



The University of
Nottingham

TOBACCO SMOKING AND MULTIPLE SCLEROSIS

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*With thanks to Dr Ali
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Learning objectives

1. To gain knowledge in the role of smoking in the susceptibility to MS
2. To gain knowledge in the role of smoking in the progression of MS
3. To gain knowledge in the effect of smoking on MS treatments
4. To gain knowledge in the role of smoking in the mortality in MS
5. To gain knowledge in potential benefits of smoking cessation in MS

Tobacco smoking and MS (findings from Nottingham MS clinics)

1. Effect on the occurrence of MS
2. Effect on the disease progression
3. Effect on mortality rates and survival

Effects of smoking cessation and scope for cessation interventions

Occurrence of MS:

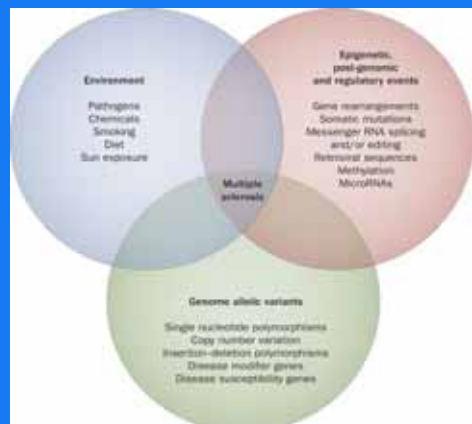
It is commonly believed that the development of MS is due to some environmental trigger in genetically susceptible people (gene-environment hypothesis).

Known environmental factors influencing MS risk:

1. Vitamin D
2. Infectious (e.g. EBV)
3. Diet (e.g. fatty acids)
4. Smoking

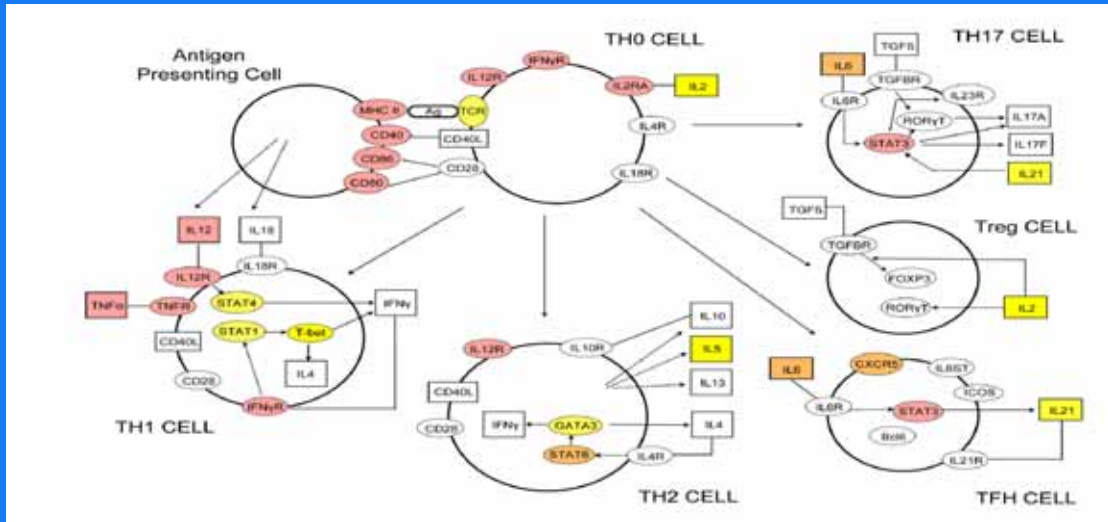
Known genetic factors:

1. HLA-DRB1*15:01 (the most strongly linked genetic factor)
2. IL7R
3. IL2RA
4. CYP27B1
5. TNFRSF1A



Picture from: Oksenberg, J. R. & Baranzini, S. E. (2010) Multiple sclerosis genetics—is the glass half full, or half empty? *Nat. Rev. Neurol.* doi:10.1038/nrneuro.2010.91

VIRTUALLY ALL GENES OF MS SUSCEPTIBILITY ARE IMMUNE RESPONSE GENES



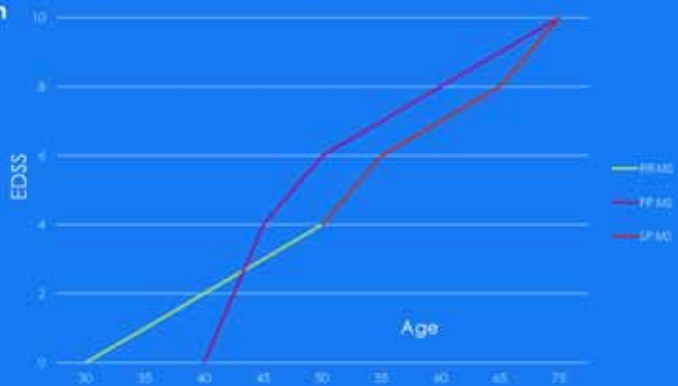
Steven Sawcer, International MS Consortium, 2011

Progression:

Like the disease onset, the mechanism underlying progression of the disease is yet to be identified.

Known factors influencing progression in MS:

- Age (perhaps the most important factor)
- Gender (males have disadvantages)
- Ethnicity (black people usually do worse)
- Vitamin D
- Infection (e.g. urinary and upper respiratory tracts infections)
- Smoking



Mortality:

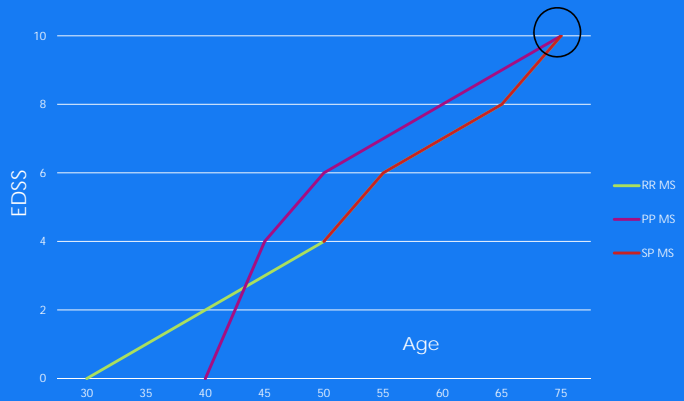
It has been shown that patients with the diagnosis of MS usually live 7 to 14 years shorter than their counterparts in the general population [1].

Common causes of death:

1. MS related causes (e.g. aspiration Pneumonia, sepsis)
2. Cardiovascular diseases
3. Cancer
4. Suicide

Notes:

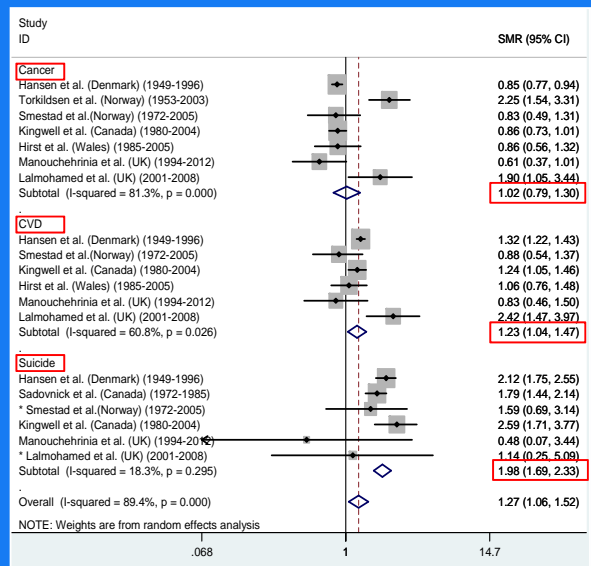
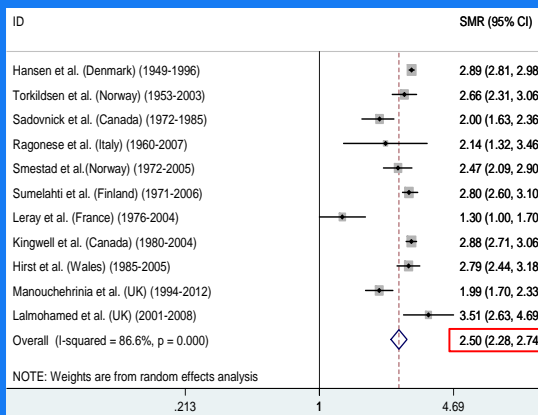
There is no survival advantage for any type of MS



1. Scalfari, A., V. Knappertz, G. Cutter, D. S. Goodin, R. Ashton and G. C. Ebers (2013). "Mortality in patients with multiple sclerosis." *Neurology* **81**(2): 184-192.

Mortality:

Pooled analysis of standardised mortality ratios (SMR)



Nottingham MS clinics:

- Clinics were started in 1994
- Over 3,000 patients are registered
- 1,245 patients were routinely followed up
- In 2013 we sent out a comprehensive questionnaire to study the influence of smoking on disease progression.

| | |
|-----------------------------|----------------------|
| Age (mean(SD)) | 52.89 (\pm 11.33) |
| Sex(female) | 71.47 % |
| Disease phenotype | |
| RR MS | 57.2 % |
| SP MS | 33.3 % |
| PP MS | 9.4 % |
| DMT (%) | 54 % |
| Disease duration (mean(SD)) | 19.28 (\pm 10.44) |
| Latest EDSS score | 5.5 (3.5 to 6.5) |



Smoking

Michael Eriksen
Judith Mackay
Hana Ross

THE TOBACCO ATLAS

FOURTH EDITION
Completely Revised and Updated



SOME NUMBERS ABOUT SMOKING

20% of the world's population

900 million men and 200 million women

>16 million Americans live with a disease caused by smoking

Worldwide 900000 people die of second hand smoke (75% women and children)

1 in 5 deaths in the USA caused by smoking

Life expectancy 10 years shorter in smokers than in never smokers

Diseases linked to smoking

Almost any organ

Cardiovascular

Cancer

Diabetes

COPD

Inflammatory –e.g. Rheumatoid arthritis

Infectious (increased susceptibility to Tb)

Smoking-related illness in the United States costs more than \$300 billion each year, including: Nearly \$170 billion for direct medical care for adults. More than \$156 billion in lost productivity, including \$5.6 billion in lost productivity due to secondhand smoke exposure.

8 Apr 2016 CDC

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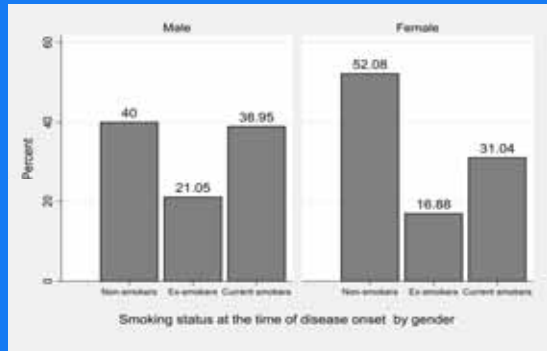
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| Disease duration (mean(SD)) | 19.28 (\pm 10.44) |
| Latest EDSS score | 5.5 (3.5 to 6.5) |



Tobacco smoking in our cohort:

1. Mean age at the start of regular smoking was **17.5** (SD \pm 4.4).
2. Our patients smoked for an average duration of **22.8** (SD \pm 13.4).
3. Average smoking intensity was **18.7** (SD \pm 12.5) cigarettes per day.

At the age of EDSS score 4 and 6, still **20%** were smoking.



Tobacco smoking and risk of MS: a case-control study

Background:

There is ample epidemiological evidence that tobacco smoking is a significant trigger in the development of MS.

1. Tobacco smoking increases the risk of MS by **50%** [1].
2. Presence of DRB1*15 and absence of A*02 and smoking is shown to increase the risk of MS by 13.5 times [2]
3. Decreased risk of MS was found in the Swedish snuff-takers (Smokeless tobacco) [3].
4. The risk of MS for ever-smokers was only significant among the cases with high anti-EBNA titers [4].

* Exposure to parental and environmental tobacco smoke has also been shown to increase the risk of MS

1. Handel, A. E., A. J. Williamson, et al. (2011). "Smoking and multiple sclerosis: an updated meta-analysis." PLoS One **6**(1): e16149
2. Hedstrom, A. K., et al. (2011). "Smoking and two human leukocyte antigen genes interact to increase the risk for multiple sclerosis." Brain **134**(Pt 3): 653-664.
3. Hedstrom, A., J. Hillert, T. Olsson and L. Alfredsson (2013). "Nicotine might have a protective effect in the etiology of multiple sclerosis." Mult Scler **19**(8): 1009-1013.
4. Simon, K. C., et al. (2010). "Combined effects of smoking, anti-EBNA antibodies, and HLA-DRB1*1501 on multiple sclerosis risk." Neurology **74**(17): 1365-1371.

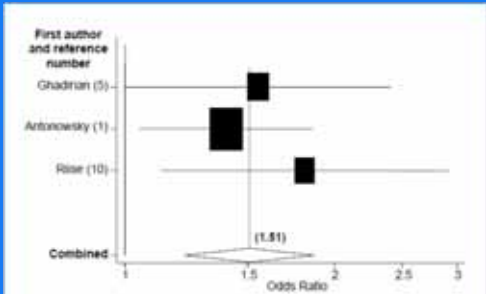


Figure 1 Metanalysis of retrospective studies using ever:never smoking prior to MS onset. The size of the black rectangles is inversely proportional to the confidence interval.

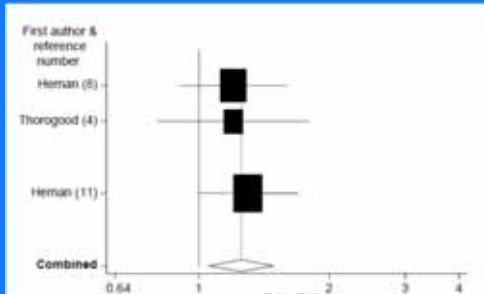


Figure 2 Metanalysis of prospective studies using most conservative analysis. The size of the black rectangles is inversely proportional to the confidence interval.

Hawkes MSJ 2007

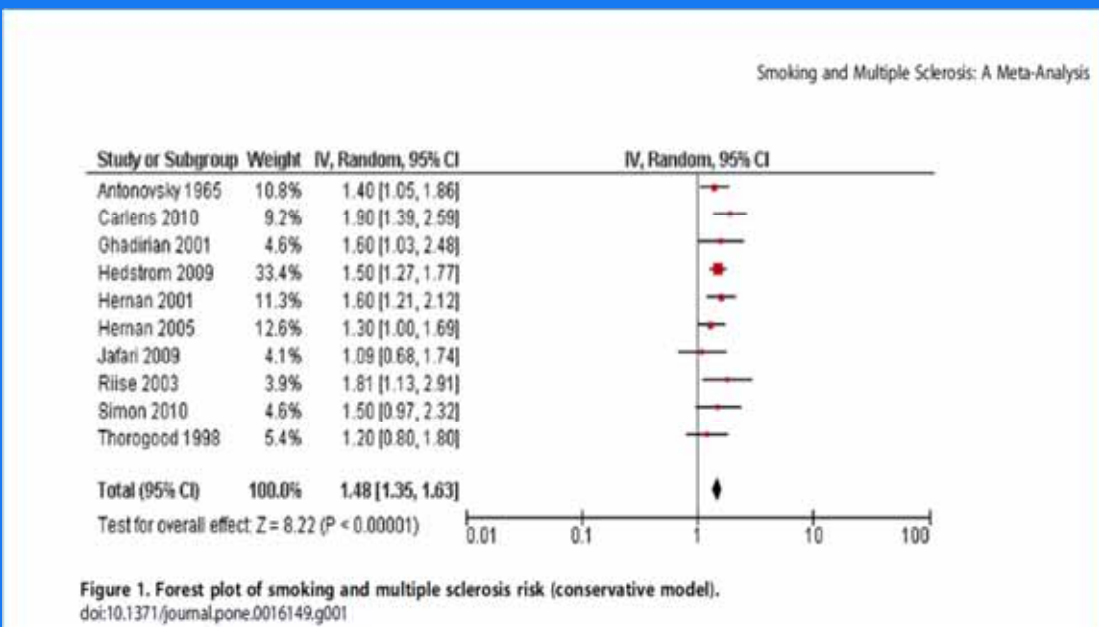


Figure 1. Forest plot of smoking and multiple sclerosis risk (conservative model).
doi:10.1371/journal.pone.0016149.g001

Handel et al 2011 PlosOne

1. Tobacco smoking and risk of MS: a case-control study
2. Tobacco smoking and risk of MS progression: a cohort study
3. Tobacco smoking and risk of premature death: a cohort study

Tobacco smoking and risk of MS: a case-control study

Results:

| | | Male | Female | Total |
|---------|------------|-------|--------|-------|
| Control | Number | 386 | 966 | 1349 |
| | Age (mean) | 54.55 | 52.30 | 52.94 |
| Case | Number | 193 | 483 | 676 |
| | Age (mean) | 54.55 | 52.26 | 52.93 |

1. Individual smoking:

1. Regular smokers were **64%** (OR 1.64, 95%CI: 1.35 to 1.99, $P < 0.001$) more likely to develop MS than non-smokers.
2. Ever-smoking was associated with **44%** (95%CI: 1.19 to 1.74, $P < 0.001$) increase in risk of MS.

2. Parental smoking:

- No influence of parental smoking during patients' childhood on the risk of MS was observed.

HOWEVER, MS patients were **50%** more likely to become regular smokers if either of parents smoked regularly during their childhood. They were **85%** more likely to smoke if both parents were smokers.

Tobacco smoking and risk of MS: a case-control study

Interpretation:

1. There is a modest but significant influence of smoking on the risk of MS.
2. It is unlikely that smoking alone can explain the development of MS.
3. Based on our findings, parental smoking during patients' childhood is unlikely to influence the risk of MS , HOWEVER, an indirect influence may exist.

1. Tobacco smoking and risk of MS: a case-control study
2. Tobacco smoking and risk of MS progression: a cohort study
3. Tobacco smoking and risk of premature death: a cohort study

Tobacco smoking and risk of MS progression: a cohort study

Background:

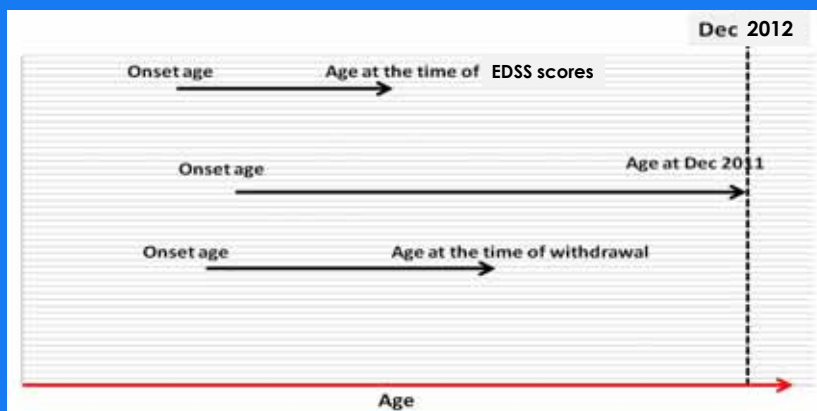
Studies have reached contradicting conclusions.

1. Studies have shown higher risk of transition to SP MS (3.5 times) [1].
2. Higher level of disability was observed [2].
3. Higher disease activity on MRI of smokers was shown [3].
4. Higher risk of transition to CD MS [4].

1. Hernan, M. A., et al. (2005). "Cigarette smoking and the progression of multiple sclerosis." *Brain* **128**(Pt 6): 1461-1465.
2. Pittas, F., et al. (2009). "Smoking is associated with progressive disease course" *J Neurol* **256**(4): 577-585.
3. Zivadinov, R., et al. (2009). "Smoking is associated with increased lesion volumes and brain atrophy in multiple sclerosis." *Neurology* **73**(7): 504-510.
4. Di Pauli, F., et al. (2008). "Smoking is a risk factor for early conversion to clinically definite multiple sclerosis." *Mult Scler* **14**(8): 1026-1030

Tobacco smoking and risk of MS progression: a cohort study

Method:



Tobacco smoking and risk of MS progression: a cohort study

Outcome measures:

1. Risk of PP MS
2. Risk of reaching EDSS scores 4 and 6
3. Risk of transition to SP MS
4. Disease severity (MSSS, range 0–9.5)
5. PDDS and MSIS-29 Scores
6. Effects of comorbidities

| In the past two weeks, how much has your MS limited your activities | Not at all | A little | Moderately | Quite a bit | Extremely |
|--|------------|----------|------------|-------------|-----------|
| <input type="checkbox"/> 3 Gait Disability: MS does interfere with my activities, especially my walking. I can work a full day, but athletic or physically demanding activities are more difficult than they used to be. I usually don't need a cane or other assistance to walk, but I might need some assistance during an attack. | | | | | |
| <input type="checkbox"/> 4 Early Cane: I use a cane or a single crutch or some other form of support (such as touching a wall or leaning on someone's arm) for walking all the time or part of the time, especially when walking outside. I think I can walk 25 feet in 20 seconds without a cane or crutch. I always need some assistance (cane or crutch) if I want to walk as far as 3 blocks. | | | | | |
| <input type="checkbox"/> 5 Late Cane: To be able to walk 25 feet, I have to have a cane, crutch or someone to hold onto. I can get around the house or other buildings by holding onto furniture or touching the walls for support. I may use a scooter or wheelchair if I want to go greater distances. | | | | | |
| 25. Feeling anxious or tense? | 1 | 2 | 3 | 4 | 5 |

Risk of developing PP MS:

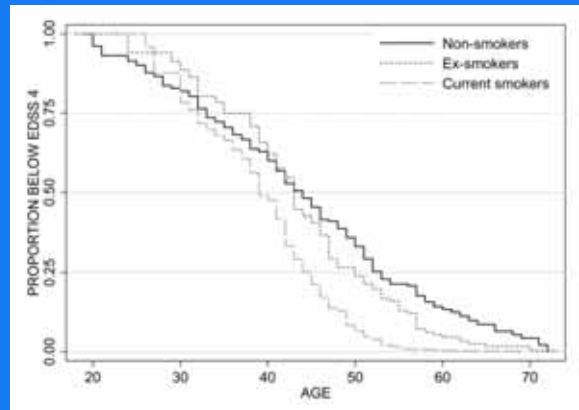
- We could not find any association between smoking and having progressive onset MS (PP MS).

| | <i>n</i> | Odds ratio (95%CI) | P-value |
|---------------------------------|----------|---------------------|---------|
| Smoking (ever vs. never) | 1166 | 0.82 (0.54 to 1.24) | 0.36 |
| Pack-years smoked | 615 | 1.00 (0.98 to 1.02) | 0.90 |
| Gender (female vs. male) | 1166 | 0.34 (0.22 to 0.52) | < 0.001 |
| Onset age | 1166 | 1.09 (1.07 to 1.11) | < 0.001 |

Risk of reaching EDSS score milestones 4 and 6:

1. Risk of reaching EDSS 4:

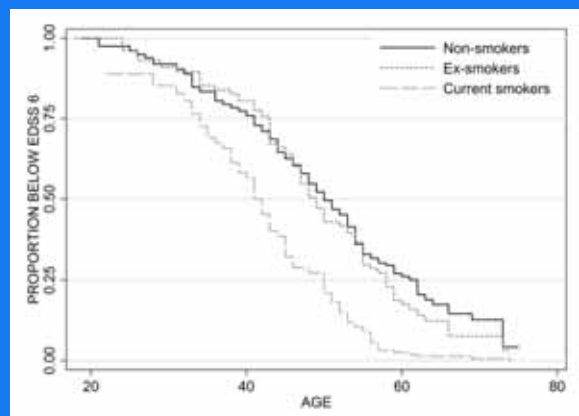
1. Current smokers had **88%** (95%CI: 1.43 to 2.48, $P < 0.001$) higher risk of reaching EDSS score 4 compared with non-smokers.
2. Ex-smokers had no increased risk of reaching EDSS score 4 compared with non-smokers (**HR: 0.93**, 95%CI: 0.72 to 1.20, $P = 0.6$).



Risk of reaching EDSS score milestones 4 and 6:

2. Risk of reaching EDSS 6:

1. Current smokers had **66%** (95%CI: 1.17 to 2.35, $P = 0.004$) higher risk of reaching EDSS score 6.
2. There was no increased risk of reaching EDSS score 6 in ex-smokers (**HR: 0.81**, 95%CI: 0.58 to 1.12, $P = 0.21$) whether they quit before or after MS onset.

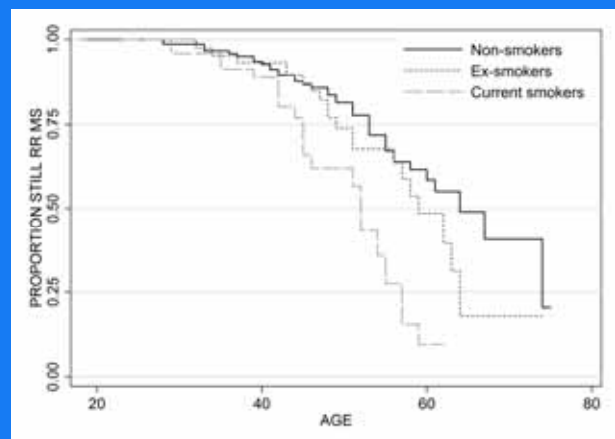


Age at the time of EDSS score milestones 4 and 6:

| Smoking status | Median time to EDSS 4 from onset (95%CI) | Median time to EDSS 4 from birth (95%CI) |
|-----------------|--|--|
| Non-smokers | 16 (14 to 19) | 50 (48 to 51) |
| Ex-smokers | 15 (12 to 18) | 51 (47 to 52) |
| Current-smokers | 11 (9 to 12) | 45 (42 to 47) |
| | Median time to EDSS 6 from onset (95%CI) | Median time to EDSS 6 from birth (95%CI) |
| Non-smokers | 22 (19 to 25) | 54 (53 to 55) |
| Ex-smokers | 20 (15 to 23) | 54 (52 to 55) |
| Current-smokers | 16 (13 to 20) | 50 (47 to 53) |

Risk of transition to SP MS:

- We found that current smokers have **2.38 times** (95%CI: 1.39 to 4.08, $P = 0.001$) higher risk of developing SP MS.
- The risk of transition to SP MS was not increased amongst ex-smokers compared with non-smokers (HR: **0.9**, 95%CI: 0.54 to 1.51, $P = 0.71$).
- Each unit increase in the pack-years smoking was associated with **1%** (95%CI: 1.001 to 1.02, $P = 0.03$) increased risk of developing SP MS



Disease severity (MSSS):

- the average MSSS was **0.8** (95%CI: 0.26 to 1.35, $P = 0.004$) and **0.35** (95%CI: -0.07 to 0.77, $P = 0.1$) higher in current and ex-smokers respectively
- Those with pack-years smoked* more than 10 had an average **0.62** (95%CI: 0.17 to 1.06, $P = 0.006$) MSSS higher than non-smokers (zero pack-years).

We looked at the odds of being in upper quartile MSSS (MSSS > 7.5) compared with lower quartile (MSSS < 2.5)

| | Odds ratio (95%CI) | P-value |
|-----------------------|---------------------|---------|
| Smoking status | | |
| Non-smokers | --- | --- |
| Ex-smokers | 1.3 (0.7 to 2.42) | 0.39 |
| Current smokers | 2.88 (1.29 to 6.43) | 0.01 |
| Pack-years | | |
| Non-smokers | --- | --- |
| 1 to 10 | 1.06 (0.45 to 2.49) | 0.88 |
| More than 10 | 2.17 (1.17 to 4.02) | 0.01 |

* Number of pack-years = (number of cigarettes smoked per day × number of years smoked)/20 (1 pack has 20 cigarettes)

PDDS and MSIS-29 score:

- PDDS:** The average PDDS score was **0.71** (95%CI: 0.25 to 1.17, $P = 0.002$) score and **0.27** (95%CI: -0.07 to 0.63, $P = 0.12$) score higher in current and ex-smokers compared with non-smokers respectively.
- MSIS-29:** MSIS-29, MSIS psychological scale and MSIS physical scale scores were significantly higher amongst ever-smokers.

| | Never-smoked | | Ever-smoked | | P-value * |
|--|--------------|--------------|--------------|--------------|-----------|
| | Mean (SD) | Median (IQR) | Mean (SD) | Median (IQR) | |
| Feeling unwell? | 2.40 (±1.24) | 2 (1 to 3) | 2.74 (±1.30) | 3 (2 to 4) | < 0.001 |
| Problems sleeping? | 2.45 (±1.40) | 2 (1 to 4) | 2.66 (±1.37) | 3 (1 to 4) | = 0.020 |
| Feeling mentally fatigued? | 2.92 (±1.34) | 3 (2 to 4) | 3.36 (±1.31) | 4 (2 to 4) | < 0.001 |
| Worries related to your MS? | 2.38 (±1.27) | 2 (1 to 3) | 2.73 (±1.39) | 3 (2 to 4) | = 0.001 |
| Feeling anxious or tense? | 2.44 (±1.28) | 2 (1 to 4) | 2.78 (±1.34) | 3 (2 to 4) | < 0.001 |
| Feeling irritable, impatient, or short tempered? | 2.43 (±1.26) | 2 (1 to 3) | 2.92 (±1.33) | 3 (2 to 4) | < 0.001 |
| Problems concentrating? | 2.68 (±1.34) | 2 (2 to 4) | 3.06 (±1.30) | 3 (2 to 4) | < 0.001 |
| Lack of confidence? | 2.48 (±1.39) | 2 (1 to 4) | 2.84 (±1.44) | 3 (2 to 4) | < 0.001 |
| Feeling depressed? | 2.11 (±1.29) | 2 (1 to 3) | 2.61 (±1.40) | 2 (1 to 4) | < 0.001 |

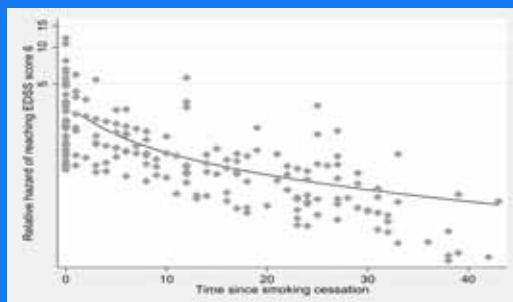
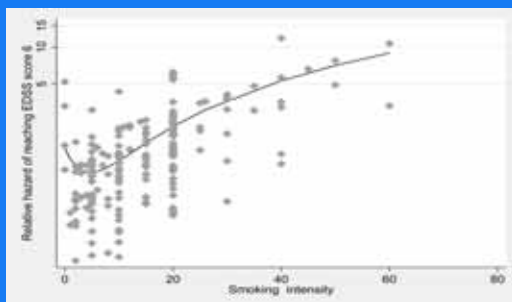
* P-values from Wilcoxon-Mann-Whitney test

Effects of comorbidity:

- As expected the prevalence of concomitant comorbid diseases was significantly higher in ever-smokers (58% in ever-smokers vs. 42% in never-smokers, $P = 0.002$).
- When the analysis was limited to the patients with no concomitant medical condition:
 1. the average MSSS was still significantly higher in ever-smokers compared with never-smokers (Coef: **0.89**, 95%CI: 0.46 to 1.32, $P < 0.001$).
 2. Average PDDS score was also significantly **0.77** (95%CI: 0.31 to 1.23, $P = 0.001$) score higher in ever-smokers compared with never-smokers.
 3. Ever-smokers had **34%** (95%CI: 1.02 to 1.75, $P = 0.03$) higher risk of reaching EDSS score 6.

Effects of smoking intensity and time since smoking cessation:

- As seen, the risk of progression in ex-smokers were similar to non-smokers.
- We found that each cigarette smoked was associated with **3%** (95%CI: 1.01 to 1.05, $P < 0.001$) increased risk of reaching EDSS score 6.
- Each year increase in the time since cessation of smoking was associated with **5%** (HR: 0.95, 95%CI: 0.93 to 0.97, $P < 0.001$) decreased risk of reaching EDSS score 6.



Tobacco smoking and risk of MS progression: a cohort study

Interpretation :

1. Current smokers reach EDSS scores 4 and 6 in shorter time.
2. Smokers have higher levels of physical and psychological disability.
3. Disease was more severe in smokers.
4. Although smokers had higher levels of comorbid conditions, it appeared that the influence of smoking is independent of the presence of comorbid conditions.
5. Those who gave up smoking could do as well as non-smokers



Manouchehrinia, A., C. R. Tench, J. Muxted, R. H. Bibani, J. Britton and C. S. Constantinescu (2013). "Tobacco smoking and disability progression in multiple sclerosis: United Kingdom cohort study." *Brain*.

Tobacco smoking: effects on disease modifying treatments for MS

Increased risk of NABs to natalizumab and IFN-beta (*Hedstrom et al 2013; Hedstrom et al 2014*)

Increased risk of side effects of fingolimod (decreased lung capacity)

No clear effect on progression in BENEFIT

1. Tobacco smoking and risk of MS: a case-control study
2. Tobacco smoking and risk of MS progression: a cohort study
3. Tobacco smoking and risk of premature death: a cohort study

Tobacco smoking and risk of premature death: a cohort study

Background:

Mortality in patients with MS has been studied in several populations but not many studies have evaluated environmental factors associated with increased mortality risk.

1. The two largest survival studies in MS estimated an almost 3-fold increased mortality risk in MS patients relative to the general population [1,2]
2. In the UK, it has been suggested that current smokers with MS have **6.7**-fold increased mortality rate compared with the sex- and age-matched counterparts without MS [3].

1. Bronnum-Hansen H, et al. Trends in survival and cause of death in Danish patients with multiple sclerosis. *Brain : a journal of neurology*. 2004 Apr;127(Pt 4):844-50.
2. Kingwell E, van der Kop M, Zhao Y, et al. Relative mortality and survival in multiple sclerosis: findings from British Columbia, Canada. *JNNP*. 2012 Jan;83(1):61-6.
3. Lalmohamed A, et al. Causes of death in patients with multiple sclerosis and matched referent subjects: a population-based cohort study. *European journal of neurology* 2012 Jul;19(7):1007-14.

Tobacco smoking and risk of premature death: a cohort study

Results:

1. We studied 923 patients.
2. The 923 patients contributed a total of 18,717 person-years of data.
3. There were 80 (46 males and 34 females) deaths recorded in our cohort.

| | Deceased (n = 80) | Alive (n = 843) | P-value |
|----------------------------------|-------------------|-----------------|---------|
| Sex (female %) | 34 (42%) | 610 (72%) | < 0.001 |
| Last recorded EDSS (median(IQR)) | 7.5 (±1.5) | 5.5 (±3.5) | < 0.001 |
| Age at the onset (mean) | 35 (±10.67) | 32(±9.74) | = 0.02 |
| Disease duration (median) | 20 (±17) | 15 (±14) | < 0.001 |
| Type of MS | | | |
| Relapsing-remitting | 9 (11%) | 445 (52%) | < 0.001 |
| Primary-progressive | 16 (20%) | 87 (10%) | |
| Secondary-progressive | 55 (69%) | 311(37%) | |
| DMT ≥ 1 year | 13 (16%) | 384 (45%) | < 0.001 |

Tobacco smoking and risk of premature death: a cohort study

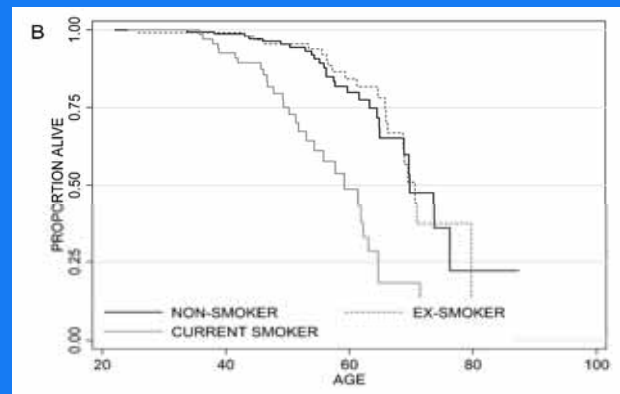
Results:

1. Survival age and role of smoking

- Estimated survival age was 76 years (95% CI: 74 to 79) for all patients.
- Estimated survival age was:
 - **81** (95%CI: 78 to 83) years in non-smokers,
 - **78** (95% CI: 75 to 81) years in ex-smokers and
 - **71** (95% CI: 68 to 74) in current smokers (P < 0.001).

2. Risk of premature death:

1. Current smokers were at higher risk of death, with a hazard ratio relative to never smokers of **2.70** (95% CI: 1.59 to 4.58; P < 0.001) and
2. The hazard ratio was **1.30** (95% CI: 0.72 to 2.32; P = 0.37) for ex-smokers.



Survival compared with the UK general population.

Results:

- Our patients had 2-fold increased risk of premature death compared with people without MS in the UK general population
- When stratified by smoking status never-smokers did not have any excess mortality

| | SMR (general population) | SMR (male British doctors) |
|-----------------|--------------------------|----------------------------|
| Overall | 1.99 (1.70 to 2.33) | ----- |
| Male | 2.41 (1.95 to 2.96) | ----- |
| Female | 1.80 (1.40 to 2.30) | ----- |
| Non-smokers | 1.27 (0.87 to 1.86) | 1.12 (0.63 to 1.97) |
| Ex-smokers | 1.96 (1.27 to 3.0) | 0.54 (0.26 to 1.14) |
| Current smokers | 3.83 (2.71 to 5.42) | 1.84 (1.24 to 2.72) |

Tobacco smoking and risk of premature death: a cohort study

Interpretation :

- In our MS population current smoking was associated with more than 2.5-fold increased risk of death.
- Current smokers and ex-smokers with MS had a reduction of about 10 and 3 years in their life expectancy relative to non-smokers with MS.
- Non-smokers with MS could live as long as people in the general population.

In general:

1. Smoking is associated with higher risk of MS development.
2. Smoking influences progression of disability.
3. Smoking is associated with higher risk of premature death.
4. Smoking results in a significant reduction in patients life expectancy.

Clinical Implications:



Smoking cessation in MS

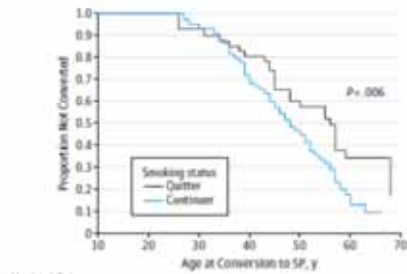
JAMA Neurol. 2015;72(10):1117-1123. doi:10.1001/jamaneurol.2015.1788
Published online September 8, 2015.

Original Investigation

Effect of Smoking Cessation on Multiple Sclerosis Prognosis

Ryan Ramanujam, PhD; Anna-Karin Hedström, MD; Ali Manouchehrinia, PhD; Lars Alfredsson, PhD

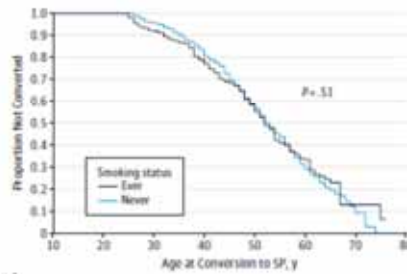
Figure 2. Kaplan-Meier Plot of Quitters and Continuers



| No. at risk | 0 | 10 | 20 | 30 | 40 | 50 | 60 | 70 |
|-------------|---|----|----|----|----|----|----|----|
| Quitter | 0 | 0 | 28 | 30 | 22 | 8 | | |
| Continuer | 0 | 1 | 57 | 98 | 92 | 19 | | |

A Kaplan-Meier plot with the age at conversion to secondary progressive (SP) disease for smokers at diagnosis who quit smoking completely (n = 118) and smokers at diagnosis who smoked continuously (n = 332).

Figure 3. Kaplan-Meier Plot of Never Smokers and Ever Smokers

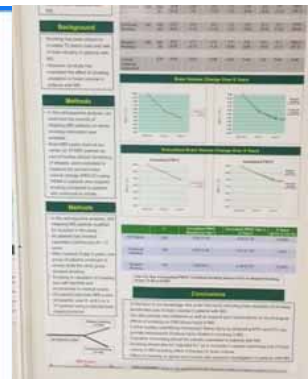
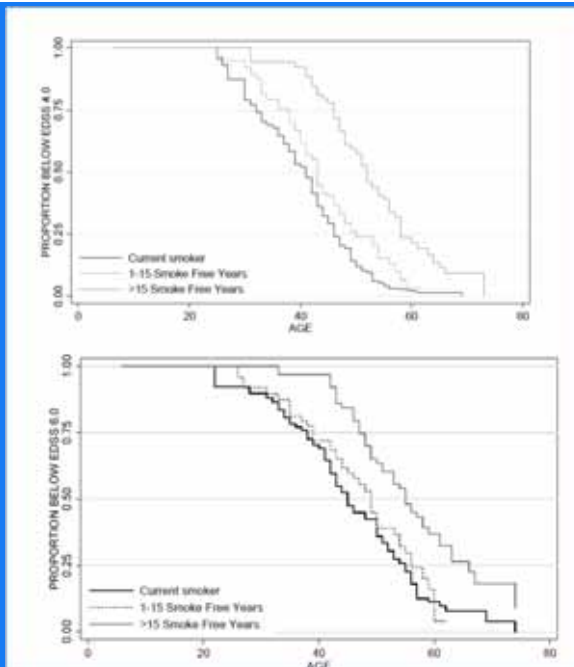


| No. at risk | 0 | 10 | 20 | 30 | 40 | 50 | 60 | 70 | 80 |
|-------------|---|----|-----|-----|-----|-----|----|----|----|
| Never | 0 | 1 | 218 | 371 | 191 | 54 | 2 | | |
| Ever | 0 | 2 | 258 | 455 | 362 | 110 | 4 | | |

A Kaplan-Meier plot of age at conversion to secondary progressive (SP) disease for never smokers (n = 1012) compared with ever smokers (n = 1346).

Each smoke-free year was associated with 0.96 (95% CI: 0.95 to 0.97) times decreased risk of reaching EDSS 4.0 and 0.97 (95% CI: 0.95 to 0.98) times decreased risk of reaching EDSS 6.0. Current smokers showed a significantly higher level of disability in all the self-reported outcomes with the highest negative impact of smoking on the MSIS-29 psychological scale where current and ex-smokers had a 0.8 (95% CI: 0.41 to 1.19) and 0.56 (95% CI: 0.18 to 0.94) increase in the median score compared with non-smokers.

Manouchehrinia A, Tanasescu R, Constantinescu C, manuscript in preparation



Omar Khan, ECTRIMS poster 2015

Work in progress:

1. Further investigation into major aspects of smoking (e.g. the effects of age at smoking initiation)
2. A qualitative assessment of smoking cessation programmes



3. Clinical trials of smoking cessation
4. Active and effective intervention strategies.

"The battle is far from being over. Unless the prevalence of smoking is reduced substantially, the number of smokers will increase in the world in the next several decades, mostly due to population expansion in low- and middle-income countries. Measures to tackle the epidemic remain seriously under-funded."

Margaret Chan, Director-General, WHO, 2012

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Thank you for your attention