evidence here to make any definitive conclusions, the evidence that does exist suggests that further research may highlight specific damaging effects of smoking on MS symptoms and that smoking cessation could reduce the burden of worsening symptoms for people with MS.

3.3 Smoking effects clinical prognosis 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}.

Also, as mentioned earlier some studies did not find that smoking affected EDSS scores in people with MS, though most of these studies did not examine current smokers in particular^{7, 16, 29, 30}. One study did focus on current smoking and, while no difference in EDSS progression was found between smokers and non-smokers, this study did identify an increase in brain lesions and brain atrophy in current smokers compared to non-smokers¹⁶. This may reflect a worsening of sub-clinical prognosis, which is damage that is occurring in the brain where it is not noticed in EDSS or symptoms but can be seen in MRI scans.

However, the effect of smoking on brain lesions may be a result of underlying damage from smoking. 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 this brain damage could have taken place before MS diagnosis 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 worse symptoms earlier for people with MS. Also, 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, suggesting that the brain can begin to heal itself once the threat of smoking has been removed¹⁶.

3.4 Faster progression to SPMS in people who smoke

Accelerated conversion to SPMS in people with RRMS who smoke has been reported in multiple studies^{5, 6, 11, 13, 14, 16}. A meta-analysis by Degelman and Herman identified five studies looking at progression from RRMS to SPMS, and three of these were suitable to be combined to review the evidence in their meta-analysis⁴. The analysis showed a significant effect of smoking on conversion from RRMS to SPMS. However, the statistical criteria used in this meta-analysis, the Bradford Hill criteria, only scored this as moderate evidence for causality, likely due to the small number of studies available for analysis. This effect appears to be linked to the number of cigarettes smoked⁶- the more smoked the greater the effect.

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, and each additional year of smoking post-diagnosis of MS was found to result in accelerated time to conversion from RRMS to SPMS⁵. However, quitting can change this prognosis. While one study found that SPMS occurred approximately four years earlier in 'ever-smokers' 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 diagnosed in the first instance did not find any link between smoking and an increased risk of diagnosis of RRMS or PPMS^{7, 11, 13, 14, 16, 37}.

3.5 Smoking may increase the 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) and those that have used varied methodologies and provide varied results.

The 2017 meta-analysis by Degelman and Herman, mentioned above, identified only three papers looking at this aspect of disease progression. Two of these were excluded due to different outcome measures and analysis procedures, and due to this small number of studies no strong evidence was found⁴. In research for this paper seven studies that examined conversion from CIS to CDMS were identified^{1, 2, 3, 8, 9, 10, 12}, two of which similarly measured smoking at CIS diagnosis to determine if it was a predictor of future CDMS diagnosis^{1, 2}. While one of these studies found smoking to be predictive, the other did not. Also, interestingly, the study that found smoking at time of CIS to be a significant predictor for CDMS did not see the same effect in ex-smokers¹.

This supports the finding mentioned above for MS progression, that ex-smokers show a reduction in risk to that seen in never-smokers, and therefore quitting could reduce the risk of conversion from CIS to CDMS to that of non-smokers.

3.6 Increased relapses during treatment in people with MS who smoke

Unfortunately, while disease modifying treatments (DMTs) aim to reduce the number of relapses and slow down disease progression, studies have shown that the effectiveness of at least two DMTs is 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}. This figure controlled for relapse rate history, and is therefore a reflection of DMTs working less well in people with MS who smoke.

3.7 Smoking, and passive smoking, linked to increased risk of getting MS

For decades research has pointed to a link between smoking and increased MS risk. Two large reviews of studies looking into MS and smoking both estimated that the relative risk of smokers developing MS is around 50% higher than for non-smokers^{37, 38, 59}. In 2017 a large review of the research was conducted to examine the quality of evidence and the strength of the causal link between smoking and MS. This review identified a strong causal association between smoking and the risk of getting a MS diagnosis⁴.

One of the studies examined in this review used records from the General Practice Research Database where each MS case was matched with 10 controls. That study identified a 40% increase in risk of being diagnosed with MS for current smokers, however those who had stopped smoking showed a reduction to the same level of risk of those who had never smoked¹⁴. This again highlights the potential benefit that may be achieved by those who choose to stop smoking.

There is a substantial amount of evidence that smoking is a risk factor for MS, especially current smoking, which is also linked to conversion from CIS to CDMS^{1, 4, 37, 38}. This has raised concerns about the effects of passive smoking. While there are very few studies that examine the links between passive smoking and MS risk, those that do show that passive smoking contributes to MS risk in a dose dependent manner, where 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, including 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}. Numerous studies have shown that nicotine itself is not the cause of this increased risk^{17, 21, 22, 47}, and though there are many theories as to how smoking exerts this effect on MS risk no definitive evidence to explain how smoking has this effect has been identified.

3.8 Vaping may also have a negative impact on MS

As mentioned above there is growing evidence that nicotine does not have a negative impact on risk of being diagnosed with MS, disability accumulation or disease progression^{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.

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 respectively, found that nicotine free cigarette smoke and nicotine-free vapour condensate both caused cell damage^{24, 36}. Furthermore, the study examining the effects of the heated 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.

Therefore, while vaping is a useful tool to aid quitting smoking, it is still a new practice that may in itself lead to damage and only the future will tell.

3.9 Effects of smoking cannabis

While we have been campaigning to see cannabis for medicinal use available on the NHS since 2017 we strongly advise against smoking cannabis because of the known risk associated with smoking and MS. There are many different ways that cannabis as a symptom management could be prescribed if made legal. We will be working with decision makers and health care professionals to establish how cannabis should be made available. It is currently unclear whether vaping cannabis would be advisable and we will be seeking to address this question while working to see access to medicinal cannabis become a reality.

4 Barriers and support to stop smoking

Nicotine is extremely addictive and most smokers find it hard to give up without help. Only about 5% of unaided quit attempts result in smokers giving up for good but effective smoking cessation support can increase the chances of success more than fourfold⁶⁰.

A number of barriers to quitting smoking exist amongst the general population of smokers and the literature available on this subject is vast. It includes a large number of studies based on qualitative research (often conducted via semi-structured interviews) as well as randomised control trials testing smoking cessation interventions. However, one specific gap that emerged in this review was a lack of research looking at specific barriers to giving up smoking for those who have long-term health conditions.

Across the literature review the following barriers emerged as the most common reasons stopping people giving up:

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

The cost of smoking in England alone is at least £2 billion to the NHS and over £12 billion to wider society⁶¹. While the government has targets to reduce the smoking prevalence rate in England to 12% by 2022 this is unlikely to happen due to NHS smoking cessation services having been reduced in the past decade. The British Lung Foundation has found that⁶²:

- in England, levels of nicotine replacement therapy prescribed in primary care in 2016-17 were around 25% of 2005-06 levels
- in Wales, the number of all stop smoking products prescribed in 2016-17 was a third of that of 2007-08
- in Scotland, levels of stop smoking products prescribed fell by 40% between 2012-13 and 2014-15.

They also found that there is a postcode lottery in accessing smoking cessation services across the UK, with some areas having no official routes at all for doctors to prescribe support to quit smoking.

5 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. Despite the recognised need for further research to draw clear and definitive conclusions about how smoking impacts specific MS symptoms or how it is affecting underlying processes in MS, overall the evidence shows that there is undoubtedly a negative impact and that quitting can dramatically reduce these effects.

Furthermore, our research suggests that people with MS are not familiar with the risks of smoking related to MS. Recent research commissioned by us and conducted by Headstrong Thinking Ltd. found that people with MS who smoked reported not having been told by health care professionals of the importance of quitting or not having seen any information on this issue from other sources. This is despite the fact that the NICE guidelines clearly state that people with MS should be advised that they should not smoke as 'it may increase the progression of disability'.

We are taking a position to inform people with MS of the links between smoking and MS. This is a result of considering the detrimental effects of smoking on MS prognosis, as described above, and the NICE guidelines recommendation to advise people with MS not to smoke.

We recommend that:

1. We need to further promote smoking cessation amongst people with MS, highlighting the risks involved and promoting the importance of quitting smoking
2. Opportunities to signpost people to support to stop smoking should be used, as people who quit for a month are more likely to quit long term⁶³
3. People with MS should be able to access the most up to date information on smoking and MS
4. Vaping should be considered as a route towards quitting only rather than a replacement to smoking long term

5. 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
6. Health professionals should bring up the importance of giving up smoking as soon as appropriate near the time of diagnosis and at annual reviews.
7. The UK government should reverse cuts to public health funding for local authorities to allow for people to access smoking cessation services.
8. Those who are related to someone with MS are more likely to be diagnosed with MS, smoking may increase this risk further. We will be highlighting this risk in our information resources to encourage people at greater risk of an MS diagnosis to quit.

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