Factors Affecting Outcomes Among People With MS

Written by Jill Shuman

Factors such as smoking, obesity, and mental health comorbidities play an important role in the etiology and well-being of patients with multiple sclerosis (MS), as well as their families.

According to Ruth Ann Marrie, MD, PhD, University of Manitoba, Winnipeg, Manitoba, Canada, there is growing evidence that smoking may confer ≤50% greater risk in the development of MS, particularly among Caucasian men (Figure 1) [O'Gorman C, Broadley SA. *J Neurol*. 2014]. Some data also suggest that people who begin smoking earlier than age 15 may have a worsened prognosis as the disease progresses [Sundström P, Nyström L. *Mult Scler*. 2008].

Dr Marrie then discussed adolescent obesity as a risk factor for MS. In a Swedish case-control study, people with a body mass index >27 kg/m^2 at age 20 were twice as likely to develop MS when compared with their normal-weight counterparts [Hedström AK et al. *Mult Scler*. 2012]. In the Nurses' Health Study, women who self-described themselves as obese at age 18 were at twofold greater risk of MS ($P < .001$) [Munger KL et al. *Neurology*. 2009]. Age-adjusted risk for body size at age 20 was associated with a 96% increased risk of MS ($P < .009$). No significant risk was evident for a large body size at age 5 ($P < .46$) or 10 ($P < .15$). Dr Marrie also highlighted a study suggesting that female adolescent obesity increases the risk of developing pediatric MS [Langer-Gould A et al. *Neurology*. 2013].

A small percentage of people with MS who are treated with natalizumab develop antidrug antibodies, which is associated with a suboptimal clinical response [Calabresi PA et al. *Neurology*. 2007]. Tomas Olsson, MD, PhD, Karolinska Institutet, Stockholm, Sweden, spoke next about the relationship between smoking and the development of these antinatalizumab antibodies.

Data were drawn from 1338 patients with MS who were treated with natalizumab in 2 large ongoing clinical trials [EIMS; GEMS], both of which have collected information on participants' smoking habits. Treatment-related information was obtained from the Swedish national MS registry and antibody status before the start of therapy and again at 6, 12, and 24 months. Logistic regression was then used to compare the risk of developing antinatalizumab antibodies among smokers versus those who never smoked.

Among the 1338 patients, 4.8% developed antibodies to natalizumab [Hedstrom A et al. *Mult Scler*. 2013]. Compared with never smokers, patients who smoked at the time of screening were more than twice as likely to develop antinatalizumab antibodies (OR, 2.4; 95% CI, 1.2 to 4.4; $P = .008$). For patients who smoked within 2 years of the screening, the odds ratio of developing antinatalizumab antibodies was 2.7 (95% CI, 1.5 to 5.1; $P = .001$). There was no significant association between people who had stopped smoking at least 2 years prior to screening and the risk of developing the antibodies ($P = .09$)

Prof Olsson hypothesized that smoking irritates the lungs, which initiates a reaction that increases the risk of an immune response to natalizumab, as well as interferon β and monoclonal antibodies. He closed his session by emphasizing the clinical implications of these findings and highlighting the importance of smoking cessation among people at risk of MS.

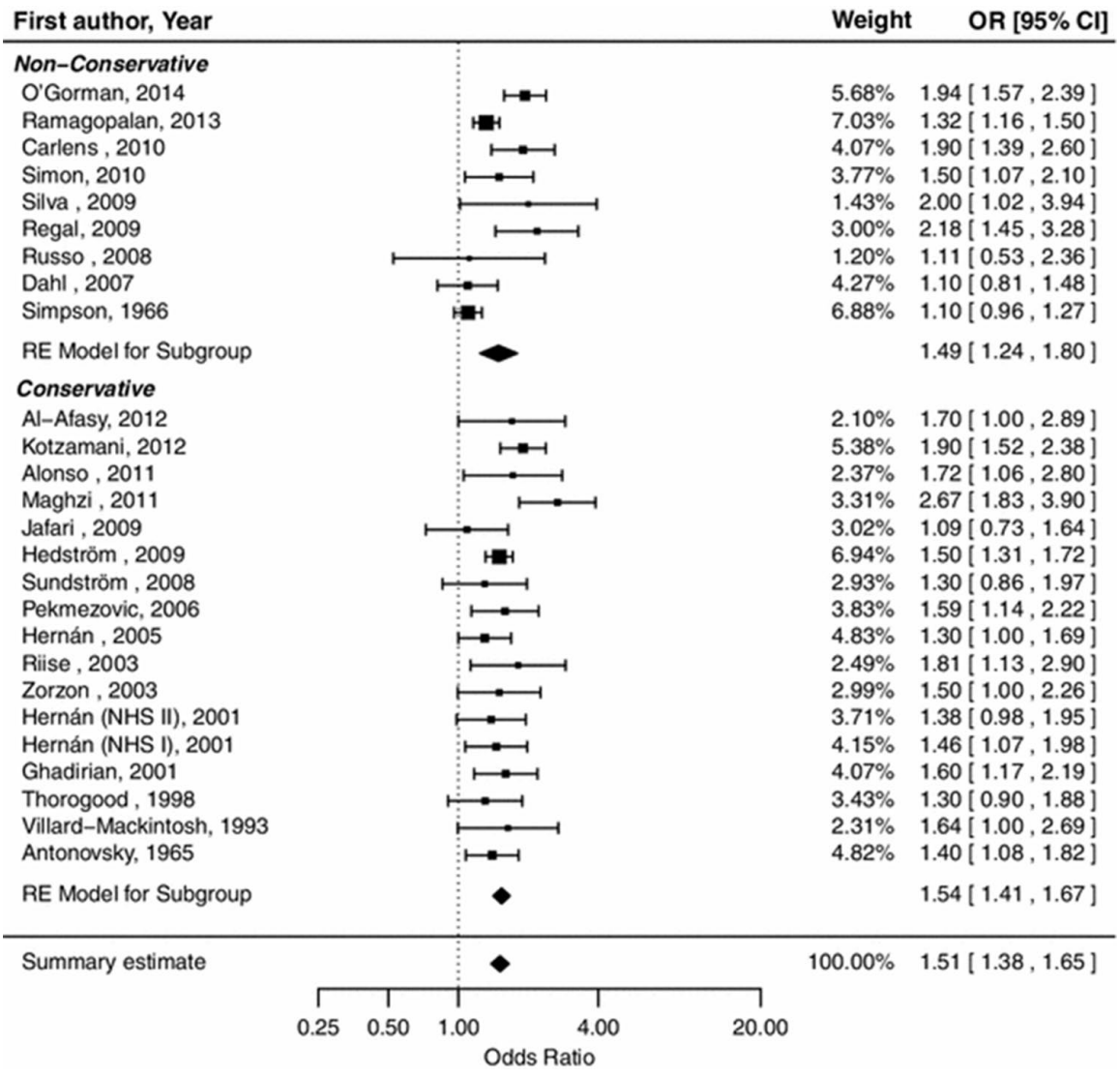
Although children who have a parent with a chronic disease may be at risk of developing social, emotional, or behavioral difficulties [Sieh DS et al. *Clin Child Fam Psychol Rev.* 2010], there is little consensus as to whether children who have a parent with MS are at this same risk [Razaz N et al. *BMC Neurol.* 2014]. Neda Razaz, MPH, University of British Columbia, Vancouver, British Columbia, Canada, described a study designed to examine the association between parental MS and childhood developmental outcomes.

Peer-Reviewed Highlights From the

2014 Joint ECTRIMS-ACTRIMS Meeting

September 10–13, 2014
Boston,
Massachusetts, USA

Figure 1. Meta-analysis of the Association Between Smoking and Multiple Sclerosis



Reproduced from O'Gorman C et al. Smoking and multiple sclerosis: evidence for latitudinal and temporal variation. *J Neurol.* 2014;261:1677-1683. Figure 1. © Springer-Verlag Berlin Heidelberg 2014. With kind permission from Springer Science and Business Media.

This was a retrospective cohort study that collected data from hospital discharges, pharmacy claims, physician claims, census and income bureaus, and child development data. The outcome of interest was the absence or presence of vulnerability on 5 outcomes of childhood development measured by the Early Development Instrument (EDI) when administered to a child at 5 years of age. The 5 domains of interest were social competence, physical health and well-being, language and cognitive development, emotional maturity, and communication skills.

Among 3116 adults with MS, 153 had a child who had taken the EDI. These children and their parents were then matched with 876 controls from the general population. The characteristics of the MS group are shown in Table 1.

Adjusted odds ratios were calculated with multivariable logistic regression that adjusted for potential confounders, such as socioeconomic status, maternal age at birth, age of the child when the EDI was administered, number of siblings per child, and whether parents had comorbid

Table 1. Characteristics of Parents with MS, n = 153

Factors	%	Median (Range)
Female	85	
Ever on MS disease-modifying treatment	51	
Beta-interferon	83.3	
Glatiramer acetate	16.7	
Age of parent at MS onset		29.4 (10.3 to 43.8)
Parental MS disease duration at EDI		6.3 (< 0.1 to 24.5)
Child exposure to MS at the time of EDI		5.3 (< 0.1 to 5.3)
Parental MS onset occurred after child birth	58.8	

EDI, Early Development Instrument; MS, multiple sclerosis.

mental health issues. Compared with the controls, parents with MS were older at time of childbirth, achieved a higher socioeconomic status, and were significantly more likely to have mental comorbidity (50.3% vs 35.3%; $P < .001$).

According to Razaz, children with an MS parent showed no significant differences in any of the 5 EDI domains when compared with the control children. However, there was a relationship between the duration of a child's exposure to parental MS and vulnerability on the physical health and well-being domain of the EDI (adjusted OR, 1.49; 95% CI, 1.03 to 2.15). Parents with MS and a mental health comorbidity were more likely to have children vulnerable on the social competence domain (adjusted OR, 5.06; 95% CI, 1.02 to 25.1) and emotional maturity domain (adjusted OR, 3.0; 95% CI, 1.04 to 8.67). Razaz also noted that although the study was limited by its small size and a lack of access to information about the course of the parental MS, health professionals should be aware that a parent with MS and mental comorbidity might have an effect on childhood development over time.